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The role of surgery in stage IV breast cancer: Clinical experiences of 62 patients

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Ethics Committee Approval

The study was approved by the Karamanoğlu Mehmet Bey University Clinical Research Ethics Committee (Date: August 31, 2022, Decision No: 08-2022/10).

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

Conflict of Interest

No conflict of interest was declared by the authors.

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Abstract

Background/Aim: The effect of surgical intervention on the quality of life and survival of patients presenting with metastatic breast cancer is a controversial issue. In this study, we aimed to reveal the survival, clinical, and pathological differences in patients with breast cancer who had metastatic disease at diagnosis and who underwent and did not undergo surgery for the primary tumor in our clinic and to evaluate the efficacy of surgical approach on the course of the disease.

Methods: In this retrospective cohort study, the data of patients with metastatic breast cancer in our clinics between January 2000 and June 2021 were retrospectively analyzed. The study included those with primary metastatic disease. The study did not include male patients, patients with primary non-breast tumors, those who died of causes unrelated to breast cancer, those who underwent surgery for metastatic foci other than the primary tumor, and those who could not be followed up regularly for various reasons. In our study, there were two groups; those who received only systemic therapy were assigned to Group 1, while those who underwent surgical treatment for the primary tumor were assigned to Group 2. The clinicopathological and survival data of the groups were examined.

Results: Surgical intervention was performed on 62 of our patients. The 4-year survival rates were higher than those who did not undergo surgery (Group 1: 59.6 [14.7%], Group 2: 83.5 [6%]). The comparison of the two groups showed a longer median survival in patients in Group 2 who underwent surgery, albeit not statistically significant (77 [11.23] months in Group 1 and 84 [18.91] months in Group 2 [$P=0.16$]).

Conclusion: In conclusion, our study showed that surgical treatment may have positive effects on survival.

Keywords: breast cancer, metastasis, surgery, survival

Introduction

Breast cancer remains the most common type of cancer in women [1]. Despite intensive efforts and screening programs for early diagnosis, 25% of newly diagnosed patients still present with metastatic disease at diagnosis [2]. The standard approach for the treatment of this patient population is systemic therapy. With a better understanding of tumor biology and developments in the drugs used for adjuvant therapy, the survival of these patients presenting with metastatic disease has improved over time [3].

The effect of surgical intervention on patients presenting with metastatic breast cancer is a controversial issue [4,5]. Some experimental studies suggest that there may be an increase in the release of some growth factors and angiogenic factors due to the removal of the primary tumor. It is believed that this may lead to the emergence of new metastases and a more aggressive course of existing metastatic foci [6]. However, no clinical data supporting these studies could be obtained. In contrast, the majority of recent clinical studies have shown that surgical treatment of the primary tumor, especially in selected cases of primary metastatic breast cancer, not only halts local progression but also prolongs overall and disease-free survival [7,8].

In this study, we aimed to reveal the survival, clinical, and pathological differences in patients with breast cancer who had metastatic disease at diagnosis and who underwent and did not undergo surgery for the primary tumor in our clinic and to assess the efficacy of surgery on the course of the disease.

Materials and methods

This study was approved by the Karamanoğlu Mehmet Bey University Clinical Research Ethics Committee (Date: August 31, 2022, Decision No: 08-2022/10), and patient files were reviewed with the approval of the ethics committee. The data of patients with metastatic breast cancer who were treated and followed up in our clinics (Karamanoğlu Mehmet Bey University Faculty of Medicine and Necmettin Erbakan University Meram Faculty of Medicine, General Surgery clinics) between January 2000 and June 2021 were analyzed retrospectively. Patient files were reviewed with the approval of the ethics committee. No additional consent was required from the patients. Patient data were collected from the hospital information management system. The study included those with primary metastatic disease. The presence of distant metastases was diagnosed by imaging techniques or histopathological methods. The groups were those who received only systemic therapy without any surgical intervention and were assigned to Group 1 (n=51), while those who underwent surgery for the tumor and then received adjuvant systemic therapy were assigned to Group 2 (n=62). This study did not include male patients, patients with primary non-breast tumors, those who died of causes unrelated to breast cancer, those who underwent surgery for metastatic foci other than the primary tumor, or those who could not be followed up regularly for various reasons.

Demographic data, site of metastasis, surgical and medical treatments, clinical and histopathological findings of the tumor, mortality rates, and overall survival of the patients were evaluated. The differences between Group 1 and Group 2 in terms

of these data and the variables that may have an effect on overall survival were statistically analyzed.

Statistical analysis

The analyses of the study were carried out using the SPSS (Statistical Package for the Social Sciences, IBM Corp. Armonk, NY, USA) version 21.0 software package. The level of error was set at $P<0.05$. The normality of data distribution was evaluated by the Kolmogorov-Smirnov test. Frequency table results were given for categorical variables and descriptive measures for numerical variables. Student's t-test or Mann-Whitney U test was used to compare the groups. Chi-square analysis was used to test whether two categorical variables were independent or related to one another. Disease-free survival and overall survival were calculated using the Kaplan-Meier method. The log-rank test was employed to test whether there was a difference between the survival times of the groups. Risk factors that could affect survival were analyzed with the Cox proportional hazards model.

Results

Of the patients who had distant metastases at diagnosis and were included in our study, 51 underwent no surgical intervention and received only systemic therapy, while 62 underwent surgical treatment for the primary tumor. Comparative clinical and demographic outputs of the groups are in Table 1. The groups were the same in terms of age distribution (52.29 [13.43] and 52.14 [13.54], respectively; $P=0.95$). Twenty-four (47.1%) of the patients in Group 1 and 34 (54.8%) of the patients in Group 2 were postmenopausal ($P=0.41$). There was no difference between the groups in terms of birth rates (46 [90.2%] and 55 [88.7%], respectively; $P=0.79$). The groups were statistically the same in terms of variables such as alcohol use, rate of having any comorbidity, most common comorbid condition (hypertension), and family history of malignancy ($P>0.05$). The rate of smoking was higher in the non-surgical group (7 [13.7%] and 2 [3.2%], respectively; $P=0.04$).

The evaluation of tumor laterality revealed that both groups were similar ($P=0.51$). Of the patients in Group 1, 25 (49%) had right-side, 25 (49%) had left-side, and 1 (2%) had bilateral tumor. In Group 2, the tumor location in 29 (46.8%) patients was on the right side, and in 33 (53.2%) patients on the left side. In both groups, the most frequent site of involvement was the upper outer quadrant (25 (49%) and 27 (43.5%), respectively), while the least frequent site of involvement was the lower inner quadrant (4 (7.8%) and 3 (4.8%), respectively) (Figure 1). The groups were similar in terms of the quadrants of involvement ($P=0.83$).

Figure 1: Bar chart showing the localization of the tumors in both groups ($P=0.83$)

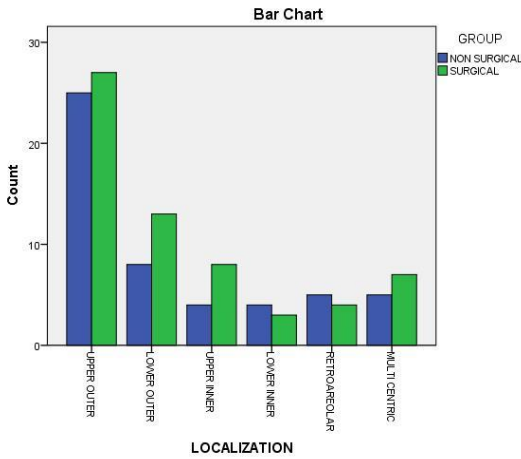


Table 1: Analysis and comparison of demographic and selected clinical characteristics between Non-surgical and Surgical metastatic breast cancer patients.

| | Non-surgical group n (%) | Surgical group n (%) | P-value (chi-square) |
|--------------------------------|-----------------------------|-------------------------|-------------------------|
| Age | 52.29 (13.43) | 52.14 (13.54) | 0.95 |
| Follow-up time (months) | 25.66 (20.44) | 38.33 (24.22) | 0.004 |
| Comorbidity | | | 0.95 |
| No | 31 (60.8%) | 38 (61.3%) | |
| Yes | 20 (39.2%) | 24 (38.73%) | |
| Alcohol | | | 0.80 |
| No | 48 (94.1%) | 59 (95.2%) | |
| Yes | 3 (5.9%) | 3 (4.8%) | |
| Smoking | | | 0.04 |
| No | 44 (86.3%) | 60 (96.8%) | |
| Yes | 7 (13.7%) | 2 (3.2%) | |
| Malignancy in family | | | 0.59 |
| No | 40 (78.4%) | 46 (74.2%) | |
| Yes | 11 (21.6%) | 16 (25.8%) | |
| Childbirth | | | 0.79 |
| No | 5 (9.8%) | 7 (11.3%) | |
| Yes | 46 (90.2%) | 55 (88.7%) | |
| Tumor side | | | 0.51 |
| Right | 25 (49%) | 29 (46.8%) | |
| Left | 25 (49%) | 33 (53.2%) | |
| Bilateral | 1 (2%) | 0 (0%) | |
| Tumor localization | | | 0.83 |
| Upper outer | 25 (49%) | 27 (43.5%) | |
| Lower outer | 8 (15.7%) | 13 (21%) | |
| Upper inner | 4 (7.8%) | 8 (12.9%) | |
| Lower inner | 4 (7.8%) | 3 (4.8%) | |
| Central | 5 (9.8%) | 4 (6.5%) | |
| Multicentric | 5 (9.8%) | 7 (11.3%) | |
| Metastasis site | | | 0.07 |
| Bone | 14 (27.5%) | 30 (48.4%) | |
| Liver | 4 (7.8%) | 4 (6.5%) | |
| Lung | 6 (11.8%) | 4 (6.5%) | |
| Multi-organ | 21 (41.2%) | 13 (21%) | |
| Others | 6 (11.8%) | 11 (17.7%) | |
| Mortality | | | 0.77 |
| No | 40 (78.4%) | 50 (80.6%) | |
| Yes | 11 (21.6%) | 12 (19.4%) | |

Among the diagnostic biopsy techniques, the tru-cut biopsy technique was the most frequently used technique in both groups (30 [58.8%] and 30 [48.4%], respectively). Fine-needle aspiration biopsy was the least preferred technique (6 [11.8%] and 6 [9.7%], respectively). The groups were statistically similar in terms of the biopsy techniques used ($P=0.38$). In both surgical and non-surgical groups, the most common histological type was infiltrative ductal carcinoma (37 [72.5%] and 51 [82.3%], respectively), followed by infiltrative lobular carcinoma and mixed type (has features of both infiltrative ductal and infiltrative lobular carcinoma), respectively (Figure 2). The groups were statistically similar in terms of histopathological types ($P=0.31$). In addition, both groups had statistically similar rates of tumor grade, estrogen receptor positivity, progesterone receptor positivity, Cerb-B2 positivity, triple negativity, and triple positivity ($P>0.05$). The histopathological features of the tumors in the Groups are summarized in Table 2. The evaluation of the groups in terms of the site of metastasis showed that Group 1 most

frequently had multi-organ metastasis ($n=21$ [41.2%]), while Group 2 most frequently had bone involvement ($n=30$ [48.4%]) (Figure 3). The least frequent site of metastasis was the liver in both groups (4 [7.8%] and 4 [6.5%], respectively). Despite the proportional difference between Groups 1 and 2 in terms of the site of metastasis, there was no statistical difference ($P=0.07$).

