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EDITORIAL

Dear Readers,

In this first issue in 2023, we have received 12 original articles from different fields of medicine. The interest in our journal, and therefore both the number and quality of our articles, is increasing day by day. Recently, our journal Journal of Medicine and Palliative Care (JOMPAC) entered TR-Dizin ULAKBİM, and strong indexes. We thanks our valuable colleagues who contributed as authors, and to everyone who contributed to the journal.

Best Regards

Prof. Aydın ÇİFCİ, MD
Editor-in-Chief

CONTENTS

Original Article

Original Article

MEDICINE PALLIATIVE CARE

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J Med Palliat Care 2023; 4(1): 1-6

Children with ADHD were affected in terms of mental health and quality of life during the COVID-19 pandemic

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ABSTRACT

Aim: COVID-19 pandemic has had negative effects on the lives of many children and adolescents with psychiatric disorders. This research aims to investigate the effects on the mental status and quality of life of children with ADHD during the COVID-19 pandemic.

Material and Method: This study was conducted at the child and adolescent psychiatric outpatient clinic of a university hospital, between April and May 2020. The research group consisted of 113 children and adolescents with ADHD, and the control group consisted of 45 children and adolescents. The depression and anxiety symptoms of the children were assessed using the Child Depression Inventory (CDI) and the Screen for Child Anxiety-Related Emotional Disorders (SCARED), respectively. Child-reported and parent-reported Pediatric Quality of Life Inventories (PedsQL) were used to evaluate the health-related quality of life of the children.

Result: Depressive symptoms and anxiety levels were found to be statistically higher in the ADHD group. According to PedsQL-P scale, psychosocial and scale total scores were statistically significantly lower. According to the regression analysis, the SCARED scores predicted negative physical, psychosocial, and total scores of the PEDsQL-C scale. The CDI scores, however, predicted negative physical, psychosocial, and total scores of the PEDsQL-P scale.

Conclusion: This study revealed that in the COVID-19 pandemic, children with ADHD are more affected in terms of depression, anxiety and quality of life than children without any psychiatric disease. The study findings suggest that further studies are needed to better understand the psychological conditions and difficulties that children with ADHD experience during the COVID-19 pandemic.

Keywords: Attention-deficit/hyperactivity disorder, children, COVID-19, depression, anxiety, life of quality

INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by problems with attention deficit, mobility, impulsiveness and executive functions, starting in childhood (1,2). Around the world, 5-12% of children are known to be affected by ADHD (3). Due to this high prevalence, ADHD is also defined as a public health problem (4,5).

The COVID-19 pandemic directly causes widespread anxiety, fear, and panic in all age groups and segments of society (6-9). Children and young people, and individuals with chronic physical and psychiatric illnesses are especially vulnerable in this regard (10). The inability of children and young people to attend school, being subjected to physical restrictions, and the negative effects of the quarantine process on both children and their parents leads to significant negative mental effects experienced by families. (8,11-14).

In a recent study, Fonseca et al. (15) found that patients with schizophrenia were at serious risk both physically and psychologically during this pandemic. Research conducted by Hao et al. (16) with patients who received treatment for psychiatric diagnoses revealed that the pandemic worsened their psychiatric symptoms.

It is known that carelessness, mobility, and executive dysfunction in individuals with ADHD are directly linked to individuals' quality of life and daily functionality (17,18). However, mood disorders, such as depression and anxiety, are known to have negative effects on irritability, emotional liability, and core symptoms of ADHD in individuals with ADHD (19,20). Moreover, daily functionality and quality of life have negative effects on the relationship between ADHD and mood symptoms (21). Therefore, the effects of physical and social restrictions on children's mental health during the COVID-19 pandemic and

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the management strategies for the resulting problems are of importance in a disease such as ADHD, where social communication and mobility are at the forefront (22). A study investigating the stress levels, behavioral symptoms, and mood levels of school-age children with ADHD during the pandemic has shown that negative mood levels are associated with ADHD symptoms and that parents' mood affects the child's ADHD symptoms (23). In a literature review, there was no other research investigating the psychological effects of the pandemic process on individuals with ADHD.

It is of great importance to respond to the psychological effects of the COVID-19 pandemic, in a timely manner, in every age group and every disease group (24). When planning these interventions, it is necessary to determine the effects of the pandemic in individuals receiving psychiatric treatment. This research aims to investigate the effects of the COVID-19 pandemic on the psychological state and quality of life of children with ADHD.

MATERIAL AND METHOD

The study was carried out with the permission of Necmettin Erbakan University Meram Faculty of Medicine Non-Pharmaceutical and Medical Device Researches Ethics Committee (Date: 08.05.2020, Decision No: 2020/2482). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Participants

The study group consisted of patients with ADHD in aged 7-17 years and their parents. A total of 113 children and adolescents with ADHD and 45 healthy controls were included in this study. The patients were diagnosed in the pediatric and adolescent psychiatric outpatient clinic of a university hospital, according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria and were followed up and treated for at least 6 months. Inclusion criteria for the study group were to be under follow-up and medication with the diagnosis of ADHD, and to be between the ages of 7-17. The exclusion criteria included the presence of major physical, endocrine or neurologic disorders, autism spectrum disorder, psychotic disorder, bipolar disorder, substance use disorder, severe head injury, intellectual disabilities and comorbid psychiatric disorders. The control group comprised healthy, volunteer children and adolescents aged 7-17 years and their parents. Children with normal cognitive and social development were included in the control group of the study. The same exclusion criteria were also applied to the control group. Those who previously received a psychiatric diagnosis and treatment were not included in the control group.

This study was conducted between May – June 2020. Children and adolescents followed up with the diagnosis of ADHD were re-evaluated between these dates. Written and oral consents were obtained from the participants and the parents after the researchers explained the purpose and course of the research.

Procedure

In order to determine the depression and anxiety levels of the participants who received ADHD treatment, who had no comorbid psychiatric disorders, and were diagnosed as having ADHD according to the Schedule for Affective Disorders and Schizophrenia for School-Aged Children, Present and Lifetime Version (K-SADS-PL) in our clinic, they were asked to complete the Children's Depression Inventory (CDI), and the Screen for Child Anxiety-Related Disorders (SCARED). Then, both children and adolescents and their parents were asked to complete the Pediatric Quality of Life Inventory.

Schedule for Affective Disorders and Schizophrenia for School-aged Children–Present and Lifetime Version

The K-SADS-PL is a semi-structured interview method that was developed by Kaufman et al. (25) to identify psychiatric disorders that children and adolescents experience in the past and present. The K-SADS-PL is implemented by interviewing the child and the parent face-to-face, and as a result, data are collected from various sources (parents, children, and schools), evaluated, and finalized. If there is a discrepancy in the data from different sources, the physician uses their clinical opinion to solve the problem. The validity and reliability study of the Turkish version of this interview form was conducted by Gökler et al. (26). The DSM-5 adaptation study of the K-SADS-PL for Turkey was performed by Ünal et al. (27).

Children's Depression Inventory (CDI)

This scale, developed by Kovacs, is used to measure the level of depression in children. It is a self-assessment scale and can be applied to children and adolescents aged 6-17 years (28). The scale consists of a total of 27 items. Each item contains three sentences in which the child evaluates their last two weeks and chooses the most appropriate statement. The answers given are scored between 0 and 2 points. The depression score is obtained by summing up these scores. The highest score possible on the scale is 54. An increased total score indicates an increased severity of depression. The cut-off score of the scale for a diagnosis of depression is 19 points. Its Turkish adaptation was conducted by Öy (29).

Screen for Child Anxiety Related Disorders (SCARED)

SCARED is used to measure anxiety levels in the children and adolescents. It was developed by Birmaher

(30). Each item in the 41-item scale is rated 0, 1 or 2 according to the severity of the symptoms. The higher the total score, the more severe the level of anxiety. The validity and reliability study for the Turkish population was conducted by Karaceylan(31).

Pediatric Quality of Life Inventory (PedsQL)

PedsQL is an overall quality of life scale that assesses the physical and psychosocial experiences of children in the 8-18 years' age group. There are two separate forms of the scale that assess 8-12-year-olds and 13-18-year-olds. Scoring is performed in three areas on the scale. The first is the scale total score, the second is the physical health total score, and the third is the psychosocial health total score, which assesses social and school functionality. On this scale of 23 items, each item is scored in the range of 0-100. The score taken is 100 if all the responses are 'never', 75 if all are 'rarely', 50 if all are 'sometimes', 25 if all are 'frequently', and 0 if all are marked as 'almost always'. The Turkish validity and reliability study of both parts was conducted by Memik et al (32,33).

Data Evaluation and Statistical Analysis

Statistical analysis of the data was performed using the Statistical Package for the Social Sciences (SPSS) version 23.0. Skewness and Kurtosis statistics were used to evaluate the normality of distribution of the data. Student's t-test was used to evaluate quantitative data. The Chi-square ($\chi 2$) test or Fisher's exact Chi-square test was used for intergroup comparisons of quantitative data. Pearson's and Spearman correlation tests were used to investigate the relationship between two measured values in the groups. $P<0.05$ was accepted as the level of statistical significance in all analyses. The effects of different variables on the occurrence of quality of life variables in the patients with ADHD in univariate analysis were analyzed, and the variables for which the unadjusted p-value was <0.10 in logistic regression analysis were identified as potential risk markers and included in the full model. We reduced the model by using backward conditional elimination multivariate logistic regression analyses and eliminated potential risk markers by using likelihood ratio tests.

RESULTS

The study included 113 children and adolescents with ADHD, and 45 children and adolescents in the control group. There was no significant difference between the patients and the control group in terms of age, sex, and maternal and paternal education levels. The demographic characteristics of the study population are presented in **Table 1**.

Table 1. Demographic and clinical characteristic of patients and healthy controls

	Patient (n=113)	Control (n=45)	t or x^2	p
Age (year)	11.89 (3.38)	12.27 (3.64)	-.611	0.54
Sex, male/ female	59/54	19/26	1.285	0.25
Education (year)				
Mother	10.44 (3.39)	9.61 (3.01)	1.222	0.22
Father	12.56 (2.69)	11.81 (2.32)	1.398	0.16

Depressive symptoms and anxiety levels were found to be statistically higher in the ADHD group (**Table 2**). There was no statistically significant difference between the groups in terms of total and sub-scale PedsQL-C scores (**Table 2**). According to the PedsQL-P scale, psychosocial and scale total scores were statistically significantly lower. However, there was no statistically significant difference in terms of physical levels. In addition, the quality of life and psychological variables of the children and adolescents in the ADHD group were also compared with each other. According to this, the depressive symptom level of adolescents (16.06±8.17) was statistically higher than that of children (11.75±6.96) (z= -2.99, p=0.003). In terms of the levels of anxiety and quality of life, there was no statistically significant difference between the children and adolescents in the ADHD group.

Table 2. Quality of life and levels of psychological variables in ADHD and Control group

	Patient (n=113)	Control (n=45)	t or z	p
CDI	13.73 (7.8)	8.18 (5.23)	-4.25[b]	<0.001
SCARED	31.79 (15.74)	25.48 (11.92)	2.72[a]	0.007
PedsQL-C				
Physical	81.94 (12.24)	81.38 (13.30)	-0.21[b]	0.82
Psychosocial	79.57 (9.72)	82.59 (9.45)	-1.77[a]	0.07
Total	80.39 (8.93)	82.17 (9.09)	-0.95[b]	0.34
PedsQL-P				
Physical	71.14 (19.13)	78.19 (14.26)	-1.83[b]	0.06
Psychosocial	61.95 (19.21)	82.81 (11.55)	-8.03[a]	0.016
Total	65.27 (16.43)	81.20 (10.76)	-5.94[a]	<0.001

PedsQL-C, Pediatric quality of life inventory child version; PedsQL-P, Pediatric quality oflife inventory parent version; CDI, Child depression inventory; SCARED, Screen for child anxiety-related emotional disorders. [a] Student'st-test. [b] Mann–Whitney test.

The correlation between PedsQL scores and psychological variables of children with ADHD was also evaluated. A negative correlation was found between the total and sub-scale scores of both PedsQL-C and PedsQL-P scales and the CDI and SCARED scores (**Table 3**).

Table 3. Correlation between PEDsQL and psychological variables in ADHD group

PedsQL-C	CDI		SCARED	
	r	p	r	p
Physical health	-.255**	0.006	-.266**	.004
Psychosocial	-.2630**	0.005	-.354**	<0.001
Total	-.369**	<0.001	-.394**	<0.001
PedsQL-P				
Physical health	-.356**	<0.001	-.246*	0.014
Psychosocial	-.482**	<0.001	-.290**	0.004
Total	-.479**	<0.001	-.302**	0.002

PedsQL-C, Pediatric quality of life inventory child version; PedsQL-P, Pediatric quality oflife inventory parent version; CDI, Child depression inventory; SCARED, Screen for child anxiety-related emotional disorders. *<0.05 **<0.01

The effects of the psychological variables on PEDsQL were evaluated using linear regression analysis. According to the analyses, the SCARED score predicted negative physical, psychosocial, and total scores of the PEDsQL-C scale (β= -0.236, p<0.001, β= -0.198, p=0.008, β= -0.211, p=0.002, respectively). The CDI score, however, predicted negative physical, psychosocial, and total scores of the PEDsQL-P scale (β= -0.672, p=0.033, β= -1.243, p<0.001, β=-1.023, p<0.001, respectively).

DISCUSSION

In this study, depressive symptoms and anxiety levels were higher in the ADHD group than in the control group. According to the parental form of the Quality of Life scale, psychosocial and total health scores were lower in the ADHD group than in the control group. However, the physical health score was low compared with the controls. Similarly, there were no differences between the groups in terms of total and sub-scale scores, according to the pediatric form of the Quality of Life scale. In addition, the distribution of psychiatric factors in the children was assessed to investigate whether they affected the quality of life outcomes. Regression models showed that the anxiety symptoms in the children affected the quality of life reported by the children. Moreover, it was found that depressive symptoms in children affected the quality of life reported by the parents.

The anxiety and fear caused by the pandemic is one of the important negative effects of this situation, in addition to the deadly effects of the COVID-19 pandemic (8). Although these effects have an impact on all segments of society, it is an undeniable fact that children and young people are more vulnerable in this regard (13,34). However, individuals experiencing physical or psychiatric problems, in particular, are more vulnerable in this regard (9). Current psychiatric symptoms may increase during this process and may become difficult to treat. Therefore, it is essential to apply timely and appropriate mental interventions. For appropriate interventions to be implemented, it is of importance to know the effects of the pandemic, especially in selected disease groups. However, data on these populations are highly limited. In diseases such as ADHD, which are known to be more affected by symptoms of anxiety and depression than the normal population, it is important to determine the level of exposure to the pandemic for appropriate interventions (school holiday and curfew). The study of Zhang et al. (23) the only study in the literature that we could find, found that children's negative mood was associated with ADHD symptoms, and the parents' mood also affected the symptoms of ADHD. However, this study did not make a comparison with healthy children, so it is not possible to determine how much the patients with ADHD were affected compared with the normal population. Moreover, the symptoms of anxiety were not fully determined and the quality of life and daily functioning of the children who had severe difficulties during the quarantine processes were not evaluated. Our research provides the first data in the literature in this context; both anxiety and depression symptoms were statistically significantly higher in children and adolescents with ADHD than in the healthy control group. These results show that children and adolescents with ADHD experience more symptoms of depression and anxiety compared with general society during the pandemic.

The COVID-19 pandemic has led to changes in children's daily routines in many countries, such as attending school and spending time with friends. Given the importance of adequate social functionality and healthy peer relationships for the optimal development of children, the COVID-19 pandemic can be stated as affecting children mentally and socially (35). Children with ADHD are reported to have lower quality of life and greater difficulties in their daily lives compared with their peers (36). In this study, parents of children with ADHD reported a worse quality of life in physical and total areas compared with the control group. This may indicate significant difficulty in staying at home in the ADHD group, where mobility and disorganization are prominent. The absence of differences in psychosocial quality of life in children with ADHD may be due to the fact that children are maintaining both academic and peer relationships through the Internet during the COVID-19 pandemic. This is because children with ADHD are reported to have greater difficulties in social skills and have excessive use of the Internet and technology (37). In contrast to their parents, children with ADHD reported no worsening in their quality of life in this study. This may suggest that, given the disorganization, distraction, and difficulty in planning and organization in children with attention-deficiency (17,18), they may have trouble fully interpreting the possible ongoing effects of the COVID-19 pandemic process on their lives. As far as we can assess,

no study in the literature has investigated the quality of life of children with ADHD during the pandemic. However, a recent study that evaluated children with immunodeficiency reported that quality of life was worse in children at risk of depression/anxiety (10).

The present study showed that increased anxiety and depression scores were associated with worsening in the quality of life in children with ADHD and their parents. Moreover, increased depression scores predict a related worsening in children's physical and psychosocial quality of life, according to their parents. Increased anxiety scores, however, were associated with worsening physical and psychosocial quality of life of children with ADHD, according to children's self-reports. Given this information, it can be suggested that the children's quality of life worsens, according to their own views, as their anxiety increases during the pandemic, whereas this process does not lead to a negative manifestation of the children's quality of life, according to their parents. In contrast, increased depressive symptoms in children may make the deterioration in children's quality of life more visible to parents. In line with our findings, a systematic review reported that psychiatric conditions such as anxiety and depression in children with ADHD worsened their quality of life (38).

As far as we know, this study is the first to investigate the quality of life of children with ADHD during the COVID-19 pandemic. Moreover, the study is of importance as being the first study in which the depression and anxiety levels in children are compared with a control group. The most important limitation of this study is that it does not reveal causality because it is a cross-sectional study. In addition, as a limitation, the effects of any psychiatric conditions of the parents on their children were not evaluated in the study.

CONCLUSION

Finally, the findings of this study have important implications. The study findings suggest that further studies are needed to better understand the psychological conditions and difficulties that children with ADHD experience during the COVID-19 pandemic. In addition, the problems in psychological conditions and quality of life seen in the ADHD group will contribute to the planning of preventive interventions for these children.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Necmettin Erbakan University Meram Faculty of Medicine Non-Pharmaceutical and Medical Device Researches Ethics Committee (Date: 08.05.2020, Decision No: 2020/2482).

Informed Consent: Written and oral consents were obtained from the participants and the parents after the researchers explained the purpose and course of the research.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: No conflict of interest was declared by the author

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Author Contributions: The author declares that he has responsible for the design, execution, and analysis of the paper and that he has approved the final version.

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Original Article

MEDICINE PALLIATIVE CARE

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Effect of relaxation exercises on dyspnea and sleep quality in chronic obstructive pulmonary disease

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ABSTRACT

Aim: Sleep disorders is one of the most common problems after respiratory symptoms in patients with COPD. The probability of sleep disorders increases at the same rate with the severity of COPD symptoms. The aim of our study is to evaluate the effect of relaxation exercises on dyspnea and sleep quality in COPD patients receiving optimal bronchodilator therapy.

Material and Method: This is a randomized controlled clinical study. The study was conducted with 67 voluntary patients with COPD who admitted to the Muğla Traininng and Research Hospital Chest Dieseases Outpatient Clinic. The study was planned as pretest and posttest clinical trial which included COPD patients with severe dyspnea and patients were randomly distributed to the intervention and control groups. Patients in the intervention group (n=34) were given relaxation exercises to be practiced at home for six weeks. Patients in the control group (n=33) were given breathing exercises. During this period, all patients continued to receive routine medical treatments. At baseline and after the intervention dypsnea and sleep quality was assessed.

Results: There was a significant decrease in the posttest Modified Borg Scale-MBS, Modified Medical Research Council Scale-mMRC medians ($p<0.001$) in intervention group. Additionally a significant improvement in Global Pittsburgh Sleep Quality Index (PSQI) ($p<0.001$) and also some sleep quality subscales including subjective sleep quality ($p<0.001$), sleep latency ($p=0.029$), sleep duration ($p<0.001$), sleep efficiency ($p=0.047$) and daytime dysfunction ($p<0.001$) were found in the intervention group.

Conclusion: We think that relaxation exercise, which is simple and an easy-to-apply method would provide a decrease in the dyspnea severity and an improvement in sleep quality of the patients with COPD when added to the optimal medical treatment.

Keywords: COPD, relaxation exercises, dyspnea, sleep quality

Our research's data was presented in 24. National Congress of Turkish Thoracic Society as 'E-poster Presentation' on November 2021.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is an is a preventable and treatable chronic inflammatory lung disease with permanent airflow limitation, airway and alveolar abnormalities (1). COPD is characterized by long-term respiratory symptoms. COPD is an increasing public health problem. It causes serious incapacity and economic burden in the societies where it is seen. As a result of airflow limitation in COPD, patients admit to hospitals with various symptoms such as shortness of breath, chronic cough, sputum, weakness and fatigue. Sleep disturbance is one of the most common symptoms reported by COPD patients (2). Sleep duration, effectiveness and quality may decrease due to the degree of dyspnea, which is the most important symptom in COPD. Sleep quality is often impaired in patients with COPD, which is likely to be an important factor in the chronic fatigue, sleepiness and overall impairment in quality of life reported by these patients (3).

The main purpose of the pharmacological treatment of COPD is improve a patient's functional status and quality of life by preserving optimal lung function, improving symptoms, and preventing the recurrence of exacerbations. Currently, none of the pharmacological treatments have been shown to significantly improve lung function or decrease mortality (4-7). There is an increasing interest in non-pharmacological treatment methods of COPD. Pulmonary rehabilitation is one of these non-pharmacological treatment methods in patients with COPD. Pulmonary rehabilitation is a central aspect of the treatment of COPD, for which treatment other than smoking cessation and long-term oxygen therapy largely aims at improving symptoms.

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Pulmonary rehabilitation is described as an 'individually tailored and designed, multidisciplinary programme of care' for patients with chronic respiratory impairment. The Global Initiative for Chronic Obstructive Disease suggests that pulmonary rehabilitation be included in the management of patients with chronic obstructive pulmonary disease (COPD) categories B, C, and D (1). Pulmonary rehabilitation programs in COPD are usually personalized programs (8). The best results come from 6-8 week programs those are performed in rehabilitation clinics. As an alternative to pulmonary rehabilitation, the relaxation exercises those can be done at home are used for the patients who can not require going to any special center.

In this study, we aimed to demonstrate the effectiveness of relaxation and breathing exercises on sleep related disorders in COPD patients with severe dyspnea who were under optimal bronchodilator treatment.

MATERIAL AND METHOD

For this study, the approval of Muğla University Faculty of Medicine Clinical Researches Ethics Committee (Date: 05.09.2019, Decision No: 11/VI) was received. All procedures were carried out in accordance with the with the ethical rules and the principles of the Declaration of Helsinki. This randomized controlled study was conducted with COPD patients who applied to the Chest Diseases Outpatient Clinic at Muğla Training and Research Hospital between September 2019–January 2020. The sample size was calculated by using G Power 3.1.9.4. Considering possible losses (10%), it was planned to reach approximately 72 COPD patients (36 patients for intervention and 36 patients for control). Dyspnea severity was assessed by Modified Medical Research Council (MMRC) Dyspnea Scale ≥2. Seventy eight COPD patients with high dyspnea score were interviewed between September 2019 and January 2020. The exclusion criterias were having hearing, neurological or psychological problems, presence of immunosuppressive state, oncological disease, decompensated heart failure or acute myocardial infarction. Also, the patients who participated another rehabilitation program were excluded. Six patients who did not meet the research criteria and did not want to participate were excluded from the study. Seventy two COPD patients of our outpatient clinic were included. The demographic data, smoking status, mMRC scores, spirometry parameters and oxygen saturation (SpO_2) were recorded. The participants were randomized 1:1 to either a supervised training intervention group (INT, n=37) or a control group (CON, n=35). The baseline Modified Borg Scale (MBS) and Pittsburgh Sleep Quality Index (PSQI) of the all participants were calculated. Training with relaxation exercises were given to 37 COPD patients who were determined as the intervention group. The control group had training for only breathing exercises.

Relaxing Exercises

Content of relaxation exercises was formed as lower extremity exercises, upper extremity exercises and breathing exercises. The appropriate number and set of repetitions of each exercise were adjusted to the patient. The continuation of the exercise program was ensured for about 30 minutes a day and for 6 weeks. Lower extremity exercises consisted of ankle pumping exercise and bedside knee flexion-extension exercises. In the ankle pumping exercise performed to control the circulation and prepare the patient for the exercise program, the individual was arranged to breathe while pulling his foot towards himself (dorsiflexion) and to exhale while pushing his foot (plantar flexion). Similarly, in the bedside knee flexion-extension exercise, he was shown to inhale while bending the knee (flexion) and exhale while straightening the knee (extension). Upper extremity exercises consisted of shoulder abduction, shoulder flexion and circumduction movements to be performed with breath control. The degree of joint range of motion was determined according to the patient, and he was taught to breathe in each exercise in which the rib cage expanded and to exhale while relaxing.

Breathing Exercises

Breathing exercises were composed of pursed-lip breathing, thoracic expansion exercises, and diaphragmatic breathing components. For pursed lip breathing, the patient was taught to breathe deeply through the nose and exhale through the mouth. Training was given for respiratory control so that the exhalation time was twice the inhalation time. Thoracic expansion exercises were given to help the patient's lung segment especially needed to be ventilated. For diaphragmatic breathing exercises, in order to stimulate deep breathing and increase breathing volume, the patients were asked to put their hands on their stomach while they were in the supine position and inflate the bottom of their hands with the breath they took through their noses.

Exercise trainings were given practically for 30 minutes in a quiet room by a physiotherapist. Illustrated hand brochures explaining the exercises were distributed to the patients at the end of the education. They were asked to take notes of the time of daily exercise for both groups. All of the participants were called two weeks after the initial training. They were asked whether they did the exercises correctly and whether they repeated each day. Those who exercised for about 20-30 minutes

every day were considered to be fully compatible with the program. Those who exercised for less than 20 minutes, not less than 5 days a week, were considered as partially compliant. Those who exercised less than 5 days a week and for less than 20 minutes were considered as non-compliant with the program. Two patients in the intervention group left the study due to hospitalization with COPD exacerbation. One patient was excluded from the intervention group because of newly diagnosed neurological disorder. Two patients in the control group left the study because one of them was admitted to the intensive care unit due to COPD exacerbation and the other one did not want to be followed up. Thirty four patients in the intervention group, thirty three patients in the control group completed the research process. At the end of six weeks, patients in both groups were called to the clinic for the application of spirometry, SpO_2 measurement, mMRC, MBS and PSQI scales as a post-test. Data were collected by the researcher through face-to-face interviews. Each interview lasted approximately 25-30 minutes for a single patient.

Statistical analyzes and figures were performed with "Jamovi project (2020), Jamovi (Version 1.1.9.0) with [Computer Software] (Retrieved from https://www.jamovi.org). The significance level was taken into account as 0.05 (p-value) in statistical analyzes. Descriptive statistics were shown as mean ± standard deviation and median values. Categorical variables were summarized as a percentage. Independent Samples t-test was used in two independent group comparisons if it showed normal distribution. In other cases, the Mann Whitney U test was used if it did not show normal distribution. Changes between two measurement values taken from the same individuals were evaluated with Paired Samples t-test when numerical variables showed normal distribution. Wilcoxon test was used in cases where it did not show normal distribution. Differences between categorical variables were compared in 2x2 tables with Pearson Chi-Square and Fisher's Exact Test. The relationship between numerical variables were examined with Spearman's Rho Correlation coefficient.

RESULTS

A total of 67 patients completed the study. Sixty five (97%) were male and two (3%) were female. The mean age was 68.5±8.3 years. The general demographic data of the groups were summarized in **Table 1**. There was no significant demographic difference between the groups. It was determined that there was a statistically significant difference in smoking status between the groups (p=0.027). There was not any statistically significant difference in the comparison of some other clinical data of individuals. **Table 2** includes the smoking status, comorbidities and some clinical data of the individuals included in the study. The mMRC and MBS scores of the intervention group after six weeks of training with relaxing exercises were lower than the control group. The decrease in the post mMRC score and the increase in the post SpO2 were significant in the intervention group. The changes in FEV1 (%), FVC (%), SpO2 (%), mMRC and MBS scores summerized in **Table 3**. The post total PSQI, sleep quality and daytime dysfunction scores were significantly low in the intervention group (**Table 4**). The changes in sleep latency, sleep duration and sleep efficiency scores were significant after training with relaxing exercises (**Table 4**). It was seen that there was a statistically significant, linear, same-sided and moderate relationship between the pre-test PSQI scores and MBS values (rho=0.423 p<0.001) while there was a weak correlation between the pre-test PSQI scores and mMRC values (rho=0.308 p=0.011). A statistically significant, linear, same-directional and moderate correlation was found between post-test PSQI scores, mMRC and MBS values (p<0.001 for each and rho=0.454, rho=0.517, respectively). In other words, it can be said that as the pretest and posttest PSQI scores increased, the mMRC and MBS values also increased. It was observed that there was no statistically significant and linear relationship between disease duration (years) of the individuals and the pretest and posttest values of mMRC, MBS and PSQI (p>0.05 for each). There was no statistically significant difference between the mMRC and MBS mean scores of individuals with and without comorbidity (p>0.05 for each).

Table 1. Demographic data of the participants

	Group		p
	Intervention	Control	
Age, years	69.6±8	67.3±8.5	0.267***
Gender, n (%)			0.999**
Female	1 (2.9)	1 (3)	
Male	33 (97.1)	32 (97)	
Education, n (%)			0.186**
Primary school	28 (82.4)	26 (78.8)	
Secondary school	0 (0)	4 (12.1)	
High School	3 (8.8)	2 (6.1)	
University	3 (8.8)	1 (3)	
Income rate, n (%)			0.375*
Low	18 (52.9)	21 (63.6)	
Intermediate	16 (47.1)	12 (36.4)	
Living place, n (%)			0.664*
City	22 (64.7)	23 (69.7)	
Urban	12 (35.3)	10 (30.3)	
Living conditions, n (%)			0.512**
Alone	4 (11.8)	6 (18.2)	
Family	30 (88.2)	27 (81.8)	

* Pearson Chi-Square test, ** Fisher's Exact test, *** Mann-Whitney U test

Table 2. Clinical data of the participants

	Group		p
	Intervention	Control	
Smoking status, n (%)			0.027[b]
Smoker	4 (11.8)	12 (36.4)	
Non-smoker	1 (2.9)	2 (6.1)	
Ex-smoker	29 (85.3)	19 (57.6)	
Cigarette pack/year [IQR]	43.5 [38-60]	50 [40-55]	0.849[c]
Comorbidity, n (%)	13 (38.2)	9 (27.3)	0.339[a]
Hypertension, n (%)	12 (35.3)	8 (24.2)	0.323[a]
Diabetes, n (%)	2 (5.9)	3 (9.1)	0.673[b]
CAD, n (%)	8 (23.5)	4 (12.1)	0.223[a]
Dyslipidemia, n (%)	8 (23.5)	4 (12.1)	0.223[a]
Heart failure, n (%)	0 (0)	3 (9.1)	0.114[b]
COPD duration (year)	6 [2-10]	7 [5-10]	0.645[c]
LTOT, n (%)			0.548[a]
Yes	11 (32.4)	13 (39.4)	
No	23 (67.6)	20 (60.6)	
NIV, n (%)			0.803[a]
Yes	7 (20.6)	6 (18.2)	
No	27 (79.4)	27 (81.8)	
Annual exacerbation [IQR]	1.5 [1-5]	2 [1-3]	0.573[c]
Treatment, n (%)			0.201[b]
LAMA	7 (20.6)	2 (6.1)	
LAMA+LABA	3 (8.8)	6 (18.2)	
LABA+ ICS	3 (8.8)	1 (3)	
LAMA+LABA+ICS	21 (61.8)	24 (72.7)	

[a] Pearson Chi-Square test, [b] Fisher's Exact test, [c] Mann-Whitney U test, IQR: Interquartile Range, CAD: Coronary artery disease, LTOT: Long-term oxygen therapy, NIV: Non-invasive mechanical ventilation

Table 3. Comparision of pre and post-test values of FEV1, FVC, mMRC, MBS and SpO2

	Group		p
	Intervention	Control	
FEV1 (%)			
Pre test	40.5 [28-54]	35 [28-45]	0.444 a
Post test	38.5 [27-51]	32 [29-41]	0.324 a
px	0.623	0.458	
FVC (%)			
Pre test	58±15.9	55.9±18.6	0.613 b
Post test	55.9±13.9	54±19.8	0.645 [b]
p z	0.285	0.222	
mMRC			
Pre test	2.5 [2-3]	2 [2-3]	0.628 a
Post test	2 [1-3]	2 [2-3]	0.016a
p x	<0.001	0.564	
MBS			
Pre test	5 [4-7]	6 [5-7]	0.533 a
Post test	4 [3-5]	5 [5-6]	0.010a
p x	<0.001	0.029	
SpO2 (%)			
Pre test	91.9±4	92.3±2.6	0.612 b
Post test	92.9±3.6	92.3±3	0.458 b
p z	0.023	0.929	

Descriptive statistics, depending on the distribution; numerical variables were given as mean±SD or median [IQR], x, z: Comparison between repeated measures within group, a, b: Comparison between groups,a: Mann-Whitney U test, b: Independent Samples T test, x: Wilcoxon test, z: Paired Samples T test, IQR: Interquartile Range

Tablo 4. PSQI scores of the groups

	Group		p[a]
	Intervention	Control	
PSQI total			
Pre test	9 [5-12]	8 [5-12]	0.743
Post test	6 [3-8]	8 [5-11]	0.015
px	<0.001	0.024	
Sleep quality			
Pre test	1 [1-2]	1 [1-2]	0.180
Post test	1 [1-1]	1 [1-2]	<0.001
px	0.001	0.058	
Sleep latency			
Pre test	1 [0-2]	2 [1-3]	0.091
Post test	1 [0-2]	2 [1-2]	0.054
px	0.029	0.166	
Sleep duration			
Pre test	1 [1-3]	1 [1-3]	0.963
Post test	1 [0-2]	1 [1-2]	0.057
px	0.001	0.197	
Sleep efficiency			
Pre test	1 [0-3]	1 [0-2]	0.865
Post test	1 [0-1]	1 [0-1]	0.573
px	0.047	0.079	
Sleep disturbances			
Pre test	1,5 [1-2]	2 [1-2]	0.727
Post test	1 [1-2]	2 [1-2]	0.069
px	0.132	0.480	
Use of sleeping medications			
Pre test	0 [0-0]	0 [0-0]	0.200
Post test	0 [0-0]	0 [0-0]	0.344
px	0.414	0.999	
Daytime dysfunction			
Pre test	1 [0-1]	1 [0-2]	0.664
Post test	0,5 [0-1]	1 [0-2]	0.034
px	<0.001	0.480	

x: Wilcoxon test (Comparison between repeated measures within group), a: Mann-Whitney U test (Comparison between groups)
IQR: Interquartile Range

DISCUSSION

This study shows that, after the exercise training given by a physiotherapist, the relaxation exercises applied at home for 30 minutes at a time, every day for six weeks, are effective in reducing dyspnea and increasing sleep quality in COPD patients with high dyspnea score.

