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Editorial Office

Ordu University

Institute of Health Sciences

Cumhuriyet Campus

52200, Ordu, TURKEY

Tel: +90 (452) 234 5010-6105

Fax: +90 (452) 226 52 28

E-mail: ukaraman@odu.edu.tr

Correspondence Address: Ulku KARAMAN, PhD, Assoc. Prof. Dr.
Institute of Health Sciences,
Ordu University,
Cumhuriyet Campus,
52200 Center/ Ordu TURKEY

Phone: +90 452 234 50 10
Fax: +90 452 226 52 55
Email: ukaraman@odu.edu.tr
ulkukaraman44@hotmail.com

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The aim of the journal is to contribute to the international literature with clinical and experimental research articles, case reports, reviews and letters to the editor in the field of health sciences.

The target audience of the journal is all scientists working in the field of health, graduate students and researchers in this field.

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Cumhuriyet Campus
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Conclusion
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DECEMBER 2021 **VOLUME 7** **ISSUE 3**

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EDITORIAL

As we enter 2022,

We have finished another year with Covid-19.

We would like to thank the researchers who supported this issue with their articles and refereeing.

Hope to see you in a healthy, peaceful and happy working year...

PhD, Assoc. Prof. Ülkü KARAMAN

Editor

Middle Black Sea Journal of Health Science / Mid Blac Sea J Health Sci **December 2021; 7(3):312-319**

RESEARCH ARTICLE **DOI:** 10.19127/mbsjohs.911429

The Evaluation of Posterior Urethrovesical Angle, Urethral Length, Bladder Wall Thickness, and Residual Volume with Transperineal Ultrasonography in Women with Urinary Incontinence

Nihal Callioglu[1(ID)],Keziban Dogan[1(ID)], Cemal Ark[2(ID)],Sema Baghaki [1(ID)]

[1]Department of Obstetrics and Gynaecology. Sadi Konuk Research and Training Hospital,Istanbul,Turkey
[2]Department of Obstetrics and Gynaecology. Kanuni Sultan Süleyman Research and Training Hospital,Istanbul,Turkey.

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Objective: In the recent decades, transperineal ultrasonography has been used to examine patients in urogynaecology practice. In this study, we aimed to evaluate the function of transperineal ultrasonography in women with urinary incontinence.
Methods: Forty-five patients who were admitted to our institution between December 2012 and May 2013 and clinically and urodynamically diagnosed as having urinary incontinence (SUI n=20, DI+UUI n=13, MUI n=12) were included in the study. Additionally, 25 clinically and urodynamically continent women were included as the control group.
The patients were evaluated using transperineal ultrasonography (USG) in the supine position during rest and straining. An abdominal probe was placed in the perineum vertically and sagittally; when the symphysis pubis, urethra, bladder, vagina, and rectum could be seen clearly on the monitor, the image was frozen. Posterior urethrovesical angle (PUVA), urethral length, bladder wall thickness, and residual urine volume were measured on the image. All measurements were compared statistically between the SUI, UUI, MUI groups, and control group. The post-void residual volume measured using transperineal ultrasonography was compared with the post-void residual volume measured using a catheter during urodynamics.
Results: PUVA was significantly different in the SUI and MUI groups at rest than in the control group ($p<0.05$). During Valsalva maneuvers, PUVA was statistically significantly different in the SUI and MUI groups than in the UUI and control groups ($p<0.01$).
Conclusion: The measurement of PUVA and bladder wall thickness by transperineal ultrasonography is shown to be useful in diagnosis of patients with suspected detrusor instability and structural defects in pelvic floor. Therefore, transperineal USG may be an easy and reliable method which could be an alternative to urodynamic studies in patients who cannot undergo urethral catheterization.
Key words: urinary incontinence, ultrasonography, urinary sphincter

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Address for correspondence/reprints:

Sema Baghaki

Telephone number: +90 (537) 733 08 99

E-mail: semabaghaki@hotmail.com

Introduction

Urinary incontinence (UI) is defined as involuntary leakage of urine by the International Continence Society (ICS) (1). It is known that approximately 50% of adult women have urinary incontinence, but only 25% to 61% of these consult a physician (2,3). Risk factors for UI include obesity, parity, type of delivery, advanced age, and family history (3-7). The major clinical types of UI include stress incontinence (SUI), incontinence with maneuvers with increased intraabdominal pressure; urge incontinence (UUI), incontinence together with feelings of urgency; and mix incontinence (MUI), which is a combination of stress and urge incontinence (8,9).

Methods such as the Q-type test, fluoroscopy, X-ray cystourethrography, and video-urethrocystography, which are used to evaluate the bladder neck and urethra mobility and are the necessary parameters for the diagnosis and treatment of UI, are difficult to apply, costly, and some require the use of ionizing radiation (10,11). In the last few decades, transperineal ultrasonography has been used for the diagnosis of UI, in the determination of the surgical method, and objective evaluations of postoperative success. The bladder neck, urethrovesical junction, and urethral hypermobility can be seen with transvaginal and transperineal ultrasonography (USG), which is a noninvasive and safe method (12-15).

The aim of the study was to present the importance of transperineal USG in the diagnosis of incontinence by evaluating the length of the urethra, bladder wall thickness, posterior urethrovesical angle (PUVA), and post-operative residual volume.

Methods

The study was conducted in our institution between December 2012 and May 2013 after obtaining Ethics Committee approval. Women age between 40 and 55 years were included in the study. The study group consisted of 45 patients who were diagnosed as having urinary incontinence clinically and urodynamically, and the control group comprised 25 healthy women who were clinically and urodynamically continent. Twenty patients with SUI, 13 with detrusor instability and UUI, and 12 patients with MUI were included in the incontinence group. The procedures to be performed were explained verbally and consent was obtained. Those who had major pelvic surgery, pelvic organ prolapses, diabetes mellitus and glucose intolerance, and high calcium levels were excluded from the study. Those with urinary infections were included in the study after receiving treatment.

Age, height, weight, number of births, type of delivery (vaginal birth, cesarean-section), history of birthweight over 4000 g, chronic diseases, menopausal status, and previous urogynecologic surgery were examined. Urine analysis, urine culture, serum calcium levels, and fasting and postprandial blood glucose levels were assessed before the study. In addition, gynecologic and neurologic examinations were performed, and pelvic organs were assessed using transvaginal USG.

In this study, an LOGIQ 200 PRO (Healthcare Korea/2008) ultrasound device and central 3.5 Mhz convex abdominal probe were used for transperineal USG. Urodynamic examinations were performed using a multichannel urodynamic device (Life-Tech, Inc., Texas/USA, 2009).

The patients were examined on a gynecology table with a 45-degree angle between the body axis and the legs in the supine position during rest and the Valsalva maneuver. The probe was placed sagittally to the perineum; when the symphysis pubis, urethra, bladder, vagina, and rectum could be seen clearly on the monitor, the image was frozen. In cases where these anatomical structures could not be clearly displayed at the same time, it was aimed to include only the symphysis pubis, urethra, and bladder in the image area (16).

Measurements were taken on the image for the calculation of the posterior urethrovesical angle (PUVA, ß angle), Dx, Dy distances, urethral length, bladder thickness, and residual volume. Gynecologic examinations and ultrasonographic measurements were performed by the same physician.

While the urethral length measurement was performed, the abdominal probe was placed in the perineum without pressure on the urethral meatus and the distance between the bladder neck and the external urethral meatus was measured in the bladder with residual urine.

In order to measure Dx and Dy distances, two parallel lines passing through the central and internal os of the pubis were used, and a third line (dotted line) that crossed these lines at an angle of 90 degrees and passed through the inferior corner of the symphysis pubis were used (Figure 2). The Dy distance was measured as the urethral length between two parallel lines. The Dx distance was measured as the distance between the internal os and the line passing through the pubis inferior (17,18).

When measuring PUVA(ß), the angle between a line passing through the urethral axis and a second

line passing through the posterior of the bladder base was measured. The patient was asked to perform a Valsalva maneuver without disturbing the position. PUVA was measured by freezing the image at the time of maximum descent.

Urine volume measurement was performed within 10 min after micturition. Three patients with pathologic values residual urine volumes of more than 50 mL were excluded from the study to ensure standardization. To calculate the residual urine volume, post-micturition measurements were performed by imaging the bladder in transverse and sagittal planes with a probe placed a few centimeters below the pubis. The longest oblique diameter (H), transverse width (W), and sagittal anterior-posterior length (D1) were measured in each patient. The formula 0.65xHxWxD1 was used to calculate the bladder volume (19). While the bladder wall thickness was measured, the abdominal probe was placed vertically in the perineum and the anterior bladder wall thickness corresponding to the internal urethra meatus was measured.

Urethral length, bladder wall thickness and residual volume in supine position and at rest, and PUVA in the supine position and at rest and during the Valsalva maneuver are recorded to examine the variability between each group and the control group.

Statistical analysis

Statistical analysis was performed using the SPPS ver. 12.0 program. One-way analysis of variance (ANOVA) was used for normally distributed numerical parameters, and Tukey's honestly significant difference (HSD) test was used as a post-hoc test. The Kruskal-Wallis test was used for comparisons between three or more groups in non-normally distributed numerical parameters. Cross-table statistics were used to compare categorical variables (Chi-square). Statistical significance was identified as p=0.05

Results

Forty-five (64.28%) patients aged between 40 and 55 (mean age, 46.4±9.2) years, who were clinically and urodynamically diagnosed as having urinary incontinence and had no major pelvic surgery or pelvic organ prolapse, and 25 (35.72%) patients with a mean age of 45.4±6.9 years who were accepted as being urodynamically and clinically continent (control group) were included in our study. Twenty (28.6%) patients with stress urinary incontinence (SUI), 13 (18.6%) with detrusor instability (DI) and urge urinary incontinence (UUI), and 12 (17.1%) with mixed urinary incontinence (MUI) comprised the incontinence group. The demographic findings of the participants are presented in Table 1. No statistically significant difference was found between the groups in terms of age, body mass index (BMI), parity, type of delivery (p> 0.05).

The transperineal USG findings are presented in Table 2. When the measurements made with transperineal ultrasound were compared, no statistically significant difference was observed between the patients in the control group and the SUI, UUI, MUI groups in terms of urethral length, bladder wall thickness, and posterior residual urine volume measured in the supine position (p>0.05). There was no significant difference in terms of residual urine volume measured with the catheter during urodynamics between the continent and urinary incontinent groups (p>0.05). However, the residual urine volume measured using transperineal USG was 10.8% higher than the urine volume measured with urodynamics. There was no statistically significant difference between the patients with urinary incontinence and controls in terms of D-PUVA, which expressed the change of PUVA during rest and straining (p>0.05).

Statistical comparisons between the groups in terms of PUVA are presented in Table 3. PUVA was significantly higher at rest and in the Valsalva maneuver in the SUI and MUI groups than in the control group (p<0.001). However, no significant difference was found between the UUI group and the control group, or between the SUI and MUI groups during rest and the Valsalva maneuver (p>0.05).

There was a significant difference between the SUI and UUI groups during the Valsalva maneuver (p<0.001), and between the MUI and UUI groups during rest and the Valsalva maneuver (p<0.006, p<0.001).

Table 1. Demographic data

	SUI n=20 (28.6%)	UI n=13 (18.6%)	MUI n=12 (17.1%)	Control n=25 (35.7%)	p- value
Age (mean±SD)	47.1±7.7	45.4±12.9	46.9±7.3	45.4±6.9	[b]0.897
BMI (mean±SD)	32.2±5.2	29.8±4.8	30.5±6.6	29.0±5.6	[b]0285
Parity (mean±SD)	3.3±1.6	3.4±1.6	4.6±3.4	3.0±1.2	[c]0.777
Delivery Type					
Cesarean section (n,%)	2 (10%)	1 (7%)	2 (16%)	2 (8%)	[a]0.188
Vaginal (n,%)	18 (90%)	12 (93%)	10 (84%)	23 (92%)	[a]0.879
4000 g Over Birth	5 (25%)	3 (23%)	4 (33.3%)	6 (24%)	[a]0.124
Menopause	8 (40%)	5 (38%)	4 (33%)	7 (28%)	[c]0.702

a Chi-square and, b One-way-ANOVA, c Kruskal-Wallis tests were used for the statistical analysis.
* p<0.05, significantly different groups.
SUI: stress urinary incontinence; UUI: urge urinary incontinence; MUI: mixed urinary incontinence; BMI: body mass index

Table 2. Perineal ultrasonography data

		SUI n=20 (28.6%)	UUI n=13 (18.6%)	MUI n=12 (17.1%)	Control n=25 (35.7%)	p-value*
Length of Urethra (Mm)	Mean±Sd	32.5±1.8	33.1±3.2	33.5±2.0	32.7±2.8	[b] 0.697
	Median-(Min-Max)	32.8-(27.9-35.4)	34.2-(27.5-38.8)	33.6-(29.5-36.7)	31.7-(27.9-37.5)	
Bladder Thickness (Mm)	Mean±Sd	*2.04±0.33*	*2.28±0.44*	2.17±0.33	*2.1±0.4*	*[b] 0.325*
	Median-(Min-Max)	2.1-(1.5-2.8)	*2.2(1.7-3.3)*	2.1-(1.7-2.9)	*2-(1.5-2.9)*	
Prv (Usg)	Mean±Sd	*2.7±4.1*	*6.5±10*	*2.6±2.5*	*3.7±6.4*	*[b] 0.791*
	Median-(Min-Max)	*0.25-(0-13)*	1-(0-28)	2-(0-8)	1-(0_28)	
Prv (Catheter)	Mean±Sd	*3.2±4.7*	*3.4±4.3*	*5.2±9.4*	*2.6±4.3*	*[b] 0.795*
	Median-(Min-Max)	*1-(0-20)*	*0-(0-12)*	*1-(0-33)*	*0-(0-15)*	
Puva (Rest)	Mean±Sd	*115.3±12.9*	*107.5±12*	*122±9*	*103.8±8.3*	*[a] 0.001*
	Median-(Min-Max)	*116-(95-139)*	*110-(92-133)*	*122.5-(107-141)*	*105-(92-118)*	
Puva (Valsalva)	Mean±Sd	*143.9±10.1*	*128.2±8.9*	*148.4±7.4*	*127.6±9.2*	*[b] <0.001*
	Median-(Min-Max)	*144.5-(121-160)*	*125-(117-145)*	*148-(138-163)*	*125-(110-155)*	
D-Puva	Mean±Sd	*28±10*	*20.7±7.1*	*26.4±5.3*	*24±7.3*	*[c] 0.096*
	Median-(Min-Max)	*27-(12-46)*	*20-(11-33)*	*26-(18-39)*	*23-(13-47)*	

a chi-square, b one-way-ANOVA and c Kruskal-Wallis tests were used for the statistical analysis.
* p<0.05 means significantly different groups
SUI: stress urinary incontinence; UUI: urge urinary incontinence; MUI: mixed urinary incontinence; BMI: body mass index PRV: Post-void residual volume PUVA: posterior urethrovesical angle

Table 3. Statistical comparisons between groups for PUVA

	Test	P (rest)	P (Valsalva)
SUI and Control	Tukey HSD	[b] **0.004**	[b] **<0.001**
UUI and Control	Tukey HSD	[b] 0.739	[b] 0.998
MUI and Control	Tukey HSD	[b] **<0.001**	[b] **<0.001**
SUI and UUI	Tukey HSD	[b] 0.185	[b] **<0.001**
SUI and MUI	Tukey HSD	[b] 0.311	[b] 0.534
UUI and MUI	Tukey HSD	[b] **0.006**	[b] **<0.001**

[b]One-way ANOVA p<0.001

Discussion

The main result of our study was that PUVA measured using perineal USG was significantly higher in the SUI and MUI groups during rest and the Valsalva maneuver compared with the UUI and control group. However, the D-PUVA value, which indicates the change of PUVA with the Valsalva maneuver, showed no significant difference in our study and control groups.

Perineal ultrasonographic imaging has an important role among the radiodiagnostic methods in a wide area, ranging from the simple cotton swab test to magnetic resonance imaging (MRI) for the evaluation of the lower urinary tract system and the diagnosis of stress urinary incontinence. The advantages of USG are that it is easy to use, reliable, real-time, with no X-ray risk, no contrast agent, and it can be performed in office conditions. It takes a place

among other radiologic diagnostic methods for the assessment of the pelvic floor (10-15). Numerous studies and classifications have been made to detect the etiology of urinary incontinence to date. First, Green et al. attributed the cause of stress incontinence to PUVA changes based on clinical experience, defined PUVA as the angle between the urethral axis and the axis of the bladder base, and expressed that PUVA might be important for the selection of the appropriate surgical method in patients with SUI in 1962 (20). Koelbl et al. (21) measured PUVA and the urethral angle (alpha angle) using perineal USG and cystourethrography and found a correlation between the two methods, showing that non-invasive perineal USG was superior to cystourethrography in terms of ease of use and adverse effects. It has also been suggested that perineal USG was more reliable than transvaginal USG (22).

Similar to our study results, PUVA was found to be different in patients with SUI during rest and the Valsalva maneuver when compared with continent women, and it was suggested that perineal USG and PUVA measurements could be used for the diagnosis of patients with SUI (23,24). It has also been suggested that preoperative evaluation of SUI using PUVA measurements with perineal USG might be useful in cases of surgical failure or complications and physicians interested in urogynecology should use this method more frequently (22). We think that perineal USG, which still only has limited use in our country, should be used routinely in the evaluation incontinent women.

In our study, the PUVA value of the patients with SUI and MUI during the Valsalva maneuver was statistically different and greater than those with UUI and normal continence. In conclusion, although PUVA measurements with transperineal USG did not determine the type of incontinence, we found that it could detect patients with anatomic defects (23-25).

In a study in which Yalçın et al. investigated the role of PUVA in determining the type of urinary incontinence, PUVA values were measured during rest and straining using transperineal USG, and D-PUVA values were significantly higher during straining than at rest ($p<0.01$). When compared with SUI and MUI, there was no statistically significant difference between PUVA values while straining and at rest in patients who had DI ($p>0.05$). With these results, it was thought that the PUVA values during rest and with straining or the change of angle during straining in patients with urinary incontinence were not effective parameters in the differential diagnosis of incontinence types (26).

In our study, the mean urethra length was 32.8 ± 2.5 cm. There was no significant difference between the groups and it was found to be shorter than the reported average in the literature. De Souza et al., who measured the length of urethra using MRI and determined the mean value as 3.1 cm, found this difference to be associated with a slight forward twist of the urethra in the supine position and with the flattening and elongation of the urethra in surgical and cadaveric measurements. Contrary to the normal anatomic position, examinations in the supine position do not allow the evaluation of the dynamic changes in the urethra, retropubic cavity, and vesicourethral angle with changes in intra-abdominal pressure as in the natural position and it measures shorter its actual length (27).

In our study, bladder wall thickness measured using USG in patients with SUI, UUI, MUI, and continent women, was measured as 2.04, 2.28, 2.17, and 2.10 mm, respectively. Although the bladder wall thickness was greater in the group with UUI than the other groups, no statistical difference was found between them. However, unlike our data, in many studies bladders wall thickness was measured thicker in transvaginal USG measurements in patients with a diagnosis of overactive bladder (28,29). This difference may be related to the bladder wall thickness depending on age and urine volume in the bladder or may be related to the transperineal USG method we used (30).

Measurement of residual urine volume helps in the detection of post-micturition residual urine and distinguishing urinary retention and overflow incontinence. Although the residual urine volume can be determined using USG, this method has a standard error of 15-20%. Similar to our study results, there are studies that found the difference between the mean residual urine volume measured using a urethral catheter and the volume of urine estimated using pelvic USG formulae (31,32). On the other hand, an approximate measurement of bladder urine volume can be performed using real-time USG, but the measurement obtained in cases where changes in residual urine need to be measured more accurately may not be sufficiently reliable (33). In terms of the residual urine volume in our study, no statistically significant difference was found between the study and control groups in terms of the values calculated using transperineal USG and vesical catheter during urodynamics. A 10.8% standard error was found for the value we detected using transperineal USG. This value is close to the standard error in the literature and lower than that value. Although residual urine

measurement with a catheter is the gold standard, using transperineal ultrasound is an easy, non-invasive, and may be an alternative method for urethral catheterization (32).

The main limitation of our study was the difficulty in standardizing the maximum straining of patients during the Valsalva maneuver when PUVA was measured. Although the patients were warned about maximum straining before the examination, subjects who did not strain at the desired level made the evaluation difficult. In this case, the image with maximum straining was taken into consideration.

Conclusion

Transperineal USG is a simple and non-invasive method that provides detailed visualization of the bladder, urethra, and pelvic support structures in patients with urinary incontinence. It could demonstrate structural changes in the pelvic floor structure with examinations at rest and during the Valsalva maneuver. The measurement of PUVA using transperineal USG could not determine the type of incontinence but it could detect patients with anatomic defects. Measurement of bladder wall thickness can be performed to help in diagnosis in patients with suspected detrusor instability. Transperineal USG could be an easy and reliable alternative method for residual urine volume measurements in cases where catheterization cannot be performed.

Main Points

•The main result of our study was that posterior urethrovesical angle (PUVA) measured using perineal USG was significantly higher in the SUI and MUI groups during rest and the Valsalva maneuver compared with the UUI and control group.

•Transperineal USG and PUVA measurements can be used for the diagnosis of patients with SUI and MUI.

•Although residual urine measurement with a catheter is the gold standard, using transperineal ultrasound is an easy and non-invasive method to support the diagnosis of SUI or MUI and it can be an alternative method to urethral catheterization.

Ethics Committee Approval: This study was performed on the extracted human teeth. Clinical Studies Ethics Committee of Ordu University, Faculty of Medicine was not needed.
Peer-review: Externally peer-reviewed.
Author Contributions:
Concept: N.Ç, C.A , *Design:* N.Ç, C.A, *Literature search:* N.Ç, K.D, S.B, *Data Collection and Processing:* N.Ç, K.D, *Analysis or Interpretation:* N.Ç, K.D, *: Writing:* N.Ç, C.A, K.D, S. B.
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Evaluation of Knowledge Levels of Ordu University Faculty of Dentistry Students about Hepatitis B: Cross-Sectional Survey Study

Cigdem Guler [1(ID)], Ihya Cakmakci [1(ID)]

[1]Department of Pediatric Dentistry, Faculty of Dentistry, Ordu University, Ordu,Turkey.

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Abstract

Objective: To evaluate the knowledge levels of Ordu University Faculty of Dentistry students about Hepatitis B Virus (HBV), preventive measures, and compare differences between academic classes.

Methods: Students from Ordu University Faculty of Dentistry (1th to 5th year from 2019-2020 academic year) were asked to respond a one-page questionnaire form measuring their knowledge about HBV. The questionnaire was created online and a total of 417 students were asked to respond. Data were analyzed using descriptive statistics, chi-square test and Fischer's exact test. Significance level was set at a $P<0.05$.

Results: In this study, 318 of 417 students participated. In total, 97.8% of 318 students knew that HBV can be transmitted through dental treatments. In addition, 85.2% of students stated that HBV can be transmitted through saliva. 94.7% of students who answered the questionnaire knew that HBV vaccination program consisted of 3 doses. In the question of standard universal precautions for HBV contagiousness, 28% of students selected the option 'I do not know', and there was a statistically significant difference between academic classes in this question ($P<0.05$).

Conclusion: According to the results of this study, although students had better knowledge about HBV when compared to similar studies, it is recommended that knowledge of students, especially on standard universal measures, should be reviewed. In addition, the vaccination and immune status of the students should be followed regularly.

Key words: Hepatitis B virus, Dental students, Questionnaire

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Address for correspondence/reprints:

Ihya Cakmakci

Telephone number: +90 (507) 687 05 10

E-mail: ihyagundogdu@hotmail.com

Introduction

Hepatitis B is a serious life-threatening liver infection caused by Hepatitis B virus (HBV), which is one of the DNA viruses (1). Hepatitis B is both highly contagious and can turn into a chronic infection that can cause fatal diseases such as cirrhosis and hepatocellular carcinoma (2).

HBV can be transmitted in many ways. Some of these include contact with infected blood and body fluids, mother to baby at birth, with parenteral route, and with sex with an infected partner (3). According to 2015 data, there are more than 2 billion infected

people in the world and 257 million of them are chronic hepatitis patients (1). Epidemiological studies reveal that Hepatitis B surface antigen (HBsAg) positivity in Turkey has been reported between 4% and 5% (4). Although there is an effective vaccine, the current numbers show that there is still a considerable number of patients in our country and in the world.

Dentists are at higher risk of HBV infection compared to both general population and other healthcare professionals (5). Likewise, dentistry students are at higher risk than other health care students. When all these risks are combined with the lack of protective measures, the situation becomes even more serious, considering the greater possibility of occupational injury compared to other professions in dentistry.

The main preventive measure against Hepatitis B infection is vaccination. HBV vaccine is highly effective and safe. Currently, 3-dose HBV vaccine routine has reached 85% worldwide (1, 6). In particular, the dental community should pay attention to immunity of Hepatitis infections.

HBV vaccination of health care workers in Turkey has been implemented since 1987. As a result, HBV carrier rates approximately decreased by half. Immunization rates by vaccination in health care workers have up to 75% in Turkey (7). It is known that similar rates are observed in dentistry students.

It is very important to raise awareness of dentistry students about the measures to be taken against the transmission of Hepatitis B infection. Before starting a clinical practice, the vaccinations of students should be applied fully and immunization follow-ups should be done. In addition, sufficient information should be obtained about the precautions to be taken in the dental clinic.

The aim of this study is to evaluate the knowledge level of dental students of Ordu University Faculty of Dentistry about HBV and preventive measures and compare the differences between academic classes.

Methods

This study was a cross-sectional survey study of Ordu University Faculty of Dentistry students in the 2019-2020 academic year. The questionnaire form in our study was prepared based on another previous study and applied online via the Google Forms application (8). Participants were able to access this online questionnaire via their e-mails. A total of 417 dentistry students in the 2019-2020 academic year were invited online to participate in the questionnaire and participation was voluntary. Considering the target audience of the survey (417), the sample size was calculated as 301 at the level of 95% confidence and 3% margin of error. While 318 of students participated in our survey, 99 did not.

The questionnaire form consisted of three parts. In the first part, demographic information of the participants such as age, gender, and classes were questioned. The second part questions aim to measure the students' knowledge about HBV, transmission routes and vaccination. There were 15 questions in this section and 13 of them were yes / no questions. There were four options in one question and participants were asked to choose their level of knowledge. In the third and last part, there were six questions and the protective measures against HBV and the vaccination status of participants were questioned.

Statistical analysis

The database collected in the Google forms application were converted to Excel format (Microsoft Corp., Redmond, WA, USA) for further analysis. The data were analyzed using IBM SPSS Statistics Package (Version 22.0. Armonk, NY: IBM Corp.).

Descriptive analysis, chi-square test and Fischer's exact test were used to analyze the data. Statistical significance level was set at $P<0.05$.

Ethics of the Study

This study was approved by Ordu University Clinical Research Ethics Committee with the 2020/35 numbered decision. All participants were informed in detail about the objective of the study and gave written consent. The study was performed in accordance with the ethical principles of the Declaration of Helsinki.

Results

Demographic data were obtained in the first part of the questionnaire. Table 1 presents the distribution of demographic data of participants. In this study, 35.5% of participants were male and 64.5% were female. While 17% of students were in the 16-20 age range, 56.6% were in the 20-22 age range and 26.4% were over 22 years old. The distribution of participating students according to the years was as follows (Table 1): 65 students in the 1st year (20.4%), 59 students in the 2nd year (18.6%), 75 students in the 3rd year (23.6%), 62 students in the 4th year (19.5%), 57 students in the 5th year (17.9%). Table 2 presents the distribution of gender according to years. Male participating students (113) according to the years were as follows (Table 2): 22 students in the 1st year (19.5%), 22 students in the 2nd year (19.5%), 31

students in the 3rd year (27.4%), 22 students in the 4th year (19.5%), 16 students in the 5th year (14.2%). Female participating students (205) according to the years were as follows (Table 2): 43 students in the 1th year (21%), 37 students in the 2nd year (18%), 44 students in the 3rd year (21.5%), 40 students in the 4th year (19.5%), 41 students in the 5th year (20%).

Table 1. The distribution of demographic data of the participants

Age	16-20	54 (17%)
	20-22	180 (56.6%)
	>22	84 (26.4%)
Gender	Male	113 (35.5%)
	Female	205 (64.5%)
Year	1	65 (20.4%)
	2	59 (18.6%)
	3	75 (23.6%)
	4	62 (19.5%)
	5	57 (17.9%)

Table 2. The distribution gender of the participants acording to year

Year	Male	Female	Total
1	22 (19.5%)	43 (21%)	65 (20.4%)
2	22 (19.5%)	37 (18%)	59 (18.6%)
3	31 (27.4%)	44 (21.5%)	75 (23.6%)
4	22 (19.5%)	40 (19.5%)	62 (19.5%)
5	16 (14.2%)	41 (20%)	57 (17.9%)
Total	113 (%100)	205 (%100)	318 (%100)

In the second part of the questionnaire, students' knowledge about HBV was tested with 15 questions. According to the data of the first question, 85.2% of students knew that HBV could be transmitted by saliva. In the second question, 301 students (94.7%) knew that HBV could be transmitted from the dentist to the patient. In addition, students correctly answered that HBV could be transmitted from patient to patient and from patient to dentist with 98.4% and 97.8%, respectively. The answers and statistical information of the questions in the second part according to the years were shown in Table 3. In the second part of the questionnaire, the 7th question was 'A considerable proportion of dentists experience needlestick injuries frequently' and 86.8% of participating students marked 'yes'. There was a statistically significant difference between the preferences of 1st and 5th year students (P=0.001).

Another important question of the second part was 'Level of knowledge about standard universal precautions'. While 26.1% of students stated that they were educated, 28% of students stated that they did not have information about standard universal measures. In the comparison between years, the answers of the 4th and 5th years were significantly different from the 1st and 2nd years separately (P<0.005).

In the first question of the third part, 83% of students stated that they always wore gloves as protective equipment. This rate was determined to be 53.8% for 1st year students and a statistically significant difference was found when compared to other years (P<0.005). Preferences for the use of protective equipment were shown in Table 4.

In the second question of the third part, 214 students stated that they were always recapping the needles after they used it (67.3%). The answers of the 4th and 5th years were significantly different from the 1st and 2nd years separately (P=0,001) (Table 5). Regarding the approach to patients with HBV infection, 42 students (13.2%) stated that they did not treat HBV-infected patients, 236 students (74.2%) stated that there was no difference between HBV infected patients and other patients, 40 students (12.6%) stated that infected patients delayed their treatment (Figure 1). In the comparison between years, it was seen that 5th year students' preferences showed a statistically significant difference compared to 1st year and 2nd year students' preferences (P <0.005).

On the other hand, 94.7% of the students participating in the questionnaire knew that the HBV vaccine consisted of 3 doses and 195 students (61.3%) had 3 doses of vaccine. In terms of administered vaccination dose, a statistically significant difference was found between the 2nd year students and the other years, and the 1st year students and the 4th and 5th years separately (P<0.005). Only 157 (80.5%) of the students who completed 3 doses of vaccine stated that they controlled their immunity. While 76.4% of these students had antibody titers of 100 and above, 15.9% of them were between 10 and 100, and 7.6% were between 0 and 10 (Table 6).

When the answers were compared according to gender, a statistically significant differences were found in some questions. In the first question of the second part (HBV can be transmitted through saliva), 79.6% of male participants marked yes, while 88.3% of female participants marked yes, and this was a statistically significant difference (P = 0.038). The questions with a statistically significant difference when compared according to gender, were shown in Table 7.

Table 3: Students' knowledge of HBV infection-related topics, by year and total

Question (Q)	Answers	1th Year N%	2nd Year N%	3th Year N%	4th Year N%	5th Year N%	Total N%	P-Value
Q1-HBV can be transmitted through saliva	Yes No	56 (86.2%) 9 (13.8%)	45 (76.3%) 14 (23.7%)	66 (88%) 9 (12%)	53 (85.5%) 9 (14.5%)	51 (89.5%) 6 (10.5%)	271 (85.2%) 47 (14.8%)	.281
Q2-HBV can be transmitted from dentist to patient	Yes No	59 (90.8%) 6 (9.2%)	55 (93.2%) 4 (6.8%)	71 (94.7%) 4 (5.3%)	59 (95.2%) 3 (4.8%)	57 (100%) 0	301 (94.7%) 17 (5.3%)	.248
Q3-HBV can be transmitted from patient to patient	Yes No	64 (98.5%) 1 (1.5%)	57 (96.6%) 2 (3.4%)	74 (98.7%) 1 (1.3%)	61 (98.4%) 1 (1.6%)	57 (100%) 0	313 (98.4%) 5 (1.6%)	.701
Q4-HBV can be transmitted from patient to dentist	Yes No	61 (93.8%) 4 (6.2%)	58 (98.3%) 1 (1.7%)	74 (98.7%) 1 (1.3%)	61 (98.4%) 1 (1.6%)	57 (100%) 0	311 (97.8%) 7 (2.2%)	.170
Q5-There is a confirmed risk of HBV transmission through dental treatments	Yes No	62 (95.4%) 3 (4.6%)	57 (96.6%) 2 (3.4%)	74 (98.7%) 1 (1.3%)	61 (98.4%) 1 (1.6%)	57 (100%) 0	311 (97.8%) 7 (2.2%)	.437
Q6-Dentists are at higher risk of HBV infection than the general population	Yes No	53 (81.5%) 12 (18.5%)	53 (89.8%) 6 (10.2%)	70 (93.3%) 5 (6.7%)	59 (95.2%) 3 (4.8%)	55 (96.5%) 2 (3.5%)	290 (91.2%) 28 (8.8%)	**.024***
Q7-A considerable proportion of dentists experience needlestick injuries frequently	Yes No	47 (72.3%) 18 (27.7%)	50 (84.7%) 9 (15.3%)	68 (90.7%) 7 (9.3%)	56 (90.3%) 6 (9.7%)	55 (96.5%) 2 (3.5%)	276 (86.8%) 42 (13.2%)	**.001***
Q8-There is a higher risk of HBV than HIV transmission through needlestick injury	Yes No	44 (67.6%) 21 (32.3%)	47 (79.6%) 12 (20.3%)	64 (85.3%) 11 (14.6%)	55 (88.7%) 7 (11.2%)	50 (87.7%) 7 (12.2%)	260 (81.8%) 58 (18.2%)	**.012***
Q9-There is a higher risk of HBV than HCV transmission through needlestick injury	Yes No	45 (69.2%) 20 (30.7)	45 (76.2%) 14 (23.7)	63 (84%) 12 (16%)	50 (80.6%) 12 (19.3%)	42 (73.6%) 15 (26.3%)	245 (77%) 73 (24.2%)	.275
Q10-HBV can persist in plastery casts for up to 7 days	Yes No	55 (84.6%) 10 (15.3%)	50 (84.7%) 9 (15.2%)	62 (82.6%) 13 (17.3)	46 (74.1%) 16 (25.8%)	32 (56.1%) 25 (43.8%)	245 (77%) 73 (24.2%)	**.001***
Q11-HBV transmission from dentist to patient can be prevented with the use of gloves	Yes No	58 (89.2%) 7 (10.7%)	46 (79.3%) 12 (20.6%)	63 (84%) 12 (16%)	51 (82.2%) 11 (17.7%)	50 (87.7%) 7 (12.2%)	269 (84.5%) 49 (15.4%)	.557
Q12-HBV transmission from patient to dentist can be prevented with the use of gloves	Yes No	57 (87.6%) 8 (12.3%)	49 (83%) 10 (16.9%)	65 (86.6%) 10 (13.3%)	53 (85.4%) 9 (14.5%)	53 (92.9%) 4 (7%)	277 (87.1%) 41 (12.8%)	.594
Q13-Level of knowledge about standard universal precautions	Don't know Have heard something Being educated Following an educatable protocol	30 (46.1%) 32 (49.2%) 3 (4.6%) 0	21(35.5%) 37 (62.7%) 1 (1.6%) 0	16 (21.3%) 40 (53.3%) 19 (25.3%) 0	11 (17.7%) 16 (25.8%) 29 (46.7%) 6 (9.6%)	11 (19.2%) 8 (14%) 31 (54.3%) 7 (12.2%)	89 (27.9%) 133 (41.8%) 83 (26.1%) 13 (4%)	**.000***
Q14-What is the risk of HBV transmission to a healthy person when a HBV infected needle is sank? (%)	0.1 3 30	6 (9.2%) 22 (33.8%) 37 (56.9%)	18 (30.5%) 17 (28.8%) 24 (40.6%)	6 (8%) 36 (48%) 33 (44%)	9 (14.5%) 27 (43.5%) 26 (41.9%)	16 (28%) 29 (50.8%) 12 (21%)	55 (17.2%) 131 (41.1%) 132 (41.5%)	**.000***
Q15-Hepatitis B vaccination program consists of 3 doses	Yes No	56 (86.1%) 9 (13.8%)	55 (93.2%) 4 (6.7%)	72 (96%) 3 (4%)	62 (100%) 0	56 (98.2%) 1 (1.7%)	301 (94.6%) 17 (5.3%)	**.005***

Table 4: Students' use of personal protective equipment, by year

	Year	Always	Mostly	Sometimes	Rarely	Never	P-value
Gloves	1	35(53.8%)	9(13.8%)	9(13.8%)	11(16.9%)	1(1.5%)	
	2	47(79.6%)	11(18.6%)	1(1.6%)	0	0	
	3	65(86.6%)	10(13.3%)	0	0	0	**.000***
	4	61(98.3%)	1(1.6%)	0	0	0	
	5	56(98.2%)	1(1.7%)	0	0	0	
	Total	264 (83%)	32(10.1%)	10(3.1%)	11(3.5%)	1(0.3%)	
	Year	Always	Mostly	Sometimes	Rarely	Never	P-value
Face Masks	1	29(44.6%)	15(23%)	11(16.9%)	9(13.8%)	1(1.5%)	
	2	41(69.4%)	14(23.7%)	1(1.6%)	3(5%)	0	
	3	61(81.3%)	12(16%)	2(2.6%)	0	0	**.000***
	4	58(93.5%)	2(3.2%)	0	1(1.6%)	1(1.6%)	
	5	53(92.9%)	4(7%)	0	0	0	
	Total	242(76.1%)	47(14.7%)	14(4.4%)	13(4%)	2(0.6%)	
	Year	Always	Mostly	Sometimes	Rarely	Never	P-value
Protective Gowns	1st	21(32.3%)	13(20%)	10(15.3%)	15(23%)	6(9.2%)	
	2nd	23(38.9%)	13(22%)	15(25.4%)	5(8.4%)	3(5%)	
	3th	27(36%)	13(17.3%)	27(36%)	5(6.6%)	3(4%)	**.004***
	4th	21(33.8%)	31(50%)	8(12.9%)	2(3.2%)	0	
	5th	17(29.8%)	27(47.3%)	13(22.8%)	0	0	
	Total	109(34.2%)	97(30.5%)	73(22.9%)	27(8.4%)	12(3.7%)	
	Year	Always	Mostly	Sometimes	Rarely	Never	P-value
Protective Shields	1st	18(27.6%)	10(15.3%)	16(24.6%)	16(24.6%)	5(7.6%)	
	2nd	32(54.2%)	16(27.1%)	8(13.5%)	3(5%)	0	
	3th	27(36%)	12(16%)	23(30.6%)	11(14.6%)	2(2.6%)	**.041***
	4th	15(24.1%)	20(32.2%)	16(25.8%)	8(12.9%)	3(4.8%)	
	5th	10(17.5%)	21(36.8%)	18(31.5%)	7(12.2%)	1(1.7%)	
	Total	102(32%)	79(24.8%)	81(25.4%)	45(14.1%)	11(3.4%)	

Table 5: Students' practice of recapping needles, by year

Year	Rarely	Mostly	Always
1	11 (16.9%)	20 (30.7%)	34 (52.3%)
2	9 (15.2%)	20 (33.8%)	30 (50.8%)
3	5 (6.6%)	20 (26.6%)	50 (66.6%)
4	1 (1.6%)	9 (14.5%)	52 (83.8%)
5	1 (1.7%)	8 (14%)	48 (84.2%)
Total	27 (8.4%)	77 (24.2%)	214 (67.2%)

The answers of the 4th and 5th years were significantly different from the 1st and 2nd years separately (P=0.001)

Discussion

HBV is one of the leading infectious diseases. Although has a long history and has been effectively tackled by both vaccines and preventive measures, HBV is still an important issue for dentistry (9). As mentioned in previous studies, percutaneous injuries are more common in dental students than in other healthcare fields. In addition, dental students are among the riskiest occupational group in terms of transmission risk of HBV infections (5,10). When we looked at the literature, we saw that this issue was not studied much, especially for dental students in Turkey. Therefore, in this study, we aimed to measure the knowledge of our school's dental students about HBV and preventive measures.

Considering the findings of our study, we can say that students of Ordu University Faculty of Dentistry have satisfactory knowledge about HBV and preventive measures. It was observed that most of the questions in the second part of the questionnaire were given correct answers to a large extent. However, our students, who gave highly correct answers to most questions, gave contradictory answers to some questions.

As it is known, saliva, which is one of the transmission routes of HBV, has a moderate level of infectiousness (7). In our questionnaire, 85.2% of the students stated that HBV could be transmitted by saliva. In a similar study conducted with Iranian students, the same rate was found to be 81.7% (8). Our students gave a high rate of the correct answer

and it was compatible with the literature. On the other hand, 79.6% of male participants and 88.3% of female participants marked the correct answer. Difference between the rates of the correct answer according to gender was statistically significant (p=0,038). In recent study, 5th year students had the highest number of correct answers with 89.5%. This outcome may have resulted from the increase in the knowledge level of the students as the last period of education approaches. In a similar study, final year students of the Tehran University of Medical Sciences stated the correct answer in the same question with 81.7% and this was lower than junior students' rates of the correct answer (8). The sample size of the study was smaller than ours, and the academic years studied were not similar, which may be the reason for this result.

It is a known fact that HBV can be transmitted by dental treatments. In our study, 97.8% of students gave the correct answer this question. In similar studies conducted with Iranian students and Italian dentists, the same rate was found to be 74,6% and 44.1%, respectively8,11. Based on these rates, we can say that our students are well aware of the importance of HBV in dentistry.

Healthcare workers are always faced with infection by bloodborne pathogens due to their occupational contact with blood and infected body fluids. Needlestick injuries are frequently encountered in dentistry. HBV transmission through injuries during dental procedures ranges from 6% to 30% (11). In our study, there was a question stating that 'A considerable proportion of dentists frequently experience needlestick injuries', and 86.8% of the participating students answered 'yes' to this question. When we look at the similar study, only 59.9% of Iranian students answered yes to the same question (8). The difference between the current rates is remarkable and the students included in our study think that needlestick injuries are more common among dentists.

In serological studies, it has been found that HBV infection in healthcare personnel is approximately 10 times higher than in the general population (12). Our students gave the correct answers at the rate of 91.2%, in line with the rates in similar studies. The risk of developing clinical hepatitis in needlestick injuries contaminated with HBV-containing blood has been reported as 22-31%, and it has been determined that these injuries are mostly caused by re-capping the needle tips in dentistry (13,14). Unfortunately, only 41.5% of our students correctly answered the HBV transmission rate as a result of an infected needlestick. Because of this rate, we can say that more than half of our students do not know the HBV transmission rates through needlestick injuries.