Figure 2: Bar chart showing the histological types of the tumors in both groups ($P=0.31$)

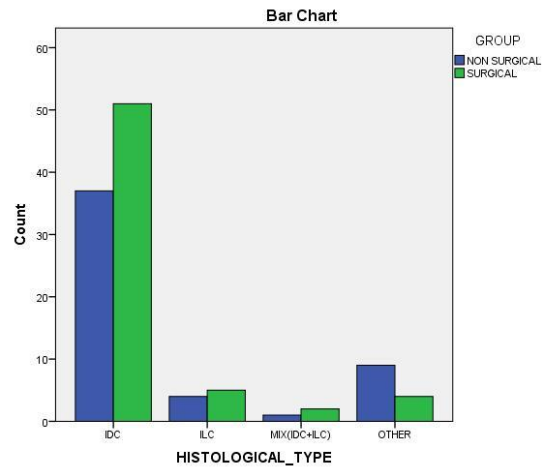
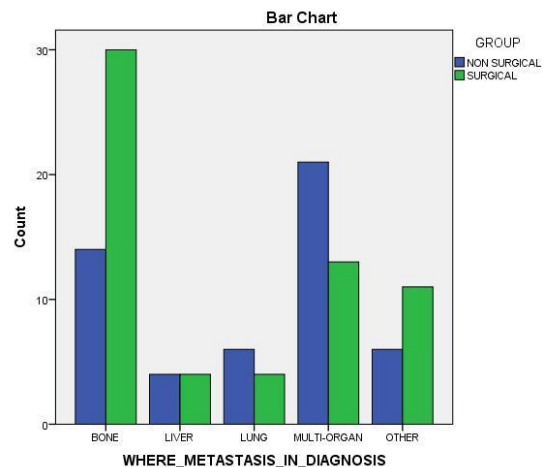


Table 2: Analysis and comparison of histopathological characteristics between Non-surgical and Surgical metastatic breast cancer patients.

| | Non-surgical group n (%) | Surgical group n (%) | P-value (chi-square) |
|------------------------------|-----------------------------|-------------------------|-------------------------|
| Tumor size (cm) | | 25.66 (20.44) | |
| Histological grading | | | 0.09 |
| Grade 1 | 0 (0%) | 0 (0%) | |
| Grade 2 | 16 (88.9%) | 38 (69.1%) | |
| Grade 3 | 2 (11.1%) | 17 (30.9%) | |
| Type of biopsy | | | 0.38 |
| Excisional | 15 (29.4%) | 26 (41.9%) | |
| Tru-cut | 30 (58.8%) | 30 (48.4%) | |
| Fine needle | 6 (11.8%) | 6 (9.7%) | |
| Histological Type | | | 0.31 |
| IDC | 37 (72.5%) | 51 (82.3%) | |
| ILC | 4 (7.8%) | 5 (8.1%) | |
| Mix (IDC+ILC) | 1 (2%) | 2 (3.2%) | |
| Others | 9 (17.6%) | 4 (6.5%) | |
| Estrogen receptor | | | 0.89 |
| Negative | 13 (30.2%) | 17 (31.5%) | |
| Positive | 30 (69.8%) | 37 (68.5%) | |
| Progesterone receptor | | | 0.52 |
| Negative | 17 (39.5%) | 18 (33.3%) | |
| Positive | 26 (60.5%) | 36(66.7%) | |
| Cerb-B2 | | | 0.28 |
| Negative | 13 (30.2%) | 22 (40.7%) | |
| Positive | 30 (69.8%) | 32 (59.3%) | |
| Triple-positive | | | 0.43 |
| No | 27 (62.8%) | 38 (70.4%) | |
| Yes | 16 (37.2%) | 16 (29.6%) | |
| Triple-negative | | | 0.81 |
| No | 41 (95.3%) | 52 (96.3%) | |
| Yes | 2 (4.7%) | 2 (3.7%) | |

IDC: Infiltrative Ductal Carcinoma, ILC: Infiltrative Lobular Carcinoma

Figure 3: Bar chart showing the metastasis sites in both groups ($P=0.07$)



The treatment types of the patients in the Groups are summarized in Table 3. Of the patients in Group 2, 56 (90.3%) underwent a modified radical mastectomy, 4 (6.5%) underwent breast-conserving surgery, and 2 (3.2%) underwent a simple mastectomy. The groups were statistically similar in terms of chemotherapy types ($P < 0.001$). The patients in both groups most frequently received palliative chemotherapy (30 [58.8%] and 23 [37.1%], respectively), followed by neoadjuvant ($n=20$ [39.2%]) and adjuvant ($n=1$ [2%]) chemotherapy in Group 1 and adjuvant ($n=18$ [29%]) and neoadjuvant ($n=17$ [27.4%]) chemotherapy in Group 2. Twenty-eight (54.9%) patients in Group 1 and 26 (41.9%) in Group 2 did not receive radiotherapy. Palliative radiotherapy was applied more in Group 1 ($n=18$ [35.3%]), while the rate of adjuvant therapy ($n=18$ [29%]) was higher in Group 2. The groups were significantly different in terms of radiotherapy types ($P=0.04$). The groups were statistically the same in the rates of hormone therapy and Herceptin ($P > 0.05$).

Table 3: Analysis and comparison of treatment options between Non-surgical and Surgical metastatic breast cancer patients.

| | Non-surgical group n (%) | Surgical group n (%) | P-value (chi-square) |
|-------------------------|-----------------------------|-------------------------|-------------------------|
| Surgery | | | |
| MRM | 0 (0%) | 56 (90.3%) | <0.001 |
| BCS | 0 (0%) | 4 (6.5%) | |
| SM | 0 (0%) | 2 (3.2%) | |
| Not applied | 51 (100%) | 0 (0%) | |
| Chemotherapy | | | |
| No | 0 (0%) | 4 (6.5%) | <0.001 |
| Palliative | 30 (58.8%) | 23 (37.1%) | |
| Adjuvant | 1 (2%) | 18 (29%) | |
| Neoadjuvant | 20 (39.2%) | 17 (27.4%) | |
| Radiotherapy | | | |
| No | 28 (54.9%) | 26 (41.9%) | 0.04 |
| Palliative | 18 (35.3%) | 18 (29%) | |
| Yes | 5 (9.8%) | 18 (29%) | |
| Hormonal therapy | | | |
| No | 30 (58.8%) | 28 (45.2%) | 0.14 |
| Yes | 21 (41.2%) | 34 (54.8%) | |
| Herceptin | | | |
| No | 33 (64.7%) | 46 (74.2%) | 0.27 |
| Yes | 18 (35.3%) | 16 (25.8%) | |

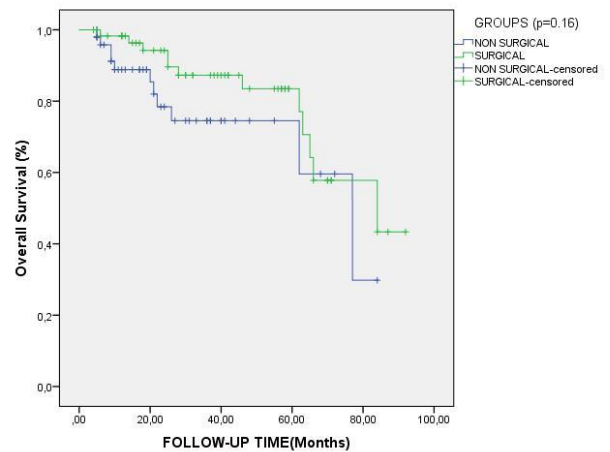
MRM: Modified Radical Mastectomy; BCS: Breast-Conserving Surgery; SM: Simple Mastectomy

The mean follow-up time was 25.66 (20.44) months in Group 1 and 38 (24.22) in the second group. This duration of Group 2 was statistically significantly higher ($P=0.004$). Eleven patients (21.6%) in Group 1 and 12 (19.4%) in Group 2 died during the follow-up. Although the mortality rate was lower in Group 2, groups were statistically similar in mortality rates ($P=0.77$).

Survival times were calculated using the Kaplan-Meier method. Figure 4 shows the overall survival curves of both groups. The estimated 4-year overall survival was 59.6 (14.7%) in the first and 83.5 (6%) in the second group. The median survival was 77 (11.23) months in Group 1 and 84 (18.91) months in Group 2. Despite the longer survival time of Group 2, the log-rank test showed no statistically significant difference in survival time between both groups ($P=0.16$).

Whether being in Group 1 or Group 2 was a risk factor that may affect survival was analyzed with the Cox proportional hazards model, which revealed that being in Group 1 or Group 2 had no statistically significant effect on overall survival ($P=0.17$). Among the many models created, only the model in which the group variable and the hormone therapy variable were used together was significant, and hormone therapy (Hazard Ratio: 2.75, 95% CI: 1.18–6.57, $P=0.003$) was associated with decreased mortality.

Figure 4: Kaplan-Meier curves of overall survival in the Non-Surgical ($n=51$) and the Surgical group ($n=62$).



Discussion

Surgical treatments for metastatic breast cancer have two basic goals: improving quality of life and prolonging survival [9]. The surgical intervention may aim at the primary tumor or may be performed as metastasectomy in some selected cases [10]. Today, the concept of “treatment” has lost its relatively more aggressive implication of eliminating all cancerous cells and has been defined more often as providing prolonged survival without obvious symptoms [10]. This approach has increased the tendency to prefer more aggressive methods for these patients [10].

The long-established and adopted approach to metastatic breast cancers was that surgery of the primary tumor was an inappropriate method [11]. The general approach has been surgery of the primary tumor only in cases of uncontrolled local disease and patient complaints [12]. In line with this view, 51 of 113 patients included in our study did not undergo any surgical intervention and received only systemic therapy. It has been assumed that surgical intervention activates growth factors in such patients, leading to a more aggressive metastatic disease and a decrease in survival [13]. However, it has been observed that the survival time is quite short after treatments are performed by adopting this approach, with an increase in the rates of progressive local disease that may impair the quality of life of the patients as well as associated disorders such as ulceration, pain, and bleeding [14]. Thereupon, local surgical treatment of the primary tumor has been performed more frequently, and the outcomes of surgical interventions, especially before adjuvant chemo-radiotherapy have been satisfactory in terms of quality of life and survival [11]. Surgical intervention was performed on 62 of our patients, with the 4-year survival rates being higher than those who did not undergo surgery. The comparison of the two groups showed a longer median survival in patients in Group 2 who underwent surgery, albeit not statistically significant.

The initial historical approach to breast cancer was the progression of the disease by spreading to adjacent tissues. Based on this view, it was believed that a broader and more aggressive treatment would be more positive in terms of local control of the disease and survival [15]. However, in the early 21st century, contrary to this view, it has been accepted that breast cancer has a more complex form of spread via the bloodstream and lymphatic system rather than in the form of local spread [16]. For this reason, it has been considered that local control is insignificant and has no

effect on secondary metastases that may develop [16]. Current studies have led to the development of an opinion of a combination of these views that have evolved over time. Early radiotherapy studies have yielded results supporting this view. These studies have shown that the treatment of residual or recurrent disease not only provides local control but also prevents the emergence of new metastases and reduces the risk of mortality [12]. The results of our study showed a higher survival rate in the surgical group, which supports this view.

Although experimental studies have proposed breast cancer stem cell theory, genetic repair model, parallel mutation hypothesis, increased angiogenic activity hypothesis, surgical trauma-induced increase in growth factors hypothesis, clonal dominance theory, immune system theory, and theory of metastatic disease due to surgical treatment of the primary tumor, they are no longer accepted as they cannot be supported by clinical studies [17]. Some hypotheses have also been put forward about by what mechanism the removal of the primary tumor leads to an improvement in survival, including the elimination of growth factors, which are secreted from the primary tumor and thought to be effective on metastatic disease, by primary tumor surgery; the elimination of immunosuppression caused by the tumor after surgery; an increase in the efficacy of adjuvant treatment methods due to the decrease in the possible necrotic tissue load in the tumor as a result of surgery [17].

There are numerous recent academic studies that support the positive effects of surgical intervention. The study by Copelci et al. concluded that surgical resection performed in selected patients with stage IV breast cancer increased survival [3]. Moreover, other studies show that resection of the primary tumor is an independent risk factor for survival, reduces mortality risk, is effective in preventing local symptoms of primary cancer, and can positively affect the quality of life [3,7,11,12,18,19]. Our study also yielded results supporting surgical intervention, similar to these studies in the literature. According to the results of another literature review by Rüterkamp et al. [20], patients with metastatic breast cancer, especially young individuals with a single metastasis, benefit more from surgical treatment of the primary tumor, and mastectomy or lumpectomy may be preferred as a surgical technique for these patients, provided that adequate resection can be achieved. Contrary to all these studies, there are also published papers suggesting that primary surgery does not provide the benefit of improving quality of life and overall survival in stage IV breast cancer and that the data are insufficient to determine the efficacy of local surgical treatment [1,21,22].

