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From the Editor

Dear Readers,

We are pleased to present you with the second issue of 2023, which contains a variety of articles that we believe will be of interest to healthcare professionals, particularly primary care physicians. Our aim is to provide a useful guide for healthcare professionals, so we have prepared 6 research articles, a case report and a review that highlight new developments in important areas of healthcare.

Our research articles cover a range of topics, including the latest advances in vitamin D testing, the management of endocrine disorders in primary care, and approaching geriatric patients. Our case report provides a detailed analysis of a rare but important case, while our review article examines the current state of post-traumatic stress disorder.

As the most cited primary care journal in Turkey, we are honoured to continue to serve as a valuable resource for healthcare professionals in the region. We are grateful for your growing interest in our journal and look forward to continuing to bring you the latest research and evidence in primary care.

Please stay tuned for the next issue, which we are confident will be as informative and thought-provoking as this one.

Assoc. Prof. Dr. Ahmet Keskin

Contents

THE CHANGE OF THE VITAMIN D TEST REQUEST NUMBER AFTER THE REGULATION BY THE MINISTRY OF HEALTH

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Abstract

Objectives: There has been an increase in 25-hydroxy vitamin D (25(OH)D) test requests and laboratory costs in recent years. At the end of 2019, the General Directorate of Health Information Systems issued a regulation calling for restricting vitamin D requests in primary care. We aimed to investigate the effect of this regulation on the requested numbers of 25(OH)D tests with the big data obtained from the national information health system of the Turkish Ministry of Health.

Materials and Methods: Between 2016-2022, all inpatient and outpatient tests and 25(OH)D tests in all medical biochemistry laboratories in Turkey were determined based on department and institution type. Distribution among health institutions and test request rates were calculated.

Results: The total number of 25(OH)D tests requested was increased from 2016 to 2022, except for 2020 and 2021, probably related to the COVID-19 pandemic. The yearly increase rate in 2017, 2018, 2019, and 2022 was 137%, 56%, 16%, and 5%, respectively. The number of 25(OH)D tests requested in primary care institutions decreased after the regulation. The total number of 25(OH)D tests requested in 2nd and 3rd Stage Public Health Facilities and private hospitals increased in 2022 compared to 2019.

Conclusion: Our findings showed that the request for 25(OH)D testing decreased in primary care and increased in 2nd and 3rd Stage Public Health Facilities and private hospitals after the regulation was released. Despite the decrease in the yearly increase rate in the number of test requests, the annual number of tests requested is still high, suggesting that different measures should be taken.

Keywords: 25-hydroxyvitamin D, medical biochemistry laboratory, big data, laboratory tests, national health data, ministry of health.

Introduction

Vitamin D is a hormone known to be vital for bone development and strength. Vitamin D is found to be associated with multiple conditions such as autoimmune diseases, cardiovascular disorders, multiple sclerosis, diabetes, cancer, and infection risk without a proven causal relationship.[1] Moreover, a very large proportion of the population has low vitamin D levels, which may be due to a normal variation in vitamin D metabolism.[2]

On the other hand, the role of vitamin D in the pathogenesis of many diseases has prompted doctors and patients to request more vitamin D tests, increasing the number of tests exponentially.[3] Who should be tested for vitamin D deficiency is still a matter of debate. Although vitamin D deficiency is common, universal testing is not recommended because due to the high cost of the test materials. Additionally, extensive studies demonstrated that vitamin D supplementation in vitamin D-replete individuals did not improve overall health status.[4] National and international guidelines suggest vitamin D testing only in certain risk groups.[5,6]

The use of laboratory tests is vital in diagnostic decision-making, and approximately 70% of these decisions are based on the results of diagnostic tests.[7] As a result of the increased use of laboratory testing, the associated costs have increased considerably.[8] Several studies have been done in recent years to find a better solution to improve the appropriate use of laboratory tests in hospital and primary care settings.[9] The impact of different interventions to decrease laboratory test requests was evaluated in these studies. These modifications are classified as weak, moderate, or strong based on the strength of their effect on decreasing inappropriate testing.[10] Educational approaches, such as reference to evidence-based guidelines, are considered weak tools; however, various restrictions in the ordering process, such as limiting or completely eliminating test availability, test ordering algorithms, and reflex testing, as well as the design of the ordering process, including decision support and the use of pop-ups, are considered moderate and strong tools.[9] In Turkey, total health expenditure was $12,467,468,000 in 2002 and increased to $39,662,184,539 in 2016 while spending on medical laboratory services in 2002 was approximately $100 million (0.802% of the entire budget), 2016 it increased by about 3.5-fold, exceeding $350 million (approx. 0.882% of the overall budget) and the 25-hydroxyvitamin D (25(OH)D) test was one of the most striking tests of recent years.[11]

At the end of 2019, the Turkish Ministry of Health imposed a regulation that prevented the request for vitamin D testing by primary care physicians. The present study aims to describe the effect of this circular on vitamin D test request numbers among different health facilities and specialties.

Materials and Methods

The health records of individuals who were admitted to public, private, and university health institutions were collected via the Turkish Ministry of Health National electronic database. E-Health uses information and communication technologies for health and includes the data of health information systems, including electronic health records, telemedicine, mobile devices, e-learning tools, and decision support system.[12] This retrospective study included 25(OH)D measurements from 2016 to 2022. Laboratory results were presented to the author group under the supervision of the Ministry of Health to encourage data sharing and scientific research with the scientific community. The National Health Database provided information about laboratory services and testing processes. The test name, test result, test unit, and reference range were all included in the test process information. Demographic information of individuals was included in laboratory service information. Chromatographic methods, especially the immunoassay method, were generally used for vitamin D testing in Turkey (approximately 95%). All of the test measurements were presented as mg/L.[13]

At the end of 2019, the Turkish Ministry of Health imposed a regulation regarding vitamin D testing, preventing the request for vitamin D testing by primary care physicians. At the beginning of 2020, this Regulation was launched. Although by the regulation, every physician could order a free vitamin D test for inpatients and intensive care patients, only certain specialists were allowed to order vitamin D tests in the outpatient and emergency departments. Family physicians working in primary care could no longer request vitamin D testing. Additionally, the vitamin D test ordering interval has been established as 90 days, and it has been made mandatory for the Hospital Information System (HIS) to send a message to remind of this interval. A restriction was also imposed on requesting more than two tests per year.

Statistical analysis

Study data were analyzed by the SPSS program (version 20). Statistics output was presented as numbers and percentages.

Results

The total number of 25(OH)D tests requested between 2016 and 2022 were 2,826,997, 6,722,430, 10,506,144, 12,216,974, 5,477,206, 9,704,615 and 12,823,842 for consecutive years respectively. The total number of 25(OH)D tests requested in primary care institutions increased from 732,246 in 2017 to 2,714,443 in 2019, decreasing to 36,130 in 2022. The total number of 25(OH)D tests requested in 2nd and 3rd Stage Public Health Facilities and private hospitals increased in 2022 compared to 2019. There is a decrease in 25(OH)D testing in 2020 and 2021 compared to 2019 among all institutions (Table 1 and Figure 1). The yearly distribution of the number of Vitamin D requests by primary care institutions is shown in Figure 1. We excluded the year 2020 and 2021 because of the COVID-19 pandemic and calculated the yearly increase rate in the test requests. The yearly increase rate in 2017, 2018, 2019, and 2022 were 137%, 56%, 16%, and 5%, respectively. Despite the restriction on vitamin D requests with the regulation, the fact that the number of test requests has not decreased to zero in primary care institutions shows that the restriction could not be applied in some centers. However, it should be underlined that there is a substantial decrease in test request numbers.