Cigarette smoking is the most important risk factor for the development of COPD. Smoking worsens the health status of patients, increases the severity of dyspnea and adversely affects their quality of life. Several studies have shown that increasing the amount and duration of smoking increases the severity of dyspnea in individuals with COPD (9-11). It was determined that the patients with high dyspnea severity had an average of 48.3±22.7 pack/year of cigarette smoking in our study. However, the patients were not similarly distributed in the two groups in terms of smoking. This

is one of the limitations of our study. Therefore, based on our study, it is not possible to comment on the effects of smoking and relaxation exercises on dyspnea and sleep quality. Dyspnea is the most common symptom in patients with COPD and causes the individual to consult a physician. Dyspnea is usually chronic and has a progressive course. Studies have shown an increase in the severity of the disease and an increase in the perception of dyspnea symptoms in COPD patients (12,13). We included the COPD patients with high dyspnea scores in our study. In our study, MBS and mMRC scales were used to evaluate the severity of dyspnea. Our results show that relaxation exercises significantly reduce the dyspnea symptom perception of individuals after a 6-week exercise program. Yılmaz et al. (14) found a statistically significant improvement in post-test mMRC and SpO2 values in 68 patients with moderate and severe COPD who practiced relaxation exercises. In our study, mMRC and MBS were used to evaluate the severity of dyspnea. There was a significant decrease in mMRC and MBS post-test medians in the intervention group. In addition, a significant increase was observed in the post-test SpO2 of the individuals in the relaxation exercise group. It has been shown that the severity of dyspnea assessed by MBS was related to respiratory rate and pulmonary function tests (15). However, we could not find an increase in FEV1% of the patients because of the small number of patients in our study. This may be an other limitation of our study.

Comorbidities have a significant influence on the dyspnea severity, morbidity and mortality in patients with COPD (9). In our study, it was observed that the dyspnea severity of our patients with COPD was not adversely affected by comorbid diseases.

It is thought that respiratory changes seen during sleep in healthy adults may be more severe in individuals with COPD. In COPD, respiratory control center activity decreases and there is an increase in upper airway resistance and serious deterioration in gas exchanges. These changes those lead to severe hypoxemia and hypercapnia are more common in the REM period (16-18). Decreased muscle contractility and diaphragmatic dysfunction seen during the daytime in individuals with COPD become more pronounced during sleep (19). The severity of COPD symptoms increases the likelihood of patients experiencing sleep problems at the same rate (20). More severe nocturnal desaturations are seen in COPD patients with daytime hypoxemia and an FEV1/FVC below 60% (16). In individuals with COPD, total sleep time decreases, sleep efficiency decreases, sleep latency increases, and REM sleep decreases (18). As a result, sleep quality decreases.

In a randomized controlled clinical study (21) which investigated the effect of relaxation exercises during 8 weeks on fatigue and sleep quality in COPD patients, there was not reported any significant difference between the mean pretest and posttest PSQI global scores of the intervention and control groups. However, subjective sleep quality, sleep latency, sleep duration and sleep efficiency sub-components of PSQI were found to be significantly different between the groups. In our study, the difference between the post-test median scores of the global PSQI score, subjective sleep quality, sleep latency, sleep duration, sleep efficiency, and daytime dysfunction between the groups were found to be statistically significant. Şahin et al. (22) reported similar results to our study in the study they conducted with 45 COPD patients in a single group for 6 weeks. Our study, like previous studies investigating the effect of relaxation exercises in individuals with COPD, was carried out with individuals with COPD in a stable period (14,21,22). Future studies may be planned with COPD patients in the exacerbation episode.

CONCLUSION

Relaxation exercises can be used as a non-pharmacological treatment method in addition to pharmacological treatments in patients with advanced stage and high symptom perception. There is a need for studies examining the effects of relaxation exercises on dyspnea and sleep quality in individuals with COPD in exacerbation. The use of telemedicine methods to evaluate patients' compliance with the relaxation exercise program and to facilitate their follow-up may be determined for future studies.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Muğla University Medical Faculty Clinical Researches Ethics Committee (Date: 05.09.2019, Decision No: 11/VI).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: No conflict of interest was declared by the author

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Author Contributions: The author declares that he has responsible for the design, execution, and analysis of the paper and that he has approved the final version.

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Original Article

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Analysis of some measurement parameters that may predict the risk of developing obesity: a clinical study

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ABSTRACT

Aim: Obesity is a severe and chronic disease, which is currently increasing rapidly. The aim of this study was to reveal some parameters that can predict the risk of obesity and to create a new scale using these parameters.

Material and Method: The demographic information of the study subjects was recorded, together with the anthropometric measurements of Body Mass Index (BMI), blood pressure, height, body weight, waist circumference, and hip circumference were recorded.

Results: Evaluation was made of 74 subjects, comprising 11 (14.9%) females and 63 (85.1%) males with a median age of 34 years (24-45). Mean body weight was measured as 77.3±12.46 kg, height as 174.3±8.86 cm, waist circumference as 84 (66-103) cm, hip circumference as 97 (83-121) cm, and BMI as 25.4±3.21 kg/m². It was seen that the risk of developing obesity could increase when age and duration of work increased, with an increased frequency of eating outside the home, in the absence of regular exercise, and when the waist and hip circumference values increased. Regression analysis showed that body weight, waist, and hip circumference measurement values could be used to predict the obesity development risk. Finally, a valid and reliable scale called OBEZRISK was created that would easily predict the risk of obesity development in individuals.

Conclusion: The study results showed that body weight, waist, and hip circumference measurement values could be used to predict the risk of obesity development in individuals. It was also concluded that the OBEZRISK scale could be used to predict the risk of developing obesity.

Keywords: BMI, hip circumference, waist circumference, obesity, risk of developing obesity

INTRODUCTION

Obesity is a multifactorial chronic disease, which diminishes quality of life, causes a shortening of life, and is currently tending to increase gradually throughout the world (1). According to World Health Organisation (WHO) data (2), obesity affects over 300 million people and approxmately one billion people are classified as overweight. In addition to environmental factors such as a sedentary lifestyle and changes in eating habits, some inherited features also play an important role in the increase in obesity prevalence (3). At least 2.8 million people die annually due to being overweight and obese, and the risk of diseases such as heart disease, stroke, diabetes, and cancer increases gradually due to the increase in body mass index (BMI). Therefore, raising awareness about obesity, shifting daily eating habits in a healthy direction, increasing physical activity, and acquiring healthy living habits are important in obesity prevention and obesity treatment (4).

Although BMI values can show whether people are obese, they cannot predict the risk of an individual classified as overweight becoming obese. Therefore, there is a need for a new scale that can predict the risk of obesity developing in people who are in the overweight category and which will enable precautions to be taken for these people. The aim of this study was to draw attention to the need to predict the risk of obesity development and to provide a solution for this need by creating a new scale that can predict this risk.

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MATERIAL AND METHOD

The study was carried out with the permission of Batman Regional State Hospital Non-Invasive Clinical Researches Ethics Committee (Date: 12.12.2014 and Decision No: 56). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Participants

The study participants were selected from volunteers, who were informed about the aims of the study and all those included in the study signed the Informed Consent Form. A questionnaire was then completed for each participant to collect the study data of age, gender, marital status, working time, comorbid diseases (smoking and alcohol use and dosage, diabetes mellitus, chronic lung disease, chronic liver disease, etc.), and lifestyle (frequency and type of exercise, nutrition habits). Blood pressure, body height, body weight, waist circumference, hip circumference, and BMI measurements were also recorded.

Methods

The BMI value of the patients was calculated using the "body weight (kg)/height (m^2)" formula and classified using the WHO BMI classification (5). Patients with BMI ≥30 kg/m^2 were classified as obese, 25.0 <BMI <29.9 kg/m^2 as overweight, 18.5 <BMI <24.9 kg/m^2 as normal, and BMI <18.5 kg/m^2 as thin.

Measurements were taken of each patient wearing light clothing using the same instruments and on an empty stomach, and an empty bladder. Body weight measurement was made with a standard scale device, and height measurements were made with bare feet, the backs of the participants turned and perpendicular to the measuring instrument, and the gluteus and back area tangent to the wall.

Waist circumference was measured at the level of the navel, using a fixed tension-supported tape measure, with the participant standing upright and without contracting the abdominal muscles. For the diagnosis of abdominal obesity, a waist circumference measurement >88 cm in females and >102 cm in males was taken as the baseline value (3,6). Hip circumference was measured from the most prominent point of the gluteus maximus muscle and the line passing over the pubis using a fixed tension-supported tape measure. After sitting and resting for approximately 15 minutes, systolic and diastolic blood pressure values were measured in both arms with a standard blood pressure monitor.

Statistical Analysis

The data obtained from the study were analyzed using SPSS vn. 20.0 software (Statistical Package for the Social Sciences Inc, IBM). The normal distribution of the study data was evaluated using the Kolmogorov-Smirnov test, and parametric data were presented as mean±standard deviation (SD) values, non-parametric data as median (minimum-maximum) values, and categorical data as number (n) and percentage (%). Parametric data were compared using the Independent Samples t-test, non-parametric data using the Mann Whitney U test, and categorical data using Pearson's Chi-square test. A value of $p<0.05$ was considered statistically significant.

Spearman's rho Correlation test was used to test the relationships between study data. ROC-Curve analysis was applied to determine parameters that could predict the risk of obesity, and Logistic Regression analysis was used to determine the best parameter to predict the risk of obesity. The Odds Ratio test was applied to the study data to show the factors that increase the obesity risk.

In addition, to create a scale (OBEZRISK) to predict obesity risk and to evaluate the validity and reliability of this scale, Factor analysis (ie Principal Component Analysis), and a Reliability test were applied.

RESULTS

Evaluation was made of a total of 74 participants, comprising 11 (14.9%) females and 63 (85.1%) males, with a maximum age of 45 years, 39 (52.7%) aged < 35 years, and 35 (47.3%) >35 years. Of the participants, 29 (39.2%) were single, 44 (59.5%) were married, and 1 (1.4%) was widowed. Duration of employment was reported as <10 years by 48 (64.9%) participants and > 10 years by 26 (35.1%). A chronic disease was determined in 6 (8.3%) participants. Alcohol consumption was reported by 13 (17.5%) participants, and 38 (51.4%) were smokers with average smoking of 1 pack-day. Regular exercise was taken by 14 (18.9%) participants (3 female, 11 male) with walking being the most common form at 23%, followed by football at 13.5%, and indoor sports at 2.7%. In response to the lifestyle questions, 34 (46%) participants stated that they always used elevators when available, 34 (45.9%) that they used them sometimes, and 6 (8.1%) that they did not use elevators. When means of transport were questioned, 61 (82.4%) participants drove to the workplace and 9 (12.2%) walked. In respect of general eating habits, 55 (74.4%) participants ate home-cooked

meals and 12 (17.6%) ate restaurant meals. Breakfast was reported not to be eaten by 25 (33.8%), and always eaten by 10 (13.5%) (**Table 1**).

The mean anthropometric measurements of the participants were determined as height 174.1±8.86 cm, body weight 77.3±12.46 kg, waist circumference 84 (66-103) cm, hip circumference 97 (83-121) cm, and BMI 25.4±3.21 kg/m² (**Table 2**). It was seen that 5 (6.8%) participants (1 female and 4 male) had a BMI value of ≥30 kg/m² in the obesity category, and 34 (45.9%) males had a BMI value between 25-29.9 kg/m² in the overweight category. The participants were asked whether they had had their blood pressure measured before, and 44.6% of the participants stated that they had had their blood pressure measured before. The measurements taken in this study showed that the systolic blood pressure of none of the participants exceeded the limit of 140 mm Hg, while the diastolic blood pressure of 5 participants (6.8%) was 90 mmHg (**Table 2**).

In the comparisons of the findings of the male and female groups, it was found that most females were aged <35 years (Z=-2.713, p=0.007). When the duration of employment was compared according to gender, males had a longer duration of employment (Z=-2.051, p=0.044). In the comparisons of smoking status according to gender, no significant difference was found between the groups (X2=2.999, p=0.083). The male participants were deterrmined to have higher values of height (t=-5.529, p<0.001), body weight (t=6.253, p<0.001), waist circumference (t=-2.963, p=0.004), and BMI (t=3.242, p=0.002) than those of females. No difference was determined between male and female participants in terms of exercising, using elevators, using vehicles, nutrition, and breakfast habits (**Table 3**, **Figure 1**).

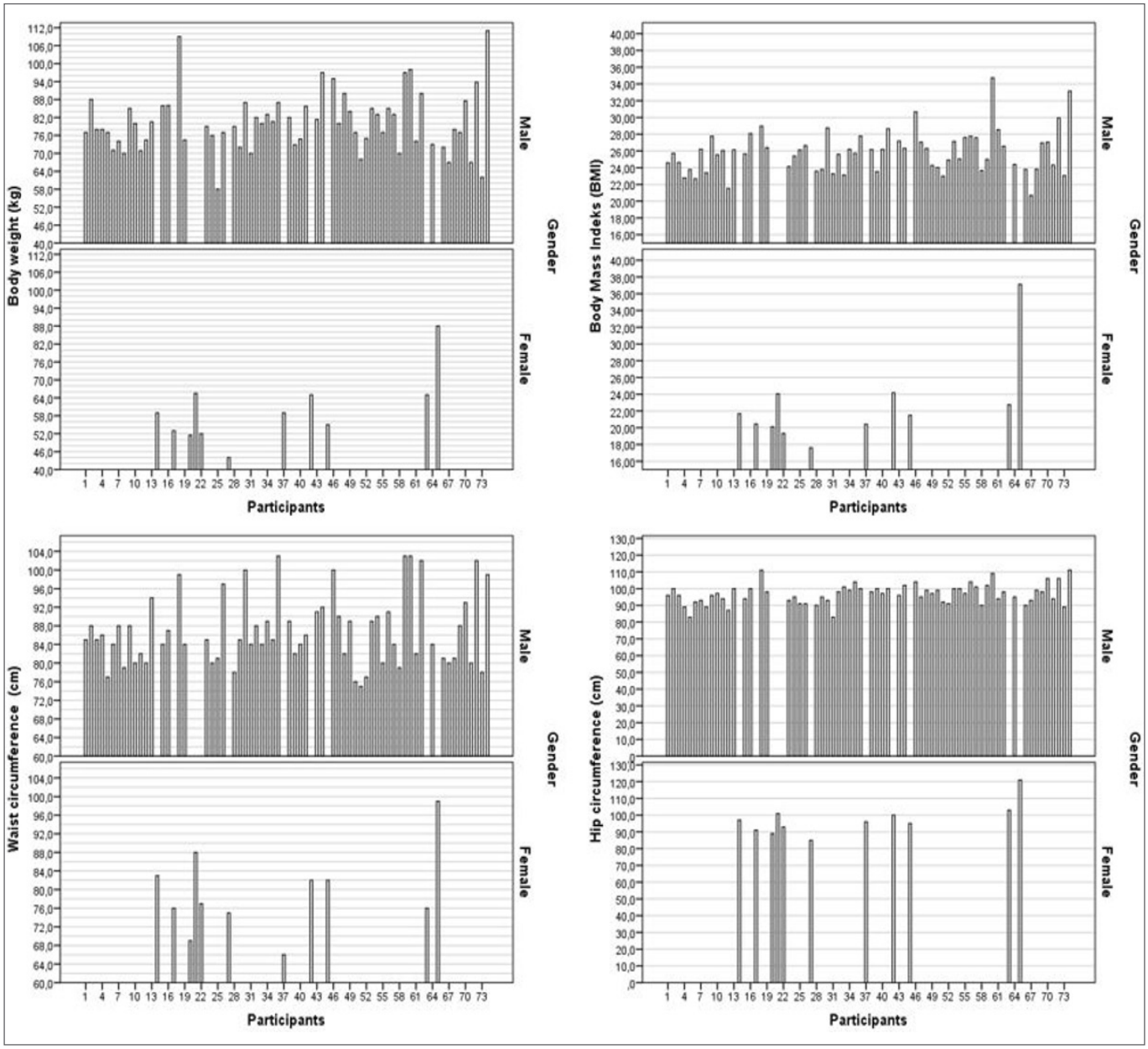

Figure 1. The distribution of gender in different groups

Table 1. The characteristics of the study sample

Variable	N (%)
Age (year)	34 (24-45)
Age group	
<35-year-old	39 (%52.7)
≥35-year-old	35 (%47.3)
Gender	
Female	11 (%14.9)
Male	63 (%85.1)
Marital status	
Single	29 (%39.2)
Married	44 (%59.5)
Widow	1 (%1.4)
Working time in the profession	
<10 years	48 (%64.9)
≥10 years	26 (%35.1)
Comorbidity	
No	68 (%91.9)
Diabetes mellitus	1 (%1.4)
Chronic lung disease	3 (%4.1)
Chronic liver disease	1 (%1.4)
Osteogenesis imperfecta	1 (%1.4)
Smoking	
No	36 (%48.6)
Yes	38 (%51.4)
Alcohol consumption	
No	61 (81.5)
Yes	13 (%17.5)
Habit of exercising	
No	60 (%81.1)
Yes	14 (%18.9)
Elevator use	
No	6 (%8.1)
Yes	34 (%45.9)
Always	34 (%46.0)
Type of transportation	
Walk	9 (%12.2)
Vehicle	61 (%82.4)
Mixed	4 (%5.4)
Breakfast habit	
No	25 (%33.8)
Sometimes	18 (% 24.3)
Often	21 (%28.4)
Always	10 (%13.5)
Eating place habit	
House	55 (%74.4)
Restaurant	12 (%17.6)
Mixed	6 (%8.1)

Table 2. The mean anthropometric measurements of the study

Variable	N (%)
Body height (cm)	174.2±8.86
Body weight (kg)	77.3±12.46
Waist circumference (cm)	84 (66-103)
Hip circumference (cm)	97 (83-121)
Body Mass Index (kg/m²)	25.4±3.21
Systolic blood pressure (mmHg)	110 (80-130)
Diastolic blood pressure (mmHg)	70 (50-90)

Table 3. The distribution (in %) for gender according to the demographic characteristics (i.e., body mass index, habit of exercising and age).

Variable	Female	Male	t / Z/ X²	p
	Mean±SD/ Median (min-max)/ N (%)	Mean±SD/ Median (min-max)/ N (%)		
Age (year)	29 (23-38)	35 (21-45)	-2.713†	0.007
Body height (cm)	162.73±4.71	176.23±7.83	-5.529*	<0.001
Body weight (kg)	59.73±11.54	80.37±9.85	-6.253*	<0.001
Waist circumference (cm)	79.36±9.06	86.84±7.49	-2.963*	0.004
Hip circumference (cm)	96 (85-121)	97 (83-111)	-0.110†	0.913
Body Mass Index	22.65±5.18	25.85±2.51	-3.242*	0.002
Marital status			1.378‡	0.502
Single	6 (20.7%)	23 (79.3%)		
Married	5 (11.4%)	39 (88.6%)		
Widow	0 (0.0%)	1 (100.0%)		
Working time (year)	4.95±3.05	8.05±4.82	-2.051*	0.044
Comorbidity			0.017‡	0.897
No	10 (14.7%)	58 (85.3%)		
Yes	1 (16.7%)	5 (83.3%)		
SBH (mmHg)	100 (80-130)	120 (90-130)	-3.060†	0.002
DBH (mmHg)	60 (50-90)	70 (60-90)	-2.224†	0.026
Smoking			2.999‡	0.083
No	8 (22.2%)	28 (77.8%)		
Yes	3 (7.9%)	35 (92.1%)		
Smoking (pack/ day)	0 (0-1)	0.5 (0-2)	-2.156†	0.031
Alcohol consumption			3.015‡	0.221
No	11 (18.1%)	50 (81.9%)		
Yes	0 (0.0%)	13 (100.0%)		
Habit of exercising			0.588‡	0.443
No	8 (13.3%)	52 (86.7%)		
Yes	3 (21.4%)	11 (78.6%)		
Exercise duration (hours/week)	0 (0-5)	0 (0-10)	-0.682	0.495
Elevator use			1.432‡	0.698
No	0 (0.0%)	6 (100.0%)		
Yes	6 (17.6%)	28 (82.4%)		
Always	5 (14.7%)	29 (85.3%)		
Type of transportation			7.108‡	0.069
Walk	2 (22.2%)	7 (77.8%)		
Vehicle	9 (14.8%)	52 (85.2%)		
Mixed	0 (0.0%)	4 (100.0%)		
Breakfast habit			5.489‡	0.139
No	7 (28.0%)	18 (72.0%)		
Sometimes	2 (11.1%)	16 (88.9%)		
Often	1 (4.8%)	20 (95.2%)		
Always	1 (10.0%)	9 (90.0%)		
Eating place habit			2.371‡	0.668
House	10 (18.2%)	45 (81.8%)		
Restaurant	1 (7.7%)	12 (92.3%)		
Mixed	0 (0.0%)	6 (100.0%)		

(*) t value, Independent Samples t test; (†) Z value, Mann Whitney U test, (‡) X2 value, Pearson's chi-square test, p<0.05

The correlation analysis revealed a positive correlation between BMI and age (r=0.454, p<0.001), gender (r=0.421, p=0.001), marital status (r=0.274, p=0.018), time in occupation (r=0.334, p=0.004), eating habits (r=0.294, p=0.011), waist circumference (r=0.732, p<0.001) and hip circumference (r=0.583, p<0.001) values, and a negative correlation was found between BMI values and exercise habits (r=0.262, p=0.024). The ROC-Curve analysis showed that if body weight was >87 kg, this parameter could be 100% sensitive and 92% specific in predicting the risk of obesity (AUC=0.972, p<0.001). When waist circumference was measured >98 cm, this parameter was found to be 100% sensitive and 95% specific in predicting the risk of obesity (AUC=0.979, p<0.001). When hip circumference was measured >104 cm, it was found that this parameter could be 100% sensitive and 94% specific in predicting the risk of obesity (AUC=0.982, p<0.001). The Logistic Regression analysis determined that the hip circumference measurement value could be used as the best parameter to predict the risk of developing obesity (B=0.503, Wald=7.639, p=0.006) (**Table 4**, **Figure 2**). However, the Odds Ratio analysis showed that no parameter alone would be sufficient to increase the risk of obesity.

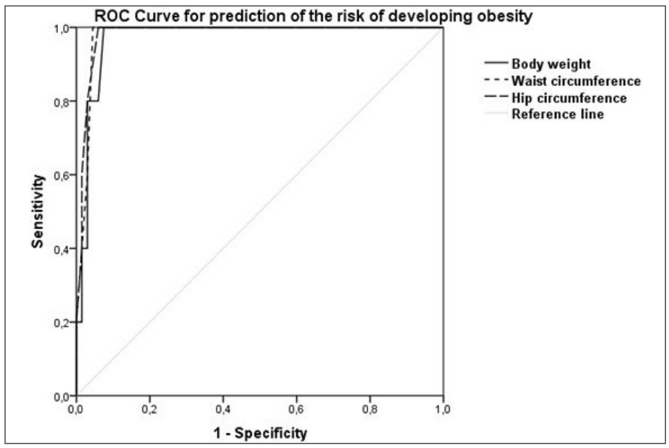

Figure 2. ROC Curve for prediction of the risk of developing obesity

The factor analysis results confirmed that the sample size of this study was sufficient to develop a scale that can measure the risk of developing obesity (Kaiser-Meyer-Olkin Measure of Sampling Adequacy test value = 0.626). Test results based on the correlation matrix table suggested that only "body weight", "waist circumference", "hip circumference", "exercise habit", and "duration of exercise" could be components of the OBEZRISK scale (Bartlett's Test of Sphericity value=199.795, p <0.001). The results of the analysis also showed that the OBEZRISK scale scores were equally distributed under two different factors (explained variance was 83.88%). The variance explained by the Factor 1 (i.e. anthropometric risk) scores was higher than the variance explained by the Factor 2 (i.e. habits risk) scores (31.68% versus 52.20%, respectively). The 2-factor variation in factor analysis showed that this scale could predict both the risk of anthropometric measurements and the risk of exercise habits (Eigenvalues=2.61 and 1.58). The reliability analysis test showed that this scale had moderate reliability as the Cronbach's alpha value was between 0.60 and 0.80 (Cronbach's alpha=0.642, intraclass correlation=0.642, 95% CI=0.499-0.755). The F test revealed no similarity between the parameters constituting this scale (F=2.791, p<0.001) (**Table 5**, **Table 6**).

Table 6. The cut off prediction results among anthropometric measurements and habit risk

Prediction	Variable	Cut-off value	Score	Person's score
Anthropometric risk				
	Body height	>87 kg	1	
	Waist circumference	>98 cm	1	
	Hip circumference	>104 cm	1	
Habit risk				
	Do you exercise regularly?	No	1	
	How many hours a week do you exercise?	No	1	
Total Score				

Table 4. ROC-Curve and Logistic Regression analysis for risk of developing obesity

ROC-Curve analysis for risk of developing obesity

Variable	AUC	Cut-off value	p	Sensitivity	Specificity	95 CI	
						Lower	Upper
Body height	0.972	>87 kg	<0.001	%100	%92	0.934	1,000
Waist circumference	0.979	>98 cm	<0.001	%100	%95	0.948	1.000
Hip circumference	0.982	>104 cm	<0.001	%100	%94	0.954	1.000
OBESRISK	0.993	Score >3	<0.001	%100	%94	0.975	1.000

Logistic Regression analysis for risk of developing obesity

			Obesity risk		
		Observed	Predicted		Percentage
			No	Yes	
Hip circumference	Obesity risk	No	68	1	98.6%
		Yes	2	3	60.0%
		Overall percentage			95.9%
			B	Wald	p
Hip circumference			0.503	7.639	0.006

Table 5. Analysis results of Factor Test and Reliability Test

	Factor test	
	Factor 1 (Anthropometric risk)	Factor 2 (Habit risk)
"Body weight"	0.907	
"Waist circumference"	0.879	
"Hip circumference"	0.842	
"Do you exercise regularly?"		0.953
"How many hours a week do you exercise?"		0.955
Eigenvalues	2.61	1.58
% of Variance	52.20	52.20
Cumulative %	31.68	83.88
Kaiser-Meyer-Olkin measure of sampling adequacy		0.626
Bartlett's test of Sphericity		199.795 (df=10, p<0.001)

Reliability test						
Variable	Cronbach's Alpha	Intraclass Correlation	95% CI		F Test	
			Lower	Upper	F	p
OBEZRİSK scale	0.656	0.656	0.515	0.766	2.911	<0.001

DISCUSSION

Obesity and obesity-related problems are currently considered one of the most important public health problems today. Obesity is known to be the main risk factor for Type 2 Diabetes, and an increase of one kilogram in body weight increases the risk of diabetes by 5%. This relationship leads to the risk of developing metabolic syndrome (7, 8, 9, 10, 11). Although metabolic syndrome is mostly known as a problem in adults, it has emerged as an important social problem in childhood, especially in adolescence. It has been stated that this situation is closely related to nutrition, exercise habits, and advancing age (12, 13, 14). There has also been shown to be a higher risk of early mortality for individuals with a sedentary lifestyle compared to those who are more active. A study in Turkey reported that 40% of the study participants stated that exercise was important, but a very low rate of those performed sports effectively. Studies in the literature have shown that obesity rates can vary according to the mobility of society and eating habits (15). As obesity is increasing in Turkey and throughout the world, it is now accepted as necessary to follow national and international policies for the prevention of this disease. The need to increase societal awareness about obesity has begun to be accepted with the identification of gaps in the existing knowledge gaps, and educational tools to fill these gaps have been created (5, 16).

The majority of the current study participants were male, married, and had been employed for less than 10 years. Type II diabetes mellitus type II was present in 1 participant, chronic lung disease in 3, chronic liver disease in 1, chronic bone disease in 1, and the rest were healthy. It was observed that most of the participants did not exercise regularly, used the elevator instead of climbing the stairs, used a motor vehicle instead of walking, did not eat breakfast regularly, but most preferred home-cooked meals for other meals. The number of smokers and non-smokers was similar and the smokers consumed approximately 1 pack of cigarettes per day. Most of the participants did not consume alcohol. In the light of these findings, it was observed that although most of the study participants did not have any comorbid disease, a high percentage preferred a sedentary lifestyle without exercise and smoked.

Waist circumference measurements vary in different populations, so it has been suggested that waist circumference should be determined for each society and the criteria should be adjusted accordingly to determine the real risk (17). There is no acceptable study on this subject in Turkey as yet. In the current study, the prevalence of abdominal obesity was 45.5% in females and 15.9% in males. Although there was a difference between these rates, there was no statistically significant difference between the genders in terms of detecting abdominal obesity, which was thought to be due to the low number of female participants in the study. The mean BMI value of the whole study group was 25.4±3.21 kg/m², which was between the upper limit of normal and the overweight limit. However, when the data were examined in detail, it was seen that the BMI value of 5 participants was >29.9, placing them in the obesity category, and almost half of the participants were in the overweight category and all of these subjects were male. When the relationship between obesity and the study parameters was examined, it was seen that the risk of developing obesity could increase with increased age, waist and hip circumference values, duration of working, frequency of eating outside the home, and in the absence of regular exercise. Thus, excess body weight could be associated with more ready-to-eat food consumption and insufficient physical activity due to working conditions.

When the study participants were evaluated according to male and female gender, it was observed that males were older, had worked for longer, and had higher height, body weight, BMI, waist circumference, systolic and diastolic blood pressure measurement values, and smoked more than females. However, no differences were observed between the genders in terms of hip circumference measurement values, alcohol consumption, marital status, comorbid diseases, exercise habits, elevator and vehicle usage habits, and general eating and breakfast habits.

As a result of the ROC-Curve analysis applied to predict the risk of obesity, it was determined that body weight, and waist and hip circumference values could predict the risk of developing obesity. It was concluded that no other study parameters could be a predictive marker. The results of the logistic regression analysis applied to find out which of the parameters obtained in the ROC analysis could be the best predictor for obesity risk, showed that the hip circumference measurement value could be the best parameter to be used for the prediction of the risk of obesity. However, from the Odds ratio analysis applied to test the parameters that may increase the obesity risk, it was concluded that none of the demographic and measurement-based parameters used in the study directly increased the risk of developing obesity.

Finally, at the end of this study, it was seen that a new and simple scale was needed to easily predict the risk of developing obesity. Therefore, to meet this need, a new scale named "OBEZRISK" was developed using the parameters of this study. It was thought that the "body weight (kg)", "waist circumference (cm)", "hip circumference (cm)" "exercise habit", and "exercise duration" parameters in this scale could predict the risk of developing obesity. The results of the Factor analysis and Reliability test showed that the OBEZRISK scale created in this study can be accepted as a valid and reliable scale.

The ROC-Curve analysis showed that a scale score >3 points indicated a higher risk of developing obesity (**Table 4**). According to these findings, the scoring of this scale and the interpretation of the scores can be as follows: the risk of developing obesity may increase when body weight, waist, and hip circumference measurement values are all measured high on this scale. If more than four parameters are scored on this scale, it can be concluded that the risk of developing obesity may be almost certain. Therefore, at the end of the study, it was thought that this newly produced scale could be used as a valid and reliable scale to safely and easily predict the risk of developing obesity in individuals. Nevertheless, further studies with larger samples and a greater variety of parameters are required to re-test and confirm the reliability and validity of the scale.

Limitations

This study had some limitations. First, this study was retrospective and had a small number of participants. Therefore, the power to reflect the results obtained from this study to the general population was low. Second, metabolic syndrome markers were not included in this study, as blood biochemistry analysis data and radiological imaging (such as abdominal ultrasonography) were not available. Finally, during the creation of the OBEZRISK scale obtained from this study, the participants included in the study were cross-sectional (people with a university education level) and remained far from reflecting the general population. However, the factor analysis test results revealed that the number of participants was sufficient to create the scale. Therefore, the results obtained from the study and the scale created can be accepted as enlightening for future studies. However, it was also accepted that this scale should be retested for reliability and validity by conducting studies with larger samples and a greater variety of evaluation parameters.

CONCLUSION

In conclusion, the results of this study demonstrated that although most participants did not have a comorbid disease, a high percentage had a sedentary and non-exercise lifestyle and smoked. In addition, it was seen that the risk of developing obesity could increase when age increased, the duration of working increased, the habit of eating outside the home increased, the values of waist and hip circumferences increased, and there was a pattern of not exercising. Finally, it can be suggested that the newly created scale called OBEZRISK could be used as a valid and reliable scale to safely and easily predict the risk of developing obesity.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Batman Regional State Hospital Non-Invasive Clinical Researches Ethics Committee (Date: 12.12.2014, Decision No: 56)

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

MEDICINE PALLIATIVE CARE

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Association of serum uric acid/albumin ratio with completely occluded infarct-related artery in patients with non-ST-segment elevation myocardial infarction

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ABSTRACT

Aim: Infarct-related artery (IRA) patency before primary percutaneous coronary intervention (pPCI) is linked to improved clinical outcomes and lower mortality in patients with acute coronary syndrome. The purpose of this research was to examine the association between serum uric acid/albumin ratio (UAR) and IRA patency in patients with non-ST-segment elevation myocardial infarction (NSTEMI).

Material and Method: We evaluated 430 consecutive patients with NSTEMI in total retrospectively. The study population was divided into 2 groups according to the IRA patency as assessed by the degree of Thrombolysis in Myocardial Infarction (TIMI) flow before pPCI. As a result, completely occluded IRA was defined as TIMI grade 0-1, while patent IRA was defined as TIMI grade 2-3.

Results: IRA was found to be occluded in 110 (25.5%) patients prior to the procedure. UAR level (p=<0.001) was found to be higher among the patients with IRA occlusion when compared to the patent group. Regression analysis revealed that UAR (OR:3.125; 95% CI:1.186-8.232, p<0.001), left ventricular ejection fraction (OR:0.917, 95% CI:0.885-0.951, p<0.001) and culprit artery diameter (OR:0.917, 95% CI:0.885-0.951, p<0.001) were independent predictors for an occluded IRA. An UAR cut-off value of >1.40 was detected to prognosticate the occluded IRA with 62.7% sensitivity and 63.8% specificity (AUC: 0.722, 95% CI: 0.671-0.773, p<0.001).

Conclusion: UAR is an independent predictor of preprocedural IRA patency in patients with NSTEMI. Thus, UAR may be an easily accessible parameter to diagnose high-risk NSTEMI patients who would benefit from an immediate invasive strategy (<2 hours).

Keywords: Serum uric acid/albumin ratio, infarct-related artery, non-ST elevation myocardial infarction

INTRODUCTION

ST-segment elevation myocardial infarction (STEMI) is characterized by fully enclosed or almost fully enclosed occlusion of the infarct-related artery (IRA). Early restoration of coronary flow in IRA is associated with better clinical outcomes and lower mortality (1). Therefore, primary percutaneous coronary intervention (pPCI) is currently preferred as the best treatment process for STEMI (2). As a matter of fact, non-ST-segment elevation myocardial infarction (NSTEMI) represents a wide range of clinical conditions that are usually associated with atherosclerotic plaque rupture and result in intermittent or incomplete thrombotic occlusion of IRA (3). In particular, it has been hypothesized that the adverse clinical outcomes associated with STEMI are due to complete occlusion of IRA (4). Moreover, previous studies have reported that approximately 30% of NSTEMI patients had completely occluded infarct-related arteries, as they experienced angiographic features similar to those of STEMI patients (5,6). Finally, each patient with NSTEMI underwent a postponed revascularization procedure based on the absence of ST elevation on the electrocardiogram (ECG), despite a completely occluded infarct-related artery (6).