Limitations

Our study has some inevitable limitations. First, the level of evidence is not strong enough because of the retrospective design of the study. Second, the data were collected from patient records and operative notes. Third, there were no objective examination findings. Fourth, the standardization in follow-up and treatment methods could not be strictly adhered to due to reasons such as advanced age and patient preference. Lastly, the relevant detailed information on chemotherapeutic agents and radiotherapy procedures could not be obtained.

Conclusion

In conclusion, our study showed that surgery of the primary tumor in these patients may have positive effects on

survival. We are of the opinion that patients should be encouraged to participate in randomized controlled studies in order to eliminate the doubts caused by studies that have yielded contrary results and to provide standardization in the treatment of this disease.

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Evaluation of the use of hormonal contraceptive methods and awareness of a group of women with cardiological symptoms and diseases

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Ethics Committee Approval

The study was approved by the SBU Istanbul Training and Research Hospital Clinical Research Ethics Committee (Decision No: 1995, Date: September 27, 2019), and institutional permission was obtained from Beylikdüzü State Hospital. All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest

No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Hormonal contraceptives can carry risks, particularly for women with chronic conditions such as heart disease and diabetes. A wide range of basic science, animal, and human studies indicate an enduringly heightened risk of venous thromboembolism, hypertension, myocardial infarction, and ischemic stroke associated with birth control hormones (estrogen and progestogen). According to the guidelines, women aged 35 and over considering hormonal contraceptives should be evaluated for vascular diseases and cardiovascular risk factors. However, the number of studies on this subject is insufficient. This study aimed to assess the use of hormonal contraceptive methods and the knowledge levels of women with cardiological symptoms and diseases attending a cardiology outpatient clinic.

Methods: A descriptive and cross-sectional study was conducted with cardiological problems (diagnosed or being treated at the Cardiology Polyclinic) of women between the ages of 18 and 45. Data were collected through face-to-face interviews using the Sociodemographic Characteristics Form and the Structured Contraception Knowledge Level Form. The study sample consisted of 190 women visiting a state hospital's Cardiology Polyclinic in Istanbul between October 2019 and January 2020.

Results: Among the participants, 24.8% used hormonal contraceptives, and 15.8% reported facing problems while using them, most commonly experiencing constant headaches (53.3%) and iron deficiency (30%). The study revealed that 7.9% of the participants had cardiovascular disease, with 52.1% experiencing cardiological symptoms, such as palpitations and rapid heartbeat. A total of 24.7% had received family planning counseling, and 59.6% believed that counseling influenced their contraceptive choices. Those who received counseling showed greater knowledge regarding the safety of progesterone-only birth control pills for women with heart disease.

Conclusion: Women with cardiovascular disease should be well informed about the risks associated with hormonal contraceptives. The study emphasizes the importance of counseling services provided by nurses in cardiology and obstetrics clinics to guide women toward safer contraceptive options. Continuous monitoring and education are essential to ensure women's health and safety in contraceptive choices.

Keywords: hormonal contraceptives, cardiologic disease, cardiologic symptoms, contraceptive counseling, progesterone

Introduction

The main objectives of contraceptives include preventing pregnancy-related risks in women, reducing fetal mortality, preventing sexually transmitted diseases such as human immunodeficiency virus / acquired immune deficiency syndrome (HIV/AIDS), reducing unwanted pregnancies and induced abortions, improving education, reducing adolescent pregnancies, and slowing down population growth [1]. In particular, hormonal contraceptives should be used selectively in cases of chronic diseases such as heart disease and diabetes [2,3]. Due to their estrogen and progestogen content, hormonal contraceptives play a crucial role in developing conditions such as venous thromboembolism, hypertension, myocardial infarction, and ischemic stroke [4]. The estrogen functions by increasing the plasma levels of particular coagulation factors (Factor II, Factor VII, and Factor X) and lowering the plasma levels of antithrombin III. These effects are dose-dependent, and the risk increases within four months after starting the medication [3].

The World Health Organization (WHO) has published a guide called "Medical Eligibility Criteria for Contraceptive Use (WHO-MEC)" to ensure the safety of various contraceptive methods for individuals with specific health conditions and characteristics. According to the guidelines, combined oral contraceptives (OCs) from the WHO-MEC Stage 4 contraceptive group are not recommended and/or contraindicated in risk factors, such as venous thromboembolism, obesity (BMI >35), smoking in women over 35 years of age, ischemic and cyanotic heart disease, heart failure, arrhythmia, and the use of bosentan [5].

Oral contraceptives may increase the risk of vascular disease by acting directly on the vessel wall, disrupting fat and carbohydrate metabolism, affecting the hemostatic system, and influencing blood pressure. COC use in smokers over 35 has an anti-synergistic effect on the cardiovascular system [4,6]. It also increases the risk of arterial thrombosis and hypertension. On the other hand, contraceptives containing only progesterone do not increase the risk of venous thromboembolism, hypertension, ischemic stroke, or myocardial infarction, because they lack estrogen. Progesterone-containing oral contraceptives are suitable for almost every woman, and for those with hemodynamically unstable heart disease, the intrauterine device (IUD) is safe and highly effective. Thus, informing women diagnosed with cardiovascular disease about hormonal contraceptives is necessary [4,7] and of public health importance for women. It is essential for nurses to offer guidance on preventive health services to patients. However, previous studies have not adequately addressed this issue. This study aims to investigate the use of hormonal contraceptive methods and the knowledge levels of women with cardiovascular symptoms and diseases.

Materials and methods

The study was conducted as a descriptive and cross-sectional research to evaluate the characteristics and knowledge level of women with cardiological symptoms and diseases using hormonal contraceptive methods.

The study sample consisted of 190 women who applied to the Cardiology Polyclinic of a state hospital in Istanbul between October 2019 and January 2020. In the study, the 3-month average

number of patients attending the outpatient clinic was determined, and the plan was to involve 190 patients. Consequently, when working with 190 patients and considering Cohen's medium effect size ($d=0.5$) with a margin of error of 0.05, the statistical power of the study was calculated to be 95%. Participants were selected using a simple random sampling method, which is a non-probability sampling method. All patients attending the outpatient clinic were included in the research.

The study included women between the ages of 18 and 45 who had the ability to communicate verbally, were sexually active and had cardiological problems diagnosed or being treated at the Cardiology Polyclinic. Participants were required to have no diagnosis of any psychiatric disorder and express willingness to participate verbally or in writing. Those who did not meet the mentioned criteria were excluded from the study.

Data were collected through face-to-face interviews, with an average duration of 15-20 minutes, on weekdays when both the patients and the researchers were available. Data collection tools included the Sociodemographic Characteristics Form and the Structured Contraception Knowledge Level Form. The Sociodemographic Characteristics Form consisted of questions about the patient's age, height, weight, marital status, education level, and income status. The Structured Contraception Knowledge Level Form was prepared by the researchers based on the literature and was presented to three nursing faculty members for their expert opinions.

A pilot test was conducted with a group of 20 individuals, and their feedback was obtained to measure the adequacy of the surveys. It included questions about contraceptive use and experienced symptoms, cardiovascular disease and related symptoms, and the awareness of women with cardiovascular disease and/or symptoms regarding the use of hormonal contraceptive methods.

The accuracy of information provided by participants regarding dependent variables, such as medication use, lifestyle habits, and other medical conditions, as well as their willingness to consciously provide misleading responses is a common source of bias in studies of this nature. However, it is believed that conducting the study face-to-face and employing a pilot study minimizes such issues. While it was essential to have a larger sample size in the study, the study group's need to have characteristics such as cardiovascular disease and symptoms prevented this.

Statistical analysis

Statistical analyses were performed using the IBM SPSS Statistics 26 package program. Frequencies (number, percentage) were provided for categorical variables, while descriptive statistics (mean, standard deviation) were given for numerical variables. Chi-square analysis was used to interpret relationships between two independent categorical variables. Fisher's Exact test results were utilized when the expected value assumption was not met in the chi-square analysis. A statistical significance level of 0.05 was considered in the analyses.

Ethics

The study was approved by the SBU Istanbul Training and Research Hospital Clinical Research Ethics Committee (Decision No: 1995, Date: September 27, 2019), and institutional permission was obtained from Beylikdüzü State Hospital.

Participants were informed about the purpose of the study, the procedures involved, and their rights as participants. Written and verbal consent was obtained from all participating women.

Results

As seen in Table 1, the average age of the participants is 35.80 (7.27) years, with an average BMI of 25.80 (4.61). In terms of education level, 25.8% of the participants have completed high school, 25.8% have a college education, and 25.8% have postgraduate education. Regarding economic status, the majority reported being in good economic condition. The overwhelming majority of the participants are married.

Table 1: Distributions by sociodemographic characteristics (n=190)

| | Mean | SD |
|------------------------------------|-------|-------|
| Age | 35.80 | 7.27 |
| Weight | 68.49 | 12.85 |
| BMI | 25.80 | 4.61 |
| | n | % |
| Education Status | | |
| Primary education | 27 | 14.2 |
| High school | 49 | 25.8 |
| College | 49 | 25.8 |
| License | 16 | 8.4 |
| Postgraduate | 49 | 25.8 |
| Economic Status | | |
| My income is less than my expenses | 7 | 3.7 |
| My income is equal to my expenses | 78 | 41.1 |
| I'm in good condition | 105 | 55.3 |
| Marital status | | |
| Married | 174 | 91.6 |
| Single | 16 | 8.4 |

SD: standard deviation

Upon examining Table 2, it becomes apparent that within the group of hormonal contraceptive users, 22% opt for progesterone mini-pills, 16.2% prefer monthly injections, and the majority, 59.4%, choose estrogen-progesterone combination pills. It is noteworthy that 15.8% of the participants encountered difficulties with birth control pills. Among these participants, the most frequently reported issue was persistent headaches, reported by 53.3%, followed by iron deficiency, reported by 30%.

Table 2: Contraceptive use and symptoms experienced

| (n=190) | n | % |
|---|-----|------|
| Current Contraception Status | | |
| Yes | 177 | 93.2 |
| No | 13 | 6.8 |
| Contraceptive Method | | |
| Monthly Injections | 6 | 3.4 |
| Vaginal Ring | 1 | 0.6 |
| Hormone Intrauterine Devices | 19 | 10.7 |
| Birth Control Pills | 20 | 11.3 |
| Male Condom | 60 | 33.9 |
| Protective gel | 1 | 0.6 |
| Calendar method | 16 | 9.0 |
| Withdrawal method | 38 | 21.5 |
| Tube ligation | 8 | 4.5 |
| Hormonal contraceptives (n=37) | | |
| Mini Pills with Progesterone | 8 | 21.6 |
| Monthly Injections | 6 | 16.2 |
| Pills Containing Estrogen-Progesterone Combination | 22 | 59.4 |
| Vaginal Ring | 1 | 2.78 |
| Having Problems Using Oral Contraceptives | | |
| Yes | 30 | 15.8 |
| No | 160 | 84.2 |
| * Problems Experienced While Using Birth Control Pill (n=30) | | 13.3 |
| Migraine | 7 | 23.3 |
| Persistent Headache | 16 | 53.3 |
| Vertigo | 2 | 6.7 |
| Anemia | 7 | 23.3 |
| Psychiatric Discomfort | 4 | 13.3 |
| B12 Deficiency | 5 | 16.7 |
| Iron Deficiency | 9 | 30.0 |
| Heart Disease | 1 | 3.3 |
| No Problem | 19 | 40.4 |

* In this variable, the participants were able to give more than one answer.

Table 3 indicates that 46.7% of those with cardiovascular disease use drugs related to cardiovascular disease. Of these

participants, 52.1% experienced cardiological symptoms; 40.4% complained of palpitations; and 28.3% reported unexplained rapid heartbeat. Family planning counseling had previously been received by 24.7%, and 59.6% of those women indicated that this counseling affected the method of protection they use.