Table 1. Distribution of the number of Vitamin D requests by institutions and by years

Year	Institutions				Total
	Primary care institutions	2nd and 3rd Stage Public Health Facilities	Private Institutions	University Hospitals	
2016	9,219	2,127,364	380,031	310,383	2,826,997
2017	732,246	4,489,953	723,596	776,635	6,722,430
2018	1,830,337	6,492,303	1,097,516	1,085,988	10,506,144
2019	2,714,443	6,758,801	1,420,031	1,323,699	12,216,974
2020	89,738	3,246,971	1,478,096	662,401	5,477,206
2021	8,752	6,314,894	2,371,408	1,009,561	9,704,615
2022	36,130	8,935,703	2,464,049	1,387,960	12,823,842

The total number of individuals who had three or more tests per year is shown in Figure 2. There was an increase in the number of individuals who had three or more tests per year from 2016 to 2019. By the regulation, a decrease was observed in the number of individuals who had three or more tests per year (Table 2 and Figure 2).
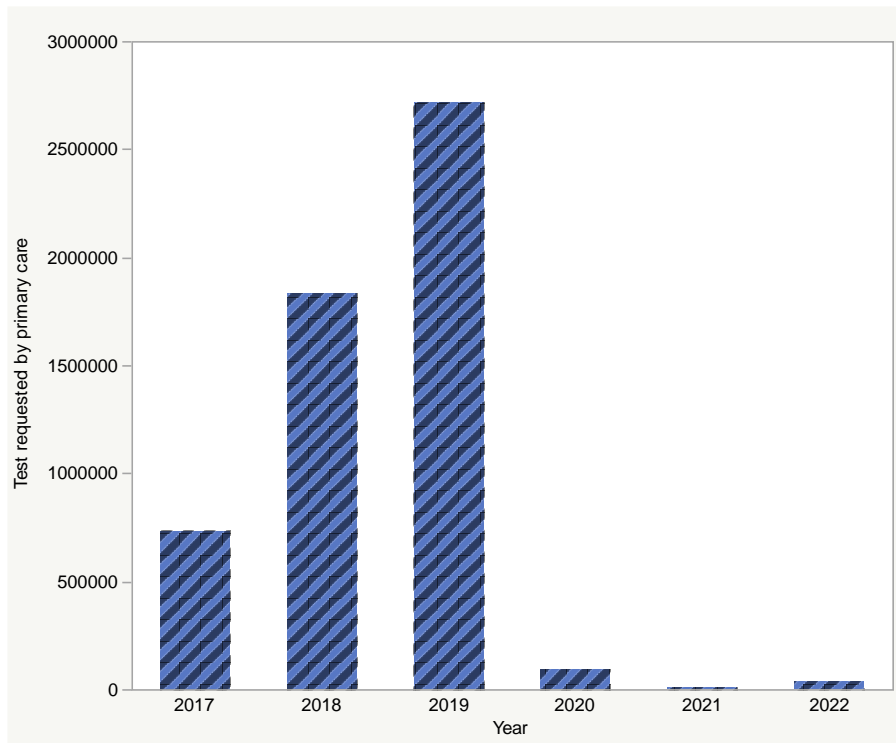
Figure 1. Yearly distribution of the number of Vitamin D requests by primary care institutions
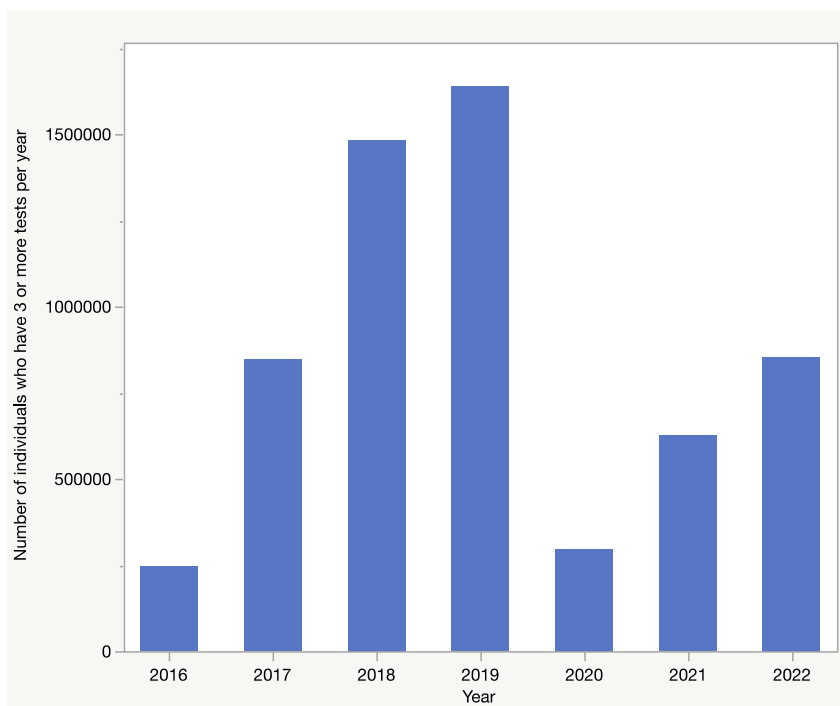
Figure 2. Number of individuals who had ≥3 tests per year

Table 2. Distribution of test request numbers by year

	Number of patients who were given a test only once a year	%	Number of patients for whom testing was requested twice a year	%	Number of patients who were asked to be tested ≥3 times a year	%	Total
2016	2,008,551	71	576,252	20	242,194	9	2,826,997
2017	4,281,303	64	1,600,384	24	840,743	13	6,722,430
2018	6,431,140	61	2,604,705	25	1,470,299	14	10,506,144
2019	7,502,170	61	3,089,549	25	1,625,255	13	12,216,974
2020	4,180,491	76	1,005,494	18	291,221	5	5,477,206
2021	6,933,119	71	2,151,595	22	619,901	6	9,704,615
2022	8,926,439	70	3,049,329	24	848,074	7	12,823,842

The distribution of the top 10 branches with the highest demand for vitamin D tests by year is shown in Table 3. In general, most of the 25(OH)D tests were requested by internal medicine, pediatrics, and their subspecialties. Family medicine was in the top 10 list before the regulation, and family medicine was not in the top 10 list after the regulation.

Table 3. Distribution of the top 10 branches with the highest demand for vitamin D tests by years

	2016	2017	2018	2019	2020	2021	2022
1.	Internal Medicine	Internal Medicine	Internal Medicine	Internal Medicine	Internal Medicine	Internal Medicine	Internal Medicine
2.	Subspecialties of Medicine	Family Medicine	Family Medicine	Family Medicine	Pediatrics	Pediatrics	Pediatrics
3.	PTR	Subspecialties of Medicine	Subspecialties of Medicine	Pediatrics	Subspecialties of Medicine	Subspecialties of Medicine	Subspecialties of Medicine
4.	Pediatrics	PTR	Pediatrics	Subspecialties of Medicine	PTR	PTR	PTR
5.	Medical Biochemistry	Pediatrics	PTR	PTR	Neurology	Neurology	Neurology
6.	Neurology	Neurology	Neurology	Neurology	Subspecialties of Pediatrics	Subspecialties of Pediatrics	Subspecialties of Pediatrics
7.	Family Medicine	Subspecialties of Pediatrics	Subspecialties of Pediatrics	Subspecialties of Pediatrics	Obstetrics and Gynecology	Obstetrics and Gynecology	Obstetrics and Gynecology
8.	Subspecialties of Pediatrics	General Surgery	Dermatology	Dermatology	Family Medicine	Medical Biochemistry	Medical Biochemistry
9.	General Surgery	Dermatology	Obstetrics and Gynecology	Obstetrics and Gynecology	Orthopedics	Orthopedics	Orthopedics
10.	Dermatology	Obstetrics and Gynecology	General Surgery	General Surgery	Cardiology	Cardiology	Cardiology

(PTR: physical therapy and rehabilitation)

Discussion

This study showed that the regulation of vitamin test requests led to a substantial reduction in vitamin D requests among primary care physicians. The decrease in vitamin D requests may be related to the change in the request screens of the medical software used by primary care physicians. This link between change in requesting behavior and laboratory request forms has been previously demonstrated in the literature.[14–16] The number of vitamin D tests ordered in general practice has increased substantially in developed countries in recent years, possibly due to its relationship with diseases, increasing scientific publications, and the influence of the media.[17] Vitamin D testing is an expensive test and imposes a significant financial burden, especially due to inappropriate testing and retesting. Clear and precise guidance for evaluating vitamin D status in primary care settings is needed. It is known that a substantial proportion of vitamin D tests are retested unnecessarily. Although guidelines suggest retesting after 3-6 months, 20% of retests were performed within three months.[18] The regulation restricted requesting more than two tests per year in our country. The total number of individuals who had three or more tests per year decreased after the regulation.

