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Research article

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Restorative effects of *Acetobacter ghanensis* on the pathogenicity of gliadin-induced modulation of tight junction-associated gene expression in intestinal epithelial cells

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Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: At present, a gluten-free diet is the only efficient way to treat celiac disease (CD). The development of novel approaches to lessen or counteract the pathogenic effects of gluten remains crucial for the treatment of CD. The aim in this investigation was to examine the restorative effects of *Acetobacter ghanensis* as a novel probiotic against gliadin-induced modulation in the barrier integrity of an intestinal epithelial cell (IEC) model (Caco-2).

Methods: Fully differentiated Caco-2 cell monolayers were subjected to enzymatically digested gliadin with a pepsin and trypsin (PT) in the presence or absence of *A. ghanensis* for 90 min. The relative amounts of zonulin, zonula occludens-1 (ZO-1), claudin-1, and occludin mRNA expression were determined by quantitative real-time polymerase chain reaction (qRT-PCR). Transepithelial electrical resistance (TEER) was evaluated to monitor the barrier integrity of cell monolayers. Statistical analyses were carried out using one- or two-way ANOVA followed by Tukey's post-hoc analysis for multiple pairwise comparisons.

Results: A significant upregulation (4.7-fold) of zonulin was noted in the PT-gliadin treated Caco-2 cells in comparison with the untreated controls (P<0.001). Conversely, gliadin-induced zonulin expression was markedly downregulated in the Caco-2 cells following exposure to *A. ghanensis* in the presence of PT-gliadin (P<0.001). Furthermore, prominent decreases in the mRNA expression levels of ZO-1 (45%) and occludin (40%) were seen in the PT-gliadin exposed Caco-2 cells compared to the untreated control cells (P<0.001). PT-gliadin in the Caco-2 cells did not significantly alter the mRNA levels of claudin-1 (P=0.172). Similarly to zonulin expression, the decreasing effect of PT-gliadin on ZO-1 was completely attenuated in the PT-gliadin-administrated Caco-2 cells following exposure to *A. ghanensis* (P<0.001).

Conclusion: *A. ghanensis* restored the pathogenicity of PT-gliadin on intestinal barrier integrity.

Keywords: celiac disease, gluten, probiotic, *Acetobacter ghanensis*, caco-2 cells

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Introduction

Celiac disease (CD) is a chronic inflammatory disorder induced by the cells of the natural and acquired immunity in genetically predisposed individuals following consumption of dietary prolamins such as gluten, hordein, and secalin in wheat, barley, and rye, respectively [1]. The disease is characterized by malabsorption due to progressive degrees of inflammation in the intestinal epithelial cells (IECs) resulting in the flattening of the villi, which are specialized cells that carry out absorption of nearly all nutrients. Besides intestinal symptoms, CD is characterized by various signs, namely iron deficiency anemia, osteoporosis, night blindness, muscle weakness, and weight loss [2]. Furthermore, CD is correlated with raised risk for other autoimmune disorders including itchy skin disease (dermatitis herpetiformis), alopecia, and type-1 diabetes [3,4].

Gliadin, a main ingredient of wheat gluten, has been implicated as the primary cause of the increased IEC permeability and inflammatory processes associated with CD [5,6]. Under physiological conditions, the homeostasis of the integrity of the IECs as the physical blockage against exterior factors is facilitated by tight connections between each enterocyte through tight junction (TJ) proteins containing claudin, occludin, and zonula occludens (ZO) [7]. In genetically vulnerable people having human leukocyte antigen (HLA)-DQ2 and/or HLA-DQ8 alleles, however, the interaction of gliadin with chemokine receptor CXCR3 on the apical location of enterocytes initiates a signaling cascade that results in TJ disassembly [8]. During this process, the synthesis of zonulin, a crucial protein contributing to the regulation of TJs in IECs, is upregulated and it is liberated to the gut lumen following exposure to dietary gliadin. The binding of zonulin to protease activated receptor 2 (PAR2) and epidermal growth factor receptor (EGFR) in IECs then leads to the dismantling of TJ proteins from the junctional structure by activating the phosphorylation processes of target proteins including ZO followed by impairment in barrier integrity and function [9,10].

At present, a gluten-free diet is the only efficient way to treat CD. Thus, the investigation of novel therapeutic strategies to lessen or counteract the pathogenic effects of gluten remains crucial for the treatment of CD. In the last few years, there has been a rapid rise in interest in applications of various probiotics that confer health benefits. Specifically, *in vivo* and *in vitro* investigations have shown promising results from the use of probiotic strains including *Bifidobacterium and Lactobacillus* to treat CD [11,12].

In the current study, the novel probiotic strain examined, *Acetobacter ghanensis*, was obtained from kefir, a home-made fermented dairy product; its probiotic characteristics based on antibiotic resistance, antimicrobial activity, hydrogen peroxide and hydrogen sulfide production, and endurance in an extremely acidic environment. However, the physiological health benefits of *A. ghanensis* remain uncertain. The current research was thus undertaken to investigate the potential restorative effects of *A. ghanensis* against gliadin-induced intestinal barrier dysfunction due to modulation in the expression levels of genes encoding TJ-related associated proteins participating in the formation and integrity of IECs *in vitro*.

Materials and methods

Cell cultivation and treatment conditions

Caco-2 cells obtained from the American Type Culture Collection (ATCC) were cultivated in minimal essential medium (Corning™ cellgro™; 10-010-CV) comprising 15% (v/v) fetal bovine serum (Sigma; F3135), streptomycin (10,000 µg/mL), and 1% penicillin (10,000 IU/mL) and an antibiotic mixture (Corning™ cellgro™; 30-002-CI), 1% nonessential amino acid mixture (Corning™ cellgro™; 25-025-CI), and 1% sodium pyruvate (Corning™ cellgro™; 25-000-CI) at 37 °C in a humidified 5% CO_2/O_2 atmosphere. For the experimental setup, Caco-2 cells plated at a concentration of 1×10^5 viable cells were grown as monolayers on 12-mm collagen-coated membrane inserts (Corning® Transwell®) and cultivated for 21 days for full differentiation. The cultivation medium was replaced every 2 days. Before the experimental treatment, fully differentiated Caco-2 cells were kept in complete medium without antibiotic for 2 days. PT-gliadin obtained from wheat was prepared as described previously [13]. For the experimental setup Caco-2 cells were treated with or without the addition of viable *A. ghanensis* suspension (1×10^8 CFU/mL), and then the cells were incubated for 90 min. Untreated Caco-2 cells were also included as a control of the experimental approaches.

Total RNA extraction, cDNA synthesis, and qRT-PCR analysis

Total RNA extraction was carried out using RNAzol® RT reagent (Molecular Research Center, Inc.) in accordance with the manufacturer's directions following the experimental approaches employed for Caco-2 cells for 90 min. An iScript cDNA synthesis kit (Bio-Rad; 170889) was used to synthesize complementary DNA (cDNA) from the isolated RNA samples as described in the manufacturer's instructions.

To assess the relative abundances of the gene products of interest and a housekeeping gene, cyclophilin A (*CYPA*), expressed at comparatively steady levels among the experimental groups as an internal control qRT-PCR method, was applied using a LightCycler® 2.0 real-time PCR system and SYBR® Green Master Mix (Bio-Rad). Comparative C_T ($2^{-\Delta\Delta CT}$) analysis was conducted to assess the relative mRNA expression levels of target genes normalized to *CYPA* mRNA levels. Sequences of gene-specific primer pairs used for qRT-PCR are described as reported previously [14].

Bacterial cultivation

Acetobacter ghanensis, the species examined in the present study, was previously obtained from kefir, a home-made fermented dairy product manufactured without the use of commercial starter culture, and was identified by DNA sequencing. The bacterial stock maintained at -80 °C was thawed at room temperature. It was then plated on a cultivation medium containing HS broth and left to stand at 32 °C for 72 h. After centrifugation at 10,000 × *g* for 10 min, the bacterial cells were collected in the pellet and then washed twice with sanitized phosphate-buffered saline (PBS) with re-centrifugation and were resuspended in MEM cell culture medium. A Den1B McFarland densitometer was used to count bacterial cell numbers.

Evaluation of transepithelial barrier resistance in Caco-2 cells

For *in vitro* monitoring of the barrier integrity of IEC monolayers in real time, TEER values were evaluated at 30-min periods for a total of 90 min using an epithelial volt/ohm meter (World Precision Instruments) as described earlier [15]. Only TEER values greater than 250 Ω/cm^2 were considered acceptable, indicating fully formed IEC barrier integrity with TJs. The TEER levels of the IEC monolayers at the beginning were reflected to be TEER values of 100%.

Statistical analysis

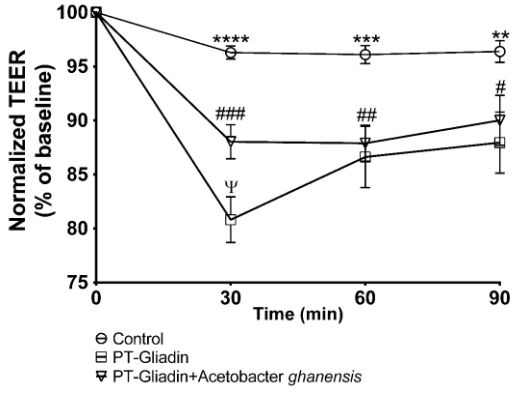
Data from the gene expression analysis and TEER values were analyzed by one- and two-way ANOVA, respectively, using GraphPad Prism (version 6.0 for Windows). Tukey's multiple-comparison post-hoc test was used to determine the differences between the experimental groups. The data were presented as the mean (SEM) of duplicate measures established in two distinct experiments with three replicates. A *P*-value of 0.05 or less was considered significant.

Results

Effects of *Acetobacter ghanensis* on PT-gliadin-induced impairment in the barrier integrity of Caco-2 cells

The exposure of fully differentiated Caco-2 cell monolayers to PT-gliadin led to a considerable decrease of 20% in TEER values in comparison to the untreated control cell monolayers at 30 min ($P<0.001$) (Figure 1). Although the TEER values of the Caco-2 cells exposed to PT-gliadin started to increase over time, they were significantly lower than those of the untreated control cells at 60 and 90 min ($P=0.005$ and $P=0.002$, respectively). In contrast, TEER levels were significantly greater in the *A. ghanensis*-treated Caco-2 cells in the presence of PT-gliadin compared to the PT-gliadin treated Caco-2 cells exposed to PT-gliadin alone at 30 min ($P=0.009$). However, no significant alterations in TEER values were obtained between the PT-gliadin-treated groups in the presence or absence of *A. ghanensis* at 60 and 90 min ($P=0.852$ and $P=0.658$, respectively). Although *A. ghanensis* attenuated PT-gliadin-dependent decreases in TEER values at 30 min, the TEER values were still significantly lower in comparison to the control Caco-2 cell monolayers ($P=0.003$).

Figure 1: The restorative effects of *A. ghanensis* on the IEC barrier.



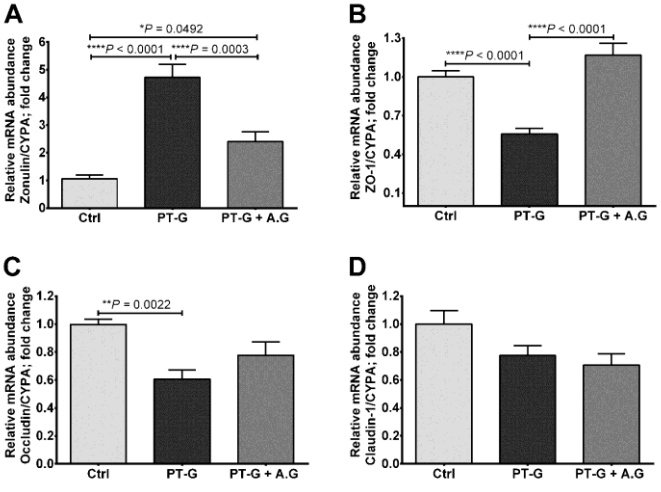
TEER levels were ascertained in PT-gliadin exposed Caco-2 cells with or without addition of *A. ghanensis* (10^8 CFU/mL). $^{**}P=0.019$, $^{***}P=0.001$, and $^{****}P<0.001$ (untreated control group vs. PT-gliadin treated group); $^{\#}P=0.024$, $^{\#\#}P=0.002$, and $^{\#\#\#}P=0.003$ (untreated control group vs. *A. ghanensis* and PT-gliadin co-administrated group); $^{\Psi}P=0.009$ (*A. ghanensis* and PT-gliadin co-administrated group vs. PT-gliadin treated group) at the same measurement time intervals.

Effects of *Acetobacter ghanensis* on TJ gene expression

The mRNA expression of zonulin was significantly upregulated by approximately 4.7-fold when Caco-2 cells were administered with PT-gliadin for 90 min in comparison to untreated control cells ($P<0.001$) (Figure 2A). The increasing impact of PT-gliadin on the mRNA levels of zonulin was significantly suppressed by 50% when *A. ghanensis* was administered to Caco-2 cells in the presence of PT-gliadin ($P<0.001$). Although the presence of *A. ghanensis* attenuated the increasing effects of gliadin, the zonulin expression was still significantly greater (2-fold) than that of the untreated control group ($P=0.049$).

Significant downregulation of ZO-1 (45%) and occludin (40%) was noted in the Caco-2 cells after incubation with PT-gliadin compared to the untreated control cells ($P<0.001$ and $P=0.002$, respectively) (Figure 2B). Importantly, the ZO-1 mRNA expression level in the Caco-2 cells following exposure to *A. ghanensis* and PT-gliadin was significantly higher, by 57%, compared to those of the Caco-2 cells subjected to PT-gliadin alone ($P<0.001$). Taken together, these findings indicate that administration of *A. ghanensis* to Caco-2 cells in the presence of PT-gliadin prevented PT-gliadin-stimulated alterations in the zonulin mRNA levels (~50%) and ZO-1 (~100%) mRNA. Although the mRNA levels of occludin in the *A. ghanensis* and gliadin exposed Caco-2 cells were 28% higher than those of the PT-gliadin-administrated Caco-2 cells, these differences did not reach statistical significance ($P=0.217$) (Figure 2C). Again, while the mRNA expression levels of claudin-1 in the PT-gliadin exposed Caco-2 cells were slightly lower (23%) than those of the untreated control cells, the change was not statistically significant ($P=0.172$) (Figure 2D). On the other hand, administration of *A. ghanensis* to the Caco-2 cells did not change claudin-1 expression in those cells ($P=0.803$).

Figure 2: Expression of the genes involved in the regulation of IEC barrier permeability and function.



The mRNA expression levels of zonulin (A), ZO-1 (B), occludin (C), and claudin-1 in PT-gliadin treated Caco-2 cells in the presence or absence of *A. ghanensis* (10^8 CFU/mL) for 90 min. Ctrl: Untreated control; PT-G: a pepsin and trypsin digested wheat gliadin; A.G: *Acetobacter ghanensis*.

Discussion

Studies have revealed that the incidence of CD has risen dramatically over the last two decades worldwide [16,17]. Although the current global prevalence of CD is considered to be about 1-2%, most individuals with CD (80-90%) are

undiagnosed but still experience high disease burden [18]. Nutrient deficiency-related diseases are commonly seen in patients with CD due to inappropriate inflammatory response in the IECs, which build a chemical and physical barrier in addition to roles in nutrient absorption. Intestinal permeability is controlled by the collaborations of proteins involved in the establishment of TJs between neighboring IECs. In 2008, Lammers et al. [8] elucidated the mechanism that increases the levels of zonulin proteins in IECs following exposure to gliadin, which leads to loss of barrier integrity and permeability, by regulating junctional structures between epithelial cells. In the last decade, scientific attention towards the use of probiotics in therapeutic cure of CD has increased dramatically because of their general health benefits [19-21]. Understanding the mechanisms by which probiotics reduce the toxicity of gluten peptides for the intestinal epithelial barrier in CD is essential for developing efficient approaches for health promotion.

In the present study, we demonstrated *in vitro* that *A. ghanensis*, a novel probiotic strain, attenuated the pathogenicity of PT-gliadin peptides in IECs by decreasing the modulatory impacts of gliadin on the expression of genes essential in the development of TJs. Consistent with our findings, previous reports [9,22,23] demonstrated that the mRNA expression levels of zonulin were upregulated in Caco-2 cells following PT-gliadin exposure. The early effects of gliadin on zonulin release were shown in rat IECs (IEC-6 cell line) by Clemente et al. [22]. In 2006, Drago et al. [9] revealed that exposure to gliadin induced rapid synthesis of zonulin in IEC-6 and Caco-2 cells. An *ex vivo* study conducted by Hollon et al. [23] showed increasing effects of gliadin on zonulin expression in the intestinal biopsy explants of patients with active CD. Collectively, the outcomes of these investigations provide evidence that the modulatory role of zonulin in the formation of TJ proteins is interconnected with CD. In 2014, Orlando et al. [24] reported that the expression levels of zonulin in Caco-2 cells rapidly rose and reached the highest levels following PT-gliadin exposure for 60 min. It was also shown that the expression levels of zonulin decreased after 60 min of incubation in a time-dependent manner. In line with that observation, it was reported that TEER values started to increase after 90 min. Similar observations were reported by Lindfors et al. [25] and Silano et al. [26], who found an increasing tendency for reduced TEER values in Caco-2 cells following incubation with PT-gliadin after 60 min of incubation. Consistent with these findings, we demonstrated that PT-gliadin treatment for 90 min caused a marked increase in the expression levels of zonulin. Since zonulin is a key regulator in the formation of TJs, the elevated levels of zonulin led to a notably rapid decrease in the TEER values of Caco-2 cells exposed to PT-gliadin for 30 min, but the TEER values increased following longer incubation times, consistent with the findings of previous reports.

In the present study, we showed that Caco-2 cells exposed to PT-gliadin exhibited significant decreases in the mRNA expression levels of ZO-1 and occludin in line with elevated levels of zonulin and decreased levels of TEER, but no significant alteration was found in the release of claudin-1. Similar outcomes were reported by Sander et al. [27], who demonstrated that exposure of Caco-2 cells to PT-gliadin (1 mg/mL) resulted in low expression levels of ZO-1 but did not alter claudin-1 protein expression.

The present study was designed to assess the protective roles of *A. ghanensis* against gliadin-induced modulation of TJ formation in IECs. Notably, the administration of *A. ghanensis* to PT-gliadin treated Caco-2 cells decreased the mRNA expression levels of zonulin compared to PT-gliadin incubated Caco-2 cells. On the other hand, the decreasing effect of PT-gliadin on ZO-1 expression was completely attenuated in Caco-2 cells following *A. ghanensis* exposure. This observation supports findings from an earlier investigation in which the zonulin synthesis stimulated by gliadin in Caco-2 cells was suppressed by subsequent *Lactobacillus rhamnosus* GG exposure [24]. It was also reported that the presence of *Lactobacillus rhamnosus* GG in Caco-2 cells incubated with PT-gliadin increased the release of occludin and ZO-1 expression but did not cause a considerable difference in the expression levels of claudin-1 [24]. Similar findings from an *in vivo* study reported by Orlonda et al. [28] demonstrated that exposure of newborn Wistar rats fed with gliadin to the same probiotic strain attenuated the gliadin-induced decrease in the expression levels of ZO-1, occludin, and claudin-1 at the mRNA and protein levels. Similarly, Bhat et al. [29] revealed that the expression levels of ZO-1 and occludin were upregulated by subsequent incubation of Caco-2 cells with *L. rhamnosus* (LR: MTCC-5897). Other research, performed by Anderson et al. [30], showed that the expression levels of TJ proteins visualized by fluorescent microscopy including ZO-1/2 and occludin were higher in Caco-2 cells exposed to *Lactobacillus plantarum* MB452 than in untreated control cells.

In our previous report, we demonstrated that PT-gliadin exposure of Caco-2 cells co-cultivated with peripheral blood mononuclear cells (PBMCs) collected from patients with CD caused a rapid and significant reduction in TEER levels with simultaneous rises in the mRNA expression levels of zonulin in parallel with decreases in the expression levels of occludin and ZO-1 [14]. On the other hand, the administration of *A. ghanensis* to Caco-2 cells co-cultured with PBMCs in the presence of PT-gliadin attenuated the gliadin-induced changes related to intestinal barrier formation and integrity [14]. We also revealed that *Acetobacter ghanensis* was able to metabolize gluten peptides in a medium supplemented with gluten as the major nitrogen supply for survival. The gluten-digesting features of *A. ghanensis* may explain why it can counteract the toxic consequences of gliadin peptides for the maintenance of intestinal homeostasis. A previous study evaluating proteolytic activities against gluten by bacteria localized in the human small intestine demonstrated that a minimum of 85 bacterial strains mainly belonging to the genus *Lactobacillus* and the phylum Firmicutes can digest gluten peptides [31]. This is consistent with the observation that *Lactobacillus* species are involved in the proteolytic digestion of gluten peptides throughout the fermentation process of wheat flour with sourdough [32,33].

Limitation

In the present investigation, the mRNA expression levels of zonulin and TJ associated gene expression levels were determined after 90 min of PT-gliadin exposure with or without addition of *A. ghanensis.* PT-gliadin induced a significant increase in intestinal permeability following incubation with PT-

gliadin for 30 min, and intestinal permeability tended to decrease and then became stable over time (60 min and 90 min). Thus, the expression levels of zonulin as a key regulator of gut permeability at 30 and 60 min of the experimental treatments could be considered to provide a mechanistic explanation for increased intestinal permeability at the early time point. Furthermore, even though no marked alteration in the expression of claudin-1 was observed among the treatment groups, claudin-2, which is another mediator of leaky gut, should be investigated to test the conclusion.

Conclusion

The evidence provided by the present study has emphasized the potential suppressive characteristics of *A. ghanensis* on gliadin-induced cellular responses through alterations in the expression of genes involved in the maintenance of IEC barrier permeability. The gluten-digesting properties of *A. ghanensis* offer a possible explanation for the improvements in maintaining the TJs between IECs. However, more precise mechanistic data from further *in vivo* and *in vitro* investigations and clinical trials are needed to fully elucidate the functional significance of *A. ghanensis in vivo*.

References

1. Lindfors K, Ciacci C, Kurppa K, Lundin KEA, Makharia GK, Mearin ML, et al. Coeliac disease. Nat Rev Dis Primers. 2019;5(1):3. doi: 10.1038/s41572-018-0054-z.
2. Uche-Anya E, Lebwohl B. Celiac disease: clinical update. Curr Opin Gastroenterol. 2021;37(6):619-24. doi: 10.1097/MOG.0000000000000785.
3. Jalilian M, Jalali R. Prevalence of celiac disease in children with type 1 diabetes: A review. Diabetes Metab Syndr. 2021;15(3):969-74. doi: 10.1016/j.dsx.2021.04.023.
4. Naveh Y, Rosenthal E, Ben-Arieh Y, Etzioni A. Celiac disease-associated alopecia in childhood. J Pediatr. 1999;134(3):362-4. doi: 10.1016/s0022-3476(99)70466-x.
5. Chirdo FG, Auricchio S, Troncone R, Barone MV. The gliadin p31-43 peptide: Inducer of multiple proinflammatory effects. Int Rev Cell Mol Biol. 2021;358:165-205. doi: 10.1016/bs.ircmb.2020.10.003.
6. Falcigno L, Calvanese L, Conte M, Nanayakkara M, Barone MV, D'Auria G. Structural Perspective of Gliadin Peptides Active in Celiac Disease. Int J Mol Sci. 2020;21(23). doi: 10.3390/ijms21239301.
7. Chelakkot C, Ghim J, Ryu SH. Mechanisms regulating intestinal barrier integrity and its pathological implications. Exp Mol Med. 2018;50(8):1-9. doi: 10.1038/s12276-018-0126-x.
8. Lammers KM, Lu R, Brownley J, Lu B, Gerard C, Thomas K, et al. Gliadin induces an increase in intestinal permeability and zonulin release by binding to the chemokine receptor CXCR3. Gastroenterology. 2008;135(1):194-204.e3. doi: 10.1053/j.gastro.2008.03.023.
9. Drago S, El Asmar R, Di Pierro M, Grazia Clemente M, Tripathi A, Sapone A, et al. Gliadin, zonulin and gut permeability: Effects on celiac and non-celiac intestinal mucosa and intestinal cell lines. Scand J Gastroenterol. 2006;41(4):408-19. doi: 10.1080/00365520500235334.
10. Fasano A. Zonulin, regulation of tight junctions, and autoimmune diseases. Ann N Y Acad Sci. 2012;1258:25-33. doi: 10.1111/j.1749-6632.2012.06538.x.
11. Håkansson Å, Andrén Aronsson C, Brundin C, Oscarsson E, Molin G, Agardh D. Effects of. Nutrients. 2019;11(8). doi: 10.3390/nu11081925.
12. Marasco G, Cirota GG, Rossini B, Lungaro L, Di Biase AR, Colecchia A, et al. Probiotics, Prebiotics and Other Dietary Supplements for Gut Microbiota Modulation in Celiac Disease Patients. Nutrients. 2020;12(9). doi: 10.3390/nu12092674.
13. Gujral N, Suh JW, Sunwoo HH. Effect of anti-gliadin IgY antibody on epithelial intestinal integrity and inflammatory response induced by gliadin. BMC Immunol. 2015;16:41. doi: 10.1186/s12865-015-0104-1.
14. Doguer C, Akalan H, Tokatlı Demirok N, Erdal B, Mete R, Bilgen T. Protective effects of *Acetobacter ghanensis* against gliadin toxicity in intestinal epithelial cells with immunoregulatory and gluten-digestive properties. Eur J Nutr. 2022. doi: 10.1007/s00394-022-03015-6.
15. Gulec S, Collins JF. Silencing the Menkes copper-transporting ATPase (Atp7a) gene in rat intestinal epithelial (IEC-6) cells increases iron flux via transcriptional induction of ferroportin 1 (Fpn1). J Nutr. 2014;144(1):12-9. doi: 10.3945/jn.113.183160.
16. Gujral N, Freeman HJ, Thomson AB. Celiac disease: prevalence, diagnosis, pathogenesis and treatment. World J Gastroenterol. 2012;18(42):6036-59. doi: 10.3748/wjg.v18.i42.6036.
17. Ludvigsson JF, Murray JA. Epidemiology of Celiac Disease. Gastroenterol Clin North Am. 2019;48(1):1-18. doi: 10.1016/j.gtc.2018.09.004.
18. Makharia GK, Singh P, Catassi C, Sanders DS, Leffler D, Ali RAR, et al. The global burden of coeliac disease: opportunities and challenges. Nat Rev Gastroenterol Hepatol. 2022;19(5):313-27. doi: 10.1038/s41575-021-00552-z.
19. Su GL, Ko CW, Bercik P, Falck-Ytter Y, Sultan S, Weizman AV, et al. AGA Clinical Practice Guidelines on the Role of Probiotics in the Management of Gastrointestinal Disorders. Gastroenterology. 2020;159(2):697-705. doi: 10.1053/j.gastro.2020.05.059.
20. Seiler CL, Kiflen M, Stefanolo JP, Bai JC, Bercik P, Kelly CP, et al. Probiotics for Celiac Disease: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Am J Gastroenterol. 2020;115(10):1584-95. doi: 10.14309/ajg.0000000000000749.
21. Cristofori F, Indrio F, Miniello VL, De Angelis M, Francavilla R. Probiotics in Celiac Disease. Nutrients. 2018;10(12). doi: 10.3390/nu10121824.
22. Clemente MG, De Virgiliis S, Kang JS, Macatagney R, Musu MP, Di Pierro MR, et al. Early effects of gliadin on enterocyte intracellular signalling involved in intestinal barrier function. Gut. 2003;52(2):218-23. doi: 10.1136/gut.52.2.218.
23. Hollon J, Puppa EL, Greenwald B, Goldberg E, Guerrerio A, Fasano A. Effect of gliadin on permeability of intestinal biopsy explants from celiac disease patients and patients with non-celiac gluten sensitivity. Nutrients. 2015;7(3):1565-76. doi: 10.3390/nu7031565.
24. Orlando A, Linsalata M, Notarnicola M, Tutino V, Russo F. Lactobacillus GG restoration of the gliadin induced epithelial barrier disruption: the role of cellular polyamines. BMC Microbiol. 2014;14:19. doi: 10.1186/1471-2180-14-19.
25. Lindfors K, Blomqvist T, Juuti-Uusitalo K, Stenman S, Venäläinen J, Mäki M, et al. Live probiotic Bifidobacterium lactis bacteria inhibit the toxic effects induced by wheat gliadin in epithelial cell culture. Clin Exp Immunol. 2008;152(3):552-8. oi: 10.1111/j.1365-2249.2008.03635.x.
26. Silano M, Vincentini O, Luciani A, Felli C, Caserta S, Esposito S, et al. Early tissue transglutaminase-mediated response underlies K562(S)-cell gliadin-dependent agglutination. Pediatr Res. 2012;71(5):532-8. doi: 10.1038/pr.2012.4.
27. Sander GR, Cummins AG, Henshall T, Powell BC. Rapid disruption of intestinal barrier function by gliadin involves altered expression of apical junctional proteins. FEBS Lett. 2005;579(21):4851-5. doi: 10.1016/j.febslet.2005.07.066.
28. Orlando A, Linsalata M, Bianco G, Notarnicola M, D'Attoma B, Scavo MP, et al. GG Protects the Epithelial Barrier of Wistar Rats from the Pepsin-Trypsin-Digested Gliadin (PTG)-Induced Enteropathy. Nutrients. 2018;10(11). doi: 10.3390/nu10111698.
29. Bhat MI, Sowmya K, Kapila S, Kapila R. Potential Probiotic Lactobacillus rhamnosus (MTCC-5897) Inhibits Escherichia coli Impaired Intestinal Barrier Function by Modulating the Host Tight Junction Gene Response. Probiotics Antimicrob Proteins. 2020;12(3):1149-60. doi: 10.1007/s12602-019-09608-8.
30. Anderson RC, Cookson AL, McNabb WC, Park Z, McCann MJ, Kelly WJ, et al. Lactobacillus plantarum MB452 enhances the function of the intestinal barrier by increasing the expression levels of genes involved in tight junction formation. BMC Microbiol. 2010;10:316. doi: 10.1186/1471-2180-10-316.
31. Herrán AR, Pérez-Andrés J, Caminero A, Nistal E, Vivas S, Ruiz de Morales JM, et al. Gluten-degrading bacteria are present in the human small intestine of healthy volunteers and celiac patients. Res Microbiol. 2017;168(7):673-84. doi: 10.1016/j.resmic.2017.04.008.
32. Greco L, Gobbetti M, Auricchio R, Di Mase R, Landolfo F, Paparo F, et al. Safety for patients with celiac disease of baked goods made of wheat flour hydrolyzed during food processing. Clin Gastroenterol Hepatol. 2011;9(1):24-9. doi: 10.1016/j.cgh.2010.09.025.
33. Francavilla R, De Angelis M, Rizzello CG, Cavallo N, Dal Bello F, Gobbetti M. Selected Probiotic Lactobacilli Have the Capacity to Hydrolyze Gluten Peptides during Simulated Gastrointestinal Digestion. Appl Environ Microbiol. 2017;83(14). doi: 10.1128/AEM.00376-17.

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Prognostic value of lymphovascular and perineural invasion in colorectal cancer

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Ethics Committee Approval
The study was approved by the Hitit University Clinical Research Ethics Committee with the decision numbered 2022-86.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Lymphovascular and perineural invasion (LVI and PNI, respectively) are associated with poor prognosis in various cancers. We sought to identify clinical variables associated with LVI and PNI in colorectal cancer (CRC) and their effects on survival.
Methods: Our study design is consistent with a retrospective cohort study. Data from 237 patients with documented LVI or PNI who underwent surgery for colorectal cancer between 2017 and 2021 were retrospectively reviewed. Demographic characteristics, surgery and pathology reports, disease-free and overall survival (DFS and OS, respectively) of the patients were examined.
Results: When the DFS duration of the patients were evaluated, The mean DFS of the LVI-negative group was 27.4 (15.09) months, and the mean of the LVI-positive patients was 20.45 (13) months. DFS was longer in the LVI-negative group (P<0.001). DFS was 52.26 (1.89) months in PNI-negative patients and 34.29 (2.71) months in PNI-positive patients. DFS expectation of PNI-positive patients was approximately 18 months less than that of negative patients (P<0.001). When the patients were evaluated in terms of OS duration, no significant difference was observed in LVI-negative and -positive patient groups, while the estimated OS duration was 52.29 (1.84) months in PNI-negative patients, and 40.10 (2.49) months in PNI-positive patients. OS was 12 months shorter in PNI-negative patients (P<0.001).
Conclusion: The use of PNI and LVI together was found to have a significant impact on the survival rates of patients with colorectal cancer. Documenting LVI and PNI status in biopsy specimens can aid in the management, prognosis, and decision-making for treating colorectal tumors.

Keywords: colorectal cancer, lymphovascular invasion, perineural invasion

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Introduction

Colorectal cancer (CRC) is one of the most common cancers and the fifth leading cause of cancer-related death [1]. Despite advances in technology and treatment, recurrence and metastases continue to cause reductions in patient survival [2]. The extent of the disease is important in terms of treatment choices and prognosis of CRC. It is based on the American Joint Committee on Cancer (AJCC) staging. This classification (TNM) includes various histopathological features, such as tumor invasion depth (T), lymph node metastasis (N), and the presence of metastatic disease (M) [3]. However, TNM classification is insufficient to predict the prognosis of CRC as patients with the same TNM stage may experience different survival times and recurrence rates [4,5].

Various risk factors for poor prognosis have been identified: (1) T4 tumor, (2) perforation, (3) obstruction, (4) high-grade tumor, (4) lymphovascular invasion (LVI) or perineural invasion (PNI), (5) positive resection margin, and/or (6) removal of less than 12 lymph nodes [6,7]. Various international guidelines, including those of the American Society of Clinical Oncology (ASCO), the National Comprehensive Cancer Network, and the European Society of Medical Oncology, recommend adjuvant chemotherapy for stage II patients with these risk factors [8–10]. However, no conclusive evidence supporting the efficacy of adjuvant chemotherapy in this patient group has been presented. In addition, several conflicting results have been reported about the benefits of adjuvant chemotherapy even in high-risk patients [11,12].

LVI is the involvement of small lymphatic or blood (typically venous) vessels in the tumor, while PNI is defined as the involvement of nerve cells and the nerve sheath around the organ with the tumor [13,14]. Histopathological identification of LVI has long been considered a potential prognostic indicator and predictor of patient outcomes because of its association with increased lymphatic metastasis [15–17]. PNI has been associated with more aggressive tumor phenotypes and poor prognoses in various cancers [14].

In this study, we aimed to evaluate the prognostic significance of LVI and PNI in patients with CRC.

Materials and methods

Our study was planned as a retrospective cohort study after it was approved by the Hitit University Clinical Research Ethics Committee with the decision numbered 2022-86. Data were collected by examining patient files and computer records.

Between 2017 and 2021, we screened 354 CRC patients who underwent surgery at the Department of General Surgery. Two-hundred thirty-seven patients were included in the study after the study excluded several types of patients: (1) those under the age of 18, (2) those with known hematological and oncological diseases other than colon carcinoma, (3) those with pre-operative metastases, those with post-operative pathology other than adenocarcinoma, and those whose records could not be reached. Patients' age, gender, operation type, operation technique, pathology result, tumor size, number of metastatic lymph nodes, T-and M-stages, length of hospital stay, duration of operation, pre-operative serum lymphocytes, platelets, neutrophils, carcinoembryonic antigen and cancer antigen 19 (CEA and CA 19-9 levels, respectively) presence of lymphovascular and/or perineural invasion in pathology reports, presence of recurrence and/or metastasis during follow-up, disease-free survival (DFS), overall survival (OS) duration, and the presence of cancer-related mortality and all-cause mortality were obtained by retrospectively scanning records from the archive system.

Statistical analysis

IBM SPSS Statistics for Windows program was used for all statistical analysis (version 26; IBM Corp., Armonk, N.Y., USA). For descriptive statistics, numbers and percentages were used for categorical variables, and means (standard deviations [SD]) were used for numerical variables. Normal data distribution was evaluated using the Shapiro–Wilk test. Relationships between variables were investigated with Pearson's or Spearman's correlation coefficient based on data distribution. Comparison of numerical measurements for two independent groups' ages, tumor sizes, number of metastatic lymph nodes, lengths of hospital stay, operation times, pre-operative serum lymphocytes, platelets, neutrophils, CEA and CA19-9 levels, DFS, OS using the Mann–Whitney U test were evaluated.

Categorical variables, such as gender, operation type, operation technique, pathology result, T- and M-stages, presence of lymphovascular invasion in pathology reports, presence of perineural invasion, presence of recurrence and/or metastasis during follow-up, presence of cancer-related mortality, and all-cause mortality frequency and distribution were determined by research groups. Ratio comparisons were evaluated using the chi-squared test. Estimated DFS and OS times of the patients according to LVI and PNI status were determined and compared using the Kaplan–Meier analysis and log-rank test. For the statistical significance level, $P<0.05$ was accepted.

Results

The mean age of the patients in the whole group was 69.84 (10.82) years. Of these patients, 151 (63.71%) were male, and 86 (36.29%) were female (Table 1). No statistical difference in terms of operation type and technique ($P=0.453$ and $P=0.211$, respectively) were found. Of the extracted materials, 59 were well differentiated (24.89%),164 were moderately differentiated (69.20%), and 14 were poorly differentiated (5.91%). The mean tumor diameter was 4.99 (2.12) cm. The mean number of metastatic lymph nodes in the excised material was two.

When the patients were examined in terms of T-stage, nine patients were in T1 (3.80%), 27 patients were in T2 (11.39%),150 patients were in T3 (63.29%), and 51 patients were in T4 (21.52%). One-hundred fifteen patients were N0 (48.52%), 86 (36.29%) N1, and 36 patients were N2 (15.19%). The mean hospital stay of the patients in the whole group was 16.03 (8.85) days, and the mean operation time was 157.51 (53.62) min.

When the laboratory values were examined, the mean lymphocyte count of the patients in the whole group was 1.63 (0.68), the mean platelet count was 271.54 (93.54), and the mean neutrophil count was 5.7 (3.25). The mean of the CEA was 26.49 (175.64) µg/L, and the mean of CA19-9 was 28.56 (79.33) U/mL.

