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Evaluation of spinal instrumentation following organ transplantation: A retrospective cohort study

Organ nakli sonrası spinal enstrumantasyon sonuçları: Retrospektif kohort çalışma

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Abstract

Aim: Improvements in transplantation medicine and surgery, anesthesiology, and postoperative care paved the way for successful procedures for transplant patients. The aim of the present study is to describe the results of surgical correction for spinal deformities in patients who underwent several types of organ transplantation.

Methods: The study group consisted of ten patients with a history of organ transplantation who require spinal surgery with different etiologies. Seven (70%), two (20%) and one (10%) patient had lung, liver, and lung transplantations, respectively. The etiology for spinal surgery was spinal stenosis in six (60%), vertebra fracture in three (30%), and vertebral metastasis in one (10%) patient. Pre-intra- and postoperative radiological, clinical, and functional outcomes were noted.

Results: The mean age of the patients was 57.1 (8.9) years, ranging between 38-62 years. Six of the patients were male, and four were female. Surgery time following the transplant surgery was 15.6 (2.1) months. The blood requirement in the operating room was 5.6 (0.8) units of erythrocyte suspension. Hospital length of stay was 8.5 (5.6) days following the spinal instrumentation surgery. Two patients had mild complications in the postoperative period. The preoperative VAS score significantly decreased from 6.4 (0.8) to 3.1 (1.6) after the surgery (P<0.001).

Conclusions: Posterior spinal instrumentation on transplanted patients can be an effective treatment which improves the life quality of the patients. A multidisciplinary approach with an experienced team is highly required.

Keywords: Organ transplantation, Hepatocellular carcinoma, Spinal surgery, Spine metastasis, Instrumentation

Öz

Amaç: Organ nakli cerrahisi, anestezi ve postoperatif bakımdaki gelişmeler transplant hastalarında ek cerrahi girişimlerin de yapılabilmesinin önünü açmıştır. Bu çalışmanın amacı farklı organ nakilli hastalarda omurga cerrahisinin sonuçlarını incelemektir.

Yöntemler: Farklı etiyolojilerle omurga cerrahisi uygulanan 10 transplant hastası çalışmaya dahil edildi. Yedi hasta (%70) böbrek nakli, 2 hasta (%20) karaciğer ve 1 hasta (%10) akciğer nakli olmuştu. Hastaların 6'sı (%60) spinal stenoz, 3'ü (%30) vertebra kırığı ve 1'i (%10) vertebra metastazı sebebi ile omurga cerrahisi geçirmişti. Hastaların ameliyat öncesi ve sonrası radyolojik, klinik ve fonksiyonel durumları ve ağrı skorlamaları incelendi. Ameliyat süreleri, kan transfüzyon ihtiyacı ve hastanede kalış zamanları not edildi.

Bulgular: Hastaların yaş aralığı 38-62 yıl ve yaş ortalaması 57,1 (8,9) idi. Hastaların altısı erkek, dördü kadındı. Transplant cerrahisinden omurga ameliyatına kadar geçen süre ortalama 15,6 (2,1) ay bulundu. Hastalara ameliyat esnasında ortalama 5,6 (0,8) ünite eritrosit süspansiyonu verildi. Hastanede kalış süresi ortalama 8,5 (5,6) gündü. İki hastada ameliyat sonrası minör komplikasyon gelişti. Hastaların ameliyat öncesi 6,4 (0,8) olan VAS ağrı skorlarının 3,1'e (1,6) düştüğü gözlendi (P<0.001).

Sonuç: Posterior spinal enstrumantasyon, transplant hastalarında da yaşam kalitesini arttırmada etkili bir yöntemdir. Tecrübeli bir ekip ve multidispliner yaklaşım şarttır.

Anahtar kelimeler: Organ nakli, Hepatosellüler karsinom, Omurga cerrahisi, Omurga metastazı, Enstrumantasyon

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Introduction

Organ transplantation has become the essential treatment modality for medically suitable patients with organ failure. Improvements in transplantation medicine and surgery, anesthesiology, and postoperative care have led to increased success ratios of different procedures on transplant patients [1,2].

Multiple factors contribute to the pathogenesis of a spinal defect on this patient group, including organ metastasis, prolonged use of medications, restriction in movement and immobilization, the effect of the systemic disease on bone morphology [3,4]. Life quality of these patients is impaired due to the spinal defect, and correction of the deformity is crucial, especially for severe cases.

There are a limited number of articles on spinal instrumentation surgery on transplant patients. The aim of the present study is to describe the results of surgical correction for spinal deformities in transplant patients who underwent different types of organ transplantation.

Materials and methods

Following approval from the Ethical Committee of Istanbul Yeni Yuzyil University (04.03.2019, number 2019/3), records of organ transplanted patients who underwent spinal instrumentation were retrospectively evaluated. Informed consent was obtained from all patients. The study group consisted of ten patients with a history of organ transplantation who required spinal surgery with different etiologies. Seven, one and two patients had kidney, lung and liver transplantations, respectively. The etiology for spinal surgery was spinal stenosis in six, vertebra fracture in three, and vertebral metastasis in one patient. Of those, only one patient with previous kidney transplantation had congenital scoliosis. Four patients in the kidney transplantation group had stenosis, and two suffered from fractures. Among those who underwent liver transplantation, one patient had metastatic bone disease (Figure 1), and one had stenosis due to immunosuppressant therapy. One patient with lung transplantation had vertebral fractures.

All patients underwent operations through the posterior surgical approach. Polyaxial pedicle screws were placed under fluoroscopic control. Laminectomy and partial facetectomy was performed for decompression in patients with spinal stenosis. The solitary case with metastatic lesion required *en bloc* laminectomy, dural decompression, right pediculectomy, and marginal posterior corpus resection following posterior instrumentation (Figure 2).

The duration between the transplantation and instrumentation surgery, intraoperative blood products, postoperative follow-up data were collected and recorded. Postoperative radiological, clinical, and functional outcomes were also noted. Patients' VAS for pain at 1 month after surgery were recorded and compared to baseline values.

Statistical analysis

The results were presented as mean (standard deviation) for continuous variables. Categorical variables were described as frequency and percentage. Continuous variables were compared using paired samples t-test. A *P*-value <0.05 was considered as significant. All statistical analyses were performed with IBM SPSS ver. 23.0 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.).

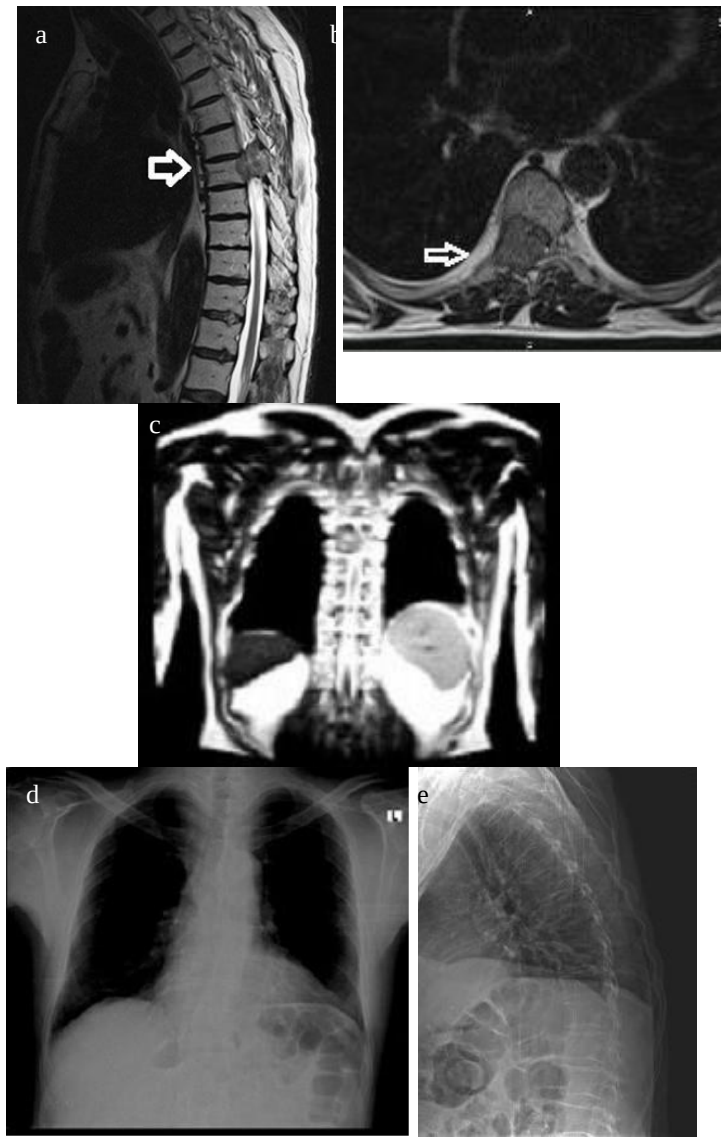

Figure 1: Preoperative sagittal views of T1-weighted (a), axial (b), and coronal (c) magnetic resonance images. Anteroposterior (d) and lateral (e) X-rays show the T7 metastasis (arrow)

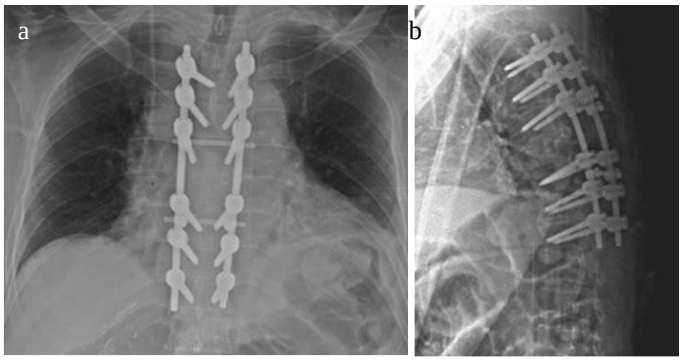

Figure 2: Postoperative anteroposterior (a) and lateral (b) X-rays after posterior wide resection and spinal instrumentation for T7 metastasis

Results

The mean age of the patients was 57.1 (8.9) years ranging between 38-62 years. Six of the patients were male, and four were female. Six patients had moderate, and four patients had mild neurological deficits. All patients had a history of pain that non-prescription analgesics could not relieve.

Surgery time following the transplant was 15.6 (2.1) months. The blood requirement in the operating room was 5.6 (0.8) units of erythrocyte suspension. Hospital length of stay was 8.5 (5.6) days following the spinal instrumentation surgery. All

patients were taking various doses of the immunosuppressive agent, Tacrolimus, since their transplantation surgery. Four cases were previous smokers, and none used alcohol.

All patients achieved ambulatory status following surgery. The preoperative VAS score significantly decreased from 6.4 (0.8) to 3.1 (1.6) after the surgery ($P<0.001$). Two patients returned to work, and the remaining cases could perform daily activities at home. There were no implant failures, screw loosening or loss of reduction during the follow-up period. Sagittal and coronal alignment was within normal limits in 9 cases.

Two patients had complications in the postoperative period. A cerebrospinal leak in one patient was repaired by suturing the dura mater and augmenting with fibrin glue. Superficial infection of another improved with antibiotics and regular dressing. No patients developed nosocomial infection. There were no graft rejections or transplant related complications during the study period. At month-10, positron emission tomography (PET)-CT of the patient with hepatocellular carcinoma showed a 39 mm left sacroiliac joint metastatic lesion that was treated by radiotherapy (Figure 3). The patient developed no further symptoms or recurrence and was able to perform all daily activities at the 21st month. All patients were alive as of 2019.

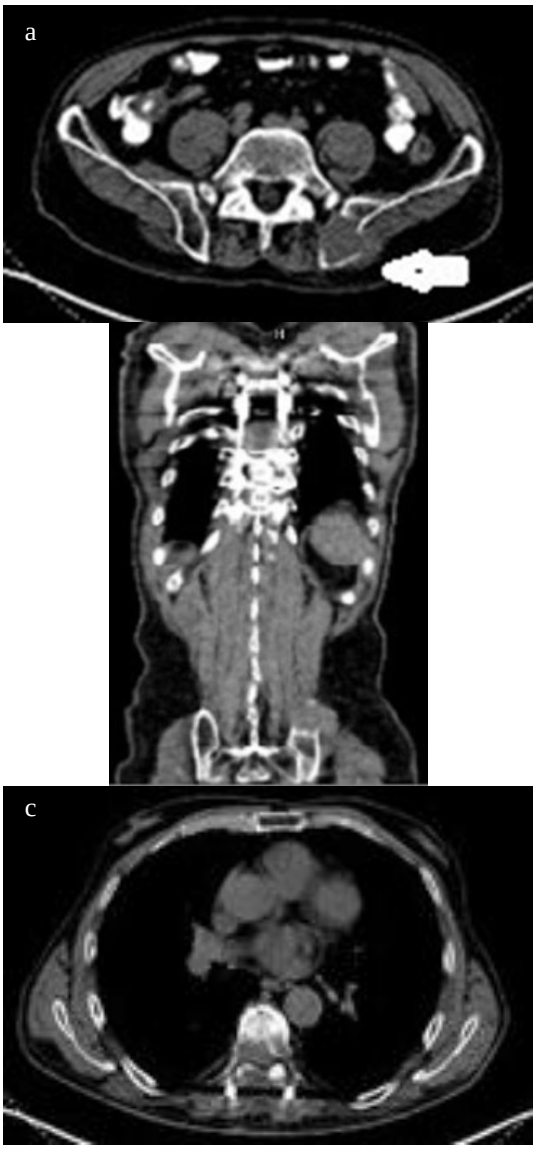

Figure 3: PET-CT images at month-20 after surgery. Note the 39 mm metastatic lesion at the left sacroiliac joint (arrow; a, b) and the intact T7 vertebra (c)

Discussion

With the developments in the field of spinal surgery, the number of transplanted patients undergoing instrumentation and fusion surgery increase gradually. There are several reports demonstrating efficient outcomes in this patient group for the hip or knee replacement surgery [5-7]. Additionally, the establishment of minimally invasive surgical techniques and regional blocks especially in patients with organ failure increases the success rate of surgeries in this specific patient group [8,9]. Our results present additional data for the literature stating that transplanted subjects might be treated for spinal fusion and instrumentation without major side effects.

Spinal problems requiring surgery in patients after organ transplantation might be observed because of various conditions. The need for spinal surgery was vertebra metastasis in one patient who underwent liver transplantation due to hepatocellular carcinoma. Three patients had spinal fractures due to prolonged use of immunosuppressant and corticosteroids, and their detrimental effects on the bone structure. Besides these, patients with renal transplantations might have a syndrome, and vertebra abnormalities might be a component of their syndrome [10,11]. We did not detect a growth abnormality in any of the cases, and all patients are adults with a moderate level of skeletal growth. We also did not observe a visible sign of genetic deformity or mental retardation, however, the cases were not evaluated by a medical genetics consultant. For those cases, a genetic study should be employed to better understand likely future complications.

Spinal deformity or increased kyphosis in the patient with lung transplants might cause restrictive lung disease, thus, immediate surgery was planned to prevent decreased compliance or elevated pulmonary artery pressure. Spinal metastases of the hepatocellular tumors may require embolization before the operation due to their hypervascular nature. Tan et al. stated that the preoperative embolization of spinal HCC metastases is useful for decreasing intraoperative blood loss [12]. However, another study reported that preoperative embolization had no effect on blood loss but did decrease surgery time [13]. The single patient with spinal metastasis in our study required 9 units of erythrocyte transfusion during surgery. We did not perform preoperative embolization because of the conflicting results of previous studies. Multidisciplinary approaches should be considered for the treatment of spinal metastases, including conventional-stereotactic radiation therapy, radiofrequency ablation, trans-arterial chemo-embolization, chemotherapy (sorafenib), immunotherapy, vertebroplasty-kyphoplasty, cement augmentation, and various types of surgery [14].

As a result of their specific condition, transplanted patients are more likely to develop any kind of complications in the postoperative period. Although Yoshihara et al. reported an increased incidence of neurological complications in this patient group, only two patients in our cohort experienced complications: One dural leak, and one superficial infection, which were resolved in the postoperative period during the hospital stay [15]. Despite their long-term use of immunosuppressant and steroids, none of the patients in our study group developed an infection caused by nosocomial pathogens.

During the hospital stay, we closely monitored the cardiac and renal functions of the patients, and the postoperative period was event free. Since urinary tract infections are commonly observed in transplant patients who underwent spinal surgery, we obtained urine culture specimens on a daily basis and did not observe a bacterial colony growth during the hospitalization [4].

Although the dose of steroids might complicate the healing and fixation process, we did not observe a complication caused by the osteoporotic bone structure during the follow-up period. Because of the increased prevalence of comorbidities and complications in this patient group, a multidisciplinary team should be employed during the pre- and postoperative period. The dose of the immunosuppressant drugs and the agents used for the anesthesia and analgesia management should be carefully adjusted and prescribed to prevent any avoidable adverse event. The additional comorbidities in our patients were spinal stenosis in six, vertebra fracture in three, and vertebral metastasis in one patient. The patients with renal transplantation might have an altering state of fluid retention and distribution in the body compared to the other organ transplants, and special consideration should be given to this population.

Reports suggest that the hospitalization period for this patient group is longer than the patients without a transplanted organ [16]. In our study, the mean postoperative length of stay was 8.5 (5.6) days, and four patients were discharged within a similar number of days compared to the patients without a previous history of transplant surgery.

The mean blood loss during the surgery was slightly higher than the patients without transplantations. The reason for the increased amount of blood loss might be caused by longer operation time. When the need for blood product transfusion arises, the metabolic condition of the patients should be closely monitored, preferably by an anesthesiology team experienced on transplanted patients. Also, a nephrologist should be a member of the team with instructions on the proper use of medications and other interventions.

Limitations

The main limitation of our study is low number of patients. This fact may be expected, since this is a very special group with emphasis on survival of the patient and the transplanted organ. Surgical interventions are largely omitted in these immunosuppressed patients to avoid complications, unless absolutely necessary. Retrospective design and lack of inter and intra group analyses are among other limitations of this study. Further studies with larger patient cohort are needed to derive conclusions supported by statistical analysis.

Conclusion

In conclusion, our report presents a rare case of a patient with hepatocellular carcinoma who received living donor transplantation, with nine other transplanted patients. Our successful treatment modality and low rate of complications indicate that spinal fusion and instrumentation is a safe and convenient approach in transplant patients in a well-equipped hospital setting with an experienced multidisciplinary team under special circumstances.

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Research article
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A novel method for treatment of persistent colorectal anastomotic strictures: Magnetic compression strictureplasty

Tekrarlayıcı kolorektal anastomoz striktürlerinin tedavisinde yeni bir teknik: Manyetik kompresyon striktüroplasti

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Abstract

Aim: Colonic anastomotic strictures are usually caused by staple use, anastomotic leakage, intestinal or suture line ischemia and radiotherapy. Endoscopic treatments should be the first choice. Resection of the stricture line and re-anastomosis form the basis of surgical treatment. Compared to endoscopic approaches, the morbidity rate of surgical treatments for strictures are higher. In patients with stricture and history of multiple pelvic surgeries who don't allow endoscopic treatments, magnetic compression strictureplasty (MCS) may be a good choice for lower morbidity.

Methods: The study population included patients with colorectal anastomotic stricture who had failed endoscopic treatments and for whom a tertiary resection and anastomosis was also considered as having high morbidity. Firstly, the MCS technique was planned by colonoscopic approach. It was aimed to place the magnet proximal to the stenotic colon with the colonoscope, which has a ring-shaped magnet attached at the tip, through the ileostomy entrance. This endoscopic approach failed. Then, laparotomy was performed. A 1-cm colotomy was performed from the proximal site of the stricture, and the magnet was left inside the intestine. Another magnet was placed distally to stricture from the anus. The two magnets were observed to compress the stricture by magnetic attraction, and the operation was terminated. Patient demographics, surgical history, MRI results, colonoscopic examination results were recorded. The follow-up conditions of the patients were noted.

Results: MCS was performed on two male patients mean aged 70 (14.14) years. All patients had multiple abdominal surgeries in their surgical history. Colonoscopy showed fully obstructing anastomotic stricture in patients. The mean distance from the anal verge to the stricture in colonoscopic examination was 7±1.41 cm. Mean stricture length in MRI was 12±2.82 mm. In follow up, control rectosigmoidoscopies revealed that the magnets had fallen into the rectum lumen and the stricture line was fully patent for all patients.

Conclusion: MCS might be preferred as a safe surgical technique with low morbidity in patients with previous multiple colorectal surgeries and a full obstructive stricture in the colorectal anastomosis line.

Keywords: Stricture, Magnet, Low-Morbidity, Low anterior resection, Redo surgery

Öz

Amaç: Anastomoz kaçakları, anastomozun stapler ile yapılmış olması, anastomoz hattında oluşan iskemi ve radyoterapi uygulamaları kolonik anastomotik darlıkların en önemli sebepleridir. Striktür tedavisinde endoskopik girişimler ilk tercih olmalıdır. Striktür hattının rezeksiyonu ve yeniden anastomoz cerrahi tedavinin temelini oluşturur. Endoskopik yaklaşımlarla karşılaştırıldığında, darlıklara yönelik cerrahi tedavilerin morbidite oranı daha yüksektir. Endoskopik tedavilere izin vermeyen darlık ve çoklu pelvik cerrahi öyküsü olan hastalarda, manyetik kompresyon strikürüoplastisi (MCS) düşük morbidite için iyi bir seçim olabilir.

Yöntemler: Çalışma popülasyonu kolorektal anastomotik darlığı olan ilave bir rezeksiyon-anastomoz girişiminin yüksek morbiditeye sahip olduğu ve endoskopik tedavilerin başarısız olduğu hastaları içermekteydi. İlk olarak MCS yöntemi kolonoskopik olarak planlandı. İleostomi açıklığından girerek ucunda halka şeklinde bir mıknatıs olan kolonoskop ile mıknatısın kolondaki darlığın proksimaline yerleştirilmesi hedeflendi. Bu endoskopik girişim başarısız oldu. Daha sonra hastalara laparotomi yapıldı. Striktürün proksimal bölgesinden yapılan 1 cm'lik kolotomiden sirküler yapıda 1,5 cm çaplı mıknatıs bağırsağın içine bırakıldı. Anüsten de striktürün distaline başka bir mıknatıs yerleştirildi ve iki mıknatısın, manyetik çekimle striktüre kısmı sıkıştırarak birbirine yapıştığı gözlendi ve ameliyat sonlandırıldı. Hastaların demografik bilgileri, cerrahi geçmişleri, MRG sonuçları, kolonoskopik muayene sonuçları kaydedildi. Hastaların postoperatif takip bilgileri kaydedildi.

Bulgular: İki erkek hastaya MCS uygulandı. Yaş ortalaması 70 (14,14) saptandı. Tüm hastalar daha önce geçirilmiş multipl abdominal cerrahi öyküsüne sahipti. Kolonoskopide, hastalarda tamamen tıkanmış anastomotik darlık gözlendi. Kolonoskopik incelemede anal girimden striktüre olan ortalama mesafe 7±1,41 cm saptandı. Manyetik rezonans görüntülemede ortalama striktür uzunluğu 12±2,82 mm saptandı. Postoperatif takipte kontrol rektosigmoidoskopide mıknatısların rektum lümenine düştüğü ve darlık hattının tamamen açıldığı gözlendi.

Sonuç: MCS, daha önce multipl kolorektal cerrahi geçirmiş olan ve kolorektal anastomoz hattında tam tıkayıcı striktüre sahip hastalarda güvenli ve düşük morbiditeli bir cerrahi teknik olarak tercih edilebilir.

Anahtar kelimeler: Striktür, Mıknatıs, Düşük morbidite, Aşağı anterior rezeksiyon, Redo cerrahi

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Introduction

Benign anastomotic strictures on the anastomotic line after colorectal surgery lead to lumen narrowing. These strictures are usually caused by staple use, anastomotic leakage, intestinal or suture line ischemia and radiotherapy [1,2]. The diagnosis of strictures in a patient is based on the clinical findings of partial or complete intestinal obstruction, the presence of stenosis that does not allow the passage of a colonoscope and the thickening of the anastomotic line on radiological examinations [3]. Benign anastomotic strictures occur in 2%–7% of patients after colonic anastomoses and may range from 5% to 22% in colorectal anastomoses performed using staples [4-6]. Strictures lead to serious clinical conditions requiring endoscopic treatments or multiple surgical treatments in the majority of patients. Surgical procedures increase the morbidity of the disease.

Surgical treatments for strictures in colonic anastomoses include resection of the stricture line and re-anastomosis. Endoscopic treatment methods such as balloon dilation and stent application should be preferred in patients with partially obstructing strictures through which a guidewire can be passed [6]. In patients with complete obstruction, surgical resection and re-anastomosis are the only alternatives.

Various studies in the literature report performance of magnetic strictureplasty in anastomotic strictures after upper gastrointestinal (GI) surgery [7]. In this study, we aimed to define a new surgical technique based on creating an anastomosis with magnetic attraction for stenosis in the colonic anastomosis line.

Materials and methods

Patients with a fully obstructing anastomotic stricture and a history of low anterior resection were included the study. Surgical histories of the patients were recorded. Magnetic resonance imaging (MRI) and colonoscopic examination were performed in all patients preoperatively. Stricture length in MRI, the distance from anal verge to stricture in colonoscopic examination and follow up results were noted. All patients were treated with MCS.

Patients

We operated two male patients with ages of 80 and 60 years during the study period. Both patients had multiple colorectal surgeries due to anastomotic leakage after low anterior resection surgery. Final colorectal anastomoses of the patients were performed with circular staples. Colonoscopy showed fully obstructing anastomotic stricture which did not allow even a guidewire to pass in both patients (Figure 1). The distance from the anal verge to stricture in colonoscopic examination was 7 (1.41) cm. Stricture length in MRI was 12 (2.82) mm (Figure 2) (Table 1).

Surgical technique

Patients were scheduled for MCS, which was initially attempted colonoscopically. A neodymium magnet ring with a diameter of 15-mm was attached to the tip of the colonoscope and advanced distally through the ileostomy entrance (Figure 3). This colonoscopic procedure failed due to the dense fecal content of the ascending colon, and the ileocecal valve contraction. Therefore, the patients underwent laparotomy. A 1-cm colotomy was performed proximally to the stricture, and the magnet was left inside the intestine. Another magnet was placed distally to the stricture through the anus, and the two magnets were observed to compress the stricture by magnetic attraction. After primary closure of the colotomy, the surgery was terminated.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 22.0 (IBM, Armonk, NY, USA). Variables were expressed as mean (standard deviations [SD]) or as medians (range) depending on their distribution, and categorical variables were expressed as frequencies and percentages.

Table 1: Patients characteristics who were treated with magnetic compression strictureplasty

Demographics	
Age, mean (SD)	70 (14.14)
Gender, male/female	2/0
Surgical History	
Patient 1	-Low anterior resection due to benign colorectal disease -Resection of anastomotic segment and re-anastomosis and diverting ileostomy due to anastomotic stricture (four months after the first surgery)
Patient 2	-Low anterior resection due to rectum tumor -Hartmann colostomy due to anastomotic leakage (Ten days after the first surgery) -Colostomy closure with diverting ileostomy (After adjuvant treatment)
Colonoscopic findings	Fully obstructing stricture in the colorectal anastomotic area
Stricture length in MRI, mean (SD), (min-max), (mm)	12 (2.82) (10-14)
The distance from anal verge to stricture in colonoscopic examination, mean (SD), (min-max), (cm)	7 (1.41) (6-8)

SD: standard deviation, MRI: magnetic resonance imaging

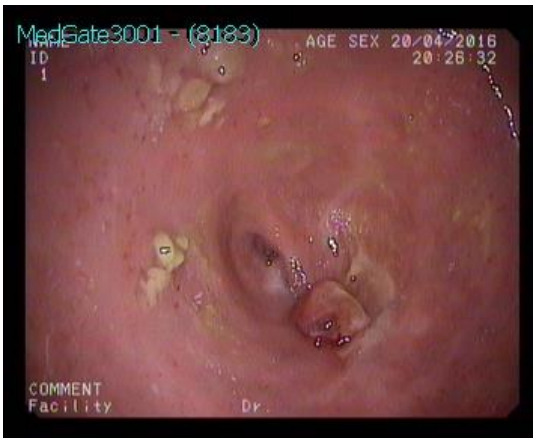

Figure 1: Colonoscopic appearance of strictured colonic segment

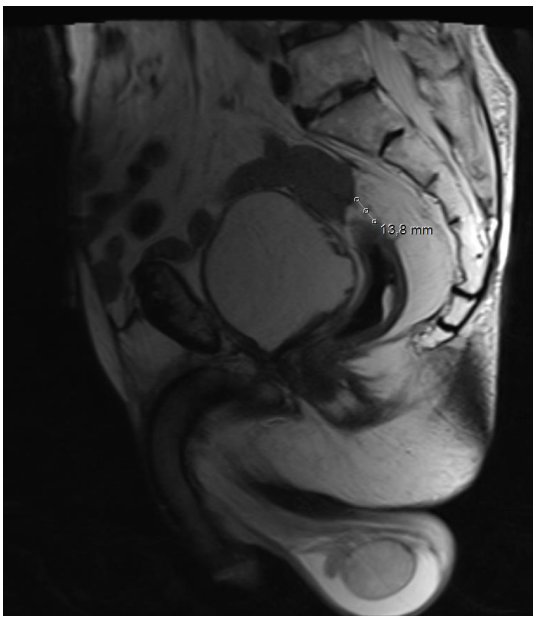

Figure 2: Magnetic resonance imaging of strictured colonic segment

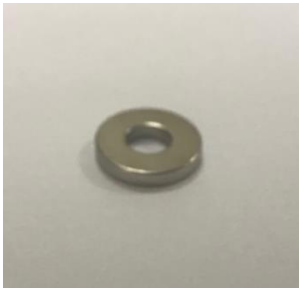

Figure 3: Image of circular mid-spaced magnet with a 15-mm diameter

Results

In the first postoperative week, control rectosigmoidoscopy showed that the lumen was completely patent (Figure 4). Due to the pressure exerted by the magnets on the stricture line, the stricture line had dissolved, and the magnets were free in the lumen. An endoscopic examination performed on the first postoperative month revealed that the anastomotic line was patent. One of the patients needed a fully covered stent placement due to slightly narrowing. The stent was removed after 4 weeks. Both ileostomies were closed on postoperative third month uneventfully following rectosigmoidoscopic examination.

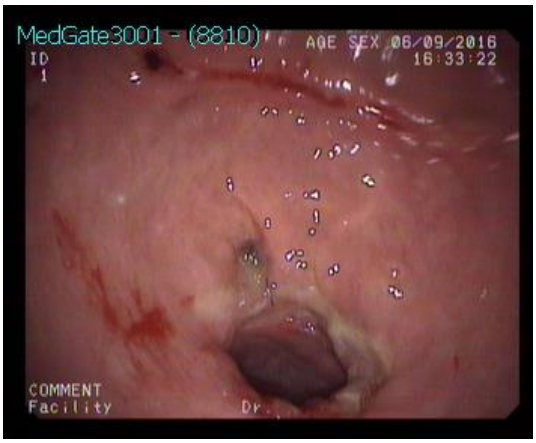

Figure 4: Colonoscopic appearance after magnetic compression strictureplasty

Discussion

Anastomotic strictures usually develop after colorectal surgery secondary to ischemia, leakage, inflammation, or hemorrhage from anastomosis. The majority are observed in the first 6 months after surgery [8,9]. Some researchers have argued that the possibility of a stricture increases when anastomoses are performed using a stapler [10]. Literature suggests treating anastomotic strictures through which a colonoscope cannot pass proximally [8]. In both of our cases, the strictures were fully obstructive. Endoscopic procedures should be the primary choice of treatment for anastomotic strictures, and surgical treatment should be considered when endoscopic procedures fail. Endoscopic dilatation with a balloon or stent application requires passing a guidewire proximally through the stricture. However, it is not possible to apply these treatment modalities in completely obstructing strictures.

Surgical treatments for strictures include resection of the stricture and re-anastomosis of the remaining bowel. Repeated resection of the stricture line and re-anastomosis are often technically very difficult and highly morbid, particularly if the patient has undergone more than one surgical procedure in the same region in pelvic strictures. The first patient in our study had undergone two resections and anastomoses in the distal pelvic region and stricture had recurred. In the second patient, anastomosis was performed twice in the distal pelvic region due to tumor resection and colostomy closure and stricture had developed in the anastomotic line. Similar to our case, in patients with a history of multiple pelvic anastomoses, resection and anastomosis may lead to several problems. In these patients, reaching the pelvic region may not be possible and bleeding may occur during adhesiolysis. The reliability of reconstructed anastomoses will also decrease. There is also the possibility of recurrent strictures in the new anastomotic line. For the reasons mentioned, applying MCS in this group of patients to may reduce morbidity and make surgical technique easier. The principle of this magnet-involved strictureplasty technique compresses the stricture by the magnetic attraction of the magnets placed distally and proximally to the stricture, inducing ischemia in this area. We believe that the technique with which we achieved successful results in both of our cases can be improved by conducting studies in a selected, wider group of patients.

Limitations

Nevertheless, the current study has some limitations. The first of these restrictions is the limited number of patients in our study. Since we recommend the applicability of MCS in selected patients, we believe that we will achieve more effective results over time by applying this technique to more patients. In addition, while planning our technique, although it was intended to place the proximal magnet colonoscopically, we achieved this by laparotomy due to the stool content of the ascending colon and ileocecal valve stenosis, as we noted in this article. We think this is the developable side of the MCS technique.

Conclusion

Consequently, in patients with colorectal anastomotic strictures and previous multiple colorectal anastomosis histories, MCS can be performed instead of re-resection and re-anastomosis, which has more morbidity in case of unsuccessful endoscopic interventions.

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The effect of COVID-19 pandemic on sleeping status

COVID-19 pandemisinin uyku durumu üzerine etkisi

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Abstract

Aim: Sleep is a physiological condition that is needed by the animal organism and required for the regular function of organ systems and mental health. The recent COVID-19 pandemic caused widespread anxiety worldwide with health-related, economic, and social burdens. The aim of this study is to determine the sleep-related perturbances and the level of anxiety in a Turkish population and compare the outcomes between the genders and working status of the subjects during the COVID-19 pandemic.

Methods: We performed a phone-based cross-sectional semi-structured questionnaire on 100 adult volunteers in May 2020. Sociodemographic data, the responses for ten questions on sleep performance and their level of anxiety and life satisfaction were noted and reported.

Results: Male subjects reported a higher incidence of change in their waking hours, and an increased need for sleep during daytime (P=0.008). The anxiety level was significantly higher among female subjects, and the main causes of the anxiety were different between the two groups (P=0.035, P<0.001, respectively). Female subjects described a higher rate of change in their well-being (P<0.001), and the overall scores for well-being and life satisfaction were significantly lower among the females (P<0.001). The non-working group had an increased incidence of severe anxiety and an increased ratio of change in their lifestyle in comparison to usual (P=0.006, P<0.001, respectively).

Conclusions: To our knowledge, this report is the first survey analysis on anxiety and sleep performance following the COVID-19 infections in Turkey. We report a high incidence of impaired sleep status, change of lifestyle, satisfaction, and increased anxiety in the population independent from the gender and current working status.

Keywords: COVID-19, Pandemic, Sleeping status, Anxiety

Öz

Amaç: Uyku, organizma tarafından ihtiyaç duyulan ve organ sistemlerinin ve zihinsel sağlığın düzenli işlevi için gerekli olan fizyolojik bir durumdur. Son zamanlarda COVID-19 salgını dünya çapında sağlık, ekonomik ve sosyal sorunlar ile ilgili yaygın endişeye neden olmuştur. Bu çalışmanın amacı, Türk toplumundaki uyku ile ilgili sorunları ve kaygı düzeyini belirlemek ve katılımcıların cinsiyetleri ile COVID-19 pandemisi sırasında aktif olarak çalışma durumları arasındaki sonuçları karşılaştırmaktır.

Yöntemler: 100 adet yetişkin, gönüllü birey üzerinde telefon temelli kesitsel yarı yapılandırılmış bir anket uygulandı. Sosyodemografik veriler, uyku performansı, kaygı düzeyleri ve yaşam memnuniyeti ile ilgili on soruya verilen yanıtlar analiz edilerek raporlandı..

Bulgular: Erkek katılımcıların uyanıklık saatlerindeki değişim ve gündüz uykusuna artmış düzeyde gereksinimi daha yüksek oranda saptandı (P=0,008). Anksiyete düzeyi kadınlarda anlamlı olarak daha yüksekti ve anksiyetenin ana nedenleri iki grup arasında farklıydı (sırasıyla P=0,035, P<0,001). Kadın katılımcılar, sağlık durumlarında daha yüksek oranda bir değişim tanımladılar (P<0,001) ve sağlık durumu ile yaşam memnuniyeti için toplam puan kadınlar arasında anlamlı olarak daha düşük olarak saptandı (P<0,001). Pandemi döneminde aktif olarak çalışmayan grubun anksiyete oranı daha yüksek ve yaşam tarzında meydana gelen değişikliklerin oranı anlamlı olarak daha yüksek saptandı (sırasıyla P=0,006, P<0,001).

Sonuç: Bu çalışma, Türkiye'de COVID-19 enfeksiyonlarını takiben ortaya çıkan kaygı ve uyku bozukluğu üzerine yapılan ilk araştırma analizidir. Çalışmamız ile, Türk toplumunda cinsiyet ve mevcut çalışma durumundan bağımsız olarak uyku bozukluğu, yaşam tarzı değişikliği, memnuniyet ve artan kaygı insidansının yüksek olduğunu bildirmekteyiz.

Anahtar kelimeler: COVID-19, Pandemi, Uyku durumu, Kaygı

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Introduction

Sleep is a physiological state that is needed for the regular performance of daily activities, mental and physical health, and good life quality. Sleep disorders have been announced as a public health epidemic by the Centers for Disease Control and Prevention (CDC), and according to data, chronic sleep loss and disturbances in sleeping behavior have been related to serious metabolic, endocrine, and systemic diseases including obesity, diabetes mellitus, coronary heart disease, cancer, and stroke [1-3]. Also, the risk of developing Alzheimer's disease is 1.5 times greater in individuals with low sleep quality [4]. Short-term sleep deprivation leads to cognitive impairment, diminished concentration, and impaired intellectual capacity, which might lead to accidents, depressive symptoms, as well as psychotic behavior in individuals with a neuropsychological tendency [5].

As of May 12, 2020, more than 4 million cases with 200 thousand resulting in mortality have been reported globally. In Turkey, a total of 139771 COVID-19 cases were confirmed and 3841 individuals died from the disease [6]. The ongoing COVID-19 pandemic have led to widespread anxiety among the populations, and as the regular precautions are taken with increasing alarm levels, people experienced a great psychological pressure considering the health-related, economic and social outcomes of the process.

As the main point of view of the current reports are on the pathogenesis and treatment of the COVID-19 infection, there is limited data on the anxiety level and related conditions during the COVID-19 pandemic. The reports from the previous pandemics and epidemics suggested an increased rate of insomnia, anxiety, depression, and suicidality, as well as seizures, encephalitis, encephalopathy, and demyelinating diseases [7,8].

Besides the high-risk populations with chronic systemic disease, older age, prolonged use of immunosuppressive medications, health-care workers and disease survivors are also at-risk populations for anxiety and mental health problems [9]. In addition, inadequate amounts of sleep and rest impair the immune system, and COVID-19 has been reported to increase the infection and mortality rates in individuals with disturbed immune systems [10].

The aim of this study is to determine the sleep status and sleep-related perturbances in a selected population including healthcare professionals and compare the outcomes between the genders and working status of the subjects during the COVID-19 pandemics.

Materials and methods

Study design and participants

We designed a phone-based cross-sectional semi-structured questionnaire on one hundred adult volunteers. The study was conducted in May 2020. The participants with impaired sleep and increased level of anxiety were assessed with a neurological consultation and referred for psychological evaluation when necessary.

Sociodemographic data including age, gender, marital, accommodation and graduation status, occupation, presence of any chronic diseases, drug use, smoking status, and regular alcohol intake were collected from all participants.

In the second part, the subjects answered ten questions on sleep performance and their level of anxiety and life satisfaction. The participants were asked if they worked during the pandemic, and compared in terms of change in sleeping behavior, such as difficulty in falling asleep during bedtime, causes of difficulty of sleeping, presence of any trouble staying asleep, rested state at wake-up in the morning, the total amount of sleep, along with personal evaluation of anxiety and well-being, the main reasons of anxiety, and changes in the lifestyle during the COVID-19 pandemics.

This study was conducted in accordance with the Declaration of Helsinki. The ethical board approval was obtained from İstanbul Yeni Yuzyil University, Science, Social and Non-Interventional Health Sciences Research Ethics Committee (Number: 2020/04-05). Verbal informed consent was obtained from all participants.

Statistical analysis

GraphPad Prism v 8.0 was used for the statistical analyses. The data were presented as mean (standard deviation [SD]) and number and percentage. The qualitative variables were compared using the Student's t-test. Chi-square test ($\chi 2$) or 2-sided Fisher's exact t-test were used to compare the categorical variables between the groups. A *P*-value of less than 0.05 was considered statistically significant.

Results

A power analysis was conducted with a Type II error rate of 0.05 and power level of 0.80. Thus, a total of 100 individuals with a mean age of 45.3 (12.6) years completed the questionnaire.

The participants consisted of 52 female and 48 male subjects. The comparison of the demographic data between male and female individuals are presented in Table 1. The ratio of the married participants was significantly higher among the female population (P=0.038), whereas the ratio of males residing in a family-based household was significantly higher than females (P=0.006). We also observed occupational differences between female and male populations (P=0.025). The ratio of regular alcohol intake was significantly higher among male subjects (P=0.003). On the sleep questionnaire, male subjects reported a higher incidence of change in their waking hours, and they reported an increased need for sleep during the daytime (P=0.009).

Anxiety level was significantly higher in the female subjects, and the main causes of anxiety were different between the two groups (P=0.018, P<0.001, respectively). Female subjects described a higher rate of change in their well-being (P<0.001), and the overall score for well-being and life satisfaction was significantly lower among females (P<0.001).

The overall prevalence of impaired sleep was 42.3% and 39.61% in the female and male populations, respectively. Among the participants who answered, the most common reason of difficulty falling asleep was "change of habits" and "All of the above" in both groups. The ratio of individuals who reported trouble staying asleep was 34.6% among females, and 22.9% among males (Table 2).

Table 1: Sociodemographic classification of the study population according to gender

	Female (n=52)	Male (n=48)	*P*-value
Age	46.6 (13.9)	43.3 (11.3)	0.71
Married/Single	26/26 (1.0)	39/9 (4.3)	0.038
Number of children	1.21 (1.18)	1.36 (1.07)	0.32
Accommodation			
Alone	5 (9.6%)	0 (0%)	0.006
Family home	47 (90.4%)	48 (100%)	
Graduation status			
Non-schooled	2 (3.8%)	0 (0%)	0.48
Primary school	5 (9.6%)	4 (8.3%)	
Elementary school	1 (1.9%)	2 (4.2%)	
High school	11 (21.2%)	8 (16.6%)	
University	33 (63.5%)	34 (70.9%)	
Occupation			
Lawyer	1 (1.9%)	0 (0%)	0.025
Own company-Private sector	5 (9.6%)	26 (53.8%)	
IT	0 (0%)	1 (2.1%)	
Health	25 (54.6%)	10 (21.0%)	
Teacher	1 (1.9%)	1 (2.1%)	
Architect/Engineer	5 (9.6%)	5 (10.5%)	
Finance	0 (0%)	3 (6.3%)	
House woman	10 (10.9%)	0 (0%)	
Retired	6 (11.5%)	2 (4.2%)	
Chronic disease			
DM	4 (7.6%)	2 (4.2%)	0.38
HT	12 (23%)	3 (6.3%)	
Thyroid cancer	1 (1.9%)	0 (0%)	
Ulcerative colitis	1 (1.9%)	1 (2.1%)	
CVD	3 (5.8%)	4 (8.4%)	
Breast cancer	1 (1.9%)	0 (0%)	
Thyroid disease	8 (15.4%)	0 (0%)	
Sarcoidosis	0 (0%)	1 (2.1%)	
Behcet's Disease	0 (0%)	1 (2.1%)	
Epilepsy	0 (0%)	1 (2.1%)	
Psoriasis	0 (0%)	1 (2.1%)	
Prostate cancer	0 (0%)	1 (2.1%)	
Hepatitis	0 (0%)	1 (2.1%)	
Migraine	1 (1.9%)	0 (0%)	
MS	1 (1.9%)	0 (0%)	
Drug use			
Yes	22 (42.3%)	16 (33.3%)	0.41
No	30 (57.7%)	32 (66.7%)	
Smoking status			
Yes	14 (26.9%)	22 (45.8%)	0.07
No	38 (73.1%)	26 (54.2%)	
Alcohol use			
Yes	2 (3.8%)	10 (21%)	0.003
No	50 (96.2%)	38 (79%)	

The mean age of the working population during the pandemic was significantly lower than the rest (P=0.003). Among the subjects who worked during the pandemic, 71.1% were university graduates, and 21.0% had graduated from high school. Fifty percent of the working participants were health care workers, and 36% worked in the private sector or ran their own business.

The ratio of having at least one chronic disease and prolonged and regular use of medications was higher in the non-working population (P=0.018, P=0.006, respectively). Smoking behavior was significantly lower in the working population (P=0.004) (Table 3).

The participants in home confinement reported a higher incidence of a change in their working hours, and they further stated that their waking hours were later than the usual (P<0.001, P=0.004, respectively). The need for sleep during the daytime and the total amount of sleep was also higher in the non-working population (P=0.022, P=0.009, respectively). The anxiety levels were different between the groups, and the non-working group had an increased incidence of severe anxiety (P=0.005). They also reported an increased ratio of change in their lifestyle in comparison to usual (P<0.001). The overall prevalence of impaired sleeping was 47.3% in the working population and 37.1% in the non-working population.

Table 2: Evaluation of the questionnaire data according to genders

	Female (n=52)	Male (n=48)	*P*-value
Worked during pandemics			
Yes	20 (38%)	19 (39.6%)	0.92
No	32 (62%)	29 (60.4%)	
How would you describe the way you currently fall asleep in comparison to usual?			
Similar	28 (53.9%)	26 (54.1%)	0.98
Worse	22 (42.3%)	19 (39.6%)	
Better	2 (3.8%)	3 (6.3%)	
What is the main reason for your difficulty fall asleep?			
Thoughts	2 (3.8%)	3 (6.3%)	0.81
Fear	2 (3.8%)	1 (2.1%)	
Anxiety	5 (9.6%)	1 (2.1%)	
Change of my habits	7 (13.5%)	7 (14.6%)	
All	7 (13.5%)	7 (14.6%)	
Don't want to answer	1 (1.9%)	3 (6.3%)	
Would you describe trouble staying asleep?			
Yes	18 (34.6%)	11 (22.9%)	0.27
No	34 (65.4%)	37 (77.1%)	
If above question is answered as "Yes"; Would you describe difficulty in falling asleep again?			
Yes	8 (15.4%)	5 (10.4%)	0.86
No	10 (19.2%)	6 (12.5%)	
Did you experience a change in your waking hours?			
Yes	23 (44.2%)	31 (64.5%)	0.009
No	29 (55.8%)	17 (35.5%)	
If above question is answered as "Yes"; How would you describe your waking status in comparison to usual?			
Later than usual	20 (38.5%)	26 (54.2%)	0.94
Earlier than usual	3 (5.8%)	5 (10.4%)	
How do you feel when you wake up in comparison to usual?			
Similar	30 (57.7%)	29 (60.4%)	0.74
More tired	22 (42.3%)	19(39.6%)	
Would you need for sleep during the day in comparison to usual?			
Yes	17 (32.7%)	25 (52.0%)	0.003
No	35 (67.3%)	23 (48.0%)	
Would you describe a change in total amount of your sleep in comparison to usual?			
Similar	33 (63.5%)	25 (52.0%)	0.12
More hours	10 (19.2%)	14 (29.2%)	
Less hours	9 (17.3%)	9 (18.8%)	
Would you describe anxiety in comparison to usual?			
Yes	42 (80.8%)	34 (70.8%)	0.16
No	10 (19.2%)	14 (29.2%)	
How would you score your anxiety?			
None	1 (1.9%)	5 (10.4%)	0.018
Mild	24 (46.2%)	19 (39.6%)	
Moderate	22 (42.3%)	21 (43.8%)	
Severe	5 (9.6%)	3 (6.2%)	
What is the main reason for your anxiety and disturbance in sleep?			
Health issues	36 (69.2%)	20 (43.8%)	<0.001
Social issues	14 (27.0%)	9 (18.8%)	
Financial issues	1 (1.9%)	13 (27.0%)	
None	1 (1.9%)	5 (10.4%)	
Would you describe a change in your well-being in comparison to usual?			
Yes	38 (73.0%)	24 (50.0%)	<0.001
No	14 (27.0%)	24 (50.0%)	
How would you score your well-being and life satisfaction? (0-Lower; 5-Highest)			
0	1 (1.9%)	0 (0%)	<0.001
1	1 (1.9%)	1 (2.1%)	
2	10 (19.0%)	5 (10.5%)	
3	23 (44.5%)	16 (33.3%)	
4	14 (27.0%)	20 (43.6%)	
5	3 (5.7%)	5 (10.5%)	
Would you describe a change in your lifestyle in comparison to usual?			
Yes	36 (69.2%)	38 (79.0%)	0.17
No	16 (30.8%)	10 (21.0%)	

Among the participants who stated a reason for difficulty in falling asleep, the most common answer was "change of habits" in the working population, and "All of the above" in the non-working population. The ratio of individuals who reported trouble staying asleep was 36.8% in the working population, and 24.2% in the non-working population (Table 4).

All subjects reported a higher rate of fatigue when they wake up in the morning, an increased rate of anxiety, where approximately half of the participants in each study group reported a moderate level of anxiety. The most common reason for anxiety and sleep disturbance was health-related issues, followed by social and financial discomfort. More than half of the participants reported a change in their well-being in comparison to usual.

Table 3: Sociodemographic data of the study population according to working status during the pandemic

	Yes (n=38)	No (n=62)	*P*-value
Age	39.3 (9.51)	48.6 (13.3)	0.003
M/F	18/20	30/32	0.97
Married/Single	24/14	41/21	0.79
Number of children	1.16 (1.24)	1.36 (1.05)	0.86
Accommodation			
Alone	5 (13.2%)	6 (9.7%)	0.48
Family home	33 (86.8%)	56 (90.3%)	
Graduation status			
Non-schooled	0 (0%)	2 (3.2%)	0.72
Primary school	3 (7.9%)	6 (9.6%)	
Elementary school	0 (0%)	3 (4.8%)	
High school	8 (21.0%)	11 (17.7%)	
University	27 (71.1%)	40 (64.7%)	
Occupation			
Lawyer	0 (0%)	1 (1.6%)	0.32
Own company-Private sector	14 (36.8%)	20 (32.3%)	
IT	1 (2.6%)	0 (0%)	
Health	19 (50%)	16 (25.8%)	
Teacher	1 (2.6%)	1 (1.6%)	
Architect/Engineer	3 (7.8%)	2 (3.2%)	
Finance	0 (0%)	3 (4.8%)	
House woman	0 (0%)	10 (16.0%)	
Retired	0 (0%)	8 (12.9%)	
Chronic disease			
DM	2 (5.2%)	4 (6.5%)	0.018
HT	3 (7.9%)	14 (22.6%)	
Thyroid cancer	0 (0%)	1 (1.6%)	
Ulcerative colitis	0 (0%)	1 (1.6%)	
CVD	2 (5.2%)	5 (8.0%)	
Breast cancer	0 (0%)	1 (1.6%)	
Thyroid disease	3 (7.9%)	5 (8.0%)	
Sarcoidosis	0 (0%)	1 (1.6%)	
Behcet's Disease	0 (0%)	1 (1.6%)	
Epilepsy	1 (2.6%)	0 (0%)	
Psoriasis	0 (0%)	0 (0%)	
Prostate cancer	0 (0%)	1 (1.6%)	
Hepatitis	1 (2.6%)	0 (0%)	
Migraine	0 (0%)	1 (1.6%)	
MS	0 (0%)	1 (1.6%)	
Drug use			
Yes	17 (44.7%)	19 (30.6%)	0.006
No	21 (55.3%)	43 (69.4%)	
Smoking status			
Yes	14 (26.9%)	22 (45.8%)	0.004
No	38 (73.1%)	26 (54.2%)	
Alcohol use			
Yes	6 (15.8%)	6 (9.7%)	0.31
No	32 (84.2%)	56 (90.3%)	

Table 4: Evaluation of the questionnaire data according to working status during the pandemic

	Yes (n=38)	No (n=62)	*P*-value
How would you describe the way you currently fall asleep in comparison to usual?			
Similar	19 (50%)	35 (56.5%)	0.19
Worse	18 (47.3%)	23 (37.1%)	
Better	1 (2.7%)	4 (6.4%)	
What is the main reason for your difficulty fall asleep ?			
Thoughts	2 (5.4%)	3 (4.8%)	0.14
Fear	4 (10.8%)	0 (0%)	
Anxiety	1 (2.7%)	5 (8.1%)	
Change of my habits	8 (21.6%)	6 (9.7%)	
All	5 (13.2%)	9 (14.5%)	
Don't want to answer	18 (47.4%)	39 (62.9%)	
Would you describe trouble staying asleep?			
Yes	14 (36.8%)	15 (24.2%)	0.08
No	24 (63.2%)	47 (75.8%)	
If above question is answered as "Yes"; Would you describe difficulty in falling asleep again?			
Yes	10 (26.3%)	9 (14.5%)	0.28
No	4 (10.5%)	6 (9.7%)	
Did you experience a change in your waking hours?			
Yes	14 (36.8%)	56 (90.3%)	<0.001
No	24 (63.2%)	6 (9.7%)	
If above question is answered as "Yes"; How would you describe your waking status in comparison to usual?			
Later than usual	11 (28.9%)	50 (80.6%)	0.004
Earlier than usual	3 (7.9%)	6 (9.7%)	
How do you feel when you wake up in comparison to usual?			
Similar	22 (57.9%)	37 (59.7%)	0.88
More tired	16 (42.1%)	25 (40.3%)	
Would you need for sleep during the day in comparison to usual?			
Yes	12 (31.6%)	30 (48.4%)	0.022
No	26 (68.4%)	32 (51.6%)	
Would you describe a change in total amount of your sleep in comparison to usual?			
Similar	26 (68.6%)	32 (51.6%)	0.009
More hours	4 (10.8%)	19 (30.6%)	
Less hours	8 (21.0%)	11 (17.8%)	
Would you describe anxiety in comparison to usual?			
Yes	27 (71.0%)	49 (79.0%)	0.26
No	11 (29.0%)	13 (21.0%)	
How would you score your anxiety?			
None	2 (5.4%)	4 (6.4%)	0.005
Mild	18 (47.4%)	25 (40.3%)	
Moderate	17 (44.7%)	26 (41.9%)	
Severe	1 (2.7%)	7 (11.3%)	
What is the main reason for your anxiety and disturbance in sleep?			
Health issues	21 (55.3%)	35 (56.4%)	0.42
Social issues	8 (21.0%)	15 (24.2%)	
Financial issues	7 (14.4%)	7 (11.3%)	
None	2 (5.4%)	5 (8.0%)	
Would you describe a change in your well-being in comparison to usual?			
Yes	24 (63.2%)	38 (61.3%)	0.83
No	14 (36.8%)	24 (38.7%)	
How would you score your well-being and life satisfaction? (0-Lower; 5-Highest)			
0	1 (2.7%)	0 (0%)	0.13
1	1 (2.7%)	1 (1.6%)	
2	7 (18.4%)	9 (14.5%)	
3	12 (31.6%)	27 (43.5%)	
4	14 (36.8%)	20 (32.2%)	
5	3 (7.9%)	5 (8.0%)	
Would you describe a change in your lifestyle in comparison to usual?			
Yes	18 (47.4%)	56 (90.3%)	<0.001
No	20 (52.6%)	6 (9.7%)	

Discussion

In worldwide epidemics such as the SARS outbreak in 2003 and Spanish flu in 1926, an increased incidence of anxiety and neuropsychological complications during and after the incident were reported. Recently, the World Health Organization (WHO) announced the status of a pandemic due to the worldwide spread of COVID-19 [11].

A dramatic change in the lifestyle during the pandemic and its consequences are expected. However, individuals had to cope with not only health-related but also financial and social disturbances during this period, worldwide.

Our phone-based study shows a high prevalence of anxiety and impaired sleep in the adult Turkish population during the COVID-19 pandemic. Anxiety symptoms manifested in a higher degree among females than males, however, all subjects reported a higher level of anxiety and related symptoms compared to usual, irrespective of their gender. With the

increasing ratio of people losing their jobs due to lock-down and government policy related restrictions, a high number of people lack knowledge about their future working status and financial stability. Supporting this condition, in our study, we observed that almost half of the subjects reported increased impaired sleep, difficulty in sleeping and staying asleep, and more than moderate levels of anxiety.