Many studies observed that the 25(OH)D test is unnecessarily requested by primary care physicians worldwide as a screening test, regardless of clinical diagnosis or pre-diagnosis. Bastemur et al. investigated 25(OH)D levels of 772.525 of healthy children requested by family physicians from 2000-2014, and they reported an increase in both test demand and prescriptions. Additionally, this increase was more pronounced, especially after 2008, and increased by 15 times from 2008 to 2013.[19] Rodd et al. compared the numbers of 25(OH)D tests in 2006/2007 and 2012/2013 and reported an increase in test numbers from 4,854 to 20,089. Additionally, they stated that family physicians were responsible for this increasing trend.[20] Another study conducted in the UK demonstrated that the demand for 25(OH)D tests in primary care increased by 11 times.[18] Bilinski et al. also reported that the need for 25(OH)D tests increased by 94 times from 2000 to 2010, and they stated that family physicians are responsible for this increase.[21] Our study observed a yearly increase in demand for the 25(OH)D test from 2016 to 2019, which is much more pronounced in primary care facilities. At the beginning of 2020, this Regulation by the Turkish Ministry of Health was launched. There was a decrease in demand for the 25(OH)D test between 2020 and 2021. The decreases in test demands during 2020-2021 were probably due to the Covid-19 pandemic, but not the regulation. In 2022, the effect of the Regulation became more evident, there was a significant decrease in the increase rate of 25(OH)D test demand compared to 2019. We think that the main factor as a reason for this decrease in tests was the restriction imposed on primary care physicians by the regulation released at the end of 2019.

Wong et al. observed that the combination of educational courses and the removal of laboratory tests on request forms could lead to a decrease in the use of thyroid function tests by 60%.[22] Shalev et al. showed that physician test ordering practices could be influenced by changes in laboratory order forms, either by adding or

deleting tests.[16] Patel et al. showed that a simple, pragmatic redesign of the electronic request form for vitamin D tests significantly decreased vitamin D requests without affecting the quality of care in primary care settings.[23] Munk JK et al. observed that a compulsory pop-up form decreased the number of vitamin D requests from general practitioners by 25%.[9]

Hofstede H et al. aimed to investigate the barriers and facilitators for reducing the number of unnecessary orders of vitamin D and B12 laboratory tests. They suggested that updating GPs' knowledge with guidelines with clear and uniform recommendations on evidence-based indications for vitamin testing, combined with regular (individual) feedback on test-ordering behavior, was necessary to facilitate a sustainable decrease in vitamin testing. Furthermore, the education of the general public to access clear and reliable information on vitamin testing is also necessary.[24]

One limitation of this study was that we could not have information on patient's medications, including vitamin D supplementation. Moreover, the database does not contain any information related to measurement methods. Therefore, we were not able to compare the vitamin D measurement methods used in various laboratories. Finally, patients with chronic diseases (e.g., cardiovascular disorders, diabetes mellitus, and cancer) could not be excluded.

Unnecessary, inadequate, and uncontrolled test requests may lead to harmful treatments that may have an adverse impact on healthy individuals.[25,26] With the regulation issued to reduce the number of tests, although a decrease in the yearly increase rate in test request number was provided, it did not provide a decrease in the total number of test requests.

Our findings showed that the request for 25(OH)D testing decreased in primary care and increased in 2nd and 3rd Stage Public Health Facilities and private hospitals after the regulation letter released at the end of 2019. The regulation allowed the follow-up of vitamin D deficiency in secondary and tertiary health institutions. Despite the decrease in the rate of increase in the number of test requests, the annual number of tests requested is still high, suggesting that different measures should be taken. The possible negative effects on costs of performing vitamin D tests in more expensive 2nd and 3rd stage health facilities instead of primary care facilities, which are inherently much cheaper, should be investigated. We think that all physicians should know that the 25(OH)D test should not be used as a screening test and that this test will be requested only in suitable patients, which will reduce the demand for 25(OH)D tests in the future. It is clear that there are different interventions to decrease laboratory test requests, such as educational-based approaches (evidence-based guidelines), various restrictions in the requesting process, and using of pop-ups; however, the general public needs access to clear and reliable information on vitamin testing. Additionally, all physicians, not just family

physicians, should be aware that the 25(OH)D test is not a screening test, which will reduce the demand for 25(OH)D tests in the future.

Ethical Considerations: This study conforms to the ethical norms and standards in the Declaration of Helsinki. The Ministry of Health's Ethical Board Committee approved the study protocol (IRB number: 95741342020/27112019).

Conflict of Interest: The authors declare no conflict of interest.

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EVALUATION OF MALNUTRITION IN GERIATRIC PATIENTS RECEIVING HOME CARE SERVICES

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Abstract

Objectives: In our study, it was aimed to determine the frequency of malnutrition and assess risk factors related to malnutrition in elder individuals receiving home care services.

Materials and Methods: This cross-sectional, descriptive study was conducted on patients who were registered to Home Care Services of Samsun Training and Research Hospital. All patients assessed sociodemographic characteristics, comorbid diseases, level of dependence, presence of pressure sore, use of nutrition supplement and nutritional status were assessed by Mini Nutritional Assessment-Short Form (MNA-SF) using face-to-face interview method.

Results: Overall, the study included 356 subjects (218 female, 61.24%). The mean age was 79.31±8.60 years. Of the subjects, 42.14% (n=150) were in the age group of 75-84 years. The mean MNA-SF score was 9.20±2.85. Based on the MNA-SF score, 27.52% (n=98) of the subjects had malnutrition, while 42.69% had a risk of malnutrition. The MNA-SF score was significantly lower in males (p=0.009), in those aged ≥85 years (p=0.035), in those with oncological disease (p=0.002), in those with cerebrovascular disease (p=0.003), in those with dementia (p<0.001), in the presence of pressure sore (p<0.001) and in bedridden (p<0.001). In the logistic regression analysis, it was found that being gender (p=0.002), bedridden (p<0.001), oncologic disease (p<0.001), cerebrovascular disease (p=0.002), dementia (p<0.001) and presence of pressure sore (p=0.002) were independent risk factors for malnutrition.

Conclusion: The risk of malnutrition was increased in male gender, in patients aged≥85 years and in those with cerebrovascular disease and dementia. The malnutrition prevalence was found to be high in patients with oncologic disease, in the presence of pressure sore and in bedridden patients.

Keywords: Malnutrition, aged, home care services.

Introduction

Malnutrition is a condition that results in regression of physical and mental functions, delayed healing, alterations in body components and several clinical consequences due to insufficient or excessive intake of protein, energy, and other nutritional elements.[1] Again, malnutrition is a clinical condition that is commonly seen with proven effects on morbidity and mortality in the geriatric population.[2] At old age, the mortality rate is increased by 9-38% due to malnutrition alone within 1 to 2.5 years after the onset of weight loss for any reason.[3] Nutrition is affected by many changes associated with physiological, physical, psychological, cognitive, social, and environmental aging.[1] In old age, nutritional status has an important role in the development and course of diseases. The "malnutrition" and "malnutrition" risk in old age aggravate diseases already present, impair quality of life, reduce treatment success and increase healthcare costs.[4]

The malnutrition studies have been mostly conducted in elderly individuals, reporting varying malnutrition prevalence. The malnutrition prevalence varies from 2% to 32% in community-dwelling elderly, whereas 25-60% in geriatric facilities and 35-65% in hospitalized elderly.[5] It is higher among patients receiving home care services when compared to the normal population. In studies on patients receiving home care services, it was found that the prevalence of malnutrition risk and malnutrition were 38.2-39.3% and 33.1-48.3%, respectively.[3]

In a study on community-dwelling elderly individuals, six risk factors were identified for malnutrition, including aging alone, requiring assistance in daily living activities, depression, chronic disease or disability, receiving home care services, and receiving care from family.[6] Inadequate nutrition and resultant malnutrition are common in patients receiving home care services. This leads to impaired body immunity, fall and hip fracture, prolonged recovery period, increased infection, delayed wound healing, increased compression ulcers, prolonged hospitalization, and increased healthcare costs in elderly individuals.[7] Therefore, this warrants assessment of nutritional status, risk factors for malnutrition and potential consequences of malnutrition in elderly individuals.