On the other hand, 67.3% of our students answered the question 'Would you recap the needle tips again after use?' as 'always'. In a study conducted with Egyptian health care workers, it is stated that 40% of the reported needlestick injury cases were related with behaviour of manipulation of the needle after injection15. It is clear that our students should refresh their knowledge on this subject. The risk of Hepatitis C Virus (HCV) and Human Immunodeficiency Virus (HIV) contamination after percutaneous contact is 1.8% and 0.3%, respectively (15,16). In related questions, we can see that 77% of our students knew that HBV can be transmitted at a higher rate than HCV, and 81.8% of the students knew that HBV can be transmitted at a higher rate than HIV. The correct answer rates of Iranian students to the same questions were 95.8% and 72.5%, respectively (8). Therefore, we can say that the rates are satisfactorily correct in these questions.

Vaccination is the most effective and easiest method of protection against HBV. The vaccine is usually given as 3 or 4 injections in 6 months. With vaccination, protection is provided against HBV as well as from diseases such as liver cancer and cirrhosis caused by HBV (6). Our students knew that HBV vaccine consisted of 3 doses (%94.7). In the study conducted with Brazilian students, 87.9% of the students chose the 3 dose option, and our results were almost similar to this study (17). In addition, 61,3% of our students had completed 3 doses of vaccine, and these results were similar to the study conducted with Brazilian students (62.2%) (17). In a study conducted with Turkish dentists, 87.9% of the participating clinicians stated that they were completely vaccinated according to the schedule (18). If an anti-HBs antibody level of 10 mIU / ml is achieved after three doses of vaccine, there is no need for booster doses or monitoring of antibody titers (19). Antibody titers of 92.3% of the students participating in our survey who completed 3 doses of vaccines were found to be 10 mIU / ml or more.

In the first question about the use of protective equipment, 83% of our students stated that they always wore gloves as a protective measure. It is thought provoking that the options such as 'never', 'rarely', 'sometimes' were marked, even if there were a small number of participants. Rates of the glove use was 89.4% in Iranian students, 90.9% in Canadian students, and 95% in Turkish dentists (8,18,20). In the question of face mask use, 76.1% of our students selected the 'always' option and it was observed that

they used it at a higher rate than similar publications (8).

In the Ordu University Faculty of Dentistry, dental students are given training on infectious diseases and preventive measures starting form the first year. HBV, which is the most common source of cross infection especially in dentistry, is taught in all academic years. In the question about standard universal precautions related to HBV contagion, 28% of our students ticked 'I don't know' and 41.8% marked 'I heard something'. These rates are similar to analogous studies and unfortunately reducing the reliability of the answers given to other questions.

This study was conducted under limited conditions as it was a single center study and could not ensure the participation of all students studying in Turkey. It is recommended that a similar survey is conducted countrywide among dental students to evaluate and define Turkish dental students' knowledge on hepatitis b infections.

Conclusions

Our students, who gave highly correct answers to most questions, gave contradictory answers to some questions. In this situation, we cannot say that dental students of Ordu University Faculty of Dentistry have a very good level of knowledge about HBV infections and preventive measures. The education curriculum should be developed and students' knowledge should be tried to be increased with questioning and inquiry education methods. In addition, it will be safer to follow the vaccination and antibody levels of the students more closely to protect against HBV.

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Vitamin D and Psychological Status in Dialysis Patient

Kubra Gokalp [1](ID), Mevra Aydin Cil[2](ID), Aysegul Yayla[3](ID)

[1]Department of Psychiatric Nursing, Nursing Faculty, Atatürk University, Erzurum, Turkey
[2]Department of Nutrition and Dietetic, Faculty of Health Sciences, Atatürk University, Erzurum, Turkey
[3]Department of Surgery Nursing, Nursing Faculty, Atatürk University, Erzurum, Turkey

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Abstract

Objective: The study was conducted to determine the association between vitamin D level and psychological status in dialyzed patients.

Methods: The population consisted of dialysis patients in a university hospital dialysis center in Eastern Turkey between March and May 2017. The study's sample involved in 90 dialysis patients (59 hemodialysis, 31 continuous ambulatory peritoneal dialysis). 25(OH) D levels measured in a university hospital. Psychological status was evaluated by Brief Symptom Invantory. Minimum-maximum values, percentage, mean and standard deviation, average, frequency, Kruskal–Walli's test and Pearson's Correlation Analysis were used to evaluate the data.

Results: Mean age was 53.74±14.83 years, 61.6% of patients were female, 38.4% of patients were male. Mean Vitamin D was 23.51±29.50 ng/mL. The vitamin D levels of 72.2% of the patients were below 30ng/mL. There was statistically significant negative correlation between vitamin D and somatization, obsessive compulsive disorder, interpersonal sensivity, depression, anxiety, hostility, phobia, paranoid thought, psychotization, other and total scores. Patients who low vitamin D level has had high scores of psychological statuses.

Conclusion: Vitamin D level has effect on psychological status in participants. Vitamin D is essential for psychological wellness in dialysis patients. While clinicians will assess, and therapy of these patient's psychological status should take into account patients's vitamin D status

Key words: Medical science, Psychosocial care, Dialysis patient, psychological status

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Address for correspondence/reprints:

Kubra Gokalp

Telephone number: +90 (442) 231 14 48

E-mail: kubragungormus2010@hotmail.com

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Introduction

Chronic Kidney Disease (CKD) is an important public health problem increasingly prevalent in our country as it is in the world. The prevalence of chronic kidney disease in our country was found 15.7%. This means one out of every 6-7 adults has kidney disease (1). When the creatin clearance falls to 12-15 ml / min in chronic renal disease patients should be initiated replacement therapies such as hemodialysis, peritoneal dialysis, or renal transplantation to maintain survival (2). Hemodialysis and peritoneal dialysis patients constitute 87% of the patients who receive replacement therapy (1).

Depression and anxiety are comorbid diseases most associated with end-stage renal disease (3). The prevalence of depression in dialysis patients changes 22.8% -39.3%. (4). In particular, depression and anxiety prevalence in hemodialysis patients is up to 70% (3). Depression episodes increase the pre-existing inflammation in dialysis patients, that is facilitate the occur of other medical problems such as cardiovascular diseases (5). Meanwhile psychological problems may lead to difficulty in compliance with treatment and increase in morbidity and mortality rates (6). Renal 1-α hydroxylase activity decreases due to reduction of renal mass in chronic renal failure and as a result, 1-25 hydroxycholecalciferole levels, active vitamin D form, are decreased. (2). The Kidney Dialysis Outcomes Quality Initiative Guidelines are suggested vitamin D supplementation when the 25 hydroxy vitamin D (25 (OH) D) levels are below 30 ng / ml (7). Vitamin D is important for calcium homeostasis and bone health, also it is essential for brain development and functions. Vitamin D receptors are found in various regions of the brain. One of the regions, where vitamin D receptors are located, is the amygdala where emotions and behaviors are regulated. At the same time, vitamin D shows neuroprotective effects by regulating calcium concentrations (8). In clinical trials, 25 (OH) D levels were determined to be associated with low cognitive function (9,10), anxiety (11), and depression (9).

In a randomized double-blind study with patients receiving vitamin D supplementation, in participants with levels of vitamin D<40 ng / dl the Beck Depression Scale (BDI) scores were found higher than levels of vitamin D>40 ng / dl. In addition, improvement in BDI scales was observed in the supplemented group (12). A systematic review of 17 trials in 2013 indicated that depressed patients should be offered daily 1000-2000 IU vitamin D supplementation (12).

In another study, it was determined that CKD patient's vitamin D deficiency was a significant predictor of depression (13). On the other hand, a study conducted in China, vitamin D supplementation in dialysis patients did not have any effect on the symptoms of depression (5).

In the course of dialysis, the nurses are the health workers who most communicate and gives care to patients. Nurses give care according to the requirements of patients which is helping, educating, and raising the quality of life of the patient for improve of their physical and psychological well-being (14). For this reason, it is important that the nurses who are working as a member of the treatment team have an awareness about emphases of vitamin D when questioning the psychological status and well-being of the patients.

Although the prevalence of serum vitamin D deficiency and depression is high in dialysis patients, there is a limited number of studies on the relationship between vitamin D level and psychological status. The study was planned to determine the relationship between serum vitamin D level and psychological status in patients with dialysis taking into consideration taking into account this shortcoming in the literature.

Methods

Study Design and Sample

This descriptive study was completed between March 2017 and May 2017 in a university hospital dialysis center in Eastern Turkey. The population consisted of dialysis patients in a university hospital dialysis center (96 hemodialysis, 52 continuous ambulatory peritoneal dialysis patients). This study sample group consisted of 59 hemodialysis, 31 continuous ambulatory peritoneal dialysis patients who met the inclusion criteria and accepted to participate in the study. Inclusion criteria of the study; 1) Do not use psychiatric or sleeping medicine 2) Being over 18 years of age 3) Being dialysis disease at least 6 mounts.

Data Collection Tools

1. Personal Information Form: The Personal Information Form was involved three questions regarding sociodemographic characteristics of participants.

2. Vitamin D: Patients's serum 25 (OH) D level was measured by using electrochemiluminescence immunoassay on a Beckman Coulter Autoanalyzer in a university hospital laboratory in Turkey (15)

3. Brief Symptom Inventory (BSI): The BSI was developed by Derogatis and Melisaratos (16) evaluates psychological or psychiatric pathology in person. The inventory is a 53 item and the 5-point Likert scale ("not at all" (0) "a lot" (4)). (16). The Turkish validity reliability study was conducted by Sahin, and Durak (17).

Ethical Considerations

The Ethics Committee of Faculty of Health Sciences was approved (Decision No:2017/03/09)

and legal permission. The participants were informed about the purpose and their questions were answered. Since the use of human fact in this study requires protection of individual rights, "Protection of Confidentiality Principle", "Informed Consent Principle" and "Voluntary Basis" and which are relevant ethical principles were realized.

Statistical analysis

The study to assess the data was used Statistical Package for the Social Sciences (SPSS 22.0. Normal distribution of variables was examined by the Kolmogorov–Smirnov, Shapiro–Wilk tests and normality plots. Descriptive analysis (minimum-maximum values percentage, mean and standard deviation, average, frequency) were used to evaluate the data. As well as Kruskal–Wallis test and Pearson's Correlation Analysis were used to analyze relationships among serum vitamin D level and psychological status in participants. The level of significance was set at $p<0.05$.

Results

This study was conducted with 90 dialysis patient (59 hemodialysis, 31 continuous ambulatory peritoneal dialysis). Mean age was 53.74±14.83 (18-81) years, 61.6% of patients were female, 38.4% of patients were male. Mean Vitamin D was 23.51±29.50 ng/mL (3-118) (Table 1)

Table 1. Demographic status of patients

Demographic Status (N=90)	n	%
Dialysis Type		
Hemodialysis		65.6
Peritondialysis	31	34.4
Gender		61.1
Women	35	38.9
Man		
Age		Min±Max
	53.74±14.83	18-81
Vitamin D	23.51±29.50	3-118

M:Mean, Sd:Standart deviation

Table 2. Levels of Vitamin D

Vitamin D Group (N=90)	n	%
VD <20 ng/ mL	57	63.3
VD 20-30 ng/ mL	8	8.9
VD >30 ng/ mL	25	27.8

Table 3. The relationship between patients' Vitamin D levels and BSI score averages

Scale	Vitamin D Grup	M ±Sd		KW	p
Somatization	**VD <20ng/mL**	8.16±5.25	r=-0.263	5.141	0.076
	VD 20-30 ng/mL	7.00±1.87			
	VD >30 ng/mL	5.39±4.47	p=0.012		
Obsessive compulsive disorder	**VD <20 ng/mL**	7.55±3.76	r= -0.378	11.094	**0.004**
	VD 20-30 ng/mL	6.25±4.46			
	VD >30 ng/mL	4.79±4.23	p=0.000		
Interpersonal sensivity	**VD <20 ng/mL**	4.66±2.99	r=-0.284	6.855	**0.032**
	VD 20-30 ng/mL	4.00±1.07			
	VD >30 ng/mL	2.91±2.48	p=0.007		
Depression	**VD <20 ng/mL**	7.28±4.71	r=-0.330	9.894	**0.007**
	VD 20-30 ng/mL	6.00±1.60			
	VD >30 ng/mL	3.87±2.67	p=0.001		
Anxiety	**VD <20 ng/mL**	7,07±4.77	r=-0.319	10.709	**0.005**
	VD 20-30 ng/mL	4,50±2.78			
	VD >30 ng/mL	3.56±2.65	p=0.002		
Hostility	**VD <20 ng/mL**	5.89±3.97	r=-0.232	6.873	**0.032**
	VD 20-30 ng/mL	3.75±2.31			
	VD >30 ng/mL	3.43±2.51	p=0.028		
Phobia	**VD <20 ng/mL**	5.89±3.97	r=-0.291	7.057	**0.029**
	VD 20-30 ng/mL	3.75±2.31			
	VD >30 ng/mL	3.38±2.43	p=0.005		
Paranoid thought	**VD <20 ng/mL**	5.89±3.97	r=-0.247	4.790	0.091
	VD 20-30 ng/mL	3.75±2.32			
	VD >30 ng/mL	3.85±2.93	p=0.019		
Psychotization	**VD <20 ng/mL**	5.89±3.97	r=-0.248	6.713	**0.035**
	VD 20-30 ng/mL	3.75±2.31			
	VD >30 ng/mL	3.64±3.20	p=0.018		
Other	**VD <20 ng/mL**	4.71±3.17	r=-0.293	8.485	**0.014**
	VD 20-30 ng/mL	3.00±1.85			
	VD >30 ng/mL	2.58±3.20	p=0.005		
Total	**VD <20 ng/mL**	6.01±35.46	r=-0.329	8.768	**0.012**
	VD 20-30 ng/mL	45.75±17.56			
	VD >30 ng/mL	37.44±22.58	p=0.002		

M:Mean, Sd:Standart deviation

As seen of Table 2, 63.2% of patients were levels of Vitamin D<20 ng/mL, 8.9% of patients were levels of Vitamin D 20-30 ng/mL, %27.8 of patients were levels of Vitamin D >30 ng/mL.

According to the Table 3, negatif correlation was found between Vitamin D and psychological status in participants (p=0.002). There was significant relation between Vitamin D and somatization (p=0.012), obsessive compulsive disorder (p=0.000), interpersonal sensivity (p=0.007), depression (p=0.001), anxiety (p=0.002), hostility (p=0.028), phobia (p=0.005), paranoid thought (p=0.019), psychotization (p=0.018) and other (p=0.005).

Patients who low Vitamin D level has had high scores.

Discussion

The study was conducted to determine the association between vitamin D level and psychological status in dialyzed patients. To our best knowledge, this study was the first that association between vitamin D level and psychological status in dialyzed patients in Turkey. End-stage renal failure affects the physical, mental, and social well-being of patients (18). Psychiatric disorders such as depression and anxiety are most commonly comorbid diseases associated with end-stage renal disease (3). It has been shown that in a previous study more than 50% of dialysis patients had depression and depression reduced the quality of life and increased mortality (18).

In the present study, we found a high rate of prevalence of serum vitamin D deficiency. Many factors such as physiological, biochemical, psychosocial, nutrition contribute to the development and progression of depression in dialysis patients (19). It has been showed that vitamin D deficiency, which is frequently seen in dialysis patients, can be one of the causes of depression (5). In parallel with this study, vitamin D deficiency was determined about 80% of the dialysis patients (20). In another study, level of vitamin D was condected about 87.1% of dialysis patients had levels <30 ng/ml (21).

In studies of the relationship between vitamin D and depression, low levels of vitamin D were associated with depression (22,13). In a study about the relationship between depression prevalence and vitamin D levels, the prevalence of depression in individuals with 25 (OH) D level <30 ng / mL was 22.6%; 25.8% for <20 ng / mL and 35.0% for <10 ng / mL (23). Zhang et al. was shown that 44% of the 484 dialysis patients had depression and the average serum vitamin D level was 17.6 ± 7.7 nmol / L. Depressive symptoms were more common in dialysis patients with low D vitamin levels, but D vitamin supplementation didn't effect on the psychological status. Researchers have noted that the dose of vitamin D supplementation and follow-up time may be inadequate for the treatment of depression (5). In this study, it was shown that the score of depression was higher in patients with low levels of seum vitamin D. Vitamin D receptors are found in many regions of the brain. It has been suggested that they have many functions in the brain, such as neuroprotection, neuroplasticity, inflammation, and regulation of neurotrophic factors. The presence of vitamin D receptors in dopaminergic cells and vitamin D-responsive elements in promotor regions of tryptophan hydroxylase and serotonin receptor genes that this supports the possible biological association between psychiatric disorders and D vitamin deficiency (24).

In the present study, obsessive compulsive disorder, interpersonal susceptibility, depression, anxiety, hostility, psychoticism and phobia scores were found to be higher in patients with low vitamin D levels. It has been reported that total scores, somatization, obsessive compulsive disorder, interpersonal sensitivity, depression, anxiety, and paranoid thinking scores were similar in dialysis patients whereas hostility, phobic anxiety and psychosis scores were higher in patients with peritoneal dialysis (25,26). Furthermore, depression, anxiety, hostility, and interpersonal susceptibility scores were found to be higher in the dialysis treatment subjects compared to the control group in a study comparing end-stage renal patients receiving without receiving dialysis treatment (27).

In this study, for the first time in the literature, the relationship between serum vitamin D levels and other depressive psychological disorders such as somatization, anxiety, obsessive compulsive disorder, phobia, paranoid thought, psychosis, hostility, interpersonal sensitivity in dialysis patients has been shown.

Conclusion

Vitamin D level has significant effect on psychological status in dialysis patients. While clinicians will assess, and therapy of dialysis patient's psychological status should take into account patients's vitamin D status and vitamin D may be used to replace or improve the efficacy of medical treatment. For this reason, while health

professionals' recommendations to patients in this respect, need to have knowledge and awareness about the studies on vitamin D. The results here may provide a basis for future research with regard to evaluating the use of vitamin D in the management of psychological status of dialysis patients. In this regard, there is need for more randomized controlled trials.

Ethics Committee Approval: The Ethics Committee of Faculty of Health Sciences was approved (2017/03/09) and legal permission.
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The Effect of Diagnosis of Covid-19 on Sleep Quality in Emergency Service Personnel: A Comparative Study

Serdar Derya[1](ID), Bora Tetik[2](ID)

[1]Department of Traumatology and Emergency Medicine, Malatya Training and Research Hospital, Malatya / Turkey
[2]Deparment of Neurosurgery, Inonu University School of Medicine, Malatya / Turkey.

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Abstract

Objective: The COVID-19 pandemic, is an important health problem that affects our lives in social, political, economic and psychological areas In this study, it was aimed to determine the effect of diagnosis of COVID-19 on sleep quality in emergency service personnel.

Methods: In this comparative study, 66 personnel providing emergency services and diagnosed with COVID-19 were compared with 66 personnel providing emergency services who were not diagnosed with COVID-19. The data were obtained through the Personal Information Form and Pittsburgh Sleep Quality Index (PSQI).

Results: The average time after diagnosis in personnel diagnosed with COVID-19 (n=66) was 5.52±2.27 months. It was determined that the mean total score of PSQI was 18.03±1.73 in emergency service personnel diagnosed with COVID-19 and 16.71±2.28 in emergency service personnel who were not diagnosed with COVID-19, and the difference between the groups was statistically significant (p=0.000). As the time passed after the diagnosis of COVID-19, it was determined that the mean total score of PSQI decreased statistically significantly, that is, the quality of sleep increased (p=0.027).

Conclusion: It was observed that the sleep quality of the emergency service personnel diagnosed with COVID-19 was worse compared to the personnel who were not diagnosed, however, the sleep quality increased significantly as the time passed after the diagnosis.

Key words: Emergency service personnel, COVID-19 diagnosis status, sleep quality.

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Address for correspondence/reprints:

Bora Tetik

Telephone number: +90-(422) 341 06 60-3207

E-mail: drboratetik@hotmail.com

Introduction

The COVID-19 pandemic, which started in China and affected the whole world, is an important health problem that affects our lives in social, political, economic and psychological areas (1). Although there is not enough evidence yet, there is increasing evidence in the scientific literature that COVID-19 disease is increasingly associated with mental and neurological symptoms, including delirium, anxiety, sleep disorders, and depression (2,3). It is stated that factors such as precautions, compulsory changes related to work and education, and economic difficulties play a role in this increase in psychological health problems, as well as the effect of quarantine and treatment processes and unavoidable death rates (4,5).

The fact that the cause of the emergence of COVID-19 is not known exactly, the virus cannot be controlled and all individuals in the world are at potential risk have turned the epidemic into a global trauma (1). As the prevalence and death rate of infectious diseases increase, it is inevitable that individuals' fear, depression and anxiety levels will increase (6). There are cross-sectional studies emphasizing that the prevalence of stress-related psychiatric symptoms in the general population causes an increase in depression, anxiety, and sleep problems (5,7).

The COVID-19 epidemic has affected the social and business environments in various ways (2). COVID-19 has psychological effects on health workers, as in many occupational groups, and it is emphasized in the literature that especially frontline workers are at risk (5,8,9). Healthcare professionals dealing with the diagnosis, treatment and care of patients diagnosed with COVID-19 may show symptoms of stress, depression and insomnia more frequently (1). In this process, negative emotions such as worry, depression and anxiety may impair the sleep quality of individuals (6,10). Sleep is a vital process for quality of human life and maintaining homeostasis.

Good sleep quality has effects on physical and mental health (11). For this reason, it is important that health workers who provide treatment and care for individuals diagnosed with COVID-19 have good sleep quality (6). In the literature, it is stated that the physical and psychological health levels of health personnel are at risk due to their working conditions, and that the anxiety and stress experienced may negatively affect sleep (12). The possibility that problems such as post-traumatic stress disorder, depression, anxiety and sleep disorders affect healthcare professionals, especially those who are in contact with the public at the front, increases the importance given to the issue (2). It can be thought that the impact on emergency service personnel who are in contact with the public, especially on the front, will be inevitable and higher. Based on this information, it was aimed to determine the effect of diagnosis of COVID-19 on sleep quality in emergency service personnel. The secondary aim is to compare the demographic characteristics and sleep quality of 112 personnel diagnosed with covid-19.

Methods

This study was designed as a comparative study to determine the effect of diagnosis of COVID-19 on sleep quality in emergency service personnel. The universe of the research consisted of all Emergency Medical Technicians (EMT), Paramedics and Doctors serving under the Provincial Ambulance Service Chief Physician in a province in the east of Turkey. The number of personnel diagnosed with COVID-19 during the pandemic process is approximately 130. The research was carried out in April 2021 and 66 emergency service personnel diagnosed with COVID-19 were compared with 66 emergency service personnel not diagnosed with COVID-19. Personnel without any diagnosed sleeping disorder were included in the study. Emergency service personnel included in the study were selected from the relevant population by simple random sampling method.

Data Collection Tools

Personal Introduction Form and Pittsburgh Sleep Quality Index are used to obtain the data.

Personal Introduction Form

This 8-question form prepared by the researchers consists of questions questioning the introductory characteristics (age, gender, education level, income status, etc.) of the 112 emergency service personnel included in the study and their diagnosis during the COVID-19 pandemic process.

Pittsburg Sleep Quality Index (PSQI)

Pittsburgh sleep quality index (PSQI) is a measuring tool that provides knowledge about sleep quality and the type and severity of sleep disorder in the last month, and is used to determine sleep quality. It was developed by Buysse and his friends in 1989 (13). 19 of 24 questions in the scale, which was adapted into Turkish by Ağargün and his friends, are self-report questions. The total PSQI score ranges from 0-21. High scores define poor sleep quality and high level of sleep disturbance. The Cronbach's alpha coefficient of the Pittsburgh Sleep Quality Scale was found to be 0.80 (14). In this study, the Cronbach's alpha coefficient of the Pittsburgh Sleep Quality Scale was found to be 0.69.

Data Collection

The data collection phase of this research was carried out using the Google Form method (Google Forms®). Emergency service personnel were reached via the Internet on WhatsApp and data collection forms were sent to the participants using the Google Form method. Emergency service personnel who agreed to participate in the study were first asked to approve the informed consent form, and the personnel who gave consent were directed to the data collection forms via the internet. All data obtained by the online self-report method was recorded with the Google Form method.

Statistical analysis

The data were evaluated using the SPSS 24.0 statistical package program. In the evaluation of the data, descriptive statistics (min-max values, mean, standard deviation, number and percentage) as well as one-way anova test, independent groups t test and Pearson correlation analysis were used. The results were evaluated at the 95% confidence interval and the significance was evaluated at the $p<0.05$ level.

Results

In Table 1, the distribution of the descriptive characteristics of the emergency service personnel is given. 53% of the personnel diagnosed with covid-19 are male, 43.9% have a associate degree, 45.5% are EMT, and the rate of those who state that their income is equal to their expenses is 56.1%. 63.6% of the personnel who are not diagnosed with covid-19 are women, 47% have a associate degree, 48.4% are EMT, and the rate of those who state that their income is less than their expenses is 54.5% (Table 1).

In Table 2, the comparison of the sleep quality of the emergency service personnel with and without the diagnosis of COVID-19 is given. It was determined that the mean total score of PSQI was 18.03±1.73 in emergency service personnel diagnosed with COVID-19, and 16.71±2.28 in emergency service personnel who were not diagnosed, and the difference between the groups was statistically significant ($p<0.001$). High values obtained from PSQI indicate poor sleep quality and high level of sleep disturbance (Table 2).

In Table 3, it was seen that the time passed after the diagnosis of COVID-19 in the emergency service personnel diagnosed with COVID-19, the time passed after the diagnosis of COVID-19, and the total score of PSQI increased as the time passed after the diagnosis of COVID-19, the average of the total score of PSQI decreased, that is, the quality of sleep increased (Table 3). In addition, no relationship was found between age and working year and sleep quality.

Table 4 shows comparison of descriptive characteristics and sleep quality in emergency service personnel diagnosed with COVID-19. No difference was found between gender, education level, profession and perceived income status and sleep quality of the personnel who had diagnosed with COVID-19 ($p>0.05$).

Table 1. Distribution of descriptive characteristicsof emergency service personnel (n=132)

Variables	Diagnosed With COVID-19 (n=66) n(%)	Not Diagnosed With COVID-19 (n=66) n(%)
Gender		
Female	31(47.0)	42(63.6)
Male	35(53.0)	24(36.4)
Education		
High school	8(12.2)	19(28.8)
Associate degree	29(43.9)	31(47.0)
Bachelor degree	29(43.9)	16(24.2)
Profession		
Paramedic	28(42.4)	30(45.5)
EMT	30(45.5)	32(48.4)
Doctor	8(12.1)	4(6.1)
Perceived income status		
My income less my expense	23(34.8)	36(54.5)
My income equivalent to my expense	37(56.1)	27(41.0)
My income more than my expense	6(9.1)	3(4.5)
	Mean±SD	**Mean±SD**
Age (year)	29.22±5.74	31.39±9.13
Working year	7.86±4.01	8.69±7.24
Time/Month after COVID-19 diagnosis	5.52±2.27	-

Table 2. Comparison of sleep quality of emergency service personnel with and without COVID-19 diagnosis (n=132)

COVID-19 Diagnosis Status	PSQI Mean±SD	Test and p value
Yes (n=66)	18.03±1.73	t=3.731
No (n=66)	16.71±2.28	**p=0.000***

*p<0.001 t=Independent groups t test Mean±SD= Mean and standard deviation

Table 3. The relationship between the time passed after COVID-19 diagnosis, age and working year and sleep quality in emergency service personnel diagnosed with COVID-19 (n=66)

Variables	PSQI
Age/ Year	r= 0.058 p= 0.644
Working year	r= 0.054 p= 0.669
Time/Month after COVID-19 diagnosis	r= -0.275 **p= 0.027***

*p<0.05 r=Pearson correlation analysis

Table 4. Comparison of descriptive characteristics and sleep quality in emergency service personnel diagnosed with COVID-19 (n=66)

Variables	n	PSQI (Mean±SD)	Test and p value
Gender			
Female	31	18.00±1.93	t= -0.312
Male	35	18.05±1.57	p=0.895
Education			
High school	8	18.12±1.88	F=0.150
Associate degree	29	17.89±1.54	p=0.861
Bachelor degree	29	18.13±1.92	
Profession			
Paramedic	28	17.64±1.68	F=2.063
EMT	30	18.13±1.61	p=0.136
Doctor	8	19.00±1.13	
Perceived income status			
My income less my expense[a]	23	18.73±1.91	F=0.501
My income equivalent to my expense[b]	37	17.48±1.42	p=0.608
My income more than my expense[c]	6	18.66±1.86	

EMT: Emergency Medical Technician, t=Independent groups t test, F=One-way anova test, Mean±SD= Mean and standard deviation

Discussion

Individuals with COVID-19 have to cope with many sources of stress, such as uncertainty about the process, fear of infecting their relatives, and exclusion from society, as well as the physical effect of the disease. Health workers, especially those who have the closest contact with infected people, carry a high risk of transmission while fighting the epidemic. Especially the mental health of the health personnel working in intensive care units, 112 emergency service command center and emergency services is severely affected and this causes psychiatric problems such as sleep disorders, depression and anxiety. In the literature, it has been reported that psychological effects are higher in high-risk groups, primarily healthcare workers (4).

Sleep; It is the time period when the immune system continues to work, the nervous system rests, individuals are freed from complex thoughts and go to rest (6). In the current pandemic period, it is obvious that the working conditions of healthcare workers have become more difficult, their shifts have increased and their sleep patterns have been disturbed (3). Although there is not enough evidence yet, there is evidence in the literature that COVID-19 disease is increasingly associated with mental and neurological symptoms, including delirium, anxiety, sleep disorders, and depression. Studies conducted in the last ten years have gradually increased the view that sleep disorders have a strong effect on the risk of infectious diseases, the occurrence and progression of a number of diseases, and the incidence of depression (11). In Liu and his friends' study during the pandemic period, the rate of those who thought their sleep patterns were very good and good was 80 %, and the rate of those who slept more than 7 hours was 53 % (15). In the study conducted by Cansel et al. across Turkey, it was found that 53% of the participants slept for more than 8 hours, there was no disturbance in their sleep quality, and their anxiety levels were lower (16). In our study, it was found that those diagnosed with COVID-19 from the PSQI, the scale by which we evaluate sleep quality, received higher scores and had worse sleep quality. Sleep quality is an important indicator of health. Good sleep quality for clinical staff not only enables them to work more effectively to treat patients, but also maintains optimal immune function to prevent infection. Therefore, sleep quality is an important indicator for health (12). In addition, in our study, it was observed that as the time passed after being diagnosed with COVID-19 increased, the PSQI score decreased and sleep quality increased. Therefore, in order to improve the sleep quality of healthcare personnel with COVID-19, a comprehensive approach should be provided.

The authors found that anxiety was associated with stress and poor sleep quality, and that the combination of anxiety and stress reduced sleep quality. In a study conducted during the pandemic process, it was reported that 50.4% of healthcare professionals experienced depression, 44.6% had anxiety and 34.0% had insomnia (10). In a study conducted by Xiao et al. on healthcare professionals in China who were involved in the treatment of patients with COVID-19 infection; determined that anxiety level is a related factor that negatively affects sleep quality (12). In addition, in the literature, it is stated that the COVID-19 pandemic may increase sleep disorders and damage the function of the immune system (11). Work-related stress, sleep deprivation, shift work and fatigue often cause sleep disturbances and poor sleep quality in healthcare workers (17). Based on these data, it is necessary to improve the working conditions of health workers in order to provide sleep quality during the pandemic period.

Conclusion

It was observed that the sleep quality of the emergency service personnel who were diagnosed with COVID-19 was worse compared to the personnel who were not diagnosed, but the sleep quality increased significantly as the time passed after the diagnosis increased. In line with these results; It can be said that there is a need for action plans to reduce the effects of COVID-19 on mental health in order to protect sleep quality and psychological health of healthcare workers during and after the epidemic. Of course, although psychological impact is an expected result in an extraordinary situation like a pandemic, the continuation of the danger and restrictions will cause permanent psychological and biological effects. Therefore, while evaluating the pandemic in healthcare professionals, it will be important to determine the psychological problems and related factors that may develop afterwards, to determine the target group and to take the necessary precautions, and to direct the aid.

Limitation

This study has some limitations; firstly, sleep quality don’t relate only to infectious disease. Other factors haven’t been investigated for this study. In addition, the other limitation of the study is that the

data were obtained from emergency service personnel working in only one province.

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Author Contributions:

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Urgent Thoracotomy Operations In COVID-19 Era

Baris Hekimoglu[1](ID),Muhammet Ali Beyoglu[2](ID), Mehmet Furkan Sahin[2](ID)

[1]Department of Thoracic, Surgery Faculty of Medicine, Ordu University, Ordu, Turkey,
[2]Department of Thoracic, Surgery Faculty of Medicine, Ankara City Hospital, Ankara, Turkey,

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Abstract

Objective: This study has aimed to share the perioperative management practices and respective outcomes in patients; who underwent urgent thoracotomy due to traumatic hemothorax during the pandemic.

Methods: In a single-center, 18 patients; who underwent urgent thoracotomy due to traumatic hemothorax in March 2020 to March 2021, were included in the study retrospectively. Patient data were retrieved from digital archive files. The initial evaluation was performed in the emergency room while wearing complete personal protective equipment. Patients were taken into the operating room under emergency conditions without waiting for the results of the nucleic acid tests performed on oropharyngeal and nasopharyngeal swabs. The operation was carried out by involving the minimum number of personnel. In the postoperative period, patients were followed up in a negative pressure intensive care room. Isolation measures were maintained until two novel coronavirus nucleic acid tests on oropharyngeal and nasopharyngeal swabs collected 48 hours apart were reported as negative.

Results: During the one-year period in the COVID-19 pandemic, 18 patients were operated on with the indication of urgent thoracotomy. Of the patients, 14 were men (77.8%), and 4 were women (22.2%). Nucleic acid test results were negative in 17 patients (94.5%). The nucleic acid test result was reported positive in one patient (5.5%) for samples taken at the 48th hour. Nucleic acid tests were performed on the oropharyngeal and nasopharyngeal swabs obtained on the fifth and seventh days from the operation personnel. No novel coronavirus transmission occurred in the healthcare personnel. In the postoperative period, 15 patients (83.3%) were successfully treated and discharged from the hospital, but 3 patients (16.7%) died. No morbidity or mortality occurred due to COVID-19.

Conclusion: Urgent thoracotomies can be successfully performed during the COVID-19 pandemic. Novel coronavirus transmissions can be avoided if relevant healthcare personel comply with isolation measures and use complete personnel protective equipment.

Keywords: COVID-19, Thoracotomy, Surgery

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E-mail: drbarishekimoglu@yahoo.com

Address for correspondence/reprints:

Barış Hekimoğlu

Telephone number: +90 (452) 212 72 45

Introduction

The coronavirus disease-2019 (COVID-19) pandemic, caused by coronavirus type 2 (SARS-CoV-2), was declared a pandemic by the World Health Organization (WHO) on 11 March 2020. Although it has been 15 months since the declaration, the pandemic continues to challenge healthcare systems globally. According to WHO, 113 million people have been infected with SARS-CoV-2, and 2.5 million of these infected people died as of March 2021 (1). In many countries, healthcare services other than emergency and oncological treatments had to be postponed due to the pandemic. Even the postponement of oncological procedures has been discussed, especially when the density of cases was high (2,3). The Republic of Turkey (T.R.) Ministry of Health directive issued on April 2020 instructed that surgical operations other than emergency and cancer surgery should be postponed in our country (4). Implementing necessary adjustments according to the requirements emerged due to the pandemic, emergency, and oncological surgical interventions of thoracic surgery continued in the period after the directive.

Urgent thoracotomy is the most common non-elective intervention in thoracic surgery. Urgent thoracotomy is a surgical procedure performed in cases where excessive bleeding occurs in the hemithorax following thoracic trauma. Generally accepted urgent thoracotomy indications include the state of shock developing after thoracic trauma, the presence of a major repairable intrathoracic injury, and continuous thoracic hemorrhage (5). Continuous thoracic hemorrhage is defined as the occurrence of hemorrhagic drainage of >1500 ml (20 ml/kg) during tube thoracostomy or the drainage of >250 ml/hour within 3 hours after tube thoracostomy (5). This study has aimed to share the implemented measures and obtained outcomes in patients; who underwent urgent thoracotomy due to traumatic hemothorax during the COVID-19 pandemic.

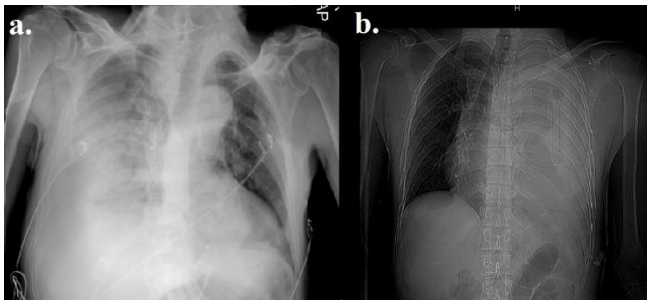

Figure 1. a) Chest radiography of patient 6 reveals right side hemothorax. b) Chest radiography of patient 9 reveals left side hemothorax.

Methods

This study was designed as a retrospective, descriptive, and cross-sectional study. In the one year between March 2020 and March 2021, patients; who underwent urgent thoracotomy in a secondary stage health center were retrospectively included in the study. A total of 18 patients admitted to the emergency department due to blunt or penetrating chest trauma and on whom urgent thoracotomy and bleeding control were performed due to massive intrathoracic hemorrhage were included in the study. Patient information was obtained from digital and physical archives.

Patients were evaluated in the emergency room in compliance with the T.R. Ministry of Health guideline about the examination of patients suspected of having COVID-19 or diagnosed with COVID-19. Each patient was evaluated by a thoracic surgeon wearing personal protective equipment (PPE). PPE included a bonnet, a face shield, goggles, an N-95 mask, a surgical mask, double gloves, and coveralls or a disposable surgical gown. After taking the anamnesis, performing a physical examination, and laboratory tests including a complete blood count, serum biochemistry, coagulation parameters, blood type tests, direct chest radiography, and thoracic computed tomography (CT) were performed in patients with stable hemodynamics (Figure 1). Patients were inquired not only about the history of the trauma but about COVID-19 as well. Patients were asked whether they had any fever, fatigue, chills, shivering, headache, loss of smell, generalized muscle pain, and diarrhea in the ten days preceding the trauma. Patients were also inquired about whether they visited any places known to be densely populated with COVID-19 cases or whether they had any contact with persons diagnosed with COVID-19 or suspected of having COVID-19 in the last two weeks. Nasopharyngeal (NP) and oropharyngeal (OP) swabs were obtained from patients to perform the SARS-CoV-2 Reverse Transcriptase Polymerase-Chain-Reaction (RT-PCR) test. In patients with stable hemodynamics, tube thoracostomy was performed for the treatment of hemothorax. Immediately after the tube thoracostomy, patients with a hemorrhagic drainage volume of 1500 ml or 20 ml/kg underwent urgent thoracotomy without waiting for the results of the SARS-CoV-2 RT-PCR test. Anamnesis could not be obtained from patients who had unstable hemodynamics and were in a severe hemorrhagic shock. Such patients underwent surgery without undergoing any radiological imaging tests. Immediately after the operation, an anesthesiologist or a surgeon wearing full PPE took NP and OP swabs

from patients whose samples could not be taken in the emergency room for the SARS-CoV-2 RT-PCR test.

Urgent thoracotomy was performed through a posterolateral incision under general anesthesia while the patient was lying in the lateral decubitus position. The same surgical team performed all operations. The fewest possible personnel were involved in the operations. A high-efficiency particulate air (HEPA) filter was applied to the draining channel of the thoracostomy drainage bottles before the patients were moved to the intensive care unit (ICU) after the operation. In order to prevent the aerosol generation, all patients were extubated after being transferred to intensive care rooms equipped with negative air pressure. Patients with stable hemodynamics and patients, who did not need mechanical ventilation, were transferred to single rooms in the inpatient unit after 24 hours of intensive care follow-up. All patients were assumed to have suspected COVID-19 until negative results were reported for two consecutive SARS-CoV-2 RT-PCR tests performed 48 hours apart. All interventions were performed by personnel wearing PPE until the suspicion of COVID-19 was ruled out. Patients were followed up through daily postoperative chest radiography images, complete blood counts, and tube thoracostomy drainages. In the presence of fever, leukopenia, and heterogeneous pneumonic infiltration on chest X-rays during the follow-up period, patients underwent nucleic acid tests for the differential diagnosis of COVID-19.

Statistical analysis

Statistical data were calculated using the SPSS 22.0 software (SPSS Inc., Chicago, IL, USA). Descriptive data were expressed as mean (standard deviation) for the continuous variables and number (%) for the categorical variables. The Mann-Whitney U test was used to determine discrepancies between two classes based on the continuous variables' nonparametric data attributes. A p-value of < 0.05 was considered statistically significant.

Results

In the period between March 2020 and March 2021, 18 patients were operated on by the same surgical team in a single-center because of the indication of urgent thoracotomy. Of the patients, 14 were males (77.8%), and 4 were females (22.2%). The mean age of the patients was 34.9 years (min-max.=8-77 years, SD ±16.3). Descriptive patient information is shown in the Table 1. Of the patients, 13 (72.2%) reported penetrating thoracic traumas, and 5 (27.8%) reported blunt thoracic traumas in the medical history. Penetrating traumas occurred due to penetrating stab traumas (n=7; 38.9%), firearm injuries (n=3; 16.7%), and foreign body penetrations (n=3; 16.7%). Causes of blunt trauma included falling from height (n=3; 16.7%), falling off a bicycle (n=1; 5.5%), and in-vehicle traffic accidents (n=1; 5.5%) (Figure 2)

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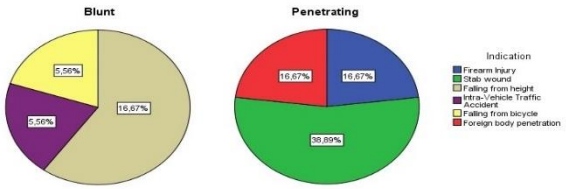

Figure 2: Patient distribution according to the trauma etiology.