The non-working population in our study group refers to individuals who were not working before the pandemic, owners of small businesses and those working in restaurants or other closed enterprises. The reported rate of life-style change, the total amount of sleep, and sleeping late hours were more common in the non-working population during the pandemic. Besides, being in home-confinement with children, home-schooling, managing to balance food supply, and house errands during the lockdown contribute to an increasing level of anxiety in the non-working population. Although a priority for financial issues would be an expected outcome for this group, we observed that financial instability was the third cause of their anxiety and disturbance in sleep after health-related and social insecurity.

On the other hand, 50% of the individuals in our study group were health care workers who continued working during the pandemic, and it is a known fact that they experience a close look at COVID-19 cases and related complications during the working hours. Reports from recent studies on healthcare workers during the pandemic stated increased anxiety for their potential role of the disease spread among their family members and people in contact.

A report from China showed that nearly one in four healthcare workers experienced sleep problems during the COVID-19 pandemic despite their long and intense working hours which would be exhausting [12]. A cross-sectional questionnaire survey among Chinese healthcare workers using the Pittsburgh sleep quality index (PSQI), Zung's self-rating anxiety scale (SAS) and self-rating depression scale (SDS) during the COVID-19 pandemic revealed that sleep disturbance was highly prevalent among the pediatric healthcare workers as well [13]. Another Chinese study with 1563 participants revealed that more than one-third of the medical staff suffered insomnia symptoms during the COVID-19 outbreak and that insomnia symptoms were associated with an education level of high school or below [14]. In our study, 33% of the participants were graduates of high school and below, and not having an academic degree might be a reason for the increased anxiety and sleep disorders in this population. Besides, uncontrolled information distributed through the mainstream and social media, and disagreement and conflict between the academics on the news and papers further contribute to increased anxiety due to the rising level of uncertainty about health-related issues and the future. Also, physicians defined a novel term in psychiatry literature, "Coronaphobia", which is an excessive fear of being infected by the novel coronavirus (2019-nCoV) [15]. There are several reports on the increasing ratio of obsessive-compulsive symptoms in the community, because of the preventive precautions including cleaning, washing hands, and regular use of disinfectants [16,17]. Although there are possible pharmacological treatment options for anxiety and sleep disorders including benzodiazepines, benzodiazepine receptor agonists, and sedating antidepressants, their potential adverse effects on the mood, behaviors, and concentration during work should be carefully concluded [18].

It is a known fact that individuals with impaired immunity are more vulnerable to COVID-19 infection as well as other infectious diseases. Thus, impaired sleep and anxiety might be risk factors for being infected with COVID-19 due to their effect on decreasing the immune response.

Limitations

Our study has several limitations to report. First, our data is limited to the COVID-19 pandemic and there is a possibility of selection bias. Secondly, the psychological condition of the participants was not scored. However, the participants reporting a decline in their life satisfaction compared to usual might be a consequence of the recent pandemic status. Third, we did not subgroup the subjects depending on the sectors they are working in, thus the working conditions during the pandemic might be a cause of the increased rate of anxiety and impaired sleep among different occupational groups. One other limitation to report is that we used a semi-structured survey, and possible bias might be of concern due to the current nature of our questionnaire.

Conclusions

To our knowledge, this report is the first survey analysis on the anxiety and sleep performance following the COVID-19 infections in Turkey after the first observed case in the country in March 2020. We report a high incidence of impaired sleep, change of lifestyle, satisfaction, and increased anxiety in the population independent from gender and current working status. Further research on specific populations with a higher number of subjects using multiple evaluation questionnaires might yield a more thorough assessment of the situation and its neuropsychological effects on the Turkish community. However, as a result of cultural bias, reports from different countries might also contribute to better understanding of the effects of this pandemic.

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Frequency and factors affecting the development of acute kidney injury following open heart surgery

Açık kalp cerrahisi sonrası akut böbrek yetmezliği gelişme sıklığı ve akut böbrek yetmezliği gelişmesine etki eden faktörler

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Ethics Committee Approval: The study was approved by the Ethics Committee of Ege University, Faculty of Medicine (decision no:13-4/40, date: 4/6/2011). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.
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Abstract

Aim: Acute kidney injury after cardiac surgery (CSA-AKI) is one of the most common complications in adult patients and associated with high mortality and morbidity. We aimed to evaluate the factors affecting the development of postoperative acute kidney injury, and frequency of hemodialysis in patients with normal preoperative renal function tests, and those with high preoperative renal function tests but no need of dialysis.

Methods: Patients who underwent elective coronary artery bypass, valve surgery, or both surgeries in the Department of Thoracic and Cardiovascular Surgery of the university hospital between January 2009 and December 2009 were retrospectively examined in this cohort study. Preoperative data such as age, gender, body mass index, previous cardiac surgery, history of unstable angina, myocardial infarction and cardiogenic shock, preoperative drug use, history of comorbid diseases, left ventricular ejection fraction (%), intraoperative data such as type of surgery, the total time of surgery and cross-clamping time, postoperative data such as length of hospital and intensive care stay, the requirement of revision surgery and hemodialysis and mortality rates were recorded retrospectively.

Results: Advanced age, long surgery and cross-clamp times were risk factors for CSA-AKI (P=0.002, P=0.03, P=0.02). There was no difference between the groups in terms of previous cardiac surgery, gender, left ventricular ejection fraction, preoperative nephrotoxic drug use and surgery type (P=0.69, P=0.10, P=0.19, P=0.66, P=0.86). The length of hospital and intensive care stay of patients with acute renal failure was longer (P=0.001, P=0.001). The requirement of hemodialysis after surgery was 1.3%, and mortality rate was 2%.

Conclusion: We think that thorough examination of the patients who are at risk for CSA-AKI during the preoperative period and planning the optimal treatment will aid in decreasing postoperative mortality and morbidity.

Keywords: Acute kidney injury, Cardiac surgical procedures, Risk factors

Öz

Amaç: Açık kalp cerrahisi geçirecek yetişkin hastalarda, kardiyak cerrahi ilişkili böbrek hasarı gelişmesi en yaygın komplikasyonlardan biridir ve bu durum yüksek mortalite ve morbidite ile ilişkilendirilmektedir. Kardiyak cerrahi sonrası akut böbrek yetmezliği sıklığı, akut böbrek yetmezliğine, kronik böbrek hasarı üzerine gelişen akut böbrek yetmezliğine yol açan faktörler ve hemodiyaliz gereksinim sıklığının saptanması amaçlanmıştır.

Yöntemler: Üniversite hastanesi Göğüs Kalp Damar Cerrahisi Anabilim Dalı'nda Ocak 2009 ile Aralık 2009 tarihleri arasında elektif koroner arter bypass, kapak cerrahisi veya her iki cerrahiyi geçiren hastalar, bu retrospektif kohort çalışmada incelendi. Hastaların preoperatif yaş, cinsiyet, body mass index, eski kardiyak cerrahi, unstabil anjina, myojard enfarktüs, kardiyojenik şok öyküsü olması, preoperatif ilaç kullanımı, ek hastalık öyküsü, sol ventrikül ejeksiyon fraksiyonu, intraoperatif geçirdiği cerrahi tipi, cerrahi süresi, kros-klemp süresi, postoperatif hastane ve yoğun bakım kalış süresi, revizyon cerrahisi, hemodiyaliz gereksinimi, mortalite verileri retrospektif olarak kaydedildi.

Bulgular: İleri yaş, cerrahi süresinin ve aort kros klemp süresinin uzun olması, açık kalp cerrahisi geçiren hastalarda renal hasar gelişmesi açısından risk faktörleri olarak bulunmuştur (P=0,002, P=0,03, P=0,02). Geçirilmiş kardiyak cerrahi, cinsiyet, sol ventriküler ejeksiyon fraksiyonu, preoperatif ilaç kullanımı, cerrahi tipi ile ilgili gruplar arası farklılığa rastlanmamıştır (P=0,69, P=0,10, P=0,19, P=0,66, P=0,86). Akut böbrek yetmezliği gelişen hastaların hastanede ve yoğun bakımda kalış süresi daha uzun bulunmuştur (P=0,001, P=0,001). Cerrahi sonrası hemodiyaliz ihtiyacı %1,3, mortalite %2 oranında gözlenmiştir.

Sonuç: Sonuç olarak preoperatif dönemde hastaların ayrıntılı incelenmesi ve mümkün olan optimal sağaltımın yapılmasının, operasyon planının iyi yapılarak renal hasar gelişebilecek hastaların önceden tahmin edilerek yaklaşımın buna göre değiştirilmesinin postoperatif mortalite ve morbiditeyi azaltma konusunda önemli bir yer tutacağı kanısındayız.

Anahtar kelimeler: Koroner arter bypass grefleme, Akut böbrek yetmezliği, Risk faktörleri

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Introduction

Acute kidney injury (AKI) is the most common serious complication seen between 3.5-31% of patients undergoing cardiac surgery. Complications based on non-cardiac etiology such as fibrillation, ventricular dysfunction requiring inotropic support, infection, gastrointestinal system disease, acute lung injury, and renal dysfunction may develop frequently after cardiac surgery. In addition, low flow, hypothermia, non-pulsatile perfusion with hemodilution reduce renal blood flow and associated glomerular filtration rate [1,2].

Many studies show that renal blood flow gets impaired, renal vascular resistance and renal blood flow (25-75%) severely decrease, and glomerular filtration rate diminishes in patients after cardiac surgery [3]. The incidence and prevalence of CSA-AKI differ in the literature. The reasons for this difference are the accepted diagnostic values for AKI, differences in inclusion / exclusion criteria, different study designs, patient profile diversity, and treatment differences [4]. It is important that even the smallest postoperative serum creatinine concentration (sCr) increase shown in these studies increases the risk of mortality [5].

Mortality is estimated at 8% in patients after cardiac surgery, and this rate may range from 4% to 22% in patients with CSA-AKI. It reaches 88% in patients requiring RRT (renal replacement therapy). This makes CSA-AKI an independent risk factor that can increase the risk of death up to 8-fold [5,6].

We aimed to evaluate the development of postoperative acute kidney injury, frequency of dialysis treatment and the factors affecting the development of this damage in patients with normal preoperative renal function tests, and those with high preoperative renal function tests but no need for dialysis.

Materials and methods

Study population

This was a retrospective cohort study of patients who underwent coronary artery bypass grafting (CABG), valvular replacement or both between January 2009 and December 2009 in the Department of Thoracic and Cardiovascular Surgery of the University Hospital.

Exclusion criteria

Patients under 18 years of age, those who underwent preoperative renal replacement therapy and off-pump coronary artery bypass grafting were not included in the study.

We reviewed the medical records of 336 patients who underwent cardiac surgery during the specified period. After the exclusion criteria were implemented, 298 patients were included in the study. The upper limit of normal sCr was accepted as 1.5mg / dL, which is the highest value in our laboratory. The estimated glomerular filtration rate (eGFR) was measured automatically using the short MDRD (Modification of Diet in Renal. Disease) formula from the Turkish Society of Nephrology [7]. We defined CSA- AKI as any patient who underwent a cardiac surgery in the past week and who fulfills the KDIGO criteria stage I with an increase in serum creatinine ≥0.3 mg/dL within 48 hours. Postoperative eGFR of each patient was also calculated. We divided the patients into 3 groups:

Group 1: Preoperative sCr <1.5mg/dL, eGFR >60ml/dk, No AKI postoperatively (Two patients with postoperative sCr <1.5 mg/dL but eGFR <60ml/dk were excluded.)

Group 2: Preoperative sCr <1.5mg/dL eGFR <60ml/dk, postoperative AKI (Eleven patients without postoperative AKI were excluded.)

Group 3: Preoperative sCr >1.5mg/dL eGFR <60ml/dL without RRT, postoperative AKI (Thirteen patients without postoperative AKI were excluded.)

Variables studied

The preoperative period was defined as the time from the scheduling of the surgery until the arrival of the patient in the operating room. The preoperative data as age, gender, body mass index (BMI, kg/m²), surgical diagnosis, previous history of cardiac surgery, unstable angina, myocardial infarction (MI), cardiogenic shock, history of drug use such as diuretics, ACEinh (angiotensin converting enzyme inhibitors), statins, nonsteroidal anti-inflammatory drugs (NSAIDs), history of comorbidities such as diabetes mellitus (DM), hypertension (HT), chronic obstructive pulmonary disease (COPD), congestive heart failure, left ventricular ejection fraction (LVEF;%), sCr, eGFR during 48 hours were retrospectively recorded.

The intraoperative period was defined as the time from the arrival of the patient in the operating room until the ICU admission. The type of surgery, such as coronary artery bypass grafting (CABG) or valvular surgery, or both, the total time of surgery and cross-clamp time, the lowest intraoperative hemoglobin value, and the need for blood transfusion were recorded.

The postoperative period was defined as the time from ICU admission to hospital discharge. As postoperative data, duration of mechanical ventilation, presence of complications in intensive care unit, need for revision surgery, sCr, eGFR, the need for renal replacement therapy, length of hospital stay, in-hospital mortality data were recorded retrospectively. When necessary, hemodialysis was intermittent because this is the only type of service available.

Ethics

The study was approved by the Ethics Committee of Ege University, Faculty of Medicine (decision no: 13-4/40, date: 06.04.2011). This study complies with the standards defined by the Declaration of Helsinki.

Sample size

We calculated a-priori study sample size using GPower 3 software. We found the minimum required sample size as 207 patients for ANOVA test to compare numerical variables among three groups of the study with a medium effect size of 0.25, type 1 error of 0.05 and a power of 0.90, and 183 patients for Chi-square test to compare the categorical variables among the groups with a medium effect size of 0.30, type 1 error of 0.05 and a power of 0.90. In the light of these findings, we approved the sample size of the study as 207 patients.

Statistical analysis

Statistical analysis was performed using SPSS 17 software. Descriptive data is presented as mean and standard deviation for numerical variables, and frequency and percentage for categorical variables. ANOVA test was used for comparing

numerical data, and Pearson Chi-Square was used to compare categorical data among three study groups. Mann-Whitney U test was utilized in the comparison of two independent groups of non-parametric data that do not show normal distribution. Kruskal –Wallis test was used for more than two groups. Multivariate Analysis (Logistic Regression) test was used for the variables potentially associated with the risk of developing AKI. *P*-value <0.05 was considered statistically significant.

Results

We reviewed the records of 273 patients. Demographic, preoperative, and postoperative data of the patients are presented in Tables 1 and 2. A flow diagram is shown in Figure 1.

The mean age of the patients was 58.5 (11.7) years, the mean BMI was 26.7 (3.7) kg/m², and 69.2% of the patients were male. Groups 2 and 3 were significantly older than Group 1 (*P*<0.001). Also, patients with AKI were older than those without AKI (*P*=0.002). There were no differences between the groups in terms of BMI and gender (*P*=0.13, *P*=0.10).

Fourteen patients had a history of unstable angina and 15% had a history of preoperative myocardial infarction (MI). Preoperative diuretic (furosemide, mannitol) use was 59.3%. ACE inhibitors and statins were used by 14.6% and 47%, respectively (Table 1). There were no significant differences between the groups with regards to a history of previous cardiac surgery, previous myocardial infarction, and drug use preoperatively such as diuretics, ACE inhibitors and statins (*P*=0.69, *P*=0.84, *P*=0.66, respectively). The mean LVEF (left ventricular ejection fraction) was 50.6 (9.6) %, which was similar between the groups (*P*=0.19) (Table 2).

Diabetes mellitus (DM) was detected in 27.8% of patients, hypertension (HT) in 49.8%, and chronic obstructive pulmonary disease (COPD) in 8.7%. There were no differences between groups in terms of comorbidities (*P*=0.57, *P*=0.27, *P*=0.31, respectively).

CABG was performed in 188 patients (68.8%), valvular surgery was performed in 71 patients (26 %), and both surgeries were performed in 14 patients (5.1%). The mean aortic cross-clamp time was 69.7(31.8) minutes (Table 3). In our study, there were no differences between the groups with regards to the type of surgery (*P*=0.86, *P*=0.38, *P*=0.57).

The total time of surgery was 293.2 (34.1) minutes (min) in Group 1, 299.8 (56.5) min in Group 2, 299.3 (40.5) min in Group 3. Mean cross-clamping time was 67 (27.2) min in Group 1, 77.9 (43.5) min in Group 2, 69.5 (29.7) min in Group 3. The total time of surgery and the cross-clamping time was much longer in Group 2 than Groups 1 and 3 (*P*=0.03, *P*=0.02, respectively). The relationship between the duration of surgery, cross-clamping time and AKI was evaluated, and CSA-AKI was seen to develop more in Group 2.

Complications such as sepsis, embolism and hypotension were observed in 44 patients (16.1%) in the postoperative period. CSA-AKI developed more in patients with complications (*P*<0.001). The length of hospital and intensive care stay in Group 2 was significantly longer than Groups 1 and 3 (*P*<0.001) (Table 4). Postoperatively, 15 patients (5.4%) underwent revision surgery, 3 patients (0.7%) needed hemodialysis and the mortality rate was 2.1% (6 patients) (Table 4).

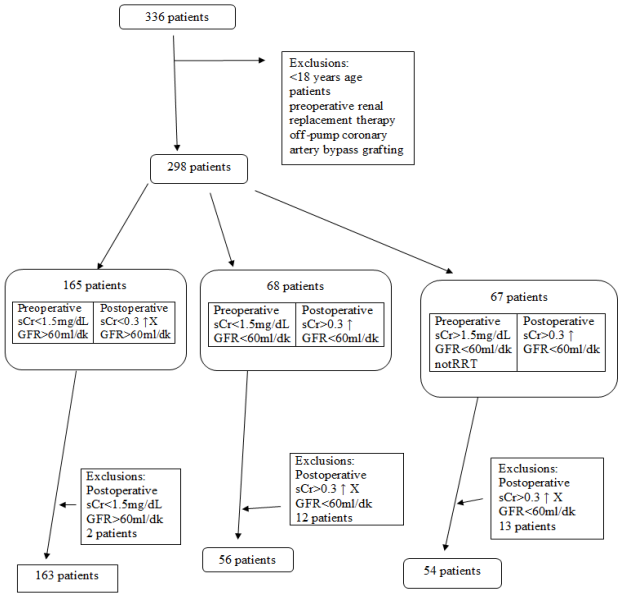

Figure 1: Flow diagram of study patients shows 273 were enrolled in the study after exclusions. Patients were categorized into those with normal kidney function and preexisting CKD without RRT by preoperative and postoperative sCr and eGFR. (RRT: Renal replacement therapy, CKD: chronic kidney disease, sCr: serum creatinine, ↑X: not elevated)

Table 1: Preoperative drug use of patients between groups

	Group 1 n=163	Group 2 n=56	Group 3 n=54	n=273	*P*-value
ACE inh	29 (17.7%)	6 (10.7%)	5 (9.2%)	40 (14.6%)	0.66
Diuretics	95 (58%)	36 (64%)	31 (57.4%	162 (59.3%)	0.19
Statins	27 (16.5%)	15 (26.7%)	5 (9.2%)	47 (17.2%)	0.37

ACE inh: Angiotensin converting enzyme inhibitors

Table 2: Demographic data of patients

Characteristics	Group 1 n=163	Group 2 n=56	Group 3 n=54	n=273	*P*-value
Age(year)	54 (11)	61(8)	67(8)	58.5(11.7)	0.002
Gender (male/female)	M:109 (66.9%) F:54 (33.1%)	M: 43 (76.8%) F:13 (13%)	M:37 (68.5%) F:17 (31.5%)	M: 189 (69.2%) F: 84 (30.8%)	0.10
BMI (kg/m²)	27.1 (3.9)	26.6 (3.5)	25.7(3.3)	26.7 (3.7)	0.13
Preop sCr mg/dL	0.86 (0.18)	0.94 (0.22)	1.40 (0.34)		
Preop eGFR mL/min/1.73 m²	103.7 (27.7)	81.4 (22.4)	48.5 (8.9)		
Postop sCr mg/dL	0.94 (0.2)	1.75 (0.9)	2.1 (1.7)		
Postop GFR mL/min/1.73 m²	94.5 (22.7)	4 (16)	40.4 (12)		
Comorbidities					
DM	41 (25%)	13(23%)	22 (40%)	76 (27.8%)	0.57
HT	72 (44%)	30(53%)	34 (64%)	136 (49.8%)	0.27
COPD	11 (6%)	12(21%)	1 (1.8%)	24 (8.7%)	0.31
Preop history of unstable angina	12 (7.4%)	2(3.6%)	0	14(5.1%)	0.26
Preop history of MI	19 (11.7%)	9 (16.1%)	13 (24%)	41(15%)	0.84
LVEF %	51.3 (9.2)	50.5 (8.7)	48.5 (11.2)	50.6 (9.6)	0.19

Preop: Preoperative, Postop: Postoperative, BMI: body mass index, eGFR: estimated glomerular filtration rate, MI: myocardial infarction, DM: diabetes mellitus, COPD: chronic obstructive pulmonary disease, HT: hypertension, LVEF: Left ventricular ejection fraction

Table 3: The surgery type and time of surgery between groups

	Group 1 n=163	Group 2 n=56	Group 3 n=54	n=273	*P*-value
History of previous cardiac surgery (n %)	22 (13.5%)	10 (17.9%)	7 (13%)	39 (14.2%)	0.69
CABG (1)	111 (68.1%)	37 (66.1%)	40 (74.1%)	188 (68.8%)	0.86
Valvular surgery (2)	49 (30.1%)	16 (28.6%)	6 (11.1%)	71 (26%)	0.38
1+2	3 (1.8 %)	3 (5.4%)	8 (14.8%)	14 (5.1%)	0.57
Total time of surgery (min)	293.2 (34.1)	299.8 (56.5)	299.3 (40.5)	295.47 (40.8)	0.03
Aortic cross- clamp time (min)	67 (27.2)	77.9 (43.5)	69.5 (29.7)	69.7 (31.8)	0.02

CABG: coronary artery bypass grafting, min: minutes

Table 4: Postoperative data of groups

	Group 1 n=163	Group 2 n=56	Group 3 n=54	n=273	*P*-value
Postop complications (sepsis, embolism, hypotension)	16 (9.8%)	14(25%)	14(25.9%)	44 (16.1%)	0.001
Length of intensive care stay(day)	1.6(0.9)	3.5(4.9)	3.35(4.1)	4.8(6.9)	0.001
Revision surgery	6 (3.6%)	3 (5.4%)	6 (11.1%)	15 (5.4%)	0.2
Length of hospital stay(day)	12.1(4.9)	15.4(8.3)	15.2(7.5)	10.4 (7.1)	0.001
Mortality in hospital	1 (0.6%)	2 (3.6%)	3(5.6%)	6 (2.1%)	0.76
RRT	0	0	3(5.6%)	3 (0.7%)	0.34

Postop: Postoperative, RRT: Renal replacement therapy

Discussion

AKI is the most common complication of cardiac surgery. The incidence of CSA-AKI varies from 5% to 42%. CSA AKI is the second most common cause of AKI after sepsis in intensive care patients. It increases intensive care stay, hospitalization time and cost of care. It is characterized by a rapid loss of renal function within hours to days, with a wide range of triggering agents [8,9].

No clear consensus exists on the definition of CSA-AKI. There are over 35 different definitions in the literature. The authors used AKIN (Acute Kidney Injury Network) and RIFLE (Risk, Injury, Failure, Loss, End stage kidney disease) criteria. KDIGO group (the Kidney Disease: Improving Global Outcomes) defined AKI as an increase in serum creatinine by ≥ 0.3 mg/dL within 48 hours (h), or an increase in serum creatinine to ≥ 1.5–1.9 times baseline levels, which is known or presumed to have occurred within 7 days or urine output < 0.5 ml/kg/h for 6 hours [10]. However, the use of these criteria may cause problems in patients who have undergone cardiac surgery due to the widespread use of fluid resuscitation and fluid overload during priming in CPB with a pump. Serum creatinine values may vary according to fluid balance, which leads to underdiagnosis of AKI. sCr is not an ideal marker for assessing renal injury because it may be normal with a greater than 50% reduction in eGFR and may not rise as soon as tubular injury has occurred. eGFR<60 mL/min/1.73 m^2 is the best definition of reduced renal function, and the lower the value, the higher the risk of worsening. Although sCr is not an ideal biomarker, it is still the only reliable marker for the diagnosis of AKI [11,12]. In our study, we used both sCr and eGFR for diagnosing CSA-AKI.

AKI is considered an independent risk factor for postoperative mortality. The mortality rate can reach up to 60%. In retrospective studies, a 30% decrease in GFR increased mortality by 4-6% in patients after cardiac surgery [11-14]. In a prospective cohort study of 43,642 patients after CABG and valvular surgery, the 30-day mortality was 64 % in patients needing hemodialysis after surgery, and 4% in patients without renal injury [15]. Welten et al. [16] reported that a 10 % reduction in creatinine clearance in patients after CABG that was transient (improved within 3 days) and CSA-AKI increased the risk of mortality by 4 -7-fold within 30 days. The need of hemodialysis after cardiac surgery occurs in approximately 1% and most of these patients remain dialysis dependent. In our study, the rate of hemodialysis in the postoperative period was 1.3%, while mortality rate was 2%.

Renal dysfunction following cardiac surgery is multifactorial and its pathogenesis is not clearly understood [17-19]. The combination of tissue ischemia-reperfusion, inflammatory processes, nephrotoxicity and atheroembolic mechanisms is thought to cause this condition [4]. Renal hypoperfusion is the most common factor leading to AKI after cardiac surgery. Renal medulla is already known to be susceptible to hypoxia and hypoperfusion [19]. Recent cardiac damage or severe cardiac valve diseases which reduce cardiac output and hypotension cause renal hypoperfusion. Low cardiac output is a common trigger for AKI development in the early postoperative period. Renal damage due to hypoperfusion in GFR occurs if low cardiac output or low hypotension persists. Prolonged renal ischemia causes structural tubular damage and tubular dysfunction. Renal hypoperfusion and tubular damage are also seen in case of oxidative damage and inflammation [20]. Wang et al. [21] evaluated 4603 patients after cardiac surgery. They found 28% patients' CrCl <60 mL/min/1.73 m² with normal sCr levels. In these patients, mortality and renal replacement therapy rate had increased, along with the comorbidity rate of cardiovascular, respiratory, neurological, and infectious complications. Wijeysundera et al. [22] reported that 13% of the patients developed AKI although sCr was within normal limits. They found that mortality rate and dialysis requirement increased by 3-fold in these patients. Common preoperative risk factors for the development of cardiac surgery-related AKI are female sex, advanced age, presence of comorbidities (previous cardiac surgery history, chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), hypertension(HT), hypercholesterolemia, congestive heart failure, LVEF < 35% and obesity [23,24]. Chertow et al. [20] reported the perioperative risk factors for the development of AKI as female gender, LVEF <35%, preoperative intra-aortic balloon pump (IABP), DM, COPD and high preoperative sCr. Chywinski et al. [18] found no differences in the development of AKI in patients with DM. O'Neil et al. [25] stated that patients with HT, DM, recent MI, left ventricular dysfunction and COPD were at increased risk for AKI after cardiac surgery. Magro et al. [26] reported that patients undergoing cardiac surgery were older and had more comorbidities than before. Therefore, they stated that the prognosis of the patients may deteriorate, and the recovery process may go slower. Santos et al. [27] suggested the age of 63 years or older was an independent risk factor for AKI because GFR decreased due to diminished renal functional reserve with age. In our study, patients in which postoperative AKI developed were older than the others, but we found no significant differences between groups in terms of gender, LVEF, previous cardiac surgery or comorbidities such as DM, COPD, HT.

Patients become more susceptible to CSA-AKI by the frequent administration of NSAIDs, diuretics, ACE inhibitors, or angiotensin receptor blockers, which also contribute to impaired glomerular hemodynamics. ACE inhibitors are routinely used in the standard treatment of heart failure due to their beneficial effects on impaired left ventricular function after myocardial infarction, reducing mortality and morbidity. They cause renal tubular damage [20]. We found no significant differences in terms of preoperative ACEinh usage. Potentially nephrotoxic drugs (such as NSAII, aminoglycosides, radiocontrast agents, ACEinh, Angiotensin receptor blockers) are recommended to be discontinued in patients scheduled for cardiac surgery, if possible [14]. A retrospective study indicated that prophylactic use of statins in the preoperative period would have a prophylactic effect on the prevention of postoperative AKI. However, other large randomized controlled trials in the literature found that statin use did not reduce hospital mortality due to postoperative AKI or cardiac surgery [28-31]. We found no significant differences in patients with preoperatively used statins.

Common intraoperative risk factors for AKI after cardiac surgery include surgery type (valvular, valvular and coronary, emergent or redo surgery), cardiopulmonary bypass

time greater than 100-120 minutes, presence of hemodilution, hemolysis and embolism [11]. Jang et al. [14] reported that surgery type was not a risk factor for AKI after cardiac surgery. In this retrospective study, 30.6% CABG, 40% isolated valvular surgery and 4.8% both surgeries were performed. Rodrigues et al. [32] suggested that valvular surgery is a risk factor for AKI because of the complexity and the long duration. Ramos et al. [33] found no significant difference between the patients with and without AKI with respect to surgical procedure performed. In their study, CABG was performed in 19 (30.64%) of the 62 patients with AKI and in 37 (46.25%) of the 80 patients without. Valve replacement alone was performed in 40 patients (64.51%). We found no significant differences between the groups regarding the type of surgery.

Suen et al. [34] observed that significant risk factors for CSA-AKI were cardiopulmonary bypass time (CPB) >140 min, preoperative congestive heart failure, and diabetes mellitus. Ninni et al. [35] stated that increased duration of surgery is a risk factor for CSA-AKI. Prolonged duration of CPB and aortic cross-clamping are accepted as some factors that influence renal blood flow and trigger renal ischemia. In our study, total surgery time and cross-clamping time were significantly different between the groups. Group 2 had a longer total time of surgery than Groups 1 and 2. CSA-AKI developed more in patients with longer surgery and cross-clamping times.

Renal dysfunction after cardiopulmonary bypass is a common finding affecting ICU and hospital stay times and raising hospital costs [2,8]. In our study, patients with renal dysfunction were found to have longer hospital and intensive care unit stays. Avoidance of AKI by preventive measures remains the mainstay management in patients with an elevated risk [11].

Limitations

Our study has several limitations. First, our study outcomes are short term outcomes, which are probably not sufficient to estimate long-term efficiency, success, and side effects of surgery. Second, our study is a single-center study with a relatively small sample size, which limits the generalization of the outcomes to the entire patient population. This causes a validity issue for the study. The retrospective design of the study gives us limited chance to consider causation between effects (preoperative renal function tests and preoperative need for dialysis treatment) and outcomes (presence of postoperative acute kidney injury, postoperative complications, preoperative radio-contrast exposure etc.). The estimations directly affect the validity, exactness, and reliability of the retrospectively gained data, and these limitations should be kept in mind when interpreting the results.

There are so many potential bias sources in retrospective studies such as inappropriate inclusion and exclusion criteria for selection bias, and irregular or missed patient records for information bias. We defined the inclusion and exclusion criteria at the planning stage. We adhered strictly to these criteria in the patient enrollment stage. We gathered study data from patient records, which gave us a chance to avoid some type of information biases, such as recall bias. Nevertheless, missing data is a big issue for the accuracy and the validity of the outcomes of the studies in which data are obtained from patient file records. Because of this, we had to exclude the patients with missing data from the study.

Conclusion

In our study, advanced age, longer surgery time and cross-clamping time were risk factors for CSA-AKI. Patients with AKI after surgery had longer intensive care and hospital stays. There is no pharmacological or non-pharmacological specific treatment for acute renal injury due to cardiac surgery. Preservation of the patient's existing renal function, prevention of AKI and continuation of effective supportive treatment are cornerstones of treatment management.

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Investigation of dose related effects of propolis on anxiety and some biochemical parameters with sympathetic skin response and increased T-maze

Propolisin anksiyeteye ve bazı biyokimyasal parametrelere etkilerinin sempatik deri cevabı ve yükseltilmiş T labirent ile araştırılması

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Abstract

Aim: Propolis has been shown to have anti-microbial, antioxidant, anti-tumor, anxiolytic and anti-inflammatory effects. However, to the best of our knowledge, there are no studies on its anxiogenic effects. In this study, we aimed to investigate the effects of different doses of propolis on anxiety in rats with cold stress via sympathetic skin response (electrodermal activity) and elevated T maze.

Methods: Forty Wistar albino male rats were used in the study, divided into four groups: The control group, low dose (10 mg/kg PRO), medium dose (30 mg/kg PRO) and high dose propolis groups (50 mg/kg PRO). Propolis was administered via gavage to all rats except the control group. Twenty minutes after injection, the anxiety scores of the rats were evaluated with an elevated T-maze, and their electrodermal activities (EDA) were measured. At the end of the experiment, some enzymatic and lipid values were measured with malondialdehyde (MDA) in blood samples.

Results: The percentage of time spent on open arms and the number of open arm entries were lower in the 10mg/kg PRO group, while an increase was observed in the 30 mg/kg PRO group. EDA values were lower in the 30 mg / kg PRO (P=0.012; P=0.02, respectively) and 50 mg / kg PRO (P=0.013, P=0.02, respectively) groups as compared to the control group. MDA was significantly lower in the 30 mg/kg PRO and 50 mg/kg PRO groups. While AST value increased in the 30 mg / kg PRO group, ALT value decreased. Total cholesterol and triglyceride values were significantly lower in the 50 mg / kg PRO group. HDL value increased significantly after administration of propolis and LDL value decreased significantly only in the 10 mg/kg PRO group.

Conclusions: According to the results obtained by EDA and T labyrinth methods, while low and high dose propolis, which was administered to rats after cold stress, showed an anxiogenic effect, medium dose propolis exerted an anxiolytic effect. It also decreased MDA values in the medium and high dose groups and influenced enzymatic and lipid values in favor of the rat. It was concluded that the anxiety-related effects of propolis were dose-dependent.

Keywords: Propolis, EDA, Anxiety, T-maze

Öz

Amaç: Propolisin anti-mikrobiyal, antioksidan, anti-tümör, anksiyolitik ve anti-inflamatuar etkilere sahip olduğu gösterilmiştir. Ancak literatürde propolisin anksiyojenik etkisi konusundaki çalışmalara rastlanılmamıştır. Bu çalışmamızda, soğuk stresi oluşturulmuş sıçanlarda propolisin farklı dozlarının anksiyeteye etkilerinin sempatik deri cevabı (elektrodermal aktivite) ve yükseltilmiş T labirent ile araştırılması amaçlandı.

Yöntemler: Çalışmada 40 adet Wistar albino erkek sıçan kullanıldı. Kontrol grubu, düşük doz (10 mg/kg PRO), orta doz (30 mg/kg PRO) ve yüksek doz propolis (50 mg/kg PRO) grupları oluşturularak, kontrol grubu hariç diğer gruplara propolis gavaj yoluyla uygulandı. Enjeksiyondan 20 dakika sonra, sıçanların anksiyete skorları yükseltilmiş T-labirent ile değerlendirildi ve daha sonra da elektrodermal aktiviteleri (EDA) ölçüldü. Deney sonunda kan örneklerinde, spektrofotometrik olarak malondialdehit (MDA) ile bazı enzimatik ve lipid değerleri ölçüldü.

Bulgular: 10 mg/kg PRO grubunda açık kolda harcanan zamanın yüzdesi ve açık kola giriş sayısı, diğer gruplara göre daha düşük bulunurken 30 mg/kg PRO grubunda artış gözlendi. EDA, 30 mg/kg PRO (sırasıyla, P=0,012, P=0,02) ve 50 mg/kg PRO (sırasıyla, P=0,013, P=0,02 gruplarında kontrole kıyasla daha düşüktü. MDA'nın 30 mg/kg PRO ve 50 mg/kg PRO gruplarında önemli oranda düşük olduğu görüldü. 30 mg/kg PRO grubunda AST değeri artış gösterirken ALT değerinde azalmanın olduğu görüldü. Toplam kolesterol ve trigliserit değerleri 50 mg/kg PRO grubunda anlamlı olarak düşüktü. HDL değerinin düşük doz propolisten uygulamasından itibaren anlamlı yükseldiği, LDL değerinin ise sadece 10 mg/kg PRO grubunda anlamlı azaldığı olduğu görüldü.

Sonuçlar: EDA ve T-labirent yöntemleriyle elde edilen sonuçlara göre düşük ve orta doz propolis anksiyetik etki yaparken, yüksek doz propolis anksiyolitik etki göstermiştir. Ayrıca sıçanlara soğuk stres sonucunda uygulanan propolisin MDA değerlerini orta ve yüksek doz gruplarında düşürdüğü, enzimatik ve lipid değerlerinde ise organizma lehine olumlu değişimlere sebep olduğu görüldü. Dolayısıyla propolisin anksiyeteye ilişkin yanıtlarının, doza bağlı etkilerine göre değiştiği sonucuna varılmıştır.

Anahtar kelimeler: Propolis, EDA, Anksiyete, T-labirent

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Introduction

Anxiety disorders, one of the most common psychiatric diseases worldwide, constitute an important health problem [1]. There are many types of anxiety, including post-traumatic stress disorders, phobias, panic disorders, and obsessive–compulsive disorders, all of which usually share important mental and physical symptoms such as nervousness, tremor, racing thoughts, agitation, emotional discomfort, and insomnia [2]. Although new drug types have not been adopted since the introduction of selective serotonin uptake inhibitors (SSRIs) and other antidepressants for the treatment of anxiety, advancement in anxiolytic drugs has been a major focus of the pharmaceutical industry and academic neuropsychiatric investigations [3]. Anxiety research relies on similarities between human emotional behavior and behaviors in animals, such as the rat and the mouse [4]. There are many rodent behavioral paradigms that aim to model anxious behavior, such as anxiety-related defense behavior (ARDEB), the elevated plus maze (EPM), the light-dark box (LD) and the open field (OF) [3].

In psychological research, one of the most utilized indices of the autonomic nervous system is electrodermal activity (EDA), which usually measures the level of skin conductivity (SCL) [5]. SCL reflects tonic arousal [6]. EDA, for which the change in skin potential or resistance of sweat gland reaction that is controlled by the sympathetic nervous system (SNS), is measured, has been used in studies examining emotion [7], attention [8], and psychopathology. The relationship between anxiety and sympathetic skin response (SSR), in other words, SCL, has been widely studied. The results of studies on human subjects and animals indicate that anxious subjects have greater sweat gland activity [9,10]. However, data are limited in animals. These studies were conducted to define the anxiolytic activities of some drugs, and to measure anxiety, fear response, stress, and arousal [11,12].

The elevated T maze test is a widely used anxiety measurement method based on the natural avoidance of rodents from high and open fields. Untreated animals usually spend more time in closed arms. The percentage of time spent in open arms is regarded as an index of anxiety. It is generally known that anxiolytic drugs increase the number of entries in open arms (OAEs) and the time spent in there (TSOA), while the anxiogenic drugs decrease these parameters. Certain pharmacological compounds may affect anxiety-related behaviors depending on the dose [9].

Natural products have been used in medicine for various purposes for centuries. Propolis, which is a natural product, is gaining increasing importance due to its antioxidant effect against pathogenic microorganisms [13]. Propolis has antibacterial, antifungal, anti-inflammatory, antioxidative, adaptogenic, and anxiolytic effects [14-19].

Studies investigating the effect of propolis on anxiety have generally been studied in one or two doses. These studies were conducted directly on the rats without anxiety, and anxiety was measured in the open area, forced swimming test and plus maze. In the literature, there is no study investigating the effect of different doses of propolis on anxiety by creating an anxiety model. The aim of this study was to determine the effect of propolis on the behavioral scores of rats, assessed by elevated plus-maze (ETM) and EDA, and which mechanism plays a more effective role on anxiety.

Materials and methods

Experimental animals

All protocols were approved by the Animal Care and Use Committee (3/11/2015, 15/65 Ethics Committee) of Erciyes University. About 3-4 months-old male Wistar albino rats (average body weight of 250-300 g) were supplied by the Laboratory Animal Unit of Experimental and Clinical Research Center, Erciyes University and kept under controlled conditions (25±1°C temperature, 55% relative humidity and 12 h dark/light cycles). Food and water were allowed ad libitum during the experimental period. All animal experiments were conducted in the Laboratory of Brain Dynamics, Erciyes University Faculty of Medicine, Department of Physiology.

Preparation of propolis

1.2 g of propolis extract was weighed on a precision scale. It was placed in the measuring cup and dissolved in a magnetic stirrer. Propolis was prepared for each subject with ethanol and distilled water at a dose of 0.012 g/ml/kg. First, 50 ml of ethanol was added slowly. Then, a total of 500 ml of water was added and the propolis was allowed to dissolve in the magnetic stirrer for 40 minutes. The undissolved particles were passed through filter paper and mixed after re-addition to the medium. Following these procedures, the mouth of the container was left open for 1 week to remove alcohol. For low dose propolis, medium dose propolis and high dose groups, 50 µl, 75 µl and 250 µl were withdrawn from the propolis solution and completed to 5 ml with distilled water.

Cold stress

Animals were kept in a cold room (+4ºC) between 08:00 and 10:00 for 2 hours each day during the 5-day experiment. The body weights of the rats were measured to determine the effect of the cold stress procedure. Also, the rectal temperatures of the animals exposed to cold were measured immediately after this application [20]. The rat groups and each of the rats were studied individually. In cold-exposed rats, propolis was administered after cold exposure, when rectal temperatures normalized. Propolis was administered 30 minutes prior to the ETM. The sympathetic activity via skin conductivity was then recorded with A/AgCl electrodes attached to the plantar surfaces of the posterior extremities for EDA measurement.

Forming the experimental groups

In the study, 40 male rats, 10 rats in each group, were used.

Control group: Physiological saline was administered by gavage to each rat.

Low dose propolis group (10 mg/kg PRO): 10 mg/kg of propolis was administered by gavage to each rat.

Medium dose propolis group (30 mg/kg PRO): 30 mg/kg of propolis was administered by gavage to each rat.

High dose propolis group (50 mg/kg PRO): 50 mg/kg of propolis was administered by gavage to each rat.

Elevated T-maze test (ETM)

The rats were subjected to an ETM, to determine if propolis affected anxiety-related behavior [12]. Briefly, the ETM

consisted of a central platform (5 cm×5 cm), with two open arms (50 cm×10 cm×50 cm), and one closed arm (50 cm×10 cm×40 cm). The arms were arranged in such a way that each type was opposite each other. The maze was 50 cm above floor level and tests were conducted under a dim red light. The animals were placed individually on the central platform of the T-maze facing an open arm. Two observers recorded the number of times spent in the open and closed arms and the number of entries into each arm during a 5-minute period. The percentage of time spent in the open arms and the number of entries into these arms were used to measure anxiety [9].

Electrodermal activity (EDA)

The physiological recordings took place in a dimly lit, electrically and acoustically shielded experimental room. EDA was measured using the MP30 system (MP30, Biopac Systems Inc, Santa Barbara, CA). EDA was recorded between the paw pads of both hindlimbs using 2 Ag/AgCl electrodes after ETM. NaCl electrode (0.05 M) jelly was placed between the skin and the electrodes. The two electrodes were connected to the MP30 system. The signals received from the skin were converted to digital signals by MP30 data acquisition unit and processed for off-line analysis on an IBM-AT computer located in a separate room. Digital signals were stored in the computer for data analysis. The mean of skin conductance (SC) was expressed as SCL [ln (μmho)/cm^2 per electrode area]. Two recordings were obtained in 2 sections for all animals. Tonic section was recorded over 2 minutes without any stimuli. The phasic section was recorded by giving 15 auditory stimuli, which were of 1-second duration, 1000 Hz tones with 50-ms rise and fall times. The sound chip of a computer produced the tones. They were amplified with an audio amplifier (Harvard). The intensity of the tones was 90 dB as measured by a sound level meter positioned at the approximate location of the rat's ear. The tones were presented against a 50-dB pink noise background. They occurred at pseudorandom intervals ranging from 30 s to 65 s and averaging 45 s. The mean SCL values were also calculated off-line for phasic EDA. Values of phasic SCL averaged at 10 rats per group during the test period, which used 15 auditory stimuli [9].

Procedure

The animals were conscious during the recordings. Propolis was administered to the rats in three different doses at once. The ETM measurements started 30 min after the gavage. The ETM apparatus was wiped clean with a sponge and dried with a cloth between tests. After ETM, SCL was recorded, without losing any time.

Collection and analysis of blood samples

Blood was collected from anesthetized rats to measure total cholesterol, HDL-LDL cholesterol, phospholipid, triglyceride, total protein, albumin, glucose, AST and ALT enzyme levels and transferred to heparinized polyethylene tubes for determination of lipid peroxidation level +4°C at 3000 rpm. They were centrifuged for 10 minutes and their plasma was obtained, which were stored at -20°C until analysis. -80°C was used for the storage of plasma separated for MDA measurements. The determination of the specified biochemical values was studied by spectrophotometric method using an auto analyzer. Blood plasma MDA values were also determined spectrophotometrically (UV-2100 Shimadzu, Japan) with the help of Oxis Research (Bioxytech) test kits.

Statistical analysis

The distribution of the data was evaluated by histogram, q-q graphs, and Shapiro-Wilk test. Values were expressed as means (Standard deviation). Data from the T-maze test and EDA were analyzed with Mann-Whitney U test and independent t-test was used for comparison of 2 groups. One-way analysis of variance was used for comparison of biochemical parameters between the groups, and Tukey and Tamhane tests were used for multiple comparisons. SPSS program was used to analyze the data. A *P*-value of less than 0.05 was considered statistically significant.

Results

Effects of propolis rats in the T-maze

The number of entries into open (NEOA) and closed arms (NECA), total time and the percentage of time spent (% TSOA) in the open arms were measured in the T-maze test (Table 1).

Table 1: Distribution of parameters evaluated in T-maze test according to experiment groups. Mean (SD)

	NEOA	NECA	TSOA	% TSOA
Control	1.5(0.52)	2.4(0.69)	38(11.83)	14.5(3.43)
10mg/kg PRO	0.5(0.52)*#	1.4(0.56)*#	6.5(3.01)*#	2.2(1.09)*#
30mg/kg PRO	2.6(0.84)	2.7(0.42)	24(6.41)	9.6(2.66)
50mg/kg PRO	0.6(0.96)*#	1.3(0.63)*#	0.6(0.83)*#	0.6(0.34)*#
P-value	<0.011	<0.001	<0.001	<0.001

* Different from the control group, PRO: propolis, # Different from the medium dose group (*P*<0.05, Kruskal-Wallis, post-hoc Mann-Whitney U), NEOA: Number of entries into open arms, NECA: Number of entries into closed arms, TSOA: Time spent in open arms, % TSOA: Percentage of time spent in open arms

The NEOA, NECA, TSOA, and % TSOA values of the control group were significantly different from the propolis groups except for the 30 mg/kg PRO.

The number of entries into the open arms and percentage of time spent there were lower in 10 mg/kg PRO group than in the other groups. The open and closed arm entries (*P*<0.001, *P*<0.001, respectively), time spent in the open arms (*P*<0.001) and the percentage of time spent in the open arms (*P*<0.001) decreased significantly in the 50 mg/kg PRO group as compared to the control group. This finding indicated that administration of 50 mg/kg PRO increased anxiety and sympathetic activity. Administration of 30 mg/kg propolis increased the number of open arm entries (*P*=0.011), the number of enclosed arm entries (*P*=0.013), time spent in the open arms (*P*=0.009) and percentage of time spent in the open arms (*P*=0.009), when compared with administration of 50 mg/kg propolis. The anxiolytic potential of 30 mg/kg PRO was stronger than that of other groups in the elevated T-maze model. There were no significant differences between the 30 mg/kg PRO and the control groups (Figure 1, 2).

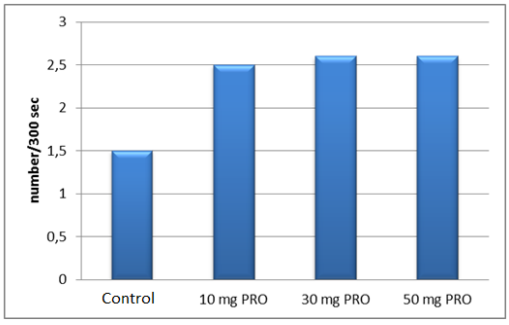

Figure 1: Distribution of NEOA (The number of entries into open arms)

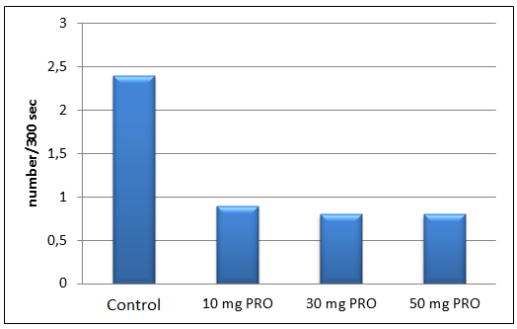

Figure 2: Distribution of NECA (The number of entries into closed arms)

Effects of propolis on skin conductance level (SCL)

The increase in SCL in Tonic EDA, which is independent of the stimuli, and the phasic EDA measured by stimulating, indicate increased anxiety.

Tonic and Phasic SCLs were statistically higher in the 50 mg/kg PRO group than the control (P=0.02, P=0.04, respectively) and 30 mg/kg PRO groups (P=0.013, P=0.02, respectively). Tonic and Phasic SCLs were statistically lower in the 30 mg/kg PRO group than the control (P=0.012, P=0.02, respectively) and 50 mg/kg PRO group (P=0.013, P=0.02, respectively). These findings showed that 50 mg/kg PRO exhibited an anxiogenic effect, while 30 mg/kg PRO showed an anxiolytic effect (Table 2).

The results of biochemical parameters

Evaluation of lipid peroxidation product MDA to measure antioxidant revealed that it was significantly lower in the 30 mg/kg PRO and 50 mg/kg PRO groups. This decrease was more pronounced in 30 mg/kg PRO (P<0.001) group. AST value increased in the 30 mg/kg PRO group, while a decrease in ALT was observed. No differences were observed between the groups in terms of LDH values (Table 3).

There was a decrease in triglyceride and total cholesterol values, especially in 50 mg/kg PRO group (P<0.001). It was observed that HDL value increased significantly starting from the administration of high dose propolis and LDL value decreased significantly in the 10 mg/kg PRO group only (P<0.001). A significant increase was observed in the phospholipid values in the 30 mg/kg PRO and 50 mg/kg PRO groups (Table 3).

Table 2: Tonic and phasic SCL values of the groups.

SCL (µmho)	10 mg/kg PRO	30 mg/kg PRO	50 mg/kg PRO
Tonic SCL	9.53(1.46)	6.32(0.23)*	12.12(1.12)
Phasic SCL	8.74(2.15)	5.75(1.22)*	11.17(1.19)
P-value	<0.001	<0.001	<0.001

Mean (Standard deviation), * Compared with 30 mg/kg PRO, # Compared with 50 mg/kg PRO

Table 3: Average blood values and statistical results of rats

Parameter/Group	Control group	10 mg/kg PRO	30 mg/kg PRO	50 mg/kg PRO	*P*-value
MDA (µM)	2.46(0.37)^{a}	2.25(0.26)^{a}	1.83(0,27)^{b}	0.76(0.16)^{c}	<0.001
AST (IU/L)	116.59(21.30)	114.48(15.21)	112.07(21.34)	114.14(19.74)	0.874
ALT (IU/L)	57.68(10.24)^{a}	58.34(7.44)^{a}	52.14(10.72)^{ab}	48.32(8.57)^{b}	0.018
LDH (IU/L)	1502(294.14)	1633(314.72)	1672(201.24)	1508(276.12)	0.248
Triglycerides	169.04(43.01)^{a}	145.27(32.76)^{ab}	141.25(25.42)^{bc}	114.13(11.78)^{c}	0.001
Total cholesterol	97.25(6.28)^{ab}	101.14(9.8)^{a}	92.23(4.8)^{b}	76.94(10.48)^{c}	<0.001
HDL	24.28(4.89)^{a}	31.76(8.75)^{b}	39.89(5.85)^{c}	41.23(4.28)^{c}	<0.001
LDL	36.27(3.89)^{a}	30.27(6.57)^{b}	21.54(7.98)^{c}	16.49(6.21)^{c}	<0.001
Phospholipids	178.43(17.25)^{a}	154.76(22.58)^{b}	216.23(24.89)^{c}	230.49(22.76)^{c}	<0.001

Data are expressed as mean (standard deviation), The same letters in the same line indicate the similarity between the groups and the different letters indicate the difference between the groups, MDA: malondialdehyde, AST: Aspartate Aminotransferase, ALT: Alanine aminotransferase, LDH: Lactate dehydrogenase, HDL: high density lipoprotein, LDL: low density lipoprotein

Discussion

Emotional, cognitive, and physical behaviors include changes in peripheral autonomic activity. Electrodermal activity (EDA), the so-called galvanic skin response or sympathetic skin response, reflects sympathetic tone, and is therefore frequently used as an indirect measure of attention, cognitive effort, or emotional arousal [21]. EDA is a multisynaptic sympathetic reflex that may be evoked by a variety of internally generated or externally applied arousal stimuli. It is considered an index of psychological processing properties of stimuli, such as significance, novelty or emotional relevance, and effortful processing [22]. Skin conductance level (SCL) is a parameter of EDA. A high SCL may result from increased eccrine sweat gland activity and sympathetic activity [5].

Anxiety can be explained as fear, tension, distress during daily life and is part of a widely spread group of psychiatric illnesses which are a cause of major concern [1]. The defense behavior assays of rodents have usually been used as preclinical models of anxiety. The EPM and EDA are established methods for testing animal anxiety.

Studies examining the effects of propolis on sympathetic nerve activation and blood pressure are very limited. In the literature, there is no study on whether propolis affects anxiety. Thus, in our study, it was investigated whether different doses of propolis affect anxiety level and electrodermal activity, which is considered an indicator of sympathetic nervous system activity.

Considering the role the autonomic nervous system plays in its formation, EDA can be evaluated as the window of the central nervous system (CNS) opening to the periphery. From this point of view, it is possible to extract information about CNS through observations made in the periphery. It is also stated that EDA can be used to study the effectiveness of various anesthetic conditions and drugs in the CNS. Dolu et al. [23] reportedly used EDA and plus maze methods in their studies to investigate the acute effects of L-tryptophan on anxiety in different doses. Anxiety mainly stems from the CNS. The attention and perception centers of CNS, which are also responsible for anxiety, play a significant role in EDA formation. Therefore, according to the level of anxiety, the electrical activity of the skin changes as a result of variable emotional sweating in the sweat glands innervated by the sympathetic nervous system, which is controlled by the autonomic nervous system in CNS. The reflection of the changing electrical activity of the skin in the DIS is measured by EDA.

According to the results of EDA measurements in our study, the anxiety levels of 30 mg/kg PRO and 50 mg/kg PRO groups were found to have significantly changed. In the 30 mg/kg PRO group, tonic and phasic SCL were quite low. This showed us that propolis suppresses sympathetic activation and reduces anxiety levels. The results obtained by EDA measurements were supportive of the behavior scoring in the T-maze test.

MDA measurements for determination of antioxidant levels revealed that it was significantly lower in the 30 mg/kg PRO and 50 mg/kg PRO groups. This decrease was thought to stem from propolis flavonoids. Mohammadzadeh et al. [24] reported that the samples with low flavonoid concentrations were more effective in MDA inhibition in their studies comparing the flavonoid contents (mg/g propolis) and MDA formation inhibition values (%) of the propolis samples they collected from different regions. They emphasized that the structural type of

flavonoid may be more important than the total flavonoid amount in the antioxidant effect expected from flavonoids. Hosnuter et al. [25] similarly reported a significant decrease in MDA values compared to the control group with the administration of CAPE, an important compound of propolis, in rats.

AST enzyme did not change significantly in intergroup averages, while ALT activity decreased in the 50 mg/kg PRO group. A similar situation was observed when examining the regulatory effect of long and short-term propolis supplementation by applying sodium fluoride, and it is noteworthy that the ALT enzyme is higher and the AST enzyme is lower in the groups treated with propolis compared to the sodium fluoride group [26]. In the studies of Kolankaya et al. [27] on alcohol-induced hepatotoxicity, the AST activity of the alcohol-administered group increased significantly more than ALT, whereas it was observed that this increase reached a normal course in the alcohol+propolis group. No such relationship could be detected in the mentioned groups in terms of ALT levels. Similarly, Mani et al. [28] reported that did not detect any changes in AST levels in rats which were administered 1, 3 and 6 mg/kg/day propolis.

The level of MDA and ALT values decreased in 30 mg/kg PRO group. No significant difference was observed in intra-group and inter-group comparisons of LDH. While Mani et al. [28] did not find any differences in LDH enzyme values in rats which were administered propolis for a short and long time, Newairy et al. [29] reported that there was a significant decrease in LDH activity in the rat group with AlCl3 toxicity which were given propolis. Kolankaya et al [27] found that LDH activity was low in rats that were administered alcohol compared to the propolis group.

There was a decrease in triglyceride and total cholesterol values and a statistically significant decrease in the 30 mg/kg PRO group only. It was observed that HDL value increased significantly after administration of low dose propolis and LDL decreased significantly only in the PRO-30 mg/kg group. A significant increase was observed in the phospholipid values in the 30 mg/kg PRO and 50 mg/kg PRO groups. The results are compatible with many other studies on this subject [27,29,30].

Limitations

Blood samples could have been evaluated at the beginning and end of the experimental study, along with other biochemical parameters such as TAS, and TOS. However, due to lack of time and funding, it could not be done. We believe that this study will contribute to future work as a basis.