In elderly individuals, anthropometric measurements, laboratory tests, clinical examination and dietary content can be used as parameters to determine nutritional status.[8] Although body mass index (BMI) is the most used anthropometric measure, BMI does not allow differentiating losses from fat tissue and muscular tissue or central obesity. Albumin and pre-albumin are the most used laboratory parameters; however, they have low specificity and sensitivity.[9] Although recording daily dietary content is a valuable tool, it is difficult to apply and obtain accurate data.[3] The European Society for Clinical Nutrition and Metabolism (ESPEN) recommends routine nutritional screening in elderly individuals.[1] It was found that Mini Nutritional

Assessment (MNA) and Mini Nutritional Assessment-Short Form (MNA-SF) can sufficiently detect inadequate nutrition.[10]

In Turkey, home care services are provided under the supervision of family practitioners, given that the continuity of preventive and rehabilitative care should be given effectively. As home care services have increasingly become more available in Turkey, it has become possible to plan measures and nutrition programs for the nutritional care of patients in need of special nutritional intervention. Thus, we planned to conduct a prevalence study to guide such efforts in Turkey. Our study, it was aimed to determine the frequency of malnutrition and assess risk factors related to malnutrition in elder individuals receiving home care services.

Materials and Methods

This cross-sectional, descriptive study was conducted on patients who were registered to Home Care Services of Samsun Training and Research Hospital between January 1, 2022, and March 1, 2022. The patients who were fed by oral route were included in the study after obtaining informed consent from patients and/or primary caregivers (in patients with cognitive dysfunction). Patients aged <65 years, those receiving parenteral or enteral nutrition (via nasogastric route, nasojejunal route, gastrostomy or jejunostomy), those declining participation and patients at terminal period were excluded. The study universe included 3500 patients who registered with Home Care Services of Samsun Training and Research Hospital. Participants were selected by random sampling method, and the sample size was calculated as at least 296 with 80% power, 95% confidence interval and 5% acceptable margin of error when malnutrition prevalence was accepted as 30%. In all patients assessed, sociodemographic characteristics, comorbid diseases, level of dependence, presence of pressure sore, use of enteral nutrition supplement and nutritional status were assessed by MNA-SF using face-to-face interview method.

The MNA is the most used tool to assess nutrition in elderly individuals.[11] The MNA was first developed in 1997, and its validity in assessing nutritional risk in elderly individuals was proven.[12] The original questionnaire includes 18 items; however, a shorter version, including six items, was developed (MNA-short form). The MNA-SF includes the following items: final weight loss, mobility, psychological stress or acute disease, neuropsychological problems, and body mass index (BMI).[11] The specificity and sensitivity of MNA-SF are comparable to the original MNA. The newer, shorter version has a sensitivity of 98%, specificity of 100% and diagnostic accuracy of 99% for prediction of malnutrition.[13] Total MNA-SF score is defined as follows: 12-14 points, adequate nutrition; 8-11 points, risk of malnutrition; and 0-7 points, malnutrition. Authors have shown that MNA can adequately identify inadequate nutrition when compared to other screening tools.[10] The validation study for the Turkish version was proven by Sarikaya et al.[14]

Data analysis

The program International Business Machines Corporation Statistical Package for the Social Sciences (IBM SPSS) version 26.0 was used in the statistical analysis of data. Descriptive statistics are presented with mean and standard deviation values for continuous data; they are presented with numbers and percentages for categorical data. The compliance of continuous data with a normal distribution was evaluated by Kolmogorov-Smirnov test. Independent groups t-test was used to compare two independent groups with parametric characteristics. Pearson Chi-square test was used to compare categorical groups. Finally, a multivariate logistic regression model was created to identify risk factors associated with malnutrition. A P value of .05 or less was used to determine statistical significance.

Results

Overall, the study included 356 subjects (218 female, 61.24%). The mean age was 79.31±8.60 years. Of the subjects, 42.14% (n=150) were in the age group of 75-84 years. Of the subjects, care was given by offspring in 55.89% (n=199) and by a spouse in 19.10% (n=68). Of the subjects, 49.16% (n=175) were bedridden, while 47.47% (n=169) were semi-dependent. There was hypertension in 70.22% (n=250), cardiovascular disease in 37.07% (n=132), diabetes in 34.83% (n=124), dementia in 35.11% (n=125) and cerebrovascular disease in 33.42% (n=119). Of the subjects, 16.29% used enteral nutritional supplements. There was a pressure sore in 20.22% (n=72). The mean MNA-SF score was 9.20±2.85. Based on the MNA-SF score, 27.52% (n=98) of the subjects had malnutrition, while 42.69% had a risk of malnutrition. The nutrition was normal in 29.79% of the subjects (n=106) (Table 1).

The MNA-SF score was significantly lower in male subjects (p=0.041), in those aged ≥85 years (p=0.027), in those with oncological disease (p=0.005), in those with cerebrovascular disease (p=0.021), in those with dementia (p<0.001), in the presence of pressure sore (p<0.001) and in bedridden subjects (p<0.001). The risk of malnutrition was higher in male subjects, those aged ≥85 years, those with cerebrovascular disease and those with dementia (p<0.001). The malnutrition prevalence was increased in subjects with oncologic disease, in the presence of pressure sore and in bedridden subjects (Table 2). In the logistic regression analysis, it was found that being male gender (p=0.002), bedridden (p<0.001), oncologic disease (p<0.001), cerebrovascular disease (p=0.002), dementia (p<0.001) and presence of pressure sore (p=0.002) were independent risk factors for malnutrition (Cox-Snell R^2=0.263, Nagelkerke R^2=0.297) (Table 3).

Table 1. Demographic and clinical characteristics of participants (n=356)

Variables	n	%
Gender		
Female	218	61.24
Male	138	38.76
Age		
65-74	105	29.49
75-84	150	42.14
≥ 85	101	28.37
Level of dependence		
Independent	12	3.37
Semi-dependent	169	47.47
Bedridden	175	49.16
Caregiver of patient		
Offspring	199	55.89
Spouse	68	19.10
Other relatives	42	11.79
Paid caregiver	47	13.22
Chronic diseases		
Hypertension	250	70.22
Diabetes	124	34.83
Chronic renal disease	44	12.36
Cardiovascular disease	132	37.07
Chronic pulmonary disease	54	15.16
Oncological disease	34	9.55
Cerebrovascular disease	119	33.42
Dementia	125	35.11
Other diseases*	87	24.44
Pressure sore		
Present	72	20.22
Absent	284	79.78
Use of enteral nutrition supplement		
Present	58	16.29
Absent	298	83.71
MNA classification**		
Malnourished	98	27.52
At risk	152	42.69
Normal	106	29.79
BMI category***		
Underweight	5	1.40
Normal weight	170	47.76
Overweight	137	38.48
Obese	44	12.36

(Abbreviations: BMI, body mass index; MNA, Mini Nutritional Assessment.)

* Other diseases: Thyroid disease, epilepsy, Parkinson's disease, benign prostate disease, chronic rheumatic diseases, liver disease.

** MNA-SF classification: 0-7 = malnourished; 8-11 = at risk for malnutrition; 12-14 = normal nutritional status.

*** BMI category: <18.5 = underweight, 18.5–24.9 = normal weight, 25.0–29.9 = overweight, ≥30 = obese.

Table 2. Evaluation of demographic and clinical data of participants according to nutritional status

Variables	MNA classification*			P**
	Normal (n=106)	**At risk (n=152)**	**Malnourished (n=98)**	
Gender				
Female	73 (33.49%)	94 (43.11%)	51 (23.40%)	
Male	33(23.91%)	58(42.02%)	47 (34.07%)	**0.041**
Age				
65-74	36 (34.29%)	48 (45.71%)	21 (20.00%)	
75-84	45 (30.00%)	63 (42.00%)	42(28.00%)	**0.027**
≥ 85	25 (24.75%)	41 (40.60%)	35 (34.65%)	
Chronic diseases				
Hypertension	70 (28.00%)	108 (43.20%)	72 (28.80%)	0.489
Diabetes	39 (31.45%)	54 (43.55%)	31 (25.00%)	0.721
Chronic renal disease	18 (40.90%)	14 (31.83%)	12 (27.27%)	0.175
Cardiovascular disease	47 (35.60%)	48 (36.36%)	37 (28.04%)	0.112
Chronic pulmonary disease	15 (27.77%)	26 (48.14%)	13 (24.09%)	0.669
Oncological disease	3 (8.82%)	15 (44.18%)	16 (47.10%)	**0.005**
Cerebrovascular disease	26 (21.84%)	51 (42.86%)	42 (35.29%)	**0.021**
Dementia	17 (13.60%)	62 (49.60%)	46 (36.80%)	**<0.001**
Other diseases***	24 (27.58%)	44 (50.57%)	19 (21.83%)	0.201
Pressure sore				
Present	9 (12.50%)	28 (38.90%)	35 (48.60%)	
Absent	97 (34.15%)	124 (43.66%)	63 (22.19%)	**<0.001**
Level of dependence				
Independent	7 (58.33%)	4 (33.33%)	1 (8.34%)	
Semi-dependent	66 (39.05%)	78 (46.15%)	25 (14.80%)	
Bedridden	33 (18.85%)	70 (40.00%)	72 (41.15%)	**<0.001**
Caregiver of patient				
Offspring	61 (30.65%)	84 (42.21%)	54 (27.14%)	
Spouse	21 (30.88%)	28 (41.18%)	19 (27.94%)	
Other relatives	10 (23.80%)	20 (47.62%)	12 (28.58%)	0.989
Paid caregiver	14 (29.79%)	20 (42.55%)	13 (27.66%)	

* MNA-SF classification: 0-7 = malnourished; 8-11 = at risk for malnutrition; 12-14 = normal nutritional status.