Table 1. Patient demographics and clinical characteristics

Cases	Gender	Age	Cause of Trauma	Trauma Type	Localization	Hemodynamic status	Preop Hmg	Postop Hmg	Surgical Repair	RT-PCR	LOS (days)	Status
1	M	40	Firearm Injury	Penetrating	Right	Stable	8.0	10.1	ICA+ LP	Neg/Neg	22	Exitus
2	F	30	Firearm Injury	Penetrating	Left	Non-stable	7.3	3.6	ICA + Lingular Artery	Neg/Neg	26	Alive
3	M	50	Stab Wound	Penetrating	Left	Stable	10.6	10.9	LIMA	Neg/Neg	13	Alive
4	M	22	Foreign Body Penetration	Penetrating	Right	Non-stable	4.5	12.1	ICA+ LP	Neg/Neg	5	Alive
5	M	38	Stab Wound	Penetrating	Left	Stable	11.7	11.0	ICA	Neg/Neg	3	Alive
6	M	77	Falling from height	Blunt	Right	Stable	7.6	9.2	ICA + LP	Neg/Neg	6	Alive
7	M	35	Foreign Body Penetration	Penetrating	Left	Stable	12.1	13.4	LP+ Diaphragma Artery	Neg/Neg	7	Alive
8	M	59	Falling from height	Blunt	Right	Stable	6.1	8.2	LP	Neg/Neg	58	Exitus
9	M	45	Stab Wound	Penetrating	Left	Stable	7.4	10.2	LIMA + ICA	Neg/Neg	5	Alive
10	M	26	Stab Wound	Penetrating	Left	Stable	8.2	9.9	LP+ Diaphragma Artery	Neg/Neg	4	Alive
11	F	32	Intra-vehicle Accident	Blunt	Left	Stable	7.1	8.5	ICA+ LP	Neg/Neg	7	Alive
12	F	34	Falling from height	Blunt	Right	Non-stable	6.8	9.0	ICA+ LP	Neg/Neg	5	Alive
13	M	8	Falling from height	Blunt	Right	Non-stable	8.0	9.5	ICA+ L.P	Neg/Neg	8	Alive
14	F	11	Foreign Body Penetration	Penetrating	Right	Non-stable	7.1	10.2	L.P	Neg/Neg	6	Alive
15	M	26	Stab Wound	Penetrating	Left	Stable	4.5	7.0	ICA+ LP + Diaphragma Artery	Neg/Neg	5	Exitus
16	M	40	Stab Wound	Penetrating	Right	Stable	6.5	10.3	RIMA	Neg/Neg	6	Alive
17	M	31	Stab Wound	Penetrating	Right	Stable	8.4	11.0	ICA+ LP	Neg/Pos	11	Alive
18	M	24	Fire-arm Injury	Penetrating	Left	Stable	7.9	9.0	ICA+ IPV	Neg/Neg	10	Alive

Abbreviations: Preop: Pre-operative, Postop: Post-operative, RT-PCR: Novel Coronavirus Reverse Transcriptase Polymerase-Chain-Reaction Test, LOS: Length Of Stay, M: Male, F: Female, ICA.: Inter Costal Artery, LP: Lung Parenchyma, LIMA: Left Internal Mammarian Artery, RIMA: Right Internal Mammarian Artery, IPV: Inferior Pulmonary Vein, Neg: Negative, Pos: Positive.

Of the patients, who underwent urgent thoracotomy (n=18), 9 (50%) had right hemothorax, and 9 (50%) had left hemothorax. Right posterolateral thoracotomy was performed in 9 patients (50%); left posterolateral thoracotomy was performed in 9 patients (50%), and bleeding was controlled. It was found out during the operations that bleeding occurred due to traumas to the following structures, including an intercostal artery in 12 (66.6%) patients, the lung parenchyma in 12 (66.6%) patients, a phrenic artery in 3 (16.7%) patients, the left internal mammary artery in 2 (11.1%) patients, the right internal mammary artery in 1 (5.5%) patient, the inferior pulmonary vein in 1 (5.5%) patient, and the lingular pulmonary artery in 1 (5.5%) patient. During operations, an average of 3.6 units of erythrocyte suspension (minimum-maximum=2-12, SD±2.5) and an average of 3.8 units of fresh frozen plasma (minimum-maximum=2-8, SD±1.9) were administered to patients for replacement. The mean hemoglobin value was 7.7 g/dl in the preoperative complete blood counts (min-max.=4.5-12.1, SD±2.0), and the mean hemoglobin value was 9.6 g/dl (min-max=3.6-13.4, SD±2.1) in the postoperative complete blood counts. There was a statistically significant difference between the preoperative and postoperative hemoglobin values (p=0.013).

In the postoperative period, patients were followed up in an intensive care room equipped with negative pressure. Thirteen patients (72.2%) were extubated just after they were transferred to the intensive care room, and 2 patients (11.1%) were extubated at the postoperative 24th hour because blood pressure stabilization could not be achieved in the early postoperative hours. The remaining 3 patients (16.7%) were followed under invasive mechanical ventilation for a mean of 27.3 days. These patients were those with severe preoperative blood loss and needed massive blood transfusions during and after surgery. They were followed up on a mechanical ventilator for a long time because of developing respiratory and metabolic acidosis. Of these 3 patients, 2 (11.1%) died due to bacterial sepsis of unknown origin. The other patient (5.5%) died due to disseminated intravascular coagulation. 15 patients (83.3%) were moved to single rooms in the inpatient unit after 24 hours of intensive care follow-up.

Any condition to raise a suspicion of COVID-19 was not observed in the preoperative anamnesis of 13 patients (72.2%) who were conscious and did not have a severe hemorrhagic shock. No suspicious conditions were detected in the anamnesis of 5 patients (27.8%), whose medical history could only be obtained in the postoperative period because these patients were confused or lethargic due to a severe hemorrhagic shock and impaired consciousness.

Radiologic examinations such as chest x-ray and computed tomography were performed in 13 patients (72.2 %) who were hemodynamically stable when they first came to the emergency department, in order to show the severity of the trauma. 5 patients (27.8%) who were unstable were taken directly to the operating room. No findings associated with COVID-19 were detected in the thoracic CT scans of these patients. Tube thoracostomy was performed on these patients in the emergency department. A mean volume of 1738 milliliters (min-max=1200-2500 ml, SD±333) hemorrhagic drainage occurred just after the tube thoracostomy.

Only in 1 patient (5.5%), the result of the RT-PCR test was positive for the swabs taken for the second time 48 hours after the first samples in the postoperative period. This patient, whose SARS-CoV-2 RT-PCR test result was reported as positive, had no history of contact with a COVID-19 patient, and had no symptoms associated with COVID-19 as revealed in the anamnesis that could be taken in the postoperative period. In the thoracic CT images, there were no findings in favor of COVID-19. Favipiravir (2x1600mg, 2x400 mg-4 days) therapy was started, and the patient was transferred to the unit, where COVID-19 patients were followed up. No statistically significant difference was obtained in the comparison of the patient with a positive COVID-19 test with other patients in terms of drain termination, hospital stay, and additional complications. NP and OP swab samples for SARS-CoV-2 RT-PCR tests were obtained from the personnel involved in this patient's operation on the 5th and 7th postoperative days. The test results were reported as negative for all of the involved healthcare personnel.

Patients were followed up for COVID-19 in the postoperative period with daily chest radiography, follow-up of the body temperature, and symptom inquiries. In 3 patients (16.7%), thoracic CT was performed due to postoperative fever; however, no COVID-19-associated findings were observed in the thoracic CT images. The SARS-CoV-2 RT PCR tests on the OP and NP swabs taken from these patients were resulted as negative. The mean length of hospital stay was calculated as 11.8 days (SD±13.0), and the mean length of intensive care stay was 5.4 days (min-max: 1-58 days, SD±13.8). In the postoperative period, 2 patients (11.1%) died due to bacterial sepsis, and 1 patient (5.5%) died due to disseminated intravascular coagulation. 15 patients

(83.4%) were discharged without the development of any morbidity.

Discussion

The COVID-19 pandemic caused the postponement of many elective medical and surgical procedures. While continuing the treatment of COVID-19 patients, measures had to be taken to protect healthcare workers and non-COVID-19 patients treated for other reasons in hospitals. In many countries, hospitals are classified as pandemic and non-pandemic hospitals. In areas where the allocation of pandemic hospitals was not possible, isolation measures have been implemented in the hospital. In the early stages of the outbreak, a retrospective study reported that 41.3% of patients diagnosed with COVID-19 contracted the disease through in-hospital transmission (6). Concerning the density of COVID-19 patients in emergency departments, arrangements have been recommended to protect and treat non-COVID-19 patients and healthcare workers (7-9).

Major trauma patients requiring emergency interventions emerged as a difficult group to manage in this process. Traumatic hemothorax is one of the leading causes of emergencies of thoracic surgery. Traumatic hemothorax is associated with high mortality rates, but timely interventions can be lifesaving. Traumatic hemothorax has become more complex and critical as a condition requiring emergency interventions during the pandemic period, parallel to protecting healthcare workers from this highly infectious infection. There is not an adequate number of papers about the management and outcomes of chest trauma patients who have severe intrathoracic bleeding and face such a life-threatening condition in the literature. Taking necessary preventive measures with the anticipation that each patient could be COVID-19 positive, we performed the necessary interventions on our patients unhesitatingly when emergency surgery was needed during the pandemic.

SARS-CoV-2 is transmitted through droplets when the individual is in close contact with an infected person and through the aerosol particles in the same indoor environment (10). Since SARS-CoV-2 has a limited incubation period and can be transmitted by asymptomatic patients, it is highly contagious. Therefore, it is necessary to treat trauma patients as suspected COVID-19 patients in order to protect both healthcare workers and patients (11). Patients should be evaluated by personnel wearing full PPE. Patients with stable hemodynamics and patients not receiving mechanical ventilation support should wear surgical masks. A HEPA filter should be used in the breathing circuit for patients who are mechanically ventilated. If possible, direct radiography should be taken in the room where the patient is. Patients in the present study were examined in the trauma room in the emergency department by healthcare workers wearing full PPE. The transport of the patients to imaging facilities and the operating room was performed by involving the minimum number of personnel. The SARS-CoV-2 transmission was not detected in the emergency room staff and the surgeons of the cases.

It is recommended that patients diagnosed with COVID-19 or who were suspected of having COVID-19 should undergo surgery in operating rooms equipped with negative pressure if possible (11-13). Medical supplies and equipment that may be required should be made available for use in the room in advance so that the door of the room should be kept closed throughout the procedure after the patient is admitted to the room (13). General anesthesia and endotracheal intubation are imperative procedures for major surgical procedures such as urgent thoracotomy. General anesthesia and endotracheal intubation are procedures that generate high rates of aerosol (12,14). The management of these procedures should be carried out by the fewest possible personnel wearing full PPE. The cases in our study were managed by a surgical team wearing full PPE. Entrances and exits to the operating room were restricted, and operations were performed with the minimum number of personnel. The door was kept closed during the operation.

Equipment not used in routine operations, such as N95 masks, goggles, face shields, and overalls, cause discomfort for the surgical team during procedures that will take at least two hours. Therefore, the surgeon can be distracted and try to end the operation in a short time (13). Sweating and an inability to retain clear vision due to fogging on the surfaces of goggles and face shields are the most common causes of discomfort for surgeons. As a result, some steps should be taken to combat the surgical team's propensity to not completely use PPE and to avoid premature procedure termination. Airtightness should be ensured around the nose to prevent the formation of fog on the surfaces of goggles. Anti-fog solutions should be applied to goggles and face shields. The ambient operating room temperature should be kept low to help the surgical teamwork comfortably while wearing full PPE. Previous studies have shown that some viruses can survive in surgical smoke (15). Therefore, it is recommended to use energy devices at low power levels, and the surgical smoke should be evacuated continuously. In the present study, the

aforementioned precautions were taken to prevent the fog formation, maintain the ambient room temperature, and evacuate the surgical smoke so that the surgical team would work comfortably during operations without compromising the use of complete PPE. The healthcare personnel involved in the operation of the patient, who was reported to have a positive nucleic acid test result in the postoperative period, were followed up and underwent the SARS-CoV-2 RT-PCR test on NP-OP swabs on the 5th and 7th days after the operation of the patient. No transmission of SARS-CoV-2 was seen in any personnel.

Tube thoracostomy with closed underwater drainage is one of the thoracic surgery procedures that should be adjusted to the conditions of the pandemic. Via the closed underwater drainage, the air in the thorax is moved to the indoor environment, mixing with the air in the room. Implementation of various procedures has been recommended to prevent aerosol dispersion into the room air (16,17). The most widely used steps are to apply sodium hypochlorite to the bottle fluid and to install a HEPA filter in the bottle's draining tube. In order to prevent the aerosol generation, a HEPA filter was added to the draining channel of the drainage bottles of the study patients.

Extubation of the patient after the operation is a procedure that causes intense aerosol generation. Patients should be extubated by personnel wearing full PPE. In order to prevent the aerosol spread during the transport of the patients, our study patients were extubated after they were transferred to an intensive care room equipped with negative aspiration. In ICU, the provision of treatment and patient visits were performed by personnel wearing full PPE.

A second NP-OP swab sample was taken from each patient at the 48th hour after surgery, and the SARS-CoV-2 RT-PCR test was performed. The test results were negative in all patients except one. The patient, whose test result was positive, was transferred to the COVID-19 inpatient unit and was discharged on the 10th postoperative day without any complications. Thanks to the precautions taken, no transmission of SARS-CoV-2 occurred in the ICU staff and thoracic surgery personnel involved in the provision of treatment and care to the patient.

Conclusion

Wearing full PPE and compliance with isolation measures in the emergency department, operating rooms, ICU, inpatient units, imaging facilities, transport activities, and disinfection procedures significantly reduce the risk of SARS-CoV-2 transmission. Urgent thoracotomy, which is one of the leading non-elective surgical interventions that cannot be postponed due to the conditions of the COVID-19 pandemic, can be performed safely and successfully if sufficient precautions are taken. Until proven otherwise, trauma patients should be considered suspected COVID-19 cases. At the same time, trauma patients should be protected from SARS-CoV-2 transmission during treatment and follow-up.

Limitations

The retrospective nature of the research, the small number of cases included, and only one positive SARS-CoV-2 RT-PCR test result in the postoperative period appear to be limiting factors in completely reflecting the interventions' real protective efficacy as mentioned earlier. There is a need for large-scale prospective studies about surgical procedures performed on patients diagnosed with COVID-19.

Ethics Committee Approval: The study was approved by the decision of Ordu University Clinical Research Ethics Committee dated 03/06/2021 with the decision number 128.

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Validity and Reliability of the Turkish Version of the Family Empowerment Scale for Caregivers of Adults with Mental Health Issues (FES-AMT)

Hatice Durmaz [1](ID), Esra Yildiz [2](ID)

[1]Department of Pysciatric Nursing, Ataturk University Faculty of Nursing, Erzurum, Turkey
[2]Department of Public Health Nursing, Ataturk University Faculty of Nursing, Erzurum, Turkey

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Abstract

Objective: This study aimed to adapt the Family Empowerment Scale for family caregivers of adults with mental health issues to the Turkish context.

Methods: The study data is collected from 1 January 2019 to 15 April 2020. The FES was originally developed by Koren et al.and, Kageyama et al. adapted it to assess the empowerment of family caregivers of adults with mental health issues, and they tested its validity and reliability. The study sample comprised 223 caregivers whose families of patients staying at the psychiatry clinic of a research and training hospital and those who had applied to the polyclinic. The scale has 34 items rated on a 5-point Likert-type scale. The scoring was subjected to a two-phase cluster analysis to obtain detailed information about the caregiver's empowerment.

Results: Confirmatory factor analysis was applied to examine the goodness of fit and construct validity of the structure, which was determined to consist of 3 factors by explanatory factor analysis. Factor loading range from 0.722 (item 20) to 0.008 (item 22). Exploratory factor analysis was conducted. Kaiser - Meyer - Olkin sampling adequacy value was determined as 0.894. The Cronbach's alpha coefficient of internal consistency was .908. The scale has three subscales: Family, Service System, and Community/Political. The total variance explained by the scale was 47.78%. The Cronbach's alpha coefficient for the whole scale was .927.

Conclusion: The Turkish version of the Family Empowerment Scale for caregivers of adults with mental health issues (FES-AMT) is a valid and reliable measurement tool. This scale can be used to evaluate patient relatives in the clinical practice of nurses.

Key words: Family, Empowerment, Turkish, Validity

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Address for correspondence/reprints:

Hatice Durmaz

Telephone number: +90 (530) 921 85 27

E-mail: haticedurmaz_25@hotmail.com

Introduction

Research emphasizing the difficulties experienced by primary caregivers of individuals with chronic diseases has increased (1). Family empowerment is gaining importance, especially in situations that cause disability (2). Empowerment is an important concept for the status of parents within health care services (1) because family empowerment has been shown to

have a positive effect on different patient populations in various cultures (1, 3-5) Researchers have used various approaches and measurement tools to assess family empowerment (6). In cases of psychiatric disorders, family caregiver empowerment is a significant factor in coping with the nature of the disease. Family empowerment in social, political, and service-related matters can facilitate the work of caregivers (7, 8).

Additionally, the empowerment of family caregivers has emerged as a new objective of family interventions. This includes disease management required for patient care as well as finding social roles through interaction with other family caregivers and participating in advocacy (7). The 34-item Family Empowerment Scale (FES) was developed by Koren, DeChillo, and Friesen in 1992 to measure empowerment among the parents of children with emotional disability. The reliability and validity of this scale have been verified in various languages and cultures (7-10). The FES has been used and validated in various populations, including children with diabetes (1, 9). Kageyama et al. (7) developed a Japanese version of the FES for family caregivers of adult patients with mental disorders and verified its validity and reliability (7). Due to the nature of psychiatric patients' illnesses, strong caregivers are essential for care. In some cases, the caregiver needs to make a decision instead of the patient. In order to use this authority, the caregiver must be strong. Therefore, there is a need for a measurement tool to evaluate the strengths of caregivers, especially of psychiatric patients.

No studies have assessed the empowerment of family caregivers in the Turkish context. Thus, this study aimed to adapt the FES for caregivers of adults with mental health issues to the Turkish context and verify its validity and reliability.

Methods

This methodological study was conducted to adapt the FES for caregivers of adults with mental health issues to the Turkish context and test its validity and reliability. The study was conducted in three stages: 1) translation of the scale into Turkish and back-translation into English, 2) assessment of the content validity of the scale by a group of experts, and 3) psychometric analyses (factor analysis and calculation of Cronbach's alpha, validity coefficient, and fit indices).

Erzurum is located east of Turkey. The hospital where the research was conducted provides services to patients in both the rural areas and the city center of 11 cities located around Erzurum. It is close to the Iranian border. The city has an average population of 762,000. The study sample comprised the families of patients staying at the psychiatry clinic of a research and training hospital and those who had applied to the polyclinic. To adapt a scale to another culture, the sample should be at least 5 to 10 times larger than the number of scale items. Therefore, this study was carried out with 223 caregivers. The study data were collected from 1 January 2019 to 15 April 2020, after obtaining approval from the ethics committee of the local and official ethics committee.

The study included caregivers of patients diagnosed with a psychiatric disorder who had no problem communicating. Data were collected using the Turkish version of the Family Empowerment Scale for Caregivers of Adults with Mental Health Issues through face-to-face interviews.

Data collection tools

Data were collected through face to face using the Turkish version of the FES for caregivers of adults with mental health issues. The authors obtained permission from Kageyama, Koren, DeChillo, and Friesen to develop a Turkish version of their scale.

Evaluation of data

Data were analyzed using SPSS and AMOS software. The study used exploratory factor analysis to test the structural validity and confirmatory factor analysis to test the accuracy of the factor structure. Fit indices and Cronbach's alpha coefficients were calculated.

FES for caregivers of adults with mental health issues

The FES was originally developed by Koren et al. (2) to assess the empowerment of parents of children with mental health issues (2). Kageyama et al. (6) adapted it to the Japanese context to assess the empowerment of family caregivers of adults with mental health issues, and they tested its validity and reliability (7). They changed "child" to "the person," "children" to "people with disorders," and "parent" to "family" (referring to the family caregiver). In addition, "grow and develop" was changed to "recovery" (items 4 and 27), and "special education laws" was revised to "the law related to the disorders" (item 24). However, the dimensions of the Japanese version are the same as those of the original scale. The FES divides empowerment into two dimensions. The first refers to the levels of empowerment: service system and community/political. The second refers to how empowerment is expressed in the form of attitudes and knowledge.

Each item is scored on a Likert-type scale from 1 (not true at all) to 5 (very true). The FES assesses empowerment based on three subscales: Family (12 items), Service System (12 items), and Community/Political (10 items). See Table 1

Table 1. Dimensions of the Family Empowerment Scale

		Level		
		Family	*Service System*	*Community/Political*
Expression	*Attitudes*	4, 9, 21, 34	1, 18, 32	3, 17, 25
	Knowledge	7, 16, 26, 33	5, 11, 12, 23, 30	10, 14, 22, 24
	Behaviors	2, 27, 29, 31	6, 13, 19, 28	8, 15, 20

The Family subscale assesses parents' management of everyday matters in the home. Service System refers to the professionals and institutions providing services to the patient; this subscale primarily concerns parents collaborating with the service system to provide sufficient care for their children. The Community/Political subscale refers to legislative bodies, policymakers, agencies, and community members; it primarily concerns caregivers' advocacy for the relevant population.

The mean score of each subscale is calculated by summing the scores for each item and dividing the total score by the number of questions. Although all subscale scores can be added to obtain a total score ranging from 3 to 15, it is recommended that each subscale score be used since they measure different areas.

The language validity of the scale was examined, and the scale was then translated into Turkish and reviewed by eight health professionals who speak English as a second language. The content validity index was calculated as 0.80.

Statistical analysis

Data were analyzed using SPSS and AMOS software. The study used exploratory factor analysis to test the structural validity and confirmatory factor analysis to test the accuracy of the factor structure. Fit indices and Cronbach's alpha coefficients were calculated.

Results

Participants' sociodemographic characteristics

The study was conducted with 223 participants. Their mean age was 39.70 ± 11.42. Ninety participants (52.5%) were male, 76 (34.1%) were bachelor graduates, 170 (76.2) were married and 125 (56.1%) had a job. Participants are spouses, siblings or parents of people with mental illness.

Factor analysis

Exploratory factor analysis was conducted. Kaiser - Meyer - Olkin sampling adequacy value was determined as 0.894. As Bartlett's significance test level is $p < 0.05$ and the KMO coefficient approaches are 1, the sample should be considered sufficient. The scale was weighted in three subscales and explained 47.78% of the total variance.

We did rotated component matrix (Table 2). Varimax rotation was used to determine the factors that scale items weighted.

Table 2. Factor loading of the Turkish version of the Family Empowerment Scale for caregivers of adults with mental health issues

		Items	Item Factor Loading		
Family	*Attitudes*	R4	**.599**	-.037	-.313
	Attitudes	R9	**.350**	-.042	.299
	Attitudes	R21	**.617**	.017	-.005
	Attitudes	R34	**.416**	.168	.041
	Knowledge	R7	**.552**	.240	.317
	Knowledge	R16	**.323**	.175	.526
	Knowledge	R26	**.115**	.144	.422
	Knowledge	R33	**.217**	.553	.298
	Behaviors	R2	**.534**	.274	-.008
	Behaviors	R27	**.581**	.240	.350
	Behaviors	R31	**.553**	-.099	.417
	Behaviors	R29	**.125**	.072	.605
Community/Political	*Attitudes*	R17	.160	**.706**	-.023
	Attitudes	R3	.534	**.274**	-.008
	Attitudes	R25	.199	**.695**	-.126
	Knowledge	R10	.672	**.426**	.080
	Knowledge	R24	.828	**.043**	.073
	Knowledge	R14	.633	**.328**	.144
	Knowledge	R22	.675	**.008**	.319
	Behaviors	**R8**	**.461**	**-.098**	**.163**
	Behaviors	R15	.133	**.530**	.294
	Behaviors	R20	.318	**.722**	-.093
Service System	*Attitudes*	R32	.031	.637	**.117**
	Attitudes	R1	.029	.079	**.445**
	Attitudes	R18	-.089	.741	**.175**
	Knowledge	R23	.770	.262	**.035**
	Knowledge	R12	.658	-.103	**.349**
	Knowledge	R11	.373	.451	**.353**
	Knowledge	R5	.694	.192	**.301**
	Knowledge	R30	.712	.375	**.031**
	Behaviors	R6	.001	-.101	**.755**
	Behaviors	R19	.204	.742	**.122**
	Behaviors	R28	.338	-.013	**.598**
	Behaviors	R13	.620	-.329	**.451**

Factor loads are between -0.098 and 0.722. All items other than items 8 was positively weighted in the same subscales as in the original scale. Item 8 of the Community/Political subscale were negatively weighted. These three items were positively weighted in the family subscale. Factor loading range from 0.722 (item 20) to 0.008 (item 22) (Table 3).

Table 3. Fit indices of the Turkish version of the Family Empowerment Scale for caregivers of adults with mental health issues

Acceptable Fit Indices	Measured Fit Indices
$\chi 2/sd < 5$	3,745
GFI >0.90	0.936
AGFI >0.90	0.910
CFI >0.90	0.912
TLI>0.90	0.931
RMSEA <0.08	0.077

Confirmatory Factor Analysis is an extension of explanatory factor analysis that evaluates the underlying structure of the data. Exploratory Factor Analysis tries to provide a determination function, to obtain information for establishing a hypothesis. Confirmatory Factor Analysis is used to test whether there is a sufficient relationship between these determined factors. In addition, Confirmatory Factor Analysis is used to test which variables are related to which factors, whether the factors are independent from each other, and whether the factors are sufficient to explain the model. Confirmatory factor analysis was applied to examine the goodness of fit and construct validity of the structure, which was determined to consist of 3 factors by explanatory factor analysis. Fit index analyses showed that the model was compatible with the data, as $\chi 2/df$ was lower than 5, indicating a good model fit. The goodness-of-fit index and Tucker-Lewis index were above 0.90, the adjusted goodness-of-fit index was above 0.85, and the root mean square error of approximation was below 0.08, indicating an acceptable model fit.

Reliability

The Cronbach's alpha coefficients were 0.736 for the Family subscale, 0.905 for the Service System subscale, and 0.773 for the Community/Political subscale. The Cronbach's alpha coefficient for the whole scale was 0.927 Cronbach alpha values above 0.70 value. These values indicate a good level of reliability.

Discussion

This study aimed to determine the validity and reliability of the Turkish version of the FES for family caregivers of adults with mental health issues (FES-AMT).

Factor analysis was conducted to search for correlations between the variables. The result of Bartlett's test was significant, indicating that the variables were correlated. The data had multiple normal distributions. The KMO value was above 0.80, which is excellent for a sample of this size (11).

In this study, we found that many items were not weighted at the required subscale. Items 8, 22 and 24 were the lowest-weight items. However, we found that items other than item 8 were not weighted negatively. For this reason, we did not remove items from the scale. The scale items 8, 22, and 24 were weighted differently compared to the original scale. Kageyama et al. (7) found that the weighting of these items differed on community-political subscale in the original scale (7). Koren et al. (2) found that items 22 and 24 were weighted higher than .40 on service system and community-political subscales of the original scale (2). Items 8 and 22 featured the word "legislator." Koren et al. (2) stated that these items are relevant to parents who can contact legislators and make a legal complaint. However, Kageyama et al. (7) cautioned that the Japanese may have difficulty understanding these two items because they are unlikely to encounter legislators (7). The results of the present study show similarities between the Turkish and Japanese contexts. Like the Japanese, Turkish people rarely have the opportunity to meet legislators. Items 8, 22, and 24 were modified in studies conducted with the parents of child patients (1, 4). These items should also be modified for validity and reliability studies among family caregivers of adult patients. Item 24 involves knowing the rights of people and families who are subject to laws on disorders. This result showed that Turkish people may be not aware of their rights. And item 26 has lower factor loading. It involves being able to ask for help from others when assistance with family problems is needed. Turkish people cannot ask for help from others when it comes to mental illnesses. These findings showed that up to us who care nurses in psychiatric nursing in Turkey demonstrates the need for more strength in the policy areas of the patients' relatives. Nurses can increase the effectiveness of their interventions by knowing the areas where their relatives need to be strengthened. These results, obtained in Turkey reveals similarities to Japanese and American culture. These similarities in societies also present the commonness of

international problems to nurses in evaluating patient relatives. These problems can also provide a source of data for intercultural nursing.

Also, Segers et. all. (1) In the validity and reliability study of the scale in the Netherlands, they found that there were differences in understanding in the translation of the items in our scale into a new language. For example, they described the term service system in item 23 as incomprehensible (1). This finding; suggested that this may be the reason for the low factor loadings of some items in our study. According to Zolmajd et al. (8) found that the factor loads of similar items of the scale were low. Similar to the results of this study, the factor load of the items is below .30. This finding may suggest that the Persian culture and the region where this study was conducted show similarities (8).

In fact, since the sub-dimensions of the items of the scale were predetermined, we focused on the fit index data for validity. We can say that the scale has validity because the fit index data are acceptable. According to the fit indices from the confirmatory factor analysis, the scale has a good level of validity. Therefore, it can be concluded that the Turkish version of the FES is a valid measurement tool.

The fact that the $\chi 2$ / sd value is below 5 indicates that the data obtained and the model fit are acceptable. The GFI value that obtained in this study is a good fit value. This value is a measure of the amount of variance and covariance that can be explained by the model. AGFI is a criterion sensitive to the sample volume. The AGFI value that obtained indicates perfect fit. The CFI value shows the mismatch between the data and the hypothetical model. The CFI value that obtained from this study is a good fit value. The TLI value and RMSA values also show a good fit (12).

The Cronbach's alpha coefficients were calculated to test the reliability of the scale. The Cronbach's alpha coefficients for the whole scale and the three subscales were above .70, similar to the results of Kageyama et al. (7). This indicates that the Turkish version of the scale is a reliable measurement tool (7). The high reliability of the scale indicates that this scale can be used by psychiatric nurses to evaluate caregivers

Implications for caregiving

• Empowerment of families that care for adults with mental health problems has increased interest in among mental health nurses in Turkey. Even this interest has even turned into a purpose for planned interventions for families.

• The scale is suitable for all families that have adults with mental health problems with inpatient or outpatient treatment.

• It is easy to apply, understandable and purposeful.

• The scale offers tips to families for reducing of caregiving burdenLimitations and future researches

Conclusion

The Turkish version of the FES for family caregivers of adults with mental health issues is a valid and reliable measurement tool. Further research could also verify the validity and reliability of the scale for the family caregivers of children.

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Evaluation of the Perception and Management of the Terminal Process by Nurses in Terminal Patients

Guler Eraslan Doganay[1(ID)], Mustafa Ozgur Cirik[1(ID)]

[1]Department of Anesthesiology and Reanimation, Ministry of Health University Atatürk Chest Diseases and Thoracic Surgery Training and Research Hospital, Ankara, Turkey

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Abstract

Objective: It is important that nurses can perceive and control their feelings about the disease, life, death and loss in order to perform the 'good death' process in terminal patients and to provide better care to patients. In this study, we aimed to evaluate the perception of the terminal process by the nurses and how they manage this process.

Methods: The study was conducted at Ataturk Chest Diseases and Thoracic Surgery Training and Research Hospital with the ethical approval numbered 05.03.2020/665. Nurses who currently work or who have worked before in intensive care or palliative service were asked to answer the questionnaire "Perception and Management of the Terminal Process by Nurses". The answers were evaluated and interpreted statistically.

Results: The total number of volunteer nurses participating in the study was 55. The mean age of the nurses was 30.05±6.4, of which 21.8% were male and 78.2% were female. 30.9% had more than 10 years of professional experience.

The participants (89.1%) thought that care for the terminal stage patient was a right and comfort-peace, but they were reluctant to provide care due to sadness. They are reluctant to communicate with patients and their relatives in the terminal process and they often directed the patient and their relatives to talk to the doctor.

Conclusion: Nurses are reluctant to care and avoid communicating with the patient and their families. Therefore, terminal process, patient communication and emotion management awareness should be increased with in-service training. The terminal process should be ensured to be better manageable for auxiliary medical personnel. Patients waiting to die should be ensured to have the good death they deserve.

Key words: Terminal Stage, Death, Palliative, Nurse

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Address for correspondence/reprints:

Guler Eraslan Doganay

Telephone number: +90 (533) 218 27 47

E-mail: gulerdoganay@hotmail.com.tr

Introduction

The terminal period is when death occurs within weeks, due to diseases or advancing age. Patients or their relatives, who cannot manage this period at home due to pain or difficulty in care, prefer hospitals. Therefore, many terminal stage patients spend this period in the intensive care or palliative service. In order for nurses to provide better care to these patients, they should know what the physical and psychological needs of the patients are and accept the death event. In order to fully assist a dying patient and his family, the nurse must first recognize her own feelings (1,2).

Natural death is accepted as a "good death", where the privacy of the person is respected, pain and other symptoms can be kept under control, emotional, spiritual, and religious needs are met, and there is time to say goodbye to loved ones. In the terminal period, patients' expectations are to eliminate their current complaints, especially pain, improve their quality of life, and spend their remaining time with their loved ones. A terminally ill patient experiences mixed emotions after learning that he or she will die. The psychological care of the dying patient is as important as the physical care (3). In patients with fear of death, the level of anxiety increases, changes in attitudes and behaviors may develop and it becomes difficult to adapt to the environment (4).

In the terminal period, nursing care and management consist of managing the patient's anxiety, fear of death, depressive mood, trying to reduce the patient's symptoms such as pain by complying with the treatment, increasing the quality of life and strengthening the patient's hope as much as possible (5). Studies show that nurses are afraid of death and facing the terminally ill patients and they prefer to work in wards where there are no terminally ill patients (1,2). Nurses are the health professionals who spend the most time with the patient for the realization of the 'good death' process in terminal patients. Nurses' ability to perceive and control their own feelings about illness, life, death and loss will be effective in providing better care to patients.

The aim of this study is to evaluate how the terminal process is perceived by nurses, how they manage this process, and to determine the perceptions and concerns of nurses in the terminal process.

Methods

The study was performed at Atatürk Chest Diseases and Thoracic Surgery Training and Research Hospital, with the ethical approval numbered 05.03.2020/665.

The study is a face-to-face volunteer-based survey study and all nurses who worked or currently working in the intensive care and palliative service were invited for the survey, only two of them did not participate in the survey because they did not volunteer and were excluded from the study. A total of 55 nurses participated in the survey. Nurses participating in the survey were asked face-to-face to choose one of the multiple choice answers for 19 questions in the "Questionnaire of Nurses' Perception and Management of the Terminal Process in Terminal Patients". The answers were interpreted statistically.

The criteria for participation in the questionnaire were volunteering and having previously worked or currently working in the intensive care or palliative service.

The exclusion criteria are, those who work in the intensive care or palliative service and did not volunteer to participate in the survey.

Statistical analysis

Statistical analyzes were evaluated with the SPSS 22.0 (Statistical Program Social Sciences) package program.

In the evaluation of data, frequencies and percentages were given for qualitative data. Kolmogrow Smirrov test was used to determine the normal distribution of quantitative data. For quantitative data, mean and standard deviation values were given from descriptive statistical methods, and for qualitative data, their frequency and percentage (%) were given.

Results

The total number of volunteer nurses participating in the study was 55. Only two nurses were excluded because they did not volunteer to participate in the survey.

The mean age of the interviewers was 27.7, and 21.8% were male and 78.2% were female. 23.6% of them are in the first year of their professional life. 45.5% have 2-10 years of experience and 30.9% have more than 10 years of professional experience. The units in which the interviewers worked at the time they answered the questionnaire; 14.5% were in the service, 16.4% were in palliative care and 69.1% were in intensive care. According to the working years of the interviewers in the unit where they worked, 3 people had been working in the same unit for 7 years and 49 participants for 1-2 years . 54.5% of the nurses participating in the survey were married and 47.3% had children (Table 1).

Table 1. Distribution of Demographic Characteristics of Participants

		n	(%)
Age, $\bar{x}$ ± SS (Min-Max)		30.05 ± 6.40 (21-45)	
Gender	Female	43	(78.2)
	Male	12	(21.8)
Education Status	High School	9	(16.4)
	College	18	(32.7)
	University	28	(50.9)
Working year in the profession	0-1 year	13	(23.6)
	2-10 years	25	(45.5)
	More than 10 years	17	(30.9)
Department	Service	8	(14.5)
	Palliative care	9	(16.4)
	Intensive care	38	(69.1)
Working year in current department	1 year	20	(36.4)
	2 years	29	(52.7)
	3 years	3	(5.5)
	7 years	3	(5.5)
Marital Status	Married	30	(54.5)
	Single	25	(45.5)
Status of having children	Yes	26	(47.3)
	No	29	(52.7)

81.5% of the nurses were involved in the death process of any of their relatives. 40.6% of them had experienced the death process of their first degree relative (spouse, mother-father-child-sibling), 34.5% of them had experienced the death process of a family's elder such as grandparents. 85.4% of them stated that they were very sorry for the loss they experienced (Table 2).

The 52.7% of nurses received terminal patient care training. The answers given by the nurses to the questions about terminal patient perception and management were evaluated and the following results have emerged (Table 3).

To the question "How do you treat a patient who's worried about death?", 58.2% do not want to take responsibility by directing the patient to a doctor or psychologist. 27.3% of them believe that they can manage the process of death.

58.1% of the nurses think that the patient in the terminal process should not be forced for treatment and nutrition, and even that the treatment is torture for the patient. 52.7% of nurses said they were reluctant to treat terminally ill patients because they were worried that the treatment was causing pain to the patient, and 21.6% of them thought that the treatment increased the hope of the relatives of the patients.

Table 2. Distribution of Participants' Thoughts About Death and Their Situations of Encountering Death

		n	(%)
11. What do you think about death?	The last process of a person's life, extinction	24	(43.6)
	The beginning of another life	30	(54.5)
	We don't have enough information about death yet.	1	(1.8)
12. Have you ever lost a loved one or someone close to you?	Yes	44	(81.5)
	No	11	(18.5)
12a. If you lost. what was the degree of closeness of your lost relative with you?	First-degree relatives such as parents, children, siblings	16	(29.7)
	Spouse	6	(10.9)
	Family elders like grandparents	19	(34.5)
	Second degree relatives such as uncle and aunt	9	(16.4)
	Friend	1	(1.8)
12b. How did you handle the loss?	I thought of my own death, I got scared.	3	(6.3)
	I was very sad and cried because I couldn't see him/her.	41	(85.4)
	I was worried for her, I felt anxiety that I couldn't help her anymore.	4	(8.3)

For the care of the patient in the terminal process, the vast majority of nurses (89.1%) believe that care for the patient is a right and comfort-peace. However, the majority (85.4%) stated that they were aware that their efforts would not change the result and that they were reluctant to give care due to sadness and weariness.

Only 5.5% are emotionally affected by the loss of their patient in the terminal process. 94.5% evaluate the process as normal and think that it is a positive outcome for the patient.

The 43.4% of participants are reluctant to communicate with patients and their relatives in the terminal process. 55.6% stated that they directed patients and their relatives to talk to the doctor.

Table 3. Distribution of Participants' Approach to The Terminal Patient

		n	(%)
9. Have you ever had a relative who couldn't meet the personal needs you had to look after?	Yes	13	(23.6)
	No	42	(76.4)
10. Have you received training on terminal period patient care?	Yes	29	(52.7)
	No	26	(47.3)
13. What is your attitude towards the terminal patient who is worried?	I ask him to talk to his doctor or psychologist about such issues related to his concerns.	32	(58.2)
	I'll tell him it's nothing, he'll get better, it's just a process..	7	(12.7)
	I'll tell him to accept that he's going to die anyway, that fear and anxiety won't help anymore.	1	(1.8)
	I have received the necessary training regarding the circumstances of death and I believe I can give the full support necessary to the patients and their relatives.	15	(27.3)
14. What is your approach to the treatment of the terminal patient?	If I think that the treatment does not help, I think that the treatment is torture for the patient.	24	(43.6)
	I think all treatment should be continued until the moment of death	21	(38.2)
	I think that interventions and drugs for treatment are unnecessary and that their nutrition is enough.	2	(3.6)
	I think that the patient should not be forced either in terms of treatment or nutrition.	8	(14.5)
15. What challenges you most when treating a terminal patient?	I think the patient is in pain, I'm worried about hurting him/her.	29	(52.7)
	I'm concerned that the patient's relatives won't accept the patient's condition.	12	(21.8)
	I don't have a hard time in this proces and I keep my job routine.	14	(25.4)
16. How do you feel when you witness the death of your patient?	I take it natural and think it's a fact of life.	38	(69.1)
	I think his/her pain is over.	13	(23.6)
	I cry and/or I get very sad	3	(5.5)
	I get scared	-	
	I'm not emotionally affected, I do my job.	3	(5.5)
17. What are your reasons for wanting to care for your terminal patient?	The dying patient has the right to receive quality care and it is the duty of the nurse to provide care	24	(43.6)
	Ensuring the patient's relaxation and peace of mind	25	(45.5)
	Thinking that death is a natural process	8	(14.5)
18. What are your reasons for not wanting to care for your terminal patient?	Causing a feeling of helplessness and sadness	16	(29.1)
	The process is exhausting and tiring	10	(18.2)

Discussion

This survey study showed that; although nurses see care as a right, peace and service for the patient in the terminal process, they are reluctant to give care due to pain and inability to change the outcome. Although they are involved in the terminal process, they also avoid communicating with patients and their families. The good death process, which is the natural right of the terminal ill patients, can be realized by the understanding and management of terminal process by the nurses. The increase of anxiety of nurses working with the terminal ill patient, will negatively affect the care they will give. Understanding their feelings about death first will be useful for nurses to manage the process (1,6). Terminal process management is an issue that must be supported by in-service training.

For health professionals, the situation of individuals who have experienced loss and it's important to understand their feelings. Reactions to death significantly affected by their physical, emotional and social experiences (7,8).

Stehle reported that; Holschach defined mental stres in nurses as the inability to recover from the disease, the fear of losing the patient (9).

Our study shows that nurses cannot work in the same unit for a long time due to the fact that they get more tired and wear out spiritually in the special units. In Unsal's study, it was found that as the working year increased, anxiety decreased (10). Although anxiety decreases with experience, we think that working in specialized units for many years causes fatigue and burnout.

In our study approximetly half of nurses do not want to take responsibility, they are reluctant to communicate with patients and their relatives and directing the patient to a doctor. We believe that this rate is insufficient for auxiliary medical staff working in specialized units. Because these units are where terminal process patients receive intensive treatment and care.

“Good death” which can also be defined as receiving treatment to reduce symptoms in patients in the terminal process, reducing invasive procedures, maintaining effective communication with their relatives and being able to say goodbye to the patient's relatives, receiving peaceful and good care in a safe environment, is the fundamental right of every patient (11). In this process, it is extremely important for the nurses, who spend the most time with the patient, to actively participate in the process and to manage the care and process by including the family (12).

The nurses, 50% of participating in the survey received training on the terminal process. Although 85% of them have experienced the death process of any of their relatives, they see "death" as a difficult process. Nurses who do emotional labor in addition to their job responsibilities tend to stay away from the process, patients and their relatives.

Nurses state that they do not know what to say to patients and their relatives during the death process. An article states that the most appropriate approach to death may be to say, "I don't know what to say, but I want to be with you" (13).

Our study showed that the nurses working in the special units of the hospital abstained and had difficulties in managing the terminal process. According to Hurtig WA (14), nurses avoid facing death and communicating with dying patients and their families, despite working with dying patients.

Behaviors expected from nurses such as "continuous communication", "being the person to be reached at all times", "giving patients the feeling that they are safe", "constantly trying to be friendly", "empathizing" and "giving service without expecting anything in return" also cause burnout. In this respect, working continuity is difficult in specialized units. In our study, only 11% of the participants stated that they had worked in the same unit for more than 2 years.

In order to provide the necessary support to the dying patient and their relatives, it is important for the nurse to know her own feelings about death and to determine her attitudes towards death before completing the education process (4,15). In our study 50% of nurses participating in the survey received training on the terminal process. We agree with this conclusion that nursing education programs are insufficient to prepare nurses for this process (16).

Managing and caring for the terminal patient requires many skills. Patient care becomes more difficult during this period, which does not benefit from treatment, whose general condition is getting worse, symptoms become difficult to control, difficult questions are asked by patients and their relatives, and emotional and spiritual requirements increase. However, the death of a patient is also a difficult process for the nurse, and it is experienced as a loss. The reactions of the patient and his/her family also make it difficult for nurses. All these difficulties may negatively affect the terminal patient's receiving the care and treatment that he or she deserves (17).

The limitations of our study are that it is single-centred and only palliative service and intensive care nurses were included as a sample.

We could not create a control group because in our hospital, patients in the terminal process were followed only by intensive care and palliative service nurses, not by wards nurses. Another reason is the low number of participants.

We suggest survey studies to be conducted in larger sample groups before and after the training.

Conclusion

Although nurses see care as a right, peace and service for the patient in the terminal process, it has been observed that they refrain from giving care due to pain and inability to change the result and avoid communicating with patients and their families.

