ACTA MEDİCA RUHA

INTERNATIONAL JOURNAL OF MEDICINE AND HEALTH SCIENCES

E-ISSN: 2980-1184

Web: https://actamedicaruha.com

E-mail: editor@actamedicaruha.com

Acta Medica Ruha

International Journal of Medicine and Health Sciences

ISSN: 2980-1184

Web: www.actamedicaruha.com
E-mail: editor@actamedicaruha.com

CILT/VOLUME: 2 **SAYI/ISSUE: 3** **YIL/YEAR: 2024**

EYLÜL/SEPTEMBER 2024

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Bişar Amaç Yayıncılık Basım Organizasyon Ticaret İthalat Ve İhracat Anonim Şirketi
Yayınevi Sertifika No/Publisher Certificate Number: 72941
Yayınevi Adresi/Publisher Address: Seyrantepe District. 8076 St. No: 14/22 Karaköprü / Şanlıurfa, Türkiye.
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ISSN: 2980-1184

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Acta Medica Ruha
International Journal of Medicine and Health Sciences
E-ISSN: 2980-1184

ORIGINAL ARTICLE
Volume:2 Issue:3 Year:2024
https://doi.org/10.5281/zenodo.13340894

Retrospective Analysis of Spontaneous Pneumothorax Cases Associated with COVID-19

COVİD-19 ile İlişkili Spontan Pnömotoraks Vakalarının Retrospektif Olarak Analizi

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ABSTRACT

Introduction: Spontaneous pneumothorax is the presence of air in the pleural space without a history of trauma. The risk of developing spontaneous pneumothorax was 40 to 100 times higher in patients with COVID-19 compared to those without.
Objective: Within the scope of this research, we aimed to elucidate spontaneous pneumothorax cases associated with COVID-19 in a retrospective manner.
Method: Patients diagnosed with COVID-19 and spontaneous pneumothorax at our were included in this retrospective analysis. The patients' admission complaints, comorbidities, COVID-19, RT-PCR results, laboratory findings, imaging results, treatment methods applied, and hospitalization or discharge were recorded.
Results: A total of 31 patients aged between 21 and 90 were included in the analysis. Patients were divided into two subgroups: discharge (n=20) and exitus (n=11). While the average hospitalization period of the discharge group was 14.7±22/days, the average hospitalization period of the exitus group was calculated as 2.6±2.1/days ($p<0.001$). While 15 (75%) patients in the discharge group required intensive care follow-up, all in the exitus group required intensive care follow-up ($p=0.133$). A statistically significant difference was detected between the mean values of hemoglobin, INR, D-Dimer, and PLT in the laboratory examinations of the discharge group and the exitus group (p-value; 0.022, 0.004, 0.005, and 0.042, respectively). It was found that there was a strong positive relationship between the length of hospital stay of the patients and laboratory findings, PLR, and NLR (correlation coefficient: 0.818 and 0.818, respectively).
Conclusion: Although many different clinical conditions that develop during COVID-19 infection are in the literature, cases of pneumothorax and pneumomediastinum have been rarely reported. In addition, the possibility of high mortality in these clinical conditions that may be seen in the actively ongoing COVID-19 pandemic should also be taken into consideration.

Keyswords: Pneumothorax, COVID-19, Intensive Care Unit, D-dimer, Acute Respiratory Distress Syndrome.

ÖZET

Giriş: Spontan pnömotoraks, travma öyküsü olmaksızın plevral boşlukta hava bulunmasıdır. Spontan pnömotoraks gelişme riski, COVID-19 hastalarında olmayanlara göre 40 ila 100 kat daha yüksektir.
Amaç: Bu araştırma kapsamında, COVID-19'a bağlı spontan pnömotoraks vakalarının retrospektif olarak aydınlatılması amaçlandı.
Yöntem: Hastanemizde COVİD-19 tanısı alan ve spontan pnömotoraks tanısı alan hastalar bu retrospektif analize dahil edildi. Hastaların başvuru şikayetleri, yandaş hastalıkları, COVİD-19, RT-PCR sonuçları, laboratuvar bulguları, görüntüleme sonuçları, uygulanan tedavi yöntemleri, hastaneye yatış veya taburculuk durumları kaydedildi.
Bulgular: Analize yaşları 21 ile 90 arasında değişen toplam 31 hasta dahil edildi. Hastalar taburculuk (n=20) ve ölüm (n=11) olmak üzere iki alt gruba ayrıldı. Taburcu olan grubun ortalama yatış süresi 14,7±22/gün iken, ölüm grubunun ortalama yatış süresi 2,6±2,1/gün olarak hesaplandı ($p<0,001$). Taburcu olan grupta 15 (%75) hastanın yoğun bakım takibine ihtiyacı olurken, ölüm grubundaki hastaların tamamının yoğun bakım takibine ihtiyacı vardı ($p=0,133$). Taburcu edilen grup ile ölüm grubunun laboratuvar incelemelerinde ortalama hemoglobin, INR, D-Dimer ve PLT değerleri arasında istatistiksel olarak anlamlı fark saptandı (p değeri sırasıyla 0,022, 0,004, 0,005 ve 0,042). Hastaların hastanede kalış süresi ile laboratuvar bulguları, PLR ve NLR arasında güçlü pozitif ilişki olduğu belirlendi (korelasyon katsayısı: sırasıyla 0,818 ve 0,818).
Sonuç: Sonuç olarak, COVID-19 infeksiyonu sırasında gelişen birçok farklı klinik durum literatürde olmakla birlikte pnömotoraks ve pnömomediastinum olguları nadiren bildirilmiştir. Ayrıca aktif olarak devam eden COVID-19 pandemisinde görülebilecek bu klinik durumlardaki olası yüksek mortalite ihtimali de göz önünde bulundurulmalıdır.

Anahtar Kelimeler: Pnömotoraks, COVİD-19, Yoğun Bakım Ünitesi, D-dimer, Akut Respiratuar Distres Sendromu.

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Received: 05.05.2024, Accepted: 15.07.2024, Published Online: 20.09.2024
Cited: Kılıç Ş, et al. Retrospective Analysis of Spontaneous Pneumothorax Cases Associated with COVID-19. Acta Medica Ruha. 2024;2(3):139-145. https://doi.org/10.5281/zenodo.13340894

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INTRODUCTION

Pneumothorax is defined as free air between the visceral and parietal pleural layers. Spontaneous pneumothorax is the presence of air in the pleural space without a history of trauma. It is divided into primary and secondary spontaneous pneumothorax. While primary spontaneous pneumothorax is more common in young people, secondary spontaneous pneumothorax is mostly observed in the elderly (age>55) population (1). Although the incidence of spontaneous pneumothorax varies in various studies, it is reported as 2.2/100.000 in women and 12.3/100.000 in men. It is known that this peaks especially in young men between 16 and 25 (2). The most common presenting symptoms are sudden chest pain and shortness of breath. Contrary to popular belief, no relationship exists between physical activity and spontaneous pneumothorax (3). Although the pathophysiology of primary spontaneous pneumothorax is unclear, pulmonary bullae and the bursting of subpleural blebs are most blamed (4). The recurrence rate in a patient with pneumothorax increases after each attack. For this reason, surgery is recommended after the second pneumothorax attack (1).

The goal in pneumothorax treatment is to remove the air in the pleural space and prevent pneumothorax from occurring again. For this, tube thoracostomy is performed in the first stage. However, patients with a first attack of pneumothorax who are clinically stable can be monitored by giving O2 therapy without intervention. Publications report that simple thoracentesis and aspiration are as effective as air drainage with a traditional chest tube and have an 80% success rate in these patients. After the second pneumothorax attack, the widely accepted view is to remove the bulla and bleb structures, if any, surgically, and today, the most commonly used method for this is video-assisted thoracoscopic surgery (VATS). Whether surgery is performed or treatment is provided with simple drainage, pleurodesis is recommended (5).

The most blamed factor in the pathogenesis of pneumothorax is the bulla and bleb structures found in the parenchyma. The new coronavirus disease 2019 (COVID-19) may also disrupt the lung parenchyma structure and cause blisters and blebs. The clinical spectrum of the disease varies widely, from asymptomatic cases to severe pneumonia and severe respiratory failure. The incidence of spontaneous pneumothorax development in COVID-19 has been reported as 1%. Most of the reported cases of pneumothorax associated with COVID-19 do not have traditional risk factors or underlying predisposing lung disease (6). The risk of developing spontaneous pneumothorax was 40 to 100 times higher in patients with COVID-19 compared to those without. However, COVID-19 pneumonia, unlike other viral pneumonia, has been associated with an increased incidence of pneumothorax (7).

Pneumothorax or pneumomediastinum may occur spontaneously or due to applied mechanical ventilation in patients with acute respiratory distress syndrome (ARDS) due to COVID-19. In non-COVID-19 ARDS patients, pneumothorax and pneumomediastinum are observed at 2-15% rates, while this was 5-55% in COVID-19 patients (7, 8). A higher rate of pneumothorax and pneumomediastinum is observed in patients with COVID-19 infection who require invasive mechanical ventilation than those without COVID-19 (8). However, the mortality rate was similarly higher in patients with and without COVID-19 who develop pneumothorax and pneumomediastinum (7, 8).

Within the scope of this research, we aimed to elucidate spontaneous pneumothorax cases associated with COVID-19 in a retrospective manner.

METHOD

Patients diagnosed with COVID-19 and spontaneous pneumothorax at Sakarya Training and Research Hospital Emergency Medicine Clinic between March 2020 and March 2022 were included in this retrospective analysis. The patient data were obtained from patient files and data in the hospital automation system. The patients' admission complaints, comorbidities, COVID-19, RT-PCR results, laboratory findings, imaging results, treatment methods applied, and hospitalization or discharge were recorded.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval has been granted from our institution with protocol number E-

71522473-050.01.04-216241-28. As this was retrospective research, no informed consent was obtained from participants.

Statistical Analysis

Patient data collected within the scope of the study were analyzed with the IBM Statistical Package for the Social Sciences (SPSS) for Macos 29.0 (IBM Corp., Armonk, NY) package program. Frequency and percentage for categorical data and mean and standard deviation for continuous data were given as descriptive values. For comparisons between groups, the “Independent Sample T–test” was used for two groups, and the “Pearson Chi-Square Test” was used to compare categorical variables. Normality testing of variables was evaluated with the Kolmogorov Smirnov test. In comparisons between groups, "Independent Sample T-Test" was used for variables showing normal distribution for two groups, "Mann Whitney U-Test" is used for variables that do not show normal distribution, "Chi-Square or Fisher's Exact Test" is used for comparing categorical variables, and "Chi-Square or Fisher's Exact Test" is used for examining the relationship between continuous variables. “Spearman's Correlation Analysis” was utilized. The results were considered statistically significant when the p-value was less than 0.05.

RESULTS

A total of 31 patients aged between 21 and 90 were included in the analysis. Patients were divided into two subgroups: discharge (n=20) and exitus (n=11). There was no statistically significant difference between the discharge and exitus groups regarding additional diseases (malignancy, diabetes mellitus, hypertension, chronic pulmonary obstructive disease, palsy, and chronic kidney disease). While the average hospitalization period of the discharge group was 14.7±22/days, the average hospitalization period of the exitus group was calculated as 2.6±2.1/days, and a statistically significant difference was found between them (p<0.001). While 15 (75%) patients in the discharge group required intensive care follow-up, all in the exitus group required intensive care follow-up (p =0.133). The distribution of demographic and clinical findings of the patients according to their final status is denoted in Table 1. When the table is examined, no statistically significant difference was seen in all demographic and clinical findings, except the length of stay, according to the final status of the patients.

Table 1. Distribution of Demographic and Clinical Characteristics of Patients

Variables	Total (n=31)	Discharged (n=20)	Deceased (n=11)	p-value
Spontaneous PNX	27 (87,1)	16 (80)	11 (100)	0,269
Age (year)				0,241
Mean±SD	50,9±22,6	47,4±22	57,5±23,3	
Median (Min-Max)	50 (21-90)	48,5 (21-86)	57 (21-90)	
Duration of Hospitalization				**<0,001**
Mean±SD	10,4±18,5	**14,7±22**	**2,6±2,1**	
Median (Min-Max)	5 (1-99)	**9 (1-99)**	**2 (1-6)**	
Comorbid Diseases				
Malignity	4 (12,9)	2 (10)	2 (18,2)	0,601
DM	16 (51,6)	8 (40)	8 (72,7)	0,171
Hypertension	12 (38,7)	7 (35)	5 (45,5)	0,705
COPD	12 (38,7)	6 (30)	6 (54,5)	0,255
Palsy	3 (9,7)	1 (5)	2 (18,2)	0,281
CKD	7 (22,6)	3 (15)	4 (36,4)	0,210
CORADS				0,088
CORADS-2	3 (9,7)	2 (10)	1 (9,1)	
CORADS-3	8 (25,8)	6 (30)	2 (18,2)	
CORADS-4	9 (29)	8 (40)	1 (9,1)	
CORADS-5	11 (35,5)	4 (20)	7 (63,6)	
PNX				0,707
Left	14 (45,2)	10 (50)	4 (36,4)	
Right	17 (54,8)	10 (50)	7 (63,6)	
Pneumomediastinum	1 (3,2)	0 (0)	1 (9,1)	0,355
Intensive Care Unit	26 (83,9)	15 (75)	11 (100)	0,133
Thoracic Tube	30 (96,8)	19 (95)	11 (100)	1,000
Thoracotomy	1 (3,2)	1 (5)	0 (0)	1,000

PNX: Pneumothorax; SD: Standard Deviation; DM: Diabetes Mellitus; COPD: Chronic Obstructive Pulmonary Disease; CKD: Chronic Kidney Disease.

The distribution of laboratory measurements according to the final status of the patients is elaborated in Table 2. When the table was examined, it was observed that there was a statistically significant difference in hemoglobin, international normalized ratio (INR), D-Dimer, and platelet (PLT) measurements between the two groups. A statistically significant difference was detected between the mean values of hemoglobin, INR, D-Dimer, and PLT in the laboratory examinations of the discharge group and the exitus group (p-value; 0.022, 0.004, 0.005, and 0.042, respectively). It was found that there was a strong positive relationship between the length of hospital stay of the patients and laboratory findings, platelet-to-lymphocyte ratio (PLR), and neutrophil-to-lymphocyte ratio (NLR) (correlation coefficient: 0.818 and 0.818, respectively).

Table 2. Distribution of Patients' Laboratory Findings

Laboratory	Total(n=31)	Discharged(n=20)	Deceased(n=11)	p-value
Hemoglobin				**0,022**
Mean±SD	13,1±2,2	**13,8±1,8**	**11,8±2,4**	
Median (Min-Max)	13,7 (8,7-16,6)	**14,2 (9,1-16,6)**	**11,2 (8,7-15,7)**	
WBC				0,353
Mean±SD	14,7±7,8	13,4±5	16,9±11,3	
Median (Min-Max)	13,3 (2-37,5)	12,6 (5,9-23,6)	13,8 (2-37,5)	
Lymphocyte				0,934
Mean±SD	2,8±3,4	2,3±1,8	3,6±5,3	
Median (Min-Max)	1,8 (0,2-18,9)	1,8 (0,4-6,7)	1,8 (0,2-18,9)	
CRP				0,510
Mean±SD	77,5±86,1	73,2±83,3	84,2±94,1	
Median (Min-Max)	35 (1,6-331,7)	31 (3,7-256)	60 (1,6-331,7)	
PLR				0,173
Mean±SD	187±189,4	207,6±181,8	149,7±206,1	
Median (Min-Max)	125,7 (10,9-750)	138,6 (32,4-652,3)	72,5 (10,9-750)	
Troponin				0,087
Mean±SD	66,1±181,5	25,7±67,8	139,5±284,4	
Median (Min-Max)	8 (0,1-872)	6,7 (0,1-309)	11,3 (4,6-872)	
Ferritin				0,591
Mean±SD	453,5±551,6	306±338,2	721,5±756,9	
Median (Min-Max)	185 (13-1941)	186,5 (35-1461)	167 (13-1941)	
INR				**0,004**
Mean±SD	1,3±0,2	**1,2±0,1**	**1,4±0,2**	
Median (Min-Max)	1,3 (1,1-1,7)	**1,2 (1,1-1,6)**	**1,4 (1,2-1,7)**	
NLR				0,804
Mean±SD	8,3±8,9	8,2±8,8	8,4±9,4	
Median (Min-Max)	4,3 (0,3-33)	4,6 (0,3-28,4)	4,3 (0,3-33)	
GFR				0,087
Ortalama±SS	100,7±44,5	106,8±23	89,6±68,7	
Medyan (Min-Max)	106 (12,6-259)	111,4 (63-132,1)	96,3 (12,6-259)	
D-Dimer				**0,005**
Mean±SD	2358,3±3353,2	**1535,5±2170,5**	**3854,3±4578,6**	
Median (Min-Max)	895 (103-14400)	**664,5 (103-8360)**	**1647 (884-14400)**	
Lactate				0,066
Mean±SD	2,9±2,5	2,1±0,8	4,5±3,6	
Median (Min-Max)	2 (1,1-10,6)	1,8 (1,1-3,7)	2,7 (1,1-10,6)	
Neutrophil				0,478
Mean±SD	10,6±6,3	9,9±4,6	12±8,8	
Median (Min-Max)	9,3 (1,2-31,9)	9,5 (3,2-20,5)	7,7 (1,2-31,9)	
PLT				**0,042**
Mean±SD	243,1±106	**271,5±103,3**	**191,4±94,2**	
Median (Min-Max)	226 (25-545)	**246,5 (146-545)**	**182 (25-377)**	

SD: Standard Deviation; WBC: White Blood Cell; CRP:C-reactive Protein; PLR: Platelet-to-lymphocyte Ratio; INR: International Normalized Ratio; NLR: Neutrophil-to-lymphocyte Ratio; GFR: Glomerular Filtration Rate; PLT: Platelet.

The correlation analysis evaluated the relationship between the length of stay and laboratory measurements of the patients (Table 3). As a result of the significant relationship between the variables, a positive correlation coefficient indicates a positive linear relationship between the variables, and a negative correlation indicates a reverse linear relationship. The value ranges of the correlation coefficient are expressed as follows;

Correlation coefficient;

- If it is between 0.00-0.29, the relationship is weak,
- If it is between 0.30-0.49, the relationship between two variables is low,
- If it is between 0.50-0.69, the relationship between two variables is medium,
- If it is between 0.70-0.89, the relationship between the two variables is strong and
- The fact that it is between 0.90 and 1.00 indicates that the relationship between the two variables is very strong.

Table 3. Investigation of the Relationship between Length of Stay and Laboratory Findings

		Duration of Hospitalization	PLR	NLR	D-Dimer	Ferritin
Duration of Hospitalization	Correlation Coefficient	1,000	0,062	-0,114	**-0,438**	-0,054
	p-value		0,742	0,541	**0,014**	0,772
PLR	Correlation Coefficient	0,062	1,000	**0,818**	-0,317	-0,069
	p-value	0,742		**<0,001**	0,082	0,711
NLR	Correlation Coefficient	-0,114	**0,818**	1,000	0,000	-0,090
	p-value	0,541	**<0,001**		0,998	0,631
D-Dimer	Correlation Coefficient	**-0,438**	-0,317	0,000	1,000	**0,359**
	p-value	**0,014**	0,082	0,998		**0,047**
Ferritin	Correlation Coefficient	-0,054	-0,069	-0,090	**0,359**	1,000
	p-value	0,772	0,711	0,631	**0,047**	

PLR: Platelet-to-lymphocyte Ratio; NLR: Neutrophil-to-lymphocyte Ratio.

When the table was examined, it was determined that there was a low inverse relationship between the length of stay and D-dimer, a strong linear relationship between PLR and NLR, and a low linear relationship between D-dimer and ferritin.

DISCUSSION

The mortality rate in COVID-19 patients who developed pneumothorax and pneumomediastinum was approximately 10% higher than in COVID-19 patients who did not develop these complications (60% vs. 53%) (9). This situation appears to be similar in patients without COVID-19 (7,8). The median hospital stay of patients who developed pneumothorax and pneumomediastinum was found to be 39.5 days, and their mortality was high at 75%. COVID-19-related pneumothorax appears to be associated with an increased likelihood of long-term hospitalization and death (10). Pneumothorax associated with COVID-19 tends to be right-sided (11). Miro et al. stated that COVID-19-related pneumothorax was 3.8 times more likely to occur in the right hemithorax among COVID-19 patients (12).

Cases of pneumothorax, pneumomediastinum, and subcutaneous emphysema developing based on COVID-19 pneumonia are rarely reported in the literature and generally in the form of case reports. The largest series in the literature is a study that was obtained by collecting data from 16 separate centers in England and included 71 patients (60 with pneumothorax and 11 with pneumomediastinum) (13). In this study, pneumothorax and pneumomediastinum developing in patients under 70 did not affect mortality due to COVID-19. However, it has been reported that significantly lower survival occurs in patients over the age of 70 who develop pneumothorax and pneumomediastinum.

Alveolar destruction and spontaneous alveolar rupture caused by destructive damage to the lung parenchyma, as well as alveolar damage and rupture caused by positive pressure air given by respiratory support devices, be effective in the mechanism of pneumothorax, pneumomediastinum and subcutaneous emphysema that develop based on COVID-19 (14, 15). Some studies in the literature have reported that complications in COVID-19 patients without comorbidities may occur as a result of widespread parenchymal involvement with progressively developing severe pneumonia (14, 16, 17). In support of these data, our study examined cases of pneumothorax, pneumomediastinum, and subcutaneous emphysema that developed due to the effect of barotrauma during ICU treatment and included cases of COVID-19 complications that were thought to be the result of spontaneous alveolar rupture during home treatment.

In the study conducted by Martinelli et al. (16), it was reported that pneumothorax development based on COVID-19 increased the mortality level in patients with comorbidities such as diabetes mellitus, hypertension, and heart failure, but there was no statistically significant difference. In the case report of Quincho-Lopez et al. (18), 2 patients were evaluated, and the condition of a 55-year-old female patient became critical after the development of pneumothorax due to COVID-19 infection and mortality. The other patient was discharged without any problems. Despite the limitations of a single case report, the observation of mortality in this 55-year-old patient with no comorbidities is noteworthy.

In the case report of Elhakim et al. (19), a COVID-19 patient who developed pneumothorax, pneumomediastinum, and subcutaneous emphysema, which was not related to smoking, comorbidities, and barotrauma with high flow oxygen or mechanical ventilation, was presented. It was reported that this patient was discharged home due to treatment. In our study, it was determined that 8 out of 15 patients who developed pneumothorax, pneumomediastinum, and subcutaneous emphysema during home treatment developed only complications arising from COVID-19 pneumonia, without any additional risk factors for the development of pneumothorax and pneumomediastinum. In the other 7 patients in this group, There were additional risk factors such as asthma, smoking, bullous lung disease, and obesity.

In the study of Vega et al. (20) showing the mortality of pneumothorax, pneumomediastinum, and subcutaneous emphysema due to COVID-19 pneumonia, it was reported that the follow-up of 3 patients with the findings resulted in mortality. What makes this study different from other studies is that it is possible to make a diagnosis directly with thorax CT in case of sudden changes in the general condition of patients during hospital treatment. Transport of seriously ill COVID-19 patients followed in the ICU to thorax CT was not deemed appropriate due to the life-threatening situation it could cause. These cases could be diagnosed with portable chest radiographs taken at the bedside.

In our study, a statistically significant difference was achieved in the mean values of hemoglobin, INR, D-Dimer, and PLT in the laboratory examinations of the discharge group and the exitus group. It was found that there was a strong positive relationship between the length of hospital stay of the patients and laboratory findings, PLR, and NLR. As a result of the significant relationship between the variables, a positive correlation coefficient indicates a positive linear relationship between the variables, and a negative correlation indicates a reverse linear relationship. A low inverse relationship was observed between the length of stay and D-dimer, a strong linear relationship between PLR and NLR, and a low linear relationship between D-dimer and ferritin.

CONCLUSION

As a result, although many different clinical conditions that develop during COVID-19 infection are in the literature, cases of pneumothorax and pneumomediastinum have been rarely reported. In addition, the possibility of high mortality in these clinical conditions that may be seen in the actively ongoing COVID-19 pandemic should also be considered.

DESCRIPTIONS

No financial support.

No conflict of interest.

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Acta Medica Ruha
International Journal of Medicine and Health Sciences
E-ISSN: 2980-1184

ORIGINAL ARTICLE
Volume:2 Issue:3 Year:2024
https://doi.org/10.5281/zenodo.13353751

Evaluation of the Relationship Between Vitamin D Levels and Glycemic Parameters in Prediabetic Individuals

Prediyabetik Bireylerde D Vitamini Düzeyi ile Glisemik Parametreleri Arasındaki İlişkinin Değerlendirilmesi

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ABSTRACT

Objective: Prediabetic condition is a precursor clinical picture that poses a significant risk for the development of diabetes. Early diagnosis and treatment are crucial for preventing micro and macro complications. Numerous studies have been conducted to explore the relationship between Vitamin D and the development of diabetes, attempting to clarify this connection. We planned this study to examine the relationship between Vitamin D and glycemic parameters in prediabetic individuals and to lay the groundwork for future research in this direction.
Method: Our study included 192 patients aged 24-65 who presented to internal medicine clinics. The study retrospectively examined 93 prediabetic individuals and 99 healthy individuals without any diseases, drug use, Vitamin D supplementation, or any other significant characteristics. The selected patients' demographic data, fasting glucose levels, HbA1C, insulin, HOMA-IR, 25(OH)D vitamin, calcium, and albumin levels were analyzed using chromatography equipment, HPLC method. The Chi-Square test was used to determine the differences in categorical data between groups. The level of statistical significance was set at $p<0.05$.
Results: The mean age was 53.18±12.71 in the prediabetic group and 42.44±14.72 in the control group. No statistically significant difference was observed in gender distribution between the two groups (p=0.9072). When comparing Vitamin D levels between the two groups, it was found to be 14.62±6.87 ng/mL in the prediabetic group and 17.53±11.02 ng/mL in the control group, which was statistically significant (p=0.029).
Conclusion: Our study found a significant difference in Vitamin D levels between prediabetic individuals and healthy individuals with normoglycemic progression. Observational studies suggest a significant relationship between Vitamin D and diabetes mellitus, and similar findings are observed in prediabetic individuals. We believe that Vitamin D supplementation in the prediabetic population could have significant effects on public health and glucose metabolism.

Keyswords: Prediabetes, Vitamin D, Glycemic Parameters.

ÖZET

Amaç: Prediyabetik durum diyabet gelişimi açısından büyük risk oluşturan öncül klinik tablo olup erken tanı ve tedavi ile mikro-makro komplikasyonların önlenmesi açısından önemli yer tutmaktadır. D vitamini ile diyabet gelişimi arasında birçok çalışma yapılmış ve arasındaki ilişki aydınlatılmaya çalışılmıştır. Prediyabetik bireylerde D vitamini ile glisemik parametreleri arasındaki ilişkini irdelenmesi ve bu yönde ileriye dönük çalışmaların ortaya konması adına bu çalışmayı planladık.
Yöntem: Çalışmamıza iç hastalıkları polikliniklerine başvuran 24-65 yaş arası 192 hasta dahil edildi. Çalışmada 93 prediyabetik birey ile herhangi bir hastalığı olmayan ilaç kullanımı olmayan D vitamini desteği almayan ek bir özelliği olmayan 99 sağlıklı birey retrospektif olarak incelendi. Seçilen hastaların demografik verileri, açlık glukoz seviyesi, HbA1C, insülin, HOMA-IR, 25(OH) D vitamini, kalsiyum, albümin düzeyleri kromotografi cihazında, HPLC yöntemi ile çalışılmış olan veriler analiz edildi. Gruplar arasındaki kategorik veri farklılıklarını belirlemek için Ki-Kare testi kullanılmıştır. İstatistiksel anlamlılık düzeyi $p<0,05$ olarak belirlenmiştir.
Bulgular: Yaş ortalaması prediyabetik grubunda 53,18±12,71 iken kontrol grubunda 42,44±14,72 olarak bulunmuştur. Cinsiyet dağılımlarına bakıldığında ise her iki grup arasında istatistiksel açıdan anlamlı bir fark saptanmamıştır (p=0,9072). Her iki grubun D vitamini düzeyleri karşılaştırıldığında prediyabetik grubunda 14,62±6,87 ng/mL iken kontrol grubunda 17,53±11,02 ng/mL olarak ölçülmüş olup istatistiksel açıdan anlamlı derece farklı olduğu saptanmıştır (p=0,029).
Sonuç: Çalışmamızda prediyabetik bireyler ile normoglisemik seyreden sağlıklı bireylerin D vitamini düzeyleri arasında anlamlı fark olduğu görüldü. Yapılan gözlemsel çalışmalarda D vitamini ile diyabet mellitus arasında anlamlı bir ilişkinin olduğu gibi prediyabetik bireylerde de sonuçların aynı doğrultuda olduğu görülmüştür. D vitamini desteğinin prediyabetik popülasyonunda değerlendirildiğinde toplum sağlığı ile glukoz metabolizması üzerine önemli etkilerin olabileceğini düşünmekteyiz.

Anahtar Kelimeler: Prediyabet, D Vitamini, Glisemik Parametreler.

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Received: 14.05.2024, Accepted: 21.08.2024, Published Online: 20.09.2024
Cited: Ergün U. Evaluation of the Relationship Between Vitamin D Levels and Glycemic Parameters in Prediabetic Individuals. Acta Medica Ruha. 2024;2(3):146-149. https://doi.org/10.5281/zenodo.13353751
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INTRODUCTION

Diabetes mellitus (DM) represents one of the most significant health challenges in our society. It is a heterogeneous and complex disease characterized by insulin resistance, insufficient secretion, metabolic disturbances causing reduced effectiveness, or complete lack of secretion (1). The complications it causes lead to chronic health problems due to progressive organ and functional losses. It significantly impairs quality of life, being a major cause of morbidity and mortality. Prediabetes, which includes impaired glucose tolerance and impaired fasting glucose, represents elevated glucose levels that are above normal but below the diagnostic threshold for diabetes. Prediabetes is particularly a major risk factor for type 2 DM, with the risk of developing diabetes being approximately six times higher than in individuals with normal glycemic values (2,3). From this perspective, prediabetes has become a precursor to the complications that can occur due to DM. The pathogenesis of prediabetes is similar to type 2 DM and includes factors such as genetic predisposition, environmental factors, defects in insulin secretion, and insulin resistance.

There is evidence suggesting that Vitamin D influences insulin sensitivity and plays a role in glucose regulation (4). Pancreatic beta cells, by expressing the Vitamin D receptor (VDR), affect insulin sensitivity. Pancreatic beta cells lacking VDR exhibit impaired insulin secretion in response to an increased glucose load, contributing to the prediabetic condition. Furthermore, studies indicate that insulin secretion in prediabetic patients could be affected through genomic and non-genomic pathways, although the pathogenesis is not entirely clear (5). Vitamin D enhances insulin receptor expression, thereby increasing insulin sensitivity. Given the current literature, there is a clear correlation between Vitamin D and type 2 DM (6). The significance of Vitamin D levels in prediabetic conditions, which are a significant risk factor for type 2 DM, is evident. Since prediabetes is a persistent condition that may evolve into DM over time, early detection of its causes and combating it with proper treatment before it becomes a chronic health issue is crucial. This study aims to examine the impact of Vitamin D on glycemic parameters in prediabetic individuals.

METHODS

Our study included 192 patients aged 24-65 who visited the internal medicine clinics at Balıkesir Atatürk City Hospital between January 1, 2022, and October 2, 2023. The study retrospectively examined 93 prediabetic individuals who met the following criteria: no diagnosed DM, no current medication use, no intake of Vitamin D or calcium supplements, and oral glucose tolerance test criteria or HbA1C levels between 5.7 and 6.5. Additionally, 99 healthy individuals with no diseases, no medication use, and no Vitamin D supplementation were included. The findings from previously conducted anamneses and physical examinations (age, weight, height, body mass index, etc.) were analyzed. The selected patients' demographic data, fasting glucose levels, HbA1C, insulin, insulin resistance index (HOMA-IR), 25(OH) Vitamin D, calcium, and albumin levels were analyzed using chromatography equipment through the High-Performance Liquid Chromatography (HPLC) method. Patients' 25(OH) Vitamin D levels were categorized as follows: >30 ng/ml as sufficient, 20-29 ng/ml as deficient, 10-19.9 ng/ml as insufficient, and <10 ng/ml as severely insufficient. Data collected during the study were recorded for further analysis.

Statistical Analysis

In this study, the demographic and clinical characteristics of the evaluated cases were examined using descriptive statistical analyses (numbers, percentages, etc.). The data were processed using the SPSS-22 software package. The Chi-Square test was utilized to determine the differences in categorical data between groups. The Shapiro-Wilk and Kolmogorov-Smirnov tests were applied to assess whether the data followed a normal distribution. For comparing measurements of a specific variable between two different groups, the Student's t-test was used for data that followed a normal distribution, while the Mann-Whitney U test was used for data that did not. The level of statistical significance was set at $p<0.05$. Box-Plot graphs were arranged for biochemical variables that showed significant differences between the patient and control groups.

Ethics Committee Approval

This study received approval from the Ethics Committee of Balıkesir Atatürk City Hospital for Scientific Research (Approval Date: 23/11/2023, Decision No: 2023/11/68).

RESULTS

In our study, various biological and physiological parameters were compared between the prediabetic individuals (n=93) and the healthy control group (n=99). The average age was 53.18±12.71 in the prediabetic group and 42.44±14.72 in the control group, with no statistically significant difference identified between the two groups (p=0.333).

Similarly, no significant differences were observed in terms of average weight and height; the prediabetic group weighed 59.92±6.9 kg, while the control group weighed 60.08±7.01 kg. The average heights were 164.14±7.12 cm and 160.72±6.85 cm, respectively, with no statistically significant differences found (p=0.441 and p=0.922). The body mass index (BMI) was 23.01±1.98 kg/m² in the prediabetic group and 22.5±1.79 kg/m² in the control group, which was not statistically significant (p=0.283). No statistically significant difference was observed in gender distribution between the two groups (p=0.9072) (Table 1).

Regarding glycemic parameters, significant differences were identified between the prediabetic and control groups in fasting glucose, HOMA-IR, HbA1C, albumin, and Vitamin D levels (Table 1). The average fasting glucose in the prediabetic group was 109.75±11.68 mg/dL, compared to 89.68±6.55 mg/dL in the control group, and this difference was statistically highly significant (p<0.001). The HOMA-IR was 6.96±3.67 in the prediabetic group and 1.67±0.47 in the control group, showing a statistically significant difference (p<0.001). HbA1C levels were 6.09±0.25% in the prediabetic group and 5.35±0.21% in the control group, with a statistically significant difference (p<0.001). Albumin levels were 4.39±0.28 g/dL in the prediabetic group and 4.51±0.29 g/dL in the control group, which was statistically significant (p=0.006). When comparing Vitamin D levels, the prediabetic group had 14.62±6.87 ng/mL, whereas the control group had 17.53±11.02 ng/mL, and this difference was statistically significant (p=0.029).

DISCUSSION

Prediabetic individuals are known as a significant public health concern due to their substantial risk of developing DM, which in turn leads to complications, morbidity, and mortality. The pathogenesis of prediabetes involves pancreatic beta-cell dysfunction, resulting in insufficient insulin production and hyperglycemia due to tissue resistance to this hormone (7). While Vitamin D is commonly associated with bone mineralization and diseases such as osteoporosis, its role in common conditions like type 2 DM, prediabetes, depression, and obesity is less understood. The literature provides strong evidence that Vitamin D influences the pathways involved in the pathogenesis of type 2 DM; it is thought to play a critical role in calcium flux in beta cells, cellular viability, and the regulation of insulin secretion (8). According to another hypothesis, the relationship between Vitamin D and glucose metabolism is thought to be linked to the Vitamin D Receptor (VDR) in the pancreas (5). An experimental clinical study in rats has shown that Vitamin D deficiency leads to damage in pancreatic beta cells and insulin deficiency, which can be reversed with Vitamin D supplementation (9). Other studies have also reported that Vitamin D's anti-inflammatory effects positively impact insulin secretion, potentially preventing the development of diabetes. Additionally, numerous studies have associated low Vitamin D levels with decreased insulin sensitivity (10). To date, many studies have documented the relationship between type 2 DM and Vitamin D; our study investigates this connection in prediabetes, a precursor to DM. In this study comparing glycemic parameters and Vitamin D levels, significant differences were found between prediabetic individuals and the healthy group.

We observed that the relationship between glycemic parameters and Vitamin D levels in prediabetic individuals yielded similar results to those studies conducted with DM patients. We found that the fasting glucose levels, HbA1C, and HOMA-IR levels in prediabetic individuals aligned with other studies in the same direction. When comparing Vitamin D levels, those in prediabetic individuals were lower and significantly different statistically compared to the healthy group. In a study by Mitri et al.,

improvements in pancreatic beta-cell functions were demonstrated with Vitamin D and calcium supplementation over 16 weeks. The same study showed that community-wide Vitamin D supplementation reduced the risk of developing type 2 DM by lowering the increase in HbA1c levels (11). Once again, Vitamin D supplementation has proven significant for prediabetic individuals, who are at high risk of developing DM. While the pathogenesis of Vitamin D on glucose metabolism is not yet fully elucidated, its importance is evident. This study demonstrates the potential effect of Vitamin D in prediabetic individuals, similarly to those with DM.