Table 1: Descriptive characteristics and association of both lymphovascular and perineural invasion with clinicopathological features

Variables		All Patients	LVI negative (n=121)	LVI positive (n=116)	*P*-value	PNI negative (n=154)	PNI positive (n=83)	*P*-value
Age		69.84(10.82)	70.2(10.87)	69.38(10.78)	0.354	69.92(10.66)	69.7(11.17)	0.715
Gender	Male	151 (63.71%)	69 (57.02%)	82 (70.69%)	0.029	96 (62.34%)	55 (66.27%)	0.549
	Female	86 (36.29%)	52 (42.98%)	34 (29.31%)		58 (37.66%)	28 (33.73%)	
Operation type	Hemicolectomy, right-sided	72 (30.38%)	34 (28.10%)	38 (32.76%)	0.654	45 (29.22%)	27 (32.53%)	0.453
	Hemicolectomy left-sided	44 (18.57%)	26 (21.49%)	18 (15.52%)		33 (21.43%)	11 (13.25%)	
	Low anterior resection	102 (43.04%)	51 (42.15%)	51 (43.97%)		65 (42.21%)	37 (44.58%)	
	Abdominoperineal resection	19 (8.02%)	10 (8.26%)	9 (7.76%)		11 (7.14%)	8 (9.64%)	
Operation technique	Open	202 (85.23%)	103 (85.12%)	99 (85.34%)	0.962	128 (83.12%)	74 (89.16%)	0.211
	Laparoscopic	35 (14.77%)	18 (14.88%)	17 (14.66%)		26 (16.88%)	9 (10.84%)	
Pathologic type	Adenocarcinoma, well-differentiation	59 (24.89%)	35 (28.93%)	24 (20.69%)	0.010	50 (32.47%)	9 (10.84%)	0.001
	Adenocarcinoma, moderate-differentiation	164 (69.20%)	84 (69.42%)	80 (68.97%)		97 (62.99%)	67 (80.72%)	
	Adenocarcinoma, poor-differentiation	14 (5.91%)	2 (1.65%)	12 (10.34%)		7 (4.55%)	7 (8.43%)	
Tumor size (cm)		4.9(2.12)	4.8(2.27)	5.18(1.93)	0.077	4.7(2.17)	5.38(1.97)	0.011
Metastatic lymph node count (n=120)		2 (1-13)	1 (1-12)	2 (1-13)	0,038	2 (1-12)	2 (1-13)	0.020
T stage	T1	9 (3.80%)	9 (7.44%)	0 (0,00%)	<0.001	9 (5.84%)	0 (0.00%)	<0.001
	T2	27 (11.39%)	23 (19.01%)	4 (3.45%)		25 (16.23%)	2 (2.41%)	
	T3	150 (63.29%)	77 (63.64%)	73 (62.93%)		94 (61.04%)	56 (67.47%)	
	T4	51 (21.52%)	12 (9.92%)	39 (33.62%)		26 (16.88%)	25 (30.12%)	
N stage	N0	115 (48.52%)	97 (80.17%)	18 (15.52%)	<0.001	94 (61.04%)	21 (25.30%)	<0.001
	N1	86 (36.29%)	22 (18.18%)	64 (55.17%)		49 (31.82%)	37 (44.58%)	
	N2	36 (15.19%)	2 (1.65%)	34 (29.31%)		11 (7.14%)	25 (30.12%)	
Hospitalization duration (days)		16.03(8.85)	16.45(8.77)	15.59(8.94)	0.453	15.73(7.99)	16.58(10.29)	0.643
Operation duration (minutes)		157.51(53.62)	153.92(47.51)	161.25(59.31)	0.453	155.86(51.31)	160.5(57.86)	0.580
Lymphocyte count		1.63(0.68)	1.61(0.66)	1.66(0.69)	0.563	1.58(0.6)	1.74(0.78)	0.233
Platelet count		271.54(93.54)	261.07(93.53)	282.47(92.7)	0.086	259.29(85.3)	294.28(103.95)	0.011
Neutrophile count		5.7(3.25)	5.46(3.25)	5.94(3.24)	0.094	5.35(2.94)	6.33(3,69)	0.024
CEA		26.49(175.64)	8.49(22.23)	45.26(249.2)	0.038	25.6(208.25)	28.15(88.7)	0.159
CA19-9		28.56(79.33)	22.49(36.25)	34.88(107.07)	0.813	27.58(92.16)	30.37(47.49)	0.511
Lymphovascular invasion	LVI negative	121 (51.05%)				104 (67.53%)	17 (20.48%)	<0.001
	LVI positive	116 (48.95%)				50 (32.47%)	66 (79.52%)	
Perineural invasion	PNI negative	154 (64.98%)	104 (85.95%)	50 (43.10%)	<0.001			
	PNI positive	83 (35.02%)	17 (14.05%)	66 (56.90%)				
Disease status	Disease-Free	169 (71.3%)	108 (89.3%)	61 (52.6%)	<0.001	128 (83.1%)	41 (49.4%)	<0.001
	Recurrence or Metastasis	68 (28.7%)	13 (10.7%)	55 (47.4%)		26 (16.9%)	42 (50.6%)	
Disease free survival duration (months)		24(14.5)	27.4(15.09)	20.45(13)	<0.001	26.26(15.04)	19.8(12,47)	<0.001
Overall survival (months)		27.97(14.5)	29.02(14.77)	26.89(14.21)	0.237	28.88(14.99)	26.3(13.49)	0.254
Cancer related mortality	No cancer related mortality	204 (86.1%)	111 (91.7%)	93 (80.2%)	0.010	141 (91.6%)	63 (75.9%)	0.001
	Cancer-related Mortality	33 (13.9%)	10 (8.3%)	23 (19.8%)		13 (8.4%)	20 (24.1%)	
All Causes Mortality	Alive	179 (75.53%)	96 (79.34%)	83 (71.55%)	0.163	126 (81.82%)	53 (63.86%)	0,002
	Exitus	58 (24.47%)	25 (20.66%)	33 (28.45%)		28 (18.18%)	30 (36.14%)	

PNI: perineural invasion, LVI: lymphovascular invasion

When the patients were examined in terms of lymphovascular invasion, there were 121 patients with negative LVI (51.05%) and 116 patients with positive LVI (48.95%). Considering PNI, 154 PNI-negative patients (64.98%) and 83 PNI-positive patients (35.02%) were found. In the post-operative follow-up period, 169 (71.3%) patients showed no signs of relapse, but recurrence or metastasis was observed in 68 (28.7%) patients.

The mean DFS of the patients in the study group was 24 (14.5) months, and the mean OS was 27.97 (14.5) months. When the patients were examined in terms of cancer-related mortality, cancer-related mortality was observed in 33 patients (13.9%). When all-cause mortality was evaluated, mortality was observed in 58 patients (24.47%).

Lymphovascular invasion

No statistical significance was found when the patients were compared in terms of age (*P*=0.354). When the gender distribution was examined, the male ratio was higher in LVI-positive patients (*P*=0.029) as shown in Table 1. No statistical significance in terms of the operation type and surgical techniques used for the patients (*P*=0.654 and *P*=0.962, respectively).

When the pathology results were examined, the rate of poorly differentiated carcinoma was higher in the second group (*P*=0.01), and was considered a statistically significant different.

No statistical significance between the two groups in terms of the mean tumor diameter of LVI-negative and positive patients (*P*=0.077) was found. The number of removed metastatic lymph nodes was higher in LVI-positive patients (*P*=0.038).

When the relationship between PNI and LVI was examined, 104 (85.95%) patients in the LVI negative group were PNI negative, 17 (14.05%) were PNI positive, in the LVI positive group 50 (43.10%) patients were PNI negative, and 66 (56.90%) patients were found to be PNI positive. LVI positivity and PNI positivity were more common together, which would be statistically significant (*P*<0.001).

Recurrence or metastasis was observed in only 13 (10.7%) patients in the LVI negative group, this rate increased in the LVI positive group, and recurrence or metastasis was observed in 55 (47.4%) patients, which was statistically significant (*P*<0.001).

When the DFS was evaluated in the patients, the mean of the LVI-negative group was 27.4(15.09) months, and the mean of the LVI-positive patients was 20.45 (13) months. Statistical significance (*P*<0.001) was noted. When OS was examined, the mean survival time of LVI-negative patients was 29.02 (14.77) months, and the mean OS of LVI-positive patients was 26.89 (14.21) months, and no statistically significant difference was found (*P*=0.237).

In the LVI-negative group, mortality was observed in 10 (8.3%) patients due to cancer-related causes. In the LVI-positive group, this rate increased and cancer-related mortality was observed in 23 (19.8%) patients, and a statistically significant difference was observed (*P*=0.01). When compared in terms of overall mortality, 25 (20.66%) patients died in the LVI negative

group, and 33 (28.45%) died in the LVI positive group. Although an increase in the rate was observed; however, statistical significance could not be determined (*P*=0.163).

Perineural invasion

When the patients were compared in terms of age, no statistical significance in terms of age and gender was found (Table 1).

No statistically significant difference was found between the type and surgical technique (*P*=0.453 and *P*=0.211, respectively).

The mean tumor diameter of PNI-negative patients was 4.78 (2.17) cm and that of PNI-positive patients was larger at 5.38 (1.97) cm. A statistically significant difference (*P*=0.011) was found. More metastatic lymph nodes were dissected in PNI-positive patients (*P*=0.02).

A comparison in terms of T-stages is summarized in Table 1. When the mean duration of hospitalization and operation time of PNI-negative and positive patients were compared between the groups, no statistically significant difference was found (*P*=0.643 and *P*=0.580, respectively). Similarly, no statistically significant difference was observed between the serum lymphocyte, CEA, and CA19-9 levels of the patients in the two groups (*P*= 0.233, *P*=0.159, and *P*=0.511, respectively).

The mean platelet count of the patients in the PNI-negative group was 259.29 (85.3), while it was 294.28 (103.95) in the PNI-positive patients. A statistically significant difference (*P*=0.011) was detected. When evaluated in terms of neutrophil count, the mean of PNI-negative patients was 5.35 (2.94) while it was 6.33 (3.69) in PNI-positive patients, and a statistically significant difference was observed (*P*=0.024).

When the relationship between PNI and LVI was in terms of PNI, in the PNI-negative group, 104 (67.53%) patients were LVI negative, and 50 (32.47%) patients were LVI positive. In the PNI positive group, 17 (20.48%) patients were LVI negative, and 66 (79.52%) patients LVI was found to be positive, which was statistically significant. The incidence of LVI positivity increased in PNI positivity (*P*<0.001).

In the PNI-negative group, 128 (83.1%) patients remained disease-free. Recurrence or metastasis was observed in 26 (16.9%) patients in the PNI-negative group, and in 42 (50.6%) patients in the PNI-positive group, which resulted in a significant increase in the recurrence rate (*P*<0.001).

The mean DFS was found to be 26.26 (15.04) months in PNI-negative patients and 19.8 (12.47) months in PNI-positive patients (*P*<0.001). When the OS was examined, the mean OS time of PNI-negative patients was 28.88 (14.99) months and that of PNI-positive patients was 26.3 (13.49) months. No statistical significance between groups was found (*P*=0.254).

In the examination of cancer-related death (CRD) rates, 13 (8.4%) of PNI-negative patients died due to cancer-related causes, while this rate increased in 20 (24.1%) patients in the PNI-positive group, and statistical significance was observed (*P*<0.001). When the patients were evaluated in terms of overall mortality, it was observed that 28 (18.18%) patients died in the PNI-negative group, while the mortality rate in the PNI-positive group increased. A statistically significant difference was found, and 30 (36.14%) patients were passed away (*P*=0.002).

Estimated disease free survival and overall survival analyzes

As a result of the Kaplan–Meier survival analysis and log-rank test to determine the estimated overall survival (OS) of the patients in the study, the mean estimated OS expectation of the whole group was found to be 48.26 (1.60) months (95% confidence interval [CI] 45.120–51.390) as shown in Table 2. The mean estimated OS of LVI-negative patients was 49.09 (1.98) months (95% CI 41.086–50.589) while it was 45.84 (2.42) months (95% CI 45.200–52.977) in LVI-positive patients. No statistically significant difference was observed between the durations (*P*=0.127). When evaluated for PNI, the estimated OS was 52.29 (1.84) months (95% CI 48.690–55.889) in PNI-negative patients and 40.10 (2.49) months (95% CI 35.220–44.971) in PNI-positive patients. PNI positivity shortened OS expectation by 12 months; thus, a statistically significant difference was fond (*P*=0.001) as shown in Figures 1 and 2.

Table 2: Estimated overall survival times of both lymphovascular and perineural invasion

Variables		Estimated OS duration	%95 CI	*P*- value
Lymphovascular invasion	LVI Negative	49.09(1.98)	45.200–52.977	0.127
	LVI Positive	45.84(2.42)	41.086–50.589	
	Estimated OS	48.26(1.60)	45.120–51.390	
Perineural invasion	PNI Negative	52.29(1.84)	48.690–55.889	0.001
	PNI Positive	40.10(2.49)	35.220–44.971	
	Estimated OS	48.26(1.60)	45.120–51.390	

OS: overall survival, PNI: perineural invasion, LVI: lymphovascular invasion, CI: confidence interval

Figure 1: Lymphovascular invasion & overall survival

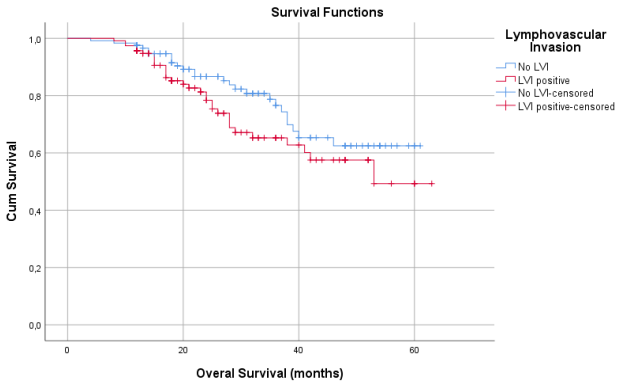
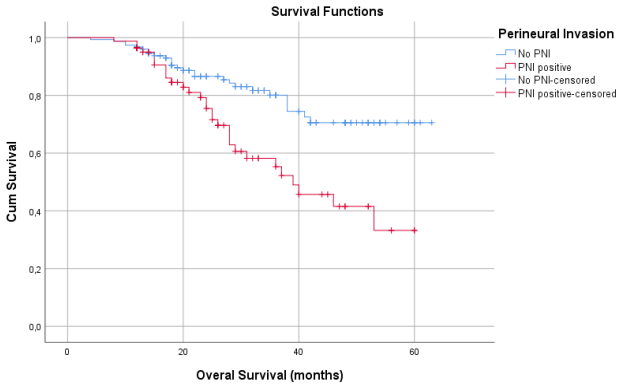


Figure 2: Perineural invasion & overall survival



When evaluated in terms of estimated DFS, the mean estimated DFS expectation of the whole group was found to be 47.34 (1.77) months (95% CI 43.872–50.803). While the mean DFS expectancy of LVI-negative patients was calculated as 48.73 (2.10) months (95% CI 44.608-52.848), it was observed as 44.08 (2.85) months (95% CI 38.493–49.667) in LVI-positive patients with a statistically significant difference (*P*=0.027) as shown in Table 3. The estimated DFS expectancy of PNI-negative patients was calculated as 52.26 (1.89) months (95% CI

48.562–55.954). The estimated DFS expectancy of PNI-positive patients was found to be 34.29 (2.71) months (95% CI 28.986–39.588), and the DFS expectancy of positive patients was approximately 18 months less than negative patients. The difference was considered statistically significant (P<0.001) as shown in Figures 3, and 4.

Table 3: Estimated disease-free survival times of lymphovascular invasion and perineural invasion

		Estimated DFS duration	%95 CI	*P*-value
Lymphovascular invasion	LVI Negative	48.73(2.10)	44.608–52.848	0.027
	LVI Positive	44.08(2.85)	38.493–49.667	
	Estimated DFS	47.34(1.77)	43.872–50.803	
Perineural invasion	PNI Negative	52.26(1.8)	48.562–55.954	<0.001
	PNI Positive	34.29(2.71)	28.986–39.588	
	Estimated DFS	47.34(1.77)	43.872–50.803	

DFS: disease free survival, PNI: perineural invasion, LVI: lymphovascular invasion, CI: confidence interval

Figure 3: Lymphovascular invasion & disease free survival

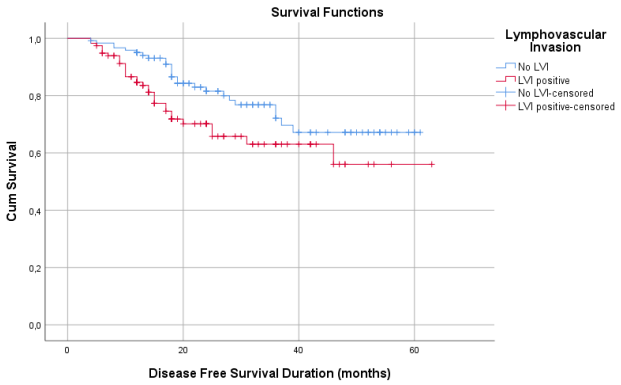
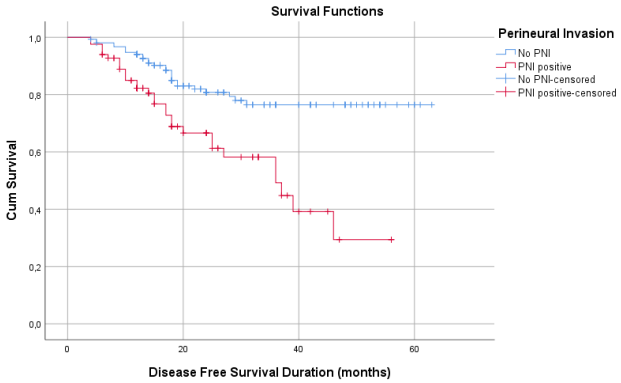


Figure 4: Perineural invasion & disease free survival



Discussion

In this study, it was found that LVI had a prognostic effect on DFS but had no effect on OS in CRC patients. It was observed that PNI affected both DFS and OS, and the DFS expectation was 18 months lower in the patient group with PNI than in the one without PNI.

Metastasis formation pathways in CRC has been investigated in many studies. It has been shown that the first step in metastasis formation is the invasion of vascular and neural structures. PNI represents tumor invasion of the space surrounding a nerve. Many studies have investigated the relationship between PNI and cancers. Beard et al. [18] reported that PNI is associated with recurrence and metastases in patients with prostate cancer. Harnden et al. [19] also reported that PNI leads to an increase in recurrences and is a prognostic marker in prostate cancer patients. Mendenhall [20] showed that PNI is associated with an increase in the risk of regional and distant metastases in head and neck cutaneous squamous cell carcinoma in addition to an increase in the risk of local recurrence, most prominently including recurrences in both the skin and cranial nerves.

In colorectal cancer, the incidence of PNI ranges from <10% to 35% from series to series [14,21,22]. Liebig et al. observed an average of 22% of PNI in stage I–IV colorectal cancer [14] as also found in our study. The incidence of patients with the disease was found to be 35%, which is consistent with reports in the literature. Detection of PNI is important for treatment decisions since PNI is an indicator of poor prognosis in patients with CRC in previous studies [23]. In a series of 269 stages I–IV patients with CRC, 5-year DFS and OS in those with PNI-positive tumors were significantly higher, and PNI proved to be both an overall cancer-specific and an independent prognostic factor for disease [14]. In a study of Sun et al. [24], the risk of poor survival was found to be 4.8 times higher in patients with PNI. In our study, a statistically significant difference was observed in PNI in terms of both DFS and OS, and the DFS expectation was 18 months in the patient group with PNI compared to the patient group without PNI, which was observed to be lower.

LVI is defined as tumor invasion in the vascular and lymphatic structures. Since it is not possible to distinguish between lymphatic and venous vessels histologically, the term LVI is often used to refer to any of these structures [25]. The presence of LVI in the literature ranges from 10% to about 90% [26,27]. Zhong et al. [28] reported the presence of LVI in 20% of patients. However, the results of Yuksel et al. [29] are similar to those in our study in which 48.95% of patients had LVI. Differences in the presence of LVI in studies may be due to the heterogeneity of the study population. Differences may also be due to differences in interpretation of LVI as some authors refer to LVI as lymphatic invasion, angiolymphatic invasion, or venous invasion [13,30].

In many studies it has been reported that LVI is an important prognostic factor for OS and DFS. In a study by Nakamura et al. [31] with a series of 316 patients, they concluded that LVI has a negative effect on OS and DFS and is associated with peritoneal recurrence in stages II and III, and liver metastasis of colon cancer after curative resection. In contrast, Osterman et al. [32] concluded that LVI did not affect OS and DFS in their study. Zhang et al. [33] found that LVI did not affect OS in their study evaluating the effect of adjuvant chemotherapy. No statistically significant difference was observed. The DFS expectancy of LVI-positive patients was approximately four months less than that of negative patients and was statistically significantly different. Our results were similar to those found by Zhang et al. [33].

Limitations

Our study has some limitations. One is the retrospective design, and the fact that some selection bias exists. The sample size was not large enough, and more samples may be needed to further validate our model. In addition, the inability of pathologists to evaluate samples independently may have caused errors in the ratios of PNI and LVI.

Conclusion

As a result, the DFS duration of the patients was longer in the LVI-negative group. The DFS expectancy of PNI-positive

patients was approximately 18 months less than that of negative patients. In addition, no significant difference was observed in LVI-negative and -positive patient groups in terms of OS durations. OS was 12 months shorter in PNI-negative patients than in PNI-positive patients.

References

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA Cancer J Clin. 2022;72:7-33.
2. Guyot F, Faivre J, Manfredi S, Meny B, Bonithon-Kopp C, Bouvier A. Time trends in the treatment and survival of recurrences from colorectal cancer. Ann Oncol. 2005;16(5):756-61.
3. Edge, Stephen B, Carolyn C. Compton. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol. 2010;17(6):1471-74.
4. McLeod HL, Murray GI. Tumour markers of prognosis in colorectal cancer. Br J Cancer. 1999;79(2):191-203.
5. Schneider NI, Langner C. Prognostic stratification of colorectal cancer patients: current perspectives. Cancer Manag Res. 2014 Jul 2;6:291-300.
6. Benson AB, Venook AP, Al-Hawary MM, Arain MA, Chen YJ, Ciombor KK, et al. Colon Cancer, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2021 Mar 2;19(3):329-59.
7. Argilés G, Tabernero J, Labianca R, Hochhauser D, Salazar R, Iveson T, et al. Localised colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2020 Oct;31(10):1291-305.
8. Benson AB, Schrag D, Somerfield MR, Cohen AM, Figueredo AT, Flynn PJ, et al. American Society of Clinical Oncology recommendations on adjuvant chemotherapy for stage II colon cancer. J Clin Oncol. 2004;22:3408–19.
9. Labianca R, Nordlinger B, Beretta GD, Mosconi S, Mandalà M, Cervantes A, et al. Early colon cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2014;24(6):64–72.
10. Benson AB 3rd, Venook AP, Cederquist L, Chan E, Chen YJ, Cooper HS, et al. Colon cancer, version 1.2017, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw. 2017;15(3):370–98.
11. Weiss JM, Schumacher J, Allen GO, Neuman H, Lange EO, Loconte NK, et al. Adjuvant chemotherapy for stage II right-sided and left-sided colon cancer: analysis of SEER-medicare data. Ann Surg Oncol. 2014 Jun;21(6):1781-91.
12. Booth CM, Nanji S, Wei X, Peng Y, Biagi JJ, Hanna TP, Krzyzanowska MK, Mackillop WJ. Adjuvant Chemotherapy for Stage II Colon Cancer: Practice Patterns and Effectiveness in the General Population. Clin Oncol (R Coll Radiol). 2017 Jan;29(1):e29-e38. doi: 10.1016/j.clon.2016.09.001. Epub 2016 Sep 20. PMID: 27663601.
13. Compton CC, Fielding LP, Burgart LJ, Conley B, Cooper HS, Hamilton SR, et al. Prognostic factors in colorectal cancer. College of American Pathologists Consensus Statement 1999. Arch Pathol Lab Med. 2000 Jul;124(7):979-94.
14. Liebig C, Ayala G, Wilks J, Verstovsek G, Liu H, Agarwal N, et al. Perineural invasion is an independent predictor of outcome in colorectal cancer. J Clin Oncol. 2009; 27(31): 5131
15. Harris EI, Lewin DN, Wang HL, Lauwers GY, Srivastava A, Shyr Y, et al. Lymphovascular invasion in colorectal cancer: an interobserver variability study. Am J Surg Pathol.2008;32:1816–21.
16. Yuan H, Dong Q, Zheng B, Hu X, Xu JB, Tu S. Lymphovascular invasion is a high risk factor for stage I/II colorectal cancer: a systematic review and meta-analysis. Oncotarget 2017;8:46565–79.
17. Lim SB, Yu CS, Jang SJ, Kim TW, Kim JH, Kim JC. Prognostic significance of lymphovascular invasion in sporadic colorectal cancer. Dis Colon Rectum.2010;53:377–84.
18. Beard CJ, Chen MH, Cote K. Loffredo M, Renshaw AA, Hurwitz M, et al. Perineural invasion is associated with increased relapse after external beam radiotherapy for men with low-risk prostate cancer and may be a marker for occult, high-grade cancer. Int J Radiat Oncol Biol Phys. 2004;58:19–24.
19. Harnden P, Shelley MD, Clements H, Coles B, Tyndale-Biscoe RS, Naylor B, et al. The prognostic significance of perineural invasion in prostatic cancer biopsies: a systematic review. Cancer-Am Cancer Soc. 2007;109:13–24.
20. Mendenhall WM, Amdur RJ, Hinerman RW, Werning JW, Malyapa RS, Villaret, et al. Skin cancer of the head and neck with perineural invasion. Am J Clin Oncol. 2007;30:93–96.
21. Peng J, Lu JJ, Zhu J, Xu Y, Lu H, Lian P, Cai G, Cai S. Prediction of treatment outcome by CD44v6 after total mesorectal excision in locally advanced rectal cancer. Cancer J. 2008 Jan-Feb;14(1):54-61. doi: 10.1097/PPO.0b013e3181629a67. PMID: 18303484.
22. Matsushima T, Mori M, Kido A, Adachi Y, Sugimachi K. Preoperative estimation of neural invasion in rectal carcinoma. Oncol Rep. 1998; 5(1):73-9.
23. Knijn N, Mogk SC, Teerenstra S, Simmer F, Nagtegaal ID. Perineural Invasion is a Strong Prognostic Factor in Colorectal Cancer: A Systematic Review. Am J Surg Pathol. 2016 Jan;40(1):103-12.
24. Sun Q, Liu T, Liu P, Luo J, Zhang N, et al. Perineural and lymphovascular invasion predicts for poor prognosis in locally advanced rectal cancer after neoadjuvant chemoradiotherapy and surgery. J Cancer. 2019 May 21;10(10):2243-9.
25. Hoda SA, Hoda RS, Merlin S, Shamonki J, Rivera M. Issues relating to lymphovascular invasion in breast carcinoma. Adv Anat Pathol. 2006;13:308–15.
26. Lim TY, Pavlidis P, Gulati S, Pirani T, Samaan M, Chung-Faye G, et al. Vedolizumab in Inflammatory Bowel Disease Associated with Autoimmune Liver Disease Pre- and Postliver Transplantation: A Case Series. Inflamm Bowel Dis. 2016;22:39–40.
27. Huh JW, Lee JH, Kim HR, Kim YJ. Prognostic significance of lymphovascular or perineural invasion in patients with locally advanced colorectal cancer. Am J Surg. 2013;206:758–763
28. Zhong JW, Yang SX, Chen RP, Zhou YH, Ye MS, Miao L, et al. Prognostic Value of Lymphovascular Invasion in Patients with Stage III Colorectal Cancer: A Retrospective Study. Med Sci Monit. 2019;25:6043–50.
29. Yüksel C, Çulcu S, Gojayev A, Demirci S, Ünal A. E. Prognostic Value of Lymphovascular and Perineural Invasion in Colon Cancer. Acta Oncologica Turcica, 2021;54(2):166-74.
30. Sibio S, Di Giorgio A, D'Ugo S, Palmieri G, Cinelli L, Formica V, et al. Histotype influences emergency presentation and prognosis in colon cancer surgery. Langenbecks Arch Surg. 2019 Nov;404(7):841-51.
31. Nakamura Y, Hokuto D, Koyama F, Matsuo Y, Nomi T, Yoshikawa T, et al. The Prognosis and Recurrence Pattern of Right- and Left-Sided Colon Cancer in Stage II, Stage III, and Liver Metastasis After Curative Resection. Ann Coloproctol. 2021 Oct;37(5):326-36.
32. Osterman E, Mezheyeuski A, Sjöblom T, Glimelius B. Beyond the NCCN Risk Factors in Colon Cancer: An Evaluation in a Swedish Population-Based Cohort. Ann Surg Oncol. 2020 Apr;27(4):1036-45.
33. Zhang C, Yin S, Tan Y, Huang J, Wang P, Hou W, et al. Patient Selection for Adjuvant Chemotherapy in High-Risk Stage II Colon Cancer: A Systematic Review and Meta-Analysis. Am J Clin Oncol. 2020 Apr;43(4):279-87.

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Comparison of classical and distance histology education taken by daytime and evening education students of health services at a vocational high school

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Ethics Committee Approval
The study was conducted with ethics approval (dated 12.30.2022 and numbered 4047) obtained from the Ethics Committee of Siirt University. 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: Distance education applications can improve histology education. This study aimed to compare the classical and distance histology education given to the daytime and evening education students of the Health Services Vocational High School Medical Laboratory Techniques course. The students' academic achievement, motivation, and mood were compared.

Methods: The students (n=134) that participated in the study were divided into four groups. The daytime and evening education students to whom the classical education model was applied were identified as the control group (Groups 1 and 3). The daytime and evening education students who received distance education were identified as the experimental group (Groups 2 and 4). Before and after the study, a pretest and posttest, the State-Trait Anxiety Inventory, and the Academic Motivation Scale were applied to the students who received nervous system histology education.

Results: The state-trait anxiety scores did not differ significantly according to the groups ($P>0.05$). The state anxiety scores obtained after the posttest were significantly lower than the state anxiety scores obtained before the pretest. According to the Academic Motivation Scale scores, the extrinsic motivation - external regulation subscale was significantly lower in Group 3 compared to the other groups ($P<0.05$). For the knowledge test results, there was a significant difference between the pretest and posttest scores in all groups, and the mean posttest scores were higher than the mean pretest scores. The posttest score of the daytime education face-to-face group (Classical education, Group 1) was significantly higher than the other groups ($P=0.011$).

Conclusion: In our study, the daytime education face-to-face group was the most effective among the different teaching styles and training methods in nervous system histology education. Our finding that the efficiency of distance education applications was not as high as face-to-face education suggests that such digital applications require further optimization. The lower success rates observed in the evening education groups can be increased by integrating face-to-face and distance education.

Keywords: histology education, daytime (formal) education, distance education, evening education

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Introduction

Advances in digitalization have resulted in a new era in education, changing the duties and responsibilities of educators. Recent developments have revealed that education should not be limited within the faculty and can continue outside the faculty. It has been demonstrated that education can become independent of space. In classical education, the concept of space is limited to the environment within universities, whereas digital education can be accessed from almost anywhere. Besides face-to-face education, various digital education platforms are also established. These digital platforms provide students with a much more flexible learning opportunity [1]. Thus, distance education platforms for histology education may provide benefits in addition to those of classical education.

Daytime (formal) education students attend classes during the daytime, while evening education students attend classes in the evening [2]. It is claimed that there would be no change in the quality of education if daytime (formal) education and evening education students receiving education at similar levels and under similar conditions [3]. Furthermore, some studies have reported negative opinions about evening education. Some disadvantages regarding evening education have been reported, such as a decrease in the quality of education and the decrease in scientific studies [4]. Therefore, there is a need for more comprehensive studies evaluating daytime and evening education students in terms of academic achievement, motivation, and mood.

Histology is an important aspect of basic medical sciences education [5]. Histology addresses examines the structural organization and functions of cells that form tissues [6]. It has been stated that new technological applications and distance education options will contribute to the histology course students generally describe as difficult [5]. The coronavirus 2019 (COVID-19) pandemic has negatively affected the health system [7] and medical and health education [8]. Unexpected conditions such as pandemics necessitate the development of alternative teaching methods, including online education, in basic medical courses such as histology and anatomy [9].

To our knowledge, no study has compared histology education to different education styles (daytime and evening education), including both face-to-face and distance education. This study aimed to compare the classical and distance histology education given to the daytime and evening education students of the Department of Medical Laboratory Techniques at the Health Services Vocational High School. The students' academic achievement, motivation, and mood were compared.

Materials and methods

The study was conducted with ethics approval (dated 12.30.2022 and numbered 4047) obtained from the Ethics Committee of Siirt University. All applications were carried out considering the ethical rules and the Declaration of Helsinki. The "Research Permission Form" required for the research was obtained from the institution where the study was conducted. The students that participated in the study were informed about the study and completed the "Informed Voluntary Consent Form".

Learning environment

The students that participated in the study were divided into four groups. The daytime and evening education students receiving classical education were identified as the control group (Groups 1 and 3, respectively). The daytime and evening education students who received distance education were identified as the experimental group (Groups 2 and 4, respectively). The information in the "Nervous System Histology" section in the "General Histology" book [10] was given to both groups. Education was given to Group 1 (classical education) and Group 2 (distance education) between 10:00 and 11:00 in the morning in two different classrooms. Group 3 (classical education) and Group 4 (distance education) were given a 1-h theoretical course between 19:00 and 20:00 in the evening in two classrooms. The content of the education given to each group was prepared to be similar. The nervous system histology course given to Groups 2 and 4 was recorded before the study for distance education. The link to the relevant course was shared with the students, who accessed these recordings online. For this purpose, smart devices and internet access were provided to the students in these groups.

Data collection

Before the education, the daytime education students (Groups 1 and 2) were given a Structured Student Introduction Form that included questions regarding demographic information and a "Knowledge exam (pretest)" that they were asked to complete. After completing the pretest, the students were divided into two groups and two classes. Both groups were asked to complete the "State-Trait Anxiety Inventory (STAI)" and the "Academic Motivation Scale (AMS)" forms. Group 1 received a face-to-face classical education, and Group 2 received the same course online, accessed via the provided link to the relevant course. The students accessed the recorded lecture asynchronously by clicking on the link on their smart devices before the study. Next, the "Knowledge exam (posttest)" and the "State Anxiety Inventory" forms were distributed to both groups, and they were asked to complete these forms. The same procedures were applied to the evening education students (Groups 3 and 4), and all obtained data were analyzed.

Study participants

The research population consists of 134 students out of a total of 176 students receiving education in the second year of Siirt University Health Services Vocational School Medical Laboratory Techniques Department between September 26, 2022, and January 9, 2023. Forty-two students who did not accept to participate in the study or did not meet the criteria were excluded from the study. Daytime and evening education students studying in this department were included in the study. A power analysis was performed to create a sample and to determine the number of students required for the research. Power analysis was performed using a statistical power analysis software, G*Power, version 3.1.9.7 (Heinrich Heine University, Düsseldorf, Germany) [11]. The number of students in the groups needed to be at least 30 at the $P \leq 0.05$ level.

The sampling criteria were not having graduated from high schools providing health education, not having received any education on mobile learning, taking the histology course for the first time, and giving verbal and written consent to participate in

the study. Students who did not meet these criteria were not included in the study.

Study design and randomization

The research followed a randomized, controlled experimental design. In terms of transparency of the study, randomization was made by a researcher outside the study using a website, and the students were divided into four groups: Group 1 (daytime education, classical education: n=31), Group 2 (daytime education, distance education: n=34), Group 3 (evening education, classical education: n=35), and Group 4 (evening education, distance education: n=34).

Data collection tools

A Structured Student Introduction Form, a "Knowledge exam" on nervous system histology (pretest and posttest), the STAI, and the AMS were used for data collection.

Student introduction form

Sociodemographic information such as age, gender, and the high school the students graduated from was obtained from the students using the Structured Student Introduction Form. In addition, two close-ended and two open-ended questions were asked. The close-ended questions were about the information tools the students used the most (phone, computer, and tablet) and their opinions about using technological methods in education (useful, complex, and unnecessary). The first open-ended question prompted the students' opinions in Group 2 (daytime education, distance education) and Group 4 (evening education, distance education) about the benefit of the histology course taken by the distance education method. The second open-ended question asked the students' opinions in Group 3 (evening education, classical education) and Group 4 (evening education, distance education) about the distance or face-to-face histology course taken in the evening.

State-Trait Anxiety Inventory

The STAI was first developed in 1970. It consists of the State Anxiety Inventory (STAI-S) and the Trait Anxiety Inventory (STAI-T) subscales. These subscales were adapted to Turkish by Öner [12]. Both subscales consisted of 20 items and were scored on a four-point Likert-type scale. The scoring on the scale was between 1 and 4. Responses in the STAI-S subscale were (1) Not at all, (2) Somewhat, (3) Moderately so, and (4) Very much so. Responses in the STAI-T subscale were (1) Rarely, (2) Sometimes, (3) Often, and (4) Almost always. The score obtained from both scales varied between 20 and 80. A high score on the scale indicated a high level of anxiety, while a low score indicated a low level of anxiety.

Academic Motivation Scale

The AMS was developed by Vallerand et al. in Canada in 1992 [13] and adapted into Turkish by Karagüven [14]. The scale was used to measure the academic motivation of the participants. It consisted of 28 items and seven subscales, three of which belonged to intrinsic motivation, three to extrinsic motivation, and one to amotivation, each of which consists of four items. These subscales are Intrinsic Motivation to Know-IMBI, Intrinsic Motivation to Accomplish-IMBA, Intrinsic Motivation to Experience Stimulation-IMES, Extrinsic Motivation External-EME, Extrinsic Motivation Introjection-EMIJ, Extrinsic Motivation Identified-EMI, and Amotivation-AM. The scores on the subtests ranged from 4 to 28. Since the subscales were separately evaluated, a value close to 28 on each subscale indicated that the dimension was high in the individual. The AMS can be easily applied to large groups quickly [14]. The application was carried out over seven responses between 1 (does not correspond at all) and 7 (corresponds exactly).