Conclusions

This is the first study to investigate the effect of propolis on anxiety and electrodermal activity. According to the results obtained by EDA and T labyrinth methods, low and medium dose propolis showed anxiogenic effects while high dose propolis exerted an anxiolytic effect. In addition, positive changes in enzymatic and lipid values in favor of the organism were observed in which propolis administered to rats decreased MDA values in the middle and high dose groups. Therefore, it was concluded that the anxiety responses of propolis depend on dosage.

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A retrospective review of patients over 70 years of age undergoing pneumonectomy for non-small cell lung cancer: 10 years of experience, a cross-sectional study

Küçük hücreli dışı akciğer kanseri nedeniyle pnömonektomi uygulanan 70 yaş üzerindeki hastaların incelemesi: 10 yıllık deneyim, kesitsel çalışma

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Ethics Committee Approval: The study was approved by the Ethic Committee of Ankara City Hospital (28/05/2020-18979). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.
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Abstract

Aim: Future projections suggest that more older people will be affected by non-small cell lung cancer (NSCLC) over the next years due to longer life expectancy and aging global population. Chronological age is used to define elderly. 70 years of age is the most commonly accepted lower limit of senescence since the majority of physiological changes occur after this age. The aim of the current study was to review demographic, epidemiological and clinical characteristics of patients over the age of 70 diagnosed with NSCLC who underwent pneumonectomy at our clinic in a retrospective manner.

Methods: This cross-sectional study involved a retrospective assessment of 21 patients over 70 years of age who were diagnosed with NSCLC and underwent pneumonectomy between January 2010 and January 2020. Demographic data, symptoms, tumor types, localization of tumors, postoperative complications and stages of cancer were recorded in the database and statistically analyzed.

Results: All 21 patients were male and had a mean age of 72.5 years. The presenting symptom was dyspnea in 23.8% of the patients, cough in 28.6%, hemoptysis in 19%, chest pain in 14.3% and weight loss in 4.8% of the patients and 9.5% of the cases were detected incidentally. The tumor types included squamous cell carcinoma (57.1%), adenocarcinoma (23.8%), adenosquamous carcinoma (14.3%) and large cell carcinoma (4.8%). Tumor site was the left lung in 81% and right lung in 19% of the patients. Early postoperative complications occurred in 5 (23.8%) patients. Three of these patients developed atrial fibrillation and two patients suffered hemorrhage. Postoperative tumor stages of the patients were stage 3a (47.6%), stage 2b (19%), stage 2a (14.3%), stage 1b (9.5%) and stage 1a2 (9.5%). Multidimensional scaling analysis showed an association between the type of tumor and smoking but no association was found between tumor type and family history (P=0.024, P=0.586, respectively).

Conclusion: It should be kept in mind that surgical resection and even pneumonectomy which is associated with high mortality and morbidity can be successfully performed in older cancer patients through a good preoperative workup, tumor staging, assessment of the risk of mortality and the effects of comorbid conditions.

Keywords: Lung cancer, Surgery, Pneumonectomy, Age

Öz

Amaç: Uzayan yaşam süresi ve yaşlanan dünya nüfusu ilerleyen yıllarda daha fazla sayıda yaşlı küçük hücreli dışı akciğer kanserli (KHDAK) hastanın ortaya çıkacağını göstermektedir. Yaşlılık tanımlaması için kronolojik yaş kullanılmaktadır. 70 yaş fizyolojik değişikliklerin giderek artmaya başladığı dönem olması nedeniyle en çok kabul gören sınır olmuştur. Çalışmamızda; kliniğimizde KHDAK tanısı nedeniyle pnömonektomi uygulanmış 70 yaş üstü hastaların demografik, epidemiyolojik ve klinik özelliklerinin geriye dönük olarak incelenmesi amaçlanmıştır.

Yöntemler: Kesitsel tipteki bu çalışmada, Ocak 2010 ile Ocak 2020 arasında KHDAK tanısı alan ve pnömonektomi yapılan 70 yaş üstü 21 hastanın retrospektif olarak değerlendirilmesi yapıldı. Demografik veriler, semptomlar, tümör tipleri, tümörlerin lokalizasyonu, postoperatif komplikasyonlar ve kanser evreleri veri tabanına kaydedildi ve istatistiksel olarak analiz edildi.

Bulgular: Çalışmamızda yer alan 21 hastanın tamamı erkek ve ortalama yaş 72,5 idi. Hastaların %23, 8'i dispne, %28,6'ı öksürük, %19'u hemoptizi, %14,3'ü göğüs ağrısı, %4,8'i kilo kaybı şikayeti ile başvururken %9,5'i insidental olarak saptanmıştır. Tümör tipi %57,1 squamöz hücreli karsinom, %23,8 adenokarsinom, %14,3 adenosquamöz karsinom ve %4,8 large cell karsinom olarak tespit edilmiştir. Tümör %81 sol, %19 sağ akciğer yerleşimliydi. Postoperatif erken dönemde olguların 5'inde (%23,8) komplikasyon görülmüştür. Erken dönem komplikasyon görülen olguların 3'ünde atrial fibrilasyon, 2'sinde kanama olduğu görüldü. Hastaların postoperatif evreleri; %47,6'ı evre 3a, %19'u evre 2b, %14,3'ü evre 2a, %9,5'i evre 1b ve %9,5'i evre 1a2 idi. Çok boyutlu ölçekleme analizinde tümör tipi ile sigara kullanımının ilişkisi saptanmış ancak aile öyküsü ile tümör tipi arasında ilişki kurulamamıştır (sırasıyla P=0.024, P=0.586).

Sonuç: Cerrahi rezeksiyon olarak morbidite ve mortalitesi yüksek olan pnömonektominin bile yaşlı hastalarda iyi bir preoperatif değerlendirme, evreleme, eşlik eden hastalıkların etkileri ve mortalite tayini ile başarılı bir şekilde uygulanabileceği bilinmelidir.

Anahtar kelimeler: Akciğer kanseri, Cerrahi, Pnömonektomi, Yaş

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Introduction

Lung cancer is the leading cause of cancer death worldwide and non-small cell lung cancer (NSCLC) accounts for more than 80% of all lung cancers [1]. Surgical treatment is the first-line treatment for early stage non-small cell lung cancer [2]. Increased life expectancy is associated with higher numbers of patients diagnosed with lung cancer and older patients [3]. Aging leads to physiological changes in cardiovascular and respiratory systems, resulting in increased rate of comorbidities, and older patients are more likely to develop life-threatening complications following surgical resection [4].

Future projections suggest that there will be more older people affected by NSCLC over the next years due to longer life expectancy and aging global population. It is not possible to determine the real biological age of a person and therefore, chronological age is used to define elderly. Different cut-offs for chronological age have been used in studies to define elderly including 65, 70 and 75 years of age. 70 years of age is the most accepted lower limit of senescence since most physiological changes occur after this age [5]. Studies on optimal treatment of NSCLC patients have mostly enrolled patients under 65 years of age [6]. Older patients with lung cancer are less likely to receive conventional cancer treatments compared to younger patients [7]. Toxicity, the presence of coexisting conditions associated with increased morbidity and mortality, difficulties in access to healthcare services and patient and physician preferences may present barriers to patients in getting maximal therapy. Age is not the sole criterion to decide whether a patient may or may not tolerate cancer treatment. Outcomes of lung cancer therapy in most elderly patients are generally comparable to those in younger patients [8,9]. Comorbid conditions, age-related physiological losses, chronic medication use, and smoking status of the patients should be considered when determining the therapeutic options. In brief, functional status and physiological capacity of the patient should be carefully evaluated in older patients with lung cancer while making treatment plans.

The aim of the current study was to review demographic, epidemiological and clinical characteristics of patients over the age of 70 diagnosed with NSCLC who underwent pneumonectomy at our clinic in a retrospective manner.

Materials and methods

The study involved a retrospective assessment of 21 patients diagnosed with NSCLC and underwent pneumonectomy between January 2010 and January 2020 at the clinics that we provided medical service. Epidemiological, demographic, clinical, laboratory, histopathological and treatment data were retrieved from the medical files of the patients and statistical analyses were performed on these data. Gender, age, presenting symptom, smoking status, family history, preoperative diagnostic method, anatomical location of the mass, lymph node involvement on preoperative PET-CT and maximum standardized uptake values (SUVmax) of the tumor, operated side and type of surgery, early postoperative complications, tumor size, results of postoperative histopathological examination and pathological staging of the patients were reviewed. Cardiology and internal medicine departments had evaluated all patients preoperatively.

Preresection pulmonary assessment included respiratory function tests, DLCO (diffusing capacity for carbon monoxide), the six-minute walk test, postoperative FEV1 measurement and cardiopulmonary exercise testing (vo2 max) for borderline values. The type of tumor, family history and smoking status were also examined using multidimensional scaling and correspondence analysis.

Statistical analysis

Recorded data were analyzed using the SPSS for Windows, version 23.0 software package. Descriptive statistics of studied numerical variables were reported using mean as a measure of central tendency and standard deviation as a measure of dispersion. Mann-Whitney U and Wilcoxon tests were used to compare study variables between groups. A *P*-value of less than 0.05 was considered statistically significant.

Results

All 21 patients were male, with a mean age of 72.5 years. The presenting symptom was dyspnea in 23.8% of the patients, cough in 28.6%, hemoptysis in 19%, chest pain in 14.3% and weight loss in 4.8% of the patients, and 9.5% of the cases were detected incidentally. Among patients, 66.7% were current smokers 4.8% never smoked and 28.6% had quit smoking. Family history was absent in 81% of the patients. Preoperative diagnosis was established with bronchoscopy in 71.4%, transthoracic biopsy in 19% and intraoperative frozen section procedure in 9.5% of the patients. When the respiratory reserve of the patients was evaluated, only one patient had a FEV1 value less than 2 L/min (1.89 L) who was subjected to further assessment by postoperative FEV1 measurement and 6-minute walk test. Upon pulmonary clearance for pneumonectomy, the patient underwent resection.

The tumor types included squamous cell carcinoma (57.1%), adenocarcinoma (23.8%), adenosquamous carcinoma (14.3%) and large cell carcinoma (4.8%). Tumor site was the left hilum in 61.9% and right hilum in 14.3% of the patients, the upper left lobe in 14.3%, the upper right lobe in 4.8% and the left lower lobe in 4.8% of the patients. The mean tumor SUVmax value was 16.15 (5.9-42.92). Among all, 57.1% of the patients underwent left pneumonectomy, 19% had mediastinoscopy and left pneumonectomy, 14.3% had right pneumonectomy, 4.8% had mediastinoscopy and right pneumonectomy and 4.8% had left pneumonectomy and thoracic wall resection.

Early postoperative complications occurred in 5 (23.8%) patients. Three of these patients developed atrial fibrillation and two patients suffered hemorrhage. Emergency treatment was initiated in patients with atrial fibrillation upon consultation with the cardiology department, with no additional arrhythmia-related complications occurring until discharge. Among patients with bleeding, the volume of hemorrhagic fluid drained within 24 hours was 800 cc in one patient and 500 cc in the other. One patient was on anticoagulant therapy due to coronary artery disease and anticoagulant therapy was not discontinued in the preoperative period. Patients did not undergo repeat thoracotomy but were kept under close drainage monitoring. These patients were discharged within 15 days.

Postoperative tumor stages of the patients were stage 3a (47.6%), stage 2b (19%), stage 2a (14,3%), stage 1b (9.5%) and stage 1a2 (9.5%).

Multidimensional scaling analysis showed an association between the type of tumor and smoking (P=0.024) but no association was found between tumor type and family history (P=0.586) (Figure 1). The correspondence analysis was used to analyze the relation between smoking and cancer cell type and showed strong associations with squamous (P=0.024) and adenosquamous carcinoma (P=0.017) among patients who were smokers or those who quit smoking but no associations with adenocarcinoma or large cell carcinoma (P=0.274) (Figure 2).

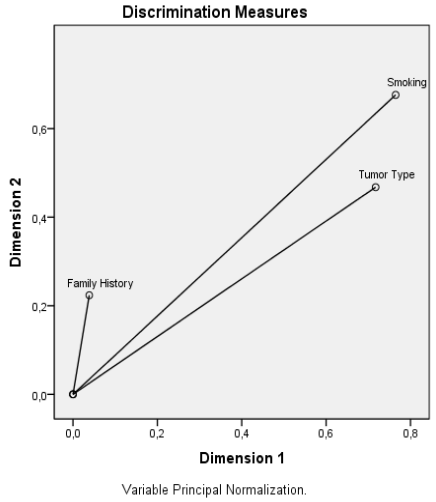

Figure 1: Association between the type of tumor, family history and smoking

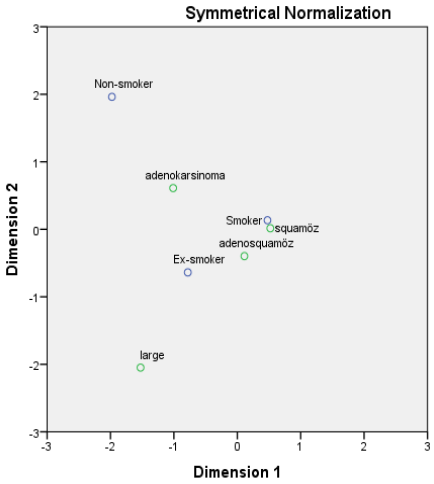

Figure 2: Association between the type of tumor and smoking

Discussion

As with patients from other age groups, surgical resection at an appropriate stage is the standard of care in patients over 70 years of age. When deciding on the suitability of a patient for surgical treatment, physical performance and comorbidities of the patient are considered rather than his/her age [10]. Consistently, the decision for surgical treatment in our patients was made based on their performance, comorbidities, and patient consent rather than their age. There is an increased likelihood of tumor resectability and an early detection of the tumor with advancing age. According to the Guideline on Preoperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgeries published by the American College of Cardiology, thoracic surgery is considered a high-risk surgery that poses cardiac risk. High-risk surgery includes major emergency surgery, particularly in the elderly; aortic and other major vascular surgery, peripheral vascular surgery, major intrathoracic surgery and anticipated prolonged procedures associated with large fluid shifts and/or blood loss. Intermediate-risk procedures include intraperitoneal, head, neck, orthopedic, urological, gynecological, and non-major thoracic surgery [11].

Following the guideline, all our patients were stratified as high-risk cases. It is known that the risk of developing lung cancer increases significantly in patients with a smoking history of more than 20 pack-years. In our study, there were 14 active smokers with a smoking history of 53 pack-years on average. The risk of lung cancer increases at least two-fold in individuals with a first-degree relative with lung cancer regardless of smoking [12]. In our study, 2 patients had a first-degree relative with lung cancer and 2 other patients had a first-degree relative with gastrointestinal malignancy.

When the chief complaints of lung cancer patients were examined, cough was found to be the primary complaint (59.3%). Other complaints included lethargy (46.4%), shortness of breath (42.5%), chest pain (35.1%) and hemoptysis (24.6%). In our study, cough was the initial symptom (28.6%), followed by shortness of breath (23.8%) and chest pain (14.3%). Symptomatology of our patients was similar to that reported in literature. The tumor location is the major determinant of the initial clinical symptom. Centrally located tumors are more likely to present with cough and hemoptysis. All of the tumors in our patients were centrally located. Bronchoscopy provides a diagnostic yield of up to 90% in central endobronchial lesions [12]. 71.4% of our patients were diagnosed with the aid of bronchoscopy. Among 4 patients diagnosed with transthoracic biopsy, the lesions could be accessed with fine needle biopsy due to the large size of the tumors (mean size of 8.6 cm) despite their central location.

In the 1980s, advanced age was considered a contraindication to thoracotomy and resection. However, more elderly patients have undergone surgery in the last 20 years due to advances in anesthesia and surgical techniques. Studies demonstrated that age alone is not a risk factor for surgical resection [13]. Two major concerns need to be considered when planning surgical treatment in older patients and these include firstly survival and secondly, postoperative morbidity and mortality [14,15]. While some studies advocated that advanced age is associated with the occurrence of postoperative complications, others did not find such an association [16,17]. On the other hand, an increased incidence of fatal complications was reported in older patients by some studies on mortality, but other studies did not support this observation [16,18,19]. In a 2011 study, Melek et al. [20] reported a morbidity rate of 32% in patients over 70 years of age and 30% in patients under 70 years of age, with no significant differences between the two groups. While both age groups developed pulmonary complications such as persistent air leak, restricted lung expansion and atelectasis, and arrhythmias in the early postoperative period, no significant difference was found between the groups in terms of comorbid conditions and postoperative morbidity. Pulmonary complications related to surgery including air leak, pneumonia,

pulmonary embolism, respiratory failure, bronchopleural fistula and bleeding following pulmonary resection have been commonly reported in literature, the most frequent complications were air leak and arrhythmia [21,22]. Among cardiac complications, rhythm disorders were reported at rates varying between 3.8% and 37% [23]. In a study from Turkey, the prevalence of cardiac complications was reported at 20% among older patients [24]. In our study, the prevalence of early postoperative complications was 23.8%, including cardiac arrhythmia in 3 (14.3%) patients and bleeding in 2 (9.5%) patients. Complications have been successfully managed with appropriate treatment strategies.

Studies have reported a resectability rate of 25% in patients over 75 years of age and 15.3% in patients under 55 years of age [25,26]. Moreover, the reported rate of surgery refusal was 30% in geriatric patients but 8% in younger patients [27]. Acceptable mortality and morbidity rates can be achieved in the geriatric patients with a good preoperative evaluation and assessment of comorbidities, as demonstrated by literature data. In a study by Aelony [28], the mortality rates were 1.2% among patients over the age of 75 undergoing early stage resection and 0.45% in younger patients. Tumor stages of our patients were stage 3a (47.6%), stage 2b (19%), stage 2a (14,3%), stage 1b (9.5%) and stage 1a2 (9.5%). Thus, stage 1 and 2 tumors were predominant in our study sample.

Limitations

The patients over 70 years of age were selected cautiously. The comorbidities they have were not considered in statistical analyses. This was the limitation of our study.

Conclusion

NSCLC is a major health problem that affects younger individuals as well as elderly population. Chronological age should not be the sole determinant when deciding on surgical treatment in older patients. It should be kept in mind that surgical resection and even pneumonectomy which is associated with high mortality and morbidity can be successfully performed in older cancer patients through a good preoperative workup, tumor staging, assessment of the risk of mortality and the effects of comorbid conditions.

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Psychological and social effects of COVID-19 pandemic on obstetrics and gynecology employees

COVID-19 pandemisinin kadın hastalıkları ve doğum kliniğindeki sağlık çalışanları üzerindeki psikolojik ve sosyal etkileri

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Abstract

Aim: COVID-19 pandemic affected most health care professionals and to the best of our knowledge, there has not been any studies on the gynecology and obstetrics department workers in the literature. In our study, we aim to investigate the psychological and social effects of the COVID-19 epidemic on the healthcare workers serving in the gynecology and obstetrics department and to help healthcare professionals improve their physical and mental health.

Methods: This cross-sectional study was conducted among healthcare professionals working in obstetrics and gynecology clinics in Mardin province. It was carried out in Mardin State Hospital and Kızıltepe State Hospital, which are considered "Pandemic Hospitals". All participants received Sociodemographic Data Form, Psychological Symptom Screening Test (SCL-90-R), Beck Anxiety Inventory and Short Psychiatric Rating Scale. These evaluation scales were applied to 13 doctors, 52 midwives and 38 nurses working in Gynecology and Obstetrics Clinics in total. They were compared in terms of occupation, gender, and age, as those under or equal to 29 (≤29) years and over 29 years (>29) of age. Twenty-nine was picked because it was the mean age of the group.

Results: Although differences did not reach statistical significance, anxiety, hostility, and phobic anxiety were higher in participants over the age of 29 years (P=0.472, P=0.549, P=0.776, respectively). According to profession groups, only phobic anxiety scores were higher among doctors (P=0.373), and somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, paranoid ideation, psychoticism, eating and gastrointestinal symptoms (GIS) were higher in midwives (P=0.166, P=0.624, P=0.531, P=0.321, P=0.147, P=0.205, P=0.359, P=0.490, P=0.696, P=0.557, respectively).

Conclusion: COVID-19 will undoubtedly have psychological consequences which may be permanent in healthcare professionals. Frontline employees will be at risk, especially in departments with emergency services. Actions are needed to alleviate the effects of COVID-19 on mental health by protecting and promoting the psychological well-being of healthcare workers during and after the outbreak.

Keywords: COVID-19, Anxiety, Healthcare professionals, Corona virus pandemic

Öz

Amaç: Bu çalışmanın amacı, Korana virüs pandemisi sürecinde kadın hastalıkları ve doğum sevisinde çalışan doktor, ebe ve hemşirelerde psikolojik ve sosyal etkilerin araştırılması amaçlanmıştır.

Yöntem: Bu kesitsel çalışma Mardin ilinde kadın hastalıkları ve doğum kliniklerinde çalışan sağlık çalışanları arasında yapıldı. Çalışma Mardin ilinde "Pandemi Hastanesi" olarak kabul edilen Mardin Devlet Hastanesi ve Kızıltepe Devlet Hastanesi'nde gerçekleştirildi. Tüm katılımcılara Sosyodemografik Veri Formu, Psikolojik Belirti Tarama Testi (SCL-90-R), Beck Anksiyete Ölçeği ve Kısa Psikiyatrik Değerlendirme Ölçeği uygulandı. Toplamda Kadın Hastalıkları ve Doğum kliniklerinde çalışan 13 doktor, 52 ebe ve 38 hemşireye bu değerlendirme ölçekleri uygulandı. Meslek, cinsiyet, 29 yaş ve altı (≤29) ve 29 yaş üstü (>29) olarak değerler karşılaştırıldı. 29 yaş katılımcıların median yaşı olduğu için seçildi.

Bulgular: Analiz istatistiksel olarak anlamlı olmamasına rağmen; kaygı, öfke-düşmanlık ve fobik anksiyete 29 yaş üzerinde daha fazla olarak saptandı (sırasıyla P=0,472, P=0,549, P=0,776). Mesleklere göre karşılaştırıldığında ise fobik anksiyete doktor grubunda daha yüksek saptanırken (P=0.373); somatizasyon, obsesif kompulsiyon, kişilerarası duyarlılık, depresyon, kaygı, öfke-düşmanlık, paranoid düşünce, psikotizm, yeme içme ve gastrointestinal semptomlar (GIS) ebelerde daha fazla saptandı (sırasıyla P=0,166, P=0,624, P=0,531, P=0,321, P=0,147, P=0,205, P=0,359, P=0,490, P=0,696, P=0,557).

Sonuç: Pandemi ile birlikte hastanelerde çalışan sağlık çalışanlarına COVID-19 salgını sırasında ve sonrasında psikolojik sorunları ele alınmalı ve yardımcı olacak stratejiler geliştirilmesini öneriyoruz.

Anahtar kelimeler: COVID-19, Anksiyete, Sağlık çalışanları, Korona virüs pandemisi

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Introduction

A pandemic is an epidemic disease caused by a factor (bacteria, virus, parasite etc.) that can spread to a wide range of areas simultaneously in multiple countries or continents all over the world. The definition of a pandemic is determined by the "World Health Organization" (WHO). The fact that the newly emerging vector spreads from person to person easily, simply, and quickly is an important indicator. The pandemic affects all people, regardless of age and economic level. The mental health of healthcare workers, who undertake all risks voluntarily and make sacrifices, can be adversely affected in these special times [1].

The COVID-19 virus, which first appeared in Wuhan, China in December 2019, has affected all countries of the world over time. It was accepted as a pandemic by the World Health Organization (WHO) about a month after the first case occurred. The epidemic continues to spread by increasing its effect day by day and causes escalating casualties. Healthcare workers constitute an important part of the patients [2].

Although the outbreak affects the lives of all people, factors such as long working hours under strict security measurements, taking more professional responsibilities, constantly wearing protective equipment and clothes, and being alert to work without loss of attention and concentration can raise healthcare workers' psychological stress levels. On the other hand, since healthcare workers are in close contact with the virus, they are considered a risk factor by the society. In response to all this, social support to healthcare workers has decreased due to the risk of transmission to families and relatives. Social isolation, anxiety and decreased self-care can occur in this stressful working environment. The fear of getting sick and dying are important stress factors that healthcare professionals face in this process [3].

Outpatient care has been reduced for non-urgent health problems all over the world and non-urgent surgeries have been delayed. These measures are not possible for those who provide health services in the department of obstetrics and gynecology. Applications continue to a considerable extent due to the high anxiety experienced by pregnant women. The maternity service continues at the same level compared to the pre-crisis period and will increase in the summer [4].

The number of pregnant women infected with the virus is increasing day by day. Given this information, those who provide healthcare services in the gynecology and obstetrics department continue to work with increasing risk and manage the crisis in this process, which has many unknowns.

We think that such crises can provide an opportunity for the development of health policies. Therefore, obstetricians play an important role in addressing this crisis as part of the current COVID-19 outbreak, just like other healthcare professionals. In our study, we aim to investigate the psychological and social effects of the COVID-19 epidemic on the healthcare workers serving in the gynecology and obstetrics department and to help healthcare professionals improve their physical and mental health.

Materials and methods

This study was conducted among healthcare professionals working in the Obstetrics and Gynecology clinics in Mardin State Hospital and Kızıltepe State Hospital, which are the two most intense pandemic hospitals in Mardin province. Approval was obtained from Mardin Provincial Directorate of Health's Ethics Committee (Document no: 37201737-806.02.02, Date: 4/22/2020) and the research was carried out in accordance with the Helsinki Declaration, published by the World Medical Association. Doctors, nurses, and midwives who agreed to participate in the study were included. All participants received Sociodemographic Data Form, Psychological Symptom Screening Test (SCL-90-R), Beck Anxiety Inventory and Brief Psychiatric Rating Scale. In total, scales were applied to 13 doctors, 52 midwives and 38 nurses working in Obstetrics and Gynecology departments.

Data Collection Tools

Sociodemographic Data Form

It is a short form which questions age, gender, and task, developed by researchers for use in this study.

Beck Anxiety Inventory (BAI)

It is a 21-item Likert-type scale (sum of degrees) used to determine the frequency of anxiety symptoms experienced by the person. The person is asked to answer the questions on the scale over the symptoms he / she has experienced during the 'last week including today'. Each item scores between 0 and 3 as none, mild, moderate, and severe, respectively. There is a direct proportion between the height of the total score obtained from the scale and the anxiety severity experienced by the person. In our country, the validity and reliability of the Turkish version of the test has been performed in studies [5-6].

Psychological Symptom Screening Test (SCL-90-R)

This Liker-type scale consists of 90 items in total and 10 different subscales. The scores are as follows: None (0), Very Low (1), Moderate (2), Fairly High (3) and Advanced (4). The subscale scores of the scale are obtained by summing up the score values of the answers given to the relevant items and dividing them by the number of items that make up that subscale. There is a positive correlation between the high score of the individual and having more advanced psychological symptoms. The overall symptom level average is obtained by dividing all scores obtained for each item by 90. Values above 1 indicate a psychological problem, 0.5 to 1 indicate a medium level problem, and values less than 0.5 indicate no problem. The validity and reliability studies of the Turkish version of the test have been performed [7-8].

Brief Psychiatric Rating Scale (BPRS)

It is a scale consisting of 18 questions used to determine the severity of psychotic and some depressive symptoms and symptoms. Each question is scored as None (0), Very Mild (1), Mild (2), Moderate (3), Moderate-Severe (4), Severe (5), Extremely Severe (6). The validity and reliability studies of the Turkish version of the test have been performed [9].

Statistical analysis

Nominal and ordinal data were presented as frequency analysis and numerical data, as mean and standard deviation. Cronbach Alpha coefficients were used for the internal consistency coefficient of the scales. Confirmatory Factor

Analysis (CFA) was performed for the validity of the scale items, and all scale items resulted above the 0.4 factor load, which is considered acceptable in the literature (Kaiser Meier Olkin KMO: 0.563; $P<0.05$). Compliance of the data to normal distribution was analyzed with the Kolmogorov Smirnov Test, according to the results of which, Independent Sample T-test was used to evaluate the difference between the two groups, and the One Way ANOVA to assess the difference between more than two groups. The Mann Whitney U and Kruskal Wallis tests were utilized for comparing non-normally distributed two and more than two groups, respectively. All analyses were performed in SPSS 17.0 for Windows program with a 95% confidence interval and 0.05 significance level.

Results

The demographic characteristics of the healthcare professionals participating in the research are presented in Table 1. The mean age of the participants was 29.38 (5.56), ranging between 21-45 years. Based on the mean age, the participants were divided into two groups as less than or equal to 29 (≤29) and over 29 years (>29). For difference analysis, these two age categories were taken into consideration, according to which 56.3% of the participants were 29 years old or younger, and 43.7% were older than 29. Female and male participants constituted 88.3% and 11.7% of the study population, respectively. There were 13 doctors (12.6%), 52 midwives (50.5%) and 38 nurses (36.9%).

The mean and standard deviation values of the responses given by the participants to the scale dimensions are presented in Table 2. The highest scoring dimension on the SCL-90 scale was the Obsessive-Compulsive dimension, followed by depression, eating, and interpersonal sensitivity. Global Severity Index (GSI) mean was 1.10 (0.84), ranging from 0.03-3.52. The mean BAI and BPRS were 14.40 (13.33) and 21.08 (21.46), respectively.

Distribution of responses to psychological symptom dimensions and difference analysis results by age groups are presented in Table 3. Somatization, obsessive-compulsive disorder, interpersonal sensitivity, depression, paranoid ideation, psychoticism, eating and drinking disorder symptoms were higher in the participants aged 29 years or younger, along with Global Severity Index (GSI), Beck Anxiety level and BPRS means. Anxiety, hostility, and phobic anxiety were higher in participants over 29 years of age. These differences were not statistically significant.

Distribution of responses to psychological symptom dimensions and difference analysis results by gender groups are shown in Table 4. Somatization, interpersonal sensitivity, and hostility averages were insignificantly higher in females, while other averages were insignificantly higher in males.

Distribution of responses to psychological symptom dimensions and difference analysis results by profession groups are presented in Table 5. Only phobic anxiety score was higher among doctors, and all other scale scores were higher in midwives, the differences between which were all statistically insignificant.

Table 1: Distribution of the participants according to their demographic characteristics

Parameter	Value
Age, Mean (SD)	29.38 (5.56)
Age, n (%)	
≤29	58 (56.3)
> 29	45 (43.7)
Gender, n (%)	
Female	91 (88.3)
Male	12 (11.7)
Occupation, n (%)	
Doctor	13 (12.6)
Midwife	52 (50.5)
Nurse	38 (36.9)

SD: Standard Deviation

Table 2: Mean and standard deviation values of the responses given by the participants to scale dimensions

SCL-90	Cronbach Alpha	Lowest	Highest	Average	SD
Somatization	0.894	0.00	3.42	1.09	0.83
Obsessive-compulsive	0.905	0.00	3.30	1.40	0.96
Interpersonal sensitivity	0.886	0.00	3.89	1.13	0.90
Depression	0.931	0.00	3.69	1.27	0.99
Anxiety	0.910	0.00	3.90	1.03	0.94
Hostility	0.889	0.00	3.83	0.95	1.00
Phobic anxiety	0.871	0.00	3.71	0.93	0.96
Paranoid ideation	0.854	0.00	4.00	1.10	1.00
Psychoticism	0.914	0.00	3.90	0.75	0.87
Eating	0.818	0.00	3.71	1.25	0.96
GIS	0.986	0.03	3.52	1.10	0.84
BAI Total	0.955	0.00	57.00	14.40	13.33
BPRS Total	0.961	0.00	94.00	21.08	21.46

Table 3: Distribution of responses to psychological symptom dimensions and difference analysis by age groups

SCL-90	Age* ≤29 (n=58)	Age > 29 (n=45)	*P*-value
Somatization	1.14(0.75)	1.03(0.94)	0.175[a]
Obsessive-compulsive	1.49(0.88)	1.29(1.05)	0.289[b]
Interpersonal sensitivity	1.22(0.80)	1.01(1.02)	0.253[b]
Depression	1.34(0.91)	1.18(1.08)	0.432[b]
Anxiety	1.02(0.83)	1.03(1.08)	0.472[a]
Hostility	0.91(0.85)	1.00(1.18)	0.549[a]
Phobic anxiety	0.89(0.92)	0.97(1.02)	0.776[a]
Paranoid ideation	1.12(0.86)	1.07(1.18)	0.192[a]
Psychoticism	0.77(0.71)	0.72(1.04)	0.075[a]
Eating	1.29(0.89)	1.20(1.05)	0.648[b]
GIS	1.14(0.72)	1.05(0.99)	0.634[b]
BAI Total	15.21(12.27)	13.36(14.67)	0.139[a]
BPRS Total	21.57(18.17)	20.44(25.29)	0.121[a]

a: Mann Whitney U Test, b: Independent Samples T-test, *mean age was 29, and patients divided into two groups as under or equal median (≤29) and over 29 ages (>29)

Table 4: Distribution of responses to psychological symptom dimensions and difference analysis by gender

SCL-90	Female (n=91)	Male (n=12)	*P*-value
Somatization	1.10 (0.83)	1.08 (0.94)	0.833[a]
Obsessive-compulsive	1.39 (0.95)	1.50 (1.03)	0.710[b]
Interpersonal sensitivity	1.14 (0.90)	1.07 (1.01)	0.826[b]
Depression	1.26 (0.96)	1.37 (1.26)	0.725[b]
Anxiety	1.01 (0.93)	1.15 (1.03)	0.761[a]
Hostility	0.95 (1.01)	0.93 (0.97)	0.979[a]
Phobic anxiety	0.90 (0.97)	1.12 (0.92)	0.352[a]
Paranoid ideation	1.09 (0.97)	1.17 (1.28)	0.749[a]
Psychoticism	0.74 (0.87)	0.84 (0.87)	0.512[a]
Eating	1.24 (0.94)	1.37 (1.10)	0.656[b]
GIS	1.09 (0.83)	1.17 (0.95)	0.765[b]
BAI Total	14.29 (13.31)	15.25 (14.09)	0.865[a]
BPRS Total	20.79 (21.14)	23.25 (24.66)	0.930[a]

a: Mann Whitney U Test, b: Independent Samples T-test

Table 5: Distribution of responses to psychological symptom dimensions and difference analysis by profession groups

SCL-90	Doctor (n=13)	Midwife(n=52)	Nurse (n=38)	*P*-value
Somatization	0.92 (0.92)	1.18 (0.73)	1.04 (0.94)	0.166[a]
Obsessive-compulsive	1.30 (0.98)	1.49 (0.91)	1.31 (1.02)	0.624[b]
Interpersonal sensitivity	0.89 (0.96)	1.20 (0.83)	1.11 (0.99)	0.531[b]
Depression	1.16 (1.15)	1.42 (0.99)	1.11 (0.92)	0.321[b]
Anxiety	1.01 (1.02)	1.14 (0.88)	0.87 (1.00)	0.147[a]
Hostility	0.78 (0.96)	1.08 (1.02)	0.83 (1.00)	0.205[a]
Phobic anxiety	1.05 (0.91)	0.97 (0.92)	0.82 (1.05)	0.373[a]
Paranoid ideation	1.01 (1.24)	1.17 (0.93)	1.04 (1.03)	0.359[a]
Psychoticism	0.69 (0.85)	0.78 (0.80)	0.72 (0.97)	0.490[a]
Eating	1.19 (1.10)	1.33 (0.95)	1.17 (0.94)	0.696[b]
GIS	1.01 (0.92)	1.19 (0.79)	1.01 (0.90)	0.557[b]
BAI Total	11.77 (13.40)	15.96 (12.09)	13.16 (14.94)	0.123[a]
BPRS Total	17.23 (20.58)	21.65 (18.82)	21.61 (25.27)	0.510[a]

a: Kruskal Wallis Test, b: One Way ANOVA Test

Discussion

After the occurrence of cases of COVID-19 in Turkey, the Turkish Ministry of Health has taken the necessary measures and put them into practice. However, following a symptomatic patient who had positive screening test results in pandemic hospitals caused a commonly shared anxiety in healthcare professionals. As a result, they worked in different moods from their normal days, even if they did not want to. It is not surprising that the issue of psychological stress on medical staff is addressed in the current COVID-19 pandemic.

In this study, an evaluation was made using the questionnaire method to determine the change in mood, anxiety and extra behaviors of the healthcare professionals in the Obstetrics and Gynecology departments in Mardin. Most of the healthcare professionals who participated in this study were female individuals. Experience before smaller scale outbreaks and emerging literature around COVID-19 show that the amount of unique stress that healthcare professionals deal with is associated with increased psychological morbidity [10].

When all participants were evaluated in the form of psychological symptoms in all groups, "closeness to COVID-19 patients" was recorded as the most important complaint in the additional symptom query. In this pandemic, social restrictions, infection protection measures, anxiety and depression are associated with psychological stress [11]. Various comments also point to the burden of mental health in the population [12]. Health care workers in the UK were given a free "digital package" and asked to relax outside of working hours [13]. In our country, various telecommunication companies tried to support this issue by loading extra internet packages to the telephone lines of healthcare workers.

In the data obtained, the most encountered psychological disease in healthcare workers, the obsessive-compulsive disorder (OCD), is followed by depression, eating and interpersonal sensitivity. Especially in midwives, maternal fluids and amniotic fluid are avoided during delivery. Later, repetitive hand washing, and increased cleaning of the clothes are seen. The night shift system caused an excessive eating during the pandemic and distance had to be kept during interventions and giving information to patients and their relatives. Also, newborns had to be intervened, which led to increased psychiatric symptoms and OCD incidence in the delivery rooms [14]. Somatization, obsessive-compulsive, interpersonal sensitivity, depression, paranoid ideation, psychoticism, eating, and drinking were higher among young participants. Increased working time and increased experience may have led to decreased or masked symptoms expected with age. Defense mechanisms and methods are gained in infancy - childhood. It should also be borne in mind that individuals may be exhibiting self-gained behaviors before acting in accordance with the scheme to approach a patient with COVID-19, as recommended during the pandemic.

Somatization, interpersonal sensitivity, and hostility were more common in women. It is exceedingly difficult to find a generally accepted definition for somatization. It is defined as " physical symptoms complaints that are not secondary to a physical illness". The genetic structure that facilitates the emergence of somatic complaints, the psychological development during infancy and adolescence, the personality structure gained from family, learned answers, all sociocultural values can be considered. Somatization disorders constitute five percent of general outpatient applications. It is highly expected and natural for these common conditions to increase during the pandemic, when special precautions are taken. We determined that phobic anxiety had increased in the doctors. In numerous studies, anxiety was reportedly more common among young, female individuals with low education levels, without jobs, with low income and in those who do not live with a partner [15]. Individuals with phobic anxiety also have minor obsessions or insignificant fears. Generally, the anxiety of "getting infected with COVID-19" was high among doctors participating in the study.

Limitations

Our sample size is limited since only medical staff working in gynecology and obstetrics in pandemic hospitals in Mardin province were included. Also, we had to arrange the age groups according to our health professionals' mean age. Our sample size's mean age was 29 but it can differ in various hospitals.

Conclusion

COVID-19 will have possibly permanent psychological effects on healthcare professionals. Frontline employees will be at risk, especially in departments with emergency services. Actions are needed to alleviate the effects of COVID-19 on mental health by protecting and promoting the psychological well-being of healthcare workers during and after the outbreak.

We recommend that healthcare professionals develop broader strategies to support their psychological well-being during and after the COVID-19 outbreak.

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Helicobacter pylori incidence of patients with gastritis in endoscopic biopsies

Endoskopik biyopsilerde gastrit saptanan hastalarda helikobakter pylori sıklığı

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Abstract

Aim: H. pylori is the most common permanent bacterial infection worldwide and an important health problem in terms of the diseases it causes. The aim of this study was to determine H. pylori incidence according to age and gender in biopsy materials of patients who were diagnosed with gastritis.

Methods: This was a cross-sectional study which examined the endoscopic and pathological reports of 1240 patients who were diagnosed with gastritis between June 2014 and October 2019 and underwent biopsy from the antrum. The incidence of H. pylori infection was evaluated according to age and gender. Based on the Sydney classification, the patients were scored as none (-), low (+), medium (++) and high (+++) in the pathological records. Patients were divided into 5 age groups: 18-34, 35-44, 45-64, 65-74 and ≥75 years.

Results: A total of 1240 patients, 664 (53.5%) females and 576 (465%) males were included in the study. The mean age of the patients was 49.9 (16.2). A total of 422 (34.0%) patients were H. pylori (+), while 818 (66.0%) were H. pylori (-). H. pylori density was low in 123 (29.1%) patients, medium in 207 (49.1%) patients, and high in 92 (21.8%) patients. There was no difference in terms of H. pylori positivity with regards to age and gender (P=0.296, P=0,812, respectively). The number of H. pylori (+) and (-) patients in the groups were as follows: Group 1: 71 (16.8%) vs. 160 (19.6%), Group 2: 125 (29.6%) vs. 186 (22.7%), Group 3: 134 (31.8%) vs. 281 (34.4%), Group 4: 60 (14.2%) vs. 120 (14.7%) and Group 5: 32 (7.6%) vs. 71 (8.7%). H. pylori positivity rates were as 30.7%, 40.2%, 32.3%, 33.3% and 31.1% for groups 1, 2, 3, 4 and 5, respectively. Although the Group 2 (35-44 years) had the highest rate, it was not statistically significant (P=0.117).

Conclusion: In our study, the incidence of H. pylori was 34%, and this rate is pleasing in terms of decreasing H. pylori incidence in our country compared to previous studies.

Keywords: H. pylori, Incidence, Age, Gender

Öz

Amaç: H. pylori dünya çapında en sık görülen kalıcı bakteriyel enfeksiyondur ve neden olduğu hastalıklar açısından önemli bir sağlık sorunudur. Bu çalışmanın amacı, endoskopik olarak gastrit tanısı alan hastaların biyopsi materyallerinde yaş ve cinsiyete göre H. pylori insidansını belirlemektir.

Yöntemler: Bu çalışma Haziran 2014-Ekim 2019 tarihleri arasında gastrit tanısı alan ve antrumdan biyopsi yapılan 1240 hastanın endoskopik ve patolojik raporlarını inceleyen kesitsel bir çalışmadır. Sydney sınıflamasına göre, hastalar patolojik kayıtlarda yok (-), düşük (+), orta (++) ve yüksek (+++) olarak skorlandı. Hastalar ; 18-34, 35-44, 45-64, 65-74 ve ≥75 olmak üzere 5 farklı yaş grubuna ayrıldı.

Bulgular: Çalışmaya 664 (%53,5) kadın ve 576 (%46,5) erkek olmak üzere toplam 1240 hasta dahil edildi. Hastaların ortalama yaşı 49,9 (16,2) idi. H. pylori (+) olanların sayısı 422 (%34,0), H. pylori (-) olanların sayısı ise 818 (%66,0)'di. H. pylori yoğunluğuna göre değerlendirildiğinde 123 (%29,1) hastada düşük, 207 (%49,1) hastada orta ve 92 (%21,8) hastada yüksekti. Yaş ve cinsiyetler arasında H. pylori pozitifliği açısından herhangi bir fark yoktu (Sırasıyla P=0,296, P=0,812). Gruplardaki H. pylori (+) ve (-) hasta sayısı şöyleydi: Grup 1: 71 (%16,8) - 160 (%19,6), Grup 2: 125 (%29,6) - 186 (%22,7), Grup 3: 134 (%31,8) - 281 (%34,4), Grup 4: 60 (%14,2) - 120 (%14,7) ve Grup 5: 32 (%7,6) - 71 (%8,7). 1,2,3,4 ve 5. gruplardaki H. pylori pozitiflik oranları sırasıyla %30,7, %40,2, %32,3, %33,3 ve %31,1 idi. En yüksek oran grup 2'de (35-44 yaş) saptanmış olmasına rağmen, bu istatistiksel olarak anlamlı değildi (P=0,117).

Sonuç: Çalışmamızda, H. pylori insidansı %34 olarak saptanmıştır ve bu oran daha önceki çalışmalarla kıyaslandığında, ülkemizde H. pylori insidansının azalması açısından memnuniyet vericidir.

Anahtar kelimeler: H. pylori, Sıklık, Yaş, Cinsiyet

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Introduction

Helicobacter pylori (H. pylori) was first described by Marshall and Warren in the stomach epithelium of patients with chronic atrophic gastritis in 1983 and also it has been shown to play roles in other gastrointestinal system diseases in the next years [1]. It is a gram-negative, spiral-shaped, motile, and flagellate bacteria that produces urease enzymes, usually found under the gastric mucus layer, close to epithelial cells, and damages them [2].

It is estimated that approximately 50% of the global population is infected with H. pylori [3] and it is one of the major risk factors for diseases such as chronic gastritis, peptic ulcer disease, gastric carcinoma, and gastric mucosal associated lymphoid tumor (MALT lymphoma) [4]. Although the transmission routes for H. pylori are not exactly known, low socioeconomic levels, poor hygiene, living in crowded environments, iron deficiency anemia, poor nutrition, coronary artery disease, 0 blood group and low education level of the mother are considered risk factors [5]. In recent years, it has become less common due to socioeconomic development, smaller family sizes, improved sanitation, and the frequent use of antibiotics [3].

The diagnosis of H. pylori is made by either non-invasive methods such as serology, 13C urea breath test and stool antigen test, or by the invasive methods including the examination of endoscopic biopsy specimens with histopathological, culture and rapid urease tests and polymerase chain reaction test [6]. In pathological diagnosis, hematoxylin eosin and modified giemsa dyes are preferred because they are sensitive, easy, and accessible [7].

In this study, we aimed to determine the distribution of the frequency of H. pylori according to age and gender in biopsy materials of patients who were diagnosed with gastritis endoscopically and underwent biopsy from antrum.

Materials and methods

For this study, endoscopic and pathological reports of patients who were diagnosed with gastritis between June 2014 and October 2019 at the gastroenterology clinic of Acıbadem Kayseri Hospital and underwent biopsy from the antrum were evaluated retrospectively. Esophagogastroduodenoscopy was performed to all patients with a white light video endoscopy using high definition system (Olympus Evis Exera II CV180, NBI) by the same endoscopist. This study was approved by the Acibadem University Ethics Committee (ATADEK, 1/9/2020, 2020-01/31).

The patients who had at least 3 biopsies from the antrum were included in the study. Patients with active bleeding or an evidence of malignancy were excluded. Biopsy specimens of the patients obtained from the antrum were stained with hematoxylin eosin and giemsa and examined under light microscopy. Based on the Sydney classification, the patients were scored as none (-), low (+), medium (++) and high (+++) in the pathological records. The frequency of H. pylori infection was evaluated according to gender and age groups. Patients were divided into 5 age groups: Group 1: Patients between the ages of 18-34 years, Group 2: Patients between the ages of 35-44 years, Group 3: Patients between the ages of 45-64 years, Group 4: Patients between the ages of 65-74 years, Group 5: Patients ≥75 years.

Statistical analysis

Statistical Package for the Social Sciences [SPSS] v 22 was used for statistical analyses. We reported continuous variables as mean **(**standard deviation [SD]), and categorical variables as numbers (n) and percentages (%). While groups were compared with chi-square test, student t test was used to calculate the mean age of each group. *P*-values <0.05 were considered significant.

Results

A total of 1240 patients, aged between 18-97 years, were included in the study. The mean age of the patients was 49.9 (16.2) years. Among 1240 patients included in the study, 664 (53.5%) were females and 576 (46.5%) were males. The mean age of the females and males were 50.0 (16.6) and 49.7 (15.8) years, respectively.

The number of H. pylori (+) and H. pylori (-) patients were 422 (34.0%) and 818 (66.0%), respectively. H. pylori density was low in 123 (29.1%) patients, medium in 207 (49.1%) patients, and high in 92 (21.8%) patients (Table 1).

The number of H. pylori (+) and (-) females were 224 (33.7%) and 440 (66.3%), respectively while the number of H. pylori (+) and (-) males were 198 (34.4%) and 378 (65.6%), respectively. There was no difference in terms of H. pylori positivity between age and genders (*P*=0.296, *P*=0.812, respectively) (Table 2).

The number of H. pylori (+) and (-) patients in the age groups were as follows: Group 1: 71 (16.8%) vs. 160 (19.6%), Group 2: 125 (29.6%) vs. 186 (22.7%), Group 3: 134 (31.8%) vs. 281 (34.4%), Group 4: 60 (14.2%) vs. 120 (14.7%) and Group 5: 32 (7.6%) vs. 71 (8.7%). H. pylori positivity rates were as 30.7%, 40.2%, 32.3%, 33.3% and 31.1% for groups 1, 2, 3, 4 and 5, respectively There was no difference in terms of H. pylori positivity between the groups (*P*=0.122) (Table 3).

In addition, when patients were grouped as <50 years of age and ≥50 years of age, there was no significant difference in terms of H. pylori positivity (233 vs. 139, *P*=0.07).

Table 1: The prevalence of H. pylori

H. pylori	Negative (-)	Total Positive	Positive (+)	Positive (++)	Positive (+++)
n	818	422	123	207	92
%	66	34	29.1	49.1	21.8

Table 2: Distribution of H. pylori by gender

	Total	H. pylori (+)	H. pylori (-)	*P*-value
n	1240	422	818	
Gender				
Female n (%)	664 (53.5)	224 (33.7)	440 (66.3)	0.812
Male n (%)	576 (46.5)	198 (34.4)	378 (65.6)	
Age mean (SD)	49.9 (16.2)	49.7 (15.4)	50.0 (16.6)	0.296

Table 3: H. pylori distribution by age groups

Age groups	HP (-)	HP (+)	*P*-value
Group 1 (18-34) n %	160 (69.3)	71 (30.7)	0.122
Group 2 (35-44) n %	186 (59.8)	125 (40.2)	
Group 3 (45-64) n %	281 (67.7)	134 (32.3)	
Group 4 (65-74) n %	120 (66.7)	60 (33.3)	
Group 5 (>=75) n %	71 (68.9)	32 (31.1)	

Discussion

H. pylori is the most common permanent bacterial infection worldwide and an important health problem in terms of the diseases it causes. At the beginning of 2000s, the prevalence of adults infected by H. pylori was believed to be more than 80%

in developing nations and 20% to 50% in industrialized countries [8]. Although it is suggested that the transmission of H. pylori can occur through fecal-oral, oral-oral, or iatrogenic routes; the exact mechanism still remains uncertain [9].

H. pylori frequency differs among different geographic regions and ethnic groups [10]. An ethnic group study by Lee et al. [11] reported that the histopathological examination of endoscopic biopsy samples showed that H. pylori positivity was 48.3%, 67.4% and 77.9% in American, Korean and Japanese subjects, respectively. In the EUROGAST study conducted in asymptomatic whites between the ages of 25-34, covering 3194 individuals, H. pylori positivity was reported as 15% in Minneapolis-St. Paul Minnesota, 62% in Japan and 70% in some regions of Poland [12]. In a study by Wex et al. [13] conducted in Germany in 2010, immunoglobulin G antibodies were examined in the blood serologically and the frequency of H. pylori was 44.4%. Also, there was no difference between genders.

The prevalence of H. pylori is higher in the geographical location of our country, compared to western societies. In the study of Özardalı et al. [14] in Şanlıurfa region in 1998, H. pylori was detected in 89.8% of patients diagnosed with chronic atrophic gastritis. In a study performed by Özdil et al. [15] in 2010, the frequency of H. pylori was 71.3% in the histopathological samples of 3301 patients who underwent biopsy from both the corpus and antrum. Uyanıkoğlu et al. [16] showed the frequency of H. pylori as 71.3% in their study including 1298 endoscopic antrum biopsies. A serological study carried out in Van province and its region in 2012 by Esen et al [17] showed 87% positivity of H. pylori. This rate was 78.4% in the study of Demirtaş et al. [18] containing 1405 antrum and corpus biopsies of patients in Erzincan province, in 2014. However, in recent years, decreases in H. pylori prevalence are noteworthy in studies conducted in our country. In this context, Turan et al. [19] found the H. pylori positivity rate as 43.85% in year 2017. In our study, this rate was even lower, 34%. In our opinion, the most important reason for the decrease in H. pylori positivity rate has been the increase of awareness among physicians in recent years and the application of eradication treatment more frequently. In addition to the awareness of clinicians, the increase in the use of social media, especially in recent years, has increased the awareness of patients and the frequency of consulting a doctor about this subject. According to the results of a study published in China in 2019, the effect of social media on H. pylori treatment is quite remarkable. In this study, H. pylori (+) patients confirmed with positive carbon-14 (C14) breath tests and endoscopic biopsies and also showed the indications for H. pylori eradication treatment were divided into two groups: The intervention group used a social media platform as a reminder besides traditional instructions and the control group was only given traditional instructions verbally about the dose and method of medication, the precautions that should be taken during the medication regimen and information related to follow-ups. The results of this study were as follows: Compared to the control group, the intervention group had significantly better awareness of H. pylori, significantly higher treatment adherence and significantly higher eradication rate whereas there was no significant difference in terms of drug related adverse reactions [20].

In our study, no difference was found between genders in terms of H. pylori positivity. There are publications in the literature that do not detect gender differences similar to our study [18,19,21-23], as well as studies that show high frequency of H. pylori in men or women [24,25]. In our study, the highest positivity rate was 40.2% between the ages of 35-44 years, while the lowest positivity rate was found to be 30.7% in the 18-34-year age group. Megraud et al. [26] showed that H. pylori decreases and loses its habitat in the older age because of increased incidence of atrophic gastritis in this age group. However, in our study, we did not detect such a decrease in the older age group and there was no difference between the age groups. Similar to our study, there was an age group in the study of Marusic et al [27], where the H. pylori positivity rate was high and they reported that the number of the H. pylori infected patients were highest between the ages of 51-70.

H. pylori exhibits a patchy placement in the stomach and is mostly located in the antrum [28]. In our study, all biopsy samples were taken from at least 3 different points of the antrum. Although this seems to be a restrictive point in our study, there are many publications in the literature that support the higher rates of H. pylori positivity in the antrum than in the corpus [29,30].

As a result, in our study, we found the H. pylori positivity rate as 34% in the biopsy samples taken from antrum. In the literature review, this rate seems to be quite low for our country compared to the studies in previous years. Although many causative factors can be considered for this decrease, we think that the worthiest among them is the increase of awareness among physicians in recent years and the application of eradication treatments more frequently. Another key factor of this decrease is the increased use of social media in recent years, thus increased awareness of patients and the frequency of consulting a doctor about this subject. We think that improving the socioeconomic status and ensuring compliance with hygiene conditions will further pull these figures backwards, and therefore a reduction in many H. pylori related diseases can be achieved.

Limitations

The most important limitation of our study is that no biopsy was obtained from the corpus. Meticulously designed clinical studies that will be performed by taking biopsies from both the antrum and corpus will be more useful in determining the incidence of H. pylori.

Conclusion

In recent years, the frequency of H. pylori has been decreasing in our country. We found the H. pylori frequency as 34% in our study and this was one of the lowest among the studies in our country. Based on the available data and considering the obvious changes in the epidemiological features of H. pylori infection, we think that the local prevalence of H. pylori infection should be investigated by focusing on specific age groups.

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Management of distal unstable radius fractures with volar locking plates: A retrospective cohort study

Unstabil radius distal uç kırıklarının volar kilitli plak ile yönetimi: Retrospektif kohort çalışma

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Abstract

Aim: Unstable distal radius fractures are difficult to manage. Volar locking plate screw is a better option than the other treatment methods (external fixator, K pin, etc.). The aim of this study is to present the radiographic and functional clinical results of patients with lower end unstable radius fractures who were treated with volar locking plate screws in our clinic.

Methods: A total of 52 patients (29 males, 23 females, mean age 42; the distribution 18-77) who underwent volar locking plate fixation due to an unstable distal radial end fracture were examined. Based on the AO classification, six patients (11.5%) had B2, five patients (9.6%) had B3, four patients (7.6%) had C1, 29 patients (55.7%) had C2 and 8 patients had (15.3%) C3 fractures. Twenty-one (77.8%) of the fractures had dorsal angulation, while six (22.2%) had volar angulation. The fracture was accompanied by an elbow dislocation and/or fracture in four patients (14.8%). Eleven patients (21.1%) had distal radioulnar joint problems. In fifteen patients (28.8%), autogenous crista iliac graft was used in addition to fracture fixation. The patients' range of motion and grip strength were measured. Evaluations were made according to the Stewart criteria. In the functional evaluation, the Quick-DASH-T (Disabilities of the Arm, Shoulder and Hand-Turkish) questionnaire and the Gartland-Werley evaluation form were used. The average duration of follow-up was 15 months (range: 12-34 months).

Results: All bones healed smoothly in approximately 7 weeks (range: 6-8 weeks). The average radiographic score was 0.5 (0-3) in the Stewart rating scale. The ulnar variance value was approximately -0.4 (between 0 and -2.5 mm) in 30 patients (57.6%). The average positive ulnar variance level was 0.5 mm (between 0-2.5 mm) in 12 patients (23%). A neutral variance level occurred in ten patients (19.2%). In 32 patients (61.5%) whose radial inclination angles were not equalized, the intact side was 28.5° (the interval 21°-30°) while the average angle for the side that underwent surgery was 22.3° (the interval 18°-27°). The radial inclination angle of fifteen patients (28.8%) gradually equaled the intact side. In other patients, the average radial inclination angle was 5.9° towards the volar direction (dorsal 2°- volar 13°) on the intact side. In twenty-five patients (48%), the loss of radial height was 1.3 mm (0-5 mm) on the side that underwent surgery. The grip strength of the side treated was approximately 69% (18 kg) of the intact side. The average Quick-DASH-T score was found as 8.3 (the distribution being 0-70.5), and the average Gartland-Werley score was found as 4.7 (the distribution 0-16). According to the Gartland-Werley evaluation, the results were excellent in 25 patients (48%), good in 25 (48%) and moderate in 3 (4%).