As the most common and important protein of human serum, serum albumin (SA) plays a vital role in many important biological functions. Albumin is a circulating antioxidant protein and its decreased synthesis and increased catabolism indicate an increased inflammatory state (7). The pathophysiological mechanism of hypoalbuminemia in coronary artery disease (CAD) can be essentially related to its inefficacy in performing antioxidant, anti-inflammatory and anti-platelet aggregation activities, which consequently results in intensified blood viscosity, decreased endothelial function, oxidative stress, and narrowing in coronary artery due to large numbers of platelets (8). On the other hand, as a byproduct of purine metabolism, serum uric acid (UA) promotes the probability of atherosclerosis,

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as high levels contribute inevitably to the occurrence and prognosis of coronary artery disease (9). Moreover, UA has been shown to be a mediator of inflammation, endothelial dysfunction, and vascular disease (10). Latest researches have revealed that serum uric acid/albumin ratio (UAR) as a novel inflammatory marker is associated with severe clinical symptoms in patients with acute coronary syndrome (ACS) (11,12).

Although the presence of a fully occluded IRA is relatively common in NSTEMI, limited data are available on factors related to IRA patency. Therefore, we tried to evaluate the association between serum UAR and IRA patency in patients with NSTEMI before pPCI.

MATERIAL AND METHOD

The study protocol was approved by the Yozgat Bozok University Clinical Researches Ethics Committee (Date: 13.10.2022, Decision No: 2017-KAEK-189_2022.10.13_01). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. This current study was a retrospective analysis; therefore, patients were not required to give informed consent.

Study Population

The cross-sectional and single-centered study encompassed 430 consecutive patients in total that were admitted to the department of emergency with the diagnosis of NSTEMI and underwent pPCI from May 2021 to September 2022. NSTEMI was diagnosed as the absence of ≥ 2 mm ST segment elevation consistent with myocardial infarction in the adjacent chest leads and the absence of ≥ 1 mm ST segment elevation in the two standard leads with new left bundle branch block and positive markers of cardiac necrosis (3). Exclusion criteria include the inability to reach serum UA or albumin levels, history of coronary artery bypass grafting, STEMI, hypo/hyperthyroidism, acute decompensated heart failure, severe hepatic or renal dysfunction, hematological or autoimmune diseases, malignancies, presence of active infection, chronic inflammatory diseases, use of medication which may increase serum UA levels or patients with high serum UA such as gout, patients with unidentified IRA or multiple IRAs, and myocardial obstruction within non-obstructive coronary arteries.

Each patient involved in the research was evaluated in terms of age, gender, and cardiovascular risk variables based on their folders recorded in the hospital database.

Laboratory Measurements

Blood sampling of peripheral venous catheters was provided from the patients by means of atraumatic puncture from the antecubital vein during diagnosis, prior to sending them to the catheter lab examination. We used Beckman Coulter AU 5800 autoanalyzer in order to measure ratios of blood biochemical elements such as creatinine, potassium, uric acid, lipid panel, albumin, and sodium. Complete blood count variables were analyzed using an automated blood cell counter (Beckman Coulter LH 750; Beckman Coulter Inc., USA), while UAR was measured through the division of the serum UA level by the albumin level. The neutrophil/lymphocyte ratio (NLR) was calculated by dividing the total neutrophil count by the lymphocyte count using the same blood samples collected at admission. In addition, platelet/lymphocyte ratio (PLR) was measured through the division of the platelet count by the lymphocyte count.

Transthoracic echocardiography (Vivid 7 GE Medical System) was applied on each patient just followed by pPCI in the coronary intensive care unit, whereas left ventricular ejection fraction (LVEF) was identified through Simpson's method.

Angiographic Analysis

We used the Standard Judkins technique (Expo; Boston Scientific Corporation, Natick, Massachusetts, USA) and Siemens Axiom Sensis XP device (Munich, Germany) so as to observe the coronary angiography. Each coronary artery was visualized in at least two perpendicular planes. Just before the intervention, all patients received 180 mg of ticagrelor or 600 mg of a loading dose of clopidogrel and 300 mg of acetylsalicylic acid. During the PCI procedure, a bolus of 70 IU/kg unfractionated heparin was administered to the patients. The use of the stent type (naked or drug-coated) and the glycoprotein IIb/IIIa receptor inhibitor tirofiban was left to the operator's choice. PCI processes were conveyed using iopromide (low osmolarity and nonionic contrast agent) in accordance with the NSTEMI guidelines declared by the European Society of Cardiology (3). All patients enrolled in the study were required to undergo cardiac catheterization within 72 hours of admission together with PCI, surgical revascularization, or medical management, depending on the assessment of the operator in charge.

Just after completing patient recruitment, two experienced interventional cardiologists who were blinded to the study recorded all coronary angiographic images digitally in order to assess the rate of IRA flow. The culprit artery was defined mainly by angiographic findings [presence of obvious or suspected thrombus, ulcerated or ruptured plaque, and Thrombolysis in Myocardial Infarction (TIMI) flow grade ≤ 2]. In addition, ECG and echocardiogram recordings supported angiography data in the assessment of IRA in case of uncertainty.

Prior to coronary intervention, the antegrade flow of IRA for each patient was visually calculated according to

the TIMI study classification (13). Thus, TIMI flow was rated as follows: TIMI flow Grade 0: no antegrade flow; TIMI flow Grade 1: partial contrast penetration beyond an occlusion with incomplete distal filling; TIMI flow Grade 2: patent epicardial artery with opacification of the entire distal artery (but with delayed contrast filling and/or washout); TIMI flow Grade 3: patent epicardial artery with normal flow (13). Based on the findings of this rating system, the research groups were separated into two different groups those with TIMI 0-1 flow with a completely occluded IRA (n=110) and those with TIMI 2-3 flow with a patent IRA (n=320). There was no difference among interventional cardiologists for calculated TIMI flow grades.

Statistical Analysis

All findings were obtained through the use of the SPSS 22.0 Statistical Package Program for Windows (SPSS Inc., Chicago, IL, USA), followed by testing the data for normality using the Kolmogorov-Smirnov test. Normally distributed continuous data were shown as mean±standard deviation, while non-normally distributed continuous data were displayed as median (interquartile range 25-75). Qualitative variables were displayed in numbers and percentages. We compared parametric continuous variables using the Student t-test, whereas non-parametric continuous variables were evaluated through the Mann-Whitney U test. In addition to comparing categorical variables using chi-square and Fisher's exact test, we used the receiver operating characteristic (ROC) analysis to define the optimum cutoff level of UAR to predict occluded IRA. As multivariate logistic regression was used to determine the independent predictors of occluded IRA, a two-sided $p < 0.05$ was considered statistically significant for all analyzes.

RESULTS

The research encompassed 430 patients (male: 301; mean age: 62.8±10 years) in all, as the study groups were divided into two different groups according to the baseline antegrade flow of the IRA including 110 patients (male: 80; mean age: 61.3±10.7 years) with totally occluded IRA (pre-PCI TIMI flow 0-1) and 320 patients (male: 221; mean age: 63.3±9.8 years) with patent IRA (pre-PCI TIMI flow 2-3). Fundamental attributes and laboratory parameters of the study population are listed in **Table 1**. There was no statistically remarkable difference among patients with and without occluded IRA in terms of age, gender, hypertension, the frequencies of diabetes mellitus, dyslipidemia, familial history, tobacco use, and history of CAD (**Table 1**). Additionally, SBP and LVEF were significantly lower while length of hospital stay and peak troponin I level were remarkably higher in obstructed IRA group (**Table 1**). Moreover, NLR [3.7 (2.05-5.96) vs. 2.71 (1.9-4.26); p=0.005] and UAR [1.53±0.26 vs. 1.29±0.29; p<0.001] were remarkably higher in the occluded IRA group when compared to the patent IRA group (**Table 1**).

Angiographic characteristics of the study population regarding the presence or absence of occluded IRA are listed in **Table 2**. Here, no significant difference was detected in terms of IRA lesion length and number of diseased vessels between the groups (**Table 2**). However, time from admission to PCI was significantly higher while culprit artery diameter was remarkably lower in patients with occluded IRA (**Table 2**). On the other hand, the left circumflex artery (LCx) was the major culprit artery (43.6%) in the occluded IRA group, while the left anterior descending artery (LAD) was more common (49.1%) in the patent IRA group. Additionally, proximal localization for culprit lesion was more common in the patent IRA group than that of the occluded IRA group (51.9% vs. 40%; p=0.036).

Agents that were found to be noteworthy in univariate analyses were assessed by means of the multivariate logistic regression model so as to determine independent predictors of occluded IRA. As a result, it was observed that the UAR was an independent predictor of IRA patency. Moreover, we determined that values of LVEF and culprit artery diameter served as independent predictors of occluded IRA (**Table 3**).

As revealed by the ROC curve analysis; the cut-off value of 1.40 for UAR predicted the occluded IRA with a sensitivity of 62.7% and specificity of 63.8% (AUC: 0.722; 95% confidence interval: 0.671-0.773; p<0.001) (**Figure**).

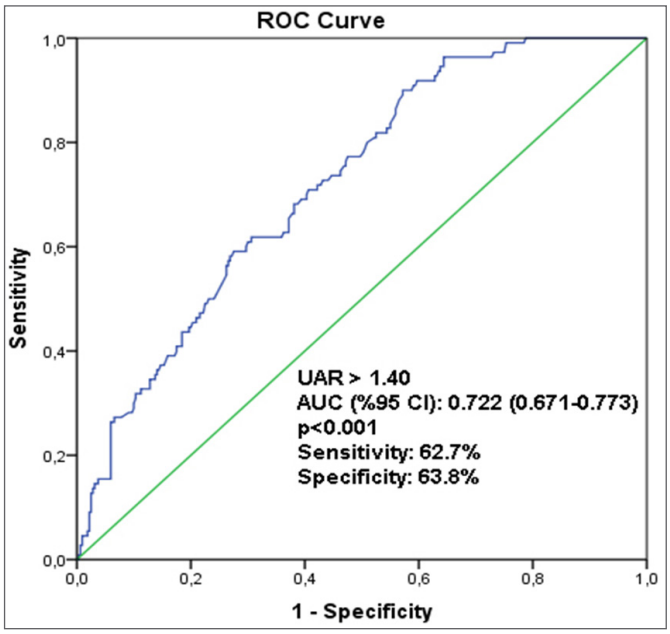

Figure. The receiver operating characteristic (ROC) curve analysis of serum uric acid/albumin ratio for the prediction of occluded infarct-related artery

Table 1. Baseline characteristics and laboratory parameters of the study groups

Total study population (n=430)			
Variables	**Occluded IRA group (n= 110) Pre-PCI TIMI flow 0/1**	**Patent IRA group (n=320) Pre-PCI TIMI flow 2/3**	**p value**
Baseline characteristics			
Age, years	61.3±10.7	63.3±9.8	0.099
Male gender, n (%)	80 (72.7)	221 (69.1)	0.547
Diabetes Mellitus, n (%)	41 (37.3)	121 (37.8)	0.920
Hypertension, n (%)	53 (48.2)	173 (54.1)	0.320
Dyslipidemia, n (%)	45 (40.9)	142 (44.4)	0.578
Current smokers, n (%)	59 (53.6)	140 (43.8)	0.077
Previous CAD, n (%)	24 (21.8)	81 (25.3)	0.521
Family history of CAD, n (%)	20 (18.2)	62 (19.4)	0.888
Left ventricle EF, %	48.5±8.2	53.5±6.5	**<0.001**
SBP at admission, mmHg	125±21	129±19	**0.010**
Heart rate at admission, bpm	76±15	77±14	0.900
Length of hospital stay, day	2.55±1.01	2.36±1.00	**0.038**
Laboratory parameters			
Glucose, mg/dl	135 (112-195)	125 (104-183)	0.080
Creatinine, mg/dl	0.85±0.23	0.83±0.22	0.822
Sodium, mmol/L	136 (135-139)	136 (134-138)	0.839
Potassium, mmol/L	4.3±0.99	4.24±0.83	0.338
Uric acid, mh/dl	6.13±1.04	5.33±1.23	**<0.001**
Albumin, g/dl	4.06 (3.8-4.2)	4.1 (3.9-4.3)	**0.002**
Total cholesterol, mg/dl	193 (164-230)	190 (163-221)	0.443
HDL-C, mg/dl	40.8±9.5	42.2±12.7	0.313
LDL-C, mg/dl	125 (106-159)	124 (101-152.5)	0.317
Triglycerides, mg/dl	137.3±92.9	145.4±124.4	0.805
WBC count, x103/µL	9.5 (8-12)	9.05 (7.4-10.9)	**0.018**
Neutrophil count, x103/µL	6.5 (5.2-8.8)	5.6 (4.6-7.6)	**0.003**
Lymphocyte count, x103/µL	1.9 (1.3-2.5)	2.1 (1.5-2.8)	0.140
Hemoglobin, g/Dl	14.4±1.6	14±1.6	0.051
RDW, fL	13.8 (13.4-14.5)	13.9 (13.4-14.5)	0.693
Platelet count, x103/µL	232 (197-259)	234 (196-276)	0.600
Peak troponin I, ng/L	10927 (4723-19816)	2313 (637-7479)	**<0.001**
NLR	3.7 (2.05-5.96)	2.71 (1.9-4.26)	**0.005**
PLR	120.5 (85.2-178.4)	109.7 (80.6-158.3)	0.174
UAR	1.53±0.26	1.29±0.29	**<0.001**

All values are expressed as mean±standard deviation, median (25th and 75th interquartile range), and number (%). Abbreviations: CAD: Coronary artery disease; EF: Ejection fraction; HDL: High-density lipoprotein; IRA: Infarct-related artery; LDL: Low-density lipoprotein; NLR: Neutrophil to lymphocyte ratio; PLR: Platelet to lymphocyte ratio; RDW: Red cell distribution width; SBP: Systolic blood pressure; TIMI: Thrombolysis in Myocardial Infarction; UAR: Uric acid to albumin ratio; WBC: White blood cell. p values in bold signify statistically significant differences.

Table 2. Angiographic features of all patients according to the presence or absence of occluded IRA

	Total study population (n=430)		
Variables	**Occluded IRA group (n= 110) Pre-PCI TIMI flow 0/1**	**Patent IRA group (n=320) Pre-PCI TIMI flow 2/3**	**p value**
Infarct-related artery, n (%)			
LAD	36 (32.7)	157 (49.1)	**0.004**
LCX	48 (43.6)	92 (28.7)	**0.005**
RCA	26 (23.6)	71 (22.2)	0.792
Proximal location for culprit lesion, n (%)	44 (40)	166 (51.9)	**0.036**
Extent of CAD, n (%)			
Single-vessel disease, n (%)	47 (42.7)	135 (42.2)	0.921
Two-vessel disease, n (%)	43 (39.1)	130 (40.6)	0.822
Three-vessel disease, n (%)	22 (20)	57 (17.8)	0.669
Culprit artery diameter, mm	2.70±0.43	2.96±0.50	**<0.001**
IRA lesion length, mm	29.7±13.7	27.7±12.3	0.198
Time from admission to PCI, hour	3.20±2.44	3.67±2.41	**0.021**

All values are expressed as mean±standard deviation and number (%). Abbreviations: CAD: Coronary artery disease; IRA: Infarct-related artery; LAD: Left anterior descending; LCX: Left circumflex; PCI: Percutaneous coronary intervention; RCA: Right coronary artery; TIMI: Thrombolysis in Myocardial Infarction. p values in bold signify statistically significant differences.

Table 3. Univariate and multivariate logistic regression analysis for assessment of predictors of occluded infarct-related artery

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p value	OR (95% CI)	p value
Systolic blood pressure	0.987 (0.976-0.999)	0.028	0.993 (0.980-1.005)	0.258
NLR	1.072 (1.019-1.128)	0.008	1.046 (0.942-1.160)	0.400
PLR	1.002 (1.000-1.005)	0.038	0.999 (0.994-1.004)	0.647
UAR	4.238 (1.516-12.872)	<0.001	3.125 (1.186-8.232)	<0.001
LVEF	0.914 (0.886-0.942)	<0.001	0.917 (0.885-0.951)	<0.001
Culprit artery diameter	0.260 (0.143-0.473)	<0.001	0.307 (0.164-0.574)	<0.001
Proximal location for culprit lesion	0.618 (0.398-0.960)	0.032	0.605 (0.355-1.031)	0.065

Abbreviations: CI: Confidence interval; LVEF: Left ventricular ejection fraction; NLR: Neutrophil to lymphocyte ratio; OR: Odds ratio; PLR: Platelet to lymphocyte ratio; UAR: Uric acid to albumin ratio.

DISCUSSION

Through this research, we evaluated the connection between UAR and patency of IRA in patients with NSTEMI, revealing that UAR is a remarkable and independent marker of preprocedural IRA patency in individuals with NSTEMI.

The number of NSTEMI patients is increasing worldwide, and approximately 30% of them are thought to experience complete obstruction of a coronary artery (5,6). In our study, the prevalence of occluded IRA was detected as 25.5%, consistent with the literature. These patients experience more severe clinical symptoms and display a poor prognosis than those with non-occlusive culprit arteries. Meta-analyses have suggested that delayed invasive approach can have adverse cardiovascular consequences on prognosis (5,6). As suggested by Stone et al. (1) found, patients exhibiting IRA TIMI flow grade 3 can expect improved results in terms of heart failure, preservation of EF, and clinical endpoint at 6 months when compared to those with TIMI grades 0 to 2. Advantages of early IRA patency include a reduction in enzymatic infarct size, fatal arrhythmic events, and in-hospital mortality (14).

The emergence of an occluded IRA in patients with NSTEMI may not be merely detected through clinical or electrocardiographic measurements. It has not been figured out yet why the typical ST segment elevation does not manifest itself despite complete occlusion of the artery in patients with NSTEMI. Decreased sensitivity of the standard 12-lead ECG in detecting acute occlusion changes in the inferolateral distribution, the presence of good collaterals, acute total occlusion in an area with double blood supply, and chronic total occlusion, which are misclassified as acute, may be listed as possible mechanisms (5,6).

Previous studies in the literature have shown differences in the anatomical distribution of the culprit artery between the occluded IRA and patent vessels in the NSTEMI groups. Khan et al. (6), evaluating the data obtained from 6 studies, reported that RCA was the most common culprit artery. In contrast, Huang et al. (5) reported that LCx was the most commonly involved artery in NSTEMI patients with occluded IRA. In addition, in another study led by Hwang et al. (15), it was shown that the distal vascular bed is more frequently involved as being the anatomical location of the lesions in patients with occluded IRA. Similarly, our study has revealed that proximal vessel involvement is more common in patients with patent IRA.

Albumin level is an independent and readily available cardiovascular prognostic biomarker. A reduction in SA has been found to be associated with poor in-hospital survival, in-stent restenosis, and coronary artery disease severity (16,17). Furthermore, decreased SA concentrations are closely linked to the emergence and growth of coronary atherosclerosis (18). Loss of the antioxidant properties of albumin can lead to an advanced risk of clotting in the coronary capillary lumen (19).

Serum UA is a byproduct of purine metabolism (19), thus it can initiate local inflammatory responses by forming monosodium urate crystals in various tissues. It has been reported that these activities involving UA crystals are significantly increased in patients with CAD (9). Human atherosclerotic plaque contains significant amounts of UA, thus high serum UA can promote thrombus formation via purine metabolism (20). In addition, UA can give rise to oxidative stress and induce inflammation, vasoconstriction, and endothelial dysfunction (21). As observed in patients with hyperuricemia, almost all elements mentioned above can play a significant role in the progression of atherosclerosis and can potentially result in the progression of CAD.

As the role of UAR in patients with cardiovascular disease has been studied, it can clearly indicate the presence of inflammation and oxidative stress. Kalkan et al. (12) found that STEMI patients with a higher UAR have an increased risk of death. Çakmak et al. (22) showed that a high UAR level is a more reliable predictor of the extent of CAD (using the SYNTAX score) in patients with NSTEMI than the C-reactive protein/albumin ratio. In another recent research, a high UAR level was reported to be an independent marker of the emergence of contrast-induced nephropathy after pPCI in patients with STEMI (23).

Taking into account the relevant findings, it can be suggested that UAR has a close relationship with the coronary flow in patients with NSTEMI. Thereby, we showed that UAR was remarkably higher in NSTEMI patients with an occluded IRA, and a high UAR level was an independent predictor of an occluded IRA. Yet, further studies can clarify whether a higher UAR value in NSTEMI patients is an indicator of IRA.

Nevertheless, this study has some restrictions. Firstly, the single-center, retrospective design may have led to biases. Therefore, it failed to fully control for confounding factors, including undocumented drug history, nutritional status linked by serum albumin level, and comorbidities. The small sample size is a second and important limitation. Thus, the values regarding the incidents and the data obtained did not allow us to evaluate measures reflecting NSTEMI prognoses, such as TIMI score, GRACE score, Killip class, or BNP levels. Also, we were unable to collect data on ECG changes at admission, so it was unclear whether posterior ECG leads were applied or not. We calculated UA and SA levels merely at admission, thus the use of a spot laboratory value prevented us from using values obtained over some time. Another limitation is that the findings are not predictive for patients with other acute coronary syndromes because only NSTEMI patients were included.

CONCLUSION

We revealed that there is a remarkable association between UAR and pre-procedural infarct-related arterial patency in NSTEMI patients. UAR was an independent predictor of an occluded IRA in patients undergoing PCI for NSTEMI. Thus, UAR may be an easily accessible parameter to diagnose high-risk NSTEMI patients who would benefit from an immediate invasive strategy (<2 hours).

ETHICAL DECLARATIONS

Ethics Committee Approval: The study protocol was approved by the Yozgat Bozok University Clinical Researches Ethics Committee (Date: 13.10.2022, Decision No: 2017-KAEK-189_2022.10.13_01).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: No conflict of interest was declared by the author.

Financial Disclosure: The author declared that this study had received no financial support.

Author Contributions: The author declares that he has responsible for the design, execution, and analysis of the paper and that he has approved the final version.

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Original Article

MEDICINE PALLIATIVE CARE

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Is it possible to reduce treatment costs in distal radius torus fractures?

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ABSTRACT

Aim: The aim of the study was to evaluate the effect of parental information on the number of radiological examinations, the number of orthopedics outpatient visits, the duration of early orthopedic outpatient admission, the fracture recovery scores of reduction, and the cost of treatment of torus fractures in children in in the emergency service.

Material and Method: A total of 85 patients having stable torus fractures, aged between 0-16 years have been included to the longituidinal study during the period of first of April 1, 2020 and first of September, 2022. A total of 44 patients whose parents are not informed were evaluated in the emergency department and were transfered to the Orthopedics polyclinic (No Information group- No-INF), whereas 41 patients were evaluated by the Orthopedist in the emergency department and their parents were informed directly (Information group-INF). The groupd were compared in terms of the duration of the first admission to the orthopedic polyclinic, the number of applications to the orthopedic polyclinic, the number of radiological examinations performed, whether reduction has been performed, fracture healing scores and current treatment costs and correlation was analyzed.

Results: The MAYO Wrist Score (p=0.80), age (p=0.712), gender (p=0.815), and complications (p=0.482) did not differ significantly between the No-INF and INF groups. Patients in the INF group whose parents have been directly informed in the emergency department had lower orthopedic polyclinic application rates (p<0.001), longer delay for the first orthopedic polyclinic admission (p<0.001) and a lower probability and/or less number of X-Ray evaluation(p<0.001). Correlation between the variables such as Patient's Modified MAYO Wrist Scores, the number of orthopedic polyclinic visits, the first orthopedic polyclinic admission time, the reduction procedure and the number of X-Rays was not ststistically significant (p>0.05). Findings show that additional tests and procedures such as radiography has increased the costs of 6-41% in the present study.

Conclusion: It can be concluded that adequate information in the emergency services for parents of children with stable torus fractures might provide a reduction in treatment costs due to lower orthopaedic polyclinic admission and reduced radiographic examination. Wrist MAYO scores have not been affected application of reduction, radiographic evaluation, polyclinic admission and time.

Keywords: Distal radius, torus fracture, parents information, polyclinic application frequency, radiography frequency, treatment cost

INTRODUCTION

The pediatric torus fractures (TF) are frequently seen at the junction of the metaphyseal diaphysis in the distal radius and are stable in nature having a good prognosis and usually heal well. When the load on the bone exceeds the plastic deformation threshold, the cortex apex swells outward. TF is usually not displaced, but it can rarely be angulated (1). Thus, non-rigid immobilization methods such as removable braces and bandages are prefered instead of rigid immobilization methods such as plaster and splint for fracture fixation (2-7). In TF, pediatric orthopedists prefer to fix with 30% brace (14). TF resembles the common cold that does not require medical treatment, and frequent radiographs are unnecessary in the follow-up period (8,9). For TF treatment, only pain control is recommended, whereas any hard immobilization and serial radiographic (X-Ray) requests are accepted as excessive treatment (9-11).

Undoubtedly, the information obtained by educated parents and the cooperation with the physician plays a key role in the management of TF (11-13). However, to omit fixation with rigid immobilization, to change the routine clinical follow-up and to coordinate the process with the parents is very challenging and difficult in developing countries. Unnecessary radiation exposure, decreased cost and time loss can be avoided with better prognosis of TF in children. For this reason, we aimed to evaluate the effect of parental information on the number of radiological examinations, the number of orthopedics outpatient visits, the duration of early orthopedic outpatient admission, the fracture recovery scores of reduction, and the cost of treatment of torus fractures in children in in the emergency service.

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MATERIAL AND METHOD

The procedures of the longituidinal study were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki and with the permission of Hitit University Non-interventional Clinical Researches Ethics Committee (Date: 4.11.2022, Decision No: 2022-23).

The population of the study are patients diagnosed with stable TF that did not show angulation between April 1, 2020 and September 1, 2022. The sample of the study consisted of a total of 85 patients which were classified as a) No-INF group (n=44) who are patients evaluated in the emergency department and were transfered to the Orthopedics polyclinic and parents did not receive information in the emergency department, and b) INF group (n=41) patients who were evaluated by the Orthopedist in the emergency department and their parents were informed directly in the emergency department. The diagnoses of the patients admitted to the emergency department were confirmed by bidirectional wrist X-Ray (**Figure 1**). A short arm splint was applied to all patients, while manual traction was applied to certain patients who needed reduction in their treatment. The information about TF was shared verbally with parents either in the emergency clinic by the orthopeadist (INF group) or at the orthopaedic clinic where the patients were send from the emergency clinic (No-INF group). Information shared verbally with parents was as follows; "Torus fractures are simple, fast-healing non-displaced fractures specific to children. A three-week short arm splint is required for treatment. In the third week, the split will be removed under the control of an orthopedist in the orthopedic polyclinic. There might be mild pain for a few days. There is no need to take an X-ray again.". The splint of the patients were removed in the orthopedics polyclinic at the end of three weeks. Wrist functions were evaluated with the Mayo wrist scoring system which evaluates range of motion, grip strength, satisfaction level, and pain as well in children (14) (**Table 1**).

Data of all patients was reviewed retrospectively from hospital records in terms of the number of orthopedic polyclinic visits, the number of radiographs, the day of admission to the orthopedics polyclinic, and clinical recovery scores and were compared between the groups with and without parental information, INF and No-INF groups respectively. The number of orthopedics polyclinic visits, X-Rays, orthopedics polyclinic admission days and clinical recovery scores were compared between the patients who received reduction treatment and patients who do not.

Table 1. Mayo modified wrist score

Category	Score	Findings
Pain (25 points)		
	25	No pain
	20	Mild pain with vigorous activities
	20	Pain only with weather changes
	15	Moderate pain with vigorous activities
	10	Mid pain with activities of daily living
	5	Moderate pain with activities of daily living
	0	Pain at rest
Satisfaction (25 points)		
	25	Very satisfied
	20	Moderately satisfied
	15	No satisfied, but working
	0	No satisfied, unable to work
Range of motion (25 points)		
	25	100% percentage of normal
	20	75%-99% percentage of normal
	15	50%-74% percentage of normal
	10	25%-49% percentage of normal
	0	0%-24% percentage of normal
Grip strenght (25 points)		
	25	100% percentage of normal
	20	75%-99% percentage of normal
	15	50%-74% percentage of normal
	10	25%-49% percentage of normal
	0	0%-24% percentage of normal
Final result(total points)		
	90-100	Excellent
	80-89	Good
	65-79	Fair
	<65	Poor

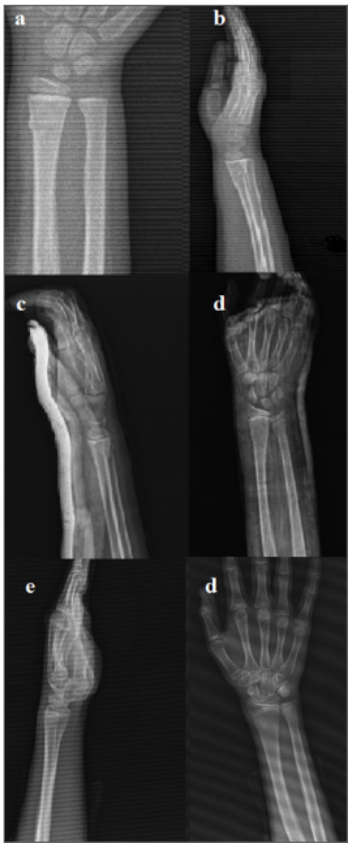

Figure 1. Anteroposterior and lateral radiograph demonstrating a torus fracture of the distal radius (a, b: X-Ray images of the first examination, c,d: X-Ray images with splint, e, f X-Ray image of the 3rd week)

Statistical Analysis

Statistical analysis of the data was performed with the SPSS (Version 22.0, SPSS Inc., Chicago, IL, USA, Undergraduate) package program. Kolmogorov-Smirnov test and Shapiro-Wilk test were used to test the normality of data distribution. Descriptive statistics for numerical data was presented as mean±standard deviation (SD) and median (Q1-Q3), depending on data distribution, whereas categorical variables were presented as frequency and percentage (%). Two groups were compared by using Student's t-test for normally distributed variables, whereas Mann Whitney U test was used as parametric test for independent sample comparisons. Correlations between numerical data were investigated using the Spearman correlation coefficient based on the assumption of normal distribution at a significance level of $p<0.05$.

RESULTS

A total of 85 patients were analyzed desriptively and the frequency of males was 67.1% (57), whereas 32.9% (28) of the patients were females with a mean age of 103.6±38.2 months for the whole sample. Only one pediatric patient had an angulation of approximately 20° in the fracture as a complication due to falling again. Descriptive demographic and clinical characteristics of the patients are presented in detail in **Table 2**. The MAYO Wrist Score (p=0.80), age (p=0.712), gender (p=0.815), and complications (p=0.482) of the INF group (n=41) and No-INF group (n=44) did not differ significantly as shown in **Table 3**.

Table 2. Descriptive statistics on the socio-demographic and clinical information of the patients

		n (%)
Gender	Male	57 (67.1%)
	Female	28 (32.9%)
Parent notification	No	44 (51.8%)
	Yes	41 (48.2%)
Reason for application	Control	55 (64.7%)
	Termination of treatment	29 (34.1%)
	Falling again	1 (1.2%)
Complication	No	84 (98.8%)
	Yes	1 (1.2%)
Reduction	No	40 (47.1%)
	Yes	45 (52.9%)
Splint	No	0
	Yes	85 (100%)
		Mean±SD / **Median (Q1-Q3)**
Age (month)		103.6±38.2 / 99 (69.5-133.5)
Follow-up time		6±0 / 6 (6-6)
Number of polyclinic admissions		2.247±1.1 / 2 (1-3)
First polyclinic admissions time (days)		9.564±8.098 / 5 (3-20.5)
Number of X-Rays taken		2.4±1.399 / 2 (1-3)
Splint duration (weeks)		2.976±0.21 / 3 (3-3)
Modified Mayo Wrist Score		93.94±4.16 / 95 (90-95)

SD: Standard deviation

Table 3. Statistical findings on the comparison of socio-demographic and clinical information between patients with and without parental notification.

		No-INF group (n=44)	INF group (n=41)	P values
Gender	Male	29 (65.9%)	28 (68.3%)	0.815[a]
	Female	15 (34.1%)	13 (31.7%)	
Complication	No	44 (100%)	40 (97.6%)	0.482[b]
	Yes	0 (0%)	1 (2.4%)	
Splint	No	0 (0%)	0 (0%)	-
	Yes	44 (100%)	41 (100%)	
Age (month)		105.1±35.6	102±41.1	0.712[c]
Modified MAYO Wrist Score		95 (90-95) (94.09±4.21)	95 (90-95) (93.78±4.15)	0.800[d]

[a]Chi Square, [b]Fisher Exact test with n (%), [c]Student's t-test with mean±standard deviation, [d]Mann-Whitney U test with median (Q1-Q3) and (mean±standard deviation) SD: Standard deviation

The reason for applying to the orthopedic polyclinic in the INF group was found as control, termination of the treatment and falling once again, whereas for No-INF group, the purpose of visiting the polyclinic was control and a significantly correlation was found between the reasons for admission and the information ($p<0.001$). In addition, the number of orthopedic polyclinic admissions of the patients in the INF group was significantly lower ($p<0.001$), while the first orthopedic polyclinic admission time was significantly later ($p<0.001$) and the number of X-Rays taken was significantly lower ($p<0.001$) compared to the No-INF group. (**Table 4**) .

The MAYO Wrist scores of patients with and without reduction in the emergency clinic did not differ significantly (p=0.903) (**Figure 2**, **Table 6**), whereas no statistically significant correlation was found among the MAYO Wrist Scores of the patients, the number of admissions to the orthopedics polyclinic, the time to the first orthopedics polyclinic admission, and the number of X-Rays taken ($p>0.05$) (**Table 5**).