Knowledge Exam on Nervous System Histology

Nervous system histology exam questions were prepared according to the literature [10] and consisted of ten multiple-choice questions. The score for each question was calculated as 1. The lowest score that could be obtained from the exam was 0, and the highest score was 10 (100%). Exams were applied to all groups in the same format. The pretest and posttest exam questions included the same questions.

Statistical analysis

The data were analyzed using the IBM SPSS Statistics 23 package program. Categorical variables were given as frequencies (number and percentage), and numerical variables were presented as descriptive statistics (standard deviation and mean). For the numerical variables (scale and subscale scores) to be statistically tested, the normality test was performed separately for the control and experimental groups, and skewness and kurtosis coefficients were checked. Parametric methods were used for the normally distributed features, and non-parametric statistical methods were used for the non-normally distributed features.

The groups' pretest and posttest knowledge scores were compared using the dependent samples t-test. The mean knowledge test scores of the groups and whether the difference between them was significant were examined using a one-way analysis of variance (ANOVA). The Tukey test was applied to determine from which group a difference originated. The mean state and trait anxiety levels of the groups and whether the difference between them was significant were examined using one-way ANOVA. The state anxiety scores of the groups were compared using the dependent samples t-test. The mean motivation levels of the groups and whether the difference between them was significant were examined using one-way ANOVA, and then the TUKEY test was performed to determine from which group the difference originated.

Results

The research population consisted of 134 students receiving education at the Department of Medical Laboratory Techniques at the Siirt University Health Services Vocational High School between September 26, 2022, and January 9, 2023 (fall semester of the 2022–2023 academic year). The demographic data of the students participating in the study were analyzed. The mean age of the students was 21.21 years. Of the students, 76 (56.7%) were female and 58 (43.3%) were male. Seventy-two (53.7%) of the students were Anatolian high school graduates, and the rest were general (26.1%) and vocational (20.2%) high school graduates. For information tools, the students in the study mostly used smartphones (87.6%), computers (7%), and tablets (5.4%). Of the students, 105 (78.4%) found technological methods useful, 23 (17.2%) found these methods complex, and six (4.4%) found these methods unnecessary.

The results of the descriptive analysis of the data obtained from the two open-ended questions are given below.

1. What are your opinions on the benefit of the histology course given by distance education? Compared with face-to-face education.

Two main themes were identified based on the answer to this question, which was asked to Group 2 (daytime education, distance education) and Group 4 (evening education, distance education). The first main theme had three sub-themes, and the second had five sub-themes (Table 1).

The students' opinions about the sub-themes of the main themes are given below:

1a) "I think it will be useful, especially for students whose home is far away."

1b) "Sometimes we get distracted while listening to the lecture, or we may not understand at first. It would be nice to have the opportunity to listen for the second time."

1c) "Sometimes we do not attend the lecture for private reasons. It would be nice to watch the lecture we missed."

2a) "It would be better if I had the opportunity to ask questions to the educator."

2b) "Constantly watching the video prevents me from concentrating over time."

2c) "I always have difficulty accessing technological applications. This repulses from distance education."

2d) "In face-to-face education, I feel it is compulsory to attend the lecture. The same seriousness does not exist in distance education."

2e) "In face-to-face education, the educator's gestures and acts or how he uses the board makes the lecture more efficient and enjoyable. I find distance education more boring because there are no such opportunities."

Table 1: Themes and sub-themes regarding the question: "What are your thoughts on the benefit of the histology course given by distance education?"

Themes	Sub-themes
1. Positive aspects of the method (distance education)	a. Ease of access to the lecture from anywhere b. Opportunity to listen repeatedly c. Ability to make up for the missed lecture
2. Negative aspects of the method (distance education)	a. inability to communicate effectively b. Problems in concentrating on the lecture c. Difficulty accessing technological tools d. Failure to ensure course discipline e. Boring learning style

2. What are your opinions on the distance or face-to-face histology course in evening education? What are the advantages or disadvantages?

Two main themes were identified based on the answer to this question, which was asked to Group 3 (evening education, classical education) and Group 4 (evening education, distance education). The first main theme had two sub-themes, and the second main theme had three sub-themes (Table 2).

The students' opinions about the sub-themes of the main themes are as follows:

1a) "I don't experience sleep problems because I don't need to get up early in the morning. I can also come to class rested."

1b) "I can spare more time for my personal work and social activities during the day."

2a) "I have problems because the time I leave the faculty is late. I have a hard time finding public transportation, especially at late hours. Coming home is tiring."

2b) "I think that the lectures taken in the morning will be more bearable in mind. I also feel more absent-minded in the evening."

2c) "Educators are more tired in the evening hours because they teach all day long. They are less efficient in lectures."

Table 2: Themes and sub-themes regarding the question: "What are your opinions on the distance or face-to-face histology course taken in evening education?"

Themes	Sub-themes
1. Advantages of evening education	a. More comfortable b. Allowing other activities during the day
2. Disadvantages of evening education	a. Continuation of education until late hours b. Less lecture efficiency c. Fatigue-related low performance among educators

Change in STAI scores by group

The mean state and trait anxiety levels of the groups and whether the difference between them was significant were examined using one-way ANOVA. According to the one-way ANOVA results, the state and trait anxiety scores of the groups did not differ significantly ($P>0.05$). In other words, the state and trait anxiety levels of the groups were similar (Table 3).

Table 3: Analysis of STAI levels

		n	Mean	SD	F	*P*-value
State anxiety inventory	Group 1	31	51.19	15.02	0.300	0.826
	Group 2	34	49.38	13.05		
	Group 3	35	49.97	15.64		
	Group 4	34	52.62	16.89		
	Total	134	50.76	15.10		
Trait anxiety inventory	Group 1	31	36.19	12.06	0.233	0.658
	Group 2	34	34.38	8.26		
	Group 3	35	34.97	12.28		
	Group 4	34	37.62	14.55		
	Total	134	35.76	14.98		
State anxiety inventory - 2	Group 1	31	42.04	12.14	0.710	0.548
	Group 2	34	41.03	7.96		
	Group 3	35	42.94	10.71		
	Group 4	34	44.56	10.41		
	Total	134	42.68	10.26		

Comparison of State Anxiety Inventory

The state anxiety inventory scores of the groups were compared using the dependent samples t-test. There was a significant difference between the state anxiety scores in all four groups before the pretest and after the posttest. The state anxiety scores after the posttest were significantly lower than the state anxiety scores before the pretest (Table 4).

Table 4: Comparative analysis of the state anxiety inventory scores before and after the study

	State		State 2		*P*-value
	Mean	SD	Mean	SD	
Group 1	51.19	15.02	42.04	12.14	<0.001
Group 2	49.38	13.05	41.03	7.96	<0.001
Group 3	49.97	15.64	42.94	10.71	<0.001
Group 4	52.62	16.89	44.56	10.41	<0.001

Change in AMS scores by group

The mean AMS levels of the groups and whether the difference between them was significant were examined using one-way ANOVA. According to the one-way ANOVA results, the extrinsic motivation - external regulation subscale differed significantly between the groups ($P<0.05$), but the other subscales did not differ significantly. According to the results of the Tukey test, which was performed to determine which group the difference originated from, the mean scores of Groups 1, 2, and 4 were significantly higher than that of Group 3 (evening education, classical education) (Table 5).

Table 5: Analysis of AMS scores of the groups

		n	Mean	SD	F	*P*-value
Intrinsic motivation to know	Group 1	31	21.15	5.40	0.914	0.436
	Group 2	34	21.41	4.90		
	Group 3	35	19.43	5.85		
	Group 4	34	20.74	5.25		
	Total	134	20.64	5.36		
Intrinsic motivation to accomplish	Group 1	31	15.62	5.34	0.458	0.712
	Group 2	34	16.82	4.98		
	Group 3	35	15.89	5.90		
	Group 4	34	16.82	4.36		
	Total	134	16.33	5.14		
Intrinsic motivation to experience stimulation	Group 1	31	17.04	5.35	0.342	0.795
	Group 2	34	16.24	5.45		
	Group 3	35	15.83	5.83		
	Group 4	34	16.94	5.72		
	Total	134	16.47	5.56		
Extrinsic motivation identified	Group 1	31	19.81	5.28	0.633	0.595
	Group 2	34	20.38	5.16		
	Group 3	35	18.86	6.58		
	Group 4	34	20.47	4.67		
	Total	134	19.88	5.47		
Extrinsic motivation introjection	Group 1	31	15.85	4.97	0.182	0.908
	Group 2	34	16.09	5.74		
	Group 3	35	16.83	6.64		
	Group 4	34	16.03	5.53		
	Total	134	16.22	5.75		
Extrinsic motivation external	Group 1	31	22.19	3.45	3.840	0.011*
	Group 2	34	22.88	4.26		
	Group 3	35	19.37	5.43		
	Group 4	34	21.59	4.47		
	Total	134	21.45	4.67		
Amotivation	Group 1	31	10.12	4.93	1.174	0.322
	Group 2	34	8.76	5.20		
	Group 3	35	10.26	5.83		
	Group 4	34	11.26	5.94		
	Total	134	10.10	5.54		

* $P<0.05$

Comparison of knowledge test scores

The pretest and posttest knowledge scores of the groups were compared using the dependent samples t-test. There was a significant difference between the pretest and posttest scores in all four groups, and the mean posttest scores were significantly higher than the mean pretest scores (Table 6).

Table 6: Comparative analysis of the pretest and posttest scores of the groups

	Pretest		Posttest		*P*-value
	Mean	SD	Mean	SD	
Group 1	2.15	0.97	4.81	0.80	<0.001
Group 2	2.12	0.81	4.03	1.60	<0.001
Group 3	2.14	1.17	3.83	1.62	<0.001
Group 4	2.18	1.09	3.56	1.52	<0.001

Comparison of knowledge test scores according to groups

The mean knowledge test scores of the groups and whether the difference between them was significant were examined using one-way ANOVA. According to the one-way ANOVA results, the posttest knowledge scores of the groups differed significantly ($P<0.05$). According to the Tukey test results performed to determine which group the difference originated from, the posttest knowledge score of Group 1 (daytime education, classical education) was significantly higher than that of the other groups. There was no significant difference between the other groups (Table 7).

Table 7: Analysis of the significance of the knowledge tests between the groups

		n	Mean	SD	F	*P*-value
Knowledge pretest	Group 1	31	2.15	0.97	0.019	0.996
	Group 2	34	2.12	0.81		
	Group 3	35	2.14	1.17		
	Group 4	34	2.18	1.09		
	Total	134	2.15	1.01		
Knowledge posttest	Group 1	31	4.81	0.80	3.853	0.011*
	Group 2	34	4.03	1.60		
	Group 3	35	3.83	1.62		
	Group 4	34	3.56	1.52		
	Total	134	4.01	1.51		

* $P<0.05$

Discussion

This study evaluated the success of students who took the nervous system histology course via distance and face-to-face (classical) education using pre- and posttests. The most significant difference was found in the group who received face-to-face education in daytime education. The posttest results were significantly higher in all groups than in the pretest. There was no significant difference between the groups in terms of STAI scores. It was observed that the state anxiety scores obtained after the posttest were significantly lower compared to the state anxiety scores before the pretest. There was no significant difference for the AMS except for the extrinsic motivation - external regulation subscale.

During university education, stress and anxiety are common among many students. Psychosocial stress may occur in students receiving education in health fields such as medicine due to the lecture load, exam anxiety, and communication problems with patients and their relatives [15]. It is known that exam anxiety harms the academic achievement of students. A study found in the literature reported that students who did not have methods for coping with test anxiety had higher anxiety levels [16]. Furthermore, the increase in social expectations regarding students and concerns for their professional future are the main factors that increase students' anxiety levels during the university period [16,17]. Therefore, it may be beneficial to implement supportive measures to reduce individuals' stress and anxiety levels [18].

In this study, the state anxiety inventory scores of the students were examined before the pretest and after the posttest, and the posttest state anxiety level was low in all groups (Table 4). Therefore, the high state anxiety level observed before the education significantly decreased after the education. This result can be explained by the fact that the students were relaxed and self-confident after their education. The trait anxiety score of the students was also compared between the groups, and no significant difference was observed. Considering that mood factors may affect students' academic achievement [19], the fact that the groups had similar characteristics in terms of state and trait anxiety levels (Table 3) is important for the reliability of the knowledge test (pretest/posttest).

Motivation is a key factor that arouses interest in students and ensures that they actively participate in a lecture. Successful termination of academic education and professional progress is possible with motivation [20]. This concept can be examined in three ways: intrinsic, extrinsic, and amotivation [21]. It has been reported that there was a positive relationship between extrinsic motivation and academic achievement [22]. In another study conducted with university students, it was determined that there was a significant difference in extrinsic motivation in individuals who were aware of their department in high school compared to individuals who were not [21]. On the contrary, several studies have also stated a negative relationship between extrinsic motivation and academic achievement [23].

In this study, no significant difference was found between the groups in terms of academic motivation in general (except for extrinsic motivation – external regulation subscale in Group 3). On the other hand, only the score of Group 1 (daytime education, classical education) was significantly higher than the

other groups for the posttest knowledge scores. Based on these data, it is difficult to reach a conclusion regarding extrinsic motivation and its effect on academic achievement among daytime and evening education students. Considering the contradictory results in the literature regarding extrinsic motivation and academic achievement [22,23], more comprehensive studies are required on this subject.

Today, besides daytime (formal) education, alternative methods such as distance education and evening education are applied to expand university education. Evening education following the end of formal daytime education brings some difficulties and shortages [24]. In this study, the evening education students expressed their concerns about this method (e.g., low lecture efficiency, low educator performance), which can be an example of these shortages. In a study conducted with students learning foreign languages, it was reported that the students enrolled in the daytime education (formal) program were more successful than the students enrolled in the evening education program [25]. Therefore, both students and academic staff participating in evening education experience fatigue. This disadvantage harms the implementation of courses and students' perception of field proficiency [2]. With today's rapidly developing technology, the involvement of distance education applications can solve the problems experienced in evening education. The positive approaches of some students in the present study about distance education (e.g., ability to access the lecture anywhere and anytime, the opportunity to make up) support the authors' opinion.

Distance education models, such as mobile learning and technological applications, are applied in cases where face-to-face education cannot be appropriately provided, such as during the pandemic [26-28]. The development of internet technologies and the increased use of smart devices have extended distance education. Although these practices are not as effective as face-to-face education, they contribute to students' learning [27]. In a study in which histology and anatomy education was facilitated with face-to-face and mobile learning methods, it was reported that the most successful group was the group that received education using both methods, suggesting that face-to-face and digital education models would be more successful when integrated [29]. During the development of distance education applications, it is also important to structure courses by obtaining feedback from students [27]. In the current study, some students stated they had concerns about distance education (e.g., inability to communicate effectively with educators, insufficient technological structure). Therefore, to maximize academic achievement in education, it can be said that it would be more beneficial to minimize the disadvantages of distance education and integrate it with face-to-face (classical) education.

This study compared face-to-face and distance education to different education styles (daytime and evening education). It was seen that the most successful group was the group that received face-to-face education in daytime education (Group 1). Although there was a significant difference between the pretest and posttest scores in all groups, the most significant difference was observed in the group receiving face-to-face daytime education. In another study, it was reported that the efficiency of distance anatomy education was lower than that of traditional (face-to-face) anatomy education [30], supporting the results of the current study. Another remarkable finding of the current study was that the posttest scores for daytime education (face-to-face and distance) were higher than those for evening education (face-to-face and distance). A study showed that melatonin positively affects daytime-dependent synaptic plasticity and learning efficiency [31], which may explain this situation. In a study carried out with medical faculty students and educators, it was stated that the lectures given during the daytime were more productive than the lectures given in the evening [32], supporting these results. According to all these data, it can be stated that evening or distance education is not as effective as formal and face-to-face education but does not prevent academic achievement. Moreover, it can be considered that hybrid education models in which distance education methods are integrated to support face-to-face education will further increase the quality of education. The flipped learning model applied to nurse students was reported to increase learning skills and academic achievement more than traditional methods [33], supporting the opinions of the current study's authors.

Limitations

This study was conducted with the Health Services Vocational High School students at Siirt University. Similar studies could be carried out in other health-related faculties (e.g., medicine and dentistry) to support the study's results. Secondly, the effectiveness of face-to-face (classical) and distance education in the study groups was evaluated separately. The scope of the study can be expanded with hybrid education models in which both models are applied together.

Conclusion

In our study, we show that among the different teaching styles and training methods in histology education, the most effective was the daytime education, face-to-face group. The fact that the efficiency of distance education applications was not as high as face-to-face education suggests that such digital applications require further optimization. Furthermore, the lower success rates observed in the evening education groups can be increased by integrating face-to-face and distance education. Therefore, we recommend applying hybrid education models so that students can show similar success performances in different teaching styles. The fact that similar findings were obtained from the groups regarding the state-trait anxiety inventory and the academic motivation scale is important for the reliability of the study.

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References

1. Ataş H, Gündüz S. Digital Transformation with its Economic and Social Dimensions. Digital Transformation in Higher Education. In: Çelik İE, eds. Ankara: Gazi Bookstore; 2019. pp. 1-28.
2. Kahramanoğlu R, Ay Y. Examination of the Primary Teacher Candidates' Special Field Competence Perceptions as to Different Variables. TLCE. 2013;2(2):285-301.
3. Doğan Y, Özçakmak H. Evaluation Of Pre-Service Turkish Language Teachers' Summarizing Skills For The Texts Listened. Mustafa Kemal University Journal of Social Sciences Institute. 2015;11(28):153-76.
4. Tanrıogen A, Baştürk R. Opinions of evening course student on the evening education program. Pamukkale University Journal of Education. 2005;18(18):51-9.
5. Taş F. Health sciences students' viewpoint on innovative approaches in histology courses. J Surg Med. 2022;6(12):981-5.

6. Cheng X, Chan LK, Li H, Yang X. Histology and embryology education in China: the current situation and changes over the past 20 years. Anat. Sci. Educ. 2020;13(6):759-68.
7. Taş F, Yılmaz M, Erdemci F, Aşır F, Deveci E. Examining the long-term effects of COVID-19 on the umbilical cord. JHSM. 2022;5(5):1371-7.
8. Güneş S, Bolatlı G, Taş F, Üyüklü M. Views Of Physicians On The Persistence And Efficiency Of Basic Medical Sciences Education. Gevher Nesibe Journal of Medical & Health Sciences. 2021;6(15):65-72.
9. Saverino D, Marcenaro E, Zarcone D. Teaching histology and anatomy online during the COVID-19 pandemic. Clin Anat. 2022;35(1):129-34.
10. Eşrefoğlu M. General Histology. 2nd ed. Istanbul Medical Bookstore; 2016. pp. 305-38.
11. Faul F, Erdfelder E, Lang AG, Buchner A. G* Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav. Res. Methods. 2007;39(2):175-91.
12. Öner N, LeCompte A. The handbook of the state-trait anxiety inventory. İstanbul: Bogazici Publications; 1983. pp. 26-42.
13. Vallerand RJ, Pelletier LG, Blais, MR, Briere NM, Senecal C, Vallieres EF. The Academic Motivation Scale: A measure of intrinsic, extrinsic, and a motivation in education. Educ Psychol Meas. 1992;52(4):1003-17.
14. Karagüven M, Ünal H. The Adaptation of Academic Motivation Scale to Turkish. Educ. Sci. Theory Pract. 2012;12(4):2599-620.
15. Ertek IE, Özkan S, Candansayar S, İlhan MN. Stress, Burn-Out and Depression in Medical Students. Gazi Journal of Health Sciences. 2020;5(1):10-20.
16. Vural PI, Korpe G. Kadın sağlığı ve hastalıkları hemşireliği uygulamasında öğrencilerin baş etme yöntemleri sınav kaygısını etkiler mi? Van Med. J. 2020;27(2):118-24.
17. Geylani M, Yıldız CÇ. Development of "Future Anxiety Scale in University Students": Validity and Reliability Study. JHVS. 2022;10(1):284-300.
18. Sakaoğlu HH, Orbatu D, Emiroglu M, Çakır Ö. Spielberger State and Trait Anxiety Level in Healthcare Professionals During the Covid-19 Outbreak: A Case of Tepecik Hospital. Journal of Tepecik Education and Research Hospital. 2020;30(2):1-9.
19. Kuzay D. Effects Of Depression On Family-Friend Relationship And Academic Success In Medical Faculty, Health High School And Vocational Health High School. AUHSJ. 2019;4:576-80.
20. Uyulgan MA, Akkuzu N. An Overview of Student Teachers' Academic Intrinsic Motivation. Educ. Sci. Theory Pract. 2014;14(1):24-32.
21. Terlemez B, Şahin D, Dilek F. Opinions of health services vocational school students at Namık Kemal university academic motivation levels. Pamukkale j. eurasian socioecon. stud. 2015;2(2):67-78.
22. Moneta GB, Siu CMY. Trait İntrinsic And Extrinsic Motivations, Academic Performance, And Creativity İn Hong Kong College Students. J. Coll. Stud. Dev. 2002;43: 664-83.
23. Lepper RM, Corpus JH, Iyengar SS. Intrinsic and Extrinsic Motivational Orientations in the Classroom: Age Differences and Academic Correlates. J. Educ. Psychol. 2005; 97(2):184-96.
24. Çınar NF. Evaluation of The Future Problem of Secondary Education in Public Universities Vocational Schools In Turkey. Bilge International Journal of Social Research. 2018;2(1):21-5.
25. Aydın S. Examining the level of success in learning English as a second language according to some variables. Journal of Graduate School of Social Sciences. 2006;8(2):273-85.
26. Bolatlı G, Taş F. Student opinions about the training set consists of smart interactive mockups and application program used in anatomy and histology education. EJOSAT. 2023;(46):90-7.
27. Keskin M, Derya O. Evaluation of Students' Feedbacks on Web-Based Distance Education in the COVID-19 Process. Izmir Katip Celebi University Faculty of Health Sciences Journal. 2020;5(2):59-67.
28. Erbeke E, Bolatli G. The Effect of Mobile Learning in Anatomy Education on Learning Skills and Motivation of Students: Systematic Review. EJOSAT. 2022;(41):269-84.
29. Taş F, Bolatlı G. A new model in medicine education: smart model education set. Surg Radiol Anat. 2022;1-9.
30. Hizay A, Şenol Y. Evaluation of Traditional and Online Anatomy Teaching of Medical Students in the Covid 19 Pandemic. World of Medical Education. 2022;21(65):5-17.
31. Jilg A, Bechstein P, Saade A, Dick M, Li TX, Tosini G, et al. melatonin modulates daytime-dependent synaptic plasticity and learning efficiency. Journal of pineal research. 2019;66(3):e12553.
32. Bahşi İ, Çetkin M, Kervancıoğlu P, Orhan M, Ayan H, Sayın S. Evaluation of the efficiency of the medical faculty courses, the way they are taught and the attendance control of the students. J. Gen. Med. 2018;28(3):89-95.
33. Chi M, Wang N, Wu Q, Cheng M, Zhu C, Wang X, et al. Implementation of the Flipped Classroom Combined with Problem-Based Learning in a Medical Nursing Course: A Quasi-Experimental Design. Healthcare. 2022;10(12):2572.

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Orthopedic surgeons' attitudes and expectations toward artificial intelligence: A national survey study

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Ethics Committee Approval
The study was approved by Dokuz Eylul University Non-interventional Clinical Research Ethics Board with protocol number 2021/16-01 on May 27, 2021.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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Abstract

Background/Aim: There is a lack of understanding of artificial intelligence (AI) among orthopedic surgeons regarding how it can be used in their clinical practices. This study aimed to evaluate the attitudes of orthopedic surgeons regarding the application of AI in their practices.
Methods: A cross-sectional study was conducted in Turkey among 189 orthopedic surgeons between November 2021 and February 2022. An electronic survey was designed using the SurveyMonkey platform. The questionnaire included six subsections related to AI usefulness in clinical practice and participants' knowledge about the topic. It also surveyed their acceptance level of learning, concerns about the potential risks of AI, and implementation of this technology into their daily practice
Results: A total of 33.9% of the participants indicated that they were familiar with the concept of AI, while 82.5% planned to learn about artificial intelligence in the coming years. Most of the surgeons (68.3%) reported not using AI in their daily practice. The activities of orthopedic associations focused on AI were insufficient according to 77.2% of participants. Orthopedic surgeons expressed concern over AI involvement in the future regarding an insensitive and nonempathic attitude toward the patient (53.5%). A majority of respondents (80.4%) indicated that AI was most feasible in extremity reconstruction. Pelvis fractures were found in the region where the AI system is most needed in the fracture classification (68.7%).
Conclusion: Most of the respondents did not use AI in their daily clinical practice; however, almost all surgeons had plans to learn about artificial intelligence in the future. There was a need to improve orthopedic associations' activities focusing on artificial intelligence. Furthermore, new research including the medical ethics issues of the field will be needed to allay the surgeons' worries. The classification system of pelvic fractures and sub-branches of orthopedic extremity reconstruction were the most feasible areas for AI systems. We believe that this study will serve as a guide for all branches of orthopedic medicine.

Keywords: artificial intelligence, attitudes, orthopedic surgeons, survey

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Introduction

The use of artificial intelligence (AI) in health care has gained interest in recent years [1]. AI represents health-related research and clinical care with enhanced qualities and abilities that exceed those naturally found in clinicians. AI has been applied in a wide range of fields in medicine including cardiology, radiology, dermatology, and mental health [1,2].

The application of AI systems has high potential in orthopedics. Digital imaging and documentation are steadily increasing, resulting in a large database for algorithms. Therefore, the use of AI is inevitable in improving the quality of patient care through management, research, and diagnosis [3].

There is a lack of AI understanding among orthopedic surgeons as to how it can be utilized in their clinical practice [4]. AI in the orthopedic area is still in its infancy compared to other areas of medicine [1]. Orthopedic surgery has recently begun adopting AI systems, and in the literature it is possible to see the increase in research for AI applications in recent years. Hip fractures [5,6], and pediatric elbow fractures [7] have been diagnosed with image-based algorithms. Radiographic measurements, such as acetabular component position [8] and coronal knee alignment [9] can also be performed with AI systems. These programs have been used for the pre-operative templating total knee arthroplasty to improve the accuracy and efficiency of surgery [10-12].

In addition, we believe that new projects and research are still needed to figure out the potential and logic of AI systems. With this need in mind, we designed a national multicenter survey to evaluate the views and attitudes of orthopedic surgeons regarding the application of AI in their practices.

Materials and methods

This questionnaire was approved by the Dokuz Eylul University Non-interventional Clinical Research Ethics Board with protocol number 2021/16-01 on May 27, 2021. The research was carried out as a descriptive observational study among orthopedic surgeons in Turkey. A search of the Council of Higher Education Theses Center database [https://tez.yok.gov.tr/UlusalTezMerkezi/] was performed. In conducting a detailed search, the subject division was filtered using "orthopedics and traumatology," and the time was limited between 1980 and 2020. The list of surgeons was numbered one by one, starting with the number one. The participants of the survey were randomly selected by generating random numbers in Microsoft Excel.

An electronic survey was designed using the SurveyMonkey platform. Between November 2021 and February 2022, an electronic survey was distributed via email to 650 orthopedic surgeons. The invitation email included the aim of the study and a link to participate in the survey. The email was sent three times, one week apart. Data collection was completed anonymously. Informed consent including the nature and aim of the survey was provided, and participants were notified that it was always possible to withdraw from the survey.

The survey included six subsections. The first subsection aimed to gather general demographic data including age, gender, title/degree, the institution of residency training, years of experience, and the institution where currently working. The second subsection evaluated the level of awareness of artificial intelligence. Answers were scored using two types of five-point Likert scales (strongly disagree, disagree, undecided, agree, strongly agree; and never, slightly, moderately, adequately, and completely). The third subsection aimed to analyze the preference of treatment steps in which AI would be used. The fourth subsection assessed surgeons' concerns about the potential risks of AI involvement in daily practice. The fifth subsection explored the sub-branches of orthopedics in which AI would be useful. The last subsection included the surgeons' preference level of AI usage according to the classification of fracture type.

Statistical analysis

The distributions of data were checked using the Kolmogorov-Smirnov normality test. Categorical data were analyzed with the chi-square test and represented as numbers and percentages. The differences in the questionnaire responses according to working places and daily practices were analyzed using the Mann-Whitney test. All analyses were done on SPSS for Windows (version 22.0; IBM Corp, Armonk, NY, USA). A *P*-value below 0.05 was accepted as a statistical difference.

Results

The demographic data including age, gender, title/degree, the institution of residency training, years of experience, and the institution where currently working is shown in Table 1. A total of 650 registrants and 189 surgeons filled out the questionnaire (response rate: 29.1%).

Table 1: Descriptive characteristics of the participants

Characteristics	n(%)
1) Gender	
Male	186 (98.4)
Female	3 (1.6)
2) Age (years)	
25 – 29	1 (0.5)
30 – 34	41 (21.7)
35 – 39	61 (32.3)
40 – 50	66 (34.9)
>50	20 (10.6)
3) Title/Degree	
Specialist	81 (42.9)
Chief resident	6 (3.2)
Assistant professor	28 (14.8)
Associate professor	48 (25.4)
Professor	26 (13.8)
4) The institution of orthopedics and traumatology residency training	
Training and research hospital	75 (39.7)
University hospital	104 (55)
Foundation university hospital	10 (5.3)
Abroad	0 (0.0)
5) Experience in orthopedic surgery (years)	
<5	53 (28)
5 – 9	51 (27)
10 – 14	38 (20.1)
15 – 20	24 (12.7)
>20	23 (12.2)
6) The institution of current working for	
State Hospital	26 (13.8)
Training and research hospital	55 (29.1)
University hospital	44 (23.3)
Foundation university hospital	16 (8.5)
Private hospital	34 (18)
Specialty hospital	0 (0.0)
Private clinic	14 (7.4)

The results of evaluating the level of awareness of artificial intelligence are indicated in Table 2. This table shows 33.9% of participants thought that they were adequately or completely familiar with the concept of AI. On the other hand, 82.5% of participants planned to learn about artificial

Table 2: Responses rate to questions about the level of awareness of AI (n, [%])

Evaluating the level of awareness of artificial intelligence that orthopedists have					
Question	**Never**	**Slightly**	**Moderately**	**Adequately**	**Completely**
▪ **How familiar do you think you are with the concept of artificial intelligence?**	6 (3.2)	41 (21.7)	78 (41.3)	48 (25.4)	16 (8.5)
▪ **How much information are you planning to learn about artificial intelligence in the coming years?**	2 (1.1)	1 (0.5)	30 (15.9)	93 (49.2)	63 (33.3)
▪ **To what extent do you use AI in your day-to-day clinical practices?**	68 (36)	61 (32.3)	48 (25.4)	7 (3.7)	4 (2.1)
	Strongly disagree	**Disagree**	**Undecided**	**Agree**	**Strongly agree**
▪ **I think, compared to clinical experience, AI will be better at making accurate and rapid diagnoses.**	6 (3.2)	44 (23.3)	62 (32.8)	62 (32.8)	15 (7.9)
▪ **I think I will be out of a job in the future because of the widespread use of artificial intelligence.**	61 (32.3)	113 (59.8)	8 (4.2)	5 (2.6)	2 (1.1)
▪ **I think that the activities that orthopedic associations conduct focusing on information technologies, such as artificial intelligence, are sufficient.**	39 (20.6)	107 (56.6)	33 (17.5)	7 (3.7)	3 (1.6)
▪ **I think the subject of artificial intelligence should be included in the curriculum of orthopedic specialty training.**	2 (1.1)	13 (6.9)	39 (20.6)	94 (49.7)	41 (21.7)

Table 3: Participants' consideration of using AI in which treatment steps (n, [%])

To what extent would you consider using the AI in the treatment steps mentioned below?					
Question	**Never**	**Slightly**	**Moderately**	**Adequately**	**Completely**
▪ **Diagnosis**	8 (4.2)	14 (7.4)	61 (32.8)	65 (32.3)	39 (20.7)
▪ **Radiographic evaluation**	2 (1.1)	4 (2.1)	31 (16.4)	81 (42.9)	71 (37.6)
▪ **Surgical planning (Templating)**	2 (1.1)	0 (0.0)	32 (16.9)	94 (49.7)	60 (31.7)
▪ **Prognostic management**	5 (2.6)	16 (8.5)	59 (31.2)	76 (40.2)	32 (16.9)
▪ **Evaluation of treatment success**	5 (2.6)	9 (4.8)	46 (24.3)	84 (44.4)	44 (23.3)
▪ **Literature review**	0 (0.0)	3 (1.6)	10 (5.3)	54 (29.6)	121 (64.0)

Table 4: Distribution of participants' concerns about potential situations when AI will be involved in many fields of their daily practice in the future (n, [%])

With the likelihood/possibility/probability of AI involvement in many fields of our daily practice in the future, to what extent are you concerned about the following potential situations?					
Question	**Never**	**Slightly**	**Moderately**	**Adequately**	**Completely**
▪ **Who will be responsible in the case of AI-related malpractice**	19 (10.1)	31 (16.4)	55 (29.1)	42 (22.2)	40 (21.2)
▪ **Cognitive dissonance**	5 (2.6)	25 (13.2)	83 (43.9)	54 (28.6)	20 (10.6)
▪ **Inability to adapt to real-world practice**	8 (4.2)	30 (15.9)	83 (43.9)	48 (25.4)	17 (9)
▪ **Having an insensitive and nonempathic attitude toward the patient and not being able to evaluate the patient's thoughts and expectations**	11 (5.8)	24 (12.7)	50 (26.5)	44 (23.3)	57 (30.2)
▪ **Going beyond serving just as a complementary component in diagnosis and treatment and becoming the decision-maker of the entire process**	20 (10.6)	33 (17.5)	63 (33.3)	38 (20.1)	32 (16.9)

Table 5: Relationship between sub-branches of orthopedics and feasibility of AI (n, [%])

To what extent do you think that AI is useful and feasible in the sub-branches mentioned below?					
Question	**Never**	**Slightly**	**Moderately**	**Adequately**	**Completely**
▪ **Arthroplasty**	2 (1.1)	1 (0.5)	45 (23.8)	79 (41.8)	60 (31.7)
▪ **Foot and Ankle**	4 (2.1)	25 (13.2)	76 (40.2)	64 (33.9)	19 (10.1)
▪ **Hand and Microsurgery**	26 (13.8)	62 (32.8)	55 (29.1)	30 (15.9)	15 (7.9)
▪ **Extremity Reconstruction and the Ilizarov**	2 (1.1)	6 (3.2)	28 (14.8)	66 (34.9)	86 (45.5)
▪ **Shoulder and Elbow**	7 (3.7)	31 (16.4)	87 (46)	43 (22.8)	19 (10.1)
▪ **Spine**	3 (1.6)	10 (5.3)	36 (19)	80 (42.3)	59 (31.2)
▪ **Pediatric**	7 (3.7)	61 (32.3)	73 (38.6)	32 (16.9)	15 (7.9)
▪ **Sports Injury – Arthroscopic Surgery**	6 (3.2)	39 (20.6)	81 (42.9)	45 (23.8)	17 (9)
▪ **Trauma**	7 (3.7)	27 (14.3)	64 (33.9)	56 (29.6)	34 (18)
▪ **Tumor**	6 (3.2)	27 (14.3)	56 (29.6)	47 (24.9)	52 (27.5)

Table 6: Participants' opinions how AI system is needed for fracture classification according to region (n, [%])

To what extent do you think you need an AI system to classify the fracture type of the following regions?					
Question	**Never**	**Slightly**	**Moderately**	**Adequately**	**Completely**
Vertebrae	9 (4.8)	21 (11.1)	60 (31.7)	60 (31.7)	39 (20.6)
Humerus	23 (12.2)	48 (25.4)	71 (37.6)	30 (15.9)	15 (7.9)
Radius	23 (12.2)	36 (19)	77 (40.7)	39 (20.6)	14 (7.4)
Ulna	26 (13.8)	50 (26.5)	71 (37.6)	27 (14.3)	15 (7.9)
Carpal	18 (9.5)	39 (20.6)	59 (31.2)	46 (24.3)	27 (14.3)
Pelvis	7 (3.7)	11 (5.8)	41 (21.7)	67 (35.4)	63 (33.3)
Femur	20 (10.6)	30 (15.9)	93 (49.2)	28 (14.8)	16 (8.5)
Tibia	20 (10.6)	33 (17.5)	85 (45)	31 (16.4)	19 (10.1)
Fibula	23 (12.2)	52 (27.5)	72 (38.1)	26 (13.8)	15 (7.9)
Tarsal	18 (9.5)	36 (19)	74 (39.2)	36 (19)	25 (13.2)

intelligence in the coming years. The majority (68.3%) of surgeons expressed that they did not use AI in their daily clinical practices. Additionally, participants who were working in training hospitals (training and research hospitals, university hospitals, foundation university hospitals) were more likely to use AI in their daily clinical practice than other center workers (P=0.045).

A total of 40.7% of participants thought that AI would be better than clinical experience in making accurate and rapid diagnoses. Surgeons in non-academic positions (34.6%) and those in academic positions (45.4%) agreed that AI has a superior diagnostic ability for clinical experiences. The majority of surgeons (92.3%, n=174) did not believe that their jobs would be replaced by AI in the future. The activities that orthopedic associations conduct focusing on AI were not believed to be sufficient according to 77.2% of participants. In addition, 71.4% of surgeons expressed the need for AI in the curriculum of orthopedic specialty training.

Participants' consideration of using AI in relation to treatment steps is shown in Table 3. Most surgeons would consider using AI in the treatment steps of diagnosis, radiographic evaluation, surgical planning (templating), prognostic management, evaluation of treatment success, and literature review. Among all the treatment steps mentioned, the literature review had the highest agreement with 93.6%, followed by surgical planning (81.4%) and radiographic evaluation (80.5%). The diagnosis had the least agreement with 53%.