Therefore, by organizing in-service training, the awareness of the death of nurses for the terminal process, patient communication and emotion management should be increased. It should be aimed both to ensure that the terminal process is manageable for them and to ensure that patients waiting for death get the good death they deserve.

Ethics Committee Approval: Ethics committee approval was received for this study from Research Ethics Committee of University of Health Sciences, Ataturk Chest Diseases and Thoracic Surgery Training and Research Hospital (approval date & number: 03/05/2020-665).
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Determination of Factors Related to Coronary Heart Diseases by Associative Classification Technique

Zeynep Kucukakcali[1](ID) Ipek Balikci Cicek[1](ID)

[1]Department of Biostatistics and Medical Informatics, Faculty of Medicine, Inonu University, Malatya,

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Abstract

Objective: The goal of this study is to categorize CHD using the relational classification approach on a CHD dataset made up of open access patients with and without CHD, as well as to disclose the disease's relationship to the risk factors that cause CHD.

Methods: The associative classification model was applied to the open-access data set "CHD" in this study. The performance of the model was evaluated by accuracy, specificity, negative predictive value. According to the results of the associative classification model, the factors associated with the disease were determined by specific rules. groups, examined using Mann-Whitney U, Pearson Chi-square test, and Fisher's Exact test. $p<0.05$ values were considered statistically significant.

Results: For the associative classification model applied to the data set, the results of the performance metrics that specificity, accuracy, and negative predictive value were calculated as 0.995, 0.852, 0.854, respectively.

Conclusion: The conclusions of this investigation revealed that the study conducted on the CHD data set with the associative classification model yielded successful results. Since the results obtained from the associative classification model reveal certain rules, it is very easy for users to understand and the results can be easily interpreted. Thus, the findings obtained with this model can be used quite easily in preventive medicine practices.

Key words: CHD, classification, association rules, associative classification.

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Address for correspondence/reprints:

İpek Balikci Cicek

Telephone number: +90 (422) 341 06 60-1337

E-mail: ipek.balikci@inonu.edu.tr

Introduction

In parallel with the developments in science, medicine, and technology in the world, life expectancy increases with the increase in the level of perception of disease/health. With the prolongation of life expectancy, the prevalence of chronic diseases is also increasing (1, 2). According to the 2008 data of the World Health Organization, 63% of deaths in the world are caused by chronic diseases. Among the causes of death due to chronic diseases, cardiovascular diseases (48%) take first place with the highest rate (3). Coronary heart diseases (CHD), which is among the cardiovascular diseases, is the most important cause of morbidity and mortality in the World (4). Coronary heart disease (CHD), which

is the most common cause of death due to cardiovascular diseases, is a progressive, systemic and inflammatory disease in which atherosclerosis plays a role in its etiology and can cause clinical events ranging from asymptomatic to acute myocardial infarction and sudden death. Often atherosclerotic plaques cause narrowing of the coronary artery (5). It presents as acute myocardial infarction or sudden cardiac death without symptoms in a significant part of the patients. Therefore, it is very important to know, prevent, and diagnose the risk factors of CHD (6).

Simply put, data mining is the process of finding usable information concealed in large amounts of data (7). With tools from several disciplines such as artificial intelligence, machine learning, statistics, and optimization, data mining allows researchers to make effective and well-informed conclusions. It also allows for the discovery of hidden, implicit, beneficial links, patterns, relations, or trends that would be difficult to uncover using traditional method (8).

Under the associative analysis model, which is one of the data mining models, there is an association rules model. Because of their simplicity and utility, association rules are commonly employed in data mining. Association rules are used while doing this analysis to express the occurrence of events along with their probabilities. The association rules' aim is to give relationships and associations as rules (9, 10) .

When developing a model, the associative classification uses the logic of merging the classification and association rule models, which are two data mining methodologies. Classification models are generated using the set of rules obtained from association rule analysis in associative classification. The response/target variable being on the right side of the obtained rule makes it easier to understand and interpret in the associative classification approach (11).

This study, it is aimed to classify CHD by applying the relational classification method on the CHD dataset consisting of open access patients with and without CHD, and to reveal the disease relationship with the risk factors that cause CHD.

Methods

Dataset

The associative classification model, a data mining method that combines classification and association rules methodologies, was used in the study to analyze an open-access data set called "CHD." The open-access data set "Cardiovascular Study Dataset" was obtained from the address https://www.kaggle.com/christofel04/cardiovascular-study-dataset-predict-heart-disea.

Association Rules

One of the data mining method is association rules, which use probabilistic expressions to explain the presence of certain occurrences in the database (12). Association rules that are unsupervised data mining methods are used to find hidden links in huge data sets. Potential data relationships can be defined by association rules. The goal is to uncover the rules that govern the occurrence of occurrences that are likely to occur at the same time. A series of operations are applied in bulk to the records in the databases, and the rules explaining the link between the records are derived using this method (13).

Associative Classification

Associative classification is a novel supervised learning approach that seeks to predict scenarios that haven't been encountered before. An associative classification, in particular, is a method for creating classification models that employs rules derived from association rules. Associative classification combines classification and association rule mining to can produce give more accurate results than other data mining classification techniques. Only the class/response / dependent variable categories make up the right side of association rules in associative classification. The rules of the association are derived using if-then clauses, which are precursor-successor clauses. Therefore, the user will have an easier time understanding and interpreting the results. As a result of this circumstance, associative classification is more advantageous than traditional classification methods (11).

Associative classification uses and develops a variety of algorithms. In this study, the classification based on the association rules (CBA) method was applied.

Statistical analysis

Quantitative data are summarized by median (minimum-maximum) and qualitative variables are given by number and percentage. Normal distribution was evaluated with the Kolmogorov-Smirnov test. In terms of input variables, the existence of a statistically significant difference and relationship between the categories of the output variable, " 10-year risk of coronary heart disease (yes) " and " 10 year risk of coronary heart disease (no) " groups, was examined using Mann-Whitney U,

Pearson Chi-square test, and Fisher's Exact test. $p<0.05$ values were considered statistically significant. In all analyzes, IBM SPSS Statistics 26.0 for the Windows package program was used.

Results

The table showing the distribution of the dependent variable in the data set used in this study is given below (Table 1).

Descriptive statistics of the independent variables in this study are given in Table 2. According to this table; There is a statistically significant difference between the groups of the dependent variable (TenYearCHD) in terms of age, tot Chol, sys BP, dia BP, BMI, glucose and cigs Per Day variables ($p<0.05$).

However, there was no statistically significant difference between the groups of the dependent variable (TenYearCHD) in terms of the heart Rate variable ($p>0.05$).

Table 3 shows that; there is a statistically significant relationship between the sex, education, is smoking, BP Meds, prevalent Stroke, prevalent Hyp and diabetes variables and the dependent variable (TenYearCHD) groups ($p<0.05$).

Table 4 shows the classification matrix for the associative classification model that was used to classify the Cardiovascular Work Dataset in this study

Table 1. Table showing the distribution of the dependent variable

No		Yes	
Count	Percentage (%)	Count	Percentage (%)
2879	84.9	511	15.1

Table 2. Descriptive statistics table of quantitative independent variables

Variables	TenYearCHD (have 10 year risk of coronary heart disease (CHD or not))		p-value*
	No	Yes	
	Median (min-max)	Median (min-max)	
Age	48 (32-70)	55 (35-70)	**<0.001**
Tot Chol	232 (113-696)	243 (107-600)	**<0.001**
Sys BP	127 (83.5-243)	139 (83.5-295)	**<0.001**
Dia BP	81 (50-142.5)	85 (48-135)	**<0.001**
BMI	25.23 (16.48-51.28)	26.19 (15.96-56.8)	**<0.001**
Glucose	78 (40-386)	80 (45-394)	**0.001**
Cigs Per Day	0 (0-70)	4 (0-60)	**0.001**
Heart Rate	75 (45-143)	75 (50-120)	0.358

*: Mann Whitney U test

Table 3. Descriptive statistics for qualitative independent variables

Variables	Categories of Variables	TenYearCHD		p-value
		No	Yes	
		Number (%)	Number (%)	
Sex	Female	1684 (58.5)	239 (46.8)	**<0.001***
	Male	1195 (41.5)	272 (53.2)	
Education	1	1135 (40.5)	256 (51.4)	**<0.001***
	2	872 (31.1)	118 (23.7)	
	3	479 (17.1)	70 (14.1)	
	4	319 (11.4)	54 (10.8)	
is smoking	No smoke	1467 (51.0)	236 (46.2)	**0.047***
	Yes smoke	1412 (49.0)	275 (53.8)	
BP Meds	No Meds	2775 (97.6)	471 (93.5)	**<0.001***
	Yes Meds	67 (2.4)	33 (6.5)	
Prevalent Stroke	No stroke	2867 (99.6)	501 (98.0)	**0.001****
	Yes stroke	12 (0.4)	10 (2.0)	
Prevalent Hyp	No Hyp	2065 (71. 7)	256 (50.1)	**<0.001***
	Yes Hyp	814 (28.3)	255 (49.9)	
Diabetes	No diabetes	2825 (98.1)	478 (93.5)	**<0.001***
	Yes diabetes	54 (1.9)	33 (6.5)	

*: Pearson chi-square test, **: Fisher's Exact test

Table 4. The associative classification model's classification matrix

Prediction	Reference		
	No	Yes	Total
No	2471	421	2892
Yes	12	23	35
Total	2483	444	2927

Table 5 shows the results of the classification performance criterion for the associative classification model. The model's specificity was calculated to be 0.995, the accuracy to be 0.852, and the negative predictive value to be 0.854.

Table 5. The model's classification performance criteria's values

Metric	Value
Specificity	0.995
Accuracy	0.852
Negative predictive value	0.854

The classification algorithm's association rules are shown in Table 6. As expressed in Table 6, when age=[32,55.5), is smoking=no smoke, prevalent hyp=no hyp and glucose=[40,122) are considered, the probability of not having 10 year risk of coronary heart disease is 94.7%. Similarly, as age=[32,55.5), is smoking=no smoke, sys bp=[83.5,145) and BMI=[16,28.8) are taken into account, the probability of not having 10 year risk of coronary heart disease is 94.6%. In the same way, age=[32,55.5), is smoking=no smoke, tot chol=[113,256) and dia bp=[48,99.2) are regarded, the probability of not having 10 year risk of coronary heart disease is 94.6%. If age=[32,55.5), is smoking=no smoke, prevalent stroke=no stroke, prevalent hyp=no hyp are considered, the probability of not having 10 year risk of coronary heart disease is 94.6 %. Other rules derived from the classification based on association rules model can be interpreted in the same way as the previously described rules. (Table 6).

Table 6: The classification algorithm's association rules

Left-hand side rules	Right-hand side rules	Support	Confidence	Frequency
{Age=[32,55.5), is smoking=No smoke, Prevalent Hyp=No Hyp, Glucose=[40,122)}	{Tenyearchd=No}	0.224	0.947	657
{Age=[32,55.5), is smoking=No smoke, Sys Bp=[83.5,145), BMI=[16,28.8)}	{Tenyearchd=No}	0.205	0.946	599
{Age=[32,55.5), is smoking=No smoke, Tot Chol=[113,256), Dia Bp=[48,99.2)}	{Tenyearchd=No}	0.215	0.946	629
{Age=[32,55.5), is smoking=No smoke, Prevalent Stroke=No stroke, Prevalent Hyp=No Hyp}	{Tenyearchd=No}	0.225	0.946	660
{Age=[32,55.5), is smoking=No smoke, Prevalent Hyp=No Hyp, Diabetes=No diabetes}	{Tenyearchd=No}	0.224	0.945	656
{Age=[32,55.5), Sex=Female, Prevalent Hyp=No Hyp, Tot Chol=[113,256)}	{Tenyearchd=No}	0.231	0.943	675
{Age=[32,55.5), is smoking=No smoke, Bp Meds=No Meds, Sys Bp=[83.5,145)}	{Tenyearchd=No}	0.247	0.94	724
{Age=[32,55.5), is smoking=No smoke, Tot Chol=[113,256), Glucose=[40,122)}	{Tenyearchd=No}	0.228	0.94	668
{age=[32,55.5), Cigs Per Day=[0,17.5), Prevalent Hyp=No Hyp, Tot chol=[113,256)}	{Tenyearchd=No}	0.271	0.94	792

Discussion

Today, cardiovascular diseases are quite common and one of the leading causes of death. Although death from coronary heart disease, a cardiovascular disease in which atherosclerosis plays a role and can cause clinical events ranging from asymptomatic to acute myocardial infarction, has fallen significantly, it remains the single leading cause of death for adults worldwide. This evidence demonstrates the need to implement effective primary prevention approaches worldwide and to identify risk groups and potential areas of improvement, with the fact that mortality from CHD is expected to continue to rise in developing countries. For this reason, accurate and timely diagnosis of coronary heart disease is very important in terms of treatment and reducing mortality rates (14, 15). Therefore, it is very important to determine the factors associated with the disease.

Association rules are methods for analyzing the coexistence of events, and they are one of the descriptive models in data mining. These connections are based on the coexistence of data items and express the co-occurrence of occurrences as well as certain possibilities. One of the most basic approaches of machine learning is classification analysis, which is employed by a vast scientific community (16). Classification is a rule-based estimate procedure that

assigns each observation in a dataset to one of several specified classes. Associative classification combines two common data mining approaches, association rules, and classification methods, to provide categorization. In associative classification, association rules methods have been effectively employed to construct proper classifiers in recent years (17,18). Furthermore, when applied to medical data sets, associative classification stands out as a novel approach that makes it easier for users to interpret (19,20).

An open-access CHD data set was used in this work to test an associative classification model. In this context, the associative classification model was used to estimate distinct factors (explanatory variables) that may be connected with CHD (the dependent variable), and rules were established. According to the findings, the accuracy, specificity, and negative predictive value derived from the associative classification model were 85.20 %, 99.50%, and 85.40 %, respectively.

As a result, the associative classification model utilized in the study with the CHD data set yielded successful findings. Furthermore, this model has yielded specific disease-related criteria that might be applied in preventative medicine practices.

Ethics Committee Approval: This study does not require ethical approval because the open-source data set is used
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Perception of Individualized Care and Satisfaction with Nursing Care of Women Who Give Birth by Cesarean Section

Ezgi Yildiz [1](ID), Nilufer Tugut[2](ID)

[1]Department of Nursing, Sivas Cumhuriyet University Susehri School of Health, Sivas, Turkey,
[2]Department of Gynecology and Obstetrics Nursing, Sivas Cumhuriyet University Faculty of Health Sciences, Sivas, Turkey,

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Abstract

Objective: This descriptive cross-sectional study aims to determine the perception of individualized care and satisfaction with the nursing of women who underwent cesarean section.

Methods: The population of this study consists of women undergoing cesarean section in a university hospital between 15 August and 15 December 2018 (N=260). The sample consists of 156 women giving birth by cesarean section who have agreed to participate in this study. The data have been collected by using the Personal Information Form and the Individualized Care Scale (ICS) and the Newcastle Satisfaction with Nursing Scale (NSNS).

Results: It has been found that the women who gave birth by cesarean section have good ICSA (3.50±0.99), ICSB (3.82±1.18), and NSNS (70.53±16.27) mean scores. There is a significant, positive, and moderate relationship between the ICS and NSNS scores. It has been found that there is a statistically significant difference between the place of residence and the level of satisfaction with nursing. It has been determined that the women whose income is higher than their expenses are more satisfied with nursing care, and their individualized care perception is higher.

Conclusion: It has been determined that women who gave birth by cesarean section have a good level of individualized care perception and nursing satisfaction. It has been found that women's satisfaction with nursing increases.

Key words: Individualized care; satisfaction with nursing care; cesarean section

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Address for correspondence/reprints:

Ezgi Yildiz

Telephone number: +90 (543) 423 61 18

E-mail: ezgiyildiz58@hotmail.com

Introduction

Cesarean section, which is a surgical intervention, should be preferred in case a condition threatens the health of both the woman and the baby. In cesarean section, maternal mortality and morbidity rate is higher than it is in vaginal delivery. Cesarean delivery is increasing all over the world (1-3). According to the data released by Turkey's Ministry of Health and the Organization for Economic Cooperation and Development (OECD), Turkey takes the first place

among the countries in the world where cesarean section is performed most (4).

Regardless of the mode of delivery, the birth and postpartum period is the most sensitive period in a woman's life because in this period, the mother experiences intense physiological and psychological changes and possible health problems (5). Health problems are widespread in the postpartum period, especially in the first days, and most of these problems are likely to persist for up to six and eight weeks or even a year (6). The postpartum is a period when mother and baby need nursing care a lot. During this period, nurses, who are directly responsible for care, assume significant responsibilities in preventing problems observed in the mother and baby (7). Especially the risks of cesarean section on maternal and infant health make the individualized nursing care given to women who have undergone cesarean section more important, because it is only possible to talk about quality care when an individual's needs and desires are met. Individualized care is provided to improve the quality of care, to determine the direction of care, to establish clinical guidance, to create positive patient outcomes and to maximize all these.

The more an individual's personal characteristics, values, beliefs, and cultural characteristics are taken into account in the provision of care, the more the individuality of the care increases (8). Providing and maintaining individuality in the provision of care is possible as the problems determined are solved by evaluating all the dimensions of an individual, implementing interventions specific to the individual and allowing the patient to participate in care decisions. Individualized care, offered by taking into account characteristics unique to an individual, can yield positive results such as the improvement and functioning of personal health, quality care, autonomy, provision of satisfaction, improvement of the person's use of autonomy, and increase in the quality of life of individuals.

Individualized care is thought to be related to the patient's satisfaction with nursing care. Given the diversity of health problems after cesarean section, the wide variety of care and needs, and the wide variety of perspectives and expectations of women receiving health services, the importance of individualized care planned through cooperation between the patient and nurse, and of patient satisfaction comes to the fore (9). The basis of patient satisfaction is the cooperation between the patient and nurse (10).

Measurement of patient satisfaction related to nursing care plays an important role in determining the patient's needs, planning appropriate nursing interventions, evaluating the results and making changes in the provision of care according to their preferences (11,12). Providing nursing care in line with the needs of the mother and family until the postpartum period is over is very important for the healthy management of this process. Therefore, this study was conducted to determine how women who underwent cesarean section perceived individualized care and whether they were satisfied with the nursing care they were given.

Methods

Type and Place of the Study

This descriptive cross-sectional study was conducted in the obstetrics and gynecology service with a capacity of 31 beds where 11 nurses and 2 midwives worked. Each nurse looks after an average of 10-15 patients per shift.

Study Population and Sample

The population of the study consisted of women who were hospitalized in the gynecology and obstetrics service of a university hospital between August 15, 2018, and December 15, 2018 (N = 260). In the present study, no sampling method was implemented. Of the women in the study population, 156 who received inpatient care in this clinic between the aforementioned dates, who could answer questions independently when they were discharged from the hospital, who did not have psychiatric problems, and who volunteered to participate in the study constituted the study sample.

Measures

The following three forms were used to collect the study data: Personal Information Form, Individualized Care Scale (ICS) and Newcastle Satisfaction with Nursing Scale (NSNS).

Personal Information Form

The form prepared by the researchers based on the pertinent literature includes eight closed-ended questions on the patient's age, income level, education status, place of residence, health insurance, employment status, the number of hospitalizations, and the number of cesarean deliveries (1,13).

Individualized Care Scale (ICS)

The scale developed by Suhonen et al. to evaluate individualized care from the patients' point of view was adapted to Turkish by Acaroglu et al. (14,15). The ICS has two parts each containing 17 items: the ICS-A used to assess the patient's awareness of

nursing interventions, the ICS-B used to assess the patient's perception of individuality in the care given to her. The Cronbach's alpha coefficient of the ICS-A and ICS-B was determined as 0.92 and 0.93, respectively. Responses given to the items are rated on a 5-point Likert type scale ranging from 1 to 5. The scores of the ICS-A and ICS-B are calculated by summing the item scores obtained from their subscales and dividing them by the number of the items for each subscale separately. Therefore, the mean score for each subscale also varies between 1 and 5. The higher the score obtained from the ICS-A is the more individualized the nursing interventions provided for the individual are. Similarly, the higher the score obtained from the ICS-B is the higher the level of the patient's perception of individuality for the care given to her. In the present study, the Cronbach' alpha coefficient for the ICS-A and ICS-B was 0.94 and 0.95 respectively.

Newcastle Satisfaction with Nursing Scale (NSNS)

The NSNS developed by Thomas et al. to determine patients' satisfaction with nursing care was by Akin and Erdogan (11,16). The scale consists of 19 items whose responses are rated on a 5-point Likert-type scale ranging from 1 to 5 (Not at all satisfied = 1, Barely satisfied = 2, Quite satisfied = 3, very satisfied = 4, completely satisfied = 5). The minimum and maximum possible scores to be obtained from the scale are 19 and 95 respectively. The higher the total score obtained from the scale is the more satisfied the patient with the nursing care is. The Cronbach's alpha coefficient of the scale was 0.96 in Akin and Erdogan's study and 0.97 in the present study.

Implementation of the Study and Ethical Issues

To conduct the study, Ethics Committee approval from Cumhuriyet University Non-Interventional Clinical Research Ethics Committee, (Decision No: 2018-04 / 02) and written permission from the institution where the study was to be conducted were obtained. The patients who met the inclusion criteria and volunteered to participate in the study were informed about the study and then the Informed Consent Form was administered to them to obtain their consent to participate in the study. A suitable environment (quiet, calm, etc.) was established for patients whose discharge procedures were initiated. After they were given information on the data collection tools, the tools were administered to them and they were asked to fill in the forms, which took approximately 10 minutes.

Statistical analysis

The data obtained were analyzed using the SPSS 23.0 software program. In the analysis, the numeric data (women's education level, the number of cesarean deliveries, place of residence, etc.) were given as frequency distribution, and the data obtained by measurement (perceived individualized care and the level of satisfaction with the nursing care) were given as arithmetic mean and standard deviation. In the analysis of the normally distributed data, the t-test was used for two groups and the ANOVA was used for more than two groups. When the mean scores of independent groups not showing normal distribution were compared, Mann Whitney-U test was used for the two groups and if the number of the independent groups was more than two, Kruskal Wallis analysis was used. Spearman correlation analysis was used to determine the direction and level of the relationship between the scales, and the margin of error was taken as 0.05.

Results

In Table 1, the descriptive characteristics of the women who gave birth by cesarean section are given. Their mean age was 30.49 ± 6.46 years. Of them, 44.2% were primary school graduates, 60.3% lived in a city, 78.8% did not work in any paid job, 75% had income equal to their expenses, 94.6% had health insurance, 53.2% had one cesarean delivery and 26.9% were hospitalized twice.

In Table 2, the distribution of the mean scores obtained from the overall ICS-A and ICS-B dimensions of the Individualized Care Scale and their subscales, and the overall Newcastle Satisfaction with Nursing Scale was given. The mean scores the participating women obtained from the overall ICS-A and its Individuality in clinical situation, individuality in personal life situation and individuality in participating in decision making subscales were 3.50 ± 0.99, 3.50 ± 0.99, 3.16 ± 1.24 and 3.50 ± 1.03 respectively. The mean scores the participating women obtained from the overall ICS-B and its Individuality in clinical situation, individuality in personal life situation and individuality in participating in decision making subscales were 3.82 ± 1.18, 3.75 ± 1.24, 3.25 ± 1.39, 4.13 ± 1.01 and 70.53 ± 16.27 respectively.

Table 1. Descriptive Characteristics of the Women Having Undergone Cesarean Section

Variables	**X̄±SD**
Age	30.49±6.46
	Min-Max 18-45
Educational status	**n(%)**
Primary school graduate	**69(44.2)**
High school graduate	50(32.1)
University graduate	37(23.7)
Place of residence	
Village	28(17.9)
District	34(21.8)
City	**94(60.3)**
Economic status	
Income less than expenses	18(11.5)
Income equal to expenses	**117(75.0)**
Income more than expenses	21(13.5)
Health insurance	
Yes	**148(94.9)**
No	8(5.1)
Employment status	
Employed	33(21.2)
Not employed	**123(78.8)**
The number of Cesarean deliveries	
1	**83(53.2)**
2	39(25.0)
≥3	34(21.8)
The number of hospitalizations	
1	40(25.6)
2	**42(26.9)**
3	41(26.3)
≥4	33(21.2)

Table 2. Mean scores obtained from the overall ICS-A and ICS-B dimensions of the Individualized Care Scale and their subscales, and the overall Newcastle Satisfaction with Nursing Scale (NSNS)

Subscales	**X̄±SD**	**Range**
ICS-A*	3.50±0.99	1-5
Individuality in clinical situation	**3.70±1.06**	1-5
Individuality in personal life situation	3.16±1.24	1-5
Individuality in participating in decision making	3.50±1.03	1-5
ICS-B**	3.82±1.18	1-5
Individuality in clinical situation	3.75±1.24	1-5
Individuality in personal life situation	3.25±1.39	1-5
Individuality in participating in decision making	**4.13±1.01**	1-5
NSNS ***	70.53±16.27	0-100

*Awareness of nursing interventions **Perception of individuality ***Newcastle Satisfaction with Nursing Scale

In Table 3, the correlation between the mean scores obtained from the ICS-A and ICS-B dimensions of the Individualized Care Scale (ICS) and the Newcastle Satisfaction with Nursing Scale was given. There was a significant, positive and high correlation between the mean scores the participating women obtained from the ICS-A and ICS-B dimensions of the Individualized Care Scale. On the other hand, the correlation between the mean scores obtained from the Individualized Care Scale and the Newcastle Satisfaction with Nursing Scale was significant, positive and moderate.

Table 3. Correlation between the mean scores obtained from the ICS-A and ICS-B dimensions of the Individualized Care Scale (ICS) and the Newcastle Satisfaction with Nursing Scale (NSNS)

Scales	ICS				NSNS	
	ICS-A		ICS-B			
	r	p	r	p	r	p
ICS-A	--	--	0.832	0.001*	0.493	0.001*
ICS-B	0.832	0.001*	--	--	0.490	0.001*

*p<0.05

In Table 4, the distribution and comparison of the introductory characteristics of women who gave birth by cesarean section and the mean scores obtained from the Individualized Care Scale and the Newcastle Satisfaction with Nursing Scale were given. As is seen in table 4, there was a statistically significant correlation between the economic status of the women and the mean scores they obtained from the scales ($p < 0.05$). Of them, those whose income was more than their expenses were more satisfied with nursing care and their individualized care perception level was higher ($p < 0.05$).

Discussion

Postpartum is a period when mother and baby need nursing care a lot (13). In this period, women's perception of individualized care is of great importance. In the present study, the mean scores obtained by the participating women who underwent cesarean section from the ICS-A related to awareness of nursing interventions aimed at supporting the individuality (3.50 ± 0.99) and ICS-B related to perceived individuality in the care given to them (3.82 ± 1.18) were at a good level. In line with this result, we can say that the nurses were aware of individualized care and treatment needs of the patients and that the nursing care process was used appropriately, which was supported by the fact that the women who participated in our study were satisfied with nursing care. In the literature, although several studies in which patients' perception of individualized care was investigated by using the ICS were conducted (17-20), there is a gap regarding studies in which women's perception of individualized care was investigated. The findings of our study are consistent with those of studies conducted with different study groups.

Table 4. Distribution and comparison of the mean scores obtained by the participating women from the ICS-A and ICS-B dimensions of the Individualized Care Scale (ICS) and the Newcastle Satisfaction with Nursing Scale in terms of their descriptive characteristics

	ICS-A	ICS-B	NSNS
	X̄±SD	M(Min-Max)	X̄±SD
Educational status			
Primary school graduates (n = 69)	3.52±1.06	4(1-5)	70.57±16.12
High school graduates (n = 50)	3.57±0.96	4(1-5)	71.18±14.74
University graduates (n = 37)	3.38±0.90	4(1-5)	60.56±18.73
Test significance value	F=0.415 p=0.661	KW=1.486 p=0.476	F=0.104 p=0.902
Place of residence			
Village (n = 25)	3.37±1.17	4(1-5)	65.07±19.31
District (n = 34)	3.41±1.09	4(1-5)	78.08±11.77
City (n = 94)	3.57±0.88	4(1-5)	69.42±15.89
Test significance value	F=0.637 p=0.530	KW=0.590 p=0.745	F=5.798 **p=0.004***
Economic status			
Income less than expenses (n = 18)	2.78±1.17	3(1-5)	63.94±17.59
Income equal to expenses (n = 117)	3.58±0.94	4(1-5)	70.08±15.63
Income more than expenses (n = 21)	3.69±0.84	4(1-5)	78.66±16.13
Test significance value	F=5.788 **p=0.004***	KW=9.928 **p=0.007***	F=4.321 **p=0.015***
Health insurance			
Yes (n=148)	3.50±0.97	4(1-5)	70.37±16.49
No (n=8)	3.49±1.33	4(1-5)	73.37±11.89
Test significance value	t=0.037 p=0.971	Z=-0.244 p=0.807	t=0.506 p=0.613
Employment status			
Employed (n=33)	3.58±0.72	4(2-5)	74.03±14.67
Not employed (n=123)	3.48±1.05	4(1-5)	69.59±16.60
Test significance value	t=0.494 p=0.622	Z=-0.236 p=0.813	t=1.395 p=0.165
The number of cesarean deliveries			
1 (n=83)	3.57±1.06	4(1-5)	70.78±18.78
2 (n=39)	3.44±0.89	4(1-5)	68.33±14.60
≥3 (n=34)	3.39±0.90	4(1-5)	72.44±12.90
Test significance value	F=0.471 p=0.625	KW=0.461 p=0.794	F=0.597 p=0.552
The number of hospitalizations			
1 (n=40)	3.46±1.01	4(1-5)	68.12±20.74
2 (n=42)	3.57±0.93	4(1-5)	70.78±15.28
3 (n=41)	3.31±0.98	4(1-5)	69.53±12.42
≥4 (n=33)	3.70±1.03	4(1-5)	74.36±15.53
Test significance value	F=1.046 p=0.374	KW=5.343 p=0.148	F=0.955 p=0.415

***p<0.05**

Nurses are healthcare professionals who spend the most time with patients and are in closest contact with them (21). Therefore, nurses are the leading source for patients to obtain information and responses to their questions. In the literature, in studies in which satisfaction with nursing is evaluated, the mean scale score ranges between 67.82 ± 16.13 and 76.59 ± 15.11 (9,22-24). In the present study, the mean score regarding satisfaction with nursing was 70.53 ± 16.27, which suggests that the participating women who underwent cesarean section were generally satisfied with nursing care. In Bulut and Timur Tashan's, Karabulutlu and Yavuz's studies, nursing care satisfaction levels of women who underwent cesarean section were good too (1,25). There are also several studies indicating that women were satisfied with nursing during their hospitalization after delivery (26,27). The findings of the present study and those of the studies in the literature are similar, which indicates that the participants were satisfied with the nursing care. This situation can be explained by developing factors that increase satisfaction in the postpartum period, taking preventive measures for reducing factors, improving care policies, and continuing in-service training for nurses in recent years. On the other hand, the mean scores varied from one study to another, which may have stemmed from the differences between the health institutions where the studies were conducted, sample groups and the quality of health service. Although the satisfaction levels of the women in the present study were above average, it is noteworthy that these levels were well below the targeted level in nursing care.

The mean scores the participating women obtained from the subscales of the ICS-A were as follows: 3.70±1.06 for the clinical situation, 3.1 ±1.24 for the personal life situation, and 3.50±1.03 for participating in decision making about care. These results indicate that individuality is more noticed in nursing activities in clinical situations. This suggests that the patients perceived individuality in nursing

practices more when there was deterioration in their clinical condition.

The mean scores the participating women obtained from the subscales of the ICS-B were as follows: 3.75±1.24 for the clinical situation, 3.25±1.39 for the personal life situation, and 4.13±1.01 for participating in decision making about care. This result indicates that the clinical characteristics of the women were taken into account while they were given care, and that their participation in decision making about care was ensured, but that the least considered factor was their characteristics related to their personal life situation. Within this context, it can be said that the factor regarding patients' personal life situation should be improved. The study results of Ogut and Uyar Hazar support our findings (20). On the contrary, Abdelati et al. found that women who underwent cesarean section were not satisfied with their decision-making processes in participating in their care (28).

In the present study, no statistically significant correlation was determined between the variables such as the women's educational status, place of residence, having health insurance, employment status, the number of cesarean births and the number of hospitalizations, and their levels of individualized care perception and nursing care satisfaction. This result is consistent with those of the studies conducted by Ceylan and Eser, Ogut and Uyar Hazar, Kaya and Vural (17,20,29). Contrary to the findings of our study, in some studies, individual characteristics negatively affected the perception of care and satisfaction with nursing care (30,31). However, Singla et al. reported that there is no statistically significant relationship between educational status and the level of satisfaction with postpartum nursing care (32). These findings suggest that the women's socio-demographic characteristics did not affect the evaluation of nursing services in the early postpartum period.

The results obtained in the present study indicate that there was a statistically significant correlation between the place of residence and the level of satisfaction with nursing, and that satisfaction levels of the women whose place of residence was the district were higher than were of those the women whose place of residence was the city center or villages. This result is consistent with that of Sise's study (12) but different from that of Temizyurek Yavuz and Basaran Acıl's study (31). This suggests that patients' expectations of nursing services were affected by their place of residence.

In the present study, a statistically significant correlation was determined between the economic status of the participants and the mean scores they obtained from the scales. Participants whose income was higher than their expenses were more satisfied with nursing care and their perception of individualized care was higher than those with lower expenses. In the literature, there are studies whose results support this finding (31,33). This suggests that the expectations of women with good income may decrease because they themselves can meet most of their needs in the hospital.

A patient's previous experiences and information obtained from external sources can affect their expectations of healthcare professionals responsible for their treatment and care (34). In the present study, the correlation between the previous hospitalization status of women who had cesarean delivery and their satisfaction with nursing care was not statistically significant ($p > 0.05$; Table 4). The results of studies conducted by Sise and Ogut and Uyar Hazar are consistent with our findings (12,20). This result can be explained by the fact that the number of the women who had only one hospitalization experience was high. However, it also suggests that the hospitalization of women with more than one previous hospitalization experience did not affect their perception and satisfaction with nursing care, because their expectations of nursing care were the same each time they were hospitalized.

In the present study, the number of cesarean deliveries had no effect on the participants' perception of individualized care and nursing care satisfaction. Although our search for studies in which the relationship between the perception of individualized care and cesarean section was investigated demonstrated a gap in the literature, in their study, Ogut and Uyar Hazar (20) stated that women's levels of perception of individuality in the care given to them (ICS-B) decreased significantly as the number of births they gave increased. In the literature, there are several studies conducted on the effect of the number of cesarean deliveries on the satisfaction with nursing care whose results support the findings of our study. For instance, no significant correlation was determined between the number of pregnancies and satisfaction with nursing care in Christiaens and Bracke's study and between the number of cesarean deliveries and satisfaction with nursing care in Kaya and Vural's study ($p > 0.05$) (29,35). These results in our study can be explained by the fact that the number of women who had only one cesarean delivery was high. In addition, it can be said that previous birth history did not affect current individualized care perception and satisfaction with nursing care.

In the present study, a strong positive correlation was determined between the level of satisfaction with nursing care and the mean scores obtained from the ICS-A and ICS-B. As the patients' awareness of nursing activities increased, so did their perception of individuality in the care given to them and their satisfaction with nursing. A moderate positive correlation was determined between perception of individuality in the patients' own care, and awareness of nursing activities and satisfaction with nursing care. In the present study, it was observed that as the patients' level of perception of individualized care increased, so did their levels of awareness of nursing activities and their satisfaction with nursing care. In the literature, there is a gap related to studies in which the relationship between perception of individualized care and satisfaction with nursing care among women who underwent cesarean section was investigated. However, in Ogut and Uyar Hazar's, a positive relationship was found between women's perception of individuality in their postpartum self-care and satisfaction with midwifery care (20). A positive relationship was determined between perception of individualized care and satisfaction with nursing care in patients in Acaroglu et al.'s study, and in patients who underwent orthopedic surgery in Tekin and Yildiz Fındık's study (36,37). The results of both studies were consistent with those of our study. Snyder and Engstrom stated in their study that the results of patient participation were patient satisfaction, health care cost and health care outcomes (38). Similarly, Prey et al. stated that satisfaction with nursing care and patient participation were related, but there were deficiencies in practice, and patient participation was inadequate (39). In Tambuyzer et al.'s study, a statistically significant relationship was determined between patient participation and satisfaction (40). As determined by Abdelati et al., women who underwent cesarean section were not satisfied with the psychological care, continuity of care, and participation in decision-making processes in the provision of care (28). All these suggest that there is a need for regulations aimed at encouraging patient participation in the provision of care and increasing patients' satisfaction with nursing.

Conclusion

It was determined that the women who underwent cesarean section had a good level of perception of individualized care and satisfaction with nursing. As the rate of awareness of nursing activities among the participants increased, so did their perception of individuality in the care given to them and, as the patients' awareness of nursing activities and the level of individuality in perceiving nursing care increased, so did the rate of satisfaction with nursing care. It can be said that the satisfaction of women who had cesarean delivery with nursing care is influenced more not by their demographic characteristics but by whether their care needs are met. Although participation in patient care is a mutual relationship, our study reveals only patient views. Therefore, it is recommended that in future studies, not only the opinions of patients who receive care from nurses but also those of nurses who give care to patients regarding patient participation should be investigated.

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Investigation of Self-Esteem and Assertiveness Levels among Emergency Healthcare Personnel

Gulhan Kurtoglu Celik[1(ID)], Gul Pamukcu Gunaydın[1(ID)], Cagdas Yildirim [1(ID)], Servan Gokhan[1(ID)],

[1]Department of Emergency Medicine, Faculty of Medicine, Ankara Yıldırım Beyazıt University, Ankara, Turkey

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Abstract

Objective: It has been determined that self-esteem and assertiveness level of the individual significantly affect his/her environment. In this study, our goal is to determine the self-esteem and assertiveness levels of healthcare personnel in Emergency Department.

Methods: Our study is a prospective analytical observational study. The study population included nurses, emergency medicine residents, specialists and faculty member working in the Emergency Department. The three-part questionnaire form consists of 54 questions. Data were collected using a personal information form containing socio-demographic characteristics (14 questions), the Rosenberg Self-Esteem Scale (RSES) form (10 questions) and the Rathus Assertiveness Schedule (RAS) (30 questions).

Results: 217 participants were included. The median of RSES scores of the individuals was found to be 31 (10-40) and the median RAS of 20 (-42-69). Most of the participants did not receive any training on self-esteem or assertiveness (79.3% and 88%, respectively). Majority of participants stated that they did not have difficulty expressing themselves. RSES scores of those who stated they needed self-esteem training were found to be lower ($p < 0.001$). RAS scores of those who needed assertiveness training were found to be lower than those who did not, and this difference was statistically significant ($p < 0.001$).

Conclusion: Self-esteem and assertiveness levels of the healthcare professionals working in the emergency department are high. Although individuals' education about self-esteem or assertiveness does not change their self-esteem and assertiveness, those with low self-esteem and assertiveness feel a need for these issues.

Key words: Self-Esteem, Assertiveness, Emergency Medicine

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Address for correspondence/reprints:

Cagdaş Yildirim

Telephone number: +90 (505) 710 66 14

E-mail: cyildirim@ybu.edu.tr

Introduction

Self-esteem positively affects the therapeutic communication of healthcare professionals with patients and helps them cope with crises (1-3). A high level of self-esteem reduces individuals' anxiety levels and the number of negative consequences caused by stress (3). Also, healthcare personnel with low self-esteem may display negative behaviors and attitudes in the workplace in addition to other negative consequences of low levels of self-esteem (2,3).

Assertiveness can be defined as confidence, effective self-assertion, behaving appropriately and being firm in a positive manner (4). Assertive people are easy to communicate with and do not ignore the rights of others while defending their own (5,6).

The goal of this study is to determine and compare the self-esteem and assertiveness levels of the emergency medicine residents, specialists and nurses. To the best of our knowledge this topic has not been investigated in the literature.

Methods

Our study is a prospective analytical observational study. The local ethics committee approval was obtained for this study (Date 4 June 2020). It was conducted between 10 and 30 June 2020 in Ankara City Hospital which is an urban hospital that has 450.000 emergency department visits per year.

Study Population

The study population consisted of nurses, emergency medicine residents, emergency medicine specialists and faculty members working at the Emergency Department. Inclusion criteria: to work at emergency department as health care personnel. Exclusion criteria: not willing to participate in the survey. There were 65 residents, 24 specialist, 18 faculty members, 247 nurses in the department at the time**.**

Data Collection

A three-part questionnaire form consisting of 54 questions was used. Data were collected using a personal information form aimed at obtaining data regarding the socio-demographic characteristics of the participants (14 questions), the Rosenberg Self-Esteem Scale (RSES) (10 questions) and the Rathus Assertiveness Scale (RAS) (30 questions). The scales were applied to participants online via Google Forms. The personal information form consisted of questions designed to obtain information about the participants' demographic characteristics (i.e. age, gender, marital status, number of children, parents' living status and opinions on their income levels); the nature of their work (i.e. position in the institution, period of professional experience); self-esteem levels; history of participation in any training on assertiveness and self-esteem and opinions on assertiveness and self-esteem.

RSES and RAS scores

The RSES is used to measure individuals' self-esteem levels and reflect their views on their worth as a person. It consists of 10 statements, of which 5 are positive and 5 are negative. The total score can be between 10 and 40. The higher the mean score, the higher is the self-esteem. RAS is a scale that consists of 30 6-point Likert-type items and consists of 13 positive and 17 negative statements. A score between −90 and +10 indicates timid behavior, while a score between +10 and +90 indicates assertive behavior.

Statistical analysis

The analysis of the data obtained was conducted using IBM SPSS16.0 (Chicago, IL, USA) statistical software. Whether the distribution of discrete and continuous numerical variables is suitable for normal distribution was investigated using the Kolmogorov–Smirnov test. Because the data did not conform to the normal distribution, they were presented as the median and the minimum/maximum and categorical variables as the number of cases and (%). Categorical variables were evaluated using Chi-square and continuous variables with Mann–Whitney U and Kruskal–Wallis tests. The Cronbach's α internal consistency score was calculated as 0.866 for RSES and 0.871 for RAS. With $p < 0.05$, the findings were considered statistically significant.

Results

350 healthcare personnel work at the Emergency Clinic of Ankara City Hospital. Of these, 128 did not want to participate in the study, and 5 could not be included in the study because they were on annual leave or sick leave; thus, the study was conducted with 217 people. Demographic characteristics of the participants are as followed: 51.6% (n=112) of the participants were male. 28.1% (n=61) of participants were between ages 18-24, 53% (n=115) were between 25-34 and 41% (n=41) of them were 35 and above. Regarding job status 24.4% (n=53) of the participants were emergency medicine residents, 7.8% (n=17) were emergency medicine specialists, 7.4% (n= 16) were faculty members and 60.4% (n=131) were nurse or paramedics. 67.7% (n=147) of the participants had 0-5 years of work experience, 14.7% (n=32) had 6-10 years, 10.6% (n=23) had 11-

15 years and 6.9% (n=15) had over 15 years of work experience. 42.4% (n=92) of the participants were married and rest of them were single. 71% (n=154) of the participants had no children, 13.8% (n=30) had 1 child, 15.2% (n=33) had 2 or more children. 91.2% (n=198) of the participants' both parents were alive. 8.8% (n=19) had at least one parent deceased. 66.8% (n=145) of the participants had positive opinions on their income where 33.2% (n=72) had negative opinions.