Conclusion: Volar locking plate applications are efficient in correcting and protecting the distal radius end anatomy.

Keywords: Open reduction, Locking plate, Unstable fracture, Distal radius fracture

Öz

Amaç: Unstabil distal Radius kırığının tedavi yönetimi zordur. Voler kilitli plak uygulamaları diğer yöntemlere kıyasla (external fiksatör, k teli vb.) daha iyi bir yöntemdir. Bu nedenle, bunu göstermek için, merkezimizde Volar yerleşimli kilitli plak vida tespitleri ile tedavi edilen instabil radius alt uç kırıklarının radyografik ve fonksiyonel klinik sonuçları değerlendirildi.

Yöntemler: Radius dital uç instabil kırığı nedeniyle volar yerleşimli kilitli plak tespiti uygulanan 52 hasta (29 erkek, 23 kadın, ort. Yaş 42; dağılım 18-77) incelendi. AO sınıflamasına göre altı hastada B2 (%11,5), beş hastada B3 (%9,6), dört hastada C1 (%7,6), yirmi dokuz hastada C2 (%55,7) ve sekiz hastada C3 (%15,3) olarak sınıflandırıldı. Kırıkların 21'inde (%77,8) dorsal, altısında (%22,2) volar açılanma vardı. Dört hastada (%14,8) kırığa dirsek çıkığı ve/veya kırık eşlik etmekteydi. On bir hastada (%21,1) distal radioulnar eklem sorunları vardı. On beş hastada (%28,8) kırık tespitine ek olarak otolog krista iliaka grefti kullanıldı. Hastaların hareket açıklıkları, kavrama kuvvetleri ölçüldü, Stewart ölçütlerine göre radyografik değerlendirmeleri yapıldı. Fonksiyonel değerlendirmede Quick-DASH-T (Disabilities of the Arm, Shoulder and Hand-Türkçe) sorgulaması ve Gartland-Werley değerlendirme formu kullanıldı. Ortalama takip süresi 15 ay (dağılım 12-34 ay) idi.

Bulgular: Kırıkların tümü ortalama 7 haftada (dağılım 6-8 hafta) sorunsuz kaynadı. Stewart derecelendirme skalasındaki ortalama radyografik skor 0.5 (0-3) idi. Otuz hastada (%57,6) ulnar vayans değerleri ortalama olarak -0,4 (0 ila -2,5 mm arası) oluştu. On iki hastada (%23) 0.5 mm (0-2,5mm aralığı) ortalama pozitif ulnar varyansı değeri oluştu. On hastada (%19,2) nötral varyans değeri oluştu. Radial inklünasyon açıları eşitlenmemiş olan 32 hastada (%61,5); sağlam taraf 28,5° (Aralık 21 ° -30°) iken ameliyat edilen taraf için ortalama açı 22,3° (Aralık 18°-27°) idi. On beş hastada (%28,8) radyal inklünasyon açısı sağlam tarafla eşitlendi. Diğer hastalarda, sağlam tarafta ortalama radyal inklünasyon açısı volar yönüne (dorsal 2° - volar 13°) doğru 5,9° idi. Yirmi beş hastada (%48) radial yükseklikteki kayıp ameliyat edilen tarafta 1,3 mm (0-5 mm) idi. Tedavi edilen tarafta kavrama gücü, sağlam tarafın ortalama %69'ü (18 kg) idi. Quick-DASH-T skoru ortalaması 8,3 (dağılım 0-70,5), Gartland-Werley puanı ortalaması 4,7 (dağılım 0-16) bulundu. Gartland-Werley değerlendirmesine göre, 25 hastada (%48) mükemmel, 25 (%48) hastada iyi, üç has tada (%4) ise orta sonuç alındı.

Sonuç: Volar yerleşimli kilitli plak uygulamaları radius distal uç anatomisinin düzeltilmesinde ve korunmasında etkilidir.

Anahtar kelimeler: Açık redüksiyon, Kilitli plak, Unstabil kırık, Distal radius kırığı

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Introduction

Distal radius fractures are frequently seen. The main purpose of treatment is to reestablish the anatomical integrity and functions. In unstable intra-articular fractures, it is usually not possible to reestablish the integrity of the wrist's inner joints and maintain the radial length with closed methods. In these cases, open surgical procedures are required. Various surgical methods and fixation materials can be used [1,2]. Recent studies providing a better understanding of the anatomy of the wrist and its functioning, as well as the increasing expectations of patients, have extended indications for surgical treatment. In addition, the developments in fixation materials have provided new opportunities [3,4].

Due to its intra-articular and unstable structure, distal radius fractures, classified as B and C by AO criteria, were treated surgically. Today, open surgery plate fixation is one of the common methods for these types of fractures [2,5]. Locking plates have replaced conventional support plates. The screws locking into the plate gives the advantage of more biomechanical endurance against forces applied to the fracture surfaces [6,7]. Due to their biomechanical endurance, locking plates are preferred in osteoporotic and multi-fragmented fractures [2,5,8]. On the other hand, there is not a consensus about placing these plates on the distal radius [3,6,9,10]. In recent years, volar approach has become more popular.

In this study, the radiographic and functional results of volar plate fixations on unstable distal radius fractures were evaluated.

Materials and methods

The ethical approval for our study was obtained from Adana City Hospital ethics committee (date: 11/6/2019, number: 605). Volar locking plate fixation was performed on a total of 52 patients (29 males, 23 females) with a mean age of 42 years, with unstable distal radius fractures between 2018-2019 in our clinic. These patients were followed up for about 15 months. The fracture was on the right side in 38 patients (73%). Based on the AO classification, six patients (11.5%) had B2, five patients (9.6%) had B3, four patients (7.6%) had C1, 29 patients (55.7%) had C2 and 8 patients had (15.3%) C3 fractures. Twenty-one (77.8%) of the fractures had dorsal angulation while six (22.2%) had volar angulation. The fracture was accompanied by an elbow dislocation and/or fracture in four patients (14.8%).

As a first intervention, closed reduction and splinting were performed on the patients in the emergency room. The pre-treatment fracture angulation was approximately 29° (18°-44°). There were comorbid distal radioulnar joint problems in eleven patients (21.1%). A comorbid fracture in the contralateral extremity was present in five patients (9.6%).

Patients who had a comorbid ulnar fracture or a multi-fragmented unstable radius distal fracture as surgical treatment indications were included in our study. Age, occupation, hobbies, the patient's accompanying lesions and active or passive life were evaluated as additional factors in terms of selecting a treatment. Unstable fractures with inner joint cascading were evaluated as one of the open surgery and locking plate fixation indications. Locking plates were preferred because of their biomechanical advantages and earlier start of movement.

The average pre-operative duration was 3 days (1-7). All surgical interventions were conducted under a tourniquet with the volar Henry approach and radioscopy control was ensured in every surgery.

Grafts were obtained from the crista iliaca autogenously in fifteen patients (28.8%) who required them. A temporary Kirschner wire fixation was performed on six patients who had compatibility problems in the distal radioulnar joint. An additional bone fixation procedure was not performed for patients with an ulnar styloid fracture, who were observed to have a stable distal radioulnar joint during the surgery. A short arm splint was made after the surgery. The splint and sutures were taken off after two weeks and active wrist exercises were started after 20 days. After radiological and clinical union was observed, exercises were started to increase the joint's range of motion and muscle strength. Open fracture treatment protocol was applied to three patients (5.7%) with a Gustilo type I open fracture. Comorbid fractures were also treated surgically.

Post-operative control graphs (anterior-posterior and lateral x-ray) were examined to evaluate the relationship between distal screws and the joint.

In control visits, if there was no pain in the fractured area, bone union was considered to have occurred. Patient follow-ups were performed on the 2^{nd} and 6^{th} weeks and 6^{th} and 12^{th} months. The radiographic controls were examined by comparing with the intact side. The radial inclination angle, radial height and ulnar variance were measured. They were evaluated according to the Stewart criteria [11]. Joint movement angles were measured using a standard goniometer. Grip strength was measured using a dynamometer (Saehan Smedley firm, South Korea) and compared with the healthy side. The functional subjective results were evaluated with the Turkish Version of Quick DASH (Disabilities of the Arm, Shoulder and Hand) and the Gartland-Werley evaluation form [12]. The average length of follow-up was 15 months (12-28 months).

Statistical analysis

Independent samples t test was used for comparison of normally distributed data, and Wilcoxon rank sum test (Mann-Whitney U test) was used for comparing nonparametric data. The Fisher exact test was used for comparison of two proportions. The paired t test and Wilcoxon signed-rank test were used to compare paired data. Kendall τ-b was used to measure associations of ranked variables. *P*-value <0.05 was considered significant. Mean values, percentages, and ORs were presented with 95% confidence intervals (CI). Statistical evaluations of the data were performed with SPSS computer software.

Results

All fractures healed in approximately 7 weeks (between 6-8 weeks). The average radiographic score on the Stewart Rating Scale was found as 0.5 (0-3). The ulnar variance levels were approximately -0.4 (between 0 and -2.5 mm) in thirty patients (57.6%). Twelve patients (23%) had an average positive ulnar variance level of 0.5 mm (between 0-2.5 mm). Ten patients (19.2%) had a neutral variance level. Almost half of the patients' radial tilt angles equalized with the intact side. In 32 patients

(61.5%) whose tilt angles were not equalized, the average angle was 28.5° (the interval 21°-30°) on the intact side and 22.3° (the interval 18°-27°) on the side that underwent surgery. The radial inclination angle equalized with the intact side in fifteen patients (28.8%). In other patients, the average radial inclination angle was 5.9° towards the volar direction (dorsal 2°- volar 13°) on the intact side. In twenty-five patients (48%), the loss of radial height was 1.3 mm (0-5 mm) on the side that underwent surgery.

In their final controls, the range of motion of the patients were as follows: Average flexion angle was 55° (the interval 0°-70°), average extension angle was 40° (the interval 35°-70°), average radial deviation was 18° (the interval 10°-26°), average pronation was 86° (the interval 0°-90°) and average supination angle was 83° (the interval 0° -90°). Synostosis development and loss in forearm rotations were observed in three patients (5.7%).

During the dynamometric evaluations, the average grip strength of the healthy side was measured as 69% (18 kg, 5-30 kg on average). The average Quick DASH-T score was 9.7 (the interval 0-70.5). Twenty-five patients (48%) were excellent, 25 patients (48%) were good and 2 patients (4%) were moderate in the Gartland-Werley evaluation scale. The average Gartland-Werley score was 5.6 (the interval 0-16).

To provide radial height, fifteen (28.8%) metaphyseal gaps were filled by taking grafts from crista ilica, supporting the plate fixation. Supportive (osteoconductive) or uniting stimulant (osteoinductive) instillation was not deemed necessary for the other patients.

There was a statistically significant difference between pre- and post-operative radial inclination angles, volar tilt and radial heights (P=0.009); however, these parameters were similar with the healthy sides, except for volar tilt angles (P=0.18). The increase in the Stewart radiographic scores was believed to negatively affect Gartland-Werley functional scores (r=0.35, P=0.006) and cause an increase in the DASH-T scores (r=0.53, P=0.18). In addition, a significant relationship between Quick DASH-T and Gartland-Werley evaluation scores was observed (r=0.827, P<0.001) (Table 1).

A statistically significant difference in muscle strength between the intact side and fractured side was found. The difference in joint movements was significantly different from the intact side (Table 2).

Table 1: Clinical outcomes

	3rd month	12th month	*P*-value
DASH score	21.3	9.7	0.27
VAS score	1.8	0.9	0.18

DASH: Percentage values for limb limitation (low values indicate less limitation), VAS: Visual analogue scale (low values indicate less pain)

Table 2: Mean limitation radiocarpal joint in degrees

	Outcomes	*P*-value *
3rd month		
Flexion	18.4°	0.16
Extension	29.5°	0.22
Ulnar deviation	9.2°	0.34
Radial deviation	6.3°	0.19
Pronation	18.7°	0.25
Supination	15.5°	0.17
12th month		
Flexion	6.5°	0.25
Extension	3.9°	0.27
Ulnar deviation	2.9°	0.35
Radial deviation	2.2°	0.22
Pronation	3.3°	0.30
Supination	3.6°	0.24

Units of measurement is degrees, * *P*-value for the intact side vs. the fractured side

Discussion

Osteoporosis reduces trabecular thickness and connectivity in bone mass and microarchitecture, leading to increased vertebral fragility and fracture risk [13]. Based on the Stewart criteria, important anatomical restorations were obtained for our study in terms of post-operative evaluation for fractures. After nearly a one-year follow-up, approximately 80% recovery in the wrist's range of motion and approximately 60% recovery in grip strength was observed compared to the healthy side. The Quick DASH-T score used for measuring daily functions was 8.3. In the Gartland-Werley evaluation scale, 25 patients were excellent, 25 patients were good, and 2 patients were moderate. In addition, graft use was not deemed necessary for 71.2% of the patients.

Locking plates provide successful results especially in the treatment of intra-articular unstable fractures [1,5,8,14,10]. The effectiveness of this method in anatomical reduction allows early joint movement through its fixation strength [11,15]. Its biomechanical advantages include ability to screw close to the joint surface and in different directions. The volar approach ensures fixation by creating minimal surgical trauma in the distal radius and adapting better to the surrounding soft tissues [2,5,6,8,9,14,16,17]. In our study, successful anatomical restoration was achieved in our patients with the volar approach, regardless of the direction of the fracture angle. The patients, who were mostly young adults, went back to their daily activities with 90% recovery. The effect of restoration of distal radius joint alignment angles on functional outcomes is controversial. Despite studies showing a direct correlation between anatomical and functional outcomes, it is seen that functional outcomes are satisfactory despite deformity in elderly patients with low functional expectations.

Collapse and loss of reduction on the joint surface is the most frequently seen early stage complication of treatment with plates [3-7,16-18,21,22]. Radiographic evaluations of correction loss revealed that the radiological outcomes of surgical treatment were superior to conservative treatment, even though adequate anatomical restoration can be achieved with closed reduction.

We believe that our study will provide additional information and experience regarding the treatment of unstable distal radius fractures.

Limitations

Patients with additional complications, pathologies, and multi-trauma were not included in our study. Patients with a bone metabolism disease except for primary osteoporosis, malignant disease, chronic cortisone use, history of wrist fracture or surgery, patients with insufficient improvement (x-ray), and patients with missing data or incomplete follow-up were excluded from the study. The patient exclusion criteria for our study was: Volar angulation not exceeding 10°, radial inclination not being lower than 15°, loss of radial height not exceeding 5 mm, intra-articular cascades not exceeding 2 mm.

Conclusions

Locking plates are effective in the restoration and protection of the distal radius anatomy. Joint movement and daily functions are regained by using locking plates in distal radius unstable fractures within a shorter period.

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Clinical and basic cardiovascular features of patients with COVID-19 admitted to a tertiary care center in Turkey

Türkiye'de bir üçüncü basamak sağlık merkezine başvuran COVID-19'lu hastaların klinik ve temel kardiyovasküler özellikleri

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Ethics Committee Approval: An official study permit was obtained from Amasya University Medical Faculty Sabuncuoglu Serefeddin Research and Training Hospital with issue number 62949364-929. In addition, a system registration was created with the number 2020-05-05T14-08-05 to the Ministry of Health. All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.
Etik Kurul Onayı: Amasya Üniversitesi Tıp Fakültesi Sabuncuoğlu Şerefeddin Araştırma ve Eğitim Hastanesi'nden 62949364-929 sayılı resmi çalışma izni alındı. Ayrıca çalışma için, Sağlık Bakanlığı'na 2020-05-05T14-08-05 numaralı bir sistem kaydı oluşturuldu. İnsan katılımcıların katıldığı çalışmalardaki tüm prosedürler, 1964 Helsinki Deklarasyonu ve daha sonra yapılan değişiklikler uyarınca gerçekleştirilmiştir.

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Abstract

Aim: COVID-19 is a new zoonotic infectious disease that can cause acute respiratory failure, which first occurred in Wuhan, China in December 2019. The aim of study was to analyze cases with COVID-19 admitted to a tertiary care center in Turkey.

Methods: We evaluated demographic characteristics, clinical symptoms or signs, comorbidities, laboratory results, chest computed tomography (CT) findings and outcomes including hospitalization, intensive care unit (ICU) admission and survival of 49 patients (20 females, 29 males) diagnosed with COVID-19 disease.

Results: Twenty (40.9%) of the cases were female and 29 (59.1%) were male. The mean age of the patients was 56.20 (17.65) years. The most common symptom was cough (75.5%). Hypertension (26.5%) was the most prevalent comorbid disease. Troponin I result of 42 (85.7%) patients were negative (reference value <0.1 ng/mL). Ten patients (18.4%) were admitted to the ICU and overall mortality rate was 4.1% (n=2). The important characteristics of two non-survivors were as follows: 1) A 67-year-old-man, high fever (38.5^{0}C), current smoker, diabetes mellitus (+), chronic obstructive pulmonary disease (COPD) (+), congestive heart failure (+), first admission to ICU, bilateral infiltration on chest CT, troponin I: 4.01 ng/L. 2) A 38-year-old-man, current smoker, COPD (+), first admission to ICU and high CRP (120.86 m/L).

Conclusion: The clinical parameters that determine the prognosis of COVID-19 are currently acute respiratory tract exacerbation and accompanying cardiovascular diseases such as hypertension and coronary artery disease. Cardiac enzyme monitoring is important in patients with cardiovascular risk factors.

Keywords: COVID-19, Clinical profile, Tertiary care center

Öz

Amaç: COVID-19 akut solunum yetmezliğine neden olabilen, ilk kez Aralık 2019'da Çin'in Wuhan şehrinde ortaya çıkan yeni zoonotik bir enfeksiyöz hastalıktır. Bu çalışmanın amacı Türkiye'de bir üçüncü basamak hastaneye başvuran COVID-19'lu hastaları analiz etmektir.

Yöntemler: Çalışmada, COVID-19 hastalık tanısı almış 49 hastanın (20 kadın, 29 erkek) demografik özellikleri, klinik semptom ve bulguları, komorbiditeleri, laboratuvar sonuçları, toraks bilgisayarlı tomografi (BT) bulguları ve sağkalım, yoğun bakım ünitesine (YBÜ) ve servis yatışlarını değerlendirdik.

Bulgular: Vakaların 20'si (%40,9) kadın ve 29'u (%59,1) erkekti. Hastaların ortalama yaşı 56,20 (17,65) idi. En sık görülen semptom öksürüktü (%75,5). Hipertansiyon en sık eşlik eden hastalıktı (%26,5). 42 hastanın (%85,7) troponin I değeri negatifti (referans değer <0,1 ng/mL). 10 hasta YBÜ'ye başvurmuştu ve genel mortalite oranı %4,1 idi (n=2). Ölen iki hastanın önemli karakteristik özellikleri şöyleydi: i) 67 yaş erkek hasta, yüksek ateş (38,5^{0}C), sigara içici, diabetes mellitus (+), kronik obstrüktif akciğer hastalığı (KOAH) (+), konjestif kalp yetmezliği (+), ilk başvuru YBÜ'ye, toraks BT'de bilateral infiltrasyon ve troponin I (4,01 ng/L). ii) 38 yaş erkek hasta, sigara içici, KOAH (+), ilk başvuru YBÜ'ye ve yüksek c-reaktif protein (120,86 m/L).

Sonuç: Mevcut bilgilerimize göre COVID-19'da prognozu belirleyen klinik parametreler akut solunum yolu alevlenmesi ve hipertansiyon veya koroner arter hastalığı gibi kardiyovasküler hastalıkların eşlik etmesidir. Kardiyovasküler risk faktörleri olan hastalarda kardiyak enzim takibi önemlidir.

Anahtar kelimeler: COVID-19, Klinik profil, Üçüncü basamak merkez

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Introduction

An infectious new zoonotic coronavirus disease (COVID-19), which first occurred in Wuhan, China in December 2019, was declared as a pandemic in March 2020 and since April 2020, thousands of people have been affected by the disease and died in more than a hundred countries [1-3]. COVID-19 has become a serious public health problem causing socio-economic collapse all over the world. The first positive case in Turkey had contact with Europe and was announced on 11 March 2020 [4-6]. New positive cases and deaths due to this highly contagious disease continue in many countries, including ours. The numbers of COVID-19 patients in Turkey are as follows: Total number of tests: 889,742, number of positive cases: 110,130, number of deaths: 2,805, number of cases admitted to intensive care unit (ICU): 1,776, number of intubated patients: 883, number of cases recovered from the disease 29,140 [7].

Vaccine and drug studies have been conducted in several countries of the world, including our country, to no avail [5]. In the literature, there are studies reporting the clinical progress and outcomes of patients with COVID-19 and it is reported that the disease is directly and indirectly associated with cardiovascular complications [2,3,5,8].

In the study, we aimed to evaluate the clinical and basic-simple cardiovascular features of patients with COVID-19 infection admitted to a tertiary care center in Turkey.

Materials and methods

Study design and population

We performed a retrospective cohort study with 49 COVID-19 cases from a tertiary hospital in Turkey. The study was conducted in accordance with the Declaration of Helsinki guidelines. An official study permit was obtained from Amasya University Medical Faculty Sabuncuoglu Serefeddin Research and Training Hospital with issue number 62949364-929. In addition, a system registration was created with the number 2020-05-05T14-08-05 in the Ministry of Health. The study included patients with laboratory-confirmed COVID-19 infection who were hospitalized and treated in Amasya University Sabuncuoglu Serefeddin Research and Training Hospital in Turkey from March 14 to April 13, 2020. Nasopharyngeal swab samples were obtained, and patients with laboratory-confirmed positive test results of reverse-transcriptase-polymerase-chain-reaction (RT-PCR) were considered to have definitive diagnoses of COVID-19 infection. We summarized the epidemiological characteristics and examined the prognosis of the disease. Hospital archive records and computer database were reviewed and demographic characteristics, clinical symptoms, comorbidities (smoking, hypertension, chronic obstructive pulmonary disease, diabetes mellitus, coronary artery disease, congestive heart failure, malignancy), vital signs, laboratory test results, chest computed tomography (CT) imaging findings and outcomes (hospitalization, ICU admission and survival) of patients were recorded.

Computed tomography and nasopharyngeal swab were obtained for the definitive diagnosis of COVID-19 from suspected patients. A suspected patient was defined as any of the followings: i) exhibiting any one of fever, cough or sputum complaints, ii) the clinical status cannot be explained by another disease except COVID-19, iii) a history of travel to other countries in his/her relatives or himself/herself within 14 days before the beginning of symptoms, iv) contact history with COVID-19 with an accurate diagnosis within 14 days before the beginning of symptoms [3].

Patients who required hospitalization or ICU admission due to definitive diagnosis of COVID-19 were included in the study in the presence of at least one of following findings: i) any lesion on the radiological imaging (chest x-ray or CT), ii) severity of the symptoms and findings (temperature 38^0C, dyspnea, cough, sputum, malaise, altered mental status, increased respiratory rate (≥30 per minute), shortness of breath, peripheral cyanosis, oxygen saturation below 93%, arterial blood oxygen partial pressure (PaO_2)/oxygen concentration (FiO_2) ≤300 mmHg), iii) critically ill patients (acute respiratory failure, requiring endotracheal intubation, sepsis or shock, admission to ICU and organ failure), iv) coexisting diseases (hypertension, diabetes mellitus, chronic obstructive pulmonary disease, asthma, coronary artery disease, neoplastic disease, chronic renal-liver disease, congestive heart failure, cerebrovascular diseases, nursing home resident), v) patients who cannot provide their own isolation (soldiers, crowded family, elderly patients, lack of space in the house, nursing home resident, dormitory-dwellers) [3].

Patients who had pneumonia agents or clinical findings other than COVID-19, positive patients to which home isolation is recommended according to the guideline of the Scientific Committee of Turkish Ministry of Health and those diagnosed with COVID-19 but not requiring hospitalization per the decision of an infectious disease specialist or pulmonologist (based on severity of the symptoms, radiological imaging, physical examination) were excluded from the study [3].

Recovery discharge criteria included regression of respiratory symptoms, decreased fever, regression of pulmonary findings on chest CT, and a negative RT-PCR result [9].

Statistical analysis

All statistical analyses were performed with SPSS 23.0 (SPSS for Windows, Chicago, IL, SA). Continuous variables were expressed as mean (standard deviation) and categorical variables were defined as percentages (%).

Results

Between March 22 and April 13, 2020, we obtained 855 nasopharyngeal swabs from suspicious cases and evaluated 49 patients with RT-PCR confirmed COVID-19 infection in the hospital. Twenty (40.9%) of the cases were females and 29 (59.1%) were males. The mean age of the patients was 56.20 (17.65) years, ranging between 17-88 years. Two patients had international contact (Saudi Arabia and France). Six of the patients had family contact and two cases were healthcare professionals. Fifteen (30.6%) cases were current smokers, 31 (61.3%) were non-smokers and 3 (6.1%) were ex-smokers. There were no patients who resided in nursing homes or were homeless. The fever of the cases ranged from 36 to 39 ^{o}C, with a mean of 36.75^{o}C (0.66). The respiratory rate of the patients ranged between 18 and 32 breaths per minute with a mean of 21.19 (3.47) breaths. The mean systolic blood pressure of cases

was 110.20 (9.01) mmHg, ranging between 100 and 130 mmHg. The heart rate of the cases varied between 58 and 105 beats per minute, with a mean of 76.89 (8.95) beats. The mean oxygen saturation was 92.71 (5.63) (range: 82-99%) on room air. Clinical symptoms and signs of patients and their comorbidities are presented in Table 1. The most common symptom was cough (75.5%). Hypertension (HT) (26.5%) was the most prevalent coexisting disease. Demographics of the patients admitted to ICU are shown in Table 2.

Table 1: Clinical symptoms and signs of patients and their comorbidities

		COVID-19 patients (n=49)	
		No.	%
Gender	Male	29	59.1
	Female	20	40.9
Smoking status	Current smoker	15	30.6
	Non-smoker	31	63.3
	Ex-smoker	3	6.1
Hypertension		13	26.5
Diabetes mellitus		3	6.1
Coronary artery disease		4	8.2
COPD		5	10.2
Asthma		-	-
Nursing home resident		-	-
Neoplastic disease		2	4.1
Chronic liver diseases		-	-
Congestive heart failure		2	4.1
Cerebrovascular diseases		-	-
Chronic renal diseases		-	-
Confusion		1	2.05
Pleural effusion		3	6.1
ICU admission		10	20.4
Mortality		2	4.1
	Min-Max	Mean	SD
Respiratory rate (min)	18-32	21.19	3.47
Systolic blood pressure (mmHg)	100-130	110.20	9.01
Temperature (^{o}C)	36-39	36.75	0.66
Heart rate (min)	58-105	76.89	8.95
Age (years)	17-88	56.20	17.65

Table 2: Demographics of patients admitted to ICU

		COVID-19 patients (n=10)	
		No.	%
Gender	Male	8	80
	Female	2	20
Smoking status	Current smoker	5	50
	Non-smoker	3	30
	Ex-smoker	2	20
Hypertension		2	20
Diabetes mellitus		2	20
Coronary artery disease		3	30
COPD		3	30
Neoplastic disease		1	10
Congestive heart failure		1	10
Confusion		1	10
Pleural effusion		2	20
Mortality		2	20
	Min-Max	Mean	SD
Systolic blood pressure (mmHg)	100-120	107	6.74
Temperature (^{o}C)	36-39	37.2	1.06
Heart rate (min)	72-90	79.4	7.12
Age (years)	38-80	62.7	12.9
Albumin, g/L	20-38.1	28.2	5.91
Creatinine, mg/dL	0.52-1.26	0.82	0.24
Troponin I, ng/L	0.04-4.01	0.49	1.23
CRP, mg/L	3.97-246.9	108.8	70.6
Hemoglobin, g/dL	5.7-14.9	11.8	2.45
Lymphocyte, 10*9 L	0.4-1.73	1.07	0.46
Platelet, 10*3/uL	153-503	298	123
Neutrophil, 10*3/uL	0.93-26.92	9.93	7.74
D-dimer	0.88-2.53	1.46	0.74

Table 3 presents the blood results of patients including renal functions (urea, creatinine), liver tests (alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin), lactate dehydrogenase (LDH), sodium, glucose, c-reactive protein (CRP), albumin and complete blood count (white blood cell (WBC), neutrophil, hemoglobin, platelets, eosinophil, basophil. Troponin I result of 42 (85.7%) patients were negative (reference value <0.1 ng/mL). In Table 4, chest CT findings of the cases are presented. Three patients (6.1%) had pleural effusion and 14 patients (28.5%) had bilateral lung infiltration. Ground glass densities were detected in 28 (57.1%) and consolidation in 7 (14.2%) patients. Ten patients (18.4%) were admitted to the ICU and the overall mortality rate was 4.1% (n=2). The important characteristics of two non-survivors were as follows: i) A 67-year-old-man, high fever (38.5^{0}C), current smoker, diabetes mellitus (+) and chronic obstructive pulmonary disease (+), congestive heart failure (+), first admission to ICU, bilateral infiltration on the chest CT, lower serum albumin level (20 g/L), CRP:3.97 mg/L and higher AST (6755 U/L), and ALT (256 U/L), troponin I: 4.01 ng/L, LDH: 1058 U/L, ii) A 38-year-old-man, current smoker, chronic obstructive pulmonary disease (+), first admission to ICU and higher CRP (120.86 m/L). The samples of CT findings of six patients are shown in Figures 1a-1f.

Table 3: Blood parameters of the cases

	n	Minimum	Maximum	Mean (SD)
Albumin, g/L	39	20	47.6	37.24 (6.86)
Creatinine, mg/dL	49	0.52	1.29	0.84 (0.19)
AST, U/L	47	14	6755	173.93 (98.94)
ALT, U/L	47	6	256	29.85 (37.35)
Total bilirubin, mg/dL	46	0.16	1.54	0.48 (0.26)
LDH, U/L	46	142	1058	320.28 (164.67)
Sodium, mmol/L	47	134	146	139.68 (3.03)
Glucose, mg/dL	47	76	427	118.34 (54.4)
CRP, mg/L	49	0.46	246.9	54.06 (58.58)
Eosinophil, 10*9 L	47	0	0.7	0.08 (0.12)
Hemoglobin, g/dL	49	5.7	15.5	12.83 (1.65)
Neutrophil, 10*3/uL	47	0.93	26.9	5 (4.55)
Platelet, 10*3/uL	49	108	503	227.5 (87.02)
Lymphocyte, 10*9 L	47	0.40	2.93	1.47 (0.57)
Troponin I, ng/L	49	0.04	4.01	0.119 (0.55)
D-dimer, ng/mL	31	0.40	310	11.14 (55.47)

Table 4: Chest CT findings of the patients

	n	%
Pleural effusion	3	6.1
Bilateral infiltration	14	28.5
Infiltration		
Right lung upper lobe	19	38.7
Right lung middle lobe	12	24.4
Right lung lower lobe	24	48.9
Left lung upper lobe	17	34.6
Left lung lower lobe	20	40.8
Left lung lingula	12	24.4
Consolidation	7	14.2
Ground glass densities	28	57.1

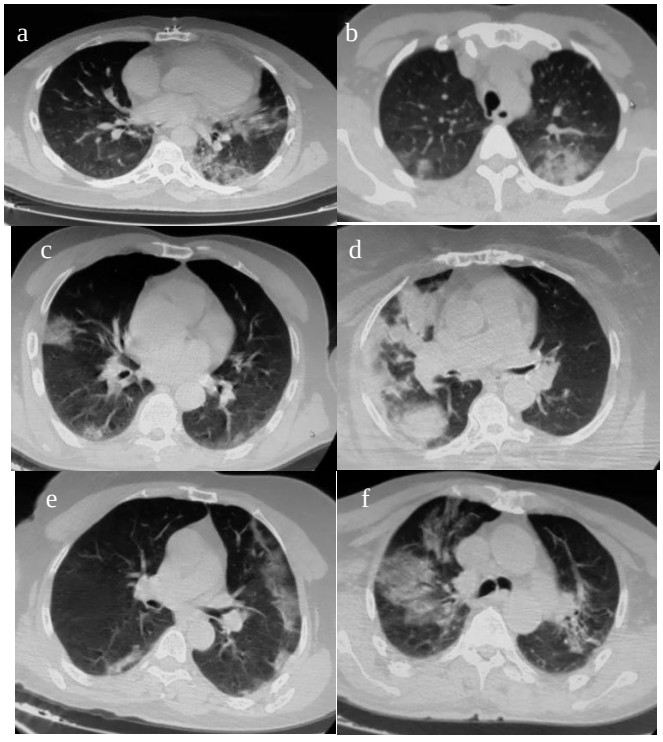

Figure 1: Chest CT samples of the patients (a: consolidation and peribronchial thickening in the left lower lobe, b: ground glass densities and alveolar consolidation in the posterior segment of the right lung upper lobe and the apicoposterior segment of the left lung lobe, c: patchy infiltration and ground glass densities in the right lung, d: consolidation and ground glass densities in right lung parenchyma, e: multifocal patchy infiltration and ground glass densities in the right and left lung, f: diffuse ground glass densities and multifocal pneumonic infiltration)

Discussion

In our hospital, the fever of all patients admitted to emergency department is measured first in the triage and patients demonstrating any of the fever, cough or sputum complaints are considered as patients with suspected COVID-19. Typical symptoms in patients with COVID-19 are commonly known as fever, cough, dyspnea, muscle weakness, malaise, sore throat and respiratory symptoms (cough, dyspnea), but some patients are also known to present with chest pain and palpitations [1,11]. The diagnostic test usage, demographics and mortality rates of COVID-19 can differ between countries [1]. We particularly focused on clinical and basic-simple cardiac features of our patients.

Cardiac arrhythmias and elevation of troponin I can be seen with COVID-19, and the specific effect of this disease on the cardiovascular system remains uncertain [8]. Based on our current knowledge, the pathophysiology of the high pathogenicity of COVID-19 is not fully understood in elderly patients or those with severe comorbidities, but it is stated that there is a relationship between increased age, cardiovascular disease and COVID-19 [8]. In a study, it is stated that the overall case-mortality rate associated with the disease in China is 2.3%, however, this rate increased to 8.0% in patients between the ages of 70-79 years and to 14.8% in patients over the age of 80 [8,11]. In this study, the mean age of patients was 56.20 (17.65) years and the mortality rate was 4.1%. One of our patients who died due to COVID-19 was a 67-year-old male, current smoker, with DM, CHF and COPD, and a high serum troponin value (4.01 ng/L). The other non-survivor was 38-year-old male, current smoker, with COPD and he had a high serum CRP level (120.86 m/L). Although only mild signs of infection are seen in the majority of patients, increased troponin level, which indicates the cardiac complication of COVID-19, is seen in 20-30% of patients, especially in the elderly with hypertension, heart failure, CAD and DM [1,12,13]. It is reported that in patients with COVID-19, mortality rate increases up to 70% in case of high troponin level and CAD [1,13]. Ventricular dysfunction and increased inflammatory markers including CRP and NT-proBNP are also associated with poor prognosis [1,13]. In another meta-analysis including patients with COVID-19, the presence of HT was reported as 17.1%, the presence of cardiovascular and cerebrovascular disease was 16.4%, and the rates of comorbid HT and CAD in our study were 26.5% and 8.2%, respectively [8,14].

Several studies in hospitalized patients in China report that heart damage is more common and may be associated with a poor prognosis in patients who are followed up and die in the ICUs [8,15-17]. In our study, the number of patients admitted to ICU was 10 (20.4%) and two (20%) of those died. Seven (80%) patients recovered from the ICU and were discharged, including one patient who was intubated and resuscitated due to cardiopulmonary arrest, and the other, a current smoker who had previously received a coronary artery bypass-graft. The troponin levels of five (10.2%) patients in our study were relatively high, and this may be due to the low average age of our group and their relatively low comorbidities such as CAD and DM (8.2% and 6.1%, respectively). One of the two patients (50%) who died had a high troponin value and three of five patients (60%) with increased troponin needed ICU. The frequency of cardiac arrhythmia is twice as high in patients with COVID-19 admitted to ICU [8,15].

Previous studies showed that patients with COVID-19 had prominent levels of proinflammatory cytokines [8,17]. In one of our two patients who died, CRP value was very high (120.86 mg/L) and ICU was needed in 24.3% (n=9) of 37 patients whose CRP value was above the reference value (0-5 mg/L). Cytokine discharge associated with systemic inflammation may lead to atherosclerotic plaque instability, rupture, and myocarditis [1,18]. The mean CRP value in our patients was 54.06 (58.58) mg/dL, and this relatively low value may be due to less coexisting diseases such as CAD and DM.

Limitations

This single-centered study had some limitations. To begin with, the size of the patient population was relatively small, and we could not compare the data of survivors and non-survivors. Only patients diagnosed with COVID-19 and treated in the hospital were included in the study, and patients with home isolation were excluded. In the future, multicenter and large-scale studies are needed in Turkey.

Conclusions

According to our current knowledge, clinical parameters that determine the prognosis of COVID-19 are acute respiratory exacerbation, accompanied by cardiovascular diseases such as hypertension and coronary artery disease. We think that cardiac enzyme monitoring including troponin is important especially in patients with cardiovascular risk factors.

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Evaluation of peripheral vascular injuries treated with surgery: A retrospective cohort study

Cerrahi tedavi yapılan periferik vasküler yaralanmalarda değerlendirme: Retrospektif kohort çalışma

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Etik Kurul Onayı: Çalışmanın retrospektif doğası nedeniyle etik kurul onayı alınmadı. İnsan katılımcıların katıldığı çalışmalardaki tüm prosedürler, 1964 Helsinki Deklarasyonu ve daha sonra yapılan değişiklikler uyarınca gerçekleştirilmiştir.

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Abstract

Aim: Vascular injuries constitute 2-3% of the total injuries. Early diagnosis and emergent management of peripheral vascular injuries, which have high mortality and morbidity rates if inadequately managed, are particularly important. In this study, we aimed to evaluate the etiology and treatment results of patients who underwent surgical treatment due to peripheral vascular injury.

Methods: This research was designed as a retrospective cohort study. The etiologies, localizations, accompanying injuries, surgical methods, and results of 57 cases operated due to peripheral arterial injury in Yozgat State Hospital and Bozok University Research Hospital between 2012 and 2019 were evaluated.

Results: Fifty-two patients were male (91.23%) while 5 were female (8.77%). The mean age of all patients was 27.6 (10.5) years (range: 4 - 63 years). Among etiologies, injury due to sharp objects and firearms were significantly higher (n=34 (59.6%) and n=16 (28%), respectively). Traffic accidents were the cause in 5 (8.7%) cases and occupational accidents had occurred in 2 (3.5%) patients. Arterial injuries were detected in 33 (56.89%) upper extremities and 24 (41.87%) lower extremities. End-to-end anastomoses were performed in 29 cases, lateral arteriorrhaphy (primary repair) was performed in 24, autogenous saphenous vein interposition in 4 and ligation was performed in one patient. No cases required fasciotomy or amputation and one patient with a multi-trauma died. A secondary operation was needed for hematoma, thrombectomy, and anastomosis revision in seven, five and three cases, respectively.

Conclusion: In vascular injuries, after ensuring hemodynamic stability, the primary aim is providing the accurate operation approach in the shortest time to reduce morbidity and mortality.

Keywords: Vascular trauma, Vessel repair, Peripheral arterial injury

Öz

Amaç: Tüm travmaların %2 ila %3'ünü vasküler travmalar oluşturmaktadır. Etkin tedavi edilmediğinde mortalite ve morbidite oluşturan periferik damar yaralanmalarında erken tanı ve acil tedavinin önemi büyüktür. Bu çalışmada periferik vasküler yaralanmayla cerrahi tedavi uyguladığımız olguların etiyolojisi ve tedavi sonuçlarının değerlendirilmesini amaçladık.

Yöntemler: Bu çalışma retrospektif kohort çalışması olarak tasarlanmıştır. 2012 ve 2019 tarihleri arasında Yozgat Devlet Hastanesi ve Bozok Üniversitesi Araştırma Hastanesinde periferik arter yaralanması ile operasyona alınan 57 olgu etiyolojileri, lokalizasyonları, eşlik eden yaralanmalar, uygulanan cerrahi yöntemler ve sonuçları retrospektif olarak değerlendirildi.

Bulgular: Hastaların 52'si erkek (%91,23), 5'i kadın (%8,77), yaş ortalaması; 27,6 (10,5) (4-63 yaşları arasında) idi. Yaralanma etiyolojilerine bakıldığında kesici delici alet yaralanmalarında ve ateşli silah yaralanmalarında önemli bir artış izlendi. Kesici delici vakaların 34'ünde (%59,6) kesici delici alet, 16'sında (%28) ateşli silah yaralanmaları mevcuttu. Buna karşın, vakaların 5'inde (%8,7) vasküler yaralanmaya yol açan trafik kazası, 2'sinde (%3,5) iş kazası yaralanması gözlendi. Olguların, 33'ünde (%56,89) üst ekstremitede, 24'ünde (%41,37) ise alt ekstremitede arter yaralanması tespit edildi. 29 Vakada uç-uca anastomoz, 24'ünde lateral reperasyon (primer tamir), 4'ünde otojen safen ven interpozisyonu ve 1 hastada ligasyon uygulandı. Multi-travmalı olan bir hastada mortalite gözlendi. Hiçbir hastada fasiyotomi ihtiyacı olmadı ve ampütasyon yapılmadı. 7 vakada hematom, 5 vakada postoperatif trombektomi, 3 vakada anastomoz revizyonu gerekti.

Sonuç: Vasküler yaralanmalarda, hemodinamik stabilitenin sağlanarak en kısa sürede en doğru operasyon yaklaşımının sağlanması morbidite ve mortalitenin azaltılmasında esastır. Zaman tetkik ikileminde, vakaya göre karar verilmesi hastalık yoktur hasta vardır ilkesi doğrultusunda her vakaya özel yaklaşımı gerekli kılmaktadır.

Anahtar kelimeler: Vasküler travma, Damar onarımı, Periferik arter yaralaması

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Introduction

The main cause of death and disability under the age of 45 years is injury, which shows an increasing incidence due to global sociocultural corruption [1,2]. Vascular injuries constitute 2-3% of total injury cases [3]. Early diagnosis and emergent management of peripheral vascular injuries, which have high mortality and morbidity rates if inadequately managed, are particularly important [4,5].

Illegal individual armament and violence are rising problems all around the world. Injuries, even loss of lives caused by violence is increasing day by day. Owing to the recent improvements in vascular surgery, extremity loss has reasonably decreased. In cases which multiple tissues, such as muscle, tendon, bone, and nerve tissue, are at risk, a multidisciplinary management strategy is necessary.

This study was conducted to investigate the contemporary epidemiology and patient outcome of vascular injuries in Turkey.

Materials and methods

This retrospective cohort research, conducted in Yozgat State Hospital and Bozok University Research Hospital, complies with the standards of Declaration of Helsinki. The etiologies, localizations, accompanying injuries, surgical methods, and results of 57 cases operated due to peripheral arterial injury between 2012 and 2019 were retrospectively evaluated.

Colored Doppler Ultrasonography (CDUS) was performed in every patient in addition to anamnesis taking and physical examination for diagnosis. In seven cases, computerized tomographic angiography (CTA) was used. All patients underwent surgery after hemodynamic stabilization. After exploration of the traumatic zone, injured vessels were clamped proximally and distally. In case of suspected emboli, embolectomy was performed. Before clamping the injured vessels, 40-90 IU/Kg Heparin was administered intravenously. Each patient received tetanus prophylaxis along with antibiotic drug treatment for seven days starting from the preoperative period. The patients were prescribed wide spectrum antibiotics and 150 mg acetylsalicylic acid at discharge if there were no contraindications. All patients were re-evaluated on the 10^{th} postoperative day.

Statistical analysis

Statistical analysis was conducted using the SPSS for Windows software package (ver. 17; SPSS Inc., Chicago, IL, USA). All variables were evaluated using visual (histograms, probability plots) and analytical (Kolmogorov Smirnov test) methods to determine normality of distribution. Continuous variables were reported as mean (SD) for normally distributed, and median with interquartile ranges for non-normally distributed variables. Categorical variables were presented as numbers and percentages.

Results

Fifty-two patients were male (91.23%) while 5 were female (8.77%). The mean age of all patients was 27.6 (10.5) years (range: 4 - 63 years) (Table 1).

Among etiologies, injury due to sharp objects and firearms were significantly higher (n=34 (59.6%) and n=16 (28%), respectively). Traffic accidents were the cause in 5 (8.7%) cases and occupational accidents had occurred in 2 (3.5%) patients (Table 2).

Arterial injuries were detected in 33 (56.89%) upper extremities and 24 (41.87%) lower extremities (Table 3). A. ulnaris was the most frequently injured artery, as seen in 32% (n=16) of the cases. In lower extremities a. femoralis was the most frequently injured artery, as observed in 18.96% (n=16) of the cases. V. femoralis was the most frequently injured vein, as observed 3.44% (n=2) of the cases. Among 57 cases, 55 arterial and 3 venous injuries were observed.

End-to-end anastomoses were performed in 29 cases (50%), lateral arteriorrhaphy (primary repair) was performed in 24 (41.4%), autogenous saphenous vein interposition in 4 (6.9%) and ligation was performed in one (1.7%) patient (Table 4). No cases required fasciotomy or amputation and one patient with a multi-trauma died. A secondary operation was needed for hematoma, thrombectomy, and anastomosis revision in seven, five and three cases, respectively. One patient had a wound infection and was treated with antibiotics. Postoperative complications are listed in Table 5. Mean hospitalization time was 7.4 (1.8) days (range: 5-15 days).

Table 1: Distribution of gender

Gender	Number (n)	Percent (%)
Male	52	91.23
Female	5	8.77

Table 2: Etiology of vascular trauma

Type of injury	Number (n)	Percent (%)
Sharp object injury	34	59.6
Firearm injury	16	28.0
Traffic accident	5	8.7
Occupational accident	2	3.5
Total	57	100

Table 3: Injured vessels

Injured vessel	Number (n)	Percent (%)
Upper Extremity Arterial Injury	33	56.89
A. Axillaris	1	1.72
A. Brachialis	5	8.62
A. Ulnaris	19	32.75
A. Radialis	7	12.06
A.Radialis+ A.Ulnaris	1	1.72
Lower Extremity Arterial Injury	24	41.37
A. Femoralis	11	18.96
A. Poplitea	8	13.79
A. Tibialis Posterior	3	5.17
A. Tibialis Anterior	2	3.44
Venous Injury	3	5.17
V. Femoralis	2	3.44
V. Brachialis	1	1.72

Table 4: Operational techniques

Operational techniques	Number (n)	Percent (%)
End to end anastomosis	29	50.0
Lateral reparation	24	41.4
Saphenous vein interposition	4	69
Ligation	1	1.72
Total	58	100

Table 5: Peroperative complications

Complication	Number (n)	Percent (%)
Hematoma	7	12.1
Postoperative thrombosis	5	8.62
Revision of anastomosis	3	5.17
Wound infection	1	1.72
Mortality	1	1.72

Discussion

Peripheral vascular injuries remain a serious health problem despite the decreased mortality and morbidity rates compared to the past. Etiology of vascular injury differ with region. The most common causes of peripheral vascular injuries

are firearms in the US, blunt traumas and iatrogenic causes in European countries and sharp objects in Turkey [3, 8-10].

In our study, sharp object injuries were the most frequent, followed by firearm injuries, while occupational accidents and traffic accidents were the rarest. Traffic density and industrial structure of our region is less in comparison to other regions. These results show that economic structure and vascular traumas may be related. According to numerous studies, vascular traumas are mostly seen in the young male population [6,7,10], just as in our study.

The first step in a vascular trauma is to achieve hemodynamic stability. Airway should be kept open; volume should be replaced, and active bleeding should be stopped. A direct pressure on the bleeding area is more beneficial than a tourniquet to maintain collateral circulation. The external compression should be sustained until traumatic vascular tissues are surgically managed [4,6,7,9,11]. Decreased traffic density and relatively low population of our region are the main advantages in the transportation of patients with vascular injuries. According to the data derived from Yozgat Local Health Authorities, the mean time of an ambulance reaching a patient in the city center is 6 minutes, which is lower than the country average of 10 minutes.

In extremity traumas, vascular repair should be performed primarily. Otherwise, serious complications may be observed [3-6,11]. All patients were managed with multidisciplinary involvement in the emergency unit. Orthopedic and Neurosurgery Clinics were consulted in case of related tissue injuries. However, vascular management was prioritized.

In most of the cases diagnosis is based on physical examination [3,6,9,11-14]. Radiological imaging is a crucial step in localizing the traumatic tissues. Therefore, color Doppler ultrasonography (CDUS) was our first option due to the practicality and needlessness of contrast material use. However, in blunt traumas CDUS may remain incapable and angiographic imaging is more beneficial [6,7-12]. The time lapse between diagnosing imaging and surgical management maybe lifesaving and life threatening.

There are many revascularization techniques, such as autologous and artificial graft use. However, the first choice should always be arteriorrhaphy (primary repair). End to end anastomosis and lateral arteriorrhaphy are the most used techniques [3-6,8,11,13].

In our patients, we preferred end to end anastomosis and lateral arteriorrhaphy. For interposition, we used the saphenous vein. In one patient we ligated the artery. The first aim should be to maintain the viability of original tissue.

Parry et al. claim that patency rate following venous repair is 73% [16]. Although we did not observe any vascular complications after venous repair among our patients, we think that the number of our cases is not adequate to generalize our results.

Postoperative wound infections are one of the serious complications following surgery among these patients. Antibiotherapy administered peroperatively both for prophylaxis and according to the culture antibiogram is crucial. It is important to be alert about resistant infections, especially those resulting from firearm injuries.

Limitations

As a result of the retrospective nature of the study, certain variables specifically related to peripheral vascular injury are not available, including specific vascular imaging or diagnostic tests. Another limitation of our study is the lack of autopsy of sudden deaths following a multi-traumatic vascular injury, which were impossible to include. Further multi-center studies involving larger number of cases would provide more realistic and meaningful statistical results.

Conclusion

In vascular injuries, providing the most accurate operation approach in the shortest time after ensuring hemodynamic stability is essential in reducing morbidity and mortality. In case of dilemma, it must be kept in mind that the patient, rather than the disease, must be cured, and a different approach may be required for each case.

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Effect of preoperative radiotherapy and emergent surgery on conversion in laparoscopic colorectal surgery: A retrospective cohort study

Preoperatif radyoterapi uygulanmasının ve acil cerrahinin laparoskopik kolorektal cerrahide açığa geçiş üzerine etkisi: Retrospektif kohort çalışma

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Abstract

Aim: The effects of preoperative radiotherapy and emergent surgery on conversion in laparoscopic colorectal surgery is not clear. We therefore aimed to determine the effects of neoadjuvant radiotherapy and emergent surgery on conversion.

Methods: The data of 67 patients, who were operated for familial adenomatosis polyposis coli, colon, and rectum malignant neoplasms by the same surgical team between October 2016 and January 2018 were evaluated retrospectively. Among them, fifty-five laparoscopically finished or converted to open surgery cases were included in the study. The exclusion criteria included cases which began as open surgery, history of previous colorectal surgery for benign or malignant diseases, morbid obesity (body mass index >40 kg/m^2) and missing data. Demographic values (age, gender), localization of tumor, whether it was an emergent or elective surgery, history of preoperative chemotherapy and radiotherapy, and causes of conversion were evaluated.

Results: Among 55 patients, 35 were male (63.6%) and 20 were female 20 (36.4%), with a mean age of 58.4 (13.4) (22 – 80) years. Mean ages of conversion and laparoscopically finished cases were 62.86 (8.91) (53 – 73) and 57.71 (13.84) (22 – 80) years, respectively (*P*=0,216). The reason for operation was right colon cancer in three patients (5.5%), left colon cancer in six (10.9%), rectum cancer in thirty-seven (67.3%), rectosigmoid junction cancer in five (9.1%) and adenocancer due to familial adenomatous polyposis coli in four patients (7.3%). In seven patients (12.7%), the need for conversion to open surgery arose. Among 55 patients, 47 patients were operated electively (85.5%) and 8 were operated under emergent conditions (14.5%). Of the 7 conversion patients, 5 were operated under emergent conditions and 2 were operated electively (*P*<0,001). This result showed that conversion rates were higher in emergent surgery patients. Neoadjuvant radiotherapy wasn't administered to 38 patients (69.1%) (chemotherapy was administered alone to 3 of the patients and 35 patients were not treated with any neoadjuvant therapy), and neoadjuvant chemoradiotherapy combination was administered to 17 patients (39.1%). Among 7 conversion patients, 1 had been administered neoadjuvant radiotherapy while 6 had not (*P*=0.308). This result showed no statistical differences between patients to whom preoperative radiotherapy were and were not administered.

Conclusion: Laparoscopic colorectal surgery can be performed as successfully as conventional open surgery under elective conditions. Preoperative radiotherapy is not related to conversion.

Keywords: Rectum cancer, Colon cancer, Laparoscopic surgery, Conversion, Radiotherapy, Emergent surgery

Öz

Amaç: Laparoskopik kolorektal kanserlerde açığa geçiş üzerinde neoadjuvan radyoterapi uygulanmasının ve acil şartlarda operasyon yapılmasının etkisi açık değildir. Bu nedenle Neoadjuvan radyoterapi alınması ve acil cerrahinin preoperatif açık cerrahiye geçiş üzerine etkilerini değerlendirmek amaçlandı.

Yöntemler: Ekim 2016 – Ocak 2018 tarihleri arasında aynı cerrahi ekip tarafından ailesel polipozis koli, kolon malign neoplazisi ve rektum malign neoplazisi nedeniyle aynı cerrahi ekip tarafından opere edilen 67 hastanın dosyaları retrospektif olarak incelendi. Laparoskopik tamamlanan veya laparoskopik başlanıp açık cerrahiye geçilen 55 hasta çalışmaya dahil edildi. Çalışmadan çıkarılma kriterleri; direk açık cerrahi uygulanmak, benign veya malign sebeplerle daha önce kolorektal cerrahi uygulanmış olmak, morbid obezite (vücut kitle indeksi >40 kg/m^2) ve verilere ulaşılamamaktır. Hastalar demografik özellikleri (yaş, cinsiyet), tümör lokalizasyonu, cerrahinin acil ya da elektif olarak yapılması, preoperatif kemoterapi ve radyoterapi uygulanması, açığa geçiş nedenleri açısından değerlendirildi.

Bulgular: Çalışmaya dahil edilen 55 hastanın 35'i erkek (%63,6), 20'si kadın (%36,4) hastaydı. Hastaların yaş ortalaması 58,4 (13,4) (22 – 80) yaştı. Açığa geçilen hastaların yaş ortalaması 62,86 (8,91) (53 – 73) ve laparoskopik tamamlanan hastaların yaş ortalaması 57,71 (13,84) (22 – 80) yaştı (*P*=0,216). Hastaların operasyon nedenleri; 3 sağ kolon kanseri (%5,5), 6 sol kolon kanseri (%10.9), 37 rektum kanseri (%67,3), 5 rektosigmoid bölge tümörü (%9,1) ve 4 familiyal polipozis koli sendromu zemininde gelişen adenokarsinomdu (%7,3). 7 hastada cerrahiye laparoskopik başlandı ancak açık cerrahiye geçilmek zorunda kalındı (%12,7). 47 hasta elektif şartlarda (%85,5) opere edilirken 8 hasta acil şartlarda (%14,5) opere edildi. Açığa geçilen 7 hastanın 5'i acil şartlarda opere olurken 2 hasta elektif şartlarda opere edildi (*P*<0,001). 38 hasta (%69,1) neoadjuvan radyoterapi almamışken (3'ü sadece kemoterapi, 35'i hiçbir neoadjuvan tedavi almadı), 17 hastaya (%39,1) neoadjuvan kemoterapi ve radyoterapi kombinasyonu verilmişti. Açığa geçilen 7 hastadan 1'inde neoadjuvan radyoterapi uygulanmışken, 6'sı neoadjuvan radyoterapi almamıştı (*P*=0,308).

Sonuç: Laparoskopik kolorektal cerrahi, elektif şartlarda konvansiyonel açık cerrahi kadar başarı ile uygulanabilen bir cerrahidir. Preoperatif radyoterapi alınması ile açığa geçiş arasında ilişki yoktur.

Anahtar kelimeler: Rektum kanseri, Kolon kanseri, Laparoskopik cerrahi, Açığa geçiş, Radyoterapi, Acil cerrahi

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Introduction

Colorectal cancers are the most common cancers of the gastrointestinal tract, the third most common malignancy after prostate and lung cancer for men and second leading cancer after breast cancer for women in cancer-related deaths [1-3]. Treatment options include endoscopic or surgical interventions (laparoscopic and conventional surgery), depending on the tumor stage, along with chemotherapy, radiotherapy, and their combinations when necessary. With these additional therapies, local recurrences and distant organ spreads can be controlled [2,4].