The distribution of participants' concerns about potential situations in which AI will be involved in their daily practice in the future can be seen in Table 4. The most possible situation of AI involvement in the future that concerned orthopedists were having an insensitive and nonempathic attitude

toward the patient and not being able to evaluate the patients' thoughts and expectations (53.5%) followed by who will be responsible in the case of AI-related malpractice (43.3%) and cognitive dissonance (39.2%).

The relationship between sub-branches of orthopedics and the feasibility of AI is revealed in Table 5. Of all respondents, 80.4% thought that AI was the most useful and feasible in extremity reconstruction and in the Ilizarov procedure followed by arthroplasty and spine with rates of 73.5%. Hand and microsurgery had the lowest rate (23.8%). In sports injury–arthroscopic surgery—there was a statistical difference between the participants who employed at least a moderate use of AI in their day-to-day clinical practices and those who used it slightly or not at all (P=0.043).

Participants' opinions on how an AI system is needed for fracture classification according to the region is seen in Table 6. Pelvis fractures were found in the region where the AI system is most needed in the fracture classification (68.7%), followed by vertebrae (52.3%) and carpal (38.6%) fractures. Fibula fractures were reported as having the least need for an AI system (21.7%).

Discussion

Our study has shown that less than half of our participants are familiar with AI systems. Nevertheless, the majority would like to learn about artificial intelligence in the coming years. Furthermore, only almost 30% use AI in their daily clinical practices. Nearly all of the participants believe that they will not be replaced by AI.

In this study, we assessed whether AI is superior to clinical experience in diagnosis. Less than half of the participants thought that AI would be better at diagnosis. Doctors in non-academic positions were less likely than surgeons in academic positions to agree that AI has superior diagnostic capacity. On the other hand, Oh et al. [13] showed that academicians were less likely than medical students and training physicians to agree that AI is diagnostically superior. We found that doctors in academic positions were more knowledgeable about AI technology in the orthopedic area, thus making them more aware that AI systems had great potential and could perform tasks that could not be done by humans.

There are some important aspects of the doctor-patient relationship. Doctors can interact with patients to gain their trust, reassure them, and have an empathic attitude toward them [14]. AI systems can collect important information to facilitate diagnoses and treatment plans; furthermore, there is always a need to integrate interaction between the doctor and patient, collect the medical history, perform a physical exam, and help further discussion [15]. Our results supported that more than half of the participants believe that AI cannot take the doctors' place in the doctor-patient relationship.

Almost half of the orthopedists believed that the future involvement of AI in many fields will bring about some problems. The most likely concerns who would be responsible in the case of AI-related malpractice in the future. These results are consistent with a study by Sarwar et al. [16] that the legal implications of AI in medicine, both from a regulator and malpractice standpoint, were a common theme among pathologists. Hence, regulatory authorities and principles should be defined to prevent ethical and legal problems in medicine caused by AI.

The alignment of extremities is quantified by defining several anatomic landmarks [17]. Traditionally, the plan of extremity reconstruction is done with the radiographic evaluation of extremities, and this method takes a great deal of time, whereas AI can process data very quickly. When we combine these two pieces of information, it is not surprising that most of the participants believe that AI is useful and feasible in extremity reconstruction and the Ilizarov procedure.

The literature review process includes both creative and mechanical issues, which are useful areas for AI systems. By avoiding time-consuming and repetitive tasks, researchers can dedicate more time to other issues [18]. In the current study, most of the respondents preferred using AI in the literature review followed by surgical planning and radiographic evaluation. These results were not surprising, considering the large volume of digital imaging data that AI models can interpret. Federer et al. [19] reported in a review study that almost half of the publications related to AI and orthopedics were interpreted using diagnostic imaging modalities.

During the last decades, there have been several studies reported on AI for fracture recognition with very promising results [20-23]. However, its applications and limitations are still large and unsolved questions [24]. We asked the participants about the classification of which region fractures have superiority for the use of AI systems. Pelvis fractures had the highest agreement that AI systems would be the most useful. These responses could suggest that the classification of severe pelvic ring fractures is extremely difficult, partly due to their complexity and the absence of imaging in important patient subgroups. Therefore, the industry must pay attention to integrating AI systems in the classification of pelvis ring fractures.

A large majority of participants expressed an interest in integrating AI into residency training. They supported the belief that the orthopedics community must, in fact, extend a greater effort to ensure AI's future role in this field. Training and education programs should be planned to teach orthopedic surgeons how to use AI-based applications in their daily clinical practice. This was also mentioned by most participants in previous studies [25,26].

Orthopedic surgeons were extremely confident about their future. On the statement: "I think I will be out of a job in the future because of the widespread use of artificial intelligence," 92.1% of orthopedic surgeons responded with strongly disagree or disagree. However, these results were not consistent with previous studies. Abdullah et al. [27] indicated that most respondents were concerned that their jobs would be replaced by AI. In another study, 48.3% of participants reported that they believed certain specialties would be replaced by AI [28]. However, the study by Oh et al. [13] reported that doctors did not believe they would be replaced.

Limitations

This study, of course, has some limitations. Firstly, we only included a fraction of Turkish orthopedic surgeons, and not all surgeons worldwide are represented in our cohort. We did not evaluate the participants' technical level of AI technology, which

might cause different AI conceptualizations. The nature of survey-based studies is that there is always the possibility of recall bias. The response rate is low, and the sample size is small. Therefore, an increase in the risk of selection bias can be expected. However, the distribution of participants' age, years of experience, and current working places were homogenous.

Conclusion

In conclusion**,** most of the respondents did not use AI in their daily clinical practice, but almost all surgeons had plans to learn about artificial intelligence in the coming years and there was a need to improve the activities that orthopedic associations conduct focusing on artificial intelligence. Furthermore, new research including medical ethics issues will be needed to overcome the orthopedic surgeons' worries. The classification system of pelvic fractures and sub-branches of orthopedic extremity reconstruction were the most feasible areas for AI systems. We believe that the results we determined will serve as a guide in all branches of orthopedic medicine.

References

1. Cabitza F, Locoro A, Banfi G. Machine learning in orthopedics: A literature review. Front Bioeng Biotechnol. 2018;6:75.
2. Choy G, Khalilzadeh O, Michalski M, Do S, Samir AE, Piankh OS, et al. Current applications and future impact of machine learning in radiology. Radiology. 2018;288(2):318–28.
3. Panchmatia JR, Visenio MR, Panch T. The role of artificial intelligence in orthopedic surgery. Br J Hosp Med. 2018;79(12):676–81.
4. Federer SJ, Jones GG. Artificial intelligence in orthopedics: A scoping review. PLoS ONE. 2021;16(11):e0260471. doi: 10.1371/journal.pone.0260471.
5. Urakawa T, Tanaka Y, Goto S, Matsuzawa H, Watanabe K, Endo N. Detecting intertrochanteric hip fractures with orthopedist-level accuracy using a deep convolutional neural network. Skelet Radiol. 2019;48:239–44.
6. Yamada Y, Maki S, Kishida S, Nagai H, Arima J, Yamakawa N, et al. Automated classification of hip fractures using deep convolutional neural networks with orthopedic surgeon-level accuracy: ensemble decision-making with antero-posterior and lateral radiographs. Acta Orthop. 2020;91:699–704.
7. Choi JW, Cho YJ, Lee S, Lee J, Lee S, Choi YH, et al. Using a dual-input convolutional neural network for automated detection of pediatric supracondylar fracture on conventional radiography. Investig Radiol. 2020;55:101–10.
8. Rouzrokh P, Wyles CC, Philbrick KA, Ramazanian T, Weston AD, Cai JC, et al. A deep learning tool for automated radiographic measurement of acetabular component inclination and version after total hip arthroplasty. J Arthroplasty. 2021;36(7):2510–7.e6. doi: 10.1016/j.arth.2021.02.026
9. Schock J, Truhn D, Abrar DB, Merhof D, Conrad S, Post M, et al. Automated analysis of alignment in long-leg radiographs by using a fully automated support system based on artificial intelligence. Radiol Artif Intell. 2021;3(2):e200198.
10. Lambrechts A, Ganapathi M, Wirix-Speetjens R. Clinical Evaluation of Artificial Intelligence-based Preoperative Plans for Total Knee Arthroplasty. CAOS 2020 - The 20th Annual Meeting of the International Society for Computer Assisted Orthopedic Surgery: EasyChair; 2020;169–73.
11. Li Z, Zhang X, Ding L, Du K, Yan J, Chan MTV, et al. Deep learning approach for guiding three-dimensional computed tomography reconstruction of lower limbs for robotically-assisted total knee arthroplasty. Int J Med Robot. 2021;17(5):e2300. doi: 10.1002/rcs.2300.
12. Jacofsky DJ, Allen M. Robotics in Arthroplasty: A Comprehensive Review. J Arthroplasty. 2016;31(10):2353–63. doi: 10.1016/j.arth.2016.05.026
13. Oh S, Kim JH, Choi SW, Lee HJ, Hong J, Kwon SH. Physician Confidence in Artificial Intelligence: An Online Mobile Survey J Med Internet Res. 2019;21(3):e12422.
14. Inkster B, Sarda S, Subramanian V. An empathy-driven, conversational artificial intelligence agent (Wysa) for digital mental well-being: real-world data evaluation mixed-methods study. JMIR Mhealth Uhealth. 2018;23;6(11):e12106. doi: 10.2196/12106
15. Krittanawong C. The rise of artificial intelligence and the uncertain future for physicians. Eur J Intern Med. 2018;48:e13-4. doi: 10.1016/j.ejim.2017.06.017
16. Sarwar S, Dent A, Faust K, Richer M, Djuric U, Ommeren RV, et al. Physician perspectives on integration of artificial intelligence into diagnostic pathology. NPJ Digit Med. 2019;2:28. doi: 10.1038/s41746-019-0106-0
17. Paley D, Herzenberg JE, Tetsworth K, McKie J, Bhave A. Deformity planning for frontal and sagittal plane corrective osteotomies. Orthop Clin North Am. 1994;25(3):425-65.
18. Tsafnat G, Glasziou P, Choong MK, Dunn A, Galgani F, Coiera E. Systematic review automation technologies. Systematic Reviews. 2014;3:1–15.
19. Federer SJ, Jones GG. Artificial intelligence in orthopedics: A scoping review. PLoS ONE. 2021;16(11): e0260471. doi: 10.1371/journal.pone.0260471
20. Kim DH, MacKinnon T. Artificial intelligence in fracture detection: transfer learning from deep convolutional neural networks. Clin Radiol. 2018;73(5):439–45. doi: 10.1016/j.crad.2017.11.015
21. Olczak J, Fahlberg N, Maki A, Razavian AS, Jilert A, Stark A, et al. Artificial intelligence for analyzing orthopedic trauma radiographs Deep learning algorithms-are they on par with humans for diagnosing fractures? Acta Orthopedica. 2017;88(6):581–6. doi: 10.1080/17453674.2017.1344459
22. Chung SW, Han SS, Lee JW, Oh KS, Kim NR, Yoon JP, et al. Automated detection and classification of the proximal humerus fracture by using deep learning algorithm. Acta Orthop. 2018;89(4):468–73. doi: 10.1080/17453674.2018.1453714
23. Gan KF, Xu DL, Lin YM, Shen Y, Zhang T, Hu K, et al. Artificial intelligence detection of distal radius fractures: a comparison between the convolutional neural network and professional assessments. Acta Orthopedica. 2019;90(4):394–400. doi: 10.1080/17453674.2019.1600125
24. Langerhuizen DWG, Janssen SJ, Mallee WH, Van Den Bekerom MPJ, Ring D, Karkhoffs GMMJ, et al. What Are the Applications and Limitations of Artificial Intelligence for Fracture Detection and Classification in Orthopedic Trauma Imaging? A Systematic Review. Clin Orthop Relat Res. 2019; 477(11):2482-91. doi: 10.1097/CORR.0000000000000848
25. Liang S, Tang F, Huang X, Yang K, Zhong T, Hu R, et al. Deep-learning-based detection and segmentation of organs at risk in nasopharyngeal carcinoma computed tomographic images for radiotherapy planning. Eur Radiol. 2019;29(4):1961–7. doi: 10.1007/s00330-018-5748-9
26. Wong K, Gallant F, Szumacher E. Perceptions of Canadian radiation oncologists, radiation physicists, radiation therapists and radiation trainees about the impact of artificial intelligence in radiation oncology–national survey. J Med Imaging Radiat Sci. 2021;52(1):44–8. doi: 10.1016/j.jmir.2020.11.013
27. Abdullah R, Fakieh B. Health Care Employees' Perceptions of the Use of Artificial Intelligence Applications: Survey Study. J Med Internet Res. 2020;22(5):e17620. doi: 10.2196/17620
28. Sit C, Srinivasan R, Amlani A, Muthuswamy K, Azam A, Monzon L, et al. Attitudes and perceptions of UK medical students towards artificial intelligence and radiology: a multicentre survey. Insights Imaging. 2020;11:14. doi: 10.1186/s13244-019-0830-7

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Biochemical predictors of complicated diverticulitis: A case-control study evaluating white cell count and C-reactive protein in the assessment of acute diverticulitis

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

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Abstract

Background/Aim: Acute diverticulitis represents a common surgical condition and one of the leading gastrointestinal causes of surgical admissions in Western societies. Complicated diverticulitis increases the length of the hospital stay and the risk of requiring surgical intervention. In areas of limited availability or long waiting times for CT scanning, biochemical predictors of complicated diverticulitis might be valuable. In the available literature, there is no consensus on cut-off values of C-reactive protein or the value of a white cell count in the diagnosis of complicated diverticulitis. Additional studies among different populations are required to add to the existing literature to reach a consensus on diagnostic cut-off levels of inflammatory markers to diagnose complicated diverticulitis. The aim of the present study is to evaluate the predictive value of a white cell count and C-reactive protein, and their sensitivity and specificity in differentiating complicated from uncomplicated diverticulitis.

Methods: This case-control study was performed for patients with acute diverticulitis in Lyell McEwin Hospital in Adelaide, South Australia. Data were collected for consecutive patients admitted from January 2015 to December 2017. Patients with acute diverticulitis confirmed by computed tomography were included in the study. Data of patients with complicated diverticulitis were compared to those of patients with uncomplicated diverticulitis as a control group. Patient characteristics, symptoms, number of attacks of diverticulitis, presence of immunosuppression, past history of complicated diverticulitis, inflammatory markers (white cell count and C-reactive protein), and computed tomography findings were collected and compared.

Results: A total of 106 consecutive cases were recruited for the period from 2015 to 2017. There were 44 cases of complicated diverticulitis and 62 cases with uncomplicated diverticulitis (control group). A white cell count (WCC) and C-reactive protein (CRP) were collected at the time of presentation from the clinical records and pathology reports. A receiver operating characteristic (ROC) analysis was performed and multiple cut-off values for both WCC and CRP were reported. For WCC, the area under curve (AUC) was 0.69 (0.582-0.797) with a *P*-value of 0.001. At a cut-off of 14, sensitivity was found to be 56.8% and specificity of 80.7%. The sensitivity gradually decreased and specificity gradually increased as the cut-off value increased. At 18 the sensitivity was 25% and specificity was 79%. The positive predictive value for the study sample at WCC of 18×10^9/L or above is 79.5%. For CRP, the AUC was 0.828 (0.729-0.927) with a *P*-value of <0.001. At a cut-off value of 100 mg/L, the sensitivity was 72.7% and specificity was 80.6%. Sensitivity gradually decreased and specificity increased as the cut-off increased in value. At 160 mg/L, sensitivity was 36.36% and specificity was 97.22% with a positive predictive value of 76%.

Conclusion: Contrary to what has been previously reported in the literature, we found that WCC remains a significant test in diagnosing complicated diverticulitis. A high cut-off value of 18×10^9/L is useful in predicting complicated diverticulitis with high positive predictive value. When compared to WCC, CRP is a more sensitive test in detecting complicated diverticulitis. We recognized a cut-off value of 160 mg/L to be a significant value to rule in complicated diverticulitis with a significant positive predictive value. WCC and CRP are very specific predictors of complicated diverticulitis with high positive predictive value at high cut-off values of 18×10^9/L and 160 mg/L, respectively.

Keywords: acute diverticulitis, white cell count, C-reactive protein, biochemical predictors

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Introduction

Diverticular disease represents a common surgical condition with a rising incidence in Western societies. It is expected that 30% of people above age 60 have diverticular disease. The prevalence rises to 60-80% of people above 80 years of age. Symptoms develop in 10-20% of people [1].

Both the incidence of acute diverticulitis and the number of cases requiring hospital admissions are increasing [2]. This is particularly true among the younger age group (18 - 44 years) which accounts for 82% of cases [3].

Diverticular disease is a common cause of hospital admissions, which results in a significant burden on the health care system in Western societies [4,5]. It is one of the most common gastrointestinal conditions that requires hospitalization and the leading indication for elective colon resection in the United States [6-8].

The modified Hinchey classification is a well-recognized classification system that is used to describe perforated diverticular disease. The classification includes multiple stages: Stage Ib (pericolic abscess), Stage IIa (distant abscess amenable to percutaneous drainage), Stage IIb (complex abscess associated with/without fistula), Stage III (generalized purulent peritonitis) and Stage IV (fecal peritonitis) [9].

There is no clear distinction between uncomplicated and complicated diverticulitis in terms of clinical and laboratory findings[9]. The use of inflammatory markers as biochemical predictors of complicated diverticulitis has been studied in multiple previous studies. The findings of WCC as a predictor of perforated diverticulitis are conflicting. One study found variable accuracy of WCC in predicting complicated diverticulitis [10]. Another study found no correlation between WCC and complicated diverticulitis [11]. Another report indicated that WCC was found to correlate with complicated diverticulitis, but no further diagnostic evaluation was done [12]. The diagnostic value of WCC was found to be poor with area under curve of only 0.58 in another study [13].

A great deal of research has been conducted to investigate the usefulness of C-reactive protein as an inflammatory marker in predicting complicated diverticulitis; however, there was no consensus on a cut-off level of CRP as a diagnostic test of complicated diverticulitis. Most of these studies, showed that CRP is a useful predictor in detecting complicated diverticulitis [14]. Some studies suggested CRP> 200 mg/L with a positive predictive value (PPV) of 69%. In another study CRP >200 mg/L had a PPV of 90% and negative predictive value (NPV) of 59% for complicated diverticulitis [15]. A cut-off of 150 mg/L was reported in a later study [15]. CRP was reported to be higher in patients who needed emergency surgery (171.8 mg/L) compared to those who were managed conservatively (101.5 mg/L) [11]. Another study recommended a CRP cut-off of 175 mg/L with a PPV of 36%, a NPV of 92%, a sensitivity of 61%, and a specificity of 82% [13]. This was a similar finding to other research with a CRP cut-off value of 170 mg/L to distinguish patients who needed surgery. The sensitivity was 87.5% and the specificity was 91.1% [16]. Only one report found no significant difference in CRP levels between uncomplicated and contained perforation [17].

The aim of the present study is to evaluate the predictive value of white cell count and C-reactive protein in detecting complicated diverticulitis, and their sensitivity and specificity in differentiating complicated from uncomplicated diverticulitis at different cut-off values.

Materials and methods

This case-control study was conducted in Lyell McEwin Hospital in Adelaide, South Australia. The Human Research Ethics Committee (HREC Australia) issued approval HREC/18/CALHN/38. Both HREC approval and site-specific approval were obtained following the ethical approval process guidelines. Data were obtained from records of consecutive patients admitted for inpatient management of acute diverticulitis from January 2015 to December 2017.

Patients with diverticular disease were identified by using medical condition specific codes available in hospital records. Patients with CT diagnosis of acute diverticulitis were included in the study. Patients with diverticular bleeding, no CT confirmation, and incidental diverticular disease on colonoscopy were excluded.

The study sample was divided into a case group and a control group. Patients with a Hinchey Ia diverticulitis classification were designated as “uncomplicated diverticulitis. Patients with Hinchey Ib and above were described as having “complicated diverticulitis.” This determination was made based on radiological diagnoses.

Baseline characteristics, previous diverticulitis, immunosuppression, previous complicated diverticulitis, white cell count, C-reactive protein, and computed tomography findings were obtained and reported. These parameters were extracted from the patient’s clinical, laboratory and radiology records.

Statistical analysis

Binary and continuous data were used in the study. White cell count and C-reactive protein were analyzed as continuous data. Analysis of binary variables was performed using 2 x 2 tables and calculating odds ratios with 95% confidence intervals and using Chi-squared as the test of significance. Diagnostic test analysis was performed by using receiver operating characteristic curves and area under the curve with 95% confidence intervals for both white cell count and C-reactive protein. In addition, the sensitivity, specificity, PPV, and NPV of multiple cut-off values for both white cell count and C-reactive protein were calculated and reported. The calculation of PPV and NPV was performed using the prevalence of complicated diverticulitis in the study group. This, in turn, was calculated from data of all consecutive patients admitted to the hospital with acute diverticulitis in 2015.

Results

For the period of 2015-2017, 116 consecutive cases were collected; 10 cases had no CT diagnosis and were excluded, leaving a total of 106 consecutive cases, which were recruited for the study. There were 44 cases of complicated diverticulitis and 62 cases with uncomplicated diverticulitis. Uncomplicated diverticulitis cases were allocated as the control group. Table 1 summarizes the characteristics of the study groups and other

factors that were expected to be relevant in determining outcomes.

Table 1: Characteristics of the study groups

	Complicated (Case) group	Uncomplicated (Control) group
Frequency	44	62
Sex (%)		
Male	26 (59%)	32 (52%)
Female	18 (41%)	30 (48%)
Mean age (SD)	56.7 (17)	56.2(14.6)
First episode	23 (52.3%)	24 (38.7%)
Recurrent episode	21 (47.7%)	38 (61%)
Immune suppression	3 (6.8%)	5 (8%)
Previous complicated diverticulitis	8 (18.2%)	11 (17.8%)

The inflammatory markers, namely WCC and CRP, were the biochemical markers of interest in this study. WCC and CRP at time of presentation were collected from clinical and pathology reports. ROC analysis was performed. In addition, multiple cut-off values for both WCC and CRP were reported. Sensitivity and specificity were calculated for each cut-off. PPV and NPV were calculated based on the prevalence of the complicated diverticulitis in the study population. The prevalence of complicated diverticulitis was 20%. An odds ratio with 95% confidence interval was also calculated to assess the increase in risk for each cut-off value (Table 2).

For WCC, the ROC was obtained (Figure 1). The AUC was 0.69 (0.582-0.797) with a *P*-value of 0.001. This was a statistically significant result with a fair diagnostic value. To help in recognizing appropriate diagnostic cut-off value, sensitivity and specificity along with PPV, NPV and odds ratio (OR) of multiple cut-off values were reported. Table 2 summarizes the diagnostic test parameters for cut-off values of 14, 15, 16, 17 and 18 ($\times 10^9$/L). At cut-off of 14, sensitivity was found to be 56.8% and specificity 80.7%. The sensitivity was found to gradually decrease and specificity gradually increase as the cut-off value increased. At 18 the sensitivity was 25% and specificity was 79% (Table 2). A PPV of WCC of 18 or above was present in 79.5% in the study population.

Figure 1: White cell count ROC curve

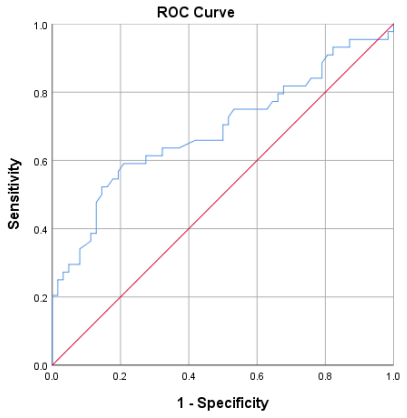


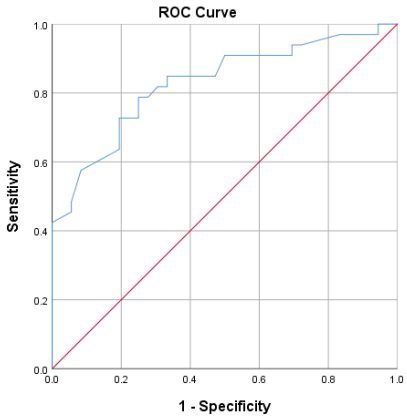
Table 2: Evaluation of multiple cut-off values of WCC and CRP in predicting complicated diverticulitis

Cut-off values	Sen	Spe	PPV	NPV	OR	CI 95%
WCC ($\times 10^9$/L)						
14	56.8	80.7	42.3	88.2	5.482	2.302 – 13.055
15	50	85.5	46.3	87.2	5.889	2.344 – 14.794
16	38.6	87.1	42.8	85	4.25	1.629 – 11.088
17	27.3	95.2	58.5	84	7.375	1.938 – 28.062
18	25	98.4	79.5	84	20.33	2.514 – 164.47
CRP (mg/L)						
100	72.7	80.6	48.3	92	11.048	3.583 – 34.067
120	57.6	91.7	63.3	89.6	14.929	3.798 – 58.676
140	45.5	94.4	67.2	87.4	14.167	2.912 – 68.927
160	36.36	97.22	76.6	85.94	20	2.42 - 166.67

Sen: sensitivity, Spe: specificity WCC: white cell count, CRP: C-reactive protein, PPV: positive predictive value, NPV: negative predictive value , OR: odds ratio, CI: confidence interval

For CRP, there were 37 missing data, and these were for patients who did not have CRP done during admission. Sixty-nine cases were available for analysis. The ROC curve was obtained as shown in Figure 2. The area under the curve was 0.828 (0.729-0.927) with a *P*-value of <0.001. This was a statically significant result with a high diagnostic value. Diagnostic test parameters of cut-off values of 100, 120, 140 and 160 (mg/L) were reported (Table 2). At cut-off value of 100 the sensitivity was 72.7% and the specificity was 80.6%. Sensitivity decreased and specificity increased as the cut-off increased in value. At 160 mg/L, sensitivity was 36.36% and specificity was 97.22% with PPV of 76% in the study population.

Figure 2: C-reactive protein ROC curve



Discussion

In this study we examined the diagnostic value of both WCC and CRP in detecting complicated diverticulitis. We found that both WCC and CRP have a diagnostic value in predicting complicated diverticulitis. The AUC for WCC was 0.69 (0.582-0.797) and the *P*-value was 0.001. This represents a significant finding compared to the existing literature. Accordingly, WCC has a fair value as a predictive test of complicated diverticulitis. This result supported the usefulness of WCC as a predictive test of complicated diverticulitis. This finding was contrary to current literature conclusions of no correlation, variable accuracy, or poor value of WCC in predicting complicated diverticulitis [10,11,13].

CRP as a predictive test of complicated diverticulitis had a higher AUC of 0.828 (0.729-0.927) with a *P*-value of <0.001. This represents a very significant result and high value in predicting complicated diverticulitis. This finding confirms similar results of previous studies of high value of CRP as a predictor of complicated diverticulitis [11,13-16].

Choosing a effective cut-off value for use in clinical practice depends on the clinical scenario. It must be determined whether a higher sensitivity is required to detect more cases of complicated diverticulitis or a higher specificity is needed to achieve greater accuracy in predicting complicated diverticulitis.

For WCC, a cut-off value of 18 in the study population had a specificity of 98.4% with positive predictive value of 79.5%. This means the chances of having complicated diverticulitis for cases with WCC of 18 or above is almost 80% within the study population. At this cut-off value, the odds of having complicated diverticulitis are 20 times higher than that of uncomplicated diverticulitis. Sensitivity at this cut-off is only

25%, making this cut-off value more useful in determining complicated diverticulitis.

For CRP, all the cut-offs examined showed higher sensitivities compared to those for WCC. At a cut-off of 160, specificity was 97.22% and a positive predictive value of 76.6% was seen in the study population. The means that at CRP of 160 mg/L and above, the chances of having complicated diverticulitis is 76.6%. Once again, the estimated odds of having complicated diverticulitis were 20 times the odds of uncomplicated diverticulitis in the study population. Sensitivity at this cut-off was only 36%, making this cut-off value more useful in ruling on cases of complicated diverticulitis. Compared to the current literature we found that a CRP cut-off value of 160 mg/L has a significant specificity and PPV, making it useful in clinical practice as a predictor of complicated diverticulitis. This result was very close to studies in the available literature with findings of a cut-off of 150 mg/L or slightly higher 175 mg/L, but significantly lower than the cut-off of other study findings of 200 mg/L [11,13-16].

Both WCC and CRP are highly specific tests in predicting complicated diverticulitis at higher cut-off values. This makes high cut-off of WCC and CRP a dependable test to use as a determinant in complicated diverticulitis, and hence, a strong predictor. However, the drawback of high cut-off values of inflammatory markers is reduced sensitivity and a considerable percentage of complicated diverticulitis cases being missed.

One recognized limitation of this study is its small sample size. Even within the small sample size, the results of the study have achieved statistical significance and internal validity was ensured. A larger sample size would have alleviated doubts in generalizability of the study findings. We collected data from consecutive patients in a complicated diverticulitis group over the period of the study and also used consecutive patients for the control group to avoid sampling bias. The findings of the study are probably valid for Western and industrial societies where the prevalence of diverticulitis and complicated diverticulitis is similar to the study population.

Conclusion

Contrary to what has been previously reported in the literature, we found that WCC remains a significant test in diagnosing complicated diverticulitis. A high cut-off value of 18 $\times 10^9$/L is useful in predicting complicated diverticulitis with high positive predictive value. When compared to WCC, CRP is a more sensitive test in detecting complicated diverticulitis. We recognized a cut-off value of 160 mg/L to be a suitable level to determine complicated diverticulitis with a significant positive predictive value.

WCC and CRP are very specific predictors of complicated diverticulitis with high positive predictive values at high cut-off values of 18 $\times 10^9$/L and 160 mg/L, respectively. However, at these high cut-off values the sensitivity of the tests suffers significantly and a considerable portion of complicated diverticulitis will be missed. For that reason, using radiological diagnosis continues to be important part of the assessment of patients with acute diverticulitis.

Both WCC and CRP are very useful predictors of complicated diverticulitis. Further studies can be implemented to formulate a predictive model of complicated diverticulitis, which can be useful in areas where CT scanning availability is limited.

References

1. Sheth AA, Longo W, Floch MH. Diverticular disease and diverticulitis. The American journal of gastroenterology. 2008;103(6):1550-6. Epub 2008/05/16. doi: 10.1111/j.1572-0241.2008.01879.x. PubMed PMID: 18479497.
2. Etzioni DA, Mack TM, Beart RW Jr, Kaiser AM. Diverticulitis in the United States: 1998-2005: changing patterns of disease and treatment. Annals of surgery. 2009;249(2):210-7. Epub 2009/02/13. doi: 10.1097/SLA.0b013e3181952888. PubMed PMID: 19212172.
3. John H Pemberton M, Lawrence S Friedman, MD, Shilpa Grover, MD, MPH, AGAF. Colonic diverticulosis and diverticular disease: Epidemiology, risk factors, and pathogenesis. Uptodate. 2021.
4. Everhart JE, Ruhl CE. Burden of digestive diseases in the United States part II: lower gastrointestinal diseases. Gastroenterology. 2009;136(3):741-54. Epub 2009/01/27. doi: 10.1053/j.gastro.2009.01.015. PubMed PMID: 19166855.
5. Shaheen NJ, Hansen RA, Morgan DR, Gangarosa LM, Ringel Y, Thiny MT, et al. The burden of gastrointestinal and liver diseases, 2006. The American journal of gastroenterology. 2006;101(9):2128-38. Epub 2006/07/20. doi: 10.1111/j.1572-0241.2006.00723.x. PubMed PMID: 16848807.
6. Peery AF, Dellon ES, Lund J, Crockett SD, McGowan CE, Bulsiewicz WJ, et al. Burden of gastrointestinal disease in the United States: 2012 update. Gastroenterology. 2012;143(5):1179-87.e3. Epub 2012/08/14. doi: 10.1053/j.gastro.2012.08.002. PubMed PMID: 22885331; PubMed Central PMCID: PMC3480553.
7. Anaya DA, Flum DR. Risk of emergency colectomy and colostomy in patients with diverticular disease. Archives of surgery (Chicago, Ill : 1960). 2005;140(7):681-5. Epub 2005/07/20. doi: 10.1001/archsurg.140.7.681. PubMed PMID: 16027334.
8. John H Pemberton M, Martin Weiser, MD, Krishnan Raghavendran, MD, FACS. Acute colonic diverticulitis: Medical management. Uptodate. 2022.
9. Köhler L, Sauerland S, Neugebauer E. Diagnosis and treatment of diverticular disease: results of a consensus development conference. The Scientific Committee of the European Association for Endoscopic Surgery. Surgical endoscopy. 1999;13(4):430-6. Epub 1999/03/27. doi: 10.1007/s004649901007. PubMed PMID: 10094765.
10. Reynolds IS, Heaney RM, Khan W, Khan IZ, Waldron R, Barry K. The Utility of Neutrophil to Lymphocyte Ratio as a Predictor of Intervention in Acute Diverticulitis. Digestive surgery. 2017;34(3):227-32. Epub 2016/12/13. doi: 10.1159/000450836. PubMed PMID: 27941316.
11. Käser SA, Fankhauser G, Glauser PM, Toia D, Maurer CA. Diagnostic value of inflammation markers in predicting perforation in acute sigmoid diverticulitis. World journal of surgery. 2010;34(11):2717-22. Epub 2010/07/21. doi: 10.1007/s00268-010-0726-7. PubMed PMID: 20645093.
12. Tursi A, Brandimarte G, Giorgetti G, Elisei W, Maiorano M, Aiello F. The Clinical Picture of Uncomplicated Versus Complicated Diverticulitis of the Colon. Digestive Diseases and Sciences. 2008;53(9):2474-9. doi: 10.1007/s10620-007-0161-2.
13. van de Wall BJ, Draaisma WA, van der Kaaij RT, Consten EC, Wiezer MJ, Broeders IA. The value of inflammation markers and body temperature in acute diverticulitis. Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland. 2013;15(5):621-6. Epub 2012/10/24. doi: 10.1111/codi.12072. PubMed PMID: 23088216.
14. Tan JP, Barazanchi AW, Singh PP, Hill AG, Maccormick AD. Predictors of acute diverticulitis severity: A systematic review. International journal of surgery (London, England). 2016;26:43-52. Epub 2016/01/19. doi: 10.1016/j.ijsu.2016.01.005. PubMed PMID: 26777741.
15. Mäkelä JT, Klintrup K, Takala H, Rautio T. The role of C-reactive protein in prediction of the severity of acute diverticulitis in an emergency unit. Scandinavian journal of gastroenterology. 2015;50(5):536-41. Epub 2015/02/11. doi: 10.3109/00365521.2014.999350. PubMed PMID: 25665622.
16. Kechagias A, Rautio T, Kechagias G, Mäkelä J. The role of C-reactive protein in the prediction of the clinical severity of acute diverticulitis. The American surgeon. 2014;80(4):391-5. Epub 2014/06/03. PubMed PMID: 24887672.
17. Elsing C, Ernst S, Stremmel W. Value of lipopolysaccharide binding protein, interleukin-6 and C-reactive protein as biomarkers of severity in acute diverticulitis: a prospective study. Clinical laboratory. 2012;58(1-2):145-51.

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Can biomarkers predict the risk of cardiovascular disease in patients with obstructive sleep apnea syndrome?

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Ethics Committee Approval
The study was approved by the Ethical Committee of Binali Yildirim University (Decree No: 21/06/2021, 08/11).
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: Obstructive sleep apnea syndrome (OSAS) is a clinical syndrome characterized by recurrent partial or total obstruction of the upper airway. Cardiovascular disease (CVD) is more common in OSAS patients. Biomarkers can predict the progression of OSAS disease and the occurrence of CVD. Here we investigate the effects of age, gender, body mass index (BMI), comorbidities, neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), platelet-to-lymphocyte ratio (PLR), systemic inflammatory index (SII), atherogenic index of plasma (AIP), C-reactive protein-to-albumin ratio (CAR) and monocyte to HDL cholesterol (MHR) on the severity of OSAS and the occurrence of CVD in OSAS patients.

Method: This cross-sectional study included 172 OSAS patients presenting to Erzincan Binali Yildirim University Mengucek Gazi Training and Research Hospital, Sleep Service between 01.01.2021 and 31.08.2022. Polysomnography (PSG) was applied to patients participating in the study, and routine complete blood and biochemistry tests were performed. Comorbidities and demographic data of the participants were recorded.

Results: The frequency of CVD, chronic pulmonary disease (CPD) and hyperlipidemia increased as the severity of OSAS increased (P=0.005, P<0.001, P=0.016, respectively). As the severity of OSAS disease increased, only the MHR indices increased (P=0.009). When OSAS groups with and without CVD were examined, OSAS patients with CVD were older and had higher BMI (P<0.001, P=0.001, respectively). In addition, tended to be females with hyperlipidemia, diabetes mellitus (DM) and high Charlson Comorbidity Index (CCI) scores (all P<0.001). When the polysomnography of OSAS patients with CVD was evaluated, apnea-hypopnea index (AHI), non-rapid eye movement (NREM)-AHI (NREM-AHI), respiratory disorder index (RDI) and oxygen desaturation index (ODI) values were higher and sleep efficiency (SE) values were lower than patients with OSAS without CVD (P=0.002, P=0.002, P=0.003, P<0.001, P<0.001, respectively).

Conclusion: CVD is common in OSAS patients. As the severity of OSAS increases, the risk of developing CVD increases. Elderly female OSAS patients with hyperlipidemic, DM, high BMI, and Charlson Comorbidity Index (CCI) constitute a relatively risky group for CVD. OSAS patients with high AHI, NREM-AHI, RDI, ODI, and low SE values should be monitored more closely for CVD.

Keywords: OSAS, cardiovascular disease, biomarker, AHI

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Introduction

Obstructive sleep apnea syndrome (OSAS) is a disease that affects 3–7% of the middle-aged population [1]. OSAS is a clinical syndrome characterized by recurrent partial or total upper airway obstruction. Its main symptoms are snoring, excessive daytime sleepiness, and witnessed apnea [2]. OSAS is diagnosed using nocturnal polysomnography (PSG) testing. The diagnostic criteria for OSAS are an apnea-hypopnea index (AHI) >5 on PSG in the presence of symptoms or an AHI >15 for an asymptomatic patient [3].