Table 3: Information on having cardiovascular disease and experiencing symptoms

| (n=190) | n | % |
|---|-----|------|
| Do You Have Cardiovascular Disease? | | |
| Yes | 15 | 7.9 |
| No | 175 | 92.1 |
| Diagnosis of Cardiovascular Disease (n=15) | | |
| Heart valve diseases | 3 | 20.0 |
| Rhythm Disorders | 6 | 40.0 |
| Hypertension | 6 | 40.0 |
| Drug Use for Cardiovascular Disease (n=15) | | |
| Yes | 7 | 46.7 |
| No | 8 | 53.3 |
| Experiencing Cardiological Symptoms for the First Time | | |
| Yes | 99 | 52.1 |
| No | 91 | 47.9 |
| * Symptoms (n=99) | | |
| Leg Swelling, Redness Pain | 17 | 17.2 |
| Blue Purple Red Color on Skin | 4 | 4.0 |
| Shortness of breath | 14 | 14.1 |
| Chest Pain | 4 | 4.0 |
| Unexplained Cough | 1 | 1.0 |
| Unexplained Fast Heartbeat | 28 | 28.3 |
| Sweating Restlessness Fear of death | 11 | 11.1 |
| Feeling of fainting | 9 | 9.1 |
| Nausea | 27 | 27.3 |
| Palpitation | 40 | 40.4 |
| Fatigue quickly | 19 | 19.2 |
| Other | 2 | 2.0 |
| Getting Family Planning Counseling Before | | |
| Yes | 47 | 24.7 |
| No | 143 | 75.3 |
| Did the Counseling Received Affect the Method Used? | | |
| Yes | 28 | 59.6 |
| No | 19 | 40.4 |

* In this variable, the participants were able to give more than one answer.

According to Table 4, the utilization rate of hormonal intrauterine devices among patients with cardiovascular disease is 28.6%, which is significantly higher than the rate among patients without cardiovascular disease.

Table 4: Hormonal birth control methods used by cardiovascular disease status

| | Cardiovascular Disease | | Chi-square | P-value |
|-------------------------------------|------------------------|------|------------|---------|
| | Yes | No | | |
| | n | % | n | % |
| Vaginal Ring | | | | |
| Yes | 1 | 7.1 | 0 | 0.0 |
| No | 13 | 92.9 | 163 | 100.0 |
| Hormone Intrauterine Devices | | | | |
| Yes | 4 | 28.6 | 15 | 9.2 |
| No | 10 | 71.4 | 148 | 90.8 |
| Birth Control Pills | | | | |
| Yes | 1 | 7.1 | 19 | 11.7 |
| No | 13 | 92.9 | 144 | 88.3 |

* P<0.05

In Table 5, 41.7% of women answered “yes” in agreement to the statement, “Women with heart disease (those who have had clots before, etc.) should not use birth control pills containing estrogen hormone”. In addition, 19.5% answered “yes” to “Birth control pills (mini-pills) containing only progesterone hormone are safer for women with heart disease”.

Table 6 applies the statistical analysis, which shows a statistically significant relationship between the status of previously receiving family planning counseling and the answers given to the statement “Only birth control pills (mini-pills) containing only progesterone hormone are safer for women with heart disease” (P=0.005). Accordingly, the proportion of those who previously received family planning counseling responding “yes” to the statement compared to those who had not previously received family planning counseling was significantly higher than the rate of those who said “yes” to the statement “The pill is safer for women”.

Table 5: Findings of women’s awareness of the use of hormonal methods by heart patients

| | (n=190) | % |
|--|---------|------|
| Women Over 35 Who Smoker Should Not Use Estrogen Containing Estrogen Hormone | | |
| Yes | 80 | 42.1 |
| No | 8 | 4.2 |
| I don't know | 102 | 53.7 |
| Birth Control Pills Containing Estrogen Hormone May Cause Clot Formation In Women With Heart Disease | | |
| Yes | 65 | 37.1 |
| No | 1 | 0.6 |
| I don't know | 109 | 62.3 |
| Women with Heart Disease (Those Who Have Had a Clot Before. etc.) Should Not Take Birth Control Pills Containing Estrogen Hormone | | |
| Yes | 73 | 41.7 |
| No | 2 | 1.1 |
| I don't know | 100 | 57.1 |
| Containing Progesterone Only Birth Control Pills (Mini Pills) Are Safer For Women With Heart Disease | | |
| Yes | 37 | 19.5 |
| No | 10 | 5.3 |
| I don't know | 143 | 75.3 |

Table 6: Knowledge levels on hormonal contraceptive use

| | Getting Family Planning Counseling Before | | | | Chi-square | P-value |
|--|---|------|---------|------|------------|---------|
| | Yes | | No | | | |
| | (n=190) | % | (n=190) | % | | |
| Women Over 35 Who Smoker Should Not Use Estrogen Containing Estrogen Hormone | | | | | 2.134 | 0.344 |
| Yes | 24 | 51.1 | 56 | 39.2 | | |
| No | 2 | 4.3 | 6 | 4.2 | | |
| I don't know | 21 | 44.7 | 81 | 56.6 | | |
| Birth Control Pills Containing Estrogen Hormone May Cause Clot Formation In Women With Heart Disease | | | | | 3.055 | 0.217 |
| Yes | 21 | 47.7 | 44 | 33.6 | | |
| No | 0 | 0.0 | 1 | 0.8 | | |
| I don't know | 23 | 52.3 | 86 | 65.6 | | |
| Women with Heart Disease (Those Who Have Had a Clot Before. etc.) Should Not Take Birth Control Pills Containing Estrogen Hormone | | | | | 1.369 | 0.504 |
| Yes | 20 | 46.5 | 53 | 40.2 | | |
| No | 1 | 2.3 | 1 | 0.8 | | |
| I don't know | 22 | 51.2 | 78 | 59.1 | | |
| Containing Progesterone Only Birth Control Pills (Mini Pills) Are Safer For Women With Heart Disease | | | | | 10.691 | 0.005* |
| Yes | 16 | 34.0 | 21 | 14.7 | | |
| No | 4 | 8.5 | 6 | 4.2 | | |
| I don't know | 27 | 57.4 | 116 | 81.1 | | |
| I Can Explain the Side Effects of Birth Control Pills and Hormonal Methods | | | | | 2.492 | 0.288 |
| Yes | 12 | 60.0 | 66 | 42.0 | | |
| No | 7 | 35.0 | 84 | 53.5 | | |
| Yes But Not Enough | 1 | 5.0 | 7 | 4.5 | | |
| I Know the Side Effects of Birth Control Pills and Hormonal Methods | | | | | 0.074 | 0.853 |
| Yes | 14 | 70.0 | 113 | 72.0 | | |
| No | 6 | 30.0 | 44 | 28.0 | | |
| I'm undecided | 0 | 0.0 | 0 | 0.0 | | |
| I Know What To Do When I Have A Side Effect With Birth Control Pills And Hormonal Methods | | | | | 0.387 | 0.534 |
| Yes | 10 | 50.0 | 90 | 57.3 | | |
| No | 10 | 50.0 | 67 | 42.7 | | |
| I'm undecided | 0 | 0.0 | 0 | 0.0 | | |

Discussion

In this study, 24.8% (n=46) of the participants were using hormonal contraceptives. This percentage aligns with the findings of a previous study by Acar et al [8], where 21% of the respondents reported using hormonal contraceptives. In our study, 15.8% (n=30) of the participants reported experiencing problems while using birth control pills, similar to the findings of Acar et al’s study, where women using birth control pills complained of headaches, amenorrhea, and weight gain [8].

Studies have established a link between hormonal contraceptives and risks, such as thromboembolism, myocardial infarction, and ischemic and hemorrhagic stroke [9]. In this study, 7.9% of the participants had previously had cardiovascular disease, and these patients should be protected from the abovementioned risks. Data from the Chronic Diseases and Risk Factors Study in Turkey provided important information on chronic diseases, revealing that the incidence of coronary heart disease in women aged 15 and over was 2.3% [10,11]. The difference may be attributed to the fact that this study was conducted specifically in the cardiology outpatient clinic. Among the participants, 52.1% (n=99) experienced cardiological symptoms, with 40.4% reporting palpitations and 28.3% experiencing an unexplained rapid heartbeat. Considering

cardiovascular diseases rank first among the most common chronic diseases worldwide (37%) [11], our findings support this. Of the total participants, 24.7% had previously received family planning counseling, and among those, 59.6% believed that it influenced their choice of contraceptive method. In a study of women who received counseling, 95.2% preferred the method suggested by the family planning counseling service staff, indicating a significant influence of counseling on women’s preferences [12]. The difference in our study may be attributed to the fact that women with cardiological symptoms sought a safer contraceptive method, leading to a relatively higher use of condoms (33%) in our study.

The rate of using hormonal intrauterine devices in patients with cardiovascular disease was 28.6%, whereas it is 9.2% in patients without cardiovascular disease. In another study, IUD use among women aged 15-49 was 21%, which aligns with our results [13]. Additionally, the rate of using birth control pills in patients with cardiovascular disease was 7.1%, whereas it was 11.7% in those without cardiovascular disease. This difference may be due to heart patients’ preference for contraceptive methods with fewer side effects [12].

It was explained to 42.1% of the participants that women over 35 years of age should not use estrogen-containing preparations. Additionally, most participants were aware that

individuals with heart conditions should avoid using combined oral contraceptives and that contraceptives containing progesterone were more reliable than combined ones.

Counseling services provided to women may have contributed to these results. In one study, 95.2% of women preferred the method first suggested by the family planning counseling staff. It was observed that family planning counseling services significantly influenced women's preferences [12]. As both venous and arterial thrombosis are the most common serious side effects of combined oral contraceptives, modifications have been made to the hormonal components of contraceptive pills in the last decade to reduce harmful thrombotic risks. However, an increase in the CRP level is still evident [14]. On the other hand, third-generation low-dose combined OCs can cause myocardial infarction in young women, even in the absence of other cardiovascular risk factors [15]. Therefore, as these risks are explained during counseling services, it is likely that women will turn to mini-pills.

Findings indicate that there are significant differences between those who received counseling about hormonal contraceptives and those who did not, with women who received counseling demonstrating greater knowledge about contraceptives [12]. As a result of the statistical analyses applied, a statistically significant relationship was found between receiving family planning counseling and the answers given to the statement, "Only birth control pills (mini-pills) containing only progesterone hormone are safer for women with heart disease". Progestin-only pills (POP) have a progestin dose very close to the contraceptive efficacy threshold, with a failure rate of 0.3% in perfect use and 8-9% in typical use [16]. The women's responses to this question also indicate their awareness that progesterone pills are not associated with myocardial infarction or stroke risk. Accordingly, the proportion of those who answered "yes" to the statement "Only birth control pills (mini-pills) containing only progesterone hormone are safer for women with heart disease" among those who received family planning counseling is significantly higher than those who did not receive family planning counseling. This result suggests that family planning counseling contributes to an important awareness of progesterone-only contraceptives in women with heart disease.

Limitations

The sample size in the study was limited to 190 women. Conducting future research with a larger sample size and in more centers may be more beneficial for generalizing the results. Although the researchers prepared the questions, the objectivity could have been influenced. However, the pilot study conducted on the questions alleviated this concern. Participants may not have disclosed their other medications, lifestyle habits, or other medical conditions. They might have attempted to provide socially acceptable answers and conceal their actual situations, which could affect the accuracy of the data.

Conclusion

The results of this study highlight that palpitations were the most frequently reported symptom among participants, with the majority of birth control pill users experiencing persistent headaches. The study also revealed that male condoms are the prevailing choice for birth control among the participants. Furthermore, there is a notably higher usage of estrogen-

progesterone combination birth control pills in hormonal contraceptive use among the participants. Statistical significance further emphasizes the participants' greater preference for hormonal intrauterine devices. Additionally, the study underscores that counseling enhances awareness of hormonal contraceptives among women with cardiovascular disease.