CONCLUSION

Our study observed a significant difference in Vitamin D levels between prediabetic individuals and healthy individuals with normoglycemic progression. Given that prediabetes may progress to DM over time, it is evident that early screening and treatment methods will lead to a decrease in the incidence of DM. Observational studies have shown a significant relationship between Vitamin D and the development of diabetes, and similar results have been observed in prediabetic individuals. We believe that Vitamin D supplementation in the prediabetic population could have significant effects on public health and glucose metabolism.

DESCRIPTIONS

No financial support.

No conflict of interest.

Acknowledgments: We would like to thank Uzm. Dr. Ahmet Güleç for his contributions to the statistical analysis of our study.

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Acta Medica Ruha
International Journal of Medicine and Health Sciences
E-ISSN: 2980-1184

ORIGINAL ARTICLE
Volume:2 Issue:3 Year:2024
https://doi.org/10.5281/zenodo.13364892

Akciğer Kanserli Hastalarda Çevresel Faktörlerin, Uyku Kalitesinin, Fonksiyonel Bağımsızlığın ve Postür Anatomisinin Değerlendirmesi

Assessment of Environmental Factors, Sleep Quality, Functional Independence, and Posture Anatomy in Lung Cancer Patients

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ÖZET

Giriş: Akciğer kanseri yaygın bir hastalıktır. Bu hastaların karşılaştığı zorluklara çok sayıda faktör katkıda bulunabilir.
Amaç: Çalışmanın amacı, akciğer kanserli hastalarda çevresel faktörler, uyku kalitesi, bağımsızlık düzeyi ve duruş anatomisi gibi bir dizi faktörü değerlendirmektir.
Yöntem: Akciğer kanseri tanısı almış hastaların dahil edildiği çalışmada bireylerin demografik bilgileri sorgulanmıştır. Katılımcılara Medical Research Council Skalası, Pittsburgh Uyku Kalitesi İndeksi, Vizüel Analog Skalası, Barthel Günlük Yaşam Aktiviteleri İndeksi ve New York Postür Analizi uygulanmıştır.
Bulgular: Klinik bulgular arasında katılımcıların %77'sinde öksürük, %72,5'inde balgam çıkarma, %42,5'inde göğüs ağrısı, %62,5'inde dispne ve %37,5'inde ses kısıklığı tespit edilmiştir. Katılımcıların %27,5'inin 4 değerinde dispne, %22,5'inin 3 değerinde dispne belirtisi gösterdiği, %12,5'inin ise dispne belirtisi göstermediği görülmüştür. Katılımcıların tıbbi geçmişlerinde en sık görülen sistemik hastalık diabetes mellitus (%22,5) olmuştur. Barthel İndeksi ile değerlendirildiğinde, katılımcıların %75'inin uyku kalitesinin kötü olduğu, %25'inin şiddetli bağımlılık, %35'inin ise orta derecede bağımlılık sergilediği belirlenmiştir.
Sonuç: Öksürük, nefes darlığı ve ağrı akciğer kanserli hastalarda sık görülen semptomlardır ve uyku kalitesi üzerinde önemli bir etkiye sahiptir. Bu bulgular, rehabilitasyonun bu hastalar için tedavi planının önemli bir yönü olduğu sonucunu desteklemektedir. Ailesinde kanser öyküsü olmayan bireylerin sayısının yüksek olması, halk sağlığı girişimlerinde çevresel faktörlerin de dikkate alınması gerektiğini göstermektedir.

Anahtar Kelimeler: Akciğer Kanseri, Postür Anatomisi, Uyku Kalitesi, Fonksiyonel Bağımsızlık Düzeyi.

ABSTRACT

Introduction: Lung cancer is a prevalent disease. A multitude of factors can contribute to the challenges faced by these patients.
Objective: The objective of the study was to evaluate a number of factors, including environmental factors, sleep quality, independence level and posture anatomy, in patients with lung cancer.
Method: In the study, the demographic information of the individuals diagnosed with lung cancer was ascertained through questioning. The participants were assessed using a number of standardized instruments, including the Medical Research Council Scale, Pittsburgh Sleep Quality Index, Visual Analogue Scale, Barthel Activities of Daily Living Index and New York Posture Analysis.
Results: Among the clinical findings, 77% of the participants presented with a cough, 72.5% exhibited sputum production, 42.5% reported chest pain, 62.5% demonstrated dyspnoea, and 37.5% displayed hoarseness. It was observed that 27.5% of the participants exhibited dyspnoea with a value of 4, 22.5% with a value of 3, and 12.5% demonstrated no dyspnoea symptoms. The most prevalent systemic disease in the participants' medical histories was diabetes mellitus (22.5%). It was determined that 75% of the participants exhibited poor sleep quality, 25% demonstrated severe dependence, and 35% exhibited moderate dependence, as assessed by the Barthel Index.
Conclusion: Cough, dyspnoea, and pain are common symptoms in patients with lung cancer and have a significant impact on sleep quality. These findings support the conclusion that rehabilitation is an important aspect of the treatment plan for these

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Received: 15.05.2024, Accepted: 28.07.2024, Published Online: 20.09.2024
Cited: Arğalı Deniz M, et al. Assessment of Environmental Factors, Sleep Quality, Functional Independence, and Posture Anatomy in Lung Cancer Patients. Acta Medica Ruha. 2024;2(3):150-158. https://doi.org/10.5281/zenodo.13364892
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patients. The high number of individuals without a family history of cancer suggests that environmental factors should be considered in public health initiatives.

Keyswords: Lung Cancer, Posture Anatomy, Sleep Quality, Functional Independence Level.

GİRİŞ

Kanser, yaygın bir küresel sağlık sorunu ve önde gelen bir ölüm nedenidir (1). Tüm kanser türleri arasında akciğer kanseri dünya çapında en yüksek insidansa sahiptir (2). İleri evre akciğer kanserinde en sık görülen semptomlar ağrı, nefes darlığı, öksürük, iştahsızlık, kilo kaybı, yorgunluk ve halsizlik, uyku sorunları ve duygusal sorunlar olarak bildirilmektedir (3-5).
Hastalığın belirtileri ve tedavisinde kullanılan yöntemlerin yan etkileri hastaların günlük aktivitelerini olumsuz etkileyebilmektedir (6). Kanser tedavisinde kullanılan kemoterapi ve radyoterapi tüm vücut sistemleri üzerinde önemli bir etkiye sahiptir ve günlük aktivitelerin sürdürülmesinde önemli zorluklara neden olur (7). Literatürde, kemoterapötik ilaçların tedavi sırasında kullanılmasının sitotoksisite ve yan etkilere bağlı olarak uyku kalitesinde azalmaya yol açabileceği bildirilmiştir (8-10).
Literatür, akciğerle ilişkili hastalıklarda akciğer kapasitesinin azalması ve solunum kaslarının aktivasyonu nedeniyle omuzlarda, göğüste ve omurgada postüral anormalliklerin ortaya çıkabileceğini göstermektedir (11-13). Ancak, akciğer kanseri popülasyonunda kanser tutulumuna bağlı olarak zorlu vital kapasitede azalma gözlenmesine rağmen (14) postüral anormallikler üzerine herhangi bir çalışma yapılmamıştır. Sonuç olarak, çeşitli popülasyonlarda postüral kontrol ile bağlantılı olan uyku kalitesinin (15) akciğer kanserli bireylerde değerlendirilmesi çok önemlidir.
Bu çalışmada amacımız, ileri evre primer akciğer kanserli hastalarda çevresel faktörleri, uyku kalitesini, fonksiyonel bağımsızlık düzeyini ve postüral bozukluğu incelemektir.

YÖNTEM

Araştırmanın Tipi

Çalışma tanımlayıcı, kesitsel ve prospektif non-invaziv bir araştırmadır.

Araştırmanın Evreni Ve Örneklemi

Araştırmaya Hatay Mustafa Kemal Üniversitesi Sağlık Uygulama ve Araştırma Hastanesinde akciğer kanseri teşhisi konan ve bilgilendirilmiş onam veren 40 katılımcı dahil edilmiştir. 18 yaşından küçükler, hamileler, emzirenler ve imza yetkisi olmayanlar dışlanmıştır.

Veri Toplama Araçları

Katılımcıların demografik bilgileri, sigara öyküleri, operasyon geçmişi, hastalık semptomları, hastalığın tipi, yerleşim yeri, yayılımı ve tedavi bilgileri sorgulandı. Dispne düzeyleri Medical Research Council Skalası (MRCS) ile uyku kaliteleri Pittsburgh Uyku Kalitesi İndeksi (PUKİ) ile ağrı düzeyleri Vizüel Analog Skalası (VAS) ile bağımsızlık düzeyleri Barthel Günlük Yaşam Aktiviteleri İndeksi ile ve postürleri New York Postür Analizi ile değerlendirildi.

Medical Research Council Skalası (MRCS): Dispne düzeyini değerlendirmek için kullanılan skala 6 kategoriden oluşmakta olup; 0, dispne yok; 1, hafif derecede dispne (düzde koşarken veya hafif bir yokuş yukarı çıkarken nefes darlığından rahatsız olur); 2, orta derecede dispne (nefes darlığı nedeniyle aynı yaştaki insanlardan daha yavaş yürür); 3, orta derecede şiddetli dispne (seviyede kendi hızınızda yürürken nefes darlığı nedeniyle durması gerekir); 4, şiddetli derecede dispne (yaklaşık 100 yard yürüdükten veya düz yolda birkaç dakika sonra nefes almak için durur); 5, çok şiddetli derecede dispne (evden çıkamayacak kadar nefes darlığı veya giyinirken veya soyunurken nefes darlığı) olarak değerlendirilmektedir (16).

Pittsburgh Uyku Kalitesi İndeksi (PUKİ): Uyku kalitesini değerlendirmek amacıyla geliştirilen ölçek 24 maddeden oluşmaktadır. Maddelerin 19'u öz bildirimdir, 5'i ise bir eş ya da ev arkadaşı tarafından yanıtlanabilir. Ölçekten alınabilecek puan 0-21 arasındadır. Toplam puanın 5 ten küçük olması kötü uyku kalitesini gösterir (17). Çalışmada ölçeğin geçerli ve güvenilir bulunan Türkçe versiyonu kullanılmıştır (18).

Vizüel Analog Skalası (VAS): Ağrı şiddetini değerlendirmek amacı ile kullanılan skala ağrı düzeyini 10 cm'lik ölçek ile değerlendirilmekte olup; 0-3 puan hafif ağrı, 3-6 puan hafif-orta ağrı, 6 ve üzeri orta-şiddetli ağrı olarak değerlendirilir (19).

Barthel Günlük Yaşam Aktiviteleri İndeksi: Mahoney ve Barthel tarafından 1965 yılında geliştirilmiş ve Küçükdeveci ve arkadaşları tarafından Türkçeye uyarlanmıştır (20,21). Ölçekte beslenme, yıkanma, öz bakımını yapabilme, giyinme, dışkılama kontrolü, idrar kontrolü, tuvalete gitme, yataktan tekerlekli sandalyeye geçebilme yetisi, yürüme ya da tekerlekli sandalyeye bağımlı olma gibi hareketlilik durumu ve merdiven çıkma işlevleri sırasındaki bağımsızlık düzeyleri değerlendirilmektedir. Ölçekten 0-100 arası puan alınabilmekte; 0-20 puan tam bağımlı, 21-61 puan ileri derece bağımlı, 62-90 puan orta derece bağımlı, 91-99 puan hafif derece bağımlı, 100 puan tam bağımsız olarak tanımlanmaktadır.

New York Postür Analizi: Bu yöntem 13 farklı vücut bölgesindeki postür değişikliklerini değerlendirmektedir. Postür doğruysa beş, orta derecede bozuksa üç ve ciddi derecede bozuksa bir puan verilir. Analiz sonucunda alınan toplam puan maksimum 65, minimum 13 olmaktadır (22).

İstatistiksel Analiz

Çalışmanın verileri SPSS 22.0 versiyonu kullanılarak analiz edilmiştir. Tanımlayıcı istatistikler ve kategorik değişkenler frekans ve yüzde değer olarak verildi.

Araştırma Etiği

Çalışmanın protokolü Hatay Mustafa Kemal Üniversitesi Tayfur Ata Sökmen Tıp Fakültesi Klinik Araştırmalar Etik Kurulu tarafından onaylanmıştır (2015/17).

BULGULAR

Çalışma popülasyonunun %22.5 kadın, %77.5 erkeklerden oluşmaktadır. Bireylerin %22.5 ev hanımı, %27.5 emekli idi. Öğrenim durumlarına göre ilköğretim mezunu %57.5'ini oluşturmakta ve gelir düzeyi durumlarına bakıldığında %85'i asgari ücret almaktaydı. Bireylerin vücut kitle indeksi (VKİ) değerlerine bakıldığında %7.5 aşırı zayıf, %17.5 zayıf, %35 normal vücut ağırlığında, %32.5 şişman, %5 aşırı şişman ve %2.5 obezdi. Ailede kanser öyküsü olan %12.5, sigara kullanım durumu %62.5 sigarayı bırakmış, kan grubunda kanser tanısı almış hastaların %52.5 A grubu olduğu belirlendi (bknz Tablo 1). Katılımcılara demografik verilerine ait detaylı bilgiler Tablo 1'de sunulmuştur.

Tablo 1. Hastaların Demografik Verileri

		n	%
Yaş	36-45	1	2.5
	45-65	26	65
	65 ve Üstü	13	32.5
Cinsiyet	Kadın	9	22.5
	Erkek	31	77.5
Meslek	Ev Hanımı	9	22.5
	Memur	1	2.5
	Emekli	11	27.5
	Serbest	1	2.5
	Diğer	18	45
Öğrenim Durumu	Okur Yazar Değil	11	27.5
	İlk Öğretim	23	57.5
	Orta Öğretim	6	15
Gelir Düzeyi	Asgari Ücret	34	85
	Asgari Ücret-2000	5	12.5
	2000-3000	1	2.5
Medeni Hali	Evli	39	97.5
	Boşanmış	1	2.5
VKİ (kg/m^2)	Aşırı Zayıf	3	7.5
	Zayıf	7	17.5
	Normal	14	35
	Şişman	13	32.5
	Aşırı Şişman	2	5
	Obez	1	2.5

Tablo 1'in devamı			
Tanı Konulduktan Sonraki Vücut Ağılık Kaybı	Yok	4	10
	<5	10	24
	5-10	8	20
	10-15	11	27.5
	>15	7	17.5
İştahsızlık	Evet	29	72.5
	Hayır	11	27.5
Ailede Kanser Öyküsü	Var	5	12.5
	Yok	35	87.5
Sigara	Evet	7	17.5
	Hayır	8	20
	Bırakmış	25	62.5
Sigara İçme Durumu (paket/gün/yıl)	İçmiyor	33	82.5
	1 Paketten Az/0-1 Yıl	4	10
	1 Paketten Fazla/1-5 Yıl	3	7.5
Kan Grubu	A	21	52.5
	B	3	7.5
	AB	5	12.5
	0	10	25.0
	Bilmiyor	1	2.5
Rh	Pozitif	37	92.5
	Negatif	2	5.0
	Bilmiyor	1	2.5
Sistemik Hastalık	Diabetes Mellitus	9	22.5
	Hipertansiyon	7	17.5
	Kalp Yetmezliği	3	7.5
	Hiperkolesterolomi	2	5
	Diğer Sistemik Hastalıklar	4	10

Verilerimiz katılımcıların %42,5'inin bahçeli bir evde yaşadığını ve %45'inin ilçede yaşadığını ortaya koymuştur. Ayrıca, katılımcıların %90'ı birincil ev ısınma kaynağı olarak soba ile ısınmaktadır (bknz. Tablo 2). Tüm bireylerin çevresel faktörleri Tablo 2'de verildi.

Tablo 2. Hastaların Yaşadığı Çevre Verileri

		n	**%**
Ev	Apartman	7	17.5
	Tek Katlı	16	40.0
	Bahçeli Ev	17	42.5
Yaşadığı Yer	Köy	13	32.5
	İlçe	18	45.0
	Merkez	9	22.5
Evde Kullanılan Isınma Aracı	Soba	36	90.0
	Kalorifer	2	5.0
	Doğalgaz	2	5.0

Katılımcıların hastalık süresi değerlendirildiğinde %30'u 10-16 ay, %27.5'nin 5-9 ay ve %20'sinin 0-4 ay olduğu, kemoterapi tedavisi %92.5'un aldığı ve %45'inin 1-4 aylık süredir kemoterapi aldığı ve %12.5'unun 5-6 kür aldığı, klinik bulgulardan %77'sinde öksürük, %72.5'unda balgam, %42.5'unda göğüs ağrısı, %62.5'unda nefes darlığı, %37.5'unda ses kısıklığı olduğu belirlendi. Hastalık evresi 4 olan hastalar %70'ini oluşturmaktaydı. Akciğer kanser türü %50'sinde adenokarsinom idi. Hastalığın daha çok akciğer sağ lobunda olduğu (%60) özellikle sağ orta lobda (%32.5) metastaz durumunun en fazla kemikte (%32.5) olduğu görüldü (bknz. Tablo 3). Tüm bireylerin hastalık ve klinik bilgileri Tablo 3'te verilmiştir.

Tablo 3. Hastalık Bilgileri ve Klinik Bulguları

		n	**%**
Hastalık Süresi (ay)	0-4	8	20.0
	5-9	11	27.5
	10-16	12	30.0
	17-24	4	10.0
	24 Üstü	5	12.5

Tablo 3'ün devamı				
Akciğer Kanser Tedavisi	Kemoterapi		37	92.5
	Radyoterapi		1	2.5
	Kemoterapi ve Cerrahi Operasyon		1	2.5
	Kemoterapi, Radyoterapi Cerrahi Operasyon		1	2.5
Klinik Bulgular	Öksürük	Evet	31	77.5
		Hayır	9	22.5
	Balgam	Evet	29	72.5
		Hayır	11	27.5
	Göğüs Ağrısı	Evet	17	42.5
		Hayır	23	57.5
	Kan Tükürme	Evet	3	7.5
		Hayır	37	92.5
	Nefes Darlığı	Evet	25	62.5
		Hayır	15	37.5
	Yaygın Vücut Ağrısı	Evet	9	22.5
		Hayır	31	77.5
	Baş ağrısı	Evet	15	37.5
		Hayır	25	62.5
	Ses Kısıklığı	Evet	15	37.5
		Hayır	25	62.5
Hastalığın Evresi	Evre 1		4	10.0
	Evre 2		3	7.5
	Evre 3		5	12.5
	Evre 4		28	70.0
Akciğer Kanser Türü	Epidermoit		13	32.5
	Adeno CA		20	50.0
	Küçük Hücreli		7	17.5
Akciğer Kanser Tutulumu	Sağ Taraf		24	60.0
	Sol Taraf		11	27.5
	Bilateral		5	12.5
Metastaz	Meme		1	2.5
	Gırtlak		1	2.5
	Mide		5	12.5
	Kemik		13	32.5
	Lenf Nodu		4	10.0
	Beyin		2	5.0
	Karaciğer		1	2.5
	Plevra		2	5.0
Akciğer Tutulum Yeri	Sağ Orta Lob	Tutulum Var	13	32.5
		Tutulum Yok	27	67.5
	Sağ Alt Lob	Tutulum Var	2	5
		Tutulum Yok	38	95
	Sol Üst Lob	Tutulum Var	11	27.5
		Tutulum Yok	29	72.5
	Sol Lingular Lob	Tutulum Var	2	5
		Tutulum Yok	38	95
	Sol Alt lob	Tutulum Var	5	12.5
		Tutulum Yok	35	87.5
Kemoterapi Alma Süresi	Almıyor		1	2.5
	<1 ay		5	12.5
	1-4 ay		18	45.0
	5-8 ay		11	27.5
	9-12 ay		1	2.5
	13-18 ay		4	10.0
Radyoterapi Kür Sayısı	Almayan		30	75.0
	1-2		2	5.0
	3-4		3	7.5
	5-6		5	12.5
Kemoterapi Kür Sayısı	Almayan		30	75.0
	1-2		2	5.0
	3-4		3	7.5
	5-6		5	12.5

Bireylerin dispne düzeyleri MRCS'ye göre değerlendirildiğinde %27.5'unun 4, %22.5'unun 3 değer aldığı ve dispne semptomunun yalnızca %12.5'unda olmadığı görüldü. Uyku kalitesi değerlendirildiğinde %75'inin kötü uyku kalitesine sahip olduğu, Barthel indeksine göre ise %25'inin ileri derecede, %35'inin ise orta derecede bağımlı olduğu belirlendi. Postür analizine göre ise %80'ninde postüral deformasyonun olmadığı görüldü (bknz. Tablo 4).

Tablo 4. Hastaların Nefes Darlığı, Uyku Kalitesi, Fonksiyonel Bağımsızlık Düzeyi ve Postür Analizi Sonuçları

		n	%
MRCS	0	5	12.5
	1	9	22.5
	2	6	15.0
	3	9	22.5
	4	11	27.5
PUKİ	İyi	10	25
	Kötü	30	75
Barthel İndeksi	Tam Bağımlı	1	2.5
	İleri Derece Bağımlı	10	25.0
	Orta Derecede Bağımlı	14	35.0
	Hafif Derecede Bağımlı	5	12.5
	Tam Bağımsız	10	25.0
New Yor**k** Postür Analizi	Çok İyi	32	80.0
	İyi	5	12.5
	Orta	2	5.0
	Zayıf	1	2.5

Medical Research Council Skalası: MRCS, Pittsburgh Uyku Kalitesi İndeksi: PUKİ.

TARTIŞMA

Uluslararası Kanser Araştırma Ajansı verilerine göre dünya genelinde yaklaşık 19,3 milyon yeni kanser vakası ve 10,0 milyon kansere bağlı ölüm gerçekleşmiştir. Akciğer kanserinin, bu vakaların %11,4'ünü oluşturarak en yaygın ikinci kanser türü olduğu bildirilmektedir. Ayrıca, Akciğer kanseri tahmini 1,8 milyon ölümle (%18) kansere bağlı ölümlerin önde gelen nedenidir (23).

Akciğer kanseri için risk faktörlerinin hem genetik hem de çevresel faktörlerle ilişkili olduğu bildirilmiştir (24). Kanser hastalığı ülkelerin sağlık sistemleri üzerinde önemli bir ekonomik yük oluşturmaktadır (25). Bu yükün azaltılması için hastaların farklı açılardan değerlendirilmesi ve tespit edilen semptomlara yönelik etkin tedavi yöntemlerinin sunulması önemlidir. Bu nedenle çalışmamızda akciğer kanseri hastalarında çevresel faktörler, uyku kalitesi, bağımsızlık düzeyi ve postürün araştırılması amaçlanmıştır.

Kanser insidansının erkeklerde kadınlardan daha yüksek olduğu bilinmektedir (26). Ancak, özellikle akciğer kanseri için farklı vaka-kontrol çalışmalarının sonuçları tutarsızdır ve cinsiyet hormonlarının rolü henüz açıklığa kavuşturulmamıştır (27). Sigara içmek akciğer kanseri için önemli bir risk faktörüdür ve sigara bağımlılığının erkeklerde daha yüksek olduğu bilinmektedir (28). Bu nedenle insidansın erkeklerde daha yüksek olması beklenebilir. Bununla birlikte, östrojen hormonunun etkileri nedeniyle sigara içen kadınlarda akciğer kanseri insidansının daha yüksek olabileceğini düşündüren kanıtlar vardır (27). Bu konudaki literatür oldukça çelişkilidir. Mevcut literatürle uyumlu olarak, çalışma popülasyonunun %77,5'i erkektir. Bununla birlikte, cinsiyetler arasındaki insidans farkını daha net bir şekilde ortaya koymak için daha geniş örneklemli çalışmaların yapılmasını önermekteyiz.

Ailesel akciğer kanseri riski hem genetik hem de çevresel faktörlerden etkilenmektedir. Önceki çalışmalar aile öyküsünde kanser varlığının riski artırdığını göstermiştir (24,29). Ancak, çalışmamızdaki olguların %87,5'inde ailede kanser öyküsü bulunmaması dikkat çekicidir. Bu nedenle, akciğer kanserine katkıda bulunan çevresel faktörlerin aydınlatılması için daha fazla araştırma yapılması gerekmektedir.

Literatürde akciğer tutulumu olan hastalıklarda düşük eğitim düzeyi, düşük sosyoekonomik düzey, iç ve dış ortam hava kirliliği ve yetersiz beslenmenin hastalığın gelişimi ile ilişkili olduğu vurgulanmaktadır (30-32). Bu çalışmada da literatürle uyumlu olarak %27,5'inin okur-yazar olmadığı, %57,5'inin ilkokul mezunu olduğu ve sosyoekonomik düzey olarak genellikle asgari ücretle geçimini sağladıkları görülmüştür. Kanserli bireyler daha özenli bakıma ve yaşam standartlarının iyileştirilmesine ihtiyaç

duymaktadır. Ancak hastalık belirtileri nedeniyle performansları düşebilmekte ve çalışma olanakları kısıtlanabilmektedir. Düşük gelir düzeyleri, hastalığa özgü ihtiyaçlarını tam olarak karşılamalarını engelleyebilir. Bu durum, gelir düzeyinin ağrı, uyku kalitesi ve semptom kontrolü gibi faktörleri dolaylı olarak etkileyebileceğini düşündürmektedir.

Çevresel faktörlerin başında gelen ikamet edilen bölge açısından çalışmamızdaki bireylerin %22,5'i şehir merkezinde, %42,5'i ise bahçeli evlerde yaşamaktadır. Ev ortamında ısınma amaçlı soba kullanım oranının yüksek olması (%90) iç ortamın hastalıkta etken olabileceği hipotezini desteklemektedir.

Literatürde kanserli bireylerin %50'sinde tıbbi tedavi gerektirecek düzeyde uyku bozukluğu olduğu vurgulanmaktadır (33). Bizim çalışmamızda da ileri evre akciğer hastalarının uyku kalitesinin %75 oranında etkilendiği saptanmıştır.

Akciğer kanserli hastaların ağrı, nefes darlığı, öksürük ve yorgunluk gibi semptomlarla başvurduğu ve bunların toplu olarak yaşam kalitesinde azalmaya neden olduğu rapor edilmiştir (34,35). Yaşam kalitesindeki düşüşün ve semptom şiddetindeki artışın hastaların bağımsızlık düzeyini etkileyebileceğini varsaymaktayız. Çalışmamızda yer alan hastalarımızda da literatürle uyumlu olarak ağrı, öksürük, balgam, nefes darlığının yüksek oranda olması ve hastaların %2.5'nin tam bağımlı, %25'inin ileri düzeyde bağımlı, %35'inin ise orta düzeyde bağımlı olması bu varsayımımızı destekler niteliktedir. Kanser hastaları, semptomlar ve kemoterapi, radyoterapi gibi tedavi süreçlerinin zorlu yapısı nedeniyle günlük yaşam aktivitelerini yerine getirmekte zorluk yaşamaktadır. Nitekim yapılan bir çalışmada akciğer kanseri hastalarında günlük yaşam aktivitelerinde bağımlılık yaygınlığının %13-49 olduğu bildirilmektedir (36). Çalışmamızda literatüre benzer şekilde semptomatik hasta veya kemoterapi alan hasta sayısının fazla olması günlük yaşam aktivitelerinin etkilendiğini göstermektedir. Şu anda akciğer kanseri popülasyonunda bağımsızlık düzeyine ilişkin literatürde eksiklik bulunmaktadır. Bu nedenle araştırmacıların değerlendirmelerinde bağımsızlık düzeyine yer vererek mevcut literatüre katkıda bulunmalarını talep etmekteyiz.

Literatürde akciğer etkilenimi olan hastalıklarda postür bozukluklarının olduğu tespit edilmiştir (11-13). Ancak bu konu akciğer kanserli popülasyonda kontrol edilmemiştir. Verilerimiz doğrultusunda %75'lik kötü uyku kalitesine ve %35'lik oranda orta derece bağımlılığa rağmen %80 oranında çok iyi postür olduğu görülmüştür. Diğer hastalık gruplarından farklı olarak akciğer kanserine bağlı uyku kalitesindeki düşüşün nedeni postür bozuklukları değildir. Aksine, akciğer kanseri hastalarının bağımsızlık düzeylerinin ve uyku kalitelerinin hastalığın semptomlarından etkilendiği görüşündeyiz. Bununla birlikte, verilerimizde yer alan yüksek kemik metastazı (%32,5) ve kansere bağlı kas disfonksiyonu dikkate alındığında postüral etkilenim risk oluşturmaya devam etmektedir (37).

SONUÇ

Öksürük, nefes darlığı ve ağrı akciğer kanserli hastalarda sık görülen semptomlardır ve uyku kalitesi üzerinde önemli bir etkiye sahiptir. Bu bulgular, rehabilitasyonun bu hastalar için tedavi planının önemli bir yönünü oluşturduğu sonucunu desteklemektedir. Klinisyenlerin akciğer kanserli bireylerde duruşu göz önünde bulundurmaları faydalı olacaktır. Ailesinde kanser öyküsü olmayan bireylerin prevalansının yüksek olması, halk sağlığı müdahalelerinde çevresel faktörlerin de dikkate alınması gerektiğini göstermektedir.

AÇIKLAMALAR

Finansal destek yoktur.

Çıkar çatışması yoktur.

Not: Bu makale 5. Uluslarası Fizyoterapi ve Rehabilitasyon Kongresi (20.05.2015)'nde sözel bildiri olarak sunulmuştur.

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Acta Medica Ruha
International Journal of Medicine and Health Sciences
E-ISSN: 2980-1184

ORIGINAL ARTICLE
Volume:2 Issue:3 Year:2024
https://doi.org/10.5281/zenodo.13370776

Bibliometric And Visual Analysis of Video Assisted Thoracoskopic Surgery

Video Destekli Torakoskopik Cerrahi Segmentektominin Bibliyometrik ve Görsel Analizi

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ABSTRACT

Introduction: The video-assisted thoracoscopic surgery (VATS) method has been used in thoracic surgery for the last three decades, and segmentectomy operations performed by VATS have an increasingly broader area of usage including thoracic surgery, oncologic surgery, lung cancer, and metastatic lung tumors. The definition and applicability of VATS segmentectomy are dynamically broadening over time, and the number of published reports in this field is increasing. However, no bibliometric analysis of the segmental anatomy in VATS segmentectomy procedures was encountered.
Objective: In this study, keywords and phrases including "VATS segmentectomy" were searched in the Web of Science (WoS) Core Collection, and the collected data were analyzed using the RStudio and VOSviewer programs.
Method: The analyses focused on the current state of research on VATS segmentectomy, previous studies, recent studies, and expectations for the future.
Results: A total of 693 publications were found. The average number of publications per year was 8.16. The most productive countries were respectively China and the US. The country with the highest number of citations was the US. The two most prominent WoS categories were surgery and the respiratory system. The most involved institution was Tongji University (China).
Conclusion: In the keyword analyses, it was seen that the keywords segmentectomy and lung cancer were frequently used, and there were strong connections between the two. It was seen that the recent trend in research in this field involved video-assisted thoracoscopies and robotic surgery, but strong connections indicating the controversial nature of the outputs of research were identified.

Keyswords: VATS, Segmentectomy, Bibliometrics.

ÖZET

Giriş: Video yardımlı torakoskopik cerrahi (VATS) yöntemi göğüs cerrahisinde son otuz yıldır kullanılmakta olup, VATS ile yapılan segmentektomi ameliyatları göğüs cerrahisi, onkolojik cerrahi, akciğer kanseri ve metastatik akciğeri de kapsayacak şekilde giderek daha geniş bir kullanım alanına sahiptir. VATS segmentektominin tanımı ve uygulanabilirliği zamanla dinamik olarak genişlemekte ve bu alanda yayınlanan raporların sayısı artmaktadır. Ancak VATS segmentektomi işlemlerinde segmental anatominin bibliyometrik analizine rastlanmamıştır.
Amaç: Bu çalışmada Web of Science (WoS) Core Collection'da "VATS segmentektomi"yi içeren anahtar kelimeler ve ifadeler araştırılmış ve toplanan veriler RStudio ve VOSviewer programları kullanılarak analiz edilmiştir.
Yöntem: Analizler, VATS segmentektomi ile ilgili araştırmaların mevcut durumuna, önceki çalışmalara, son çalışmalara ve geleceğe yönelik beklentilere odaklandı.
Bulgular: Toplam 693 yayın bulundu. Yıllık ortalama yayın sayısı 8,16 oldu. En verimli ülkeler sırasıyla Çin ve ABD oldu. En çok atıf alan ülke ise ABD oldu. En öne çıkan iki WoS kategorisi cerrahi ve solunum sistemiydi. En çok katılan kurum Tongji Üniversitesi (Çin) idi.
Sonuç: Anahtar kelime analizlerinde segmentektomi ve akciğer kanseri anahtar kelimelerinin sıklıkla kullanıldığı ve aralarında güçlü bağlantıların olduğu görüldü. Bu alandaki araştırmalarda son dönemdeki eğilimin video yardımlı torakoskopiler ve robotik cerrahi olduğu görülmüş, ancak araştırma çıktılarının tartışmalı niteliğine işaret eden güçlü bağlantılar tespit edilmiştir.

Anahtar Kelimeler: VATS, Segmentektomi, Bibliyometri.

INTRODUCTION

Surgical resection is the best therapeutic option for non-small cell lung cancer in terms of both survival and cure rate. However, some patients may not be able to get intensive surgical treatment even though their lung cancer is operable due to their inadequate cardiopulmonary reserves and related comorbidities. Surgical treatment options are now available to these patient groups with low cardiopulmonary reserve thanks to advancements in postoperative care and increased surgical experience, particularly in

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Received: 24.07.2024, Accepted: 25.08.2024, Published Online: 20.09.2024
Cited: Acıpayam A, et al. Bibliometric And Visual Analysis of Video Assisted Thoracoskopic Surgery. Acta Medica Ruha. 2024;2(3):159-165. https://doi.org/10.5281/zenodo.13370776
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parenchyma-preserving resections that can be carried out with minimally invasive interventions. Furthermore, new research has been released indicating that sublobar resection may be carried out even in cases where pulmonary capacity is adequate, particularly in individuals with early-stage lung cancer. Following these research efforts, interest in sublobar resections amongst thoracic surgeons has increased significantly (1-3). Although it is stated in the National Comprehensive Cancer Network (NCCN) guideline that sublobar resections are a suitable option for patients with poor lung reserve or who cannot tolerate lobectomy due to comorbidities, patients with pure adenocarcinoma in-situ histology, a ground glass solid ratio greater than 50%, peripheral nodules smaller than 2 cm, and doubling times longer than 400 days are considered as acceptable candidates for this surgical alternative (4).

In their study evaluating the advantages of sublobar resections to the patient, Nomori et al., argued that the real functional benefit occurs in single segment resections, and this advantage is limited in other multiple segmentectomies (5). If all of these evaluations lead to the decision to execute a segmentectomy, then anatomical segmentectomy preserving the relevant segment's artery, vein, and bronchus should be carried out without violating oncological principles. Furthermore, sufficient parenchymal surgical margins, a methodical lymph node sampling protocol, and an intraoperative assessment of the tumor's histological characteristics should all be part of the surgical process.

By examining and comprehending the organization of knowledge, bibliometric analysis sheds light on both developmental and qualitative tendencies. In order to assess the state of lung surgery and related research, the goal of this study was to conduct a thorough analysis of segmentectomy research.

METHOD

The keyword “VATS segmentectomy” was used to reach publications for bibliometric analyses. To prevent changes in the dataset as new publications would be added, the information for the relevant articles was downloaded in May 2024 from the Web of Science Core Collection (WoSCC) database. Research articles and books published in any language and listed on WoSCC were included in the analyses. The search results were saved in “tab delimited file” and BibTex” format (6).

Data Analysis

Analyses in different categories, including bibliometric analysis, general outlook, countries/regions, authors/institutions, journals, documents/references, keywords, and trends, were carried out. The data were visualized using WoS, Biblioshiny (R version 4.4.2; Vienna, Austria; www.r-project.org), and VOSviewer (1.6.20; Leiden, Netherlands) (6,7).

RESULTS

Table 1. Category and count of documents according to WOS

Category	Record Count
Surgery	363
Respiratory System	333
Cardiac-Cardiovascular Systems	200
Oncology	123
Medicine - General Internal	27
Medicine - Research, Experimental	18
Anesthesiology	8
Critical Care Medicine	5
Health Care Sciences, Services	4
Orthopedics	4

In the examinations conducted for the bibliometric data analyses, based on searches made for publications using the keyword “VATS segmentectomy” made between November 1966 and May 2024 included in the WoS database, 693 publications were identified. Among these, 493 were research articles, 1 was a book chapter, 41 were conference manuscripts, and 91 were reviews. Moreover, 1098 Keywords Plus (ID) and 736 Author's Keywords (DE) were identified. The first year of publication according to the WoS database was 1996, and only 2 articles on “VATS segmentectomy” were published in that year. The increasing trend of publications over the years is shown in Figure 1/A. This progress, which started with 2 studies in 1966, reached double-digit yearly numbers in the 2000s, and it continued

to grow by showing a fluctuating curve. The highest number of publications was in 2022, whereas small decreases were seen in 2023 and 2024. The three WoS categories in which the highest numbers of publications were made were the “surgery”, “respiratory system”, and “cardiac-cardiovascular systems” categories, which were followed by oncology, biochemistry, and molecular biology, while the average number of publications per year was 8.16 (Table 1).