**Pearson Chi-Square Tests

*** Other diseases: Thyroid disease, epilepsy, Parkinson's disease, benign prostate disease, chronic rheumatic diseases, liver disease.

Table 3. Logistic regression analysis of variables*

Variables	OR	95% CI	p
Gender	2.906	1.460-5.781	**0.002**
Age	0.524	0.236-1.163	0.112
Bedridden	0.309	0.154-0.619	**0.001**
Oncological disease	0.068	0.017-0.278	**<0.001**
Pressure sore	0.244	0.100-0.597	**0.002**
Cerebrovascular disease	0.341	0.170-0.683	**0.002**
Dementia	0.222	0.106-0.466	**<0.001**
Abbreviations: OR, Odds Ratio; CI, Confidence interval.			
* Cox-Snell R^2=0.263, Nagelkerke R^2=0.297			

Discussion

This cross-sectional study showed that malnutrition prevalence was high in patients (aged≥65 years) who were registered to Home Care Services of Samsun Training and Research Hospital between January 1, 2022, and March 1, 2022. Of 356 subjects included, malnutrition was found in 27.52% and the risk of malnutrition in 42.69%. The malnutrition prevalence and risk of malnutrition were significantly higher in male subjects, in those aged ≥85 years, in those with oncologic disease, in those with cerebrovascular disease, in those with dementia, in the presence of pressure sore and in bedridden subjects.

In our study, it was found that malnutrition prevalence and risk of malnutrition were high in elder individuals receiving home care services, in agreement with the literature. In a study on patients receiving home care services, Tüzün et al. found malnutrition prevalence at 28.8% and risk of malnutrition at 36.3%.[15] In a systematic review by Guigoz et al., it was found that malnutrition prevalence was 2% and risk of malnutrition was 24% in elder individuals (21 trials, n=14,149; range: 0-8% and 8-76%, respectively). These rates increased up to 9% and 45% in patients receiving home care services, respectively (25 trials, n=3,119; range: 0-30% and 8-65%, respectively).[16] In a study by Cevik et al., it was found that there was malnutrition in 33.1% and risk of malnutrition in 39.3% of individuals aged ≥65 years who were receiving home care services.[3] In the International SENECA study, the malnutrition prevalence was found to be 19-38% in healthy elderly individuals, 5-12% in elder individuals receiving home care services, 26-65% in hospitalized elderly individuals and 5-85% in those residing in nursing homes.[17] Given the high prevalence of malnutrition, it can be suggested that in-home care services settings, early recognition of individuals at risk for malnutrition and timely management play important roles in the prevention of malnutrition and in the prognosis of related clinical conditions.

In our study, it was found that malnutrition prevalence was significantly higher in male gender. In the literature, there are contradictory results regarding malnutrition prevalence according to gender. In a study including patients receiving home care services, it was found that malnutrition frequency was higher in female subjects.[18] However, there are studies indicating no significant difference in malnutrition prevalence according to gender.[2,3,15] In our study, it was found that malnutrition prevalence was significantly higher in patients aged ≥85 years. In many studies, it was reported that malnutrition prevalence increased with advancing age[19,20]; however, in some studies, no significant correlation was detected between malnutrition prevalence and age.[3,15,18]

In our study, the presence of oncologic disease, cerebrovascular disease and dementia were found to be associated with malnutrition and risk of malnutrition. In cancer patients, weight loss occurs in 30-80% during the disease process. In these patients, malnutrition develops when food intake is decreased due to the tumor itself or complications or when metabolic demand is increased.[21] In previous studies, it was reported that malnutrition and weight loss are poor prognostic factors in cancer patients.[22] Cerebrovascular disease is an important neurological problem that may lead to dysphagia and swallowing disorders. In patients with cerebrovascular disease, malnutrition develops due to insufficient food and fluid intake. The food and fluid intake is decreased as a result of altered consciousness level in swallowing mechanism, physical weakness and coordination problems. In these patients, malnutrition is associated with poorer functional status and higher complication rates.[23] The malnutrition prevalence can increase up to 45% during the acute rehabilitation period following cerebrovascular disease.[24] In patients with dementia, decreased food intake and weight loss may occur due to impaired cognitive functions, alterations in the sense of smell and taste, neuroendocrine disorders, and dysphagia. In previous studies, dementia was linked to poor nutritional status.[25,26] Yilmaz et al. found a significant correlation between dementia and malnutrition and reported that malnutrition prevalence was increased by increasing dementia symptoms.[27] Tüzün et al. found that the risk of malnutrition was high in patients with dementia, in agreement with our study.[15]

In our study, malnutrition prevalence was higher in bedridden subjects when compared to semi-dependent or non-dependent subjects. It was also found that the risk of malnutrition was increased in semi-dependent subjects. Previous studies reported that malnutrition prevalence and risk of malnutrition were increased in bedridden individuals.[3,18,28] In a study on patients receiving home care services, malnutrition prevalence was found to be higher in bedridden patients, while the risk of malnutrition was in semi-dependent patients.[15] In our study, it was found that malnutrition prevalence was significantly higher in subjects with pressure sores. Malnutrition is one of the major risk factors for the development of pressure sore. A low MNA score was reported as a potential predictor in the presence of a pressure sore.[9] Weight loss and hypo-albuminemia due to inadequate food intake play a role in the development of pressure sore.[29] In the literature, it was reported that malnutrition prevalence is increased by the presence of pressure sore.[18,30]

This study has some limitations. Since it is a single-center study, our results cannot be generalized to the general population. The study also has some strengths, including prospective design and inclusion of elderly individuals with physical and/or cognitive regression.

The malnutrition prevalence was higher among elder individuals receiving home care services. The risk of malnutrition was increased in male gender, in patients aged≥85 years and in those with cerebrovascular disease and dementia. The malnutrition prevalence was found to be high in patients with oncologic disease, in the presence of pressure sore and in bedridden patients. In-home care settings, screening patients for malnutrition using appropriate tools and correction of nutritional status with appropriate interventions will positively affect general health status, quality of life and disease-related complications.

Ethical Considerations: Ethics committee approval was obtained with of Samsun University Samsun Training and Research Hospital Clinical Research Ethical Committee.

Conflict of Interest: The authors declare no conflict of interest.

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SCREENING OF CARDIOVASCULAR RISKS IN ACTIVE ATHLETES WITHIN THE PROVINCIAL DIRECTORATE OF YOUTH AND SPORTS

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Abstract

Objectives: This study aimed to assess the cardiovascular risks of athletes engaged in sports activities in various branches.

Materials and Methods: In this cross-sectional study, a 20-item questionnaire including demographic information and sports history was applied to 181 athletes. In addition to physical examinations, complete blood count, biochemistry, lipid profile, TSH, T4, ECG and ECHO tests were conducted.

Results: Of the athletes, 25 (13.81%) had a pathology that could impede them from doing sports was detected. When the data was examined by comparing participants with and without the pathological status, statistically significant differences were found in terms of cardiac rate, the presence of ventricular hypertrophy, T-wave, deviation in cardiac axis, HDL, LDL, calcium, ALT, diastolic blood pressure and the frequency of training per week.