The study shows that nurses in cardiology and obstetrics polyclinics and clinics have essential advisory roles in family planning options. Close monitoring of women with heart disease or symptoms is crucial for safeguarding their health. Future comprehensive research should delve deeper into this subject, providing valuable insights to assist women in making well-informed choices regarding family planning methods that best suit their health status.

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The relationship between intervertebral disc pathologies and the use of digital devices and lack of physical activity in adolescents

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Ethics Committee Approval

The study was approved by the Altınbaş University Clinical Research Ethics Committee (Decision No: 70212) on June 27, 2024. All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest

No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Existing research on herniated discs in adolescents primarily focuses on surgical interventions and outcomes, with fewer studies investigating the effectiveness of non-surgical therapies. The correlation between obesity, facet tropism, lumbosacral transitional vertebrae, trauma, certain sports activities, and herniated discs in adolescents is well-documented. Comparable to adults, a sedentary lifestyle in adolescents potentially carries a significant risk of developing disc degeneration and herniation. Consequently, this study aims to examine the relationship between increased digital device usage, decreased physical activity, and the onset of disc pathologies in adolescents.

Methods: The study group included 94 patients aged between 10 and 16 years diagnosed with cervical (CDH), thoracic (TDH), and lumbar (LDH) disc disease. For each participant, the individual daily usage time spent on desktop computers, tablets, laptops, and mobile phones and the total time spent on all digital devices were evaluated. Their level of physical activity was also assessed using the International Physical Activity Questionnaire – Short Form (IPAQ-SF). The study eliminated causes such as listhesis, facet tropism, lumbosacral transitional vertebra, trauma, and sports injuries that could prompt the development of these spinal pathologies. Additionally, other conditions that might cause spinal pain, such as scoliosis, rheumatological diseases with spinal involvement, tumors, and myofascial pain, were also ruled out.

Results: The average age of all patients was 13.44 (2.07) years. A majority were women (n=55), comprising 58.50% of the sample. Of the patients, 60.64% had CDH, 12.77% had TDH, and 75.53% had LDH. The amount of physical activity and time spent on digital devices were similar across both genders ($P=0.194$ and $P=0.770$). A significant correlation was found between CDH and the time spent on tablets, laptops, and mobile phones ($P<0.001$). Again, a significant correlation was observed between LDH, usage of desktop computers, total time spent on all digital devices, and the IPAQ-SF score for low physical activity ($P<0.001$).

Conclusion: The prevalence and duration of digital device use among adolescents are increasing, while physical activity is decreasing. Our study indicates that this situation may be linked to the development of disc degeneration and hernias. Understanding this association can help reduce treatment and rehabilitation costs and prevent the potential loss of workability and quality of life resulting from a herniated disc. Consequently, additional comparative research on this topic is crucial.

Keywords: adolescents, disc pathologies, digital devices, physical activity

Introduction

Neck/shoulder pain (NSP) and lower back pain (LBP) are increasingly recognized as significant issues in many countries, with social and economic ramifications for both individuals and governments. These conditions not only deteriorate the quality of life for those afflicted but also escalate the cost of treatment and rehabilitation, placing a substantial financial burden on the state. Adolescents suffering from LBP are likely to continue experiencing pain into their economically active years, thereby leading to inflated indirect costs through absenteeism, reduced productivity, early retirement, and sick leave. These indirect costs account for approximately 85% of total expenses [1,2].

LBP starts in childhood and adolescence, with prevalence rates mirroring that of adults [3,4]. Recently, there has been an uptick in studies examining the prevalence of NSP and LBP in these age brackets. These studies suggest an increased prevalence and higher lifetime prevalence rate than those observed in prior years [5-8].

Lumbar disc herniation (LDH) and cervical disc herniation (CDH) are significant contributors to lower back and neck pain, though they are less common in adolescents. Primarily, publications exist regarding the relationship between obesity, facet tropism, lumbosacral transitional vertebrae, trauma, certain sports activities, and LDH in adolescents [9-12].

Current studies predominantly utilize survey methods and disclose that the use of digital devices and insufficient physical activity are significant, rising contributors to spinal pain in adolescents [13-14]. Consequently, a sedentary lifestyle could be a factor in the development of disc herniations among adolescents, mirroring adults [15]. We posit that this correlation deserves attention, to mitigate future losses of workforce productivity, quality of life, and higher treatment and rehabilitation costs due to disc herniations.

Most studies on herniated discs in adolescents concentrate on surgical treatment methods and outcomes [16-19]. Non-surgical treatment results receive far less attention [20]. Only one study to date has highlighted a potential connection between excessive smartphone use and degeneration of the cervical spine [21].

In this study, we aimed to examine the relationship between digital device use and lack of physical activity, not only as causes of spinal pain but also as contributors to the development of intervertebral disc pathologies.

Materials and methods

Approval was granted by the clinical ethics committee of our institution: the Altınbaş University Health Sciences Scientific Research Ethics Committee. The Ethics Committee approved the study on 27 June 2024, with the protocol number 70212. The research took place between December 2021 and December 2023 at the Physical Medicine and Rehabilitation Centre and the Orthopedic Clinic of Altınbaş University Medical Park Bahçelievler Hospital. In this cross-sectional study, permission was obtained from the families of 94 patients, aged between 10 and 16 years, who had reported spinal pain and whose Magnetic Resonance Imaging (MRI) scans showed

bulging, protrusion, and extrusion. As none of the parents refused, all patients were included in the study.

All surveys and inquiries were personally administered to the patients and completed by them in a separate setting from their families. Therefore, special care was taken to ensure that the participants were mentally healthy and not depressed. The Mini-Mental Test was used to gauge their mental abilities, while the Beck Depression Scale assessed their depression levels. All the patients were native Turkish speakers who could both read and write in the language. The data were recorded in the outpatient clinic files by orthopedists and physical therapy doctors. Entries of the data into Excel were made by a third person unassociated with the study.

The duration of digital device use and physical activity levels were probed during clinical examinations of patients with spine pain. Patients were asked about their daily usage time for each digital device, including tablets, laptops, desktop computers, and mobile phones. They were also asked to provide the total daily usage time for all devices, in hours.

The level of physical activity was evaluated using the International Physical Activity Questionnaire-Short Form (IPAQ-SF) [22]. The Turkish validity and reliability of this scale were analyzed by Saglam et al. [23] in 2010. The IPAQ-SF is a questionnaire featuring seven items that determine the frequency and duration of moderate to vigorous physical activity, as well as daily walking, during the past week. The final question probes the amount of time spent sitting daily. Individuals' level of physical activity is gauged based on the responses to the questionnaire, using the Metabolic Equivalent of Task (MET) method, a measure of a person's oxygen consumption in mL/kg/min. A person's overall MET value is computed by considering the duration and type of physical activity performed over the week. Participants are subsequently categorized into three groups – low, medium, or high – according to their total calculated MET values [22].

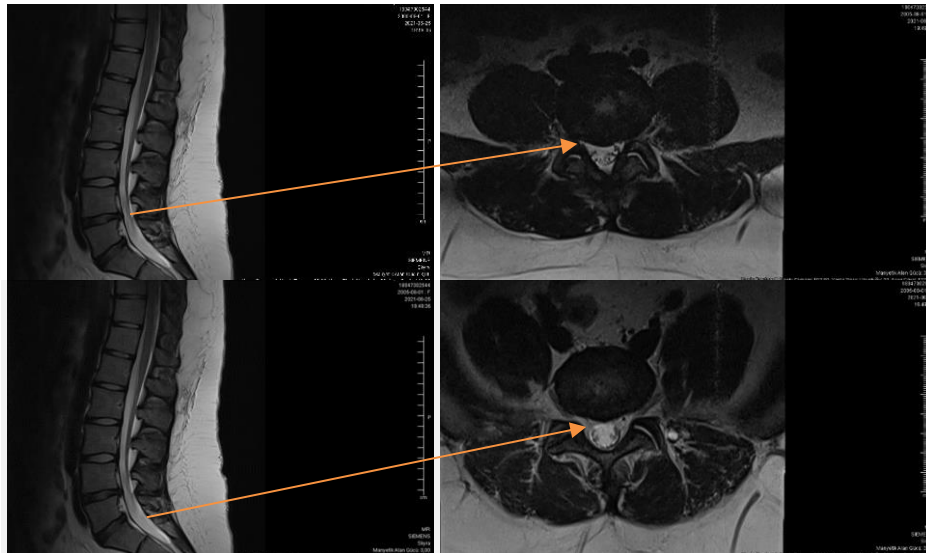
Furthermore, along with age and gender, the presence of disc pathologies in the spine was documented. A family history of disc disease was gathered from the first-degree relatives of the participants.

Exclusion criteria include causes like listhesis, facet tropism, lumbosacral transitional vertebra, trauma, and sports injury, which may lead to the development of disc pathology in the spine. Other pathologies that may cause spinal pain, such as scoliosis, rheumatological diseases resulting in spinal involvement, spinal tumors, and myofascial pain, are also considered. Additionally, a Mini-Mental score below 24 and a Beck Depression score above 7 are part of the exclusion criteria.

Statistical analysis

In conducting the statistical analysis of the study, descriptive statistics for the numerical data were provided in terms of mean and standard deviation, while categorical data were presented as numbers and percentages. The distribution of numerical data was analyzed using a skewness test and histogram graphs. Numerical data were evaluated using both the Student's t-test and the Mann-Whitney U-test for two independent groups, whereas the Chi-square test was used to analyze the categorical data. Correlations were determined using the Pearson correlation test, with a *P*-value accepted as <0.05.

Figure 1: Lumbar MRI L4-5 and L5-S1 central disc protrusion (arrows)



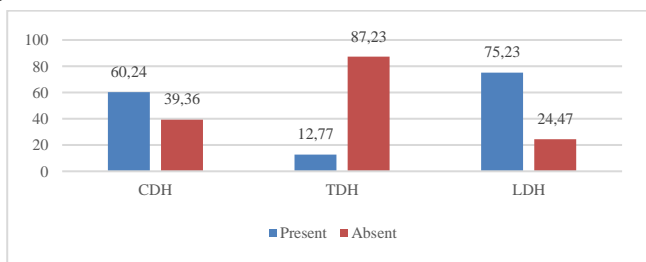
All analyses were carried out using the SPSS 23.0 software program.

Results

Out of the 116 individuals who had spinal pain, 12 were identified with scoliosis and ten with myofascial pain, and as a result, they were excluded from the research. Eventually, a total of 94 people whose MRI showed swelling, protrusion, and extrusion (sample MRI image, Figure 1) were enrolled in the study.

The average age of the patients was 13.44 (2.07) years. The study included 55 women and 39 men. Among the participants, 60.64% (n=57) had CDH, 12.77% (n=12) had thoracic disc herniation (TDH), and 75.53% (n=71) had LDH (Figure 2).

Figure 2: Distribution of disc herniation areas



None of the patients had a previous medical record of sports injuries, falls, or trauma, and no abnormalities such as listhesis, facet tropism, or lumbosacral transitional vertebrae were observed on the imaging. All participants were intellectually sound, non-depressed adolescents with Beck Depression Scores below 7, and Mini-Mental Scores above 24. There were 18 occurrences of hernias among first-degree relatives, accounting for 19% of the total.

In analyzing the number of bulging, protrusions, and extruded hernias in the cervical, thoracic, and lumbar regions, it was found that the cervical and thoracic regions had a high incidence of bulging. The number of bulging and protrusions in the lumbar region was similar, while all cases of extruded hernias were observed in the lumbar region (Figure 3). The cervical spine was most commonly affected at the C5-6 and C6-7 disc levels, the thoracic spine at the T10-T11 level, and the lumbar spine at the L4-5 and L5-S1 levels (Figure 4).