The mean RSES score of the participants was found to be 31 (10–40), and the mean RAS score was found to be 20 (−42–69). The data on whether the participants received any training on self-esteem and assertiveness and whether they feel the need to receive training on these issues are presented in Table 1.

Table 1: Self-esteem and assertiveness training and feeling of need

	n	%
Receiving training on self-esteem		
Never	172	79.3
Once and/or more	45	20.7
Feeling the need to receive training on self-esteem		
Yes	54	24.9
No	78	35.9
Sometimes	85	39.2
Receiving training on assertiveness		
Never	191	88
Once and/or more	26	12
Feeling the need to receive training on assertiveness		
Yes	65	30
No	77	35.5
Sometimes	75	34.6
Difficulty expressing oneself around colleagues		
Yes	10	4.6
No	121	55.8
Sometimes	86	39.6

No difference was found between the participants' RSES scores by age, gender, position, the period of professional experience, parents' living status and income levels ($p > 0.05$ for all values). However, a difference was found in the self-esteem levels of the participants in terms of their marital status. RSES scores of married people were found to be higher, and this difference was statistically significant ($p = 0.024$) (Table 2). As for the RAS scores, no difference was found between the participants' scores by age, gender, position, the period of professional experience, parents' living status, participants' opinions on their income levels and marital status ($p > 0.05$ for all values) (Table 2).

It was found that the mean RSES and RAS scores of the participants who stated that they do not have difficulty expressing themselves around colleagues are higher than of those who stated that they do, and these differences were statistically significant ($p < 0.001$ for both values) (Table 2).

When the relationship between receiving training on self-esteem and the RSES scores of the

the RAS scores of the participants was examined, it was found that the difference between the RAS scores of those who received training on assertiveness and those who did not ($p = 0.067$) was not statistically significant. (Table 3)

Table 2. Comparison of the self-esteem and assertiveness scores of the participants

	Rosenberg Self-Esteem Scale score	p	Rathus Assertiveness Scale score	p
Age				
18–24	31 (20–40)	0.518	23 (−26–61)	0.748
25–34	31 (10–40)		18 (−42–69)	
35 and above	31 (23–40)		12 (−14–57)	
Gender				
Male	31 (10–40)	0.907	18 (−42–67)	0.336
Female	31 (13–40)		21 (−30–69)	
Task				
Emergency medicine assistant	31 (22–40)	0.443	20 (−42–62)	0.506
Emergency medicine specialist	31 (24–40)		33 (−13–69)	
Clinical educator	31 (26–40)		11 (−14–41)	
Nurse/paramedic	31 (10–40)		20 (−31–67)	
Period of experience				
0–5 years	31 (10–40)	0.670	21 (−42–69)	0.718
6–10 years	31 (13–39)		19 (−30–62)	
11–15 years	32 (23–40)		17 (−14–64)	
Over 15 years	31 (26–35)		15 (−13–37)	
Marital status				
Married	31 (23–40)	0.024	20.5 (−28–69)	0.659
Single	30 (10–40)		20 (−42–67)	
Number of children				
No children	31 (10–40)	0.531	20 (−42–69)	0.938
1 child	31 (25–40)		21.5 (−14–64)	
2 children or more	31 (23–40)		17 (−21–56)	
Parents' living status				
Both Alive	31 (10–40)	0.082	20.5 (−42–69)	0.875
One or both Deceased	33 (23–40)		13 (−14–61)	
Opinions on Income Level				
Positive	31 (20–40)	0.165	21 (−42–64)	0.162
Negative	30 (10–40)		12.5 (−31–62)	
Difficulty expressing oneself around colleagues				
Yes	25 (13–31)	<0.001	−10.5 (−30–26)	<0.001
No	32 (10–40)		29 (−23–69)	
Sometimes	30 (20–40)		10.5 (−42–61)	

Table 3: Comparison of scale scores with receiving self-esteem and assertiveness training and feeling the need to receive such training

	Rosenberg Self-Esteem Scale score	p		Rathus Assertiveness Scale score	p
Receiving training on self-esteem			**Receiving training on assertiveness**		
Never	31 (10–40)	0.378	Never	18 (−42-69)	0.67
Once and/or more	31 (22–40)		Once and/or more	22 (−23-61)	
Feeling the need to receive self-esteem training			**Feeling the need to receive assertiveness training**		
Yes	29 (13–40)	<0.001	Yes	8 (−31–67)	<0.001 *
No	33 (10–40)	*	No	34 (−23–69)	
Sometimes	30 (21–40)		Sometimes	17 (−42–52)	

* Statistically significant differences were found between all patient groups in terms of values in posthoc tests.
* After Bonferroni correction, a new p-value was accepted as 0.016]

When the relationship between participants feeling the need to receive self-esteem training and RSES scores was evaluated, it was found that the RSES scores of those who felt the need for such training were lower than those who did not, and this difference was statistically significant ($p<0.001$) (Table 3). Similarly, when the relationship between participants feeling the need to receive assertiveness training and RAS scores was evaluated, it was found that the RAS scores of those who felt the need for such training were lower than those who did not, and this difference was statistically significant ($p < 0.001$) (Table 3).

Discussion

Healthcare personnel who have self-esteem and are assertive establish better communication with patients and other people, cope with the crises that occur in their work lives more easily, say no when necessary and feel more satisfied with their jobs and the quality of the health services they provide.

The majority of the participants in our study did not attend a self-esteem training programme and majority of the participants declared a need for training on self-esteem. (Only 35.9% of participants declared they did not need training; the rest of the participants expressed a needed for training) Likewise most of the participants stated they had no training on assertiveness and majority of them stated the needed a training about assertiveness. (Only 35.5% of participants declared they did not need training and the rest declared a need for training) It was observed that the participants have not attended any training on self-esteem and assertiveness neither as students nor as part of their professional lives and that healthcare personnel either always or sometimes feel the need to receive training on this issue. It is predicted that training programs will positively affect the self-esteem and assertiveness levels of healthcare personnel (6-10).

Half of the participants in our study described themselves as assertive. The mean RAS score of the participants was found to be 20, which is close to the minimum score needed to classify participants as assertive. This can be interpreted as participants being aware of their own assertiveness levels. Küçük et al.found that 68.6% of the participants in the study conducted with nursing students stated that they are assertive. These findings in the literature are similar to the findings of our study (11).

55.8% of the participants said that they do not experience any difficulty in engaging in communication with their colleagues. The findings of the studies in the literature show that assertive individuals express themselves more easily (2, 7, 12-14). This finding is supported by the RAS scores of the participants, which indicate that they are assertive.

The mean RAS score of the participants is 20 (min. −42, max. 69), which indicates that the participants are assertive. Kahriman found the mean assertiveness score of health college students to be 20.90 ± 25.00 (5). These study results support the findings of the present study.

The mean self-esteem and assertiveness scores of the participants do not differ significantly by age. The difference between other studies findings and our findings can be explained by the age range of the participants being narrow in our study (11, 15).

The mean self-esteem and assertiveness scores of the participants do not differ significantly by gender. The desired result in our study was similar or equal self-esteem and assertiveness levels between males and females. The fact that the self-esteem levels of males and females are high and similar is a positive indicator for emergency healthcare personnel.

The self-esteem and assertiveness scores of the participants do not differ significantly by the period of professional experience ($p > 0.05$). In our study, a decrease was observed in the assertiveness scores of the participants as the period of professional experience increased. A significant difference was not found because the average age of participants is low and similar.

Self-esteem can be positively or negatively affected by the developments that occur in people's lives (2, 3). Self-esteem is not an innate and unchanging phenomenon (10). In literature, the self-esteem levels of healthcare personnel can be strengthened while they are students by adding appropriate courses and training programs to their curriculum (16). In our study, no difference was found between the RSES scores of those who received training on self-esteem and those who did not. 79.3% of the participants stated that they did not attend such training, and 20.7% stated that they attended such training once or twice only. The rate of participation in such training programs is low among the participants and those who participated at all did so only once or twice therefore receiving training did not affect the self-esteem levels of emergency healthcare personnel in our study.

The RSES scores of the participants who feel the need to participate in self-esteem training were lower, and the difference was statistically significant. Those with low self-esteem scores are eager to receive training on self-esteem.

Several studies have shown that individuals with passive (timid) behavior became assertive after receiving assertiveness training (6-8, 17). These findings in the literature show that the quality of assertiveness can be improved with training. However, our findings suggest no significant difference between the RAS scores of those who received assertiveness training and those who did not. This is because most of the participants who received assertiveness training stated that they attended such training only once or twice, and we think that this little amount of training did not have an influence on the participants of this study.

The mean RAS score of those who felt the need to receive assertiveness training was 8 (min. −31, max. 67), of those who stated that they sometimes feel the

need to participate in such training was 17 (min. −42, max. 52) and of those who did not feel the need to participate in such training was 34 (min −23, max 69). There is a statistically significant difference between the groups in terms of RAS scores ($p < 0.001$). This finding suggests that the participants are aware of their level of assertiveness. Training programs should be organized especially for those who do not feel assertive enough.

In our study we found that those who do not have difficulty expressing themselves exhibit more assertive behavior than others (4, 5, 13, 18, 19). It is easier for assertive people to say no, to make requests more confidently, to express their positive and negative feelings more comfortably and to initiate interpersonal communication more easily (7, 8). These findings in the literature support the findings of our study.

It was stated in relevant studies that as the self-esteem levels of healthcare personnel increase their levels of assertiveness increase. Further, as their levels of assertiveness increase, their levels of self-esteem increase (2, 5, 7, 16).

Limitations

The limitations of our study are as follows: our study is conducted in a single center and this limits the generalizability of our results, we have only included health care personnel that works in emergency department and cannot compare our findings with personnel that works in other departments.

Conclusion

In this study, we determined that the self-esteem and assertiveness levels of healthcare personnel working in the Emergency Clinic. We found that emergency department personnel had high levels of self-esteem and assertiveness and also married emergency healthcare personnel have higher levels of self-esteem.

Emergency healthcare personnel should be tested for self-esteem and assertiveness at regular intervals, and supportive training should be provided as needed.

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Evaluation of Knowledge Level and Awareness of Parents About Avulsion and Crown Fracture

Cigdem Guler[1(ID)], Nihal Belduz Kara[1(ID)], Didem Turken[2(ID)]

[1] Department of Pediatric Dentistry, Faculty of Dentistry, Ordu University, Ordu, Turkey
[2] Pediatric Dentist, Private Clinic, Ordu,Turkey

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Abstract

Objective: The aim of this study was to evaluate the knowledge levels and awareness of avulsions and crown fractures of the parents. The study is important to understand how to improve parents' knowledge level related to dental treatment of avulsion and crown fracture.

Methods: The parents of pediatric patients who applied to Ordu University Faculty of Dentistry, Department of Pediatric Dentistry during April-June 2017 were the target group for this study. A questionnaire was formulated to evaluate the parents' knowledge levels and awareness of avulsions and crown fractures. Five hundred and seventy-five parents answered the questionnaire. The participation rate was 68.3%. Data were analyzed statistically.

Results: Approximately one-half of the parents in this study were in their thirties, and 61.9% of the parents were males. Only 29.9% of the parents were university graduates, and more than one-half had not attended a first aid course. The chi-squared test indicated that there was no statistically significant difference between the correct answer percentage and the age, gender, and affected by dental trauma ($P>0.05$). However, a statistically significant difference was found between the correct answer percentage and the educational level, first aid course attendance, see a dental trauma, and preferred institution for emergency dental treatment ($P<0.05$). The parents' level of knowledge and awareness of avulsions and crown fractures was 40.2% or "poor".

Conclusion: The parents' knowledge levels and awareness of avulsions and crown fractures should be increased through educational programs.

Key words: Dental trauma, knowledge level, parents, questionnaire

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Address for correspondence/reprints:

Cigdem Guler

Telephone number: +90 (452) 212 12 86

E-mail: cigdem_zehir@yahoo.com

Introduction

Traumatic dental injuries occur frequently in children and young adults, accounting for 5% of all injuries (1). Dental trauma is an important and prevalent oral health problem in children, and it can cause pain and distress (2). Epidemiological studies have indicated that dental trauma is a significant problem in young people, and that in the near future, the trauma incidence will exceed that of dental caries and periodontal disease in the young population (3). The general causes of these

dental injuries include falls, collision, fighting and pushing/shoving (4). Luxation injuries are the most common traumatic dental injuries seen in the primary dentition, whereas crown fractures are more commonly reported for the permanent teeth (1).

The majority of dental injuries occur in children between the ages of 8 and 11 years old (5). When considering the dentition periods that are affected by trauma, 30% of the primary dentition and 20% of the permanent dentition is affected (4). The primary and permanent anterior teeth are important not only for aesthetics, but also for phonetics, chewing, supporting tissues integrity, and the psychological and mental health of children (6). Therefore, the proper diagnosis, treatment planning, and follow up are important to assure a favorable outcome (1). International Association for Dental Traumatology has published dental trauma guidelines that include three sections about primary and permanent traumatic dental injuries, which also offer recommendations for their diagnosis and treatment. Prompt and pertinent emergency management is not only the responsibility of the dentist, but also of lay people, such as the parents and the teachers available at the site of accident (6). Most traumatic dental injuries occur at home, followed by school (7,8). So mothers play important roles in the appropriate decision-making (9). Most children with avulsed teeth present for treatment late due to lack of awareness and knowledge among parents, and this can result in an unfavorable long-term prognosis (10).

There have been many studies conducted to determine school teachers' knowledge levels of dental trauma (11-14). However, a literature review revealed that there have been only a few studies on the parents' knowledge levels of dental trauma (15,16). Moreover, there were no studies dedicated to evaluating the parents' knowledge levels and awareness of both avulsions and crown fractures. Therefore, the aim of this study was to evaluate the knowledge levels and awareness of avulsions and crown fractures of parents whose children were admitted to the Faculty of Dentistry, Department of Pediatric Dentistry, Ordu University in Turkey.

Methods

This study was approved by the Faculty of Medicine, Clinical Research Ethics Committee, Ordu University (2017-137). The parents of patients who applied to Faculty of Dentistry, Department of Pediatric Dentistry, Ordu University during April-June 2017 were the target group for this study. A questionnaire was formulated to evaluate the parents' knowledge levels and awareness of avulsions and crown fractures. The contents and aim of the study were explained verbally to the parents, and the confidentiality of those parents who were agreeing to participate in the questionnaire was ensured. Five hundred and seventy-five parents answered the questionnaire. The participation rate was 68.3%.

The questionnaires were distributed by the same person and collected on the same day. The questionnaire was made up of two parts, modifying the questionnaire used in the study of Mehrabkhani et al. (17) Part 1 "Personal and Professional Information," was created to obtain the participants' sociodemographic information. This section consisted of 7 questions about the basic demographic information, including the age, gender, educational level, attendance in a first aid course that included dental injuries, see any dental trauma, any past experiences with dental trauma, and the preferred institution in case of emergency dental treatment.

Part 2, "Knowledge," was created to determine the parents' knowledge levels and awareness of avulsions and crown fractures. This part was made up of 15 questions about two dental trauma types: fractured teeth and avulsed teeth. Some of the multiple-choice questions in this section had more than one correct answer (Table 1).

Every correct answer to a question in the questionnaire was assessed as 1 point, and the gradating of the knowledge level to the total score was as follows: poor = 0–5, moderate = 6–8, and good = 9–15. A chi-squared test was used to detect the relationship between the knowledge level and the age, gender, educational level, attended first aid training, experience with a dental trauma, and the preferred institution for dental treatment. The results were expressed as the number of participants and the correct response percentage. Correct answers were calculated to assess the parents' knowledge levels and awareness as follows: < 50% = bad, 50%–75% = moderate, and 75% = good.

Table 1. Part 2 of the study questionnaire: "Knowledge"

1- Can you distinguish whether a broken tooth is primary or permanent tooth?
- Yes
- No

2- Do you believe it is possible to glue a piece of a tooth back into place that was fractured due to a traumatic injury?
- Yes
- No

3- What is the best storage media for a fractured tooth prior to seeing a dentist?
- Dry
- Tap water
- Milk
- Saline
- Do not know

4- What is the first thing that you must do when your child has a broken tooth?
- After calming the child down, take him/her to the dentist without wasting time
- After calming the child down, search for the broken tooth part and take it to the dentist without delay
- Give the child sugar water to help him/her calm down
- Go to the dentist without wasting time
- Go to the nearest emergency service

5- Which type of trauma situation requires EMERGENCY dental treatment?
- If only the corner of the tooth is broken
- If 1/3 of the tooth is broken,
- If 1/2 of the tooth is broken,
- If the tooth has completely avulsed
- All of the above
- Do not know

6- If a tooth came completely out of the socket, could you distinguish whether it was a primary or permanent tooth?
- Yes
- No

7- When the permanent tooth is completely avulsed, would you replant the tooth (put it back) into the socket?
- Yes
- No

8-When the primary tooth is completely avulsed, would you replant the tooth (put it back) into the socket?
- Yes
- No

9- If you answered yes to the seventh question, when do you think professional treatment is needed?
- Immediately
- Within 30 minutes
- Within a few hours
- Within 1-2 days

10-If you decide to replant a tooth back into its socket, but it has fallen onto the ground and is covered with dirt, what would you do?
- Scrub the tooth gently with a toothbrush
- Rinse the tooth under tap water
- Put the tooth right back into the socket without doing anything else
- Do not know

11- As the time between the onset and the treatment of the tooth injury increases, the treatment success of this tooth .....
- Increases
- Diminish
- Fixed
- Do not know

12- What do you prefer if you must choose a liquid to transport an avulsed tooth to the dentist?
- Tap water
- Milk
- Child's saliva
- Alcohol
- Ice
- Juice
- Saline
- Antiseptic solution

13- If you want to clean a tooth, which part of the tooth do you hold?
- The portion of the tooth in the mouth.
- From the root
- Anywhere
- Do not know

14- If your child has contact with soil or a dirty floor after a tooth injury, what vaccination may be needed?
- Tetanus
- DPT (diphtheria, pertussis, and tetanus).
- Polio
- There is no need for vaccination

15- Which type of dentition is more important to you related to dental trauma?
- Primary teeth
- Permanent teeth
- Both of them
- Do not know

Statistical analysis

The questionnaire data was analyzed statistically using IBM SPSS Statistics for Windows version 19 (IBM Corp., Armonk, NY, USA). The findings were expressed as percentages and n values, and the significance level was set at 0.05.

Results

The distribution of the sociodemographic data of the participants and Participants' socio-demographic information distribution (Part 1: Personal and Professional Information) and statistically significant difference between the correct answer percentage is presented in Table 2.

No statistically significant difference was found between the correct answer percentage and the age, gender, and affected by dental trauma (P>0.05). However, a statistically significant difference was found between the correct answer percentage and the educational level, first aid course attendance, see a dental trauma, and preferred institution for emergency dental treatment (P<0.05).

As shown in Table 3, the demographic characteristics of the participating parents indicated that 219 (38.1%) were females and 356 (61.9%) were males. Of the total parents, 277 (48.1%) were 30–39 years old, and 172 (29.9%) had graduate and postgraduate degrees. When the relationship between the educational level and the correct answer percentage was examined, it is found that the contingency coefficient was 28%. In addition, when compared with the other educational levels, the correct answer percentage for the graduate and postgraduate degrees was the highest, in the "good" category (30.8%).

One hundred and ninety-two of the participants' (33.3%) had received first aid training, but only 28 (4.8%) reported that the training course included first aid for dental injuries. When the relationship between the first aid course attendance and the correct answer percentage was examined, it was determined that the contingency coefficient was 26%. It was found that the rate of responding to the first aid course involving dental injury intervention was the highest in the "good" category (50%).

When examining the relationship between the dental trauma experience and correct answer percentage, the contingency coefficient was 16%. The correct response percentage distribution of the participants with previous dental injury experiences was 25.8% in the "good" category, while 13% were in the "good" category in the correct response percentage distribution of the participants without dental injury experiences. Therefore, the correct response rate for those with dental injury experiences was approximately twice as high as that of those without dental injury experiences.

The rate of choosing a dental health center (45%) was higher than the rate of choosing the Faculty of Dentistry (26.7%). However, the "good" category percentage for the participants who preferred the Faculty of Dentistry was 22.7%, while the "good" category percentage was 11.2% for those who preferred dental health centers. When the relationship between the preferred institution and the correct answer percentage was examined, the contingency coefficient was 17%. Therefore, even though the Faculty of Dentistry preference rate was lower than that of the dental health center, when the accuracy distribution of the answers was examined, it was found that the patients who consulted the Faculty of Dentistry were more conscientious about the dental health center.

The parents' level of knowledge and awareness of avulsions and crown fractures was 40.2% or "poor." The distribution of the correct response percentage for Part 2 of the participants' questionnaire is shown in Table 3.

Discussion

Most dental trauma in children occurs when they are at home (18). When considering this situation, it becomes clear how important it is for parents to be informed about dental trauma and its treatment approaches. For this reason, this study was designed to assess the parents' knowledge levels and awareness of dental trauma. The results of present study showed that the knowledge levels and awareness of avulsions and crown fractures of parents was "poor" in Middle Black Sea Region, Turkey. This result was in accordance with two other studies of parental knowledge performed in Kuwait and Singapore (19,20). More than one-half of parents could not distinguish whether a traumatized tooth was a member of the permanent or primary dentition, suggesting that many parents do not discern the transition from primary dentition to exfoliation to permanent eruption. This rate was little higher than those reported in previous studies performed in Indian and the United Arab Emirates (21,22).

The gender and age of the parents did not affect their knowledge and awareness, and there

Table 2. Participants' socio-demographic information distribution (Part 1: Personal and Professional Information) and statistically significant difference between the correct answer percentage

Sociodemographic Information		N	%	P
Age (Year)	20-29	128	22.2	
	30-39	277	48.1	
	40-49	131	22.7	0.635
	50 and over	39	6.7	
Gender	Female	219	38	
	Male	356	61.9	0.195
Education level	Primary school	130	22.6	
	Secondary school	111	19.3	
	High school	161	28	**<0.001**
	University+	172	2.9	
First-aid course attendance	No	383	66.6	
	Yes, tooth injury does not involve intervention	164	28.5	**<0.001**
	Yes, it includes intervention for dental injuries	28	4.8	
See a dental trauma	Yes	151	26.2	
	No	424	73.7	**<0.001**
Affected by dental trauma	Yes	108	18.7	
	No	467	81.2	0.623
Preferred institution for emergency dental treatment	To any hospital's emergency department	77	13.3	
	To the dental health center	262	45.5	
	To the private dental examination office	60	10.4	**0.015**
	Health center	22	3.8	
	Dental medical faculty	154	26.7	
Total		575	100	

Table 3. Participants' distribution of percentage of responding correctly to survey questions (Part 2: Knowledge)

Question (Q) Number	Correct Answer	
	N	%
Q 1	268	46.6
Q 2	232	40.3
Q 3	154	26.8
Q 4	129	22.4
Q 5	268	46.6
Q 6	244	42.4
Q 7	131	22.8
Q 8	484	84.2
Q 9	164	28.5
Q 10	112	19.5
Q 11	334	58.1
Q 12	368	64
Q 13	160	27.8
Q 14	248	43.1
Q 15	171	29.7
Mean		**40.2**

was no significant difference regarding the dental trauma history according to our results. The lack of significance in the correct answers between those with and without such experience indicated that a dental trauma history did not seem to increase the parents' knowledge of the correct emergency procedures. These findings are in accordance with those of other parental studies (10,23). Additionally, witnessing someone having dental trauma increased the knowledge level and awareness a little bit. A high educational level reflected positively on the attitude and perceived importance of the immediate management of the dental trauma, and an increase in the parents' educational level increased their knowledge level of dental trauma management. Similar findings have been reported in a few previous studies (20,24).

In our study, the knowledge level among the parents participating in a first aid training course involving dental trauma management was higher than in those who did not attend such a course. This shows that participating in this type of course can improve the knowledge and skills needed to manage dental trauma. Most of the parents (83%) are aware of the necessity of going to the dentist after an emergency tooth injury, and the preferred dental institution was the dental health center (45.5%). However, the parents responded to the questionnaire correctly at a lower rate (11.2%), which showed that information provided by dentists in the dental health center is inadequate.

Most of the parents (40.3%) said that they would look for the lost tooth piece according to our results. 49.5% of the parents believed that it was possible to glue a piece of a tooth that was fractured due to a traumatic injury. These findings were in accordance with the study of Cosme-Silva et al. (18). This shows that many people are aware of the possibility of replacing the broken pieces, and the presence of the tooth part is more aesthetic and economical for restoration. However, the parents did not know much about the media in which they needed to carry their child's broken tooth piece.

According to Andreasen and Hjorting-Hansen teeth that are replanted within 30 min are exhibit a success rate of 90%, but there is only a 5% chance of long-term retention in those teeth replanted after 2 h (25). In our study, only 28.5% of the parents reported that they would intervene within 30 minutes in cases of avulsion. Most of the parents were not aware of the critical importance for success of replanting avulsed teeth “immediately” or “within half an hour.” The cause of this delay may be due to the parents caring for the primary bleeding and pain control. However, this lack of information can seriously affect the prognosis. Furthermore, 77.2% of the parents reported that it was not necessary for them to reimplantation an avulsed permanent tooth into the socket by themselves. Most avulsed teeth can be successfully replanted with a good prognosis by taking simple precautions. A lack of information, fear of harming the child, and intervention avoidance may have prevented the parents from permanent tooth replantation. Therefore, parents should be informed about the importance of an emergency intervention after a tooth trauma.

Dental trauma accompanied by bleeding and pain is an alarming situation for the parents. In addition, sterilization is very important, along with bleeding control, and 43.1% of the parents reported the need for a tetanus vaccination after contact with the soil or dirt after a tooth injury. Loh at al. (26) reported that only 26.8% of dental hygienists were correct in their choice of the need for a tetanus injection in cases of a replanted avulsed tooth. This low rate was accordance with our study. However, 73.5% of the parents reported the necessity of a tetanus vaccination in a similar study by Kaul et al. (21) The reason for this difference may have been the differences in their socioeconomic statuses and educational backgrounds, or the country’s vaccine awareness.

This study is considered to have some limitations. First, this study is a questionnaire study conducted in one institution. Therefore, the findings may not reflect the experiences of parents consulting other institutions and in other geographic areas. Second, the participation rate or questionnaire data range was low. This study population may not have covered the full range of perceptions and experiences of all parents in Ordu, Turkey. Finally, no dental trauma education was given to the parents. Additional research should be conducted to evaluate the parents' knowledge level related to dental treatment of avulsion and crown fracture.

Within the limitations of the present study, the parents were found to have a low knowledge levels and awareness regarding the procedures to follow in emergencies related to tooth avulsion and crown fractures. Educational campaigns must be organized to improve the emergency management of dental trauma among parents. The knowledge of emergency treatment methods for traumatized teeth should be increased by providing both educational and preventive programs.

Conclusion

The parents’ level of knowledge and awareness of avulsions and crown fractures was 40.2% or “poor.” The parents’ knowledge levels and awareness of avulsions and crown fractures could be increased through educational programs.

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The Effects of Variable Selection and Dimension Reduction Methods on the Classification Model in the Small Round Blue Cell Tumor Dataset

Fatma Hilal Yagin[1](ID), Zeynep Kucukkakcali[1](ID), Ipek Balikci Cicek[1](ID), Harika Gozde Gozukara Bag[1] (ID)

[1]Department of Biostatistics and Medical Informatics, Faculty of Medicine, Inonu University, Malatya, Turkey.

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Abstract

Objective: The purpose of this study is to investigate and compare the effects of different dimension reduction methods (PCA, ICA, PCA + Forward Selection, ICA + Forward Selection) on the K-NN classifier using open access gene expression data of small round blue cell tumor types.

Methods: In this study, open access gene expression data of small round blue cell tumor types was used for investigate and compare the effects of different dimension reduction methods. In the study, PCA, ICA, PCA + Forward Selection, ICA + Forward Selection were used as different dimension reduction methods together with K-NN classification method.

Results: Accuracy values obtained from the dimension reduction model made with PCA on K-NN model; for EWS, BL, NB, and RMS type tumors with 93.51%, 91.14%, 92.31%, and 94.74% respectively. Accuracy values obtained from the dimension reduction model made with PCA + Forward Selection on K-NN model; for EWS, BL, NB, and RMS type tumors with 96.25%, 96.25%, 95.06% and 95.47%, respectively. Accuracy values obtained from the dimension reduction model made with ICA on K-NN model; for EWS, BL, NB, and RMS type tumors with 91.89%, 90.67%, 88.31% and 89.47% respectively. Accuracy values obtained from the dimension reduction model made with ICA+ Forward Selection on K-NN model; for EWS, BL, NB, and RMS type tumors with 93.51%, 91.14%, 92.31% and 94.74% respectively.

Conclusion: In this study, the model created with PCA gives higher results than the model created with ICA. In addition, according to the results of the models obtained by applying the Forward selection method on these 2 models, the forward selection method has increased the classification performance.

Key words: Dimension reduction, principal component analysis, independent component analysis, K-NN, Small round blue cell tumor.

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Address for correspondence/reprints: **E-mail:** zeynep.tunc@inonu.edu.tr

Zeynep Kucukakcali

Telephone number: +90 (422) 341 06 60-1337

Introduction

Small round blue cell tumor was first described by Gerald and Rosai in 1989 (1). Although its histogenesis is not known exactly, it is thought to originate from the progenitor cell with multiphenotypic differentiation potential (2). Small round blue cell tumor involves the abdominal and pelvic peritoneum diffuse and is usually observed in childhood and young adulthood. Tumors detected more in men show a rather aggressive clinical course. Although it is composed of slightly differentiated round cells, small round blue cell tumor can be differentiated from other primitive round cell tumors with morphological, immunohistochemical and genetic findings (3).

Small round blue cell tumors are four different childhood tumors with similar appearances, making accurate clinical diagnosis extremely difficult and difficult to distinguish. However, accurate diagnosis is important because treatment options, response to treatment, and prognoses differ greatly depending on the diagnosis. These include Ewing's tumors (EWS), neuroblastoma (NB), non-Hodgkin lymphoma (Burkitt lymphoma, BL), and rhabdomyosarcoma (RMS) (4).

Bioinformatics is a research field that includes the use of various computer-aided methods, retrieves and stores data to solve biological problems, and interprets data with the help of statistical analysis. Within the framework of these purposes, one of the fields of study of bioinformatics is DNA microarrays. DNA microarray technology is a method used to discover the functions of gene functions. In order to obtain more efficient results when working with microarrays, it is necessary to use an effective and robust dimension reduction algorithm to reduce the increasing feature size of the data. Dimension reduction algorithms contribute to reducing computation time in high dimensional data such as microarrays, improving prediction performance obtained by machine learning methods, and facilitating the interpretation of results (5).

Principal Component Analysis (PCA), one of these methods, is a multivariate technique that analyzes a data table in which observations are defined by several interrelated dependent variables. In other words, PCA is a transformation technique that enables the size of the data set containing a large number of related variables to be processed in a smaller size by protecting the variables in the data set (6). Independent Component Analysis (ICA) is a new method for finding the linear, orthogonal (not mandatory) coordinate system in a multivariable data set. It makes the projections of the input data on the existing coordinate system independent from each other and minimizes the relationship between them. The purpose of the ICA is to make a linear transformation that reduces the relationship between resources (7).

Forward selection, one of the frequently used methods for feature selection in gene expression data sets, is an iterative method. With each iteration, the most contributing feature is added to the model until adding a new feature does not improve the performance of the model. It is a method that creates a feature subset by testing the effect of the feature with a classifier at each step (8).

The K-nearest neighbor algorithm (K-NN) is widely used in classification due to its simple and easy implementation and the powerful and useful learning process. The K-NN method is one of the supervised learning algorithms used in classification problems and calculates the proximity of the test sample to the samples in the training set according to a predetermined distance criterion. After this process, it determines the k closest samples and includes the test sample to the class which these samples belong to the most (9).

The aim of this study is to investigate and compare the effects of different dimension reduction methods (PCA, ICA, PCA + Forward Selection, ICA + Forward Selection) on the K-NN classifier using open access gene expression data of small round blue cell tumor types.

Methods

Dataset

In this study, the Small Round Blue Cell Tumor data set was examined inclinometers (10). Small Round Blue Cell Tumor data set consists of gene expressions of four different pediatric tumors. The data set was created to facilitate tumor diagnosis by using gene expressions. Accurate clinical diagnosis is difficult due to the similar appearance of the tumors in their histology. Due to the treatment options, it is important to make the correct diagnosis, as the responses in terms of treatment and prognosis vary depending on the common diagnosis. The data set consists of 2308 variables and 83 observations. The dependent variable classes in the data set are given in Table 1.

Table 1. Distribution of the dependent variable

Dependent Variable	Count (%)
Ewing sarkomu (EWS)	29 (34.9)
Burkitt lenfoma (BL)	11 (13.3)
Nöroblastom (NB):	18 (21.7)
Rabdomiyosarkom (RMS)	25 (30.1)

In the study, firstly, the K-NN classifier was applied to the data set whose dimensions were reduced separately by PCA and ICA. A 10-fold cross validation method was used in the training and testing phase. The purpose of this process is to obtain more reliable results from the created model. Then, in order to compare the results; After the forward selection method, one of the feature selection methods, was applied to the data set whose size was reduced by PCA and ICA, the models was created with the K-NN classifier. The classification performance of the models was evaluated using Accuracy, Precision, Sensitivity, Specificity, F1-score, Matthews's correlation coefficient (MCC), and G-mean criteria.

PCA and ICA

Dimension reduction is used in a variety of computer science fields, including computer vision, pattern recognition, and machine learning. The advantages of dimension reduction are as follows: first, it typically enables the whole method to be implemented in a more computationally efficient manner. Second, it typically results in an improvement in the method's accuracy or right amount (11).

In this paper, we propose to exploit principal components analysis (PCA) and independent component analysis (ICA) for dimension reduction. PCA is commonly used in image processing, pattern recognition, data compression, data mining, machine learning, and computer vision, among other fields (12). In data mining, principal component analysis (PCA) is commonly used to investigate data structure. By maximizing the variance of the data, new orthogonal variables (latent variables or principal components) are obtained in PCA. The number of latent variables (factors) is significantly smaller than the number of original variables, allowing the data to be visualized in a low-dimensional PC space. Although PCA reduces the dimensionality of the space, it does not reduce the number of original variables because it generates new latent variables using all of the original variables (principal components). Reducing the number of variables is often beneficial for interpretation or potential inquiries (13).

Independent component analysis (ICA) is a multiple statistical method which seks to uncover disguised variables in high-dimensional data. ICA, which is a statistical computational method, is employed to find underlying hidden factors among a set of random vectors. The main aim of ICA method is to obtain the independent components (ICs), which are linearly independent or as independent as possible. In this way, ICA can be seen as a extension of Principal Components Analysis (PCA). ICA, on the other hand, is founded on statistical independence rather than unrelatedness, which is a much stronger function than unrelatedness (14).

Forward Selection

The first variable chosen for inclusion in the built model in forward selection is the one with the highest association with the dependent variable. After the variable has been chosen, it is assessed using a set of parameters. Mallows' Cp and Akaike's knowledge criterion are two of the most popular. If the first variable chosen meets the inclusion criteria, the forward selection process begins, with the statistics for variables not in the equation being used to choose the next one. When there are no more variables that meet the entry criteria, the process ends.

K-NN

The k-Nearest-Neighbors (K-NN) classification method is a non-parametric classification method that is easy to use but useful in many situations. To classify a data record t, its k closest neighbors are retrieved, and this forms a neighbourhood of t. The classification for t is typically decided by majority voting among data records in the neighborhood, with or without consideration of distance-based weighting. However, in order to use K-NN, we must select an acceptable value for k, and the classification output is highly dependent on this value. In certain ways, the K-NN approach is influenced by k. There are many methods for determining the k value, but one of the most straightforward is to run the algorithm several times with various k values and choose the one that performs best (15).

Results

Accuracy values obtained from the dimension reduction model made with PCA on K-NN model; for EWS, BL, NB, and RMS type tumors with 93.51%, 91.14%, 92.31%, and 94.74% respectively. In this model, the highest precision value was obtained in the EWS tumor type subclass, the highest specificity value in the NB tumor type subclass, and the highest sensitivity value, F1-score value, MCC value, and G-mean value were obtained from the RMS tumor type subclass (Table 2).

Table 2. PCA+ K-NN Performance metric values calculated from created models in the testing stage

Srbct tumor / Metrics	Ewing sarkomu (EWS)	Burkitt lenfoma (BL)	Nörobl astom (NB)	Rabdomiyo sarkom (RMS)
Accuracy	0.9351	0.9114	0.9231	0.9474
Precision	0.8966	0.7273	0.8889	0.8800
Sensitivity	0.9286	0.6667	0.8000	0.9565
Specificity	0.9388	0.9552	0.9655	0.9434
F1-score	0.9123	0.6957	0.8421	0.9167
Matthew's correlation coefficient (MCC)	0.8611	0.6447	0.7934	0.8799
G-mean	0.9337	0.7980	0.8789	0.9499

Accuracy values obtained from the dimension reduction model made with PCA + Forward Selection on K-NN model; for EWS, BL, NB, and RMS type tumors with 96.25%, 96.25%, 95.06% and 95.47%, respectively. In this model, the highest precision value was obtained in the EWS type tumor subclass, the highest specificity value was obtained in the NB type tumor subclass, and the highest sensitivity value, F1-score value, MCC value and G-mean value were obtained from the RMS type tumor subclass (Table 3).

Table 3. PCA+ Forward Selection+ K-NN Performance metric values calculated from created models in the testing stage

Srbct tumor / Metrics	Ewing sarkomu (EWS)	Burkitt lenfoma (BL)	Nöroblas tom (NB)	Rabdomiyo sarkom (RMS)
Accuracy	0.9625	0.9625	0.9506	0.9747
Precision	0.9310	0.8182	0.9444	0.9600
Sensitivity	0.9643	0.900	0.8500	0.9600
Specificity	0.9615	0.9714	0.9836	0.9815
F1-score	0.9474	0.8571	0.8947	0.9600
Matthews correlation coefficient (MCC)	0.9186	0.8369	0.8646	0.9415
G-mean	0.9629	0.9350	0.9144	0.9707

Accuracy values obtained from the dimension reduction model made with ICA on K-NN model; for EWS, BL, NB, and RMS type tumors with 91.89%, 90.67%, 88.31% and 89.47% respectively. In this model, the highest precision and specificity values were obtained in the RMS subclass, the highest sensitivity, F1-score, MCC and G-mean values were obtained from the EWS type tumor subclass (Table 4).

Table 4. ICA+ K-NN Performance metric values calculated from created models in the testing stage

Srbct tumor / Metrics	Ewing sarkomu (EWS)	Burkitt lenfoma (BL)	Nöroblastm (NB)	Rabdomiy osarkom (RMS)
Accuracy	0.9189	0.9067	0.8831	0.8947
Precision	0.8621	0.6364	0.7778	0.8800
Sensitivity	0.9259	0.7000	0.7368	0.8148
Specificity	0.9149	0.9385	0.9310	0.9388
F1-score	0.8929	0.6667	0.7568	0.8462
Matthew's correlation coefficient (MCC)	0.8291	0.6135	0.6803	0.7676
G-mean	0.9204	0.8105	0.8283	0.8746

Accuracy values obtained from the dimension reduction model made with ICA+ Forward Selection on K-NN model; for EWS, BL, NB, and RMS type tumors with 93.51%, 91.14%, 92.31% and 94.74% respectively. In the model created with ICA + Forward Selection + K-NN, the highest precision value was obtained in the EWS type tumor subclass, the highest specificity value in the BL type tumor subclass, and the highest sensitivity,

F1-score, MCC and G-mean values were obtained from the RMS type tumor subclass (Table 5).

Table 5. ICA+ Forward Selection+ K-NN Performance metric values calculated from created models in the testing stage

Srbct tumor / Metrics	Ewing sarkomu (EWS)	Burkitt lenfoma (BL)	Nöroblastom (NB)	Rabdomiyosarkom (RMS)
Accuracy	0.9351	0.9114	0.9231	0.9474
Precision	0.8966	0.8182	0.8333	0.8800
Sensitivity	0.9286	0.6429	0.8333	0.9565
Specificity	0.9388	0.9692	0.9500	0.9434
F1-score	0.9123	0.7200	0.8333	0.9167
Matthews correlation coefficient (MCC)	0.8611	0.6751	0.7833	0.8799
G-mean	0.9337	0.7894	0.8898	0.9499

Discussion

Although rare in childhood, cancer is still a major cause of death in children. In developed countries, only 0.5% of cancers occur in children under the age of 15 (16). Due to the long life expectancy in childhood and high treatment success rates in these cancers, cancers seen in childhood deserve special attention (17). Although the prognosis in childhood malignant soft tissue tumors mostly varies depending on the extent of the disease at the time of diagnosis, the region of origin of the tumor and the type of treatment chosen, the diagnosis and histological type of the tumor determine the patient's morbidity and mortality (18). Small round blue cell tumor, one of the childhood tumors, is a neoplasia with well-defined features in recent years. This malignant tumor, which shows a very aggressive course, is mostly observed in the adolescent age group and young adults (19). Despite aggressive multimodal treatment, median survival ranges from 17 to 25 months, with fewer than 20% of patients achieving 5-year survival (20).

Gene expression data obtained by microarray technology generally contain a large number of gene information belonging to a small number of patients. These data sets, which can be defined as high-dimensional for the methods used in data mining, reduce the model performance during the modeling phase. For this purpose, the performance of the classification models used is increased by obtaining genes with distinctive characteristics for the disease by performing dimension reduction analyzes before performing classification analyzes in gene expression data and the results obtained can be interpreted more easily (21).

In this study, the effects of PCA, ICA and PCA + Forward Selection, ICA + Forward Selection methods, which are among the dimension reduction methods on the open access gene expression data set of small round blue cell tumor types, on the K-NN classification method were examined and the results were compared.

In a study in the literature, after dimension reduction with PCA + Discrete Wavelet Transform (DWT) in the srbct gene expression data set, K-NN and Support Vector Machine (SVM) methods were used for classification. Accuracy rates were 92.73% for K-NN and 94.86% for SVM, respectively. When the results of this study in the literature are compared with the current study, it can be said that the model created with the proposed method, PCA + Forward Selection + K-NN method, is more successful in classifying the srbct gene expression data set (22).

When the results are compared, it can be said that the model established with PCA + K-NN has higher performance than the model established with ICA + K-NN. It is seen that the selection of variables with forward selection after PCA and ICA increases the model performance. The model that best predicts these four tumor types among all created models is the model established with PCA + Forward Selection + K-NN.

Conclusion

As a result, feature selection and feature extraction methods increase the prediction performance of machine learning methods by reducing the computational cost for gene expression data.

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Evaluation of The Relationship Between Apelin 36 and Oxidative Stress in Patients with General Anxiety Disorder

Ilkay Bahceci [1(ID)], Umut Serkan Soztanacı [2(ID)] , Meltem Pusuroglu [3(ID)] ,Nuray Arslan [1(ID)] , Omer Faruk Duran [1(ID)] , Bulent Bahceci [3(ID)] , Zihni Acar Yazici [1(ID)]

[1] Department of Medical Microbiology, Faculty of Medicine, Recep Tayyip Erdoğan University, Rize, Turkey
[2] Department of Anatomy, Hamidiye Faculty of Medicine, Health Sciences University, Istanbul,Turkey
3. Psychiatry Department, Medical Faculty Hospital, Recep Tayyip Erdogan University, Rize, Turkey

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Abstract

Objective: The aim of this study was to evaluate the relationship between apelin-36 and oxidative parameters and Generalized Anxiety Disorder (GAD). Apelin which prevents hippocampal neuronal death is an endogenous ligand for G protein bound APJ receptors in the central nervous system. Oxidative Stress were occurred by free radicals which caused apoptosis in the hypothlamus, hippocampus and amygdala regions of the Central Nervous System (CNS).