Comorbid conditions, such as obesity, smoking, hypertension, hyperlipidemia, metabolic syndrome, diabetes mellitus (DM), and insulin resistance, are more common in OSAS patients compared to the general population.

Recurrent episodes of nocturnal apnea in OSAS patients cause sympathetic system activation, increased oxidative stress, endothelial dysfunction, a spike in systemic hypertension, hypoxia, and hypercapnia [3]. Intermittent episodes of hypoxia resulting from temporary respiratory arrest and ischemia-reperfusion injury during sleep are the main physiological features of OSAS. Intermittent episodes of nocturnal hypoxemia also induce the generation of oxygen radicals that cause low-grade inflammation [4]. Oxidizing radicals and proteolytic enzymes accumulate leukocytes and platelets on blood vessel walls, leading to endothelial dysfunction [5]. Inflammation is one of the main factors contributing to the initiation and progression of atherosclerosis [6]. Studies have shown that autonomic and neurohumoral abnormalities in OSAS persist during the daytime, disrupting the general circadian blood pressure rhythm and increasing short- and long-term blood pressure variability [7-9]. Absolute blood pressure elevation and fluctuations seen in OSAS have been found to cause organ damage by promoting arterial remodeling, microvascular damage, hemodynamic instability, and vascular reactivity [10-13].

Endothelial dysfunction is involved in the pathophysiology of hypertension, DM, coronary artery disease (CAD), and congestive heart failure (CHF). Endothelial dysfunction is also common in OSAS patients [14]. For these reasons, cardiovascular diseases are more common in OSAS patients [15,16]. The chronic systemic inflammation seen in OSAS may play an important role in the progression of cardiovascular disease (CVD) [17]. Studies have shown that OSAS is an independent risk factor for CVD [18].

Recent studies show that WBC and neutrophil-to-lymphocyte ratio (NLR) are good indicators of inflammation [19-23]. Studies reveal platelet/lymphocyte ratio (PLR) as a new inflammatory marker in predicting CVD [22-24]. Unlike the separate analysis of CRP and albumin, the C-reactive protein/albumin ratio (CAR) can be used as a more reliable biomarker to predict the severity and prognosis of diseases [25]. CAR was found to be significantly higher in patients with high thrombus burden. CAR can be used as a marker of proinflammation, which is closely related to the prothrombotic state. In previous studies, the systemic inflammatory index (SII) indicates inflammatory status [26]. The atherogenic index of the plasma (AIP) can be defined as a marker of atherogenic oxidized small-density LDL-cholesterol and has predictive value for cardiovascular disease risk [27]. Patients with OSAS have higher AIP and triglyceride and lower HDL-cholesterol values. The monocyte/HDL-cholesterol ratio (MHR) is a practical, cost-effective marker for determining CVD risk and may indicate endothelial dysfunction [18,28].

In our study, we aimed to investigate the relationship between inexpensive, practical, and easily obtainable complete blood and biochemistry tests and NLR, MHR, LMR, and PLR values calculated from these tests with the severity of OSAS patients and to find out their contribution in predicting CVD risk. As far as we know, very few studies have been conducted on the CVD formation of CAR, SII, and AIP values in OSAS patients. In our study, we aimed to determine CAR, SII, and AIP levels' contributions to CVD risk in OSAS patients and the severity of OSAS. In addition, we aimed to determine the effects of age, gender, and body mass index (BMI) on disease progression and CVD formation in our OSAS patients. Finally, we aimed to investigate the relationship between the severity of OSAS and comorbid conditions.

Materials and methods

This cross-sectional studies study includes 172 patients between 40 and 110 years old who were admitted to Erzincan Binali Yildirim University Mengucek Gazi Training and Research Hospital Sleep Department between 01.01.2021 and 31.08.2022 and diagnosed with OSAS according to the American Academy of Sleep Medicine (AASM). Patients younger than 18 years old, those with central sleep apnea syndrome, patients with upper respiratory tract resistance syndrome, and those with narcolepsy and movement disorders were excluded from the study. The study was carried out following the Declaration of Helsinki.

PSG evaluation of all patients was performed, and patients were grouped as mild (AHI: 5–15), moderate (AHI: 15–30), and severe OSAS (AHI) >30) according to AASM criteria (14). All patients underwent nocturnal PSG (55-channel polysomnography (Alice Sleepware; Philips Respironics, Pennsylvania, USA). Electrooculogram (two channels), electroencephalogram (four channels), electromyograms of submental muscles (one channel), anterior tibialis muscle of both legs (two channels), electrocardiograms, airflow measurements (with oronasal), thermistor and nasal cannula pressure transducer, and a snoring sensor to detect sleep and snoring vibrations were used in all patients. Using a finger probe, the thoracic and abdominal muscles' respiratory effort (two channels) was recorded using piezoelectric belts and arterial blood pressure, pulse, and oxyhemoglobin saturation (SaO2: 1 channel). Apnea was defined as a 90% reduction in airflow amplitude or 10 s relative to baseline amplitude. According to the AASM, hypopnea was defined as a 30% decrease in airflow amplitude relative to a recommended baseline and values associated with 4% oxygen desaturation lasting at least 10 s. In patients with OSAS, the number of AHI apneic plus hypopneic episodes was calculated per hour of sleep. The oxygen desaturation index (ODI) was defined as the number of measurements of -4% oxyhemoglobin desaturation within 10 s to <3 min from baseline. Mean oxygen saturation, minimum oxygen saturation, oxygen desaturation index, desaturation %,

AHI, REM AHI, NREM-AHI, sleep efficiency (SE), arousal index (AI), and respiratory disorder index (RDI) values of the patients were recorded.

Demographic characteristics, pulse rates, arterial blood pressure, sleep patterns, medical histories, cardiovascular and metabolic diseases, and drug use habits of the patients were also recorded. In the study, cardiovascular disease was diagnosed by a specialist cardiologist using an electrocardiogram, echocardiography, and coronary angiography and by evaluating the patient's medical history and drug use. CVD was used only for heart failure, coronary artery disease or arrhythmia diseases.

On the morning of PSG, patient venous blood samples were obtained after 12 h of fasting. Triglyceride, total cholesterol, LDL-cholesterol, HDL-cholesterol levels and leukocyte, neutrophil, lymphocyte and monocyte counts were determined by Sysmex XN_100 and Sysmex XN_2000 devices. Serum albumin level was analyzed using automated photometry kits (AU 2700 Backman Olympus spectrophotometric method). Serum CRP levels were measured by the nephelometric method (Siemens BN11 system). CAR was obtained by multiplying the CRP to albumin ratio by 100. The AIP value was calculated as the base 10 logarithmic conversion of the triglyceride to high-density lipoprotein-cholesterol ratio (TG / HDL-cholesterol). The systemic inflammation index (SII) was calculated using the neutrophil × platelet/lymphocyte formula. The ratio of monocytes/HDL-cholesterol found in MHR. Local Ethics Committee approval (Decree No: 21/06/2021, 08/11) was obtained from Binali Yildirim University for the study, and the study was performed per the ethical standards specified in the 1964 Declaration of Helsinki and its later amendments.

Bias

Patients with OSAS in all severity who applied to the OSAS clinic were included in the study sequentially. The cardiologist did not know the severity of OSAS in the patients.

Study size

All patients diagnosed as OSAS according to AASM criteria applied to Erzincan Binali Yıldırım University Mengucek Gazi Training and Research Hospital Sleep Service between 01.01.2021-31.08.2022 were included in the study, respectively.

Statistical analysis

Categorical variables were expressed as numbers and percentages, whereas continuous variables were summarized as mean, standard deviation, or median (Q1-Q3). The chi-square test was used to compare categorical variables between the groups. The normality of distribution for continuous variables was confirmed with the Shapiro-Wilk test. Depending on the distribution, the Student's t-test or Mann-Whitney U test was used to compare continuous variables between the two groups. The comparison between more than two groups was made by One-way ANOVA or the Kruskal-Wallis test. Logistic regression analysis was performed to determine significant predictors of CVD risk. In univariate analysis, variables significant at the P<0.25 level were entered in logistic regression analysis. All analyses were performed using IBM SPSS 20. A value of P<0.05 for all tests was considered statistically significant.

Results

One-hundred-seventy-two OSAS patients were included in our study. Age distributions were similar in all OSAS severity groups (P=0.302). The gender distribution did not affect the OSAS severity and showed a similar distribution in control, mild, moderate, and severe OSAS groups (P=0.369). BMI value, CCI score, and DM frequency were similar in all OSAS severity groups (P=0.312, P=0.062, P=0.663, respectively). CVD, CPD, and hyperlipidemia were seen more frequently as the severity of OSAS increased (P=0.005, P<0.001, P=0.016, respectively). As the severity of OSAS disease increased, only the MHR indices increased, while NLR, LMR, PLR, SII, CAR, and AIP did not change (P=0.009, P=0.134, P=0.060, P=0.796, P=0.307, P=0.187, P=0.333, respectively) (Table 1).

Table 1: Age, gender, comorbidities, laboratory values and indices of patients are seen in control and all OSAS severity groups.

	Mild OSAS (n=67)	Medium OSAS (n=52)	Severe OSAS (n=53)	*P*-value
Age	51.60 (9.36)	54.31 (10.87)	54.02 (11.76)	0.302*
Gender (M/F)	42/25	27/25	34/19	0.369^{+}
BMI	32.0 (5.9)	33.4 (7.3)	33.7 (6.1)	0.312*
CCI	1.0 (0.0-2.0)	1.0 (0.0-2.0)	1.0 (1.0-2.0)	0.062**
CVD %	21 (46.3%)^{a}	31 (59.6%)^{a,b}	40 (75.5%)^{b}	0.005^{+}
CPD %	24 (35.8%)^{a}	26 (50.0%)^{a}	39 (73.6%)^{b}	<0.001^{+}
DM %	21 (31.3%)	20 (38.5%)	20 (37.7%)	0.663^{+}
Hyperlipidemia %	11 (16.4%)^{a}	8 (15.7%)^{a,b}	18 (35.8%)^{b}	0.016^{+}
NLR	1.7 (1.3-2.1)	1.6 (1.1-2.0)	1.7 (1,5-2.4)	0.134**
LMR	3.2 (2.7-4.6)	3.7 (2.7-4.6)	2.5 (1.7-4.3)	0.060**
PLR	108.1 (88.6-128.5)	102.3 (83.5-124.0)	105.7 (84.6-123.5)	0.796**
SII	418.7 (333.0-621.9)	376.9 (327.6-518.6)	457.3 (316.8-644.9)	0.307**
CAR	7.5 (7.1-7.8)	7.7 (7.3-9.3)	7.5 (7.4-7.7)	0.187**
AIP	0.20 (0.03-034)	0.22 (-020-0.36)	0.24 (0.6-0,45	0.333**
MHR	0.02 8 (0.1-0.2)^{a}	0.01 (0.01-0.02)^{a}	0.2 (0.01-0.03)^{b}	0.009**

*One-way ANOVA, **Kruskal Wallis test and $^{+}$Chi-square test was performed. Results were presented as Mean (SD) or Median (Q1-Q3). BMI: body mass index, CCI: Charlson comorbidity index, CVD: cardiovascular disease, CPD: chronic pulmonary disease, DM: diabetes mellitus, NLR: neutrophil-to-lymphocyte ratio, LMR: lymphocyte-to-monocyte ratio, PLR: platelet-to-lymphocyte ratio, SII: systemic inflammatory index, CAR: C-reactive protein-to-albumin ratio, AIP: atherogenic index of plasma, MHR: monocyte to HDL cholesterol ratio.

The rate of OSAS patients without CVD comorbidity was 40.69% (n=70). The rate of patients with CVD comorbidity was 59.30% (n=102). We observed that OSAS patients with CVD were more commonly female, elderly, and with high BMI values (P=0.004, P<0.001, P<0.001, respectively). It was determined that the CCI score was higher, and hyperlipidemia and DM were more common in OSAS patients with CVD (P<0.001, P<0.001. P<0.001, respectively). When laboratory indices were examined in patients with and without CVD, it was observed that NLR, LMR, PLR, SII, CAR, AIP, and MHR were at similar values (P=0.366, P=0.396, P=0.689, P=0.361, P=0.803, P=0.691, P=0.994, respectively). When OSAS groups with and without CVD were examined polysomnographically, it was seen that AHI, NREM-AHI, RDI and ODI values were higher (P=0.002, P=0.002, P=0.003, and P<0.001, respectively) and SE values were lower (P<0.001) in the OSAS group with CVD, while REM-AHI and AI were similar in both groups (P=0.882 and P=0.321, respectively) (Table 2, Figure 1). Logistic regression analysis was performed using the Forward LR method to determine the potential risk factors for CVD, and variables were reported in Table 3. While age, BMI, and NREM-AHI increase, the risk of CVD increases. Also, having hyperlipidemia increased the risk of CVD by 3.9 times (95% CI: 1.3–11.6). For SE, having high sleep efficiency decreased CVD risk (OR: 0.95 [0.92–0.98]).

Table 2: Age, gender, comorbidities, indices, and polysomnographic findings are seen in OSAS patients who do not develop CVD and who develop CVD.

	CVD - (n=70)	CVD + (n=102)	*P*-value
Age	48.0 (10.3)	56.8 (9.3)	<0.001*
Gender (M/F)	(51/19)	(52/50)	0.004^{+}
BMI	30.3 (4.4)	34.8 (7.0)	<0.001*
Hyperlipidemia	7 (10.0%)	31 (30.7%)	0.001^{+}
DM	13 (18.6%)	48 (47.1%)	<0.001^{+}
CCI	0.5 (0.1-1.0)	1 (1.0-2.0)	<0.001**
NLR	1.65 (1.26-2.00)	1.71 (1.33-2.25)	0.366**
LMR	3.18 (2.35-4.65)	3.17 (2.00-4.49)	0.396**
PLR	106.36 (84.33-123.89)	105.22 (84.58-128.03)	0.689**
SII	396.90 (319.17-522.00)	437.03 (326.24-604.58)	0.361**
CAR	7.50 (7.13-8.68)	7.5 (7.32-7.89)	0.803**
AIP	0.24 (0.07-0.36)	0.22 (0.01-0.39)	0.691**
MHR	0.02 (0.01-0.02)	0.02 (0.01-0.02)	0.994**
AHI	14.3 (9.0-26.3)	21.3 (12.0-53.0)	0.002**
REM-AHI	25.3 (13.5-45.6)	28.2 (9.3-50.4)	0.882**
NREM-AHI	12.6 (7.9-27.6)	21.4 (10.6-53)	0.002**
SE%	78.9 (70.9-88.4)	73.0 (59.5-80.0)	<0.001**
AI	10.3 (6.8-18.7)	12.0 (6.7-24.7)	0.321**
RDI	14.6 (9.1-26.9)	21.6 (12.0-53.0)	0.003**
ODI	6.8 (4.0-11.1)	9.9 (5.6-23.6)	0.001**

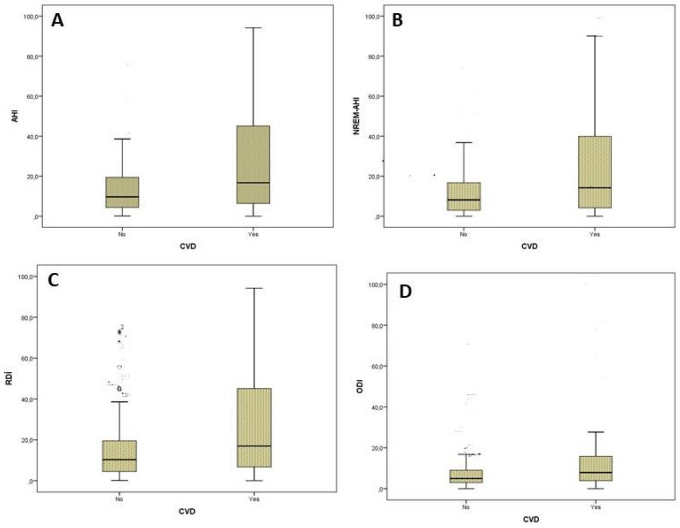
Student t-test, **Mann Whitney U test and $^{+}$Chi-square test were performed. Results were presented as Mean (SD) or Median (Q1-Q3). BMI: body mass index, CCI: Charlson comorbidity index, DM: diabetes mellitus, NLR: neutrophil-to-lymphocyte ratio, LMR: lymphocyte-to-monocyte ratio, PLR: platelet-to-lymphocyte ratio, SII: systemic inflammatory index, CAR: C-reactive protein-to-albumin ratio, AIP: atherogenic index of plasma, MHR: monocyte to HDL cholesterol ratio, AHI: apnea-hypopnea index, NREM-AHI: non-rapid eye movement AHI, RDI: respiratory disorder index, ODI: oxygen desaturation index, CVD: cardiovascular disease.

Table 3: Logistic regression results for CVD in patients with obstructive sleep apnea syndrome.

	OR	95% CI for OR		*P*-value
		Lower	Upper	
Age (years)	1.1	1.035	1.131	<0.001
BMI (kg/m^2)	1.2	1.062	1.257	0.001
Hyperlipidemia	3.9	1.298	11.642	0.015
NREM-AHI	1.03	1.012	1.052	<0.001
SE%	0.95	0.92	0.98	0.005

OR-Odds Ratio, CI- confidence interval, BMI-body mass index, NREM-AHI-non-rapid eye movement AHI, SE%-sleep efficiency. CVD- Cardiovascular Disease

Figure 1: Polysomnographic findings are seen in OSAS patients who do not develop CVD and in groups that develop CVD. AHI (A), NREM-AHI (B), RDI (C), and ODI (D).



AHI: apnea-hypopnea index, NREM-AHI: non-rapid eye movement AHI, RDI: respiratory disorder index, ODI: oxygen desaturation index, CVD: cardiovascular disease

Discussion

OSAS is characterized by recurrent narrowing of the upper airway causing intermittent oxyhemoglobin desaturation, sleep fragmentation, and daytime sleepiness.

The risk of CVD is increased in OSAS patients due to intermittent hypoxia, high BMI, excessive free radical formation, and the frequent coexistence of additional diseases, such as DM and hyperlipidemia. Predicting CVD is vital in these patients. Demographic data of patients, comorbidities, laboratory values, and polysomnographic measurements can be helpful in this regard. In a study of 2353 people, it was found that OSAS was more severe, especially in older men [29]. Our study observed that OSAS patients with CVD were older, but no significant relationship was found between OSAS severity and age.

Studies have shown that the incidence of OSAS in men is twice that of women [30]. In our study, gender did not affect the severity of OSAS. Interestingly, the frequency of CVD was higher in female OSAS patients than in males.

A study showed that BMI and DM are independent risk factors for OSAS, and central obesity may be more dangerous than BMI in this regard [29]. Another study showed that BMI is ineffective in determining the severity of OSAS [31]. In our study, BMI was similar in all OSAS severity groups. However, OSAS patients with CVD had higher BMI values.

A study showed that the most common comorbidities in OSAS patients were obesity, HT, and DM. CHF, Deep vein thrombosis (DVT), Pulmonary thromboembolism (PTE), and hypothyroidism were more common, especially in the severe OSAS group [30]. Similarly, in our study, the frequency of CVD, CPD, and hyperlipidemia was higher in the severe OSAS group than in the mild OSAS group. In addition, in our study, it was observed that hyperlipidemia and DM were more common, and the CCI score was higher in the OSAS group with CVD.

It has been reported that the relationship between OSAS and triglyceride and HDL-cholesterol is independent of obesity [32]. Another study determined that the TG\HDL-cholesterol ratio was associated with the severity of OSAS [33]. The coexistence of OSAS and dyslipidemia may be affected by genetic factors, diet, medications used by the patient, and comorbidities. Intermittent hypoxia and disruption of sleep structure may cause dyslipidemia in patients with OSAS. Sleep disturbance can also cause overeating [34]. It has been shown that REM sleep disorder more commonly causes dyslipidemia than NREM sleep disorder [35]. In our study, it was observed that the frequency of hyperlipidemia increased as the severity of OSAS increased, similar to the literature. In addition, hyperlipidemia was more common in OSAS patients with CVD.

Uygur et al. [36] found a correlation between NLR and OSAS severity and showed that NLR is an independent risk factor for CVD in OSAS patients. LMR can be used as an inflammation marker. Another study has reported a negative correlation between LMR and CAD [37]. And another study found a correlation between OSAS severity and SII values [26]. It has been shown that there is an increase in CVD risk in parallel with the increase in MHR in OSAS patients, and MHR was found to be higher in OSAS patients with CVD [38,39]. Among the indices examined in our study, only the MHR index increased with the severity of OSAS. The NLR, LMR, PLR, SII, CAR, AIP, and MHR indices were similar in OSAS patients with and without CVD.

Campos-Rodriges et al. [40] found that untreated OSAS patients had a significantly increased risk of CVD. Wang et al. [41] found a higher CVD risk in moderate and severe OSAS than in mild OSAS patients. Loke et al. [42] found that an increase in AHI of 10 or more increased the risk of CVD by 36%. In our study, it was observed that the rate of having CVD increased as the severity of OSAS increased, similar to the literature. In addition, in our study, the incidence of CVD in OSAS patients was positively correlated with AHI, NREM-AHI, RDI, and ODI

scores and negatively correlated with SE scores. AI and REM-AHI values were found to be similar in both groups.

Limitations

Our study had several limitations. A relatively small number of patients were included in our study. The fact that patients were not asked about their smoking and alcohol use is another limitation of my study. The fact that the duration of additional diseases that the OSAS patients have is not considered is another limitation.

Conclusion

The frequency of CVD is increased in OSAS patients because of intermittent hypoxia and common risk factors with CVD. As the severity of OSAS increases, the risk of developing CVD increases. Here, we found that as OSAS severity increases, CVD, CPD, and hyperlipidemia may increase, and increased NLR, SII, and MHR and decreased LMR were associated with OSAS severity. Elderly and hyperlipidemic female OSAS patients with DM and high CCI and BMI values constitute a higher risk group for CVD. In addition, OSAS patients with high AHI, NREM-AHI, RDI, ODI, and low SE values should be monitored more closely for CVD. One of the important causes of mortality in OSAS is CVD. Predicting the risk of CVD with OSAS is vital. The patient's age, gender, BMI, and additional diseases can give an idea of the formation of CVD. In addition, polysomnographic examination of patients with OSAS can be life-saving in terms of CVD risk

References

1. Duran J, Esnaola S, Rubio R, Iztueta Á. Obstructive Sleep Apnea–Hypopnea and Related Clinical Features in a Population-based Sample of Subjects Aged 30 to 70 Yr. Am J Respir Crit Care Med. 2001 Mar 17;163(3):685–9. doi: 10.1164/ajrccm.163.3.2005065.
2. Atan D, Kundi FCS, Özcan KM, Dere H. A New Predictor for Obstructive Sleep Apnea Syndrome: Monocyte to HDL Ratio. Indian J Otolaryngol Head Neck Surg. 2017 Jun 11;69(2):142–6. doi: 10.1007/s12070-016-0980-6
3. Shamsuzzaman A, Gersh B, Somers V. Obstructive sleep apnea: implications for cardiac and vascular disease. JAMA. 2003 Oct 8;290(14):1906-14. doi: 10.1001/jama.290.14.1906
4. Takama N, Kurabayashi. Influence of untreated sleep-disordered breathing on the long-term prognosis of patients with cardiovascular disease. Am J Cardiol. 2009 Mar 1;103(5):730-4. doi: 10.1016/j.amjcard.2008.10.035
5. Naruko T, Ueda M, Haze K, van der Wal AC, van der Loos CM, Itoh A, et al. Neutrophil Infiltration of Culprit Lesions in Acute Coronary Syndromes. Circulation Circulation. 2002 Dec 3;106(23):2894-900. doi: 10.1161/01.cir.0000042674.89762.20.
6. Imhof B, Aurrand-Lions M. Angiogenesis and inflammation face off. Nat Med. 2006 Feb;12(2):171-2. doi: 10.1038/nm0206-171.
7. Lattanzi S, Brigo F, Silvestrini M. Blood pressure profile and nocturnal oxygen desaturation. J Clin Hypertens (Greenwich). 2018 Apr;20(4):656-8. doi: 10.1111/jch.13259.
8. Lattanzi S, Brigo F, Silvestrini M. Obstructive sleep apnea syndrome and the nocturnal blood pressure profile. J Clin Hypertens (Greenwich). 2018 Jun;20(6):1036-8. doi: 10.1111/jch.13316.
9. Lattanzi S, Vernieri F, Silvestrini M. Blood pressure variability and neurocognitive functioning. Clin Hypertens (Greenwich). 2018 Apr;20(4):645-7. doi: 10.1111/jch.13232.
10. Wang J, Shi X, Ma C, Zheng H, Xiao J Bian H, et al. Visit-to-visit blood pressure variability is a risk factor for all-cause mortality and cardiovascular disease: a systematic review and meta-analysis. J Hypertens. 2017 Jan;35(1):10-7. doi: 10.1097/HJH.0000000000001159.
11. Tedla YG, Yano Y, Carnethon M, Greenland P. Association Between Long-Term Blood Pressure Variability and 10-Year Progression in Arterial Stiffness. Hypertension. 2017 Jan;69(1):118-27. doi: 10.1161/HYPERTENSIONAHA.116.08427.14.
12. Lattanzi S, Carbonari L, Pagliariccio G, Bartolini M. Cagnetti C, Viticchi G, et al. Neurocognitive functioning and cerebrovascular reactivity after carotid endarterectomy. Neurology. 2018 Jan 23;90(4):e307-15. doi:10.1212/WNL.0000000000004862.
13. Ribeiro A, Lotufo P, Fujita C Goulart A, Chor D G Mill J, et al Association between short-term systolic blood pressure variability and carotid intima-media thickness in ELSA-Brasil baseline. Am J Hypertens. 2017 Oct 1;30(10):954-60. doi: 10.1093/ajh/hpx076.
14. Dursunoğlu N, Dursunoğlu D. Obstructive sleep apnea syndrome, endothelial dysfunction and coronary atherosclerosis. Tuberkuloz ve Toraks. 2005 Jan 1;53(3):299-30
15. Kohler M, Stradling JR. Mechanisms of vascular damage in obstructive sleep apnea. Nat Rev Cardiol. 2010 Dec;7(12):677-85. doi: 10.1038/nrcardio.2010.145.
16. Ryan S, Taylor C, Nicholas MC W. Systemic inflammation: a key factor in the pathogenesis of cardiovascular complications in obstructive sleep apnoea syndrome? Thorax. 2009 Jul;64(7):631-6. doi: 10.1136/thx.2008.105577.
17. Nadeem R, Molnar J, Madbouly E, Nida M, Aggarwal S, Sajid H, et al. Serum inflammatory markers in obstructive sleep apnea: a meta-analysis. J Clin Sleep Med. 2013 Oct 15;9(10):1003-12. doi: 10.5664/jcsm.3070.
18. Inonu Koseoglu H, Pazarli AC, Kanbay A, Demir O. Monocyte Count/HDL Cholesterol Ratio and Cardiovascular Disease in Patients With Obstructive Sleep Apnea Syndrome: A Multicenter Study. Clin Appl Thromb Hemost. 2018 Jan;24(1):139-44. doi: 10.1177/1076029616677803.
19. Turak O, Özcan F, İşleyen A, Başar F, Gül M, Yilmaz S, et al. Usefulness of neutrophil-to-lymphocyte ratio to predict in-hospital outcomes in infective endocarditis. Can J Cardiol. 2013 Dec;29(12):1672-8. doi: 10.1016/j.cjca.2013.05.005.
20. Lattanzi S, Cagnetti C, Provinciali L, Silvestrini M. Neutrophil-to-Lymphocyte Ratio Predicts the Outcome of Acute Intracerebral Hemorrhage. Stroke. 2016 Jun;47(6):1654-7. doi: 10.1161/STROKEAHA.116.013627.
21. Lattanzi S, Cagnetti C, Rinaldi C, Angelocola S. Provinciali L, Silvestrini M. Neutrophil-to-lymphocyte ratio improves outcome prediction of acute intracerebral hemorrhage. J Neurol Sci. 2018 Apr 15;387:98-102. doi: 10.1016/j.jns.2018.01.038.
22. Lattanzi S, Cagnetti C, Provinciali L, Silvestrini M. Neutrophil-to-lymphocyte ratio and neurological deterioration following acute cerebral hemorrhage. Oncotarget. 2017 Feb 16;8(34):57489-94. doi: 10.18632/oncotarget.15423.
23. Yu S, Arima H, Bertmar C, Clarke S, Herkes G, Krause M. Neutrophil to lymphocyte ratio and early clinical outcomes in patients with acute ischemic stroke. J Neurol Sci. 2018 Apr 15;387:115-8. doi: 10.1016/j.jns.2018.02.002.
24. Dotsenko O, Chaturverdi N, Thom S, Wright AR, Mayet J, Shore A, et al. Platelet and leukocyte activation, atherosclerosis and inflammation in European and South Asian men. J Thromb Haemost. 2007 Oct;5(10):2036-42. doi: 10.1111/j.1538-7836.2007.02711.x.
25. Duman H, Çinier G, Bakırcı EM, Duman H, Şimşek Z, Hamur H, et al. Relationship Between C-Reactive Protein to Albumin Ratio and Thrombus Burden in Patients With Acute Coronary Syndrome. Clin Appl Thromb Hemost. 2019 Jan-Dec;25:1076029618824418. doi: 10.1177/1076029618824418.
26. Topuz MF, Ture N, Akdag G, Arik O, Gulhan PY. The importance of systemic immune-inflammation index in obstructive sleep apnea syndrome. Eur Arch Otorhinolaryngol. 2022 Oct;279(10):5033-8. doi: 10.1007/s00405-021-07227-0.
27. Dobiášová M, Frohlich J. The plasma parameter log (TG/HDL-C) as an atherogenic index: correlation with lipoprotein particle size and esterification rate in apoB-lipoprotein-depleted plasma (FER(HDL)). Clin Biochem. 2001 Oct;34(7):583-8. doi: 10.1016/s0009-9120(01)00263-6.
28. Karataş M, Çanga Y, Özcan K, İpek G, Güngör B, Onuk T, et al. Monocyte to high-density lipoprotein ratio as a new prognostic marker in patients with STEMI undergoing primary percutaneous coronary intervention. Am J Emerg Med. 2016 Feb;34(2):240-4. doi: 10.1016/j.ajem.2015.10.049.
29. Deng X, Gu W, Li Y, Liu M, Li Y, Gao X. Age-group-specific associations between the severity of obstructive sleep apnea and relevant risk factors in male and female patients. PLoS One. 2014 Sep 11;9(9):e107380. doi: 10.1371/journal.pone.0107380.
30. Sweed RA, Hassan S, ElWahab NHA, Aref SR, Mahmoud MI. Comorbidities associated with obstructive sleep apnea: a retrospective Egyptian study on 244 patients. Sleep Breath. 2019 Dec;23(4):1079-85. doi: 10.1007/s11325-019-01783-w.
31. Ünal M, Öztürk L, Kanik A. The role of oxygen saturation measurement and body mass index in distinguishing between non-apnoeic snorers and patients with obstructive sleep apnoea syndrome. Clin Otolaryngol Allied Sci. 2002 Oct;27(5):344-6. doi: 10.1046/j.1365-2273.2002.00592.x.
32. Gündüz C, Basoglu OK, Hedner J, Zou D, Bonsignore MR, Hein H, et al. Obstructive sleep apnoea independently predicts lipid levels: Data from the European Sleep Apnea Database. Respirology. 2018 Dec;23(12):1180-9. doi: 10.1111/resp.13372.
33. Wu W Te, Tsai SS, Shih TS, Lin MH, Chou TC, Ting H, et al. The Association between Obstructive Sleep Apnea and Metabolic Markers and Lipid Profiles. PLoS One. 2015 Jun 26;10(6):e0130279. doi: 10.1371/journal.pone.0130279.
34. Gileles-Hillel A, Kheirandish-Gozal L, Gozal D. Biological plausibility linking sleep apnoea and metabolic dysfunction. Nat Rev Endocrinol. 2016 May;12(5):290-8. doi: 10.1038/nrendo.2016.22.
35. Jun JC, Drager LF, Najjar SS, Gottlieb SS, Brown CD, Smith PL, et al. Effects of sleep apnea on nocturnal free fatty acids in subjects with heart failure. Sleep. 2011 Sep 1;34(9):1207-13. doi: 10.5665/SLEEP.1240.
36. Uygur F, Tanriverdi H, Aktop Z, Erboy F, Altinsoy B, Damar M, et al. The neutrophil-to-lymphocyte ratio in patients with obstructive sleep apnoea syndrome and its relationship with cardiovascular disease. Heart Lung. 2016 Mar-Apr;45(2):121-5. doi: 10.1016/j.hrtlng.2016.01.002.
37. Yayla Ç, Akboğa MK, Gayretli Yayla K, Ertem AG, Efe TH, Şen F, et al. A novel marker of inflammation in patients with slow coronary flow: lymphocyte-to-monocyte ratio. Biomark Med. 2016 May;10(5):485-93. doi: 10.2217/bmm-2016-0022.
38. Zhang Y, Li S, Guo YL, Wu NQ, Zhu CG, Gao Y, et al. Is monocyte to HDL ratio superior to monocyte count in predicting the cardiovascular outcomes: evidence from a large cohort of Chinese patients undergoing coronary angiography. Ann Med. 2016 Aug;48(5):305-12. doi: 10.3109/07853890.2016.1168935.
39. Gozal D, Kheirandish-Gozal L. Cardiovascular morbidity in obstructive sleep apnea: oxidative stress, inflammation, and much more. Am J Respir Crit Care Med. 2008 Feb 15;177(4):369-75. doi: 10.1164/rccm.200608-1190PP.
40. Campos-Rodriguez F, Martinez-Garcia MA, Reyes-Nuñez N, Caballero-Martinez I, Catalan-Serra P, Almeida-Gonzalez CV. Role of sleep apnea and continuous positive airway pressure therapy in the incidence of stroke or coronary heart disease in women. Am J Respir Crit Care Med. 2014 Jun 15;189(12):1544-50. doi: 10.1164/rccm.201311-2012OC.
41. Wang X, Ouyang Y, Wang Z, Zhao G, Liu L, Bi Y. Obstructive sleep apnea and risk of cardiovascular disease and all-cause mortality: A meta-analysis of prospective cohort studies. Int J Cardiol. 2013 Nov 5;169(3):207-14. doi: 10.1016/j.ijcard.2013.08.088.
42. Loke YK, Brown JWL, Kwok CS, Niruban A, Myint PK. Association of obstructive sleep apnea with risk of serious cardiovascular events: a systematic review and meta-analysis. Circ Cardiovasc Qual Outcomes. 2012 Sep 1;5(5):720-8. doi: 10.1161/CIRCOUTCOMES.111.964783.

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Preoperative advanced cardiology evaluation in adult non-cardiac surgery: A retrospective cohort study

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Ethics Committee Approval
The study was approved by the University of Health Sciences Turkey, Gülhane Non-interventional Clinical Researches Ethics Committee (Project No: 2023/24, Date: 17.01.2023).
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: Advanced cardiology evaluation (ACE) is the most frequently requested consultation during preoperative medical evaluations (PMEs) performed in anesthesia outpatient clinics. However, the efficacy and results of this ACE request are unclear. We aimed to show the frequency of ACE requested during PME of patients undergoing non-cardiac surgery (NCS) and its effect on diagnosis, treatment process, and surgical time planning.

Methods: This is a single-center, retrospective cohort study of 300 patients aged 18 years and older who need ACE. Medical charts were reviewed for patient characteristics and diagnosis, planned surgery type, surgical intervention risk, revised cardiac risk index (RCRI), other consultation records, cardiology consultation indication, risk group determined by the cardiologist, metabolic equivalent (METs), and anticoagulant use were recorded.

Results: We analyzed the data of 300 patients for whom ACE was requested from 9825 patients who underwent PME. The mean age was 66 (12) years, and the most common age range was 60–79 years (62.7%). The proportion of patients with METs ≤4 was 11% (n=33). The most common additional consultation was chest disease (10%), and the most common co-morbidity was hypertension (61.6%). The most common reason for consultation was a history of ischemic heart disease (50%). According to the revised cardiac risk index, most patients were in class 2, while according to the cardiology consultation outcome grade, most patients were in the intermediate risk group. It was observed that the cardiology consultation process was mostly completed on the same day (255 patients, 85%), and the use of anticoagulant drugs was mostly left to the individual evaluation of the surgeon (143 patients, 47.7%).

Conclusion: PME should be given due care to prevent perioperative cardiac complications in patients undergoing NCS. More careful patient assessments are needed during ACEs. This would allow for more accurate risk stratifications and, if necessary, the ordering of additional testing.

Keywords: cardiac patient, perioperative risk, preoperative evaluation, cardiology consultation

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Introduction

Preoperative medical assessment (PMA) aims to identify patient- and procedure-specific risks and optimize medical care before the procedure. Medical history, a physical examination, and personalized laboratory tests can be used to reveal preoperative risks [1]. However, some patients may require further examination and evaluation depending on variables such as co-morbidities, symptoms, and the type of surgical procedure. These patients can be consulted by the relevant clinical branches as needed. The cardiac assessment of patients scheduled for non-cardiac surgery (NCS) who have cardiac complaints and/or symptoms constitutes the largest part of these consultations [2].

Cardiovascular complications account for approximately 50% of perioperative deaths in non-cardiac surgery patients [3]. Most of the patients who develop complications have a disease of the cardiovascular system. Cardiologists examine patients at risk, and preoperative cardiac optimization is provided. The risk of cardiac complications in NCS is determined according to classifications, such as the revised cardiac risk index (RCRI) [4]. Moreover, additional drug treatments (e.g., beta-blockers) can be started for those with indications. Following the cardiology consultation recommendations may reduce perioperative morbidity and mortality [5].

Our study aims to show the frequency of cardiology consultations in PMA, further examination requirements, and their effect on the diagnosis, treatment process, and surgical time planning in patients with planned NCS.