Figure 3: Regional distribution of bulging, protrusion, and extrusion

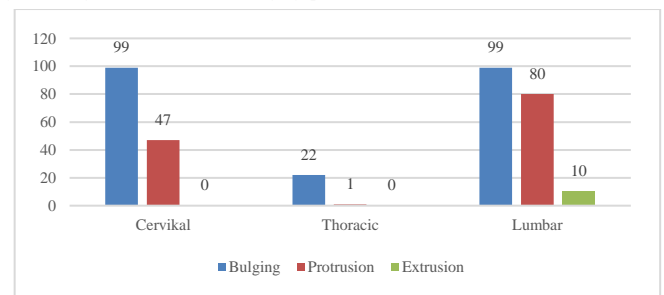
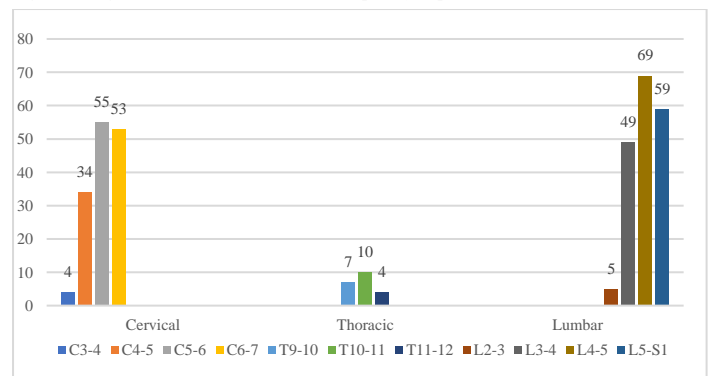


Figure 4: Regional distribution of the most frequently impacted disc levels



The distribution of disc herniations (CDH, TDH, LDH) among patients showed no significant difference by gender ($P=0.480$, $P=0.522$, $P=0.792$, [Table 1]). We found that half of the patients (50%) had a low level of physical activity, while very few (5.32%) reported a high level. The study did not reveal any statistically significant variation in physical activity level based on gender ($P=0.194$, [Table 1]).

Table 1: Evaluation of the distribution of herniated discs and physical activity by gender

| | | Gender | | | | P-value * |
|---------|----------------------------|--------|-------|--------|-------|-----------|
| | | Male | | Female | | |
| | | n | % | n | % | |
| CDH | Present | 22 | 56.41 | 35 | 63.64 | 0.480 |
| | Absent | 17 | 43.59 | 20 | 36.36 | |
| TDH | Present | 6 | 15.38 | 6 | 10.91 | 0.522 |
| | Absent | 33 | 84.62 | 49 | 89.09 | |
| LDH | Present | 30 | 76.92 | 41 | 74.55 | 0.792 |
| | Absent | 9 | 23.08 | 14 | 25.45 | |
| IPAQ-SF | Low physical activity | 19 | 48.72 | 28 | 50.91 | 0.194 |
| | Moderate physical activity | 16 | 41.03 | 26 | 47.27 | |
| | High physical activity | 4 | 10.26 | 1 | 10.82 | |

* Chi-Square Test, CDH: Cervical disc herniation, TDH: Thoracic disc herniation, LDH: Lumbar disc herniation, IPAQ-SF: International Physical Activity Questionnaire-Short Form

All 94 participants diagnosed with disc pathology had a daily routine of using desktop computers, tablets, laptops, and mobile phones. We analyzed the relationship between patients'

Table 3: Evaluation of the numerical data based on the CDH, TDH and LDH status of the patients.

| | CDH | | | TDH | | | LDH | | |
|------------------|--------------|--------------|------------------|--------------|--------------|--------------|--------------|--------------|------------------|
| | Present | Absent | P-value * | Present | Absent | P-value * | Present | Absent | P-value * |
| | Mean (SD) | Mean (SD) | | Mean (SD) | Mean (SD) | | Mean (SD) | Mean (SD) | |
| Age | 13.46 (2.19) | 13.41 (1.92) | 0.814 | 14.00 (1.86) | 13.35 (2.10) | 0.288 | 13.63 (1.99) | 12.83 (2.27) | 0.116 |
| BMI | 20.90 (2.93) | 21.13 (3.08) | 0.464 | 21.68 (1.99) | 20.89 (3.09) | 0.047 | 20.98 (2.68) | 21.01 (3.82) | 0.342 |
| Tablet | 1.54 (1.56) | 3.74 (1.00) | <0.001 | 0.83 (1.11) | 0.38 (0.51) | 0.124 | 0.39 (0.66) | 0.61 (0.50) | 0.028 |
| Laptop computer | 2.10 (1.15) | 0.20 (0.40) | <0.001 | 1.58 (1.24) | 1.32 (1.33) | 0.515 | 0.97 (0.51) | 1.00 (0.45) | 0.006 |
| Desktop computer | 0.61 (0.70) | 0.18 (0.38) | 0.009 | 2.42 (2.02) | 2.41 (1.71) | 0.988 | 3.02 (1.48) | 0.52 (0.95) | <0.001 |
| Mobile phone | 1.09 (0.55) | 0.81 (0.32) | <0.001 | 0.96 (0.14) | 0.98 (0.52) | 0.394 | 1.06 (1.25) | 2.24 (1.13) | 0.01 |
| Total duration | 5.30 (1.19) | 4.95 (1.25) | 0.174 | 5.79 (1.23) | 5.07 (1.20) | 0.055 | 5.42 (1.23) | 4.37 (0.81) | <0.001 |

* Student t-test, Mann-Whitney U-test, SD: Standard deviation, CDH: Cervical disc herniation, TDH: Thoracic disc herniation, LDH: Lumbar disc herniation, BMI: Body Mass Index. Usage time for each digital device in hours and total daily usage time of all devices in hours

body mass index (BMI), the duration of their device use (tablets, laptops, desktop computers, mobile phones), and their total device use in terms of gender distribution. While the BMI was found to be significantly higher in men ($P=0.022$), no significant difference was observed between the duration of digital device use (daily use for each device individually and total daily use of all devices) by gender ($P=0.770$, [Table 2]). Considering the length of usage time for both genders, the order is desktop computer, laptop, mobile phone, and tablet. The desktop computer had the most extended usage, with an average time of 2.41 h. Laptops were the second most-used device, with an average usage time of 1.35 h. Mobile phones noted an average use of 0.98 h, while tablet usage averaged 0.44 h. The cumulative duration of digital device use amounted to 5.16 h.

Table 2: Evaluation of the numerical data of the patients by gender

| | Gender | | | | | | P-value |
|------------------|---------|------|---------|------|---------|------|----------------|
| | Male | | Female | | Total | | |
| | Average | SD | Average | SD | Average | SD | |
| BMI | 21.88 | 3.96 | 20.35 | 1.78 | 20.98 | 2.97 | 0.022** |
| Tablet | 0.45 | 0.50 | 0.44 | 0.71 | 0.44 | 0.63 | 0.486** |
| Laptop computer | 1.31 | 1.07 | 1.38 | 1.47 | 1.35 | 1.31 | 0.789* |
| Desktop computer | 2.46 | 1.76 | 2.37 | 1.73 | 2.41 | 1.73 | 0.809* |
| Mobile phone | 0.94 | 0.38 | 1.01 | 0.56 | 0.98 | 0.49 | 0.924** |
| Total duration | 5.12 | 1.32 | 5.19 | 1.16 | 5.16 | 1.22 | 0.770* |

* Student t-test, ** Mann-Whitney U-test, SD: Standard deviation, BMI: Body Mass Index. Usage time for each digital device in hours and total daily usage time of all devices in hours

The analysis of patients' BMI, tablet, laptop, desktop computer, and mobile phone usage time, along with their overall digital device usage time, was conducted based on their CDH, TDH, and LDH statuses (Table 3). CDH patients demonstrated significantly longer durations of tablet, laptop, and mobile phone usage, but noticeably shorter desktop computer usage durations. While the BMI of individuals diagnosed with TDH was the only one showing a significant increase ($P=0.047$), there was no meaningful difference in their overall digital device usage durations. Conversely, individuals with LDH used tablets, laptops, and mobile phones for significantly shorter durations, but exhibited notably longer durations of usage with desktop computers and overall digital device usage.

No significant relationship was observed between the patients' CDH, TDH status, and IPAQ-SF scores ($P=0.318$, $P=0.162$, [Table 4]). However, a significant rise in LDH rate was noted in patients with low physical activity levels ($P=0.001$, [Table 4]).

Table 4: Evaluation of the CDH, TDH and LDH status of the patients and IPAQ-SF

| | | IPAQ-SF | | | | | | P-value * |
|-----|---------|-----------------------|-------|----------------------------|-------|------------------------|--------|--------------|
| | | Low physical activity | | Moderate physical activity | | High physical activity | | |
| | | n | % | n | % | n | % | |
| CDH | present | 32 | 68.09 | 22 | 52.38 | 3 | 60.00 | 0.318 |
| | Absent | 15 | 31.91 | 20 | 47.62 | 2 | 40.00 | |
| TDH | present | 9 | 19.15 | 3 | 7.14 | 0 | 0.00 | 0.162 |
| | Absent | 38 | 80.85 | 39 | 92.86 | 5 | 100.00 | |
| LDH | present | 43 | 91.49 | 26 | 61.90 | 2 | 40.00 | 0.001 |
| | Absent | 4 | 8.51 | 16 | 38.10 | 3 | 60.00 | |

* Chi-square test, CDH: Cervical disc herniation, TDH: Thoracic disc herniation, LDH: Lumbar disc herniation, IPAQ-SF: International Physical Activity Questionnaire-Short Form

No significant, moderate, or strong correlation was found between the duration of digital device usage by patients and their age or BMI (Table 5).

Table 5: Correlation table of age and BMI and duration of use of communication devices

| | Age (r; P-value) | BMI (r; P-value) |
|------------------|---------------------|------------------|
| Tablet | -0.025; 0.807 | 0.092; 0.380 |
| Laptop computer | 0.002; 0.982 | -0.063; 0.550 |
| Desktop computer | 0.111; 0.288 | 0.019; 0.885 |
| Mobile phone | 0.205; 0.176 | -0.006; 0.956 |
| Total duration | 0.205; 0.047 | -0.002; 0.987 |

BMI: Body Mass Index, r: Pearson correlation coefficient

Discussion

Incidences of NSP and LBP in childhood and adolescence are increasing [5-8]. LDH is a significant factor in LBP and is prevalent among adults with degenerated discs but is less typically seen in children and adolescents. Publications exist that explore the correlation between herniated lumbar discs and factors such as obesity, facet tropism, lumbosacral transitional vertebrae, trauma, and certain sports activities in adolescents [9-12].

The prevalence of spinal pain among adolescents has dramatically increased due to the widespread use of technology, including mobile phones, tablets, laptops, and desktop computers. The inclusion of these devices in educational settings contributes to a sedentary lifestyle.

In the past 2 years, we have observed an uptick in the number of adolescent patients visiting physiotherapy and orthopedic outpatient clinics due to spinal pain. Interestingly, a significant number of these patients (94 out of 102) were diagnosed with intervertebral bulging, protrusions, and extrusions – conditions that are typically rare within this age group. Most studies regarding herniated discs in adolescents are focused on surgical methods of treatment and their outcomes [16-19]. To a lesser extent, the outcomes of non-surgical treatments are discussed [20]. Only one study links the degeneration of the cervical spine discs, as shown by MRI scans, to excessive mobile phone use [21]. Consequently, our study aims to delve into the relationship between the use of digital devices, insufficient physical activity, and the onset of intervertebral disc disease.

Intervertebral discs (IVD) are anatomical structures that fill the gap between the vertebrae, contributing to their flexibility and functioning as shock absorbers [24]. Three structures comprise the IVD: the central nucleus pulposus encased between two cartilage endplates at the top and bottom, all surrounded by the annulus fibrosis (AF) ring [25,26]. A herniated disc is a medical condition whereby the annulus fibrosus, the disc's outer layer, ruptures and allows the inner part, the nucleus pulposus, to protrude. This causes the intervertebral disc to exert pressure within the spinal canal on adjacent nerves, leading to pain.

Nourishment for the intervertebral discs arrives via diffusion from the endplate, a process aided by the pumping action that occurs during movement [27,28]. If a static posture is maintained for an extended period, this impedes the pumping motion, resulting in deterioration in the nourishment of the intervertebral disc and subsequent degeneration. The potential reason for disc herniation occurring at younger ages in recent years could be youthful inactivity, which can provoke early degeneration of vertebral discs [15].