Keyword analysis

It is known that keywords can summarize a certain topic addressed by an article, provide a general overview of the publication for the researchers, and are seen as a concentrated outline of the main contents of a research article. In addition to this, keywords have an effective position in the dissemination of scientific research results to the reader in a large-scale and rapid manner. Therefore, keywords with high added value that are extracted from existing publications using bibliometric methods are important in terms of uncovering the significant topics in the scientific field in question and revealing the research hotspots around these topics. The Biblioshiny and VOSviewer programs were used to determine the simultaneous usage instances and frequencies of keywords. In the word cloud created in Biblioshiny where the size of each keyword indicated how frequently it was used, “lobectomy”, “segmentectomy”, and “resection” were found to be frequently used keywords (Figure 1/B). To understand the co-word network of keywords and the relationships among keywords, analyses were performed using the VOSviewer program. As a result of the analyses in VOSviewer, keywords were distributed in 4 clusters colored red, yellow, blue, and green, and the size of each node reflected the usage frequency of the relevant keyword in the literature. Furthermore, the thickness of the tie between two keywords (edge) represented the frequency of the co-occurrence of these two keywords. The most frequently used keywords were identified as “segmentectomy”, “lung cancer”, and “video-assisted thoracoscopic”. The largest node belonged to the keyword “segmentectomy” (blue cluster). Additionally, the keyword “segmentectomy” was determined to be strongly connected to the keyword “lung cancer”, while the keyword “video-assisted thoracoscopic” was strongly connected to the keyword “uniport VATS” (Figure1/C).

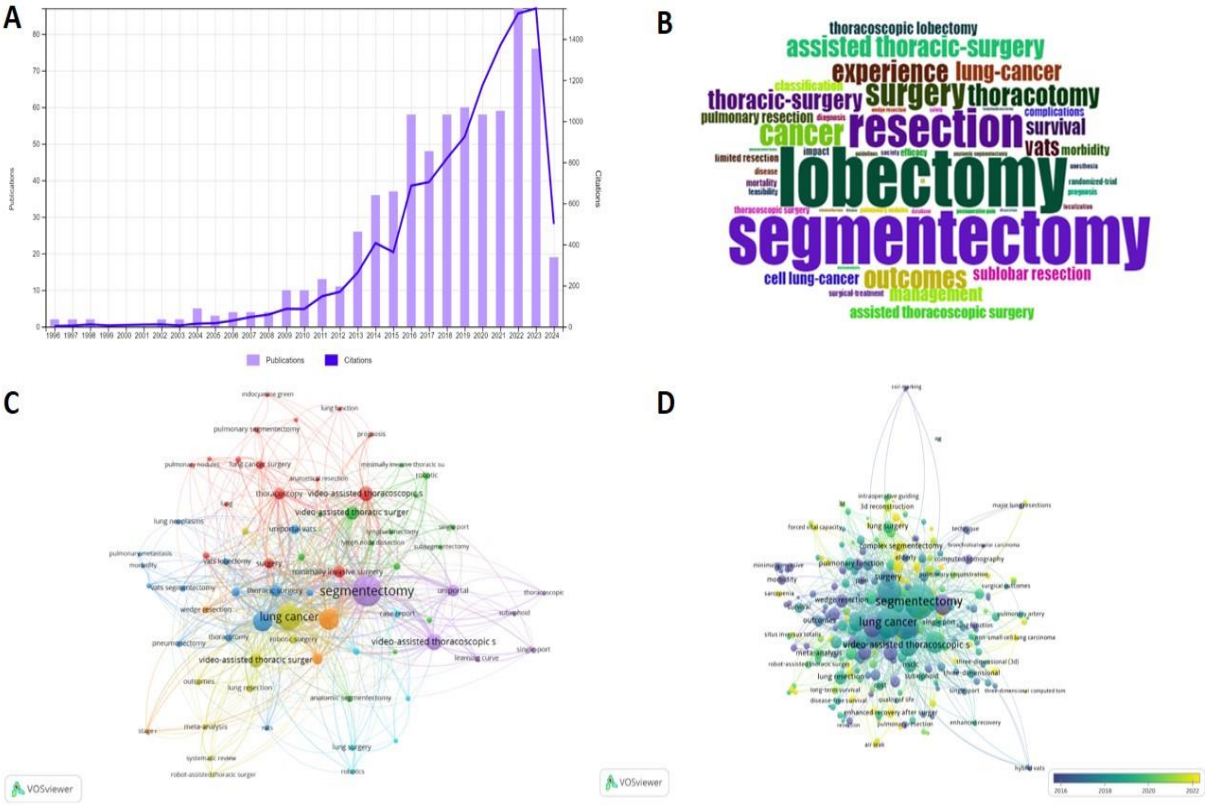

Figure 1/A. The number of documents and citations per year from 1996 to 2024, **Figure 1/B.** Visualized Word-cloud of frequently used keywords in VATS segmentectomy, **Figure 1/C.** Cluster of co-occurrence of keywords, **Figure 1/D.** Trend of keywords by year.

In studies published from 1996 to 2024, the most frequently used terms were “lobectomy” and “segmentectomy”. Here, the color purple represents the keywords that were prevalently used before and in the 2000s, while the color yellow represents those prevalently used from 2020 up to 2024. The keywords “segmentectomy” and “lung cancer” were mainly used in 2016 and before. The terms “video-assisted thoracoscopic" and “single port” were the prominent ones in 2020, while “lung surgery 3D reconstruction” and “3D” were used more frequently after 2020 (Figure 1/D).

Authorship Analysis

The analysis of citation-related data has an important place in bibliometrics. This is an important indicator of the impact of a publication and its research outputs. The impact of a certain author and article can be evaluated based on how frequently the article is cited, by whom it is cited, and the reason for its citation. The sources that are cited the most can also be used to understand the impact of a journal or a group of journals.

The number of authors who had publications with “VATS segmentectomy” as a keyword was 2925 in the examined period, and the number of single-author studies was 26. Each document was cited 15.84 times on average per year.

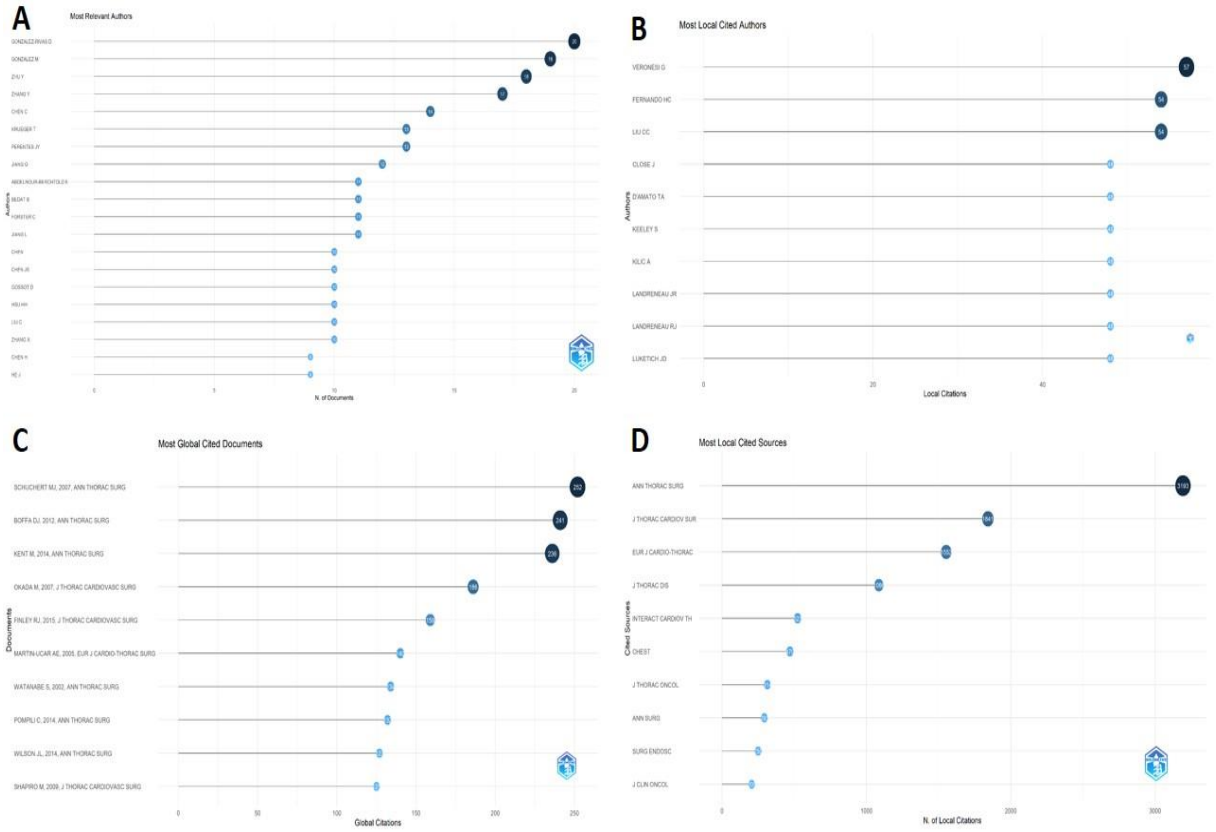

Figure 2/A. Top 20 most relevant authors of VATS segmentectomy, **Fugre2/B**. Top 10 most local cited authors of VATS segmentectomy,**Figure 2/C.** Top 10 most cited documents of VATS segmentectomy,**Figure/D.** Top 10 most local cited sourches of VATS segmentectomy.

The most relevant authors in the examined field are presented in Figure 2/A, the authors who were cited the most frequently about the topic are presented in Figure 2/B, the documents that were cited the most frequently are presented in 2/C, and their platforms of publication are presented in 2/D.

The most relevant author was Gonzalez-Rivas D., followed by Gonzalez M. (Figure 2/A). According to the total frequencies of citations, the most frequently cited author was Veronesi G. (Figure 2/B). The article that was cited the most was the one published by Schuchert M.J. in 2007 (Figure 2/C). The platform of publication that received the highest number of citations was Ann Thorac Surg, and it was followed by J Thorac Cardov Sur (Figure 2/D).

Productivity Analysis

According to the geographical distributions of the examined studies based on the data analyses of their keywords, many of them were found to involve international collaboration despite having different degrees of productivity. The most productive countries in terms of scientific knowledge production and research outputs were China, Japan, and the US. While Japan and the US were the most productive countries in the 2000s, China was in a leading position in 2020. After 2020, the productivity of Denmark and Switzerland in the field increased. In this context, China was found to have close connections with Taiwan, Spain, the UK, and especially the US. The highest numbers of citations were made to studies conducted by authors in the US and China (Figure 3/A). The views of research institutions had a strong impact. In agreement with the global data analysis results, the institution with the highest number of publications was Tongji University, followed by the National Taiwan University Hospital and the National Taiwan University (Figure 3/B). The relationships between the scientific productivity levels of countries and the citations made to studies conducted by authors from these countries (Figure 3/C) represented 4 different steps of analysis.

The publication of research outputs in the countries of the relevant authors was important in terms of explaining the active participation of researchers in research focusing on "VATS segmentectomy". According to their corresponding authors, most of the studies examined here were from China, Japan, and the US. This order did not change in the rankings based on single-country and multi-country publications (Figure 3/D).

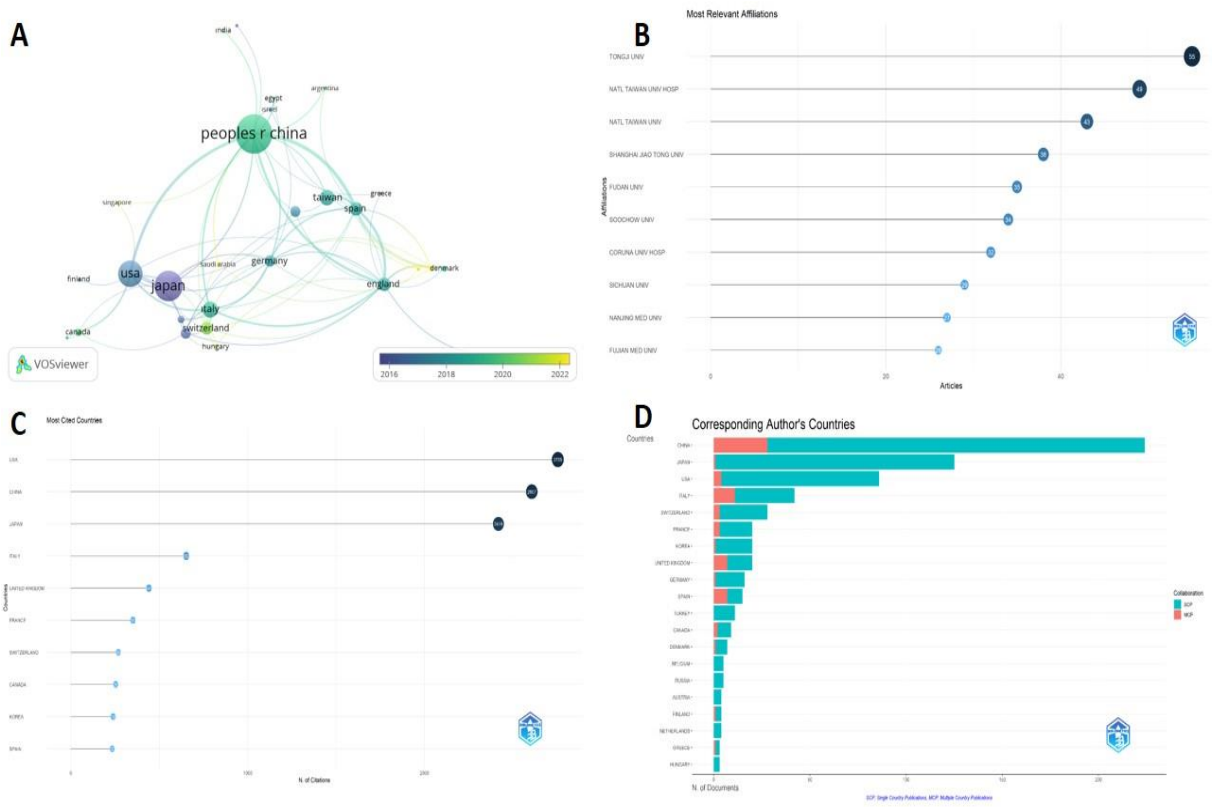

Figure 3: Analysis of national publications in VATS segmentectomy. **A)** Collaboration WorldMap, **B)** Top 10 most relevant affiliation, **C)** Top 10 most cited countries **D)** Corresponding author's countries.

DISCUSSION

Bibliometric studies have an important place in the revelation of developments in a scientific field, the productivity of scientific journals, and the impact of publications. It is known that the bibliometric method has been used in many fields in medical sciences. A bibliometric analysis of the 40 most-cited articles comparing VATS and robotic thoracic surgery in lung cancer cases was reported (8). In addition to this, although bibliometric analyses in the fields of both cancer and segmentectomy are available (9),

no such study on VATS segmentectomy could be found. The adoption of more advanced thoracoscopic surgical techniques in the last 20 years has led to a novel interest in the thoracoscopic approach in thoracic anatomic segmentectomy (VATS). Nevertheless, there is no precise consensus on the indications of VATS segmentectomy, and its role as the definitive treatment of small lesions and early-stage lung cancer is debated. It is also a more complicated procedure in comparison to standard VATS lobectomy, and the need for the surgeon to have experience in this approach is emphasized (10).

Considering the publications in this field in different countries on the continental level, Asia came first, followed by Europe and the Americas. The most productive countries were respectively China, Japan, and the US. China was discovered to have strong connections to the US, Japan, and the UK, while Denmark and Switzerland also joined the race in 2020 onward. The rapid growth of electronics and technology companies in Japan and China in the last 50 years, as well as the reflections of this growth in the field of health, may have been effective in these results (11).

According to WoS data, the first two studies published on this topic in 1996 were a study of experiences of VATS anatomic lung resections in two large hospitals in Hong Kong by Yim et al. in the journal CHEST (12) and a study on the evaluation of respiratory muscle strength following VATS by Nomori et al. in the European Journal of Cardio-Thoracic Surgery (13). The number of publications has gained considerable momentum in the last 30 years, and the highest number of publications in the field was in 2022.

Citation analysis is the most prevalently used bibliometric analysis method that allows the measurement of the impact factor of journals. It was seen that there were 11,093 citations containing the keywords that were used in relation to the topic examined in this study. The highest number of publications was in 2022. The most frequently cited study was the one conducted by Schuchert et al. titled

“Anatomic segmentectomy in the treatment of stage I non-small cell lung cancer”, which was cited 254 times. In the article published in 2007, it was stated that anatomic segmentectomy could be performed with an open approach or the VATS approach safely, and VATS was an advantageous method (14). Additionally, with their studies conducted in recent years, Gonzalez-Ravas D. had very strong authorship connections. The journal that received the highest number of citations was Ann Thorac Surg, with 3193 citations.

Considering the changes in the usage of the keyword “VATS segmentectomy”, it was seen that studies in 2023 focused on “3D reconstruction” and “long-term survival in situs inversus totalis”. In the word cloud created in this study, a strong connection was found between the terms “VATS segmentectomy” and “lung cancer”. The times when these two terms emerged were similar, and the terms associated with these in recent years were “resection”, “lobectomy”, “outcomes”, and “robot-assisted thoracic surgery”.

Despite the increasing popularity of VATS segmentectomy, it is emphasized that its oncological indications in lung cancer cases will remain controversial until long-term outcomes are reported.

In recent times, robotics has been involved in thoracic surgery, and this method was named RATS. While it was seen in our analyses that the RATS approach was not very popular, the number of reports on the surgical outcomes of segmentectomies in this field is increasing. It is observed that researchers are discussing important outcomes of both VATS and RATS such as their short- and long-term benefits and costs (15). In our analyses, there were weak connections between VATS and RATS, and the review of the relevant literature revealed the need to clarify the issue.

CONCLUSION

It was determined that the usage of the term VATS segmentectomy has increased in the last 20 years, the interest in the field has evolved toward hybrid VATS and robotic surgery, the method had advantages, but its outcomes are still a subject of debate.

DESCRIPTIONS

No financial support.

No conflict of interest.

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Acta Medica Ruha
International Journal of Medicine and Health Sciences
E-ISSN: 2980-1184

ORIGINAL ARTICLE
Volume:2 Issue:3 Year:2024
https://doi.org/10.5281/zenodo.13378662

Retrospective Evaluation of Patients Who Admitted to the Emergency Department Due to Pneumothorax

Pnömotoraks Nedeni ile Acil Servise Başvuran Hastaların Retrospektif Olarak Değerlendirilmesi

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ABSTRACT

Introduction: Spontaneous pneumothorax is a severe life-threatening situation, especially in the elderly and individuals with comorbid diseases.
Objective: In this research, we aimed to elucidate the demographic and clinical characteristics of spontaneous pneumothorax cases in a retrospective manner.
Method: Patients (n=325) diagnosed with pneumothorax at our institution's Emergency Medicine Clinic were included in this retrospective analysis. The patient data were obtained from patient files and data in the hospital automation system. The patients' admission complaints, comorbidities, laboratory findings, imaging results, treatment methods, and hospitalization or discharge were recorded.
Results: Within the scope of the study, 325 patients aged between 1 and 90 were included in the evaluation. Patients were divided into two groups according to age: <40 years (n=163) and ≥40 years (n=162). A statistically significant difference was observed in the distribution of malignancy, diabetes mellitus (DM), hypertension (HT), chronic obstructive pulmonary disease (COPD), chronic kidney failure (CKF), primary spontaneous pneumothorax (PSP), secondary spontaneous pneumothorax (SSP), traumatic pneumothorax, falls, rib fracture, thoracotomy and outcomes ($p< 0.05$). While mortality was observed in a total of 25 patients, a statistically significant difference was found in the ≥40-years-old patient group (n=21) compared to the <40-years-old patient group (n=4). The diagnosis of PSP was statistically significantly higher in the <40 age group (n=119) than in the ≥40 age group (n=79). It was observed that the hemoglobin, lymphocyte count, and estimated glomerular filtration rate (eGFR) in patients younger than 40 were higher than in patients older than 40.
Conclusion: As a result, spontaneous pneumothorax is a clinical entity that is treated according to age, clinical condition, and underlying causes, is often benign when seen in young people, and is life-threatening if not urgently intervened in elderly patients with limited pulmonary reserve. Mortality and morbidity can be prevented with timely diagnosis and appropriate treatment.

Keyswords: Spontaneous Pneumothorax, Thoracotomy, Video-Assisted ThoracicSurgery (VATS), Chronic Obstructive Pulmonary Disease (COPD), Mortality.

ÖZET

Giriş: Spontan pnömotoraks özellikle yaşlılarda ve eşlik eden hastalığı olan bireylerde yaşamı tehdit eden ciddi bir durumdur.
Amaç: Bu çalışmaya spontan pnömotoraks olgularının demografik ve klinik özelliklerini retrospektif olarak aydınlatmayı amaçladık.
Yöntem: Bu retrospektif analize kurumumuz Acil Tıp Kliniğinde pnömotoraks tanısı alan hastalar (n=325) dahil edildi. Hasta verileri hasta dosyalarından ve hastane otomasyon sistemindeki verilerden elde edildi. Hastaların başvuru şikayetleri, ek hastalıkları, laboratuvar bulguları, görüntüleme sonuçları, tedavi yöntemleri, yatış veya taburculuk durumları kaydedildi.
Bulgular: Araştırma kapsamında yaşları 1 ile 90 arasında değişen 325 hasta değerlendirmeye alındı. Hastalar yaşlarına göre <40 yaş (n=163) ve ≥40 yaş (n=162) olmak üzere iki gruba ayrıldı. Malignite, diyabetes mellitus (DM), hipertansiyon (HT), kronik obstrüktif akciğer hastalığı (KOAH), kronik böbrek yetmezliği (KBY), primer spontan pnömotoraks (PSP), sekonder spontan pnömotoraks (SSP), travmatik pnömotoraks, düşme, kaburga kırığı, torakotomi ve sonlanımlarının dağılımında istatistiksel olarak anlamlı farklılık gözlendi ($p< 0,05$). Toplam 25 hastada mortalite gözlenirken, ≥40 yaş hasta grubunda (n=21) <40 yaş hasta grubuna (n=4) göre istatistiksel olarak anlamlı fark bulundu. Spontan pnömotoraks tanısı <40 yaş grubunda (n=119), ≥40 yaş grubuna (n=79) göre istatistiksel olarak anlamlı derecede yüksekti. 40 yaş altı hastalarda hemoglobin, lenfosit sayısı ve tahmini glomerüler filtrasyon hızının (eGFR) 40 yaş üstü hastalara göre daha yüksek olduğu görüldü.

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Received: 13.05.2024, Accepted: 25.08.2024, Published Online: 20.09.2024
Cited: Çatal F, et al. Retrospective Evaluation of Patients Who Admitted to the Emergency Department Due to Pneumothorax. Acta Medica Ruha. 2024;2(3):166-172. https://doi.org/10.5281/zenodo.13378662

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Sonuç: Sonuç olarak spontan pnömotoraks yaşa, klinik duruma ve altta yatan nedenlere göre tedavi edilen, gençlerde görüldüğünde sıklıkla benign seyreden, akciğer kısıtlılığı olan yaşlı hastalarda acil müdahale edilmediği takdirde yaşamı tehdit eden bir klinik tablodur. Zamanında tanı ve uygun tedavi ile mortalite ve morbidite önlenebilir.

Anahtar Kelimeler: Spontan Pnömotoraks, Torakotomi, Video Yardımlı Göğüs Cerrahisi (VATS), Kronik Obstrüktif Akciğer Hastalığı (KOAH), Mortalite.

INTRODUCTION

Spontaneous pneumothorax is the accumulation of air in the pleural space without trauma and subsequent lung collapse. The occurrence of this condition in a healthy individual is referred to as primary spontaneous pneumothorax (PSP). If there is an underlying lung disease, it is referred to as secondary spontaneous pneumothorax (SSP). Risk factors for spontaneous pneumothorax include male gender, smoking, tall height, low body weight, and underlying lung disease. Increased neutrophil and macrophage activation in lung tissue damages elastic fibers, and bullous lesions may develop. An imbalance between protease-antiprotease and oxidant-antioxidant systems may play a role in the etiology. Sudden shortness of breath, accompanying chest pain, palpitations, and productive cough complaints may be observed. Physical examination is diagnostic (1). Management of spontaneous pneumothorax patients includes close observation, oxygen therapy, a conservative approach, aspiration, percutaneous catheter drainage, tube thoracostomy, video thoracoscopic surgery, and axillary or lateral thoracotomy treatments (2).

Patients usually have pleuritic-type chest pain or acute dyspnea on the same side. Chest pain may be very superficial or sharp. Even if pneumothorax is not treated, the pain subsides within 24 hours (3). Physical examination is normal in small pneumothoraces below 15%. Large spontaneous pneumothorax causes a decrease in vital capacity and a decrease in the alveolar-arterial oxygen gradient. Although hypoxia occurs, hypercapnia does not develop because lung function tests are generally normal. Tachycardia is the most common physical examination finding. In large pneumothorax, that side of the chest does not participate in breathing, hyperresonance is detected on percussion, and breath sounds are decreased or absent. A heart rate above 135/min, hypotension, or cyanosis should suggest tension pneumothorax (4).

In a meta-analysis of 11 series including patients who were only monitored due to PSP and treated with needle aspiration or tube thoracostomy, the recurrence rate was reported to be between 6-52%. Most recurrences occur between the first 6-24 months. This possibility is higher in cases with radiological pulmonary fibrosis, smoking habit, asthenic type, and pneumothorax occurring at a young age (5).

Pulmonary tuberculosis once again emerges as an essential factor in SSP. In a study conducted in Spain, tuberculosis was reported to be 23% of the causes of SSP (6). Pneumocystis carinia pneumonia, which develops in HIV (+) patients, is reported as one of the most common causes of pneumothorax in various countries and is associated with high mortality. Pneumothorax is reported at a rate of 25% in eosinophilic granuloma cases and 80% in lymphangiomyomatosis cases. SSP is common in older ages with the increasing frequency of chronic obstructive pulmonary disease. These patients have shortness of breath due to the underlying lung disease, even if the pneumothorax is not severe. Patients usually have pain on the same side. Hypoxia, hypercapnia, and hypotension may occur. The probability of recurrence in SSP is between 39-47% (7).

Within the scope of this research, we aimed to elucidate the demographic and clinical characteristics of spontaneous pneumothorax cases in a retrospective manner.

METHOD

Patients (n=325) diagnosed with pneumothorax at Sakarya Training and Research Hospital Emergency Medicine Clinic between January 2020 and December 2021 were included in this retrospective analysis. The patient data were obtained from patient files and data in the hospital automation system. The patients' admission complaints, comorbidities, laboratory findings, imaging results, treatment methods, and hospitalization or discharge were recorded.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval was granted from our institution on 31/01/2023 with protocol number E-71522473-050.01.04-216240-27. As this was retrospective research, no informed consent was obtained from participants.

Statistical Analysis

Patient data collected within the scope of the study were analyzed with the IBM Statistical Package for the Social Sciences (SPSS) for Windows 26.0 (IBM Corp., Armonk, NY) package program. Frequency and percentage for categorical data and continuous data were given as descriptive values. For comparisons between groups, the "Mann Whitney U Test" was used for two groups, and the "Pearson Chi-Square Test" was used to compare categorical variables. The results were considered statistically significant when the p-value was less than 0.05.

RESULTS

Table 1. Distribution of Demographic and Clinical Characteristics of Patients

Variables	Total (n=325)	<40 Age (n=163)	≥40 Age (n=162)	p-value
	n (%) or Median (IQR)	n (%) or Median (IQR)	n (%) or Median (IQR)	
Age (year)	39.00 (32.00)	25.00 (10.00)	57.00 (20.75)	**<0.001**
Comorbidity				
Malignancy	20 (6.2)	5 (3.1)	15 (9.3)	**0.02**
DM	40 (12.3)	4 (2.5)	30 (22.2)	**<0.001**
HT	50 (15.4)	5 (3.1)	45 (27.8)	**<0.001**
COPD	45 (13.8)	3 (1.8)	42 (25.9)	**<0.001**
Palsy	6 (1.8)	2 (1.2)	4 (2.5)	0.448
CKF	42 (12.9)	5 (3.1)	37 (22.8)	**<0.001**
Type of Pneumothorax				
PSP	198 (60.9)	119 (73)	79 (48.8)	**<0.001**
SSP	7 (2.2)	0 (0)	7 (4.3)	**0.007**
Traumatic pneumothorax	120 (36.9)	42 (25.8)	78 (48.1)	**<0.001**
Type of Trauma				
Falls	74 (22.8)	18 (11)	56 (34.6)	**<0.001**
Traffic accident	29 (8.9)	15 (9.2)	14 (8.6)	0.859
Penetrating injuries	7 (2.2)	3 (1.8)	4 (2.5)	0.723
Blunt injuries	3 (0.9)	2 (1.2)	1 (0.6)	1.000
Clinical Finding				
Sternum fracture	7 (2.2)	2 (1.2)	5 (3.1)	0.283
Rib fracture	92 (28.3)	30 (18.4)	62 (38.3)	**<0.001**
Pneumothorax				
Left	151 (46.5)	82 (50.3)	69 (42.6)	0.163
Right	184 (56.6)	87 (53.4)	97 (59.9)	0.237
Bilateral	10 (3.1)	6 (3.7)	4 (2.5)	0.750
Hemothorax	53 (16.3)	23 (14.1)	30 (18.5)	0.282
Pneumomediastinum	9 (2.8)	5 (3.1)	4 (2.5)	1.000
Type of Treatment				
Thorax tube	272 (83.7)	132 (81)	140 (86.4)	0.185
Thoracotomy	26 (8)	19 (11.7)	7 (4.3)	**0.015**
Refusal of treatment	7 (2.2)	2 (1.2)	5 (3.1)	0.283
Hospitalization Period (day)	6.00 (5.00)	6.00 (6.00)	6.00 (5.00)	0.112
Outcome				
Intensive care	95 (29.2)	30 (18.4)	65 (40.1)	**<0.001**
Death	25 (7.7)	4 (2.5)	21 (13)	**<0.001**
Discharge	292 (89.8)	156 (95.7)	136 (84)	**<0.001**

IQR: Interquartile range; DM: Diabetes mellitus; HT: Hypertension; COPD: Chronic obstructive pulmonary disease; CKD: Chronic kidney disease; PSP: Primary spontaneous pneumothorax; SSP: Secondary spontaneous pneumothorax.

Within the scope of the study, 325 patients aged between 1 and 90 were included in the evaluation. Patients were divided into two groups according to age: <40 years (n=163) and ≥40 years (n=162). The distribution of demographic and clinical findings of the patients according to their age groups is denoted in Table 1. A statistically significant difference was observed in the distribution of malignancy, diabetes mellitus (DM), hypertension (HT), chronic obstructive pulmonary disease (COPD), chronic kidney failure (CKF), PSP, SSP, traumatic pneumothorax, falls, rib fracture, thoracotomy and outcomes ($p< 0.05$). While there was no statistical difference between the two age groups in terms of tube thoracostomy application, it was determined that thoracotomy application was statistically more common in the < 40-years-old patient group (n=19) than in the ≥ 40-years-old patient group (n=7). While death was observed in a total of 25 patients, a statistically significant difference was found in the ≥40-years-old patient group (n=21) compared to the <40-years-old patient group (n=4). The diagnosis of PSP was statistically significantly higher in the <40 age group (n=119) than in the ≥40 age group (n=79). The diagnosis of traumatic pneumothorax is statistically significantly higher in the ≥40 age group than in the <40 age group (n=78, n=42, respectively).

The rates of PSP and thoracotomy in patients younger than 40 years of age were higher than in patients older than 40 years, the rates of patients older than 40 years were higher than those of patients younger than 40 years in other significant variables.

The distribution of laboratory measurements of the patients according to age groups is indicated in Table 2. When the table was examined, a statistically significant difference was found between the two groups in all laboratory measurements except international normalized ratio (INR) and platelet (PLT) measurements ($p <0.05$).

Table 2. Distribution of Laboratory Findings of Patients

Laboratory Parameters	Total (n=325)	<40 Age (n=163)	≥40 Age (n=162)	p-value
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	
Wbc (10^3/µL)	10.40 (5.69)	**9.70 (5.51)**	**11.23 (5.86)**	**0.008**
Hemoglobin (mg/dL)	14.00 (2.30)	**14.40 (1.82)**	**13.40 (2.10)**	**<0.001**
Neutrophil (10^3/µL)	7.14 (5.65)	**6.05 (4.60)**	**7.81 (5.41)**	**<0.001**
Lymphocyte (10^3/µL)	2.05 (1.43)	**2.08 (1.41)**	**1.85 (1.50)**	**0.020**
Platelet (10^3/µL)	223.00 (75.00)	219.00 (70.50)	228.00 (85.25)	0.899
PLR	107.69 (78.72)	**104.38 (71.87)**	**112.03 (104.66)**	**0.036**
NLR	3.22 (4.83)	**2.73 (3.69)**	**4.18 (6.37)**	**<0.001**
Crp (mg/L)	7.55 (29.54)	**2.60 (6.48)**	**18.64 (52.49)**	**<0.001**
Troponin (ng/L)	2.00 (10.50)	**0.95 (2.85)**	**5.90 (17.74)**	**<0.001**
INR	1.17 (0.16)	1.15 (0.16)	1.18 (0.17)	0.426
eGFR (mL/min/1.73m^2)	114.00 (33.11)	**125.27 (17.37)**	**98.09 (28.41)**	**<0.001**
Lactate (mmol/L)	1.80 (1.10)	**1.50 (0.90)**	**1.90 (1.29)**	**0.004**

IQR: Interquartile range; Wbc: White blood cell; PLR: Platelet-to-lymphocyte ratio; NLR: Neutrophil-to-lymphocyte ratio; Crp: C-reactive protein; INR: International normalized ratio; eGFR: Estimated glomerular filtration rate.

A statistically significant difference was detected between the two patient groups in terms of laboratory parameters such as hemoglobin, leukocyte, lymphocyte, C-reactive protein, platelet/lymphocyte ratio (PLR), troponin, neutrophil/lymphocyte ratio (NLR), estimated glomerular filtration rate (eGFR), lactate, and neutrophil count. While it was observed that the hemoglobin, lymphocyte count, and eGFR in patients younger than 40 were higher than in patients older than 40, in other significant variables, the measurements of patients older than 40 were higher than in patients younger than 40.

DISCUSSION

The incidence of spontaneous pneumothorax is reported as 7.4-28/100.000 per year for men and 1.2-6/100.000 per year for women. The majority of cases consist of PSP cases. Only about 10% are SSP cases. The most common cause of SSP development is COPD. While the recurrence rate is given as 31% for PSP, it is reported as 43% for SSP (8). The development of severe expiratory obstruction in patients and the rupture of a subpleural bulla are considered possible etiologies. The disease manifests itself with symptoms ranging from mild decrease in breath sounds to severe respiratory failure. While PSP is more common in young people, SSP is seen in middle-aged and elderly patients (9). In our study, the diagnosis of PSP was statistically significantly higher in the <40 age group (n=119) than in the ≥40

age group (n=79). The diagnosis of traumatic pneumothorax is statistically significantly higher in the ≥40 age group than in the <40 age group (n=78, n=42, respectively).

Air leakage lasts longer in patients where lung vascularity is reduced due to chronic disease. The risk of infection and empyema is higher. Surgery is not recommended before treatment of active infection in this group of patients. However, success may not be achieved with observation or aspiration treatments. The first choice should be tube thoracostomy (10). It has been reported that each pneumothorax attack can increase mortality by 4 times in patients with COPD. In our study, while death was observed in a total of 25 patients, a statistically significant difference was found in the ≥40-year-old patient group (n=21) compared to the <40-year-old patient group (n=4).

If pleurodesis is not performed, pneumothorax attacks occur again in 40-50% of patients (11). In our study, a statistically significant difference was observed in the distribution of malignancy, DM, HT, COPD, CKF, PSP, SSP, traumatic pneumothorax, falls, rib fracture, thoracotomy and outcomes ($p< 0.05$).

Treatment for SSP is more aggressive than for the primary disease. The American College of Chest Physicians guideline recommends applying tube thoracostomy when first encountered and performing pleurodesis to prevent recurrence (12). Many studies have been conducted on the risk factors in spontaneous pneumothorax cases, and many risk factors have been identified. However, it is not possible to predict relapse. Therefore, to minimize the risk of recurrence in patients with SSP, thoracoscopic surgical methods or open surgical intervention are recommended in the first pneumothorax attack if clinically appropriate (13). In previous literature, the relapse rate was 16-52%, depending on the type of treatment after the first attack. Relapses are generally seen between the first 6-24 months, and the relapse rate within the first four years is 54% (14). While it is 20-30% after the attack, it is 50% after the second attack and over 80% after the third attack (2,8). The rate of spontaneous pneumothorax development in the opposite hemithorax is 51.5% (11). Chemical pleurodesis is applied to reduce recurrences after the first attack or when recurrence occurs. However, the recurrence rate in patients who underwent pleurodesis is around 20% (12).

Guo et al. reported that the recurrence rate in cases with SSP was higher than PSP (26-50% versus 12-27%) (15). Smith et al. detected blebs and/or bullae on CT in 56% of the cases with spontaneous pneumothorax, and 44% reported no pathology (16). Ouanes-Besbes et al. detected blebs and/or bullae on CT that could not be seen on direct chest radiography in 72.5% of patients with PSP and showed that most of these lesions were located at the apices and were bilateral in 66% of the cases (17). While there are studies stating that the diameter and location of the bulla do not affect recurrence, there are also studies reporting that detecting pathology on CT is important in predicting recurrence (18, 19).