With advances in surgical instruments and surgical techniques, laparoscopic surgery has become as feasible as open surgery [5]. Compared to traditional open surgery, laparoscopic surgery has advantages such as decreased surgical trauma and pain, less intraoperative blood loss, decreased postoperative complication and faster recovery [6]. For this reason, it has been proven that it can be safely applied as an alternative surgical treatment in gastrointestinal cancers [5-7]. Although it had a narrower indication in the past, laparoscopic colorectal surgery indications have been expanded today to include not only early stage cancers but also advanced stage cancers, obese patients, and patients with a history of previous laparotomy [7]. However, despite these advantages, the rate of conversion in laparoscopic colectomies can reach up to 41% **[**8**].**

Around 10-28% of the patients are hospitalized with intestinal obstruction due to negligence of clinical symptoms, requiring emergency surgery. However, the morbidity and mortality rates of emergent colorectal surgeries are higher than elective surgeries [2].

In this study, we aimed to evaluate the effects of neoadjuvant chemoradiotherapy (chemoRT) administration and emergent surgery on conversion in laparoscopic colorectal surgery patients.

Materials and methods

This retrospective cohort study was conducted to evaluate the effect of preoperative radiotherapy and emergent surgery on conversion in laparoscopic colorectal surgery patients. The data of 67 patients who were operated by the same surgical team for familial polyposis coli (FAP), colon malignant neoplasia and rectum malignant neoplasia were retrospectively analyzed between October 2016 and January 2018. Patients' data were obtained from patient hospital records, files, and computer records. Exclusion criteria consisted of cases which began as open surgery, benign colorectal pathologies, previous colorectal or abdominal surgeries, morbid obesity (body mass index >40 kg/m^2) and missing data. Fifty-five patients who met the inclusion criteria of the study were included.

Patients were evaluated in terms of demographic characteristics (gender, age), localization of tumor, type of surgery, whether it was an emergent or elective surgery, administration of preoperative chemotherapy and radiotherapy, and reasons for conversion.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) for Windows version 22 statistical software (IBM Corp., Armonk, NY, USA). Kolmogorov-Smirnov or Shapiro Wilk tests were used to determine the normality of the results. Based on the normality of distribution, Chi-square test or Fischer's exact test were used to compare categorical data and independent sample t-test, or Mann Whitney U test were utilized for assessment of numerical results. A multivariate analysis was performed to evaluate the relationship between conversion, neoadjuvant radiotherapy, and emergent surgery. Numerical values were given as mean (standard deviation) or median (minimum – maximum values). Categorical data were given as number (n) and percentage (%). $P<0.05$ value was considered statistically significant.

Results

Among 55 patients included in the study, 35 were males (63.6%) and 20 were females (36.4%), with an overall mean age of 58.4 (13.4) years. The mean ages of male and female patients were 58.63 (13.23) and 57.9 (13.92) years, respectively. The mean age of patients who required conversion to open surgery and of those whose surgeries were finished laparoscopically were 62.86 (8.91) and 57.71 (13.84) years, respectively, with no significant difference ($P=0.216$).

The tumor localization of 14 patients were colon [3 right colon cancers (5.5%), 6 left colon cancers (10.9%), 5 rectosigmoid junction cancers (9.1%)], 37 patients, rectum (67.3%) and 4 patients, adenocarcinoma developing on the basis of familial adenomatosis polyposis syndrome (7.2%). Surgical interventions of patients included 31 laparoscopic low anterior resections (56.4%), 2 laparoscopic intersphincteric rectum resections (3.6%), 4 laparoscopic abdominoperineal resections (7.3%), 2 laparoscopic total colectomies (3.6%), 3 laparoscopic proctocolectomies (5.5%), 3 laparoscopic right hemicolectomies (5.5%), and 3 laparoscopic left hemicolectomies (5.5%). Forty-seven patients were operated electively (85.5%) and 8 patients were operated emergently (14.5%).

In 7 patients, surgery was started laparoscopically, but due to various reasons (intestinal dilatation in 3, iatrogenic jejunum injury in 1, distal rectal injury in 1, peritoneal carcinomatosis in 1 and brids in 1) converted to open surgery (12.7%). Five of the 7 patients were operated under emergent conditions, and 2 patients were operated electively ($r^2=0.38$; $P<0.001$) (Table 1 and Figure 1). Operation under emergent conditions showed a positive correlation with conversion.

While 38 patients (69.1%) had not received neoadjuvant radiotherapy (3 patients received only chemotherapy, 35 patients received no neoadjuvant therapy), 17 patients (39.1%) had received neoadjuvant chemoRT (Figure 2). One of the 7 converted patients had received neoadjuvant chemoRT, and the remaining 6 did not ($P=0,308$; $r^2=0,028$) (Table 2). Administration of preoperative radiotherapy did not correlate with conversion. Median neoadjuvant RT dosage was 5000 (4500 – 5490) centigray (cGy) in the chemoRT group. Selected chemotherapeutetic agent for the chemoRT group was 5–florourasil (5-FU).

Table 1: Demographic values

		Emergent surgery		Total	*P*-value
		Yes	No		
Gender (n %)	Male	5 (9.1%)	30 (54.5%)	35 (63.6%)	0.617
	Female	3 (5.5%)	17 (30.9%)	20 (36.4%)	
Total		8 (14.5%)	43 (84.5%)	55 (100%)	
Age (Years)		61.13 ± 10.64	59.35 ± 12.36		
Localization of tumor (n %)	Colon (Right or left)	3 (5.5%)	11 (20%)	14 (25.5%)	0.473
	Rectum	5 (9.1%)	32 (58.2%)	37 (67.3%)	
	FAP	0 (%0)	4 (7.3%)	5 (7.3%)	
Total		8 (14.5%)	47 (85.5%)	55 (100%)	
Conversion (n %)	Yes	5 (9.1%)	2 (3.6%)	7 (13.7%)	<0.001
	No	3 (5.5%)	45 (81.5%)	44 (86.3%)	
Total		8 (12.7%)	47 (87.3%)	55 (100%)	

FAP: Familial Adenomatous Polyposis

Table 2: Demographic parameters of preoperative chemotherapy and radiotherapy

		Preop ChT and RT			Total	*P*-value
		ChT	ChT + RT	None		
Gender (n %)	Male	3 (5.5%)	9 (16.4%)	23 (41.8%)	35 (63.6%)	
	Female	0 (0%)	8 (14.5%)	12 (21.8%)	20 (36.4%)	0.166
Total		3 (5.5%)	17 (30.9%)	35 (63.6%)	55 (100%)	
Age (years)		61 (51 – 78)	61 (33 – 74)	56 (22 – 80)		
Localization of tumor (n %)	Colon (Right or Left)	0 (0%)	1 (2%)	13 (25.5%)	14 (27.5%)	
	Rectum	3 (5.9%)	16 (31.4%)	18 (35.3%)	37 (72.5%)	0.081
	FAP	0 (0%)	0 (0%)	4 (7.3%)	4(%7.3)	
Total		3 (5.9%)	17 (33.3%)	31 (60.8%)	51 (100%)	
Conversion (n %)	Yes	0 (0%)	1 (1.8%)	6 (10.9%)	7 (12.7%)	
	No	3 (5.5%)	16 (29.1%)	29 (52.7%)	48 (87.3%)	0.308
Total		3 (5.5%)	17 (30.9%)	35 (63.6%)	55 (100%)	

ChT: Chemotherapy, RT: Radiotherapy, FAP: Familial Adenomatosis Coli Syndrome

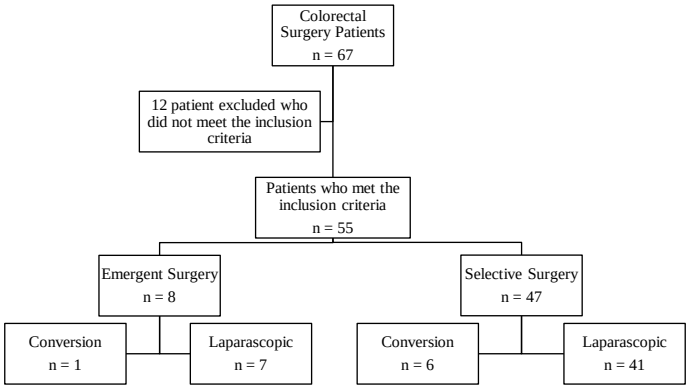

Figure 1: Number of conversion and laparoscopically finished cases due to emergent and selective surgery

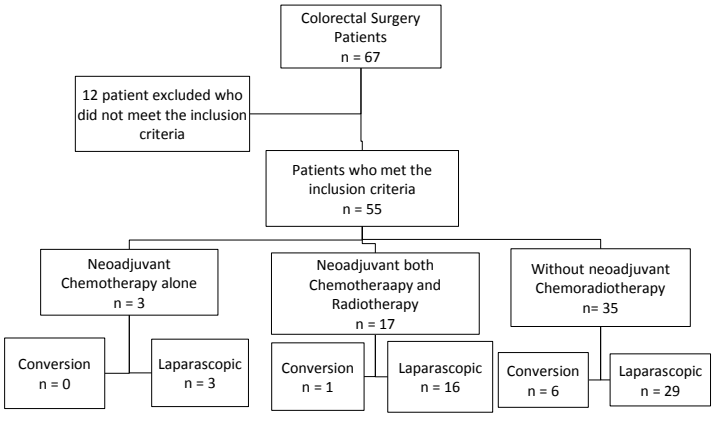

Figure 2: Number of conversion and laparoscopically finished cases due to preoperative radiotherapy application

Discussion

Since it was first described in 1991, the laparoscopic approach in the treatment of benign and malignant colorectal diseases became widely accepted [9]. Compared with open surgery, laparoscopic colorectal surgery is associated with better short-term results such as faster recovery, shorter postoperative ileus times, lower wound infection rates, shorter hospital stay, decreased postoperative pain, and faster enteral feeding [9-13]. Additionally, postoperative adjuvant therapies can be started early [13]. Moreover, no difference was noted between the two methods in terms of overall survival, oncological results, recurrence rates, complication rates, or reoperation rates [13,14].

The term "Conversion" means the termination of the laparoscopic procedure and continuing with a midline incision and should not be considered as a complication of minimally invasive surgeries. Therefore, its etiology and number should be independent from open surgeries [13]. The conversion rates are 7 - 25% in large series and 2 - 41% in smaller series [15-17]. Like the previous results, our conversion rate was 12.7%. Reasons of conversion can be classified as patient-related causes (male gender, obesity, history of abdominal surgery, tumor size and neoadjuvant therapies), surgeon-related factors (surgical experience, technical skills, patient volume), resected surgical area (narrow pelvis, especially in male patients), intraoperative complications (organ injuries, uncontrolled bleeding, anastomotic difficulties) [13, 18-20]. The conversion etiology of our study included intestinal dilatation, iatrogenic injuries (jejunum, distal rectum), abdominal adhesions thought to be related with peritonitis carcinomatosis and chemoRT.

Up to 15% of colon cancer patients present with obstructive symptoms. Acute abdomen can be observed due to abdominal distention or perforation (because of fecal contamination due to colonic perforation). This is related with increased mortality and morbidity rates and decreased oncological success [21]. The relative contraindications of laparoscopic colonic resections include intestinal obstructions, large tumors, tumor invasions to adjacent organs and pregnancy [22]. Due to obstruction, dilated bowel loops cause restriction in the field of view. In addition, tissues are more easily injured due to excessive edema [22]. In our study, conversion rates were significantly higher in emergent cases compared to elective ones. This was due to the lack of vision as a result of dilated loops and resulted with intestinal injuries.

In colorectal cancers, local recurrences have required additional treatment options. RT and CT have been included in the treatment plan in order to provide cure with additional treatment, especially in patients with local recurrence in rectum cancers, to prevent disease recurrence, provide organ-preserving treatment and improve disease-free survival period. RT, initially added as adjuvant therapy, is included in neoadjuvant applications in local advanced stage tumors in current approaches [4]. Although there is no definitive neoadjuvant protocol for colon cancers, preoperative RT alone or with CT (chemoRT) in rectum cancers as a combined treatment (such as according to clinical staging anterior and fairly low T2, T3 tumors according to clinical staging, or T4 tumors according to pelvic magnetic resonance imaging) has become gold standard [23-25]. RT is administered to decrease tumor size or stage for an effective oncological resection. After the use of surgery and chemoRT combinations, survival rates in patients with regional rectal cancer have increased from 45% to 70% since the 1970s [26]. If complete pathological response is obtained in some selected patients, surgery may not even be required after neoadjuvant chemotherapy [24]. However, as a result of these applications, various complications related to chemoRT may occur (such as excessive tissue edema causing loss of surgical

plans, wound separation, surgical site infections, anastomotic leaks, fistulas, proctitis, diarrhea, surgical interventions related with obstructions, anorectal or genitourinary dysfunctions) [24]. Apart from these postoperative effects, it is necessary to evaluate the effects of chemoRT on conversion and intraabdominal adhesions in colorectal surgery. A study conducted by Rezvani et al. on 60 patients with rectum surgery reported that neoadjuvant chemotherapy increased the rate of conversion [27]. In contrast to their findings, in our study, conversion and neoadjuvant chemoRT administration were not related. This led us to believe that administration of neoadjuvant chemoRT has no effect on conversion rates. However, our limited number of patients prevent us from reaching a certain result.

Limitations

The most important limitations of our study are the small number of cases, its retrospective and single center nature, and lack of randomization. Elimination of patients with other risk factors that may be effective on conversion (such as morbid obesity, previous abdominal surgery, surgery for benign colorectal diseases) resulted in both a limited number of patients and high rates of rectum surgery.

Conclusion

Laparoscopic colorectal surgery can be performed as successfully as conventional open surgery under elective conditions. Neoadjuvant chemoRT administration does not affect conversion in laparoscopic colorectal surgery.

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Relationship between blood pressure levels during thrombolytic therapy and functional outcomes in patients with middle cerebral artery infarction

Orta serebral arter enfarktüslü hastalarda trombolitik tedavi sırasındaki kan basıncı düzeyleri ile fonksiyonel sonuçlar arasındaki ilişki

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Abstract

Aim: Previous studies have investigated the relationship between blood pressure (BP) level before and after intravenous (IV) thrombolytic therapy, and functional outcomes of acute ischemic stroke (AIS). However, the relationship between BP level during thrombolytic infusion and functional outcomes has not been well studied. Therefore, in this study, we investigated the relationship between BP levels during thrombolytic therapy and functional outcomes at the 3rd month in AIS patients with middle cerebral artery (MCA) infarction.

Methods: This case-control study was conducted on 60 patients with infarcts in more than 1/3 of MCA. Among these, 20 patients underwent IV thrombolytic therapy after giving informed consent (study group). Forty patients who did not receive thrombolytic therapy were included in the control group. Patients undergoing IV thrombolytic therapy were divided into two groups according to modified Rankin Scale (mRS) at the 3rd month: Those with good functional outcomes (mRS score=0–2) and poor functional outcome (mRS score=3–6).

Results: The poor functional outcome group had a higher mean diastolic BP than the good functional outcome group (P=0.01). Systolic BP was <140 mmHg and diastolic BP was <75 mmHg in the good functional outcome group. A significant, positive, and moderate correlation was found between the mRS score and diastolic BP at the time of admission to the emergency department (r=0.679, P=0.001), immediately before (r=0.580, P=0.007), and during IV thrombolytic therapy (r=0.643, P=0.002).

Conclusion: In AIS patients with MCA infarction, high diastolic BP levels during IV thrombolytic therapy are associated with poor functional outcomes.

Keywords: Acute ischemic stroke, Blood pressure, Intravenous thrombolytic therapy, Middle cerebral artery infarction, Functional outcomes, Modified Rankin scale

Öz

Amaç: Önceki çalışmalar, intravenöz (IV) trombolitik tedavi öncesi ve sonrası kan basıncı (KB) düzeyi ile akut iskemik inme (Aİİ)'nin fonksiyonel sonuçları arasındaki ilişkiyi araştırmıştır. Bununla birlikte, trombolitik infüzyonu sırasındaki KB düzeyi ile fonksiyonel sonuçlar arasındaki ilişki iyi araştırılmamıştır. Bu nedenle, bu çalışmada orta serebral arter (MCA) enfarktüslü Aİİ hastalarında trombolitik tedavi sırasındaki KB düzeyleri ile 3.'üncü aydaki fonksiyonel sonuçlar arasındaki ilişki araştırıldı.

Yöntemler: Bu vaka-kontrol çalışması, MCA'nın 1/3'ünden daha büyük enfarktüsü olan 60 hasta üzerinde gerçekleştirildi. Bunlardan 20'si aydınlatılmış onam alındıktan sonra IV trombolitik tedavi yapılmış hastalardı (çalışma grubu). Trombolitik tedavisi yapılmayan 40 hastada da kontrol grubu olarak alındı. IV trombolitik tedavi yapılan hastalar 3.'üncü aydaki modifiye Rankin Skalasına (mRS) göre iki gruba ayrıldı: iyi fonksiyonel sonuç (mRS skoru=0-2) ve kötü fonksiyonel sonuç (mRS skoru=3-6).

Bulgular: Kötü fonksiyonel sonuç grubu iyi fonksiyonel sonuç grubuna göre daha yüksek ortalama diyastolik KB'ye sahipti (P=0,01). İyi fonksiyonel sonuç grubunda sistolik KB <140 mmHg ve diyastolik KB <75 mmHg idi. Acil servise girişteki (r=0,679; P=0,001), IV trombolitik infüzyonundan hemen önceki (r=0,580; P=0,007) ve infüzyon sırasındaki ortalama diyastolik KB düzeyleri (r=0,643; P=0,002) ile mRS arasında anlamlı, pozitif ve orta düzeyde bir korelasyon vardı.

Sonuç: MCA enfarktüslü Aİİ hastalarında, IV trombolitik tedavi sırasındaki yüksek diyastolik KB düzeyleri kötü fonksiyonel sonuçlarla ilişkilidir.

Anahtar kelimeler: Akut iskemik inme, Kan basıncı, İntravenöz trombolitik tedavi, Orta serebral arter enfarktüsü, Fonksiyonel sonuçlar, Modifiye Rankin skalası

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Introduction

Alteplase, a recombinant tissue plasminogen activator, is used in intravenous (IV) thrombolytic therapy for the treatment of acute ischemic stroke (AIS) [1]. Although there are certain limitations to its use, e.g., blood pressure (BP), and some negative treatment outcomes, it has become important in the treatment of AIS in recent years [2,3]. Regardless of whether mechanical thrombectomy is performed, IV thrombolytic therapy is the first-line treatment that should be administered to patients who meet the treatment criteria [3]. The American Heart Association/American Stroke Association (AHA/ASA) guidelines [3] specify that one of the criteria for commencing IV thrombolytic therapy is a systolic BP of <185 mmHg and diastolic BP of <110 mmHg because BP slightly below these values may negatively affect prognosis. A meta-analysis showed that high pre-thrombolysis systolic BP was associated with worse outcomes in thrombolysed patients with acute ischemic stroke [4]. For ensuring good prognosis in patients undergoing IV thrombolytic therapy, it may be better to maintain BP within the normal limits accepted by international standards during the therapy [5].

Stroke severity, atrial fibrillation, coronary artery disease, diabetes mellitus, pneumonia and advanced age are known to be poor prognostic factors for AIS [6]. However, the relationship between blood pressure and functional outcomes during IV thrombolytic therapy infusion has not been well studied. The aim of the present study was to investigate the relationship between BP levels during IV thrombolytic therapy and functional outcomes in patients who developed an infarct in more than 1/3 of the MCA irrigation area.

Materials and methods

Study population

This retrospective case-control study was conducted on patients with MCA infarction treated at Aksaray University Training and Research Hospital between December 2016 and March 2019. A total of 60 patients with MCA infarction who were clinically eligible for IV thrombolytic therapy [National Institutes of Health Stroke Scale (NIHSS) of ≥5 or presence of aphasia or homonymous hemianopsia] were included in the study. Among these, 20 patients underwent IV thrombolytic therapy after giving informed consent (study group), and 40 patients who did not receive thrombolytic therapy due to contraindications were included in the control group. These patients were treated with non-thrombolytic treatment methods (antiaggregants and/or anticoagulants).

Generally, in the emergency department of our hospital, anamnesis is first obtained from patients presenting with a preliminary diagnosis of stroke or from their relatives. The onset time of symptoms, time of arrival to the emergency department, and time of IV thrombolytic therapy administration are routinely recorded. Vital signs (BP, fever, pulse, and arterial oxygen saturation) are rapidly measured, and blood glucose measurement is performed using a fingerstick. During rapid neurological examination, blood samples are concurrently collected for hemogram, activated partial thromboplastin time (aPTT), international normalized ratio (INR), and biochemical analyses. Brain computed tomography or magnetic resonance imaging is performed for brain parenchymal imaging. In patients with an indication for IV thrombolytic therapy after the diagnosis of AIS, based on neurological examination and brain imaging, and in case of no contraindications, alteplase was intravenously administered at a dose of 0.9 mg/kg (maximum dose: 90 mg/kg; 10% of the total dose via IV bolus and the remaining dose via 1-h infusion) after obtaining informed consent [1,3]. In all patients with AIS, BP measurement, vital signs monitoring, and neurological evaluation are performed before IV thrombolytic therapy, every 15 min during the therapy, every 30 min within 6 h after the therapy, and every 60 min between 6 and 24 h. The modified Rankin Scale (mRS) score and other clinical findings are routinely recorded in our database before discharge and at the 3-month follow-up.

The hospital database was used to obtain information regarding the patients' BP measured at the time of admission to the emergency department, immediately before IV thrombolytic therapy, and every 15 min during the therapy, pre-treatment and 3-month mRS scores, baseline NIHSS scores, symptom-to-door, door-to-needle, and onset-to-needle times, Alberta Stroke Program Early Computed Tomography Score scores, clinical and laboratory findings, risk factors and other demographic characteristics. This information was recorded for statistical analysis. Patients with incomplete data and those aged <18 years were excluded.

The mRS, the most used outcome measure for post-stroke disability rating, is scored from 0 to 6 as follows: 0-No symptoms. 1-No obvious disability, despite the symptoms, the patient can perform daily activities and duties. 2- Mild disability, he cannot do all the usual tasks and activities he did in the past, but he can do his own work without help. 3- Moderate disability, he needs partial help to do his own work, but he can walk on his own without help. 4-Severe disability, unable to walk without help and meet physical needs. 5-Very severe disability, bed-dependent, incontinent, and needing constant care, and attention. 6- It is defined as "death" [7,8]. The functional outcomes of the study patients were evaluated with mRS scores at the 3rd month. Patients undergoing IV thrombolytic therapy were divided into two groups according to their 3-month mRS score: Good functional outcome (mRS score: 0–2) and poor functional outcome (mRS score: 3–6) [9,10].

The study was approved by the Aksaray University Human Research Ethics Committee (4/24/2020, 2020/03-66) and conducted in compliance with the Declaration of Helsinki.

Statistical analysis

The normality of continuous variables was investigated using the Shapiro–Wilk test. Descriptive statistics are expressed as mean, standard deviation, median, and minimum-maximum. Non-parametric statistical methods were used for values with skewed distribution. Mann–Whitney U-test was used for the comparison of two non-normally distributed independent groups. Fisher's exact test was used for categorical variables, and the results are expressed as count (and percentages). A two-sided *P*-value <0.05 was considered statistically significant. Spearman's rho correlation coefficient was used to investigate the relationship among non-normally distributed parameters. Statistical analysis was performed using the MedCalc Statistical

Software (version 12.7.7; MedCalc Software bvba; Ostend, Belgium; http://www.medcalc.org; 2013).

Results

As shown in Table 1, the mean age of the study and control group were 62.8 and 75.1 years, respectively. A significant difference was observed between these two groups in terms of age and baseline NIHSS scores (P=0.003), with the mean age being higher and baseline NIHSS score being lower in the control group. There were no significant differences between these groups in terms of hypertension (P=0.481), diabetes mellitus (P=0.560), hyperlipidemia (P=0.136), atrial fibrillation (P=0.154), coronary artery disease (P=0.753), congestive heart failure (P=0.165), heart valve disease (P=1.000), stroke and transient ischemic attack history (P=0.707) and gender (P =1.000). Among the patients clinically eligible for IV thrombolytic therapy (n=60), 33.33% were treated with alteplase infusion (n=20) and 66.7% were not (Table 1).

Table 2 shows the comparison of BP between the good and poor functional outcome groups. A significant difference was found between the groups in terms of diastolic BP at the time of admission to the emergency department, immediately before IV thrombolytic therapy, and at the 15th, 30th, 45th and 60th minutes during the therapy (P=0.025, P=0.047, P=0.039, P=0.004, P=0.005 and P=0.002, respectively). The mean diastolic BP was higher (P=0.01) in the poor functional outcome group (85.92 mmHg) than in the good functional outcome group (71.43 mmHg). Similarly, the mean systolic BP was higher in the poor functional outcome group than in the good functional outcome group (152 mmHg and 136.98 mmHg, respectively), although this difference was not statistically significant (P=0.181) (Table 2).

In Table 3, univariate analysis was performed with age, gender, stroke subtype, obstructed artery, and recanalization variables. Since there was no statistically significant difference in univariate analysis, multivariate analysis was not performed.

Table 1: Comparison of clinical characteristics and risk factors of the study and control groups

Characteristics		Study group n	Study group %	Control group n	Control group %	P-value
Sample size	60	20	33.3	40	66.7	
Gender	Male	9	45.0	18	45.0	1.000
	Female	11	55.0	22	55.0	
HT	Yes	15	75.0	34	85.0	0.481
	No	5	25.0	6	15.0	
DM	Yes	5	25.0	14	35.0	0.560
	No	15	75.0	26	65.0	
Hyperlipidemia	Yes	3	15.0	14	35.0	0.136
	No	17	85.0	26	65.0	
AF	Yes	4	20.0	16	40.0	0.154
	No	16	80.0	24	60.0	
CAD	Yes	4	20.0	11	27.5	0.753
	No	16	80.0	29	72.5	
CHF	Yes	0	0.0	6	15.0	0.165
	No	20	100.0	34	85.0	
Heart valve disease	Yes	1	5.0	2	5.0	1.000
	No	19	95.0	38	95.0	
Atrial thrombus	Yes	0	0.0	0	0.0	-
	No	20	100.0	40	100.0	
Stroke or TIA history	Yes	2	10.0	6	15.0	0.707
	No	18	90.0	34	85.0	
Functional outcome	Good functional outcome (mRS:0-2)	8	40.0	12	30	0.268
	Poor functional outcome (mRS:3-6)	12	60.0	28	70	-
		Mean (SD)		Mean (SD)		P-value
Age, years		62.8 (16.4)		75.1 (10.2)		0.003
Basal NIHSS		12.3 (4.6)		9.3 (5.8)		0.003

HT: Hypertension, DM: Diabetes mellitus, AF: Atrial fibrillation, CAD: Coronary artery disease, CHF: Congestive heart failure, TIA: Transient ischemic attack, mRS: modified Rankin Scale, NIHSS: National Institutes of Health Stroke Scale, SD: Standard deviation

Table 2: Comparison of blood pressures of patients grouped according to functional outcome

	Good functional outcome Mean (SD)	Poor functional outcome Mean (SD)	P-value
Systolic BP at first admission	140.63 (27.18)	155.25 (17.73)	0.181
Diastolic BP at first admission	71.63 (14.37)	86.08 (9.37)	0.025
Systolic BP level just before infusion	137.38 (25.4)	151.08 (15.44)	0.208
Diastolic BP level just before infusion	71.88 (13.28)	84.58 (7.14)	0.047
Systolic BP at 15th minute of infusion	136 (25.86)	152.17 (10.03)	0.057
Diastolic BP at 15th minute of infusion	72.13 (17.85)	85.83 (8.53)	0.039
Systolic BP at the 30th minute of infusion	135.13 (25.01)	152.92 (13.37)	0.082
Diastolic BP at the 30th minute of infusion	69.5 (14.51)	88.17 (7.99)	0.004
Systolic BP at the 45th minute of infusion	138.63 (24.31)	150.5 (11.47)	0.238
Diastolic BP at the 45th minute of infusion	72 (10.06)	85.83 (8.07)	0.005
Systolic BP at the 60th minute of infusion	137.75 (20.25)	153.33 (16.1)	0.115
Diastolic BP at the 60th minute of infusion	71.63 (8.6)	85.17 (7.9)	0.002
Mean systolic BP level during infusion	136.98 (22.57)	152 (11.95)	0.181
Mean diastolic BP level during infusion	71.43 (11.29)	85.92 (6.86)	0.010

BP: Blood pressure, SD: Standard deviation, mRS: modified Rankin Scale

Table 3: Univariate analysis of parameters that may affect functional outcome

		Good functional outcome	Poor functional outcome	P-value
Age, mean (SD)		60.8 (16.8)	64.3 (16.7)	0.792
Gender, n (%)	Male	4 (50.0)	7 (58.3)	0.714
	Female	4 (50.0)	5 (41.7)	
Subtype of Stroke, n (%)				0.652
	Great artery atherosclerosis	2 (25.0)	4 (33.3)	
	Cardioembolic	2 (25.0)	3 (25.0)	
	Cryptogenic	3 (37.5)	5 (41.7)	
	Other	1 (12.5)	0	
	Lacunar syndromes	-	-	
Occluded vessel, n (%)				0.106
	M1 segment of the MCA	0	5 (41.7)	
	M2 segment of the MCA	5 (62.5)	4 (33.3)	
	M3 segment of the MCA	3 (37.5)	3 (25.0)	
Recanalization, n (%)				0.101
	Present	5 (62.5)	2 (16.7)	
	Absent	3 (37.5)	10 (83.3)	

SD: standard deviation, MCA: Middle cerebral artery

There was a significant, positive, and moderate correlation between the 3-month mRS score and diastolic BP at the time of admission to the emergency department and immediately before and during IV thrombolytic therapy (r=0.679, P=0.001; r=0.580, P=0.007; r=0.643, P=0.002, respectively) (Figure 1). Further, there was a significant, positive, and moderate correlation between systolic BP at the time of admission to the emergency department and 3-month mRS score (r=0.471, P=0.036; Figure 1). However, there was no correlation between systolic BP immediately before and during IV thrombolytic therapy and 3-month mRS score (P=0.104 and P=0.107) (Table 4). Figure 2 shows the course of BP during infusion in patients with good and poor functional outcomes.

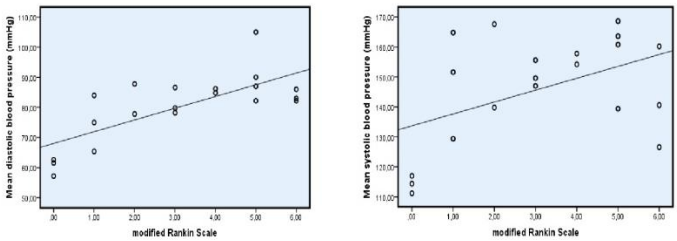

Figure 1: Correlation of mean diastolic blood pressure (r=0.643; P=0.002) and mean systolic blood pressure (r=0.372; P=0.107) during IV thrombolytic infusion with modified Rankin Scale score in the 3rd month

Table 4: Correlation analysis showing the relationship between blood pressure values during infusion and the modified Rankin Scale 3 months after intravenous thrombolytic therapy

		mRS after 3 months
Systolic BP level just before infusion	r	0.374
	P	0.104
Diastolic BP level just before infusion	r	0.580
	P	0.007
Systolic BP at 15th minute of infusion	r	0.431
	P	0.058
Diastolic BP at 15th minute of infusion	r	0.612
	P	0.004
Systolic BP at the 30th minute of infusion	r	0.312
	P	0.180
Diastolic BP at the 30th minute of infusion	r	0.565
	P	0.010
Systolic BP at the 45th minute of infusion	r	0.354
	P	0.126
Diastolic BP at the 45th minute of infusion	r	0.636
	P	0.003
Systolic BP at the 60th minute of infusion	r	0.425
	P	0.062
Diastolic BP at the 60th minute of infusion	r	0.661
	P	0.001
Mean systolic BP level during infusion	r	0.372
	P	0.107
Mean diastolic BP level during infusion	r	0.643
	P	0.002
Systolic BP at first admission	r	0.471
	P	0.036
Diastolic BP at first admission	r	0.679
	P	0.001

Spearman's rho correlation, BP: Blood pressure, mRS: modified Rankin Scale

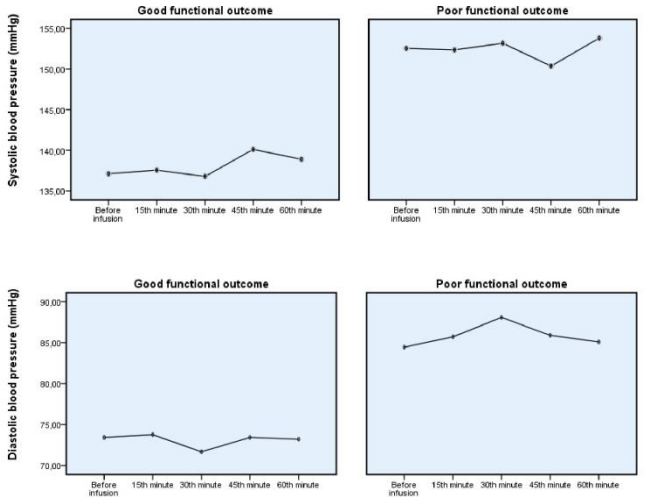

Figure 2: The course of blood pressure during infusion in patients with good and poor functional outcome

Discussion

In this study, a positive correlation was found between diastolic BP of patients undergoing IV thrombolytic therapy at the time of admission to the emergency department and immediately before and during the therapy with the 3-month mRS score and between systolic BP at the time of admission to the emergency department with the 3-month mRS score. In addition, systolic BP immediately before and during IV thrombolytic therapy was found to be insignificantly high in patients with a high mRS score. The insignificance of the difference was attributed to the small sample size. Systolic BP was <140 mmHg and diastolic BP was <75 mmHg in the good functional outcome group.

This study consists of population of patients with large MCA infarction. Patients with large subcortical and cortical infarcts due to large vessel occlusion have a lower efficacy of IV thrombolytic therapy and a higher risk of symptomatic intracerebral hemorrhage (sICH), thereby resulting in poorer therapy outcome [10]. sICH increases mortality rate and is the most feared complication of IV thrombolytic therapy [11,12]. It occurs within the initial 24 h after IV thrombolytic therapy, particularly within the initial 12 h, and tends to be fatal [11]. It is known that high BP increases the risk of sICH [12]. Although the results of the present study demonstrated that maintaining BP within the normal limit during IV thrombolytic therapy is associated with good functional outcome, the optimal BP limits remain to be identified. Nevertheless, maintaining BP within the normal limit or close to the upper limit during IV thrombolytic therapy may prove to be safe in patients with large MCA infarction. AHA/ASA guidelines [3] state that IV thrombolytic therapy can be administered if systolic and diastolic BP are <185 and <110 mmHg, respectively. However, a previous study found that IV thrombolytic therapy resulted in sICH in 25% of their patients with a systolic BP of 165 mmHg [12]. In another study, it was shown that even in cases without sICH, the results obtained at the 3rd month following IV thrombolytic therapy were negatively affected by elevated BP [13]. In their study, Liu et al. [14] found that systolic BP variability within 6 h after IV thrombolytic therapy was positively associated with sICH. In the ENCHANTED study conducted in 2019, although intensive blood pressure reduction was found to be safe due to the decrease in intracranial hemorrhage, it did not lead to better clinical results compared to guideline therapy [15]. This may be different for large vessel infarctions. The present study showed that diastolic BP levels being close to the normal limit during IV thrombolytic therapy, as indicated in clinical practice guidelines [5], results in a good prognosis, whereas higher diastolic BP results in a poor prognosis. Future studies should determine the optimal BP limit that should be maintained during and after IV thrombolytic therapy.

Almost 50% of the patients that undergo IV thrombolytic therapy tend to have good functional outcome at the end of the 3rd month following treatment [16]. In the present study, 40% of the patients had good functional results after the 3rd month following treatment. There may be two reasons for the low rate of patients with good functional outcome, i.e., all patients who underwent IV thrombolytic therapy had large infarcts due to large vessel occlusion and small sample size, which may have affected the results.

In this study, only 33.33% of the patients who were clinically eligible for IV thrombolytic therapy were treated with alteplase therapy after all contraindications were excluded. In other words, 66.67% of the patients who could possibly undergo IV thrombolytic therapy were unable to do so due to various contraindications. In their study, Hess et al. [17] found that the most common reason for not administering IV thrombolytic treatment in rural communities is that the onset-to-needle time exceeds the therapeutic time limit. The California Acute Stroke Pilot Registry study also found that the most common reason that prevented the administration of IV thrombolytic therapy was pre-hospital delay [18]. A low level of awareness about stroke and IV thrombolytic therapy in the general population is thought to play a significant role in this delay [19]. The number of patients who can benefit from IV thrombolytic therapy can be increased through efforts aimed at increasing public awareness about stroke (including the effective use of media) and by government health policies, raising awareness among physicians, and training of first aid and emergency unit personnel.

Limitations

Although we believe that this study will make an important contribution to the existing literature, there are still certain limitations to this study. The most important limitation is the small sample size. Another limitation is its retrospective nature.

Conclusion

It was concluded that there is a possible relationship between diastolic BP level during IV thrombolytic therapy and functional outcomes in patients with large MCA infarction. Further studies are needed to determine the optimal BP limits during IV thrombolytic therapy in patients with AIS.

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Urinary incontinence frequency, type, severity, and risk factors in female patients undergoing physical rehabilitation: A single center experience

Fizik tedavi uygulanan kadın hastalarda idrar kaçırma sıklığı, türü, şiddeti ve risk faktörleri: Tek merkez deneyimi

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Ethics Committee Approval: Ethics committee approval was not received due to the retrospective design of the study. All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.
Etik Kurul Onayı: Etik kurul onayı çalışmanın retrospektif dizaynından dolayı alınmamıştır. İnsan katılımcıların katıldığı çalışmalardaki tüm prosedürler, 1964 Helsinki Deklarasyonu ve daha sonra yapılan değişiklikler uyarınca gerçekleştirilmiştir.

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Abstract

Aim: Urinary incontinence (UI) is a health problem with important psychological, hygienic, and socio-economic consequences. The aim of this study is to determine the frequency, severity, and risk factors of urinary incontinence in women.

Methods: In this retrospective cohort study, we evaluated the frequency and risk factors of UI in 62 women over the age of 18 who were referred to the Physical Medicine and Rehabilitation outpatient clinic between August 2019 and February 2020. The data, socio-demographic characteristics of the patients and the results of the Urogenital Distress Inventory-6 (UDI-6) were analyzed.

Results: The mean age of 62 patients included in the study was 57.2 (15.4) years, with the mean duration of symptoms of 7.6 (4.82) years. Stress UI, urge UI and mixed UI were present in 28 (45.2%), 13 (20.9%), and 21 (33.9%) patients, respectively. UI was detected more frequently in patients over 40 years of age (30.6%) than in patients between the ages of 18 and 40 (69.4%) years, in those who gave birth at least once (80.7%) compared to those who had never given birth (19.3%), and in patients with Body Mass Index (BMI) values over 25 kg/m2 than in patients with BMIs between 18.5-25.0 kg/m2 (72.5% vs. 22.5%, respectively).

Conclusion: UI is an important health problem which negatively affects the quality of life of many women. Various socio-demographic and medical factors affect the frequency of urinary incontinence. Therefore, especially the elderly patient group should be informed of the treatability of this condition and be directed to a physician.

Keywords: Urinary incontinence, Frequency, Female

Öz

Amaç: Üriner inkontinans (Üİ), önemli psikolojik, hijyenik ve sosyo-ekonomik etkileri olan bir sağlık sorunudur. Bu çalışmanın amacı kadınlarda idrar kaçırma sıklığı, ciddiyeti ve risk faktörlerini belirlemektir.

Yöntemler: Bu retrospektif kohort çalışmada, Ağustos 2019 ve Şubat 2020 arasında Fiziksel Tıp ve Rehabilitasyon polikliniğine başvuran 18 yaş üstü 62 kadında Üİ sıklığı ve risk faktörlerini değerlendirdik. Polikliniğe başvuran hastaların verileri, sosyodemografik özellikleri ve Ürogenital Sıkıntı Envanteri-6 (UDI-6) sonuçları geriye dönük olarak incelendi.

Bulgular: Çalışmaya dahil edilen 62 hastanın yaş ortalaması 57,2 (15,4) yıl, ortalama semptom süresi 7,6 (4,82) yıl idi. 28 hastada (%45,2) stres tip Üİ, 13 hastada (%20,9) sıkışma tip Üİ ve 21 hastada (%33,9) karışık tip Üİ vardı. Uİ, 40 yaş üstü hastalarda (%30,6), 18-40 yaş arası (%69,4) hastalara göre daha sık saptandı. Uİ insidansı bir veya daha fazla doğum yapan hastalarda (%80.7) hiç doğum yapmayan hastalara göre (%19,3) daha yüksekti. Uİ, vücut kitle indeksi (VKİ) 25'in üzerinde olan hastalarda VKİ 18,5-25,0 arasında olanlara göre daha yüksekti (sırasıyla; %72,5'e karşılık %22,5).

Sonuç: İdrar kaçırma pek çok kadının yasam kalitesini hafif-orta derecede olumsuz olarak etkileyen önemli bir sağlık problemidir. Çeşitli sosyo-demografik ve tıbbi faktörler üriner inkontinans sıklığını etkilemektedir. Bu nedenle, özellikle yaşlı hasta grubu bu sorunun tedavi edilebilir bir durum olduğu konusunda bilgilendirilmeli ve bir doktora yönlendirilmelidir.

Anahtar kelimeler: Üriner inkontinans, Sıklık, Kadın

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Introduction

Urinary incontinence (UI) is defined by the International Continence Society (ICS) as an involuntary urinary incontinence that can be demonstrated objectively, resulting from lower urinary system dysfunction, causing social and hygienic problems [1].

UI cases can be classified in various forms according to pathophysiological and etiological features. Stress urinary incontinence (SUI) is involuntary urine loss during activities that increase intra-abdominal pressure (laugh, cough, sneeze, exercise, etc.). SUI is generally caused by insufficient urethral functions [2]. A patient with urge incontinence (UUI), which occurs due to the excessive activity of the bladder muscles, is incontinent before he/she reaches the toilet [3]. The coexistence of stress incontinence urge incontinence is called mixed type urinary incontinence (MUI) [4]. Other types of UI are enuresis nocturna, UI that occurs after a person falls asleep, and continuous urinary incontinence [5].

It has been reported that the prevalence of urinary incontinence in women increases with age until the age of 65, and the prevalence varies between 12% and 53% [6].

Risk factors associated with urinary incontinence are age, gender, race, smoking, birth, sex hormones, menopause, drugs, family history, previous pelvic surgery, pelvic prolapse, obesity and chronic constipation [7].

Urinary incontinence is an important health problem that is frequently seen in the female patient group but underestimated by patients and not adequately questioned by doctors. For this purpose, we planned this study to determine the prevalence and risk factors of UI in women aged 18 years and older who were referred to our Physical Medicine and Rehabilitation outpatient clinic.

Materials and methods

We evaluated the frequency and risk factors of UI in women over the age of 18 years who were referred to the Physical Medicine and Rehabilitation outpatient clinic between August 2019 and February 2020.

The data, socio-demographic characteristics of 62 patients and the results of the Urogenital Distress Inventory-6 (UDI-6) that we filled out during routine practice in case of UI were analyzed retrospectively.

Patients under the age of 18 years, those who had undergone medical or surgical treatment for UI, spinal cord injury, cerebrovascular accident, multiple sclerosis, patients with neurogenic bladder diseases and patients with infection were excluded from the study.

Patients with urinary incontinence were considered SUI if it occurred during events that caused increased intra-abdominal pressure, such as laughing, straining, coughing, and sneezing. Patients who wet their laundry until they reached the toilet after feeling the urge to urinate were considered UUI. Those with both stress type and urge type urinary incontinence were considered to have MUI.

UDI-6 is a popular inquiry form used to assess the presence and degree of distress of lower urinary tract symptoms [8]. It consists of 6 questions regarding frequent urination, urge-type incontinence, stress incontinence, drip-style incontinence, difficulty urinating and dysuria, respectively. Turkish validity and reliability have been shown [9].

All procedures in the studies involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Statistical analysis

The data was analyzed with IBM SPSS Statistics 22.0 (IBM Corporation, Armonk, NY, USA) package program. Continuous variables were presented as mean (standard deviation) (SD) and categorical data, as number and percentages.

Results

All demographic and clinical data of the patients are presented in Table 1. The mean age of 62 patients included in the study was 57.2 (15.4) years and the mean duration of symptoms was 7.6 (4.82) years. Among all, 11 patients (17.7%) had hypertension (HT), 7 patients (11.2%) had Diabetes Mellitus (DM), 3 patients (4.8%) had asthma-chronic obstructive pulmonary disease (COPD), and 2 patients (3.2%) had coronary artery disease (CAD). Twelve (19.3%) of the patients had abdominal surgery, 4 (6.4%) had Total Abdominal Hysterectomy (TAH) + Bilateral Salpingo-opherectomy (BSO). Thirty-seven patients (59.7%) were primary school graduates. SUI was present in 28 (45.2%), UUI in 13 (20.9%) and MUI in 21 (33.9%) patients.

UI was detected more frequently in patients over 40 years of age (30.6%) than in patients between the ages of 18 and 40 (69.4%) years, in those who gave birth at least once (80.7%) compared to those who had never given birth (19.3%), and in patients with Body Mass Index (BMI) values over 25 kg/m^2 than in patients with BMIs between 18.5-25.0 kg/m^2 (72.5% vs. 22.5%, respectively) (Table 2).

Table 1: Patient demographic and clinical characteristics

Variables	Value
Patients, n	62
Mean (SD) age, years	57.2 (15.4)
Mean (SD) duration of symptoms, years	7.6 (4.82)
Education, n (%)	
Primary education	38 (61.2%)
High school	20 (32.3%)
University	4 (6.5%)
Comorbidity, n (%)	
Hypertension	11 (17.7%)
Diabetes mellitus	7 (11.2%)
Chronic obstructive pulmonary disease	3 (4.8%)
Coronary artery disease	2 (3.2%)
Previous surgery	
Abdominal surgery	12 (19.3%)
Hysterectomy	4 (6.4%)
Urinary incontinence type, n (%)	
Stress	28 (45.2%)
Urge	13 (20.9%)
Mixed	21 (33.9%)

n: Number, SD: Standard deviation

Table 2: Risk factors according to urinary incontinence type

Variables		Stress, n (%)	Urge, n (%)	Mixed, n (%)
Age, years	18-40	8 (12.8%)	6 (9.7%)	5 (8.1%)
	≥40	20 (32.4%)	7 (11.2%)	16 (25.8%)
Number of births	0	5 (8.1%)	3 (4.8%)	4 (6.4%)
	≥ 1	23 (37.1%)	10 (16.1%)	17 (27.5%)
BMI	18.5-25.0	6 (9.7%)	5 (8.1%)	6 (9.7%)
	≥ 25	22 (35.5%)	8 (12.8%)	15 (24.2%)
Previous surgery	Yes	9 (14.5%)	5 (8.1%)	6 (9.7%)
	No	19 (30.7%)	8 (12.8%)	15 (24.2%)
Education	Primary education	18 (29.1%)	8 (12.8%)	11 (17.8%)
	High school	8 (12.8%)	4 (6.4%)	8 (12.8%)
	University	2 (3.3%)	1(1.7%)	2 (3.3%)
Total, n (%)		28 (45.2%)	13 (20.9%)	21(33.9%)

n: Number, BMI: Body Mass Index

Discussion

UI is a health problem with significant psychological, hygienic, and socio-economic consequences on both the patients and their families. Urinary incontinence decreases the quality of life of the person and imposes significant socio-economic burdens on public health [10].

In the literature, the rate of urinary incontinence in women varies over a wide range. In a meta-analysis involving forty-eight epidemiological studies, the prevalence of UI in women was reported between 12% and 53% [6]. In a more recent review in which UI prevalence studies in Europe were evaluated, rates varying from 16.1% to 68.8% were reported in women, with increasing rates in the elderly. In this study, pregnancy, birth age ≥ 35, obesity, familial urinary incontinence history and increased parity were shown as risk factors [11]. There are also differences in studies evaluating the incontinence subtype. While in some studies SUI was identified as the leading incontinence form [12,13], in others, MUI was the most common type identified in women [14,15]. These variable results obtained in urine incontinence researches are related to the differences in the definition of urinary incontinence, inquiry forms, and data collection methods, along with the heterogeneity of the age groups studied.

In a meta-analysis involving epidemiological studies, UI prevalence rates in Turkish women were reported between 20.5% and 68.8%. In these studies, the prevalence of SUI, UUI, and MUI ranged from 15% to 42.3%, 9.8% to 32.3%, 10.3% to 70.1%, respectively [16]. A recent cross-sectional study evaluating the UI prevalence rates in Turkish women stated that it ranged between 16.4%- 49.7%, which was parallel to the literature. MUI ranged from 7.8% - 64%, UUI 2.9% - 43% and SUI rates ranged from 20.8% to 68%. In this meta-analysis, SUI was reported most frequently, which was followed by MUI, and UUI was the rarest [17]. In our study, the most common subtype was SUI (45.2%), followed by MUI (33.9%). UUI (20.9%) was less frequent. All these findings were consistent with previous studies.

The incidence of UI increases with age. In their meta-analysis examining 17 epidemiological studies, Milsom [18] reported that prevalence increased proportionally with age. Hunskaar et al. [5] stated that the prevalence of UI peaked especially in the fifth (30%), eighth (35%) and ninth (90%) decades of life. In our study, the incidence of UI was higher ≥ 40 years of age, which was consistent with the literature.

Numerous obstetric risk factors also play a key role in the development of urinary incontinence, such as mode of delivery, multiple pregnancy, and large baby birth. In their study, Thom et al. [19] reported a linear relationship between the number of births and UI. According to their results, an increase in UI was observed in women who gave birth four or more times. Victurp et al. [20] determined that there was a significant relationship between episiotomy during vaginal delivery and SUI developing in the early period. In our study, we found that while the frequency of UI was 19.3% in patients who had never given birth, it was 80.7% in patients who had given birth at once or more.

Obesity constitutes a major public health challenge because of its comorbidities [21]. The increase in BMI can cause an increase in the severity of urinary incontinence. Bump et al. [22] showed that the risk of UI increased by 3.29 times in those with a BMI of 40 kg/m^2 or above. Dwyer et al. [23] stated that SUI was higher in people with higher BMIs. Similar to this study, we found that the incidence of UI was higher in patients with BMI≥25 kg/m^2.

It was reported that damage to pelvic facial support and pelvic floor muscles occurring during gynecological surgeries may pose a risk of urinary incontinence [24]. In our study, the incidence of UI was higher in patients who had previous surgeries, such as an abdominal surgery and hysterectomy.

In the study of Ozerdoğan et al. [25], the incidence of UI was higher in women with low levels of education. We found that there was a low incidence of UI in high school or university graduates. We think that this significant difference is due to the lower number of births in women with higher education levels.

Limitations

This study has various limitations, the major one being its retrospective nature. Other limitations are the relatively low number of patients, and its single centered design.

In this study, we showed the frequency, type, and risk factors of UI. We found that the findings were consistent with the literature. This article will lead future, multicenter prospective studies with more patients.

Conclusion

UI is a widespread problem affecting women's social lives. The feeling of shame in women, the fact that urinary incontinence is a natural result of aging and them being unaware of the available treatment options delay its treatment. For this reason, women with UI should be encouraged to apply to the physician and informed about the treatability of this condition.

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Eight-year experiences in penetrating cardiac injury: A multi-center retrospective cohort study

Penetran kalp yaralanmalarında sekiz yıllık tecrübelerimiz: Çok merkezli retrospektif kohort çalışma

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Abstract

Aim: Penetrating cardiac injuries (PCI) are mostly caused by sharp objects and comprise pericardial and myocardial deformation, which lead to myocardial dysfunction. Fifty percent of overall mortality in penetrating chest injuries are caused by PCIs. The aim of this study is to evaluate the results of patients who underwent cardiac surgery due to PCIs.

Methods: In this retrospective cohort study, twenty-seven cases undergoing cardiac surgery due to PCI in Van Yuzuncu Yil University Hospital, Yozgat City Hospital and Bozok University Hospital between 2012 and 2019 were evaluated in terms of clinical findings, treatment methods and surgical techniques.

Results: There were 3 females and 24 males. The mean age was 34.2 (13.2) years (range: 14-65 years) years. Firearms caused two and penetrating stab wounds caused twenty-five injuries, respectively. The patients were transported to the hospital within a mean time of 29.7 (14.6) minutes (range: 15-98 minutes). 29 injuries were observed in 27 patients, 18 (62.06%) of which were isolated cardiac injuries, and 11 (37.94%) were mixed type. Fourteen patients (51.8%) were operated following a transthoracic echocardiography, 12 patients (44.5%) due to clinical findings and one patient (3.7%) due to the contrast-enhanced thoracic computed tomography (TCT) result. The mean pericardial blood volume was 290 mL (range 140-460 mL) in patients with a cardiac tamponade. The most frequently injured cardiac section was the right ventricle, followed by the left ventricle. Coronary artery injuries were observed in two patients. Overall mortality rate was 44%.

Conclusion: Early diagnosis, fast and safe transport, providing qualified surgical equipment, and a multidisciplinary approach are mandatory to decrease mortality and morbidity rates. It is also crucially important to prevent individual armament in preventing penetrating cardiac surgery cases.

Keywords: Penetrating cardiac injury, Mortality

Öz

Amaç: Penetran kalp yaralanmaları (PKY) sıklıkla kesici-delici alet yaralanmaları sonucu gelişir ve perikard ile miyokard hasarına sebep olarak miyokardial disfonksiyona yol açar. Penetran göğüs yaralanmalarında görülen mortalite oranının %50'den fazlasından PKY sorumludur. Bu çalışmanın amacı PKY sebebiyle kalp cerrahisi uygulanan hastaların sonuçlarını değerlendirmektir.

Yöntemler: Bu çalışma retrospektif kohort çalışması olarak tasarlanmıştır. Van Yüzüncü Yıl Üniversitesi Hastanesi, Yozgat Şehir Hastanesi ve Bozok Üniversitesi Hastanesinde 2012 ve 2019 yılları arasında PKY sebebiyle kalp cerrahisi uygulanan 27 hasta klinik bulguları, tedavi ve cerrahi teknikleri açısından retrospektif olarak değerlendirilmiştir.

Bulgular: Hastaların 24'ü erkek 3'ü kadın, 24'ü erkek idi. Yaş ortalaması 34,2 (13,2) (14 ila 65 yaş aralığında) idi. İki vakada ateşli silah yaralanması, 25 vakada kesici delici alet yaralanması mevcuttu. Hastaneye olay yerinden intikal süresi 29,7 (14,6) (15 ila 98 dakika aralığında) dakikaydı. 27 hastada 29 kardiyak yaralanma mevcuttu. Bu vakaların 18'inde (%62,06) izole kalp yaralanması, ve 11'inde (%37,94) birden fazla yaralanma mevcuttu. İki hastada koroner arter yaralanması vardı. On dört hasta (%51,8) transtorasik ekokardiyografi, 12'si (%44,5) klinik bulgular ve bir hasta (%3,7) kontrastlı toraks tomografisi sonrası operasyona alındı. Tamponat kliniği veren vakalarda perikardiyal kan hacmi ortalama 290 ml (140-460 ml aralığında) idi. En sık yaralanan kalp bölgesi sağ ventrikül idi ve ikinci sırada sol ventrikül gelmekteydi. İki hastada koroner arter yaralanması tespit edildi. Genel mortalite oranı %44 olarak tespit edildi.

Sonuç: Mortalite ve morbiditenin azaltılmasında olay yerinden başlayarak erken tanı, doğru ve hızlı transport, deneyimli cerrahi travma ekipleri ile multidisipliner yaklaşım faydalı olacaktır. PKY'de hayatta kalmayı artırmamız için sağlık hizmetlerinin geliştirilmesinin yanı sıra bireysel silahlanmanın önlenmesine özellikle dikkat çekmek isteriz.

Anahtar kelimeler: Penetran kalp yaralanmaları, Mortalite

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Introduction

Penetrating cardiac injuries (PCI) are mostly caused by sharp objects and comprise deformation of pericardium and myocardium, which lead to myocardial dysfunction. PCI is life-threatening due to bleeding, cardiac tamponade, coronary arterial and valvular injuries. Fifty percent of the overall mortality rate of penetrating chest injuries are caused by PCIs. Clinical presentation may range from a stable condition to cardiac arrest [1,2]. Hemodynamic stability strongly depends on the kind and volume of trauma, time of transportation to the hospital, intravascular volume loss, and the occurrence of cardiac tamponade [3].

In this multicenter study, we evaluated 27 patients undergoing cardiac surgery due to PCI in terms of associated traumas, the means of the trauma, operational techniques, clinical outcomes, and results.