Conclusion: The presence of conditions posing any health risk among actively engaged athletes suggests that some risky situations can be overlooked in the examinations necessary for entry into sports. Family physicians should take a full anamnesis when evaluating people who want to do sports, and accordingly carry out a detailed examination, and predicate their findings on laboratory findings.

Keywords: Athletes, cardiovascular risk, general practice, risk management, screening.

Introduction

In recent years, the number of young and adult sports professionals has been increasing. Sport is considered to be a useful activity in the physical and mental development of individuals due to its positive contribution to the continuation of health status, prevention of obesity and diseases that may develop due to sedentary life and to the person's social life.[1,2] Regular exercise has proven to be an effective method to prevent obesity, cardiovascular diseases, diabetes, and breast, colon, rectal and prostate cancers.[1,3-7] Physical activity is known to reduce depression, lower blood pressure, positively affect bone health, improve symptoms in fibromyalgia patients, and reduce the risk of dementia.[8-12]

Various screening and risk classification tools are used before participation in sports activities. Leading institutions such as the American Heart Association (AHA), the American College of Sports Medicine (ACSM), and the American Society of Cardiovascular and Pulmonary Rehabilitation (AACVPR) have developed important screening recommendations for the general population. Screening and risk classification prior to participation in sports or physical education activities is accepted as a standard practice. In the 'Physical Activity Reading Questionnaire for All (PAR-Q +)' and 'Electronic Physical Activity Preparedness Questionnaire' (ePARmed-X +) developed for this purpose, the barriers to physical activities have been greatly reduced, and it has led to an increase in participation in physical activities for apparently healthy individuals and people with chronic health problems.

Although the benefits of exercise for staying healthy are undeniable, it is a fact that it brings some risks. Loading the organism above a certain level can trigger unexpected cardiac deaths.[13] The underlying silent pathologies are usually responsible for such events.[14] Although the incidence of sudden cardiac death (SCD) during sports and exercise activities is difficult to pinpoint, the general rate is 1-3 per 100 000.[15] However, although not very high, unexpected sudden deaths cause deep sorrow and anxiety in the community and family members. It is possible to identify most of these sudden deaths by pre-accession health assessments. On the other hand, exercise overloads can also cause musculoskeletal injuries. The importance of these evaluations in determining and monitoring these cannot be denied.

Health fitness reports for sports are organized by family physicians, sports physicians and cardiologists in Turkey. This necessitates a systematic approach for physicians beyond being a legal and professional responsibility. A medical report is required only for sports licenses in Turkey. However, like many reports, a health report is sometimes considered a formality. Therefore, some families and sports clubs do not give the necessary importance to the health control of the athletes. Family doctors have a great responsibility in this regard. If the family physician approves the medical report, he or she takes full legal responsibility.

Unfortunately, there is no guide or form available to family physicians prior to physical education activities. The effectiveness of the evaluations made before the sporting activities is also discussed.

The aim of this study is to make cardiovascular risk assessments of athletes engaged in sports activities in various branches of the Youth Center operating within the Provincial Directorate of Youth and Sports and to reveal the importance of laboratory studies before sports activities.

Materials and Methods

This research was conducted as a cross-sectional study. The reporting of the study was carried out in accordance with the STROBE criteria.[16] At the same time, approval was obtained from the Academic Board of the medical faculty of a university (Date: 06.02.2019, issue: 08).

The athletes who accepted to participate in the study were invited to the Family Medicine Polyclinic of the medical faculty of a university. A 20-item questionnaire including the anamnesis of the athletes was prepared by scanning the literature and was conducted on participants between November 2018 and April 2019. The questionnaire was completed by face-to-face interview method in the family medicine policlinic. Anthropometric measurements were taken by the researcher, physical examinations were performed, and the findings were recorded on cardiovascular risk screening forms in athletes. Hemogram, biochemistry and electrocardiographic (ECG) examinations of the participants were also requested. The ECGs of the athletes were analyzed by the cardiologist, and the findings were recorded on the same screening form. Athletes with pathological findings were referred to the relevant departments.

The population of the research consisted of 4400 athletes operating in Kahramanmaraş Provincial Directorate of Youth and Sports. From the list received from the Directorate, 200 of these athletes were identified using a table of random numbers, and they were sent a written invitation to participate in the research. A total of 181 people agreed to participate in the study, and the data of all participants were analyzed; there was no data loss (Figure 1).

The inclusion criteria of the study were determined to be active in moderate and heavy sports activities at least three days a week and at least 1 hour regularly with the coaches of Kahramanmaraş youth and sports provincial directorate and to be between the ages of 6-65.

The sample calculation was based on the presence of any pathology that could prevent sports in athletes. In a sample of 4400 individuals with a population of 179, an estimated 14% prevalence is required to determine

the 5% error margin and 95% confidence interval.[17] Considering data loss and the possibility of rejecting the invitation, the sample of the study was determined as 200 athletes.
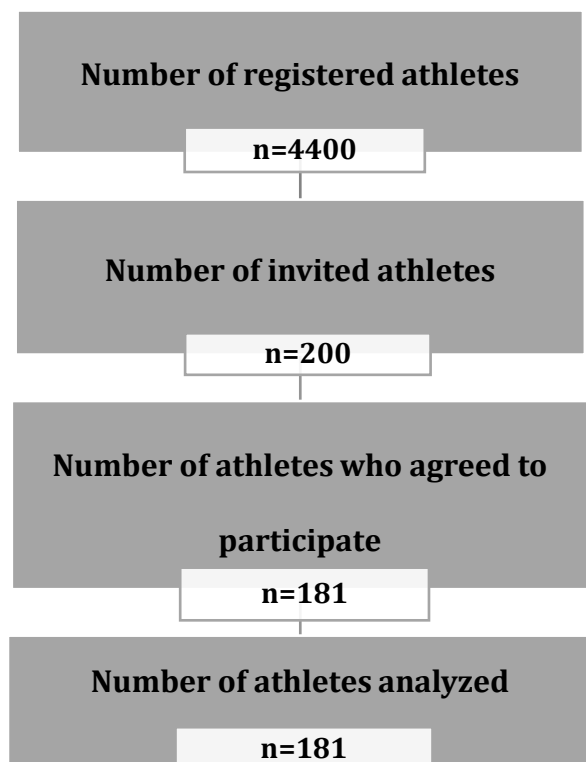
Figure 1. Participant flowchart of the study.

The dependent variable of the study is whether there is a pathology that may pose a risk for sports in physical examination, laboratory and ECG examinations. Other variables; include dizziness, blackout, fainting, chest pain or shortness of breath during or after exercise, fatigue before friends, heart rate different or faster than normal when resting, high blood pressure and high cholesterol levels, heart murmur in the family before the age of 50, death due to heart disease, family history of the sudden death of unknown cause at a young age, heart-related infectious disease in the last month, having close relatives of SCD, the type of sport performed and how many years of the sport.

The body weight of the patients was measured with Tanita SC 30 bioelectrical impedance analyzer, and the lengths were measured with a 1mm spacing. BMI values were calculated using the following formula using body weight and height.

BMI (kg / m2) = Body Weight (kg) / Length (m) ^{2})

Data were entered into the computer and analyzed with SPSS 25.0 program (Chicago, IL, USA). The findings of the study were presented as numbers and percentages for categorical variables and as the mean and standard deviation for numerical variables. The suitability of the numerical variables to the normal distribution was evaluated by looking at the skewness and kurtosis coefficients. Comparisons of the groups were made by independent samples t-test for parametric test conditions. In cases where parametric test conditions were not met, the Mann-Witney U test was used. The chi-square test was used in cases where categorical data should be compared. Statistical significance was taken as $p < 0.05$.

Results

When the data of the participants were examined, it was seen that 148 (81.77%) were male, 33 (18.23%) were female, and the mean age was 21.27±6.72 years (10-45 years). None of the participants had been smoking.

The mean±SD of QTc (msn), QRS (msn) and PR (msn) were 392.55±21.94; 85,31±10,14 and 133.02±17.50, respectively. The mean±SD of systolic and diastolic blood pressure were 102.63±12.07 and 65.45±8.30, respectively. Descriptive statistics of numerical variables are given in Table 1.

When the distribution of the participants was examined according to their sports branch, it was seen that football was the most preferred branch, with 16.57%, followed by volleyball and swimming (Table 2).