Materials and methods

This is a single-center, retrospective cohort study of patients referred for cardiology consultation during preoperative medical evaluation at Ankara Health Sciences University Gülhane Training and Research Hospital Anesthesiology outpatient clinic between July 2022 and December 2022. Our study was approved by the University of Health Sciences Turkey, Gülhane Non-interventional Clinical Researches Ethics Committee (Project No: 2023/24, Date: 17.01.2023) and conducted following the ethical principles stated in the Declaration of Helsinki. As the study is retrospective, no voluntary informed consent was obtained from the patients. In our hospital, all patients ≥18 years scheduled for elective non-cardiac surgery are assessed by an anesthesiologist for the anesthesia approval process. The Anesthesia Practice Guidelines for Preoperative Assessment of the Turkish Anesthesiology and Reanimation Society (TARS) are used for the preoperative medical assessment [6]. The anesthesiologist included only the patients whose cardiology consultation requests after the preoperative anesthesia examination. A total of 9825 patients were screened preoperatively during the 6 months. It was determined that 300 patients were referred to the cardiology clinic for further cardiac evaluation and were included in this study.

In the anesthesia outpatient clinic, the basic characteristics of each patient are recorded after anamnesis, physical examination, and laboratory examination control. Patients who need additional consultation after the examination are referred to the relevant clinics. The Revised Cardiac Risk Index is routinely calculated for each patient requiring further cardiac evaluation in the anesthesia outpatient clinic [7]. In our study, age (year), gender (female/male), height (cm), weight (kg), body mass index (BMI) (kg/m^2), American Society of Anesthesiologists (ASA) physical score (I/II/III/IV), diagnosis and planned surgery type, surgical intervention risk (low/moderate/high), RCRI (class I/II/III/IV), and other non-cardiology consultation records of the patients were reviewed. Cardiology consultation indication, risk group determined by the cardiologist (low/low-moderate/moderate/medium-high/high), functional metabolic equivalent (MET) value (below 4/above 4), and anticoagulant use were recorded. The number of days the cardiology consultation request delayed the anesthesia approval process, and the recommendations after the assessment were recorded.

Statistical analysis

Data were analyzed with the SPSS (Statistical Package for Social Science) 25.0 software. All data were categorized. Categorical data were presented using numbers (n) and percentages (%). No group comparisons were made in the single cohort sample. Additional recommendations were presented using a bar chart.

Results

The data of 9825 patients who applied to the anesthesia outpatient clinic for PMA in 6 months between July 2022 and December 2022 were analyzed retrospectively. The data of 300 patients, who were requested an ACA, were analyzed. More than half (55%) of the patients were male, and 45% were female. The mean patient age was 66 (12) years, the most common age range was 60–79 years old (62.7%), and the least common age range was less than 40 years old (3%). While the ASA2 patients (n=139, 46.3%) constituted the majority of the patients in the ASA physical status classification, the rate of patients below 4 METs was 11% (n=33) (Table 1).

Table 1: Distribution of gender, age, ASA Physical status and functional capacity classifications of patients for whom cardiology consultation was requested (n=300)

	Number of patients n (%)
Gender	
Female	135 (45)
Male	165 (55)
Age distribution	
<40	9 (3)
40-59	65 (21.7)
60-79	188 (62.7)
>79	38 (12.7)
ASA physical status	
ASA I	17 (5.6)
ASA II	139 (46.3)
ASA III	127 (42.3)
ASA IV	17 (5.6)
Functional capacity	
≤4 METs	33 (11)
>4 METs	267 (89)

ASA: American Society of Anesthesiologists, METs: Metabolic Equivalents

In addition to cardiology consultations, the most frequently requested consultations were in chest diseases, endocrinology, and nephrology (10%, 7.3%, and 3.7%), respectively (Table 2). Besides the ischemic heart disease history of the patients, the most common co-morbidities were hypertension, diabetes mellitus, and COPD (61.6%, 46%, and 36%), respectively (Table 3).

Table 2: Distribution of consultations requested from other clinics (n=300)

Clinic name	Number of patients n (%)
None	223 (74.3)
Pulmonology	30 (10)
Endocrinology	22 (7.3)
Nephrology	11 (3.7)
Hematology-Oncology	4 (1.3)
Neurology	4 (1.3)
Infectious Diseases	3 (1)
Rheumatology	2 (0.6)
Cardiovascular Surgery	2 (0.6)
Head and Neck Surgery	2 (0.6)
Psychiatry	1 (0.3)
Neurosurgery	1 (0.3)

Table 3: Distribution of additional diseases of patients (n=300)

Name of disease	Number of patients n (%)
Hypertension	185 (61.6)
Ischemic Heart Disease	138 (46)
Diabetes Mellitus	108 (36)
CABG	39 (13)
Atrial Fibrillation	35 (11.6)
None	31 (10.3)
COPD	24 (8)
Heart failure	24 (8)
Hypothyroid	15 (5)
Bronchial Asthma	13 (4.3)
Chronic Kidney Disease	12 (4)
SVE	10 (3.3)
Cardiac Valve Replacement	10 (3.3)
Non-AF Arrhythmia	7 (2.3)
ICD	6 (2)
Cardiac Valve Failure	5 (1.6)
Parkinson's Disease	3 (1)
Aortic Aneurysm	2 (0,6)

CABG: Coronary Artery Bypass Grafting, COPD: Chronic Obstructive Pulmonary Disease, SVE: Cerebrovascular Events, AF: Atrial Fibrillation, ICD: Implantable Cardioverter Defibrillator

According to the risk classification of the patients by the type of surgery, 147 (49%) low-risk, 130 (43.3) medium-risk, and 23 (7.66) high-risk surgeries were planned. When the distribution of surgical procedures was examined, gastroenterological endoscopic procedures were the most common, with 67 (22.3%) patients, followed by cataract surgeries (14.3%) and inguinal hernia operations (6%) in third place (Table 4). According to the consultation indications, the history of ischemic heart disease was the most common cause of request in 150 (50%) patients, followed by general evaluation in 52 (17.3%) patients, and non-AF ECG changes in 39 (13%) patients (Table 5).

According to the RCRI calculated in the anesthesia outpatient clinic, most patients were in class 2 with 107 patients, while the least number of patients were in class 4 with 34. According to the post-examination risk assessment by cardiology physicians, the highest number of patients were in the medium-risk group, with 129 patients, while the least number of patients were in the high-risk group, with 6 patients (Table 6).

Table 4: Surgical risk estimation by type of surgical intervention and distribution of surgical procedures (n=300)

	Number of patients n (%)
Surgical risk estimation by type of surgical intervention	
Low Risk: < 1%	147 (49)
Intermediate Risk: 1–5%	130 (43.3)
High Risk: > 5%	23 (7.66)
Surgical Procedure Name	
Endoscopy-Colonoscopy-ERCP	67 (22.3)
Cataract Surgery	43 (14.3)
Herniography	18 (6)
TUR-P Cystoscopy	18 (6)
Amputation Surgery	16 (5.3)
Others	14 (4.6)
Kidney Stone Surgery	11 (3.6)
Excision-Biopsy	10 (3.3)
TAH-BSO- Myomectomy - Ovarian Cystectomy	10 (3.3)
Cholecystectomy	8 (2.6)
Thoracotomy -VATS	7 (2.3)
LDH-CDH	7 (2.3)
Anal Fissure-Fistula-Hemorrhoidectomy	6 (2)
Carpal Tunnel Syndrome.	6 (2)
Posterior Stabilization	6 (2)
Thyroidectomy	6 (2)
TOT-Adnexal Masses- Hysteroscopy	6 (2)
Unspecified	5 (1.6)
EBUS	5 (1.6)
TKA	5 (1.6)
Nephrectomy	5 (1.6)
Rhinoplasty-Septoplasty	5 (1.6)
Liver RF	4 (1.3)
Colon-Rectum CA	4 (1.3)
EVLA	3 (1)
Eye Surgery	2 (0.6)
Over CA	2 (0.6)

ERCP: Endoscopic Retrograde Cholangio Pancreatography, TUR-P: Transurethral resection of the prostate, TAH-BSO: Total abdominal hysterectomy and bilateral salpingo-oophorectomy, VATS: Video-Assisted Thoracic Surgery, LDH: Lumbar Disk Hernia, CDH: Cervical Disk Hernia, EBUS: Endobronchial Ultrasonography, TKA: Total Knee Arthroplasty, RF: Radio-Frequency, CA: Cancer, EVLA: Endovenous Laser Ablation

Table 5. Distribution of cardiology consultation reasons (n=300)

Cardiology consultation reasons	Number of patients n (%)
History of ischemic heart disease	150 (50)
General evaluation	52 (17.3)
ECG changes (non-AF arrhythmias)	39 (13)
Atrial fibrillation	26 (8.6)
Valve abnormality	17 (5.6)
Dyspnea	9 (3)
Angina pectoris	4 (1.3)
Additional disease (HT)	3 (1)

ECG: Electrocardiogram, AF: Atrial Fibrillation, HT: Hypertension

Table 6: Distribution of cardiology consultation results and revised cardiac risk index classification

		Revised Cardiac Risk Index Classification n (%)			
		Class 1	**Class 2**	**Class 3**	**Class 4**
Cardiology consultation result risk assessment (n)	**Low Risk (44)**	29 (39.7)	13 (12.1)	1 (1.2)	1 (2.9)
	Low-Intermediate Risk (88)	29 (40.2)	34 (31.8)	22 (25.5)	3 (8.8)
	Intermediate Risk (129)	14 (19.2)	53 (49.5)	52 (60.4)	10 (29.4)
	Intermediate-High Risk (33)	1 (1.4)	7 (6.5)	8 (9.3)	17 (50)
	High Risk (6)	0 (0)	0 (0)	3 (3.5)	3 (8.8)
	Total (300)	n=73 (100)	n=107 (100)	n=86 (100)	n=34 (100)

In cardiology consultation requests, it was determined that the consultations of 255 patients (85%) were completed on the same day, while the operations of nine patients (3%) were delayed due to cardiological reasons (Table 7). The most common reason for the delay in cardiology consultations that could not be completed on the same day was echocardiography in 24 patients, MPS in six patients, CAG in four patients, CT-angiography in three patients, and an exertion test in two patients.

It was observed that in patients with a history of anticoagulant and antiplatelet drug use, the drug management process was left to the discretion of the surgeon in 143 patients; it was decided to continue in 28 patients, it was recommended to interrupt it directly and start after the procedure in 23 patients,

and it was decided to apply bridge therapy in 22 patients (Table 7). It was found that five intraoperative and nine postoperative cardiology consultation requests were made from the 300 patients included in the evaluation (Table 8).

Table 7: Distribution of cardiology consultation results (n=300)

	Number of patients n (%)
Consultation time	
Ended the same day	255 (85)
Ended after 1 day	5 (1.7)
Ended in more than 1 day	31 (10.3)
Surgery delayed	9 (3)
Anticoagulant, antiplatelet drug usage recommendations	
Surgeon's decision (bleeding thrombosis balance)	143 (47.7)
It is recommended to stop	23 (7.7)
Definitely recommended to continue	28 (9.3)
Bridge Therapy recommended	22 (7.3)
Not using	84 (28)

Table 8: Distribution of intraoperative cardiac events and postoperative cardiological procedures (n=300)

	Number of patients n (%)
Intraoperative cardiac events	
None	295 (98.3)
Uncontrolled hypertension	4 (1.3)
AF with rapid ventricular response	1 (0.3)
Postoperative cardiological procedures	
None	290 (96.7)
Anticoagulant was started	4 (1.3)
Antihypertensive was started	5 (1.7)
CABG was applied	1 (0.3)

AF: Atrial Fibrillation, CABG: Coronary Artery Bypass Grafting

Discussion

Our study evaluated patients who needed advanced cardiac assessment during PMA for NCS. We found that a cardiology consultation was requested for 3.05% of the patients who applied to the anesthesia outpatient clinic. We found that further examinations and treatment were needed in 16.6% of these patients and that decisions on postponing procedures were made in 3% for cardiac reasons. While the ACA process in our hospital was mostly completed on the same day, we found that around 15% of assessments lasted more than 1 day. We believe that the requested ACA process in PMA has a minimal effect on the timing of pre-planned surgical procedures.

The mean age of the population is increasing due to improved living conditions and medical treatments. Age alone is not a risk factor for cardiological complications that may develop in the perioperative period.. However, it can be considered a risk factor along with concomitant diseases, such as hypertension, diabetes mellitus, and coronary artery disease, the incidence of which increases with advanced age [8]. The rate of undergoing surgery increases with age [9]. This increase in additional diseases and surgeries also increases the risk of morbidity and mortality, which requires more careful preoperative preparation and advanced assessment. Gündüz et al. [1] showed that ACA rates increase with age in NCS. Similarly, we found that co-morbidities, cardiac risk factors, and preoperative ACA rates increased with age.

Gender is another factor in cardiac assessment; males are at increased risk of cardiac diseases. Carrol et al. [10] showed that 19% of men and 12% of women had cardiovascular disease. Our study found that the rate of ACA was higher in males (accounting for 55%) than in females.

A preoperative medical assessment is performed to ensure that the surgical process is completed under the best conditions by choosing the most accurate anesthesia method with the fewest complications. At this stage, patients are thoroughly assessed with anamnesis, physical examination, laboratory testing, and imaging. If necessary, consultation from other clinics can be requested. ACA is the most frequently requested consultation [8]. In our study, ACA was the most frequently requested consultation, with a rate of 3.05%.

Unnecessary consultations cause loss of labor and time. That the dates for surgical procedures are planned far in advance adds to the importance of these losses. Katz et al. [11] found that few consultation outcome notes affect perioperative patient management. Our study found that the procedure was delayed in only nine patients due to ACA. Additionally, we found that the process was prolonged for more than 1 day in 31 (10.3%) patients due to additional examination and treatment. To minimize these losses, we believe that consultations should be requested according to certain guidelines and risk assessment scales [12].

The most common cause of mortality during the perioperative period in non-cardiac surgeries is complications of cardiac origin [9]. Factors such as age, gender, co-morbidity, and the urgency of the procedure play a role in triggering cardiac complications. The oxygen requirement of the myocardium increases with the addition of factors such as blood loss, hypotension, and tachycardia in the perioperative period [13]. Adding this to the coagulation system further increases the cardiovascular system's burden. The type and duration of surgery directly affect all these changes [14]. Some classifications predict surgical risks according to the type of surgical intervention. In our outpatient clinic, we use the classification that includes three risk groups (low, medium, and high) to predict the surgical risk according to the type of surgical intervention [6]. According to this classification, we determined that among the 300 patients, 147 (49%) were planned for low-risk surgery, 130 (43.3%) were planned for medium-risk surgery, and 23 (7.66%) were planned for high-risk surgery. The most frequently planned surgical procedure was a gastroenterological endoscopic procedure with 67 patients. The type of surgical intervention must be considered when requesting an ACA in PMA. We believe a routine surgical risk estimation classification according to the type of surgical intervention should be used to establish a standard.

The preoperative medical assessment is the phase in which co-morbidities, history of medication use, and functional capacity are determined through anamnesis and physical examination and surgical and anesthesia histories are assessed. Functional capacity is an index used in clinical practice and is assessed quantitatively with MET. The MET value is calculated based on the approximate value obtained from the answers to the questions asked to the patient. A value of >7 MET is a good prognosis indicator, 4–7 MET is a moderate prognosis indicator, and ≤4 MET is a poor prognosis indicator [8]. The patient's inability to climb two flights of stairs or run a short distance is one of the indicators of insufficient functional capacity. The likelihood of a perioperative cardiac event increases significantly in patients with MET ≤4 [15]. In our study, the MET value was ≤4 in 33 patients. According to the cardiology consultation score, a significant number of these patients were in the high-risk

group. Accordingly, we believe a low MET value is important for showing the possibility of perioperative cardiac events.

Various risk scores are used in the preoperative risk assessment of patients with cardiac disease. One is the RCRI classification of the American College of Cardiology/American Heart Association [7]. This classification assesses six factors: high-risk surgery, ischemic heart disease history, congestive heart failure, cerebrovascular event history, preoperative insulin use, and a preoperative creatinine value of >2 mg/dL [4]. Using these six factors, one of the four risk classes is determined. Class 1 indicates the lowest-risk class, and class 4 indicates the highest. Hulme et al. [7] examined the 90-day mortality rates of patients undergoing colon cancer surgery and found that the mortality rates increased with the increase in class, according to RCRI. Our study examined the RCRI values of 300 patients who underwent an ACA. According to the RCRI, 73 (24.3%) of patients were in class 1, 107 (35.6%) of patients were in class 2, 86 (28.6%) of patients were in class 3, and 34 (11.3%) of patients were in the class 4 risk group. We believe that the RCRI class should be determined in the PMA and that ACA should be requested in high-risk patients.

Cardiologists determine a patient's risk class due to the examination and any additional examinations they perform on patients scheduled for surgery. Using Lee's risk scoring, they often use classification with low, low-medium, medium, medium-high, and high groups [16]. The type of surgery, gender, age, co-morbidities, and risk score values are very important in recognizing perioperative cardiac events. Lee et al. [4] reported a 2.1% risk of MI and death in patients undergoing major NCS. According to the ACA results for the 300 patients we examined in our study, 44 patients were in the low-moderate risk category, 88 patients were in the low-moderate category, 129 patients were in the medium-high category, 33 patients were in the medium-high category, and six patients were in the high-risk category. It is seen that the majority of patients were in the moderate-risk group, and most of these patients were in classes 2 or 3 based on their RCRI.

One of the requests in the ACA for patients with a history of cardiological disease is a history of anticoagulant and antithrombotic drug use. Since hemorrhagic complications will increase in the perioperative period, these treatments are usually interrupted. Additionally, considering the severity of the cardiological disorder, the type and duration of the surgical procedure, and the type/amount of medication used, the medication can be continued according to the benefit/harm ratio [14]. Some patients switch to low molecular weight or non-fractionated heparin and return to drug treatment after surgery [17]. Our study recommended discontinuing anticoagulant therapy in 22 (7.3%) patients and switching to low molecular weight heparin. Moreover, the decision to discontinue the drug was left to the surgeon performing the procedure based on a benefit/harm ratio according to the procedure performed in 143 (47.7%) patients.

Limitations

There are some limitations of this study. The retrospective design of the study can be considered the first limitation. The study could be repeated prospectively. Another limitation of our study is that it is single-centered. The small sample size can also be considered a limitation. Therefore, the results may need further validated by a larger sample size test. Since our institution is a university hospital, the high number of doctors working in the anesthesia polyclinic may be one of the limitations. Also, due to the nature of our study, no firm conclusions can be drawn as to whether preoperative consultation should be omitted.

Conclusion

As a result, the contribution of the correct indications during PMA and requested consultations to perioperative processes is significant. However, unnecessary consultations cause serious loss of labor and time. Before requesting a consultation, attention should be given to preoperative risk stratification and perioperative medical management strategies. This requires good communication and teamwork between the anesthesiologist, surgeon, and consultant physician during the PMA process. More comprehensive multicenter studies are needed to reduce unnecessary consultations and costs that do not contribute to medical management.

References

1. Gündüz E, Coşkun FN, Arıcı G, Akbaş M. Effectiveness of preoperative cardiac assessment methods in patients with non-heart surgery. Akdeniz Med J. 2019;119(1):92–9.
2. Groot MW, Spronk A, Hoeks SE, Stolker RJ, Van Lier F. The preoperative cardiology consultation: Indications and risk modification. Netherlands Hear J. 2017;25(11):629–33.
3. Yıldız ŞB, Gürsoy MO. Kalp dışı cerrahi girişim uygulanacak kalp hastalarında preoperatif değerlendirme. Koşuyolu Hear J. 2015;18(1):39–44.
4. Lee TH, Marcantonio ER, Mangione CM, Thomas EJ, Carisi A, Cook EF, et al. Prediction of cardiac risk of major non-cardiac surgery. Circulation. 1999;100(10):1043-9.
5. Zambouri A. Preoperative evaluation and preparation for anesthesia and surgery. Hippokratia. 2007;11(1):13–21.
6. Preoperative Evaluation (2015). Turkish Society of Anesthesiology and Reanimation Anesthesia Practice Guidelines. https://www.tard.org.tr/assets/kilavuz/preoperatifdegerlendirme.
7. Hulme RA, Forssten MP, Pourlotfi A, Cao Y, Bass GA, Matthiessen P, et al. The Association Between Revised Cardiac Risk Index and Postoperative Mortality Following Elective Colon Cancer Surgery: A Retrospective Nationwide Cohort Study. Scand J Surg. 2022;111(1):14-21.
8. Doğu H, Doğu D. Nonkardiyak preicerrahi uygulanacak kardiyak hastalardaki peri operatif risk faktörlerinin belirlenmesi. Kartal Eğit ve Araşt Hast Tıp Derg. 2001;12(3):120-5.
9. Naughton C, Feneck RO. The impact of age on 6-month survival in patients with cardiovascular risk factors undergoing elective non-cardiac surgery. Int J Clin Pract. 2007;61(5):768-76.
10. Carroll K, Majeed A, Firth C, Gray J. Prevalence and management of coronary heart disease in primary care : population-based cross-sectional study using a disease register. J Public Health Med. 2003;25(1):29-35.
11. Katz RI, Cimino L, Vitkun SA. Preoperative medical consultations: impact on perioperative management and surgical outcome. Can J Anaesth. 2005;52(7):697-702.
12. Poldermans D, Bax JJ, Boersma E, De Hert S, Eeckhout E, Fowkes G, et al. Guidelines for preoperative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery: the Task Force for Preoperative Cardiac Risk Assessment and Perioperative Cardiac Management in Non-cardiac Surgery of the European Society of Cardiology (ESC) and endorsed by the European Society of Anaesthesiology (ESA). Eur J Anaesthesiol. 2010;27(2):92-137.
13. Maggio C, Bonzano A, Conte E, Libertucci D, Panarelli M, Bobbio M, et al. Preoperative evaluation in non-cardiac surgery: Cardiac risk assessment. Int J Qual Heal Care. 1992;4(3):217–24.
14. Gündüz E. Kalp dışı cerrahide kardiyak hastaların preoperatif değerlendirilmesi [dissertation]. Akdeniz University Faculty of Medicine, Antalya; 2011.
15. Mendes DA, Silva da I, Ramires V, Reichert F, Martins R, Ferreira R, et al. Metabolic equivalent of task (METs) thresholds as an indicator of physical activity intensity. PLoS One. 2018;13(7):1–10.
16. Fleisher LA, Fleischmann KE, Auerbach AD, Barnason SA, Beckman JA, Bozkurt B, et al. Perioperative beta blockade in non-cardiac surgery: a systematic review for the 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing non-cardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. Circulation. 2014;130(24):278-333.
17. Santangelo G, Faggiano A, Toriello F, Carugo S, Natalini G, Bursi F, et al. Risk of cardiovascular complications during non-cardiac surgery and preoperative cardiac evaluation. Trends Cardiovasc Med. 2022;32(5):271-84.

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Impact of COVID-19 fear on Hepatitis C management

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Ethics Committee Approval
This study was approved by the ethics committee of Ondokuz Mayıs University Faculty of Medicine (Decision no: 2022/377 Date: 26.10.2022).
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: Hepatitis C virus (HCV) infection, a major cause of cirrhosis worldwide, is the most common cause of cirrhosis and hepatocellular carcinoma in Turkey. Today, HCV infection can be treated effectively and safely using direct-acting antiviral drugs, and therefore, the World Health Organization has announced elimination targets by 2030. During the pandemic, many social and personal restrictions were applied for fear of increasing the prevalence of coronavirus disease 2019 (COVID-19) infection. Here we investigate the effects of these restrictions on managing HCV infection in internal medicine departments that deal with both infections.

Methods: Patients who applied to the internal medicine departments of our hospital and tested for anti-HCV between 11 March 2020 and 09 April 2022, which was the time interval when official restrictions were applied in Turkey during the COVID-19 pandemic, were included in the study. Patients who were not tested for anti-HCV were excluded from the study. The study was planned as a retrospective cohort study, and patients' files tested for anti-HCV were scanned. Anti-HCV positivity, HCV RNA PCR testing, and treatment status in HCV RNA-positive patients were evaluated.

Results: During the official pandemic period when social restrictions were applied, anti-HCV positivity was revealed in 400 (1.9%) of 21,501 patients for whom anti-HCV tests were performed in internal medicine departments. HCV RNA was not tested in 64 of 400 patients with positive anti-HCV test (16%), and 83 (24.7%) of 336 patients tested for HCV RNA were found to be positive. It was determined that 17 (20.5%) of the HCV RNA-positive patients did not receive antiviral treatment.

Conclusion: In studies conducted in Turkey in the pre-pandemic period, it was determined that HCV RNA was not tested in approximately half of the anti-HCV-positive patients, while this rate was found to be only 16% during the pandemic period. This can be explained by the fact that patients infected with the COVID-19 virus were mostly followed-up by internal medicine clinics, where the awareness of viral hepatitis was high. It was determined that 20.5% of the patients with positive HCV RNA PCR tests remained untreated. This finding suggested that the social and personal restrictions applied during the pandemic led to patient follow-up and treatment disruptions.

Keywords: hepatitis C, management, pandemic

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Introduction

Viral hepatitis due to the hepatitis C virus is accepted as a major public health problem today. The worldwide prevalence of hepatitis C (HCV) is estimated to be 1% [1,2]. The prevalence of the disease is especially high in the Eastern Mediterranean Region, Egypt, and China [1]. In the United States, HCV is recognized as the most common cause of chronic liver disease, hepatocellular carcinoma, and liver transplantation [3]. In Turkey, the prevalence of HCV is between 1% and 1.9% [4], and HCV is the most common cause of chronic liver disease and liver transplantation after the Hepatitis B virus [5,6].

A spontaneous eradication of acute HCV infection occurs in 15–45% of patients within 6 months, while 50–85% become chronic [2,7,8]. In 20–30% of chronic cases, chronic liver disease and cirrhosis develop over time [9–11]. HCV infection may also cause many immune-related extrahepatic clinical manifestations, such as cryoglobulinemic vasculitis, polyarthritis, monoarthritis, peripheral neuropathy, immune thrombocytopenic purpura, Sjogren's syndrome, and membranoproliferative glomerulonephritis [12].

Significant progress has been made in treating HCV using direct-acting antivirals (DAA), which provide virus elimination and cure with fewer side effects and better toleration [13,14]. DAA drugs significantly reduce HCV-related mortality and the need for liver transplantation, but it is estimated that only 20% of individuals with HCV infection know their diagnosis, and only 15% of those with known HCV infection have been treated [15].

The World Health Organization (WHO) aims to reduce new chronic HCV infections by 90% and mortality by 65% by 2030 through newly developed effective treatments [16]. One of the most important obstacles to reaching this goal is the low awareness of both patients and healthcare providers about chronic hepatitis C in Turkey and worldwide. During the pandemic, various restrictions – such as the obligation to wear a mask, curfew, intercity travel ban, and online education – were implemented by the national health authorities due to the concern about the increase in the prevalence of the coronavirus disease 2019 (COVID-19) infection. In addition, patients and healthcare professionals applied some personal restrictions in addition to these due to the fear of contamination. Restrictions and changes in the delivery of health services during this period shifted clinicians' attention to COVID-19 and related conditions. In the pre-pandemic period, internal medicine departments were clinics where the diagnosis and treatment of patients with HCV infection were made frequently, and they also played an important role in the diagnosis and treatment of COVID-19 patients during the pandemic period when restrictions were applied.

Here we examine the effects of the restrictions during the pandemic on the diagnosis, follow-up, and treatment of HCV in patients who applied to the internal medicine departments of our hospital.

Materials and methods

During the COVID-19 pandemic in Turkey, official restrictions were implemented between 11 March 2020 and 09 April 2022. During this period, the files of the patients who applied to the internal medicine departments of our hospital were retrospectively reviewed. Patients tested for anti-HCV were included in the study, and those without anti-HCV testing were excluded. Then, the files of the patients included in the study were scanned retrospectively. The clinics visited by anti-HCV-positive patients and HCV RNA PCR testing status were recorded. The patients with HCV RNA positivity who received antiviral treatment and who remained untreated were investigated in the e-pulse system of the Ministry of Health (a database integrated into the social health system). Anti-HCV-positive patients who died without receiving treatment were retrieved from the death notification system (a database integrated into the social health system). Patients who were alive and needed treatment were reached using the phone numbers registered in the hospital database. After obtaining verbal consent from the patients, they were asked whether they had knowledge about the diagnosis of HCV infection. After informing the untreated patients about the diagnosis and treatment, it was explained that they could apply to the appropriate centers if they were interested.

Approval of the ethics committee

The study protocol was permitted by the ethics committee of Ondokuz Mayıs University Faculty of Medicine (decision no:2022/377, date:26.10.2022), and the procedures were in accordance with the Helsinki Declaration.

Statistical analysis

Statistical analysis was performed using the Windows SPSS program (version 22.0, SPSS Inc., Chicago, IL). In our study, the Kolmogorov-Smirnov test was applied for age, which was the only numerical data, and it was expressed as mean (SD) since it showed a normal distribution. Categorical data were expressed as n (%).

Results

We reviewed 21,501 anti-HCV tests performed in the department of internal medicine, Ondokuz Mayıs University Faculty of Medicine, between 2020 and 2022 during the COVID-19 pandemic. Anti-HCV positivity was revealed in 400 of these patients. Of the patients, 220 (55%) were female, and 180 (45%) were male. The mean age was 64.3 (14.0) years. HCV RNA was not tested in 64 of 400 cases with positive anti-HCV test (16%). Of 336 patients tested for HCV RNA, 83 (24.7%) were positive, and 253 (63%) were negative. Of the patients with HCV RNA positivity, 27 (32.5%) died without receiving treatment, 38 (45.8%) were able to receive antiviral treatment, 17 (20.5%) could not receive any treatment, and 1 (1.2%) became negative spontaneously without treatment. This patient was evaluated as having acute hepatitis C (Figure 1).

When the distribution of anti-HCV-positive patients was considered by clinical departments of internal medicine, as can be expected, most cases (227 patients) were detected in the Gastroenterology clinic. The lowest percentage of patients who did not have HCV RNA testing (10%) were also in Gastroenterology. The distribution of anti-HCV-positive patients by departments of internal medicine is shown in Table 1.

Figure 1: Distribution of anti-HCV positive patients, HCV RNA results, and antiviral treatment status.

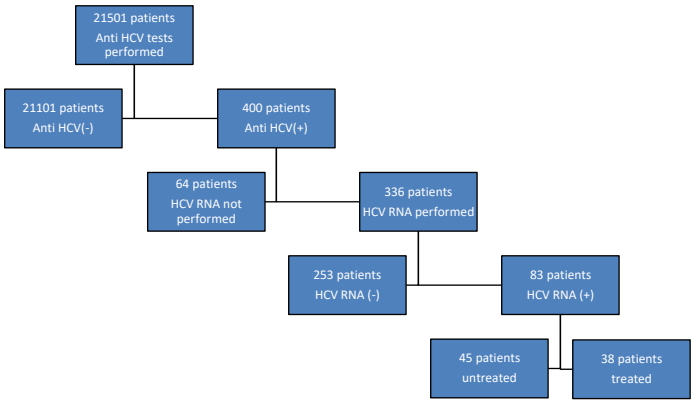

Table 1: Distribution of anti-HCV positive patients by departments of internal medicine

	HCV RNA (-) n=253	HCV RNA (+) n=83	HCV RNA (?) n=64	Total n=400
Gastroenterology	145 (63.9%)	58 (25.6%)	24 (10.6%)	227 (100%)
Nephrology	31 (60.8%)	8 (15.7%)	12 (23.5%)	51 (100%)
Hematology	30 (56.6%)	10 (18.9%)	13 (24.5%)	53 (100%)
Oncology	33 (73.3%)	5 (11.1%)	7 (15.6%)	45 (100%)
Rheumatology	10 (55.6%)	2 (11.1%)	6 (33.3%)	18 (100%)
Endocrinology	4 (66.7%)	0 (0%)	2 (33.3%)	6 (100%)

Discussion

HCV is a viral infection that causes chronic infection in 70 million people worldwide and is one of the most common causes of chronic liver disease, cirrhosis, and hepatocellular carcinoma in Turkey [4]. Recently used combinations of direct-acting antiviral agents lead to the eradication of HCV in 99% of cases [17]. Considering the role of HCV in chronic liver disease and clinical manifestations associated with extrahepatic immunity, no patient should be denied the chance to access treatment for this highly curable disease in today's conditions. A study investigating HCV awareness in the community found that only 49% of 393 patients infected with HCV knew the diagnosis, and only 80% consulted a doctor for anti-HCV positivity [18].

In the studies conducted in two different tertiary centers in Turkey before the COVID-19 pandemic, patients with positive anti-HCV test results were retrospectively evaluated, and the reported rates of HCV RNA PCR testing were 52.5% and 53.1% [19,20]. In our study, this rate was determined as 84% in internal medicine departments during COVID-19. Different inclusion criteria can explain this in other studies. The study was conducted in internal medicine departments with relatively higher awareness of HCV than other clinics and increased awareness due to the viral pandemic. Even in the gastroenterology department, which primarily deals with HCV infection, the presence of patients with anti-HCV positivity but no HCV RNA testing indicated that the awareness of HCV infection decreased during the pandemic period. It is known that people socially avoided entering communities during the COVID-19 pandemic, and restrictions increased this behavior. In a study conducted in China, it was demonstrated that most of the people in the Hubei region preferred e-health services to avoid social environments and comply with restriction rules during the pandemic period, and 79% of those who participated in the study applied to these services to minimize the risk of contact with COVID-19 [21].

Although the pre-pandemic HCV infection data from Turkish tertiary centers was similar to our hospital, an important limitation is that these tertiary center reports did not include our hospital's data and only included those patients who applied to internal medicine clinics. However, we believe our study holds value in light of the finding that roughly 20% of patients with HCV RNA positivity were unable to begin treatment, even at our tertiary gastroenterology clinic, during the COVID-19 pandemic.

Conclusion

Based on our findings, Turkey fell behind national and global targets in terms of HCV diagnosis, follow-up, and treatment during the COVID-19 pandemic. This was likely because of patients' reluctance to come to the hospital during the pandemic, difficulties in reaching the doctor, travel restrictions, increased workload of doctors, changes in working patterns, and difficulty in accessing treatment. It may still be possible to achieve national and global targets for treating HCV infection with retrospective HCV case screenings for the pandemic and identifying and treating cases needing treatment.

References

1. Blach S, Zeuzem S, Manns M, Altraif I, Duberg AS, Muljono DH, at al. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. The Lancet Gastroenterology & Hepatology. 2017;2(3):161-76.
2. Manns MP, Buti M, Gane E, Pawlotsky JM, Razavi H, Terrault N, at al. Hepatitis C virus infection. Nat Rev Dis Primers. 2017;3(1):17006.1-19.
3. Kim D, Li AA, Perumpail BJ, Gadiparthi C, Kim W, Cholankeril G, et al. Changing Trends in Etiology-Based and Ethnicity-Based Annual Mortality Rates of Cirrhosis and Hepatocellular Carcinoma in the United States: Hepatology. Hepatology. 2019;69(3):1064-74.
4. Barut HŞ, Günal Ö. Dünyada ve Ülkemizde Hepatit C Epidemiyolojisi. Klimik Dergisi. 2009;22(2):38-43.
5. Tozun N, Ozdogan O, Cakaloglu Y, Idilman R, Karasu Z, Akarca U, et al. Seroprevalence of hepatitis B and C virus infections and risk factors in Turkey: a fieldwork TURHEP study. Clinical Microbiology and Infection. 2015;21(11):1020-6.
6. Idilman R, Aydogan M, Oruncu MB, Kartal A, Elhan AH, Ellik Z, et al. Natural History of Cirrhosis: Changing Trends in Etiology Over the Years. Dig Dis. 2021;39(4):358-65.
7. Alter MJ, Gao F. The Prevalence of Hepatitis C Virus Infection in the United States, 1988 through 1994. The New England Journal of Medicine. 1999;341(8):556-62.
8. Conry-Cantilena C, VanRaden M, Gibble J, Melpolder J, Shakil AO, Viladomiu L, et al. Routes of Infection, Viremia, and Liver Disease in Blood Donors Found to Have Hepatitis C Virus Infection. N Engl J Med. 1996;334(26):1691-6.
9. Yano M, Kumada H, Kage M, Ikeda K, Shimamatsu K, Inoue O, et al. The long-term pathological evolution of chronic hepatitis C. Hepatology. 1996;23(6):1334-40.
10. Seeff LB, Miller RN, Rabkin CS, Buskell-Bales Z, Straley-Eason KD, Smoak BL, et al. 45-Year Follow-up of Hepatitis C Virus Infection in Healthy Young Adults. Ann Intern Med. 2000;132(2):105-11.
11. Poynard T, Bedossa P, Opolon P. Natural history of liver fibrosis progression in patients with chronic hepatitis C. The Lancet. 1997;349(9055):825-32.
12. Tampaki M. Extrahepatic immune related manifestations in chronic hepatitis C virus infection. WJG. 2014;20(35):12372-80.
13. EASL Recommendations on Treatment of Hepatitis C 2016. Journal of Hepatology. 2017;66(1):153-94.
14. AASLD-IDSA HCV Guidance Panel, Chung RT, Ghany MG, Kim AY, Marks KM, Naggie S, et al. Hepatitis C Guidance 2018 Update: AASLD-IDSA Recommendations for Testing, Managing, and Treating Hepatitis C Virus Infection. Clinical Infectious Diseases. 2018;67(10):1477-92.
15. Roudot-Thoraval F. Epidemiology of hepatitis C virus infection. Clinics and Research in Hepatology and Gastroenterology. 2021;45(3):101596.1-6.
16. Waheed Y, Siddiq M, Jamil Z, Najmi MH. Hepatitis elimination by 2030: Progress and challenges. WJG. 2018;24(44):4959-61.
17. Pawlotsky JM. Treatment failure and resistance with direct-acting antiviral drugs against hepatitis C virus. Hepatology. 2011;53(5):1742-51.
18. Denniston MM, Klevens RM, McQuillan GM, Jiles RB. Awareness of infection, knowledge of hepatitis C, and medical follow-up among individuals testing positive for hepatitis C: National Health and Nutrition Examination Survey 2001-2008. Hepatology. 2012;55(6):1652-61.
19. Daniş N, Arslan A, Buyruk M, Günşar F, ZeytiNoğlu A, Altuğlu İ, et al. Cerrahi prosedürler öncesi anti-HCV taraması: Hastalar yeterince bilgi sahibi mi? Akademik Gastroenteroloji Dergisi. 2021;20(1):8-12.
20. Balaban HY, Dağ O, Alp A, Tseveldorj N, Vahabov C, Göktaş MA, et al. Retrospective Evaluation of Hepatitis C Awareness in Turkey Through Two Decades. Turk J Gastroenterol. 2021;32(1):88-96.
21. Wang W, Sun L, Liu T, Lai T. The use of E-health during the COVID-19 pandemic: a case study in China's Hubei province. Health Sociology Review. 2022;31(3):215-31.