As a surgical treatment, VATS, limited thoracotomy, or axillary thoracotomy are preferred depending on the surgical conditions and the patient's condition (20). In our study, the rates of PSP and thoracotomy in patients younger than 40 years of age were higher than in patients older than 40 years, the rates of patients older than 40 years were higher than those of patients younger than 40 years in other significant variables. In some publications, it has been reported that VATS was preferred due to the low morbidity, mortality, and recurrence rate after the first attack. In cases where bleb and/or bulla were detected on CT, significant intrathoracic adhesions were observed, making VATS difficult to perform. Freixinet et al. reported that they did not detect any difference between the two methods regarding surgical time, postoperative pain and complications, and hospital stay. They even observed recurrence in two patients who underwent VATS (21). In our analysis, while there was no statistical difference between the two age groups in terms of tube thoracostomy application, it was determined that thoracotomy application was statistically more common in the < 40-year-old patient group than in the ≥ 40-year-old patient group.

The recurrence rate after surgical treatment is 0-6.8% in those who underwent thoracotomy or axillary thoracotomy and 3-13% in those who underwent VATS. The high recurrence rate in VATS was due to less tissue trauma and less formation of pleural adhesions. In cases where video-assisted thoracoscopic surgery was performed, it would be helpful to perform pleural abrasion additionally. Many studies have been conducted on the risk factors in spontaneous pneumothorax, and many risk factors have been identified, but no method has been developed to predict recurrence. To minimize the risk of recurrence,

surgical options other than tube thoracostomy (axillary thoracotomy, VATS, etc.) should be considered at the first pneumothorax attack if the patient's clinical condition is appropriate, considering the risk factors (22).

CONCLUSION

As a result, spontaneous pneumothorax is a clinical entity that is treated according to age, clinical condition, and underlying causes, is often "benign" when seen in young people, and is life-threatening if not urgently intervened in elderly patients with limited pulmonary reserve. Mortality and morbidity can be prevented with timely diagnosis and appropriate treatment. Surgical treatment methods are quite successful in the treatment of recurrent spontaneous pneumothorax.

DESCRIPTIONS

No financial support.

No conflict of interest.

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Acta Medica Ruha
International Journal of Medicine and Health Sciences
E-ISSN: 2980-1184

ORIGINAL ARTICLE
Volume:2 Issue:3 Year:2024
https://doi.org/10.5281/zenodo.13384258

Investigation of Risk Factors Related to The Use of Non-Prescription Proton Pump Inhibitors in Patients Referred to A Tertiary Health Care Institution

Üçüncü Basamak Sağlık Kuruluşuna Başvuran Hastalarda Reçetesiz Proton Pompa İnhibitörü Kullanımına Ait Risk Faktörlerin İncelenmesi

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ABSTRACT

Introduction: Proton pump inhibitors are benzamidazole derivative drugs that act by inhibiting gastric acid secretion controlled by parietal cells in the gastric epithelium through neuroendocrine pathways. Today, they are widely used worldwide for the treatment of all gastric acid-related diseases, especially gastroesophageal reflux disease.
Objective: It is known that proton pump inhibitors, which are most commonly prescribed to patients in our society, have recently been prescribed for inappropriate and unnecessary indications as well as being used without a prescription. Within the scope of rational drug use, correct and effective use of drugs in this group is important. The aim of this study was to investigate the risk factors for the use of non-prescription proton pump inhibitors in outpatients admitted to a tertiary health care institution.
Method: In this cross-sectional and analytical study, a questionnaire was administered face-to-face by the investigators to 300 volunteer patients who applied to the Internal and Surgical Outpatient Clinics of Balıkesir Atatürk City Hospital.
Results: It was found that 115 (38.3%) and 26 (8.7%) of the participants were male. It was found that 283 (94.3%) of the cases were prescription drugs, and when the reasons for use were analysed, it was determined that 116 (38.7%) were multiple drug use and 125 (41.7%) were dyspepsia in the first two. It was determined that an increase in age decreased the risk of using non-prescription proton pump inhibitors at a statistically significant level, and a higher level of education increased the risk of using non-prescription proton pump inhibitors 5.791 times at a statistically significant level.
Conclusion: In this study, it was observed that the use of proton pump inhibitors was extremely common in outpatients admitted to tertiary health care institutions. Off-label prescription use of these drugs as well as over-the-counter use was found to be high. For this reason, it is obvious that new multicenter studies should be conducted in order to examine the factors affecting the use of over-the-counter medication within the scope of rational drug use.

Keyswords: Proton Pump Inhibitor, Use Of Non-Prescription Drugs, Rational Drug Use.

ÖZET

Giriş: Proton pompa inhibitörleri mide epitelindeki parietal hücreler tarafından nöroendokrin yollarla kontrol edilen gastrik asit salınımını inhibe ederek etki eden benzamidazol türevi ilaçlardır. Günümüzde tüm dünyada, başta gastroözofageal reflü hastalığı olmak üzere gastrik asitle ilişkili tüm hastalıklarda yaygın olarak tedavi amaçlı kullanılmaktadır.
Amaç: Toplumuzda hastalara en çok reçete edilen proton pompa inhibitörlerin son zamanlarda uygun olmayan gereksiz endikasyonlar nedeniyle reçete edildiği gibi reçetesiz de kullanımının olduğu bilinmektedir. Akılcı ilaç kullanımı kapsamında bu gruptaki ilaçlarının doğru ve etkin kullanımı önem arz etmektedir. Bu çalışmada üçüncü basamak sağlık kuruluşuna ayaktan başvuran hastalardaki reçetesiz proton pompa inhibitörü kullanımına ait risk faktörlerin incelenmesi amaçlanmıştır.
Yöntem: Kesitsel ve analitik tipte olan bu çalışmada Balıkesir Atatürk Şehir Hastanesi dahili ve cerrahi polikliniklerine başvuran gönüllü 300 hasta katılım sağlanmış ve araştırıcılar tarafından yüz yüze soru-cevap şeklinde anket uygulanmıştır.
Bulgular: Çalışmaya katılanların 115'inin (%38,3) erkek olduğu, 26'sının (%8,7) olduğu bulundu. Vakaların 283'ünün (%94,3) ilaçların reçeteli olduğu, kullanım nedenlerine bakıldığında da 116'sının (%38,7) çoklu ilaç kullanımı, 125'inin (%41,7) dispepsi olarak ilk ikide tespit edildi. Yaş değerlerindeki artışın istatistiksel açıdan anlamlı seviyede reçetesiz proton pompa inhibitörü kullanma riskini azalttığı, eğitim seviyesinin yüksekliği istatistiksel açıdan anlamlı seviyede reçetesiz proton pompa inhibitörü kullanma riskini 5,791 kat arttırdığı tespit edilmiştir.
Sonuç: Yapılan bu çalışma ile üçüncü basamak sağlık kuruluşuna ayaktan başvuran hastalarda proton pompa inhibitör kullanımının son derece yaygın olduğu görülmüştür. Bu ilaçların endikasyon dışı reçeteli kullanımı olduğu gibi reçetesiz kullanımınında fazlaca olduğu tespit edilmiştir. Bu sebeple akılcı ilaç kullanımı kapsamında ileriye yönelik reçetesiz ilaç kullanımına etki eden faktörlerin incelenmesi amacıyla çok merkezli yeni çalışmaların yapılma zorunluluğu aşikadır.

Anahtar Kelimeler: Proton Pompa İnhibitörü, Reçetesiz İlaç Kullanımı, Akılcı İlaç Kullanımı.

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Received: 07.07.2024, Accepted: 28.08.2024, Published Online: 20.09.2024
Cited: Ergün U. Investigation of Risk Factors Related to The Use of Non-Prescription Proton Pump Inhibitors in Patients Referred to A Tertiary Health Care Institution. Acta Medica Ruha. 2024;2(3):173-178. https://doi.org/10.5281/zenodo.13384258
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INTRODUCTION

Proton pump inhibitors (PPIs) are benzamidazole derivative drugs that act by inhibiting gastric acid secretion controlled by neuroendocrine pathways in the parietal cells of the gastric epithelium. Currently, these widely used drugs are the most commonly prescribed group for the treatment of conditions such as peptic ulcer, gastroesophageal reflux disease, esophagitis, and functional dyspepsia (1). While their use is generally considered safe due to correct indications, long-term use of these drugs can lead to complications such as pneumonia, bone fractures, vitamin B12 and iron deficiency, gastric polyp development, and enterocolitis. Their use has further increased due to their strong effects in preventing gastrointestinal side effects of non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and other drugs used in the treatment of diseases such as atherosclerotic heart disease, osteoarthritis, and rheumatoid arthritis (2,3). Studies have reported that PPIs are among the most frequently prescribed medications in many health institutions and that their use without a prescription has also increased recently. Often, they are prescribed by various specialties for inappropriate and unnecessary indications (4). It has been observed that PPIs, which are used in an uncontrolled and increasingly frequent manner, can be obtained without a prescription by patients themselves, their relatives, or through other means. Therefore, the widespread use of over-the-counter PPIs has been noted, and few studies have examined the risk factors contributing to this situation. This widespread use is contrary to rational drug use principles, posing a significant economic burden on healthcare institutions and potential long-term adverse effects for patients. This study aims to analyze the main risk factors influencing the use of over-the-counter PPIs and ensure the correct and effective use of this drug group. The development of advanced methods to prevent the extensive prescription of PPIs, raising awareness among physicians regarding prescription practices, and increasing awareness were planned with this study.

METHODS

This cross-sectional and analytical study included 300 voluntary patients, aged between 18 and 80 years, of both genders who visited the internal medicine and surgical outpatient clinics of Balıkesir Atatürk City Hospital. The sample of the study consisted of patients using PPIs between December 2023 and February 2024. Informed consent forms were prepared in advance and provided to the patients, who were then informed about the study. The evaluation questionnaire, pre-determined for this study, was administered face-to-face in a question-and-answer format to patients who were mentally competent and consented to participate.

The survey collected demographic data (age, gender, marital status, education level, etc.), information on chronic diseases, the regularity of PPIs usage (in our study, appropriate use was defined as taking the medication approximately 30 minutes before meals and regularly once a day before symptoms began), whether the medication was prescribed by a physician, the specialty of the prescribing physician, the duration and indication for use, and the effectiveness of usage. The responses were recorded through the questionnaire form.

Statistical Analysis

The demographic and clinical characteristics of the cases evaluated in the study were examined using descriptive statistical analyses (e.g., numbers, percentages). Factors influencing the risk of using PPIs without a prescription or unnecessarily were analyzed using univariate and multivariate binary logistic regression analyses. The significance level for all analyses was set at $p<0.05$. The normal distribution of the data was checked using kurtosis and skewness values (±1.5). IBM SPSS 26.0 software was used to perform the analyses.

Ethics Committee Approval

Our study was approved by the Scientific Research Ethics Committee of Balıkesir Atatürk City Hospital with the decision dated 23/11/2023 and number 2023/11/75.

RESULTS

In the study, it was found that 115 (38.3%) of the patients using PPIs were male, 26 (8.7%) were single, 43 (14.3%) had deceased spouses, and 231 (77%) were married. Additionally, 16 (5.3%) were illiterate, 41 (13.7%) were literate, 86 (28.7%) had primary education, 40 (13.3%) had secondary education, 51 (17%) had high school education, and 66 (22%) had a university education. Regarding economic status, 3 (1%) were very well-off, 71 (23.7%) were well-off, 201 (67%) were average, and 25 (8.3%) were poor (Table 1).

Table 1. Demographic Characteristics of Cases Using PPIs

		n	%
Sex	Male	115	38.3
	Female	185	61.7
Marriage Status	Single	26	8.7
	Wife passed away	43	14.3
	Married	231	77.0
Education Status	No Literate	16	5.3
	Literate	41	13.7
	Primary School	86	28.7
	Middle School	40	13.3
	High School	51	17.0
	University	66	22.0
Economic Situation	Very good	3	1.0
	Good	71	23.7
	Little	201	67.0
	Bad	25	8.3
Smoker	Yes	74	24.7
	Nok	226	75.3
Alcohol Consumption	Yes	21	7.0
	No	279	93.0

It was found that 283 (94.3%) of the patients had PPIs prescribed. The reasons for PPIs use included polypharmacy in 116 (38.7%), dyspepsia in 125 (41.7%), gastritis in 4 (1.3%), peptic ulcer in 12 (4%), reflux in 27 (9%), gallstones in 1 (0.3%), and irritable bowel syndrome in 15 (5%). Among the patients, 163 (54.3%) occasionally paid attention to PPIs use, 105 (35%) paid attention, and 32 (10.7%) did not pay attention. It was found that 30 (10%) had previously been informed about PPIs use, and 5 (1.7%) experienced side effects from PPIs use.

Table 2. Factors Affecting The Risk of Over The Counter PPIs Use

				95%CI					95%CI	
	βa	p	OR	LL	UL	βb	p	OR	LL	UL
Age	**0.088**	**<0.001**	**0.916**	**0.880**	**0.953**	**-0.098**	**0.003**	**0.907**	**0.850**	**0.968**
Marriage Status	0.031	0.957	0.969	0.305	3.074	1.401	0.094	4.060	0.788	20.917
Education	**1.756**	**0.001**	**5.791**	**2.111**	**15.886**	0.325	0.626	1.385	0.374	5.132
Economic Situation	**1.328**	**0.009**	**3.773**	**1.399**	**10.173**	0.849	0.173	2.338	0.689	7.934
Smoker	0.545	0.300	1.725	0.615	4.838	-0.461	0.439	0.630	0.196	2.028
Alcohol Consumption	0.617	0.435	1.853	0.394	8.703	-0.002	0.998	0.998	0.180	5.532
Chronic Disease	**2.836**	**0.006**	**17.051**	**2.231**	**130.309**	1.660	0.128	5.260	0.620	44.612

a=Univariate Binary Logistic Regression Analysis, b= Multivariate Binary Logistic Regression Analysis.

Regarding the prescribing departments, it was found that 2 (0.7%) prescriptions came from emergency medicine, 45 (15%) from family medicine, 1 (0.3%) from neurosurgery, 1 (0.3%) from physical therapy, 15 (5%) from gastroenterology, 9 (3%) from general surgery, 6 (2%) from pulmonary diseases, 1 (0.3%) from ophthalmology, 148 (49.3%) from internal medicine, 37 (12.3%) from cardiology, 2 (0.7%) from otolaryngology, 4 (1.3%) from neurology, 1 (0.3%) from oncology, 12 (4%) from orthopedics, and 1 (0.3%) from psychiatry. It was found that 3 (1%) had asthma, 4 (1.3%) had COPD, 50 (16.7%) had diabetes, 78 (26%) had hypertension, 9 (3%) had hypothyroidism, 23 (7.7%) had coronary heart disease, and 6 (2%) had other clinical conditions.

According to univariate binary logistic regression analysis, an increase in age was found to statistically significantly reduce the risk of using PPIs without a prescription (p<0.001). Higher education level was found to statistically significantly increase the risk of using PPIs without a prescription by 5.791 times (p=0.001). Better economic status was found to statistically significantly increase the risk of using PPIs without a prescription by 3.773 times (p=0.009). Additionally, the absence of comorbidities was found to statistically significantly increase the risk of using PPIs without a prescription by 17.051 times (p=0.006) (Table 2).

Table 3. Factors Affecting The Risk of PPIs Use for Unnecessary Indication

				95%CI					95%CI	
	βa	p	OR	LL	UL	βb	p	OR	LL	UL
Age	**0.072**	**<0.001**	**1.074**	**1.053**	**1.095**	**0.050**	**<0.001**	**1.052**	1.027	1.077
Marriage Status	0.337	0.225	0.714	0.414	1.230	0.134	0.717	0.875	0.424	1.803
Education	**1.534**	**<0.001**	**0.216**	**0.105**	**0.443**	0.049	0.926	0.952	0.337	2.686
Economic Situation	0.690	0.019	0.502	0.282	0.893	0.401	0.306	0.670	0.311	1.444
Smoker	**1.483**	**<0.001**	**0.227**	**0.116**	**0.444**	0.997	0.029	0.369	0.151	1.902
Alcohol Consumption	0.749	0.155	0.473	0.168	1.328	0.982	0.157	2.669	0.686	10.393
Chronic Disease	**1.825**	**<0.001**	**0.161**	**0.096**	**0.272**	**1.365**	**<0.001**	**0.255**	0.143	0.457

a=Univariate Binary Logistic Regression Analysis, b= Multivariate Binary Logistic Regression Analysis.

According to univariate binary logistic regression analysis, an increase in age was found to statistically significantly increase the risk of unnecessary PPIs use by 1.074 times (p<0.001). Higher education level was found to statistically significantly reduce the risk of unnecessary PPIs use (p<0.001). The absence of comorbidities was found to statistically significantly increase the risk of unnecessary PPIs use (p<0.001). According to multivariate binary logistic regression analysis, an increase in age was found to statistically significantly increase the risk of unnecessary PPIs use by 1.052 times, while the absence of comorbidities was found to statistically significantly decrease the risk (p<0.001) (Table 3).

DISCUSSION

The frequency of PPIs usage is increasing, and numerous studies have been conducted on this topic. When examining the demographic data of our cross-sectional study, it was shown that the rate of PPIs usage was higher in women at 61.7%. A study conducted by Susanna et al. in Sweden also demonstrated a higher rate of PPIs usage among women (5). Similarly, another study in the literature reported a higher proportion of PPIs usage in women (6). Thus, it is evident that the publications support our study in this regard.

When examining the clinical characteristics of patients using PPIs, it was found that 94.3% of the medications were prescribed, while 5.7% were obtained without a prescription. Many studies have shown that numerous medications are excessively and inappropriately prescribed for incorrect indications (4). PPIs are known to be among these medications. Despite various activities, announcements, and other efforts to reduce unnecessary PPIs usage and prescriptions in many communities, the prescription rates remain high. Therefore, various announcements and measures have been emphasized in our country regarding the importance of rational drug use, similar to antibiotics. Another study reported that the rate of PPIs usage without a physician's prescription was 14%. In a randomized cross-sectional study related to rational drug use conducted by Ozdinç et al., it was shown that 54% of participants used medication without any physician's prescription, and 26.5% consulted a family member, neighbor, or relative (7). In our study, the rate of PPIs usage without a physician's prescription was found to be 5.7%, which does not support the results of other studies. It is thought that the measures and practices organized in our society to prevent the use of non-prescription drugs within the scope of rational drug use may be related to our findings. Moreover, in our study, the increase in age was found to decrease non-prescription PPIs usage, while higher education level and better economic status were found to significantly increase non-prescription PPIs usage. The literature does not report studies showing the effect of better economic status and higher education level on PPIs usage. The notable finding in our study may be related to patients having both physician supervision and easy access to healthcare facilities. As in most studies, the rate of prescribed PPIs usage is high. A study by Ozdemir et al. reported a high rate of prescribed PPIs usage among elderly individuals, but it did not examine non-prescription PPIs usage (6).

It is known that many medications are inappropriately and unnecessarily prescribed for indications that are not suitable. PPIs are among these medications, as evidenced by their widespread prescription by various specialties. When examining the findings of our study, it was found that the prescription status of PPIs by specialty was in line with other studies, with internal medicine being the most common at 49.3%. Regarding the indications for use, it was shown that 41.7% of the usage was for dyspepsia and 38.7% for polypharmacy. According to current information, using PPIs for polypharmacy without gastrointestinal risk factors is an unnecessary indication and not a correct approach. However, the literature shows the widespread prevalence of inappropriate and unnecessary PPIs usage (8-12). Supporting our study, the findings of a randomized study by Chia et al. showed that the rate of off-label usage was 54.1%.

Other findings from our study showed that an increase in age was associated with an increase in unnecessary PPIs usage. Similarly, higher education level was found to reduce unnecessary PPIs usage. This can be explained by patients being more conscious and rational in their medication usage and remaining under physician supervision. Additionally, the absence of comorbidities was found to increase the risk of unnecessary PPIs usage.

In our study, the excessive use of PPIs due to unnecessary indications, and the increase in non-prescription PPIs usage associated with higher education level and better economic status, were found to be significant. To prevent this situation, individuals can be encouraged through accessible, easy, and up-to-date information campaigns within the scope of rational drug use. Since our study was single-centered and conducted with patients visiting outpatient clinics, it may not reflect the true values of non-prescription drug usage.

CONCLUSION

As a result, it is evident that PPIs therapy is frequently initiated for both necessary and unnecessary indications, followed by a significant amount of usage without physician supervision and without a prescription. This study demonstrated that the prevalence and inappropriate usage rate of these medications are in line with the results of other studies in the literature. However, there is a clear need for new multicenter studies to investigate the non-prescription use of PPIs and the factors influencing this behavior. Therefore, we believe that encouraging contributions to other actions within the scope of rational drug use are important.

DESCRIPTIONS

No financial support.

No conflict of interest.

Ethical Declaration: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval has been granted from our institution. Informed consent was obtained from all participants.

Acknowledgements: We sincerely thank Prof. Dr. Erkan CAGLAR for his unwavering support and for sharing his experience with us throughout the study.

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Acta Medica Ruha
International Journal of Medicine and Health Sciences
E-ISSN: 2980-1184

ORIGINAL ARTICLE
Volume:2 Issue:3 Year:2024
https://doi.org/10.5281/zenodo.13640193

Individual-Level Abortion Stigma and Affecting Factors in Women with Abortion Experience

Kürtaj Deneyimi Olan Kadınlarda Bireysel Düzeyde Kürtaj Damgalanması ve Etkileyen Faktörler

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ABSTRACT

Introduction: Women may decide to have an abortion for various reasons such as not wanting a child, maternal/fetal health problems, age, financial difficulties, family or partner pressure and lack of social support. Therefore, many women face psychological problems as a result of the individual-level abortion stigma they experience for sociodemographic and cultural reasons. Measuring individual-level abortion stigma is important in terms of preventing individual stigma and the health problems it may cause.
Objective: This study aims to determine the individual-level abortion stigma and the factors affecting this situation in women with abortion experience.
Method: The population of this cross-sectional study consisted of women who applied to the gynaecology and obstetrics outpatient clinic of a hospital. The sample consisted of 127 participants who met the inclusion criteria and agreed to participate in the study. Data were collected using Personal Information Form and Individual Level Abortion Stigma Scale.
Results: In the study, 77.2% of the participants were between the ages of 18-35, 89.0% had at least one living child, and 92.9% had 3 or less abortions. Among women, 95.3% of abortions were for medical reasons and 89.3% of these were due to fetal indication. The mean score of the Individual Level Stigma in Abortion Scale was 1.61±0.57. There was no significant relationship between socio-demographic and obstetric characteristics and scale score ($p>0.05$).
Conclusion: The individual-level abortion stigma was found to be at a moderate level in women with abortion experience. Individual-level abortion stigma was found to be independent of individual and environmental factors.

Keyswords: Abortion, Abortion Stigma, Individual Stigma.

ÖZET

Giriş: Kadınlar çocuk istememe, anne/fetüs sağlığı sorunları, yaş, maddi zorluklar, aile veya eş baskısı ve sosyal destek eksikliği gibi çeşitli nedenlerle kürtaj yaptırmaya karar verebilmektedir. Dolayısıyla birçok kadın sosyodemografik ve kültürel nedenlerle yaşadıkları bireysel düzeydeki kürtaj damgalanması sonucunda psikolojik sorunlarla karşılaşmaktadır. Bireysel düzeydeki kürtaj damgalanmasının ölçülmesi, bireysel damgalanmanın ve yol açabileceği sağlık sorunlarının önlenmesi açısından önemlidir.
Amaç: Bu çalışma, kürtaj deneyimi olan kadınlarda bireysel düzeyde kürtaj damgalanmasını ve bu durumu etkileyen faktörleri belirlemeyi amaçlamaktadır.
Yöntem: Bu kesitsel çalışmanın evrenini bir hastanenin kadın hastalıkları ve doğum polikliniğine başvuran kadınlar oluşturmuştur. Örneklem, dahil edilme kriterlerini karşılayan ve çalışmaya katılmayı kabul eden 127 katılımcıdan oluşmuştur. Veriler Kişisel Bilgi Formu ve Bireysel Düzeyde Kürtaj Damgalanma Ölçeği kullanılarak toplanmıştır.
Bulgular: Çalışmada katılımcıların %77,2'si 18-35 yaş aralığında, %89,0'ı yaşayan en az bir çocuğa sahip ve %92,9'u 3 veya daha az kürtaj yaptırmış. Kadınların %95,3'ü tıbbi nedenlerle kürtaj yaptırmış ve bunların %89,3'ü fetal endikasyon nedeniyle gerçekleşmiştir. Kürtajda Bireysel Düzeyde Damgalanma Ölçeği puan ortalaması 1,61±0,57'dir. Sosyo-demografik ve obstetrik özellikler ile ölçek puanı arasında anlamlı bir ilişki bulunmamıştır ($p>0,05$).
Sonuç: Kürtaj deneyimi olan kadınlarda bireysel düzeydeki kürtaj damgalanmasının orta düzeyde olduğu bulunmuştur. Bireysel düzeydeki kürtaj damgalanmasının bireysel ve çevresel faktörlerden bağımsız olduğu bulunmuştur.

Anahtar Kelimeler: Kürtaj, Kürtaj Damgalanması, Bireysel Damgalanma.

INTRODUCTION

Abortion is defined as the process of termination of pregnancy due to the woman's own will or a maternal/fetal medical necessity (1). According to World Health Organisation data, approximately 73 million elective abortions occur worldwide every year. 61% of unwanted pregnancies and 29% of all pregnancies result in elective abortion (2). According to Turkey Demographic and Health Survey 2018

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Received: 31.07.2024, Accepted: 03.09.2024, Published Online: 20.09.2024
Cited: Özgen HN, et al. Individual-Level Abortion Stigma and Affecting Factors in Women with Abortion Experience. Acta Medica Ruha. 2024;2(3):179-185. https://doi.org/10.5281/zenodo.13640193
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data, the level of abortion on demand in Turkey is 5.6% (3). Women are more likely to have abortions for individual and socio-cultural reasons such as not wanting children, financial difficulties (4), age (very young or advanced age), family or partner pressure, lack of social support, lack of readiness to become a mother (5), medical reasons related to fetal (6, 7), and maternal (5, 8, 9) health problems. Many women experience various types and levels of stigmatisation as a result of these decisions (10).

The term 'abortion stigma' is used to describe the negative attitudes and beliefs held by some people towards women who have undergone or are considering an abortion. These attitudes are often expressed in ways that mark women as inferior to the ideals of femininity (1).Women who have abortions are exposed to abortion stigma by their husbands/partners or family and social circles with different expressions such as irresponsible/careless (11). This type of stigmatisation, which also negatively affects social life, may cause women who have voluntary abortion to experience negative emotions such as loss of social status (12), being judged by family members or loved ones (13), guilt and shame (11, 14, 15). In addition, (1) women who associate the abortion experience with the rejection of the maternal role may define themselves as immoral (11) or consider themselves as sinful or evil due to their religious beliefs or cultural norms (16). All these negativities cause women who have abortion to experience individual abortion stigma (11-14, 16).

Individual abortion stigma is defined as the internalisation of perceived or experienced social stigma related to abortion, feelings of guilt or shame, or a response to other negative feelings about oneself (11, 16). Women's experience of individual stigma related to abortion varies depending on many factors such as age, education, religion/religiosity, race/ethnicity, social support resources or the time since the abortion (6, 10, 13, 14, 17, 18). Problems such as depression, post-traumatic stress disorder (6) and anxiety (19) can be seen in women who experience individual abortion stigma.

In the prevention of individual-level abortion stigma and the health problems it may cause, it is very important to measure the individual-level abortion stigma and to create social awareness by determining the factors affecting it. For this reason, the aim of this study was to determine the individual-level abortion and the factors affecting it in women with abortion experience in Şanlıurfa.

METHOD

Type of Research

The research is cross-sectional type.

Population and Sample of the Study

The study population comprised women who had applied to the the gynaecology and obstetrics outpatient clinic of a training and research hospital. In order to calculate the sample size, a pilot study was conducted with 30 women who applied to the hospital. The standard deviation of the individual level abortion stigma scale score obtained from the pilot study was 0.63, the margin of error was 0.11, and the required number of people was calculated as 127 with a 95% confidence level. The study was conducted between September 2023 and April 2024.

Criteria for inclusion in the sample;

- $\geq$ 18 years of age,

- Experienced an abortion within the last year and at least two weeks have passed since the abortion procedure,

- To know Turkish, and to have no communication problems related to language.

Exclusion criteria;

- Presence of a diagnosed psychiatric illness.

Ethics Committee Approval

The necessary permissions were obtained from the authors of the scale, the hospital where the study was conducted, the ethics committee of the Harran University Clinical Research Ethics Committee (dated 21.08.2023 and numbered HRU/23.15.19) and the provincial health directorate. The study was conducted in accordance with the principles set forth in the Declaration of Helsinki, and informed consent was obtained from all women who participated in the study.

Data Collection Tools

Data of the study were collected through the Personal Information Form, which was created by the researchers and included questions about the socio-demographic and obstetric characteristics of the participants, and the Individual Level Abortion Stigma Scale, using the face-to-face interview technique. The data collection forms were filled in by the literate participants themselves and by the researchers for the illiterate participants. Each interview lasted approximately 10-15 minutes.

Personal Information Form: It consists of a total of 11 questions, including 7 questions about the socio-demographic characteristics of the participants (age, educational status, marital status, language spoken, employment status, economic status, family type) and 4 questions about obstetric characteristics (number of living children, number of abortions/reason/time since last abortion).

Individual Level Abortion Stigma Scale (ILASS): It was developed by Cockrill et al to assess the individual internalised stigma perception of women with abortion experience (10). Turkish validity and reliability was performed by Çetinkaya et al (13). The Likert-type scale consists of 4 subscales and 20 items. The 8th, 9th and 10th items in the 'Isolation' subscale of the scale have a Likert-type evaluation between 0-3, and all other scale items have a Likert-type evaluation between 0-4. Scoring of the scale differs according to the subscales. The lowest-highest item score ranges that can be obtained from the total scale and its subscales are 0-3 for the 'Worries about Judgement' subscale, 0-3.5 for the 'Isolation' subscale and the 'Total Scale', and 0-4 for the 'Self-Judgement' and 'Community Condemnation' subscales. Item scores are summed and divided by the number of items, thus total scale and subscale scores are obtained. High scores obtained from the scale and subscales are evaluated as women perceiving themselves as highly stigmatised. The scoring of seven items of the scale (items 8, 9, 10, 11, 12, 13 and 15) are reversed. The Cronbach's alpha values of the scale were reported to be between 0.80-0.90 and the total scale Cronbach's alpha value was 0.88. There are no clear thresholds or cut-off points related to stigmatisation between the scale and subscales (10, 13). In this study, the Cronbach's alpha value of the scale was calculated to be 0.73.

Statistical Analysis

The data obtained from the participants were evaluated with the statistical package programme (SPSS 24.0). The dependent variable of the study is the total score of the participants from ILASS. The independent variables of the study are socio-demographic and obstetric characteristics of the participants.

In the analysis of the data, descriptive statistics, including percentage, mean, and standard deviation were used. The Mann Whitney U (MWU) test was used for univariate analyses in the comparison of two groups (age, educational level, marital status, employment status, family type, number of abortions, reason for abortion, and reason for fetal or maternal indications). The Kruskal-Wallis One-Way ANOVA test was used in the comparison of three or more groups that do not fit a normal distribution (most spoken language at home, income level). Spearman's correlation analysis was performed for ordinal data (age, number of living children, number of abortions, and time since last abortion) in groups that did not fit the normal distribution in the relationships between dependent and independent variables. The findings were interpreted at 95% confidence interval and $p<0.05$ significance level.

RESULTS

77.2% of the participants were between the ages of 18-35. 98.4% of the participants were married, 70.9% lived in a nuclear family, and 94.5% were not employed. 92.1% of the participants have completed primary education and below. 70.1% of the participants their income level as 'medium', and 78.7%

speak a language other than Turkish at home (63% Arabic, 15.7% Kurdish). The number of abortions of 92.9% of the participants was between 1-3, 95.3% of the abortions were for medical reasons, and 89.3% of these were due to fetal indications. In 70.1% of the participants, the time since the last abortion was 9-12 months (Table 1).

Table 1. Sociodemographic and Obstetric Characteristics and ILASS Scores of the Participant

			ILASS Score		
Characterics	**N**	**%**	**Median (Min-Max)**	**MWU***	**p**
Age (Years)					
Between 18-35	98	77.2	1.57 (0.40 - 3.30)	1362.000	0.735
Between 36-44	29	22.8	1.45 (0.60 - 3.15)		
Education level					
Primary school and ↓	117	92.1	1.55 (0-3)	1362.000	0.735
Secondary education and ↑	10	7.9	1.58 (1-2)		
Marital Status					
Married	125	98.4	1.55 (0.40 - 3.30)	32.000	0.072
Single	2	1.6	2.47 (2.05 - 2.90)		
Employment Status					
Yes	7	5.5	1.60 (1.20-2.60)	351.500	0.469
No	120	94.5	1.55 (0.40 - 3.30)		
Family Type					
Nuclear family	90	70.9	1.55 (0.40 - 3.30)	1651.500	0.943
Extended family	37	29.1	1.55 (0.85 - 2.90)		
Number of Abortions					
1- 3	118	92.9	1.52 (0.40 - 3.30)	518.000	0.903
4 and ↑	9	7.1	1.60 (0.60 – 3.15)		
Reason for Abortion					
Induced abortion	6	4.7	2.10 (1.20 - 2.60)	195.000	0.056
Fetal or maternal indications	121	95.3	1.50 (0.40 - 3.30)		
Reason for fetal or maternal indications (N=121)					
Maternal	13	10.7	1.55 (0.55 - 2.90)	708.500	1.000
Fetal	108	89.3	1.47 (0.4 - 3.30)		
Characterics	**N**	**%**	**Mean Rank**	**X^{2**}**	**p**
Most Spoken Language at Home					
Turkish	27	21.3	75.78	3.656	0.161
Kurdish	20	15.7	58.08		
Arabic	80	63.0	61.51		
Income Level					
High	11	8.7	63.09	1.244	0.537
Medium	89	70.1	61.99		
Low	27	21.3	70.98		
The Time Since the Last Abortion					
1-4 months	18	14.2	68.56	0.701	0.704
5-8 months	20	15.7	67.83		

*Mann Whitney U test, **Kruskal-Wallis test.

Age (MWU= 1362.000, p= 0.735), educational levels (MWU= 1362.000, p= 0.735), marital status (MWU= 32.000, p= 0.072), employment status (MWU= 351.500, p= 0.469), family type (MWU= 1651.500, p= 0.943), number of abortions (MWU= 518.000, p= 0.903) and reason for abortion (MWU= 195.000, p= 0.056), there was no significant difference between the mean ILASS scores (p>0.05). It was determined that there was no significant difference between the mean ILASS scores of the participants in terms of the most spoken language at home (X2= 3.656, p= 0.161), income level (X2= 1.244, p= 0.537) and time since the last abortion (X2= 0.701, p= 0.704) (p>0.05) (Table 1).

The mean ILASS score of the participants was 1.61±0.57. The mean scores of the subcales of the scale are 'Worries about Judgement' 0.82±0.79, 'Isolation' 2.28±0.94, 'Self-Judgement' 1.75±1.12 and 'Community Condemnation' 1.99±1.40, respectively (Table 2).

There was no significant difference (p>0.05) between the participants' age, number of living children, number of abortions and the time since the last abortion and ILASS score (Table 3).

Table 2. Women's ILASS Scores

Subscales	ILASS Score	
	Mean±SD	Range
Worries about Judgment Subscale	0.82±0.79	0-3
Isolation Subscale	2.28±0. 94	0-3.5
Self-judgment Subscale	1.75±1.12	0-4
Community Condemnation Subscale	1.99±1.40	0-4
Scale Total Score	1.61±0.57	0-3.5

Table 3. Correlation of Some Participants' Characteristics and ILASS Scores (N=127)

Characterics	ILASS Score		
	n	rho	p
Age (Years)	127	-.132	0.139
Number of Living Children	127	-.062	0.490
Number of Abortions	127	.045	0.616
Time since Last Abortion (Months)	127	-.059	0.510

DISCUSSION

In this study, which investigated the individual-level abortion stigma in women with abortion experience, it was determined that women's individual-level abortion stigma was at a moderate level (1.61±0.57). The mean ILASS score (1.46±0.56) obtained by Çetinkaya et al (13) in their study in Turkey and the mean score (1.59±0.60) obtained by Belfrage et al in their study in Mexico are compatible with our study (14). Li et al reported that the individual-level abortion stigma score in women who had abortion due to fetal indication in China was at a moderate level (1.49±0.60) (7). In Germany, Hanschmidt et al reported that women who thought that the chance of survival of the fetus was low experienced lower individual-level abortion stigma than those who did not (6). The results of our study are similar to the scores reported by women who had abortion for various reasons. In the literature, it has been stated that abortions performed for fetal or maternal indications are more acceptable than abortions performed for socioeconomic reasons (20, 21). In different studies conducted in Turkey, it is also stated that abortion is more acceptable in case of maternal or fetal health problems (13, 22, 23). In this study, 95.3% of the participants had an abortion reason for fetal or maternal indications, and 89.3% of these were due to fetal indications. The results of the studies show that individual-level abortion stigma is a universal experience for women despite the reason for abortion and cultural differences.