As a result of the study, 25 (13.81%) of the participants were identified to be inconvenient in terms of sports. The most common disorders were; triglyceride (n = 12), hemoglobin (n = 3) and TSH (n = 2) elevation. ECG revealed left ventricular hypertrophy and T negativity, left axis deviation, right bundle branch block, short PR and delta wave and short QT in one athlete.

When the relationship between the variables was examined, significant correlations were found. It is noteworthy that many variables are associated with age. It is observed that QTc tends to shorten and QRS and PR to lengthen, especially with age (p=0.001, 0.018 and 0.025, respectively).

When the data were compared in terms of the presence of pathology that may pose a risk to health, a statistically significant difference was found in terms of cardiac rate, HDL, LDL, calcium, ALT, diastolic blood pressure, and the number of training times per week, there was no significant difference in other variables (Table 3). When the categorical variables were compared, a statistically significant difference was found in terms of ventricular hypertrophy, t wave and deviation in the cardiac axis (Table 4).

Table 1. Descriptive information about the participants

	Min	Max	Mean	SD
QTc (ms)	330	453	392.55	21.94
QRS (ms)	64	121	85.31	10.14
PR (msn)	86	200	133.02	17.50
Sport time (years)	1	8	2.71	1.07
Length (cm)	130	187	169.82	8.11
Weight (kg)	35	98	67.93	11.65
Body Mass Index (kg / m2)	17.06	32.45	23.43	3.00
Systolic blood pressure (mmHg)	80	130	102.63	12.07
Diastolic blood pressure (mmHg)	50	82	65.45	8.30
Cardiac Speed (min)	58	92	72.15	7.46
Hemoglobin (g / dl)	10	18.1	14.31	1.62
Number of white spheres (mm3)	4000	14000	7171.99	1667.39
Platelets (mm3)	120000	540000	257668	59480
Glucose (mg / dL)	66	134	87.61	7.84
BUN (mg / dl)	6	20	12.01	2.80
Creatinine (mg / dL)	0.4	1	0.78	0.15
AST (IU / L)	11	39	20.07	4.43
SUB (IU / L)	9	52	18.32	6.53
Na (mmol / L)	132	145	139.69	2.54
K (mmol / L)	4	5.2	4.64	0.43
Ca (mg / dl)	8	10.3	9.40	0.56
Triglyceride (mg / dL)	39	330	93.92	39.94
LDL (mg / dL)	30	187	86.41	23.65
HDL (mg / dL)	29	74	47.06	8.79
TSH (mU / L)	0.9	7	2.32	0.85
ST4 (ng/dl)	0.9	1.7	1.09	0.15

(SD: Standard deviation.)

Table 2. Distribution of participants according to their sport

	n	%
Football	30	16.58
Volleyball	22	12.16
Swimming	21	11.60
Athletics	14	7.74
Shooting	12	6.64
Canoe	12	6.64
Tae-kwon-do	10	5.52
Basketball	10	5.52
Karate	10	5.52
Boxing	10	5.52
Wrestle	10	5.52
Barbell	10	5.52
Ping pong	10	5.52
Total	181	100.00

Table 3. Comparison of age, anthropometric, biochemistry and ECG measurement results

Variables	Result of evaluation	n	Mean	SD	t/Z	p
Age (year)	No pathology	156	21.12	6.31	-0.554	0.584
	Pathology	25	22.16	9.02		
QRS (msn)	No pathology	156	84.92	10.01	-1.282	0.201
	Pathology	25	87.72	10.85		
Training (day/week)	No pathology	156	2.42	0.45	-2.961	**0.006**
	Pathology	25	2.72	0.50		
Length (cm)	No pathology	156	169.79	8.43	-0.886	0.144
	Pathology	25	170.04	5.84		
Weight (kg)	No pathology	156	67.27	11.32	-1.915	0.057
	Pathology	25	72.04	13.07		
BMI	No pathology	156	23.20	2.71	-1.942	0.063
	Pathology	25	24.88	4.19		
Systolic Blood Pressure	No pathology	156	101.9	11.27	-1.624	0.115
	Pathology	25	107.2	15.68		
Diastolic Blood Pressure	No pathology	156	64.91	8.27	-2.199	**0.029**
	Pathology	25	68.8	7.81		
White Blood Cell	No pathology	156	7189.68	1726.78	0.356	0.722
	Pathology	25	7061.6	1256.72		
Platelets	No pathology	156	256512.8	57716.49	-0.652	0.654*
	Pathology	25	264880	70412.67		
BUN	No pathology	156	12.14	2.83	1.567	0.119
	Pathology	25	11.2	2.48		
Creatinine	No pathology	156	0.778	0.15	0.554	0.581
	Pathology	25	0.76	0.14		
AST	No pathology	156	19.94	4.51	-0.982	0.327
	Pathology	25	20.88	3.90		
ALT	No pathology	156	17.59	5.73	-3.294	**0.001***
	Pathology	25	22.88	9.12		
Na	No pathology	156	139.63	2.57	-0.826	0.410
	Pathology	25	140.08	2.36		
K	No pathology	156	4.624	0.43	-0.951	0.343
	Pathology	25	4.712	0.40		
Ca	No pathology	156	9.362	0.54	-2.390	**0.018**
	Pathology	25	9.644	0.60		
LDL	No pathology	156	81.12	16.84	-5.802	**<0.001***
	Pathology	25	119.44	32.33		
HDL	No pathology	156	47.86	8.80	3.665	**0.001**
	Pathology	25	42.08	7.05		
sT4	No pathology	156	1.086	0.15	-0.192	0.848
	Pathology	25	1.092	0.15		
Cardiac Speed	No pathology	156	71.38	7.46	-4.428	**<0.001**
	Pathology	25	76.92	5.49		

Table 4. Comparison of categorical variables according to results

Variables		Examination of pathology				p	χ2
		Not exist		Exist			
		n	%	n	%		
Sex	Male	127	85.81	21	14.19	0.756	0.097
	Female	29	87.88	4	12.12		
Delta wave	Not Exist	155	86.11	25	13.89	0.688	0.161
	Exist	1	100.00	0	0.00		
Right bundle branch block	Not exist	155	86.59	24	13.41	0.136	2.225
	Exist	1	50.00	1	50.00		
General ECG review	Normal	153	86.44	24	13.56	0.512	0.43
	Pathological	3	75.00	1	25.00		
Axis	Normal	155	86.59	24	13.41	**0.040**	6.425
	Right Axis	1	100.00	0	0.00		
	Left Axis	0	0.00	1	100.00		
T wave	Normal	156	86.67	24	13.33	**0.012**	6.275
	Pathological	0	0.00	1	100.00		
Ventricular hypertrophy	Not exist	156	86.67	24	13.33	**0.012**	6.275
	Exist	0	0.00	1	100.00		
Dizziness, blackout, or fainting during or after exercise	Not exist	150	86.21	24	13.79	0.97	0.001
	Exist	6	85.71	1	14.29		
Chest pain or shortness of breath during or after exercise	Not exist	138	85.71	23	14.29	0.600	0.274
	Exist	18	90.00	2	10.00		
Fatigue during exercise. before friends	Not exist	129	87.16	19	12.84	0.421	0.647
	Exist	27	81.82	6	18.18		
Different or fast heartbeats while resting	Not exist	145	86.31	23	13.69	0.865	0.029
	Exist	11	84.62	2	15.38		
Death due to heart disease before the age of 50 in the family	Not exist	155	86.59	24	13.41	0.136	2.225
	Exist	1	50.00	1	50.00		
Family history of the sudden death of unknown cause at a young age	Not exist	154	86.03	25	13.97	0.569	0.324
	Exist	2	100.00	0	0.00		

Discussion

Sudden athlete deaths, injuries during sports and variability in athlete performances have led to the discussion of the examination of athletes. The athletes underwent an evaluation including potential personal health history, family history, history of drug use, physical examination and possible diagnostic tests to identify potential risks for heart disease, musculoskeletal disease, neurological diseases, respiratory disease, bleeding disorders and psychiatric disorders that they kept.

The distribution of participants according to their sports branches revealed that football was the most preferred branch, followed by volleyball and swimming. Furthermore, when the data were analyzed with respect to the dependent variables, several statistically significant differences emerged. Specifically, significant variations were observed in cardiac rate, HDL, LDL, calcium, ALT, diastolic blood pressure, and the number of

training times per week. These findings indicate that engagement in different sports branches can significantly influence various physiological factors related to cardiovascular health and metabolic profiles. Moreover, the comparison of categorical variables in relation to the main outcome measures provided further insights. The results demonstrated a statistically significant difference in terms of ventricular hypertrophy, T wave alterations, and deviation in the cardiac axis. These findings suggest that participation in specific sports branches can have notable implications for cardiac structure and electrical activity.