Materials and methods

Study design and patient population

This retrospective cohort study was conducted in Van Yuzuncu Yil University Hospital, Yozgat City Hospital and Bozok University Hospital, in accordance with the standards defined by the Declaration of Helsinki. Twenty-seven cases undergoing cardiac surgery due to penetrating cardiac injury between 2012 and 2019 were evaluated. Patients with hemodynamic instability underwent emergent surgery without preoperative tests. Hemodynamically stable patients underwent electrocardiography (ECG), transthoracic echocardiography (TTE), chest radiography, and thoracic computerized tomography. Pericardiocentesis was not performed to any patient for diagnosis or treatment. Thoracotomy, sternotomy, or both were performed in some cases. Cardiac tamponade was relieved, hemorrhage was controlled, and traumatic section was repaired. Two patients required coronary artery bypass grafting due to coronary arterial injuries. 3-0 and 5-0 pledged prolene sutures were preferred in ventricular and atrial injuries, respectively. The injuries around the coronary arteries were repaired by longitudinal sutures crossing under the coronary artery. A pericardial window was formed to allow pericardial drainage through the pleural cavity. Before discharge and at the end of the 2nd postoperative month, all patients underwent TTE.

Exclusion criteria

Poisoning and toxicity cases, patients with submersion injuries, strangulation, asphyxiation, anoxic brain death and electrocution cases were excluded.

Statistical analysis

Statistical analysis was conducted with the SPSS for Windows software package (ver. 17; SPSS Inc., Chicago, IL, USA). All variables were evaluated using visual (histograms, probability plots) and analytical (Kolmogorov Smirnov test) methods to determine whether they were normally distributed. Continuous variables were reported as mean (SD) for normally distributed variables, and median with interquartile ranges for non-normally distributed variables. Categorical variables were presented as numbers and percentages.

Results

The mean age of 27 patients, out of which three were females, was 34,2 (13,2) years (range: 14-65 years). Two patients had firearm injuries, while 25 patients were injured with sharp objects. The patients were transported to the hospital within a mean time of 29.7 (14.6) minutes (range: 15-98 minutes). Twenty-one patients (77.8%) were transported to hospital by ambulance and 6 patients (22.2%) with unqualified vehicles. 29 injuries were observed in 27 patients, 18 (62.06%) of which were isolated cardiac injuries and 11 (37.94%), mixed type injuries (Table 1).

Fourteen patients (51.8%) underwent operation following TTE, 12 patients (44.5%) due to clinical findings and one patient (3.7%), due to contrast-enhanced thorax computed tomography findings. The mean pericardial blood volume was 290 mL (range 140-460 mL) in patients with a cardiac tamponade. Accompanying abdominal injury was observed in three patients. Twelve patients had hemodynamic instability and three underwent operation with cardiac resuscitation. A left anterolateral thoracotomy was performed to 14 patients, a median sternotomy was performed to eight patients and a right anterolateral thoracotomy was performed to two patients. In three patients, both a left anterolateral thoracotomy and median sternotomy were used. One patient required both left and right thoracotomy. Splenectomy was performed in three patients, and laparotomy was performed due to abdominal injuries. Injured cardiac sections are listed in Table 2.

Two patients had coronary artery injuries. The mean length of the injuries was 2.3 cm (range: 0.4-5 cm). The cardiac injuries of 25 patients were repaired primarily and two patients required a cardiopulmonary bypass. Two patients underwent a postoperative explorative laparotomy operation. Atelectasis was observed in eight patients and cerebrovascular insufficiency was seen in five patients. Mortality was encountered in 12 patients, among which three patients underwent operation with cardiac resuscitation, five patients had a cerebral infarct due to cerebrovascular insufficiency, two patients had multiple injuries and two patients had multiple cardiac injuries. Mortality rate was 44.5%.

Table 1: Type of injuries

Injured area	Number (n)	Percentage (%)
Isolated heart	18	62.06
Mixed type injury	11	37.94
*Isolated abdomen + PCI	1	3.44
*Isolated lung + PCI	7	24.13
*Abdomen + lung + PCI	2	6.89

PCI: Penetrating cardiac injury

Table 2: Localization of cardiac injuries

Localization	Number (n)
Right ventricle	14
Left ventricle	8
Right atrium	5
Left atrium	2

Discussion

Until early 1950s it was not possible even to think of cardiac suturing or repairing [4]. Cardiac injuries still have an increased rate of morbidity and mortality. In emergent operations, chest trauma is seen in 10.4% of the cases and only 1% of the cases comprise cardiac injuries [5]. Although the incidence is lower in comparison to other traumatic cases, cardiac injuries are important due to high mortality rates [6,7].

Time of transportation of the patient to the hospital is one of the major factors affecting the mortality rates. Only 6% of the PCI patients are transported to the hospital alive, and only 50% of them survive [8,9].

Naughton MJ et al. published a statistical analysis of a study consisting of peroperative exitus cases involving prehospital deaths. According to this study, 33% of the patients transported to the hospital with a helicopter, 76% of the patients transported with an ambulance and 100% of patients transported with unqualified vehicles did not survive [10]. In our study, the mean time of transportation of the patient to the hospital was 29.7 minutes; 77.8% were transported with an ambulance and 22.2% with unqualified vehicles. Overall mortality rate was 44.5%, and the mortality rate of patients transported with unqualified vehicles was 83.5%.

PCI is mostly seen in the young, male population [1,2,5]. In our study, among 27 cases, 24 (88.9%) were male and 3 (11.1%) were female. The mean age was 34.2 (13.2) years (range: 14-65 years).

The survival rates of PCI cases vary with clinical presentation. Even in asymptomatic PCI cases, the mortality rate remains high, which is why early diagnosis of a possible PCI can be lifesaving. In all injuries located between the areolas, jugulum and upper abdomen, cardiac injury must be suspected unless otherwise specified [11]. The most important means of detecting a possible cardiac injury is echocardiography. Even in thoracic traumas, cardiac injury must be eliminated via echocardiography, because it is the main factor affecting surgical success [2,4,7,12,13]. In 51.8% of cases, we performed preoperative echocardiography, and 44.5% of patients underwent emergency surgery due to clinical findings. The entrance and the exit points of the injury are important in the management of the case [2,12,14]. Hypotension, tachycardia, and congestion in cervical veins may indicate a cardiac tamponade. Pericardiocentesis can be performed for diagnosis, but it is not appropriate for treatment in PCI cases [1,14,15]. We did not perform pericardiocentesis to any of patients, and PCI suspected asymptomatic patients underwent preoperative TCT.

Firearm injuries were present in two cases and sharp object injuries were observed in 25 cases. Firearm cardiac injuries cause larger deformities in the pericardium and myocardium in comparison to sharp object injuries of the heart. Cardiac tamponade is observed in 80-90% of the sharp object injuries of the heart, but only in 20% of the firearm cardiac injuries [16,17]. The mortality of firearm injuries of the heart is much higher than that of sharp object injuries. Henderson et al. found the mortality rates of firearm and sharp object injuries were 93.5% and 62.9%, respectively, in a series of 251 cases [18]. In this study, we included two cases who were admitted to the emergency service with cardiac arrest due to firearm cardiac injury and underwent emergent surgery with CPR. They could not survive. The mortality rate of firearm cardiac injury was 100% in our study, and overall mortality of 27 cases were 44%.

Firearm cardiac injuries are more commonly seen in the USA compared to England and South Africa due to the convenience of individual armament, resulting with higher mortality rates [19-21]. In recent studies of the Turkish community, sharp object injuries of the heart are reportedly higher than firearm cardiac injuries [4-6].

Limitations

Due to the retrospective nature of the study, certain variables specifically related to cardiac injuries are not available, including specific cardiac imaging or diagnostic tests. Another limitation of our study is the lack of autopsy of sudden deaths following a cardiac injury, which could not be included in the statistical analysis. There were not any resuscitative thoracotomy cases among our patients. Further multi-center studies involving larger number of cases would provide more realistic and meaningful statistical results.

Conclusion

Technological improvements result in complicated and mixed type cardiac injuries. To decrease mortality and morbidity rates, early diagnosis, fast and appropriate transport, a multidisciplinary approach with experienced surgical teams are mandatory. In addition to improving health services, preventing individual armament would be beneficial in increasing the survival rates of PCIs.

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Relationship of orgasm with measurable dimensions of clitoris and visibility of clitoral glans

Klitorisin ölçülebilir boyutları ve glansın görünürlüğü ile orgazm arasındaki ilişki

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Abstract

Aim: The clitoris is the dominant sexual organ in the female, varies in size and plays an active role in genital sensation and orgasm. Since the importance of clitoral glans visibility is known, surgeries of clitoris are increasing day by day. However, there is insufficient literature on the subject. The aim of this study is to determine the effect of measurable dimensions of clitoris and the clitoral glans visibility on female sexual function.

Methods: Seventy-seven patients included in this cross-sectional study were examined in the lithotomy position and the measurable dimensions of the clitoris, the visibility of the clitoral glans and the length of the prepuce were noted. The Female Sexual Function Index (FSFI) was applied to all participants, which were divided into two groups, as those with normal orgasmic function and orgasmic dysfunction. One researcher made all measurements.

Results: There were no statistically significant differences in clitoral glans width, length, or prepuce length (P=0.11, P=0.63, P=0.35, respectively). Clitoral glans was visible in 41 of 51 patients in the normal orgasmic function group, which was significantly higher than the group with orgasmic dysfunction (P<0.001).

Conclusion: Since there is a significant relationship between clitoral glans visibility and orgasm, genital surgeries performed to increase clitoral glans visibility can facilitate sexual satisfaction and/or increase orgasm intensity. The fact that the relationship between measurable dimensions of clitoris, length of prepuce and orgasm cannot be shown suggests that clitoral glans visibility is more important than clitoral size for sexual stimulation.

Keywords: Sexual dysfunction, Clitoris, Orgasm

Öz

Amaç: Klitoris kadında baskın cinsel organıdır ve boyut olarak değişken olup genital duyum ve orgazmda etkin bir rol oynamaktadır. Klitoral glans görünürlüğünün önemi bilindiğinden klitoral glansı açığa çıkaracak cerrahiler gün geçtikçe artmaktadır. Ancak bu durumu destekleyecek literatür bilgisi yetersizdir. Bu çalışmanın amacı klitorisin ölçülebilir boyutları ve klitoral glans görünürlüğünün kadın cinsel fonksiyonu üzerindeki etkisini belirlemektir.

Yöntemler: Bu kesitsel çalışmaya dahil edilen 77 hastanın litotomi pozisyonunda klitorislerinin ölçülebilen boyutları ile klitoral glansın görünürlüğü ve prepisyum uzunlukları ölçülerek kaydedildi. Kadın Cinsel Fonksiyon İndeksi (FSFI) uygulandı. Hastalar normal orgazmik fonksiyonu olan ve orgazmik disfonksiyonu olan iki gruba ayrıldı. Bütün ölçümler tek araştırmacı tarafından yapıldı.

Bulgular: Klitoral glans genişliği, glans uzunluğu, prepisyum uzunluğu ölçümlerinde orgazmik fonksiyonlar açısından gruplar arasında istatistiksel olarak anlamlı bir fark izlenmedi (P=0.11, P=0.63, P=0.35). Klitoral glansın görünür olduğu 51 hastanın 41 tanesi orgazmik grupta yer aldı. Klitoral glans görünürlüğünün orgazmik grupta daha fazla olduğu izlendi (P<0,001).

Sonuç: Klitoral glans görünürlüğü ile orgazm arasında anlamlı bir ilişki olduğundan klitoral glans görünürlüğünü artıracak şekilde uygulanan genital cerrahiler cinsel tatmini kolaylaştırabilir ve/veya orgazm yoğunluğunu artırabilir. Klitorisin ölçülebilen boyutları ve prepisyum uzunluğu ile orgazm arasındaki ilişkinin gösterilememesi klitoral uyarı için boyutlardan daha çok klitoral glansın görülebilir olmasının ön planda olduğunu düşündürmektedir.

Anahtar kelimeler: Cinsel disfonksiyon, Klitoris, Orgazm

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Introduction

Sexual health is one of the most important indicators of the individual's quality of life, which is negatively affected by sexual dysfunction [1].

Sexual dysfunction classification systems are structured on the coordination of the phases of sexual response cycle, which are defined by Master and Johnson and developed by Kaplan, including desire, arousal, and orgasm [2]. According to the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) criteria, the most common female sexual dysfunction is desire / arousal and orgasmic disorders [3,4].

The frequency of orgasmic disorders in women is between 18% and 34%, which is quite high [5]. Studies have shown that only 39-47% of married women achieve orgasm in every sexual intercourse and only 12-16% are multi-orgasmic [6].

The clitoris, located in the vulva and distal vagina of the female sexual anatomy, is the dominant sexual organ of the woman. Anatomical and physiological differences can facilitate sexual satisfaction or increase the intensity of orgasm [7]. The clitoris is called the clitoral complex with the distal vagina and urethra [7]. The clitoral complex is variable in size and plays an active role in genital sensation and orgasm [8,9]. Some studies suggest that there is a relationship between the clitoral position and orgasm by measuring urethrovaginal and clitoral-urethral distances [10]. However, very few studies have addressed the relationship between clitoral size, visibility, and female sexual response. While conducting these studies, many different scales are used to detect sexual response and sexual dysfunction in women. One of the most frequently used is the Female Sexual Function Index (FSFI). Different individual domains such as desire, arousal, lubrication, orgasm, satisfaction, and pain are analyzed with this questionnaire [11].

The aim of this study is to determine the effect of measurable clitoral dimensions and clitoral glans visibility on female sexual function by comparing women with normal and dysfunctional orgasms.

Materials and methods

This cross-sectional study included 77 participants who applied to our hospital's outpatient clinic between April 2018 and January 2019 for routine gynecological examination. These participants who reflected the healthy society were premenopausal women, over the age of 18 years, had been sexually active for the past 12 months and having sexual intercourse for at least in every 15 days.

Informed consent forms were obtained from all patients. Those who did not want to participate in the study, who were not sexually active, patients with organic pathologies in their vaginal examinations, patients under the age of 18 years or over the age of 55 years, patients who underwent genital surgery for aesthetic or other reasons, postmenopausal patients or those under hormone replacement therapy, patients with symptoms that may be due to hormonal imbalances such as increased muscle mass, clitoral growth, acne development or voice thickening, those using oral contraceptives, topical estrogen or sexual enhancement drugs, patients with menstrual irregularity, primary anorgasmic patients, and morbidly obese patients with BMI >30 kg/m^2 were excluded from the study.

Ethical approval was obtained from the Ethics Committee of Düzce University Medical Faculty Hospital (Ethics Committee Number: 2017/122). All participants were informed about the study and the confidentiality of the interview before they were included. Demographic data of the patients (age, body mass index (BMI), parity, marital status, number of partners, smoking habit, and delivery type) were recorded.

The patients underwent gynecological examination in the lithotomy position. After evaluation of the clitoral glans visibility only by spontaneous inspection, it was recorded whether the glans of clitoris was visible or not. The skin fold on the clitoris was measured craniocaudally and noted. Clitoral measurements were made with the help of 'digital stainless steel vernier caliper' which can measure one tenth of a millimeter. In terms of hygiene, calipers were sterilized by ethylene oxide or used by passing into disposable pouch gloves. All clitoral glans measurements were measured by pulling the prepuce back.

The clitoral length was measured as the distance from crura insertion at the symphysis pubis to the tip of the glans, as described by Verkauff [12]. The clitoral width was recorded as the transverse diameter at the widest point. All measurements were made by the same researcher (AEK).

Female Sexual Function Index (FSFI) with a Turkish validity and reliability analysis (Cronbach's alpha coefficient of 0.95, test retest reliability of 0.75-0.95) was applied to all patients [13]. The cutoff scores for the FSFI scales were created by using the scale-specific means for women without sexual dysfunctions minus one SD as reported by Wiegel and colleagues [14]. The cutoff score was 3.75 for orgasm. Based on this value, the patients were divided into two groups, as those with and without orgasmic dysfunction according to total scores of the scale.

An FSFI total score of 26.55 is generally considered the optimal cut-off score to differentiate women with and without sexual dysfunction (maximum possible score: 36) [14].

Statistical analysis

The descriptive statistics for continuous variables were expressed as mean (standard deviation) or median (minimum-maximum), while nominal variables were expressed as number and percentage (%). The significance of the difference between the mean values of the groups was evaluated using Mann Whitney U test. A *P*-value< 0.001 was considered statistically significant. Statistical analysis was performed using SPSS for Windows version 22 software (SPSS Inc., Chicago, IL, USA).

Results

The mean age of the patients was 32.8 (7.8) years, and the mean BMI was 24.91 kg/m^2 (4.68). Age and BMI were compared between the groups with no significant differences (*P*=0,17). All patients were sexually active, 14 (18.2%) were never married, 58 (75.3%) were married, and 5 (6.5%) were divorced. Seventy-one (92.2%) patients had one partner, while 6 (7.8%) had two partners. While 41 (53.2%) patients were non-smokers, 36 (46.8%) were smoking. The mean parity of the patients was 2 (min-max 0-6). Thirty-four patients (44.2%) gave

birth by normal vaginal route. The demographic data of the patients are presented in Table 1.

The measurable dimensions of the clitoris were evaluated in patients with orgasmic dysfunction. Clitoral glans width, length and prepuce length were 0.66 (0.16) cm, 0.91 (0.24) cm and 2.00 (0.45) cm, respectively. In patients with normal orgasmic function, the glans width, length, and prepuce length were 0.59 (0.14) cm, 0.87 (0.17) cm, 2.07 (0.40) cm, respectively. There was no statistically significant difference between the measurable dimensions of the clitoris between both groups (P=0.11, P=0.63, P=0.35, respectively). The evaluation of 77 patients for clitoris glans visibility revealed that the glans was invisible in 26 patients, and visible in 51 patients.

Ten of 51 patients with a visible glans were in the group with orgasmic dysfunction, while 41 were in the orgasmic group. It was found that clitoral glans visibility was higher in the orgasmic group (P<0.001). The FSFI total scores in the groups with orgasmic dysfunction and normal orgasmic function were 16.5 (0.95) and 28.9 (0.42), respectively. The increase in total score of FSFI is significantly and directly related to the intensity of orgasm (P<0.001). In Table 2, the comparison of the measurable dimensions of the clitoris, prepuce length, clitoral glans visibility and FSFI Total scores in patients with or without orgasmic dysfunction are presented.

Table 1: Demographic data of patients

	n=77 mean (SD), median, min-max
Age mean (SD)	32.8 (7.8)
BMI mean (SD)	24.91 (4.68)
Parity (median, min-max)	2, 0-6
Marital status (n, %)	
Single/Partner	14, 18.2%
Married	58, 75.3%
Divorced	5, 6.5%
Partner count (n,%)	
One	71, 92.2%
Two	6, 7.8%
Smoking (n,%)	
No	41, 53.2%
Yes	36, 46.8%
Delivery method (n,%)	
Vaginal	
Yes	34, 44.2%
No	43, 55.8%

BMI: Body mass index, SD: Standard deviation

Table 2: Comparison of measurable clitoral dimensions, clitoral glans visibility and FSFI total scores in patients with or without orgasmic dysfunction

	OD-G (n= 28)	O-G (n= 49)	*P*-value
Clitoral Glans width	0.66 (0.16)	0.59 (0.14)	0.11
Clitoral Glans length	0.91 (0.24)	0.87 (0.17)	0.63
Prepuce length	2.00 (0.45)	2.07 (0.40)	0.35
Visibility of the Clitoral Glans			
Not visible (n = 26)	18	8	<0.001
Visible (n = 51)	10	41	
FSFI			
Total	16.5 (0.95)	28.9 (0.42)	<0.001

OD-G: Orgasmic dysfunction group, O-G: Orgasmic group, Data are expressed as mean (Standard deviation), Measurements are given in centimeters.

Discussion

There is surprisingly limited data on relationship between the measurable dimensions of the clitoris and orgasm in the literature. The most important finding of this study is to reveal the importance of clitoral glans visibility in achieving orgasm. However, no relationship was found between the measurable dimensions of the clitoris, prepuce length and orgasm.

In a study in which clitoral measurements were made, the measurement results obtained by different physicians were evaluated and no statistically significant difference was found [15]. The fact that there is no significant difference between the measurements of different physicians also shows that measurements are completely reliable in this study, in which all the measurements were done by a single physician. This study represents the first in the literature which indicates the relationship between visibility of clitoral glans and orgasm. Since the assessment may vary by person, patients were examined by a single physician who has expert publications in the field of female genital area anatomy and practiced in examination of the vulvar region (AEK).

In a study conducted by Doğan et al. [16], improvement of sexual functions has a prominent place among the reasons that motivate women towards genital aesthetic surgeries. According to a study conducted by Goodman et al. [17], it was shown that there was a significant increase in postoperative sexual satisfaction rates in patients who underwent clitoral hoodplasty in order to increase the visibility of clitoral glans. However, since combined surgeries such as labioplasty and clitoral hoodplasty were performed concomitantly in some patients, one should not incorrectly state that clitoral hoodplasty alone improves sexual satisfaction. Placik et al. [18] reported that no decrease in clitoral region sensitivity was observed in patients who underwent clitoral hoodplasty. To the best of our knowledge, there is no study that shows the negative effects of clitoral region surgeries on orgasm. In our study, among the patients who had no previous genital surgeries, a statistically significant relationship was found between clitoral glans visibility, sexual function, and orgasm. This suggests that performing genital surgery to increase clitoral glans visibility may benefit patients in improving sexual satisfaction.

In a cohort study of Vaccaro et al. [19], women with normal orgasmic function have been shown to have smaller clitoral complexes in MR examination. In contrast, another study on measurements determined by non-contrast pelvic MRI shots showed that orgasmic functions are associated with larger clitoral complexes [20]. In both MRI examinations, the entire clitoris was measured. In our study, the measurable dimensions of the clitoris were evaluated. There was no statistically significant relationship between the glans width and length, the measurable dimensions of clitoral glans, and orgasm. In the research by Oakley et al. [20], an evaluation was also made according to the location of the clitoris, that is, the distance from the entrance of the vagina. Although the absence of such a measurement in this study seems like a limitation, more studies should be conducted in larger series regarding whether the clitoral glans visibility or location of clitoris is a more prominent factor for orgasm.

Lloyd et al. [5] showed that clitoral dimensions are not related to age, parity, ethnicity, hormone use, or history of sexual activity. However, in another study, there was a relationship between high androgen and estradiol levels and the dimensions of clitoral glans, which showed that clitoral tissue responds to serum hormones [21]. Although it seems a limitation of the study to not evaluate the hormone profile, this limitation was tried to be overcome by excluding patients who are likely to have hormone irregularities. Patients with menstrual irregularities, menopausal symptoms as well as those under hormone replacement therapy, who use oral contraceptives, topical

estrogen or sexual enhancement drugs and those with symptoms related to an increase in testosterone production were not included in the study.

Limitations

Measuring only the visible parts of the clitoris, not using other imaging techniques to measure the size of the corpus and crus, and using only FSFI among all sexual assessment scales to evaluate sexual and orgasmic dysfunction are the other limitations of our study.

Conclusion

Since there is a significant relationship between clitoral glans visibility and orgasm, genital surgeries performed to increase clitoral glans visibility can facilitate sexual satisfaction and/or increase orgasm intensity. The inability to show the relationship between the measurable dimensions of the clitoris and orgasm suggests that clitoral stimulation is more related to visibility of clitoris rather than the size of it. The localization of the prepuce is more important for orgasm compared to its length: It should be localized in such a way that it does not cover the clitoris. Although this study contributes significantly to the literature, future studies with larger series are required.

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Evaluation of the efficacy and safety of levetiracetam treatment for neonatal seizures in extremely preterm infants

İleri derece preterm bebeklerde neonatal nöbetler için levetirasetam tedavisinin etkinliğinin ve güvenilirliğinin değerlendirilmesi

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Abstract

Aim: Levetiracetam (LEV) is increasingly being used to treat seizures in the neonatal period. Data about using LEV in extremely preterm infants with seizures is insufficient and limited with only a handful studies. This study aimed to evaluate the efficacy and safety of LEV in the treatment of seizures in extremely preterm infants.

Methods: This retrospective cohort study was conducted on extremely premature newborns, those who were born ≤28 weeks of gestational age, and took their first intravenous dose of levetiracetam due to neonatal seizure before their 44th gestational week between September 2017-February 2019. Loading and maintenance dosage of LEV, previously used antiepileptic medications, response to treatment and side effects of LEV were recorded.

Results: Twenty extremely preterm neonates (9 males and 11 females) who received LEV were evaluated. Gestational ages ranged from 23 to 28 weeks, with a median of 26.5 weeks. Birth weights ranged from 520-1210 gr and 15 infants (75%) had extremely low birth weights. For the treatment of seizures, 12 patients (60 %) were initially started on levetiracetam as first-line therapy and eight patients (40%) were administered levetiracetam as a second or third-line antiepileptic drug. The efficiency of seizure control with LEV was 60 % (12/20) in all patients. The median LEV dose at the time seizure control was achieved was 40 mg/kg. No side effects were observed due to LEV treatment.

Conclusion: This study shows that LEV can be efficient and safe for seizure management in extremely preterm infants. Seizure control was better achieved when LEV was given as the first-line antiepileptic medication in extremely preterm infants.

Keywords: Levetiracetam, Neonatal seizures, Preterm

Öz

Amaç: Levetirasetam (LEV), yenidoğan döneminde nöbetleri tedavi etmek için giderek daha fazla kullanılmaktadır. Nöbet geçiren ileri derece preterm bebeklerde LEV kullanımı ile ilgili veriler yetersizdir ve sadece birkaç çalışma ile sınırlıdır. Bu çalışma, ileri derece preterm bebeklerde nöbetlerin tedavisinde LEV'in etkinliğini ve güvenilirliğini değerlendirmeyi amaçlamıştır.

Yöntemler: Bu retrospektif kohort çalışma, Eylül 2017-Şubat 2019 tarihleri arasında ≤28. haftalık gebelik haftasında doğan ve yenidoğan nöbeti nedeniyle ilk doz intravenöz levetirasetamı postnatal 44. haftaya kadar alan ileri derece preterm yenidoğanlarda yapılmıştır. LEV'in yükleme ve idame dozu, daha önce kullanılan antiepileptik ilaçları, tedaviye yanıtı ve LEV'in yan etkileri kaydedildi.

Bulgular: Levetirasetam alan 20 ileri derece preterm yenidoğan (9 erkek ve 11 kadın) değerlendirildi. Gestasyonel yaşları 23 ila 28 hafta arasında değişiyordu ve ortalama 26.5 hafta idi. Doğum ağırlıkları 520-1210 gr arasında değişiyordu 15 bebek (%75) aşırı düşük doğum ağırlıklıydı. Nöbetlerin tedavisi için başlangıçta birinci basamak tedavi olarak 12 hastaya (%60) levetirasetam başlandı ve sekiz hastaya (%40) ikinci veya üçüncü basamak antiepileptik ilaç olarak levetirasetam verildi. Tüm hastalarda LEV ile nöbet kontrolünün etkinlik oranı %60 (12/20) idi. Nöbet kontrolü sağlandığında ortalama LEV dozu 40 mg/kg olarak bulundu. LEV tedavisine bağlı herhangi bir yan etki gözlenmedi.

Sonuç: Bu çalışma, LEV'in ileri derece preterm bebeklerde nöbet yönetimi için etkili ve güvenli olabileceğini göstermektedir. İleri derecede preterm bebeklerde LEV birinci basamak antiepileptik ilaç olarak verildiğinde nöbet kontrolü daha iyi sağlanmıştır.

Anahtar kelimeler: Levetirasetam, Neonatal nöbetler, Preterm

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Introduction

Seizures are one of the most common and serious neurological emergencies in the neonatal period [1,2]. Neonatal seizures occur in 1-3 per 1000 term newborns and it may increase up to 10-130 per 1000 in preterm neonates [2-4]. The neonatal period is the most important period of life for developing seizures, because neonatal seizures, especially if prolonged, were reportedly associated with poor neurodevelopmental outcomes, as it may negatively affect the immature brain of premature infants [1,5,6]. Therefore, treatment and management of neonatal seizures are particularly important to reduce neurological disabilities of children [1,5].

Neonatal seizures usually manifest with stereotypical muscular activity or autonomic changes, and are a result of abnormal electrical discharges in the central nervous system of neonates, occurring within the first 28 days after birth in full-term infants or until 44 weeks of gestational age in preterm infants [1,4,7]. The etiologies of neonatal seizures are reported in a broad spectrum, such as hypoxic-ischemic encephalopathy (HIE), infections, metabolic and electrolyte disturbances, brain injuries, intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL) and brain malformations [1,8]. Extremely preterm infants who are born ≤28 weeks gestational age may be more vulnerable to neonatal seizures than other preterm and term neonates due to the immaturity of their nervous system, and they can have a lot of comorbidities including various disorders of the brain, which may lead to the decrease of seizure threshold [7,9].

Despite a highly broad spectrum of etiologies and their importance on neurodevelopmental outcomes, we only have a few treatment options to manage neonatal seizures. In the neonatal period, phenobarbital and phenytoin are well known and the most often used antiepileptic drugs, because they are the only two drugs which have been approved by the FDA for the treatment of neonatal seizures [1-3]. However clinical studies showed that both have some side effects during the acute seizure treatment period or long-term use [2,5,10]. The use of phenobarbital may have a negative effect on long-term neurodevelopmental outcomes [2,10] . Similarly, long-term use of phenytoin in newborns is associated with some serious potential side effects such as arrhythmia, hypotension, and serious tissue necrosis if extravasated during administration [10]. On the other hand, the efficacy of phenobarbital and phenytoin in controlling neonatal seizures is around only 75-85 %, even when used together [1,11]. In addition, the intravenous form of phenobarbital to treat acute seizures cannot be found in our country. During the last decade, treatment preferences in lots of countries for neonates with seizures have begun to change towards other anti-seizure medication drugs, especially LEV.

Animal studies demonstrated that LEV may reduce apoptosis on the neonatal brain and may lead to neuroprotection, and clinical studies show that LEV is related to good neurodevelopmental outcomes of neonates with seizures [2,12]. Even though the use of LEV in neonates has not been approved by FDA yet, in the literature, studies which evaluate the use of LEV in neonatal seizures have increased in the last decade [2,13,14]. These clinical studies showed that LEV can be used to control seizures in term neonates safely and effectively [2,13]. However, data about efficacy and safety of using LEV in even preterm infants is limited, data about using LEV in extremely preterm infants with seizures is even more insufficient and is limited to only a handful studies [4,9,15]. This study aims to evaluate the efficacy and safety of LEV in the treatment of seizures in extremely preterm infants.

Materials and methods

Study population

We performed a retrospective cohort study in the neonatal intensive care unit at Adana City Training and Education Hospital, Adana/Turkey from September 2017 to February 2019. Extremely preterm newborns who were born ≤ 28 weeks of gestational age and took their first intravenous levetiracetam due to neonatal seizures until the 44th gestational week were included in the study. Infants whose seizures were caused by electrolyte disturbances or metabolic (i.e., hyponatremia, hypocalcemia, hypomagnesemia, or hypoglycemia) reasons, those who had pyridoxine-responsive seizures and all infants born later than the 28th gestational week were excluded. This study was approved by the institutional review board Ethics Committee of Çukurova University Medicine Faculty, Adana, Turkey (2019/89).

Data collection

Data was collected by a medical record review of detailed prenatal and postnatal variables of babies and mothers including maternal parity, consanguinity of parents, familial history, maternal age, type of delivery, gestational age, birth weight and gender. Perinatal disorders usually associated with premature labor were also recorded. Based on gestational age, our sample was divided into 2 subgroups: 1) <27 weeks and 2) 27-28 weeks. Small for gestational age (SGA) was defined as birth weight <10th percentile on Fenton growth curves. Birth weight less than 1000 gr was accepted as extremely low birth weight.

Apgar scores at the 1st and 5th min were recorded and whether the baby was resuscitated at birth was evaluated. Apgar scores were ranked as follows: Below or equal to three, between four and seven, and equal to or above eight. Physical and neurological examination findings of babies were noted. Detailed laboratory parameters (including complete blood count and serum sodium, glucose, blood urea nitrogen (BUN), creatinine, potassium, chlorine, calcium, serum aspartate aminotransferase (AST), serum alanine aminotransferase (ALT), arterial blood gas, total bilirubin, C-reactive protein (CRP)) were obtained from all patients**.**

Seizure protocol

Neonatal seizures were diagnosed based on the clinical observation of doctors (neonatologists, pediatricians, and pediatric neurologists) and nurses, and findings of neurological and physical examinations. Types of seizures were defined according to Volpe's classification, including subtle, tonic, clonic and myoclonic seizures, by a pediatric neurologist. The time of seizure onset was classified as occurring within the first 24 h, between 24 to 72 h, between 3 and 7 days, and over 7 days after birth. Seizure etiologies were evaluated.

Loading and maintenance dosage of LEV, previously used anti-seizure medications, concomitant treatments with other

AEDs, response to treatment, side effects during or after the loading or maintenance dosage of levetiracetam were recorded. The use of LEV as first, second- and third-line anti-seizure medication were evaluated.

At our institute, phenytoin, midazolam, and LEV are administered intravenously, but PB is given orally at our NICU because the intravenous form of PB is absent in our country. LEV is mixed with normal saline and initially loaded intravenously (IV) over one hour. Loading and maintenance dosage of levetiracetam were determined by pediatric neurologists on a case-by-case basis. The maintenance dosage of LEV after loading is administered twice daily. The anti-seizure medications were considered effective when the seizure terminated within one hour after LEV administration and did not recur for at least 24 h.

Anti-seizure medications were considered safe and tolerable if patients showed no changes in vital signs, clinical-laboratory parameters, or electrocardiography abnormalities during the treatment period. Length of hospital stay, presence of any comorbidities and complications (intraventricular hemorrhage, PVL, hydrocephalus with or without a ventriculoperitoneal shunt, etc.) and mortality rate were evaluated.

Statistical analysis

Statistical analyses were performed using SPSS version 16.0 (SPSS, Inc., Chicago, IL, USA). Qualitative and quantitative (continuous) variables were presented as the number of cases (n) with percentages (%), mean (standard deviation (SD)), median and range, respectively. Fisher's exact test was used for the evaluation of nominal variables according to the response to LEV treatment because of our small sample size. A value of P <0.05 was considered statistically significant.

Results

Within the study period, 928 infants were admitted to the NICU, 49 of which met the seizure criteria, and 29 neonates were excluded. A total of 20 neonates who were born before 28 weeks GA were included in the study (Figure 1).

We retrospectively analyzed 20 extremely preterm neonates (9 males and 11 females) who received LEV monotherapy, or a combination therapy including LEV. The median age of mothers was 26 years, and 20% of the mothers were primiparous. Eight (40%) patients were immigrants. According to the evaluation of pre-perinatal risk factors, ten patients had a least one risk factor while 4 patients had two and more. The most frequently seen prenatal risk factors were premature rupture of membranes (PROM) (n=9), and chorioamnionitis (n=4). The demographical and clinical features of the infants were shown in Table 1. Fifteen (75%) infants were delivered by C-section. Gestational ages ranged from 23 to 28 weeks, with a median of 26.5 weeks. Birth weights ranged from 520-1210 gr, with a median of 730 gr. Fifteen infants (75%) had extremely low birth weights (birth with less than 1000 gr) and two infants (10%) were SGA. Apgar scores at the 1st minute ranged from 2-7, with a median of 3.5, and Apgar scores at the 5th minute ranged from 5-9, with a median of 7. The 1st minute Apgar score was under 3 points in 10 patients and Apgar scores at the 5th minute were under 7 points in all patients except for four. Ninety percent of all patients were resuscitated at birth, and respiratory distress syndrome (RDS) was diagnosed in 16 (80%) neonates.

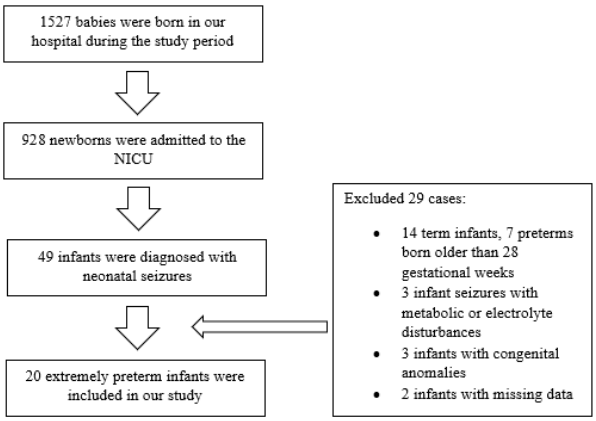

Figure 1: The flow diagram shows how patients were included in the study

The median of seizure onset was the 3rd day, and it varied between 2 and 26 days. The onset of seizure according to gestational ages ranged from 23 to 32 weeks. No patient had a seizure within the first 24 hours after the birth, 16 (80%) among all patients developed seizures within 7 days after birth (Table 2). Most patients presented with partial seizures with or without secondary generalization. The main seizure types were clonic (40%) and tonic seizures (25%), and five subjects (25%) presented with more than one type of seizures in different combinations (Table 2). Subtle type seizures were seen in six newborns (30%), majority of which were accompanied by clonic or tonic seizures. According to their etiologies of seizures, the most frequent diagnosis was germinal matrix hemorrhages (grade II to IV) which were seen in 12 (60%) of all infants.

Table 1: The characteristics of extremely premature infants (n=20)

Characteristics	Median	(Minimum - Maximum)
Gestational age (week)	26.5	23-28
Birth weight (g)	730	520-1210
Maternal age (year)	26.5	22-39
Maternal parity	3	1-5
Apgar 1st min	3.5	2-7
Apgar 5th min	5.5	5-9
Time of the seizure onset (day)	3.5	2-26
	n	Percentage
Gender (female) n, (%)	11	(65 %)
Cesarean section n, (%)	15	(75%)
Pre-perinatal complication n, (%)		
PROM	9	(45%)
Chorioamnionitis	4	(20%)
Preeclampsia	1	(5%)
Etiology of seizure n, (%)		
IVH	12	(60%)
Sepsis	4	(20%)
Meningoencephalitis	2	(10%)
HIE	2	(10%)
Accompanying comorbidities and complications		
RDS	16	(80 %)
PVL	6	(30%)
Hydrocephalus	4	(20%)
Mortality n, (%)	7	(35%)

PROM: Premature rupture of membranes, IVH: Intraventricular hemorrhage, HIE: Hypoxic-ischemic encephalopathy, RDS: Respiratory distress syndrome, PVL: Periventricular leukomalacia

For the treatment of seizures, 12 patients (60%) were initially started on levetiracetam as first-line therapy (Group 1). Group 2 consisted of eight patients, four of the which (20%) began receiving LEV as a second-line antiseizure drug because of continued seizures on phenytoin or phenobarbital, and four patients (20%) received LEV as third-line treatment because of continued seizures despite phenytoin and phenobarbital administrations (Table 2). The median first loading dose of LEV was 40 mg/kg (ranged; 20-45 mg/kg). Nine patients (45%) needed an additional loading dose to control the seizures, and the

maximum loading dosage of LEV was 70 mg/kg. The median LEV dose at the time when seizure control was achieved was 40 mg/kg (range: 20-70 mg/kg) and the median maintenance dose of LEV was 45 mg/kg/day (ranged; 20-60 mg/kg/day). The efficiency rate of seizure control with LEV was 60% (12/20) among all patients. The seizures were successfully managed in 67% (8/12) when LEV was used as the first-line drug and 50% (4/8) when LEV was used as the second or third-line drug (Figure 2). There were no statistically significant differences between the groups in terms of the rate of seizure management (P=0.64). When patients were evaluated according to favorable response to LEV treatment, we did not find any significant differences between the groups in terms of gestational age, birth weight, gender, delivery mode, Apgar scores, seizure onset, and loading dosage of LEV (P>0.05) (Table 3).

Table 2: Features of seizures and treatment of levetiracetam (n=20)

	Number of subjects	Percentage (%)
Time of seizure onset		
First 24 hours	-	-
24-72 hour	10	50
4-6 days	6	30
≥7 days	4	20
Seizure semiology		
Clonic	8	40
Tonic	5	25
Clonic - subtle	4	20
Tonic - subtle	1	5
Myoclonic	1	5
Subtle	1	5
Total	20	100
Treatment of levetiracetam		
First line	12	60
Second line	4	20
Third line	4	20
Seizure control rate with LEV	12	60
	Median	Range
Median first loading dosage of LEV	40 (mg/kg)	20-45 (mg/kg)
Median total loading dosage of LEV	40 (mg/kg)	20-70 (mg/kg)
Median maintenance dose of LEV	45 (mg/kg/day)	20-60 (mg/kg/day)
Side-adverse effects	-	-

Table 3: Characteristics of extremely preterm infants with favorable versus unfavorable response to levetiracetam

Values	Number of subjects (n, %)	Group 1 (n=12)	Group 2 (n=8)	P-value
Gestational age				0.65
23-26 week	10(50)	5	5	
27-28 week	10(50)	7	3	
Birth weight				0.69
<1000 g	15(75)	9	6	
>1000 g	5(25)	3	2	
Gender				0.19
Female	11(55)	5	6	
Male	9(45)	7	2	
Delivery mode				0.70
Cesarean	15(75)	9	6	
Spontaneous	5(25)	3	2	
Pre-perinatal complication				0.65
No	10	7	3	
Yes	10	5	5	
1-min Apgar score				0.65
0-3	10(50)	7	3	
4-7	10(50)	5	5	
8-10	0	0	0	
5-min Apgar score				0.53
0-3	0	0	0	
4-7	16(80)	10	6	
8-10	4(20)	2	2	
Seizure onset				0.69
<72hour		5	5	
≥72 hour		7	3	
Etiology				
IVH	12	7	5	
Sepsis	4	3	1	
Meningoencephalitis	2	1	1	
HIE	2	1	1	
Treatment of levetiracetam				0.648
First line	12(60)	8	4	
Second or third line	8(20)	4	4	
Median loading dosage of LEV, range (mg/kg)	40 (20-70)	40 (20-70)	40 (30-70)	
Exitus	7(35)	4	3	0.68

LEV: Levetiracetam, Group 1: Favorable response to LEV, Group 2: Unresponsive to LEV

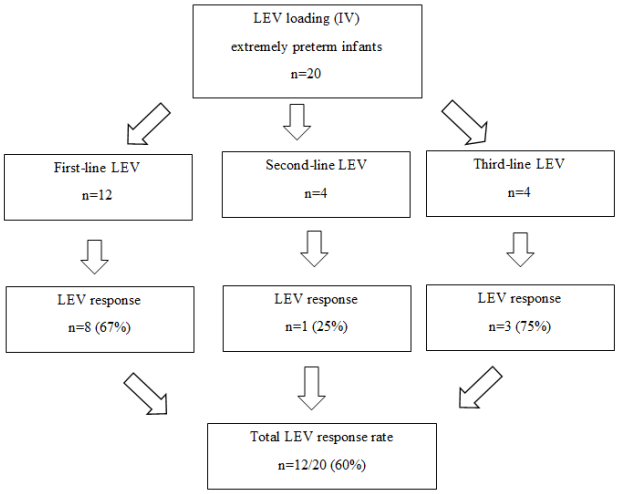

Figure 2: The efficiency rate of seizure control with LEV was 60 % (12/20) in all patients. The seizures were successfully managed in 67% (8/12) when LEV was used as the first-line drug and 50% (4/8) when LEV was used as the second-line or third-line drug (LEV: Levetiracetam)

No serious side effects were observed due to LEV infusion or oral administration in terms of clinical (changes of respiratory status, heart rate or blood pressure, somnolence, irritability, etc.) or laboratory (hepatic and renal dysfunction) parameters. The median length of hospital stay was 82 days (range; 7-142 day) and mortality rate was 35%.

Discussion

The present study conducted with 20 extremely premature neonates indicates that intravenous levetiracetam may be effective and safe in the management of acute seizures during the neonatal period. Seizure control was achieved in 60% of all patients, treatment with levetiracetam did not result in any adverse events and was generally well-tolerated in our study population.

Levetiracetam is a second-generation anticonvulsant with wide spectrum anti-seizure efficiency. In 2012, FDA approved the use of LEV in infants and children aged 1 month and older to treat focal seizures as an adjunctive antiepileptic medication. Animal studies demonstrated that LEV may reduce apoptosis on the neonatal brain and may lead to neuroprotection, and clinical studies show that LEV is related to good neurodevelopmental outcomes of neonates with seizures [12,13,16,17]. Although the use of levetiracetam in newborns has not been approved by the FDA yet, LEV has been increasingly used off label in neonates because of clinical reports in the literature showing efficiency and safety of using of levetiracetam in neonatal seizures, and animal studies showing the neuroprotective effects of levetiracetam [2,13]. The presence of side effects of phenobarbital and phenytoin during administration, the negative effects on long-term neurodevelopmental outcomes, and absence of intravenous form of phenobarbital in our country, the demonstration of the safety, well tolerability and neuroprotective effects of LEV led to a change of treatment preferences in neonates with seizures, in favor of LEV in our hospital as in the world.

Prematurely born infants, especially extremely premature infants, are more vulnerable to neonatal seizures than full-term infants [6,7,9]. They are born with a more immature central nervous system, most of the time they need longer intensive care and they may have lots of comorbidities which can

facilitate having a seizure [7]. Neonatal seizures should be monitored and treated carefully to avoid brain damage [1,5,7]. In premature babies, treatment of neonatal seizures quickly and choosing the drug with the least side effects at treatment and follow up are much more important than it is for full-term neonates in terms of long-term neurodevelopmental outcomes [7,9,15]. Also, the frequency of NEC is higher in prematures and they may not be able to take oral medicines for a long time. Therefore, the use of LEV, which has very few side effects in intravenous or oral use and is safe for a long-term treatment, may be a good option in premature cases.

Currently, some studies in the literature show that using LEV in premature infant seizures is effective and safe for neonates [2,9]. However, studies about the use of LEV in extremely preterm infants with seizures is limited with only a handful studies, the results of which highly vary [4,9,15]. Han et al. [9] conducted a retrospective analysis of 37 preterm infants (mean gestational age 31.5±1.9 weeks (range, 26 to 36+6 weeks)) who were treated with LEV as the first-line anti-seizure medication. That study population included three infants (8%) with extremely low birth weights (less than 1000 g) and 10 (27%) with very low birth weights (less than 1500 g). In their cohort, 57% of all preterm infants were seizure-free while on LEV at the end of the first week, no additional anti-seizure medication was required and they suggested that LEV can be an acceptable and safe choice for treatment of neonatal seizures in preterm infants [9]. Özelkaya et al. [15] retrospectively evaluated 26 preterm infants, including extremely preterm infants (the mean gestational was 26.7±3.3 weeks) treated with LEV. No side effects were observed during LEV treatment. They found that the seizure control rate was 11.5% when LEV was the first-line therapy and overall seizure control rate with LEV was 65%. They reported that seizure control was better achieved when LEV was given as the second antiepileptic medication in premature infants.

A recent study conducted by Kurtom et al. [4], including only extremely preterm infants, evaluated the effectiveness of monotherapy with levetiracetam as a first-line treatment in achieving seizure cessation in extremely preterm infants with seizures. This single-center study retrospectively reviewed 61 extremely preterm infants and showed that 74% of their patients did not respond to LEV monotherapy and required additional medications. Similar with the Kurthom et al. study population, our study included only extremely preterm infants. In contrast to the results of Kurthom et al. [4] and Özelkaya et al. [15] studies, we determined that seizure control was achieved in 60% of all patients, and the rate of seizure control increased to 67% when LEV was first-line treatment. Unfortunately, we could not obtain statistically significant differences between the first-line therapy group and second or third-line therapy groups in terms of the rate of seizures management. It may be related to small sample size of the groups.

The big differences in the rate of seizure control with LEV as first-line therapy between our study and Kurthom's may be related to the most important limitation of our study. They used continuous video electroencephalography to diagnose seizures, but we could not obtain electroencephalography records. Neonatal seizures at the present study were diagnosed based on clinical observation of doctors and nurses. Most likely, in the present study, we may have missed subtle seizures which are known as the most frequently seen seizure type at the neonatal period, due to us using only clinical observation to detect seizures.

Association between SGA and seizures in preterm and term infants has been reported previously [4,8]. Kurthom's study population included an important proportion of SGA patients (21%) and none of them had a favorable response to LEV treatment. We had only two SGA patients and one of them showed a favorable response to LEV treatment, which was used as first line treatment of the seizure. Another factor of differences in the rate of seizure control with LEV as first-line therapy between our study and Kurthom et al.'s study may be related to the low proportion of SGA patients in ours.

No clear recommendations about the dosage of LEV in neonates are available in the literature, where the doses range from 10-80 mg/kg [16-18]. Sharpe et al. [17] showed that LEV was well tolerated in their study of sick neonates and clearance of LEV in neonates was higher than expected on the basis of immature renal function in term infants and increased significantly during the first week of life. At the present study, the seizures were successfully managed by 67% (8/12) when LEV was used as the first-line drug and most of the patients who were given 40 mg /kg loading dosage of LEV as first loading dosage responded well to LEV (10/17 patients, 58%). Some patients needed additional loading dosage to control seizures. The maximal dosage of LEV in our study was 70 mg/ kg/day and no side effects were seen during the loading and maintenance treatment periods. Similar to our results, Han et al. used loading doses of LEV ranging from 40 to 60 mg/kg (mean: 56 mg/kg), the maintenance dosing ranging from 20 to 30 mg/kg (mean: 23 mg/kg) and no adverse effects were observed [9]. Özelkaya et al. [15] used a mean dose of 17±9.23 mg/kg LEV in preterm infants, overall seizure control rate with LEV was 65%, but seizure control rate was 11.5% when LEV was the first-line therapy. Their low efficacy rate of LEV treatment as first-line therapy may be related to lower loading LEV dosage. Although clear recommendations about loading dosage of LEV in premature infants are not available in the literature, according to our results, we think that at least 40 mg/kg loading dosage of LEV may be used to manage seizures successfully at the first loading time.

Limitations

Our study has some important limitations such as small sample size, retrospective design and the diagnosis of seizures being made only clinically, without EEG monitoring. Another important limitation of our study is that patients did not have long-term neurological follow-up. Unfortunately, we could not reach regular follow-up after the discharges of the patients at our neurology department since a significant part of our patients are immigrants or children who are from families with low socio-cultural status. Additional multicentric, larger, prospective randomized control studies are needed to define the efficacy, safety, and tolerability of the use of levetiracetam in extremely premature infants exhibiting seizures during the neonatal period.

Conclusion

Our study indicates that using levetiracetam may be effective in the management of acute neonatal seizures in

extremely preterm infants. Seizure control was better achieved when LEV was given as the first line antiseizure medication for extremely preterm infants. Treatment with intravenous levetiracetam did not result in any important adverse events and was generally well tolerated. We believe that it can be safely used as first or second-line therapy for seizure control in extremely premature infants in the NICU with limited facilities like us, despite all the limitations of our study.

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Comparison of stripping/ligation and embolization with cyanoacrylate in venous insufficiency treatment

Venöz yetmezlik ve varis tedavisinde stripping/ligasyon ve siyanoakrilat ile embolizasyon yöntemlerinin karşılaştırılması

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Abstract

Aim: Stripping/ligation (S/L) is the gold standard method used in the treatment of varicose veins. Saphenous vein ablation with cyanoacrylate (CA) is a new minimally invasive treatment method that forces this throne. Our aim is to compare these two methods in terms of patient satisfaction.

Methods: In this cross-sectional study, voluntary patients who had superficial venous insufficiency and varicose vein were divided into two groups as S/L and CA. CEAP (Clinical-Etiologic-Anatomic-Pathophysiologic-clinical score) and VAS (Visual Analogue Scale) were evaluated on the 1st, 3rd, 7th, 14th, 30th postoperative days and at the outpatient follow-up visits 1 year later. SF-36 (Short Form -36) questionnaire was applied at the first month. VCSS (Venous Clinical Severity Score) of patients were compared at 6 months after surgery. Control, color doppler ultrasonography was performed on patients with recurrent varicose veins or those who were symptomatic. SPSS 22.0 program was used for data analysis.

Results: The preoperative and postoperative VCSS scores were lower in the CA group than in the S/L group (P<0.001). In both groups, postoperative VCSS score was lower compared to preoperative conditions (P<0.001). The VAS score of S/L group was higher than the CA group, during anesthesia, on the 1st, and 3rd postoperative days (P<0.001). However, during the procedure, on the 7th (P<0.001) and 14th days (P=0.033), VAS scores were lower in the S/L group than the CA group. In short form -36, viability score was better in the S/L group (P<0.001). CA group scored higher in the other parameters (such as physical functioning, role limitations, bodily pain, general mental health, social functioning, role limitations due to emotional problems and general health perceptions) (P<0.001 for all).

Conclusion: Although the S/L method is the gold standard for varicose vein treatment, saphenous vein ablation with CA scored higher in terms of patient satisfaction.

Keywords: Venous insufficiency, Stripping and ligation, Endovenous ablation with Cyanoacrylate, Short Form-36 quality of life questionnaire

Öz

Amaç: Sıyırma/ligasyon (S/L), varisli damarların tedavisinde kullanılan altın standart yöntemdir. Siyanoakrilat (CA) ile safen ven ablasyonu, bu tahtı zorlayan yeni minimal invaziv bir tedavi yöntemidir. Amacımız bu iki yöntemi hasta memnuniyeti noktasında karşılaştırmaktır.

Yöntemler: Bu makale kesitsel bir çalışma olarak tasarlandı. Gönüllü yüzeysel venöz yetmezliği ve varisi olan hastalar, S/L ve CA grubu şeklinde ikiye ayrıldı. CEAP (Klinik-Etiyolojik-Anatomik-Patofizyolojik-klinik skor) ve VAS (vizüel ağrı skalası) 1. gün, 3. gün, 7. gün, 14. gün, 30. gün ve poliklinik takip ziyaretlerinde 1 yıl sonra değerlendirildi. Bir ay sonra SF-36 (Kısa Form-36) anketi uygulandı. Hastaların ameliyat sonrasi 6. ayda VCSS (Venöz Klinik Şiddet Skor) karşılaştırıldı. Tekrarlayan varisli veya semptomatik hastalarda kontrol renkli doppler ultrasonografi yapıldı. Veri analizi için SPSS 22.0 programı kullanıldı.

Bulgular: CA grubunda ameliyat öncesi ve ameliyat sonrası VCSS, S/L grubuna göre anlamlı olarak düşüktü (P<0,001). S/L grubunun VAS skoru anestezi sırasında, 1. ve 3. günlerde CA grubundan daha yüksekti (P<0,001). Ancak işlem sırasında, 7. günde (P<0,001) ve 14. günde (P=0,033) VAS skoru S/L grubunda CA grubuna göre daha düşüktü. S/L grubunda Kısa Form-36 canlılık skoru anlamlı olarak daha iyi bulundu (P<0,001). Diğer parametrelerde (fiziksel işlevsellik, rol kısıtlamaları, bedensel ağrı, genel ruh sağlığı, sosyal işlevsellik, duygusal sorunlara bağlı rol kısıtlamaları ve genel sağlık algıları gibi) CA grubu üstündü (P<0,001).

Sonuç: Varis tedavisinde S/L yöntemi altın standart olmasına rağmen, CA ile safen ven ablasyonu hasta memnuniyeti açısından daha üstün bulunmuştur.

Anahtar kelimeler: Venöz yetmezlik, Sıyırma ve ligasyon, Siyanoakrilat ile endovenöz ablasyon, Kısa Form-36 yaşam kalitesi ölçeği

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Introduction

Chronic venous insufficiency (CVI) is a common disease that affects almost half of the population with its high prevalence [1,2]. Various risk factors such as pregnancy, age, positive family history and high-risk occupations (such as long-standing barbers, butchers, and surgeons) trigger varicose veins [3,4].

Varicose patients are usually asymptomatic. They mostly consult a doctor for cosmetic anxiety. Symptomatic patients may have pain, feeling of weight, especially ankle edema, skin discoloration, and ultimately, venous leg ulcers [5]. The presence of reflux in the saphenofemoral junction and large saphenous vein due to valve failure is a crucial factor in the formation of varicose veins [5].

Ligation of the large saphenous vein from the saphenofemoral junction and stripping of the large saphenous vein is considered the gold standard in the treatment of varicose veins. However, minimally invasive methods such as endovenous laser ablation and radiofrequency, which developed within the last two decades, have become an alternative to surgical treatment. In both methods, multiple perivenous injections such as tumescent anesthesia and thermal complications led surgeons to search for new methods. Especially in the last decade, saphenous vein embolization with cyanoacrylate (CA) has become a rapidly shining star. Since there is no heat in this method, there are no thermal complications. Learning curve is not long, unlike tumescent anesthesia, which is a complicated method. This procedure is performed under local anesthesia. It takes about 10 minutes and return to work is fast [6].

The main purpose of our study is to compare the S/L and CA methods used in the treatment of varicose veins in the one-year follow-up period in terms of quality of life, satisfaction, pain scores and complications.