Methods: In this study, 61 patients diagnosed generalized anxiety disorder at psychiatry polyclinic and 55 control subjects were enrolled. The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and the Hamilton Anxiety Rating Scale (HARS) were used in this study and they were filled by the patients and healthy individuals. Serum apelin-36 level was measured by using an ELISA kit. Total antioxidant status (TAS) and Total Oxidant Status (TOS) in the serum was measured by an automated system. The data were analyzed by using the SPSS.

Results: It was found that serum apelin-36, TOS and Oxidative stress index (OSI) levels were significantly lower in patients' group than controls. In addition, negative correlation was detected between apelin 36 levels and HARS scores, TOS and OSI values in patients' group. TAS values were found as similar between the patient and control group. There was no correlation between TAS and Apelin 36 in the patient group.

Conclusion: In this study it was found that serum apelin-36, TOS and OSI levels were low in GAD. According to the results, Apelin-36 and oxidative stress may play a role in the etiopathogenesis of Generalized Anxiety Disorder.

Key words: Apelin-36, Generalized Anxiety Disorder, Oxidative Stress, Total Antioxidant Status, Total Oxidant Status

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Address for correspondence/reprints:

Ilkay Bahceci

Telephone number: +90 (464) 223 61 26

E-mail: mdilkaybahceci@gmail.com

Introduction

Generalized anxiety disorder (GAD) is a psychiatric disorder that significantly decreased the quality of life. The excessive fear and worry about the different life events which persist throughout the day are the clinical symptoms of the disease which happened on almost every day. Its annual prevalence is 3-8%. GAD usually begins at twenties and 30% of GAD referrals take place during this period.

The presence of other comorbid psychiatric diseases such as depression is 81% of GAD patients may cause misdiagnosing and decrease the rate of GAD diagnosis

The etiopathogenesis of GAD has not been completely understood yet (1). Neurobiological studies have shown that the level of proinflammatory cytokines is positively correlated with anxiety level (2).

It was determined that neuronal death occurred due to apoptosis based on chronic stress as a result of decreased level of anti-apoptotic protein Bcl-2 in neurons (3).

Magnetic resonance imaging studies have also showed pathological changes in brain regions such as amygdala, hippocampus and hypothalamus (4).

Apelin is a peptide that was firstly purified from bovine stomach tissue extracts. It is synthesized primarily as Pre-pro-apelin which is 77-amino acid in length. Subsequently, it breakdowns into apelin-13, 17 and 36 forms which had similar bioactivity and action as proteolytically. Apelin performs its function in the central nervous system by binding the G protein-coupled APJ receptor (5,6).

In some studies, it has been shown that apelin 36 reduces hippocampal neuronal death due to cerebral edema and infarcts more effectively than apelin-13 (7-10).

The effects of apelin peptides in the cardiovascular and endocrinological diseases in humans and animals have been studied but the roles in psychiatric diseases have been investigated to a limited extent (11-18).

Oxidative stress occurs by the accumulation of free radicals in cells due to imbalance between oxidants and anti-oxidants. Free radicals reduce synaptic plasticity, increase proinflammatory cytokine secretion and induce apoptosis in the hippocampus, amygdala and hypothalamus (19).

There are no studies investigating the contribution of the relationship between apelin-36 and oxidative stress in GAD etiopathogenesis.

The aim of this study is to investigate the role of oxidative stress and apelin-36 in the etiopathogenesis of GAD.

Methods

Participants:

This study was carried out in the outpatient psychiatry clinic of Recep Tayyip Erdoğan Education and Research Hospital. The study was approved by the Ethics Committee of the Medical School (Decision No: 2016/96, Date: 21/10/2016). The study included 61 patients, who were admitted to the outpatient clinic, and 55 healthy individuals, who were hospital staffs.

Voluntary informed consent form was signed by the patients and controls.

Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), Hamilton Anxiety Rating Scale (HARS) and sociodemographic data forms were filled by all the individuals themselves.

Individuals who were smoking, using alcohol and drug who had chronic diseases and were pregnancy excluded from the study. Their Body Mass Index ranged between 18.5 and 24.9. Individuals have psychiatric diseases in the control group are excluded and there were no psychiatric diseases except the GAD in the patient group.

Blood Samples:

After overnight fasting, 5 ml peripheral blood was drawn and then was centrifuged at 4000 rpm/5 min. and serum was stored-frozen at -20 °C until usage. Serum apelin-36 level was measured by using an ELISA kit (AP 36 test kit, Cloud-Clone Corp., Houston, USA). Sensitivity of the test is reported as <2.52 pg/mL, according to the manufacturer's protocol. The absorbance was determined at 450 nm with a microtiter plate reader (Multiskan GO, Thermo Scientific, Waltham, MA, USA) within 5 minutes.

Levels of apelin were measured by the standard curve created by Titri ELISA software. The standard curve was then used to convert the absorbance values to apelin-36 concentration.

Measurement of total antioxidant status (TAS):

TAS in the serum was measured by an automated system. The assay measure anti-oxidative effect against free radical in the serum. The results were expressed as mmol Trolox Eq/L (20).

Measurement of total oxidant status (TOS):

Serum TOS was measured by the automated method of Erel. The results are expressed as micromolar hydrogen peroxide equivalent per liter (μmol H2O2Equiv/L) (20).

Oxidative stress index (OSI):

OSI (Arbitrary unit) = TOS (mmol H2O2 Equiv.L-1)/ TAS (mmolTroloxEq/L) (20).

Evaluations of Tests:

The sociodemographic data form designed by the investigators, which was contained information for age, gender, place of residence, marital status, education level and income status (low:<500 euro,

medium:501-1500 euro, high:>1501 euro) were fulfilled by participants.

The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) was developed by First et al. in 1997 (21). The validity and reliability studies for the adaptation of the SCID-I were performed by Corapcioglu et al. in 1999 (22). The Hamilton Anxiety Rating Scale (HARS) was developed by Hamilton in 1959, which contains 14 questions that query mental and physical symptoms (23).

Each item is rated on a five-point Likert-type scale ranging from 0 to 4. It determines the level of anxiety and symptom distribution in patients. The validity and reliability study of the Turkish version of the scale was conducted by Yazici et al. in 1998 (24).

Statistical analysis

Statistical data were analyzed by using SPSS version 18.0. (SPSS Inc., Chicago, IL, USA).

Normal distribution of continuous variables was tested with Kolmogorov-Smirnov test.

Between-group comparisons with normal distribution values were tested by the student's-test.

Chi-square test was used for the comparisons of categorical variables. Correlation analysis was performed by using the Pearson correlation coefficient. Data is expressed as mean±standard deviation (SD). The significance level was determined as $p< 0.05$.

Results

Age and gender distribution were found similar between patient and control groups, respectively, in terms of age (30.86±7.61, range 24-49, and 32.86±5.25, range 23-51, p=0.342) and gender (37 F/24 M and 32 F/23 M, p=0.232) (Table 1).

Also,distribution of the place of residence, marital status, education level and income status were found similar between the patient and control groups, respectively (p=0.543, p=0.212, p=0.303, p=0.123) (Table 1).

There was a statistically significant difference between the two groups in terms of the HARS scores. The scores of the patient group were higher than the control group (23.46 ±4.10 and 3.86±1.69, respectively, ($p\leq0.01$) (Table 2).

The serum apelin-36 levels were statistically significantly lower in the patient group than control group. Levels were measured as 363.83±21.07 pg/ml and 1050.93±51.35pg/ml, respectively, ($p\leq0.01$) (Table 2 and Figure 1).

Table 1. Sociodemographic Data of Patients and Controls

Parameters		Patient (n=61)	Control (n=55)	p
Age (range)		30.86±7.61(24-49)	32.86±5.25(23-51)	0.342
Gender (F/M)		37/24	32/23	0.232
Place of residence	City Village Town	36 20 13	32 17 6	0.543
Marital status	Single Widow(er) Divorcee	38 21 2	34 19 2	0.212
Education level	Primary Middle High	10 37 14	7 35 13	0.303
Income level	Low Medium High	15 38 8	13 35 7	0.123

Table 2. Parameters measured and outcomes

	Patient	Control	p
HARS*	23.46±4.10	3.86 ±1.69	0.000
Apelin 36 (pg/ml)	363.83±21.077	1050.93±51.35	0.000
TAS* (mmol Trolox Eq/L)	1.39+0.81	1.32+0.20	0.721
TOS* (mmol H_2O_2 Equiv./L)	44.52+0.28	10.02+0.97	0.005
OSI* (arbitrary unit)	3.92+6.17	0.78+0.44	0.005

*Abbreviations: HARS (Hamilton Anxiety Rating Scale), TAS (Total Antioxidant Status), TOS (Total Oxidant Status), OSI (Oxidative Stress Index)

Table 3. The correlation of TAS, TOS, OSI and HARS scores with apelin 36 levels in patients

	Apelin 36	
	r	p
HARS*	-0.737	0.000*
TAS*	-0.126	0.233
TOS*	-0.443	0.026*
OSI*	-0.374	0.043*

Pearson correlation, p<0.05.
*Abbreviations: HARS (Hamilton Anxiety Rating Scale), TAS (Total Antioxidant Status), TOS (Total Oxidant Status), OSI (Oxidative Stress Index)

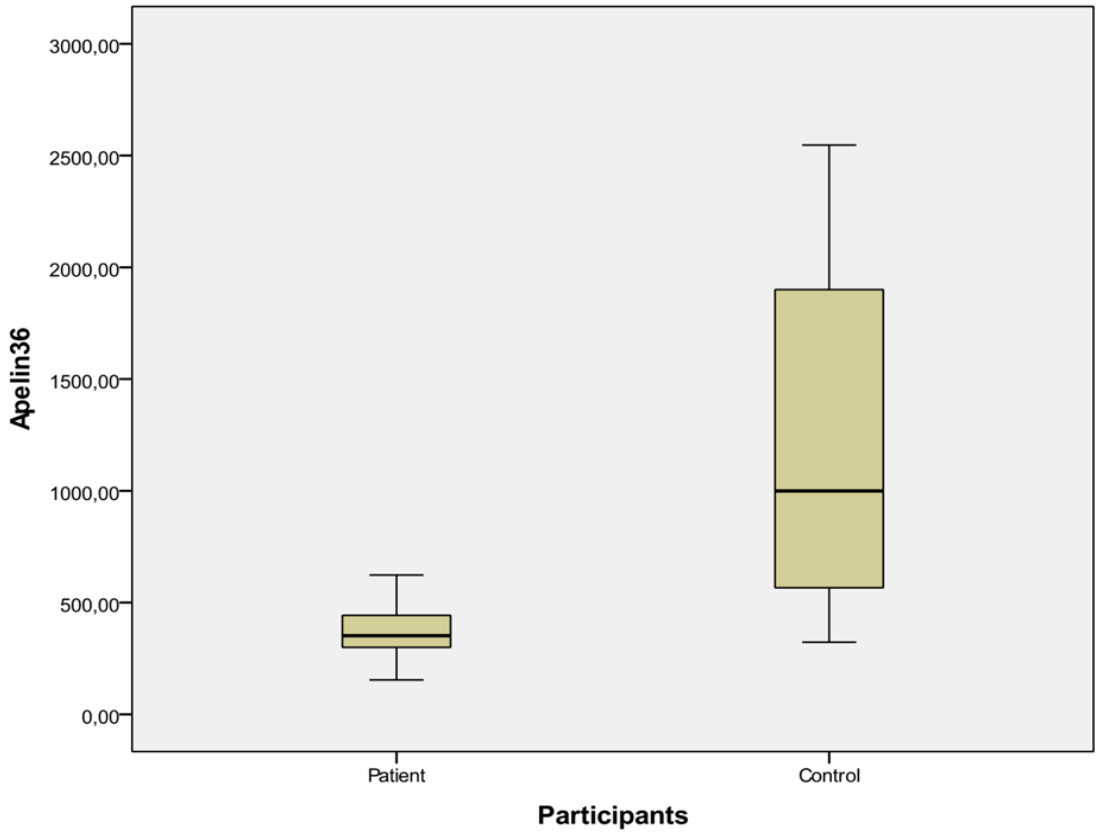

Figure 1. The distribution of apelin-36 levels (pg/ml) in the patient and control groups

While there were no significant difference between patient and control groups for TAS levels, which were1.39+0.81 and 1.32+0.20(p=0.721), respectively, the levels of TOS and the OSI were detected significantly higher in the patient group(These values were, respectively, 44.52+0.28, 10.02+0.97 ($p\leq0.01$) ; 3.92+6.17, 0.78+0.44,($p\leq0.01$) (Table 2).

In the patient group, while there was a strong negative correlation between the serum apelin-36 levels and the HARS scores (r=-0.737, p=0.000), correlation was not found between TAS and apelin 36(r=-0.126, p=0.233). TOS and OSI were negatively correlated with apelin 36 (r=-0.443, p=0.026; r=-0.374, p=0.043, respectively) (Table 3).

Discussion

There have been recent studies on investigating the role of oxidative stress and biomarkers in the etiopathogenesis of GAD. However, the precise causes have not been identified yet.

Therefore, we investigated the relationship between apelin-36 levels, oxidative stress and GAD patients in this study.The serum apelin-36 levels of the patients with GAD were compared with the healthy controls among with their respective HARS, TAS, TOS, and OSI scores.

The role of oxidative stress biomarkers in the etiopathogenesis of psychiatric disorders including GAD has been studied in previous studies. Ercan et al, showed that prolidase levels were elevated in GAD patients (25). It has been showed that molecules like prolidase, malondialdehyde, superoxide dismutase, and nitric oxide play role in the development of psychiatric conditions including schizophrenia, depression, obsessive-compulsive disorder, and adult attention-deficit hyperactivity disorder (26-30).

In this study, serum apelin-36 levels were found significantly lower in the patient group than the control group. Moreover, there was also a strong negative correlation between the serum apelin-36 levels and the HARS scores in the patient group. In some studies, GAD has been shown to be associated with a proinflammatory response. The detection of inflammatory cytokines such as IL-1, IL-6 and TNF-α in the hippocampus and amygdala indicates that they may play a role in etiopathogenesis (2,4). Apelin has been shown to inhibit the secretion of these cytokines in the same regions of the brain (7-10). In addition to its anti-pro-inflammatory cytokine effect in the brain, apelin was shown to have a neuroprotective effect by preventing neuronal apoptosis observed in patients with GAD (3,8).

Previous studies evaluating the relationship between apelin, and psychiatric diseases have focused on the sub-unit of apelin-13 (12-18). In these studies, it was reported that apelin-13 level was low in autism and may play a role in the etiopathogenesis of ADHD (13). In addition, apelin administered to mice has been shown to have anti-depressive and anxiolytic effects (14-18). No study has been found in the literature investigating the role of apelin 36 in the etiopathogenesis of generalized anxiety disorder.

It is probably that apelin prevents apoptotic processes in neuronal cells by inhibiting the release of anxiogenic and inflammatory cytokines. Therefore, apelin may have a role in the etiopathogenesis of generalized anxiety disorder. Therefore, further studies are needed to clarify the role and the relation of Apelin in GAD.

The envelope phospholipid integrity of neurones in the cortical regions, including amygdala and the hippocampus, is impaired by the accumulation of free radicals and / or the lack of anti-oxidants. These alterations affect the density and functions of catecholamine receptors such as GABA and serotonin / dopamine / noradrenaline which play a role in the pathophysiology of GAD (31-32). In addition, it can also mask serotonin binding sites of the receptor, and thus may play a role in the etiopathogenesis (33).

In this study, even though TAS was similar in both groups, TOS and OSI values were significantly higher in patients. Cenk et al, also reported that it was found similar TAS levels in GAD patients and controls. However, Emhan et al, reported that higher levels of TAS was found in GAD patients than controls (25,34). In both studies, TOS and OSI were like ours. According to these results, inflammatory cases characterized by free radical accumulation may play a role in the etiology of GAD.

Apelin and its receptors are commonly found in the structures organizing stress response such as hypothalamus, hippocampus, and amygdala (8-10). Apelin inhibits the inflammatory response by decreasing release of cytokines such as IL-1, IL-6 and TNF-α in these brain regions. Some studies have shown that apelinergic system protects neurons by preventing apoptosis and improves behavioral performance (7-10).

Free radicals cause apoptosis in the hypothalamus, hippocampus, and amygdala regions of the CNS by disrupting synaptic plasticity, stimulating / increasing inflammatory cytokine release, and triggering pre-apoptotic signaling (19).

This study also demonstrated a negative correlation between TOS and OSI and apelin-36. However, no correlation was found between TAS and

apelin-36. Despite it has a potent bioactivity in neuronal protection, the role of apelin-36 in the etiopathogenesis of GAD has not been investigated so far. The small number of participants in the study and the fact that inflammatory cytokine and apelin-36 levels were not measured before and after treatment are the limiting factors.

Conclusion

According to the results of this study it could be taken into consideration that free radical accumulation and low apelin-36 may play a role in the etiopathogenesis of GAD.

Ethics Committee Approval: This study was conducted with approval from our faculty of medicine ethics committee (Report no: 2016/96)
Peer-review: Externally peer-reviewed.
Author Contributions:
Concept: IB, USS, BB, *Design:* MP, NA, OFD, *Literature search:* IB, MP, BB *Data Collection and Processing:* USS, NA, OFD, *Analysis or Interpretation:* MP, IB, USS, *Writing:* IB, BB, ZAY
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The Role of the Integrated Pulmonary Index in Determining Respiratory Complications in Patients Undergoing Upper Gastrointestinal Endoscopy Under Sedation

Leyla Kazancıoğlu[1(ID)], Şule Batçık[1(ID)]

[1]Department of Anaesthesia and Reanimation, Faculty of Medicine, Recep Tayyip Erdogan University Rize, Turkey

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Abstract

Objective: In this study, we aimed to evaluate the respiratory complications defined by the Integrated Pulmonary Index (IPI) in patients with comorbid risk factors who underwent Upper gastrointestinal endoscopy (UGE) under sedation.

Methods: This cross-sectional, prospective study was conducted with 157 patients, aged over 18 years, in our endoscopy unit between July 2020 and December 2020. Patients' demographic data, body mass index (BMI), ASA class and comorbidities were recorded. The mean arterial pressure (MAP), and HR, RR, SpO2, EtCO2 for the IPI were measured as baseline values and 5 minutes of the procedure and compared between two groups as the patients who developed (Group I) and did not develop (Group II) complications.

Results: The mean BMI value was statistically significantly higher in Group I compared to Group II ($p<0.001$). The mean HR was statistically significantly higher and IPI score significantly lower in Group I than in Group II before the procedure ($p=0.013$, $p=0.01$; respectively). The mean SpO2, EtCO2 and IPI values were statistically significantly lower in Group I compared to Group II at 5 minutes of the procedure ($p=0.001$, $p=0.004$, $p=0.010$; respectively). The frequency of comorbidities was statistically significantly higher in Group I. In the logistic regression analysis, BMI value was found as an independent factor affecting the development of respiratory complications.

Conclusion: The mean IPI scores dropped significantly in patients who developed complications, mainly due to the decreases in EtCO2 and SpO2 values at 5 minutes of the procedure. BMI was determined as a risk factor for the development of respiratory complications. IPI monitoring can provide guidance during sedation of patients with comorbid diseases undergoing UGE.

Key words: Anesthesia, endoscopy, integrated pulmonary index, respiratory complications, monitoring

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Address for correspondence/reprints:

E-mail: leyla.kazancioglu@erdogan.edu.tr

Leyla Kazancioglu

Telephone number: +90 464 212 30 09

Introduction

Upper gastrointestinal endoscopy (UGE), also known as esophagogastroduodenoscopy (EGD), is an prominent procedure performed for screening, diagnosis and treatment of various GI diseases, demand for which is consistently increasing (1, 2). Diagnostic indications for UGE vary in a wide spectrum from persistent upper abdominal pain to chronic symptoms of gastroesophageal reflux disease (GERD), alarming symptoms such as anorexia, and surveillance for malignancy, while therapeutic indications may include removal of a foreign body, upper GI bleeding control and placement of draining or feeding tubes (3). Over 1.2 million diagnostic and therapeutic UGE procedures were performed in the United Kingdom in 2016 (4).

Although UGE can be performed without sedation, today the majority of UGE procedures are performed while the patient is sedated (5). Sedation can significantly increase cooperation and satisfaction of patients and help them to more easily undergo subsequent endoscopies by decreasing vomiting, gag reflex and dizziness (6, 7). However, especially the patients undergoing UGE under sedation should be assessed for comorbid risk factors that increase sensitivity to sedative medications, including chronic pain; advanced chronic lung disease; pulmonary hypertension; coronary artery, liver, or renal diseases; obstructive sleep apnea and anxiety disorders (8).

On the other hand, it is well known that although rare, various respiratory complications can occur in UGEs performed under sedation. Adverse respiratory events seen in UGE procedures range from minor complications such as changes in oxygen saturation to significant major complications, including respiratory arrest (9). It has been that oxygen saturation fell below 90% in 57% of the patients (19) and that short-term mask ventilation may be required in 0.4% of patients and endotracheal intubation in 0.09% of patients, especially during UGE procedures (11). Many guidelines recommend monitoring of basic vital parameters such as oxygen saturation, heart rate and blood pressure sedation applications for UGE (12, 13).

The Integrated Pulmonary Index (IPI™, Medtronic, Dublin, Ireland) combines four parameters such as ventilatory frequency (VF), EtCO2, pulse rate (PR) and SpO2 into one unitless score between 1 and 10 for real-time monitoring of vital parameters (14). This numerical value provides a quick assessment of the patient's clinical condition.

The correlation between IPI respiratory physiological parameters in patients undergoing surgery and colonoscopy has been reported (15, 16). However, there is only limited evidence on its role and usefulness in other clinical situations, including upper GI endoscopy. Therefore, in this study, evaluation of the respiratory complications defined by IPI in patients with comorbid risk factors who underwent UGE under sedation was aimed.

Methods

Study Design and Patients

Our study was designed as a cross-sectional, prospective study and conducted in the endoscopy unit of our hospital between July 2020 and December 2020. Patients aged over 18 years with physical status classified as ASA II-III according to the American Society of Anesthesiologists (ASA) guidelines were included in the study.

Patients aged under 18 years, those with ASA III-IV; patients with hypoxemia (SpO2≤ 90%), bradycardia (heart rate < 50 bpm) or hypotension (systolic blood pressure < 90 mmHg) before the procedure, pregnant patients and those without written consent were excluded from the study.

Data Collection

The UGE procedures were performed under sedation with propofol or fentanyl. Patients' demographic data such as gender and age body mass index (BMI), ASA class, doses of anesthetic agents used, procedure duration, presence of chronic obstructive pulmonary disease, diabetes mellitus (DM), hypertension (HT), ischemic heart disease (IHD), obesity and smoking status were recorded. Respiratory failure and the need for mask ventilation occurring during the procedure were monitored. The patients were evaluated in two groups as those who developed respiratory complications during the procedure (Group I) and the patients who did not develop respiratory complications (Group II).

All patients were monitored with standard electrocardiogram, non-invasive arterial blood pressure and administered 2 L/min oxygen via a nasal cannula with a port from which the exhaled CO2 content could be sampled. In addition, the patient was also monitored with the IPI index that integrates time-based CO2 graphic waveform via CO2 sampling line, end-tidal CO2 pressure (EtCO2; mmHg), respiratory rate (RR; breaths per minute), and pulse rate via an integrated pulse oximeter (SpO2). The IPI index incorporates these four parameters into one score between 1 and 10 as seen in Table 1.

Table 1. The Integrated Pulmonary Index (IPI) scoring system

IPI Scores	Patient Status
10	Normal
8-9	Within normal range
7	Close to normal range, requires attention
5-6	Requires attention and may require intervention
3-4	Requires intervention
1-2	Requires immediate intervention

IPI scores were obtained using a portable bedside monitor (Capnostream 20; Oridion Medical, Needham, MA, USA). Heart rate (HR) and peripheral oxygen saturation (SpO2) values were recorded by using an integrated pulse oximeter (Nellcor, Covidien, Boulder, CO, USA). The mean arterial pressure (MAP), and HR, RR, SpO2, EtCO2 for the IPI were measured as baseline values and 5 minutes of the procedure. The data obtained were compared between the two groups.

The primary outcome of the study was the difference between baseline and 5 minutes SpO2, EtCO2 and IPI values in the patients who experienced respiratory complications during the procedure (Group I) and the patients who did not experience respiratory complications (Group II).

Sedation Procedure

IV cannulation was carried out for sedation in patients who will undergo diagnostic UGE without premedication. The induction dose for sedation was administered with fentanyl 1 mcg/Kg (Talinat® 0.5 mg/10 mL ampul, VEM, Istanbul, Turkey) or propofol 0,5- 1 mg/Kg (Propofol® 1% 10 mL ampul, Fresenius, Uppsala, Sweden), and 10 or 20 mg propofol bolus doses were added with titration, when deemed necessary. The starting dose was 0.5-1 mg/kg and if needed 10-20 mg bolus doses were added. The patients were clinically monitored by an independent anesthesiologist throughout the procedure. Based on standard monitoring parameters and clinical observation, SpO2 < 92% and/or RR ≤ 8,20 % decrease in EtCO2 from baseline value and loss of spontaneous breathing for more than 60 seconds were considered respiratory complications. In the case of respiratory complications, the following actions were carried out: (1) patient stimulation, (2) cessation of the IV drug, (3) chin lift and jaw thrust maneuver, (4) increasing the oxygen supply, and in case of necessity (5) endotracheal intubation.

Statistical analysis

The data obtained in this study were statistically analyzed using SPSS for Windows version 22.0 (SPSS, Statistical Package for Social Sciences, IBM Inc., Chicago, IL, USA). Normality of the variables was analyzed with Kolmogorov-Smirnov test. Continuous variables are explained as mean±standard deviation or median, and categorical variables as frequency and percentage. The independent samples t test was used for the comparison of numerical data between independent groups. Logistic regression analysis was used to eliminate possible interactions of parameters that may affect respiratory complications. $p<0.05$ values were considered statistically notable.

The sample size was calculated as 150 by using the G*Power 3.1.9.7 software with 84% power, the effect size as 0.50 and $\alpha=0.05$.SPSS software (SPSS, Inc., Chicago, IL, USA).

Results

A total of 164 patients undergoing UGE under sedation were included in the study. Four patients with missing data and three patients who left were excluded from the study. Finally, the study was completed with 157 patients. The patients were divided into two groups according to development of respiratory complications as Group I (53 patients with complications) and Group II (104 patients without complications). The mean age was found as 62.64±8.01 years in Group I and 62.82±10.8 years in Group II. The female/male ratio was found as 30/23 in Group I and 46/48 in Group II. No statistically notable disparity was found between the two groups in terms of gender and age (both $p>0.05$). The mean BMI value was statistically notably higher in Group I compared to Group II ($p<0.001$) (Table 2).

The mean MAP and IPI parameters including HR, RR, SpO2 and EtCO2, and IPI scores were measured before the procedure and at 5 minutes of the procedure. The mean HR was statistically significantly higher and IPI score was notably lower in Group I than in Group II before the procedure ($p=0.013$, $p=0.01$; respectively). The mean SpO2, EtCO2 and IPI values were statistically significantly lower in Group I compared to Group II at 5 minutes of the procedure ($p=0.001$, $p=0.004$, $p < 0.001$; respectively). There was no notable disparity between the two groups in terms of the other parameters before

the procedure and at 5 minutes (for all p>0.05) (Table 3).

Table 2. Demographic features and endoscopic data of the patients

	Group I (n=53, 34%)	Group II (n=104, 66%)	p values
Gender F/M, n	30/23	46/48	0.142**
ASA II/III, n	30/23	59/45	0.988**
Age (years)	62.64±8.01	62.82±10.8	0.917*
BMI (Kg/m2)	32.87±6.46	27.77±3.66	**<0.001***
Operation time (min)	10.20±4.92	10.55±4.74	0.155*
Propofol dose (mg)	100.57±32.72	105.48±27.33	0.321*
Fentanyl dose (µgr)	46.70±18.37	46.17±19.07	0.864*

ASA: American Society of Anesthesiologists; BMI: Body Mass Index
*Independent samples t test; **Pearson's Chi-square test

Comorbidity status of the groups was analyzed (Figure 1). Accordingly, the frequency of COPD (43% vs 24%), obesity (47% vs 20%) and having risk factors ≥2 (60% vs 30%) were found to be statistically notably higher in Group I compared to Group (II) (p=0.01, p<0.01, p<0.01; respectively).

The IPI values were statistically notably lower in Group I patients with comorbidities compared to Group II patients with comorbidities at 5 minutes of the procedure (for all p<0.05) (Table 4).

Table 3. IPI scores, IPI parameters and MAP values before the procedure and at 5 minutes

Parameter	Time	Group I	Group II	p
HR (bpm)	baseline	83.47±15.67	76.98±14.23	**0.013**
MAP (mmHg)	baseline	102.87±18.67	101.38±19.61	0.642
SpO_2 (%)	baseline	96.42±2.72	97.10±2.1	0.167
RR (breaths per minute)	baseline	20.51±5.18	19.37±4.55	0.176
$EtCO_2$ (mmHg)	baseline	32.06±6.5	33.03±5.02	0.343
IPI	baseline	8.09±2.03	8.90±1.23	**0.010**
HR (bpm)	5 minutes	78.00±15.031	75.19±12.92	0.225
MAP (mmHg)	5 minutes	92.74±18.472	89.20±20.23	0.288
SpO_2 (%)	5 minutes	91.75±2.80	96.14±2.608	**0.001**
RR (breaths per minute)	5 minutes	17.94±6.386	17.87±4.752	0.938
$EtCO_2$ (mmHg)	5 minutes	28.17±8.982	32.18±5.961	**0.004**
IPI	5 minutes	4.36±0.901	8.65±1.077	**<0.001**

HR: Heart Rate, MAP: Mean Arterial Pressure, SpO2: Peripheral Oxygen Saturation, RR: Respiratory Rate, EtCO2: End-tidal Carbon Dioxide, IPI: Integrated Pulmonary Index (Independent Samples t Test)

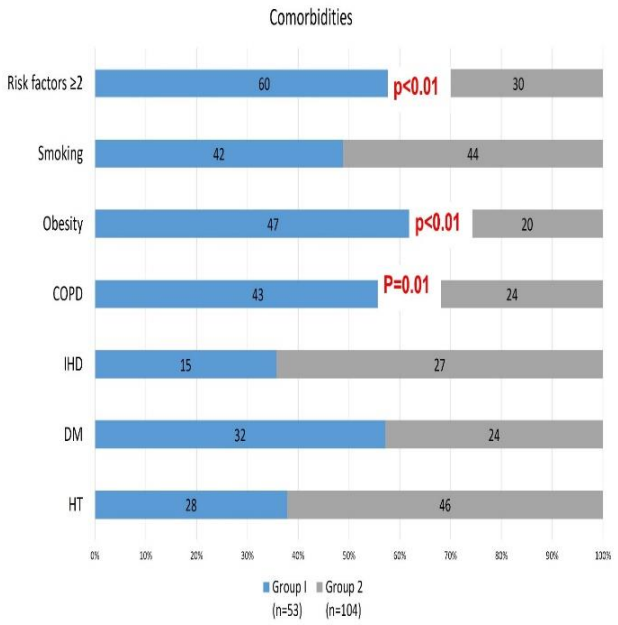

Figure 1. Frequency distribution of comorbidities between the groups

Figure Footnote:COPD: Chronic Obstructive Pulmonary Disease, IHD: Ischemic Heart Disease, DM: Diabetes Mellitus, HT: Hypertension. Chi-square test was used for the comparisons.

Table 4. IPI scores at 5 minutes of the procedure in patients with comorbidities

	IPI VALUES (5 MINUTES)		
	Group I	Group II	p
	mean ± SD	mean ± SD	
HT	4.50±0.63	8.71±1.06	**<0.001**
DM	4.00±0.86	8.68±1.03	**0.001**
IHD	4.50±0.76	8.79±1.07	**<0.001**
Smoking	4.59±0.67	8.46±1.90	**<0.001**
COPD	4.44±0.78	8.67±1.11	**<0.001**
Obesity	4.28±0.90	8.67±1.11	**<0.001**
Risk Factors ≥2	4.38±0.80	8.66±1.10	**<0.001**

COPD: Chronic Obstructive Pulmonary Disease, IHD: Ischemic Heart Disease, DM: Diabetes Mellitus, HT: Hypertension.
Mann-Whitney U test was used for the comparisons.

A logistic regression analysis was performed to determine the factors affecting respiratory complications during UGE under sedation. Age, BMI, smoking, HT, DM, IHD and COPD variables were included in the analysis. As a result, BMI value was found as an independent factor affecting the

development of respiratory complications (OR:1,274; 95% CI: 1,159-1,400; p<0.05).

Discussion

Upper GI endoscopy procedures under sedation have been associated with minor complications such as decreased oxygen saturation and heart rate. Hypoxia during UGE is a well-known complication. The incidence of hypoxia related to endoscopic sedation has been reported between 6–18% depending on the drug and dosage (17). In addition, changes in respiratory rate and end-tidal carbon dioxide may also be seen. However, it is not exactly clear whether these complications are the result of sedation or the endoscopy procedure itself. In our study, we investigated the role and usefulness of the integrated pulmonary index (IPI), which incorporates four vital parameters into a unique score between 1 and 10, in UGE procedures performed in patients with comorbidities who underwent UGE under sedation. Procedure time were similar between the group of patients who developed complications (Group I) and the group of those who did not develop (Group II).

Obesity (BMI ≥30 kg/m2) has been associated with reduced oxygen saturation and hypoventilation (18, 19). In our study, the mean BMI value was higher in the patients who developed complications (32.87 kg/m2 vs 27.77 kg/m2) during UGE, including a decrease in oxygen saturation. In addition, we found with the logistic regression analysis that BMI was an independent factor affecting the development of complications during UGE. In a study by Geng et al., BMI was found to be a useful predictor of hypoxia during GI endoscopy (20). In a retrospective study by Kilic et al. with 1,172 patients investigating the effects of obesity on sedation related complications, the rate of patients who developed desaturation <80% for 3 minutes during endoscopy procedures was found as 7.7% in patients with a BMI values of 25-30 kg/m2 and 14.7% in patients with a BMI value >30 kg/m2 (21). In another study by Wani et al., increasing BMI values were associated with increased frequency of airway maneuvers and hypoxia during advanced endoscopy procedures (22). In this context, our results were consistent with the literature.

The IPI is an algorithm that combines the benefits of ventilation monitoring and oxygenation monitoring and helps the medical team respiratory status of the patient looking at a single parameter. In our study, we used IPI scores to control respiratory events during UGE procedures under sedation and compared the IPI scores between patients who developed complications and those who did not. Based on standard monitoring parameters and clinical observation, patients with a SpO2< 92% and/or RR ≤ 8 and loss of spontaneous breathing for more than 30 seconds were considered to develop respiratory complications. In the patients with complications, the mean IPI score dropped to 4.36 at 5 minutes of the procedure from the baseline value of 8.09. In addition, the mean IPI scores were notably lower in the patients with complications compared to those without complications both at baseline and 5-minute values. In a study by Michael et al., standard monitoring was compared with standard monitoring + IPI scoring in patients undergoing percutaneous endoscopic gastrostomy under sedation. Capnography and IPI readings were recorded for all patients but were only viewable to the endoscopic staff in the standard monitoring group. the mean IPI was found as 8.82±1.62 in the standard group and 9.33±1.11 in the IPI group with no notable difference between them (p=0.06) (23). In another study by Veassen et al. the IPI value of patients undergoing UGE under sedation dropped to 8.89 ± 1.132 in the beginning of the endoscopy from 9.1±1.071 at the beginning of anesthesia induction (24). In a study by Yildirim et al. with ASA I-III patients undergoing cataract surgery under sedation, the mean IPI value was found as 8.84±1.86 at baseline and 8.1±2.48 at 5 minutes of the surgery with no significant difference (p=0.06) (15). However, these studies included no groups with and without complications. When all patients were evaluated in our study, the mean IPI value was found as 8.63±1.59 at baseline and 7.36±2.20 at 5th minute with statistically significant difference (p<0.000). We think that this difference is related to the high ASA groups of the patients included in our study.

There is no consensus on the effectiveness and usefulness of the IPI scoring in patients undergoing endoscopic procedures under sedation. In a study by Vaessen et al. evaluating IPI scores for the detection of respiratory events in patients undergoing UGE under sedation, it was reported that the use of IPI cannot be recommended in UGE, especially when CO2 was used (24). In another study by Berkenstadt et al., a limited agreement was found between respiratory physiological parameters and IPI scores (16).

In our study, the mean IPI scores were statistically significantly lower at 5 minutes of the procedure in patients with comorbidities who developed complications compared to those with comorbidities but who did not develop complications, suggesting that the presence of comorbidities did not affect IPI scores. In fact, the only factor affecting the

development of complications was found as BMI in the logistic regression analysis, supporting this opinion.

Recently, EtCO2 has been increasingly used in routine monitoring in operating rooms and intensive care units. It has been reported that EtCO2 monitoring is crucial especially during upper GI endoscopies (25). In our study, the mean 5th minute EtCO2 and SpO2 values were notably lower in the patients who developed complications (p=0.001, p=0.004; respectively), which may explain the lower IPI values at 5 minutes in these patients. In the present study also IPI values were affected by EtCO2 and SpO2, while the other two components, HR and RR did not significantly change at 5 minutes, raising questions about the utilization of the IPI. Hence, we believe that further more comprehensive prospective studies with a larger series of patients are needed to draw more definite conclusions.

Study Limitations

The main limitation of the ourstudy is the relatively small number of patients. In addition, standard monitoring could be statistically compared with the IPI scoring. Finally, the measurements were limited with baseline and 5th minutes. However, its prospective nature makes our study strong, and our results could be guiding for future prospective studies about UGE procedures that are limited in the literature.

Conclusion

IPI combines oxygenation and ventilation parameters, allowing a quick and easy assessment of patients' respiratory status. In this study, in which the ASA III-IV patient group was included, the mean IPI scores decreased significantly in patients who developed complications, especially due to the decreases in EtCo2 and SpO2 values at the 5th minute of the procedure. BMI was determined as a risk factor for the development of respiratory complications. IPI monitoring can offer guidance during sedation of patients with comorbid diseases undergoing UGE. Our results can contribute to the studies on this subject in the literature.

Ethics Committee Approval: This study was conducted with the approval of the ethics committee of Recep Tayyip Erdogan University Faculty of Medicine, Non-Invasive Clinical Research Ethics Committee. (Ethics Committee Approval Date:01.07.2020 Decision no: 2020/138)
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Outcomes of Microsurgical Clipping in Middle Cerebral Artery Aneurysms

Mehmet Secer [1](ID) Aykut Gokbel [2](ID)

[1]Department of Neurosurgery, Alaaddin Keykubat University School of Medicine, Antalya, Turkey.
[2]Neurosurgery Clinic, Derince Training and Research Hospital, Kocaeli, Turkey

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Abstract

Objective: Surgical or endovascular treatment is used in the treatment of intracranial aneurysms. Recent studies have suggested that the of endovascular treatment are superior to surgery Middle cerebral artery (MCA) aneurysm is the third most common bleeding aneurysm after anterior communicating artery and internal carotid artery aneurysms. We aimed to retrospectively evaluate the microsurgical outcomes of cases operated for MCA aneurysm.

Methods: Twenty cases with MCA aneurysm who accepted the microsurgical treatment option were included in this study. Data were obtained by retrospectively reviewing the clinical, radiological, and intraoperative findings, as well as postoperative morbidity and mortality of the cases.

Results: In total, 23 MCA aneurysms were detected in 20 cases. In 2 cases, MCA aneurysm was detected incidentally. Microsurgical clipping was performed in 23 aneurysms. In the study, the total mortality rate was 10% and the morbidity rate was 20% in MCA aneurysms.

Conclusion: It was observed that the incidence of calcification or thrombosis within the aneurysm increased and the Glasgow outcome scores at the 3rd month decreased as the width and length values of the aneurysm sac increased. In addition, presence of calcification in the aneurysm wall or thrombosis in the sac was found to be positive and strongly correlated with mortality and morbidity.

Key words: Middle cerebral artery, aneurysm, microsurgery

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Address for correspondence/reprints:

Mehmet Secer

Telephone number: +90 (505) 347 89 55

E-mail: memetsecer@yahoo.com

Introduction

Surgical or endovascular treatment is used in the treatment of intracranial aneurysms. Recent international studies have suggested that the outcomes of endovascular treatment are superior to surgery (1,2). However, microsurgical clipping is the first treatment option in most centers since middle cerebral artery (MCA) aneurysms have a wide neck and middle cerebral artery branches come out of the base or body of the aneurysm (2,3).

MCA aneurysms constitute 18%–36% of all intracranial aneurysms (3). It is the third most common bleeding aneurysm after anterior communicating artery and internal carotid artery

aneurysms (2). This study retrospectively evaluated the microsurgery results of 23 MCA aneurysms detected in 20 cases. Demographic findings, morphological structure of the aneurysm, calcification in the wall and thrombosis in the sac the effect of on outcome were evaluated.

Methods

We retrospectively evaluated consecutive cases operated for MCA aneurysm performed by a single surgeon (M.S). (Ethics committee number: 74-2021). Inclusion criteria for the study; rupture and non-rupture MCA aneurysm was detected and microsurgery was applied. Exclusion criteria were those who did not accept surgery for an MCA aneurysm and had endovascular treatment. Of the cases, 18 presented to the emergency department with symptoms of subarachnoid hemorrhage (SAH) that developed after rupture of the aneurysm. Incidental MCA aneurysm was detected on MRI in 2 patients who presented to the outpatient clinic with headache. In cases of SAH and incidental detection of MCA aneurysm, computed tomographic angiography and/or digital subtraction angiography were used to evaluate the morphology and location of the aneurysm (Fig. 1). We measured and recorded the largest width and height values of the aneurysm sac. Patients who presented following SAH were admitted to the intensive care unit.

Statistical analysis

Statistical analysis was performed using the SPSS version 25.0 for Windows (Armonk, NY: IBM Corp.). The normality of the distribution of the data was analyzed by the Shapiro Wilk test. The relationship between variables was evaluated using the Spearman correlation analysis. The results were presented as numbers (percentages) and mean ± standard deviation. Results with a p value less than 0.05 were considered statistically significant.

Results

The cases comprised 12 women and 8 men. The mean age was 53.2 ± 12.9, with the youngest and the oldest patient being 14 and 70 years old, respectively. The bilateral MCA aneurysm was found in 3 cases with SAH (Fig. 2). Morphologically; 17 aneurysms were small in size (smaller than 15 mm), one aneurysm was large (20 × 23 mm), 2 aneurysms had a giant size (48 × 34 mm and 30 × 34 mm) and partial thrombosis, and 2 aneurysm walls had calcified. Clinical, radiological, intraoperative findings, postoperative morbidity, and Glasgow outcome scale (GOS) at 3 months are shown in Table-1. Emergency surgery was performed in one patient with a large temporal hematoma. Other patients were operated under the earliest elective conditions to prevent the possibility of re-bleeding.