Table 4. Comparison of the reason for admission, the number of patient visits, the time of first patient admission and the number of X-Rays received by the patients between the patients with and without parental information

		No-INF group		INF group		P values
Reason for application	Control	44 (100%)		11 (26.8%)		<0.001[a]
	Termination of treatment	0 (0%)		29 (70.7%)		
	Falling again	0 (0%)		1 (2.4%)		
		Medyan (min max)	**Mean±SD**	**Medyan (min max)**	**Mean±SD**	
Number of polyclinic admissions		3 (2-4)	2.863±1.00	1 (1-2)	1.585±0.773	<0.001[b]
First polyclinic application time (days)		4 (3-5.75)	4.59±2.705	21 (4.5-22)	14.9±8.569	<0.001[b]
Number of X-Rays taken		3 (3-4)	3.38±1.039	1 (1-1.5)	1.341±0.854	<0.001[b]

[a]Fisher Exact test with n (%), [b]Mann-Whitney U test with median (Q1-Q3) and (mean±standard deviation)

Table 5. Correlation analysis findings between the modified MAYO wrist scores and the number of patient visits, the time of first patient admission, and the number of X-Rays received by the patients

		Number of polyclinic admissions	First polyclinic admissions time (days)	Number of X-Rays taken
Modified Mayo Wrist Score	r	-0.100	0.138	0.003
	P	0.363	0.207	0.977

Spearman correlation analysis

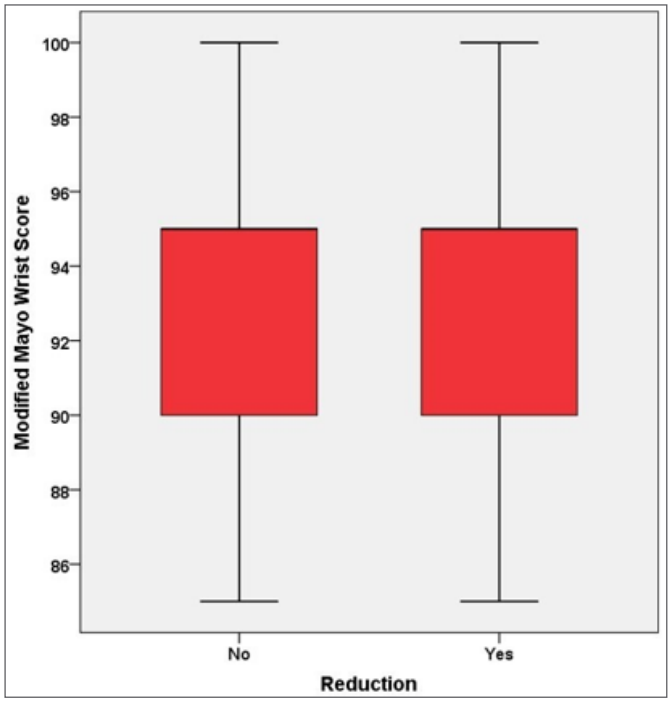

Figure 2. Box plot of the distribution of modified MAYO wrist scores between patients with and without reduction

Table 6. Comparison of Modified Mayo Wrist Scores between patients with and without reduction

	No-INF group	INF group	P values
Modified Mayo Wrist Score	95 (90-95) (94±3.95)	95 (90-95) (93.8±4.38)	0.903[b]

[b]Mann-Whitney U test with median (Q1-Q3) and (mean±standard deviation)

Emergency examination payment (EEP) is 135 TL, consultation payment (CP) is 50 TL, radiography payment (RP) is 30 TL, splint procedure payment (SPP) is 72.5 TL, orthopedics polyclinic examination payment (OPEP) is 135 TL and plaster removal payment (PRP) is calculated over 27.5 TL.

Minimum treatment payment (MTP) for a patient: EEP + CP + RP + SPP+ OPEP + PRP = 450 TL

- MTP + at least one RP=6.6% increase;
- MTP + at least one OPRP=30% increase;
- MTP + RP + OPRP = 41.1% increase

In addition to our patients, the treatment fee for the patient who comes to the control up to four times and has three radiographs is 1080 TL, causing an additional cost of 41.6%.

DISCUSSION

The time devoted to parental information in pediatric patients with TF having applied to emergency clinic plays an important role during the treatment. Providing simple information about the nature of the fracture and thereby calming parents facilitates the managment of fractures. Being selective about radiation exposure and to continue follow up with as few X-rays as possible is a key determinant for the treatment of TF in pediatric patients. It was hypothized that informing the patient's parents might reduce the number of orthopedic polyclinic applications which will reduce wasting time for the physician, decreases the costs for patients, and declines the cost for healthcare system by reducing the expenses. According to our findings, time for early orthopedic polyclinic admission, frequency of admission to orthopedics polyclinic, verbal information to parents, application of reduction procedure and the number of X-Rays requested were not effective in clinical recovery in the treatment of pediatric TF. Thus, different perspectives and practices are needed in the management of TF. We believe that this may place an excessive burden on health costs. According to the Public Health Services Price List (19) on 08.09.2022, costs can be reduced for each excessive performed transaction. According to the list, emergency room examination fee was determined as 135 Turkish Liras (TL), whereas the costs for specialist physician consultation is 50 TL, orthopedic polyclinic examination is 135 TL, short arm splint is 72.5 TL, bidirectional joint radiography is 30 TL, plaster removal is 27.5 TL, closed reduction is 939 TL. If a torus fracture admitted to the emergency service can be managed as expected, the total cost of the emergency examination, radiography, orthopedic consultation, short arm splint, orthopedic polyclinic control and splint removal costs only 430 TL. However, unneccessary additional radiography and orthopedic polyclinic applications raises the costs between 6-41% at varying rates. Findings of the study showed that there were patients who increased the cost of the treatment up to 630 TL by applying to the orthopedics polyclinic at most four times and having radiograph scanning for three times.

It has been reported that radiography does not change the course of fracture healing in TF (9,23). Our findings showed that the number of X-Rays do not play an important role in the clinical functions and healing of these fractures. In order to reduce radiological examinations, attention should be paid to informing parents in the first stage of treatment. However, the treatment proposal offered by the clinician has not been accepted by individuals with different beliefs and

sociodemographic backgrounds. Children are exposed to a radiation dose of approximately 0.05–0.005 mSv per extremity during radiography scanning (15). This dose is below the threshold for a carcinogenic effect, however, the least possible radiation exposure should be targeted, especially in children. Thus, it might be possible to reduce and prevent an unnecessary radiation exposure by informing the parents. In our study, a total of 204 bidirectional wrist radiographs (average 2.4 per person) were scanned, whereas the average of radiographs of INF group was lower compared to No-INF group, 1.3 and 3.3 respectively. Thus informing parents in the emergency clinic reduced the number of scans for approximately 60%. This means that 44 patients in the No-INF group received additionally radiographs with a mean of 2.1 scans per person.

In several countries, certain steps are taken to reduce cost loss and increase service quality in health services (16,17,22,23). We suppose that this will be achieved by preventing unnecessary examinations and patient referrals. Due to the changes in package pricing in health payments in our country, we did not have the chance to statistically compare net prices. However, the cost analysis was performed by using the rates for currency. The total expenditure of approximately 2880 TL was prevented and the costs were reduced by 64% by preventing 96 additional radiography scans as a result of briefing/informing parents in the emergency clinic. On the other hand, it can be argued that physicians have a vocation to apply frequent radiography scans during the follow-up period to avoid possible problems in fracture healing (9). The requested radiograph scans might prevent negative processes that will develop with the patient and their relatives, especially in an environment where violence against physicians and healthcare professionals might occur (18).

Literature showed that treatments of TF mainly consists of application of plaster, splint, removable splint and elastic bandage, and the use of rigid immobilization methods are not needed, especially in nowadays treatments (3,4,7,10,14). However, the advise of the physician not to use fixation in children with TF is mostly not well accepted by parents in the emergency clinic. Many families insistently prefer plaster cast, stating that they cannot keep the child stable (2,10,12). Due to the medicolegal challenges and to prevent overreaction of parents, we preferred to routinely apply splints in the TF treatments. On the other hand, families accepted the suggestions and advise that there is no need for reduction. There was a tendency to omit reduction from the treatment because of the belief that reduction is a painful procedure. Regulations are needed for the treatment of pediatric fractures to prevent loss of time and money spent in the polyclinic (20), since reduction or frequent orthopedic polyclinic follow-ups are not needed for already stable torus fractures (9,10,11). The findings of clinical improvement in patients with and without reduction were paralel with literature such that the number of orthopedic polyclinic visits and the time of early orthopedic polyclinic admission after the emergency service was not associated with clinical improvement, showing that unnecessary orthopedic polyclinic referrals can be prevented by briefing the parents of pediatric patients with fractures. When orthopedic polyclinic application reasons were considered, No-INF group outnumbered the INF group for the visit purpose for control which was reduced directly by informing parents. Another effect of the information was manifested in the significant increase in the group of patients who came for treatment termination at the end of the 3rd week. Moreover, the time of admission to the orthopedics polyclinic was shorther in the No-INF group compared to the INF group. Recently, studies focused on decreasing the appliction number of orthopedics polyclinic for fractures such as TF have reported not only decline in time and costs, but also ease of follow-up period (21). While 127 patients were admitted to the orthopedics polyclinic in the No-INF group group without parental information, this number was reduced to 64 in the INF group where parents were informed directly in the emergency clinic. The additional cost of 63 patient's admission to orthopedics polyclinic resulted in an additional cost of 8505 TL, and caused disruption in health services due to additional unnecessary examination. Considering the number of patients who are examined daily in our clinic (average 60-80 patients), it corresponds to a daily workload for each physician in the orthopedics polyclinic. Informing parents open and precise might reduce the time and costs without impairing the functional healing of torus fractures.

CONCLUSION

In pediatric patients admitted to the emergency department with a torus fracture, the time we will devote to parental information will result in less radiological examination, less radiation exposure, and fewer orthopedic outpatient referrals. This will prevent waste of time for the physician, decreases the treatment costs for the patient, and lightens the burden of healthcare system expenses. In the treatment of pediatric torus fractures, the time of early orthopedic polyclinic admission, the frequency of orthopedics polyclinic visits, and the number of radiography scans requested and also reduction of pediatric torus fractures have no effect on clinical recovery.

One of the limitations of the study is the lack of cost analysis which could not be calculated due to frequent price changes. Moreover, the waste of time for patient, parent and doctor examination could not be determined and calculated either. Since the study was retrospective, it was limited to a small sample size and the educational level of the the parents could not be determined to question whether they understood the information and recommendations during the treatment.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Hitit University Non-interventional Clinical Researches Ethics Committee (Date: 4.11.2022, Decision No: 2022-23).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: No conflict of interest was declared by the author.

Financial Disclosure: The author declared that this study had received no financial support.

Author Contributions: The author declares that he has responsible for the design, execution, and analysis of the paper and that he has approved the final version.

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Original Article

MEDICINE PALLIATIVE CARE

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Assessment of factors affecting mortality in patients with percutaneous endoscopic gastrostomy tube placement in the intensive care unit

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ABSTRACT

Aim: It was aimed to evaluate the clinical outcomes, complications, and factors affecting mortality of percutaneous endoscopic gastrostomy (PEG) applied to patients in the intensive care unit (ICU).

Material and Method: PEG procedures which were performed in the ICU between January 2016 and January 2021 and patients' age, gender, comorbidities, trauma history, serum CRP, albumin levels, CRP albumin ratios (CAR), and PEG-related complications were reviewed. Patients were divided into two groups, patients without mortality (Group 1) and patients with mortality (Group 2), and a comparison between groups was made.

Results: Of all patients, 49 (39.2%) patients had mortality. The mean age of the patients in group 2 was 69.57±16.78 years, which was higher than the other group (p<0.001). Nephrological diseases and diabetes were significantly more common in Group 2, whereas neurologic diseases were less common (p=0.005, p=0.005, 0.044, respectively). The median length of stay (LOS) of the patients in Group 1 was 50 days, while the median LOS of the patients in Group 2 was found to be significantly higher, with 81 days (<0.001). The mean CRP of Group 2 was 81.63±54.06, which was higher than the other group, while the mean of albumin was found to be 2.29±0.5 and was lower than Group 1 (p<0.001, p<0.001). The mean CAR of Group 1 was 15.96±16.81, which was significantly lower than that of Group 2 (p<0.001). The optimal CAR cut-off value for mortality discrimination was found to be 20,216 with a sensitivity of 73.5%, a specificity of 78.9%, a positive predictive value of 69.2%, a negative predictive value of 82.2%, and 76.8% test accuracy. A CAR value of ≥ 20.216 increased the odds of death 9.3-fold (OR 10.385, CI 95% 4.481-24.065, p<0.001).

Conclusion: We suggest that CAR ratio, low albumin, and high CRP levels could be predictors of early mortality. Considering that PEG is an elective procedure, we believe that it can be a safe and effective procedure when nutritional support is provided by alternative means and appropriate conditions are met.

Keywords: Percutaneous endoscopic gastrostomy, complications, CRP/albumin ratio, mortality

INTRODUCTION

The primary indication for enteral and parenteral nutrition is to provide nutritional support to meet metabolic requirements in patients with inadequate oral intake. Enteral feeding is generally the preferred method over parenteral feeding in patients with a functional gastrointestinal (GI) tract due to the associated risks of the intravenous route, higher cost, and the inability of parenteral feeding to provide enteral stimulation and subsequent disruption of the intestinal defense barrier (1,2). It has also been shown that enteric feeding can reduce the risk of bacterial translocation and associated bacteremia. Tube feeding through the gastrointestinal tract is mainly considered in patients with inadequate oral intake who have a functional GI tract and for whom tube placement in the digestive tract can be safely maintained.

Percutaneous endoscopic gastrostomy (PEG) is a common procedure indicated for patients with a normal gastrointestinal function who are expected to require long-term enteral nutrition. However, patients requiring PEG typically have underlying chronic diseases and fragile general health. Although there are currently no established standardized criteria for patients requiring PEG, guidelines published by the American Gastroenterological

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Association recommend that PEG be performed only in patients expected to survive more than 30 days after the procedure (3). Despite ongoing efforts to investigate risk factors associated with PEG-related complications and mortality, there have been many studies that have reported different risk factors (4-7). Furthermore, it should be noted that although the PEG has been shown to be a safer option than radiologic or surgical placement, acute and chronic complications have been reported as well. The 30-day mortality rate after PEG has been reported to be 3.3-23.9% (8). The complication rate with PEG has been reported to be 13.2-42.9% (9,10). Complications, including bleeding, wound infection, tube occlusion, tube leakage, aspiration pneumonia, perforation, and buried bumper syndrome, are associated with PEG (11).

Both high CRP and low albumin levels have been shown to be associated with significantly higher mortality in patients undergoing PEG. High CRP and low albumin levels undoubtedly pose a mortality risk for all surgical procedures (7,12,13)

High serum CRP levels have been associated with inflammatory conditions (14). According to studies, both low albumin levels and high CRP levels are associated with malnutrition (7,15). Furthermore, PEG is performed because low albumin levels are an indicator of malnutrition. However, patients who die within 30 days do not benefit from PEG. Therefore, underlying acute conditions should be identified and mitigated, based on albumin and CRP results.

The combination of albumin and CRP in a single index has previously been suggested, and subsequent studies have demonstrated that the CRP/albumin ratio is more indicative of prognosis than either CRP or albumin alone (16). There has been extensive research on the CRP/albumin ratio as an independent prognostic marker in patients with infections, malignancies, and other diseases (16,17). Kim et al. (17) showed that the CRP/albumin ratio at admission was positively correlated with prognosis in patients with severe sepsis or septic shock treated with early targeted therapy. In a study of elderly patients admitted to the emergency department, a high sensitivity-CRP/albumin ratio at admission to the emergency department was associated with all-cause in-hospital mortality in patients older than 65 years (18). CAR has been shown to be a predictor of mortality in patients with acute pancreatitis (19). Furthermore, CAR has predicted overall survival in various malignancies (20-24). However, there are relatively few studies focusing on critical care patients in the ICU (16). There is only one study in the literature about CAR in patients who underwent a PEG in the ICU, and in this study, it was revealed that CRP/albumin ratio could be used to predict complications and early mortality after PEG placement (25).

The aim of this study was to evaluate the clinical outcomes, complications, and factors affecting mortality of PEG performed in critically ill patients in the ICU of the 3rd level Anesthesia and Reanimation Unit, although it is safe and minimally invasive.

MATERIAL AND METHOD

This study was approved by the Hitit University Non-Interventional Researches Ethics Committee (Date: 02.07.2021, Decision No: 2021-73). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Only the PEG procedures performed by the General Surgery Clinic in the 3rd Stage Anesthesia and Reanimation Intensive Care Unit at Hitit University Medical Faculty Erol Olçok Training and Research Hospital between January 2016 and January 2021 and related patients were reviewed. Of these patients, 125 patients were included in the study excluding patients under the age of 18 years, patients with known hematologic diseases, patients without progression records according to hospital records, and patients with a history of upper gastrointestinal obstructive malignancy. 125 patients' age, gender, known neurological, respiratory, gastrointestinal, nephrological, urological, cardiovascular system diseases, trauma history, length of hospitalization, pre-PEG placement serum CRP and albumin levels, CRP albumin ratio (CAR), intubation status of the patient, tracheostomy status and complications due to the PEG were obtained by retrospectively scanning from the archive system. When evaluating the mortality, the follow-up periods of the patients until discharge from the ICU were taken, and patients who developed mortality during the follow-up period (group 1) and patients who did not develop mortality (group 2) were divided into 2 groups, and these groups were compared.

It was designed as a retrospective study. All statistical analyses were conducted using IBM SPSS Statistics for Windows software (version 26; IBM Corp., Armonk, N.Y., USA). Descriptive statistics were expressed as numbers and percentages for categorical variables, and mean ± standard deviation and median in parentheses for numerical variables. The normal distribution of the data was analyzed via the Shapiro-Wilks test. The relationships between variables were investigated using Pearson or Spearman correlation coefficients depending on the distribution normality of the data. Comparison of numerical measurements according to the study groups for two independent groups was evaluated by Mann Whitney U test for age, LOS, pre-PEG placement serum CRP and albumin levels depending on the data distribution. Ratio comparisons of categorical

variables such as gender, known neurological, respiratory, gastrointestinal, nephrological, urological, cardiovascular system diseases, presence of trauma history, rate of need for change after PEG placement, presence of PEG-related infection, intubation status of the patient, and tracheostomy rates according to research groups were analyzed using chi-square test. ROC curve was used to show the discriminating power of CAR, which was significant in terms of mortality, and cut-off values for markers were found using the area under the curve and Youden's index. The sensitivity, specificity, PPV, NPV, and accuracy values were calculated for these cut-off values. Odds ratio values were calculated according to these cut-offs. The level of statistical significance was considered as p<0.05.

RESULTS

The mean age of 109 patients in the whole group was 62.54±17.93 (65) years. 76 (60.8%) patients were male and 49 (39.2%) were female. Patients' comorbidities, LOS, CRP, albumin, and CAR ratios are shown in **Table 1**.

Complications that developed during and after PEG in patients are shown in **Table 2** and indications for the procedure are shown in **Table 3**. Of all patients, 48 (38.4%) patients underwent tracheostomy during the procedure and 28 (22.4%) patients were intubated during the procedure. Mortality developed in 49 (39.2%) patients. No PEG-related mortality was observed.

Comparison of Patients with and without Mortality

Patients were divided into 2 groups without mortality (group 1) and with mortality (group 2) and comparisons were made between the variables. The mean age of group 1 patients was 58±17.27 (61.5) years and that of group 2 patients was 69.57±16.78 (74) years. Group 2 patients were older with a significant difference (p<0.001). When compared in terms of comorbidities, the incidence of neurological and nephrological diseases was significantly higher in group 1 patients compared to group 2 (p=0.044, p=0.005). The median LOS of group 1 patients was 30 (1-730) days, while it was 81 (4-539) days in the other group. It was longer, with a significant difference (p=<0.001). No significant difference was found between the groups in terms of other comorbidities (**Table 1**).

Table 2: Complications due to PEG

Acute complications	
Bleeding	1 (0.8%)
Ileus	2 (1.6%)
Chronic complications	
Wound infection	2 (1.6%)
Leak-Leakage	4 (3.2%)
Tube blockage	3 (2.4%)
Spontaneous tube removal	2 (1.6%)
Aspiration pneumonia	1 (0.8%)
Buried bumper syndrome	1 (0.8%)

Table 3: Indications for PEG Insertion

Diseases	n=125
Neurological Diseases	63 (50.4%)
Lung Diseases	18 (14.4%)
Malignant Diseases	13 (10.4%)
Nephrological diseases	8 (6.4%)
Cardiovascular Diseases	11 (8.8%)
Trauma	12 (9.6%)

The mean CRP of group 1 patients was 44.67±41.64 (34.84) and that of group 2 was 81.63±54.06 (64.9),

Table 1: Demographic characteristics, comparison between patient groups with and without mortality

Variables	All patients (n=125)	Without mortality (Group 1) (n=76)	With mortality (Group 2) (n=49)	Statistical Significance
Age	62.54±17.93 (65)	58±17.27 (61.5)	69.57±16.78 (74)	<0.001
Gender				0.051
Male	76 (60.8%)	41 (53.95%)	35 (71.43%)	
Female	49 (39.2%)	35 (46.05%)	14 (28.57%)	
Neurological Disease	96 (76.8%)	63 (82.89%)	33 (67.35%)	0.044
Respiratory Disease	18 (14.4%)	8 (10.53%)	10 (20.41%)	0.124
Nephrological Disease	21 (16.8%)	7 (9.21%)	14 (28.57%)	0.005
Malignancy	17 (13.6%)	13 (17.11%)	4 (8.16%)	0.189
Diabetes Mellitus	21 (16.8%)	7 (9.21%)	14 (28.57%)	0.005
Cardiovascular Disease	50 (40%)	26 (34.21%)	24 (48.98%)	0.100
Trauma	12 (9.6%)	8 (10.53%)	4 (8.16%)	0.763
Length of stay (days)	50 (1-730)	30 (1-730)	81 (4-539)	<0.001
CRP	59.16±50.08 (44.2)	44.67±41.64 (34.84)	81.63±54.06 (64.9)	<0.001
Albumin	2.89±1.27 (2.6)	3.28±1.45 (2.95)	2.29±0.5 (2.3)	<0.001
CAR	24.65±23.39 (16.56)	15.96±16.81 (11.02)	38.12±25.82 (30.24)	<0.001
PEG replacement	16 (12.8%)	10 (13.16%)	6 (12.24%)	0.881
PEG-associated infection	2 (1.6%)	0 (0%)	2 (4.08%)	0.152
Number of intubated patients	28 (22.4%)	10 (13.16%)	18 (36.73%)	0.002
Number of patients with tracheostomy	48 (38.4%)	23 (30.26%)	25 (51.02%)	0.020
Mortality	49 (39.2%)			

which was significantly higher (p<0.001). The mean albumin level of group 1 patients was 3.28±1.45 (2.95), while it was 2.29±0.5 (2.3), which was significantly lower than that of the other group patients (p<0.001). The mean CAR was 15.96±16.81 (11.02) in group 1 patients and 38.12±25.82 (30.24) in the other group, with a significant difference (p<0.001) (**Table 1**). No significant difference was found between the two groups in terms of PEG replacement and complications (**Table 1**).

While 10 (13.16%) patients in group 1 were intubated, in the other group, 18 (36.73%) patients were intubated, and a significant difference was found between the two groups, in terms of the intubation rates (p=0.002). 23 (30.26%) patients in group 1 had the tracheostomy, while, in the other group, 25 (51.02%) patients had the tracheostomy, and a significant difference was found between the groups (p=0.02) (**Table 1**).

The efficiency of CAR Value to Predict Mortality

The optimal CAR value to discriminate the groups with and without mortality was analyzed using the area under the ROC curve and Youden's index (AUC 0.792 (0.041), 95% CI 0.710-0.873, p<0.001). The optimal CAR cut-off value for mortality discrimination was found to be 20.216 with a sensitivity of 73.5%, a specificity of 78.9%, a positive predictive value of 69.2%, a negative predictive value of 82.2%, and test accuracy of 76.8%. A CAR value of ≥ 20.216 was found to increase the odds of death 9.3-fold (OR 10.385, CI 95% 4.481-24.065, p<0.001) (**Table 4**, **Figure 1**).

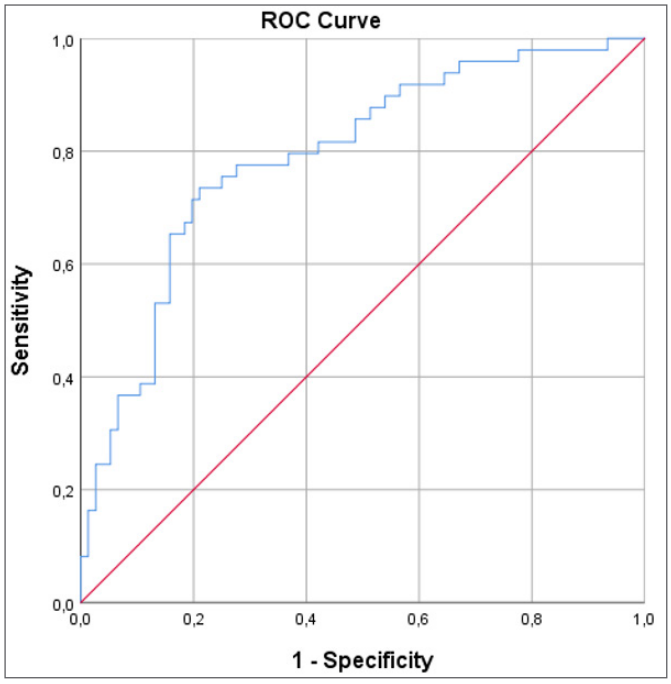

Figure 1: CAR cut-off point and diagnostic values for mortality

DISCUSSION

PEG is usually performed in patients with severe disease, elderly and nearing the end of life. In our study, the median age of the patients who underwent PEG in our study was 65 years. Several studies (4,8,26) have reported comparable results with a median age ranging from 66 to 80 years. The PEG is placed for a variety of conditions that prevent the patient's oral intake or require gastric decompression. It is necessary to define realistic goals and objectives given the indication and the patient's overall medical condition. It is placed to maintain or improve the patient's quality of life (even in the short term), reduce the patient's pain and suffering, and provide access to hydration or medication administration. In the PEG study applied to 80,000 patients, the most common indications for gastrostomy tube placement were a cerebrovascular disease, neoplasms, fluid and electrolyte disturbances, and aspiration pneumonia (27).In this study, neurological diseases (50.4%), pulmonary diseases (14.6%), and malignancy (10.09%) were the most common indications for PEG tube placement. Neurologic dysphagia is one of the most common reasons for PEG tube placement (11, 28).

PEG tube insertion is generally considered a safe procedure, but complications may occur at varying rates depending on the study population. Although procedure-related mortality was low in most studies, the mortality may increase in patients with underlying comorbidities (29). Despite ongoing efforts to assess risk factors associated with PEG-related complications and mortality, several studies have reported different risk factors (4-7). Moreover, although PEG has been shown to be a safer approach than radiologic or surgical placement, the complication rate with PEG has been reported to be 13.2%-42.9% (5,9,10). Complications such as bleeding, wound infection, tube occlusion, tube leakage, aspiration pneumonia, perforation, and buried bumper syndrome (BBS) are associated with PEG (11). In this study, complications developed in 16 (12.8%) patients. This was consistent with the literature.

Bleeding following gastrostomy tube placement is rare. It is usually caused by perforation of the left gastric or gastroepiploic arteries or one of their branches (30). Most bleeding can be controlled by applying simple pressure to the abdominal wound. Endoscopy or surgery should be performed if bleeding persists or if there are significant signs of bleeding such as decreased hemoglobin,

Table 4: CAR cut-off point and diagnostic values for mortality

Variables	Cut-Off	Diagnostic Values					ROC Analysis			Odds Ratio		
		Sensitivity	Specificity	PPV	NPV	Accuracy	Area (SE)	95% CI	p	OR	95% CI	p
CAR	≥20.216	73.5%	78.9%	69.2%	82.2%	76.8%	0.792 (0.041)	0.710-0.873	<0.001	10.385	4.481-24.065	<0.001

aspiration of pure blood from the stomach, melena, hematochezia, or hemodynamic instability. In this study, bleeding occurred in one patient, and gastroscopy was performed due to a decrease in hemoglobin. Besides, it was found that it was not from the stomach and blood products and fluid replacement were performed in the follow-up and it was under control.

Ileus rarely occurs after PEG and the reported incidence is 1%-2% (31). In this study, ileus developed in 2 (1.6%) patients and all patients improved after conservative treatment.

Diabetes mellitus (DM) and old age are considered important risk factors associated with the wound infection after invasive procedures and surgery. Furthermore, DM alters immunity by suppressing polymorphonuclear leukocyte function and cutaneous responses to antigen threats (32).In this study, wound infection developed in 2 (1.6%) patients in the chronic period after PEG. Considering that PEG is an invasive procedure penetrating through the skin into the stomach, wound healing is crucial to prevent infection and tube leakage. In this study, elderly patients with DM who underwent showed significant increases in chronic complications associated with wound healing, with tube leakage being the most common chronic complication in 4 (3.2%) patients.DM and old age may have contributed to tube leakage, which was observed in four patients who presented with signs of inflammation such as redness, pain, swelling, and pus-like discharge at the insertion site. In this study, mortality in patients with DM was significantly higher in Group 2. They found that increased mortality risk after PEG was associated with advanced age, male gender, and diabetes mellitus (8,33).In other studies, various risk factors including high CRP level, low albumin level, advanced age, low BMI, and diabetes mellitus have been reported to be associated with early mortality after PEG (4-8). Our study also supports these studies.

The incidence of feeding tube occlusion has been reported as high as 23%-35%. Risk factors for occlusion include the use of thick enteral feeding formulas, the use of bulking agents, and the use of a smaller diameter feeding tube (8-9 Fr). In this study, occlusion developed in 3 (2.4%) patients. We attribute the lower incidence than the literature to the use of an 18 Fr feeding tube with a larger diameter.

BBS is a serious complication of PEG tube placement that occurs when the internal tampon moves along the stomal tract and outside the stomach wall. This typically occurs as a result of excessive compression between the internal tampon and the external support. The incidence of BBS has been recorded to be approximately 1% (0.3%-2.4%). It occurred in 1 (1.2%) patient in the study and was consistent with the literature.

In this study, no mortality occurred due to the PEG procedure. A mortality rate of 49 (39.2%) was observed in patients with PEG, and it was found that this mortality was associated with high CRP levels, low albumin, elevated CAR, old age, nephrological diseases, diabetes mellitus, intubated patients with and patients with tracheostomy, longer hospitalization, and neurological diseases. Bloomberg et al. (7) found that a CRP level of >10 mg/L and albumin < 3.0 g/dL are independent risk factors for mortality after PEG. Moreover, using these cut-off points, the authors demonstrated 20.5% mortality in patients with high CRP and low albumin levels. In a similar study, the mortality was found to be approximately 60% in patients with a CRP of >21.5 mg/L and albumin of <3.15 g/dL (10). In another study that identified post-PEG CRP elevation as an independent risk factor, an 18% mortality rate was reported at CRP levels >50 mg/L. The cut-off point for low albumin level as an independent risk factor for mortality after PEG in dementia patients has been reported to be 2.8 g/dL (34). In another study, the cut-off points were 78.3 mg/L for CRP and 2.71 g/dL for albumin. Consistent with previous studies, these biomarkers were identified as an independent risk factor for mortality, with 73.1% of patients with high CRP/low albumin levels survived less than 30 days after PEG, which was identified as an independent risk factor for mortality (13). In this study, high CRP and low albumin values were predictive of mortality, which is consistent with the literature.

In this study, the optimal CAR cut-off value for mortality discrimination was 20.216 with a sensitivity of 73.5%, a specificity of 78.9%, a positive predictive value of 69.2%, a negative predictive value of 82.2% and 76.8% test accuracy (OR 10.385, CI 95% 4.481-24.065, p<0.001). A CAR value of 20.216 and higher increased the odds of mortality by 9.3 times. This is consistent with the literature, and in a study supporting this, it has been suggested that the CRP/albumin ratio can be used to predict complications and early mortality after PEG insertion, and that higher CRP/albumin ratios may help in decision-making in patient selection for the procedure, since PEG is elective (25).

CAR ratio, low albumin and high CRP levels have been previously reported as indicators of malnutrition, inflammation and postoperative infection (7,14,15). Since PEG is not an emergency procedure, it can be postponed; The authors reported that it can be done after investigating an underlying acute condition. In the meantime, nutritional support can be provided with less invasive methods such as parenteral nutrition

or nasogastric catheter (7). PEG should therefore be considered cautiously, particularly in patients with high CRP levels and low albumin levels, as with any elective surgical procedure.

The limitation of this study was that some data were missing from the medical records due to the retrospective design of the study. Besides, the complication and mortality rates were determined by reviewing file alone. Therefore, the possibility of misjudgment of complications and cause of death cannot be ruled out.

CONCLUSION

We suggest that the CAR ratio, low albumin and high CRP levels could be predictors of early mortality. Therefore, underlying acute conditions should be identified and alleviated under the guidance of CAR, albumin and CRP. Considering that PEG is an elective procedure, we believe that it can be a safe and effective procedure when nutritional support is provided by alternative means and appropriate conditions are met.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Hitit University Non-interventional Researches Ethics Committee (Date: 02.07.2021, Decision No: 2021-73)

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: No conflict of interest was declared by the author

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Author Contributions: The author declares that he has responsible for the design, execution, and analysis of the paper and that he has approved the final version.

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Original Article

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Relationship between hemoglobin, albumin, lymphocyte, and platelet (HALP) score and 28-day mortality in very elderly geriatric critically ill patients with acute ischemic stroke

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ABSTRACT

Aim: In this study, we aimed to evaluate the relationship between the HALP score, calculated by hemoglobin, albumin, lymphocyte and platelet values, and 28-day mortality in very elderly geriatric critically ill patients with acute ischemic stroke.

Material and Method: The study was designed retrospectively and patients aged 85 years and older admitted to the general intensive care unit with the diagnosis of acute ischemic stroke were evaluated. Demographic data, laboratory data and HALP scores of these patients were recorded. Patients who died within 28 days in intensive care follow-up were defined as the Non-Survival group, and patients who did not die were defined as the survival group.

Results:There was a statistically significant difference between the groups in terms of hemoglobin values admitted to the intensive care unit (p:0.00). For albumin, patients in the Non-Survival group had lower values, but there was no statistically significant difference between the groups (p: 0.054). Non-Survival group had lower values for lymphocytes and there was a statistically significant difference between the groups (p: 0.00). For platelet value, patients in the Non-Survival group had higher values and there was no statistically significant difference between the groups (p: 0.164). Patients in the Non-Survival group had lower values for HALP score and there was a statistically significant difference between the groups (p: 0.00)

Conclusion: The HALP score is associated with 28-day mortality in very elderly geriatric critically ill patients with acute ischemic stroke. However, it has low sensitivity (30.1%) and specificity (27.9%).

Keywords: HALP Score, very elderly geriatric patient, acute ischemic stroke

INTRODUCTION

Acute ischemic stroke (AIS) is one of the leading causes of mortality (1). The incidence of AIS increases with aging, and age is an important risk factor (2). Inflammation is known to occur in the pathophysiology of AIS. Necrotic cells, which are formed in the brain due to vascular occlusion, trigger inflammation in acut ischemic stroke (3). In addition, abnormal blood clotting, poor nutritional status and inflammation are associated with a poor prognosis of AIS (4,5).

Lymphocytes have an essential role in inflammation, and since inflammation is also involved in the pathophysiology of AIS, the lymphocyte values of these patients should be considered (6).

Platelet hyperactivity increases the risk of atherosclerosis and thromboembolism . Problems, abnormal thrombosis occurs and causes an increase in inflammation (7). Anemia and hypoalbuminemia are risk factors for AIS and are parameters associated with malnutrition (8).