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Evaluation of vestibular evoked myogenic potential values in elder patients with hip fractures: A prospective controlled study

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Ethics Committee Approval
The study was approved by the Kastamonu University clinical research ethical committee, Turkey, (Decision no. 2020-KAEK-143-123 dated 20.10.2021).
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: Hip fractures among the elderly are a major public health problem that cause high rates of morbidity and mortality. There are many studies regarding prevention and defining the underlying causes of hip fractures. The purpose of this study was to evaluate the cervical vestibular evoked myogenic potential (cVEMP) test responses of elderly patients without vestibular symptoms hospitalized due to fall-related hip fractures in order to evaluate the subclinical vestibular dysfunction rates in patients with hip fractures.

Methods: Twenty-two patients aged 67-79 hospitalized due to fall-related hip fractures and 24 control patients presenting to the orthopedic clinic due to knee pain were included in the study. The participants underwent detailed otological examination and cVEMP tests. The two groups' cVEMP records were then compared.

Results: The demographic characteristics of the participants in the patient and control groups including age, gender, and race were similar. There was no statistically significant difference between the groups' absent VEMP response rates. No significant difference in terms of P1 and N1 latencies was determined between the right and left ears in either group. The hip fracture group (study group) had significantly increased P1 and N1 latencies in cVEMP which is associated with central vestibular dysfunction. (P=0.008 and P=0.007, respectively).

Conclusion: The rate of subclinical peripheral vestibular dysfunction, which can be identified by cVEMP evaluation, is increased in elderly patients with hip fractures caused by low energy trauma. Precautions like vestibular rehabilitation can be a preventive measure for hip fractures in the elderly.

Keywords: cVEMP, hip fracture, balance disorder, vestibular dysfunction

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Introduction

Hip fractures are a public health problem causing social and economic problems, particularly among the elderly [1,2]. The global number of hip fractures, 1.26 million in 1990, is expected to rise to 4.5 million by 2050 as the elderly population continues to grow. Although regional data vary between countries, 18% of women and 6% of men are generally expected to be affected [3]. Hip fractures generally result from low-energy traumas in the home and exhibit a high rate of mortality and morbidity within one year following hospitalization [4].

Decreased bone mineral density (BMD) is still the primary risk factor. Factors affecting BMD include genetic predisposition, advanced age, and sex. Other predisposing factors to hip fractures are impaired vision, drug use, and balance problems [5]. Severe increases in mortality and morbidity occur over time in these patients following surgery [1,4].

An increase in daily activities and a decrease in fear of falling and numbers of falls has been observed in these patients as a result of balance studies [4]. Studies of balance problems have reported hip fracture-preventing and postoperative quality of life-enhancing results [4,6]. The incidence of balance problems among the elderly population has been reported as 34% [7]. Measures routinely taken to reduce hip fractures in the elderly population include balance examinations, use of crutches, and balance exercises [7-10].

Some accidents can, therefore, be avoided by means of simple, low-cost measures aimed at serving as guides for the elderly in risky situations. These provide significant benefits in terms of quality of life and significant reductions in mortality, morbidity, and socioeconomic costs of this growing problem [7,10].

Vertigo and balance problems are seen in approximately 15-20% of the adult population. Vestibular disorders can be caused by central or peripheral pathologies. The most widespread causes of peripheral vestibular vertigo in ear, nose, and throat clinical practice are benign paroxysmal positional vertigo, vestibular neuronitis, and Meniere's disease (MD). Vertigo can also result from non-peripheral vestibular causes, such as neurological and autoimmune diseases [11].

Vestibular evoked myogenic potentials (VEMP) testing is a non-invasive and objective method permitting the electrophysiological evaluation of vestibular functions and is used in the diagnosis of vestibular diseases [11,12]. Two types of VEMP test are employed in clinical practice, cervical VEMP (cVEMP) and ocular VEMP (oVEMP) [7]. oVEMP yields information about utriculo-ocular functions, while cVEMP provides data concerning vestibulo-colic reflex functions [12]. The neural pathway tested using cVEMP begins from the saccule and provides stimulation of the sternocleidomastoid (SCM) muscle via the motor neurons of the inferior vestibular nerve, lateral vestibular nucleus, medial vestibulospinal tract, and spinal cord [11,12]. A biphasic response is elicited with the administration of acoustic stimuli. Electromyographic activity is recorded using electrodes placed over the SCM. The presence or absence and the structure and symmetry of the recording provide information about the location of peripheral pathologies of the vestibular nerve [11].

The purpose of this study was to determine the effect of balance problems, which exacerbate falls, one of the etiological causes of hip fractures, with the evaluation of cVEMP.

Materials and methods

Approval for this prospective study was granted by the Clinical Research Ethical Committee of Kastamonu University Clinical Ethical Board (Decision no. 2020-KAEK-143-123 dated October 20, 2021). Written informed consent was obtained from all the participants after the study protocol had been explained to them in detail. Twenty-two consecutive patients who were hospitalized at the orthopedic clinic due to hip fracture between November 1, 2021 and May 1, 2022 were included in the study. The control group consisted of 24 random patients with a similar age range and similar demographic characteristics admitted to the orthopedic clinic due to knee pain. All participants underwent detailed otological examinations, and their demographic characteristics, additional diseases, and clinical features were recorded. The two groups' cVEMP records were compared. Individuals with histories and complaints of vertigo, with middle and outer ear diseases, with neuropsychiatric diseases or with histories of otological surgery were not included in the study. Those using muscle relaxant drugs or hearing devices were also excluded from the study.

The VEMP test was performed in the patient's room using a Socrates device (Hedera Biomedics, Taranto, Italy). Recordings were taken with the patients in a supine position and facing the contralateral side in order to ensure sufficient and continuous tension in the SCM. Electromyographic activity was measured using an active electrode placed on the upper third of the SCM muscle, a reference electrode on the suprasternal notch, and a ground electrode on the forehead. The skin was cleaned where the electrodes were attached. The response of the ipsilateral SCM to monoaural stimuli was recorded. Acoustic stimuli (tone-burst, 500 Hz, 4.3/s stimulus rate, rise=2 ms, plateau=1 ms, and fall=2 ms) were applied by means of Etymotic ER3C insert earphones (USA). A 90 dB stimulus was applied to determine the VEMP threshold, and ipsilateral myogenic potentials were recorded. The first positive wave was recorded as P1 and the first negative wave as N1. The latencies and amplitudes of these waves were calculated and recorded. When biphasic wave forms were not recognizable and repeatable, the VEMP response was regarded as absent. The VEMP asymmetry rate (VAR) was calculated using the formula VEMP asymmetry (%)=100(Ar-Al)/(Ar+Al) and subsequently recorded.

Statistical analysis

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) version 20.0 software (IBM Corporation, New York, NY, USA). Normality of data distribution was evaluated using the Shapiro-Wilk test. Student's t test was applied in the case of normal distribution, and the non-parametric Mann-Whitney U test in the case of non-normal distribution. Data were expressed as mean (SD). The chi-square test was applied in the analysis of categorical data. *P*-values <0.05 were regarded as significant for all tests.

Results

Twenty-two patents aged 64-79 and a control group consisting of 24 individuals aged 67-83 were included in the study. The patient group was made up of 13 women and 9 men, and the control group consisted of 14 women and 10 men. No significant age or gender difference was observed between the two groups.

Eleven members of the patient group had been hospitalized due to a left hip fracture and 11 with a right hip fracture. Both groups underwent detailed otological examinations. Audiograms were not performed since the patients were immobile. However, as previously mentioned, patients with hearing loss or using hearing aids were excluded from the study.

Unilateral absent VEMP response was observed in five and bilateral absent VEMP response in three members of the patient group, while in the control group unilateral absent VEMP response was determined in two individuals and bilateral absent VEMP response in one. No significant difference in asymmetry rates was determined between the patient and control groups (P=0.505).

No significant difference was determined between the right and left ears in either group in terms of P1 and N1 latencies. However, P1 and N1 values in both the right and left ears differed significantly between the fracture and control groups (P=0.008 and P=0.007, respectively). The hip fracture group had significantly increased P1 and N1 latencies, which is associated with central vestibular dysfunction (Table 1).

Table 1: The mean values of P1 an N1 latencies evaluated cVEMP of fracture and control groups

	Control group	Fracture group	*P*-value
Right P1	15.17 (6.02)	29.20 (6.05)	0.007
Left P1	15.79 (6.07)	28.63 (6.19)	0.007
Right N1	15.33 (8.19)	29.04 (8.23)	0.008
Left N1	17.62 (8.21)	29.96 (8.38)	0.008

Discussion

Decreased bone quality due to osteoporosis is the most important cause of hip fractures in the elderly. However, balance problems that exacerbate falls represent another important risk factor [1,3,4,9,10].

A complex interaction of physiological mechanisms is involved in the safe performance of such daily activities as walking and standing. An important risk factor for falls in the elderly is an age-related decrease in balance control [10], and balance disorders are one of the causes of hip fractures. Shunney et al. [9] reported that 53% of patients had fallen at least once in the six months prior to hospitalization due to hip fracture.

Hip fractures increase with age and cause high rates of mortality and morbidity. It is, therefore, essential to identify these patients beforehand and administer the requisite fall-prevention treatment and rehabilitation. Even the use of crutches alone has been identified as a fall-preventing factor [8]. Postoperative rehabilitation and balance therapies in elderly individuals with hip fractures have resulted in early returns to daily life, faster walking, and an improved quality of life [8-10].

Significant changes in VEMP have been shown in superior semicircular canal dehiscence syndrome, an inner ear disease characterized by audiological findings, such as dizziness, imbalance, hyperacusis, autophony, pulsatile tinnitus, and conductive hearing loss occurring with pressure and loud noise [13]. Ziniga et al. [14] showed that hearing loss associated with exposure to noise can lead to falls, and suggested that it would be useful for patients to be evaluated in terms of saccular dysfunction using VEMP.

VEMP is a clinical reflex test employed in the diagnosis of vestibular diseases and involves the recording and evaluation of muscle potentials resulting from stimulating the vestibular system with different stimuli. cVEMP is an effective method that successfully shows balance functions in both humans and animals [16]. Differences in VEMP recordings appear in diseases deriving from the ear and the vestibular system [12,14,15]. Some studies have shown that VEMP is not useful in the diagnoses of MD and vestibular neuritis. This situation, known as absent response, indicates inferior vestibular nerve involvement [16].

Several studies of oVEMP and cVEMP tests have reported that no response could be obtained in elderly individuals in particular. Although up to 40% of otologically and neurologically healthy individuals over the age of 60 do not produce a cVEMP in response to an air conduction tone burst at 500 Hz, Piker et al. [17] recommended that this should be investigated at 500 or 750 Hz for obtaining cVEMP response. In a study of patients over 60, Rosengren et al. [12] reported an absence of cVEMP rate of 5-15%. In the present study, cVEMP was applied at 500 Hz to all patients. No failure to achieve a bilateral response occurred in any patient. The most consistent age-related finding is a decreased peak-to-peak amplitude and a threshold that increases in line with age (in other words, a threshold occurring at higher stimulus levels).

In a study of patients followed-up due to osteoporosis, Gargeshwari et al. [18] described the absence of oVEMP in particular as significant when they applied oVEMP and cVEMP tests. They also suggested that it should be mandatory for elderly individuals under follow-up due to osteoporosis and osteopenia to be assessed in terms of balance.

Limitations

There are also certain limitations to this study. The most important limitation of this study is the absence audiometric analysis for the patients due to their lack of mobility. The relatively low number of patients prevented us from subgrouping the patients in terms of age and fracture types. This subject might be usefully investigated in future and more extensive studies.

Conclusion

This study revealed that the rate of subclinical peripheral vestibular dysfunction, which can be identified by cVEMP evaluation, is increased in elderly patients with hip fractures caused by low energy trauma. Precautions like vestibular rehabilitation can be a preventive measure for hip fractures in the elderly.

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References

1. Sterling RS. Gender and race/ethnicity differences in hip fracture incidence, morbidity, mortality, and function. Clin Orthop Relat Res. 2011 Jul;469(7):1913-8. doi: 10.1007/s11999-010-1736-3. PMID: 21161737; PMCID: PMC3111795.
2. Ensrud KE. Epidemiology of fracture risk with advancing age. J Gerontol A Biol Sci Med Sci. 2013 Oct;68(10):1236-42. doi: 10.1093/gerona/glt092. Epub 2013 Jul 5. PMID: 23833201.
3. Veronese N, Maggi S. Epidemiology and social costs of hip fracture. Injury. 2018 Aug;49(8):1458-60. doi: 10.1016/j.injury.2018.04.015. Epub 2018 Apr 20. PMID: 29699731.

4. Neto JS, Dias CR, de Almeida JD. Epidemiological characteristics and causes of proximal femoral fractures among the elderly. Rev Bras Ortop. 2015 Nov 16;46(6):660-7. doi: 10.1016/S2255-4971(15)30322-0. PMID: 27027070; PMCID: PMC4799322.
5. Nevitt MC, Cummings SR, Hudes ES. Risk factors for injurious falls: a prospective study. J Gerontol. 1991 Sep;46(5):M164-70. doi: 10.1093/geronj/46.5.m164. PMID: 1890282.
6. Chen X, Yang W, Wang X. Balance training can enhance hip fracture patients' independence in activities of daily living: A meta-analysis of randomized controlled trials. Medicine (Baltimore). 2020 Apr;99(16):e19641. doi: 10.1097/MD.0000000000019641. PMID: 32311935; PMCID: PMC7440254.
7. Değer TB, Saraç ZF, Savaş ES, Akçiçek SF. The Relationship of Balance Disorders with Falling, the Effect of Health Problems, and Social Life on Postural Balance in the Elderly Living in a District in Turkey. Geriatrics (Basel). 2019 May 17;4(2):37. doi: 10.3390/geriatrics4020037. PMID: 31108836; PMCID: PMC6630729.
8. Ohara A, Yasuhiro M, Mochizuki F, Shinohe T, Sasano Y, Suzuki K, Mikami K, Koizuka I. Effects of using cane and vestibular rehabilitation on the walking function in elderly patients with dizziness. Auris Nasus Larynx. 2021 Aug;48(4):571-6. doi: 10.1016/j.anl.2020.10.010. Epub 2020 Nov 19. PMID: 33223340.
9. Shumway-Cook A, Ciol MA, Gruber W, Robinson C. Incidence of and risk factors for falls following hip fracture in community-dwelling older adults. Phys Ther. 2005 Jul;85(7):648-55. PMID: 15982171.
10. Halvarsson A, Dohrn IM, Ståhle A. Taking balance training for older adults one step further: the rationale for and a description of a proven balance training programme. Clin Rehabil. 2015 May;29(5):417-25. doi: 10.1177/0269215514546770. Epub 2014 Sep 8. PMID: 25200877; PMCID: PMC4419050.
11. Rosengren SM, Colebatch JG, Young AS, Govender S, Welgampola MS. Vestibular evoked myogenic potentials in practice: Methods, pitfalls and clinical applications. Clin Neurophysiol Pract. 2019 Feb 26;4:47-68. doi: 10.1016/j.cnp.2019.01.005. PMID: 30949613; PMCID: PMC6430081.
12. Wu HJ, Shiao AS, Yang YL, Lee GS. Comparison of short tone burst-evoked and click-evoked vestibular myogenic potentials in healthy individuals. J Chin Med Assoc. 2007 Apr;70(4):159-63. doi: 10.1016/S1726-4901(09)70350-8. Erratum in: J Chin Med Assoc. 2008 Apr;71(4):221. PMID: 17475597.
13. Fife TD, Colebatch JG, Kerber KA, Brantberg K, Strupp M, Lee H, et al. Practice guideline: Cervical and ocular vestibular evoked myogenic potential testing: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2017 Nov 28;89(22):2288-96. doi: 10.1212/WNL.0000000000004690. Epub 2017 Nov 1. PMID: 29093067; PMCID: PMC5705249.
14. Zuniga MG, Dinkes RE, Davalos-Bichara M, Carey JP, Schubert MC, King WM, Walston J, Agrawal Y. Association between hearing loss and saccular dysfunction in older individuals. Otol Neurotol. 2012 Dec;33(9):1586-92. doi: 10.1097/MAO.0b013e31826bedbc. PMID: 23064383; PMCID: PMC3498596.
15. Negishi-Oshino R, Ohgami N, He T, Ohgami K, Li X, Kato M. cVEMP correlated with imbalance in a mouse model of vestibular disorder. Environ Health Prev Med. 2019 Jun 1;24(1):39. doi: 10.1186/s12199-019-0794-8. PMID: 31153359; PMCID: PMC6545207.
16. Murofushi T, Halmagyi GM, Yavor RA, Colebatch JG. Absent vestibular evoked myogenic potentials in vestibular neurolabyrinthitis. An indicator of inferior vestibular nerve involvement? Arch Otolaryngol Head Neck Surg. 1996 Aug;122(8):845-8. doi: 10.1001/archotol.1996.01890200035008. PMID: 8703387.
17. Piker EG, Jacobson GP, Burkard RF, McCaslin DL, Hood LJ. Effects of age on the tuning of the cVEMP and oVEMP. Ear Hear. 2013 Nov-Dec;34(6):e65-73. doi: 10.1097/AUD.0b013e31828fc9f2. PMID: 23673615; PMCID: PMC3748259.
18. Gargeshwari A, Jha RH, Singh NK, Kumar P. Behavioural and objective vestibular assessment in persons with osteoporosis and osteopenia: a preliminary investigation. Braz J Otorhinolaryngol. 2018 Nov-Dec;84(6):744-53. doi: 10.1016/j.bjorl.2017.08.013. Epub 2017 Sep 21. PMID: 29030130; PMCID: PMC9442882.

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Impact of prenatal physical preparation program on respiratory parameters of pregnant women

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The study was approved by School of Public Health of the Faculty of Medicine of the University of Kinshasa (date and number: 17 September 2019). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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Abstract

Background/Aim: Pregnancy is a condition that alters a woman's respiratory parameters. We aimed to verify the impact of a prenatal physical preparation program on respiratory parameters of pregnant women.
Methods: A quasi-experimental study was conducted with 38 pregnant women over a period of 8 months. It consisted of measuring the respiratory parameters (using the New MIR Spirolab Spirometer) of pregnant women who participated in the prenatal physical preparation program. Each session lasted 45 minutes and took place once a week. The sessions involved low to moderate intensity and assessed the forced expiratory volume second, the vital capacity force, and the peak expiratory flow.
Results: After the intervention program in prenatal physical preparation, there was a significant change in the vital capacity force (74 (3.65) before vs 79 (0.54) after; P=0.003); forced expiratory volume (68 (0.63) vs 76 (0.45), P=0.002); and peak expiratory (69 (1.77) before vs 78 (1.12) after; P=0.001) The Tiffeneau index showed (72.8 (4.2) vs 76.19 (13.3), P=0.001). The number of pregnant women with normal spirometry doubled from 47.4% at the start of the program to 94.7% at the end of the program. Similarly, the proportion of pregnant women with mild restriction increased from 42.1% at the start of the program to 2.6% at the end, indicating a total improvement of the obstructive disorders.
Conclusion: The regular practice of physical activity allows for improvement of the respiratory parameters of pregnant women. This program must continue to enable these women to maintain their respiratory capacity after childbirth.

Keywords: physical preparation, prenatal, pregnant women, spirometry

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Introduction

Pregnancy is a critical period for pregnant women. Several adaptations are necessary to meet the increased metabolic needs of the mother and the fetus. Significant anatomical and functional changes in the cardiorespiratory system occur during pregnancy due to hormonal factors and the progressive increase in the size of the uterus [1].

It is not always easy to distinguish the physiological changes of pregnancy from the pathophysiological states associated with pre-existing cardiopulmonary disease or issues that may occur during pregnancy or in the postpartum period.

Physical exercise is defined as a structured modality of physical activity aimed at maintaining or increasing fitness [1]. The practice of moderate physical exercise during pregnancy is advised in order to increase or maintain a reasonable level of physical fitness. This is why several countries (France, Canada, United States, Norway, Denmark) have established recommendations for health professionals to better inform women about the benefits of physical activity. The Haute Autorité de Santé (HAS), the American College of Obstetricians and Gynecologists (ACOG) [2] and the Society of Obstetricians and Gynecologists of Canada (SOGC) recommend encouraging pregnant women with no contraindications (medical or obstetric) to initiate or continue the practice of moderate physical activity, regular and included in their lifestyle, up to 30 minutes a day, between three and five times a week (depending on the trimester of pregnancy) [3].

We found that despite the recommendations of learned institutions, Congolese pregnant women with no medical contraindication to the practice of physical exercises always remained sedentary. It is for this reason that we were motivated to design a physical preparation program to help these women stay active throughout the pregnancy period.

Materials and methods

This study was conducted among pregnant women recruited from the prenatal consultations of the Mont Amba Hospital Center in Kinshasa, Democratic Republic of Congo, from September 2020 to April 2021.

The pregnant women followed a prenatal physical preparation program. The selection criteria included:

- having a gestational age of at least 20 weeks gestation;
- having a chronological age between 20 and 39 years;
- agreeing to regularly attend prenatal consultation (PNC) at the Mont Amba Hospital Center in Kinshasa;
- not presenting pathologies or abnormalities that might limit the practice of exercise or physical activity that could influence the well-being of the mother and the fetus.

Through the use of convenience sampling, 38 pregnant women agreed to participate in the study at the Mont Amba Hospital Center.

The variables studied were:

- the forced expiratory volume second (FEV1);
- the vital capacity force (FVC);
- the peak expiratory flow (PEF);
- the Tiffeneau index (FEV1/FVC).

All these measurements were carried out using the New MIR Spirolab Spirometer. (Medical, Ref. JFB-246) (MIR Medical International Research).

Spirometry procedure for the 38 pregnant women

Prior to the measurement, a short questionnaire was administered to collect a profile of the pregnant woman. This included age, weight, sex, height, race, and physical activity.

Subsequently, the pregnant women carried out following steps in the examination:

- The pregnant woman was seated comfortably on a chair, with her head straight to optimize breathing. A nose clip was used so that all the air from the lungs passed in a single tube.
- Afterwards, the measurement took place in three stages: the first two stages involved a deep inspiration followed by the slow exhalation. The third stage consisted of a deep inspiration followed by a strong and fast exhalation in the mouthpiece with nose pliers.

Physical and respiratory exercises constituted the treatment to fight against respiratory disorders in some pregnant women and to maintain good physical condition and good breathing. The pregnant women walked on the spot with swinging arms, then walked with displacement in a room of six square meters.

In decubitus position:

- Diaphragmatic and thoracic inspiration-expiration, synchronized or alternated with the movements of the upper limbs (five series);
- Lifting the head from the mat while exhaling and returning to the initial position while inhaling (three times);
- Knees drawn while lifting the head and exhaling; returning to the initial position while inhaling (two times);
- Finally continue with normal breathing

Sitting or standing:

- Alternately make the lateral inclination of the trunk to the left and to the right, synchronizing with the exhalation during the movement and the inspiration during the return to the initial position (five times).
- Raising both arms forward, laterally or up while inhaling and lowering arms while exhaling (four times).

Quadripedal position:

- Hollowing the back while inhaling and rounding the back while exhaling (three times);
- Contracting while exhaling and relaxing while inhaling the abdominals (five times);
- Alternately raising one arm (four times);
- Deep inspiration followed by slow expiration (four times).
- Return to normal breathing.

The program lasted 16 weeks for each pregnant woman, from the 20th to the 36th week of amenorrhea.

Operational definitions (Spirometry)

Normal:

- FEV >80%
- FVC >80%
- FEV/FVC >75%

Mild Obstruction:

- FEV 60-79%
- FVC 60 -79%
- FEV1/FVC 60-79%

Moderate Obstruction:

- FEV1 41-59%
- FVC 51-59%
- FEV1/FVC 41-59%
- Mild restriction: PEF <70%.
- Moderate restriction: PEF >50%

Ethical considerations

The study was submitted and approved by the Ethics Committee of the E School of Public Health of the Faculty of Medicine of the University of Kinshasa under number ESP/CE/254/2019 on September 17, 2019. Written informed consent was obtained from each pregnant woman.

Statistical analysis

Quantitative data was presented as mean and standard deviation while qualitative data was presented as frequency and percentage. The student's t-parameter test was used to compare the means before and after the intervention program, against the non-parametric chi-square test that allowed us to compare the qualitative data. *P*-value <0.05 was considered the statistical significance level.

Results

The vital capacity force, the forced expiratory volume second, the FEV1/FVC: Tiffeneau index as well as the PEF: peak expiratory flow of pregnant women were significantly modified after the intervention program (Table 1).

Table 1: Evolution and comparison of spirometric parameters at the start and at the end of the program

Parameters	Before the program	After the program	
	Mean (SD)	Mean (SD)	*P*-value
FVC (%)	74 (3.65)	79 (0.54)	0.003
FEV1 (%)	68 (0.63)	76 (0.45)	0.002
FEV1/FCV (%)	72.8 (4.2)	76.19 (13,3)	0.001
PEF (%)	69 (1.77)	78 (1.12)	0.001

FVC: vital capacity force, FEV1: forced expiratory volume second, FEV1/FVC: Tiffeneau index, PEF: peak expiratory flow

The results shown in this table indicate that the number of pregnant women with normal spirometry doubled from 47.4% at the start of the program to 94.7% at the end of the program. Similarly, the proportion of pregnant women with a light restriction fell from 42.1% at the start to 2.6% at the end. The evolution was similar to mild and moderate obstruction.

Table 2: Respiratory disorders in pregnant women at the start and end of the program

Results	Before the program	After the program
	n=38 (%)	n=38
Normal spirometry	18 (47.4)	36 (94.7)
Slight restriction	16 (42.1)	1 (2.6)
Moderate restriction	1 (2.6)	1 (2.6)
Slight obstruction	2 (5.3)	-
Moderate obstruction	1 (2.6)	-

Table 3 shows the evolution of spirometry before and after the program according to an age greater than or equal to 30 years. In fact, in the under-30 age group, pregnant women with normal spirometry increased from 52.2% at the start of the program to 95.7% at the end of the program. The evolution was the same among those aged 30 and over (40% to 93.3%). The same trend was observed for mild and moderate restriction and for mild and moderate obstruction.

Table 3: Relationship between spirometry and the age of pregnant women.

Spirometry	Before the program			After the program		
	Age (years)			Age (years)		
	Under 30	30 and older		Under 30	30 and older	
	n=23 (%)	n=15 (%)	*P*-value	n=23 (%)	n=15 (%)	*P*-value
Normal spirometry	12 (52.2)	6 (40)	0.61	22 (95.7)	14 (93.3)	0.33
Slight restriction	9 (39.1)	7 (46.7)		1 (4.3)	-	
Moderate restriction	-	1 (6.7)		-	-	
Slight obstruction	1 (4.3)	1 (6.7)		-	-	
Moderate obstruction	1 (4.3)	-		-	1 (6.7)	

Discussion

The objective of the study was to evaluate the respiratory function of pregnant women who followed the prenatal physical preparation program, specifically by evaluating spirometric parameters with the New MIR Spirolab Spirometer.

Respiratory disorders were observed in 20 pregnant women, i.e. 52.63% of all participants in this study. These data, when compared to those reported in the literature by Goslin (6.5%) are much higher [4].

This is explained by the methodological approach used, which was to examine, using the New Spirolab, all the participating pregnant women at the start of the program. While at the end of the program, comparative data are unavailable in the literature, there is a lack of prospective and longitudinal scientific studies of prenatal physical preparation including spirometry [5].

In our study, the restriction was found in 17 (44.73%) of cases at the start of the program, and 2 (5.26%) pregnant women at the end of the program. A very significant improvement in restrictive disorders and a total improvement in obstructive disorders were observed. Nevertheless, this study highlighted the contribution of specific breathing exercises to remedy this situation.

In our series, we found the modification of the Tiffeneau index, peak expiratory flow, and forced expiratory volume of pregnant women after the intervention program. According to Reimann [9], the regular practice of adapted activities in pregnant women improves respiratory parameters. The Tiffeneau index results from our study were lower than those found by Kamanga et al. [6]. This is most likely justified by the small sample of the study composed exclusively of pregnant women. It is evident that a high secretion of progesterone causes an increase in respiratory rate, leading to hyperventilation.

The respiratory rate increases and can thus lead to a feeling of shortness of breath on exertion, or even at rest. It is estimated that one in two pregnant women is dyspneic [3].

The spirometric values obtained in healthy women in the 20-29 and 30-39 age groups in a study by Kamanga et al. [5], show agreement between the results of FEV1, FVC and DEP with those of the study. [3] In our series, at the end of the program, of all women under 30 and 30 and over, had 95.7% and 93.3% of normal spirometry, respectively. Artal and Mittelmark [6] reported the frequency of 50% of pregnant women who have difficulty breathing (dyspnea), a common complaint among pregnant women. In the present study, at the start of the program, the results were slightly higher than those in the literature reported by Artal and Mittelmark [6]. In a study titled "Reference Values and Predictive Equations of Spirometry in the Moroccan Population", Khalid Bouti [7] obtained spirometric values for a sample composed of men and women. Only the age groups of women aged between 20-29 and 30-39 were taken into account. The values of FEV1, FVC and PEF agree with the results of the study. There is a clear difference between the Tiffeneau Pinelli ratio in Khalid Bouti's study according to the two age groups, the values of which were 89 [7]. This difference is explained by the fact that the study sample is exclusively composed of pregnant women [8,9].

Limitation of the study

The absence of standard values for pregnant women is a major problem for the interpretation of the results of the examination.

Strength of the study

This study is the first in the Democratic Republic of Congo to show the beneficial effects of regular physical and respiratory exercise on the spirometric parameters (FEV1, FVC, PEF, FEV1/FVC) of pregnant women.

Conclusion

This study carried out at the Center Hospitalier du Mont Amba in Kinshasa showed the effectiveness of physical and respiratory exercise in the care of pregnant women with respiratory problems. There was a marked improvement in spirometric parameters (FEV1, FVC, PEF, FEV1/FVC) at the end of the prenatal physical preparation program. We suggest that this practice should continue in order to maintain the achievements of this program.

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References

1. Biddle S, Goudas M. Sport, activité physique et santé chez l'enfant. 1994;47(2):135 44.
2. ACOG Committee on Obstetric Practice. Committee opinion 267: exercise during pregnancy and the postpartum period. Obstet Gynecol. 2002 Jan 1;99(1):171–3.
3. Clapp J, Seaward B, Sleamaker R, Hiser D. Maternal physiologic adaptations to early human pregnancy. Am J Obstet Gynecol. 1988;159(6):1456-60.
4. Gosling J. Anatomy and Physiology, Educational and Cultural Center. 1995;74(4):103-12.
5. Kamanga Mwamba B, Kayembe J, Nkiama Ekisawa C. Reference spirometric values in the Bantu population of Kinshasa. Pam. Afr Med J. 2019;5(3):33-42.
6. Artal R, Mittelmark M. Physical changes during pregnancy. Saint Louis, University School of Medicine latest revised, 2021.
7. Khalid B. Reference values and predictive equations for spirometry in the Moroccan population. 2017;56(3):131-6.
8. Bourgrida M, Ben Saad H, Kheireddinne Bourahil M, Bougmiza I, Mehdioul H. Spirometric reference equations of Algerians aged 19 to 73 years. J Obstet. 2006;7(3):66-7.
9. Riemann MK, Kanstrup HI. Effects on the foetus of exercise in pregnancy. Scand J Med Sci Sports. 2000 Feb;10(1):12-9.

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Research article

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Benefits of a prenatal physical preparation program on the condition of the perineum and Apgar scores at birth

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Ethics Committee Approval
The study was approved by School of Public Health of the Faculty of Medicine of the University of Kinshasa (date and number: September 17, 2019). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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Abstract

Background/Aim: The practice of physical activities among pregnant women remains a significant health challenge in the Democratic Republic of Congo. The aim of this study was to examine the influence of prenatal physical preparation on the state of the perineum and Apgar scores at birth.
Methods: This experimental study included 89 pregnant women, with 38 of them subjected to an 8-month prenatal physical preparation program that involved weekly sessions of 45 min of low to moderate intensity. The remaining 51 pregnant women did not participate in the program and served as a control group. The variables of interest, including episiotomy, perineal tear, intact perineum, and Apgar scores, were measured, and the chi-square statistical test was used to compare the two study groups. *P*-values <0.05 were considered statistically significant.
Results: The present study reveals that the women in labor in the experimental group (EG) had fewer perineal tears and less episiotomy compared to the control group (CG). Specifically, the incidence of perineal tear was significantly lower in the EG (5.3%) than in the CG (27.5%) with a *P*-value of 0.001, while the incidence of episiotomy was also significantly lower in the EG (7.9%) than in the CG (25.5%) (*P*=0.032). Furthermore, a significant number of women in the EG (86.8%) had an intact perineum compared to those in the CG (47%) (*P*=0.001).
Conclusion: The delivery parameters of pregnant women who followed a prenatal physical preparation program underwent significant changes compared to those who did not participate in the program. These findings suggest that the program should be continued to improve the care of women who have given birth.

Keywords: labor, physical preparation, pregnant women

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Introduction

Childbirth refers to the set of phenomena that contribute to the exit of the fetus and its annexes from the maternal genital tract at term [1-5]. These phenomena are governed by the adaptation of the fetal head and the maternal pelvis and genitals, accompanied by uterine contractions that push the fetus outward [6-10].

Despite these accommodations, complications during vaginal delivery frequently occur at the perineal level and are challenging for new mothers. These complications can alter pelvic muscles, leading to postpartum pain, dyspareunia, urinary incontinence, anal incontinence in the case of damage to the external and internal anal sphincter, prolapse, and obstetric fistula [11, 12]. Moreover, these complications can cause psychological distress, particularly after an episiotomy, leading to a sense of mutilation [11, 12]. Maternal morbidity and mortality are high due to the complications arising from vaginal delivery [13-18].

About six out of ten women experience partial perineal tears during vaginal delivery due to the tension exerted by the baby on the vagina at the time of birth [19]. Although perineal tears and episiotomy can limit fetal suffering by helping the rapid expulsion of the baby, they are traumatic and painful episodes that affect the perineal area, which is extremely sensitive and weakened by nine months of pregnancy [20]. Anal sphincter tears during childbirth represent a public health problem that has long-term medico-socioeconomic risks and a negative impact on the quality of life of young women in childbirth.

It is known that regular physical activity before and during pregnancy improves the physical condition of women. Some authors have investigated its effect on the duration of childbirth by comparing the duration of labor in active and sedentary women [21]. Bechmann and Bechmann reported a significantly reduced duration of labor at delivery for participants in the physical activity program [22]. Physical activity allows pregnant women to maintain their autonomy and psychological well-being by safeguarding their image and self-esteem [23]. Additionally, regular and appropriate physical activity during the third trimester alleviates mood disorders that can accompany pregnancy, such as anxiety and depression [24].

Although physical activity is a recommended therapy in the care of pregnant women [25-28], it is not integrated into the preparation of pregnant women for childbirth in the Democratic Republic of Congo. To reduce maternal and fetal morbidity due to traumatic lesions of the perineum during vaginal delivery in the Democratic Republic of Congo, a physical and psychological preparation program has been established. This program aims to systematically use the methods and techniques of prenatal physical and psychological preparation.

Materials and methods

Nature and period of the study

We opted for the evaluative method and conducted an experimental study of pregnant women undergoing a prenatal physical preparation program for 8 months (September 2020 to April 2021).

Study framework

The Mont-Amba hospital center in Kinshasa, Democratic Republic of Congo and the University of Kinshasa clinics served as the framework for this study.

Study population and sample

The total population of our study was composed of 138 pregnant women, including 87 in the experimental group (EG) and 51 in the control group (CG). The distribution of the groups was a function of the women's availability to join the program.

Out of a population of 87 pregnant women in the experimental group, 49 were excluded from the study. Exclusion criteria included 15 women with a gestational age of fewer than 20 weeks of amenorrhea, 8 who refused to participate in the program, 17 who were lost to follow-up, and 9 who did not attend the required number of sessions (at least 12 sessions). In the end, 38 pregnant women were included in the experimental sample, which was gradually recruited. Of these women, 8 entered the program in September, 17 in October, and 13 in November. The control group consisted of 51 pregnant women who were retained in the study.

The inclusion criteria were: a pregnancy with a gestational age greater than or equal to 5 months; agreeing to go regularly to prenatal consultations (PNCs) during the study period; absence of pathologies or anomalies contraindicated to the practice of physical activities; a chronological age between 20 and 39 years; freely agree to participate in the program from the beginning to the end of the study. Any pregnant woman who did not meet the above criteria was excluded.

Data collection techniques

The data for this study were collected from the records of pregnant women at delivery. Episiotomy, perineal tear, intact perineum, and Apgar served as variables of interest.

Support Protocol

The care protocol consisted of two parts, a conventional program and a prenatal physical preparation program.

The conventional program: The control group subjects took part in this protocol, consisting of prenatal consultations without practicing physical exercises.

The prenatal physical preparation program: The prenatal physical preparation program was led by physiotherapy experts, accompanied by trainees in Physical Medicine and Rehabilitation. Each 45-minute session, held once a week, began with warm-up and stretching exercises, followed by muscle-strengthening exercises for the lower limbs, pelvic muscles (with a focus on perineal work), abdominals, and upper limbs. Breathing exercises (deep inspiration, slow expiration) were also used to prepare for labor and maintain breathing throughout pregnancy. The session ended with relaxation exercises.

Ethical considerations

The protocol for this study was defended and approved by the ethics committee of the School of Public Health of the Faculty of Medicine of the University of Medicine under number ESPCE2542019, dated September 17, 2019. Written informed consent was obtained from pregnant women.