All individuals in our study exhibited disc degeneration. There was no record of any patients experiencing a sports injury, fall, or trauma that might have resulted in a hernia. Moreover, the imaging did not indicate any presence of listhesis, facet tropism, or lumbosacral transitional vertebra. Since the turn of the millennium, studies have started to underline that disc degeneration can also occur in adolescents, just as in adults. A histological study found that 11 out of 15 adolescents (73%) showed degenerative changes in the intervertebral discs similar to those seen in adults [29]. While previous studies highlighted the significance of trauma and history of congenital anomaly as factors in the pathogenesis of intervertebral disc prolapse among young patients, this research indicates that pre-existing disc degeneration should be considered in isolated traumatic disc herniations, similar to adults [29]. The study examined intervertebral disc degeneration (IVDD), changes in endplates, and paraspinal muscles in the lumbar spine of 214 children and adolescents who underwent MRI for LBP. In this study, severe IVDD was identified at all levels of the lumbar spine except L2-L3 [30].

Existing studies, primarily in the form of surveys, suggest that the use of digital devices and a lack of physical activity are significant and increasing factors in spinal pain among adolescents [13-14]. However, aside from one study that emphasizes the link between cervical disc degeneration and mobile phone use in teenagers, no research has yet observed the relationship between disc herniations, digital device use, and a lack of physical activity. In the study examining the connection between cervical disc degeneration and mobile phone use, the degree of cervical disc degeneration was evaluated in 2438 patients using the Cervical Disc Degeneration Scale (CDDS), which was developed based on the Pfirrmann classification. The CDDS scores of patients who excessively used smartphones were discovered to be higher than those of patients who did not use their smartphones excessively [21].

Evidence suggests that hereditary variants significantly contribute to the incidence of disk degeneration and herniations. The reported prevalence of family history ranges from 13% to 57% [31-34]. In our study, we found that 18 out of 94 patients had a first-degree relative with a hernia, a rate comparable with those reported in the literature. While some publications explore the correlation between pediatric disk herniations and the apophyseal ring fracture, we did not observe an apophyseal ring fracture in any of our study's cases [35-37].

Although women are more frequently represented in studies on pain complaints, we found no statistically significant difference between genders in the incidence of intervertebral disc disease in our research. We also discovered that physical activity

levels and digital device use were similar for both genders [9,14,38,39].

According to our study, desktop computers were the most-used device, with an average usage time of 2.41 h. Laptops were the second most commonly used device, with an average usage time of 1.35 h. Mobile phones were used for an average of 0.98 h, while tablets were used for roughly 0.44 h. The combined usage duration of all digital devices amounted to approximately 5.16 h. A literature review reveals that adolescents with back pain issues may spend almost 3 h a day using their electronic devices [1,6,38-40]. As there is no current study examining the relationship between disc herniation and duration of digital device use, a comparison cannot be drawn. However, our study suggests the total duration of digital device use is longer than that reported in studies about chronic back pain.

Our study indicated that 60.44% of patients had CDH, 12.77% had TDH, and 75.23% had LDH. Low physical activity prevalence was 50%, while moderate physical activity prevalence was 44.68%. Similar to NSP and LBP study findings in adolescents, the prevalence of high physical activity in our study was exceptionally low (5.32%). There was also a significant association between low physical activity and the presence of LDH [38-40]. This finding implies that, beyond causing spinal pain, low physical activity might be a crucial factor contributing to LDH development.

In our examination of the most frequently impacted disc levels, we observed pathology in the C5-6 and C6-7 levels of the cervical spine, the T10-T11 levels of the thoracic spine, and the L4-5 and L5-S1 levels of the lumbar spine. In a study involving 70 patients with adolescent LDHs (ages ranging from 9 to 19 years), it was found that the L4-5 level was most frequently affected, followed by the L5-S1 disc [15]. Bulging discs were discovered in 42 cases, with extruded hernias in six cases, and protrusions in 22 cases. As with our study, extrusion occurred at the lowest rate, and the most common level of involvement in the lumbar region was similar.

In our study, we found a significant relationship between CDH and the usage time of tablets, laptops, and mobile phones. The correlation between tablet use and NSP is similar to that between improper reading posture and NSP [41,42]. Stationary computers offer benefits due to their adaptability to ergonomic features, such as adjustment of screen, keyboard, table, and chair settings. However, laptops and tablets, which can be used anywhere, often fail to comply with ergonomic conditions, thereby causing spinal pain [40]. Our study indicates that similar to NSP, CDH is also caused by improper posture.

In our study, we found a significant association between LDH and the duration of desktop computer use, as well as the total time spent using digital devices. We concluded that static immobility and the total duration of inactivity during the day, compounded by a lack of physical activity, are more significant factors for LDH than poor posture. Another study that investigated the usage of digital devices concerning spinal pain found a significantly lower prevalence of LBP among mobile phone users [40]. This was attributed to the possibility of using mobile phones while standing and moving, which is consistent with our observations.

In our study involving 94 patients (10–16 years old), we found a significant relationship between CDH and the duration of tablet, laptop, and mobile phone usage. We also observed a significant association between LDH and the length of desktop computer usage. A connection was additionally detected between the total usage time of all digital devices, reduced physical activity (as measured by the IPAQ-SF score), and LDH.

Limitations

A control group could not be established, as only 22 out of 116 patients who visited our clinic with spine pain complaints lacked disc pathology. This highlights the need for future comparative studies on this subject.

Conclusion

The prevalence and duration of digital device use among adolescents is increasing, while physical activity decreases. Our study is pioneering in evaluating the relationship between the duration of digital device use, lack of physical activity, and disc pathologies in adolescents. The findings from our study group suggest that prolonged use of digital devices and a lack of physical activity appear to be significant factors contributing to intervertebral disc degeneration and hernia formation. Understanding this relationship is crucial for preventing future workforce loss, and diminished quality of life, as well as treatment and rehabilitation costs due to disc herniations.

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Hepatic artery injury in a six-year-old patient after laparoscopic cholecystectomy: A management challenge

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Informed Consent

The authors stated that the written consent was obtained from the parents of the patient presented with images in the study.

Conflict of Interest

No conflict of interest was declared by the authors.

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Abstract

Laparoscopic cholecystectomy is among the most common surgeries in adults and is increasing in the pediatric age group. However, data are lacking on complications of the surgery and their treatment in children. Although many case series can be found that address hepatic artery injury after cholecystectomy in adults, we could not find similar publications in the English literature relating to the pediatric age group. This report shares the complex diagnosis and treatment process of a six-year-old female patient who presented with jaundice eight months after laparoscopic cholecystectomy. During the treatment process, it was observed that the common bile duct went into lysis in the late period due to hepatic artery injury. The treatment continued with redo hepaticojejunostomy and catheters passed through the anastomosis line in the patient, who had anastomotic stenosis after hepaticojejunostomy. Twenty-four months after the patient's first operation, she had no active complaints. Complications may occur months after a cholecystectomy. In this case, arterial injury should be kept in mind. We wanted to contribute by presenting the first case in the literature on hepatic artery injury in the pediatric age group.

Keywords: laparoscopic cholecystectomy, hepatic artery injury, pediatric, jaundice

Introduction

Laparoscopic cholecystectomy (LC) is the gold standard in managing calculous cholecystitis in adults, and it is one of the most frequently employed abdominal surgical procedures [1]. Consequently, there is broad information on the LC approach and its complications in adults. Although currently, laparoscopic cholecystectomy is performed more frequently in children due to the rise in the rate of calculous cholecystitis, there is still limited data in the literature about this approach and its complications in children [1–4]. Almost all of the publications on both LC and its complications are series from general surgery due to the large number of patients in that branch [1,2]. Although the procedure has been employed very frequently, simple or serious complications may be encountered due to surgeon inexperience or variations of the bile ducts and liver vessels. One of the most common complications is prolonged bile leak (BL); numerous causes have been reported for this complication in adults. The diagnosis and treatment are easy for most of these causes. One of the very rare causes of prolonged BL and jaundice in adults is injuries in major hepatic vessels.

In the adult series, it has been claimed that 0.3–0.7% of the patients have biliary injuries, most of which are accompanied by vascular injuries. Although there is enough information about the diagnosis and treatment of bile duct complications due to arterial injury in adults, managing such cases is quite challenging for both physicians and patients [1–3]. In our English literature review, we found no information about prolonged BL and jaundice secondary to right hepatic artery injury in the pediatric age group. Therefore, we wanted to contribute to the literature by sharing the process and the problems experienced in the diagnosis and treatment of bile duct damage secondary to right hepatic artery injury.

Case presentation

A six-year-old female patient with no comorbid conditions had an LC for cholelithiasis in another medical center. The patient had bilious drainage on the second postoperative day. A laparoscopy was performed on the fifth postoperative day due to BL. It was observed that there was BL from the gallbladder bed, and it was clipped laparoscopically. The BL continued; therefore, laparotomy was performed three weeks after the first procedure, and the BL was repaired. The patient did not have any active complaints afterward and returned with complaints of acholic stool and scleral jaundice eight months after the first surgical procedure. The patient was referred to our clinic due to the high direct bilirubin level and magnetic resonance cholangiography (MRC) showing the absence of the common bile duct.

The physical examination was normal except for mild scleral icterus and a subcostal incision scar. Laboratory tests revealed aspartate transaminases (AST): 82 U/L, alanine transaminases (ALT): 75 U/L, total serum bilirubin (TB): 4.98 mg/dL, and direct bilirubin (DB): 3.52 mg/dL. Complete blood count and other blood biochemistry tests were within normal limits. Abdominal ultrasonography (USG) was reported as the intrahepatic bile ducts were dilated (the diameter of the right hepatic duct was 5 mm, and the diameter of the left hepatic duct was 9 mm); the echogenicity was increased at the junction of the right and left hepatic ducts and the point of junction was not observed; the common bile duct could not be clearly visualized, and there was increased echogenicity in its bed (stricture?). The patient's MRC was reinterpreted in our hospital, and the common bile duct was not observed. The stricture of the common bile duct was considered. The patient's bilirubin level continued to increase (DB: 7.6 mg/dl). Percutaneous cholangiography (PC) was performed on the third day after the patient was admitted. It was observed that the left hepatic duct terminated bluntly. The intrahepatic bile ducts were found to be dilated in the right lobe, the right and left hepatic ducts ended bluntly, and there was no transition to the common bile duct (Figure 1).

Figure 1: Percutaneous cholangiography of the patient at the first admission. The right and left common bile ducts end bluntly and there is no transition to the common bile duct.