In many recent studies, demographic characteristics such as race/ethnicity, age, education and partner support have been reported to be effective on individual-level abortion stigma (6, 10, 13, 17, 18). While studies have found that women's ILASS scores increase with age (7, 24), there are studies showing that contrary to these results, it decreases with increasing age (10, 18). In the study of Oginni et al, it was found that those with higher education had higher ILASS scores than those with primary education and below (18). In the same study, it was stated that women with higher education were more likely to express individual-level abortion stigma than other women. Hanschmidt et al reported that women with high partner support had lower individual-level abortion stigma scores (6). Similarly, Li et al reported that women who received social support had significantly lower individual-level abortion stigma scores (7). In our study, it was found that ILASS scores of women were not affected by age, education and marital status. It is thought that almost all of the women may not have been able to express individual-level abortion stigma sufficiently because they had primary education and below. In addition, it is an expected result that women in traditional and conservative societies such as Şanlıurfa experience individual-level abortion stigma regardless of their marital status. In this study, the most spoken language at home was considered as an indicator of ethnicity and the individual-level abortion stigma among women from different ethnic backgrounds was evaluated. The difference between the most spoken language at home and ILASS scores was not significant. Although the women had different ethnic backgrounds, it is thought that their individual-level abortion stigma were similar because most of them had abortions for fetal indications. Furthermore, religion may be an important common denominator between different ethnic groups. Religious beliefs about abortion may be similar among these Muslim groups, which may lead to similar individual-level abortion stigma regardless of language.

In our study, it was found that the number of living children, the number of abortions and the time since the last abortion did not affect the ILASS score. Similarly, Makleff et al. reported that the number of living children did not affect the ILASS score (24). In the study of Li et al. and Cockrill et al. it was reported that having more than one abortion did not affect the ILASS score (7, 10). In the study of Hanschmidt et al completed with 130 participants, it was reported that the time since the last abortion did not affect individual-level abortion stigma (6). In contrast to; Biggs et al., in their study with 928 participants, stated that the individual-level abortion stigma perceived in the five-year evaluations following the abortion decreased significantly as the time since the abortion increased (17). This may be due to differences in the design and locations of the studies.

Limitation of Study

In the region where the study was conducted, fertility is accepted as an indicator of femininity, while the number of children is seen as a symbol of status for women and power for men. Therefore, the data collection process took a long time in this region where abortion rates are quite low.

CONCLUSIONS AND RECOMMENDATIONS

In this study, it was found that the individual-level abortion stigma of women with abortion experience in Şanlıurfa was at a moderate level. It was determined that the individual-level abortion stigma in women was independent of sociodemographic and obstetric characteristics.

In order to reduce abortion stigmatisation at the individual level, it is recommended to carry out educational activities to raise awareness of the society, especially women, and to provide psycho-social support services to women who have had or are considering having an abortion. In addition, to reveal the factors that cause individual-level abortion stigma, it is recommended that qualitative or mixed-method studies be conducted in different sample groups, especially through in-depth interviews with women who prefer abortion on demand without fetal or maternal indication.

DESCRIPTIONS

No financial support.

No conflict of interest.

Acknowledgments: We would like to thank all the women who participated in the study.

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Acta Medica Ruha
International Journal of Medicine and Health Sciences
E-ISSN: 2980-1184

ORIGINAL ARTICLE
Volume:2 Issue:3 Year:2024
https://doi.org/10.5281/zenodo.13692382

Hemşirelerin Deprem Sonrası Sağlık Algısı, Deprem Stresi ile Baş Etme ve Uykusuzluk Durumlarının İncelenmesi

Examination of Nurses' Post-Earthquake Health Perception, Coping with Earthquake Stress and Insomnia

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ÖZET

Giriş: Depremler aniden meydana gelir. Sonraki süreçte bireylerde fizyolojik, psikolojik, sosyal sorunlara sebep olmaktadır. Hemşireler ise deprem durumlarında hem kendi sorunlarına hem de bakım verdikleri bireylerin sorunlarına çözüm üretmeye çalışmaktadırlar.
Amaç: Çalışmada hemşirelerin depremden sonra sağlık algı düzeylerini, deprem stresi ile baş etme stratejilerinin neler olduğunu, uykusuzluk yaşama durumlarını belirlemek amaçlanmıştır.
Yöntem: Tanımlayıcı tipte bir çalışmadır ve bir Eğitim ve Araştırma Hastanesi'nde çalışan hemşirelerde yapılmıştır. Çalışma Nisan 2023 – Haziran 2023 tarihleri arasında gerçekleştirilmiştir. Örneklemde 601 hemşire yer almaktadır. Verileri toplamak için tanıtıcı bilgi formu, Sağlık Algısı Ölçeği, Deprem Stresi ile Başetme Stratejileri Ölçeği ve Uykusuzluk Şiddeti İndeksi kullanılmıştır. Verilerin analizinde bağımsız gruplarda t testi, varyans analizi ve pearson korelasyon analizi yapılmıştır.
Bulgular: Sağlık algısının medeni durum ve eğitim durumundan, deprem stresi ile başetme stratejileri ölçeği alt boyutlarının eğitim durumundan etkilendiği bulunmuştur ($p<0.05$). Hemşirelerin %44.3'ünün uykusuzluk alt eşiğinde olduğu saptanmıştır. Sağlık algısı ile deprem stresi ile başetme stratejileri ölçeği dini başetme alt boyutu arasında zayıf bir ilişki saptanmıştır ($r = -.199$, $p = .000$).
Sonuç: Hemşirelerin sağlığı algılama durumlarını yükseltecek, deprem durumlarında başetme stratejilerini etkin kullanmalarını sağlayacak, uyku sorunları ile başetmeye yardımcı olacak girişimsel çalışmaların yapılması önerilmektedir.

Anahtar Kelimeler: Sağlık Algısı, Deprem Stresi ile Baş Etme, Uykusuzluk, Hemşire.

ABSTRACT

Introduction: Earthquakes occur suddenly. In the subsequent process, it causes physiological, psychological and social problems in individuals. Nurses, on the other hand, try to find solutions to both their own problems and the problems of the individuals they care for in earthquake situations.
Objective: The study aimed to determine nurses' health perception levels after the earthquake, their coping strategies with earthquake stress, and their insomnia.
Method: It is a descriptive type study. It was conducted on nurses working at Training and Research Hospital. The study was carried out between April 2023 and June 2023. There are 601 nurses in the sample. An introductory information form, Health Perception Scale, Earthquake Stress Coping Strategies Scale and Insomnia Severity Index were used to collect data. In the analysis of the data, t test, analysis of variance and Pearson correlation analysis were performed in independent groups.
Results: It was found that health perception was affected by marital status and educational status, and sub-dimensions of the earthquake stress coping strategies scale were affected by educational status ($p<0.05$). It was determined that 44.3% of the nurses were at the lower threshold of insomnia. A weak relationship was found between health perception and the religious coping sub-dimension of the earthquake stress coping strategies scale ($r =-.199$, $p = .000$).
Conclusion: It is recommended to carry out interventional studies that will increase nurses' health perception, enable them to use coping strategies effectively in earthquake situations, and help them cope with sleep problems.

Keywords: Health Perception, Coping with Earthquake Stress, Insomnia, Nurse.

GİRİŞ

Türkiye'de jeolojik, meteorolojik ve topoğrafik oluşumlar nedeniyle deprem, heyelan, sel, çığ gibi doğal afetler meydana gelmektedir (1). Deprem gibi afetler toplumun sağlığını önemli düzeyde etkilemektedir (2). Bu süreçte bireylerin sağlığını nasıl algıladığı önemlidir. Çünkü bu algı bireylerin sağlık ile ilgili davranışlarını ve düşüncelerini etkilemektedir (3). Sağlık ile ilgili algısı yüksek olan bireylerin sağlığı koruma ve geliştirmeye yönelik davranışları daha fazla olacaktır (4). Hemşirelerin sağlıklı bir bakım

Corresponding Author: Fatma Ersin, e-mail: fatmaersin1@gmail.com
Received: 12.06.2024, Accepted: 09.07.2024, Published Online: 20.09.2024
Cited: Ersin F, et al. Examination of Nurses' Post-Earthquake Health Perception, Coping with Earthquake Stress and Insomnia. Acta Medica Ruha. 2024;2(3):186-192. https://doi.org/10.5281/zenodo.13692382
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verebilmeleri için kendi sağlık algılarının farkında olmaları gerekmektedir. Bireylerin sağlık algılarını etkileyen önemli faktörlerden bir tanesi de uyku durumudur. Hemşirelerde uyku sorunları oldukça önemlidir. Ülkemizde hemşirelerde uyku ile ilgili sorunlar ikinci sırada yer almaktadır (5-7). Vardiyalı çalışmanın uyumada zorluğa neden olduğu da literatürde belirtilmiştir (5). Bu zorlu çalışma koşullarına afetlerinde eklenmesi uyku sorunlarını daha da arttırmaktadır. Bu nedenle hemşirelerin afet durumlarında baş etme becerilerini etkin kullanmaları önemlidir. Çünkü sağlık çalışanları hem kurtarma ekibi olarak çalışmakta hem de kendileri afetlere maruz kalmaktadırlar. Afet durumlarında hemşirelerin yüksek düzeyde performans sergilemeleri beklenmektedir. Bu durum hemşirelerin psikososyal yönden olumsuz etkilenmelerine neden olmaktadır (8). Hemşireler bu travmatik deneyim sonucunda sıklıkla kaygı, tükenmişlik, depresif belirtiler, empati yorgunluğu ve ikincil travmatik stres yaşamaktadırlar (9,10). Bunun yanında afet müdahalesine doğrudan dahil olmak, afet sonucunda ortaya çıkabilecek ikincil psikolojik sorunların gözden kaçırılmasına yol açabilir (11). Bu aşamada baş etme stratejileri önem kazanmaktadır. Bireylerin stres durumlarında başa çıkma stratejilerinin farklılık gösterdiği unutulmamalıdır.

Sonuç olarak afet önemli bir stres kaynağıdır. Bu nedenle hemşirelerin hem kendi sağlıklarını hem de bireylerin sağlığının korunması ve geliştirilmesinde etkili oldukları düşünüldüğünde mevcut durumun saptanması için bu çalışmanın gerekli olduğu düşünülmektedir. Ayrıca hemşirelerde deprem sonrası sağlık algısı, deprem stresi ile baş etme ve uykusuzluk ile ilgili çalışmalara ulaşılamamıştır.

Bu çalışmanın amacı hemşirelerin deprem sonrası sağlık algısı, deprem stresi ile baş etme ve uykusuzluk durumlarının incelenmesidir.

YÖNTEM

Çalışma tanımlayıcı tipte olup Nisan 2023 – Haziran 2023 tarihleri arasında bir Eğitim ve Araştırma Hastanesi'nde çalışan hemşirelerde yapılmıştır. Çalışmanın evreni 853 hemşire olup, örneklemi çalışmaya katılmayı kabul eden 601 hemşireden oluşmuştur. Verilerin toplanmasında yüz yüze görüşme tekniği kullanılmıştır. Verilerin toplanmasında tanıtıcı bilgi formu, Sağlık Algısı Ölçeği, Deprem Stresi ile Başetme Stratejileri Ölçeği ve Uykusuzluk Şiddeti İndeksi kullanılmıştır.

Tanıtıcı Bilgi Formu: Form 19 sorudan oluşmuştur ve literatür taranarak araştırmacılar tarafından oluşturulmuştur (1,4-7).

Sağlık Algısı Ölçeği (SAÖ): Diamond ve arkadaşları tarafından 2007 yılında geliştirilmiştir (12). Ölçeğin Türkçe geçerlik güvenirliği 2012 yılında Kadıoğlu ve Yıldız tarafından yapılmıştır. SAÖ 15 madde ve dört alt boyuttan oluşmuştur. Beşli likert tipi bir ölçektir. Ölçeğin 1., 5., 9., 10., 11. ve 14. maddeleri olumlu, 2., 3., 4., 6., 7., 8., 12., 13. ve 15. maddeleri olumsuz ifadeler içermektedir. Olumlu olan ifadelerin puanlaması: çok katılıyorum= 5, katılıyorum= 4, kararsızım= 3, katılmıyorum=2 şeklindedir. Olumsuz ifadeler tersten puanlanmış olup ölçekten en az puan 15 puan, en fazla ise 75 puan alınmaktadır. Toplam puanın yüksek olması bireylerin sağlık algısının yükseldiğini, düşük olması ise sağlık algısının düşük olduğunu ifade etmektedir. Ölçeğin cronbach alfa değeri 0.77 bulunmuştur (13). Bu çalışmada chronbach alpha değeri 0.70'dir.

Deprem Stresi ile Baş Etme Stratejileri Ölçeği (DSBÖ): Ölçek 2016 yılında Yöndem ve arkadaşları tarafından geliştirilmiş Türkçe geçerlilik ve güvenilirliği yapılmıştır. Ölçek üç alt boyuttan oluşmuştur (dini baş etme, olumlu yeniden değerlendirme ve sosyal destek arama). Ölçekte toplam puan hesaplanmamaktadır. Her bir madde için 1-4 arası puanlama yapılmaktadır. Dini baş etme alt boyutu 2-8-9-10-11 nolu (5-20 puan), olumlu yeniden değerlendirme alt boyutu 5-12-13-14-15- 16 nolu (6- 20 puan), sosyal destek arama alt boyutu 1-3-4-6-7 nolu maddelerden (3 ve 7. maddeler tersten hesaplanır), (5-20 puan) oluşmaktadır. Puanın yüksek olması bireylerin baş etme stratejisini daha fazla kullandığını göstermektedir. Ölçeğin Cronbach alpha katsayısı dini baş etme alt boyutunda: 0.85, olumlu yeniden değerlendirme alt boyutunda: 0.69, sosyal destek arama alt boyutunda: 0.74'dür (14). Bu çalışmada chronbach alpha değeri dini baş etmede 0.73, olumlu yeniden değerlendirmede 0.82 ve sosyal destek aramada 0.60 olarak hesaplanmıştır.

Uykusuzluk Şiddeti İndeksi (UŞİ): uykusuzluk bulgularının düzeyini belirlemek amacıyla geliştirilmiş bir ölçektir. Ölçek hem normal toplum taramalarında hem de uykusuzluğu klinik olarak

değerlendirirken de kullanılmaktadır (15). Boysan ve arkadaşları tarafından (2010) Türkçe geçerlik ve güvenirlik çalışması yapılmıştır. Yedi maddeden oluşmuştur. Beşli likert tipi bir ölçektir. Her madde 0 ve 4 arasında puanlanmaktadır. Ölçekten en az 0 en fazla 28 puan alınmaktadır. 0-7 arasında puan alınması klinik olarak önemsiz düzeyde uykusuzluk olduğunu, 8-14 puan uykusuzluk alt eşiğinde olunduğunu, 15- 21puan klinik uykusuzluk (orta düzeyde şiddetli) olduğunu, 22-28 puan ise klinik uykusuzluk (şiddetli) olduğunu göstermektedir. Ölçekten alınan puanın artması uykusuzluk şiddetinin arttığını göstermektedir. Ölçeğin Cronbach değeri 0.79 olup (16), bu çalışmada 0.97 olarak bulunmuştur.

Veriler Statistical Package For Social Sciences paket programı (SPSS 20.0) ile değerlendirilmiştir. Verilerin analizinde bağımsız gruplarda t testi, varyans analizi ve korelasyon analizi yapılmıştır. Tanımlayıcı istatistiklerden sayı, yüzde ve ortalamalar kullanılmıştır. Normallik analizlerinden Shapiro-Wilk testi yapılmıştır.

Çalışmanın bağımlı değişkenleri SAÖ, DSBÖ, UŞİ puan ortalamalarıdır. Bağımsız değişkenleri cinsiyet, eğitim durumu, medeni durumu, meslekte çalışma süresidir.

Çalışmanın yapılabilmesi için ilgili hastaneden, Etik Kurul'dan (05/05/2023 tarih ve 389 sayılı), katılımcılardan ve ölçek yazarlarından gerekli izinler alınmıştır.

BULGULAR

Hemşirelerin %55.4'ü kadın, %74.2'si lisans mezunudur. Evli olan hemşirelerin oranı %62.4, 6 yıl ve üstü süredir hemşire olarak çalışan hemşirelerin oranı ise %65.2'dir (Tablo 1).

Tablo 1. Hemşirelerin Demografik Özelliklerinin Dağılımı

Değişkenler	Sayı	Yüzde
Cinsiyet		
Kadın	333	55.4
Erkek	268	44.6
Eğitim Durumu		
Lise	108	18.0
Lisans	446	74.2
Lisans Üstü	47	7.8
Medeni Durum		
Evli	375	62.4
Bekar	226	37.6
Meslekte Çalışma Süresi		
1-5 yıl	209	24.8
6 yıl ve üstü	392	65.2

Hemşirelerin %75.2'si deprem sırasında evinde olduğunu, %37.3'ü yaşadığı alanda hasar oluştuğunu ifade etmiştir. Depremde ailesinde can kaybı olan hemşirelerin oranı %1.7, tanıdıklarından birini kaybedenlerin oranı %25.1, psikolojik destek aldığını ifade edenlerin oranı ise %9'dur. Hemşirelerin %29.6'sı önemsiz düzeyde uykusuzluk yaşamaktadır. %44.3'ü uykusuzluk alt eşiğinde, %19.6'sı orta düzeyde şiddetli uykusuzluk, %6.5 şiddetli düzeyde uykusuzluk yaşamaktadır.

Tablo 2. Sağlık Algısı Ölçeği, Deprem Stresi ile Başetme Stratejileri Ölçeği ve Uykusuzluk Şiddeti İndeksi Puan Ortalamalarının Dağılımı

Ölçekler	Ort.±SS
Sağlık Algısı Ölçeği	38.61±6.87
Deprem Stresi ile Başetme Stratejileri Ölçeği	
Dini başetme	9.84±3.26
Olumlu yeniden değerlendirme	11.47±3.54
Sosyal destek arama	10.99±2.43
Uykusuzluk Şiddeti İndeksi	11.35±6.19

Ort.±SS: Ortalama±Standart Sapma.

Hemşirelerin SAÖ toplam puan ortalamasının 38.61±6.87, DSBÖ puan ortalamaları; dini başetme alt boyutu için 9.84±3.26, olumlu yeniden değerlendirme alt boyutu için 11.47±3.54, sosyal destek arama alt boyutu için 10.99±2.43'tür. UŞİ toplam puan ortalamasının 11.35±6.19 olduğu saptanmıştır (Tablo 2).

Hemşirelerin cinsiyete göre DSBÖ sosyal destek aramayı değerlendirme alt boyutu (t=-3.487, p=.001), medeni duruma göre SAÖ toplam puan ortalamaları arasında anlamlı bir fark saptanmıştır (t=-2.914, p=.004).

Eğitim durumuna göre SAÖ toplam puan ortalamaları (F=10.874, p=.000), DSBÖ alt boyutları puan ortalamaları (dini baş etmeyi değerlendirme: F=5.560, p=.004, olumlu yeniden değerlendirme: F=3.214, p=.041), UŞİ toplam puan ortalamaları (F=3.819, p=.022) arasında anlamlı bir fark saptanmıştır (Tablo 3).

Tablo 3. Hemşirelerin Bazı Özelliklerine Göre Sağlık Algısı Ölçeği, Deprem Stresi ile Başetme Stratejileri Ölçeği ve Uykusuzluk Şiddeti İndeksi Puan Ortalamalarının Dağılımı

Ölçekler					
Değişkenler	**Sağlık Algısı Ölçeği**	**Deprem Stresi ile Başetme Stratejileri Ölçeği**			**Uykusuzluk Şiddeti İndeksi**
		Dini Başetme	**Olumlu Yeniden Değerlendirme**	**Sosyal Destek Arama**	
	Ort.±SS	**Ort.±SS**	**Ort.±SS**	**Ort.±SS**	**Ort.±SS**
Cinsiyet					
Kadın	38.22±6.89	10.00±3.10	11.68±3.55	10.68±3.43	11.21±5.99
Erkek	39.09±6.83	9.65±3.45	11.22±3.52	11.37±2.37	11.52±6.43
İstatistiki Değer	t= -1.543 p=.123	t= -1.266 p=.206	t= -1.600 p=.110	t= -3.487 **p=.001**	t= -.619 p=.536
Medeni Durum					
Evli	37.98±6.99	10.03±3.35	11.61±3.52	11.09±2.33	11.47±6.00
Bekar	39.66±6.55	9.54±3.11	11.25±3.57	10.82±2.59	11.16±6.50
İstatistiki Değer	t=-2.914 **p=.004**	t=1.758 p=.079	t=1.187 p=.236	t=1.321 p=.187	t=.590 p=.556
Eğitim Durumu					
Lise	41.34±6.44	8.90±3.03	10.70±3.03	10.87±2.57	10.19±6.41
Lisans	38.08±6.73	10.05±3.28	11.66±3.62	11.01±2.41	11.45±6.07
Lisans ve üstü	37.36±7.68	10.06±3.32	11.48±3.65	11.02±2.29	13.08±6.45
İstatistiki Değer	F=10.874 **p=.000**	F=5.560 **p=.004**	F=3.214 **p=.041**	F=.140 p=.869	F=3.819 p**=.022**
Meslekte Çalışma Yılı					
1-3 Yıl	39.25±7.89	9.93±3.09	10.84±3.22	11.05±2.96	9.74±5.62
5 yıl ve üstü	40.26±5.65	9.25±2.62	11.02±3.50	10.90±2.38	10.83±6.33
İstatistiki Değer	t=-1.031 p=.304	t=1.789 p=.089	t=-.382 p=.703	t=.399 p=.690	t=-1.288 p=.199

Ort.±SS: Ortalama±Standart Sapma.

Eğitim durumunu değerlendirmede farkın hangi gruplar arasında olduğunu belirlemek için Post Hoc analizlerinden bonferroni testi yapılmıştır. Eğitim durumuna göre SAÖ toplam puan ortalamaları değerlendirildiğinde; lise mezunu hemşireler ile lisans mezunu hemşireler arasında (p=.000), aynı zamanda lise mezunu hemşireler ile lisans üstünü tamamlayan hemşireler arasında (p=.002) anlamlı bir fark saptanmıştır. Eğitim durumuna göre DSBÖ dini baş etmeyi değerlendirme alt boyutu değerlendirildiğinde; lise mezunu hemşireler ile lisans mezunu hemşireler arasında anlamlı bir fark saptanmıştır (p=.003). Eğitim durumuna göre DSBÖ olumlu yeniden değerlendirme alt boyutu değerlendirildiğinde; lise mezunu hemşireler ile lisans mezunu hemşireler arasında anlamlı bir fark saptanmıştır (p=.034).

Tablo 4. Sağlık Algısı Ölçeği ile Deprem Stresi ile Başetme Stratejileri Ölçeği ve Uykusuzluk Şiddeti İndeksi Puan Ortalamaları Arasındaki Korelasyon

	Deprem Stresi ile Başetme Stratejileri Ölçeği			
Ölçekler	**Dini Başetme**	**Olumlu Yeniden Değerlendirme**	**Sosyal Destek Arama**	**Uykusuzluk Şiddeti İndeksi**
Sağlık Algısı Ölçeği	r= -.199 p= .000	r= .019 p= .638	r= .053 p= .194	r= -.042 p= .305

Hemşirelerin SAÖ toplam puan ortalaması ile DSBÖ dini baş etme alt boyutu puan ortalaması arasında negatif yönde çok zayıf düzeyde anlamlı bir ilişki saptanmıştır (Tablo 4).

TARTIŞMA

Çalışmada bekarların sağlık algısının anlamlı bir şekilde yüksek olduğu görülmüştür. Bu çalışmadan farklı olarak öğretmenlerde yapılan bir çalışmada da medeni durumun sağlık algısını etkilemediği belirtilmiştir (17). Bu çalışmada bekar hemşirelerin sağlık algısının yüksek olması sorumluluklarının evli bireylere göre daha az olması ile ilgili olabilir. Çünkü evli hemşirelerin işteki sorumluluklarının yanı sıra aile içindeki sorumlulukları nedeniyle kendi sağlıkları ile yeterince ilgilenemedikleri düşünülmektedir. Afet durumlarında da kendileri dışında ilgilenmeleri gereken birçok kişinin olması da sağlık algısının düşmesine neden olmuş olabilir.

Çalışmada hemşirelerin eğitim düzeyi yükseldikçe sağlık algısının yükseldiği görülmektedir. Literatürde genel anlamda eğitim durumunun yüksek olması ile sağlık algısı arasında olumlu bir ilişkinin olduğu belirtilmektedir (18,19). Bu çalışmada eğitim düzeyi yükseldikçe sağlık algısının artması beklenen bir sonuçtur.

Bu çalışmada erkeklerin DSBÖ sosyal destek arama alt boyutu puan ortalamalarının anlamlı bir şekilde daha yüksek olduğu bulunmuştur (t= -3.487, p=.001). Erdoğan ve Aksoy'un çalışmasında erkeklerin sosyal destek arama alt boyutu puan ortalaması daha yüksek olup aralarındaki fark anlamlı bulunmamıştır (20). Alkan'ın depremzedeler ile yaptığı çalışmada depremzedelerin depremden 16 ay sonra hala stres belirtileri gösterdiği belirtilmiştir. Çalışmada kadınların erkeklere göre daha fazla stres bildirdikleri ifade edilmiştir. Ayrıca bizim çalışmamızdan farklı olarak erkek ve kadınların benzer sosyal destek aradıkları belirtilmiştir (21). Literatürde sosyal destek arama duygu odaklı ele alınmaktadır. Ayrıca depresif olan bireylerin sıklıkla kullandığı bir baş etme yöntemi olarak belirtilmektedir. Bunun yanında olumlu psikolojik sonuçlarla da ilişkilendirilen bir baş etme yaklaşımıdır (22). Bu nedenle erkek hemşirelerde sosyal destek arama alt boyutu puan ortalamasının yüksek çıkması olumlu bir süreç olarak değerlendirilebilir.

Bu çalışmada medeni durum ile DSBÖ alt boyutları arasında anlamlı bir fark saptanmamıştır. Erdoğan ve Aksoy'un çalışmasında ise bu çalışmadan farklı olarak medeni durum ile dini baş etme alt boyutu arasında anlamlı bir fark saptanmıştır (20). Çalışmadan elde edilen bu sonuç evli olsun ya da olmasın bütün hemşirelerin depremden ne kadar olumsuz etkilendiğini göstermesi açısından önemlidir.

Çalışmada hemşirelerin eğitim durumunun DSBÖ alt boyutlarından dini baş etme, olumlu yeniden değerlendirme alt boyutlarını etkilediği görülmektedir. Literatürde hem sosyal destek aramanın (21) hem de olumlu yeniden değerlendirmenin (14, 23) olumlu psikolojik sonuçlarla ilişkili olduğu belirtilmektedir. Bunun yanında dini baş etmenin de bireylerin psikolojisini olumlu yönde etkilediği düşünülmektedir. Eğitim düzeyi bireylerin konulara ilişkin farkındalıklarını arttırmada önemli bir faktör olarak karşımıza çıkmaktadır. Bu nedenle eğitim düzeyinin DSBÖ dini baş etme, olumlu yeniden değerlendirme alt boyutlarını etkilemesi beklenen bir sonuçtur.

Uyku yoksunluğundan en çok etkilenen grup sağlık çalışanlarıdır. Hemşireler mesai saatlerinin uzun olması, nöbet sisteminin olması gibi nedenlerden dolayı uyku yoksunluğu yaşayabilmektedirler (24,25). Ayrıca hemşirelerin meslekleri gereği yüklenmiş oldukları sorumluluklar, aile içi sorumlulukları, yaşadıkları afetler de uyku yoksunluğu yaşamalarına neden olabilir. Bu çalışmada hemşirelerin cinsiyetinin, medeni durumunun, eğitim durumunun, meslekte çalışma yılının uykusuzluk şiddeti indeksi puan ortalamasını etkilemediği saptanmıştır. Hastalarda yapılan bir çalışmada cinsiyetin uykusuzluk şiddetini etkilediği, bu çalışmaya benzer olarak medeni durumun ve eğitim durumunun uykusuzluk şiddetini etkilemediği görülmektedir (26). Ancak bu çalışmada hemşirelerin yarıya yakınının (%44.3) uykusuzluk alt eşiğinde olduğu görülmektedir. Bu durum hemşirelerin çoğunun şiddetli uykusuzluk ile karşı karşıya kalabileceğini düşündürmektedir. Ayrıca bu sonuç yaşananların hemşirelerin uyku durumunu nasıl etkilediğini göstermesi açısından oldukça önemlidir.

Bu çalışmada hemşirelerin sağlık algısı yükseldikçe dini başetmeyi kullanma durumlarının düştüğü görülmektedir. Ayrıca bu ilişki zayıf düzeydedir. Literatür incelendiğinde dini başetme, yaşanan travmalar ya da felaketlerden sonra yaygın bir biçimde gözlediğimiz tepki biçimi olarak ele alınmaktadır. Ayrıca dini başetmenin iyi bir ruh sağlığı ve düşük stres ile ilişkili olduğu belirtilmektedir

(27). Ancak bu çalışmada hemşirelerin sağlık algısı ile dini başetme durumlarının negatif yönde olması sorunlarla başetmede dini kullanmadıklarını düşündürmektedir.

SONUÇ VE ÖNERİLER

Hemşirelerin sağlık algısının, deprem stresi ile başetme stratejilerinin düşük, uykusuzluk düzeylerinin yüksek olduğu söylenebilir. Sağlık algısının medeni durum ve eğitim durumundan, DSBÖ alt boyutlarının eğitim durumundan etkilendiği bulunmuştur. SAÖ ile DSBÖ dini başetme arasında zayıf bir ilişki saptanmıştır. Elde edilen sonuçlar doğrultusunda hemşirelerin afet durumlarında sağlık algısını yükseltecek, başetmelerini güçlendirecek girişimsel hemşirelik çalışmaları önerilmektedir. Ayrıca hemşirelerin çalışma koşullarının düzenlenmesi sağlıklı ruh sağlığını, sağlıklı uyku düzenini sağlayacak ve sağlık algısını arttıracaktır. Gerekli durumlarda hemşirelerin psikolojik destek alması sağlanmalı ve bu desteğin sürekliliğinin önemi kavratılmalıdır.

AÇIKLAMALAR

Finansal destek yoktur.

Çıkar çatışması yoktur.

Not: Bu çalışma II. Uluslararası Sağlık Bilimleri ve Multidisipliner Yaklaşımlar Kongresi'nde sözel bildiri olarak sunulmuştur.

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Acta Medica Ruha
International Journal of Medicine and Health Sciences
E-ISSN: 2980-1184

ORIGINAL ARTICLE
Volume:2 Issue:3 Year:2024
https://doi.org/10.5281/zenodo.13751912

Comparison of the Efficacies of Alteplase and Streptokinase Used for Fibrinolytic Treatment in Parapneumonic Pleural Effusion and Empyema

Parapnömonik Plevral Efüzyon ve Ampiyemde Fibrinolitik Tedavide Kullanılan Alteplaz ve Streptokinazın Etkinliklerinin Karşılaştırılması

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ABSTRACT

Introduction: Used rarely in the fibrinolytic treatment of parapneumonic pleural effusion (PPE) and empyema, alteplase is a plasminogen activator (tPA) analogue.
Objective: In our study, we divided the patients with PPE and empyema, to whom we implemented video-assisted thoracic surgery, into two groups and we implemented VATS to one group and alteplase plus fibrinolysis following VATS to the other. We compared these two groups through clinical and biochemical parameters.
Methods: Totally 66 patients were involved in the study. The patients were divided into 2 groups randomly. 5-20 mg alteplase was administered to 40 patients in the first group (Alteplase) through tube thoracostomy following VATS. And only VATS was implemented to 26 patients in the second group (Control). The chest tube removal times of the patients and their lengths of hospitalization, C-Reactive Protein (CRP) and White Blood Cells (WBC) values were compared statistically.
Results: It was determined that the groups were homogeneous statistically (P>0.05), CRP values (11.99±9.63) in the alteplase group were statistically significantly higher comparing to the control (4.07±5.10) group (P<0.05), Alteplase group was better in the comparison of the removal times of chest tubes, lengths of hospitalization and WBC values, however the findings were not statistically significant (P>0.05).
Conclusion: Alteplase is a significantly efficient fibrinolytic treatment with a success rate of 87.5%, which can be used in PPE and empyema with minimum side effects in appropriate dosages.

Keyswords: Alteplase, Streptokinase, Fibrinolytic Treatment, Parapneumonic Pleural Effusion, Empyema.

ÖZET

Giriş: Parapnömonik plevral efüzyon (PPE)ve ampiyemin fibrinolitik tedavisinde nadir kullanılan alteplaz, plazminojen aktivatör (tPA) analoğudur.
Amaç: Çalışmamızda Video yardımlı göğüs cerrahisi (VATS) uyguladığımız PPE ve ampiyemli hastaları 2 gruba ayırdık, bir gruba sadece VATS, diğer gruba VATS sonrası alteplaz ile fibrinolizis uyguladık. Bu iki grubu klinik ve biyokimyasal parametrelerle karşılaştırdık.
Metod: Toplam 66 hasta çalışmaya alındı. Hastalar rastgele seçilerek 2 gruba ayrıldı. Birinci grupta (Alteplaz) bulunan 40 hastaya VATS sonrası 5-20 mg alteplaz göğüs tüpü içinden uygulandı. İkinci gruptaki (Kontrol) toplam 26 hastaya sadece VATS yapıldı. Hastaların göğüs tüpü çekilme süreleri, hastanede kalış süreleri, C-Reaktif Protein (CRP)ve White Blood Cells (WBC) değerleri istatistiksel olarak karşılaştırıldı.
Bulgular: Grupların istatistiksel olarak homojen olduğu (P>0.05), Alteplaz grubundaki CRP (11,99±9,63) değerlerinin, kontrol (4,07±5,10) grubuna göre daha fazla olmasının istatisitksel olarak anlamlı buluğu (P<0.05), göğüs tüpü çekilme süreleri, hastanede kalış süreleri ve WBC değerlerinin karşılaştırılmasında Alteplaz grubunun daha iyi olduğu ama bulguların istatistiksel olarak anlamlı olmadığı tespit edildi (P>0.05).
Sonuç: Alteplaz PPE ve ampiyemde kolay kullanılabilecek, uygun dozlarda minimal yan etkileri olan, %87,5 başarı ile önemli ölçüde etkili fibrinolitik bir tedavidir.

Anahtar Kelimeler: Alteplase, Streptokinaz, Fibrinolitik Tedavi, Parapnömonik Plevral Efüzyon, Ampiyem.

INTRODUCTION

Parapneumonic pleural effusion (PPE) is the most frequent reason of the exudative pleural fluids that cause to inflammation of pleural capillary endothelium and permeability increase (1,2). Delay in the initiation of therapy leads to reproduction of fibrin tissues, defense cells, bacteria and bacterial products in the pleural space. As a result, serious situations may occur such as trapped lung, lung abscess, fistula, sepsis, complicated PPE or empyema (3,4). The first treatment choice of these diseases is the use of

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Received: 26.07.2024, Accepted: 10.09.2024, Published Online: 20.09.2024
Cited: Günay Ş, et al. Comparison of the Efficacies of Alteplase and Streptokinase Used for Fibrinolytic Treatment in Parapneumonic Pleural Effusion and Empyema. Acta Medica Ruha. 2024;2(3):193-198. https://doi.org/10.5281/zenodo.13751912
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antibiotics. In case of complicated situations with the progression of the disease, surgery and fibrinolytic therapies become the part of the treatment (3-5). The stage when fibrinolytic treatment is beneficial most is the fibrinopurulent phase of PPE and empyema (4,5). We can consider streptokinase, urokinase, deoxyribonuclease (DNaz) and rarely the tissue plasminogen activators (tPA) among the fibrinolytic agents used at this stage (7,8). Streptokinase is an active fibrinolytic agent that is frequently used in the thoracic surgery (7-9). Due to the decrease in streptokinase production, studies have been performed to search for alternative fibrinolytic agents in recent years. Among these agents, alteplase is a 2nd generation thrombolytic and fibrin selective agent, which is most frequently used as tPA (9,10). It affects by reducing fibrinogen and plasminogen (10). While studies about the fibrinolytic treatment with alteplase are extensive, such studies are limited for adult patients (6,9).

We designed a retrospective study to evaluate the efficacy and reliability of alteplase in fibrinolytic treatment. We divided the patients with PPE and empyema, to whom we implemented chest drain, into 2 groups and administered fibrinolysis with streptokinase to one group and with alteplase to the other and compared the groups with clinical, radiological and biochemical parameters.

METHODS

Patients with pleural effusion to fill at least one third of a hemithorax in the chest radiography and pleural fluid pH lower than 7.2, at whom multiple septations were determined in their thorax ultrasound, between the dates of March 2014 and March 2015 were involved in the study. The patients were divided into 2 groups indiscriminatingly. There were 10 (25%) females and 30 (75%) males, 40 patients in total, in the alteplase group. 32 F chest drain was implemented to the patients in this group with local anesthesia and left to closed underwater drainage. Starting from the postoperative 2nd day, 5-20 mg alteplase (0.1 mg/kg) + 50 cc saline solution was administered through the chest drain into intrapleural space once a day in 3 or 5-day periods. The drain was held flapped for 2 hours. The dosage of alteplase was arranged according to the weight, anticoagulant used and general status of the patient.