Materials and methods

Informed consent was obtained from the individuals participating in the study and the ethics committee approval was received from Adiyaman University Non-Interventional Clinical Research Ethics Committee on 16.04.2019 with the number 2019/3-8. Patients with varicose veins (related chronic venous disease) of the lower extremity who were evaluated in the Cardiovascular Surgery Policlinic of Adıyaman University Faculty of Medicine Training and Research Hospital between January 2015 and June 2019 were included in this prospective cohort-questionnaire study. The inclusion criteria in both groups were being between 18-65 years of age, reflux of more than 0.5 seconds in color doppler ultrasonography (CDUSG) and ≥C2 symptomatic varices in CEAP-clinical classification. Patients with a history of active deep venous thrombosis (DVT), pregnancy, peripheral arterial disease, arteriovenous malformation, active infection or a history of hepatitis and allergy were excluded. Patients with a saphenous diameter of over 15 mm, severely convoluting saphenous veins and obese patients were also not considered eligible for CA. A total of 856 subjects who met the criteria were included in the study on a voluntary basis. The primary endpoint was quality of life and postoperative pain after one year of follow-up. The secondary endpoint was recurrent varicose veins and complications. VCSS was applied to all patients. Venous structures were evaluated by CDUSG by a specialist radiologist. The patients were divided into two groups as S/L and CA. Decisions on the operation technique were based on physical examination findings, patient symptoms with VCSS, and 2 CDUSG findings performed by the same radiologist at 6-month intervals. Then, the treatment method was determined with the consensus of the surgeon and the patient.

Perioperative and postoperative VAS pain scale was applied to the patients. The patients were evaluated with VAS scale during anesthesia, during the procedure and on postoperative days 1, 3, 7, 14 and 30. Quality of life was evaluated by SF-36 questionnaire which included 36 questions and 8 sub-parameters. Voluntary patients who accepted to participate in this study were compared with SF-36 questionnaire in the first postoperative month in terms of quality of life. In addition, patients were evaluated with VCSS and CEAP scores in the preoperative period and the first year following the operation.

Procedural operation

S/L

All patients underwent spinal anesthesia and sedation. The saphenous vein was found distally with a 1 cm incision, made approximately 4 cm proximally to the ankle-medial malleolus and proximally with an incision of approximately 2-4 cm in the groin area. All its branches were ligated. The great saphenous vein was then ligated and divided from where it joined the main femoral vein. Then, stripping was performed with a stripper wire advanced distally. Existing packs were excised individually by miniflebectomy. After the procedure, an elastic bandage was applied for about 48 hours. The patients were hospitalized for one night, then mobilized and discharged with compression stockings to be used for at least 2 months.

Ablation with CA

Guided by CDUSG, the saphenous vein was punctured above the knee with the Seldinger technique under local anesthesia. The sheath was placed, the catheter delivered through the guide was advanced about 2-3 cm distal to the saphenofemoral junction. CA was administered with an automatic gun by applying compression to the saphenous line using the CDUSG probe. Delivery catheter was pulled 2 cm in each press. In the system we used, 0.03 cc polymer was given each time the trigger was pressed. Control CDUSG performed at the table after the procedure revealed that the saphenous vein had closed in all patients. The procedure took about 10-15 minutes. All patients were discharged with compression stockings and prophylactic LMWH to be used for one week after 2 hours of observation.

Statistical analysis

Mean, median, lowest, highest and ratio values were used to present the descriptive statistics. Categorical variables were given as frequency and percentage, and continuous variables as mean (standard deviation [SD]). The distribution of variables was measured by the Kolmogorov-Smirnov test. Mann-Whitney U test was used for the analysis of quantitative independent data. Wilcoxon test was to analyze dependent quantitative data, and chi-square test to analyze qualitative

independent data. SPSS 22.0 program was utilized for all analyses. *P*-value <0.05 was considered statistically significant.

Results

There was a total of 314 patients in the S/L group, 211 (67.2%) of which were males, and 103 (32.8%) of which were females. The mean age of the patients was 39.5 (12.1) years. Five patients had previously undergone saphenous embolization of the same leg with CA. At least one subfascial perforating vein ligation was performed in 91 patients with femoral vein valve reconstruction and 91 patients with perforator vein insufficiency who underwent CDUSG. Seven of 111 patients with Vena Saphena Parva failure underwent stripping and 104 patients underwent ligation in the same session. Patients were followed up at 2 weeks postoperatively, 297 patients had ecchymosis, 79 had superficial thrombophlebitis, 98 had transient paresthesia, and 1 had DVT. All these adverse effects were cured within a brief time with medical treatment. Preoperative demographic data and postoperative general characteristics of the patients in this group are summarized in Table 1.

There were 542 patients in CA group, 209 (38.6%) of which were males, and 333 (61.4%) of which were females. The mean age was 43,1 (12.8) years in this group. Saphenous vein embolization was performed to 250 right legs and 292 left legs by CA. The mean saphenous diameter and mean saphenous segment length were 7.5 (1.6) cm, and 29.9 (5.7) cm, respectively. In the CEAP clinical classification, 350 patients were C2, 184 patients were C3 and 8 patients were C4a in the preoperative period. Two weeks after the procedure, 69 patients had ecchymoses, 5 had superficial thrombophlebitis, 3 had transient paresthesia, and 1 had DVT. All these adverse effects were cured in a brief time with medical treatment. In the CA group, the saphenous veins were totally recanalized in 13 patients, and partially recanalized in 8 patients at the 6th postoperative month. S/L was performed in 5 of the total recanalization patients, and 3 underwent miniflebectomy in another session (Table 2).

In the CA group, age and female ratio were higher than the S/L group (P<0.001). The saphenous diameter in the CA group was lower than the S/L group (P<0.001), (Table 3).

The VAS score of S/L group was higher than the CA group on the 1st and 3rd postoperative days and during anesthesia (P<0.001). During the procedure, on the 7th (P<0.001) and 14th days (P=0.033), VAS score was significantly lower in the S/L group (P<0.001). S/L group described more pain in polyclinic controls on days 1 and 3 but interestingly, patients in the CA group had more pain on days 7 (P<0.001) and 14 (P<0.033) (Figure 1). In terms of pain, no difference was found between the groups at the end of the first month (P=0.395) (Table 3).

In SF-36 quality of life questionnaire, physical function score, pain score, general mental health score, social function score, emotional role score and general health score were higher in the CA group (P<0.001), while SF-36 vitality score (P<0.001) was lower, and time to starting daily activities, returning to work and starting active exercise were shorter.

CEAP clinical scoring showed significant improvement in both groups. The preoperative and postoperative VCSS scores were lower in the CA group than in the S/L group (P<0.001). In both groups, postoperative VCSS score was lower (P<0.001) compared to preoperative conditions (Table 3, Figure 2). Preoperative C2 was higher in CA group, while C4a was higher in S/L group. In postoperative CEAP classification, C0 (P<0.001) and C3 (P=0.01) were higher in CA group (Table 4).

Table 1: Demographic and general characteristics of S/L patients

	mean (SD) n (%)
Age(year)	39.77 (12.29)
Sex	
Female	103
Male	211
Family History	
Positive	147
Negative	167
Occupational risk factors	
Positive	181
Negative	133
Hypertension	
Positive	59
Negative	255
Body Mass Index	
Female	29.1 (4.3)
Male	28.7 (6.2)
Target leg	
Right	142
Left	172
VSM Diameter (mm)	10.1 (3.2)
CEAP Classification Clinic Category	
C2	71 (4.8%)
C3	217 (71.3%)
C4a	22 (16.6%)
C4b	4 (7.3%)
Pre-op VCSS	7.5 (2.1)
Patients who had undergone endovenous ablation with CA before	5
Post-operative	
Ecchymosis	297
Thrombophlebitis	79
Transient paresthesia	98
DVT	1
CFV insufficiency	53
CFV reconstruction performed patients	3
VSP insufficiency	111
Stripping performed in the same session patients	7
Ligation performed in the same session patients	104
Perforating Vein insufficiency (ligation)	91

S/L: Stripping/ligation, VSP: Vena Saphena Parva, VSM: Vena Saphena Magna, CEAP: Clinical- Etiologic-Anatomic-Pathophysiologic, VCSS: Venous Clinical Severity Score, CA: Cyanoacrylate, DVT: Deep Venous Thrombosis, CFV: Common Femoral Vein

Table 2: Demographic and general characteristics of CA patients

	Mean (SD) n (%)
Age (year)	43.1 (12.8)
Sex (n)	
Female	333 (61.4%)
Male	209 (38.6%)
Family History	
Positive	267
Negative	275
Occupational risk factors	
Positive	309
Negative	233
Hypertension	
Positive	112
Negative	430
Body Mass Index	
Female	28.7 (5.7)
Male	27.3 (3.9)
Target Leg:	
Right	250
Left	292
VSM Diameter (mm)	7.5 (1.6)
Treated saphenous vein length(cm)	29.9 (5.7)
CEAP Clinic Category	
C2	350
C3	184
C4a	8
Preoperative VCSS	6.0 (1.4)
Post-operative adverse events	
-In the first 2 weeks	
Ecchymosis	69 (12.7%)
Thrombophlebitis	5 (0.01%)
Transient paresthesia	3 (0.006%)
DVT	2 (0.004%)
-In the first 6 months	
Totally Re-canalized patients	13 (2.4%)
Partial Re-canalized patients	8 (1.5%)
Stripping performed in a different session	5 (0.01%)
Mini phlebectomy performed patients	3 (0.055%)

VSM: Vena Saphena Magna, CEAP: Clinical- Etiologic-Anatomic-Pathophysiologic, VCSS: Venous Clinical Severity Score, CA: Cyanoacrylate, DVT: Deep Venous Thrombosis

Table 3: Intraoperative and postoperative Quality of Life-VAS-VCSS and vitality

	S/L Mean (SD) n (%)	Median	CA Mean (SD) n (%)	Median	*P*-value	
Age (year)	39.5 (12.1)	39.0	43.1 (12,8)	43.0	<0.001	m
VSM diameter (mm)	10.1 (3.2)	9.0	7.5 (1.6)	7.0	<0.001	m
Sex Female	103 (32.8%)		333 (61.4%)		<0.001	X^2
Male	211 (67.2%)		209 (38.6%)			
Limb Right	142 (45.2%)		250 (46.1%)		0.798	X^2
Left	172 (54.8%)		292 (53.9%)			
SF-36 (postoperative 1st month)						
*Physical functioning	79.5 (8.1)	80.0	83.8 (7.2)	85.0	<0.001	m
*Role limitations	53.6 (32.1)	50.0	55.2 (25.8)	50.0	0.127	m
*Bodily pain	54.1 (9.1)	55.0	72.8 (11.9)	77.5	<0.001	m
*General mental health	64.3 (10.0)	65.0	78.1 (8.1)	80.0	<0.001	m
*Vitality. energy or fatigue	69.6 (8.2)	70.0	56.8 (6.7)	55.0	<0.001	m
*Social functioning	76.6 (9.9)	75.0	85.1 (9.6)	87.5	<0.001	m
*Role limitations due to emotional problems	53.0 (31.7)	66.7	68.7 (23.0)	66.7	<0.001	m
*General health perceptions	73.5 (6.9)	76.0	77.6 (7.1)	80.0	<0.001	m
VCSS (postoperative 6st month)						
Pre-operative	7.5 (2.1)	7.0	6.0 (1.4)	6.0	<0.001	m
Post-operative	2.2 (1.4)	2.0	1.5 (1.1)	1.0	<0.001	m
Intra group difference p VAS	0.000 w		0.000 w			
During Anesthesia Procedure	1.68 (0.91)	1.00	1.09 (0.29)	1.0	<0.001	m
During Procedure	0.26 (0.44)	0.00	2.15 (0.49)	2.0	<0.001	m
1.Day	4.10 (1.25)	4.00	2.26 (0.65)	2.0	<0.001	m
3.Day	3.12 (0.87)	3.00	2.36 (0.70)	2.0	<0.001	m
7.Day	1.72 (0.75)	2.00	2.97 (1.13)	2.0	<0.001	m
14.Day	0.60 (0.53)	1.00	0.68 (0.52)	1.0	0.033	m
1. Month	0.22 (0.41)	0.00	0.25 (0.43)	0.0	0.395	m
Start date of daily activities (days)	3.7 (1.0)	4.0	0.5 (0.5)	0.0	<0.001	m
Start date of Work (days)	4.9 (1.1)	5.0	1.2 (0.5)	1.0	<0.001	m
Start date of sports activity (days)	9.9 (2.9)	9.0	4.7 (2.4)	4.0	<0.001	m

m: Mann-Whitney u test, X^2: Chi-square test, w: Wilcoxon test, VSM: Vena Saphena Magna, SF-36: Short Form-36, VCSS: Venous Clinical Severity Score, VAS: Visual Analogue Scale, S/L: Stripping/ ligation, CA: Cyanoacrylate

Table 4: CEAP classification before and one year after the operation

	Preoperative CEAP			X^2-test	CEAP at the first postoperative year			X^2-test
	S/L	CA	Total	*P*-value	S/L	CA	Total	*P*-value
	314	542	856	<0.001	303	523	826	<0.001
C0.n(%)	0	0	0	*	83 (27.4)	229 (43.7)	312 (37.7)	<0.001
C1.n(%)	0	0	0	*	97 (32)	117 (22.4)	214 (25.9)	0.172
C2.n(%)	71 (22.6)	350 (64.6)	421 (49.2)	<0.001	45 (149)	60 (11.5)	105 (12.7)	0.143
C3.n(%)	217 (6..1)	184 (33.9)	401 (46.8)	0.099	61 (20.1)	93 (17.8)	154 (18.6)	0.01
C4a.n(%)	22 (7.0)	8 (1.5)	30 (3.5)	0.011	14 (4.6)	24 (4.6)	38 (4.6)	0.105
C4b.n(%)	4 (1.3)	0	4 (0.5)	*	3(1)	0	3 (0.4)	*

* Chi square test cannot be performed, CEAP: Clinical- Etiologic-Anatomic-Pathophysiologic, S/L: Stripping and ligation, CA: Cyanoacrylate

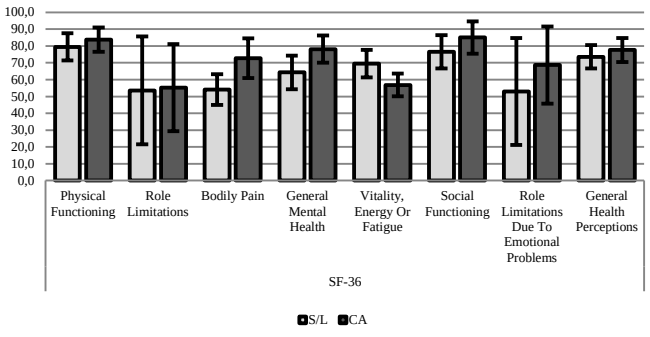

Figure 1: Comparison of SF-36 (SF-36: Short Form 36, S/L: Stripping/Ligation, CA: Cyanoacrylate)

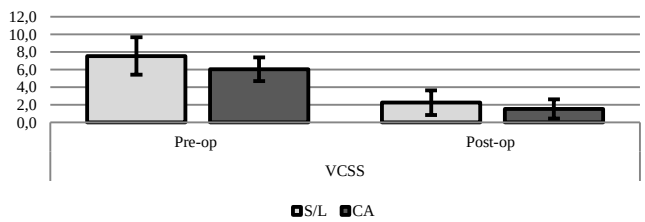

Figure 2: Preoperative and postoperative VCSS (1. Year) (VCSS: Venous Clinical Severity Score, S/L: Stripping/Ligation, CA: Cyanoacrylate)

Discussion

Because of its high prevalence, chronic venous insufficiency (CVI) causes great socioeconomic effects [6]. In recent years, minimally invasive procedures have become popular in CVI treatment for reasons such as shorter hospital stays, faster mobilization and faster return to work [7].

Although conventional or spinal anesthesia is not required as in traditional surgery, the use of thermal anesthesia in minimally invasive procedures requires preservation of perivascular tissues and skin from high temperatures [7]. However, as it is known, multiple perivascular injections related to tumescent anesthesia are difficult to apply, prolong the operation and cause possible local complications such as ecchymosis, arteriovenous fistula, pseudoaneurysm formation and paresthesia. However, as non-thermal endovenous treatment does not require an integrated anesthesia, there are no disadvantages [8,9].

N-Butyl Cyanoacrilate, which meets blood and plasma during endovenous administration in the ablation procedure, is one of the non-thermal, non-quantitative ablation methods. It rapidly solidifies and produces a rapid polymerization reaction, thus leading to ablation by the inflammatory effect on the target vessel wall [10].

Early complications (Phlebitis-Ecchymosis-Paresthesia)

In the study of Bozkurt et al., among 154 patients who underwent CA ablation, 14.2% had ecchymosis on the 3rd postoperative day, while they detected phlebitis in 7 patients. They reported that none of the patients had transient or permanent paresthesia [10].

Similar or better results were obtained in our study. Postoperative 3rd day physical examinations of 542 limbs which underwent VSM embolization with CA revealed ecchymosis in 69 (12.7%) patients, phlebitis in 5 (6.2%) patients and DVT in 1 patient. In these patients, medical treatment yielded satisfactory results at the first month visits. In 26 (4.7%) patients, transient paresthesia was detected at the first control on the 3rd day. There was no patient with complaints of paresthesia at postoperative 1st month visit. Two patients had DVT at the policlinic control at 2 weeks. Clinical findings disappeared after 3 months of warfarin treatment and recanalization occurred in CDUSG.

In our study, in line with the VSM and S/L group, ecchymosis in the first postoperative visit was observed in 297 of 314 patients who underwent the procedure and phlebitis was detected in 45 (14.3%). While 78 patients had transient paresthesia, 13 patients had permanent paresthesia at 1 month and 6 months. When the CA group in our study is examined, it is seen that thrombophlebitis rates are quite low compared to the literature [11,12]. We attribute this to the one-week LMWH we use for this group of patients. As with all minimally invasive methods, it is possible that some instrumental devices sent directly into the vessel may cause endothelial damage and that stasis in the ablated saphenous vein branches may trigger venous thromboembolism. In the literature review, LMWH was not routinely recommended or reported to be avoided to prevent post-operative complications. However, the frequency of such superficial venous thrombosis was detected between 4-5% and it was successfully treated with LMWH [12-14].

The rates of transient or permanent paresthesia secondary to nerve injury reported in S/L patient groups vary widely [15,16]. This is, of course, directly related to the technique of stripping (complete-partial, olive-olive free). Given the fact that post-operative adverse events, especially neurological damage, adversely affect the quality of life of patients, the superiority of CA ablation in this study cannot be denied.

Pain

Procedural and postoperative pain status of the patients were measured by visual analog scale (VAS). This test has been proven for a long time and is accepted in the literature. Between the two ends of a 100 mm line, the patient is asked to select the point that suits his or her condition. This test is calculated as 0 (zero): I have no pain, 10: I have the worst pain possible [17,18]. The VAS scale applied to our patients revealed less pain in the CA group during local anesthesia. This showed that spinal anesthesia caused more pain in patients than local anesthesia. During the procedure, more severe pain was detected in the CA group. We think that compression and shimic effect of cyanoacrylate during CDUSG probe use caused this pain during cyanoacrylate injection.

Discharge and return times

Ran et al. [19] reported the average discharge time of the L / S group as 3 days and the average return to work as 1 week. Chang et al. [20] reported that all patients undergoing CA were discharged on the same day of operation. Median time to return to work was 1 day (range 1-16 days). VCSS, SF-36 physical and mental scores changed from a mean of 6.91, 44.24, 54.26 at baseline to 2.43, 43.85, 52.50, respectively, at the first postoperative month. In our study, all patients who underwent CA ablation were discharged on the same day after the procedure and the mean return to work was 1.2 (0.5) days. Patients in the S/L group were discharged later. The mean time to return to work in this patient group was 4.9 (1.1) days. In addition, maintenance varicose stockings were not administered to patients in the CA group. These results were compatible with the literature.

Late complication, recanalization, efficacy, safety, and patient satisfaction:

In choosing the method, the most crucial point affecting our preferences is undoubtedly late results, as well as early results after surgery. Post-operative late-term outcomes are a particularly important indicator of the treatment efficacy. In this evaluation, re-canalization for CA ablation group and follow-up of varicose vein (vascular remodeling or neo-angiogenesis) or defective/inadequate surgical intervention are of foremost importance for the VSM S/L group. Therefore, we evaluated our patients with Venous CDUSG at their first postoperative year. We also compared pre- and post-operative VCSS values. In addition, we evaluated the satisfaction analyses of patients' quality of life with the SF-36 satisfaction questionnaire we conducted in the first month outpatient controls.

In the study of Almeida et al. [21] on long-term follow-up results of CA ablation patients in 2015, the occlusion rate was reportedly 92.0% at the 24th month follow-up. A statistically significant improvement in VCSS was reported in all patients at 24 months.

Lurie et al. [22] reported that neovascularization was observed in 4 patients during the 2-year follow-up of 36 patients who underwent S/L. In addition, cumulative rates of recurrent varicose veins were 20.9% at 1 and 2-year follow-ups. In a study by Jones et al. [23] this rate was 32%, while Creton et al. [24] reported a 12-year recurrence rate of 50%.

In our study, recurrent (neovascularization) varicose veins were found on 71(22.6%) patients in the S/L group. While 68 (95.8%) of these patients developed insufficiency in the perforated veins, 3 (4.2%) had dilatation and insufficiency in accessory saphenous veins. Among 542 patients who underwent saphenous vein ablation with CA, total and partial recanalization were observed in 13 (2.4%) and 8 (1.5%) patients, respectively. The pre-operative VCSS was 6.0 (1.4), while the post-op value reduced to 1.5 (1.1). SF-36 questionnaire form showed significant well-being in all parameters. In the S/L group, while the pre-op VCSS was 7.5 (2.1), post-op values decreased significantly to 2.2 (1.4). When both groups were evaluated in terms of VCSS, it was observed that there was statistically significant improvement in the CA group. SF-36 physical function score, pain score, general health score, social function score, emotional role score and general health score were higher in the CA group than the S/L group in the first month post-satisfaction survey. Interestingly, in the CA group, the vitality score, which was an objective assessment of vitality, energy, and fatigue, was lower than the S/L group. This showed that the patients in the S/L group felt more energetic and fuller of life, less worn, exhausted, and tired. Our results in this study were consistent and better when the literature was scanned. The following ways were followed to achieve these results: In the first policlinic examinations of the patient groups in our study, three factors were considered before choosing the method. Patient's symptoms, a detailed physical examination and detailed CDUSG findings performed by a qualified radiologist at 6-month intervals. The aim of the 6-month follow-up period was to minimize doppler examination errors, to see changes in saphenous diameter, and to encourage overweight patients to lose weight. It is evident that the weakening of the patients who are overweight, especially for S/L, will increase the comfort of the surgeon and allow a more effective S/L and a more suitable mini-phlebectomy. Patients in the CA group consisted of selected patients with lower preoperative VCSS, no dense packs, and more flat saphenous veins. The patients in the S/L group consisted of patients with dense packs, medial or lateral (sometimes both) accessory saphenous veins, and those with convoluted main saphenous veins.

Limitations

Since the aim of our study was to compare the postoperative outcomes of the patients, preoperative satisfaction surveys were not performed. In addition, although it was accepted that the patients who participated in the study voluntarily answered the questionnaire forms, we think that the answers they gave to the questionnaire forms were affected by their emotional state and physical fatigue.

Conclusion

Many factors are effective in the choice of treatment in CVI. Which method to choose in terms of patient satisfaction depends on the patient, the severity of the disease and experience

of the surgeon. Although S/L is accepted as the gold standard, minimally invasive methods seem to detract from S/L at the point of patient satisfaction, especially in patients selected for saphenous vein ablation, with non-thermal, non-tumescent CA. However, S/L + miniflebectomy remains important for patients with dense packs, tortuous, and severely extensive saphenous veins.

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Does chronic hepatitis B infection have an impact on fasting blood glucose levels and fatty liver development?

Kronik Hepatit B enfeksiyonu açlık kan şekeri düzeylerini ve yağlı karaciğeri etkiler mi?

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Abstract

Aim: The relationship between hepatitis B virus (HBV) infection and insulin resistance (IR) appears to be confusing. In this study, the goal was to compare fasting blood glucose (FBG) levels and fatty liver (FL) frequency as a reflection of IR in patients with chronic active HBV infection and to determine whether there is a relationship between liver fibrosis, FBG and FL.

Methods: In this case-control study, the study group consisted of 116 chronic HBV patients with HBV DNA levels above 2000 IU/ml. The control group included 120 healthy individuals with matching age, gender, and body mass indexes.

Results: There was no difference in FBG levels between the groups (P=0.15), but FL rates were significantly higher in patients with HBV (P=0.01; OR: 2.13, 95% CI 1.26-3.61). Although the FBG levels of groups with regards to severity of fibrosis were similar, there was a significant difference in terms of FL (P=0.07 and P<0.001, respectively). A positive correlation was found between the development of FL and the severity of fibrosis (r_s=0.216, P=0.01).

Conclusion: While FBG level appears to be unaffected by chronic active HBV infection, the frequency of FL is markedly increased in these patients. Viral factors are likely responsible for the development of FL rather than metabolic factors.

Keywords: Fatty liver, Hepatitis B, Insulin resistance, NAFLD

Öz

Amaç: Hepatit B virüsü (HBV) enfeksiyonu ile insülin direnci (ID) arasındaki ilişki kafa karıştırıcı görünmektedir. Bu çalışmada amaç, kronik aktif HBV enfeksiyonu olan hastalarda açlık kan şekeri (AKŞ) düzeyleri ile yağlı karaciğer (YK) sıklığını ID'nin bir yansıması olarak karşılaştırmak ve karaciğer fibrozunun AKŞ ve YK ile bir ilişkisi olup olmadığını belirlemekti.

Yöntemler: Bu çalışma vaka kontrol çalışması olarak planlandı. Çalışma grubu, 2000 IU/ml'nin üzerinde HBV DNA seviyesi olan 116 kronik HBV hastasından oluşturuldu. Yaş, cinsiyet ve vücut kitle indeksi uyumlu 120 sağlıklı bireyden bir kontrol grubu oluşturuldu.

Bulgular: Gruplar arasında AKŞ düzeyleri arasında fark yoktu (P=0,15), HBV'li hastalarda YK oranları anlamlı olarak daha yüksekti (P=0,01; OR: 2,13, %95 GA 1,26-3,61). Fibrozis şiddetine göre gruplar arasında AKŞ düzeyleri arasında anlamlı bir fark olmamasına rağmen, YK açısından anlamlı bir fark vardı (sırasıyla P=0,07 ve P<0,001). YK gelişimi ile fibrozisin şiddeti arasında pozitif bir korelasyon bulundu (r_s=0,216, P=0,01).

Sonuç: AKŞ düzeyi kronik aktif HBV enfeksiyonundan etkilenmemiş gibi görünse de, bu hastalarda YK sıklığı belirgin şekilde artmaktadır. Metabolik faktörlerden ziyade viral faktörlerin YK gelişiminden sorumlu olması muhtemeldir.

Anahtar kelimeler: Yağlı karaciğer, Hepatit B, İnsülin direnci, NAFLD

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Introduction

Hepatitis B, an infection of the liver, is caused by a virus (Hepatitis B virus (HBV)) that is spread through blood and body fluids. Estimations are that 350 million people worldwide are affected by the disease [1,2]. Hence, it is a major global health problem. The vast majority of people infected with HBV in adulthood are able to fight off the virus and fully recover within 1 to 3 months, although occasionally the infection can last for 6 months or more (chronic hepatitis B). In 2015, HBV resulted in an estimated 887,000 deaths, due mainly to progression to cirrhosis and hepatocellular carcinoma (HCC) [3].

Insulin resistance (IR) is when cells in muscles, body fat and liver start resisting or ignoring the signal that the hormone insulin is trying to send out. There is a worldwide rapid increase in its prevalence, and it can have serious health consequences such as metabolic syndrome (MS), fatty liver disease (FL), type 2 diabetes, cardiovascular disorders, and cancer [4]. Chronic HCV infection is linked with higher risk of diabetes mellitus and insulin resistance [5]. On the other hand, the effect of chronic HBV infection is different from chronic hepatitis C virus (HCV) infection. An experimental study indicated that the hepatitis B X protein hinders the pathway for hepatic insulin signaling, and it showed an association between HBV infection and IR [6]. The association between HBV infection and IR was further confirmed by a Korean study, which also showed that chronic HBV infected patients may require monitoring for IR and diabetes onset [7]. Many studies, however, have not shown a difference between chronic HBV infected and post-inspection healthy patients with regards to IR [8,9].

FL or hepatosteatosis, is an accumulation of fat in the liver above 5% of liver weight and it is the most common cause of chronic liver disease worldwide [11]. Many studies are investigating the link between FL and chronic HBV infection with unclear and conflicting results. Some publications report that chronic HBV infection is preventive against FL, whereas other publications report an increase in FL with HBV infection [12,13].

Considering the foregoing, the link between insulin resistance and HBV is not conclusive. Additional studies are needed on this subject, and in this study, the aim was to compare FL frequency and fasting blood glucose (FBG) levels to gain an impression of IR in patients with chronic active HBV (CAHB) infection. An additional aim was to find out whether there is a relationship between FL and liver fibrosis with FBG.

Materials and methods

This was a case control study whereby HBV patient files were reviewed for those admitting themselves into the territorial hospital gastroenterology outpatient clinic between September 2017 to March 2020. Inclusion criteria comprised HBsAg positive patients for more than 6 months, having HBV DNA > 2000 IU/ml and a liver biopsy obtained. Exclusion criteria included patients with other viral agents (such as HIV, Delta hepatitis, hepatitis C), malignancy, known diabetes, metabolic and genetic liver diseases (Wilson disease, hereditary hemochromatosis, history of hyperlipidemia, alpha-1 antitrypsin deficiency), chronic systemic disease (kidney failure, heart failure, etc.), body mass index (BMI) of 30 and above, alcohol use, and a history of drug use influencing blood sugar regulation (steroid, thiazide etc.). A control group was formed from 120 healthy individuals with matching compatible age, gender, and BMIs. Demographic data and laboratory parameters were recorded from the files of the cases.

Histopathological findings

Using the Knodell scoring between 0-6, liver biopsies in 116 patients with CAHB were noted [14]. Using the fibrosis scoring, patients with scores between 1 and 3 were classified as mild fibrosis, and above 4, as severe fibrosis.

Ultrasonography

Fatty liver was widely diagnosed with liver ultrasonography, and detection was based on thin echoes in liver parenchyma in comparison to splenic or kidney parenchyma [15]. Liver fat was classified in four groups: No liver fat, mild (G1), moderate (G2) and severe (G3) liver fat.

Ethical approval

The ethical committee of our hospital approved the study (19-2020) and it was conducted according to the Helsinki Declaration. All participants gave written informed consents prior to biopsies.

Statistical analysis

SPSS IBM 22.0 software was used for analysis, and descriptive statistics were developed for the groups. Normally distributed continuous variables were presented as mean (standard deviation), and non-normally distributed variables were given as medium (min.-max.) using categorical data and sorting via percentages and number. Group differences were analyzed with Mann-Whitney U tests and Student t-tests while multiple group comparison was performed with the Kruskal-Wallis test. Variable correlation was performed using Spearman correlation analysis and statistical significance was considered as $P<0.05$.

Results

The study and control groups consisted of 116 patients with CAHB and 120 healthy individuals. The general characteristics of the groups are presented in Table 1. The mean ages of the study and control groups were 49.60 (17.41) and 49,63(15,26) years, respectively, which were similar ($P=0.93$). While there were 72 men (62.1%) and 44 women (37.9%) in the study group, there were 62 men (51.7%) and 58 women (48.3%) in the control group. There was no difference in terms of gender distribution between the groups ($P=0.11$). Aspartate transaminase (AST) and alanine transaminase (ALT) levels were significantly higher in the study group compared to the control group (49.99 (76.14) and 27.76 (24.97), $P<0.001$; 57.02 (97.62) and 28.84 (29.55), $P<0.001$). There was no difference between the groups in terms of BMI ($P=0.31$). FBG levels in the study and control groups were 100.42 (22.76) and 102.34 (20.90), respectively ($P=0.15$).

FL rates of the groups are presented in Table 2. The frequency of FL was significantly higher in the study group compared to the control group (41.7% vs 60.3%, $P=0.01$, OR: 2.13, 95% CI 1.26-3.61).

Patients with CAHB were divided into groups according to their levels of fibrosis (absent, mild fibrosis and severe

fibrosis). Groups were compared in terms of age, gender, AST, ALT, FBG and FL (Table 3). While there was no significant difference between the FBG levels, there was a significant difference in terms of FL (P=0.07 and P<0.001, respectively).

In the correlation analysis, no relation was found between the severity of fibrosis and FBG (r_s=-0.76, P=0.27), while there was a positive correlation between the severity of fibrosis and the development of FL (r_s=0.216, P=0.01).

Table 1: General characteristics of the groups

		Control group	Study group	*P*-value
Age		49.63(15.26)	49.60(17.41)	0.93
Gender	Male	62 (51.7%)	72 (62.1%)	0.11
	Female	58 (48.3%)	44 (37.9%)	
AST		27.76(24.97)	49.99(76.14)	<0.001
ALT		28.84(29.55)	57.02(97.62)	<0.001
FBG		102.34(20.90)	100.42(22.76)	0.15
BMI		27.17(3.06)	27.78(3.10)	0.31

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, FBG: Fasting blood glucose, BMI: Body mass index

Table 2: Hepatosteatosis rates of the groups

		n	%
Control group	No FL	70	58.3
	G1	32	26.7
	G2	14	11.7
	G3	4	3.3
Study group	No FL	46	39.7
	G1	33	28.4
	G2	7	6.0
	G3	30	25.9

FL: Fatty liver

Table 3: Comparison of the groups in terms of variables according to the severity of fibrosis

	FBG	FL	AST	ALT	Age	Gender
Chi-Square	5.476	16.649	41.392	25.995	4.232	8.228
[a]*P*-value	0.065	<0.001	<0.001	<0.001	0.121	0.016

a: Kruskal Wallis Test, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, FBG: Fasting blood glucose, FL: Fatty liver

Discussion

IR is regarded as the main cause for MS and FL development and characterized by hindered insulin-mediated glucose utilization in target tissues. More studies show that IR and its related diabetes are more prevalent in chronic HBV infection [17-20]. This study's goal was to compare FBG levels and the development of FL between the control group and the CAHB group, in terms of IR. No difference could be detected between the control and study groups with regards to FBG levels or fibrosis severity. FL frequency on the other hand was higher in the CAHB group. Furthermore, a positive correlation was detected with fibrosis severity.

Important risk factor for IR is reportedly chronic hepatitis C. Hepatitis C accelerates fibrogenesis in the liver, and it is reported to cause an elevated risk of diabetes mellitus [5-21]. On the other hand, chronic HBV infections behave differently and the relationship to IR is complex. An increasing number of studies indicate that there is a positive relationship between chronic HBV infection and IR, and its underlying mechanism is that hepatitis B X protein impairs the hepatic insulin signaling path [6,7,17-20,22]. However, a study by Wang et al. [8] showed no correlation between IR in HBsAg positive patients. A meta-analysis involving 15 studies showed no risk increase for type 2 diabetes mellitus which may be due to chronic HBV infection without cirrhosis. Chronic HBV infection has been reported to elevate the risk of type 2 diabetes mellitus with cirrhosis (OR=1.74, 95% CI: 1.43-2.13), therefore the authors deduce that HBV alone may not be diabetic [23]. In their 10-year study consisting of 1233 adults, Huang et al. [9] determined that asymptomatic chronic HBV infection was not correlated with diabetes mellitus after compensation for sex, age, and BMI. In the initial medical examination of 296 non-diabetic patients, the incidence of diabetes or glucose intolerance over 10 years was not different between HBV carriers and individuals without HBV. It can be concluded that asymptomatic chronic HBV infection does not elevate the risk of diabetes. This study showed no statistically significant difference in FBG levels between the groups.

Among healthy individuals, the liver plays a particularly significant role in maintaining glucose homeostasis. Disorders in glucose metabolism, called hepatogenous diabetes, are well defined in patients with advanced cirrhosis [24]. There is also a strong relationship between the components of IR syndrome and the stage of liver fibrosis [25,26]. Therefore, as the severity of fibrosis increases, changes in the level of FBG can be expected. However, in this study, we did not find a relationship between FBG levels and the severity of fibrosis.

It is generally believed that chronic HBV infection is preventive against the development of FL [12,27]. However, the frequency of FL was higher in chronic HBV patients compared to the control group in our study. It was compatible with few other studies in the literature that gave similar results [13,28].

Limitations

Our study has various limitations, including its single center and retrospective nature, along with the small number of cases involved.

Conclusion

Our study revealed that FBG levels were similar to that of the control group as a reflection of IR in patients with CAHB, but the frequency of FL was higher. The groups were similar in terms of age, gender, and BMI; therefore, we believe that HBV infection rather than metabolic factors may play a role in the development of FL. In addition, we think that hepatic fibrosis may be associated with the development of FL, but it may not have an effect on FBG. Large-scale studies are needed for further deduction.

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Review
Derleme

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Obstructive sleep apnea syndrome (OSAS) related hypertension: A review of pathophysiology and potential therapeutic approaches

Obstrüktif uyku apne sendromu (OUAS)'na bağlı hipertansiyon: Patofizyolojisi ve tedavi yaklaşımlarına dair bir derleme

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Abstract

Obstructive sleep apnea syndrome (OSAS) is a common sleep disorder related with cardiovascular diseases, including hypertension. There are lots of evidence supporting the relationship between OSAS and hypertension, modulated by multiple factors, but the exact mechanisms underlying this complex cause and effect relationship remain unclear. The alternating pattern of OSAS-related hypertension is closely related with target organ damage, especially in the heart and brain. In this review, the etiological factors, clinical types, probable pathophysiologic mechanisms, diagnostic methods, and current therapeutic approaches to OSAS-related hypertension is discussed in the light of current literature.

Keywords: Obstructive sleep apnea syndrome, Hypertension, CPAP, Upper airway surgery

Öz

Obstruktif uyku apne sendromu (OUAS), hipertansiyon da dahil olmak üzere kardiyovasküler hastalıklarla ilişkisi olan yaygın bir uyku bozukluğudur. OUAS ve hipertansiyon arasındaki ilişkiyi destekleyen birçok kanıt mevcuttur; ancak bu kompleks sebep-sonuç etkileşiminin altında yatan kesin mekanizma halen net değildir. OUAS ile alakalı hipertansiyonun değişken yapısı, kalp ve beyinin de dahil olduğu hedef organ hasarı ile yakından ilişkilidir. Bu derlemede, OUAS ile ilişkili hipertansiyonun etyolojik faktörleri, klinik tipleri, olası patofizyolojik mekanizmaları, tanı yöntemleri ve güncel tedavi yaklaşımları güncel literatür ışığında tartışılmıştır.

Anahtar kelimeler: Obstruktif uyku apne sendromu, Hipertansiyon, CPAP, Üst havayolu cerrahisi

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Introduction

Obstructive sleep apnea syndrome (OSAS) is a prevalent disease characterized by total (apnea) or partial (hypopnea) intermittent upper airway obstruction for at least 10 seconds during sleep. During the apnea/hypopnea period, blood oxygen saturation decreases, and attacks are terminated by a hypoxia-induced sudden deep breath and awakening. This condition causes poor night-time sleep quality which is related with daytime sleepiness [1]. The American Academy of Sleep Medicine Task Force defines OSAS with an apnea-hypopnea index (AHI) >5, accompanied by excessive daytime sleepiness. The apnea-hypopnea index (AHI) is the average number of apneas and hypopneas per hour of sleep and is a parameter to indicate the severity of OSAS (AHI = 5–15 is mild, AHI = 16–30 is moderate, an AHI >30 is severe OSAS) [1,2].

Obstruction arises due to various anatomical problems in the upper airways, such as hypertrophy of palatine tonsils and adenoids (the most common cause in children), decreased tonus of the neck muscles, maxillary and mandibular retroposition, retrognathia and nasal obstruction caused by allergic rhinitis (AR) [2]. Authors also report other risk factors for OSAS, including premature birth, parental smoking for children/smoking for adults, alcohol abuse, low socioeconomic status, obesity, ageing and male gender [3,4,5]. Epidemiological studies reveal OSAS prevalence to be 3-7% and 2-5% among adult males and females worldwide, respectively [4]. Considering the substantial risk of morbidity and mortality, these rates are remarkable for health care providers. Late or undiagnosed OSAS and neglected treatment may cause significant complications, such as cognitive dysfunction, decreased work performance, and neurological, metabolic, and cardiovascular diseases [2,4,5]. Owing to its high prevalence and serious complications, OSAS is acknowledged as a public health problem.

How to diagnose OSAS?

Early diagnosis of OSAS is important to prevent serious complications. The first step of diagnosis in patients with suspected OSAS is to obtain a detailed history and conduct either the ‘Epworth Sleepiness Scale’ or ‘Berlin Questionnaire’, both of which are self-administrated. The former measures the patient's level of daytime sleepiness [6] and the latter determines the risk factors for sleep apnea [7].

The common diagnostic test for OSAS is overnight polysomnogram. It records multiple signals, including heart rate, breathing rate, electroencephalogram (EEG), electromyogram (EMG), oronasal airflow and oxygen saturation to diagnose sleep disorders in a sleep laboratory [4,8]. Because most of the patients are unaware of their pathological situation-especially patients that live/sleep alone, 70-80 % of OSAS cases remain undiagnosed [9].

OSAS and cardiovascular diseases

Polysomnographic follow-up studies indicate that hypoxia induced apnea-hypopnea periods during night sleep result in short-term changes in cardiovascular parameters, such as heart rate (HR) and blood pressure (BP) [8]. One of the most common complications of long-term untreated OSAS are cardiovascular problems, including nocturnal or persistent systemic hypertension, cardiac ischemia, pulmonary hypertension, congestive heart failure, stroke, and arrhythmia [5,10]. Vascular damage, such as increased carotid wall thickness and decreased arterial elasticity are also serious complications of OSAS related with high morbidity and mortality [11].

The mechanism underlying the relationship between OSAS and cardiovascular diseases is multifactorial. Because of many confounders such as age, obesity and smoking which take part in etiologies of both OSAS and cardiovascular diseases, it is difficult to differentiate the cause-effect relationship between the two diseases. However, there is increasing evidence that the comorbidity of OSAS and cardiovascular diseases arise independently from the confounders [5,12].

Is OSAS an independent cause of hypertension?

OSAS is known as the most common cause of secondary hypertension and remittent hypertension-related organ damage [13]. Rates of hypertension among OSAS patients range from 35% to 80%, depending on severity and duration of untreated OSAS [8]. On the other hand, 40% of hypertensive patients are also suffering from OSAS [14].

How can OSAS trigger the increase in BP? The first theory of this complex mechanism is the dysregulation of cardiovascular autonomic innervation due to sympathetic surge [8]. Apnea/hypopnea periods decrease blood oxygen levels, and hypoxia stimulates the medullary cardiorespiratory centers via chemoreceptors on the carotid body. Catecholamine surges during sleep effect autonomic cardiac modulation and cause a transient increase in heart rate and BP [15]. The indicator of severity of hypertension is considered as the hypoxia level attributed to apnea duration. Longer apnea durations cause deeper hypoxia and stronger sympathetic activation, and consequently, higher BP [13]. Also, a decrease in the sensitivity of baroreceptors and pulmonary receptors that affect cardiovascular reflexes was reported, probably due to activation of chemoreceptor reflexes [16]. Another mechanism which probably affects the sympathetic system is negative intrathoracic pressure, which occurs due to breathing against upper airway obstruction. This generates mechanical stress on the heart and large arteries by increasing left ventricular transmural pressure [1].

The second theory is oxidative stress, which increases during periodic nocturnal hypoxemia, and is thought to induce inflammatory reactions and endothelial damage. Previous studies provided lots of evidence that inflammatory process caused by OSAS takes part in the pathogenesis of hypertension. Troncoso Brindeiro et al. [17] inspected the results of sleep apnea models in rats, which were exposed to eucapnic intermittent hypoxia during sleep, and observed the secretion of excessive vascular reactive oxygen species, increased plasma endothelin-1 levels and elevated arterial BP. All were normalized after reducing oxidative stress by administration of superoxide dismutase mimetics. Endothelin-1 causes hypertension by altering endothelial function and reducing elasticity of the arterial wall. Higher levels of TNF-α (a cell-signal protein that takes part in systemic inflammation), neuropeptide-Y (a neurotransmitter in the central nervous system and a co-transmitter of noradrenaline, which increases BP) [18] and increased platelet/lymphocyte ratio

(a new biomarker for systemic inflammation) accompanying increased platelet distribution width (PDW) [19] were found in patients with OSAS-induced hypertension compared to controls and those with hypertension without OSAS.

Renin-angiotensin-aldosterone system (RAAS) activation is one of the theoretical mechanisms underlying hypertension with OSAS. There are limited data on this mechanism, but most of them point to the accuracy of this theory. A novel study [20] demonstrated that renal RAAS activity, which was measured by the level of reno-vasoconstriction, due to the effect of angiotensin II, and urine analytes associated with the RAAS signaling pathway were increased in patients with OSAS-related hypertension. In a similar study [21], alterations in effective renal plasma flow (ERPF) because of angiotensin II effect- another indicator of RAAS activity, was found to increase significantly in OSAS-related hypertension, but not in OSAS patients. OSAS can be related with several types of hypertension, which are explained below:

1. Nocturnal hypertension (NH): NH is an abnormal circadian rhythm-related BP which increases during night sleep. In normotensive subjects, nighttime BP is 10-20 % lower than daytime BP, due to the circadian rhythm of neurohumoral mechanisms. However, obstructive sleep apnea episodes trigger unusual night-time BP surges [22]. A night-time BP >110/65 is diagnosed as NH, according to the new 2017ACC/AHA guidelines [23]. Several studies indicate that remittent hypertension, especially elevations in nighttime BP levels and night-day ratio has the highest risk for end-organ damage and mortality caused by cardiovascular diseases [12,22,24].

2. Persistent hypertension (PsH): This type of hypertension is defined as high arterial BP levels (generally both systolic and diastolic) despite medical therapy with 3 antihypertensive drug combinations, including one diuretic, with all drugs at optimal doses. One third of hypertensive patients meet these criteria and OSAS is common in PsH patients. PsH is positively correlated with the severity of OSAS [1,25]. In several studies, treatment of OSAS was shown to decrease BP levels in PsH patients [25,26].

3. Masked hypertension (MH): MH is a type of hypertension with normal office BP measurements, but high ambulatory BP that can only be evaluated by ambulatory BP monitoring (ABPM). MH is often overlooked in OSAS patients, but it should be investigated in all patients with BP levels of 125/83 and above. In a current study, 30% of patients newly diagnosed with OSAS without previously known cardiovascular disease were shown to have MH by measuring 24h-ambulatory BP. This was almost equal to the rates of continuous hypertension (35.4%) [27].

4. Pulmonary hypertension (PH): OSAS-induced PH is not as common as systemic hypertension, but its prognosis is worse when untreated. Hypoxia-induced pulmonary BP elevation is thought to stem from hypoxic pulmonary vasoconstriction [28]. Pulmonary hypertension causes right ventricular distension, which affects left ventricular filling and stroke volume. Between 17-42% of OSAS patients suffer from daytime PH, and it was proven that complication rates of PH accompanying OSAS are high, including increase in right cardiac afterload, cardiac arrhythmia, or ischemic heart disease [29].

Therapeutic approach to OSAS-related hypertension

Lifestyle changes

The first and the most crucial step for attenuating severity of both OSAS and OSAS-related hypertension is weight loss. Obesity is a common risk factor for both OSAS and hypertension [1]. More than 60% of OSAS patients are overweight [30]. Follow-up studies demonstrate that weight loss increases the effectiveness of therapeutic techniques of OSAS treatment, particularly in patients with a body-mass index of (BMI) >25 [31]. The other beneficial modifications are giving up smoking, alcohol, and bedtime sedative-tranquilizers. Tobacco smoking is found to be related with sleep-disorders including snoring and OSAS, probably due to inflammation and increased reactivity of the upper airway, and it has a synergistic effect with OSAS on causing cardiovascular disease [32]. Many studies agree that alcohol and sedative-tranquilizer drug administration before bedtime decreases oropharyngeal muscle tone and disrupts nocturnal respiration by causing apnea-hypopnea periods [33,34].

CPAP (Continuous Positive Air Pressure) therapy

CPAP therapy is administered with a mask connected to a flow generator to keep airways open with the help of positive pressure. This is the most appropriate procedure for patients with moderate (AHI>20) and severe (AHI>30) OSAS, and obese patients with nocturnal hypertension. Although CPAP therapy intolerance is not rare, it is still the gold standard treatment for elective cases [35]. Researchers observed that CPAP therapy is effective in both systemic [36] and pulmonary hypertension [27] induced by OSAS. It is also shown to increase baroreceptor sensitivity [16], reduce renal RAAS activity [20], and improve endothelial function appraised by flow-mediated vasodilatation process [37] in OSAS patients with high cardiovascular risk by reduction of oxidative stress after long-term therapy.

Antihypertensive drugs

Moderate and severe OSAS patients with hypertension who develop intolerance to CPAP therapy are advised to administer antihypertensive drugs to prevent hypertension-induced target organ damage. Twenty-four hours of BP control must be provided both for nocturnal and persistent hypertension by selected daytime or nighttime doses of antihypertensives [38]. Because of inadequate evidence, there is no consensus regarding which antihypertensive drugs or which combinations should be involved in treatment protocol of OSAS-related hypertension.

Upper airway surgery

Surgical approach for OSAS is a promising option for the patients who have failed or could not tolerate CPAP therapy. The surgery basically aims to reduce or if possible, remove the obstructions in the upper airway (nasopharynx, oropharynx, or hypopharynx). The novel surgical procedures include reconstruction of nasal bones or cartilages, uvulopalatal flap (UPF), uvulopalatopharyngoplasty (removing excess tissue from palates and pharynx), laser-assisted uvulopalatoplasty, palatal implants, mandibular osteotomy, tongue reduction procedures (radiofrequency tissue reduction or reduction glossectomy), hyoid myotomy suspension, maxillomandibular advancement (enlarges retrolingual airway), adenoidectomy, tonsillectomy

etc.) [35,39]. Adenotonsillectomy is the most common first-line therapy for children with OSAS, for it improves respiratory parameters with high success rates, as measured by polysomnography [40]. In adults, reconstructive surgeries are considered Phase-1 surgeries and maxillomandibular advancement is considered Phase-2. The success rates of Phase-1 and 2 surgeries are reportedly 50-60% and 90%, respectively [41]. Resuli [42] investigated the effects of upper airway surgery on adults diagnosed with OSAS-related persistent hypertension. He evaluated 42 patients who had undergone uvulopalatopharyngoplasty (UPPP) for the treatment of mild and moderate OSAS in the 6th postoperative month and reported a significant decrease in arterial BP levels and the doses of antihypertensive drugs needed for BP control.

Conclusion

OSAS is frequently associated with a group of cardiovascular diseases including secondary hypertension. Although they have common etiological factors, such as older age, male sex, obesity, and smoking, OSAS seems to be an independent cause of hypertension. Growing number of cardiovascular morbidities is a frequent problem worldwide, and treatment of OSAS can reverse the effects of related hypertension. Therefore, early diagnosis and treatment of this combined pathology is gaining importance.

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Unilateral vocal cord paralysis following maxillofacial deformity correction

Maksillofasiyal deformite düzeltmesi sonrası gelişen unilateral vokal kord paralizi

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Abstract
General anesthesia has a low morbidity and mortality rate and is considered a safe procedure. Moderate hoarseness and sore throat are considered acceptable during the early postoperative period due to minor trauma even after first attempt noninvasive intubation. Vocal cord paralysis is an infrequent complication of endotracheal intubation. It also presents with hoarseness and that is why early diagnosis is difficult, especially if it appears after the orthognathic surgery procedure. There is only one case report of this complication after orthognathic surgery. In this case report, a 33-year-old healthy female patient who had unilateral vocal cord paralysis after bimaxillary orthognathic surgery is presented. Although hoarseness was the first symptom, it was considered as mild hoarseness due to intubation and could not be diagnosed in the early postoperative phase until the video-laryngoscopic examination was performed. Vocal cord paralysis lasted for five months and resolved spontaneously. Although very unusual, surgeons or anesthesiologists should be aware of this unpleasant complication and pay attention to vocal cord functions after orthognathic surgery. If there is no risk of aspiration, at least six months is required before performing any interventions.
Keywords: Unilateral vocal cord paralysis, Orthognathic surgery, Complication, Maxillofacial deformity

Öz
Genel anestezi, düşük morbidite ve mortalite oranına sahip, güvenli bir işlemdir. Tek seferde sağlanan, girişimsel olmayan endotrakeal entübasyon sonrası minor travma ile gelişen orta derecede ses kısıklığı ve boğaz ağrısı, erken postoperatif dönemde normal kabul edilir. Ses kısıklığı ile seyreden vokal kord paralizi ise endotrakeal entübasyonun çok nadir görülen bir komplikasyonudur. Bu nedenle özellikle ortognatik cerrahiden sonra ortaya çıkarsa erken tanı koymak zordur. Ortognatik cerrahi sonrası bu komplikasyon, sadece bir vaka raporunda bildirilmiştir. Bu olguda, 33 yaşında sağlıklı bir kadın hastada bimaksiller ortognatik cerrahi sonrası gelişen, ses kısıklığı ile seyreden tek taraflı vokal kord paralizi bildirildi. Ses kısıklığı entübasyona bağlı olarak kabul edildi ve hastada video laringoskopik inceleme yapılana kadar erken postop fazda vokal kord paralizi teşhis edilemedi. Vokal kord paralizi beş ay sürdü ve herhangi bir girişimsel tedavi uygulanmadan düzeldi. Çok nadir bir komplikasyon olmasına rağmen, vokal kord paralizi cerrahlar veya anestezi uzmanları tarafından göz ardı edilmemelidir ve ortognatik cerrahi sonrası vokal kord fonksiyonlarına dikkat etmelidir. Aspirasyon riski yoksa, herhangi bir girişimsel tedavi yapmadan önce en az 6 ay beklenmesi gerekir.
Anahtar kelimeler: Unilateral vokal kord paralizi, Ortognatik cerrahi, Komplikasyon, Maksilofasiyal deformite

Introduction

Instrumentation/manipulation of the airway is a routine part of anesthesia care. Although endotracheal intubation (EI) is associated with postoperative laryngeal morbidity, the incidence of hoarseness and vocal cord injuries is not precise [1].

Sharing the airway is one of the most problematic situations in oral and maxillofacial surgical anesthesia. Mandibular resection with EI was performed by MacEwen in 1878 the very first time. Although this method was rarely used in surgical practice before the 1960s, it is now almost as routine as placing a peripheral intravenous (IV) catheter. EI is a life-saving ventilation technique [2].

General anesthesia has a low morbidity and mortality rate and is considered a safe procedure. Among these complications, hoarseness is frequently seen in the postoperative period. Although vocal cord paralysis (VCP) is very rare, it is one of the causes of hoarseness. Factors such as the age of the patient, previous diseases, operation time, the position of the endotracheal tube and cuff pressure have been reported to cause this condition. VCP is one of the most dangerous complications of EI, resulting in severe hoarseness and aspiration [3].

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VCP must be diagnosed by video stroboscopic evaluation of laryngeal structure and function. Regarding the management, there are no studies that include a large number of these patients due to low incidence. Treatment options are voice therapy, medialization injection laryngoplasty with Hyaluronic Acid (HA) and medialization thyroplasty [3].

This report aims to present a clinical case of unilateral vocal cord paralysis (UVCP) secondary to EI for orthognathic surgery. In this case report, we are presenting a 35-year-old female who returned with the complaint of hoarseness following orthognathic surgery.

Case presentation

A 33-year-old healthy female was referred to Medipol University Mega Hospital, Department of Oral and Maxillofacial Surgery with aesthetic and functional complaints. Mandibular hypoplasia, anterior open-bite, increased overjet, decreased overbite, increased midfacial height and class II malocclusion were diagnosed. The patient was ASA-2 with no systemic diseases but a smoker. During the presurgical phase, the patient underwent leveling and alignment of maxillary and mandibular arches and removal of all prosthetic restorations.

On the day of surgery, anesthesia induction was started with aritmal® 2% (60 mg lidocaine), Dormofol® 1% (200 mg propofol), Talinat® 0.5mg/10ml (75 mcg fentanyl), and Esmeron® 50 mg/5 ml (35 mg rocuronium). One-shot nasotracheal intubation was performed despite Mallampati classification three. One mg Cezol® and 1.5 mg/kg Prednol® were administered intravenously. Local anesthesia was administered for hemostasis, for which two vials of jetocaine® (20 mg lidocaine HCl and 0.00125 epinephrine) was diluted 1:1 with a physiological saline solution. Three mm anterior and 5 mm posterior impaction for the maxilla, bilateral sagittal split ramus osteotomy and 3mm advancement for mandible and three mm anterior vertical reduction by genioplasty was achieved and surgery was terminated following hemostasis.

The patient was extubated following the observation of spontaneous respiration. She was admitted to the intensive care unit (ICU) with suspected laryngeal irritation by the suggestion of anesthesia staff and started on intravenous steroids against laryngeal edema. During the one-day ICU follow-up period, no respiratory distress was observed. As a result, the patient was discharged to a standard patient room with a relatively stable airway and vital functions. After one more day at the hospital, the patient was discharged. During intraoral suture removal at the 12th postoperative day, hoarseness was detected. The patient was consulted with the department of Otorhinolaryngology (ENT). Laryngoscopy showed normal abduction and adduction at the right vocal cord, but paralysis at the left vocal cord. Unilateral (left) VCP was the final diagnosis. There was no further pathology at oropharynx. Six months follow up was planned without any further treatment. The plan was to inject intra-chordal HA if symptoms persisted.