Surgical treatment:

ECG, invasive artery and central catheters were used in each patient for intraoperative anesthesia monitoring during aneurysm surgery. Pental was used for providing neuroprotection in cases where temporary clips were used. Surgery was performed in the form of classical pterional craniotomy in cases with thrombosed giant aneurysm and hematoma, and in the form of osteoplastic pterional craniotomy in uncomplicated cases. The patient was laid in the supine position and induced general anesthesia. Next, the head was fixed in a head holder and rotated approximately 30–45 degrees to the opposite side and a pterional skin incision was performed such that the malar eminence was in the uppermost position. The dura was opened with a C-shaped incision and toppled to the front side. Then, starting from the medial Sylvian fissure and leaving the vein group on the temporal side, dissection was performed from the frontal side to reach the internal carotid artery bifurcation. Later, after M1 was prepared for proximal control, the aneurysm was dissected distally and the aneurysm was clipped using a temporary clip when necessary (Fig. 3). Thrombectomy was performed in cases where the aneurysm was thrombosed. After clipping, the proximal and distal MCA branches were checked with a micro-Doppler probe, and papaverine-impregnated gel sponges were placed in the vascular bed. The dura was sealed watertight, and then primary closure was performed of the other layers. In patients with bilateral aneurysm, a second surgery was performed one month later for non-rupture contralateral MCA aneurysm.

Table-1: Patient demographics, characteristics of the aneurisms, and clinical outcomes.

No	Age (years)	Gender	Side	Size (mm)	Calcification / Thrombosis	Localization	Hunt& Hess	SAH	GOS 3rd month	Morbidity
1	70	Female	Left	8x4	-	Bifurcation	Grade 1	-	5	-
2	57	Female	Left	7x5	-	Bifurcation	Grade 1	+	5	-
3	14	Female	Right	5.5x4	-	M3	Grade 1	+	5	-
4	63	Female	Right	5.8x7.7	-	Bifurcation	Grade 1	+	5	-
5	65	Female	Right	6.5x5.1	-	Bifurcation	Grade 1	+	5	-
6	70	Female	Right	7x6	-	Bifurcation	Grade 1	-	5	-
7	54	Female	Right	11x10	Calcification	Bifurcation	Grade 1	+	4	Left hemiparesis
8	53	Male	Left	7.3x4.9	Calcification	Bifurcation	Grade 1	+	4	Right hemiparesis
9	54	Male	Bilateral	6.5x4 R	3.3x2.2 L	- Bifurcation	Grade 2	+		5
10	60	Female	Bilateral	6x5 R	6.4x4.5 L	- Bifurcation	Grade 2	+		5
11	35	Female	Left	5.2x5	-	Bifurcation	Grade 2	+	5	-
12	62	Male	Left	6.3x4	-	Bifurcation	Grade 2	+	5	-
13	43	Female	Right	4.1x4	-	M2	Grade 2	+	5	-
14	52	Male	Bilateral	5.2x3.4 R	1.6x1.3 L	- Bifurcation	Grade 2	+		5
15	63	Male	Right	48x34	Thrombosis	Bifurcation	Grade 3	+	5	Hydrocephaly
16	43	Male	Right	6x4	-	Trifurcation	Grade 3	+	5	-
17	45	Female	Left	30x34	Thrombosis	Bifurcation	Grade 3	+	5	Aphasia
18	35	Male	Right	20x23	-	Bifurcation	Grade 3	+	1	Fatal
19	63	Female	Right	5.6x4.3	-	Bifurcation	Grade 4	+	5	-
20	56	Male	Right	11.8X10	-	Bifurcation	Grade 5	+	1	Fatal

GOS: Glasgow outcome scale; L: left; R: right; SAH: subarachnoid hemorrhage.

Surgical Outcomes:

In a total of 20 patients, 23 MCA aneurysms were clipped. One patient with a wide hematoma and Hunt & Hess stage 3 died due to vasospasm, and another patient with a large aneurysm (size 11.8 × 10 mm) and Hunt & Hess stage 5 died due to vasospasm-related ischemic causes. In our case of giant thrombosed aneurysm located in the left MCA, transient aphasia resolved in the third month. Hydrocephalus developed during the first postoperative month in the other case with giant thrombosed MCA aneurysm. The hydrocephalus was treated with a ventriculoperitoneal (VP) shunt. Hemiparesis developed in 2 patients with MCA aneurysm with a calcified part. Both patients were able to mobilize without aid 3 months later with the support of physical therapy. In the study, the total mortality rate was 10% and morbidity rate was 20% in MCA aneurysms. The relationship between the demographic characteristics of the patients, the radiological characteristics of aneurysms, and the surgical outcomes are presented in Table-2. Age and SAH incidence were found to be negatively correlated in the cases. ($r = -0.490$; $p = 0.018$) It was observed that Hunt & Hess stages were higher ($r = 0.433$; $p = 0.039$) in the male gender. As the measured values of width and length of aneurysms increased, the incidence of calcification or thrombosis within the aneurysm increased ($r = 0.571$, $p = 0.004$ for width; $r = 0.498$, $p = 0.016$ for height) and GOS scores at the 3rd month decreased ($r = -0.507$, $p = 0.014$ in width; $r = -0.431$, $p = 0.040$ for height), and mortality and morbidity were more common ($r = 0.747$, $p < 0.001$ in width; $r = 0.679$, $p < 0.001$ for height). In addition, the presence of calcification or thrombosis in the aneurysm sac as found to be positive and strongly correlated with mortality and morbidity ($r = 0.772$; $p < 0.001$).

Table-2: Correlation coefficients of the variables.

		Male	Right / Left	Width	Height	Calcification / Thrombosis	Hunt&Hess	SAH	GOS 3rd month	Morbidity / Mortality
Age (years)	***r***	-0.239	-0.040	0.274	0.194	-0.052	-0.246	-0.490	0.223	-0.172
	p	0.273	0.855	0.206	0.376	0.814	0.257	0.018*	0.307	0.432
Gender (male)	***r***	-	0.016	0.033	-0.260	0.060	0.433	0.271	-0.310	0.278
	p	-	0.944	0.881	0.230	0.784	0.039*	0.212	0.149	0.199
Right / Left	***r***	-	-	-0.067	-0.251	0.102	-0.142	-0.069	0.153	-0.071
	p	-	-	0.761	0.248	0.643	0.518	0.755	0.487	0.749
Width (mm)	***r***	-	-	-	0.759	0.571	0.077	-0.221	-0.507	0.747
	p	-	-	-	0.000**	0.004**	0.727	0.310	0.014*	0.000**
Height (mm)	***r***	-	-	-	-	0.498	0.107	0.012	-0.431	0.679
	p	-	-	-	-	0.016*	0.627	0.958	0.040*	0.000**
Calcification / Thrombosis	***r***	-	-	-	-	-	0.000	0.142	-0.341	0.772
	p	-	-	-	-	-	1.000	0.519	0.112	0.000**
Hunt&Hess	***r***	-	-	-	-	-	-	0.369	-0.117	0.292
	p	-	-	-	-	-	-	0.083	0.596	0.176
SAH	***r***	-	-	-	-	-	-	-	-0.141	0.183
	p	-	-	-	-	-	-	-	0.521	0.402
GOS 3rd month	***r***	-	-	-	-	-	-	-	-	-0.769
	p	-	-	-	-	-	-	-	-	0.000**

GOS: Glasgow outcome scale; SAH: subarachnoid hemorrhage. *p<0.05; **p<0.01.

Discussion

The most important results of the present study are as follows. It was determined that the incidence of calcification or thrombosis in the aneurysm increased, the GOS scores at the 3rd month decreased, and mortality and morbidity were more common as the measured width and height values of the aneurysms increased. In addition, thrombosis in the aneurysm sac and calcification in the aneurysm wall were found to be positive and strongly correlated with mortality and morbidity.

Surgery for MCA aneurysm has been performed for a long time. While aneurysm occlusion at a rate of above 90% and good results at a rate of 88%–100% after surgery have been reported in nonbleeding aneurysms, results have been variable in bleeding aneurysms. There are still question marks and confusion as to the selection of the treatment method for MCA aneurysms (4). The International Subarachnoid Aneurysm Trial (ISAT) has reported that endovascular treatment is superior in the treatment of ruptured and no ruptured aneurysms (1). Microsurgical treatment comes to the fore in cases where the MCA aneurysms have a wide neck, are of dysmorphic shape, are located in the trifurcation, have MCA branches coming out of their base or body, are easily accessible surgically, and there is hematoma accompanying the ruptured aneurysm (2,4).

Ruptured aneurysms are associated with serious morbidity and mortality rates, around 60% (5,6). In the literature, the mortality rate due to microsurgical clipping ranges from 0.3% to 13% (4,7). In our study, the mortality rate was 10% when evaluated according to the number of patients, and 8.6% when evaluated according to the number of surgeries performed. The rate of major complications in MCA aneurysm surgery is between 2% and 25% (6). In this study, morbidity was 20% based on the number of cases, and 13.0% based on the number of surgeries.

In the present study; thrombosis in the aneurysm sac, large size, and calcification in the aneurysm wall are identified as risk factors leading to morbidity and mortality. In a study by Ulutaş reporting the results of intracranial aneurysm surgery; it was reported that multiple aneurysms, high Hunt & Hess stage, and presence of intracerebral hematoma affected morbidity and mortality (8). In our study, the lack of correlation between high Hunt & Hess stage and morbidity and mortality was attributed to the low number of patients in high stage. Similar to the results of the study by Ulutaş, the Hunt & Hess stage was found to be high in male patients in the present study. In our series, no mortality or morbidity was observed in patients with multiple aneurysms with bilateral MCA aneurysm. Flamm et al. reported that morbidity is high in complex aneurysms with large size and wide neck, and calcification in the aneurysm wall (9). In our study, calcification of the aneurysm wall was detected intraoperatively in both the patients who developed postoperative hemiparesis. We believe that the difficult and long duration of clip application due to calcification contributed to the development of ischemia and hemiparesis. The patient's condition following aneurysm rupture, presence of calcification in the aneurysm wall, intraluminal thrombus, and surgical accessibility are important in determining the treatment option in MCA aneurysm (10). In addition to evacuation of intraparenchymal hematoma during microsurgical clipping, it also allows decompressive hemicraniectomy when necessary (4,11,12).

The limitations of this study were the limited number of patients since it only included patients with MCA aneurysm and the failure to standardize postoperative intensive care follow-ups because it was not a controlled study.

Conclusion

In conclusion, large size of the aneurysm, presence of thrombosis in the aneurysm sac, and calcification in the aneurysm wall were found to be positive and strongly correlated with mortality and morbidity.

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The Survival Efficiency of Initial Surgical Treatment in Stage IIIa-N2 Positive Non-Small Cell Lung Cancer

Muhammet Ali Beyoglu [1(ID)] Selim Sakir Erkmen Gulhan [2(ID)], Ayperi Merzi Ozturk [3(ID)] , Leyla Nesrin Acar [2(ID)], Mehmet Furkan Sahin [1(ID)] . Gokturk Findik [2(ID)]

[1]Department of General Thoracic Surgery and Lung Transplantation, University of Health Sciences, Ankara, Turkey
[2]Department of Thoracic Surgery, Ataturk Chest Disease and Thoracic Surgery Training Hospital, Ankara, Turkey
[3]Department Interventional Pulmonology, Ataturk Chest Disease and Thoracic Surgery Training Hospital, Ankara, Turkey

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Abstract

Objective: The role of surgical treatment in the multimodal treatment of stage IIIA-N2 positive non-small cell lung cancer (NSCLC) patients is a matter of debate. We aim to investigate initial surgical treatment's survival efficiency in patients with IIIA N2 positive NSCLC**.**

Methods: The patients treated for stage IIIA N2 positive NSCLC in a single center between January 2009 and December 2014 were retrospectively analyzed. A total of 134 patients with 5 cm tumors in diameter or less and without involvements of the chest wall, mediastinal pleura, phrenic nerve, recurrent laryngeal nerve, pericardium, heart, diaphragm, vertebra, esophagus, large vessel invasion, and satellite nodule were detected. Of these patients, initial surgical treatment before chemoradiotherapy was performed in 72 (Group 1), while definitive concurrent chemoradiotherapy was performed in 62 patients (Group 2). Each patient's gender, age, physical performance status, tumors size, pathological diagnosis, lung resection types, and long-term survival data were evaluated.

Results: No statistically significant difference was found in patients' gender, physical performance, tumor size, and tumor histology. Survival rates were higher among patients aged ≤65 years and higher in Group 1 than Group 2. While one-, three, five-, and seven-year survival rates were detected as 86.1%, 62.5%, 41.6%, and 31% in Group 1, respectively, the rates were observed to be as 77.4%, 30.6%, 10.8%, and 6.7% in Group 2, respectively. However, no difference was seen between patients' survival rates with single and multiple ipsilateral mediastinal lymph node metastases.

Conclusion: Despite those advocating surgical treatment after neoadjuvant chemotherapy in treating stage IIIA N2 positive patients, others supporting surgical treatment should initially be performed. When conducted as the first step, surgical treatment achieves significant increases in survival.

Keywords: Non-small cell lung cancer, stage IIIA, N2 positive, survival**.**

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Address for correspondence/reprints: **Telephone number:** +90 (312) 552 60 60

Muhammet Ali Beyoglu **E-mail:** muhammetalibeyoglu@gmail.com

Introduction

Lung cancer is one of the leading causes of cancer-related deaths globally, and 80% of lung cancers are composed of non-small cell lung cancers (NSCLC). Additionally, almost 30% of NSCLC's are seen to be at a locally advanced stage at the time of diagnosis (1). The patients with locally advanced NSCLC are classified as stage III for the fundamental structure of the 8th TNM staging system: T for characteristics of the primary tumors, N for nodal involvement, and M for (distant) metastasis under the American Joint Commission on Cancer (AJCC) in the United States and the Union for International Cancer Control (UICC) internationally (2). Five-year survival for stage III NSCLC patients is 26% from diagnosis, and the patients at stage III constitute a very heterogeneous group (3). The presence of ipsilateral mediastinal lymph node positivity (N2 positive) independent of tumors diameter and local invasion causes the disease to be staged as III. The positivity of contralateral mediastinal lymph nodes also makes the disease be evaluated as stage III, regardless of tumors size and local invasion. Definitive concurrent chemoradiotherapy (CCRT) is recommended for stage III patients as the standard treatment (4). Although the surgical treatment after neoadjuvant chemotherapy and adjuvant chemoradiotherapy is recommended in some N2 positive patients under the National Comprehensive Cancer Network (NCCN) guidelines, the surgical treatment is not recommended the first-line modality for these patients (5). The present study aimed to evaluate the association of initial surgical treatment survival rates before chemotherapy and radiotherapy in the patients with stage IIIA N2 positive NSCLC compared to those receiving definitive CCRT.

Methods

This study was designed as a retrospective and observational study and approved by the local ethics committee (approval number: 2321/2021). An informed consent form was not obtained from the participants because of the study's retrospective design and the rendering of the patient information unrecognizable. All authors confirmed compliance with the World Medical Association Declaration of Helsinki on the ethical conduct of research involving human subjects.

The patients treated with initial surgical for stage III NSCLC in a single center between January 2009 and December 2014 were retrospectively analyzed. From the hospital records, 123 patients with the positivity of ipsilateral mediastinal lymph nodes (N2 positive) and undergoing surgical treatment were detected. Of 123 patients, 10 (8.1%) undergoing lung resection after neoadjuvant chemotherapy, four (3.3%) diagnosed with carcinoid tumor's, three (2.4%) with T4 tumor's, 18 (14.6%) with T3 tumors', 10 (8.1%) not receiving radiotherapy after lung resection, and six (4.9%) not receiving adjuvant chemotherapy were excluded from the study. Therefore, 72 (58.6%) patients treated with chemotherapy and radiotherapy following lung resection and systemic sampling of mediastinal lymph nodes were included in the study. These patients were classified as Group 1 in our study. In addition to 72 patients in Group 1, among those referred to the definitive CCRT due to N2 positivity within the pre-operative period, 62 patients with T1 and T2 tumor's and initially evaluated as respectable and operable were detected and included in the study as Group 2. As a result, of 134 patients constituting our study population, 72 (53.7%) received chemotherapy and radiotherapy after lung resection, and systemic lymph node sampling was classified as Group 1, 62 (44.3%) patients treated with definitive CCRT were put into Group 2. The patients were staged under the 8th edition of the Tumor-Node-Metastasis staging system (2). All patients (n=134) in the study were staged as stage IIIA. The follow-up period was determined to be between 60-132 months. The data of the patients were obtained from digital archive files of the hospital. Such characteristics as age, gender, date of diagnosis, pathological diagnosis, tumour location, types of pre-operative invasive mediastinal procedures, stage of the disease, and physical performance status were recorded. The patients' physical performance status was classified according to the performance status classification of Eastern Cooperative Oncology Group (ECOG) (6). The dates of the patients' deaths were also obtained from the Turkish Ministry of Health's death notification system.

Statistical analysis

The statistical analyses were carried out by using IBM SPSS Statistics for Windows, Version 22.0 (SPSS Inc., Chicago, IL, USA). The descriptive statistics of the study are presented with frequency and percentage for categorical variables and mean and standard deviations for numerical variables. Descriptive statistical methods (e.g. mean, standard deviation, median, frequency and ratio) and Shapiro-Wilks test, histogram and box plot graphics were used to evaluate the distribution of the variables. Independent group comparisons were made with the

chi-square test. The survival rates were calculated using the Kaplan-Meier method. The log-rank test evaluated the comparisons of survival curves between both groups. The effects of continuous and categorical variables on survival times were evaluated using the backward conditional method with the Cox proportional hazards regression model. The hazard ratios were estimated from the data. A $p \leq 0.05$ value was accepted to be statistically significant.

Results

Of 134 patients, 122 (91%) were male, and 12 (9%) were female. The mean age of the patients was found as 58.91±8.43 years. The findings concerning age, gender, size of tumours, number of N2 positive stations, pathological types, and physical performance status are given in Table 1. The histological investigation revealed that the most common tumours were evaluated as squamous cell carcinoma in 60 (44.7%) cases, adenocarcinoma in 51 (38%), not otherwise specified (NOS) in 14 cases (10.5%), adenosquamous tumours in 7 (5.2%) cases, and large cell carcinoma in two cases (1.6%). (Table 1)

Table 1. Baseline Characteristics of Patients

Variables	Group 1 n (%)	Group 2 n (%)	Total n (%)	P value*
Age (Years)				
≤65	59 (81.9)	49 (79)	108 (80.6)	p = 0.417
>65	13 (18.1)	13 (21)	26 (19.4)	
Gender				
Male	62 (86.1)	60 (96.7)	122 (91.0)	p = 0.029
Female	10 (13.9)	2 (3.3)	12 (9.0)	
Pathology				
Adenocarcinoma	34 (47.2)	17 (27.4)	51 (38.0)	p = 0.03
Squamous cell	31 (43.0)	29 (46.7)	60 (44.8)	
carcinoma	0	14 (22.6)	14 (10.5)	
NOS	7 (9.8)	2 (3.3)	9 (6.7)	
Others				
Metastatic mediastinal lymph node	48 (66.6)	43 (69.3)	91 (67.9)	p = 0.442
Single	24 (33.4)	19 (30.7)	43 (32.1)	
Multiple				
T status				
T1a (≤2 cm)	11 (15.3)	4 (6.4)	15 (11.2)	p = 0.413
T1b (>2cm, ≤3cm)	20 (27.8)	18 (29.0)	38 (28.3)	
T2a (>3cm, ≤4 cm)	21 (29.1)	37 (59.7)	58 (43.3)	
T2b (>4cm, ≤5 cm)	20 (27.8)	3 (4.9)	23 (17.2)	
ECOG performance status	68 (94.4)	60 (96.7)	128 (95.5)	p = 0.369
$ECOG_0$	4 (5.6)	2 (3.3)	6 (4.5)	
$ECOG_1$				

ECOG: Eastern Cooperative Oncology Group performance status, NOS: Not otherwise specified. *The distribution of the groups according to the categorical variables was analyzed with the chi-square test.

Of 72 patients in group 1, lobectomy was performed for 66 (91.6%), bilobectomy for four (5.5%), and pneumonectomy for two (2.9%) patients.

According to the Cox regression analysis, only the age (HR= 1.043, p<0.001) and the treatment groups (HR= 1.365, p<0.003) were statistically significant on survival. Gender, tumors histopathology, T status, and mediastinal lymph node metastasis (single/multiple) did not affect survival (Table 2)

When the patients in both groups were evaluated according to tumors diameter, the number of those with T1a, T1b, T2a, and T2b tumors' was 11 (15.3%), 20 (27.8%), 21 (29.1%), and 20 (27.8%) in Group 1, respectively. Even so, the number of those with the same tumours was detected as four (6.4%), 18 (29%), 37 (59.7), and 3 (4.9%) among Group 2 patients, respectively. No statistically significant difference was found between groups (p=0.91). (Table 2)

Table 2. Survival Analysis According to Categorical and Numeric Variables

	Hazard ratio	%95 CI*	p value
Gender	1.042	0.512-2.122	0.91
Age	1.043	1.017-1.070	**0.001****
Tumor histopathology	0.945	0.784-1.139	0.533
T status	1.011	0.840-1.217	0.91
N2 (Single/Multiple)	0.972	0.645-1.465	0.892
Treatment Group (Group1/2)	1.365	1.112-1.676	**0.003****

CI*: Confidence Interval

Of 134 patients, 106 (79.1%) deaths were detected, while 28 (20.9%) survived during the follow-up period as of 31st December 2019. When the survival rates were examined in both groups, median survival rates were 44 and 23 months for Groups 1 and 2, respectively. When the survival rates were evaluated by years, while one-, two-, three-, four-, and five-year survival rates were found as 86.1%, 73.6%, 63.5%, 48.6%, and 41.6% respectively for those in Group 1, the rates were calculated as 77.4%, 50%, 40.3%, 21%, and 10.3% for those in Group 2. The survival rates in Group 1 were determined to be statistically significantly higher than those in Group 2 (p<0.01). When the survival rates were examined in both genders, the average survival time was 44 months for men and 33 months for women. No statistically significant difference was found between both genders (p=0.91). (Table 2)

When the patients were divided into two groups as ≤65 years and >65 years of age, the average survival time was determined as 55.6 months among those aged ≤65 and 22.9 months among those aged >65. Based on the analyses of survival rates, a statistically significant difference was found in the survival rates of those aged ≤65 (p<0.01).

When the patients were divided into two groups as those with single N2 positive and multiple N2 positive, in light of the number of positive mediastinal lymph node stations, 91 (68%) patients were found to have single N2 positive. In contrast, 43 (32%) patients were found to be with multiple N2 positive. According to this criterion, while the mean survival rates were determined as 49.7 and 46 months for single and multiple N2 positive patients, respectively, the median survival times were calculated as 35 and 37 months. No statistically significant difference was found between those with single and multiple N2 positive (p=0.814). (Figure 1) (Table 2) However, when the survival rates of those with single and multiple N2 positive in Group 1 (n=72) were compared, the mean (median) survival times were determined as 63.5 months (median, 50 months) and 55.7 months (median, 37 months), respectively. No statistically significant difference was found between the patients with single and multiple N2 positive in Group 1 (p=0.581) regarding survival rates. (Table 3) Even so, when the survival rates of 62 patients with single and multiple N2 positive in Group 2 were compared, the mean (median) survival times were determined as 31.7 months (median, 23 months) and 32.8 months (median, 33 months), respectively. There was no statistically significant difference between single and multiple N2 positive patients in Group 2 regarding survival rates (p=0.743). (Table 3)

Table 3. Survival Analysis By Single and Multiple N2 Metastases

Survival Time Mean (Median) months			
	Single N2	**Multiple N2**	**P value**
Group 1	63.5 (50)	55.7 (37)	p = 0.581
Group 2	32.8 (33)	31.7 (23)	p = 0.743

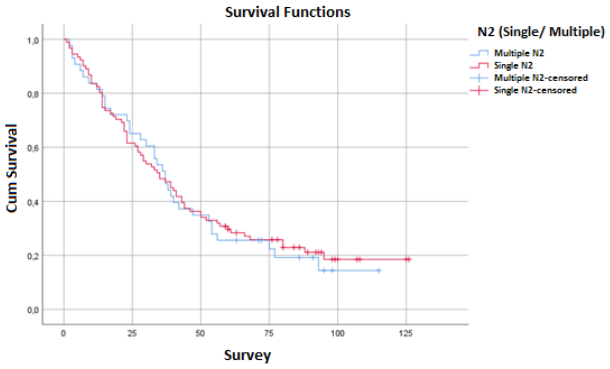

Figure 1. Analysis of survival by single and multiple mediastinal lymph node metastases

Discussion

The most critical factor determining the prognosis of NSCLC is the staging process of the disease (6). In a study, 25–30% of the patients with NSCLC were reported to be diagnosed at locally advanced stages (IIIA or IIIB). Postoperative 5-year survival rates were stated to range between 13 and 42.8% (7).

Stage III NSCLCs include a highly heterogeneous group of patients with differences in the extent and localization of the disease. Many aspects of the treatment of stage III N2 positive disease are controversial as the entities to be elucidated. The best-suggested therapy for most clinically evident N2 disease patients is definitive CCRT, using platinum-based chemotherapy plus radiotherapy. However, there is no consensus on the role of surgery in treating stage III (N2 positive) NSCLC patients. Despite definitive CCRT, survival rates require re-evaluating surgical treatment for such patients (8-10).

In previous studies, N2 positivity was the most important factor affecting prognosis negatively (11-13). Therefore, it is evident that determining the most appropriate treatment according to the stages of cancer, especially node metastasis is essential. When all patients were evaluated in our study, while the median survival time was determined as 35 months, the 5-year survival rate was 28.3 months.

The most appropriate treatment for the patients with stage IIIA N2 positive NSCLC remains controversial; however, a consensus is that utilizing a single treatment modality alone, whether surgery or radiotherapy, results in relatively low survival rates (14-17).

Definitive CCRT is recommended for those with stage IIIA (N2 positive) disease. However, surgical treatment following induction chemotherapy may also be utilized as an alternative therapy (5). In a study, overall survival (OS) was indicated better in

the patient's undergoing lobectomy than those receiving chemotherapy and radiotherapy alone (18). In other studies, postoperative radiotherapy and surgery alone were reported not to improve overall survival in the patients with IIIA N2 (positive) NSCLC, and lobectomy was stated to provide better long-term survival than pneumonectomy after induction chemotherapy, with no increase in postoperative complications or recurrence rates (19-21). In our study, the patients undergoing lung resection and systemic mediastinal lymph node sampling were considered to have no mediastinal lymph node metastasis in the pre-operative period; N2 positivity was detected intraoperative postoperative period, and so adjuvant chemoradiotherapy was performed in these patients. When the patients' survival times were examined, it was remarkable that the 5-year survival rates were like those of the patients undergoing lung resection+chemoradio therapy following neoadjuvant therapy.

Morbidity and mortality rates were determined according to the surgical resection types (20, 21). Accordingly, postoperative morbidity and mortality rates were higher in the patients undergoing neoadjuvant chemoradiotherapy after pneumonectomy than those treated with lobectomy (18). Our study demonstrated that the survival rates between the patients undergoing lobectomy and pneumonectomy were not different (p=0.635). We consider that the relatively low number of pneumonectomy patients included in the study may have affected our findings.

In the study performed it was reported that the 5-year survival rates for stages IA, IB, IIA, IIB, IIIA, IIIB, and IV in NSCLC were 82%, 66%, 52%, 47%, 36%, 19%, and 6%, respectively (20). The data released by the Japanese Lung Cancer Registry Center showed that the 5-year survival rates for stages IIA, IIB, and IIIA NSCLC were 61%, 47.4%, and 32.8%, respectively (21). In another study conducted by Cerfolio et al. (22) including similar findings to ours, the 5-year survival rate was reported to be 42% among stage IIIA N2 (positive) patients undergoing surgery after neoadjuvant treatment (22). Although surgical treatment was used as the first step of multimodal treatments in our study, our survival rates were similar to those undergoing surgery after neoadjuvant treatment reported in Cerfolio et al. (22). In our study, the 5-year survival rates were 41.6% and 10.3% in Group 1, and there was a statistically significant difference between the survival rates in Groups 1 and 2 (p<0.01). Our results indicate that combined treatments with initial surgical treatment and adjuvant chemoradiotherapy may have a higher chance for more prolonged survival in those with NSCLC. However, we consider that further studies are required to understand whether such a treatment modality can lengthen the survival rate in N2 positivity.

In the study by Misthos et al. (23) the patients with single N2 metastases were reported to have better survival rates than those with multiple N2 metastases in a relatively large group (23). There was no statistically significant difference between single and multiple N2 positive patients in our study regarding survival rates (p=0.814). When the patients in Group 1 were evaluated as single and multiple N2 positive, the mean survival times were found as 63 and 55 months, while the median survival times were calculated as 50 and 37 months, respectively. Although found to be high, the difference between the survival times was not statistically significant (p=0.581).

Conclusion

Current treatment modalities could not provide adequate survival for stage IIIA (N2 positive) NSCLC patients. Surgical treatment should be considered after neoadjuvant chemoradiotherapy and as the first step for stage IIIA N2 positive NSCLC patients' multimodal treatments. Despite the common belief that surgical treatment is not beneficial for those with multiple N2 metastases, we consider that better survival rates can be achieved in such patients, mostly when surgical treatment is performed as the first multimodal treatment step.

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GABAergic Effects of Some Food Extracts Via Inhibition of GABA-Transaminase

Sumeyye Sahin [1(ID)], Sahra Haas [2(ID)]

[1]Department of Food Engineering, Ordu University, Ordu, Turkey
[2]Food Chemistry Unit, Department of Chemistry and Pharmacy, Emil Fischer Center, Friedrich-Alexander Universität Erlangen-Nürnberg (FAU), Schuhstr, Germany

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Abstract

Objective: GABAergic system is a target for various groups of medications including sedatives, anxiolytics, muscle relaxants, antidepressants and antiepileptics. Several foods or food ingredients are able to affect the GABAergic system by the inhibition of the γ-aminobutyric acid (GABA) degrading enzymes including the GABA-transaminase and succinate semialdehyde dehydrogenase. The purpose of this study to investigate the inhibitory effects of tea (*Camellia sinensis*), coffee (*Coffea arabica L.*), peppermint (*Mentha piperita L.*), thyme (*Thymus vulgaris L.*), and cinnamon (*Cinnamomum zeylanicum*) on GABA degrading enzymes.

Methods: The inhibition of the GABA-T by aqueous extracts of tea (*Camellia sinensis*), coffee (*Coffea arabica L.*), peppermint (*Mentha piperita L.*), cinnamon (*Cinnamomum zeylanicum*), and thyme (*Thymus vulgaris L.*) was investigated using a fluorometric microplate enzyme assay. Dose-dependent inhibition of the GABA-degrading enzymes was attained by all the food extracts tested. For determination of the IC50 values of the extracts (± 95 % CI), a linear regression was performed using Origin® (Origin® 2015G von Origin Lab Corporation, Northampton, MA 01060 USA).

Results: The aqueous extract of black tea presented the strongest inhibitory activity with an IC50-value (half maximal inhibitory concentration) of 13.0 (11.0-15.3) µg/mL. The tested food extracts were successful in inhibiting the GABA-degrading enzymes even at low concentrations.

Conclusion: In conclusion, the selected food extracts could serve as natural inhibitors for GABA-degrading enzymes thus, they could increase the GABA concentration in the brain.

Key words: γ-Amino butyric acid, GABA degrading enzymes, enzyme inhibition, black tea, thyme

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Address for correspondence/reprints:

Sumeyye Sahin

Telephone number: +90 (452) 226 52 00-6305

E-mail: sumeyyesahin@odu.edu.tr

Introduction

GABA is formed from glutamate-by-glutamate decarboxylase, which is a pyridoxal phosphate-dependent enzyme, and has two isoforms (65-kDa GAD and 67-kDa) in the human organism (1-5). The degradation of GABA (Fig. 1) occurs via a transamination reaction catalyzed by the GABA transaminase (GABA-T). GABA-T catabolizes GABA to the succinic semialdehyde that is either oxidized to the succinate by a reductase enzyme, the succinic semialdehyde dehydrogenase (SSA-DH; EC 1.2.1.24)) or reduced to the γ-hydroxybutyrate by the

succinic semialdehyde reductase (SSA-R; EC 1.1.1.61)) (6-8).

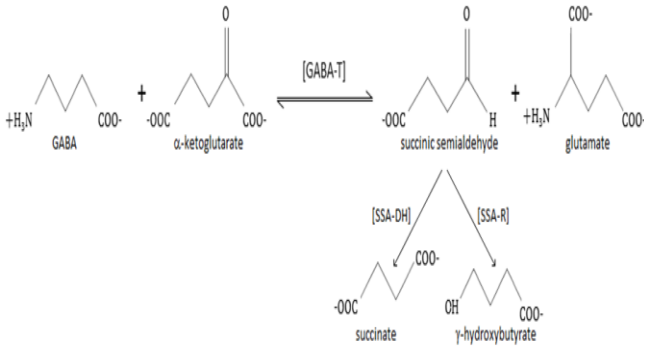

Figure 1. Schematic overview of degradation of neurotransmitter GABA; GABA-T: GABA transaminase; SSA-DH: Succinic semialdehyde dehydrogenase; SSA-R: Succinic semialdehyde reductase (6).

Low levels of GABA in the brain are associated with some neurophysiological diseases such as epilepsy, depression, panic disorders, anxiety disorders or sleep disorders (9-15). In the human study, Wood et al. (13), reported that epileptic patients have significantly low levels of GABA in cerebrospinal fluid. In the brain of depressed patients, a significantly decreased GABA concentration was also detected (14). Since the permeability of the blood-brain barrier for GABA is very low (16, 17), GABA supplementation cannot lead to an increase in GABA levels in the brain. For example, no effect on the GABA concentration in the brain of rats could be demonstrated by intraperitoneal injection of GABA (18). However, the increasing of GABA concentration is possible by the inhibition of GABA degradation (19-23).

GABA-T is a target for antiepileptic drugs, which can increase GABA levels in the brain via inhibition of GABA-T, thereby eliciting an antiepileptic or anticonvulsant effect (19, 21). Some anticonvulsants such as vigabatrin, a vinyl derivative of GABA, act as a competitive inhibitor of GABA-T (7). In addition, the inhibitory effects of several anxiolytic plants on GABA-T have been reported (24-26). Since the inhibition of GABA-T causes an increase in GABA level in the brain, there is a growing interest in the inactivation of GABA-T by foods.

Although the anxiolytic, sedative, hypnotic, and calming effects of some food plants and their ingredients have been studied in numerous studies, their physiological targets have not been completely elucidated. For example, animal model studies demonstrated that epigallocatechin gallate, a major catechin found in green tea (*Camellia sinensis*), acts as sedatives and as hypnotics in the brain (27). Coffee (*Coffea arabica L*) is consumed because coffee reduces stress, drowsiness, and neuralgia (28). Peppermint (*Mentha piperita L.*) has a relaxation effect on the muscular actions and secretory processes of the gastrointestinal tract, analgesic, and anesthetic effects in the central and peripheral nervous system (29). Some Thymus spp. are used to produce antiseptic, antispasmodic, antioxidative, and sedative effects (30). Cinnamon (*Cinnamomum zeylanicum*) exhibited anti-depressant and anti-anxiety like effect in mice (31). The present study evaluated the effects of tea, coffee, peppermint, thyme, and cinnamon on GABA-T to explain their physiological action mechanism in the central nervous system.

Methods

Chemicals

GABA, GABase from *Pseudomonas fluorescens*, and α-ketoglutarate were purchased from Sigma-Aldrich (Taufkirchen, Germany). β-nicotinamide adenine dinucleotide phosphate (NADP) disodium salt was obtained from AppliChem (Darmstadt, Germany) and vigabatrin from British Pharmacopoeia Commission Laboratory (London, United Kingdom).

Plant Material and Preparation of Extracts

Peppermint leaves (*Mentha piperita L.*), thyme leaves (*Thymus vulgaris L.*), black tea leaves (*Camellia sinensis*) and cinnamon powder (*Cinnamomum zeylanicum*) were obtained in crushed form from a local pharmacy. Roasted coffee beans (*Coffea arabica L.*) were finely ground before extraction. 100 mL of boiling water were added to 2.5 g of the test material. The mixtures were stirred (60 min at 90 °C) and filtered through filter paper. The solvents in the filtrates were removed by freeze-drying (Lyophilizer Savant Novalyphe NL150). After lyophilization, the samples were kept at -20 °C and dissolved in water (1 mg/mL) before use.

Fluorometric Microplate Enzyme Assay

The activity of GABAse composed of GABA-T and SSADH was determined spectrophotometrically according to literature (32) with some modifications. The reaction mixture contained potassium pyrophosphate buffer (150 mM, pH= 8.0), α-ketoglutarate (228,5 mM), GABA (873 mM), and GABAse (1,5-1,7 units/mg). The extracts were added to the reaction mixture and preincubated (30 min at 37 °C). After preincubation, NADP+ (26.1 mM) was added to the mixture and incubated (30 and 60 min at 37 °C). GABA-T activity was monitored by

measuring the absorbance changes at 340 nm due to the reduction of NADP+. The absorbance was measured using a microplate spectrophotometer (µQuant BioTek). Vigabatrin, an inhibitor of GABA-T, was used as the positive control. Water was used instead of the inhibitor for the negative control.

Statistical analysis

For determination of the IC50 values of the extracts (± 95 % CI), a linear regression was performed using Origin® (Origin® 2015G von OriginLab Corporation, Northampton, MA 01060 USA).

Results

Each food extract was tested for its inhibitory activity at various concentrations (4-180 µg/mL). The activity of GABA-T decreased with increasing concentrations of black tea extract (Fig. 2a). Similarly, all other plant extracts exhibited inhibitory effects on GABA-T activity in a dose-dependent manner (Fig. 2 b, c, d, e). At the concentration of 18 µg/mL, cinnamon powder, coffee beans, peppermint leaves and thyme leaves extracts led to very weak inhibition (5.1 %, 8 %, 12.8 % and 21.5 % inhibition of GABA-T, respectively), whereas the extract of black tea induced the strongest inhibitory effect (56.6 % inhibition). When black tea extract was tested at the lower concentrations of 18 µg/mL, it also showed high inhibition indicating that it is the most potent inhibitor. Black tea showed 74 % inhibition at the highest concentration tested (27 µg/mL). Interestingly, the extracts of thyme and coffee showed similar GABA-T inhibition effects (65 % inhibition) at the concentration of 108 µg/mL. Compared to thyme and coffee in the same concentration (108 µg/mL), the extracts of peppermint and cinnamon induced lower activity (55 % and 34 % inhibition, respectively). The cinnamon extract exhibited only 55% inhibition at the highest concentration used (180 µg/mL).

The inhibitory effect of each food extract was evaluated by determining its respective IC50 values (the half-maximal inhibitory concentration). The IC50 values of extracts ranged between 13 and 174.2 µg/mL (Table 1). The strongest inhibitory effect was seen with the aqueous extract of black tea (IC50=13.0 µg/mL). The extracts of coffee, peppermint and thyme showed fifty percent inhibition at concentrations lower than 100 µg/mL. On the other hands, cinnamon extract was used at a much higher concentration (174.2 µg/mL) to inhibit 50 % of the enzyme.

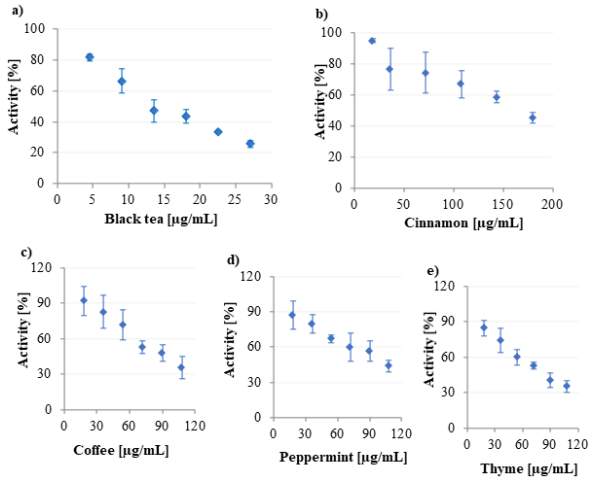

Figure 2. Dose response curve for the effect of the aqueous extract of black tea (a), cinnamon (b), coffee (c), peppermint (d), and thyme (e) on GABA-T activity expressed as percent of control. Values are the mean ± SD from triplicate analysis

Table 1. IC50 of aqueous extracts on GABA-T

Botanical	IC_{50} (with 95 % confidence interval) [µg/mL]
Black tea	13.0 (11.0-15.3)
Thyme	72.6 (60.9-86.5)
Coffee	83.9 (71.1-98.9)
Peppermint	97.5 (81.3-116.9)
Cinnamon	174.2 (135.4-224.2)

Discussion

Vigabatrin, which was designed to increase the amount of GABA in the central nervous system (7), binds as an inhibitor selectively and irreversibly at the active site of GABA-T (33). As the positive control, vigabatrin was used at the concentration of 2.7 mM (348.7 µg/mL) in the enzyme assay to confirm that detectable in vitro stimulation of total GABA-T inhibition could be measured under our experimental conditions. The food extracts showed their inhibitory effects in the concentrations of 4-180 µg/mL despite using lower concentrations than vigabatrin.

Awad et al. (24) demonstrated that the inhibitory effects of the aqueous and ethanolic extracts of traditionally used anxiolytic botanicals (*Centella asiatica, Eschscholtzia californica, Humulus lupulus, Hypericum perforatum, Matricaria recutita, Melissa officinalis, Passiflora incarnata, Piper methysticum, Scutellaria lateriflora*, and *Valeriana officinalis*) on GABA-T. They reported that IC50 values of the anxiolytic botanicals ranged from 350 to > 4000 µg/mL and the aqueous extract of M. officinalis showed the greatest inhibition of GABA-T with an IC50 of 350 µg/mL (24). Similarly, the ethanolic extracts of 34 traditional Q'eqchi' Maya plants, which used to treat some mental diseases such as

epilepsy and anxiety, were tested by Awad et al. (2009) for activity in the GABA-T. The IC50 value of the most active plant extract was 420 µg/mL (34). Compared to these anxiolytic botanicals, the aqueous food extracts tested in this study exhibited a higher inhibitory activity against GABA-T with very low IC50-values (13.0-174.2 µg/mL). Therefore, it can be concluded the aqueous food extracts (tea, thyme, coffee, peppermint, and cinnamon) may be more useful in the treatment of epilepsy and anxiety than the anxiolytic botanicals reported by Awad et al. 2007 and 2009.

Tea is consumed all over the world to relieve stress, drowsiness, and neuralgia (35). It is rich in flavonoids that have antioxidant, antitoxic, anticarcinogenic, antispastic, and antiviral activities. A study in the chick brain showed that epigallocatechin gallate, a major flavonoid of tea, acts as sedatives and as hypnotics in the brain, thereby moderating the acute stress response (27). Additionally, the anxiolytic effect of epigallocatechin gallate on mice has been reported (36). Furthermore, a human study described the anxiolytic effect of L-theanine, which is an important bioactive compound of tea (37). Like tea, coffee is consumed because coffee reduces stress (28). Peppermint, one of the most popular single ingredient herbal teas, has a relaxation effect on the muscular actions and secretory processes of the gastrointestinal tract, analgesic, and anesthetic effects in the central and peripheral nervous system, immunomodulating actions and chemo preventive potential (29). The primary constituent of peppermint oil is menthol (38) which has analgesic (39) and anesthetic activities (40). Thymol, a structural analogue of menthol, is found in thyme that is used to produce the antiseptic, antispasmodic, antioxidative, and sedative effects (30). Cinnamon showed an anti-depressant-like and anti-anxiety like effects in animal studies (31).