Recently, the scoring system called Hemoglobin, albumin, lymphocyte, and thrombocyte (HALP) has started to take place in the literature as a mortality indicator, especially in patients with malignancy. This score reflects general nutritional status and systemic inflammation (9,10). These four parameters are involved in the pathogenesis and prognosis of AIS. In this study, we aimed to evaluate the HALP score, a typical combination of these parameters, in terms of prognosis and 28-day mortality in very elderly geriatric patients with AIS.

MATERIAL AND METHOD

The study was designed retrospectively, and ethical committee approval was obtained from the Kastamonu University Clinical Researches Ethics Committee (Date: 19.10.2022, Decision No: 2022-KAEK-97). All procedures were performed by the Declaration of Helsinki and ethical rules.

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Patients aged 85 and over who were admitted to the general intensive care unit (ICU) of Kastamonu Training and Research Hospital between January/2020 and October/2022 with the diagnosis of acute ischemic stroke, admission to intensive care biochemistry values (glucose, albumin, creatinine, etc.), National Institutes of Health Stroke Scale (NIHSS) scores, demographic data (age, gender), comorbidities, and whole blood values (hemoglobin, thrombocyte) of were reviewed and recorded retrospectively from the patient file and hospital information system. The diagnosis of AIS was based on the criteria of the World Health Organization (WHO) (11).

At admission, the severity of AIS was assessed according to the National Institutes of Health Stroke Scale (NIHSS). Patients with major trauma or surgery within three months,malnutrie, neoplastic hematological disorders or using immunosuppressant drugs ,active or chronic inflammatory disease, and severe hepatic and renal dysfunction were excluded from the study. After the exclusion criteria, 179 patients were included in the study.

The HALP scoring of these patients, hemoglobin (g/L) x albumin (g/L) x lymphocytes (/L)/platelet (/L), were calculated and recorded (12).

NIHSS scoring; 1-15 points: mild; moderate between 16-20 points; A score between 21 and 42 was classified as high (13).

Of the 179 patients included in the study, 93 patients who died within 28 days in ICU follow-up were in the Non-Survival group; 86 patients who survived more than 28 days were designated as the survival group.

Statistical Analysis

All statistical analyzes were performed using SPSS Version 26.00 (SPSS Inc, Chicago, USA). Whether the data showed normal distribution was determined using Kolmogorov-Smirnov and Shapiro-Wilk tests. It was defined as the median (± standard deviation) for continuous variables and frequency (percent) for categorical variables. Chi-square for categorical variables, Student-t test for normally distributed continuous variables, and Mann-Whitney U test for non-normally distributed continuous variables. Binary logistic regression was performed for confounding factors in 28-day mortality. Roc curve analysis was performed to determine the sensitivity and specificity of the Halp score. The $p<0.05$ value was considered statistically significant.

RESULTS

A total of 179 patients were included in the study, and 93 (51.9%) patients (Non-Survival group) died within the first 28 days of intensive care follow-up. 86 (48.1%) patients (Survival group) survived longer than 28 days. Gender and mean age were similar in both groups and there was no statistical difference between the groups. When both groups were evaluated in terms of comorbidities, there was no statistically significant difference between the groups. However, hypertension was more common among additional diseases in both groups (**Table 1**).

Table 1. Demographic data and comorbidities

	Non-Survival Group (n:93)	Survival Group (n :86)	P
Gender (N/%)			0.956
Male	31 (33.3%)	29 (33.7%)	
Female	62 (66.6%)	57 (66.3%)	
Age (Mean±SD)	89.17±3.39	88.57±3.26	0.208
Hypertension (N/%)			0.645
Yes	54 (58%)	47 (54.7%)	
No	39 (42%)	39 (45.3%)	
Diabetes mellitus			0.574
Yes	34 (36.5%)	28 (32.6%)	
No	59 (63.5%)	58 (67.4%)	
Hyperlipidemia			0.663
Yes	14 (15.1%)	16 (18.6%)	
No	79 (84.9%)	70 (81.4%)	
Heart failure			0.518
Yes	39 (42%)	32 (37.2%)	
No	54 (58%)	54 (62.8%)	
Atrial fibrillation			0.607
Yes	37 (39.8%)	31 (36%)	
No	56 (60.2%)	55 (64%)	
Coronary artery disease			0.625
Yes	29 (31.2%)	23 (26.7%)	
No	64 (68.8%)	63 (73.3%)	

In terms of Apache II and Saps II scores, patients in the Non-Survival group had higher scores. For Apache II, the Median±SD value of the patients in the Non-Survival group was 29.62±8.53; Median±SD for Saps II was 44.57±7.52. There was a statistically significant difference between the groups in terms of Apache II and Saps II scores (P: 0.00 for Apache II, p: 0.00 for Saps II).

There was a statistically significant difference between the groups in the statistical analysis for the hemoglobin value admitted to the intensive care unit, and the patients in the Non-Survival group had lower values. (Non-Survival group Median±SD: 125.13±17.67, Survival group Median±SD: 134.99±11.92; p: 0.00). Patients in the Non-Survival group had lower values for albumin and there was no statistically significant difference between the groups (p: 0.054). Non-Survival group had lower values for lymphocytes and there was a statistically significant difference between the groups. (Non-Survival group Median±SD: 1.34±0.54, Survival group Median±SD: 1.96±64; p: 0.000) For platelet value, patients in the Non-Survival group had higher values

and no statistically significant difference was found between the groups (p: 0.164). For the HALP score, which is the combination of these four parameters, the patients in the Non-Survival group had lower values and there was a statistical significant difference between the groups (Non-Survival group Median±SD: 27.81±16.05, Survival group Median±SD: 48.71± 22.37; p: 0.000). In addition to these findings, nearly half of the patients in the Non-Survival group (48.3%) had a more severe acute ischemic stroke clinic than the NIHSS score, and there was a statistically significant difference between the groups (p:0.00). (**Table 2**)

Table 2. Laboratory data and HALP scoring

	Non-Survival group (n:93) Median±SD	Survival gruop (n :86) Median±SD	p
Apache II	29.62±8.53	22.20±5.19	0.000*
Saps II	44.57±7.52	34.92±7.72	0.000*
Albumin(g/L)	32.35±6.11	34.09±6.58	0.054
CRP (mg/L)	7.33±9.79	7.86±6.28	0.156
HDL (mg/dL)	43.91±9.09	45.90±10.09	0.807
LDL (mg/dL)	106.04±33.27	105.19±36.23	0.518
Triglyceride(mg/dL)	117.45±51.03	119.49±48.93	0.884
Total Cholesterol, (mg/dl)	151.86±46.80	158.41±42.49	0.248
Creatinine (mg/dl)	1.13±0.28	1.05±.0.30	0.070
Glucose (mg/dL)	154.98±76.86	138.92±39.19	0.425
White Blood Cell (103 /ul)	9.44±2.31	9.80±2.34	0.410
Hemoglobin (g/L)	125.13±17.67	134.99±11.92	0.000*
Platelet (103 /ul)	219.49±80.09	199.83±61.70	0.164
Neurophil (103 /ul)	5.71±1.29	5.75±1.22	0.814
Lymphocyte(103 /ul)	1.34±0.54	1.96±64	0.000*
NIHSS (n/%)			0.000*
Mild	10 (10.8%)	41 (47.8%)	
Moderate	38 (40.9%)	34 (39.5%)	
High	45 (48.3%)	11 (12.7%)	
HALP	27.81±16.05	48.71±22.37	0.000*

According to logistic regression analysis, there was a correlation between 28-day mortality and HALP, Saps II and NIHSS scoring. (for HALP; p: 0.001, for Saps II; p: 0.00 for NIHSS; p: 0.001). However, the HALP score had low sensitivity and specificity for 28-day mortality. (Sensitivity: 30.1%, specificity: 27.9%) (**Table 3**, **Figure**).

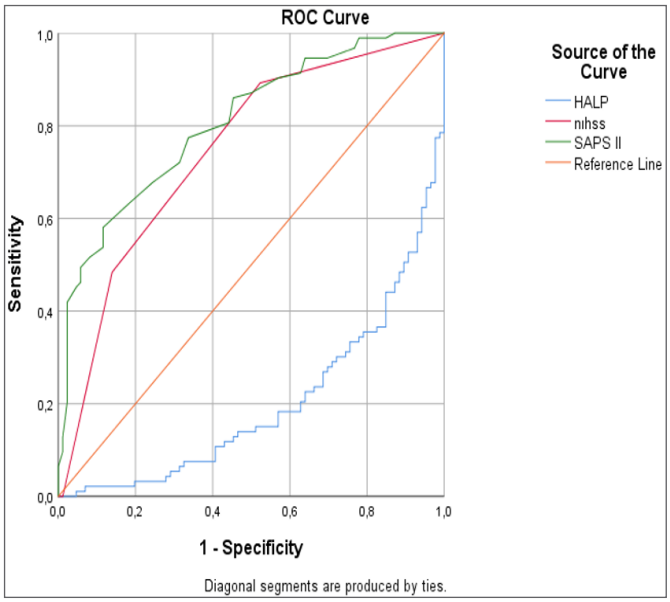

Figure. ROC curve analysis

DISCUSSION

In this study, we found a statistically significant difference between the groups in terms of Apache II score, Saps II score, NIHSS score, HALP score, hemoglobin and lymphocyte values at 28 days of mortality in advanced geriatric acute ischemic stroke patients. In addition, HALP score (p: 0.001), Saps II score (p:0.00), and NIHSS score (p: 0.001) were associated with 28-day mortality. However, the HALP score had low sensitivity (30.19%) and specificity (27.9%) for 28-day mortality.

The HALP score indicates the inflammation and nutritional status of patients. HALP score is a parameter that has been associated with survival in patients with malignancy in recent years. Peng et al. (10) showed that there is a significant correlation between HALP score and survival in patients with bladder cancer. Similar to this study, Xu et al. (12)reported that the HALP score was associated with survival and recurrence in a study conducted in patients with postoperative pancreatic cancer. In our study, we found that the HALP score was associated with 28-day mortality in very elderly geriatric critically ill patients with acute ischemic stroke.

Table 3. Logistic regression analysis

	B	S.E	Exp(B)	95%C.I.for EXP(B)		P
				Lower	Upper	
HALP	0.065	0.020	1.067	1.027	1.109	0.001
Apache II	-0.087	0.044	0.917	0.840	1.000	0.051
Saps II	-0.141	0.038	0.869	0.807	0.935	0.000
Hemoglobin (g/L)	0.017	0.018	1.017	0.982	1.054	0.346
Lymphocyte (10^3/ul)	0.509	0.462	1.664	0.673	4.114	0.270
NIHSS	-0.852	0.251	0.427	0.261	0.697	0.001
Constant	3.974	2.858	53.190			0.164

Nagelkerke R Square 0.671 NIHSS: The National Institutes of Health Stroke Scale Scores, HALP: Hemoglobin, Albumin, Lymphocyte , Platelet,APACHE: Acute Physiology and Chronic Health Evaluation, CRP: C-reactive protein, SAPS: Simplified Acute Physiology Score

Acute ischemic stroke begins with gradual or sudden cerebral hypoperfusion, including oxidative stress, hemostatic activation, and inflammation, eventually leading to a corresponding loss of neurological function (14). Low hemoglobin is a risk factor for AIS, a poor prognostic marker, and a strong parameter associated with mortality (15,16). In addition, anemia is a condition that increases inflammation (17). Albumin is a parameter associated with nutrition and inflammation produced in the liver. In addition, albumin level is also associated with the severity and prognosis of the disease in case of acute illness (18). Dziedzic et al. (19) reported that albumin level is associated with prognosis in patients with ischemic stroke. Lymphocytes are cells involved in the regression of inflammation. Low lymphocyte count causes exacerbation of inflammation. Since inflammation plays a role in the pathogenesis of acute ischemic stroke, low lymphocyte counts are associated with poor prognosis in these patients. In their study, Kim et al. (20) reported that low lymphocyte value in patients with acute ischemic stroke was associated with less recovery during the first week after admission and poor functional outcome at three months. Although platelets are mainly responsible for hemostasis, they affect the immunomodulatory system (21). Inflammation triggers the thrombosis process in which platelets participate in aggregation, release reaction and adhesion (7). Studies have shown that platelet count can be a qualified predictor of poor functional outcome ,mortality and long-term recurrent stroke. Yang et al. (22), in their study with patients with acute ischemic stroke, stated that there was a U-shaped relationship between the initial platelet count and poor functional outcome. Each parameter (hemoglobin, albumin, lymphocyte, thrombocyte) is valuable in terms of prognosis when evaluated individually. The HALP score, which is a combination of these parameters, may be a better prognostic indicator than these four parameters. In our study, there was a statistically significant difference in hemoglobin and lymphocyte values between the groups for 28-day mortality, but there was no statistically significant difference between the groups for albumin and platelet values. The HALP score, on the other hand, was statistically different between the groups and was associated with 28-day mortality.

CONCLUSION

The HALP score is an easily calculated, cost-effective parameter associated with inflammation and nutrition. The HALP score is associated with 28-day mortality in very elderly geriatric critically ill patients with AIS. However, it has low sensitivity (30.1%) and specificity (27.9%). More studies on HALP score are needed in this patient group.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Kastamonu University Clinical Researches Ethics Committee (Date: 19.10.2022, Decision No:2022-KAEK-97).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare thatthey have all participated in the design, execution, andanalysis of the paper and that they have approved the final version.

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Original Article

MEDICINE PALLIATIVE CARE

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Clinical outcomes of palliative 3-dimensional conformal external beam gastric radiotherapy: single center experience

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ABSTRACT

Aim: Patients diagnosed with locally advanced and/or metastatic gastric cancer and who cannot undergo surgery may need palliative treatment during their follow-up. There is scarce data about outcomes of palliative gastric radiotherapy (RT). In this study, we aimed to investigate the effect of 3-D external beam RT on oncological outcomes, as a non-invasive method.

Material and Method: From 2013 to 2017, sixteen gastric cancer patients treated with palliative external RT in our institutional clinic were evaluated. Only patients who received palliative gastric radiotherapy for obstruction, pain and bleeding were analyzed, and patients who had previously received RT to the abdomen or who were given RT for adjuvant purposes were not included in the analysis.

Results: Seven patients (43%) were not able to finish the planned palliative course. Thirty Gray with 10 fractions was the most planned RT schedule. Almost half of the patients (%56) received chemotherapy before RT. Overall survival was found to be median 2 months. Median survival was better in patients who were able to receive 28 Gy bioequivalent dose (4 vs 0.3 months, p≤0.00). Purpose of palliation also found to be a significant factor on survival. Patients who were referred for pain have found to be better survival rather than bleeding and obstruction (13 vs 0.7 months, p=0.03).

Conclusion: External radiotherapy is an easily applicable and effective method for palliation in gastric cancer patients. Early referral for radiotherapy in patients who need palliation may increase oncological outcomes. It has been observed that the prognosis is worse in patients who received palliative radiotherapy due to gastric bleeding and obstruction.

Keywords: Gastric cancer, radiotherapy, gastrointestinal hemorrhage

This study was accepted as Oral Presentation at 11. International Gastrointestinal Cancer Conference held in İstanbul, Turkey on 2-5 December 2021.

INTRODUCTION

Gastric cancer is the third most common cancer worldwide and also fifth in Turkey (1). 5-year overall survival is approximately 20% (2,3). Some patients still may not be approached curatively despite the improvements and new technologies in imaging, surgery and adjuvant therapies. Patients who could not have gastrectomy or locally recurred during the follow-up may need palliation for the local disease during follow-up.

Palliative radiotherapy is a non-invasive, easily applicable and successive approach that has been used for many sites, diseases and conditions like pain, obstructive symptoms and bleeding. Despite the common use of radiotherapy for gastric palliation, there is scarce data in the literature on that topic.

In this study, we tried to evaluate palliative radiotherapy outcomes in patients who were referred for symptomatic local disease, such as bleeding, pain and obstruction, as a non-invasive approach.

MATERIAL AND METHOD

All the medical records between 2013 and 2017 at Ankara Traininig and Research Hospital Radiation Oncology Department were reviewed retrospectively in which patients diagnosed with gastric cancer who were referred for palliative radiotherapy (RT) with any symptoms were included in this study. This study has been initiated after ethical approval taken from Ankara City Hospital No: 1 Clinical Researches Ethics Committee (Date: 25.08.2021, Decision No: E1-21-1954). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

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We excluded the patients who were evaluated in a definitive setting for medically inoperable newly diagnosed patients. Data was collected from the institutional registry and our local radiation oncology database. Patients who had undergone prior RT were excluded. Sixteen metastatic patients who had been treated with palliative gastric RT were included in the current study. Overall survival was calculated from the first day of radiotherapy to death. Patient characteristics were shown in **Table 1**.

Table 1. Patient Characteristics	
Median Age n, (Min-Max)	63 (12-85)
Sex n, (%)	
Female	3 (19)
Male	13 (81)
Histopathology n, (%)	
Adeno Ca	14 (88%)
Malign Epithelial Tm	2 (12%)
Metastatic Spread n,(%)	
One site	8 (50%)
At Least Two Sites	7 (44%)
Unknown	1 (6%)
Symptom n,(%)	
Bleeding	10 (62%)
Obstruction	3 (19%)
Pain	3 (19%)
Median RT Dosage (Min-Max)	4250 cGy (180-4000)
Chemotherapy before RT n, (%)	
Yes	9 (56%)
No	7 (44%)

3-dimensional conformal radiotherapy was used for all treatments. The target volume was the whole stomach and 0.5-1 cm planning target volume margins were added for setup errors and organ movements. Most of the patients were male and the most common RT protocol was 30 Gy in 10 fractions daily. α/β value was taken as 10 for bioequivalent dose (BED10) calculations.

Statistical analysis was performed using the SPSS software version 24 (IBM, Armonk, NY). Categorical data were given as numbers and proportions, Median and minimum-maximum levels were used for non-normally distributed quantitative variables. All tests were two-sided and a 0.05 p-value or less was considered statistically significant. Overall survivals were calculated from the first day of RT to death with the Kaplan-Meier estimation method. Log-rank statistics were used for analyzing the effect of symptom type, metastatic burden and RT dose on survival.

RESULTS

Patient Characteristics

In this single-center study, 16 patients were found referring to our institution for palliative gastric RT. None of the patients has prior RT history. The median age was found 63 (12-85) and 13 (81%) patients were male. All patients except one were metastatic at the time of diagnosis and no patient underwent gastrectomy before RT. Eight patients had a single metastatic disease at the time of diagnosis and the remaining seven patients had multiple metastases. While the tumor site was widespread in more than one region of the stomach in nine patients, 6 patients had a single localization. Adenocarcinoma was found as common histology and bleeding was the major referring symptom. Three thousand cGy in ten fractions was the most commonly used regimen. Chemotherapy has already begun for progression in 9 patients (56%) before palliative RT with minimal or nil response.

Outcomes

All the patients were dead, and any censored data did not exist at the time of the analysis. Median overall survival (OS) was found at 2 months for the whole cohort. After the beginning of radiotherapy, only 7 (43%) patients were able to finish the planned palliative RT schedule. The median BED10 value was 28.8 Gy. Overall survival was statistically better for those who were able to receive 2800 cGy biologically equivalent dose (p≤0.00) (**Figure 1**).

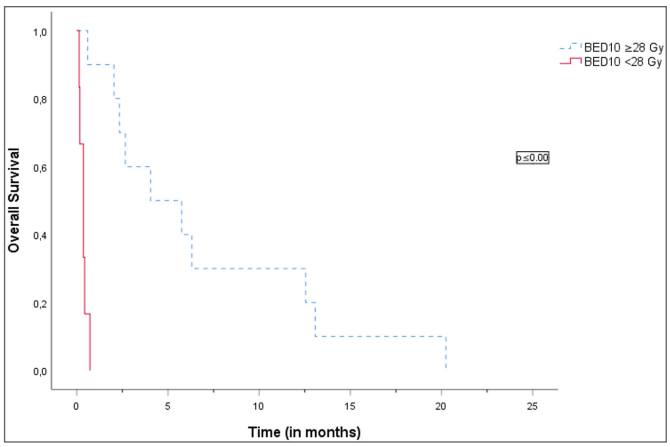

Figure 1. Kaplan-Meier Curves based on the Bioequivalent Radiotherapy Doses for α/β=10

In terms of symptom and number of metastases, OS was found worse in patients irradiated for bleeding and obstructive symptoms rather than pain (13 vs 0.7 months, p=0.03) (**Figure 2**). We also found overall survival as 5.7 months in patients with one distant metastasis and 0.6 months for multiple (p≤0.01) (**Figure 3**). We could not find any effect of previously applied chemotherapy on survival outcomes.

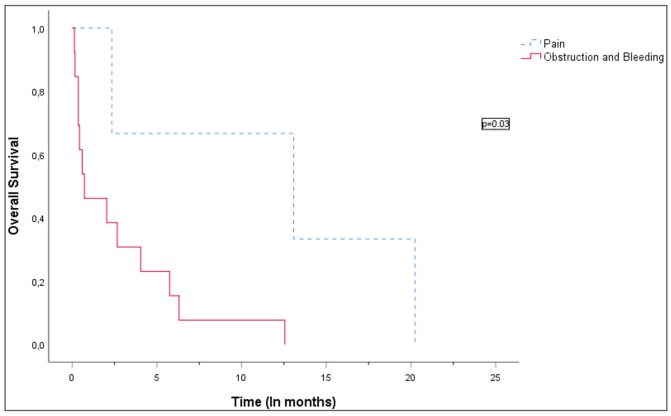

Figure 2. Kaplan-Meier Curves according to the symptoms

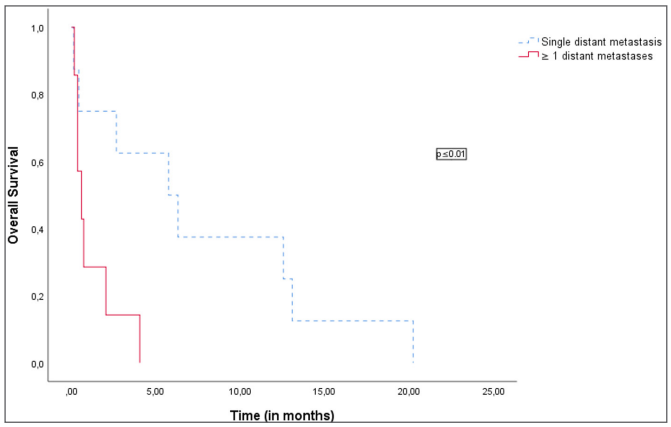

Figure 3. Kaplan-Meier curves according to the number of distant metastasis sites.

DISCUSSION

This report demonstrates that palliative radiotherapy is an effective, non-invasive approach, especially in patients referred for pain when given over 2800 cGy BED dose.

Overall survival who needs palliation in advanced gastric cancer is generally poor. It varies from 2.1 to 5.2 months in different case series despite the good responses, especially for bleeding (4-11). In most published studies on this topic, the patient population includes both metastatic and non-metastatic patient groups. Only metastatic patients were examined in the studies of Hashimoto (5) and Kondoh et al. (10) like the current study. In these studies, which included 19 and 15 patients, overall survival was found to be 3.4 months and 2.1 months, respectively. In our relatively but comparable small series with 16 metastatic patients, overall survival was found to be 2 months, and in this sense, it was found to be similar to the published data. The total applied radiation dose also seems to have a role in outcomes. In the study of Mitsuashi et al. (12) from Japan, where the incidence of gastric cancer is high, survival analysis was performed according to palliative RT dose. Here, doses with BED10 value above and below 39 Gy were compared and no contribution to survival was determined. The effect of palliative radiotherapy dose on survival was also evaluated in our study. The survival of patients who could receive 2800 cGy or higher bioequivalent dose (BED10) was found to be 4 months. Survival was found to be 0.3 months in patients who couldn't receive BED10 2800 cGy and this difference was significantly high (p=.0). When patients receiving less than 2800 cGy were examined, it was found that most of these patients were not able to receive the intended dose. This may be due to the initiation of palliative treatment with another non-invasive method, chemotherapy, in patients with gastric cancer who needs palliation. To start palliation with chemotherapy as first-line treatment may delay the start of radiotherapy. Additionally, systemic side effects of chemotherapy, which can continue during radiotherapy, may have a negative impact on outcomes in this group of patients. Therefore, early referral of patients who require palliative gastric radiotherapy may lead to the administration of planned palliative doses, which may increase oncological outcomes and palliation rates. In our series, only half of the patients were able to finish the complete planned course of RT.

Invasive procedures like endoscopic laser coagulation, gastrectomy and non-invasive palliative chemotherapy are the alternative approaches for palliation (13-16) and need better performance status. This may explain the use of RT in patients with poorer performance status and relatively low survival rates in our trial.

As we examined the relationship between the symptomatic reason for palliative RT and survival, significantly worse results were found in patients irradiated for bleeding and obstructive symptoms like less than a month. Patients who received palliative RT due to pain had a survival of approximately one year despite metastatic state. Therefore, even though the bleeding control was achieved, a lower survival rate with palliative RT has been observed for bleeding, and a relatively good survival rate of 13 months was found for pain.

Although some studies (11,12,17) have shown that radiotherapy is an effective method for bleeding, our data also shows the positive contribution of palliative RT on pain relief. In a series of 115 patients, Tey et al. (9) reported that 80.6% of patients had bleeding control, 45.5% had pain control, and 51.2% had obstruction palliation with palliative RT in the metastatic and non-metastatic patient group. There are also publications that have a relatively low 50% hemorrhagic response rate. Duration time for bleeding control varies between 1.5 and 11.4 months in the literature. Although the number of patients who underwent palliation due to pain and

obstruction were less, response rates were found 67% for pain and 68% for obstruction in other relatively small series (18). In a case series, three year long term symptom control for obstruction has also been reported (19).

In this study, the number of metastatic sites was also found to be a negative prognostic factor. While the survival rate was 5.7 in patients with metastases in a single metastatic site or organ other than primary cancer, survival was found to be 0.6 months in patients with more than a site. This result showed that, as expected, the cancer spread and survival were also inversely proportional in gastric cancer patients who needed palliation.

Chemotherapy can also be used concurrently with or without RT for palliation in gastric cancer (15). The role of concomitant chemotherapy with palliative radiotherapy has not been determined well. Fifty-six percent of our patients received chemotherapy. In the study by Asakura et al. (7), it was found that chemo radiotherapy may lead to a decrease in the re-bleeding events. Chemotherapy with concomitant radiotherapy is also the main treatment modality in advanced unresectable gastroesophageal junction and esophageal cancer and adding chemotherapy to radiotherapy in this group of patients improves survival (20, 21). Whilst, in a phase 3 study by the Trans-Tasman Radiation Oncology Group examining the contribution of adding chemotherapy to palliative radiotherapy in patients with esophageal cancer, it was found that while chemotherapy increasing toxicity, it did not change oncologic outcomes (22). In the current study, no difference in survival was found in the group receiving chemotherapy compared to those who received not.

CONCLUSION

External radiotherapy is an effective and easy applicable method for palliation in gastric cancer patients. Oncological outcomes may be improved with early radiotherapy initiation and higher bioequivalent RT doses. Current study demonstrated that the referral symptom for palliation has an impact on the oncologic outcome. Better results were shown in patients who received radiotherapy for pain compared to bleeding and obstruction. Prospective randomized studies are needed for further results.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara City Hospital No: 1 Clinical Researches Ethics committee (Date: 25.08.2021, Decision No: E1-21-1954)

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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Original Article

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The relationship between the preferences of the oral glucose screening test and the levels of health literacy and perinatal anxiety of pregnancy

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ABSTRACT

Aim: This research aimed to determine the relationship between pregnant women's oral glucose screening test preferences and their health literacy and perinatal anxiety levels.

Material and Method: The study is descriptive and cross-sectional. The sample of the study consisted of 120 pregnant women who applied to a university hospital between June and July 2022, were accepted to participate in the study, had no Turkish speaking problems, no pregestational diabetes diagnosis, no vision and hearing problems, no mental health problems, and were literate. The data were collected using face-to-face interviews with pregnant women including a questionnaire asking about the introductory characteristics of pregnant women, Turkish Health Literacy Scale-32 (TSOY-32), and Perinatal Anxiety Screening Scale (PASS). The obtained data were analyzed using one-way analysis of variance, correlation analysis, and chi-square tests.

Results: 52.5% of pregnant women believed that they do not need to have an OGT. While the effect of health personnel in this decisions is 66.1%, the effect of the closed environment is 22.9%. A statistically significant negative correlation at $p<.05$ level was found between the Turkish health literacy scale and the Perinatal anxiety screening scale scores. Participants' believes on the necessity of OGTT test has no effect on their TSOY-32 scores or PASS scores. There is no association between the preference of women and the sub-dimensions of TSOY-32 and the PASS.

Conclusion: The health literacy and perinatal anxiety levels of the pregnant women in the sample group did not affect their OGTT preferences. They stated that healthcare professionals were primarily influential in their decisions on OGTT preferences.

Keywords: Gestational diabetes mellitus, glucose tolerance test, health literacy, perinatal anxiety

INTRODUCTION

Gestational diabetes mellitus (GDM) is one of pregnancy's most common medical complications (1). It is carbohydrate intolerance that occurs in the second or third trimester of pregnancy, although the individual does not have type 1 or type 2 diabetes before. When the results of studies conducted in many countries are compared with the data in 1980, it is stated that the prevalence has doubled. One in seven births worldwide has GDM. Women diagnosed with GDM and their children experience complications caused by hyperglycemia and hyperinsulinemia in the short and long term (2). GDM is a crucial issue causing mortality and morbidity in both mothers and their babies. Obesity, maternal age, impaired glucose tolerance in previous pregnancies, and fetal macrosomia are some of the risk factors for GDM. It can lead to complications including preeclampsia, preterm delivery, polyhydramnios, malformations, shoulder dystocia, neonatal hypoglycemia, and perinatal mortality (3,4). Diabetes, insulin resistance, metabolic syndrome, cerebral palsy, and developmental disorders are among the complications expected in the long term in the babies of mothers with GDM. With early diagnosis, it is possible to treat the majority of these complications (5,6). In studies conducted in our country, the frequency of GDM varies between 1-9%. It is estimated that 21.1 million live births in 2021 have some form of hyperglycemia in pregnancy. 80.3% of these are due to gestational diabetes mellitus (2,7,8).

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The American Diabetes Association (ADA) recommends the classification of pregnant women according to risk factors and the application of screening steps accordingly. Organizations such as the American Society of Obstetricians and Gynecologists (ACOG), the World Health Organization (WHO), and the International Diabetes and Pregnancy Working Group (IADPSG) recommend screening of all pregnant women. The approach in our country; is the screening of all pregnant women for GDM with the recommendation of the Turkish Society of Endocrinology and Metabolism (TEMD) and the Turkish Society of Gynecology and Obstetrics (TJOD). Currently, there is no other proven diagnostic method for the diagnosis of GDM other than the Oral Glucose Tolerance Test (OGTT) (9-12).

Cultural dietary habits and misinformation from mass media negatively affect the rate of OGTT of pregnant women in Turkey. This might possess an increased risk of GDM and related complications. Therefore, it is important to evaluate the variables affecting the OGTT preference of pregnant women (4). Individuals' health literacy levels are an important variable that affects their health levels. The World Health Organization defines health literacy as "cognitive and social skills that determine the motivation and ability of individuals to access, understand and use information in ways that promote and maintain good health". Health literacy, the ability to access, understand, evaluate and apply health information to make appropriate health decisions, is generally accepted as a mediator in the processes that determine certain health behaviors and ultimately health status (13-16). People with a high level of health literacy are often expected to avoid risky health behaviors. When evaluated in terms of health promotion practices, health literacy means that the individual has information about his/her health status and knows how to make changes related to his/her health (17,18). Physiological symptoms of pregnancy, changes in body image, labor, anxiety about becoming a mother, and worries about the baby during pregnancy cause stress. The effort of the pregnant woman to adapt to the role of motherhood and the expectations of the people around her about being a good mother increase the level of stress. Pregnant woman Stress during pregnancy may cause the pregnant woman to have difficulty in performing daily life activities or, on the contrary, to gain healthy lifestyle habits (19).

This study aims to examine the relationship between pregnant women's oral glucose screening test preferences and their health literacy and perinatal anxiety levels. Attempts to improve the low rates of OGTT in pregnant women will be effective in ensuring the continuity of health-promoting and protective behaviors of expectant mothers and mothers. Preventing the increase in GDM rates will improve health by protecting maternal and infant health. It is thought that the potential risks of the diagnosis of GDM for the mother and the baby will decrease and the expenditures for care and treatment will thus contribute to the national economy.

Research Question

Are pregnant women's health literacy and perinatal anxiety levels effective in their OGTT preferences?

Is there a relationship between health literacy and perinatal anxiety levels of pregnant women?

MATERIAL AND METHOD

Type of Research

The research is descriptive and cross-sectional.

Place of Research

The research was carried out in the pregnant outpatient clinic of Alanya Alaaddin Keykubat University Medical Faculty Hospital between July 2022 and August 2022.

Population and Sample of the Research

The population of the study consisted of pregnant women who applied to the pregnancy polyclinic of Alanya Alaaddin Keykubat University University Medical Faculty Hospital. The sample of the study; consisted of 120 pregnant women, who did not have a Turkish speaking problem, a diagnosis of pregestational diabetes, no vision and hearing problems, no mental/mental health problems, and who could read and write. Being a health worker was accepted as an exclusion criterion.

Data Collection and Data Collection Tools

Study data were collected using a sociodemographic information form consisting of 12 questions, the Turkish Health Literacy Scale-32 to find out the health literacy levels of pregnant women, and the Perinatal Anxiety Screening Scale to determine the perinatal anxiety levels. The pregnant women who participated in the study were informed about the study and a voluntary consent form was signed. Data collection was carried out under the supervision of the researcher by interviewing the pregnant women face-to-face. It took approximately 20 minutes for the data collection forms to be filled out by the pregnant women.

Turkey Health Literacy Scale-32 (TSOY-32).

TSOY-32 is a self-report scale developed to evaluate the health literacy of literate people over the age of fifteen (20).

It is a 32-item scale developed based on the HLS-EU Study Conceptual Framework (HLS-EU CONSORTIUM, 2012). TSOY-32 consists of two dimensions: Treatment and Service and Prevention from Diseases/Promotion of Health. Each dimension includes four components: Accessing Health-Related Information, Understanding Health-Related Information, Evaluating Health-Related Information, and Using/Practicing Health-Related Information. Okyay et al. (2016) conducted a validity and reliability study in our country. Items in a 5-point Likert-type scale are expressed as 0= very easy, 1= easy, 2= difficult 3= very difficult, 4= I have no idea. In the evaluation of the scale; indices are standardized to be between 0 and 50, as in the HLSEU study. In this formula, the index refers to the index calculated specifically for the individual, and the average refers to the average of each item answered by a person. After this calculation, 0 indicates the lowest health literacy, and 50 is the highest health literacy.

As in the HLS-EU study, the index obtained was classified into four categories.