At the end of the first postoperative month, symptoms relieved and normal voice returned. History and clinical examination revealed laryngitis. However, symptoms returned after the recovery of laryngitis. We had to wait until the fifth postoperative month for totally recovery from VCP. The patient's consent was obtained to be presented as a case report.

Discussion

As in any interventional procedure, intubation has its complications, which can be classified as those occurring in the early and late periods. Hoarseness, subglottic stenosis, and VCP are examples of late-term complications. Minor injuries to the airway that cause temporary hoarseness are not considered as post-intubation complications. This is quite common, as high as 30% and is considered by most anesthesiologists and patients as a natural consequence of the procedure rather than a complication [4].

Multiple studies have shown that prolonged intubation may also result in severe laryngeal damage, which may lead to chronic laryngeal disability. One of the rare complications of intubation is VCP (<1% of intubations). VCP occurs due to compression of the recurrent nerve between the endotracheal tube and the thyroid cartilage. Therefore, the pressure of the cuff should be kept between 20mm Hg and 40 mm Hg. High cuff pressures can damage recurrent nerve even in short-term intubation. VCP associated with EI may also occur due to trauma during anesthesia induction or extubation. Laryngeal nerve injury and VCP may be unilateral or bilateral. The unilateral form is more common. Unilateral VCP should be considered if hoarseness, dysphonia, or dysphagia develops immediately after extubation. It generally resolves over days to months. Bilateral vocal cord injury is less common but more critical [5].

Early diagnosis is vital to avoid respiratory tract complications for VCP; however, poor prognostic factors complicate early diagnosis. Most studies have examined patients with unilateral VCP with various etiologies. There are many recommended treatment methods in the literature. Unfortunately, there is no appropriate study to evaluate treatment options in this complication. That is the main reason why efforts should be focused on prevention [6].

The incidence of VCP is very low [6]. Fauzdar et al. [7] reported the only case of VCP after an orthognathic surgery. The change in the voice quality of the cases is thought to be caused by injury to the recurrent laryngeal nerve during EI. In the present case report, the occurrence of VCP might be due to EI, extended cuff pressure, or deep and/or compressed insertion of the oropharyngeal pack. The last one was not stated in the literature as a possible cause of this unacceptable complication.

The patient underwent an unexpected recovery on the postoperative 28th day. First, we thought that the patient recovered. We realized that his recovery occurred due to laryngitis and symptoms returned after recovery from laryngitis. We hypothesized that laryngeal edema due to laryngitis caused enlargement at vocal cord region and vocal cords were able to close, hence relieving hoarseness. Our treatment plan was unilateral HA injection if the patient's symptoms did not resolve by the end of the sixth postoperative month.

The symptoms had disappeared in the follow-up examination on the 143rd postoperative day, and did not return by the 6th, 12th and 18th months. There were no relapses or any differences in speech. In another case that was reported previously, symptoms occurred in the sixth postoperative week

and lasted about five months. There was no aspiration nor any airway complication at any time during the follow-up period. In the other case report, the patient had hoarseness and noted a slight cough when ingesting thin fluids with no difficulty in consuming thick fluids. In the present case, although the patient's symptoms lasted longer, there was no difficulty in swallowing. Although the symptoms were not life-threatening, the patient was unable to speak appropriately for nearly five months and this complication affected her daily life and psychology dramatically.

As there is no treatment other than injection and nerve replacement surgery, gentle intubation, checking the cuff pressure at induction and during the procedure, inserting the oropharyngeal pack carefully, not too loose but without compression, and decreasing the total intubation time may help avoid this annoying complication. If doubt exists in one or more of these parameters, the anesthetist and surgeon should observe the vocal cord function immediately following extubation.

Conclusion

VCP is a very rarely observed complication following orthognathic surgery and postoperative edema due to intubation and upper airway infections may complicate the diagnosis. If the anesthesiologist or surgeon suspects that this complication may develop, the vocal cord function should be examined immediately. Although exceedingly rare, anesthesiologist and the surgeon should be aware of this unpleasant complication and be patient before performing corrective surgeries or HA injections.

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Anesthesia in Morgagni hernia with high PIP: A case report

PIP değeri yüksek olan Morgagni hernili hastada anestezi: Olgu sunumu

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Abstract
Morgagni hernia, a congenital diaphragmatic hernia, is usually asymptomatic. Surgery should be planned as soon as possible after diagnosis. The observation of variable degrees of pulmonary dysplasia and increased vascular resistance, and the presence of heart or other organ disorders make anesthesia management important. We describe the anesthetic management of a 2.5-month-old patient operated due to Morgagni hernia. Following intubation, peak inspiratory pressure was high, but rapidly returned to normal levels after the abdomen was opened. No complications were observed during this process in terms of anesthesia management.
Keywords: Congenital diaphragmatic hernia, Morgagni hernia, Anesthesia

Öz
Konjenital diyafragma hernilerinden biri de morgagni hernisi olup genellikle asemptomatik seyreder. Tanı konulduktan sonra cerrahi en yakın zamanda planlanmalıdır. Değişken derecelerde pulmoner displazi ve artmış vasküler direnç varlığının gözlenmesi, kalp veya başka organ bozukluklarının mevcudiyeti anestezi yönetimini önemli kılar. Biz de olgumuzda morgagni hernisi nedeniyle opere olan 2,5 aylık hastamızın anestezi yönetimini paylaşmayı amaçladık. Olgumuzun entübasyon sonrası ölçülen PIP değeri yüksek olup batın açıldıktan sonra normal düzeylere hızlı bir şekilde ulaştı. Bu süreçte anestezi yönetimi açısından herhangi bir komplikasyon gözlenmedi.
Anahtar kelimeler: Konjenital diyafragma hernisi, Morgagni hernisi, Anestezi

Introduction

Congenital diaphragmatic hernias (CDH) occur when the embryological development process fails to completely close the diaphragmatic muscle. The intra-abdominal organs are thus displaced into the thorax, which adversely affect the structural development of the thoracic organs. The reported incidence of the disease is between 1:2,500 and 1:3,500 [1]. Anterior diaphragmatic hernias, known as Morgagni hernias, represent one component of this group, with an incidence of 1-6% [2]. Patients are usually asymptomatic after birth and exhibit no symptoms until later ages [3]. Symptomatic patients usually exhibit pulmonary infection, dyspepsia, dysphagia, chest pain, and upper gastrointestinal obstruction [2]. In this case report, we describe the anesthetic management of a patient operated for Morgagni hernia who had high peak inspiratory pressure (PIP).

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Case presentation

A 2.5-month-old male weighing 6 kg was admitted to hospital with respiratory distress and inability to pass stool. The patient had been delivered at the 40th gestational week by cesarean section, weighing 3,600 g, and experienced neither respiratory distress nor cyanosis after birth. Posteroanterior and lateral lung radiography showed that the bowel loops were herniated into the thorax, and abdominal ultrasonography revealed omental fat tissues extending superiorly from an 8-mm wide area into the epigastric region, which led to the diagnosis of Morgagni hernia (Figure 1). Surgery was planned by the pediatric surgery department. Preoperative respiratory and cardiological examinations were normal. Laboratory parameters were within normal limits. The patient was taken to the operating room without premedication for 4 hours had passed since oral feeding, and monitored with electrocardiography (ECG), peripheral oxygen saturation (SPO_2) and end tidal carbon dioxide ($ETCO_2$) values. Vascular access was achieved, and fluid replacement was started with 1/3 Isodex at 160 ml/h. He was preoxygenated with 100% oxygen, and induction was performed with 0.5 mg/kg midazolam (Zolamid 5 mg / 5 ml, Vem Pharmaceutical Industry, Istanbul, Turkey), 1 mcg / kg fentanyl (Talinat 0.5 mg / 10ml, Vem Pharmaceutical Industry, Istanbul, Turkey) and 5 mg/kg pentothal (Pental sodium 1 g, I.E. Ulagay Pharmaceutical Industry Inc., Istanbul, Turkey). Rocuronium at a dose of 0.6 mg/kg (Muscuro 50 mg / 5 ml, Kocak Farma Pharmaceutical and Chemical Industry, Istanbul, Turkey) was administered for muscle relaxation, and positive pressure ventilation was avoided. After complete muscle relaxation, endotracheal intubation was performed without difficulty at the first attempt using an uncuffed tube with a 3 mm internal diameter. Anesthesia was maintained with a 50% -50% oxygen-air mixture and 2-2.5% sevoflurane (Sevorane, Abbott Laboratories, Istanbul, Turkey). Tidal volume was adjusted to 8 ml/kg/min, frequency to 22 breaths/min and $ETCO_2$ to 30-40 mmHg.

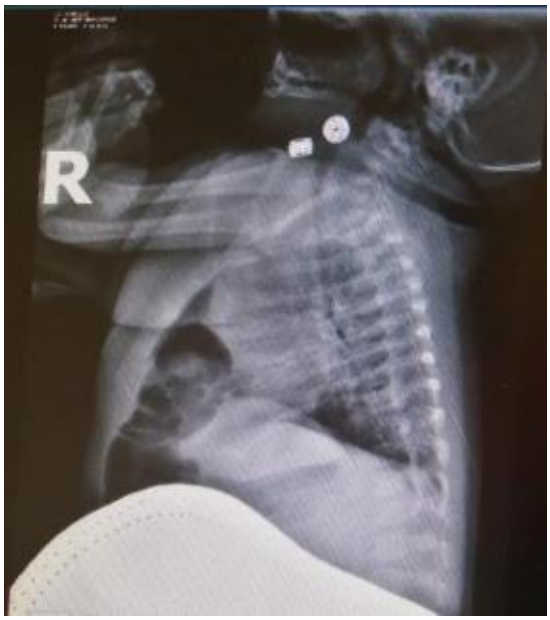

Figure 1: Lateral lung radiography showing herniated bowel loops into the thorax

Discussion

Morgagni hernia, a common entity in the pediatric age group, was first described by Morgagni in 1761. The hernia is usually located on the right and is more common in men [3,4]. Although the disease is not hereditary, comorbidity with hereditary heart diseases and other genetic diseases is present in 34-50% of cases [5]. The disease usually progresses asymptomatically until it is diagnosed incidentally in the emergency department [3]. Diagnosis is based on posteroanterior and lateral lung radiography, while thorax computed tomography (CT) and ultrasonography (USG) are also helpful [2]. Our patient was asymptomatic until presentation to the emergency department with respiratory distress and bowel disorder. Diagnosis of Morgagni hernia was based on the presence of intestinal loops in the thorax at X-ray, supported by USG.

Since patients with CDH have a high likelihood of strangulation and incarceration, which can lead to life-threatening conditions, they should be operated immediately after diagnosis [4]. According to the CDH EURO consortium consensus published in 2010 and updated in 2015, surgical repair of these patients should be performed after physiological stabilization [6].

Surgical treatment methods vary in different centers depending on the patient's clinical status, and repair is usually performed using laparotomy [7]. Although laparoscopic surgery has some advantages over open surgery, laparoscopic intervention is complicated by low mean age and body weight, the presence of varying degrees of pulmonary dysplasia, increased vascular resistance, and the presence of heart or other organ disorders [8,9]. In our case, open surgery was adopted as the surgical method because of the patient's low body weight.

The main purpose of anesthesia management in these patients is to prevent an increase in intra-abdominal pressure. Otherwise, such pressure increase will cause diaphragmatic tearing, and displaced organs to the thorax may exert pressure on the heart as a result [10]. Inhalation agents should be administered to these patients because they do not irritate the airways, prevent bronchoconstriction, and are easy to control [11]. However, the use of nitrogen protoxide should be avoided as it may cause enlargement of the intra-abdominal organs [12]. Careful adjustment of the mechanical ventilator is essential as hypoxemia and carbon dioxide retention may occur because of positive pressure ventilation [13]. At the same time, high PIP values (>35-40 cmH_2O) should be avoided to protect the patient from pressure-related complications [14]. In addition, pre-operative acid-base balance and electrolyte values should be brought to normal limits to prevent pulmonary hypertension, pulmonary vasoconstriction, hypoxemia, and hypercapnia [15]. In our case, preoperative laboratory values were normal. Consistent with the previous literature, we used inhaler general anesthetics in our case and observed PIP elevation after intubation. However, PIP values regressed to normal levels following opening of the abdomen. Vital signs were stable during surgery, and no additional problems occurred.

As in other patients undergoing thoracic surgery, postoperative pain management is important in these cases due to its restrictive effect on respiration. Otherwise, the risk of atelectasis, hypoxia and infection may increase [11]. Analgesic

control in our case was established with rectal paracetamol. No complications were encountered in the recovery room or follow-up on the ward.

Conclusions

Patients with Morgagni hernia are usually diagnosed incidentally, and the surgical procedure after diagnosis is important for anesthesia. Although there is no specific anesthetic management, selection should be made depending the clinical status of the patient and the surgery to be performed.

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An unusual cause of superficial siderosis of central nervous system: A case report of a vestibular schwannoma

Santral sinir sistemi yüzeyel siderozisin sıradışı bir nedeni: Vestibüler schwannoma olgusu

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Abstract
Vestibular schwannomas are relatively common benign tumors that account for 7-8% of all intracranial tumors. There is a limited number of cases of subarachnoid hemorrhage associated with vestibular schwannoma in the literature. The incidence of symptomatic tumor bleeding is historically reported less than 1%. Susceptibility-weighted imaging (SWI) is a relatively new Magnetic resonance imaging (MRI) sequence that is highly sensitive to compounds which distort the local magnetic field such as blood products and hemorrhage. We herein report the rare MRI findings of a 53-year-old man with unilateral vestibular schwannoma and hearing loss who was followed for 4 years. Initial diagnosis of the vestibular schwannoma was made on prior conventional MRI. We included SWI sequence in routine brain MRI protocol. During follow-up, SWI demonstrated focal superficial siderosis due to recurrent subarachnoid hemorrhage seen as hypointense blooming artifacts on the middle cerebellar peduncle-pons junction adjacent to the mass. We think that including SWI in routine MRI protocol will contribute to the initial diagnosis of acoustic schwannoma and detection of its complications such as subarachnoid hemorrhage and subsequent superficial siderosis.
Keywords: Vestibular schwannoma, Susceptibility weighted image, Superficial siderosis, MRI, Hemorrhage

Öz
Vestibüler schwannomlar, tüm intrakranial tümörlerin %7-8'ini oluşturan nispeten yaygın görülen iyi huylu tümörlerdir. Literatürde vestibüler schwannoma ile ilişkili az sayıda subaraknoid kanama vakası vardır. Semptomatik tümör kanaması insidansı %1'den daha az olarak rapor edilmiştir. Duyarlılık ağırlıklı görüntüleme (DAG), kan ürünleri ve kanama gibi lokal manyetik alanı bozan bileşiklere karşı oldukça hassas olan yeni bir Manyetik rezonans görüntüleme (MRG) sekansıdır. Bu yazıda, 4 yıllık takipteki tek taraflı vestibüler schwannoma ve işitme kaybı olan 53 yaşında erkek hastanın nadir MRG bulgularını bildirmeyi amaçladık. Olgunun vestibüler schwannoma tanısı daha önceki konvansiyonel MRG bulguları ile koyuldu. Takipte kullanılan rutin MRG protokolüne DAG sekansını dahil ettik. Takip sırasında DAG, orta serebeller pedinkül-pons bileşkesinde kitle komşuluğunda hipointens artefaktlar şeklinde izlenen, rekürren subaraknoid kanamaya bağlı fokal yüzeyel sideroz odağını gösterdi. DAG'nin rutin beyin MRG protokolüne dahil edilmesinin, akustik schwannomanın ilk teşhisine, ayrıca subaraknoid kanama ve buna bağlı yüzeysel siderosis gibi komplikasyonların tespitine katkıda bulunacağını düşünüyoruz.
Anahtar kelimeler: Vestibuler şvannom, Duyarlılık ağırlıklı görüntüleme, Yüzeyel siderozis, MRG, Hemoraji

Introduction

Vestibular schwannomas are relatively common benign tumors that account for 7-8% of all intracranial tumors [1]. Hemorrhage due to vestibular schwannoma is a very rare condition and the incidence of symptomatic tumor bleeding is historically reported less than 1% [2,3]. Bleeding may range from subarachnoid hemorrhage to massive intratumoral hemorrhage [4]. On the other hand, apart from the etiological reason, recurrent bleeding into subarachnoid space results in hemosiderin deposition along the leptomeninges in the superficial layers of the brain. This rare process is defined as superficial siderosis [5].

We herein report the rare Magnetic Resonance Imaging (MRI) findings of a 53-year-old man with unilateral vestibular schwannoma with focal superficial siderosis due to recurrent subarachnoid hemorrhage, who was followed up for 4 years.

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Case presentation

A 53-year-old man was admitted to the otorhinolaryngology department in our hospital due to progressive hearing loss on the left side. The patient did not suffer from ear discharge, pain, or fever. He and his family had no history of neurofibromatosis. Otoscopic examination was normal. The audiogram revealed sensorineural hearing loss with pure tone threshold of 78 dB in the left ear consistent with grade III (non-serviceable) hearing loss according to Gardner-Robertson Hearing Scale (Figure 1). Contrast-enhanced MRI demonstrated a vividly enhancing, lobulated left cerebellopontine lesion with extension into the intracanalicular segment of the left internal auditory canal. The mass lesion measured 23x18 mm in size and displaced and compressed the pons and the fourth ventricle (Figure 2). Susceptibility weighted imaging (SWI) was not included in our brain MRI protocol at that time. The diagnosis of vestibular schwannoma was made with conventional MRI findings. After the initial diagnosis, gamma-knife therapy was performed, and the patient was included in a follow-up program, which he dropped out of at the end of the first year to apply to another clinic. In the fourth year, he came to our department for follow-up MRI. The audiogram tests did not show any change. There was no sign of facial or trigeminal nerve paralysis. The MRI protocol included the following sequences: Axial, coronal, sagittal turbo-spin echo T2-weighted and post-contrast T1-weighted, axial gradient-echo T1-weighted, Fluid attenuation inversion recovery and SWI. A 18x15 mm residual mass lesion in the left cerebellopontine angle was observed. Findings of the pons and fourth ventricle compression were significantly regressed compared to the previous study. On SWI, there were hypointense blooming artifacts which represented focal superficial siderosis in the middle cerebellar peduncle-pons junction adjacent to the mass (Figure 3). No hypointensity compatible with an intratumoral hemorrhage was observed in the mass lesion.

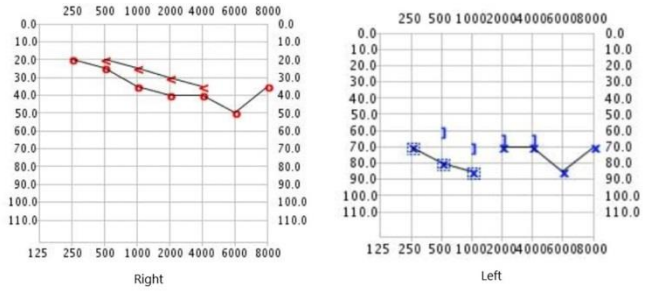

Figure 1: The audiogram of the patient

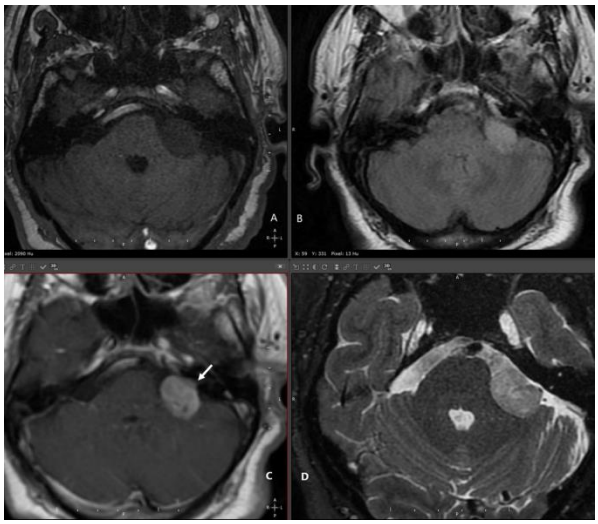

Figure 2: The first MR examination. Axial T1A (A), FLAIR (B), postcontrast T1A (C) and TSE T2A (D). Extension into the intracanalicular segment of the left internal auditory canal (white arrow)

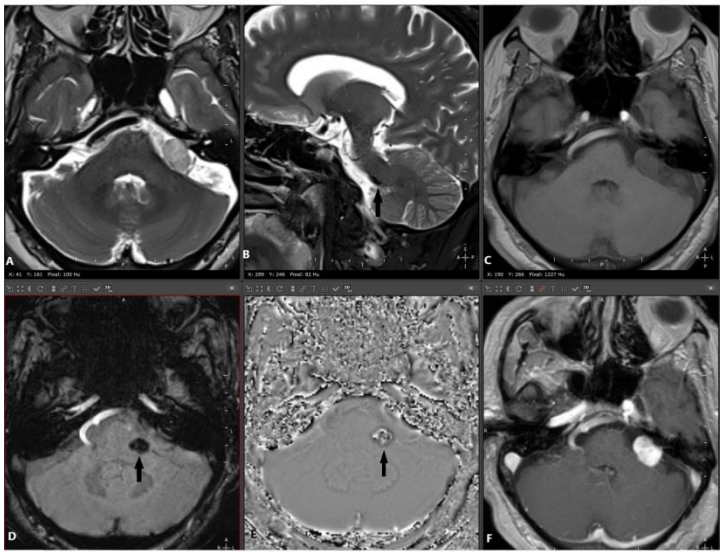

Figure 3: The last MR examination. Axial and sagittal TSE T2A (A, B), T1A (C), axial SWI and phase image (D, E), postcontrast axial T1A (F). Hypointense blooming artifacts which represent focal superficial siderosis in the middle cerebellar peduncle-pons junction adjacent to the mass (black arrows)

Discussion

Brain tumors constitute 0.4-5% of all subarachnoid hemorrhage etiologies [6,7]. Although vestibular schwannomas constitute 8% of all intracranial tumors, there is a limited number of subarachnoid hemorrhage cases associated with vestibular schwannoma in the literature. Despite the lack of an intratumoral hemorrhage finding on MRI, our patient had a focal superficial siderosis on middle cerebellar peduncle-pons junction adjacent to the vestibular schwannoma which was thought to be as a result of recurrent subarachnoid hemorrhage. In an extensive review by Kim SH et al. [2], the authors found 15 consecutive cases of subarachnoid bleeding from vestibular schwannoma. Similar to our patient, there was no intratumoral hemorrhage in 5 of 15 cases in this series.

Although the mechanisms of hemorrhage are not yet clarified, thin-walled dilated vessels, rapid tumoral growth, and cyst formation within a tumor were blamed for vascular fragility with subsequent rupture into subarachnoid space [3,8].

Clinical symptoms of hemorrhagic vestibular schwannomas depend on the size of the tumor and the type of hemorrhage. Larger tumor size (>2 cm) and presence of intratumoral hemorrhage tend to be associated with more

significant neurologic symptoms such as severe headaches, cranial nerve palsy, and even loss of consciousness due to hydrocephalus [2,9]. Our patient did not exhibit any of these symptoms.

Contrast-enhanced MRI is a valuable tool for identification of lesions in the cerebellopontine angle. Most frequent tumors of this area were meningioma and schwannoma, which account for 85–90% of all cerebellopontine angle tumors [10]. Differentiating between these two is critical because different treatment strategies need to be implemented. In their study, Mishra et al. [11] state that differentiating cerebellopontine meningioma from vestibular schwannoma with conventional imaging may be difficult. Presence of hypointense blooming artifact which represents microhemorrhages, an established histologic feature of vestibular schwannomas, is detected well by susceptibility-weighted imaging (SWI) and allows an accurate diagnosis. MRI should be the preferred modality for serial follow-up imaging in acoustic schwannomas. On MRI, residual tumor is best assessed with fat-suppressed contrast-enhanced T1-weighted images [12]. Since our cases had a history of repetitive subarachnoid bleeding with subsequent superficial siderosis, which was seen as blooming hypointensity near the middle cerebellar peduncle adjacent to the tumor on SWI, this imaging technique was thought to be one of the useful and feasible sequences for follow-up MRIs in this patient.

The treatment strategy is not different for hemorrhagic and non-hemorrhagic vestibular schwannomas, and it includes observation, surgical resection, and stereotactic radiotherapy. Especially in geriatric patients or those with small sized vestibular schwannomas with subclinical symptoms, observation is the suggested patient management strategy instead of surgical removal or stereotactic radiotherapy. Serial MRI imaging every 6-12 months is offered for observation in these patient group [3,13]. Follow-up imaging objectives could be listed as identification of recurrent or residual tumor, response to stereotactic radiotherapy, and assessment of tumor size and possible post-therapeutic complications [12]. Since our patient had grade III sensorineural hearing loss, gamma-knife radiotherapy was performed after the initial diagnosis. Serviceable hearing was preserved in first following year. The patient did not show any significant clinical symptoms or progressive hearing deterioration after stereotactic radiotherapy. MRI was chosen as the follow-up imaging modality. Unfortunately, we lost trace on him for 5 years. Six years after stereotactic radiotherapy, the patient still had a serviceable hearing. Routine follow-up MRI was suggested to the patient.

Conclusion

We believe that follow-up MRI in patients with acoustic schwannoma, SWI, is a feasible technique. It would contribute to the initial diagnosis of acoustic schwannoma and its complications, such as subarachnoid hemorrhage and subsequent superficial siderosis.

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Giant mobile left ventricular apical thrombus following silent infarction in a young patient: A case report

Genç hastada sessiz enfarkt sonrası sol ventrikül apikal dev mobil trombüs: Olgu sunumu

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Abstract
Today, percutaneous coronary treatment and anticoagulation therapies are commonly used worldwide, which is why the incidence of reported left ventricular (LV) thrombus decreased. Despite modern methods, we still encounter thromboembolic complications resulting in morbidity and mortality in a large number of patients, especially after silent infarctions. Because of high embolism risk, early detection of LV thrombus is crucial. We present the rare and interesting case of a 34-year-old patient diagnosed with a large, fragmented, very mobile left ventricular apical thrombus after silent myocardial infarction due to total occlusion of left anterior descending coronary artery.
Keywords: Silent myocardial infarction, Left ventricular thrombus, Embolism risk

Öz
Günümüzde perkütan koroner girişimler ve antikoagülan terapilerin dünya çapında yaygın kullanımı nedeniyle sol ventrikülde trombüs oluşma insidansı geçmişe göre daha azdır. Modern metodlara rağmen, özellikle sessiz enfarktlardan sonra olan ve geniş bir hasta popülasyonunda mortalite ve morbidite ile sonuçlanan tromboembolik komplikasyonlar ile karşılaşmaktayız. Yüksek emboli riski nedeniyle sol ventrikül trombüslerinin erken teşhisi kritik önem taşımaktadır. Sol ön inen koroner arterin total tıkanmasına bağlı sessiz enfarkt sonrası sol ventrikül apikal kısımda büyük, fragmante, ileri derecede mobil trombüs tanısı koyduğumuz ilginç ve nadir görülen 34 yaşındaki vakayı sunmaktayız.
Anahtar kelimeler: Sessiz miyokard enfarktüsü, Sol ventrikül trombüsü, Emboli riski

Introduction

Left ventricular (LV) thrombus mostly occurs in case of impaired LV function as a result of LV aneurysm due to prior myocardial infarction (MI). It is one of the most life-threatening complications of those conditions [1].

Patients with large anterior myocardial infarcts, LVEF value of less than 40%, severe akinesis or dyskinesis are under elevated risk of LV thrombus, which is most common in the apex and rare in the septum and the inferolateral wall [2]. The incidence of post-infarction complications is significantly reduced by percutaneous coronary intervention and effective anticoagulant therapy. Despite these widely used treatments, we still encounter complications of silent infarction. Two-dimensional echocardiography has high sensitivity (95%) and specificity (85-90%) for diagnosis and allows assessment of the embolic potential of LV thrombus [3,4].

We herein present our case diagnosed with a giant, very mobile, and fragmented LV thrombus who was successfully treated by left ventriculotomy with concomitant coronary artery bypass surgery.

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Hasta Onamı: Yazarlar çalışmada görüntüleri sunulan hastadan yazılı onam alındığını ifade etmiştir.

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Case presentation

A 34-year old male patient with no previous cardiac history was admitted to the emergency department due to difficulty breathing. His complains had continued for a year but worsened after arguing with his mother. He also had a history of admission to the psychiatry clinic because of a smoking addiction but no family history of cardiovascular, pulmonary, or hypercoagulable diseases. His general and systemic examination was unremarkable.

Electrocardiogram (ECG) showed sinus rhythm and non-specific 1 mm elevation in chest derivations V1-V3 without any reciprocal change. Creatinine kinase (CK), CK-MB, troponin I, D-dimer levels and the rest of hematological parameters were within normal range.

2D echocardiography revealed antero-apical akinesia with apical aneurysm, including a large, mobile, two-fragmented thrombus. A highly mobile component sized 24x38 mm and a less mobile component, 16x22 mm in size, was attached to the apex (Figure 1A). Both components had a very thin connection, thus, a remarkably elevated risk of embolism (Figure 1B). Inferior, posterior, and basal segments were contractile enough.

The patient was admitted to the coronary care unit and surgery was planned immediately. He underwent cardiac catheterization before surgery. It revealed 100% occlusion of proximal LAD with distal weak filling via bridge collaterals (Figure 2A), 20% plaques in left CX and normal RCA. LAD also had retrograde filling from RCA via collateral coronary arteries (Figure 2B, 2C). The patient underwent left ventricular thrombectomy with concomitant coronary artery bypass graft surgery (CABG). After the surgery he was well, and no thrombus was detected in follow-ups.

The patient was informed about the study and the consent form was signed.

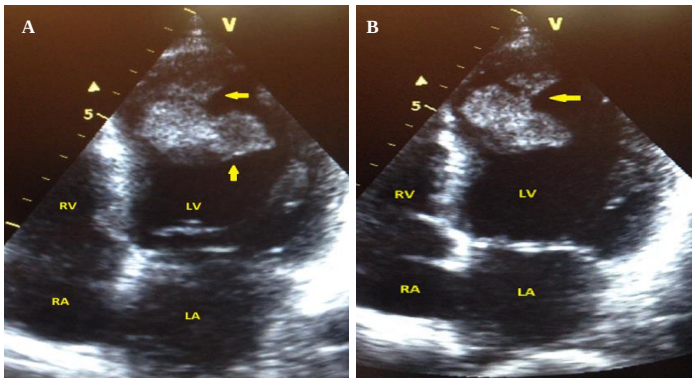

Figure 1: A: Two-dimensional transthoracic echocardiogram (apical 4-chamber view) showing the highly mobile and less mobile components of LV thrombus attached to the apex (arrow). B: Two-dimensional transthoracic echocardiogram (apical 4-chamber view) revealing the thin connection between two components of LV apical thrombus (arrow) (LA: left atrium, LV: left ventricle, RA: right atrium, RV: right ventricle)

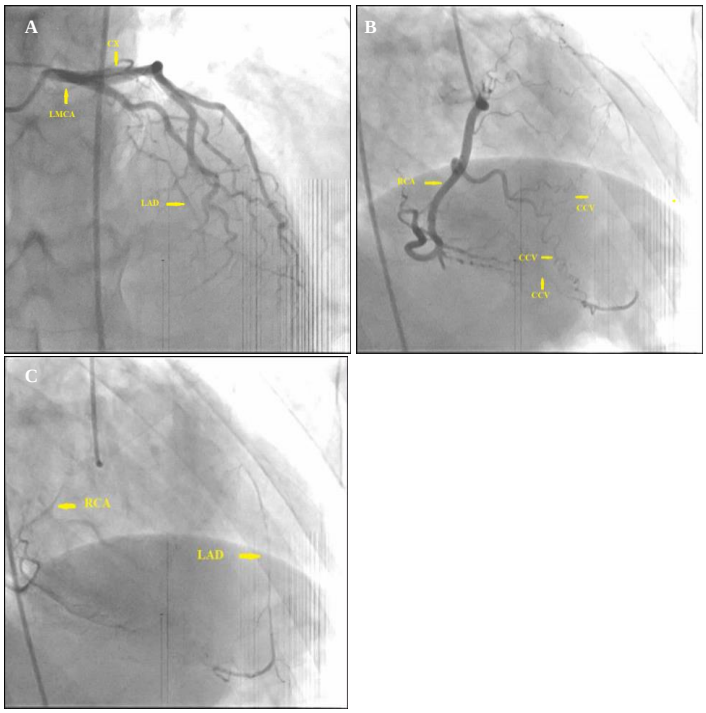

Figure 2: A: Coronary angiogram demonstrating LMCA, CX, occlusion site and distal weak filling via bridge collaterals of LAD (arrow), B: Coronary angiogram demonstrating CCA from RCA to LAD (arrow), C: Coronary angiogram demonstrating retrograde filling of LAD via CCA from RCA (arrow) (CCA: coronary collateral artery, CX: circumflex, LAD: left anterior descending, LMCA: left main coronary artery, RCA: right coronary artery)

Discussion

LV thrombus is a serious complication of large anterior MI and subsequent heart failure. There is an increased risk of thromboembolism in such patients, especially following silent infarct.

Echocardiography is important to evaluate cardiac function and scan for complications in patients who had prior MI. Patients who suffered from embolic complications, such as cerebrovascular events, should also be scanned to highlight the source of embolism [5,6].

We know that LV thrombus is mostly seen after large anterior infarction. But in our case, left anterior descending artery (LAD) was thin, which revealed that LV thrombus may occur not only after wide infarctions but after limited infarctions as well.

The most of LV thrombi are of the mural, flat and immobile type, with a lower tendency to embolize. Under anticoagulant treatment, some of them may resolve and the rate of systemic emboli may be reduced significantly [7]. Unfortunately, our patient suffered from the rare mobile type. Since the components of thrombus had a very thin connection, there was an elevated risk of systemic embolism. Therefore, immediate surgery was planned following coronary diagnostic catheterization.

The troponin level is a crucial factor to predict postoperative outcomes, such as death or in-hospital cardiac events [8]. In our patient, troponin level was within the normal range and he had an event-free postoperative period.

Conclusion

Because of the elevated risk of life-threatening embolic events, recognition, and urgent treatment of thrombotic complications due to prior myocardial infarction is crucial. Especially in young patients with silent MI and atypical symptoms, diagnosis can be difficult.

We want to emphasize that 2D echocardiography is a simple, non-invasive, inexpensive, fast, and effective technique to detect LV thrombi or any other urgent cardiac pathologies and it should be part of routine examination of even asymptomatic young patients.

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Gallbladder injury after blunt abdominal trauma: Imaging clues for diagnosis

Künt abdominal travma sonrası safra kesesi hasarı; Teşhis için görüntüleme ipuçları

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Abstract
Traumatic gallbladder injuries are rare and difficult to diagnose. Even if imaging methods including ultrasonography, computed tomography (CT) and magnetic resonance imaging (MRI) are used, it is highly challenging to detect a defect in the gallbladder wall. In a patient with blunt abdominal trauma, these clues should raise suspicion of gallbladder rupture: Hepatic laceration extending to the gallbladder area, increased abdominal distention and abdominal pain in physical examination, unfilled gallbladder and intra-abdominal increased fluid in imaging. Free fluid sampling should be performed in such patients. We herein presented the diagnostic processes of a 33-year-old woman who underwent laparotomy due to gallbladder rupture with hepatic laceration after a traffic accident.
Keywords: Blunt abdominal trauma, Gallbladder rupture, Imaging clues

Öz
Travmatik safra kesesi yaralanmaları nadirdir ve teşhis edilmesi zordur. Ultrasonografi, bilgisayarlı tomografi (BT) ve manyetik rezonans görüntüleme (MRI) gibi görüntüleme yöntemleri kullanılsa bile safra kesesi duvarındaki defektleri tespit etmek oldukça zordur. Ameliyattan önce safra kesesi rüptürünün teşhisi genellikle güçtür. Künt karın travması olan bir hastada, klinik takipte, sayılan ipuçları safra kesesi rüptüründen şüphelendirmelidir: Görüntülemesinde safra kesesi bölgesine uzanan hepatik laserasyon, takiplerinde artmış abdominal distansiyon ve abdominal ağrı, takip görüntülemelerinde hiç dolmayan safra kesesi ve karın içi artmış sıvı. Bu tür hastalara serbest sıvı örneklemesi yapılmalıdır. Burada, laparotomi uygulanan 33 yaşında trafik kazası sonrası karaciğer laserasyonu bulunan bir kadın hastanın safra kesesi rüptürü tanısı ve tanıya götüren ipuçları takdim edildi.
Anahtar kelimeler: Künt karın travması, Safra kesesi rüptürü, Görüntüleme ipuçları

Introduction

Blunt injuries to the gallbladder are exceedingly rare, while penetrating gallbladder traumas occur more frequently, because the gallbladder is protected by peripheral organs such as liver, intestines, omentum, and ribs. The diagnosis of gallbladder rupture before surgery is generally difficult. Specific symptoms are not observed, and accompanying organ injuries are frequently seen [1,2]. Gallbladder rupture is usually diagnosed in patients who are taken to emergency laparotomy due to accompanying additional organ injuries. However, even in isolated gallbladder rupture that does not require an urgent operation, early diagnosis of rupture is difficult due to the absence of specific symptoms [2]. Even if imaging methods including ultrasonography, computed tomography (CT) and magnetic resonance imaging (MRI) are used, it is highly challenging to detect the defect in the gallbladder wall. In this paper, we presented a case and discussed which clinical and imaging findings should raise suspicion for gallbladder rupture.

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Case presentation

Emergency radiology trauma records and abdomen computed tomography (CT) images obtained between 1 August 2019 and 31 January 2020 were scanned for cases of gallbladder rupture after blunt abdominal trauma and clinical-radiological findings. Abdominal CT examination was performed by using the 64-MDCT scanner (multi-slice CT Aquillion 64, Toshiba). The enhanced CT images were obtained during the portal venous phase after intravenous administration of nonionic contrast material. Enhanced CT with oral or rectal contrast was not performed, since this method was not commonly used in our radiology unit.

Only one patient who underwent laparotomy showed gallbladder rupture with hepatic laceration after a traffic accident. She was 33 years old. Medical records were examined in terms of how and when the ruptured gallbladder diagnosis was made. On admission to our emergency department, her vital signs were stable, and she was alert. Physical examination revealed right upper quadrant tenderness without signs of defense. Complete blood count revealed a white blood cell count of 21,800/mm^3 and a hemoglobin level of 12.0 g/dl. Enhanced abdominal CT suggested a liver laceration in hepatic segment 5 and a small amount of hemorrhagic ascites around the liver. The tentative diagnosis was liver injury with WSES classification grade I [3]. Since the patient's clinical and laboratory findings were stable, emergency surgery was not considered and remained conservative. However, abdominal pain increased, and distention developed over time on the 2nd and 3rd days of admission. It was noteworthy that the gall bladder was never full, including the 1st day of control abdominal tomography images. The gall bladder was contracted in 3 consecutive abdominal tomography images obtained on the 1st, 2nd and 3rd days of admission, and intraabdominal free fluid gradually increased in tomographic images. Percutaneous drainage of the ascites was performed, and the aspirated fluid was bloody and almost purely bilious. When gallbladder rupture was suspected at this stage and the CT images of contracted gallbladder was examined at magnification, a wall defect was detected (Figure 1). The patient was taken to emergency laparotomy, which showed biliary ascites in the upper right abdominal quadtrant with the gallbladder covered by edematous greater omentum. After isolating the gallbladder, a rupture was seen in the gallbladder body, as suggested by CT. Standard cholecystectomy was carried out. The postoperative course was uneventful. The consent was obtained from the patient.

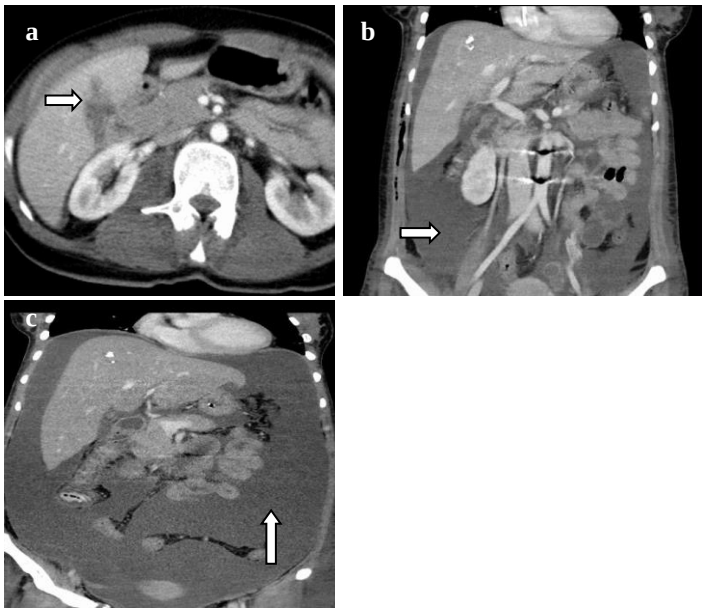

Figure 1: a: 1st day CT, enhanced abdominal CT revealed liver injury with WSES classification grade I. b: 2nd day CT, intraabdominal free fluid was gradually increasing. c: 3rd day CT, an abdominal distention developed, the gall bladder was never full.

Discussion

Gallbladder injury is most commonly caused by a penetrating wound [4]. Blunt traumatic gallbladder injury is rare, the most common causes being accidents associated with motor vehicles, falls, blows, kicks, or industrial work [4,5]. Blunt gallbladder injury is classified into three types: contusion, avulsion, and laceration (rupture or perforation), and lacerations are the most common after blunt injury [5,6]. Diagnosis of gallbladder rupture before surgery is generally difficult.

The use of imaging methods such as CT and sonography are beneficial for early diagnosis of gallbladder perforation. Sonography is a first-line modality for evaluation of intra-abdominal trauma, so awareness of sonographic findings related to gallbladder perforation are crucial for early diagnosis. These findings include a complex echogenic pericholecystic fluid collection, a thickened-edematous gallbladder wall, a collapsed gallbladder lumen despite prolonged fasting, and break of the gallbladder wall with focal loss of its reflectivity [7].

CT scan is the most useful examination when diagnosing abdominal injuries and avulsion gallbladder injuries can easily be diagnosed by CT because the gallbladder is torn from the liver and hemorrhage is obvious. However, no specific signs are revealed on CT for laceration in gallbladder injuries [6,8]. Despite the substantial leakage of bile into the peritoneal cavity in our case, we could not determine whether it was caused by a gallbladder injury or liver laceration, and further examinations and treatments were required because of the persistent high-volume bile leakage [4].

On CT images, hepatic laceration extending to the gallbladder area, unfilled gallbladder, and intra-abdominal increased fluid should raise suspicion of gallbladder rupture. Free fluid sampling should be performed in such patients when compatible with clinical findings.

A swollen postprandial gallbladder is at increased risk for a trauma, as an increased truncation force is produced between the fluid-filled gallbladder and the hepatic parenchyma [9]. Paradoxically, a chronically diseased gallbladder with a thickened wall has a preventive effect against gallbladder injury.

High serum ethanol can also raise the risk for a gallbladder injury in trauma. Tone of Oddi Sphincter is increased by alcohol, which causes gallbladder dilatation [9,10].

Laparoscopic cholecystectomy is advised as a safe and effective operation in the diagnosis and cure of traumatic gallbladder injuries [11,12]. In our patient, exploratory laparotomy and cholecystectomy were performed due to the delay in the identification.

Conclusion

Diagnosis of gallbladder rupture before surgery is generally difficult. In a patient with blunt abdominal trauma, the following clues should raise suspicious of gallbladder rupture: Hepatic laceration extending to the gallbladder area, increased abdominal distention and abdominal pain in follow-up clinical evaluation, unfilled gallbladder and intra-abdominal increased fluid in follow-up imaging. Free fluid sampling should be performed in such patients.

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Breast myofibroblastoma: Report of two cases with literature review

Meme myofibroblastom: Literatür taraması ile iki olgu sunumu

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Abstract
Myofibroblastoma (MFB) is a rare mesenchymal benign tumor that arises from the stromal structures of the breast tissue. It occurs in the elderly without sex predilection. Its clinical and radiological presentations are aspecific, thus MFB may be confounded with other malignant and benign breast lesions. However, the main histological characteristic of MFB is the presence of spindle cellsin a collagenous background. In immunohistochemistry, MFB is positive for vimentin and CD34 with a noticeable low mitotic activity. Surgical excision remains the treatment cornerstone, with excellent outcomes. We retrospectively reviewed the records of all the patients who underwent surgery of breast from 01 January 2012 to 31 December 2018. We found two cases of breast myofibroblastoma. The first was a young woman aged 17 years, and the second was a male aged 87 years. The main symptom was a palpable breast lump in both patients. The radiological work up concluded to a benign lump in the young woman, and a suspicious breast lump in the man, to whom we performed a core biopsy. Histology staining showed the features of MFB. The woman underwent a lumpectomy, and the man underwent a mastectomy. Final histological staining showed spindle cells with a collagen matrix. The cells were positive for CD34, vimentin, and actin. Those features were compatible with the diagnosis of breast MFB. The aim of this report was to describe the clinical, radiological and histological features of breast MFB.
Keywords: Myofibroblastoma, Breast, Spindle cell

Öz
Miyofibroblastom (MFB), meme dokusunun stromal yapılarından kaynaklanan nadir bir mezenkimal benign tümördür. Cinsiyet farkı olmadan yaşlılarda daha sık görülür. Klinik ve radyolojik sunumları özgündür, bu nedenle MFB diğer malign ve benign meme lezyonlarıyla karıştırılabilir. Bununla birlikte, MFB'nin ana histolojik özelliği, iş mili hücrelerinin kollajen zemininde varlığıdır. İmmünohistokimyada MFB, belirgin düşük mitotik aktiviteye sahip vimentin ve CD34 için pozitiftir. Cerrahi eksizyon, mükemmel sonuçlarla tedavi temelini korumaktadır. 01 Ocak 2012 - 31 Aralık 2018 tarihleri arasında meme ameliyatı geçiren tüm hastaların kaydını retrospektif olarak inceledik. İki meme miyofibroblastom olgusu bulduk. Birincisi 17 yaşında genç bir kadındı, ikincisi 87 yaşında erkekti. Her iki hastada da ana semptom elle tutulur bir meme yumrusuydu. Radyolojik çalışma genç kadında iyi huylu bir tümör ile sonuçlandı, ancak erkekte görüntüler şüpheli bir tümör ortaya çıkardı. Adam için çekirdek biyopsi yaptık. Histoloji boyama MFB'nin özelliklerini gösterdi. Kadına lumpektomi, erkeğe mastektomi uygulandı. Son histolojik boyama, kollajen matriksli iğ hücrelerini gösterdi. Hücreler CD34, vimentin ve aktin için pozitifti. Bu özellikler meme MFB tanısı ile uyumluydu. Bu raporun amacı, meme MFB'nin klinik, radyolojik ve histolojik özelliklerini tanımlamaktı.
Anahtar kelimeler: Myofibroblastom, Meme, İğ hücresi

Introduction

Myofibroblastoma (MFB) is a rare benign spindle cell tumor arising from mesenchymal stroma [1]. It affects older men and postmenopausal women [2]. MFB was reported in severe sites such as the head, neck, extremities, buttock, vulva, testicular region, inguinal areas, and breast [2-7]. Due to its rarity and the lack of pathognomonic clinical and radiological signs, the diagnosis may be postoperative. On the histopathological, and immunohistochemical front, MFB is characterized by the presence of spindle cells enshrined in a collagen matrix, low mitotic activity, and positivity of CD34 and vimentin [2].

We aimed to report two cases of MFB occurring in different genders with different ages and focusing on differential diagnosis.

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Case presentation

Case 1

A 17-year-old female presented with complaints of a left palpable breast mass since two years. The patient didn't have a remarkable personal or familial medical history. Physical exam revealed a well-defined, smooth and mobile mass located in the external upper quadrant of the left breast. There was no palpable lymph node in the armpit region. Ultrasonography showed a heterogeneous, hypoechoic, well-circumscribed lesion without microcalcifications (Figure 1). The mass measured 22 mm and was classified as Breast Imaging-Reporting and Data System 3 (BI-RADS). We didn't perform a core biopsy due to the probable benignity of the breast lesion. The patient underwent a lumpectomy. The histological features revealed a myofibroblastoma of the breast with free margins. The patient is currently free of disease with 8 years of regular follow-up.

Case 2

A 87-year-old male consulted for a right breast mass that had been evolving for 3 years. On physical examination, there was a voluminous, firm and mobile mass in the right breast that measured 7 cm. The contralateral breast was free of abnormalities and the lymph nodes were normal.

On breast ultrasound, a well-defined, hyperechoic, heterogeneous, voluminous mass of suspicious appearance was detected in the right breast. On mammography, the mass was hyperdense and involved the whole right breast (Figure 2). The lesion was considered BI-RADS 4c.

A micro biopsy of the mass was performed, and histological findings revealed a breast myofibroblastoma. The patient underwent a mastectomy for the large tumor's size. The definitive histological assessment showed the features of MFB of the breast, with free margins. The patient didn't experience any recurrence within a follow-up of 6 months.

Histological findings

Macroscopically, the lesions were well-defined, with a grayish color. We did not observe hemorrhage in any of the sections.

Microscopically, spindle cell was the predominant cell type. In the second case, we detected mature adipocytes without any epithelial structure. The spindle-shaped cells were arranged in irregular short bundles separated by hyalinised collagen tissue. In both cases, we found rounded cells with a pseudo-epithelial appearance without clear cytonuclear atypia (Figure 3). We didn't observe mitosis or necrosis.

The immunohistochemistry was established in both cases. These fusiform cells were positive for actin, vimentin, and CD34, and negative for Cytokeratin and βCatenin (Figure 4). The proliferation index Ki 67 was estimated at 5% in both cases. These morphological and immunohistochemical findings were compatible with the diagnosis of breast myofibroblastoma.

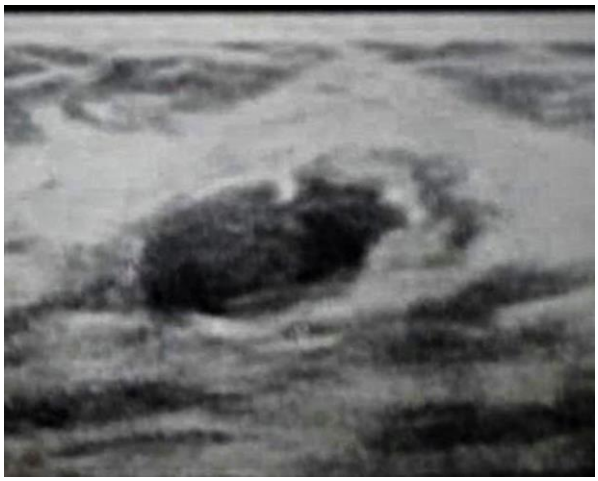

Figure 1: Ultrasonography image showing a heterogeneous, hypoechoic, well-circumscribed lesion of left breast, and measured 22mm

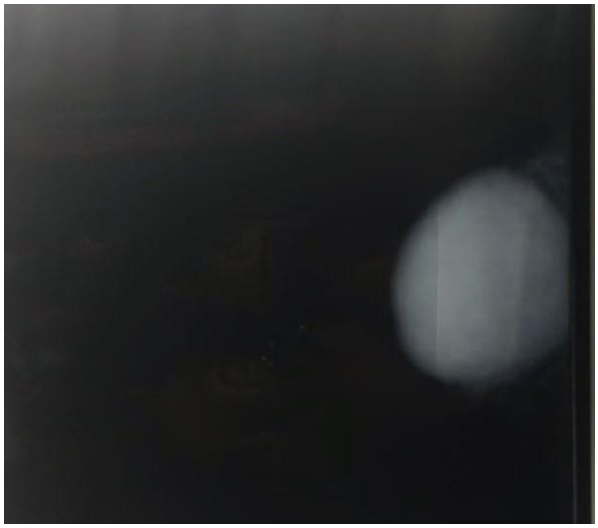

Figure 2: Mammographic image: hyperdense mass involving the whole right breast

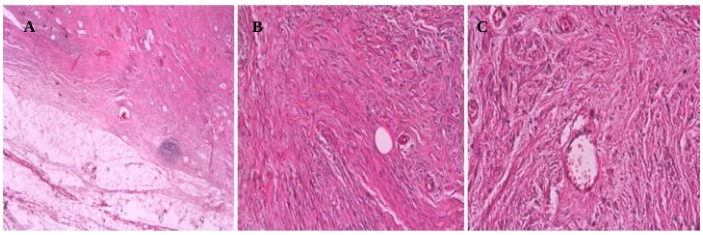

Figure 3: Microscopic image, hematoxylin-eosin staining (HES), (A) - Unencapsulated tumor with circumscribed border, (HES x 50) (B) - Fascicles of spindle cells separated by dense collagen bundles and entrapped adipocytes (HES x 100); (C) - Fibroblastic-like cells with scanty cytoplasm and elongated nuclei (HESX200)

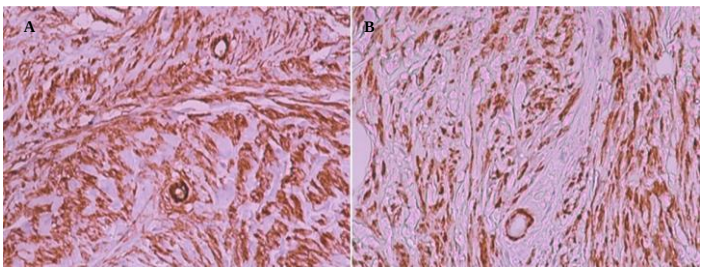

Figure 4: Immunohistochemistric image (IHC), (A) - Myofibroblast showed positivity for vimentin (IHC X200); (B) - Myofibroblast showed positivity for CD34 (IHC x 200)

Discussion

Breast myofibroblastoma is a rare, mesenchymal benign tumor firstly described by Wrgotz in 1987, who reported 16 cases [1]. Until now, only single case reports or small case series have been described in the literature.

Extra-mammary lesions are most common in older men [2]. Several extra-mammary locations have been reported, including the head, neck, extremities, buttock, vulva, and

testicular region [3-6]. The most frequent site is the inguinal region [5,7].

Magro et al. [2] studied 70 cases of breast MFB, and they witnessed that the tumor has a postmenopausal and older men's predilection. At presentation, the age ranged from 40 to 87 years. In our study, we reported a case of a 17-year-old woman, without any remarkable personal or familial history.

The risk factors for developing MFB are uncertain. However, in some reports, there was an association between renal and prostatic neoplasms with breast MFB [8]. Furthermore, some patients presented with gynecomastia, but our patient didn't have it [2,8,9]. MFB was also reported after breast cancer excision at surgical scar sites or after chest wall trauma [8,10,11].

So far, many authors suggested physiopathological explanations to understand mechanisms leading to the onset of this rare entity. Some authors suggested the role of steroid sex hormones as estrogen, progesterone and androgen receptors which were present in severe cases and associated with gynecomastia [2,9]. The second explanation was the disruptions in cytokine secretions and inflammation after trauma, leading to a transformation of tumor growth factors (TGF) in TGFβ. These findings are supported by the presence of tumor necrosis factor (TNF) and fibroblastic peptide-trophic growth factors in MFB [9]. The third explanation was the migration and transformation of fibroblasts to the surgical site after surgery [8].

Clinically, MFB may be asymptomatic and diagnosed by accident due to mammographic screening in postmenopausal women or in the context of gynecomastia [9]. However, it is usually described as a solitary, firm, slowly growing, and well-defined lump [2]. There is no documentation of axillary lymph nodes or changes in the skin and nipple.

Radiologically, there is no pathognomonic sign for the diagnosis of MFB. Ultrasonography is the first-line examination, and shows a well-defined mass, with mixed echoic patterns [10]. Mammography currently shows a heterogeneous well-defined tumor without microcalcifications. Magnetic resonance imaging (MRI) is not common to diagnose MFB, only a few cases were studied, and there were no specific signs [12].

In that regard, many differential diagnoses may arise including benign lesion as fibroadenoma, neurofibroma, lymphangioma, angiolipomas, hematoma, abscess, and malignant lesion as phyllodes tumor, carcinoma and sarcoma [10].

In our second case, we suspected a malignant lesion due to the hyperdense mass involving the entire breast. For the purpose of defining the surgical procedure, we performed a core biopsy in order to acquire a histological diagnosis.

Macroscopically, MFB is a fairly limited, firm, a whitish greyish tumor of variable size. Histologically, it consists of a proliferation of fusiform cells arranged in irregular short beams separated by thick ropes of hyalinised collagen, without atypia with a low mitotic index [1]. These cells correspond to myofibroblasts and intermediate cells between fibroblasts and smooth muscle cells [9]. In immunohistochemistry, these cells express CD 34, vimentin, actin, estrogen receptors and progesterone receptors [2,9]. Cytokeratins, c-kit, and S-100 proteins are always negative [9,11], even though the expression of desmin, SMA, bcl-2, and CD99 is variable [13].

The prognosis of MFB is excellent. Treatment remains as surgical excision. Malignant transformation of myofibroblastoma wasn't previously reported. That leads to reconsider surgical procedures in this benign neoplasm [10].

Conclusions

Myofibroblastoma is a benign, slowly growing tumor. Many differential diagnostic problems are raised and rectified by pathological and immunohistochemical examination. The treatment is based on surgical excision with excellent outcomes.

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