There were 10 female (38.5%) and 16 (61.5%) male, 26 patients in total in the streptokinase group. 32 F chest drain was implemented to the patients in this group with local anesthesia and left to closed underwater drainage. Starting from the postoperative 2nd day, 250.000 I.U streptokinase (concentration of 10 IU/mL) + 50 cc saline solution was administered through the chest drain into intrapleural space once a day in 3 or 5-day periods. The drain was held flapped for 2 hours.

Gender, ages, complications, malign and benign characteristics of the patients, chest tube removal times, durations of hospital stay were measured before the treatment and C-Reactive Protein (CRP) and White Blood Cells (WBC) values were measured on the postoperative 7th day. These values were compared statistically. Patients without fever and whose CRP levels were normal in their follow up periods were accepted successful.

Statistical Analyses

SPSS 22.0 (IBM Corparation, Armonk, New York, United States) and PAST3 (Hammer, Ø, Harper, D.A.T., Ryan, P.D. 2001) paleontological statistics programs were used in the analysis of the data. Conformity of univariate data to normal distribution was tested through Shapiro-Wilk test, Mardia (Dornik and Hansen Omnibus) test was used for the conformity of multivariate data to normal distribution and Leneve test was used for the variance homogeneity. Independent-Samples T test was used in the comparison of two independent groups together with Bootstrap results. General Linear Model-Repeated Anova test was used together with the Bootstrap results for analyzing the two repetitive measurement of dependent variables and the interaction of the repetitive measurements of the variable according to groups. Fisher Exact test was used in the comparison of categorical data with each other through Monte Carlo Simulation method. The quantitative data was expressed in the tables as mean ± sd. (standard deviation) and Range (Maximum-Minimum) values. The categorical data was expressed as numbers (n) and percentages (%). The data was analyzed at 95% confidence interval and the p value less than 0.05 was accepted significant.

RESULTS

Totally 66 patients, 20 (30.3%) females and 46 (69.7%) males, with the mean age of 43.55 ± 20.37 (85-4), who were implemented chest drain with the diagnoses of PPE and empyema between the dates of March 2014 and March 2015 were involved in the study (Table 1).

Table 1. Demographic Features of the Study Groups

	Control (n=26)	Alteplase (n=40)	Total (n=66)	P [a]
Age	47.85±20.36(85-21)	40.75±20.40 (69-4)	43.55±20.37 (85-4)	0.346
Sex (female/ Male)	10(38.5) / 16(61.5)	10(25) / 30(75)	20(30.3) / 46(69.7)	0.461
Right/Left	18(69.2) / 8(30.8)	20(50) / 20(50)	38(57.6) / 28(42.4)	0.310
Benign / Malignant	20(76.9) / 6(23.1)	36(90) / 4(10)	56(85.9) / 10(15.1)	0.276

General Linear Model Repeated Anova (Wilks' Lambda) (Bootstrap) - Independent T Test (Bootstrap) - Fisher Exact Test (Monte Carlo) Mean± Standard deviation Range (Maximum- Minimum).

It was determined that the groups were homogeneous in the demographic examination made in terms of Gender, age, side of pleural effusion and the histopathology of the effusion (benign, malign) ($p > 0.05$) (Table 1). Any difference was not seen between the groups in terms of numbers and values.

The CRP mean value of the alteplase group before treatment was measured as 16.77 ± 10.01 mg/L (43.7-4.9), and as 4.78 ± 4.15 mg/L (16.3-0.96) on the postoperative 7th day. The difference between these two values was found as 11.99 ± 9.63 mg/L and this decrease in CRP was found statistically significant ($p < 0.001$). The CRP mean value of the streptokinase group before treatment was measured as 8.92 ± 6.80 mg/L (25.6-1.65) and as 4.85 ± 2.97 mg/L (12.1-1.1) on the postoperative 7th day (Table 2). The difference between these two values was found as 4.07 ± 5.10 mg/L and this decrease in CRP was found statistically significant ($p = 0.014$). This decrease in the CRP values was found statistically significantly higher in the alteplase group ($p < 0.05$). It was determined that alteplase decreased the CRP more and recovered the infection clinics of patients better.

Table 2. WBC and CRP Value Alterations in Durations of Hospital Stay and Chest Withdrawal Times

	Control (n=26)	Alteplase (n=40)	Total (n=66)	P [a]
The durations of hospital stay	12±4.12(21-7)	11.5±3.98(21-7)	11.7±3.98(21-7)	.730
The durations of hospital stay	10.46±3.64(18-6)	10.25±3.91(19-5)	10.33±3.75(19-5)	.877
WBC				
Before(B)	11.68±5.48(24.1-5.7)	14.77±4.74(24.2-5.3)	13.55±5.19(24.2-5.3)	.115
Last(L)	8.45±2.12(12.8-5.1)	9.57±2.50(14.3-5.5)	9.13±2.39(14.3-5.1)	
Difference (B-L)	3.23±4.41(12.9-(-0.8))	5.20±4.47(13.2-(-4.8))	4.42±4.48(13.2-(-4.8))	.225
P [b]	0.022	<0.001	<0.001	
CRP				
Before(B)	8.92±6.80(25.6-1.65)	16.77±10.01(43.7-4.9)	13.68±9.59(43.7-1.65)	.015
Last(L)	4.85±2.97(12.1-1.1)	4.78±4.15(16.3-0.96)	4.81±3.68(16.3-0.96)	
Difference (B-L)	4.07±5.10(17.5-(-0.4))	11.99±9.63(36.9-(4.6))	8.87±8.96(36.9-(-4.6))	.011
P [b]	0.014	<0.001	<0.001	

General Linear Model Repeated Anova (Wilks' Lambda) (Bootsrap) - Independent T Test (Bootsrap) - Fisher Exact Test (Monte Carlo) Mean± Standard deviation Range (Maximum-Mnimum).

The WBC mean value of the alteplase group before treatment was measured as 14.77 ± 4.74 K/mm3 (24.2-5.3), and as 9.57 ± 2.50 K/mm3 (14.3-5.5) on the postoperative 7th day. The difference between these two values was found as 5.20 ± 4.47 K/mm3 and this decrease in WBC was found statistically significant ($p < 0.001$). The WBC mean value of the streptokinase group before treatment was measured as 11.68 ± 5.48 K/mm3 (24.1-5.7) and as 8.45 ± 2.12 K/mm3 (12.8-5.1) on the postoperative 7th day. The difference between these two values was found as 3.23 ± 4.41 and this decrease in WBC was not found statistically significant ($p < 0.05$). This decrease in the WBC values was found statistically significantly higher in the alteplase group ($p > 0.05$) (Table 2).

The durations of hospital stay were found as 11.5 ± 3.98 days in the alteplase group and 12 ± 4.12 days in the streptokinase group. The durations of hospital stay of the patients in the alteplase group to be lesser was not found statistically significant ($p = 0.730$) (Table 2). The drain removal times of the alteplase group were found as 10.25 ± 3.91 days and 10.46 ± 3.64 days in the streptokinase group. It was not found statistically significant the removal times of the drains to be lesser in the alteplase group ($p= 0.877$) (Table 2).

It was provided recovery in 35 (87.5%) patients in the alteplase group, it was failed in 5 (12.5%) patients (Table 3). Decortication and resection plus decortication (broncho-pleural fistula and intraparenchymal abscess) had to be implemented respectively for 2 and 3 of the 5 patients for whom it could not be provided recovery and none of the patients died during and after the treatment. When it was provided recovery in 21 (80%) patients in the streptokinase group, it was failed in 5 (20%) patients (Table 3). Decortication and resection plus decortication (broncho-pleural fistula and intraparenchymal abscess) had to be implemented respectively for 2 and 3 of the 5 patients for whom it could not be provided recovery and none of the patients died during and after the treatment.

Table 3. Efficacy of Alteplase and Streptokinase.

Parapneumonic effusions and emphyema	Alteplase	Success (n=35 ,87%)	
		Failed (n=5, 13%)	Decortication n=2
			Resection n=3
	Streptokinase	Success (n=21 ,80%)	
		Failed (n=5, 20%)	Decortication n=2
			Resection n=3

DISCUSSION

Streptokinase is the most commonly used fibrinolytic agent in recent years. Due to the decrease in streptokinase production, the alternative agents of tPA and DNAaz have started to be preferred. alteplase is a tPA that has a high fibrin affinity. Because of being a fluid, it can be used easily through the chest drain. In our study, we deemed suitable the use of alteplase, a fibrin specific agent that is easy to implement and used frequently in thromboembolism, in the comparison with streptokinase.

Our experiences with alteplase showed that there was not a definite standard to be implemented in patients. The dosage of alteplase may be adjusted can be arranged according to the weight of the patient, anticoagulant and antiaggregant (acetylsalicylic acid, warfarin) treatment used and the general status and biochemical parameters of the patient (5-10 mg). A minimal hemorrhage can be seen in patients' implemented alteplase and it can be useful to make hemogram examinations frequently in such patients. Blood transfusion was not needed in any of our patients. In the study they performed on tPA, Froudarakis et al emphasized that there was a significant decrease in WBC and CRP levels of the patients in the group they implemented tPA, they determined a rapid recovery in the clinical course of these patients and the durations of hospital stay had shortened (11). In our study, rapid reductions in CRP values were determined in both groups.

There were rapid reductions in the CRP values of both groups in our study. The more reduction in the alteplase group was statistically significant. It was determined with the clinical observations that the recovery was faster in this patient group. Also, it was seen that the WBC values decreased in both groups; however the more reduction in the alteplase group was not statistically significant.

There are studies in the literature which state that the fibrinolytic agents were effective macroscopically in the resolution of intrapleural fluid collection macroscopically, increased the pleural drainage amount and reduced the need for decortication (12). In our study, successes were achieved at the rates of 87.5% and 80% respectively in the alteplase and Streptokinase group. It was determined that the alteplase group had a better success rate and required less large surgical interventions.

Upon the determination that the viscosity of the empyema fluid was caused by the DNA; it was seen that the intrapleural application of the DNAaz enzyme would reduce the fluid viscosity and support the pleural drainage. In their study, Rahman et al divided 210 patients into 4 groups indiscriminatingly and administered 10 mg tPA to 1st group, DNAaz to 2nd, tPA and DNAaz to 3rd and double placebo to 4th group. They reported that the tPA-DNAaz group showed better results in the radiological pleural opacity resolution, necessity of surgical intervention and duration of hospital stay (8). Davied et al emphasized

that the daily drainage had increased significantly following the intrapleural fibrinolytic application comparing to the group where fibrinolytic agents were not used, and the radiologic recovery was better in the fibrinolytic implemented group (13). In our study, it was determined that the durations of hospital stay and the drain removal times were lesser in the alteplase group, however, there was no statistically significant difference between the groups ($p > 0.05$). Due to any data was not collected for the daily drainage amounts; there is no comment in this particular in our study.

The adverse effects of the fibrinolytic treatment were reported as chest pain, fever, allergic reaction and pleural bleeding (14,15). In the study they performed with tPA, Froudarakis et al determined bleeding in 3 and pain complications in 4 patients (11). In their study, Gervais et al reported that the intrapleural tPA application caused to pleural bleeding in a patient who received systemic anticoagulation (16). Taylor et al. stated that complications developed in 28 (38%) patients in a study about the effects of alteplase treatment in children with PPE and empyema. They reported that pain (21%, n = 15) ranked first and saturation reduction ranked number two among these complications (9). In our study, 700-1000 mL/day hemorrhages, which continued for 3 days, were determined from the drains of 3 patients who were administered 20 mg alteplase. A 0.2-0.4 g/dL of change was seen in the hemogram values of these patients. Blood transfusion was not performed in none of these patients. The use of 10 mg alteplase was determined to be safer in patients using anticoagulants such as acetylcysteine or warfarin due to any disease.

Limitations of the study is the retrospective design and the number of cases is relatively low.

CONCLUSION

We prepared a retroprospective study on the purpose of comparing the efficacies of alteplase and streptokinase in the fibrinolytic treatment. We compared these two groups through clinical, and biochemical parameters. In consequence of our study, we determined that (i) the (CRP) alteplase group was more effective in terms of infection control, (ii) there was not any difference between the groups in terms of duration of hospital stay, (iii) there was not any difference between the groups in terms of chest drain removal time and (iv) the 2nd surgery was needed lesser in the alteplase group.

In conclusion, with minimal side effects in proper dosages and 87.5% success, alteplase is a considerably effective fibrinolytic treatment that can easily be used in PPE and empyema.

DESCRIPTIONS

No financial support.

No conflict of interest.

Acknowledgement: The authors would like to thank the patients for granting permission for their hospital data to be included in this paper, and also Dr. Dragan Danilovski for his assistance in the statistical analyses.

Ethical Declaration: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

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Acta Medica Ruha
International Journal of Medicine and Health Sciences
E-ISSN: 2980-1184

ORIGINAL ARTICLE
Volume:2 Issue:3 Year:2024 https://doi.org/10.5281/zenodo.13766957

The Relationship Between Personality Traits and Pregnancy Adaptation: The Case of Primigravida Pregnant Women

Kişilik Özellikleri İle Gebelik Uyumu Arasındaki İlişki: Primigravida Gebe Kadınlar Örneği

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ABSTRACT

Introduction: Adaptation to pregnancy is essential for expectant mothers who will have their first experience. It includes personality traits and thus contributes to shaping the role of motherhood.
Objective: This study investigated the relationship between personality traits and pregnancy adjustment in primigravida pregnant women.
Method: This cross-sectional study was conducted with 280 women in a province in the south-eastern Anatolia region of Turkey between January and June 2024. Participants were selected randomly. The data were collected using the "Introductory Information Form," "Ten-Item Personality Inventory (TIPI)," and "Prenatal Self Evaluation Questionnaire (PSEQ)." The data were analyzed using number, percentage, mean, correlation, and regression analysis in the SPSS program.
Results: The mean scores of the participants' TIPI sub-dimensions of openness to experience, conscientiousness, extraversion, agreeableness, and emotional stability were 9.62±2.32, 10.89±2.05, 9.52±2.44, 11.43±2.88, 10.51±2.15, respectively. The mean total score of the PSEQ was 178.50±26.54, and pregnancy adjustment was moderate. There was a moderate negative relationship between pregnancy adjustment and openness to experience (r=-0.615, p=0.003), conscientiousness (r=-0.625, p=0.015), agreeableness (r=-0.605, p≤0.001), and emotional stability (r=-0.630, p≤0.001) personality traits. According to the results of the multiple linear regression model, openness to experience (β=-2.718, p=0.001) and conscientiousness (β=-3.35, p=0.004) variables are important determinants of pregnancy adjustment, and these variables explain 27.6% of the total variance in pregnancy adjustment.
Conclusion: Women who are not open to experience and have low responsibility personality traits are at-risk groups in terms of pregnancy adjustment in their first pregnancy.

Keywords: Pregnancy, Pregnancy Adaptation, Personality Traits, Primigravida.

ÖZET

Giriş: İlk deneyimini yaşayacak olan anne adaylarında gebeliğe uyum, kişilik özelliklerini içeren ve dolayısıyla annelik rolünün şekillenmesine katkı sağlayan önemli bir süreçtir.
Amaç: Bu araştırmanın amacı primigravida gebelerin kişilik özellikleri ile gebelik uyumu arasındaki ilişkinin incelenmesidir.
Yöntem: Bu kesitsel çalışma, Ocak-Haziran 2024 tarihleri arasında Türkiye'nin Güneydoğu Anadolu Bölgesi'ndeki bir ilde 280 kadın ile gerçekleştirilmiştir. Katılımcılar rastgele seçilmiştir. Veriler "Tanıtıcı Bilgi Formu", "On Maddelik Kişilik Ölçeği (OMKÖ)" ve "Doğum Öncesi Öz Değerlendirme Ölçeği (DÖÖDÖ)" kullanılarak toplanmıştır. Veriler SPSS programında sayı, yüzde, ortalama, korelasyon ve regresyon analizleri kullanılarak analiz edilmiştir.
Bulgular: Katılımcıların OMKÖ alt boyutları olan deneyime açıklık, sorumluluk, dışadönüklük, yumuşak başlılık ve duygusal dengelilik puan ortalamaları sırasıyla 9,62±2,32, 10,89±2,05, 9,52±2,44, 11,43±2,88, 10,51±2,15'tir. Prenatal Öz Değerlendirme Ölçeği toplam puan ortalaması 178,50±26,54 olup gebelik uyumu orta düzeydedir. Gebelik uyumu ile deneyime açıklık (r=-.615, p=.003), sorumluluk (r=-0.625, p=0.015), yumuşak başlılık (r=-0.605, p≤0.001) ve duygusal dengelilik (r=-0.630, p≤0.001) kişilik özellikleri arasında negatif yönde orta düzeyde ilişki tespit edildi. Çoklu doğrusal regresyon modeli sonuçlarına göre; deneyime açıklık (β=-2.718, p=0.001) ve sorumluluk (β=-3.35, p=0.004) değişkenlerinin gebeliğe uyumun önemli belirleyicileri olup bu değişkenleri gebelik uyumu üzerindeki toplam varyansın %27.6'sını açıklamaktadır.
Sonuç: Deneyime açık olmayan ve düşük sorumluluk kişilik özelliklerine sahip kadınlar ilk gebeliklerinde gebelik uyumu açısından riskli gruplardır.

Anahtar Kelimeler: Gebelik**,** Gebelik Uyumu, Kişilik Özellikleri, Primigravida.

INTRODUCTION

Most of the factors affecting women's health are encountered in the reproductive age, and pregnancy is one of the most critical factors that increase this burden (1,2). Pregnancy is a physiologic event that

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Received: 13.08.2024, Accepted: 13.09.2024, Published Online: 20.09.2024
Cited: Gül S, et al. The Relationship Between Personality Traits and Pregnancy Adaptation: The Case of Primigravida Pregnant Women. Acta Medica Ruha. 2024;2(3):199-207. https://doi.org/10.5281/zenodo.13766957
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every woman of childbearing age may experience. It is also possible to see this period as a crisis requiring changes in women's lives and adaptation to new roles (3). In this process, the woman first experiences a process of adaptation to pregnancy and then to motherhood. Although adaptation to pregnancy varies for each woman, multiple factors directly and indirectly related to each other affect this adaptation process. Especially if it is the first experience of the woman, adaptation to pregnancy includes many different variables (4,5). Among these factors, the personality characteristics of women have an essential place (5).

Personality is the active organization of an individual's physical, mental, moral, and social characteristics. It is defined as the distinctive and characteristic patterns of thought, emotion, and behavior that define the way of interaction with the physical and social environment (6). In addition, personality traits are the individual's orientations that result in certain attitudes and behaviors in certain situations (7). Therefore, to better understand the pregnancy period, personality traits should be considered in addition to the changes that pregnant women undergo (8). Because personality traits, besides defining an individual and forming the basis for predicting future attitudes, are the main factor affecting pregnant women's coping mechanisms against changes and their adaptation to pregnancy (9). In addition, personality traits, which are among the many factors that women are exposed to in terms of adaptation to pregnancy in the first pregnancy experience, constitute the most important source of personal stress (10).

The ability of the pregnant woman to adapt to her pregnancy and cope with the variables that negatively affect this period increases the health of both the expectant mother and her baby (11). In the study by Nath et al. (2020), personality traits affecting individuals' attitudes toward health and illness indicate that the psychological well-being of the expectant mother during pregnancy and the growth and development of her fetus may be practical (12). Santhi et al. (2018) revealed that pregnancy can be characterized as a source of self-realization, maturity, satisfaction, and happiness for women, as well as a source of worry, anxious waiting, and a mental burden on women. In the same study, it was determined that primigravidas, who will experience motherhood for the first time due to the fear and stress of pregnancy due to fear of the unknown, experienced more stress and negatively affected maternal attachment (13).

Adaptation to pregnancy, especially in expectant mothers who will have their first experience, is a necessary process that includes personality traits and thus contributes to shaping the role of motherhood. In this process, women have different reactions and tasks to accomplish in each pregnancy (14, 15). It is seen that personality traits are an integral part of psychosocial well-being in pregnancy. It is essential to consider the personality traits of pregnant women to make the health care services provided in this period more effective (3,15). However, when the literature was examined, it was observed that the information about the factors that would show that personality traits are an essential variable for adaptation to the first pregnancy is limited, and more scientific data is needed. In addition, revealing the relationship between personality traits and pregnancy adjustment will help prepare more comprehensive and efficient programs for expectant mothers who will experience their first pregnancy (13,15). In line with this information, this study aimed to investigate the relationship between personality traits and pregnancy adaptation in primigravida pregnant women.

METHOD

Type of Research

This research is cross-sectional and correlational.

Place and Time of the Research

This study was conducted between January and June 2024 in four family health centers (FHCs) in a province in the southeastern Anatolia center of Turkey, which were thought to reflect the general population.

Population/Sample of the Study

The study population consisted of 1035 pregnant women enrolled in four FHCs. The sample size required for the study was calculated using the Epi info program. Considering other studies, the average of 33% compliance with pregnancy was considered to be moderate (3,16). The number of individuals included in the sample was calculated as 256 with a 95% confidence interval, 5% margin of error, and 33% expected frequency. Considering the data loss, the study's sample size was rounded to 280. The number of participants to be sampled was stratified according to the number of registered pregnant women in each FHCs, and the participants who applied to the relevant FHCs and met the inclusion criteria were selected by non-probability random sampling method until the sample group determined in each cluster was reached. Inclusion criteria were being 18 or older, being at or after the 20th week of gestation, having a healthy pregnancy, not having a chronic or psychiatric disorder, being the first pregnancy, and being able to communicate.

The post hoc power analysis of the research was calculated using the G* Power 3.1.9.7 program (17). The calculation performed using the research data with a total sample size of 280 calculated the correlation value of the research as 0.785, and the power of the research was calculated as (1-β) 0.99 with a 5% margin of error (α=0.05) for correlation analysis.

Data Collection Tools

The data were collected using the Introductory Information Form, Ten-Item Personality Inventory (TIPI), and Prenatal Self Evaluation Questionnaire (PSEQ).

Introductory Information Form: This form, developed by the literature (2,3,7,12, 16), includes 13 questions that assess demographic information such as the age, education, and employment status of the woman and her husband, as well as information about the timing and planning of pregnancy and information about pregnancy.

Ten-Item Personality Inventory (TIPI): Gosling et al. (2003) and adapted into Turkish by Atak (2013) (18,19). The scale consists of ten items and has five sub-dimensions (openness to experience, conscientiousness, extraversion, agreeableness, and emotional stability). The scale is a seven-point Likert-type scale with two items in each sub-dimension. Only the average of the total score of the sub-dimensions of the scale is evaluated. In the study of the scale conducted by Tak (2013), Cronbach's alpha values were 0.83 for "openness to experience," 0.84 for "conscientiousness," 0.86 for "extraversion," 0.81 for "agreeableness," and 0.83 for "emotional stability" (19). In this study, Cronbach's alpha values were 0.85 for "openness to experience," 0.83 for "conscientiousness," 0.85 for "extraversion," 0.94 for "agreeableness," and 0.95 for "emotional stability."

Prenatal Self Evaluation Questionnaire (PSEQ): The scale developed by Lederman et al. (1979) was adapted into Turkish by Beydağ and Mete (2008) (20,21). It is a 4-point Likert-type scale with 79 items developed to evaluate the adaptation of prenatal women to motherhood. The scale has seven sub-dimensions grouped as "opinions of the individual related to the health of herself and her baby," "accepting the pregnancy," "accepting the role of motherhood," "preparation for labor," "fear of childbirth," "relationship with her mother," and "relationship with her husband." Forty-seven of the items in the PCBS are reverse items. Each item in the scale is measured on a 4-point scale. Adjustment to pregnancy is evaluated based on scores ranging from 1 to 4 (4: Very much describes, 3: Somewhat describes, 2: Somewhat describes, 1: Does not describe at all). For reverse items, the scoring is reversed. A minimum score of 79 and a maximum score of 316 can be obtained for the entire scale. Low scores indicate a high level of adaptation to pregnancy. In the study of the scale conducted by Beydağ and Mete (2008), Cronbach's alpha was found to be 0.81 (21). In this study, Cronbach's alpha was found to be 0.93.

Data Collection Method

Before the questionnaires were given to the respondents, the purpose of the research was explained, and written consent was obtained from the respondents who had volunteered to take part in the study.

Participants were provided with the questionnaire and filled in individually. The participants took approximately 15-20 minutes to complete the forms.

Data Analysis

The Statistical Package for Social Science (SPSS) 22 was used to analyze the data (IBM, Armonk, NY, USA). Number, percentile, mean ($\bar{X}$), and standard deviation (SD) were used. The Pearson Correlation test was used to compare scale scores. Linear regression analysis was used to analyze the relationship of the TIPI sub-dimensions scores with the total PSEQ score. The statistical significance level was determined as $p < 0.05$, and the 95% confidence interval level was accepted.

Ethical Considerations

The present study was carried out in the context of the Declaration of Helsinki. The ethics permission was granted by the Ethics Committee for Non-Interventional Clinical Research of Siirt University (date of application: 03/11/2023, date of approval: 29/11/2023 and assigned number: E-6002), and necessary institutional permission was obtained from the Siirt Provincial Health Directorate (Approval date: 15/12/2023, number: 98734412). In addition, the participants were informed about the study's purpose, scope, and duration, and their informed consent was received.

RESULTS

Table 1. Descriptive Characteristics of Participants (N=280)

Characteristics	n	%
Education level		
Literate	65	23.2
Primary school	105	37.5
High school	65	23.2
University degrees	45	16.1
Employment status		
Working	78	27.9
Not working	202	72.1
Perceived income level		
Poor	104	37.1
Moderate	123	43.9
Good	53	18.0
Family type		
Nuclear family	185	48.1
Extended family	199	51.9
Husband's education level		
Literate	31	11.0
Primary school	79	28.2
High school	105	37.5
University degrees	65	23.3
Husband's employment status		
Working	195	69.7
Not working	85	30.3
Gestational period		
II. trimester	132	47.2
III. trimester	148	52.8
Planning for the pregnancy		
Yes	193	68.9
No	87	31.1
Knowledge about pregnancy		
Yes	177	63.2
No	103	36.7
	Mean±SD*	**Min-Max****
Age (years)	24.11±5.12	18-29
Gestational week	30.25±4.26	20-38
Duration of marriage (years)	4.32±1.11	1-7
Husband's age (years)	30.45±6.82	23-37

*SD: Standart Deviation, **Min-Max: Minimum- Maximum.

The mean age of the pregnant women who participated in the study was 24.11±5.12 years, and the mean gestational age was 30.25±4.26 weeks. Of the participants, 37.5% were primary school graduates, 72.1% were not employed in any income-generating job, 43.9% had a medium income level, and 61.3% reported having a nuclear family structure. The mean duration of marriage was 4.32±1.11 years, the mean age of the husbands was 30.45±6.82 years, 37.5% of the husbands were high school graduates, and 69.7% were employed in any income-generating job. Of the participants, 52.8% were in the third trimester, 68.9% had a planned pregnancy, and 63.2% received information about pregnancy (Table 1).

The mean scores of the participants on the TIPI sub-dimensions of "openness to experience," "conscientiousness," "extraversion," "agreeableness," and "emotional stability" were 9.62±2.32, 10.89±2.05, 9.52±2.44, 11.43±2.88 and 10.51±2.15, respectively. The mean total score of PSEQ was found to be 178.50±26.54. The mean subscale score of the PSEQ was "opinions of the individual related to the health of herself and her baby" 26.43±4.67, the mean subscale score of "accepting the pregnancy" was 28.25±8.70, the mean subscale score of "accepting the role of motherhood" was 38.43±6.71, the mean subscale score of "preparation for labor" was 21. 41±9.45, "fear of childbirth" subscale mean score was 21.85±3.63, "relationship with her mother" subscale mean score was 22.54±5.19, and "relationship with her husband" subscale mean score was 19.59±6.74 (Table 2).

Table 2. The Distribution of Total and Sub-dimension Values of Participants' TIPI Sub-dimensions and PSEQ

Scales and Sub-dimensions	Number of Items	Score Range	Mean±SD*	Min. – Max.**
TIPI Sub-dimensions				
Openness to Experience	2	2-14	9.62±2.32	2-14
Conscientiousness	2	2-14	10.89±2.05	2-14
Extraversion	2	2-14	9.52±2.44	2-14
Agreeableness	2	2-14	11.43±2.88	2-14
Emotional Stability	2	2-14	10.51±2.15	2-14
Total PSEQ	79	79-316	178.50 ±26.54	79-245
Opinions of the Individual Related to the Health of Herself and Her Baby	10	10-40	26.43±4.67	10-36
Accepting the Pregnancy	14	14-56	28.25±8.70	14-45
Accepting the Role of Motherhood	15	15-60	38.43±6.71	15-50
Preparation for Labor	10	10-40	21.41±9.45	10-36
Fear of Childbirth	10	10-40	21.85±3.63	10-35
Relationship with Her Mother	10	10-40	22.54±5.19	10-33
Relationship with Her Husband	10	10-40	19.59±6.74	10-34

*Standart Deviation, **Min-Max: Minimum- Maximum.

There was a moderate negative correlation between the participants' total PSEQ mean and the TIPI sub-dimensions of "openness to experience" (r=-0.615, p=0.003), "conscientiousness" (r=-0.625, p=0.015), "agreeableness" (r=-0.605, p≤0.001), and "emotional stability" (r=-0.630, p≤0.001, Table 3).

Table 3. The Relationship Between Values of Participants' PSEQ and the TIPI Sub-dimensions

PSEQ		Opinions of the Individual Related to the Health of Herself and Her Baby	Accepting the Pregnancy	Accepting the Role of Motherhood	Preparation for Labor	Fear of Childbirth	Relationship with Her Mother	Relationship with Her Husband	Total PSEQ
Openness to Experience	**r***	-0.782	-0.616	-0.610	-0.652	-0.625	-0.145	-0.665	-0.615
	p	**0.012**	0.**002**	**0.001**	**0.003**	**≤0.001**	0.076	**0.001**	**0.003**
Conscientiousness	**r***	-0.396	-0.551	-0.412	-0.035	-0.691	-0.170	-0.396	-0.625
	p	**0.002**	**0.038**	**0.021**	0.150	0.065	0.785	0.093	**0.015**
Extraversion	**r***	-0.267	-0.156	-0.398	-0.125	-0.325	-0.224	-0.142	-0.256
	p	0.083	0.564	0.215	0.420	0.062	0.054	0.105	0.072
Agreeableness	**r***	-0.526	-0.639	-0.643	-0.450	-0.658	-0.625	-0.560	-0.605
	p	**0.001**	**0.004**	**0.001**	**≤0.001**	**0.003**	**≤0.001**	**≤0.001**	**≤0.001**
Emotional Stability	**r***	-0.754	-0.457	-0.652	-0.236	-0.320	-0.543	-0.694	-0.630
	p	**≤0.001**	**0.001**	**0.042**	0.078	0.052	**0.001**	**≤0.001**	**≤0.001**

*Pearson's Correlation Coefficient.

When the relationship between the sub-dimensions of the PSEQ and the sub-dimensions of the TIPI was examined, there was a high level of negative correlation between the sub-dimension "opinions of the individual related to the health of herself and her baby" and the sub-dimensions of "openness to

experience" (r=-0.782, p=0.012), and "emotional stability" (r=-0.754, p≤0.001). There was a moderate level of negative correlation between the sub-dimension "opinions of the individual related to the health of herself and her baby" and the sub-dimension of "agreeableness" (=-0.526, p=0.01). There was a low level of negative correlation between the sub-dimension "opinions of the individual related to the health of herself and her baby" and the sub-dimension of "conscientiousness" (r=-0.396, p=0.002). A moderate negative correlation was found between the PSEQ sub-dimension "accepting the pregnancy" and the TIPI sub-dimensions "openness to experience" (r=-0.616, p=0.002), "conscientiousness" (r=-0.551, p=0.038), "agreeableness" (=-0.639, p=0.004), and "emotional stability" (r=-0.457, p=0.001). A moderate negative correlation was found between the PSEQ sub-dimension "accepting the role of motherhood" and the TIPI sub-dimensions "openness to experience" (r=-0.610, p=0.001), "conscientiousness" (r=-0.412, p=0.038), "agreeableness" (=-0.643, p=0.001), and "emotional stability" (r=-0.657, p=0.042). A moderate negative correlation was found between the PSEQ sub-dimension " "preparation for labor" and the TIPI sub-dimensions "openness to experience" (r=-0.652, p≤0.001) and "agreeableness" (r=-0.450, p≤0.001). A moderate negative correlation was found between the PSEQ sub-dimension "fear of childbirth," and the TIPI sub-dimensions "openness to experience" (r=-0.625, p≤0.001), and "agreeableness" (=-0.658, p=0.003). A moderate negative correlation was found between another PSEQ sub-dimension "relationship with her mother," and the TIPI sub-dimensions "agreeableness" (r=-0.625, p≤0.001), and "emotional stability" (r=-0.543, p=0.001). A moderate negative correlation was found between the last sub-dimension "relationship with her husband" of the PSEQ, and the TIPI sub-dimensions "openness to experience" (r=-0.665, p=0.001), "conscientiousness" (=-0.560, p≤0.001), and "emotional stability" (r=-0.694, p≤0.042, Table 3).

Table 4. ***The Effect of*** the TIPI Sub-dimensions ***on the Total PSEQ***

Scale	Total PSEQ					
	B*	SD**	β***	p	95% CI****	
					Lower Limit	Upper Limit
Openness to Experience	-0.316	0.154	-2.718	**0.001**	-6.724	-2.413
Conscientiousness	-0.265	0.186	-3.355	**0.004**	-3.557	-2.145
Agreeableness	-0.045	0.090	-0.978	0.056	-1.125	0.028
Emotional Stability	-0.085	0.002	-0.054	0.750	-0.457	0.065
R: 0.526 R^2: 0.276 Adj. R^2: 0.273 **p = 0.001**						

*Coefficient B; **Standard Deviation; ***Standardized Beta Coefficient; ****Confidence Interval of 95%; R^2: R-Squared; $Adjr^2$: Adjusted R-Squared.

The regression model created with the sub-dimensions of the TIPI, which were found to have a significant relationship with the total PSEQ in the correlation analysis, found that "openness to experience" (β=-2.718) and "conscientiousness" (β=-3.355) variables were essential determinants of adjustment to pregnancy. These variables were significant predictors explaining 27.6% of the total variance in pregnancy adjustment (R2 =0.276, p=0.001, Table 4).

DISCUSSION

The personality characteristics of expectant mothers who will experience pregnancy for the first time constitute the most important source of adaptation to pregnancy (11). In this study, which we conducted to examine the relationship between personality characteristics of primigravida pregnant women and pregnancy adaptation.

In the present study; it was determined that the pregnancy adjustment of the participants was at a moderate level. When the literature was examined, Soltanı et al. (2017) examined women's life experiences adapting to the first pregnancy process. They found that adaptation to pregnancy is not easy, and planning should be made for the acceptance or responsibilities of this new role of mothers (22). In the study by Dağlar and Oskay (2022), in which the relationship between personality traits and stress and adjustment to pregnancy was examined, it was stated that the pregnancy adjustment of expectant mothers was insufficient and should be improved (3). In Demirbaş and Kadıoğlu's study (2014), in which women in the prenatal period examined the adaptation to pregnancy and related factors, it was determined that the acceptance of pregnancy was moderate (16). In the study by Küçükkaya et al. examining the relationship between body perception due to weight gain during pregnancy and acceptance of pregnancy (2020), it was found that acceptance of pregnancy was at a moderate level (23).

Our study finding is in parallel with the findings in the literature and shows that the adaptation of pregnant women to pregnancy is generally at a moderate level. These results emphasize that adaptation to pregnancy, which varies depending on various factors, should be improved in the prenatal process.

Our study found a negative and moderately significant correlation between the pregnancy adjustment of expectant mothers experiencing their first pregnancy and the personality traits of openness to experience, conscientiousness, agreeableness, and emotional stability, except for extraversion. When the literature was examined, Nath et al. (2020), in a prospective study examining the relationship between maternal personality traits, prenatal depressive symptoms, and postnatal mother-infant, found that women with high levels of personality disorder experienced depressive symptoms, and this was an important variable in reducing pregnancy adjustment (12). In the study by Hazar et al. examining the relationship between personality traits and pregnancy symptoms and health-seeking behavior (2024), personality traits were an essential variable in pregnancy adjustment (6). Dağlar and Oskay (2022) reported that as the stress level experienced by pregnant women increased, their pregnancy adjustment decreased, and especially women with emotionally unstable personality traits had higher prenatal distress levels and lower pregnancy adjustment (3). Our finding, which overlaps with the literature, suggests that personality traits are potential determinants of pregnancy adjustment.

According to the regression model in our study, it was determined that participants who were not open to experience in the postpartum period and who had low responsibility traits had lower levels of pregnancy adjustment. According to our regression model, these personality traits explained 27.6% of the change in pregnancy adjustment. When the literature was examined, Soltanı et al. (2017) stated that acceptance of responsibility for pregnancy and commitment is effective in adaptation to pregnancy and motherhood roles. The same study emphasized that primigravidas may have negative feelings toward physiological changes and a sense of uncertainty about accepting maternal responsibility due to their inexperience (22). In the study by Baştarcan and Oskay examining the relationship between personality traits on anxiety and depression levels during pregnancy (2022), it was found that pregnant women with introverted personality traits, which include not being open to experience, were more prone to anxiety and depression, which are among the critical factors affecting adaptation to pregnancy (24). We think that this finding, which supports the literature by showing that personality traits are an essential variable for adaptation to pregnancy, may shed light on interventions to improve the quality of prenatal care services.