Statistical analysis

Data were entered into Microsoft Excel 2013 software and then imported into SPSS version 22.0 for Windows. Quantitative variables were presented as the median and

interquartile range, while qualitative variables were presented as frequency and percentage in tables. The non-parametric chi-square test was used to compare qualitative variables. *P*-values <0.05 were considered statistically significant.

Results

We found that the women in the experimental group had a significantly better condition of the perineum than those in the control group (Table 1).

Table 1: Comparison of childbirth variables between the two groups.

Variables	Group		
	Experimental (n=38)	Control (n=51)	
	n (%)	n (%)	*P*-value
Torn perineum	2 (5.3)	14 (27.5)	0.001
Episiotomy	3 (7.9)	13 (25.5)	0.032
Intact perineum	33 (86.8)	24 (47)	0.001

Table 2 presents the APGAR scores of newborns in the experimental and control groups at the first, fifth, and tenth minutes. The newborns in the experimental group had APGAR scores within the lower normal limit or above the normal limit, with a median and interquartile range (IQR) of 8 at the first minute, 9 at the fifth minute, and 10 at the tenth minute. Similarly, newborns in the control group had APGAR scores within the lower normal limit or above the normal limit at the first, fifth, and tenth minutes, with a median and IQR of 2 at the first minute, 9 at the fifth minute, and 9 at the tenth minute.

Table 2: Presentation of the Apgar scores of the experimental and control groups after birth.

	Experimental group				Control group			
Apgar score	**Med***	**IQR****	**Min**	**Max**	**Med**	**IQR**	**Min**	**Max**
In the 1st min	8	2	7	10	7	2	5	9
In the 5th min	9	2	7	10	9	2	7	10
In the 10th min	10	1	9	10	9	3	9	10

*Median: **Interquartile range

Discussion

The objective of this study was to investigate the effect of a prenatal physical preparation program on vaginal delivery, with a specific focus on perineal protection. This was achieved by describing the characteristics of vaginal delivery for pregnant women in the experimental and control groups and the sociodemographic characteristics of these two groups of pregnant women at the Mont Amba Hospital Center in Kinshasa.

We found that, after childbirth, the perineum of mothers in the experimental group was in a better condition than those of the control group. Owe et al. [29] reported that the regular practice of physical activities minimizes the risk of episiotomy, perineal tears as well as cesarean sections.

Bechmann CRB and Bechmann CA [22] reported a predominance of vaginal delivery in the trained group, although the results were lower than those of our study. Lawani et al. [28] found that the trained group had a preference for vaginal delivery, with 88% having an intact perineum.

The APGAR score at the first minute had a median of 8 (range: 7–10), while at the fifth minute, it was 9 (range: 7–10), and at the tenth minute, it was 10 ± 1 (range: 9–10). All the children had a good score from the first minute. In contrast, the APGAR score for children born to mothers who did not follow the program had a median of 7 (range: 5–9) at the first minute, 9 (range: 7–10) at the fifth minute, and 9 (range: 9–10) at the tenth minute. No statistically significant difference was found between the two groups at the fifth minute.

It should be noted that the majority of children had a good score from the first minute, and all children had a very good score at the tenth minute. There was no significant difference in the APGAR scores of children whose mothers were subjected to the program and those whose mothers did not follow the program. However, the trained group had a higher APGAR score compared to the sedentary group between the first and fifth minutes of birth, which is consistent with the results of our study and those of Bachmann and Bachmann.

When comparing trained and untrained groups, Barakat et al. [30] detected no difference in the APGAR scores at the first minute and the fifth minute. All the individual values at 5 minutes were greater than or equal to 9. These results agree with those of our study, which were greater than or equal to 9 at the 5th minute of birth.

In our study, the prenatal physical preparation program was found to be very effective, with a once-a-week frequency and useful and simple exercises that could be performed at home. The hypotheses of our work were verified, and the program achieved the desired objective. The participating pregnant women benefited significantly from the program, which was positive and effective.

In Morkved et al.'s [31] program, the mothers performed at a frequency of once per week, and the ensuing results were satisfactory. Lawani et al. [28] chose a frequency of twice per week, and the results were also satisfactory.

Limitations

The small sample size of this study (38 pregnant women in the experimental group who completed the program) was limited by the number of new cases of pregnant women received per month at the PNCs of the Centre Hospitalier Mount Amba/Kinshasa during the study period.

Conclusion

Regular physical activity has beneficial effects on the health of postpartum women. Our study shows that the practice of physical activity during pregnancy can reduce the risk of tears and episiotomy during childbirth and help maintain an intact perineum. Therefore, it is recommended that this program be continued after childbirth to help postpartum women maintain their physical fitness.

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References

1. Carbrol D. Collection: Abbreviated perinatality, Ed. Masson, 2003, p.60-62.
2. Lansac J, Berger C. Obstetrics, Collection for the Practitioner, 3rd Edition, 2000.
3. Lansac J, Marret H. Practice of Childbirth, 3rd Edition. 2001;544(7):205-10.
4. Ladewing, Patricia. Nursing and Perinatal Care. 4th Ed, Saint Laurent. 2010; 1010p.
5. Brabant I. Living your pregnancy and childbirth, A happy birth, Edition Saint Martin. 2001;23(4):32-5.
6. Ageron C, Michelin JM. Practical guide to Obstetrics and gynecology. Ed. Satas, 2000.
7. Thoulon JM. Labor monitoring, Practical Collection in Obstetrics gynecology. 2003;34(6):345-75.
8. Tourris H. Illustrated summary of gynecology and of obstetrics, Ed. Masson, Paris. 2001;18(6):25-7.
9. Bernadette. Well-being and maternity, Marabout Editions. 2009;15-18.
10. Trabecchi F. Potential consequences of pregnancy and childbirth, 18th Day of gynecology of Nice and the Cte dAzur, France. May 2000;16(2):10-7.
11. Parant O, Reme J-M, Monorozis. Recent obstetric tears of the perineum and episiotomy. EMC (Elsevier Masson, Paris). Obstetrics. 1999;57(9):54-71.
12. Barot S, Tardif D. Old obstetric tears. J Gynecol. Obstet. 2010;84(3):200-10.
13. Ardon D, Reinbold D, Dregfus M. Episiotomy and recent obstetric lacerations. J Ggynecol. 2010;76(2):232-45.
14. Beucher G. Maternal complications of instrumental extractions. J Gynecol Obstet Biol Repr. 2008;37(8):244-59.
15. CNOF. Episiotomy. Text of recommendations. J Gynecol Obstet Biol. Repr. 2006;35:n1:1S77-1S80.

16. Organisation mondiale de la santé. Recent data reveals that women are victims of ill-treatment during childbirth. October 2019.
17. Faltin D. Long-term consequences of perineal tears. Swiss Med J. 2017;88(10):768-74.
18. Said Ait L, Abdelmalek H, Khalid M. Preparation of the direct sphincter: technical points, indications and results. The Pan African Medical J. 2013;44(16):134-40.
19. Tayrac Which perineal protective measures during childbirth. J Gynecol. Obstet. 2017;63(7):62-9.
20. Frenette P. Impact of episiotomy during operative vaginal delivery on obstetrical and sphincter injuries. Journal of Obstetrics and gynecology of Canada. 2019;41(12):1734-41.
21. Committee report. Physical activity guidelines Advisory. Washington, DC: US. Department of Health and Human Services, 2008.
22. Bechmann CRB, Bechmann CA. Effect of a structural antepartum exercise program on pregnancy and labor outcome in primiparas. J Repr Med. 1990;35(19);704-9.
23. American College of Obstetricians and Gynecologists (ACO). Exercise during pregnancy and postnatal period. Washington (DC). ACO, 2002.
24. Babyak M, Blumenthal M. Exercise treatment for major depression: maintenance of therapeutic benefit at 10 months. Psychoson Med. 2000;62(4):633-8.
25. Clap J.F, The effects of maternal exercise on early pregnancy out as. Am J Obstet Gynecol. 1989;16(161):1453-7.
26. Hall DC, Kaufmann DA, Effects of aerobic and strength conditioning on pregnancy outcomes. Am J Obstet Gynecol. 1987;157(76):1199-03.
27. Mersy DJ. Health benefits of aerobic exercise. Postgrad Med. 1991;90(103):110-2.
28. Lawani M.M, Alihonou E, Akplogan B, Poumart, Okou L. The effect of prenatal gymnastics on childbirth: study of 50 sedentary Beninese women during the 2nd and 3rd trimesters of pregnancy. Health. 2003;13(4):235-41.
29. Owe KM, Nystad W, Stigum H, Vangen S, Bø K. Exercise during pregnancy and risk of cesarean delivery in nulliparous women: a large population-based cohort study. Am J Obstet Gynecol. 1 déc 2016;215(6):791.e1-791.e13.
30. Virginia APAR. Evaluation of the physical health of newborns, 1953.
31. Morkved S, Bo K, Schei B, Salvesen KA. Pelvic floor muscle training during pregnancy to prevent urinary incontinence; A single-blind randomized controlled trial. Obstet Gynecol. 2003;101(2);313-9.

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Prenatal gymnastics and psychological support benefit pregnant women

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Ethics Committee Approval
The study was approved by School of Public Health of the Faculty of Medicine of the University of Kinshasa (date and number: September 17, 2019). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: The management of pregnant women is a significant public health concern. This study aims to demonstrate the benefits of prenatal gymnastics and psychological support on pain, walking, anxiety, and self-esteem during pregnancy.
Methods: A quasi-experimental study was conducted over eight months, from September 2020 to April 2021, with 38 pregnant women participating. They underwent 16 sessions of prenatal gymnastics and psychological support once a week, lasting 45 min at low to moderate intensity. Pain, six-minute walk, anxiety, and self-esteem were measured using the visual analog scale (VAS), the six-minute walk test, the Hospital Anxiety and Depression Scale (HAD Scale), and the Rosenberg scale, respectively. The parametric Student's t-test and chi-square were used to compare quantitative and qualitative variables before and after the program, with $P<0.05$ considered statistically significant.
Results: The study found that the distance traveled (377.45 m vs. 393 m; $P=0.001$) and VO2max (15.1 ml/kg/m^2 vs. 18.5 ml/kg/m^2; $P=0.001$) increased at the end of the program. However, pain (6 vs. 1.16; $P=0.001$) and walking speed (2.2 m/s vs. 1.9 m/s; $P=0.001$) decreased. The program also improved self-esteem (low: 55.3% before vs. 0% after; $P=0.001$, medium: 44.7% before vs. 13.2% after; $P=0.001$, strong: 0% before vs. 86.8% after; $P=0.001$) and anxiety (Uncertain anxiety: 31.6% before vs. 97.4% after; $P=0.001$, Questionable anxiety: 50% before vs. 2.6% after, Certain anxiety: 18.4% before vs. 0% after; $P=0.001$).
Conclusion: Regular prenatal gymnastics and psychological support positively affect oxygen consumption, pain, anxiety, and self-esteem among pregnant women. This program should be provided continuously to minimize pregnancy-related complications.

Keywords: prenatal gymnastics, psychological support, pain, walking, anxiety, self-esteem

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Introduction

Lumbo-pelvic pain is frequently mentioned by women during pregnancy [1] and typically worsens as the pregnancy progresses. As the baby grows, the body must adapt quickly to the new stress created on its ligaments, joints, muscles, and bones [2]. Pain occurs when the body can no longer adapt to the stress placed upon it. The pain may be due to muscle weakness, an asymmetry in the body, a problem with lumbopelvic stabilization, and many other sources or factors. Worsening pain can affect well-being, daily activities and sleep [3].

Finally, the baby's weight brings the center of mass more anteriorly, causing fatigue and potential weakness in the intervertebral muscles responsible for spinal self-support, ultimately leading to an accentuation of vertebral curves (e.g., increased lumbar lordosis). Studies by Dumas et al. [4], Ostgaard et al. [5], and Bullok et al. [6] have shown that at least one out of two pregnant women has lower back pain.

According to Kristiansson et al. [7], the prevalence of lower back pain varies between 49% and 61%. Recent studies on the practice of physical exercise recommend encouraging pregnant women, without contraindication, to practice aerobic exercise and muscle strengthening to maintain good physical condition. Walking evolves throughout pregnancy depending on the evolution of the static and the possible appearance of pain [8].

For better balance, the step is increased to widen the support polygon. The movements become parallel and not alternating, and hip and knee flexion amplitudes are significant [9]. Walking can become uncomfortable due to the micro-mobility of the sacroiliac joints and the pubic symphysis [10].

Standardization of the six-minute walk test (6MWT) is mandatory to ensure its reproducibility and static use. The benefits of walking during pregnancy are strengthening the lower body (thighs, glutes, calves) and greatly activating blood and lymphatic circulation. It also provides cardiovascular work and regular cardio-respiratory. It improves the body's physical condition and increases the resistance of the heartbeat and blood vessels 20 to 30 min of daily walking for the first 8 months is necessary to reinforce the benefits of exercise.

Walking offers numerous health benefits for pregnant women, including better weight management, improved blood circulation, heart rate and breathing regulation, and facilitation of childbirth and postpartum recovery. Lacoura [11] recommends walking or fast walking as a safe exercise for pregnant women that poses no risks for the baby or the mother.

Regarding psychological changes, Dayan [12] showed that the prevalence of anxiety disorders is about 14%, and the gender distribution shows an over-representation of the female population.

Capponi and Horbacz [13] report that antenatal anxiety is the most frequent psychological disorder of the perinatal period, with a frequency of 13 to 15% during pregnancy.

According to Relier [14], anxiety induces a state of alertness translated at the physiological level by a specific maternal hormonal secretion. These hormones will also permeate the fetus, which may cause clinical manifestations such as increased fetal movements or the onset of fetal tachycardia.

For Delassus and Thomas [15], the medical profession must address antenatal anxiety as a morbidity factor.

Disorders of self-esteem are a risk factor for the development of psychological disorders. Low self-esteem can lead to discomfort and difficulties in relationships with others. Individuals with low self-esteem may never feel good enough, leading to significant suffering. Valors [16] relied on the psychological aspects of pregnancy and childbirth to promote safe childbirth and optimize the duration of dilation and reduce pain intensity.

Physical activity allows pregnant women to maintain their autonomy and psychological well-being by safeguarding their image and self-esteem [17]. Also, mood disorders that can accompany pregnancy (anxiety, depression, stress, anxiety, low self-esteem) are alleviated by the practice of regular and appropriate physical activity, especially during the third trimester.

Here we test whether prenatal gymnastics and psychological support can help reduce pain, maintain walking, reduce anxiety, and improve self-esteem among pregnant women at the Center Hospitalier du Mont Amba in Kinshasa.

Materials and methods

This quasi-experimental study aimed to demonstrate the benefits of a prenatal gymnastics and psychological support program for pregnant women over 8 months from September 2020 to April 2021. The study was conducted at the Mont-Amba Hospital Center in Kinshasa, Democratic Republic of Congo.

Sample

The sample consisted of 38 pregnant women recruited from prenatal consultations at the Mont-Amba Hospital Center in Kinshasa. The study measured parameters such as anxiety, pain, maximal oxygen consumption, and self-esteem before and after the program.

Scales and measures

Visual analog scale (VAS)

Pain intensity was measured using a self-assessment visual analog scale (VAS) [18]. This scale is in the form of a 10 cm plastic ruler graduated in millimeters. During the pain assessment, the examiner presents a slider to the pregnant woman, which is moved along a straight line. One end of the line corresponds to the absence of pain, while the other represents the maximum imaginable pain. The pregnant woman then positions a cursor along the line, where the intensity of her pain can be read in millimeters. The slider's face features millimeter graduations visible only to the examiner.

Hospital Anxiety and Depression scale (HAD scale)

The Hospital Anxiety and Depression Scale (HAD) questionnaire, a standardized and reliable instrument used to screen for anxiety and depressive disorders, assessed anxiety levels among pregnant women [20]. The questionnaire was administered at the beginning and end of the program, and the scores were categorized as follows: a score of ≤7 indicated an absence of symptoms, a score of 8 to 10 indicated doubtful symptomatology, and a score of ≥11 indicated definite symptomatology.

Rosenberg Self-Esteem Scale

The Rosenberg self-esteem questionnaire was used to assess pregnant women's esteem levels [22]. Scores below 25 indicate very low self-esteem, while scores between 25 and 31 indicate low self-esteem. Scores between 32 and 34 indicate average self-esteem, while scores between 35 and 39 indicate high self-esteem. Scores above 39 indicate very high self-esteem.

Maximum oxygen consumption

Maximum oxygen consumption was measured using the six-minute walk test. Distance traveled was converted into maximum oxygen consumption (VO2max) by the following Enright and Sherill formula [19]:

VO2max = [(distance + (30 × time)/5 × time (in min)], and the average speed was obtained by the ratio of distance traveled (meters) to time taken to cover the distance (seconds).

Average speed = $\frac{\Delta \ell}{\Delta t}$ (m/s)

Support Protocol

Prenatal gymnastics

Aerobic exercise intensity was determined by maternal heart rate (HR) (220age) × 60% for each workout. The program contained: stretching exercises for the muscles of the lower limbs and back (8 min), retroversion of the pelvis and dissociation of the pelvic girdle (5 min), muscle strengthening exercises (abdominal and pectoral (5 min) and back (5 min), and breathing exercises (6 min) (normal breathing, deep inspiration and slow expiration to store enough oxygen for the future mother and child). The sessions ended with relaxation exercises.

Psychological support

This support consisted of cognitive-behavioral therapy and/or interpersonal therapy

Ethical consideration

Written informed consent was obtained from the pregnant women. The study protocol was submitted and approved by the Ethics Committee of the School of Public Health of the Faculty of Medicine of the University of Kinshasa under number ESP/CE/254/2019.

Statistical analysis

Our data was entered into a spreadsheet (Microsoft Excel 2013). The data was then exported into SPSS version 21.0 for Windows software. The comparison of the quantitative parameters was made using the student's t-test. For the qualitative parameters, we used the Chi-square test. *P*-values <0.05 were considered statistically significant.

Results

At the beginning of the program, moderate pain was most prevalent in the lumbar and dorsal spine, affecting 14 and 7 pregnant women, respectively (Table 1). However, by the end of the program, the frequency of mild pain had returned in 3 cases of pregnant women. Overall, a significant reduction in pain across all areas was observed at the end of the program.

Table 1: Distribution of pregnant women according to pain zones

	Before			After		
Area of pain	**n=38 no pain**	**pain**	**%**	**n=38 no pain**	**pain**	**%**
Dorsal spine	28	10	26.3	37	1	2.6
Lumbar spine	25	13	34.2	35	3	7.9
Bowl	31	7	18.4	37	1	2.6
Symphysis	30	8	21.1	37	1	2.6

Table 2 demonstrates that walking ability was the most negatively affected aspect of daily life by pain, affecting 18 out of 38 (47.4%) pregnant women at the start of the program. However, by the end of the program, all pain-associated traits that impacted daily life, including general activity, mood, usual work ability, relationships with others, sleep, and enjoyment of life, had disappeared in all pregnant women.

Table 2: Distribution of the negative consequences of pain on the daily life of pregnant women

Components of daily life affected by		**Before**			**After**			
	Yes	**%**	**No**	**%**	**Yes**	**%**	**No**	**%**
General activity	10	26.3	13	56.5	-	-	-	-
Mood	11	28.9	12	52.2	-	-	-	-
Ability to walk	18	47.4	5	21.7	-	-	-	-
Usual work	10	26.3	13	56.5	-	-	-	-
Relationship with others	2	5.3	21	91.3	1	2.6	22	95.7
Sleep	7	18.4	16	69.6	-	-	-	-
Taste of life	2	5.3	21	91.3	-	-	-	-

Table 3 shows that pregnant women significantly reduced their pain and speed, but their VO2max and distance traveled increased after the intervention program.

Table 3: Comparison of average pain values, distance traveled, oxygen consumption, and speed of pregnant women before and after the intervention.

	Before	**After**	***P*-value**
Parameters	**Mean(SD)**	**Mean(SD)**	
VAS	6(0.42)	1.16(0.38)	0.001
Mesured distance (m)	377.45(34.9)	393(36)	0.001
VO_2 max (ml/kg/m^2)	15.1(1.1)	18.5(1.2)	0.001
Average speed (m/sec)	2.2(0.2)	1.9(0.2)	0.001

VAS: Visual analog scale

We detected a significant difference between the parameters of self-esteem and anxiety after the intervention program (Table 4).

Table 4: Evolution of pregnant women's self-esteem and anxiety scores throughout the program.

	Before	**After**	
Parameters	**n(%)**	**n(%)**	***P*-value**
Rosen Berg			
Low	21 (55.3)	0(0%)	0.001
Medium	17 (44.7)	5(13.2)	0.001
Strong	0(0%)	33(86.8)	0.001
HAD			
Uncertain anxiety	12 (31.6)	37(97.4)	0.001
Questionable anxiety	19 (50)	1(2.6)	0.001
Certain anxiety	7 (18.4)	0(0%)	0.001

HAD: Hospital Anxiety and Depression scale

Discussion

This study aimed to demonstrate that a prenatal gymnastics program and psychological support can reduce pain, maintain walking ability, reduce anxiety, and improve self-esteem among pregnant women at the Center Hospitalier du Mont Amba in Kinshasa.

At the beginning of the program, our study recorded back pain intensities of 26.3% in the dorsal column, 34.2% in the lumbar spine, 18.4% in the pelvis, and 21% in the pubic symphysis. However, after following the prenatal physical and psychological preparation program, pregnant women experienced a significant reduction in pain across all areas, with a 97.47% reduction in the dorsal column, 94.7% reduction in the lumbar spine, 97.4% reduction in the pelvis, and 97.4% reduction in the pubic symphysis.

Furthermore, the prenatal gymnastics program and psychological support improved walking ability from 47.4% at the beginning of the program to a complete improvement by the end. The study also found that the program improved general activity, mood, habitual work, sleep, taste for life, and

relationships with others almost entirely. According to Lawani et al., back pain occurs in approximately 56% of pregnant women, with 18% of cases in the groin [20].

The literature indicates that physical activity during pregnancy can reduce the intensity and number of localized pain areas, sometimes resulting in almost complete pain relief. These findings are consistent with several studies demonstrating the positive effects of physical activity for pain relief during pregnancy [21,22].

These results demonstrate the effectiveness of the muscle-building program, which is consistent with other studies by Garshasbi et al. and Morkved et al. [23,24]. These studies also used the same types of exercises proposed in our study, but our program demonstrated significant benefits beyond those of previous studies.

Additionally, the observed decrease in pain among pregnant women after the intervention program aligns with the findings of Uthman et al. [25], who reported in a recent meta-analysis that physical activity positively affects pain.

Cardiorespiratory endurance is a physical quality that enables individuals to perform daily tasks and can be improved through regular physical activity. Our study also measured this parameter and found significant improvements in distance traveled, maximum oxygen consumption, and walking speed.

Moreover, our study found that the prenatal gymnastics program and psychological support at the Center Hospitalier du Mont Amba in Kinshasa resulted in significant improvements in self-esteem, with 86.8% of pregnant women reporting a ‘strong’ score and a substantial reduction in anxiety, with 97.4% of pregnant women showing improvement.

Previous studies have also shown that pregnant women, particularly primiparous women, benefit from education and support that boosts their confidence as women and future mothers, empowering them to manage their lives and overcome social, economic, and professional obstacles [26]. Education should be provided to improve self-esteem and reduce anxiety in pregnant women.

Limitations

The study's reduced sample size of 38 pregnant women who completed the prenatal gymnastics and psychological support program was influenced by the number of new cases of pregnant women received at the PNC of the Center Hospitalier de Mont Amba in Kinshasa.

Conclusion

The prenatal gymnastics program, when combined with psychological support, effectively minimized pregnancy-related risks, including pain, anxiety, self-esteem, and walking difficulties. Therefore, the program's ongoing implementation in the care of pregnant women is encouraged.

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References

1. Liddle SD, Pennick V. Interventions for preventing and treating low back and pelvic pain during pregnancy Cochrane. Database Syst. Rev. 2015;54(8):574-80.
2. Aldabe D, Ribeno DC, Milosaljevics, Dawn Bussey M. Pregnancy-related pelvic girdle pain and its relationship with relaxing levels during pregnancy a systematic review. European Spine J. 2012;21(9):1769-76.
3. Sinclair M, Close C, McCullough JEM, Hughes C, Liddle SD. How do women manage-pregnancy related low back and for pelvic pain Descriptive findings from an online survey. Evidence Based Midwifery. 2014;12(3):76-82.
4. Dumas G.A, Reid JG, Wolfe LA, Griffin MP, MC Grath MJM. Exercises, posture and back pain during pregnancy. Part J Clin Biomech. 1995;10(2):106-9.
5. Ostgaard HC, Andersson GBJ, Karlsson K. Prevalence of back pain in pregnancy. Spine. 1991;16(5):549-52.
6. Kristiansson P, Svardsudd K, Schoultz VB. Symphyseal pain, and back pain during pregnancy. Am J. Obstet Gynecol. 1996;175(34):1342-47.
7. Nahed M, Ezmerli MD. Exercise in pregnancy. Prim care update for Ob/Gyns. 2000;7(5):260-5.
8. Ageron C. Another way of looking at low back pain during pregnancy. 2000.
9. Lacouara C. Ten good reasons to walk during pregnancy. March, 2017.
10. Dayan J. Clinic and epidemiology of anxiety and depressive disorders of pregnancy and postpartum. J of Obst Gyn and Reproductive Biology, Masson. 2007;35(9):120-6.
11. Capponi C, Horbacz. About the indivisibility of perinatal anxiety. Psych Perspectives. October-December 2007;78(14):43-9.
12. Connect JP. Love him before he is born. Robert Lafond. Responses collection, 1993.
13. Delassus JM. The meaning of motherhood, 1997.
14. Valors M-H. The psychological side of childbirth, Article n°289, December 2000.
15. Leifer M. Psychological changes accompanying pregnancy and motherhood. Genet Psychol Monog, 1977;95(78):55-96.
16. Cleeland CS, Ryan KM. Pain assessment global use of the brief Pain inventory. Ann Acad Med Singapore. 1994;23(6):129-38.
17. Enright PL, Sherill DL. Reference equations for the six-minute walk in healthy adults. Am J Respir Crit Care Med. 1998;158(69):1384-7.
18. Zigmond AS, Smaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67(36):1-370.
19. Teichman Y. Expectant parenthood. In S-Fisher and J. Reason (Eds), Handbook of life stress. Cognition and health. 1988;18(7):3-22.
20. Rosenberg and Ekilium, Test of the self-esteem scale. 1965.
21. Lawani MM, Alihonou E, Akplogan B, Poumart G, Okou L. The effect of prenatal gymnastics on childbirth: a study on 50 sedentary Beninese women during the 2nd and 3rd trimesters of pregnancy. Health. 2003;13(4):235-41.
22. Sternfeld B, Qeensberry CP, Eskenazi B, Vewman LA. Exercise during pregnancy and pregnancy outcome. Med Sci Sports Exercise. 1995;27(3):634-40.
23. Elden H, Ladfords L, et al. Effects of acupuncture and stabilising exercises as adjunct to standard treatment in pregnant women with pelvic girdle pain: randomized single blind controlled trial. UPKOGRP, March, 2005.
24. Garshasbi, A, Zadech SF. The effect of exercise on the intensity of low back pain in pregnant women. Int J Gynecol Obstet, 2005;88(10):271-5.
25. Uhlendorf, D. Reference values for cardiopulmonary exercise testing for sedentary and active men and women. Arq Bras Cardiol. 2011;96(16):54–9.
26. Chantrain VA, Reychler G. Evaluation of exercise tolerance in pregnant and postpartum women. Revue de Physiothérapie. 2015;15(8):168-75.

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Case report

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A rare case after Nissen fundoplication: Esophageal bezoar

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Abstract

A 33-year-old female patient was admitted to our clinic with complaints of nausea and vomiting for two days and the inability to tolerate food. The patient had a Nissen fundoplication three years ago. Computed tomography (CT) showed a bezoar image in the distal esophagus. The patient stated that the symptoms began after he ate a persimmon two days ago. The patient underwent esophagogastroduodenoscopy. A bezoar was observed in the distal esophagus at the esophagogastric junction. No pathology was observed in the stomach and duodenum. After the bezoar was shredded with a snare and removed with a retrieval snare. Here, we further describe this case of a bezoar that caused ileus in the distal esophagus after a fundoplication operation.

Keywords: nissen fundoplication, esophageal bezoar, upper gastrointestinal ileus

Introduction

Bezoars are clusters of indigestible substances in the esophagus, stomach, and intestinal tract. They can be found anywhere from the esophagus to the rectum [1]. While most patients are asymptomatic, some patients may experience pain, early satiety, weight loss, and bloating. Esophageal bezoars usually present with nausea, vomiting, dysphagia, intolerance to food, retrosternal pain, and gastroesophageal reflux (GER) [2]. The main cause of esophageal bezoars is dysfunction of the lower esophageal sphincter, motility disorders, or structural abnormalities [3]. After fundoplication operations, the passage of hard-to-digest foods becomes difficult due to the relative narrowing of the lower esophageal sphincter. Here, we describe a patient who had a Nissen fundoplication operation three years ago and then developed a bezoar after eating a hard-to-digest persimmon.

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

Conflict of Interest
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Case presentation

A 33-year-old female patient applied to our clinic with complaints of nausea, vomiting, and intolerance of food that began two days prior. She stated that the symptoms began after eating a persimmon two days ago. The patient had a history of Nissen fundoplication surgery three years ago. There was no other feature in her medical history.

Physical examination was conscious-open and cooperative. Vital findings were stable. The abdominal examination had no pathological findings. She vomited 5-6 times a day. She had signs of GER. There was a feeling of obstruction in the retrosternal region. Considering the previous operation, computed tomography (CT) was performed for screening. CT examination revealed a mass of approximately 26x24 mm, which was thought to be a bezoar on the distal esophagus (Figure 1 and 2).

Figure 1: CT axial section of the bezoar distal esophagus.

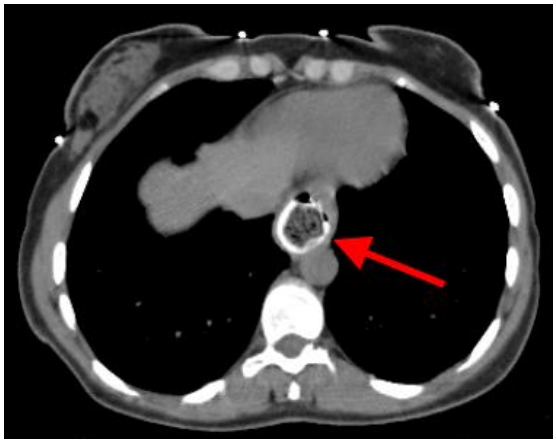
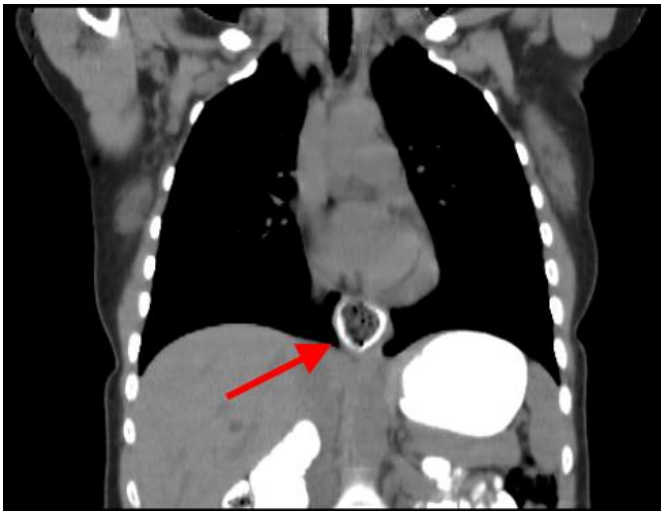


Figure 2: CT coronal section of the bezoar distal esophagus.



An esophagogastroduodenoscopy (EGD) was then planned under sedation anesthesia. This showed a bezoar seated at the esophagogastric junction (Figure 3). There were superficial ulcerated areas at the junction due to chronic irritation. The cardia endoscope was tightly wrapped. No pathology was observed in the stomach and duodenum. The bezoar was then cut into several pieces with a snare. The pieces were removed individually with a retrieval snare (Figure 4). Our patient was started on a fluid regimen on the fourth hour after the procedure and then tolerated the strict regime. The patient had oral tolerance and was discharged the same day. Written informed consent form was obtained from the patient.

Figure 3: Endoscopic view of the bezoar.

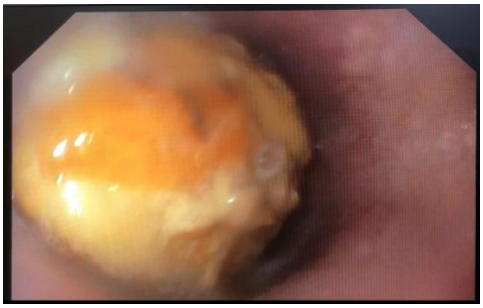
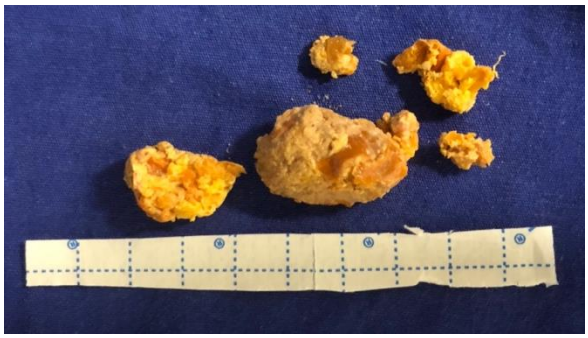


Figure 4: Bezoar removed one by one many pieces.



Discussion

Patients with food impaction often have underlying esophageal pathology. The risk is increased in people with previous gastrointestinal surgery [4]. The fact that most of the patients with esophageal bezoars have a history of Nissen fundoplication surgery showed that this surgical intervention, which is widely used in the treatment of hiatal hernia and reflux esophagitis, paves the way for esophageal bezoars [2]. Esophageal bezoars are extremely rare, and only a few case reports have described esophageal bezoars. There are very few case reports specifically seen after fundoplication [3].

Patients with bezoars in the gastrointestinal tract are usually easily diagnosed. CT is helpful in diagnosis. However, the gold standard for diagnosis is endoscopy for upper gastrointestinal bezoars [4]. CT is the most commonly used imaging method in the diagnosis of bezoars and is very useful for definitive diagnosis in patients with intestinal obstruction [5]. However, endoscopy remains the gold standard for research because it can directly visualize and treat the condition [6]. In our case, we first determined the location of the bezoar via a CT scan. We then removed the bezoar with endoscopy.

Foreign bodies and bezoars in the esophagus should be removed within 24 hours because delays in the removal may increase the risk of complications. These complications include perforation, obstruction, and narrowing [4]. We removed the bezoar by endoscopy at the sixth hour of hospitalization in our case. The procedure was completed without complications.

Bezoar removal in the esophagus is most commonly done by pushing food into the stomach or mechanically removing it. As in our patient, it may be difficult to push the bezoar into the stomach in patients who have undergone fundoplication. The use of proteolytic enzymes is also not recommended due to the risk of perforation. Mechanical dissection is recommended to safely treat esophageal bezoars [7].

The ultimate goal of bezoar treatment is removal of the mass and prevention of its recurrence. The treatment options available for this condition should be well evaluated. The minimal

benefits to patient should be considered [1]. Surgery is a difficult decision for esophageal bezoars. Rather, minimally invasive interventions with endoscopic procedures are preferred.

Conclusion

Esophageal bezoars should be considered in patients with a history of Nissen fundoplication operation when gastrointestinal obstruction is encountered with nausea, vomiting, and a feeling of obstruction in the retrosternal region. In such cases, CT may be first requested to support the diagnosis. Clearer imaging can be done with endoscopy. Endoscopy should not be delayed after a history of fundoplication and a pre-diagnosis of bezoars. More importantly, it should not be forgotten that it can be treated with endoscopy. It is safer to disintegrate the bezoar rather than push it into the stomach in patients with a history of fundoplication operation.

References

1. Mohammadi A, Mojtahedzadeh M, Ahmadi A, Imanipour MH, Saghafi F, Soltaninejad S, et al. Bowel Obstruction by Persimmon Phytobezoar. IJMTFM. 2021; 11(3):32507. doi: 10.32598/ijmtfm.v11i3.32507.
2. Gökbulut V, Kaplan M, Kaçar S, Akdoğan Kayhan M, Coşkun O, Kayaçetin E. Bezoar in upper gastrointestinal endoscopy: A single center experience. Turk J Gastroenterol. 2020 Feb;31(2):85-90. doi: 10.5152/tjg.2020.18890.
3. Georgiev YP, Karashmalakov AG, Zafirov GK. Esophageal bezoar after repeated fundoplications. Quant Imaging Med Surg. 2018 Mar;8(2):257-8. doi: 10.21037/qims.2017.06.07.
4. Ustaoğlu M, Paköz ZB. Üst Endoskopide Yabancı Cisim Saptanan Hastaların Analizi: Doğu Karadenizde Tek Merkezli Retrospektif Çalışma. Kırıkkale Üniversitesi Tıp Fakültesi Dergisi. 2020;22(1):1-6. doi: 10.24938/kutfd.586116
5. Altintoprak F, Dikicier E, Deveci U, Cakmak G, Yalkin O, Yucel M, Akbulut G, Dilek ON. Intestinal obstruction due to bezoars: a retrospective clinical study. Eur J Trauma Emerg Surg. 2012 Oct;38(5):569-75. doi: 10.1007/s00068-012-0203-0.
6. Khalil H, Parmar C, Sufi P. Conservative Managing of Bezoar in Giant Hiatus Hernia Causing Gastric Outlet Obstruction During the COVID-19 Pandemic. Obes Surg. 2021 Jun;31(6):2780-2. doi: 10.1007/s11695-021-05250-y.
7. Padhya K, Dhamija A, Carlson C, Farivar A. Post-Fundoplication Esophageal Bezoar Resolved With Endoscopic Instillation and Oral Ingestion of Cola. The American Journal of Gastroenterology. October 2019;114:S1022-3. doi: 10.14309/01.ajg.0000596816.59903.5b.