Health literacy according to the following scoring,

(0-25) points: insufficient health literacy,

(>25-33): problematic – limited health literacy,

(>33-42): adequate health literacy,

(>42-50): defined as excellent health literacy.

The reliability of the scale in Turkish; internal consistency (Cronbach Alpha) coefficient; 0.927.

The internal consistency (Cronbach's Alpha) coefficient for this study was 0.934.

Perinatal Anxiety Screening Scale (PASS)

Developed by Somerville et al. in 2014, Yazıcı et al. The Turkish validity and reliability study of the scale consists of 31 items. The four sub-dimensions of the scale are (1) acute anxiety and adjustment disorder, (2) general anxiety and specific fear, (3) perfectionism, control, and trauma, and (4) social anxiety. The questions/item answers in the scale are "never", "sometimes", "often" and "almost always" and the scores are 0, 1, 2, 3. Evaluation of the scores obtained from the scale was calculated as 0-20 for minimal anxiety symptoms, 21-41 for moderate anxiety, and 42-93 for severe anxiety (21). The Cronbach alpha value of the scale was determined by Somerville et al. 0.96 by Yazici et al. found 0.95 by Yazici et al. 2018.

Evaluation of Data

The data were evaluated by coding in the SPSS 26.0 statistical package program. Descriptive statistics such as number, percentage, mean and standard deviation were used in the analysis of the data. Normality test was used to determine the suitability of the data for normal distribution, one-way analysis of variance, correlation analysis, independent sample t-test, and chi-square tests were used to determine the difference of scale scores according to the variables. The significance level was evaluated according to p=0.05.

Ethical Aspect of Research

The study was initiated with the approval of the Alanya Alaaddin Keykubat University Health Sciences Scientific Research and Publication Ethics Committee (Date: 31.05.2022, Decision No: 2022/12), and permission from the hospital management where the research was carried out were obtained before the study to implement the study. In addition, informed consent was read from the pregnant women who participated in the study, and their written and verbal consents were obtained. The Helsinki Declaration of Principles has been complied with.

Limitations of the Research

The data obtained from this study are based on the statements of the pregnant women, and the results are valid for the group in which the study was conducted and cannot be generalized to the population.

RESULTS

In the study, which aimed to investigate the relationship between glucose screening test preferences of pregnant women and their health literacy and perinatal anxiety levels, 39% of the pregnant women forming the sample group were in the 29-33 age group, 39.8% were secondary school graduates, and 77.1% were not working. 70.3% of the pregnant women stated that they lived in the district center and 61% stated that their monthly income was above the minimum wage. One of the pregnant women who participated in the study stated that it was her 9th pregnancy, and 40.7% of them stated that it was her first pregnancy. As the number of pregnancies increased, the percentage of pregnant women in the group decreased. While 83.1% of the pregnant women stated that they did not have any health problems in their previous pregnancies, 94.1% stated that they went to regular health check-ups. When asked about the opinions of pregnant women about having OGTT, 52.5% of participants answered "No" to the question "Do you think OGTT should be done?" While the effect of health personnel in these decisions is 66.1%, the effect of the closed environment is 22.9%. The Cronbach Alpha of the Health Literacy Scale used in the study was .937; the Perinatal Anxiety Screening Scale Cronbach Alpha value was found to be .944.

Table 1. The Relationship Between Turkish Health Literacy and Perinatal Anxiety Screening Scale in Pregnants

Scales	Turkey Health Literacy Scale-32	Perinatal Anxiety Screening Scale
Turkey Health Literacy Scale-32	one	-,182*
Perinatal Anxiety Screening Scale	-,182*	One

* p < 0.05

A statistically significant negative correlation was found between the scores of Turkish health literacy scale and the scores obtained from the Perinatal anxiety screening scale, at the p<.05 level (r= -.182; p<.05) with Pearson Product Moment Correlation analysis.

In **Table 2**, there is no difference between the groups in terms of health literacy (F=,696 p>.05), and perinatal anxiety screening scale (F=,002 p>.05) scores of pregnant women.

Table 2. Anova Results of Pregnants' Health Literacy and Perinatal Anxiety Screening Scores

	Sum of Squares	sd	Mean Squares	F	p
STRAIN*					
between groups	,625	one	,625	,696	,406
within groups	104,231	116	,899		
Total	104,856	117			
PAT**					
between groups	,001	one	,001	,002	,963
within groups	75,456	116	,650		
Total	75,458	117			

* Health literacy **Perinatal anxiety screening

Health literacy mean scores of pregnant women who said that OGTT should or should not be done in **Table 3** were analyzed by Mann-Whitney U test analysis. There is no difference between the mean health literacy scores of pregnant women according to the preference variable (U = 1715,000 p=,655, z=-,446).

Table 3. Results of Pregnants' Health Literacy Scale Mean Scores by OGTT Preference Variable

OGTT Preference	n	Row Average	Row Sum	U	Z	p
Should be done	60	61,92	3715,00	1715,000	-,446	,655
Should not be done	60	59,08	3545,00			

Perinatal Anxiety Screening Scale mean scores of pregnant women who said that OGTT should or should not be performed in **Table 4** were analyzed by Mann-Whitney U test analysis. There is no difference between the Perinatal Anxiety Screening Scale mean scores according to the preference variable of the pregnant women (U = 1749,000 p=.906, z=-.119).

Table 4. U-Test Results of Pregnants' Perinatal Anxiety Screening Scale Mean Scores According to OGTT Preference Variable

OGTT Preference	n	Row Average	Row Sum	U	Z	p
Should be done	60	60,35	3621,00	749,000	-,119	,906
Should not be done	59	59,64	3519,00			

In **Table 5**, the OGTT preference of pregnant women according to sub-dimensions of health literacy and perinatal anxiety scales was evaluated with Chi-Square analysis. There is no association between the preference and the mean scores of the sub-dimensions of the Health Literacy Scale (X 2 = 3.243, p = 0.356). There is association between the preference and the mean scores of the perinatal anxiety screening scale sub-dimensions (X2=,488, p = 0.784) (**Table 5**).

Table 5. Analysis of Pregnant Women's OGTT Preferences by Health Literacy and Perinatal Anxiety Scales

				Health literacy				
	Unsatisfactory	Problem-Limited	Adequate	Excellent	Total	X2	sd	p
OGTT								
Should it be done?								
Yes	49	4	6	1	60	3,243	3	,356
No	54	4	2	0	60			
				Perinatal anxiety				
	Minimal	Moderity	Severe	Total	X2	sd	p	
OGTT								
Should it be done?								
Yes	18	24	8	60	,488	2	,784	
No	20	20	19	60				

DISCUSSION

The data of this study, which aimed to investigate the relationship between oral glucose screening test preferences of pregnant women and their health literacy and perinatal anxiety levels, were discussed by comparing them with the literature. GDM can occur at any time during the antenatal period and is not expected to persist after birth. Hyperglycemia in pregnancy is best detected in the first trimester. It is estimated that most of the cases of hyperglycemia in pregnancy (75%-90%) are GDM (22).

There is no global consensus on surveillance and diagnostic testing for GDM, thresholds for each test, or if it should be administered selectively (23,24). However, there is not enough evidence as to why testing should be done during these weeks of pregnancy; OGTT is recommended for all women between 24 and 28 weeks of pregnancy as GDM screening test. For high-risk women, screening should be done earlier in pregnancy (25). Also, earlier OGTT may reduce exposure to fetal hyperglycemia, providing opportunities for earlier treatment (26). It is estimated that women in 21.1 million (16.7%) live births in 2021 have some form of hyperglycemia during pregnancy. Of these, 80.3% are due to gestational diabetes mellitus (GDM), 10.6% to diabetes diagnosed before pregnancy, and 9.1% to diabetes diagnosed for the first time during pregnancy (including type 1 and type 2) (27).

Basbuğ et al. (28) in their studies, the frequency of GDM was found to be 7.9% in the OGTT group. In our study, 52.5% of pregnant women, according to you, should OGTT be performed? They answered no to the question. 66.1% of pregnant women stated that health workers were effective in their decisions. Dalgıç et al. (29), 51.9% of the pregnant women did not have a screening test, and some pregnant women reported that screening should be done with a method other than sugar consumption as the reason for not having the test, that their doctor did not recommend it, that they read in the media that it was harmful, that they thought it would harm their baby, and that they had no information about the test.

Turan and Toker (30), in their study, found that the socio-demographic, health and obstetric characteristics of pregnant women did not affect the OGTT behavior; It was determined that they did not have the test because they thought that the test was not necessary, they were worried that it would be harmful to themselves and their babies, and their doctors did not recommend it. Acavut et al. (31), it is noteworthy that although almost all of the pregnant women knew about the OGTT and stated that they had it done in their previous pregnancy, less than half of them would have the test done. This result suggests that the knowledge level of pregnant women is not sufficient, they are indecisive about getting tested, and the news on social media is effective in their thoughts. In the study by Hocaoğlu et al. (32), it was stated that 78.5% of pregnant women were reluctant to have the test done because they thought that OGTT was harmful to them and their babies. In Koyucu's (33) study, 64.3% of pregnant women think that OGTT screening should not be performed. The biggest reason for this is the fear that it may have harmful effects on the pregnancy process, the fetus, or the newborn after birth. In our study, a statistically significant negative correlation at $p<.05$ level was found between the scores obtained from the Turkish health literacy scale and the perinatal anxiety screening scale ($r= -.182$; $p<.05$). Nacar et al. (34), it was determined that the mean anxiety score of the pregnant women who had triple screening test and oral glucose tolerance test, which are among the perinatal screening tests, were higher than those who did not.

It is thought that this situation may be due to the possibility of getting a negative result from the test result.

Suny et al. (36) evaluated the barriers to mothers diagnosed with GDM in terms of risk follow-up for Type 2 Diabetes in the postpartum period. These barriers were stated as the mothers' perceived risk of developing Type 2 DM, the risk of T2DM and fear of its consequences, the desire to pay attention to the care of their child, and the ordering of their priorities.

In our study, when the OGTT preferences of pregnant women were examined according to health literacy and perinatal anxiety screening scale sub-dimensions, no statistically significant relationship was found. Dika et al. (13) found a strong and inversely significant relationship between blood sugar level and health literacy. It shows that mobile phone applications created considering the health literacy levels of pregnant women have the potential to prevent and improve GDM management (37). Demircan et al. (38), the GDM awareness rate of pregnant women was found to be 56.8%. In addition, it has been determined that doctors and healthcare professionals significantly lack knowledge about the pathogenesis, screening, follow-up, and treatment of GDM. In the study of Tarhan and Özaydın (35), it is stated that the education applied with the audio-visual supported pictorial training guide for pregnant women positively affects the knowledge level of patients about diabetes and their preferences for screening tests.

CONCLUSION

As a result, it was seen that the health literacy and perinatal anxiety levels of the pregnant women in the sample group did not affect their OGTT preferences. They stated that healthcare professionals were primarily influential in their decisions on OGTT preferences. Since GDM is a common health problem, early diagnosis and treatment are crucial for the prevention of maternal and fetal complications. The first step to this is the implementation of the OGTT. In our country, pregnant women, who are especially affected by visual media, oppose the screening test. It is thought that the discussions about OGTT in the media are effective in the decision process regarding the test. It is reported that not performing a test, which emphasizes the importance of doing it during pregnancy, may harm both the mother and the baby. Therefore, it is important to determine the factors that may affect the OGTT preferences of pregnant women and more studies are needed on this subject. These studies should also include the knowledge and approaches of health professionals.

It is important to plan interventions for GDM and its prevention, which are effective on infant and maternal health, through individualized support and culture-specific approaches. It is possible to support women with GDM in managing and understanding their condition, by providing multidisciplinary teams with the necessary knowledge regarding the needs and concerns of GDM patients. Also, this approach could potentially improve infant and maternal health, reduce the risk of future Type 2 diabetes in this population, and cost pressures on health systems, in the long term.liation in gastric cancer patients. Oncological outcomes may be improved with early radiotherapy initiation and higher bioequivalent RT doses. Current study demonstrated that the referral symptom for palliation has an impact on the oncologic outcome. Better results were shown in patients who received radiotherapy for pain compared to bleeding and obstruction. Prospective randomized studies are needed for further results.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was initiated with the approval of the Alanya Alaaddin Keykubat University Health Sciences Scientific Research and Publication Ethics Committee (Date: 31.05.2022, Decision No: 2022/12).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Original Article

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Prognostic factors for survival in pancreatic cancer patients received radiotherapy: a single-center experience

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ABSTRACT

Aim: To investigate survival outcomes and factors affecting the prognosis of patients with pancreatic cancer (PC) who received radiotherapy (RT).

Material and Method: A total of 73 patients with PC who received RT between 2013 and 2021 were included in the study. Clinical, demographic, and histopathological features of the patients, and the goal of RT (adjuvant, definitive, neoadjuvant, or palliative) were recorded.

Results: Median age of the patients was 62 (37-78). Male to female ratio was 1.6. In patients treated with adjuvant (n=52), definitive (n=13), and palliative (n=7) RT, median overall survival (OS) was 25.7 (11.6-39.7), 16 (7-67), and 9 (5-52) months, respectively. Survival time of 1 patient who received neoadjuvant RT was 26.6 months. Lymph node ratio (LNR) was significantly associated with OS. Patients with LNR ≤0.4 had better survival compared to those with LNR >0.4 (p=0.003). Furthermore, patients with LNR ≤0.4 and received adjuvant RT survived longer than the rest of the patients (12.1 vs. 7.7 months, p=0.001). Larger tumors (p=0.04) and LNR (p=0.003) were associated with poorer survival in univariate analysis, however, in the multivariate analysis, OS was found significantly affected only by LNR (p=0.01). Other factors were not found associated with survival.

Conclusion: LNR had a strong correlation with OS in PC patients treated with radiation. Smaller LNR was associated with better survival in patients who received RT in the adjuvant setting.

Keywords: Pancreatic cancer, prognostic factors, survival, radiotherapy

INTRODUCTION

Pancreatic cancer (PC) is the fourth malignancy resulting in cancer-related death despite being relatively less common compared to other cancers (1). Smoking, advanced age, obesity, heavy alcohol consumption, chronic diabetes mellitus, and non-O blood group are among the etiological factors of PC (2-7). Patients with PC located in the body or tail of the pancreas have lower survival rates because of more advanced disease at the time of diagnosis compared to the ones with tumors in the head of pancreas (8, 9).

Components of treatment modality of PC are surgery, chemotherapy (CT), and radiotherapy (RT). Surgery plays major role in the management of PC, however, only 15 to 20% of the patients present with operable disease at the time of diagnosis (10, 11). Following optimal resection, important prognostic factors are resection margin status, lymph node involvement, tumor size and tumor grade (12-15). CT and RT may be applied in several phases of treatment according to tumor's resectability or status of metastasis. While RT is frequently administered in adjuvant setting with CT (16-19), definitive and neoadjuvant RT with CT are the options in locally unresectable PC and resectable/borderline resectable PC, respectively (20, 21). Palliative RT is an effective option to control pain or local symptoms due to obstruction caused by primary tumor or metastatic lesions (22, 23).

In this study, the aim was to investigate the factors affecting the survival outcomes of the patients diagnosed with PC and treated with RT either as a part of multimodal management or for palliation.

MATERIAL AND METHOD

A total of 73 patients (male: 45, female: 28) diagnosed with pancreatic adenocarcinoma and attended to the department of radiation oncology between 2013 and 2021 were included in the study. Patients' data were obtained from medical recordings. The study was approved by

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the Marmara University Clinical Researches Ethics Committee (Date: 13.06.2022, Decision No: 09.2022.86) and conducted by principles of the Declaration of Helsinki. Staging was done according to AJCC (8th edition) staging system. Patients treated with neoadjuvant, adjuvant, definitive or palliative RT were recorded. Patients' characteristics are summarized in **Table 1**.

Table 1. Clinicopathologic features of the patients

Characteristics	Sex		Total % (n)	p value
	Male % (n)	Female % (n)		
Initial symptom				0.3
Weight loss	16 (7)	21 (6)	18 (13)	
Fatigue	24 (11)	14 (4)	20 (15)	
Pain	7 (3)	22 (6)	12 (9)	
Jaundice	42 (19)	25 (7)	36 (26)	
Other	11 (5)	18 (5)	14 (10)	
LNR				0.7
≤ 0.4	65 (29)	75 (21)	69 (50)	
> 0.4	4 (2)	7 (2)	5 (4)	
Unknown	31 (14)	18 (5)	26 (19)	
Blood groups				0.9
O	20 (9)	25 (7)	22 (16)	
A	44 (20)	42 (12)	44 (32)	
B	16 (7)	11 (3)	13 (10)	
AB	9 (4)	11 (3)	10 (7)	
Unknown	11(5)	11 (3)	11 (8)	
Tumor location				0.6
Head	76 (34)	79 (22)	77 (56)	
Body	11 (5)	14 (4)	12 (9)	
Tail	13 (6)	7 (2)	11 (8)	
Tumor stage				0.5
T1	9 (4)	3 (1)	7 (5)	
T2	45 (20)	36 (10)	41 (30)	
T3	42 (19)	61 (17)	49 (36)	
T4	4 (2)	-	3 (2)	
Nodal status				0.1
N0	9 (4)	21 (6)	14 (10)	
N1	45 (20)	32 (9)	40 (29)	
N2	13 (6)	29 (8)	19 (14)	
Nx	33 (15)	18 (5)	27 (20)	
Stage				0.8
I	47 (21)	54 (15)	49 (36)	
II	20 (9)	25 (7)	22 (16)	
III	22 (10)	18 (5)	21 (15)	
IV	11 (5)	3 (1)	8 (6)	
Grade				0.1
I	4 (2)	7 (2)	5 (4)	
II	45 (20)	57 (16)	49 (36)	
III	13 (6)	7 (2)	11 (8)	
Unknown	38 (17)	29 (8)	34 (25)	
CEA				0.5
< 5	44 (20)	36 (10)	41 (30)	
≥ 5	16 (7)	25 (7)	19 (14)	
Unknown	40 (18)	39 (11)	40 (29)	
CA 19-9				0.3
< 34	24 (11)	11 (3)	19 (14)	
≥ 34	38 (17)	50 (14)	43 (31)	
Unknown	38 (17)	39(11)	38 (28)	

LNR, lymph node ratio; CEA, carcinoembryonic antigen; CA 19-9, carbohydrate antigen 19-9

Initial diagnostic imaging was computed tomography in 30 patients, magnetic resonance imaging in 26, and positron emission tomography in 1 patient. Biopsy was performed in 16 patients who had unresectable or metastatic disease. Surgical procedure was distal pancreatectomy in 9 patients and Whipple procedure in 44 who underwent surgery and received adjuvant RT (n=53; 72%). Thirteen patients (18%) received definitive RT. Palliative RT was administered to 7 patients (9%) to control symptoms due to primary tumor and only one patient was treated with neoadjuvant RT (1%). Radiation fields encompassed tumor bed and regional nodes in adjuvant setting with a treatment dose of 45-50.4 Gray (Gy). In the neoadjuvant, definitive and palliative RT planning, only tumor was covered with median doses of 45, 50.4, and 30 Gy, respectively. Volumetric arc therapy was used for RT planning. Adjuvant CT regimen was gemcitabine based in 44 and fluorouracil (FU) based in 9 patients. In patients treated with adjuvant RT, concurrent CT regimens were capecitabine (n=28) and gemcitabine (n=25). For patients treated with definitive chemoradiation, gemcitabine and capecitabine were administered concomitantly in 6 and 7 patients, respectively. One patient treated with neoadjuvant chemoradiation received concurrent capecitabine.

Date of death or last follow-up time in surviving patients were recorded. Overall survival (OS) is defined as the time between the date of diagnosis and the date of death or last follow-up date of the patients.

Statistical Analyses

Statistical Package for Social Sciences (SPSS) for Windows 23.0 IBM SPSS Statistics, New York, USA was used for statistical analyses. Kaplan–Meier method, and the log-rank test was used for survival analysis. Univariate and multivariate Cox regression analyses were used to determine variables which were predictors of OS. All of the tests were two-sided, and $p < 0.05$ was considered statistically significant.

RESULTS

Median age of the patients was 62 (37-78). Male to female ratio was 1.6. Median follow up time was 19.5 (3.3-102) months. In the patients received RT in the adjuvant setting, OS was significantly better than the rest of the study population (p=0.01). Median OS of the patients treated with adjuvant and non-adjuvant RT was 25.7 (11.6-39.7) and 17 (7.9-25.1) months, respectively (p=0.01). Median OS for patients treated with definitive (n=13) and palliative (n=7) RT was 16 (7-67) and 9 (5-52) months, respectively. Survival time of 1 patient received neoadjuvant RT was 26.6 months.

The results of univariate analyses for OS are shown in **Table 2**.

Table 2. Cox regression univariate analysis for overall survival

Variables	p value	Hazard rate	95% Confidence interval	
			Lower	Upper
Age (≤65 vs. >65)	0.25	1.369	0.798	2.348
Gender (Female vs. male)	0.34	0.766	0.443	1.323
Blood groups (0 vs. non-0)	0.23	1.487	0.775	2.854
Smoking (Smoker vs. no smoker)	0.57	1.047	1.273	3.102
Tumor location (Head vs. body-tail)	0.29	1.379	0.757	2.514
Tumor stage (T1-2 vs. T3-4)	0.04	1.755	1.023	3.012
Stage (I,II vs. III)	0.51	0.766	0.346	1.696
Grade (I,II vs. III,IV)	0.73	1.133	0.561	2.288
LNR (≤ 0.4 vs. >0.4)	0.003	5.103	1.711	15.220
Surgical margins (Negative vs. positive)	0.31	2.917	0.373	2.2823
CEA (<5 vs. ≥5)	0.81	1.038	0.771	1.316
CA19-9 (<34 vs. ≥34)	0.97	1.008	0.678	1.498
Adjuvant CT regimen (Gemcitabine vs. 5-Flourouracil/ capecitabine)	0.91	1.052	0.432	2.563

LNR, lymph node ratio; CEA, carcinoembryonic antigen; CA 19-9, carbohydrate antigen 19-9; CT, chemotherapy

LNR (≤0.4 vs >0.4) was found associated with survival (p=0.003). Patients with LNR >0.4 had poorer OS compared to them with LNR ≤0.4 (**Figure 1**). Furthermore, in the subgroup analyses, patients with LNR ≤0.4 and received adjuvant RT survived longer than the rest of the patients (12.1 vs. 7.7 months, p=0.001). Additionally, advanced tumor stage (T3 and T4) was found associated with poorer survival (p=0.04) (**Figure 2**). However, in the multivariate analysis, only LNR was found significantly associated with OS in all study population (p= 0.01). Tumor grade, age, sex, tumor location, stage, blood group, smoking, carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9) levels was not associated with survival. Additionally, positive surgical margin was not significantly associated with survival in patients who underwent surgery.

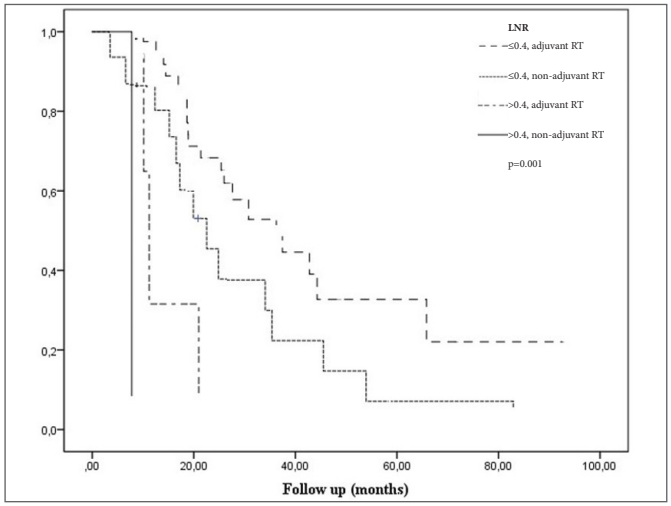

Figure 1. Association between lymph node ratio (LNR) and survival in patients treated with adjuvant and non-adjuvant radiotherapy

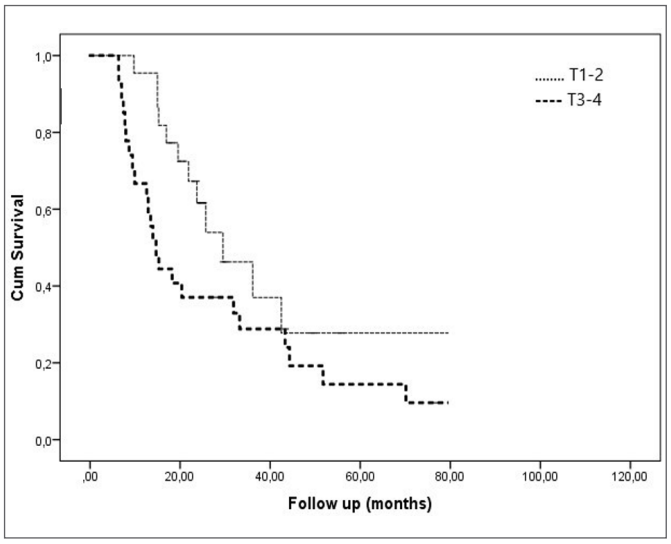

Figure 2. Association between tumor stage and survival

DISCUSSION

Pancreatic cancer is a relatively less common malignancy, however, has a worse prognosis and higher mortality compared to the other cancers (1). Several factors such as smoking, heavy alcohol use, non-O blood group, and advanced age are blamed for the etiology of PC (2-7). A two-fold increased risk of PC is reported with smoking (3). PC is more frequent in Western and industrialized countries which may be related to increased obesity and/ or higher numbers of people at advanced age (24). In this study, 51% of the patients was smokers and approximately half of the patients were at advanced age (46%). Majority of the patients was with non-O blood group (71%).

Routine screening for PC is not clearly established. Preoperative CA 19-9 levels may be useful in detecting PC, however, while CA 19-9 may increase in diseases/ disorders related to pancreaticobiliary ducts, pancreatitis or poorly controlled diabetes, it is generally used to monitor the response to therapy or detect recurrences (25). In this study, preoperative CA 19-9 levels were increased in only one-third of the patients who had available data.

Although surgery is the cornerstone of the PC treatment and optimal resection of the tumor has prognostic importance, only 15 to 20% of the patients have resectable tumors when diagnosed with PC (10, 11). In operable PC, clear resection margin is an important prognostic factor and patients with R0 resection margins have a better prognosis compared to those with R1 or R2 resection margins (26). Nevertheless, 5-year and 10-year OS rates are reported as 25% and <10%, respectively, even for patients resected with clear margins (27). In this study, survival rate of the patients with resectable PC was better than the rest of the study population as expected. However, in contrast to the previous studies, resection margin status was not found significantly associated with survival.

Radiotherapy may be applied with chemotherapy as a part of multimodal management or for palliation in PC. Neoadjuvant chemoradiation is an option in resectable and borderline resectable PC. Results of PREOPANC-1 trial, the first large phase III randomized trial, showed that neoadjuvant chemoradiation improved survival in patients with resectable or borderline resectable PC in addition to higher rates of clear resection margins (20). However, in this study, only one patient was referred for neoadjuvant management and treated with neoadjuvant chemoradiation. Locally unresectable or metastatic disease at the time of diagnosis is commonly seen in PC patients. Definitive RT with CT is an option in patients who are not suitable for surgery and generally recommended after 4-6 cycles of systemic CT. In GERCOR study, definitive RT with concurrent CT was reported to be superior to CT alone in management of non-metastatic locally unresectable pancreatic cancer (21). In this study, definitive RT was administered to one fifth of the patients and did not significantly affect survival compared to the remaining of the patients. Location of the primary tumor may cause severe symptoms. Tumors at the head of pancreas which is the most common localization of PC usually present with obstructive jaundice. Additionally, pain due to celiac plexus involvement or duodenal invasion may be observed in PC patients (28). In this study, majority of the tumors (77%) were located at the head of pancreas with a jaundice rate of 36%. Tumor related symptoms (i.e pain, biliary obstruction, or gastric outlet/duodenal obstruction) may be palliated with RT. Particularly, RT has a strong effect on pain relief derived from primary tumor in nonresponders to effective medical therapy and/or interventional procedures (22, 23). In this study, 10% of the patients needed palliation for symptoms due to primary tumor's complications.

In postoperative PC patients, lymph node involvement has a great importance in addition to clear surgical margins for predicting prognosis of the disease. Asiyanbola et al. (29) reported that LNR which is the ratio of involved lymph nodes to resected lymph nodes is an independent and most significant factor in predicting survival. They found a cutoff value of 0.4 for prediction of survival. LNR >0.4 has been reported to be associated with poor OS and high risk of local failure. In this study, the same cutoff value was used and the patients were grouped as LNR >0.4 and ≤0.4, and in consistent with Asiyanbola et al.'s study, LNR >0.4 was found strongly correlated with poorer survival (Fig. 1). Size, grade and location of the tumor also have prognostic importance for PC; larger tumor sizes are associated with shorter survival (15). Tumors located in the body or tail of the pancreas are associated with lower survival rates because of more advanced disease at the time of diagnosis (8, 9). In this study, larger tumor sizes were found associated with poorer survival by univariate analysis. However, a statistically significance for OS was not found by multivariate analysis. Additionally, majority of the tumors were located at the head of pancreas, but tumor location did not significantly affect survival of the patients. Although tumor grade is also associated with prognosis and survival of PC (30), an improved survival with lower tumor grade was not found.

Impact of multimodal treatment on disease control after maximal resection of primary tumor was shown by previous studies which demonstrated that addition of postoperative CT and RT improved survival when compared to surgery alone (16-19). Although this study does not have a homogeneous treatment population, patients treated with adjuvant RT and CT established better survival. Additionally, OS was significantly better in patients with smaller LNR and treated with adjuvant RT when compared to them received RT in non-adjuvant setting. This finding may be explained by an extra contribution of adjuvant radiation to survival in patients with less involved lymph nodes.

The study has some limitations. It is a retrospective study and despite the collection of nine years of data, it has small number of patients.

CONCLUSION

Patients with PC had poor prognosis and LNR had a strong correlation with OS in patients treated with radiation. Moreover, smaller LNR was associated with better survival in patients who received RT in the adjuvant setting.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Marmara University Clinical Researches Ethics Committee (Date: 23.06.2022, Decision No: 09.2022.86).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author has no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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Original Article

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How sedation used prior to gastrointestinal endoscopies affects patients' anxiety level for future procedures

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ABSTRACT

Aim: The application of sedoanalgesia during gastrointestinal endoscopic procedures increases the success of the procedure as well as patient comfort and safety. The aims of this study are to investigate the anxiety levels of patients and potential early complications who practised sedoanalgesia in gastrointestinal endoscopic procedures before and two days after.

Material and Method: The study was designed as a prospective, randomized, single-centre clinical trial. Patients over the age of 18 and had American Society of Anaesthesiology (ASA) physical status score 1-3 who were practised elective gastrointestinal endoscopy, between April 2022 and September 2022 were included to the study. The patients who refused to participate, were above ASA 3, and were illiterate, had an Ejection Fraction <30%, and had a diagnosis and treatment of psychiatric disease were excluded from the study. Informed consent obtained from all patients. Anxiety levels of the patients were evaluated with Beck Anxiety Inventory (BAI). Hemodynamic changes, blood test results were recorded and compared before and after the procedure.

Results: One hundred four patients included to the study with the age of 23 to 79. Preoperative and postoperative BAI scores were found statistically significant ($p<0.05$). The patients' satisfactions have seen very high after procedure. The complications have seen on 7 (%6.7) patients. All of the complications were due to nature of the procedure as epistaxis/mucosal trauma (n=3), equipment damage(n=4). There have been no serious or life-threatening complications during procedures.

Conclusion: Reducing anxiety by anaesthesia, patients will be more efficiently persuaded to execute endoscopy and by thus early diagnosis can be achieved. Patients who have undergone an endoscopy procedure while sedated have significantly fewer concerns about the future. This may increase the procedure's chances of success every time.

Keywords: Endoscopy, anaesthesia, anxiety

INTRODUCTION

Patients usually feel anxiousness during medical procedures. Unfamiliar invasive interventions, such as endoscopy, induce anxiety and fear in patients. Anxiety is a state of fear and worry that develops in response to any stimulus (1). Depending on the surgical or interventional procedure, preoperative anxiety, worry, fear and feeling of unease may develop in patients. Reducing anxiety boosts the patient's and physician's comfort throughout the procedure and the intervention's success. Thus, while the success rate of the technique increases, patients are spared from undergoing the same intervention multiple times (2).

The use of sedation in gastroenterological endoscopy has become an integral part of standard therapeutic therapy (2). Sedatives decrease anxiety and pain during trans anal endoscopy, increase patient satisfaction, and enhance examination/treatment performance (3). Also, numerous studies have demonstrated the efficacy of sedation during trans oral endoscopic examinations from the patient's perspective, and meta-analyses have demonstrated the same results (4-6). On the other hand, research suggests that the incidence of adverse outcomes, such as aspiration pneumonia, is higher during trans anal endoscopic examinations performed under general anaesthesia or anesthetic assistance compared to other examinations performed under sedation, and caution should be exercised in this regard (7,8). The American Society of Anaesthesiologists (ASA) recommends that such deep sedation applications be performed by anaesthesiologists (9). Most patients do not express their anxiety unless they are specifically questioned. In the literature has been stated that preoperatively, patients should be carefully evaluated in terms of anxiety, and their preoperative anxiety levels should be determined (10).

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Beck anxiety inventory (BAI) was developed to quantify anxiety irrespective of depressive symptoms (11). BAI includes 21 things. A two-factor model comprising 21-items of physical symptoms and emotional-cognitive symptoms was constructed for this scale. The adequacy of this model was evaluated primarily via validation experiments (12). BAI has a high overall internal consistency and a high test-retest correlation (r = 0.67) in detecting the presence of anxiety (11-15). Therefore, research indicates that the BAI is a trustworthy and valid instrument for measuring anxiety symptoms (16,17). Also, BAI is considered as the gold standard method in the measurement of anxiety due to its brevity, simplicity, and ability to effectively measure general anxiety (18).

As in many centres', in our institute, endoscopic procedures are performed with sedoanalgesia under the control of anaesthesiologists. In this study, the primary aim was to investigate the anxiety levels of patients who underwent sedoanalgesia during and two days after on gastrointestinal endoscopic procedures. Secondary aim of the study was to identify early complications in the patients.

MATERIAL AND METHOD

The study was carried out with the permission of University of Health Sciences Kartal Dr. Lutfi Kirdar City Hospital Scientific Research and Publication Ethics Committee (Date: 30/03/2022, Decision No: 2022/5 l 4/222/18). Informed consent was obtained from all the patients included in the study before they entered the operating room. This study was planned as a prospective, randomized, single-centre, clinical trial. Patients aged over 18 years that were classified as American Society of Anaesthesiologist (ASA) physical status score 1, 2, and 3 and underwent elective gastrointestinal endoscopy between April 2022 and September 2022 were included to the study.