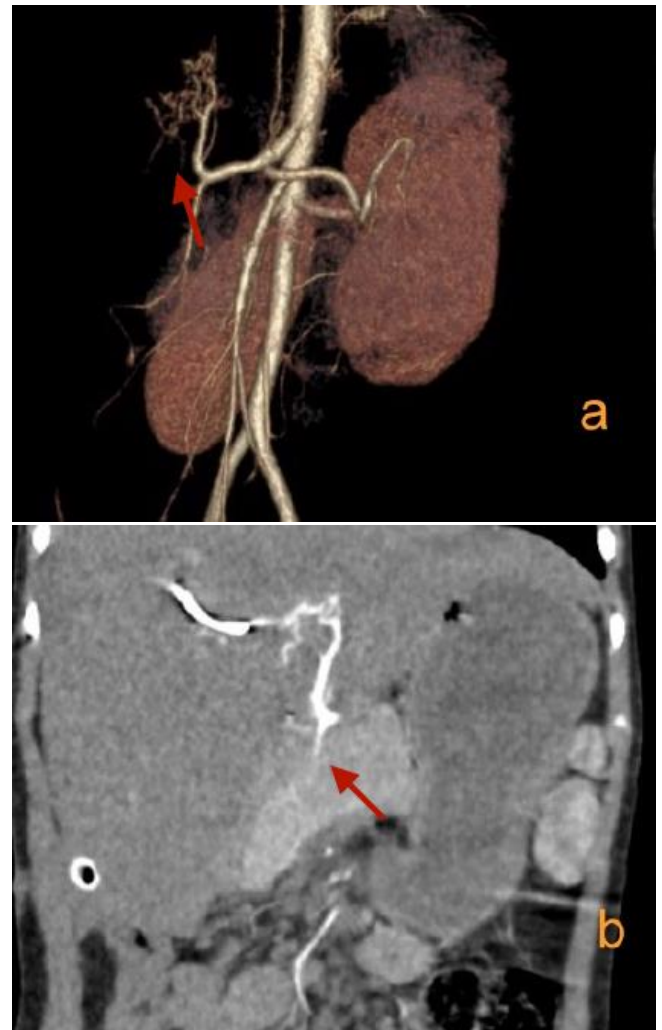


Percutaneous transhepatic drainage catheters (PTCs) were inserted into both main hepatic ducts. Laparotomy was planned since there was no passage from the right and left hepatic ducts into the common bile duct. The laparotomy performed nine months after the LC revealed that the right lobe of the liver was

darker, but the appearance was not suggestive of a blood supply insufficiency. The distal end of the fibrotic connective tissue in the location of the common bile duct was followed up to the duodenum, but luminous structures could not be seen. It was supposed that the common bile duct was lysed. The medical team chose to perform a hepaticojejunostomy (HJ). It was observed that the anterior wall of hepatic confluence was absent, but its posterior wall was intact. The right and left hepatic ducts were exposed. HJ was performed by widening the anastomosis line toward the left bile duct. However, since such a case had not been encountered before, and the right and left hepatic ducts appeared normal, vessel injury was not considered and a catheter was not placed into the biliary tract.

Postoperatively, the patient consulted with the adult hepatobiliary surgery team and the liver transplantation team. The teams stated that the patient had a typical right hepatic artery injury, that there were such cases in adult series, and that performing HJ was the right decision. They recommended that computed tomography angiography (CTA) be performed when the patient was stabilized to confirm the pathology. Postoperatively, the patient's TB values decreased to the normal limits. The right hepatic artery was not observed on CTA, and it was seen that collateral vessels had developed (Figures 2a and 2b).

Figures 2: The right hepatic artery is not observed; however, collaterals are seen.



The patient had abdominal pain four weeks after HJ, and subcapsular fluid collection that was 10 cm in diameter, determined to be a bilioma, was seen in the right lobe of the liver on USG. Interventional radiologists drained the bilioma. PC was

performed by injecting opaque material into the right and left hepatic ducts. The opaque material injected into the right hepatic duct did not pass through the HJ region. The opaque material passed into the jejunum when injected from the left side (Figure 3). The procedure was terminated by inserting a PTC into the right hepatic duct. Afterward, 200 to 400 cc/day of bile was drained from the patient's biliary catheter. Bilirubin values were within normal limits and stool was cholic.

Figure 3: Cholangiography performed one month after the first hepaticojejunostomy surgery shows a minimal transition from the left hepatic duct into the jejunum.



In the follow-up, it was observed that the patient had a biliary fistula on the skin, whose biliary catheter was incidentally removed. Three hundred to 400 cc of bile drained daily from the fistula. The fistula closed approximately four months after the hepaticojejunostomy was performed. The patient's stool became acholic, and the laboratory results showed AST: 64 U/L, ALT: 54 U/L, TB: 0.43, gamma-glutamyl transpeptidase (GGT): 101 U/L, and alkaline phosphatase (ALP): 627 U/L. PC was performed again. It was observed that there was no passage through the HJ area. A laparotomy was planned. An intraoperative cholangiography was performed. On cholangiography, there was a distance of approximately 2 cm between the right and left hepatic ducts and the previously anastomosed jejunum. On laparotomy, 1 cm-thick scar tissue was seen at the site of anastomosis. It was observed that there was no bile passage due to this stenosis. The scar tissue was removed, and an HJ was performed again. Two 8 Fr catheters were placed from the jejunum into the right and left hepatic ducts, and their opposite ends were exited through the skin. A control cholangiography was performed two weeks after the second HJ to prevent the formation of a new stricture, considering that the catheters inserted during the surgery could not be left there for a long time. Percutaneous trans anastomotic 8 Fr

catheters were inserted from the right and left hepatic ducts. The trans anastomotic catheters placed during the surgery were removed.

Afterward, the patient had no active complaints, and no free fluid was detected on the abdominal USG. The patient was discharged. Five months after discharge, PTCs were removed, and four F guides were placed. The guides were removed after two months.

Thirty-four months after the patient's LC procedure and 20 months after the second HJ, the patient had not been catheterized for 13 months, was in good general condition, and had good liver function tests.

Discussion

The prevalence of cholelithiasis has been gradually increasing in children and is reported at 0.13–1.9%. This compares to a prevalence of 3–70% in adults [4,5]. Cholecystectomy is the most common abdominal surgery in adults, and more than 80% are performed laparoscopically. Although cholecystectomy is not performed in children as frequently as in adults, the rate among children has been increasing in parallel with the increasing prevalence of cholelithiasis. LC is preferred more often in children, as in adults [2,4,5].

The major complications after cholecystectomy are bleeding, infection, wound problems, bile duct injury, vascular injury, and BL. Bile duct injury has been reported as the most common and most serious complication in both adults and children. The rate of bile duct injury has been reported as 0.3–0.7% in adults and 0.44% in children [1–3].

The causes of iatrogenic bile duct injuries are clipping, thermal injury, direct injury, and transection. These injuries are largely accompanied by vascular injuries. The most common accompanying vascular injury is the injury of the right hepatic artery [3,6].

Although Bismuth and Strasberg's classifications were used in the past for the treatment and follow-up of bile duct injuries in adult series, bile duct injuries are currently divided into two groups—low-grade and high-grade injuries, referring to the severity of BL. The cases needing aggressive treatment and having poor prognosis were included in the high-grade group [6,7]. Many articles in the literature have focused on just high-grade injuries. Our case had a biliary injury that was categorized as high-grade since its treatment required complex and repetitive interventions.

After cholecystectomy, bile duct injuries result in strictures, transections, or, most frequently, BL, which is seen at a rate of 0.3–2.7%. Stones in the biliary tract or inflammation and fibrosis due to acute cholecystitis have been reported as risk factors for BL, particularly after LC. It has been proposed that those cases mostly have high-grade bile duct injuries [6].

Treatment of BL has changed direction from surgery to minimally invasive endoscopic interventions, particularly in adults. Although the success rate for endoscopic interventions has been reported as approximately 90% in adult series, there is not enough data on this subject in the pediatric age group. In addition, the incidence and treatment of complications are often not detailed in publications on pediatric cholecystectomy [1–3,6].

Although most BL can be treated with minimal interventions, complex bile leaks may require more than one

intervention and surgery. HJ is a widely accepted procedure, particularly in the treatment of high-grade bile duct injuries. However, in some of the patients who underwent HJ, it was observed that re-intervention was required due to anastomotic stenosis. This is because most bile duct injuries are accompanied by vascular injury [3,6–8].

Bile duct problems may be secondary to intraoperative injury or may be due to ischemia. Vascular injury should be considered, especially in cases with prolonged bile duct complications. Although portal vein and arterial injuries are less frequent than biliary complications, they are serious and are often associated with biliary complications. Right hepatic artery injury is the most common vascular injury, with a rate of 92% in the adult series. However, vascular injuries are often not diagnosed without imaging or autopsy [9].

Vascular injuries are mostly diagnosed with radiological imaging after they cause serious complications. Alves et al. asserted that the vascular injury rate may be as high as 47% if angiography were performed routinely after biliary injury [3]. Although the publications on adults report a high rate of vascular injury, the lack of vascular injury in pediatric series gives the impression that vascular injury is missed in pediatric cases. Possibly children are not diagnosed with vascular injuries because hepatic artery injuries post-LC are mostly asymptomatic in childhood and angiography is not performed routinely. It has been stated that arterial injury after cholecystectomy may lead to serious problems such as abscess formation, necrosis, and atrophy in the liver, and attempts to repair the biliary tract may be unsuccessful. However, others have called these possibilities rare, and most patients with arterial injuries have been asymptomatic [10].

In our case, the common bile duct was seen to be intact during the BL repair procedure performed three weeks after the first surgery, but necrosis was observed eight months later. Contrary to the blood supply of the liver parenchyma from both the hepatic artery and the portal vein, the blood supply to the biliary system flows only from the hepatic arteries. Approximately 40% of the blood supply of the extrahepatic biliary system comes from the right hepatic artery and 60% from the gastroduodenal and retroduodenal arteries. Excessive dissection of the common bile duct during cholecystectomy may disrupt its blood supply. When the arterial blood flow of the common bile duct is impaired, the most severe ischemic damage is seen in its middle third and at the biliary confluence. Although not proven, delayed biliary stricture is explained in this way [7]. The necrosis of the intact common bile duct after eight months in our case may be explained in this way. Li et al. reported cases of right hepatic artery injury and bile duct ischemia. However, bile duct ischemia developed in a shorter time after cholecystectomy in those cases [11].

In the adult series, some authors performed routine CTA in every case with biliary complications after cholecystectomy to reveal any accompanying arterial injury; however, others performed CT angiography only in patients with prolonged BL. CTA is not performed in most cases with hepatic artery injuries [3,9].

Hepatic artery injury was not considered in the first stage, and preoperative CTA was not performed in our patient due to the lack of information about hepatic artery injury in the literature in

the pediatric age group. Although there was a demarcation line between the right and left lobes of the liver on laparotomy, the blood circulation was good. Therefore, we did not consider hepatic artery injury first. However, when we consulted with the adult Hepatobiliary Surgery Department postoperatively to reveal the etiology, we were told that the cause of common bile duct necrosis might have been right hepatic artery injury and that this condition was rarely seen in adults. The right hepatic artery was not observed on the CTA. Although hepatic artery injury has not been reported in children, CTA should be kept in mind to reveal the etiology in children with prolonged BL and obstructive jaundice that appears late after surgery. In late biliary complications, HJ is usually performed. In cases with hepatic artery injury and biliary injury, the possibility of anastomotic stenosis is high [3,8]. Therefore, several studies have investigated methods to prevent anastomotic stenosis. Some authors have recommended the placement of a trans anastomotic catheter. Although placing a trans anastomotic catheter is controversial, it is mainly recommended in cases where biliary reconstruction is complex or in cases of recurrent anastomotic stenosis [8]. Since hepatic artery injury was not initially considered in our patient, the previously placed catheters were removed and no stents were placed.

Another recommendation is the Hepp-Couinad approach—that is, widening the anastomosis toward the left hepatic duct. Here, the aim is to move away from the distal confluence, which is sensitive to ischemia in cases with right hepatic artery injury [3,9]. In our case, it was observed that the distal part of the bile duct confluence went completely into necrosis. Although hepatic artery injury was not considered in the first stage, the process was thought to be an ischemic one, and therefore anastomosis was performed by expanding it toward the left hepatic duct. However, anastomotic stenosis developed again. Therefore, when we performed a revision surgery due to anastomotic stenosis, we placed a trans anastomotic catheter, as the literature on the adult series has recommended. Afterward, these were replaced with PTC, and we tried to prevent strictures from developing. Our patient had anastomotic stenosis one month after the first surgical procedure; however, stenosis was not encountered after the second HJ procedure in which a stent was placed.

Conclusion

It should be kept in mind that there may be an accompanying arterial injury in pediatric cholecystectomy cases with biliary complications. CTA may help in managing the process more efficiently in pediatric cases with prolonged biliary complications. Even after the repair of the biliary complications, it should be kept in mind that complications may occur again after a long period in cases of concomitant arterial injury, and patients should be followed up closely. While repairing a biliary injury accompanied by arterial injury, surgeons may find that the patient may benefit from a trans anastomotic catheter that can be left in the anastomosis line for a long time. However, since the trans anastomotic catheters inserted during the surgery cannot be left in place for a lengthy time, a PTC may be inserted. These catheters should be left in place until the end of the ischemic process.

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