Limitations of the Study

The results include pregnant women living in the study's region. Therefore, generalizability is limited. The results reflect data obtained from face-to-face interviews. This quantitative research limited our ability to explore the subjective experiences of individual pregnant women. Despite these limitations, the study's results are essential to the literature because they can determine the relationship between personality traits and pregnancy adjustment in primigravida pregnant women.

CONCLUSIONS

The pregnancy adaptation of primigravida pregnant women in this study was moderate. Women who are not open to experience and have low responsibility personality traits are risky groups in terms of pregnancy adjustment in their first pregnancy. These results emphasize the importance of psychological assessment of women in terms of personality characteristics and pregnancy adaptation in preconception and antenatal care services. Among expectant mothers who will experience pregnancy for the first time or who are experiencing pregnancy for the first time, it is recommended that health professionals address in more detail and plan educational and supportive interventions for these groups, especially those who are not open to experience and have low responsibility personality traits.

DESCRIPTIONS

No financial support.

No conflict of interest.

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Acta Medica Ruha
International Journal of Medicine and Health Sciences
E-ISSN: 2980-1184

ORIGINAL ARTICLE
Volume:2 Issue:3 Year:2024 https://doi.org/10.5281/zenodo.13783567

Royal Jelly Supplementation Enhances Post-Exhaustive Exercise Energy Metabolism

Arı Sütü Takviyesi Yoğun Egzersiz Sonrası Enerji Metabolizmasını İyileştirir

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ABSTRACT

Introduction: Lactate accumulation, free radical increase and changes in the activity of regulatory enzymes in energy metabolism that occur after acute exhaustion exercise disrupt the muscle adaptation mechanism and lead to muscle damage. Royal jelly, which is considered a superfood with its cell regeneration and therapeutic effects, can compensate for the effects that occur after exercise.
Objective: In this study, the effects of royal jelly supplementation were investigated in Balb-c type mice in which an acute exhaustion exercise model was created.
Methods: Mice were randomly divided into four groups: control, royal jelly, acute exhaustion exercise, acute exhaustion exercise + royal jelly. In all groups, the levels of mitochondrial biogenesis markers Ppargc1a and TFAM, which regulate muscle adaptation, and the levels of PDHa and Slc16a1, which are effective in aerobic and anaerobic regulation, were analyzed by ELISA method.
Results: PDHa and Slc16a1 levels were statistically significant between groups (p=0.024, p=0.029, respectively), but Ppargc1a and TFAM levels were not significant between groups (p=0.087, p=0.082, respectively). It was found that PDHa, Slc16a1, Ppargc1a and TFAM levels increased in the group receiving royal jelly supplementation with acute exhaustion exercise compared to the group not receiving supplementation.
Conclusions: These findings highlight the effective potential of royal jelly in developing/improving aerobic and anaerobic respiratory pathways and in the muscle adaptation process against the impaired muscle adaptation mechanism caused by acute exhausting exercise. Based on these promising results, further research is required to explore new knowledge in exercise physiology and sports sciences.

Keyswords: Acute Exhaustion Exercise, Royal Jelly, Muscle Adaptation, Energy Metabolism.

ÖZET

Giriş: Akut tükenme egzersizi sonrası ortaya çıkan laktat birikimi, serbest radikal artışı ve enerji metabolizmasındaki düzenleyici enzimlerin aktivitesindeki değişiklikler kas adaptasyon mekanizmasını bozmakta ve kas hasarına yol açmaktadır. Hücre yenilenmesi ve terapötik etkileri ile süper gıda olarak kabul edilen arı sütü egzersiz sonrası oluşan etkileri kompanse edebilir.
Amaç: Bu çalışmada, akut tükenme egzersiz modeli oluşturulmuş Balb-c türü farelerde arı sütü takviyesinin etkileri araştırıldı.
Yöntem: Kontrol, arı sütü, akut tükenme egzersizi, akut tükenme egzersizi + arı sütü grubundan oluşan fareler rastgele dört gruba ayrıldı. Tüm gruplarda, kas adaptasyonunu düzenleyen mitokondriyal biyogenez belirteçleri Ppargc1a ve TFAM düzeyleri, aerobik ve anaerobik düzenlemede etkili olan PDHa ve Slc16a1 düzeyleri ELISA yöntemiyle analiz edildi.
Bulgular: PDHa ve Slc16a1 düzeyleri gruplar arasında istatistiksel olarak anlamlıydı (sırasıyla, p=0,024, p=0,029) ancak Ppargc1a ve TFAM düzeyleri gruplar arasında anlamlı değildi (sırasıyla, p=0,087, p=0,082). Akut tükenme egzersizi ile arı sütü takviyesi alan grupta PDHa, Slc16a1, Ppargc1a ve TFAM düzeylerinin takviye almayan gruba göre arttığı bulundu.
Sonuç: Bu bulgular akut tükenme egzersizi kaynaklı bozulmuş kas adaptasyon mekanizmasına karşı arı sütünün aerobik ve anaerobik solunum yolunu geliştirmesi/iyileştirmesi ve kas adaptasyon sürecindeki etkili potansiyelini vurgulamaktadır. Bu ümit verici sonuçlara dayanarak egzersiz fizyoloji ve spor bilimlerindeki yeni bilgileri keşfetmek için daha fazla araştırma yapılması gerekmektedir.

Anahtar Kelimeler: Akut Tükenme Egzersizi, Arı Sütü, Kas Adaptasyonu, Enerji Metabolizması.

INTRODUCTION

Acute exhaustion exercise is defined as a temporary exhaustion state that occurs after intense exercise that exceeds physical capacity. This type of exercise causes rapid depletion of energy stores in the muscles, lactate accumulation, muscle fatigue and increased oxidative stress. Increased oxidative stress and free radical production in the body can lead to cellular damage, triggering inflammation and

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Received: 13.07.2024, Accepted: 23.08.2024, Published Online: 20.09.2024
Cited: Taşkın S. Royal Jelly Supplementation Enhances Post-Exhaustive Exercise Energy Metabolism. Acta Medica Ruha. 2024;2(3):208-215. https://doi.org/10.5281/zenodo.13783567
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proteolytic processes in muscle tissue (1). In particular, microdamages occur in the muscles, triggering inflammatory responses and delaying muscle recovery. Acute depletion can also have temporary depressant effects on the immune system, increasing the risk of post-exercise infection (2). These effects may slow muscle recovery and healing.

Royal jelly, which has a rich composition of proteins, peptides, carbohydrates, fatty acids, organic acids and other bioactive compounds with high biological value, is considered a super food with functional and nutritional properties (3). It has been used for centuries in traditional Chinese medicine due to its anti-aging effects and positive effects on the immune system (4). The bioactive substances in royal jelly reduce oxidative stress and prevent cell damage, and are thus considered a potential treatment strategy in preventing many chronic diseases (3).

It is known that exercise increases fuel oxidation, mitochondrial ATP production and muscle contraction by improving muscle metabolism. These support muscle adaptation and improve muscle health. Chronic conditions such as obesity, diabetes, muscle diseases and aging are associated with a decrease in muscle function and cause these processes to progress (5,6) Considering these negative effects, understanding the molecular mechanisms of exercise and fuel metabolism is extremely critical and has significant potential (7). It has become important to identify molecular mechanisms and develop strategies that can antagonize possible adverse effects, especially in acute exhaustion exercise where muscle adaptations are impaired.

Previous studies have demonstrated that royal jelly can enhance endurance, improve mitochondrial function, and stimulate energy metabolism in animals (8). However, the potential effects of royal jelly in acute exhaustion exercise, where muscle adaptations are impaired, have not been investigated. Specific effects of mitochondrial biogenesis regulators such as Ppargc1 and TFAM, which are directly related to muscle adaptations, and metabolic enzymes such as PDHa and Slc16a1, which regulate the aerobic/anaerobic respiratory pathway, have not yet been sufficiently investigated. Royal jelly may contribute to the regulation and improvement of undesirable adaptations caused by acute exhaustion exercise by affecting the levels of these metabolic markers.

In this study, the effects of royal jelly supplementation were investigated in Balb-c mice with an acute exhaustion exercise model. These effects are discussed with the levels of mitochondrial biogenesis markers Ppargc1 and TFAM, which regulate muscle adaptation, and the levels of PDHa and Slc16a, which are effective in aerobic and anaerobic regulation.

METHOD

Animals

The study protocol was approved by the Local Ethics Committee on Animal Studies of Harran University (approval number 2024/003/09). Twenty-eight male Balb/c (8-10 weeks old) mice were supplied by Experimental Animals Application and Research Center of Harran University (Şanlıurfa, Türkiye). All animals were acclimatized for one week under standard conditions (room temperature 22 ± 2 °C and 12 h light/dark cycle). Water and standard food pellets were allowed ad libitum. All animals received human care according to the criteria outlined in the “Guide for the Care and Use of Laboratory Animals” published by the National Institutes of Health.

Experimental Procedures and Groups

The mice were randomized into four groups: control group, royal jelly (RJ) group, exercise group, and RJ+Exercise group. Royal jelly was administered to the experimental group of mice via gavage at a dose of 1 mg/g body weight for 14 days, in addition to their standard diet. The Exercise and RJ+Exercise group underwent a one-week familiarization period before starting the training intervention. During this period, animals exercised on a treadmill for 10 min at 10 m/min per session. Electric shock (0.5 mA) was also used to stimulate animals to run. Two weeks after the last familiarization session, they performed an acute exhaustive treadmill test. The test started for 5 min at 10 m/min and increased 2 m/min every 1 min. The acute exhaustive exercise protocol was implemented on a motorized treadmill at 32 m/min of speed until exhaustion. Despite all physical and electrical stimuli, the absence of any

activity or immobilization on the treadmill was considered as exhaustion and the running process was terminated. Immediately after euthanizing, muscle tissue (M. gastrocnemius) samples were collected from each group, which were stored at −80 °C. The muscle tissue samples was homogenized in ice-cold phosphate-buffered saline (gr tissue piece/10XPBS vol.). 1 mM PMSF protease inhibitor in PBS was used. The homogenates were centrifuged for 5 min. at 5000 g, and the supernatant obtained was stored at –80° C until the assays. The total protein concentration in the tissue was determined using the bicinchoninic acid assay method.

Measurement of Metabolic Analyses

The muscle tissue PDHa (Cat.No: EM1274), Slc16a1 (Cat.No: EM0793), Ppargc1a (Cat.No: EM0534), and TFAM (Cat.No: EM2518) levels were determined using a commercial ELISA kit following the manufacturer's instructions (FineTest, Wuhan Fine Biotech Co., Ltd., Hubei, China). The kits are based on the sandwich ELISA principle. The micro ELISA plate provided in those kits is pre-coated with an antibody specific to mouse PDHa (as with ELISA kits of Slc16a1, Ppargc1a, and TFAM). Muscle tissue homogenates (or Standards) are added to the micro ELISA plate wells and combined with the specific antibody. After incubation and washing process are added biotin-labeled antibody. After a second incubation and washing process are added HRP-Streptavidin Conjugate solution into each well. After incubation, artifacts are washed away. TMB substrate solution is added to each well and a final incubation is performed. The enzyme-substrate reaction is terminated by the addition of stop solution and the color turns yellow from blue. The optical density was measured with a microplate reader immediately (Varioskan LUX; Thermo Scientific) at a wavelength of 450 nm. The concentrations were calculated by comparing the OD of the samples with the standard curve. All results (except for TFAM) were expressed as ng/ mg protein, and TFAM level was expressed as pg/mg protein.

Statistical Analysis

SPSS statistical software version 24 (IBM Inc., Triangle Park, NC, USA) was used to perform all statistical analyses. The standard data distribution was tested with the Shapiro–Wilk test. Numerical variables were described using median and interquartile range values. The multi-group comparison of variables was conducted by Kruskal–Wallis test and pairwise comparisons were conducted by using Mann–Whitney U test with Bonferroni correction. For correlation, the Spearman correlation test was used. The relationship between the parameters was also shown with the heatmap matrix. A two-tailed p value < 0.05 was considered significant.

RESULTS

A total of 28 mice, 7 in each group, were included in the study. One of the mice in RJ group died during the study. The exercise protocol was completed as intended. Table 1 shows the comparison of PDHa, Slc16a1, Ppargc1a and TFAM muscle tissue levels among the control, Royal Jelly (RJ), Exercise, RJ+Exercise groups. According to Kruskal-Wallis analysis, PDHa and Slc16a1 levels was statistically significant between the groups (p=0.024, p=0.029, respectively) (Table 1, Figure 1). However, Ppargc1

Table 1. Muscle Tissue of PDHa, Slc16a1, Ppargc1a and TFAM Levels of The Subjects Within Groups

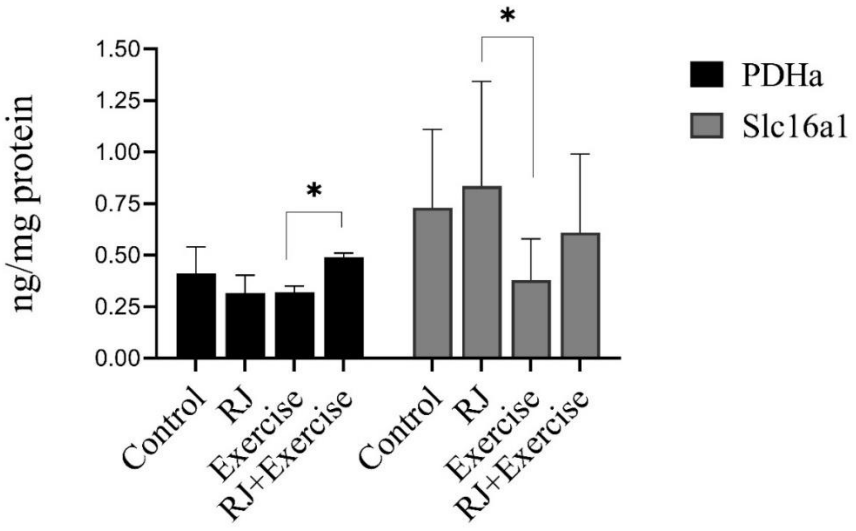
Parameters	Control n=7	RJ n=6	Exercise n=7	RJ+Exercise n=7	p*
PDHa, ng/mg protein	0.41 (0.22)	0.31 (0.11)	0.31 (0.14) α	0.49 (0.05)	0.024
Slc16a1, ng/mg protein	0.73 (0.46)	0.83 (0.76)	0.37 (0.26) β	0.60 (0.48)	0.029
Ppargc1a, ng/mg protein	0.82 (0.48)	0.49 (0.53)	0.34 (0.27)	0.53 (0.37)	0.087
TFAM, pg/mg protein	116.7 (61.37)	73.5 (77.3)	48.1 (39.9)	72.9 (60.6)	0.082

All The Data Were Expressed As The Median (Interquartile range), *Kruskal-Wallis Test, α: Exercise Group vs RJ+Excercise Group; β: Exercise Group vs RJ group. Abbreviations: RJ: Royal Jelly, PDHa: Pyruvate Dehydrogenase Alpha, Slc16a1: Monocarboxylate Transporter 1, Ppargc1a: Peroxisome Proliferator-Activated Receptor Gamma Coaktivator 1-Alpha, TFAM: Transcription Factor A, Mitochondrial.

Compared to the control group, PDHa activity was found to be lower in the RJ and exercise groups, while it was higher in the RJ+exercise group. In the intragroup comparison with Bonferroni correction, the difference between the RJ+exercise group and the exercise group was statistically significant (p=0.038). Although Slc16a1 levels varied between groups, the lowest Slc16a1 levels were in the

exercise group and the highest levels were in the RJ group. The difference between the exercise and RJ groups was statistically significant (p=0.041). Mitochondrial biogenesis parameters Ppargc1a and TFAM levels were found to decrease in the RJ, exercise and RJ+exercise groups compared to the control group. Ppargc1a and TFAM levels in the RJ+exercise group were higher than in the RJ and exercise groups, but were not statistically significant.

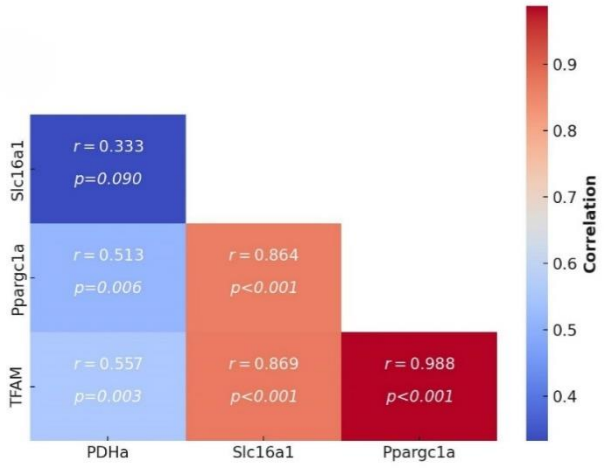
Figure I. PDHa and Slc16a1 Levels in Experimental Groups.



Median (IQR). *: p<0.05. Abbreviations: RJ: Royal Jelly, PDHa: Pyruvate Dehydrogenase Alpha, Slc16a1: Monocarboxylate Transporter 1.

The correlations between PDHa, Slc16a1, Ppargc1a, and TFAM levels are shown in Figure 2. A positive correlation was found between all parameters. As seen in the heatmap matrix, a very high level of positive correlation was found between Slc16a1 and TFAM and Ppargc1a (rho= 0.869, p<0.001; rho= 0.864, p<0.001, respectively). Also, the high correlation between TFAM and Ppargc1a, which are components of the same physiological mechanism (mitochondrial biogenesis), confirms our study results (rho= 0.98, p<0.001).

Figure 2. Heatmap Matrix Showing The Correlative Relationship Between The Parameters



Abbreviations: PDHa: Pyruvate Dehydrogenase Alpha, Slc16a1: Monocarboxylate Transporter 1, Ppargc1a: Peroxisome Proliferator-Activated Receptor Gamma Coaktivator 1-Alpha, TFAM: Transcription Factor A, Mitochondrial.

DISCUSSION

This study aimed to elucidate the effects of royal jelly supplementation on metabolic parameters by comparing them with control, royal jelly group, exercise and royal jelly+exercise groups. The findings showed that royal jelly supplementation decreased PDHa, a critical junction for aerobic respiration, whereas it significantly increased PDHa when taken in conjunction with acute exhaustive exercise. This suggests that royal jelly restores and improves the aerobic respiratory pathway during acute exhaustion exercise. Additionally, royal jelly supplementation increased the levels of Slc16a1 (MCT-1), which catalyzes the proton-coupled transport of monocarboxylates (I-lactate, pyruvate, and ketone bodies) across the plasma membrane. The level of Slc16a1, which decreased with acute exhaustion exercise, increased in the RJ+Exercise group. This finding suggests that royal jelly also activates the anaerobic respiratory pathway during acute exhaustion exercise. Correlation coefficients between Slc16a1 and PDHa levels and mitochondrial biogenesis parameters support the hypothesis about the aerobic and anaerobic mechanism of royal jelly.

Exercise is a fundamental component of cardiac rehabilitation regimens, and in particular, it reduces the risk of cardiovascular disease (9,10), supports general metabolic health (11), establishes and maintains musculoskeletal function (12), improves mental health (13), and extends life (14). The repeated deviations and changes in whole-body homeostasis caused by exercise cause different adaptations in various organs, including the brain, liver, adipose tissue, skeletal muscle, and heart (12,15). These effects may vary depending on the type of exercise (aerobic, anaerobic exercise), intensity, duration and physiological state (16). However, the molecular mechanisms by which exercise primarily improves cardiovascular health and prevents tissue injury remain unclear.

Low-intensity, rhythmic endurance-enhancing exercises involving larger muscle groups are defined as aerobic exercises (17), while short-term, high-intensity, and more strengthening exercises are defined as anaerobic exercises (18). In both types of exercise, skeletal muscle is one of the first organs to respond to homeostatic changes in adaptation to exercise and is critical for the effectiveness of exercise (19). One of the most important factors in muscle tissue during exercise is oxygen availability, which determines carbohydrate (Pyruvate) and lactate metabolism (20). Therefore, the preference of aerobic and anaerobic metabolic pathways of muscle tissue depends on this. Pyruvate dehydrogenase enzyme, one of the regulatory enzymes of carbohydrate metabolism, is regulated by the increase in ADP and pyruvate concentrations during exercise (21). It has been shown that pyruvate dehydrogenase enzyme activity increases during aerobic, sprint and isometric exercise (22). In contrast, in our study, PDHa activity was found to be low in muscle tissue after acute exhaustion exercise. This decrease is thought to be due to the active anaerobic metabolic pathway during acute exercise. However, RJ+exercise combination caused an increase in PDHa activity. This suggests that royal jelly enhances and improves the aerobic respiratory pathway during acute exhaustion exercise.

The production and utilization of lactate in muscles are strongly related to exercise performance. Increased accumulation of lactate in muscle tissue under hypoxic conditions or muscle disorders can lead to muscle fatigue and exercise intolerance (20). A decrease in pH and a significant increase in blood lactate concentration are just some of the negative effects that affect homeostasis, muscle contraction, strength, and ultimately exercise ability. On the other hand, lactate can be an important source of energy in working muscles. During exercise, it is critical to select an appropriate training intensity to maintain lactate balance and increase aerobic capacity (23). In addition, the presence and activity of certain enzymes (e.g. lactate dehydrogenase) or carrier proteins (Slc16a1/MCT1, MCT4) strongly determine the rate of lactate metabolism. Slc16a1, a proton-linked monocarboxylate transporter, facilitates rapid transfer of lactate across the cell membrane, which can be used as fuel for mitochondrial respiration in muscle tissue (24). It was found that royal jelly supplementation increased Slc16a1 levels in muscle tissue, while acute exhaustion exercise decreased Slc16a1 levels in muscle tissue. This shows that intramuscular lactate concentration increases in acute exhaustion exercise, and the lactate gradient is disrupted. However, it was found that Slc1a61 levels increased in the RJ+exercise group. Royal jelly supplementation has been shown to regulate lactate metabolism with acute exercise and to use lactate in the energy pathway.

Mitochondrial biogenesis is defined as the development of existing mitochondria and the adaptation of skeletal muscle to exercise training, induced by many signaling pathways that respond to metabolic, mechanical and hypoxic stresses occurring in myocytes during contraction (25). It has been determined that muscle mitochondrial biogenesis increases with regular exercise, and the increase in mitochondrial content increases endurance performance in individuals (26,27). It has also been reported that supplements that regulate energy metabolism contribute to this process with exercise (16). In contrast to endurance exercises, it has been reported that there is a decrease in mitochondrial volume in resistance exercises, thus decreasing mitochondrial biogenesis (28). On the other hand, some studies have stated that there is no increase or change in mitochondrial biogenesis or oxidative capacity markers after resistance exercise training (29,30) However, uncertainties on this issue still persist (31). In our study, it was found that Ppargc1a and TFAM levels, which are mitochondrial biogenesis markers, decreased after acute exhaustion exercise. Although not statistically significant, royal jelly supplementation increased mitochondrial biogenesis with exercise. Similarly, Flockhart et al. reported that excessive exercise leads to impairments in mitochondrial respiratory capacity (32). Another study indicated that short-term excessive exercise causes oxidative alterations in mitochondrial proteins, resulting in a significant reduction in mitochondrial respiration (33). These findings support the outcomes of our study. In addition, the high correlation coefficients between Slc16a1 and PDHa levels and mitochondrial biogenesis parameters support our hypothesis that royal jelly improves and regulates aerobic and anaerobic mechanisms. In general terms, the presence of varied outcomes in the literature may stem from differences in muscle activity protocols and the timing of post-exercise sample collection.

CONCLUSION

Our research emphasizes the impact of royal jelly on PDHa and Slc16a1 levels, which are crucial in the aerobic and anaerobic energy pathways. By supplementing with royal jelly, we observed an improvement in the regulation of these pathways during acute exhaustive exercise. Our findings have implications for various disciplines including exercise physiology and sports science.

Limitations and Suggestions for Future Research

Despite our contributions, there are some limitations to our research. Biochemical data along with the metabolic parameters used in this study could have contributed to the research results. Future studies can facilitate the evaluation with different tissues and a wide range of parameters to show the effects of acute exhaustion exercise and the effects of royal jelly-like supplements.

DESCRIPTIONS

No financial support.

No conflict of interest.

Acknowledgments: I would like to thank Mahmut Kılıç for his valuable contributions.

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Acta Medica Ruha
International Journal of Medicine and Health Sciences
E-ISSN: 2980-1184

REVIEW ARTICLE
Volume:2 Issue:3 Year:2024 https://doi.org/10.5281/zenodo.13784407

How Much Do Guidelines in Thoracic Surgery Influence Our Daily Practice? – A Review of the Current Routine

Göğüs Cerrahisinde Kılavuzlar Günlük Pratiğimizi Ne Kadar Etkiliyor? – Mevcut Rutinin Gözden Geçirilmesi

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ABSTRACT

Guidelines are formulated based on the results of randomised clinical trials, other non-randomized studies, and expert opinions (i.e., the opinions of most guideline committees). A randomised, multicenter, controlled trial is the ideal study to determine a patient population's mean values. However, some diseases and populations do not lend themselves easily to this format, and therefore, studies with less stringent design and enrollment criteria are often used. The latest guidelines have more reliable data and distinct subgroups and carry a higher risk of misinterpreting results than older models. Guidelines are part of a continuous educational program to facilitate a more homogeneous approach to all patients with the same disease, reduce inappropriate and unnecessary testing, ineffective treatments, and health costs, and ultimately improve care. As a result, guidelines are allegiant. The surgeon should question why and how this guideline was prepared, who supported its creation, who is on its organisation committee, and what it represents. Within the scope of this review, recommendations to improve the guidelines will be presented.

Keyswords: Thoracic Surgery, Guidelines, Randomised Controlled Trials, Clinical Practice.

ÖZET

Kılavuzlar, randomize klinik araştırmaların, diğer randomize olmayan çalışmaların sonuçlarına ve uzman görüşlerine (yani çoğu kılavuz komitesinin görüşlerine) dayanarak formüle edilir. Randomize, çok merkezli, kontrollü bir çalışma, hasta popülasyonunun ortalama değerlerini belirlemek için ideal çalışmadır. Ancak bazı hastalıklar ve popülasyonlar bu formata kolaylıkla uyum sağlamamaktadır ve bu nedenle daha az katı tasarım ve hasta alım kriterlerine sahip çalışmalar sıklıkla kullanılmaktadır. En yeni kılavuzlar daha güvenilir verilere ve farklı alt gruplara sahiptir ve öncekilere göre sonuçların yanlış yorumlanma riski daha yüksektir. Kılavuzların, aynı hastalığa sahip tüm hastalara daha homojen bir yaklaşımı kolaylaştırmak, uygunsuz ve gereksiz testleri, etkisiz tedavileri ve sağlık maliyetlerini azaltmak ve sonuçta bakımı iyileştirmek için sürekli bir eğitim programının bir parçasını oluşturduğu iddia edilmektedir. Sonuç olarak, yönergeler sadıktır. Cerrah bu kılavuzun neden ve nasıl hazırlandığını, oluşturulmasına kimlerin destek verdiğini, organizasyon komitesinde kimlerin bulunduğunu, neyi temsil ettiğini sorgulamalıdır. Bu inceleme kapsamında kılavuzların iyileştirilmesine yönelik öneriler sunulacaktır.

Anahtar Kelimeler: Göğüs Cerrahisi, Kılavuzlar, Randomize Kontrollü Çalışmalar, Klinik Uygulama.

INTRODUCTION

The doctor's mission is to protect human health. To achieve this goal, the doctor must possess the necessary knowledge and be able to apply it to an individual patient. This process must be governed by medical ethics. Therefore, the total of a physician's training should equip him/her with everything necessary to accomplish his/her mission. Some randomised prospective studies can provide data on groups of patients with small differences between them, which clinicians cannot distinguish, no matter how careful they are, and also on patients they systematically follow. Guidelines play a crucial role in our mission, with advantages and disadvantages. The accumulation of medical knowledge on diagnosis and management in the last 5-6 years has changed the course of diseases, improved clinical outcomes and increased survival. Therefore, it has been difficult for the practising physician to assess a particular therapy's long-term effects on a patient's survival. Moreover, each physician's approach to a patient with the same disease is not always uniform. Various scientific organisations have introduced clinical practice guidelines to assist physicians in applying newly acquired knowledge to patients, underscoring the significant impact of your work. Guidelines help translate new research discoveries into clinical practice (1).

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Received: 06.06.2024, Accepted: 16.08.2024, Published Online: 20.09.2024
Cited: Derdiyok O. How Much Do Guidelines in Thoracic Surgery Influence Our Daily Practice? – A Review of the Current Routine. Acta Medica Ruha. 2024;2(3):216-220. https://doi.org/10.5281/zenodo.13784407
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Randomised Clinical Trials

Evidence-based practice is the process of using the best available evidence to support clinical decisions. Guidelines are not mandatory protocols. The role of guidelines is clear in the presence of two factors. The first factor is the diversity of practices that affect patient outcomes, and the second is a strong evidence-based research base for effective therapeutic intervention. There are several limitations to the preparation of guidelines, such as the quantity and consistency of resources and the generalizability and applicability of study findings. Dr Barry Greenberg, former associate editor of the Journal of the American College of Cardiology, compares trials to music (i.e., monotonous background music, usually played in elevators or on-hold telephones). However, it is like Mozart's music, with various musical notes. The patients in daily clinical practice represent various conditions, from mild to severe, acute to chronic, and simple to very complex, with multiple medical problems. In the same way that Mozart's music cannot be made muzak, applying the results from a selected homogeneous population to complex patients with complex diseases is difficult (2).

A randomised, multicenter, controlled trial is the ideal study to determine a patient population's mean values. However, some diseases and populations do not lend themselves easily to this format, and therefore, studies with less stringent design and enrollment criteria are often used. The latest guidelines have more reliable data and distinct subgroups and carry a higher risk of misinterpreting results than older models (3).

Guidelines are often presented analytically and in detail, with the result that a person reviewing this information may not be able to determine its ultimate or core message, which extremely complicates its use by clinicians. Summary guidelines or "pocket rules" become helpful to some extent but do not solve the problem. Furthermore, guidelines in their current form are designed more often for memorisation rather than stimulating the critical ability and curiosity of the thoughtful physician. In the final analysis, guidelines are difficult to read and assimilate. Because of the procedures required to produce guidelines, they tend to be published years after the end of the clinical trial, which is a serious disadvantage (4).

DISCUSSION

Scientific societies introduced practice guidelines as a means of 'standardisation' to help physicians implement more uniform health care and bring new knowledge to each patient's care, thereby improving clinical outcomes. In 1984, the American College of Cardiology (ACC) / American Heart Association (AHA) published clinical practice guidelines for the first time. This document responded to a request from the United States Government to review the evidence on the use of cardiac pacemakers. For over 30 years, the ACC/AHA has developed more than 30 clinical practice guidelines for various conditions and procedures, with 'updates' and additional changes at intervals (5). Thus, it has become quite difficult for a single physician to assess the long-term effects of a particular treatment or intervention on 'hard' endpoints such as death, myocardial infarction, stroke, and others. Not surprisingly, each doctor's approach to an individual with the same disease is often similar but not uniform. Guidelines help translate new research discoveries into clinical practice; however, despite improvements over the years, guidelines remain controversial (6).

The concept of clinical research dates back to antiquity. In short, in randomised clinical trials, a hypothesis is formulated and based on this hypothesis- usually a null hypothesis- the study protocol is designed by a committee of experts in the field under investigation. For the conduction of a trial, overall organization and financial support are needed, and for large-scale clinical trials, the financial requirement is quite high (7). The greatest support comes from the industry in terms of limitations and costs of medical products; support should be provided by industrial firms because there are many difficulties in conducting very important studies without their support. However, companies are driven to prove that their product is better than an approved agent or placebo, and thus, they want to present 'favourable' outcomes. It is known that the way a protocol is designed can influence the results. For example, using the wrong dosage of an active control drug with unfavourable outcomes suggests the relative superiority of the study drug. Thus, industry involvement in clinical trials is associated with a risk of bias (8).

The place of these guidelines in daily use for thoracic surgery is controversial. In 2011, as a result of a meta-analysis of studies on hyperhidrosis, Cerfolio et al. revealed no standardised therapeutic approach and reported that different surgical approaches yielded nearly similar results (9). In 2014, Tschopp et al. reviewed studies on pneumothorax. They found that the rate of chemical pleurodesis, which was not included in the first options according to the 2010 pneumothorax treatment guidelines, was higher than that of mechanical abrasion and pleurectomy. However, it has been shown that chemical pleurodesis, which is not included in the first-line treatment approaches for pneumothorax in current guidelines, may come to the forefront with time in the future (10).

In the 2017 National Comprehensive Cancer Network (NCCN) mesothelioma guidelines, the survival rate of previously often preferred extrapleural pneumonectomy (EPP) was found to be lower than the other surgical treatment options, i.e. pleurectomy/decortication (P / D). Indeed, patients who underwent P/D responded better to chemotherapy and survived better. P/D is one of the first treatment options for mesothelioma (11). In the non-small cell lung cancer (NSCLC) 2017 guidelines, biopsy is recommended before surgery in stage 1 and stage 2 NSCLC. However, in the treatment stages indicated in the same guideline, it is stated that high PET uptake is sufficient to establish diagnosis in stage 1 and stage 2 NSCLC. This approach can make a serious difference in treatment options (12). Currently, the NCCN guidelines recommend "consideration of " invasive mediastinal staging for clinical stage IB-IIIA non-small cell lung cancer and invasive mediastinal staging for clinical stage IA disease. However, a recent multi-institutional prospective trial questions this approach. Of 90 patients with clinical stage I NSCLC considered at risk for occult N2 disease (T2N0 or T1N0 based on positron emission tomography with a standardised uptake value >10), mediastinoscopy detected occult N2 disease in only 1.1% of patients. The mean tumour size of 4.3 cm in diameter was considered significant and ranged from 1.3 to 12 cm. Taken together, it can be expected that in the coming years, national guidelines on invasive mediastinal staging recommendations may also consider histological subtype of the tumour, will be improved (13). Currently, the NCCN guidelines recommend sub-lobar resection as an alternative treatment for patients with peripheral nodules with an adenocarcinoma in situ pattern or glass-like appearance that is larger than 2 cm in size (12).

Although bias exists in some study designs, other studies yield negative or controversial results. Patients with stage IIIA NSCLC at diagnosis represent a very heterogeneous group, including those with limited microscopic ipsilateral mediastinal lymph node involvement discovered after surgical resection and those with radiologically evident subcarinal lymph node involvement at presentation. Different treatment options for stage IIIA disease include neoadjuvant therapy followed by surgery, primary surgery, adjuvant chemotherapy with or without sequential adjuvant radiotherapy, or definitive chemoradiotherapy without surgery. When surgery is not considered an option, a combination of chemotherapy and radiotherapy may be offered for curative purposes. For stage III NSCLC, survival after surgery alone is generally poor, between 5-10% at five years, due to the higher frequency of local and distant failure to eradicate tumour foci. Randomised trials and meta-analyses have shown a modest improvement in survival with neoadjuvant chemotherapy, but local and distant failure rates remain high. Neoadjuvant or adjuvant chemotherapy is part of multimodality treatment for stage IB-IIIB, as the risk of distant metastases after surgery alone is at a higher rate (14).

Andre et al. analysed a cohort of 702 patients with N2 NSCLC. This study identified four risk factors for clinical manifestations of N2 before surgery: multistation mediastinal lymph node involvement and T3 or T4 stage disease (15). Choi et al. found that among 19 clinical pathologic prognostic factors examined in patients with pathologic manifestations of N2 NSCLC, incomplete resection detected in CT after induction chemotherapy and persistent N2 disease were negative prognostic factors in univariate analysis. The presence of clinical manifestations of N2 disease, multistation mediastinal lymph node involvement and adenocarcinoma histology indicated poor prognosis without any statistically significant prognostic significance. Moreover, the administration of adjuvant chemotherapy did not significantly improve the prognosis (16). The results of two small, randomised trials published in early 1994 have important implications for treating patients with stage IIIA. These studies confirmed the superiority of surgery followed by induction chemotherapy after surgery for patients with stage IIIA disease (17, 18). Subsequent randomised trials and two meta-analyses compared surgery alone with surgery in patients with stage IIIA NSCLC following neoadjuvant chemotherapy and demonstrated a

significant benefit in favour of neoadjuvant chemotherapy. Data from both systematic reviews show a 6-7% absolute benefit in five-year survival in IIIA patients, improving their results from 15-35% to 21-42% (19, 20).

Thoracic surgeons are generally not inclined to use medical evidence. Guidelines are seen as accepted taboos for various reasons (being unaware of relevant medical evidence, distrust in the formulation of medical evidence, refraining from being "stigmatised" in the profession, and not being sued for malpractice, etc.). Medical oncologists may also be responsible for thoracic surgeons not being inclined to use guidelines. Indeed, medical oncologists have more say in the preparation of guidelines than the main discipline of thoracic surgery because they are more investigative and financially supported. Besides they are overprotective against their discipline and essentially keep the control of the patient flow.

CONCLUSION

As a result, guidelines are allegiant. The surgeon should question why and how this guideline was prepared, who supported its creation, who is on its organization committee, and what it represents.

DESCRIPTIONS

No financial support.

No conflict of interest.