Patients that refused to participate, ASA score above 3, were not literate, with an ejection fraction (EF) of <30%, and diagnosed with or treated for a psychiatric disease were excluded from the study. Patients in whom adequate stomach and intestinal cleansing could not be accomplished and procedure could not be finished due to difficulties were also omitted. Demographic data, such as age, gender, height, weight, comorbidities and medications used by the patients were recorded. The patients were monitored in terms of cardiac apex beat, non-invasive blood pressure (BP), and peripheral oxygen saturation (SpO2). Following cannulation, all patients received intravenous (iv) midazolam premedication, and sedation was provided by titrating the iv propofol and fentanyl combination to a dose that would allow them to experience no pain and maintain drowsiness throughout the surgery.

Preoperative and postoperative evaluations were performed using the Beck Anxiety Inventory (BAI) to determine the anxiety levels of the patients (Annex-1). Before the procedure, patients' anxiety levels were measured using the BAI scale. In addition, in an interview held on the second day after the procedure, BAI was administered to the patients again, and their satisfaction levels were also questioned based on a scale of 1 to 10. The duration of anaesthesia and procedure, length of stay in hospital and intensive care were recorded. The presence of complications was recorded preoperatively and within the first 24 hours.

Statistical Analysis

SPSS version 25 statistical software package was used for statistical analyses. Data were summarized using descriptive statistical methods (mean, frequency, percentage, minimum, and maximum values). The Shapiro-Wilk test was used to test the normality of the distribution of continuous variables. Since the variables did not show a normal distribution, the Kruskal-Wallis Test was conducted for the comparison of three groups and the Mann-Whitney U Test for the comparison of two groups. The difference between the variables obtained from the same participants was investigated using the Wilcoxon signed-rank test due to the sample being dependent and data not being normally distributed.

RESULTS

A total of 104 patients, 53 men and 52 women, who presented to Kartal Dr. Lutfi Kirdar City Hospital, were included in the study. The age of the patients ranged from 23 to 79 years. Gastroscopy was performed in 44 of the patients, colonoscopy in 25, and both (mixed) procedures in 35. According to the results, gastroscopy was the most frequently performed procedure at a rate of 42.31%. The patients were mostly evaluated as ASA class 1 and 2 (96.16%). Hypertension was the most common comorbidity (20.19%), and the rate of medication use was high (41.45%) (**Tables 1, 2**).

Table 3 presents the statistical analysis of the age, satisfaction score, and preoperative and postoperative BAI scores of the patients according to the type of endoscopy procedure performed. It was observed that the patients who underwent colonoscopy were significantly older patients ($p < 0.05$), but patient satisfaction, preoperative and postoperative BAI scores did not significantly differ between the procedures ($p>0.05$). However, there was a significant difference between the patients' preoperative and postoperative BAI scores ($p<0.05$). Accordingly, the mean preoperative BAI score of all the procedures was significantly higher than the mean postoperative BAI score ($p<0.05$). In particular, the patients that underwent gastroscopy had a much larger difference between their preoperative and postoperative BAI scores when compared to the remaining procedure types. Therefore, although the type of procedure did not

result in a significant difference between the mean BAI scores of the patients, there were significant differences in BAI scores between the preoperative and postoperative evaluations within each procedure group.

Table 1: Basic statistics of the categorical variables evaluated in the study

Variable	Group	Frequency	Percentage
Procedure			
	Gastroscopy	44	42.31
	Colonoscopy	25	24.04
	Mixed	35	33.65
Gender			
	Male	53	50.5
	Female	52	49.5
Education level			
	None	3	2.88
	Primary school	27	25.96
	Middle school	10	9.62
	High school	32	30.77
	University	32	30.77
ASA class			
	1	51	49.04
	2	49	47.12
	3	4	3.85
Hypertension			
	Absent	83	79.81
	Present	21	20.19
Diabetes mellitus			
	Absent	85	83.33
	Present	17	16.67
Hypo-hyperthyroidism			
	Absent	98	94.23
	Present	6	5.77
Psychiatric disorder			
	Absent	94	91.26
	Present	9	8.74
Gastrointestinal disease			
	Absent	97	94.17
	Present	6	5.83
Chest disease			
	Absent	97	94.17
	Present	6	5.83
Cardiac disease			
	Absent	99	96.12
	Present	4	3.88
Medication use			
	Absent	61	58.65
	Present	43	41.35
Complication			
	Absent	97	93.27
	Present	7	6.73

ASA: American Society of Anaesthesiologists

Table 2: Basic statistics on the age and anxiety and satisfactions levels of the patients

Variables	Mean	SD	Minimum	Maximum
Age	52.20	12.26	23	79
BAI score (preoperative)	6.53	7.44	0	33
BAI score (postoperative)	1.84	2.26	0	12
Satisfaction score	9.38	0.93	6	10

SD: standard deviation, BAI: Beck Anxiety Inventory

The mean BAI scores significantly differed according to medication use (Table4). The patients that used medications had a statistically higher mean postoperative BAI score than those without medication use($p<0.05$). The Wilcoxon signed-rank test was used to examine the variation in the patients' satisfaction scores according to gender. The results presented in **Table 4** indicate that the satisfaction levels of the patients did not differ between the men and women ($p > 0.05$).

Table 5 presents the results of the cross-evaluation performed to determine how the anxiety classification made according to the BAI score shifted from the preoperative period to the postoperative period. All the patients classified as having very mild anxiety in preoperative BAI evaluation were also classified in the same group in the postoperative test, while most of those that were preoperatively evaluated as having mild, moderate, or high anxiety levels shifted to the minimal anxiety and some to the mild anxiety group in the postoperative period. This demonstrates that sedoanalgesia application was very effective in reducing the patients' anxiety levels.

Table 5: Postoperative changes in patients' anxiety classification according to the BAI scores

	BAI score (postoperative), frequency and percentage	
BAI score (preoperative)	Minimal anxiety	Mild anxiety
Minimal anxiety	74 (100)	0 (0)
Mild anxiety	14 (87,5)	2 (12,5)
Moderate anxiety	8 (88,9)	1 (11,1)
Severe anxiety	4 (80,0)	1 (20,0)
Total	100 (96,2)	4 (3,8)

Table 3: Comparison of age and satisfaction and postoperative changes in anxiety levels between the endoscopic procedure groups

	Procedure			p value
	Gastroscopy	Colonoscopy	Mixed	
Age, mean (min-max)	49.36 (23-73)	58.72 (40-79)	51.11 (29-71)	0.0071
Satisfaction score	9.41(8-10)	9.12 (6-10)	9.54 (8-10)	0.3881
Mean BAI score (preoperative)	7.32	5.56	6.23	0.8961
Mean BAI score (postoperative)	2.25	1.76	1.37	0.0631
p value	0.0002	0.0002	0.0002	0.0001

1Kruskal-Wallis test, 2Wilcoxon signed-rank test, BAI: Beck Anxiety Inventory

Table 4: Mean, minimum, and maximum preoperative and postoperative BAI scores and their comparison according to the investigated variables

	BAI score (preoperative)	BAI score (postoperative)
Gender	Mean (min-max)	
Male	6.98 (0-33)	1.85 (0-12)
Female	6.08 (0-29)	1.83 (0-8)
p value	0.8242	0.7782
Education level	Mean (min-max)	
None	2.67 (2-4)	1.33 (0-3)
Primary school	7.40 (0-33)	1.85 (0-12)
Middle school	3.40 (0-8)	1.5 (0-4)
High school	7.28 (0-29)	1.53 (0-5)
University	6.38 (0-26)	2.28 (0-12)
p value	0.8151	0.6851
ASA class	Mean (min-max)	
1	5.25 (0-20)	1.47 (0-12)
2	7.53 (0-33)	2.31 (0-12)
3	10.5 (3-26)	0.75 (0-2)
p value	0.4311	0.0751
Hypertension	Mean (min-max)	
Absent	6.16 (0-33)	1.55 (0-12)
Present	8 (0-29)	2.95 (0-12)
p value	0.0752	0.0682
DM	Mean (min-max)	
Absent	6.40 (0-33)	1.81 (0-12)
Present	7.59 (0-29)	2.17 (0-12)
p value	0.5342	0.7182
Hypo-hyperthyroidism	Mean (min-max)	
Absent	7.29 (0-33)	2.29 (0-12)
Present	9.67 (0-26)	1.83 (0-5)
p value	0.5342	0.7182
Psychiatric disorder	Mean (min-max)	
Absent	6.15 (0-33)	1.80 (0-12)
Present	10.67 (0-26)	2.22 (0-5)
p value	0.1362	0.2922
Gastrointestinal disease	Mean (min-max)	
Absent	6.39 (0-29)	1.85 (0-12)
Present	9.67 (1-33)	2.00 (1-4)
p value	0.3802	0.3532
Chest disease	Mean (min-max)	
Absent	6.69 (0-33)	1.86 (0-12)
Present	5 (0-15)	2.00 (0-5)
p value	0.2672	0.7442
Cardiac disease	Mean (min-max)	
Absent	6.58 (0-33)	1.82 (0-12)
Present	6.25 (0-16)	2.25 (0-5)
p value	0.9662	0.7652
Medication use	Mean (min-max)	
Absent	5.39 (0-29)	1.44 (0-12)
Present	8.14 (0-33)	2.40 (0-12)
p value	0.0612	0.0382
Complication	Mean (min-max)	
Absent	6.57 (0-33)	1.75 (0-12)
Present	6.00 (2-16)	3.00 (1-5)
p value	0.8202	0.0212

1Kruskal-Wallis test, 2Wilcoxon signed-rank test, BAI: Beck Anxiety Inventory

The complications have seen on 7 (%6.7) patients. All of the complications were due to nature of the procedure as epistaxis/mucosal trauma (n=3), equipment damage(n=4). There have been no serious or life-threatening complications during procedures.

DISCUSSION

The early diagnosis of gastrointestinal system diseases, especially malignancies have a significant effect on patient survival. The gold standard methods for early diagnosis are esophagogastroscopy and colonoscopy for gastrointestinal system diseases (19,20). Anesthesia demand has increased due to patient and endoscopist comfort (21). Anaesthesia management of this patients requires appropriate patient evaluation before and after anaesthesia, unique knowledge, skills, experience, and equipment (22).

In a prior study, it was found that endoscopic applications induced anxiety, and that the level of anxiety was affected by gender and education level, but not by the endoscopic operation itself or patient age (23). Similarly, other studies in the literature have shown that the type of endoscopic procedure does not affect patients' anxiety levels (24,25). In our study, we also found that the type of interventional endoscopic procedure did not affect the anxiety level. Although the postoperative BAI scores were lower for all types of procedures compared to the preoperative evaluation, the decline was most significant for individuals who underwent gastroscopy. In another study, it was determined that patients who underwent gastroscopy had a significantly higher level of anxiety (34%) than those who underwent colonoscopy (26). In a study evaluating patients that underwent colonoscopy, it was observed that the patients' anxiety and post-procedural pain levels were higher among those undergoing colonoscopy for the first time (27). In our study, previous gastrointestinal interventional procedures were not questioned, and therefore we consider that there is a need to include this evaluation in future studies.

It has been stated that the anxiety level of patients depends on many factors, including age, gender, previous surgical experience, education level, type of procedure, extent of the recommended surgery, and current health status (1). A study found that female gender, never having had a gastrointestinal treatment previously, and young age enhanced anxiety during gastrointestinal procedures (24). Another study of the factors causing preoperative anxiety in 592 patients undergoing elective surgery confirmed female gender as a risk factor (28). In the current study, there was no significant correlation between anxiety levels and age, gender, or degree of education.

Similarly, another study reported no significant relationship between gender and anxiety (29). We consider that more significant results can be obtained by increasing the number and diversity of patients. In another study, the authors showed that the level of anxiety in diagnostic gastrointestinal interventional procedures performed in patients with a family history of gastrointestinal cancer was higher than those without a family history (30). The effect of family history on the level of anxiety should be further investigated in future studies.

In a study investigating risk factors that increase patient anxiety in endoscopic interventions, anxiety was higher in female patients and those with gastrointestinal symptoms, such as diarrhoea, dysphagia, and pain (31). We did not observe a significant relationship between the history of gastrointestinal disease and the level of anxiety.

In some studies, investigating the relationship between the education levels of patients and their preoperative anxiety, a significant association was reported (28, 29, 32). This was attributed to patients with higher education levels having higher awareness of anaesthesia and surgery. Other studies that did found a decrease in patients' anxiety levels as education level increased explained these findings by patients with a high education level managing their anxiety better and reducing their anxiety (1,33). In our study, no significant relationship was found between educational status and anxiety level. This can be due to the small number of patients. We consider that better results can be obtained by increasing the number of patients.

In a study, the State and Trait Anxiety Inventory (STAI) was used to compare the anxiety levels of two groups of patients based on whether or not they were going to have anaesthesia-guided endoscopic intervention (34). It was found that the anxiety levels of those who were going to have anaesthesia were lower (34). In our clinic, we routinely apply sedation in the presence of an anaesthesiologist to all our patients scheduled for gastrointestinal endoscopic interventions. Supporting our experience, previous studies showed that performing these procedures under reliable conditions accompanied by anaesthesiologists increases the success of the procedure and patient satisfaction (19,21).

This study has certain limitations. If the sample size had been greater, subgroup analyses could have been performed and provide more significant results. However, there were only limited number of patients that presented to the gastrointestinal processing unit during the study period. In addition, our study lacked a control group because gastrointestinal diagnostic procedures are routinely conducted under the supervision of an anesthesiologist and with the use of sedation in accordance with our institution's quality standards and patient safety measures. Lastly, we did not evaluate whether our patients had previous endoscopy experience, and if they did, whether these procedures had been undertaken with or without anaesthesia. Therefore, the relationship between previous endoscopy experience and anxiety should be investigated in future studies.

CONCLUSION

Considering the importance of endoscopic interventions as gold standard methods in the early diagnosis of gastrointestinal diseases, we consider that reducing anxiety by planning the procedure with sedoanalgesia positively affect the patient's decision to undergo such procedure, and thus help achieve early diagnosis. A sedoanalgesia experiment during gastrointestinal endoscopy can reduce future anxiety, especially in patients who have had multiple endoscopies, which may increase patient compliance and procedure success.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of University of Health Sciences, Kartal Dr. Lutfi Kirdar City Hospital Scientific Research and Publication Ethics Committee (Date: 30/03/2022, Decision No: 2022/5 l 4/222/18).

Informed Consent: Informed consent was obtained from all the patients included in the study before they entered the operating room.

Referee Evaluation Process: Externally peer-reviewed.

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Original Article

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The incidence and risk factors of thrombosis due to central venous catheter in SARS-CoV-2 patients in intensive care

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ABSTRACT

Aim: SARS-CoV-2 can cause an increase in both arterial and venous thrombotic events. It is thought that thrombotic events increase in patients due to deep hypoxia, which is the most serious symptom of patients, and the associated immobility.

Material and Method: 233 patients who were followed up in the 3rd Level COVID Intensive Care Unit of the hospital between 2021-2022 were retrospectively analyzed. It was determined that central venous catheter was applied to 110 patients. The age, gender, BMI, co-morbidities of the patients, and which central venous route is preferred for the catheter will be determined. In addition, the number of punctures, thrombocyte count as well as the use of anticoagulants and acetylsalicylic acid, whether or not he/she received total parenteral nutrition (TPN), and how many days the catheter was left will be recorded and thrombotic events will be determined.

Results: COVID-19 causes vascular pathologies as well as respiratory symptoms. Central venous catheter application is frequent in intensive care due to both treatment and nutritional support, and venous path preference affects the risk of thrombosis. Performing more than one catheter application from the same area, catheter duration and position of the end part of the catheter are important factors for the development of thrombosis. It has been found that thrombotic events related to femoral catheter have increased in SARS-CoV-2 patients hospitalized in intensive care. In our study, although the duration of femoral catheter use was low, the thrombosis rate was found to be high, which supports the literature. This situation has led us to reduce femoral catheter applications in intensive care SARS-CoV-2 patients hospitalized in our clinic and to prefer other catheterization methods.

Conclusion: In this study, the incidence of thrombosis was found to be higher in patients treated in the intensive care unit due to SARS-CoV-2 infection and who underwent femoral central catheterization compared to the literature.

Keywords: COVID -19, femoral vein, intensive care, SARS-COV-2, thrombosis

INTRODUCTION

SARS-CoV-2 disease commonly causes intravascular thrombosis, causing serious morbidity and mortality. The fact that patients are mostly immobile in intensive care and the increase in immobility due to desaturation by movement may also cause an increase in thrombotic events. A clear mechanism related to thrombotic events has not been proven and many theories can be proposed (1). SARS-CoV-2 accesses host cells through the angiotensin converting enzyme 2 protein, which is abundant in the lungs. This, in turn, affects the endothelial cells and leads to vascular lesions as a result of significant inflammatory syndrome and coagulation. SARS-CoV-2 virus uses angiotensin-converting enzyme 2 (ACE-2) receptors located in the endothelial layer of the respiratory tract, intestines, heart and vessels as an entry gate into the cell (2). Literature data indicate that the mediator of the serious and critical condition developing in COVID-19 patients is the state of hypercoagulation, which is characterized by micro- and macro vascular thrombotic angiopathy (3,4). It has been mentioned in research that hypercoagulation may be a consequence of viral infection caused by overexpression of ACE-2, which is used by SARS-CoV-2 as a receptor for entry into the cell in endothelial cells (3,4). In this study, we aimed to investigate peripheral vascular pathologies, the incidence of thrombosis due to central venous catheter and risk factors in SARS-CoV-2 patients in intensive care.

MATERIAL AND METHOD

The study was carried out with the permission of Ankara Atatürk Sanatoryum Training and Research Hospital Ethics Committee (Date:14.12.2022, Decision No: 2596). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

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PCR (+) patients hospitalized between 01.05.2021 and 01.08.2022 in the 3rd level COVID Intensive Care Unit in the hospital were retrospectively examined.

The age, gender, BMI, co-morbidities of the patients, and which central venous route is preferred for the catheter will be determined. In addition, the number of punctures, thrombocyte count as well as the use of anticoagulants and acetylsalicylic acid, whether or not he/she received total parenteral nutrition (TPN), and how many days the catheter was left will be recorded and thrombotic events will be determined. Thrombotic events that developed in the patients were diagnosed by the radiologist with venous Doppler ultrasonography. All patients were given anticoagulants at the treatment dose (by adjusting the Low Molecular Weight Heparin treatment dose according to kg status). Since all patients are PCR (+) and are being treated with a diagnosis of COVID pneumonia, the treatment protocol is similar in all patients. All patients were followed up until discharge from the intensive care unit or mortality. When the patients were discharged from the intensive care unit, the catheters were removed because there was no need for a catheter.

RESULTS

The patients were grouped according to the central catheter location and the evaluations were made accordingly. When the difference between the groups was evaluated, a statistically significant difference was found in terms of gender, BMI, COPD and catheter day.

The rate of COPD co-morbidity in the subclavian catheterized group was statistically significantly higher than in the femoral and jugular catheterized group. However, we believe that this is a coincidence, even though it is statistically significant. COPD comorbidity is high because the hospital is a branch hospital of Chest Diseases.

The catheter day in the group with femoral catheters was statistically significantly lower than the group with jugular and subclavian catheters. We think that the catheter could not be used for a long time due to the complications and infection that developed.

Between 01.05.2021 and 01.08.2022, 110 patients who were followed up in the COVID intensive care unit and had a central venous catheter were examined. Of these patients, 64 had a femoral catheter, 32 had a jugular central catheter, and 14 had a subclavian catheter. The mean age of patients with femoral catheters was 69.45±14.09, those with jugular catheters were 70.25±10.03 years, and the mean age of patients with subclavian catheters was 70.21±16.84 years. The gender distribution of 110 patients was 56 males and 54 females. The gender distribution in the patient group with femoral catheters was 38 males and 26 females. In the patient group with jugular catheters, there are 16 males and 16 females. In the subclavian catheter group, there were 2 males and 12 females. The number of female patients in the subclavian catheterized group was statistically significantly higher than in the femoral and jugular catheterized group. However, although it is statistically significant, we believe that this result is coincidental.

While there was no significant difference between the groups in terms of age, a difference was found in the subclavian group in terms of female gender. The BMI of the patient group who underwent subclavian catheter was statistically significantly higher than the group who underwent femoral catheter.

The presence of diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD), coronary artery disease (CAD) and malignancy were evaluated as co-morbidities of the patients. The COPD co-morbidity rate in the subclavian catheter-applied group is statistically significantly higher than in the femoral and jugular catheter-applied group. However, we believe that this is a coincidence, even though it is statistically significant. COPD comorbidity is high because the hospital is a branch hospital of Chest Diseases.

When evaluated in terms of coagulation parameters, prothrombin time (PT), international normalization ratio (INR), thrombocyte (plt) values of the patients were examined. No statistically significant difference was found between the groups.

Femoral catheter-related thrombosis was detected in 14 (21.9%) of 64 patients in the femoral catheter group. There were no complications in the jugular group. In the subclavian group, catheter-related thrombosis was observed in 1 patient. Thrombotic events that developed in the patients were diagnosed by the radiologist with venous Doppler ultrasonography.

There was no difference among the groups between the use of acetylsalicylic acid, the use of new generation oral anticoagulants and the use of low molecular weight heparin. There were no bleeding complications in any group.

The average Apache II score of the patients was 17 in the femoral group, 22 in the jugular group and 16.5 in the subclavian group, and no significant difference was found. In terms of Sequential Organ Failure Assessment Score (SOFA) averages, 10 were found in the femoral group, 11 in the jugular group, and 8 in the subclavian group. There was no statistically significant difference.

In terms of the duration of catheter use, the femoral group was used significantly shorter than the other groups. However, the rate of catheter-related thrombosis was found to be higher than the literature (**Table 1**).

Table 1: Variables according to central catheter location

	Central Catheter						p
	Femoral (n:64)		Juguler (n:32)		Subklavyen (n:14)		
	n	%	n	%	n	%	
Age, Year, $\bar{x}$±SD	69.45±14.09		70.25±10.03		70.21±16.84		0.955
Gender							0.009 [b,c]
Male	38	(59.4%)	16	(50.0%)	2	(14.3%)	
Female	26	(40.6%)	16	(50.0%)	12	(85.7%)	
BMI, $\bar{x}$±SD	27.09±3.20		27.68±3.47		29.68±3.46		0.033 [b]
TPN support							0.999
No	46	(71.9%)	23	(71.9%)	10	(71.4%)	
Yes	18	(28.1%)	9	(28.1%)	4	(28.6%)	
The use of oral anticoagulants							0.398
No	62	(96.9%)	29	(90.6%)	14	(100.0%)	
Yes	2	(3.1%)	3	(9.4%)	-		
The use of acetyl salicylic acid							0.326
No	55	(85.9%)	25	(78.1%)	10	(71.4%)	
Yes	9	(14.1%)	7	(21.9%)	4	(28.6%)	
Coronary artery disease							0.243
No	59	(92.2%)	26	(81.3%)	12	(85.7%)	
Yes	5	(7.8%)	6	(18.8%)	2	(14.3%)	
Cerebro vascular disease							0.527
No	57	(89.1%)	29	(90.6%)	11	(78.6%)	
Yes	7	(10.9%)	3	(9.4%)	3	(21.4%)	
Chronic obstructive pulmonary disease							0.021 [b,c]
No	50	(78.1%)	26	(81.3%)	6	(42.9%)	
Yes	14	(21.9%)	6	(18.8%)	8	(57.1%)	
Malignite							0.795
No	51	(79.7%)	25	(78.1%)	10	(71.4%)	
Yes	13	(20.3%)	7	(21.9%)	4	(28.6%)	
Diyabetes mellitus							0.148
No	39	(60.9%)	21	(65.6%)	5	(35.7%)	
Yes	25	(39.1%)	11	(34.4%)	9	(64.3%)	
Hypertension							0.512
No	30	(46.9%)	19	(59.4%)	7	(50.0%)	
Yes	34	(53.1%)	13	(40.6%)	7	(50.0%)	
Heart failure							0.700
No	54	(84.4%)	28	(87.5%)	11	(78.6%)	
Yes	10	(15.6%)	4	(12.5%)	3	(21.4%)	
Number of punctures							0.652
1	59	(92.2%)	28	(87.5%)	12	(85.7%)	
2	4	(6.3%)	3	(9.4%)	2	(14.3%)	
3	1	(1.6%)	1	(3.1%)	-		
Complication							0.308
No	50	(78.1%)	29	(90.6%)	11	(78.6%)	
Yes	14	(21.9%)	3	(9.4%)	3	(21.4%)	
Types of complications							0.999
Femoral tromboz	14	(100%)	3	(100%)	2	(66.7%)	
Subklavyen tromboz	-		-		1	(33.3%)	
Catheter day, med (IQR)	8 (4)		13 (7)		21 (7)		<0.001 [a,b]
Apache, med (IQR)	17 (7.5)		22 (13.5)		16.5 (13)		0.072
Sofa, med (IQR)	10 (8)		11 (9)		8 (10)		0.243
Platelet count, Med (IQR)	175 (45)		189.5 (36)		194.5 (33)		0.191

Continuous variables are expressed as either the mean ± standard deviation (SD) or as the median (IQR) and categorical variables are expressed as either frequency (percentage). Continuous variables were compared with one way anova or test by kruskal wallis test and categorical variables were compared using Pearson's chi-square test or fisher exact test. Statistically significant p-values are in bold. LSD test was performed for the binary comparisons among the groups and the p value was set at 0.05. Significant differences were found between; a: Femoral vs Juguler, b: Femoral vs Subklavyen, c: Juguler vs Subklavyen
BMI:Body mass Index TPN:Total parenteral nutrisyon

DISCUSSION

COVID-19 pneumonia is a disease that generally occurs with respiratory symptoms such as cough, fever, shortness of breath and weakness. In addition, it also causes vascular pathologies, including hypertension and an increase in thrombotic events in patients. In the autopsies of deaths caused by COVID, it has been shown that there is endothelial damage due to the virus that causes death in lung cells (2).

After the 1950s, central venous catheter applications started to increase gradually due to medical treatment applications and central venous pressure monitoring (5). Many complications related to the catheterization procedure have been described, and these are briefly hematoma formation, great vessel injury, pneumothorax, hemothorax, thrombosis, embolism, and catheter malposition. More than one factor has been held responsible for the development of thrombosis. Application of more than one catheter from the same area, the duration of the catheter and the position of the tip of the catheter are important factors for the development of thrombosis (5,6).

In COVID patients followed in the intensive care unit, there is a need for a central catheter in terms of continuous blood gas monitoring, other medical treatments and parenteral nutrition support due to oral intake insufficiency. In the studies carried out, it has been reported that procedures performed close to the patient's airway are a risk factor for transmission of COVID infection. The doctors who performed the procedure were infected despite wearing personal protective equipment (7). Intensive care physicians also preferred femoral catheters to protect themselves because the patient is further away from the airway (8). According to our clinical experience, since we think that the incidence of femoral catheter-related thrombosis is high, the frequency of internal jugular vein and subclavian catheter applications has been increased in SARS-CoV-2 patients in our clinic.

As mentioned in the literature, parenteral nutritional support is recommended for patients who cannot get enough calories, as the constant air hunger and hypoxia in COVID patients prevent patients from getting enough daily calories orally (8). Although it is found in the literature that TPN application is also effective in the development of thrombosis in the catheter and that the risk increases gradually with advanced age, TPN did not increase the risk of thrombosis in our study (9).

It may cause complications such as catheter-related thrombosis, pulmonary embolism, recurrent deep vein thrombosis, post-thrombotic syndrome and sepsis. These complications may be silent or cause severe symptoms (10). In the 1990s reported that up to 10% of patients with symptomatic catheter-related thrombosis could detect pulmonary embolism (11). However, a recently published study of 4000 patients with central venous catheters did not report any symptomatic pulmonary embolism complications (12).

Symptoms of thrombus and superior vena cava syndrome (edema in the arms, face and neck, enlargement of the chest veins, headache, cough, and dyspnea) may occur in patients undergoing central venous catheter application (13,14).

Due to the increasing number of central venous catheter applications, the rate of DVT seen in the upper and lower extremities has also increased. The incidence of thrombosis developing in the lower extremity due to femoral catheter applications has been shown to be around 21%, the highest in the literature (15). Venous Doppler ultrasonography is preferred in the diagnosis of thrombosis with the presence of clinical symptoms, because it is easy to apply, low cost, does not require any intervention, has high specificity, and distinguishes the presence or absence of flow (16). In the study, the presence of thrombosis was detected by Doppler ultrasonography.

In our study, the incidence of thrombosis in the SARS-CoV-2 patient group with femoral catheter was 21.9% and it was found to be higher than the literature. Since we saw the incidence of thrombosis in the femoral central catheter as relatively high with our clinical experience, it was no longer our preference for the femoral vein-priority central catheter in COVID -19 patients.

Removal of the catheter is important for in the treatment of central catheter-related thrombosis.

Low molecular weight heparin (LMWH) is a major choice in the treatment of central catheter-related thrombosis too. In addition, vitamin K antagonists, unfractionated heparin and fibrinolytic agents can also be used (17). Management of central venous catheter-related thrombosis may also affect developing complications. In a study, 112 patients who developed catheter-related thrombosis did not improve their symptoms when treatment was continued only without anticoagulation and without removal of the catheter (18).

Prolonged use of the same port or catheter increases the risk of symptomatic catheter-related thrombosis will occur. Therefore, international guidelines recommend removing central venous catheters as soon as they are not needed (19).

In our clinic, prophylactic LMWH dose is routinely used in intensive care for non- COVID patients, and therapeutic LMWH dose is applied in SARS-CoV-2 patients. In our clinical observations, we believe that the frequency of thrombosis is higher in SARS-CoV-2 patients, but comparative studies are needed on this subject in the COVID - non-COVID patient group.

Among the factors of catheter-related thrombosis, construction materials also gain importance. It has been reported that polyvinylchloride, Teflon, poly-ethylene catheters are more thrombotic than polyurethane and silicone catheters, and silicone catheters are also reported to be less thrombotic than polyurethane catheters (20). Polyurethane catheter is used in our clinic, but it should not be forgotten that the risk of thrombus development will not completely disappear with any catheter production material.

CONCLUSION

SARS-CoV-2 is a thrombotic disease that affects all vascular structures and causes serious mortality and morbidity. Unnecessary procedures should be avoided as vascular interventions in these patients may cause serious complications in patients. In addition, we believe that choosing the subclavian or internal jugular vein instead of the femoral vein in the application of central venous catheter will reduce the development of thrombosis. In this regard, supportive, multicenter and comparative studies are needed.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara Atatürk Sanatoryum Training and Research Hospital Ethics Committee (Date:14.12.2022, Decision No: 2596)

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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The publication language of the journal is **Turkish** and **English**, and the articles are accepted in both Turkish and English. Proper use of Turkish is important in articles written in Turkish. For this reason, the Turkish dictionary of the Turkish Language Association or www.tdk.org.tr address should also be based on a glossary of terms related to the branches of Turkish medical associations. English articles and English Abstract should be checked by a professional linguist before being submitted. The spelling and grammatical errors in the manuscript are corrected by our English language consultant and editorial committee.

STATISTICS EVALUATION

All prospective, experimental and retrospective research articles should be evaluated in terms of statistics (if required by the statistical expert) and indicated by appropriate planning, analysis and reporting.

ACCEPTANCE OF PUBLISHING

After the approval of the editors and referees, the publication date of the article is taken into consideration. A Doi number is obtained for each post.

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Manuscripts are double-spaced with Microsoft Word, and title titles (Abstract, Abstract, Introduction, Materials and Methods, Results, Discussion, References, etc.) are written in 12 pt. 2.5 cm space should be written at the top and bottom. The writing style should be Times New Roman. "System International" (SI) units should be used. Figures, tables and graphs should be referenced in the text. Abbreviations should be given in parentheses where the word first appears. Turkish articles should be 50% contiguous, and English should be 50% contiguous. A comma should be used in decimal numbers in Turkish (55.78) and a period (55.78) should be used in English manuscripts. Review articles and research articles should not exceed 4000 words, case reports 2000 words, letters to the editor should not exceed 500 words (This limits to all article types are excluding Abstract and References section). Pages should be numbered from the abstract page.

SECTIONS OF MANUSCRIPT

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This is the article that the author of the article sends to the editor of the journal. In this section, it should be noted that part or all of the article is not published elsewhere and is not in the process of being evaluated in another journal at the same time, "**Material Support and Interest Relationship**" status, language and statistical checks are made.

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The category of the article submitted at the beginning of the page should be indicated (clinical analysis, research article, experimental study, case report, review, etc.). The names and surnames of all authors should be numbered after the superscript and numbered from 1, and they should be added under the names of the institutions, clinics, cities and countries. On the title page, each author's **Orcid ID** should be his/her e-mail address. This page should include the Authorized Author (s), name, full address, telephone and **e-mail** (address information should be indicated in Turkish if the language of the article is Turkish and English if it is English). Oral or Poster presentations presented at congresses should be indicated on the title page by giving the name, place and date of the congress.

3. Article File

There should be no names of authors and institutions, only this information should be on the title page.

Title: There should be a short and clear title. It should not contain abbreviations and should be written in Turkish and English. Abstract: Turkish and English abstracts should be written. In research articles; It should be divided into sections of Aim/Introduction, Material and Method, Results/Findings and Conclusion and should not exceed 400 words. In the review, case reports and the like, Öz; it should be short and one paragraph, and should not exceed 300 words in reviews and 250 words in case reports.

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Research Article: Prospective-retrospective and all kinds of experimental studies can be published. Abstract (approximately 400 words; aim/introduction, material and method, results/findings and conclusion sections in Turkish and English), Introduction, Material and Method, Results, Discussion, Conclusion, References.

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Case Report: These are rare or different articles in diagnosis and treatment. It should be supported with sufficient number of photographs and diagrams. Abstract (about 250 words; no section; Turkish and English), Introduction, case report, discussion, conclusion.

Letter to the Editor: The articles that are published in the journal within the last year include a maximum of 500 words containing various opinions, experiences and questions of the readers. There are no Title and Abstract sections. The number of references is limited to 5 (max. 10). It should be indicated which article (number, date) is dedicated and at the end there should be the name, institution and address of the author. The answer to the letter is given by the editor or the author (s) of the article and published in the journal.

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Ethics Committee Approval: The study was carried out with the permission of ..... Ethics Committee (Date:....., Decision No. .....).

Informed Consent: Written informed consent was obtained from all participants who participated in this ....study (If study retrospective: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

Acknowledgements: If any, it should be written before references.

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SOURCE WRITING EXAMPLES

Excerpt from journals;

Cesur S, Aslan T, Hoca NT, Cimen F, Tarhan G, Cifci A. Clinical importance of serum neopterin level in patients with pulmonary tuberculosis. Int J Mycobacteriol 2014; 3: 15-8 (not 15-18).

Excerpt from the book;

Tos M. Cartilage tympanoplasty. 1st ed. Stuttgart-New York: Georg Thieme Verlag; 2009.

Excerpt from the book, which is the only author and editor;

Neinstein LS. The office visit, interview techniques, and recommendations to parents. In: Neinstein LS (ed). Adolescent Health Care. A practical guide. 3rd ed. Baltimore: Williams & Wilkins; 1996: 46-60.