Conclusion

In conclusion, since low levels of GABA in the brain are associated with some neurophysiological diseases such as epilepsy, depression, panic disorders, anxiety disorders, or sleep disorders (9-15), it can be deduced that these food plants (tea, thyme, coffee, peppermint, and cinnamon) may produce their reported sedative, anti-depressant, anti-anxiety or anxiolytic effects by increasing the level of GABA due to inhibition of GABA-T.

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Evaluation of the Relationship Between Clinical Findings and Magnetic Resonance Imaging Findings of Patients with Arthroscopic Meniscus Repair

Bekir Karagoz[1](ID), Hasan Bombaci [2](ID)

[1]Adiyaman University Training and Research Hospital Department of Orthopaedics and Traumatology, Adıyaman, Turkey
[2]Health Science University Haydarpasa Numune Training and Research Hospital Department of Orthopaedics and Traumatology, Istanbul, Turkey

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Abstract

Objective: In this study, the relationship between clinical findings and magnetic resonance imaging (MRI) findings in patients undergoing arthroscopic meniscus repair was investigated.

Methods: Seventy patients with a mean age of 29.3 ± 9.2 (range; 18-54) were included in the study. The clinical evaluation of the meniscus repairs was made according to the criteria described by Barret. MRI results were evaluated according to the classification made by Crues et al. In addition, the clinical healing and satisfaction of the patients were evaluated with preoperative and postoperative the Lysholm functional scoring. Both clinical and MRI results were compared based on age, time to surgery, type of tear, localization of the ruptured meniscus, combination with anterior cruciate ligament reconstruction.

Results: While the results of 58 (83%) patients were successful in the clinical evaluation, the number of cases that recovered according to the MRI results was found to be 39 (55.7%). The mean Lysholm functional score, which was 62.64±19.73 preoperatively, increased to 90.93±9.58 at the final follow-up. Consistency between improvement in MRI according to Kappa analysis and success or failure according to clinical evaluation was found to be insignificant. In this analysis, the sensitivity coefficient was 52.86% and the Kappa value was calculated as 0.123.

Conclusion: No correlation was found between clinical evaluation and MRI results in the statistical analysis. According to the results of this study, clinical evaluation and Lysholm functional scoring help the clinician more in case follow-up and the success of the surgery compared to the MRI results.

Key words: Meniscus repair, Lysholm, Barret criteria, Magnetic resonance

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Address for correspondence/reprints:

Bekir Karagoz

Telephone number: +90 (545) 646 89 14

E-mail: drbkr71@gmail.com

Introduction

Meniscus are anatomical formations in the fibrous cartilage structure between the tibia and femur in the knee joint (1). Its main duties are to provide load transfer with its shock absorbing feature, to increase the joint surface contact area, to contribute to joint stability and proprioception (2,3). Direct traumas, coercive movements and repetitive overloads can cause meniscus tears.

In the historical process, different surgical methods have come to the fore at different times in the treatment of meniscal tears. Among the factors that are effective in deciding the surgical technique in meniscus tears; the patient's complaint, age, the size of the tear, the morphology of the tear, the structure of the meniscus, time after injury and accompanying additional pathologies are included (1). Partial meniscectomy has been shown to cause irreversible damage to articular cartilage in the long term (4,5). Since the 1980s, arthroscopic techniques have been developed and with the recognition of the blood supply properties of the meniscus, repair has come to the fore in appropriate tears.

For the postoperative follow-up of the meniscus repair, there are various evaluations in the literature such as clinical evaluation, "secondary look" arthroscopy and magnetic resonance imaging (MRI) after meniscus repair (6-8). However, "second look" arthroscopy is not preferred because it is an invasive method. In some studies, comparing clinical evaluation and MRI results, it has been suggested that clinical evaluation has higher success rates (9). However, controversy continues regarding the congruence of MRI findings with clinical outcomes.

The aim of this study is to evaluate the relationship between clinical and MRI findings in patients who underwent arthroscopic repair due to meniscal tears. In addition, it was aimed to evaluate the success rate of the treatment method applied.

Methods

After obtaining approval from the ethics committee of our institution, patients who underwent arthroscopic meniscal tear repair between January 2011 and December 2018 were included in our study. By examining the files of the patients in the hospital archive, examination forms at the first application and functional evaluation scores used in follow-up were obtained. Inclusion criteria of the patients in the study: (1) being in the age range of 18-55 years, (2) having only meniscus tear with meniscus or anterior cruciate ligament (ACL), (3) having meniscus tear due to trauma or sports injury, (4) ACL reconstruction with hamstring tendon autograft, (5) at least six months of follow-up and regular follow-up visits, (6) patients' compliance with the standard rehabilitation process. As exclusion criteria; (1) being under the age of 18 and over 55, (2) having a history of any previous operation for the knee joint, (3) having a follow-up period of less than 6 months, (4) not following the rehabilitation process, not having regular controls. 28 of the 98 patients who underwent meniscus repair, determined from the hospital records, were not included in the study because they had exclusion criteria.

Seventy patients with inclusion criteria were included in the study. Of the cases included in the study, 57 (81.4%) were men and 13 (18.6%) were women. Average age is 29.3 ± 9.2 (range; 18-54). The mean time from trauma to surgery in patients was 12.2 ± 15.8 (range, 1-82) months, and the mean follow-up time was 35.8 ± 23.3 (range; 8-108) months. It was operated on the right side of 38 (54.3%) and the left side in 32 (45.7%). Fifty (71%) patients had medial meniscus, 15 (21%) patients had lateral meniscus, 5 (8%) patients had both medial and lateral meniscus tears. It was found that 15 of the patients (21.4%) had a complex tear with a longitudinal component, 20 (28.6%) had a bucket handle and 35 (50%) had a longitudinal tear.

Surgical Technique

All patients were operated by an orthopedic and traumatologist experienced in arthroscopic surgery. Operations were performed with a 30° slop arthroscope from Karl Storz (Karl Storz Hopkins®; Germany). In the arthroscopic technique, in addition to standard anteromedial and anterolateral portals, anterior transpatellar portal was used in some cases. After the tear area was rasped, the sutures were sent from the portal that provides the most appropriate angle to the tear line and applied horizontally, vertically or obliquely according to the shape of the tear. Two types of sutures were used in meniscus repair: Polydioxanone suture (Biomet, Warsaw; USA) was used as suture material in the inside-out technique. Meniscus was repaired completely from inside, with the help of a device, using vertical suture in the all-inside technique. Fast-fix® (Smith & Nephew, Inc. Andover, MA; USA), Maxfire (Biomet, Warsaw; USA) meniscus suture equipments were used as suture in the all-inside technique. ACL reconstruction was performed with meniscus repair in 40 of the 70 patients. Endobuttons were used for fixation on the femoral side, while an interference screw and stapler were used on the tibial side.

Rehabilitation Program

The same rehabilitation programs were applied to all patients in the postoperative period. Patients were mobilized with support from the 2nd week to the 6th week by giving partial weight. Isometric quadriceps and hamstring exercises were started on the 1st postoperative day. Full extension and flexion up to 60° were allowed for 0-2 weeks postoperatively. While maintaining the muscle strength and full extension gained between 2-4 weeks, it was tried to achieve a 90° flexion by increasing the range of motion. It was aimed to have full range of motion between 4-6 weeks. Angle adjusted brace was removed at the end of the sixth week. While the patient was allowed to have full range of motion, squatting, jumping and turning movements were not allowed before 3 months. Return to sports and training was provided with straight running for 4-6 months. In patients without ACL injuries, it was enabled to switch to contact sports between six and eight months. Patients with ACL injuries were rehabilitated according to the meniscus protocol for the first 2 months and then the ACL rehabilitation protocol was adhered to. Contact sports were allowed after 10 months.

Clinical Evaluation

Barret's criteria were checked on physical examination in all patients (10). According to Barret's criteria, the meniscus was deemed to be healed in the absence of joint tenderness, effusion, locking in the knee with meniscus repair and negative McMurray test. If one or more of these criteria were found, the result was accepted as clinical failure. In addition, Lysholm functional scoring was evaluated preoperatively and at sixth month postoperatively.

MRI Evaluation

Radiological healing of the meniscal tear was evaluated by MRI of the knee joint at the sixth month postoperatively. MRI scans were performed with a protocol for the knee joint, which is routinely used in our clinic, using a 1.5T MR imaging device (GE Healthcare: Optima MR450w) in all cases. No special preparation was made for the patients before the procedure. MRI images were evaluated by a radiologist experienced in musculoskeletal diseases. The classification made by Crues et al. was used to evaluate the MRI results (11). In this classification, meniscus healing in MRI results was divided into 4; Grade 0: Normal, Grade 1: Increased signal in the intrameniscal area, Grade 2: Intrameniscal linear or wedge-shaped signal intensity, Grade 3: Linear or spherical signal intensity extending to the joint surface. Results reported as Grade 0–1–2 whose signal intensity did not reach the joint surface were considered to be healed, while results reported as Grade 3 that reached the joint surface were considered unhealed. Both clinical and MRI results were compared based on age, tear type, number of sutures used, combination with ACL reconstruction.

Statistical analysis

Demographic and clinical characteristics of the participants who underwent meniscus repair in the study were evaluated using descriptive methods such as percentage, mean, and standard deviation. Pearson Chi-Square Analysis was used for proportional comparisons among categorical data. In addition, Fisher's Exact Chi-Square Analysis was preferred for proportional comparisons with data below 5%. "Independent groups t test" was used when comparing the average data between the groups met the normal distribution hypothesis, and the Mann Whitney U test was used if it was not met. "t test for dependent samples" was used to measure the change of preoperative and postoperative Lysholm functional scoring values. Kappa Analysis was used to measure the consistency between clinical evaluation and MRI findings. IBM SPSS 22.0 program was used to evaluate the analyzes. The level of significance was set as $p < 0.05$ for all statistical analyzes.

Results

In the clinical evaluation performed according to Barret's criteria, there was at least one physical examination finding in all patients (100%) before surgery, while this rate was found to be 17.1% after surgery. In the statistical analysis performed, this rate of healing in physical examination findings after meniscus repair was found to be statistically significant ($p < 0.05$).

Preoperative Lysholm score mean was 62.64 ± 19.73, postoperative Lysholm score mean was 90.93 ± 9.58. It was found that the Lysholm scoring mean significantly changed after treatment ($p < 0.001$).

In comparison made according to demographic characteristics; the mean postoperative Lysholm functional scores was found to be statistically significantly higher under 30 years of age than 30 years and over ($p = 0.002$). In addition, it was found that the postoperative Lysholm functional scores of the cases that were successful in the clinical evaluation made according to the Barret's criteria were statistically significantly higher than the cases without success ($p = 0.001$).

The success status of the operated patients according to the MRI results was evaluated according

to the classification by Crues et al (11). According to this evaluation, healing in MRI was detected in 39 (55.7%) patients (Grade 0-1-2), and there was no healing in 31 (44.3%) patients (Grade 3).

According to the comparison between the two groups under the age of thirty and over the age of 30, it was found that the recovery rates in MRI were not statistically significantly different (p = 0.126) among the cases who underwent meniscus repair. In addition, according to the clinical evaluation, it was observed that the success rates in treatment were not statistically significantly different than the comparison between the two groups (p = 0.743).

According to the tear patterns (complex with longitudinal component, bucket handle, longitudinal), the rates of those with healing on MRI (Grade 0-1-2) were not found to be statistically significantly different (p = 0.521). According to the MRI results, 9 (60%) of the cases with complex tear with a longitudinal component, 9 (45%) of the cases with bucket handle tear, and 21 (60%) of the cases with longitudinal tear had healed. In addition, statistical analysis performed according to clinical evaluation revealed that there was no statistically significant difference between tear patterns (complex with longitudinal component, bucket handle, longitudinal) in terms of success rates (p = 0.363) (Table 1).

In the MRI results, the mean number of sutures in non-healed (Grade 3) participants with respect to the size of the tear were found to be statistically significantly lower than the mean of those with healed (Grade 0-1-2) (p = 0.030). It was found that the success rate in clinical evaluation and the mean number of sutures were not statistically significantly different (Table 2) (p = 0.406).

It was found that the rates of cases with isolated meniscus repair and combined surgery with ACL reconstruction were statistically significantly different (p = 0.019) (Table 3). Healing was found in the MRI results in 14 (46.7%) of the cases with isolated meniscus repair, and in 25 (62.5%) of the cases who underwent combined surgery with ACL reconstruction. According to the clinical evaluation using Barret's criteria, it was found that the rates of cases with isolated meniscus repair and combined surgery with ACL reconstruction were not statistically significantly different (p = 0.363).

Statistical analysis was performed to evaluate the consistency between recovery status according to MRI results and success according to clinical assessment. According to this analysis, the sensitivity coefficient was calculated as 52.86% and the kappa value as 0.123 (Table 4). With this result, it was determined that the concordance between the improvement in MRI and success in clinical evaluation was insignificant.

Table 1. Comparison of clinical evaluation and magnetic resonance imaging results according to tear type in patients

		Tear Type						X2	p
		Complex tear		Bucket handle tear		Longitudinal tear			
		n	%	n	%	n	%		
Magnetic Resonance Imaging Result	Unsuccessful	6	40	11	55	14	40	1,302	0,521
	Successful	9	60	9	45	21	60		
Clinical Evaluation	Successful	14	93,3	17	85,0	27	77,1	2,03	0,363
	Unsuccessful	1	6,7	3	15,0	8	22,9		

Table 2. Comparison of the number of sutures according to radiological and clinical evaluation results

	Magnetic Resonance Imaging Result		
	Unsuccessful (n=31)	Successful (n=39)	p
Number of sutures	5,07±2,22	4,00±1,79	0,030
	CLINICAL EVALUATION		
	Successful (n=58)	Unsuccessful (n=12)	p
Number of sutures	4,40±2,09	4,83±1,85	0,406

Table 3. Comparison of clinical evaluation and magnetic resonance imaging results between patients with isolated meniscus repair (M) and those with combined meniscus repair and ACL reconstruction (M+ACL).

		M		M+ACL			
		N	%	N	%	X2	p
Magnetic Resonance Imaging Result	Unsuccessful	16	53,3	15	37,5	7,97	0,019
	Successful	14	46,7	25	62,5		
		N	%	N	%	X2	p
Clinical Evaluation	Successful	25	83,3	33	82,5	2,03	0,363
	Unsuccessful	5	16,7	7	17,5		

Table 4. Comparison of success between clinical evaluation and magnetic resonance imaging findings

		Magnetic Resonance Imaging Result		Total	Kappa value
		Successful	Unsuccessful		
Clinical Evaluation	Unsuccessful	9	3	12	0,123
	Successful	30	28	58	
Total		39	31	70	

Kappa <0: No consistency
Kappa between 0.00 and 0.20: Insignificant
Kappa between 0.21 and 0.40: Low
Kappa between 0.41 and 0.60: Moderate
Kappa between 0.61 and 0.80: Important
Kappa between 0.81 and 1.00: Nearly perfect

Discussion

The results of this study showed that the Barret's criteria and Lysholm functional scoring to evaluate the results of meniscus repair successful results in the follow-up and evaluation phase. When the MRI results were examined, it was found that it was not as successful as clinical evaluation in determining recovery after repair. While making a repair decision in meniscus tears; the age of the patient, the location of the tear, the pattern of the tear, the size of the tear, the stability of the knee joint, the time elapsed after the trauma, the quality of the meniscus tissue and the experience of the surgeon are factors that should be evaluated (1). The importance of these factors has been examined in many different studies (13-15).

Various evaluation methods such as clinical evaluation, "secondary look" arthroscopy and MRI have been reported in the literature after meniscus repair. "Secondary look" arthroscopy is the gold standard method for evaluating meniscus healing (16). However, its being an invasive method makes it difficult to use in routine practice (17). Miao et al. compared clinical evaluation, " secondary look " arthroscopy and MRI. The success rates of the clinical evaluation were found to be higher than the evaluation made by MRI and " secondary look " arthroscopy. Although it is an indirect method, it has been suggested that clinical evaluation with patient history and physical examination is more successful in evaluating postoperative recovery (9). In clinical evaluation, the experience of the surgeon comes to the fore, and it can be performed without any invasive procedure (16). In our study, the clinical results of meniscus repair were evaluated by physical examination methods. Physical examination was based on clinical criteria determined by Barrett et al. while there was at least one physical examination finding in all patients (100%) preoperatively, this rate was found to be 17.1% after surgery. In the statistical analysis, this healing was found significant in physical examination findings after meniscus repair. Lysholm functional scoring is one of the most used scorings for knee joint functional evaluation. It is mainly used for patients with knee ligament injury (18). All patients in our study were evaluated with preoperative and postoperative Lysholm functional scoring. It was observed that there was a statistically significant increase in the postoperative period compared to the preoperative period.

According to many studies, the most reliable imaging method for evaluating healing after meniscus repair is MRI or computed tomography arthrography (16,19,20). However, the disadvantages of both methods are that they are invasive. The fact that MRI is both noninvasive and easily accessible has increased its usability in evaluation after meniscus repair. Miao et al. combined several sequences of MRI in the radiological evaluation of meniscal healing reported 92% sensitivity and 99% specificity (21). However, edematous and fibrous tissue that occurs during the recovery period can be perceived as a pathological signal (22). When we look at the

literature, although conventional MRI is an accurate method for the diagnosis of meniscal irregularities, there are studies showing that it is less reliable in the postoperative evaluation of meniscus repairs in the short and medium term (6,23). Eggli et al. reported that tears were reported on MRI images in 24 (96%) of 25 menisci with successful healing and conventional MRI was not safe (24). Hantes et al. evaluated the healing process of meniscal repair by MRI 3, 6, and 12 months after surgery (8). Postoperative signal changes were detected in each of the 20 patients participating in the study at postoperative 3 months. There was a significant decrease in these signal changes between 3 and 12 months. However, the signal change did not disappear completely.

In our study, the radiological healing of the cases with meniscus repair was evaluated with MRI. The classification described by Crues et al. was used to evaluate the degree of signal in the repaired area. According to the classification made by Crues et al. the healing rate was found to be 55.7%. At the end of this study, our opinion; clinical evaluation and scoring method is more advantageous than MRI evaluation in postoperative follow-up, both economically and noninvasively. Negative aspects of MRI in postoperative follow-up; the presence of signal changes in MRI evaluations even after a very long postoperative follow-up period, the possibility of misleading the clinician in the follow-up of these visible signal changes, the lack of criteria for evaluating the MRI results that have yet to be clearly established in the postoperative follow-up, the high cost of the MRI method and the lack of consistency between MRI results and clinical evaluation can be counted as.

The weaknesses of our study are that male-female, internal-external meniscus subgroups were not high enough to make comparisons, meniscus sizes could not be documented in more detail, cartilage damage was not evaluated, and the number of patients included in the study was not high. Its strengths include the average follow-up period of the cases included in the study, approximately 3 years, and being operated by a single surgeon

Conclusions

According to these results, it has been determined that non-invasive and cost-free clinical evaluation gives more accurate results than MRI in the follow-up of the patients with meniscus repair. In this respect, we think that Barret's criteria and Lysholm functional scoring are effective methods to evaluate recovery. However, the long-term effects of this inconsistency in clinical evaluation and MRI findings may be a separate research topic.

Ethics Committee Approval: Ethics committee approval was received for this study from the Health Sciences University Haydarpaşa Numune Training and Research Hospital Clinical Research Ethics Committee (ethics committee date and no: 22/07/2019- HNEAH-KAEK 2019/82)

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CASE REPORT **DOI:** 10.19127/mbsjohs.975462

Mirtazapine Induced Akathisia:A Case Report

Deniz Deniz Ozturan [1(ID)], Figen Unal Demir[2(ID)]

[1]Department of Psychiatry, Ordu University Faculty of Medicine, Ordu, Turkey
[2]Tokat Mental Health and Diseases Hospital, Tokat, Turkey

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Abstract

Akathisia is a movement disorder characterized by an inner sense of restlessness and it needs attention because of the increased risk of suicidal behavior. Although akathisia may affect the trunk and arms, it predominantly affects the legs. Akathisia may occur exposure to antipsychotics and antidepressants. Mirtazapine is an antidepressant blocking presynapticα-2adrenergic receptors and 5-hydroxytryptamine (5-HT) 2A/2C, 5 HT 3 and histaminergic postsynaptic receptor. In this single case study, we aimed to present a case of akathisia which occurred after mirtazapine treatment.

Case presentation: A fifty -two-years-old woman presented with a-one-month history of decreased sleep and appetite. She had been using antidepressant medication (Fluoxetine 40 mg / day) for five months due to depressive disorder. Mirtazapine 15 mg/day was added to the patient's treatment. Three hours after the first dosage she could not sit even for few minutes and complained of inner restlessness. She reported feeling anxious. Biochemical tests for metabolic/electrolyte parameters were within reference ranges. She had no neurological disease. Mirtazapine was removed and her symptoms resolved in one day.

She consulted the department of internal medicine. Her physical examination was normal. Biochemical tests for metabolic/electrolyte parameters were within reference ranges. She had no neurological disease. Mirtazapine was removed and her symptoms resolved in one day.

Akathisia is an important side effect because of related to a subjective experience of discomfort that can lead to suicidal behavior. This case illustrates the significant of being alert to any movement disorders in patients treated with mirtazapine.

Keywords: Akathisia, mirtazapine, movement disorder

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Address for correspondence/reprints:

Deniz Deniz Ozturan

Telephone number: +90 (505) 241 91 49

E-mail: dr.denizdeniz@gmail.com

Introduction

Akathisia is recorded as "warnings and precautions" occurring in less than 1% of the population prescribed mirtazapine (1). The imbalance between dopaminergic and serotonergic/noradrenergic neurotransmitter systems has been reported as a possible mechanism of akathisia.

Mirtazapine increases noradrenaline and serotonin by blocking noradrenergic alpha 2 receptors, serotonergic 5-HT2 ,5-HT3, blocking H1 receptors (3). It has been hypothesized that the beneficial effects of this drug in akathisia are due to 5HT2A antagonism, and α2 blockade may be responsible for akathisia (4, 5,6).

We aimed to present a case of akathisia that developed after mirtazapine treatment.

Case

A 52-year-old female patient applied to our outpatient clinic with complaints of loss of appetite and insomnia lasting a month. The patient has been using fluoxetine 40 mg/day for about 5 months with the diagnosis of majör depression. Mirtazapine 15 mg/day was added to the patient's treatment because of her complaints. Four days later, the patient came with restlessness in the legs, inner restlessness and a constant desire to walk, which appeared 1-2 hours after the use of mirtazapine. Her complete blood count, liver function tests, kidney function tests, sedimentation, ferritin, iron and iron-binding capacity, thyroid function tests were normal. She did not have any neurological disease and also any chronic disease. The patient reported that she did not have any complaints on the day she did not take the drug. The patient's consent was obtained for this case study.

Discussion

Akathisia is often referred to as a feeling of inner restlessness, but many patients may not be able to describe this feeling unless asked directly, and many confuse this feeling with anxiety (7). Although the exact incidence of antidepressant-induced akathisia is unknown, it is an extrapyramidal system side effect mostly related to antipsychotic use. Drugs that increase the stimulation of serotonergic or noradrenergic receptors in the mesocorticolimbic pathway may be responsible for the induction of akathisia (8). The drugs most commonly associated with movement disorders were mirtazapine, citalopram and paroxetine, while fluoxetine, escitalopram and mianserin were also associated with movement disorders. (9). In the literature, there were case reports on the use of mirtazapine in akathisia, which generally develops after antipsychotic treatment (10). The number of patients who developed akathisia due to the use of mirtazapine is very low.

In a letter to the editor, a 52-years-old male patient who developed akathisia after mirtazapine 30 mg treatment and a 73-year-old female patient who developed akathisia after mirtazapine 30 mg was added (11). In a case report, a 72-year-old patient who developed akathisia after 20 years of mirtazapine use was presented (12). Akathisia was reported in a 42-year-old female patient who switched from fluoxetine 40 mg to 15 mg dose mirtazapine in 2015. (13). In a recent case report, a 30-year-old male patient who developed akathisia after mirtazapine use was presented, and the findings suggested that propranolol treatment was beneficial (14). In our case, akathisia was observed after adding 15 mg/day mirtazapine to the treatment of the patient who has been using fluoxetine for six months.

Although akathisia and restless legs syndrome are often confused, the inner distress and mental restlessness are not seen in restless legs syndrome. In restless legs syndrome, only the desire to move the legs is observed (15). We considered the diagnosis of akathisia because of internal restlessness in addition to the desire to move the legs in our patient.

Lipinski et al. (16) describe the successful use of propranolol ranging from 40 to 90 mg/day to treat five patients with SSRI-induced akathisia. Clonazepam, alprazolam and lorazepam are also used in the treatment of akathisia (17,18). In our case, there was no need for additional treatment, as akathisia regressed the day after the drug was discontinued.

It is stated that akathisia should be considered as an independent risk factor for self-harm and suicide (19). Thus, akathisia is a side effect that should be recognized and intervened.

Conclusion

Mirtazapine-induced akathisia is not very common but is a severe side effect. The most significant risk is to cause a suicide attempt. Although it is used in the treatment of akathisia, it should be kept in mind that mirtazapine may cause akathisia.

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Approach to Respiratory System Involvement and the Symptom of Dyspnea in Covid-19 Disease

Gulsum Hilal Demir [1(ID)], Burcu Kayhan Tetik[2(ID)]

[1]Elazığ Provincial Health Directorate, Elazığ, Turkey,
[2]Department of Family Medicine, Inonu University Medical School, Malatya Turkey

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Abstract

The Covid-19 pandemic, China at the end of 2019 and was declared a global pandemic by the World Health Organization on March 11, is still a serious public health problem. The international virus taxonomy committee named this virus as SARSCoV-2 and the disease caused by the virus as Covid-19 disease. The disease is transmitted from person to person through droplets. When the infected person coughs, sneezes, or speaks, the virus found in respiratory secretions is transmitted by direct contact with the mucosa. In addition, it can be transmitted upon bringing one's hands to the mucous membranes of the mouth, nose, or eyes after hand-to-hand contact with droplets produced by the coughing and sneezing of a sick individual.

The respiratory system is the system most affected by Covid-19 infection. The virus affects the respiratory system in 3 ways: acute respiratory distress syndrome (ARDS) with diffuse alveolar damage, diffuse thrombotic alveolar microvascular occlusion, and inflammatory mediator-associated airway inflammation. As a result of these 3 effects of the virus, impaired alveolar oxygenation, hypoxemia, acidosis and, consequently, dyspnea develops. Dyspnea occurs when breathing becomes disturbingly noticeable. Dyspnea is an important symptom that affects the prognosis of Covid-19 disease. The severity of the disease ranges from asymptomatic infection to critical illness. Dyspnea symptoms and respiratory system involvement are more common in critical illness. Primary care physicians should be familiar with respiratory system pathologies caused by the Covid-19 disease.

Keywords: Covid-19, Dyspnea, Pandemic

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Address for correspondence/reprints:

Gulsum Hilal Demir

Telephone number: +90 (552) 430 70 29

E-mail: glsm_kara90@hotmail.com

Introduction

The Covid-19 pandemic, which emerged in Wuhan, China at the end of 2019 and was declared a global pandemic by the World Health Organization on March 11, is still a serious public health problem (1).

Iatrotropic stimulus, a term frequently used in family medicine, is defined as the reason that prompts a patient to seek out the care of a physician (2). Dyspnea is an important iatrotropic stimulus in Covid-19 disease. Furthermore, dyspnea is a symptom that should be alarming for family physicians. Distinctive problem-solving skills, which is one of the leaves of the WONCA tree of competencies in general practice, is the core competency that every family doctor should have. These such problem-solving skills should be used in the management of Covid-19 disease and in managing the symptom of dyspnea due to the disease. In this context, we aimed to examine in depth the respiratory system involvement in Covid-19 disease and the symptom of dyspnea associated with this involvement.

Taxonomy and Structural Features of the Coronavirus

According to the classification determined by the International Committee on Virus Taxonomy (ICTV), coronaviruses belong to the Nidovirales class of the Riboviria kingdom. The virus that causes the Covid-19 disease is the SARS-CoV-2 strain belonging to the Betacoronavirus genus in the Coronaviridea family. The international virus taxonomy committee named this virus as SARSCoV-2 and the disease caused by the virus as Covid-19 disease (3).

Coronaviruses are 65-125 nm in diameter and contain single-stranded ribonucleic acid (RNA) and feature rod-like extensions on their surface. These viruses were named Coronavirus (crowned virus) due to these rod-like extensions, based on the Latin meaning of "corona" meaning "crown"(4).

Coronavirus Infection Chain

According to epidemiological studies, wild animals (bat?) sold in the Huanan Seafood Wholesale Market are thought to be the first source of the infection chain. The disease is transmitted from person to person through droplets. When the infected person coughs, sneezes, or speaks, the virus found in respiratory secretions is transmitted by direct contact with the mucosa. In addition, it can be transmitted upon bringing one’s hands to the mucous membranes of the mouth, nose, or eyes after hand to hand contact with droplets produced by the coughing and sneezing of a sick individual. The majority of society is susceptible to the Covid-19 disease. Health workers, people over 50 years old, people with comorbidities (hypertension (HT), heart disease, diabetes mellitus (DM), malignancy, chronic obstructive pulmonary disease (COPD), kidney disease, etc.), people in care and rehabilitation centers, schools, military barracks, prisons, people living in migrant camps, and seasonal agricultural workers are especially vulnerable groups in terms of disease (5).

Pathogenesis of Coronavirus

Coronaviruses attach to the host cells via the spike (S) protein on the outer surface and thus enter the cell. The S protein regulates the entry of the virus into the host cell by recognizing the receptor in the target cell. The life cycle of the virus begins with the binding of the S protein to the Angiotensin-Converting Enzyme 2 (ACE2) receptor on the host cell surface (6). After the virus enters the host cell, viral antigens are presented to macrophages and T lymphocytes by antigen-presenting cells (7). Thus, the chain of inflammation, the severity of which varies according to the immune system and age of the person, develops. Infection primarily affects the innate immune system and causes the release of cytokines (IFN-α, IFN-γ, IL-1β, IL-6, IL-18, etc.), especially interferon (7).

Clinical Symptoms of Covid-19 Disease

The most common symptoms in Coronavirus patients are fever, malaise, and cough. According to a study conducted in China, common clinical symptoms include fever (88.7%), cough (67.8%), fatigue (38.1%), dyspnea (18.7%), sore throat (13.9%), myalgia (14.9%), and headache (13.6%). In the same study, diarrhea (3.8%) and vomiting (5.0%) were found to be gastrointestinal symptoms of the virus (8).

Laboratory Findings of Covid-19 Disease

The most common laboratory findings in Covid-19 diagnosis were found to be lymphocytopenia (83.2%), thrombocytopenia (36.2%), and leukopenia (33.7%). High levels of infection markers such as C-reactive protein (CRP), ALT/AST in liver function tests, and D-Dimer, have also been frequently reported.

Changes in general laboratory values are summarized in the table 1 below (9).

Table 1. Changes in LaboratoryValues in Covid-19 Disease

Lab Test Name	Change in Test
Complete Blood Count	Decreased lymphocyte thrombocyte count Increase in the number of leukocytes and neutrophils
CD4+ T Cell Count	Decrease
CD8+ T Cell Count	Decrease
Ferritin	Increase
C Reactive Protein (CRP)	Increase
Sedimentation Rate	Increase
Procalcitonin	Increase
Interleukin 6 (IL-6)	Increase
CreatinineKinase	Increase
LactateDehydrogenase	Increase
D-Dimer	Increase
Troponin	Increase
AST	Increase
ALT	Increase

Radiological Findings of Covid-19 Disease

In Covid-19 pneumonia, bilateral, localized (especially in the middle and lower zone), peripherally weighted, irregularly boardered density increases and consolidation are seen on chest radiograph (10).

In the early stages of the disease, unilateral or bilateral subpleural ground-glass opacities are seen mainly in the lower lobes on Computed Tomography (CT). In the later stages of the disease, diffuse ground-glass opacities, interlobular and intralobular septal thickenings (curbstone appearance) and consolidations are detected with bilateral and multilobar distribution. Ground glass densities with more intense consolidation in a crescent or ring shape are called “reverse halo sign” and are frequently seen in Covid-19 disease (11).

Clinical Course in Covid-19 Disease

While mild infection is observed in 81% of symptomatic patients infected with Covid-19 disease, severe disease occurs in 14% of patients and critical illness occurs in 5% of patients (12).

Severe disease is predominantly seen in people with advanced age and underlying comorbidities. Studies have found that cardiovascular disease, DM, HT, chronic lung disease, cancer, chronic kidney disease, and obesity (body mass index (BMI) ≥ 30) are associated with severe disease and mortality (13). The severity of the disease ranges from asymptomatic infection to critical illness. The clinical severity of Covid-19 disease is defined in 5 groups as asymptomatic, mild, moderate, severe, and critical as indicated in the table 2 below (12,13).

Table 2. Clinical Course in Covid-19 Disease

Asymptomatic infection:	Cases with positive SARS-CoV-2 PCR test and noclinical symptoms. Asymptomatic infection is important because it increases the risk of transmission in the community. Especially asymptomatic infants and children play an important role in human-to-human transmission.
Mildillness:	Patients have mild symptoms such as fever, fatigue, myalgia, sorethroat, cough, runnynose and sneezing. There are noradiographic findings.
Moderateillness:	Pneumonia, fever and cough; patients may have wheezing, but no severe hypoxemia. Radiographic findings are present.
Severe illness:	Rapid progression, dyspnea, centra lcyanosis. Inpatients: Respiratory rate > 30 Oxygen Saturation (SpO2) < 93 There are signs of PaO 2/FiO2 < 300 mm/Hg.
Critical illness:	Akut Respiratory Distress Syndrome (ARDS), respiratory failure, sepsis, septic shock, multiple organ dysfunction are seen.

Covid-19 Disease and the Respiratory System

The course of the Covid-19 disease in the respiratory system can be categorized as early period, pulmonary period, and hyperinflammation period. In the early period, the virus is active and causes symptoms such as dry cough, fever, and weakness. In the pulmonary period, shortness of breath and hypoxemia develop. During the hyperinflammation period, the host response is dominant. During this period, ARDS, shock, and organ failure may develop (14).

Covid-19 Disease and Pneumonia

Radiological imaging shows infiltration and ground glass opacities (20). Mild cases may present with fever, chills, and dry cough. Tachypnea (>30/min), dyspnea, respiratory distress, and hypoxia (SpO2 < 90% in room air) are seen in severe cases (15).

Covid-19 Disease and ARDS

ARDS is considered according to clinical and respiratory parameters. The diagnosis of ARDS should be considered in the presence of bilateral

infiltration in radiology if acute respiratory distress cannot be explained by the association of cardiogenic edema. ARDS causes diffuse alveolar damage to the lung. In an acute situation, hyaline membrane formation in the alveoli, followed by interstitial enlargement, edema, and fibroblast proliferation develops (16).

Covid-19 Disease and Cytokine Storms

A cytokine storm is a severe immune system hyperreaction in which large amounts of cytokines are rapidly released into the systemic circulation. Chemokines and high plasma inflammatory cytokines, interleukins (IL-1, IL-6, IL-8, IL-12, IL-18), tumor necrosis factor (TNF-α), and interferon (INF) play a role in the cytokine storm. The inflammatory response caused by excessive cytokine release seen with T cell and monocyte/macrophage activation increases vascular permeability, leading to exudative fluid accumulation in the alveoli and causes respiratory failure (17).

Fever that does not decrease despite treatment, elevated D-dimer, high ferritin and CRP values, cytopenia, low fibrinogen, and abnormal liver function tests should suggest a cytokine storm. Looking at ferritin, CRP, liver enzymes, triglyceride, D-dimer, lymphocyte count, and platelet count values in terms of hyperinflammation in all severe Covid-19 cases; it is important to recognize the cytokine storm early and to identify the subgroups that may benefit from immunosuppression (5).

Treatment of Covid-19 Disease

Favipravir

Favipiravir is recommended in probable or definite cases in the Covid-19 treatment guide of the Ministry of Health. In asymptomatic, uncomplicated, mild-to-moderate pneumonia patients, a 5-day treatment is recommended as 2x1600 mg/day on the first day and 2x600 mg/day on the next 4 days. In cases aged >50 years and with comorbidities, a total of 10 days of treatment is recommended, with the dose of Favipravir being 2x1800 mg on the first day and 2x800 on the other days (18).

Anticoagulant Therapy

Thrombosis prophylaxis should be applied in all hospitalized Covid-19 patients unless there is active bleeding or thrombocytopenia (<25-30.000/µl). Low molecular weight heparin (LMWH) is preferred over standard heparin in thrombosis prophylaxis. Because LMWH causes thrombocytopenia less commonly (18).

Other Treatments:

Oxygen therapy, steroid therapy, Tocilizumab, and plasma therapy can be applied to hospitalized patients.

Definition of Dyspnea

While breathing is an unnoticed condition in normal physiology, when it becomes disturbingly noticeable, it is called dyspnea (19). It describes the feeling of difficulty in breathing. The word dyspnea is formed by the combination of the words “dys” meaning bad or difficult and “pnea” meaning breath or breathing. It is a subjective term and people may express dyspnea in different ways. Patients may express the symptoms of dyspnea as shortness of breath, chest tightness, panting, and air hunger.

The mechanisms involved in the formation of dyspnea sensation are as follows:

Increased respiratory demand: Increased ventilation at vigorous exercise levels in healthy individuals, and even mild exercise in patients with lung and heart disease causes dyspnea. This increased effort stimulates the central nervous system, resulting in an increase in motor stimulation. The dyspnea cycle results in decreased activity, decreased fitness, even less movement, and occurrence of dyspnea*. Age, nutritional disorders, and hypoxemia due to disease also cause a decrease in exercise capacity (20).

Abnormalities of the respiratory muscles: Weakness or mechanical failure of the respiratory muscles causes an incoordination between the central motor response and lung ventilation. This disharmony explains the dyspnea that occurs in neuromuscular diseases and respiratory muscle fatigue. In those with COPD, excessive inflammation of the lung and increased enlargement of the thorax lead to shortening of the inspiratory muscles and reduced pressure-generating effect. The decrease in the mechanical strength of the inspiratory muscles creates the feeling of dyspnea (20).

Conditions that prevent breathing: Increased airway resistance with narrowing of the airways in diseases such as asthma and COPD, and decreased lung elasticity in lung parenchymal diseases such as pulmonary fibrosis cause dyspnea. The emergence of conditions that prevent breathing results in central motor commands trying to increase ventilation.

Dyspnea occurs when increased respiratory effort cannot provide the necessary ventilation (20).

Blood gas abnormalities: Blood gas disorders are one of the most serious conditions to occur in heart and lung diseases. Hypoxemia increases the motor activity of respiration via chemoreceptors. Hypoxia also has a direct dyspnea-causing effect (20).

Dyspnea can also be classified as acute and chronic. Acute dyspnea develops within minutes to hours. It mostly happens in diseases that affect the heart or lungs. Pericardial tamponade and pneumothorax are examples of acute dyspnea that life threatening and often need urgent treatment. Chronic dyspnea is dyspnea lasting longer than one month. Chronic dyspnea is usually progressive. Initially, shortness of breath with exertion may increase over time and can be felt without exertion. COPD and asthma are the most common examples of chronic dyspnea (20)

The Symptom of Dyspnea in Covid-19 Disease

The respiratory system is the system most affected by the Covid-19 infection. The virus affects the lungs in 3 ways: acute respiratory distress syndrome with diffuse alveolar injury (ARDS), diffuse thrombotic alveolar microvascular occlusion, and airway inflammation associated with inflammatory mediators. As a result of these 3 effects of the virus, impaired alveolar oxygenation, hypoxemia, acidosis, and dyspnea develop as a result. (21).

Dyspnea is an important symptom affecting the prognosis of Covid-19 disease. In their meta-analysis study, which included 13 studies and 3027 patients, Zheng et al. categorized the disease as critical/mortal and non-critical. Dyspnea symptoms were significantly higher in patients categorized as critical/mortal (22). In another meta-analysis study in which 4062 patients were examined, statistically significant data was found suggesting that patients who were old, male, had a high BMI, and had dyspnea and fever symptoms experienced a more severe form of the illness (23). In a study conducted by Xie et al. in Wuhan, 49.2% of Covid-19 patients had dyspnea symptoms. As a result of this study, researchers found an independent relationship between shortness of breath and death (24). In another meta-analysis study conducted by Jain et al., in which they examined 1813 patients; dyspnea was found to be the only predictive symptom for severe Covid-19 disease and ICU admission (25).

There are studies in the literature showing that Covid-19 disease causes both acute and chronic dyspnea in patients. (26.27) In a cohort study by Lerum et al., in which they followed 103 Covid-19 patients for 3 months, it was found that dyspnea continued in 56% of the patients after 3 months. As a result of this research, they thought that Covid-19 might be the cause of chronic dyspnea (28).

The Concept of Non-Dyspneic Hypoxemia (Happy Hypoxemia, Silent Hypoxemia) in Covid-19 Disease

Hypoxemia is an insufficient amount of O2 in the arterial blood (PaO2<80 mmHg). In diseases such as pneumonia, COPD, and asthma, hypoxemia in the blood is usually seen along with the symptom of dyspnea. Likewise, in Covid-19 disease, hypoxemia is seen in the blood together with dyspnea. Silent hypoxemia (Happy hypoxemia) is severe hypoxemia without symptoms of dyspnea (29). Some COVID-19 patients have been labelled with 'happy hypoxia', in which patient complaints of dyspnoea and observable signs of respiratory distress are reported to be absent. A perplexing clinical aspect of COVID-19 is presentation of patients with pronounced hypoxemia without expected signs of respiratory distress or dyspnea, even when cyanotic. Nonetheless, these patients frequently leapfrog clinical evolution stages and suffer ARDS with concomitant cardiorespiratory arrest and death. This phenomenon is referred to as silent or 'happy' hypoxemia. Although the prevalence is not clear in Covid-19 Disease, silent hypoxemia can also be seen. There are many hypotheses in the literature regarding the pathophysiology of silent hypoxemia that can be seen in Covid-19 disease. Inability to stimulate the respiratory center due to insufficient increase in CO2 in the blood, the fact that the coronavirus binds to ACE receptors in peripheral chemoreceptors and desensitizes them, and its the relationship to thrombi in the pulmonary vessels are among the hypotheses of silent hypoxemia that occurs without the feeling of dyspnea (30, 31, 32, 33, 34).

In Summary, How Should Primary Care Physicians Approach Respiratory System Involvement and the Sympton of Dyspnea in Covid-19 Disease?

In a newly diagnosed or follow-up Covid-19 patient, shortness of breath should be questioned in the taking of medical history. Among the vital signs, respiratory rate and oxygen saturation should be checked. Patients with respiratory rate >30 and oxygen saturation <93 should be referred to a higher

level of care. In addition, since one of the causes of dyspnea in Covid-19 disease is microvascular thrombosis, the use of anticoagulants should be questioned, and anticoagulants should be started in patients who do not use anticoagulants by using the coagulopathy management guide of the Ministry of Health. In regards to the blood test results of the patient; if the blood lymphocyte count is approximately 10x the upper limit of the normal value or ferritin>500 ng/ml or D-dimer>1000 ng/ml or CRP > approximately 10x the upper limit of the normal value, the patient should be referred to an upper level of care on suspicion of cytokine storm (5.9) Physicians should not forget that in Covid-19 disease, patients may have hypoxemia without symptoms of dyspnea, and should be alert to silent hypoxemia.

In Turkey, covid-19 follow-up is not done so comprehensively by primary care physicians. However, these recommendations should be taken into account by primary care physicians.

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