Acknowledgments: The editorial support has been given by Ozan BATIGÜN MD, MBA

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Acta Medica Ruha
International Journal of Medicine and Health Sciences
E-ISSN: 2980-1184

REVIEW ARTICLE
Volume:2 Issue:3 Year:2024
https://doi.org/10.5281/zenodo.13784433

Obezite Kaynaklı İnflamasyon ve Kardiyovasküler Olaylar

Obesity-Induced Inflammation and Cardiovascular Events

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ÖZET

Obezite, hastalık ve ölüm oranlarının artmasına neden olan bir rahatsızlıktır. Bu rahatsızlık, kardiyovasküler hastalıklar başta olmak üzere tip 2 diyabet, kanser ve birçok hastalıkla ilişkilidir. Özellikle kardiyovasküler hastalıklar, obez bireylerde ölüm nedenlerinin başında gelmektedir. Ayrıca enfeksiyon, obezite ve diyabetinde içinde bulunduğu birçok hastalık inflamasyon ile bağlantılıdır. Obezite interlökin-6, tümör nekroz faktörü-α ve C-reaktif protein gibi inflamatuar sitokinlerin artması ile ilişkilidir. İnflamasyonun ateroskleroz, hipertrofik kalp yetmezliği ve miyokard enfarktüsü gibi kalp hastalıklarında da artış gösterdiği bilinmektedir. Leptin, resistin, retinol bağlayıcı protein 4 gibi adipokinler ile interlökin-1β, interlökin-6, CRP, tümör nekroz faktör-alfa, plazminojen aktivatör inhibitör-1, vb. inflamasyon medyatörleri kronik inflamasyonda yer alır. İnflamatuar sitokinler esas olarak immün sistemi hücreleri tarafından salınsa da iskemik ya da hipertrofik stres sonrasında endotel hücreler, kardiyomiyositler ve kardiyak fibroblastlar tarafından da sentezlenmektedir. Kalbin, meydana gelen inflamasyonu en aza indirgeyebilmek için endojen kökenli tabii kaynakları bulunmaktadır. Kardiyak inflamasyonu azaltmak için ya anti-inflamatuar medyatörlerin yoğunluğunu fazlalaştırmak ya da proinflamatuar medyatörlerin yoğunluğunu azaltmak gerekir. Bu yüzden kalpte bulunan endojen kökenli tabii mekanizmalar devreye girerek kardiyak işlevi olumlu yönde düzenler. Sonuç olarak; sistemik inflamasyonun azaltılması, inflamatuar immün hücrelerinin etkinliğinin minimum seviyeye indirgenmesi kardiyak inflamasyon bakımından olumlu yönde büyük katkı sağlayacaktır.

Anahtar Kelimeler: Obezite, Obezite ve İnflamasyon, Obezite ve Kardiyovasküler Olaylar.

ABSTRACT

Obesity is a condition that leads to increased morbidity and mortality. It is associated with cardiovascular diseases, type 2 diabetes, cancer and many other diseases. Cardiovascular diseases are the leading cause of death in obese individuals. In addition, many diseases including infection, obesity and diabetes are linked to inflammation. Obesity is associated with an increase in inflammatory cytokines such as interleukin-6, tumor necrosis factor-α and C-reactive protein. Inflammation is also known to be increased in heart diseases such as atherosclerosis, hypertrophic heart failure and myocardial infarction. Adipokines such as leptin, resistin, retinol binding protein 4 and inflammation mediators such as interleukin-1β, interleukin-6, CRP, tumor necrosis factor-alpha, plasminogen activator inhibitor-1, etc. are involved in chronic inflammation. Inflammatory cytokines are mainly released by cells of the immune system but are also synthesized by endothelial cells, cardiomyocytes and cardiac fibroblasts after ischemic or hypertrophic stress. The heart has natural resources of endogenous origin to minimize the inflammation that occurs. To reduce cardiac inflammation, it is necessary either to increase the concentration of anti-inflammatory mediators or to decrease the concentration of pro-inflammatory mediators. Therefore, natural mechanisms of endogenous origin in the heart come into play to positively regulate cardiac function. In conclusion, reducing systemic inflammation and minimizing the activity of inflammatory immune cells will make a major positive contribution to cardiac inflammation.

Keyswords: Obesity, Obesity and Inflammation, Obesity and Cardiovascular Events.

GİRİŞ

Obezite, hastalık ve ölüm oranlarının artmasına neden olan bir rahatsızlıktır (1,2). Bu rahatsızlık, kardiyovasküler hastalıklar (KVH) başta olmak üzere tip 2 diyabet, kanser ve birçok hastalıkla ilişkilidir. Özellikle KVH' ler, obez bireylerde ölüm nedenlerinin başında gelmektedir. Çeşitli KVH' lerin obez bireylerde büyük risk oluşturmasının altında yatan faktörler arasında hipertansiyon, tip 2 diyabet, insülin direnci vb. bulunmaktadır. Aynı zamanda obezite inflamasyonla da ilişkilidir ve bu ilişki KVH' nın risk faktörlerinin tetiklenmesine sebep olur. (1). Yaygın olarak vücut Kitle İndeksi (VKİ), bir bireyin sağlıklı bir kilo aralığında bulunup bulunmadığını tespit etmek için kullanılan bir ölçümdür. VKİ' nin hesaplanması; VKİ = Ağırlık (kg)/boy2 (m2) (2). Bu ölçüm kardiyovasküler (KV) risk altında bulunan hastaları aynı kategoride gruplandırmaz. Bu yüzden, VKİ hesaplamalarına karşın bel çevresi ve bel-

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Received: 08.12.2024, Accepted: 06.09.2024, Published Online: 20.09.2024
Cited: Hacanlı Y. Obesity-Induced Inflammation and Cardiovascular Events. Acta Medica Ruha. 2024;2(3):221-227. https://doi.org/10.5281/zenodo.13784433
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kalça oranı hesaplamalarından miyokard enfarktüsü ve metabolik rahatsızlıkların tespitine yönelik daha iyi sonuçlar elde edilebilir. (1). Çünkü bel çevresi ve bel-kalça oranı vücut yağ dağılımı ve merkezi obezite ile bağlantılıdır. Bu bağlantı aynı zamanda morbidite ile ilişkili olmasının sebebidir (2).

İnflamasyon ve Kardiyovasküler Hastalıklar

Enfeksiyon, obezite ve diyabetinde içinde bulunduğu birçok hastalık inflamasyon ile bağlantılıdır (3). Özellikle obezite interlökin-6 (IL-6), tümör nekroz faktörü-α (TNF-α) ve C-reaktif protein (CRP) gibi inflamatuar sitokinlerin artması ile ilişkilidir (4). İnflamasyonun ateroskleroz (5), hipertrofik kalp yetmezliği (6) ve miyokard enfarktüsü (7) gibi kalp hastalıklarında da artış gösterdiği bilinmektedir. Leptin, resistin, retinol bağlayıcı protein 4 (RBP4) (8) gibi adipokinler ile (9) interlökin-1β (IL-1β), IL6, CRP, TNFα, plazminojen aktivatör inhibitör-1 (PAI-1), vb. inflamasyon medyatörleri kronik inflamasyonda yer alır (3) omentum-1 ve adiponektin ise anti-aterojenik ve anti-inflamatuar etkinlik gösteren adipokinler grubundadır (9).

İnflamatuar sitokinler esas olarak immün sistemi hücreleri tarafından salınsa da iskemik ya da hipertrofik stres sonrasında endotel hücreler (10), kardiyomiyositler (11) ve kardiyak fibroblastlar (8) tarafından da sentezlenmektedir. Kalbin, meydana gelen inflamasyonu en aza indirgeyebilmek için endojen kökenli tabii kaynakları bulunmaktadır. Kardiyak inflamasyonu azaltmak için ya anti-inflamatuar medyatörlerin yoğunluğunu fazlalaştırmak ya da proinflamatuar medyatörlerin yoğunluğunu azaltmak gerekir. Bu yüzden kalpte bulunan endojen kökenli tabii mekanizmalar devreye girerek kardiyak işlevi olumlu yönde düzenler (12).

Bağışıklık hücrelerinden dolaşıma aktarılan özellikle IL-1β, IL-6 (13) ve TNFα gibi (14) inflamatuar sitokinler KV sistemdeki inflamasyon ile ilişkili olup, düzeylerinde yükselme görülmektedir. Buna karşın, İnterlökin-10 (IL-10) ve transforme edici büyüme faktör-beta' yıda (TGFβ) içeren (15) bazı anti-inflamatuar sitokinlerde ise düşüş meydana gelir. Bu durum ateroskleroz başta olmak üzere bir takım KVH' lerin meydana gelmesi ile beraber lipid yoğunluğunun artışına neden olur. Örneğin, MI hastalarında obezitenin de eşlik etmesiyle birlikte IL-1β, IL-6 ve TNFα gibi inflamatuar sitokinlerde yükselme gözlenirken; obezitesi bulunmayan MI hastalarına göre IL-10 düzeyinde ise düşüş görülmüştür (3).

İnflamasyonda Rol Oynayan Adipokinler

Leptin

Leptin, inflamasyonun başlaması ve gelişiminde yer alan önemli adipokinler arasında bulunmaktadır (16). İnflamasyonun ateroskleroza kadar uzanabilen sürecinde rol oynar. Obez olan hastalarda miyokard ve damar yapısı leptinin inflamatuar fonksiyonlarına karşı dayanıklı değildir (11). Leptin; IL-6, TNFα ve monosit kemotaktik proteinin (MCP-1) daha fazla salgılanmasını sağlar. Bu artış: endoteliyal-selektin (E-selektin), vasküler hücre adezyon molekülü 1 (VCAM-1) ve hücreler arası adezyon molekülü 1 (ICAM-1) gibi adhezyon moleküllerinin ekspresyonunu fazlalaştırarak inflamasyonu tetikler. Bu durum monositlerin vasküler endotel hücre çeperlerine doğru yönelmesine neden olur. Sonucunda ise, vasküler endotel hücre bağlantılarının geçirgenliğinin olması gerekenden daha fazla olmasına ve ateroma sebep olur (10). Ayrıca leptin, serbest radikallerin (özellikle reaktif oksijen türleri) sentezini ve endotel hücrelerin proliferasyonunu tetikler. Bu durum nitrik oksit (NO) bağımlı vazorelaksasyona zarar vererek vazokonstriksiyon ve tromboz oluşumuna katkı sağlar. Endotel fonksiyon bozukluğuna ve aterosklerozun gelişimine neden olur (12).

Retinol bağlayıcı protein 4

RBP4, fazla oranda visseral yağ bulunan kişilerde ciddi seviyede yükselir. RBP4' ün serum konsantrasyonunun artması demek trigliserit ve kolesterolün yükselmesi, HDL' nin düşmesi, metabolik sendrom, hipertansiyon ve VKİ' nin yükselerek aterosklerozla ilişkili olması demektir (17).

İnflamasyonda Rol Oynayan İnflamatuar Sitokinler

İnterlökin-1β

IL-1β; hasarlı endotel hücrelerden, bağışıklık hücrelerinden ve kardiyak hücrelerden salınmaktadır. Özellikle kardiyak inflamasyon ile bağlantılıdır. Örneğin akut miyokard enfarktüsü, kaspaz-3 aracılığıyla gerçekleşen apoptozdan dolayı kardiyak hücrelerde hasar oluşturan IL-1β' nın aracılık ettiği kardiyak inflamasyonu tetikler. (18). IL-1β' yi durdurmak kardiyovasküler inflamasyonu ciddi oranda hafifletse de inflamasyonu tam anlamı ile bloke edemeyebilir (19).

İnterlökin-6

İnterlökinler içerisinde KV inflamasyon ile ilgili en fazla çalışılan, proinflamatuar bir sitokin olan IL-6' dır. Akut iskemiden sonra kardiyak dokuda oluşan hasarda etkinliği bulunmaktadır. Organ yetmezliği ve doku hasarına neden olan proteinler akut faz proteinleridir ve bu proteinlerin sentezinin gerçekleşmesi IL-6' nın salgılanmasına bağlıdır. IL-6 ile beraber CRP seviyelerinin artması akut iskemik bir durumun olduğunu gösterir. Kalp yetmezliği (KY) yinelenmesinin belirtecidir. IL-6 düzeyi, obez ve KV riskleri bulunan hastalarda incelendiğinde yükselmiş olduğu görülür. Ek olarak, yükselmiş IL-6 seviyeleri endotel fonksiyon bozukluğunun da habercisidir. IL-6 seviyesi kalp ameliyatı olan hastalarda yükseldiği zaman mortalitenin önemli bir habercisidir (3).

Tümör Nekroz Faktör-α

TNF-α, makrofaj ve mast hücrelerinden dolaşıma aktarılmaktadır. Birçok inflamatuar sitokini tetikleyerek KV inflamasyonda yer almaktadır. Miyokardit hastalığına sahip hasta kalbinde, TNF-α' nın RNA ve protein miktarları ile reseptör I ve reseptör II' de artış gözlemlenmektedir. Kronik KY bulunan hastalarda da yine TNF-α ve reseptörlerinde artış söz konusudur. Ayrıca, TNF-α aracılığıyla matriks metalloproteinaz-3 (MMP-3) sinyal yolunun etkinliği kardiyak remodeling' de rol oynar (3).

Tablo 1. Kardiyovasküler Hastalıkta ve Obezitede İnflamasyonun Düzenleyicileri (20)

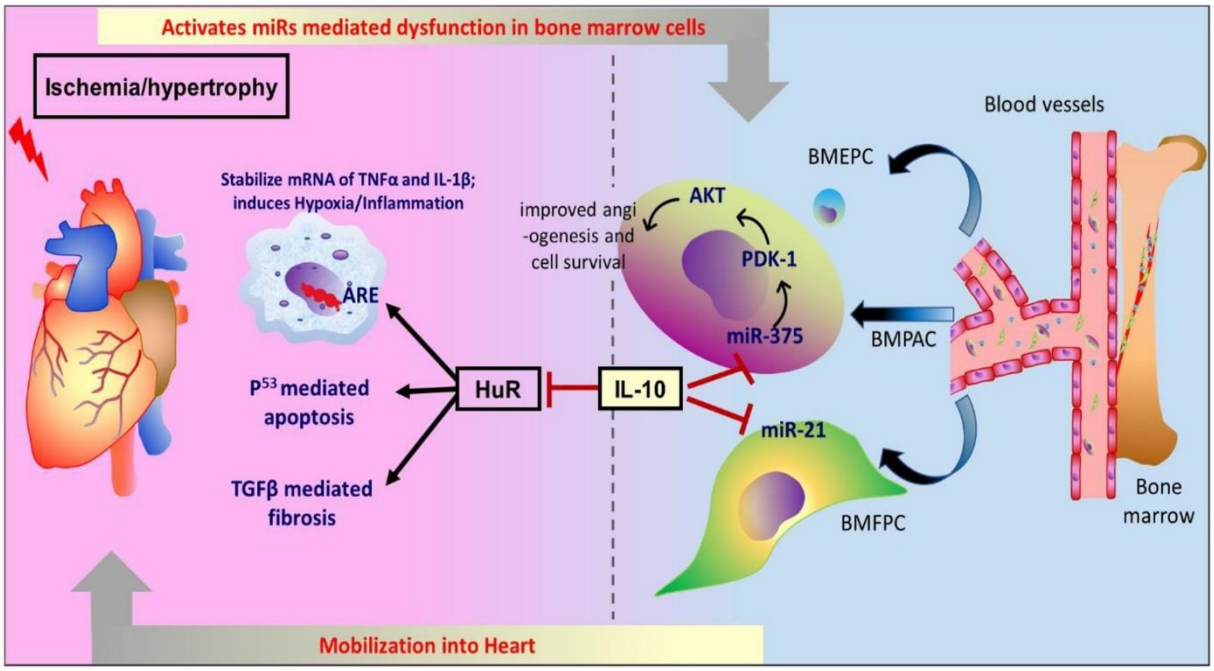
	Ateroskleroz üzerindeki etkisi	Metabolik fonksiyon üzerindeki etkisi
IL-6	Ateromlardaki enflamasyonu daha da artırmak için makrofajlar tarafından salgılanır	Genetik analizde insülin duyarlılığını bozar ve T2D riskini artırır
TNF-α	-Mendelian randomizasyon analizinde KVH ile nedensel olarak ilişkilendirilmiştir -Ateromlardaki makrofajlar ve enflamatuar hücreler tarafından salgılanarak enflamasyonu daha da artırır	Yağ dokusundaki makrofajlar tarafından salgılanır. hayvan modellerinde insülin sinyalinin azalmasında rol oynar
PAI-1	tPA'yı inhibe ederek ve fibrinoliz ve aterotromboza katkıda bulunarak intravasküler trombüs ve KVH riskini artırır	Serbest yağ asidi, abdominal yağ birikimi olan bireylerde bulunan yüksek seviyelerde üretimi artırır
Serbest yağ asidi	Makrofajlarda NLRP3 inflamazoma ve TLR4'ü aktive eder	Ektopid lipid birikimine, insülin direncine ve tip 2 diyabete katkıda bulunur

IL: İnterlökin, PAI-1: Plazminojen aktivatiör inhibitör-1, TNF-α: Tümör nekroz faktör alfa, tPA: Doku plazminojen aktivatörü.

Anti-inflamatuar Sitokin: İnterlökin-10

IL-10, sitokin grubu içerisinde bulunan pleyotropik anti-inflamatuar sitokindir. B hücreleri, makrofaj / monosit hücreleri, Th2 hücreleri, Treg hücreleri ve mast hücrelerini de içeren çeşitli bağışıklık hücrelerinden salgılanmaktadır. IL-10'un KV fonksiyonlarda anti-inflamatuar özelliği ile tanınmaktadır. Diyabetik bireylerde kardiyak inflamasyon, IL-10 sentezinin azalması ile gerçekleşir. Bu azalmanın nedeni IL-10 promotör dizisinin −1082 pozisyonundaki bir polimorfizmdir (21). IL-10 desteği ile gerçekleştirilen tedavilerde kardiyak inflamasyon hafifletilir. Bu düzelme sağlanırken IL-10 desteği; IL-1, IL-6 vb. inflamasyona neden olan sitokinlerin azaltılmasında rol oynar (22). Ayrıca MI sonrası kalbe kök hücrelerin geçişini sağlar. Bu kök hücreler kemik iliğinden aktarılan hücrelerdir (23).

Kısacası, IL-10, kardiyak inflamasyon bağlamında kapsamlı bir şekilde incelenen ve stromal hücre kaynaklı faktör-1 (SDF1) ve sinyal dönüştürücü ve transkripsiyon aktivatörü 3' ü (STAT3) etkinleştirirken HuR ve mikroRNA-21 ve mikroRNA-375' i engelleyerek kardiyak inflamasyonun azaltılmasını sağlayan anti-inflamatuar bir sitokindir. IL-10' un aktivasyonu ile fibröz ile bağlantılı kardiyak hipertrofi ve MI şiddeti düşürülür (3) (Şekil 1).



Şekil 1. IL-10' un Kalbin Rejenerasyonuna Nasıl Yardımcı Olduğunun Şematik Gösterimi (24)

TARTIŞMA

VKİ, bir bireyin sağlıklı bir kilo aralığında bulunup bulunmadığını tespit etmek için kullanılan bir ölçümdür. (2). VKİ hesaplamalarına karşın bel çevresi ve bel-kalça oranı hesaplamalarından miyokard enfarktüsü ve metabolik rahatsızlıkların tespitine yönelik daha iyi sonuçlar elde edilebilir (25). Çünkü bel çevresi ve bel-kalça oranı vücut yağ dağılımı ve merkezi obezite ile bağlantılıdır. Bu bağlantı aynı zamanda morbidite ile ilişkili olmasının sebebidir (2). Enfeksiyon, obezite ve diyabetinde içinde bulunduğu birçok hastalık inflamasyon ile bağlantılıdır (3). Leptin, resistin, retinol bağlayıcı protein 4 (RBP4) (16) gibi adipokinler ile (9) interlökin-1β (IL-1β), interlökin-6 (IL6), CRP, tümör nekroz faktör-alfa (TNFα), plazminojen aktivatör inhibitör-1 (PAI-1), vb. inflamasyon medyatörleri kronik inflamasyonda yer alır (3) omentum-1 ve adiponektin ise anti-aterojenik ve anti-inflamatuar etkinlik gösteren adipokinler grubundadır (9). El-Wakkad ve arkadaşları 86 obez hastada, merkezi obezite ile anti-inflamatuar sitokinler arasındaki ilişkiyi değerlendirdi. Hastalar iki gruba ayrıldı. Bel-kalça oranı 0,8' in üstünde olan 43 hasta çalışma grubu olurken, bel-kalça oranı 0,8' in altında olan 43 hastada da kontrol grubu olarak çalışmaya dahil edildi. Çalışma sonucunda, bel-kalça oranı 0,8' in üstünde olan çalışma grubunda IL-1β, TNF-α, leptin ve proinflamatuar sitokinlerde yükselmelerin olduğu görülmüştür. Buna karşın adiponektin seviyelerinde ise düşüş tespit edilmiştir (26). 2015' de Larsson ve arkadaşlarının yaptığı çalışmada, TNF-α ve IL-6 'nın obezitenin neden olduğu inflamasyonda önemli etkinliklerinin bulunduğu ve yoğunluklarının da VKİ ile aynı doğrultuda arttığını ortaya koymuşlardır (27). Diyabet ve/veya metabolik sendromlu ve KY bulunan obez hastalar üzerinde yapılan başka bir araştırmada, leptin ve CRP arasındaki bağlantı kanıtlanmıştır (28). Obez bireyler ile obez olmayan bireylerin KVH riski yönünden karşılaştırıldığı Framingham Sağlık araştırmasında, aterosklerotik riskin obez bireylerde daha fazla olduğu rapor edilmiştir (30). Bunun aksine, düzenli şekilde statin ilaçları kullanan veya diyetine dikkat eden bireylerde IL-6, TNF-α ve CRP gibi inflamatuar sitokinlerde düşüş gözlenirken adiponektin seviyelerinde ise yükselme olduğu görülmüştür. Bu durum aterosklerotik hastalığın azalmasını sağlamıştır (31). Ayrıca, izoproterenol müdahelesi ile kardyak hipertrofi oluşturulan farelerde IL-1β ve TNF-α inflamatuar sitokin seviyelerinin kardiyomiyositlerde fazlalaştığını, IL-10 uygulaması ile [STAT-3 vasıtasıyla nükleer faktör-kappaB (NF-κB) inhibisyonu yolu ile] bu sitokinlerin seviyelerinde azalma olduğu açıklanmıştır (32).

Yapılan bir çok çalışmada elde edilen kanıtlara göre, kronik inflamasyonun obezite ile bağlantılı metabolik disfonksiyonun patogenezinde yer aldığını ortaya koymuştur. Buna ilaveten, aterosklerotik lezyonlar ve bunun gibi çeşitli KV olayları indükleyen yüksek proinflamatuar sitokin seviyeleri arasında kesin bir ilişki olduğu kanıtlanmıştır (33).

Bilim adamları obezitenin yan etkilerini minimuma indirgeyebilmek için çok sayıda araştırma yapmıştır. Bu amaçla; deneysel araştırmalar için kemirgenleri (fareler) tercih etmişlerdir ve kemirgenler üzerinde farklı obezite protokolleri uygulamışlardır. Bu obezite protokolleri arasında; %10, %45 ve %60 yağ içeren beslenme şekilleri yer almaktadır. Olması gereken bir kemirgen diyeti yaklaşık %10 yağ ihtiva etmektedir. Bunun dışındaki %45 ve %60 yağlı besinler kemirgenler için yüksek yağlı diyet olarak adlandırılmaktadır. %45 yağ oranı bulunan beslenme şeklinde, farelerde obezite oluşturulurken; %60 yağ içeren beslenme şeklinde ise daha çabuk ve daha fazla obez fareler elde edilmektedir. Çalışma zamanının kısalması ve obezitenin arttırılmış olması araştırmacılar için önemli bir avantajdır. Çünkü bu durum hem maliyetin düşürülmesini sağlamakta hemde çalışma süresini kısaltmaktadır. Bu yüzden birçok bilim insanının tercihi, %60 yüksek yağlı diyet ile beslenme şekli olmaktadır (34).

Yağ dokusunun inflamasyonu, immün sistemin bozulmasına neden olur. Bu durum TNF-α, IL-1β, IL-6, MCP-1 ve PAI-1 ve gibi proinflamatuar sitokin düzeylerinin artması ile sonuçlanır (35). Yüksek yağlı diyetle ile beslenen farelerde epididimal beyaz yağ dokusu inflamasyonu, TNF-α ve IL-6 gibi proinflamatuar sitokinlerde yükselme gözlemlenmiştir (36). Yüksek yağlı diyet ile beslenen fareler üzerinde yapılan başka bir çalışmada, hem IL-10 nakavt farelerde hem de vahşi tip farelerde sol atriyum fibrozisinin oluştuğu, nakavt farelerde ise atriyal fibrozun daha fazla meydana geldiği görülmüştür. Obez ve IL-10 nakavt farelerde makrofaj ve monosit seviyelerinde artma görülürken; TNF-α ve IL-1β' da da aynı şekilde yükselme görülmüştür. Ayrıca, yine IL-10 nakavt farelerde MCP-1 düzeyleride de artış bulunurken; vahşi tip farelerde proinflamatuar sitokinlerin dolaşıma aktarılması daha az olmuştur. IL-10 uygulaması ile yüksek yağlı diyet kaynaklı obeziteden dolayı meydana gelen atriyal fibrilasyona karşı hassasiyet ve sol atriyum remodeling' i ciddi düzeyde iyileştirdiği kanıtlanmıştır (37).

SONUÇ

Yapılan çalışmalar sonucunda obezitenin, KVH' lerin riskinin artmasında etken olduğu ortaya konulmuştur. Çünkü yağ dokusu inflamasyonunun KVH' lerin patolojik kaynağını oluşturan bir endotel değişikliğine sebep olabileceği rapor edilmiştir (29). Ayrıca sistemik inflamasyonun indirgenmesinin de kardiyak fonksiyonların muhafazasında önemli rolü bulunmaktadır. Bu koruma bazı patolojik koşulların engellenerek olumsuz kardiyak remodeling' in azaltılması ile mümkündür. Sistemik inflamasyonun azaltılması, inflamatuar immün hücrelerinin etkinliğinin minimum seviyeye indirgenmesi kardiyak inflamasyon bakımından olumlu yönde büyük katkı sağlayacaktır (3).

AÇIKLAMALAR

Finansal destek yoktur.

Çıkar çatışması yoktur.

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Acta Medica Ruha
International Journal of Medicine and Health Sciences
E-ISSN: 2980-1184

LETTER TO THE EDITOR
Volume:2 Issue:3 Year:2024
https://doi.org/10.5281/zenodo.13784506

Prognostic Significance of Tumor Budding in Bladder Cancer: A Call for Molecular Insights

Mesane Kanserinde Tümör Tomurcuklanmasının Prognostik Önemi: Moleküler Perspektifte Bir Çağrı

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Dear Editor,

We wish to share our insights on the critical prognostic significance of tumor budding (TB) in bladder cancer (BC) and underscore the urgent necessity for further molecular-level investigations in this domain, prompted by recent studies. Tumor buds, also referred to as "sprouts," are defined as isolated single tumor cells and/or small clusters comprising fewer than five tumor cells, which originate from the invasive tumor margin and infiltrate the stroma. These entities were first characterized by Imai in the 1950s (1). The TB scoring system, established by the "International Tumour Budding Consensus Conference" (ITBCC) in 2016, has been validated as an independent predictor of lymph node metastasis in pT1 colorectal cancer cases and poor survival outcomes in stage 2 colon cancer cases, and it is now routinely reported by pathologists (2). Tumor buds are intimately associated with epithelial-mesenchymal transition (EMT) and engage in interactions with the tumor microenvironment (TME), tumor stroma, and immune system cells (3). This dynamic interaction at the molecular level in budding tumor cells establishes a distinctive signature characterized by: upregulation of MMP-7 and MMP-9 expressions, which play a role in extracellular matrix degradation; anoikis resistance through the enhanced expression of TrkB; frequent upregulation of stem cell markers such as LGR5, ALDH1, and CD44; immune evasion facilitated by the loss of MHC class I expression; increased TGFβ expression and regulation of TGFβ signaling; regulation of WNT signaling; a decrease in miRNA-200 expression, accompanied by the epigenetic upregulation of EMT-associated transcription factors, including ZEB, TWIST, and SNAIL; reduced expression of E-cadherin, particularly at the cell membrane, and β-catenin; an increase in mesenchymal markers like Vimentin, alongside a reduction in Cytokeratin expression; low levels of Ki-67 and Caspase-3 expression; and a relatively spindle-shaped morphology with podia formation (3). While it is generally accepted in solid tumors that "an increase in tumor buds correlates with a poorer clinical outcome" (3), the body of research examining TB as a prognostic marker in non-gastrointestinal tumors—particularly in BC—remains limited. As of August 8, 2024, a PubMed search using the MeSH terms "tumor budding AND bladder cancer*" yielded 34 studies, of which only 10 were found to be directly relevant to this subject.

Fukumoto and colleagues investigated the prognostic effects of TB in 121 cases of pT1 non-muscle-invasive bladder cancer (NMIBC) and demonstrated that TB positivity was statistically significantly associated with pT1 sub-staging (microinvasion/extensive lamina propria invasion) (p=0.002), tumor architecture (papillary/nodular) (p=0.023), and lymphovascular invasion (LVI) positivity (p=0.001) (4). Additionally, it was reported that the 5-year progression-free survival rate was statistically significantly higher (p=0.001) in TB-negative pT1 BC cases (88.4%), and that TB was an independent risk predictor for progression to muscle-invasive bladder cancer (MIBC) in both the entire pT1 BC cohort and the subgroup receiving intravesical BCG instillation according to Cox regression analysis (4). Building on these findings, the researchers also observed that in 86% of TB-positive cases, E-cadherin immunoexpression in the tumor center was higher than in the TB areas, highlighting the relationship between TB and EMT in pT1 BC cases (4). While Fukumoto et al. focused on the clinical implications

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Received: 23.08.2024, Accepted: 13.09.2024, Published Online: 20.09.2024
Cited: Doğan T. Prognostic Significance of Tumor Budding in Bladder Cancer: A Call for Molecular Insights. Acta Medica Ruha. 2024;2(3):228-230. https://doi.org/10.5281/zenodo.13784506
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of TB, Miyake and colleagues delved into the underlying molecular mechanisms. In their comprehensive study, they used MGH-U3, UM-UC-14, and UM-UC-3 cells in an orthotopic bladder tumor model in SCID mice and suggested that COL4A1 and COL13A1 might play a primary role in the formation of the infiltrative pattern of TB (5). However, as accurate TB analysis can be complicated by peritumoral inflammatory infiltrate or reactive stromal cells, Brieu and colleagues adopted a different approach by targeting cytokeratin, which had previously been shown to effectively distinguish TBs. They enhanced their analysis by applying machine learning and automated image analysis to IF-stained samples, thereby achieving more accurate quantification in a sample of 100 MIBC cases (6). In addition to these efforts to improve prognostic assessments, Liu and colleagues conducted a bioinformatics-based study in which they evaluated the tumor stroma ratio (TSR) and TB together in MIBC cases. By developing a TSR-TB scoring system, they reported that increased TSR-TB might be an independent poor prognostic factor for overall survival (7). In contrast, in the study conducted by Kucuk and colleagues on a sample of 60 MIBC cases, no statistically significant relationship was found between TB and tumor necrosis ($p=1.000$), LVI ($p=0.114$), or perineural invasion ($p=0.712$) (8). However, a different perspective is offered by Seker and colleagues, who, in their study involving a sample of 108 MIBC cases, found that TB was statistically significantly associated with overall survival ($p=0.004$) (9). The researchers reported that TB could be a useful parameter for predicting prognosis in MIBC cases (9). Further emphasizing the prognostic importance of TB, Soriano and colleagues quantified TB in a sample of 108 MIBC cases that had undergone pancytokeratin staining and reported that TB is an independent risk predictor for mortality (10). The researchers further noted that MIBC cases with 14 or more TBs were associated with an increased risk of mortality as well as a higher tumor stage, suggesting that each additional TB increases the cancer-specific mortality risk by approximately 2% in these cases (10). Expanding on these findings, Busquets and colleagues, in their study involving 168 high-grade stage pT1 NMIBC cases, reported that TB (when present with a count of 6 or more) ($p=0.032$, HR: 2.1), along with the presence of carcinoma in situ (CIS), endoscopic tumor pattern (papillary/solid), and the absence of BCG induction, was significant in predicting disease progression according to multivariate variance analysis (11). The researchers also emphasized that the inclusion of TB in the TNM staging system should be carefully considered and that it could assist in the decision-making process for early radical cystectomy in high-grade stage pT1 NMIBC cases (11). Eckstein and colleagues built on this by studying 92 pT1 NMIBC cases with pancytokeratin staining. They reported that, according to Kaplan–Meier analysis, TB was statistically significantly associated with worsened recurrence-free survival ($p=0.005$), progression-free survival ($p=0.017$), and cancer-specific survival ($p=0.002$) (12). The researchers also found that the presence of TB was associated with multifocal tumors ($p=0.003$) and extensive lamina propria invasion when pT1 sub-staging was performed ($p<0.001$) (12). Interestingly, among the cases that received BCG instillation, those without TB not only had better recurrence-free survival ($p=0.012$), progression-free survival ($p=0.011$), and cancer-specific survival ($p=0.022$), but also no progression or disease-related deaths were observed in this group (12). Finally, Yang and colleagues contributed further by conducting a retrospective study involving 80 BC cases (36 NMIBC and 44 MIBC) (13). They investigated the prognostic effects of EPDR1 immunoexpression and TB quantification (13). The researchers quantified TB in 44 MIBC samples, considering those with six or more TBs as positive. The study found that EPDR1 immunoexpression varied statistically significantly ($p<0.05$) with tumor stage, and MIBC cases with high EPDR1 immunoexpression were statistically significantly more likely to have increased TB ($p<0.05$) (13). Furthermore, an increased TB count was associated with a tendency toward a worse clinical status in MIBC cases ($p<0.001$) (13).

The scoring of TB varies depending on the type of solid tumor. As a result, following the development of a standardized scoring system that can be adapted to BC, the inclusion of TB as a prognostic marker in routine histopathological evaluation could provide clinicians with significant advantages in risk stratification and treatment planning, particularly in managing patients with high-grade stage pT1 NMIBC who require accurate progression prediction. Although TB scoring is more easily and reliably performed on slides stained with pancytokeratin IHC, the fact that it can also be commonly done on routine H&E stained slides makes this cost-effective marker an attractive option for clinical use in BC as well. Since tumor budding is biologically closely related to EMT and the TME, detailed investigation of the underlying molecular mechanisms holds promise for the development of actionable targets. In this context, we believe that further multicenter prospective studies and more detailed molecular

analyses are necessary to validate the clinical utility of TB and evaluate its integration into existing prognostic models. These investigations could not only validate the clinical utility of TB but also pave the way for more personalized treatment strategies in BC.

Sincerely.

DESCRIPTIONS

No financial support.

No conflict of interest.

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Acta Medica Ruha
International Journal of Medicine and Health Sciences
E-ISSN: 2980-1184

LETTER TO THE EDITOR
Volume:2 Issue:3 Year:2024 https://doi.org/10.5281/zenodo.13784551

Noninvasive Diagnostic Methods Are Useful in Malignant Pleural Effusions

Malign Plevral Efüzyonlarda Noninvazif Tanı Yöntemleri Faydalıdır

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Dear Editor,

I read with interest the case report titled "Chronic Lymphocytic Leukemia Hospitalized Due to Pleural Effusion - Case Report" written by Bahar Ağaoğlu Şanlı in the Acta Medica Ruha journal, page 1.3 (2023): 468-473. As a writer interested in pleural effusions in thoracic surgery, the case caught my attention. Pleural effusions are an area that requires research because they are a common clinical condition with multiple pathophysiologies (1).

In the case report, it is seen that the author performed diagnostic methods related to pleural effusion management, but preferred to perform a blind biopsy because the patient's general condition was not suitable for surgical biopsy. In the study, no malignant cells were observed in the pleural fluid and no malignant cells were detected as a result of blind biopsy. I believe that the author's contribution to the dark side of pleural effusions with this case resulting in mortality will bring a remarkable perspective to the literature and I congratulate the author. Currently, aspiration and cytological evaluation of pleural fluid is the main diagnostic method. However, cytological evaluation is 60% sensitive for diagnosis. The presence of tumor cells in pleural effusion has diagnostic value in malignant pleural effusions; however, the chance of finding tumor cells in the fluid is low (1). Since the pleural biopsy performed in the study was a blind biopsy, the probability of finding pathological tissue in the pleura would also be low. There is a higher chance of finding tumor markers instead (2).

In a retrospective study conducted by us in 2022, it was revealed that immature granulocyte levels contributed to the diagnosis of malignant pleural effusion (1). The author's study has shown once again that the probability of finding malignant cells in malignant pleural effusions is low even with repeated thoracentesis. Not every patient may be clinically suitable for surgical biopsy. Some malignancies may show low 18-Fludeoxyglucose uptake in positron emission tomography. In this case, less invasive peripheral markers can also be used in diagnosis.

Sincerely.

DESCRIPTIONS

No financial support.

No conflict of interest.

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Received: 21.07.2024, Accepted: 15.09.2024, Published Online: 20.09.2024
Cited: Kozanlı F. Noninvasive Diagnostic Methods Are Useful in Malignant Pleural Effusions. Acta Medica Ruha. 2024;2(3):231-231. https://doi.org/10.5281/zenodo.13784551

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