Excerpt from the book with multiple authors and editors;

Schulz JE, Parran T Jr.: Principles of identification and intervention. In: Principles of Addicton Medicine, Graem AW. Shultz TK (eds). American Society of Addiction Medicine, 3rd ed. Baltimore: Williams & Wilkins; 1998: 1-10.

If the editor is also the author of the chapter in the book;

Diener HC, Wilkinson M (editors). Drug-induced headache. In: Headache. First ed., New York: Springer-Verlag; 1988: 45-67.

Excerpt from PhD/Undergraduate Thesis;

Kilic C. General Health Survey: A Study of Reliability and Validity. phD Thesis, Hacettepe University Faculty of Medicine, Department of Psychiatrics, Ankara; 1992.

Excerpt from an internet site;

Site name, URL address, author names, access date should be given in detail.

Giving a Doi number;

Joos S, Musselmann B, Szecsenyi J. Integration of complementary and alternative medicine into the family market in Germany: Result of National Survey. Evid Based Complement Alternat Med 2011 (doi: 10.1093/ecam/nep019).

For other reference styles, see "ICMJE Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Sample References".

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Authors should declare, if any, the roles of sponsors of the study:

1. Design of the study 2. Data collection, analysis and interpretation of the results 3. Writing the report

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- Ethical Status,
- "Conflict of Interest"
- Orcid numbers and author information should be on this page.

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YAYIN KURALLARI, YAYIN POLİTİKASI, GENEL İLKELER VE GÖNDERME KURALLARI

YAZARLARA BİLGİ

Journal of Medicine and Palliative Care (JOMPAC) hakemli, açık erişimli, periyodik olarak çıkan bir dergidir. Dergi yazım kurallarına göre düzenlenmiş makaleler **DergiPark** sistemi üzerinden kabul edilmektedir. https://dergipark.org.tr/tr/pub/jompac/archive web adresinden ve **Dergipark** web sayfasından tüm sayılara ücretsiz olarak erişilebilmektedir. Amacımız uluslararası bir tabanda hastalıkların teşhis ve tedavisinde yenilikler içeren yüksek kalitede bilimsel makaleler yayımlamak ve bilime katkı sağlamaktır. Yılda dört kez (**Mart, Haziran, Eylül, Aralık**) yayımlanmaktadır. Hakemli bir dergi olarak gelen yazılar biyomedikal makalelere ait **Uluslararası Tıp Dergileri Editörleri Komitesi** (www.icmje.org) tarafından tanımlanan standart gereksinimler ile ilgili ortak kurallara uygunluğu açısından değerlendirilmektedir. Dergimizde yayımlanmış makalelerin tamamına elektronik ortamdan ulaşabilir, **DergiPark** web sitemizden (https://dergipark.org.tr/en/pub/jompac) okuyabilir, indirebilirsiniz. Amacımız siz meslektaşlarımızın göndermiş olduğu yayınların karar ve yayımlanma sürecini en kısa sürede sonuca ulaştırmaktır. Dergimizin kalitesini yükseltmek için her zaman önerilere ve yapıcı eleştirilere açık olduğumuzu ve bu konudaki bildirimlere gereken hassasiyeti göstereceğimizi belirtmek isteriz. Makale işletim sisteminde ve atıflarda derginin İngilizce adı kullanılacaktır.

Journal of Medicine and Palliative Care (JOMPAC) kapsam olarak tıbbın ve tıpla ilgili sağlık bilimlerinin her branşı ile ilgili retrospektif/prospektif klinik ve laboratuvar çalışmaları, ilginç olgu sunumları, davet üzerine yazılan derlemeler, editöre mektuplar, orijinal görüntüler, kısa raporlar ve teknik yazıları yayımlayan bilimsel, hakemli bir dergidir. Derginin dili **İngilizce** ve **Türkçe**'dir. Makaleler hem Türkçe hem de İngilizce olarak kabul edilmektedir. Türkçe gönderilen makalelerde ayrıca İngilizce Başlık, Abstract, Keywords olmalı, İngilizce olarak gönderilen makalelerde de ayrıca Türkçe Başlık, Öz, Anahtar Kelimeler olmalıdır. Başka bir dergide yayımlanmış veya değerlendirilmek üzere gönderilmiş yazılar veya dergi kurallarına göre hazırlanmamış yazılar değerlendirme için kabul edilmez. Editör, yardımcı editör ve yayıncı dergide yayımlanan yazılar için herhangi bir sorumluluk kabul etmez. Dergimizde yayımlanmış makalelerin tamamına elektronik ortamdan ulaşabilir, https://dergipark.org.tr/tr/pub/jompac web sitemizden okuyabilir, indirebilirsiniz. Yazıların tüm bilimsel sorumluluğu yazar(lar)a aittir.

DERGİ ADI

Journal of Medicine and Palliative Care

DERGİ ADININ KISALTMASI

J Med Palliat Care/JOMPAC/jompac

YAZIŞMA ADRESİ

Yazılar e-posta yoluyla sorumlu yazar tarafından, **DergiPark**'a kayıt olunduktan sonra **DergiPark** üzerinden https://dergipark.org.tr/tr/journal/3258/submission/step/manuscript/new linkine girilerek gönderilmelidir.

MAKALE GENEL YAZIM KURALLARI

Yazıların tüm bilimsel sorumluluğu yazar(lar)a aittir. Editör, yardımcı editör ve yayıncı dergide yayımlanan yazılar için herhangi bir sorumluluk kabul etmez.

EDİTÖRİYEL ÖN KONTROL DEĞERLENDİRMESİ

Journal of Medicine and Palliative Care (JOMPAC)'e gönderilen yazılar format ve intihal açısından değerlendirilir. Formata uygun olmayan yazılar değerlendirilmeden sorumlu yazara geri gönderilir. Bu tarz bir zaman kaybının olmaması için yazım kuralları gözden geçirilmelidir. Basım için gönderilen tüm yazılar iki veya daha fazla yerli/yabancı hakem tarafından değerlendirilir. Makalelerin değerlendirilmesi, bilimsel önemi, orijinalliği göz önüne alınarak yapılır. Yayıma kabul edilen yazılar editörler kurulu tarafından içerik değiştirilmeden yazarlara haber verilerek yeniden düzenlenebilir. Makalenin dergiye gönderilmesi veya yayıma kabul edilmesi sonrası isim sırası değiştirilemez, yazar ismi eklenip çıkartılamaz.

BİLİMSEL VE ETİK SORUMLULUK

Journal of Medicine and Palliative Care (JOMPAC)'in yayın ve yayın süreçleri, Dünya Tıbbi Editörler Derneği (World Association of Medical Editors (**WAME**)), Yayın Etiği Komitesi (Committee on Publication Ethics (**COPE**)), Uluslararası Tıbbi Dergi Editörleri Konseyi (International Council of Medical Journal Editors (**ICMJE**)), Bilim Editörleri Konseyi (Council of Science Editors (**CSE**)), Avrupa Bilim Editörleri Birliği (**EASE**) ve Ulusal Bilgi Standartları Organizasyonu (National Information Standards Organization (NISO)) kurallarına uygun olarak şekillendirilmiştir. Dergi, Bilimsel Yayıncılıkta Şeffaflık ve En İyi Uygulama İlkeleri'ne (Principles of Transparency and Best Practice in Scholarly Publishing (**doaj.org/bestpractice**)) uygundur.

Klinik araştırma makalelerinin protokolü Etik Komitesi tarafından onaylanmış olmalıdır. İnsanlar üzerinde yapılan tüm çalışmalarda "**Gereç ve Yöntem**" bölümünde çalışmanın ilgili komite tarafından onaylandığı veya çalışmanın **Helsinki İlkeler Deklarasyonu**'na (**https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/**) uyularak gerçekleştirildiğine dair bir cümle yer almalıdır. Çalışmaya dahil edilen tüm kişilerin **Bilgilendirilmiş Onam Formu'**nu imzaladığı metin içinde belirtilmelidir. **Journal of Medicine and Palliative Care (JOMPAC)'**e gönderilen makalelerdeki çalışmaların **Helsinki İlkeler Deklarasyonu'**na uygun olarak yapıldığı, kurumsal etik ve yasal izinlerin alındığı varsayılacak ve bu konuda sorumluluk kabul edilmeyecektir. Çalışmada "Hayvan" öğesi kullanılmış ise yazarlar, makalenin Gereç ve Yöntem bölümünde hayvan haklarını **Guide for the Care and Use of Laboratory Animals** (**https://www.nap.edu/catalog/5140/guide-for-the-care-and-use-of-laboratory-animals**) prensipleri doğrultusunda koruduklarını, çalışmalarında ve kurumlarının etik kurullarından onay aldıklarını belirtmek zorundadır. Olgu sunumlarında hastanın kimliğinin ortaya çıkmasına bakılmaksızın hastalardan "Bilgilendirilmiş rıza" alınmalıdır. Makalede Etik Kurul Onayı alınması gerekli ise; alınan belge makale ile birlikte gönderilmelidir. Makale yazarlar tarafından **akademik intihal önleme programı**ndan geçirilmelidir. Makalenin etik kurallara uygunluğu yazarların sorumluluğundadır.

Tüm makale başvuruları intihal araştırılması için taranmalı ve sonrasında dergi sistemine yüklenmelidir. İntihal, atıf manipülasyonu ve gerçek olmayan verilerden şüphelenilmesi veya araştırmaların kötüye kullanılması durumunda, yayın kurulu **COPE** yönergelerine uygun olarak hareket eder. Bakınız: **Guidance from the Committee on Publication Ethics** (**COPE**).

Yazar olarak listelenen her bireyin **Uluslararası Tıp Dergisi Editörleri Komitesi** (**ICMJE - www.icmje.org**) tarafından önerilen yazarlık kriterlerini karşılaması gerekir. **ICMJE** yazarlığın aşağıdaki 4 kritere dayanmasını önerir: (1) Çalışmanın tasarımı, verilerin elde edilmesi, analizi veya yorumlanması (2) Dergiye gönderilecek kopyanın hazırlanması veya bu kopyanın içeriğini bilimsel olarak etkileyecek ve ileriye götürecek şekilde katkı sağlanması (3) Yayımlanacak kopyanın son onayı (4) Çalışmanın tüm bölümleri hakkında bilgi sahibi olma ve tüm bölümleri hakkında sorumluluğu alma.

Bir yazar, yaptığı çalışmanın bölümlerinden sorumlu olmanın yanı sıra, çalışmanın diğer belirli bölümlerinden hangi ortak yazarların sorumlu olduğunu bilmeli ayrıca yazarlar, ortak yazarlarının katkılarının bütünlüğüne güvenmelidir. Yazar olarak atananların tümü yazarlık için dört kriteri de karşılamalı ve dört kriteri karşılayanlar yazar olarak tanımlanmalıdır. Dört kriterin tümünü karşılamayanlara makalenin başlık sayfasında teşekkür edilmelidir. Yayın kurulu yazarlık şartlarını karşılamayan bir kişinin yazar olarak eklendiğinden şüphe ederse yazı daha fazla incelenmeksizin reddedilecektir.

Journal of Medicine and Palliative Care (JOMPAC)'e gönderilen bir çalışma için bireylerden veya kurumlardan alınan mali hibeler veya diğer destekler Editör Kurulu'na bildirilmelidir. Potansiyel bir çıkar çatışmasını bildirmek için, **ICMJE Potansiyel Çıkar Çatışması Bildirim Formu**, katkıda bulunan tüm yazarlar tarafından imzalanmalı ve gönderilmelidir. Editörlerin, yazarların veya hakemlerin çıkar çatışması olasılığı, derginin Editör Kurulu tarafından **COPE** ve **ICMJE** yönergeleri kapsamında çözümlenecektir. Derginin Editör Kurulu, tüm itiraz durumlarını **COPE** kılavuzları kapsamında ele almaktadır. Bu gibi durumlarda, yazarların itirazları ile ilgili olarak yazı işleri bürosu ile doğrudan temasa geçmeleri gerekmektedir. Gerektiğinde, dergi içinde çözülemeyen olayları çözmek için bir kamu denetçisi atanabilir. Baş editör itiraz durumlarında karar alma sürecinde alınacak kararlarla ilgili nihai otoritedir. Yazarlar, dergiye bir makale gönderirken, yazıların telif haklarını **Journal of Medicine and Palliative Care (JOMPAC)**'e devretmiş olmayı kabul ederler. Yazı yayımlanmamak üzere reddedilirse veya herhangi bir sebepten geri çekilirse telif hakkı yazarlara geri verilir.Şekiller, tablolar veya diğer basılı materyaller de dahil olmak üzere basılı ve elektronik formatta daha önce yayımlanmış içerik kullanılıyorsa yazarlar telif hakları sahiplerinden gerekli izinleri almalıdır. Bu konudaki hukuki, finansal ve cezai yükümlülükler yazarlara aittir. **Journal of Medicine and Palliative Care'de (JOMPAC)** yayımlanan makalelerde belirtilen ifade veya görüşler, editörlerin, yayın kurulunun veya yayıncının görüşlerini yansıtmaz; editörler, yayın kurulu ve yayıncı bu tür materyaller için herhangi bir sorumluluk veya yükümlülük kabul etmez. Yayınlanan içerikle ilgili nihai sorumluluk yazarlara aittir.

MAKALE "BAŞKA BİR YERDE YAYIMLANMAMIŞTIR" İBARESİ

Her yazar makalenin bir bölümünün veya tamamının başka bir yerde yayımlanmadığını ve aynı anda bir diğer dergide değerlendirilme sürecinde olmadığını, editöre sunum sayfasında belirtmelidirler. Kongrelerde sunulan sözlü veya poster bildirilerin, başlık sayfasında kongre adı, yer ve tarih verilerek belirtilmesi gereklidir. Dergide yayımlanan yazıların her türlü sorumluluğu (etik, bilimsel, yasal, vb.) yazarlara aittir.

YAYIN HAKKI DEVİR FORMU

Telif Hakkı Devir Formu (https://dergipark.org.tr/tr/journal/3258/file/3177/show) linkinden temin edilebilir. Makalenin ana dilinde (makalenin dili İngilizce ise, İngilizce olmalıdır, makalenin dili Türkçe ise, Türkçe olmalıdır) doldurulmalı, makale (https://dergipark.org.tr/tr/journal/3258/submission/step/manuscript/new) adresi üzerinden yüklenirken on-line olarak gönderilmelidir 1976 Copyright Act'e göre, yayımlanmak üzere kabul edilen yazıların her türlü yayın hakkı yayıncıya aittir.

YAZIM DİLİ KONTROLÜ

Derginin yayın dili **Türkçe** ve **İngilizce**'dir, makaleler hem Türkçe hem de İngilizce olarak kabul edilmektedir. Türkçe yazılan yazılarda düzgün bir Türkçe kullanımı önemlidir. Bu nedenle Türk Dil Kurumu'nun Türkçe sözlüğü veya www.tdk.org.tr adresi ayrıca Türk tıbbi derneklerinin kendi branşlarına ait terimler sözlüğü esas alınmalıdır. İngilizce makaleler ve İngilizce Abstract gönderilmeden önce profesyonel bir dil uzmanı tarafından kontrol edilmelidir. Yazıdaki yazım ve gramer hataları içerik değişmeyecek şekilde İngilizce dil danışmanımız ve redaksiyon komitemiz tarafından düzeltilmektedir.

İSTATİSTİK DEĞERLENDİRMESİ

Tüm prospektif, deneysel ve retrospektif araştırma makaleleri istatistik yönünden (gerekirse istatistik uzmanı tarafından) değerlendirilmeli ve uygun plan, analiz ve raporlama ile belirtilmelidir.

YAYIMA KABUL EDİLMESİ

Editör ve hakemlerin uygunluk vermesi sonrası makalenin gönderim tarihi esas alınarak yayım sırasına alınır. Her yazı için bir **Doi** numarası alınır.

MAKALE YAZIM KURALLARI

Yazılar Microsoft Word programı ile çift satır aralıklı ve başlık yazıları (Makale Adı, Öz, Abstract, Giriş, Gereç ve Yöntem, Bulgular, Tartışma, Kaynaklar vs.) 12 punto olarak, makalenin diğer kısımları 11 punto olacak şekilde, her sayfanın iki yanında ve alt ve üst kısmında 2,5 cm boşluk bırakılarak yazılmalıdır. Yazı stili Times New Roman olmalıdır. "System International" (SI) unitler kullanılmalıdır. Şekil, tablo ve grafikler metin içinde refere edilmelidir. Kısaltmalar, kelimenin ilk geçtiği yerde parantez içinde verilmelidir. Türkçe makalelerde %50 bitişik yazılmalı, aynı şekilde İngilizcelerde de 50% bitişik olmalıdır. Türkçe'de ondalık sayılarda virgül kullanılmalı (55,78) İngilizce yazılarda nokta (55.78) kullanılmalıdır. Araştırma makalesi ve derleme 4000, olgu sunumu 2500, editöre mektup 500 kelimeyi (ABSTRACT/ÖZ ve REFERENCES/KAYNAKLAR hariç olmak üzere) geçmemelidir. Öz sayfasından itibaren sayfalar numaralandırılmalıdır.

Yazının Bölümleri

1. Editöre Sunum Sayfası

Journal of Medicine and Palliative Care (Tıp ve Palyatif Bakım Dergisi)'de yayımlanmak üzere değerlendirilmesi isteğinin belirtildiği, makalenin sorumlu yazarı tarafından dergi editörüne hitaben gönderdiği yazıdır. Bu kısımda makalenin bir bölümünün veya tamamının başka bir yerde yayımlanmadığı ve aynı anda bir diğer dergide değerlendirilme sürecinde olmadığı, "**Maddi Destek ve Çıkar İlişkisi**" durumu, dil ve istatistik kontrolünün yapıldığı belirtilmelidir.

2. Başlık Sayfası

Sayfa başında gönderilen makalenin kategorisi belirtilmedir (klinik analiz, araştırma makalesi, deneysel çalışma, olgu sunumu, derleme vs). Tüm yazarların ad ve soyadları yazıldıktan sonra üst simge ile 1'den itibaren numaralandırılıp, çalıştıkları kurum, klinik, şehir ve ülke yazar isimleri altına eklenmelidir. Başlık sayfasında her yazarın **Orcid no** bilgisi, **e-posta** adresi olmalıdır. Bu sayfada Sorumlu Yazar belirtilmeli isim, açık adres, telefon ve e-posta bilgileri eklenmelidir (Dergimizin formatı gereği adres bilgileri, kurumları makale dili Türkçe ise Türkçe olarak, İngilizce ise İngilizce olarak belirtilmelidir). Kongrelerde sunulan Sözlü veya Poster bildiriler başlık sayfasında kongre adı, yer ve tarih verilerek belirtilmelidir.

3. Makale Dosyası

Yazar ve kurum isimleri bulunmamalıdır, bu bilgiler sadece başlık sayfasında olmalıdır.

Başlık: Kısa ve net bir başlık olmalıdır. Kısaltma içermemeli, Türkçe ve İngilizce olarak yazılmalıdır. Öz: Türkçe ve İngilizce (Abstract) yazılmalıdır. Araştırma makalelerinde Öz; Amaç, Gereç, Yöntem, Bulgular ve Sonuç bölümlerine ayrılmalı ve 400 kelimeyi geçmemelidir. Derleme, olgu sunumları ve benzerlerinde Öz; kısa ve tek paragraflık olmalı, derlemelerde 300, olgu sunumlarında 250 kelimeyi geçmemelidir.

Anahtar Kelimeler: Türkçe Öz'ün ve İngilizce Abstract'ın sonlarında bulunmalıdır. En az 3 en fazla 6 adet yazılmalıdır. Kelimeler birbirlerinden noktalı virgül ile ayrılmalıdır. İngilizce Anahtar Kelimeler (Keywords) "**Medical Subject Headings (MESH)**"e uygun (www.nlm.nih.gov/mesh/MBrowser.html) olarak verilmelidir. Türkçe Anahtar Kelimeler "Türkiye Bilim Terimleri' ne uygun olarak verilmelidir (www.bilimterimleri.com). Bulunamaması durumunda bire bir Türkçe tercümesi verilmelidir.

Şekil, Fotoğraf, Tablo ve Grafikler: Metin içinde geçtiği yerlerde ilgili cümlenin sonunda belirtilmeli, metin içine yerleştirilmemeli, kaynaklardan sonra metin sonuna eklenmelidir. Kullanılan kısaltmalar altındaki açıklamada belirtilmelidir. Daha önce basılmış şekil, resim, tablo ve grafik kullanılmış ise yazılı izin alınmalıdır ve bu izin açıklama olarak şekil, resim, tablo ve grafik açıklamasında belirtilmelidir. Makale yazarlar tarafından akademik intihal önleme programından geçirilmelidir. Resim/fotoğraf jpeg ve en az 300 dpi çözünürlükte olmalıdır.

Metin Bölümleri: Yayımlanmak üzere gönderilecek yazı örnekleri şu şekildedir.

Editöriyel Yorum/Tartışma: Yayınlanan orijinal araştırma makaleleri ile ilgili, araştırmanın yazarları dışındaki, o konunun uzmanı tarafından değerlendirilmesidir. Dergide makalelerden önce yayımlanır.

Araştırma Makalesi: Prospektif-retrospektif ve her türlü deneysel çalışmalar yayımlanabilmektedir. Giriş, Gereç ve Yöntem, Bulgular, Tartışma, Sonuç olarak düzenlenmelidir. Öz (yaklaşık 400 kelime; amaç, gereç ve yöntem, bulgular ve sonuç bölümlerinden oluşan Türkçe ve İngilizce), Giriş, Gereç ve Yöntem, Bulgular, Tartışma, Sonuç, Kaynaklar.

Derleme: Davet edilen yazarlar tarafından veya doğrudan hazırlanabilir. Tıbbi özellik gösteren her türlü konu için son tıp literatürünü de içine alacak şekilde hazırlanabilir. Öz (yaklaşık 300 kelime, bölümsüz, Türkçe ve İngilizce), konu ile ilgili Başlıklar, Kaynaklar.

Olgu Sunumu: Tanı ve tedavide farklılık gösteren veya nadir görülen makalelerdir. Yeterli sayıda fotoğraflarla ve şemalarla desteklenmiş olmalıdır. Öz (yaklaşık 250 kelime; bölümsüz; Türkçe ve İngilizce), Giriş, Olgu sunumu, Tartışma, Sonuç olarak düzenlenmelidir.

Editöre Mektup: Dergide son bir yıl içinde yayımlanan makaleler ile ilgili okuyucuların değişik görüş, tecrübe ve sorularını içeren en fazla 500 kelimelik yazılardır. Başlık ve Öz bölümleri yoktur. Kaynak sayısı 5 (en fazla 10) ile sınırlıdır. Hangi makaleye (sayı, tarih verilerek) ithaf olunduğu belirtilmeli ve sonunda yazarın ismi, kurumu, adresi bulunmalıdır. Mektuba cevap, editör veya makalenin yazar(lar)ı tarafından, yine dergide yayımlanarak verilir.

Eğitim: Derginin kapsamı içinde güncel konularda okuyucuya mesaj veren son klinik ve laboratuvar uygulamaların da desteklediği bilimsel makalelerdir. Öz (yaklaşık 250 kelime; bölümsüz; Türkçe ve İngilizce), konu ile ilgili Başlıklar, Kaynaklar.

Kitap Değerlendirmeleri: Derginin kapsamı içinde güncel değeri olan ulusal veya uluslararası kabul görmüş kitapların değerlendirmeleridir.

KAYNAKLARDAN HEMEN ÖNCE BELİRTİLMESİ GEREKENLER

ETİK BEYANLAR

Etik Kurul Onayı (Eğer gerekiyorsa): "Çalışma için …….. Etik Kurulu'ndan .....tarih ve ..... sayı /karar no ile etik kurul onayı alınmıştır." ifadesiyle yazarlar tarafından belirtilmelidir.

Aydınlatılmış Onam: Bu çalışmaya katılan hasta(lar)dan yazılı onam alınmıştır (Olgu sunumlarında ve kişilerle yapılan prospektif çalışmalarda mutlaka olmalıdır. Eğer çalışma retrospektif ise: "Aydınlatılmış Onam: Çalışma retrospektif olarak dizayn edildiği için hastalardan aydınlatılmış onam alınmamıştır." ifadesiyle yazarlar tarafından belirtilmelidir.

Hakem Değerlendirme Süreci: "Harici çift kör hakem değerlendirmesi" ifadesiyle yazarlar tarafından belirtilmelidir.

Çıkar Çatışması: "Yazarlar bu çalışmada herhangi bir çıkara dayalı ilişki olmadığını beyan etmişlerdir." ifadesiyle yazarlar tarafından belirtilmelidir.

Finansal Destek: "Yazarlar bu çalışmada finansal destek almadıklarını beyan etmişlerdir" ifadesiyle yazarlar tarafından belirtilmelidir.

Yazar Katkıları: "Yazarların tümü; makalenin tasarımına, yürütülmesine, analizine katıldığını ve son sürümünü onayladıklarını beyan etmişlerdir." ifadesiyle yazarlar tarafından belirtilmelidir.

Teşekkür Yazısı: Varsa kaynaklardan önce yazılmalıdır.

Kaynaklar: Kaynaklar makalede geliş sırasına göre yazılmalıdır. Kaynaktaki yazar sayısı 6 veya daha az ise tüm yazarlar (soyadı ve adının ilk harfi olacak şekilde olmalı, yazar isimleri birbirinden virgül ile ayırılmalı) belirtilmeli, 7 veya daha fazla ise ilk 3 isim yazılıp ve ark. ("et al") eklenmeli, makale ismi (Tümce şeklinde sadece cümlenin ilk harfi ve özel isimlerin ilk harfi büyük olacak), kısa dergi adı, yıl, cilt, kısa sayfa no (15-8. şeklinde olacak, 15-18 olmayacak) eklenmeli ve noktalama işaretleri arasında birer boşluk bırakılmalıdır. Kaynak yazımı için kullanılan format Index Medicus'ta belirtilen şekilde olmalıdır (www. icmje.org). Kaynak listesinde yalnızca yayınlanmış ya da yayınlanması kabul edilmiş veya Doi numarası almış çalışmalar yer almalıdır. Dergi kısaltmaları **Cumulated Index Medicus**'ta kullanılan stile uymalıdır (http://www2.bg.am.poznan.pl/czasopisma/ medicus.php?lang=eng.). Kaynak sayısının araştırma makalelerinde 40, derlemelerde 60, olgu sunumlarında 20, editöre mektupta 5 (en fazla 10) ile sınırlandırılmasına özen gösterilmelidir. Kaynaklar metinde cümle sonunda nokta işaretinden hemen önce parantez kullanılarak belirtilmelidir. Örneğin (4,5). Kaynakların doğruluğundan yazar(lar) sorumludur. Yerli ve yabancı kaynakların sentezine önem verilmelidir.

4. Şekil, Grafik, Resim ve Tablo Başlıkları

Başlıklar kaynaklardan sonra yazılmalıdır. Her biri ayrı bir görüntü dosyası (en az 300 dpi çözünürlükte, jpg) olarak gönderilmelidir.

Makalenin basıma kabulünden sonra Dizginin ilk düzeltme nüshası sorumlu yazara e-posta yoluyla gönderilecektir. Bu metinde sadece yazım hataları düzeltilecek, ekleme çıkartma yapılmayacaktır. Sorumlu yazar düzeltmeleri 2 gün içinde bir dosya halinde e-posta ile yayın idare merkezine bildirecektir.

Kaynak Yazım Örnekleri

Dergilerden yapılan alıntı;

Cesur S, Aslan T, Hoca NT, Çimen F, Tarhan G, Çifci A. Clinical importance of serum neopterin level in patients with pulmonary tuberculosis. Int J Mycobacteriol 2014; 3: 15-8 (15-18 değil).

Kitaptan yapılan alıntı;

Tos M. Cartilage tympanoplasty. 1st ed. Stuttgart-New York: Georg Thieme Verlag; 2009.

Tek yazar ve editörü olan kitaptan alıntı;

Neinstein LS. The office visit, interview techniques, and recommendations to parents. In: Neinstein LS (ed). Adolescent Health Care. A practical guide. 3rd ed. Baltimore: Williams&Wilkins; 1996: 46-60.

Çoklu yazar ve editörü olan kitaptan alıntı;

Schulz JE, Parran T Jr: Principles of identification and intervention. In:Principles of Addicton Medicine, Graham AW. Shultz TK (eds). American Society of Addiction Medicine, 3rd ed. Baltimore: Williams&Wilkins; 1998: 1-10.

Eğer editör aynı zamanda kitap içinde bölüm yazarı ise;

Diener HC, Wilkinson M (editors). Drug-induced headache. In: Headache. First ed., New York: Springer-Verlag; 1988: 45-67.

Doktora/lisans tezinden alıntı;

Kılıç C. General Health Survey: A Study of Reliability and Validity. phD Thesis, Hacettepe University Faculty of Medicine, Department of Psychiatrics, Ankara; 1992.

Bir internet sitesinden alıntı;

Sitenin adı, URL adresi, yazar adları, erişim tarihi detaylı olarak verilmelidir.

Doi numarası vermek;

Joos S, Musselmann B, Szecsenyi J. Integration of complementary and alternative medicine into family prac- tice in Germany: Result of National Survey. Evid Based Complement Alternat Med 2011 (doi:10.1093/ecam/nep019).

Diğer referans stilleri için "ICMJE Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Sample References" sayfasını ziyaret ediniz.

"Bu çalışmanın içindeki materyalin tamamı ya da bir kısmının daha önce herhangi bir yerde yayımlanmadığını ve halihazırda da yayın için başka bir yerde değerlendirilmede olmadığını beyan ederim." Bu 400 kelimeye kadar olan özler hariç, sempozyumlar, bilgi aktarımları, kitaplar, davet üzerine yazılan makaleler, elektronik formatta gönderimler ve her türden ön bildirileri içerir.

Sponsorluk Beyanı

Yazarlar aşağıda belirtilen alanlarda, varsa çalışmaya sponsorluk edenlerin rollerini beyan etmelidirler:

1. Çalışmanın dizaynı 2. Veri toplanması, analizi ve sonuçların yorumlanması 3. Raporun yazılması

KONTROL LİSTESİ

Kontrol listesindekiler eksiksiz yapılmalıdır.

Makalede mutlaka olması gerekenler;

—Editöre Sunum Sayfası

—Başlık Sayfası

- Etik Durum,
- "Çıkar Çatışması Durumu" belirtir cümle,
- Orcid numaraları ve yazar bilgileri bu sayfada olmalıdır.

—Ana Metin

—Telif Hakkı Devri Formu

1. **Editöre Sunum Sayfası:** Sorumlu Yazar tarafından editöre hitaben yazılmış olmalıdır. Telefon ve E-posta eklenmelidir. Gönderilen makalenin adı, kısa adı, "Daha önceden yayımlanmamış, şu an herhangi bir dergiye değerlendirilmek üzere gönderilmemiştir ve yazarların kendi orijinal çalışmasıdır" ibaresi, "Çıkar Çatışması Beyanı" içermelidir.
2. **Başlık sayfası:** Türkçe ve İngilizce Makale başlıkları/Kısa başlıklar, Yazarlar ve Kurumları, Sorumlu Yazar posta adresi ve telefon, tüm yazarların **Orcid no** (2019 yılından itibaren zorunludur) ve **E-posta** adresleri. **Başlıkta özel isimler ve ilk harf dışında küçük harf kullanılmalıdır**.
3. **Makalenin Ana Metin sayfaları:** Türkçe ve İngilizce Makale Başlıkları/Kısa Başlıklar, Türkçe ve İngilizce Öz/Abstract ve Anahtar Kelimeler/Keywords, Makale Metni, Kaynaklar, Tablo ve Şekil Başlıkları, Tablolar. **Bu sayfada yazar isimleri, kurum bilgileri olmayacaktır.**
4. **Yazı tipi:** Başlıklarda "Times New Roman" ve 12 punto olmalı, makalenin diğer kısımlarında 11 punto, çift boşluklu satır arası ve tüm alanlarda 2,5 cm girinti ayarıyla yazılmalıdır.
5. **Öz/Abstract:** Türkçe özet **ÖZ** ile başlamalı; "**Giriş/Amaç, Gereç ve Yöntem, Bulgular ve Sonuç**" kısımlarını içermelidir. İngilizce özet **ABSTRACT** başlığıyla başlamalı "**Introduction/Aim, Material and Method, Findings/Results, Conclusion**" kısımlarını içermelidir.
6. **Anahtar Kelimeler/Keywords:** Türkçe Öz kısmının altına "**Anahtar Kelimeler**", İngilizce "Abstract" kısmının altında "**Keywords**" (birleşik) halde eklenmelidir. Anahtar kelimeler en az 3, en çok 6 kelime/sözcük olmalı, birbirlerinden virgülle ayırılmalı ve MeSH'e uygun olmalıdır.
7. **G**ereç ve Yöntem kısmında **Etik Kurul Onayı** alındığı (Alındığı yer, tarih, etik kurul no olacak şekilde yazılması önerilir) belirtilmelidir. Etik Kurul Onayı gerektirmeyen makalelerde Kurum Onayı/İzni alındığı (Çıkar Çatışması olmaması için) belirtilmelidir. İlgili belgeler talep edildiğinde gönderilmelidir. Etik problemlerde sorumluluğun yazar(lar)da olduğu unutulmamalıdır.
8. **T**artışmada istatistiksel terimler (p, r, α gibi) **kullanılmamalıdır.**
9. **"Maddi Destek/Çıkar Çatışması Durumu"** kaynakçadan önce belirtilmeli, "***Teşekkür Yazısı***" varsa kaynakçadan önce yazılmalıdır.
10. **Kaynak Gösterimi;** yazım kurallarında detaylı anlatıldığı gibi olmalıdır. Derginin sayı numarası "(2)" parantez içinde olacak şekilde bizim kaynakça gösterimimizde **bulunmamaktadır.** Altı yazara kadar yazarı olan makalelerde bütün yazarların adı yazılmalı (Soyadı ve Adının ilk harfi olacak şekilde), yedi ve daha üstü yazarlı makalelerde ilk üç yazar, et al. (ve ark.) şeklinde kaynak gösterilmelidir. Makalenin adı Tümce kullanımı şeklinde (**özel isimler ve ilk harf dışında küçük harf kullanılmalıdır**) olmalıdır. **Derginin kısa adı verilmelidir.** Dergi adından sonraki noktalama işaretleri arasında birer boşluk bırakılmalıdır.
11. **T**ablo, Şekil ve Resimler ayrı bir başlık altında kaynakçadan sonra yerleştirilmelidir. **Şekil/Resim** (En az 300 dpi çözünürlükte, **jpeg** dosyası olmalıdır) ve **Tablo**lar ayrı bir veya daha fazla dosya halinde gönderilmelidir.
12. **Telif Hakkı Devri Formu:** Makalenin asıl dilinde doldurulmalıdır. Tüm yazarlar tarafından imzalanmalıdır. Tüm yazarların imzasının olmadığı durumlarda **Sorumlu Yazar** tüm yazarlar adına sorumluluğu alarak imzalayabilir.