Blood tests and ECG can be used to assess the structure and function of the heart and the health status of the organs. Abnormal findings detected in history, physical examination, blood tests, or ECG may lead to further diagnostic tests and evaluations.[18] In our study, pathology was detected in the light of these findings in 13.81% of the participants (25 people) and referred to internal medicine, cardiology and pediatric hematology departments for further diagnostic tests and evaluations. However, it was concluded that the pathologies identified as a result of the analyzes did not prevent the participants from doing sports.

The fact that there are many interested in football among the participants may be due to the interest in football in our country as well as the fact that it requires more team players compared to other branches. The relatively high number of those who are interested in swimming among the participants in the study may be due to the ease of access to semi-Olympic swimming pools in the city.

There is solid evidence showing that adequate and regular physical activity can have positive cardiovascular, endocrine, metabolic and neurological effects.[19,20] However, it has also been shown that excessive and strenuous physical training forms can generally damage the cardiovascular system.[21] In our study, hemoglobin level was found to be significantly higher in the group with pathology. The fact that the number of training days per week was higher in the group with pathology was considered a finding compatible with the literature.

An important reason for pre-accession screening in athletes is the effort to prevent sudden deaths. The main cardiac causes of sudden death in athletes are; hypertrophic cardiomyopathy, cardiac conduction problems, coronary artery anomalies, cardiac arrest due to severe blows to the chest, and upper respiratory tract infection may be considered carditis.[22] Hypertrophic cardiomyopathy (20.6%), idiopathic left ventricular hypertrophy (13.4%) and coronary anomalies (12.0%) were found in the top three in a study that investigated sudden deaths in 331 competing athletes in the United States.[23]

Both the American Heart Association (AHA) and the European Cardiology Association (ESC) panel recommendations agreed that young competing athletes should be screened for cardiac exposure.[24,25] However, there are differences in screening methods. While AHA recommends a complete medical history and family history with physical examination, ESC recommends the routine use of a 12-lead ECG in the initial screening.[26]

Hypertrophic cardiomyopathy or right ventricular cardiomyopathy shows various ECG changes, including straight or deeply inverted T waves and deep Q waves (including a dramatic increase in R or S wave voltage), indicating the presence of structural cardiovascular disease. In a study conducted with 1005 individuals from 38 different sports branches comparing ECG with echocardiography, 40% of the participants had abnormal ECG findings, and 5% had structural heart problems.[27]

In our study, ECG findings were interpreted pathologically in 4 people (2.20%); one person had delta wave, two had right bundle branch block (one with axial deviation), and one had short QTc. It appears that the pathological ECGs are interpreted as belonging to men. This may be due to the fact that most of the participants (81.83%) are men. On the other hand, it has been considered that the male gender is a risk factor in itself for sudden cardiac death.[22] Also, in our study, it was found that QTc shortening with increasing age was consistent with the literature.[20] Therefore, it can be said that age is an independent risk factor for athletes. However, it was understood that these findings did not predict the important pathologies that would prevent the individuals from continuing their sports life.

There are different applications for screening methods. The main reason for this difference is the variability in the cost approach. According to a study conducted in the USA in 2012, the cost of more than $ 10 million is saved in every case where sudden death is prevented by ECG.[28] In the same study, it is strangely argued that ECG is a financial burden on the US economy and may hinder the implementation of some methods that can be used to prevent cardiac death. In addition, according to another study led by Italian researchers, a screening program in which ECG will not be used will be both more expensive and insufficient to identify heart disease.[29] It is thought that this difference in opinion on cost-effectiveness depends on different structuring of health systems. In this regard, the health system in terms of cost-effectiveness of screening with ECG in Turkey closer to European Union countries that have been evaluated would be more useful.

The existence of family medicine practice in our country can be used as a great advantage in this respect. From birth to death, it will be very easy for a family physician to monitor and record at least one ECG record for participation in sports to a person with records. In addition, 12-lead ECG is not widely used and interpretable in our country.[30] It is considered that it would be beneficial to take measures to eliminate the lack of education in this regard.

It will be necessary to interpret this research with some limitations. First, the age range of athletes is distributed over a wide range. The possibility of such a wide range of influences should be kept in mind. On the other hand, muscle-building protein contents and anabolic steroids that athletes may use are not considered. In addition, the lack of examination and laboratory data of athletes before starting sports can be considered a limitation.

The presence of conditions that may pose a risk to the health of athletes in people who are engaged in active sports suggests that some findings have been missed in the examinations for entry to sports. This research shows that health screening is important for the health of the athlete. Although a health report is obtained to start sports in the current practice, some pathologies can be omitted. On the other hand, only anamnesis and physical examination may not be sufficient to determine the health problems, and basic laboratory tests should be performed. Based on this research, a national guide for sports entry examinations and screening of athletes should be developed with larger samples and multi-center studies.

The following conclusions and recommendations can be drawn from our research:

- Although screening tests do not fully capture diseases, they are very helpful in identifying those who can perform sports.

- Laboratory and ECG can be used to increase the sensitivity in sports examinations.

- Family medicine practice can provide a significant advantage in terms of cost-effectiveness.

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Ethical Considerations: Ethical approval for the study was obtained from Kahramanmaraş Sütçü İmam University Faculty of Medicine Clinical Research Ethics Committee on 06.02.2019 with approval number 08.

Conflict of Interest: The authors declare no conflict of interest.

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ARE PITUITARY FUNCTIONS DIFFERENT IN OBESE PATIENTS ACCORDING TO BODY MASS INDEX CLASSES?

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Abstract

Objectives: In this study, we aimed to evaluate whether there is a difference in the pituitary functions in obese patients according to the different body mass index (BMI) classes

Materials and Methods: We retrospectively evaluated 192 patients with obesity. According to the obesity degree, patients were divided into class I (BMI;30.0-34.9 kg/m^2), class II (BMI; 35.0-39.9 kg/m^2) or class III (BMI; ≥40 kg/m^2) obesity. The demographic data of the patients (sex, age), thyroid function tests, estrogen (E2), follicle-stimulating hormone (FSH), luteinizing hormone (LH), growth hormone (GH), insulin-like growth factor-I (IGF-I), total and free testosterone, cortisol, adrenocorticotrophic hormone (ACTH) levels were measured. Also, 24-hour urine-free cortisol levels and a 1 mg dexamethasone suppression test were performed.

Results: Total of the 192 patients, 44 (22.92%) were male, 148 (77.08%) were female. According to BMI classes, 12 (6.25%) patients were in class I, 38 (19.79%) patients were in class II and 142 (73.96%) patients were in class III obesity. No significant difference was found between the groups in hormonal parameters except the IGF-I level. 1 mg dexamethasone suppression test was suppressed in all patients.

Conclusion: In our study, we found that there was no difference in pituitary functions according to obesity classes, except for the IGF-I level. Further studies are needed to investigate these functions in different classes of obesity.

Keywords: Obesity, body mass index, pituitary functions, insulin-like growth factor-I.

Introduction

The prevalence of obesity, especially severe obesity, is increasing in a threatening state worldwide.[1] Obesity is associated with some disorders such as type 2 diabetes mellitus (DM), dyslipidemia, hypertension (HT), cardiovascular and respiratory system diseases, and some cancer types. Also, it can lead to some endocrine dysfunctions, and all endocrine organs/systems can be affected directly/indirectly due to excessive fat content.[2] Increase in adipocyte size leads to inflammation, cytokine production, and release of adipokines. These changes play an important role in the pathophysiology of endocrine dysregulation, which is seen in obesity.[3] Therefore, obesity is associated with adaptive and sensitive changes that lead to various biochemical and clinical changes and are tightly regulated by the feedback loops of these systems.[4] In addition, obesity is thought to be both cause and a consequence of endocrine dysfunction.[5,6] This bidirectional relationship is complex and not fully understood.[6,7]

In our study, we aimed to evaluate whether there is a difference in the pituitary functions in obese patients according to the different body mass index (BMI) classes.

Materials and Methods

We retrospectively evaluated the patients with a body mass index ≥30 kg/m^2 and who have admitted to our endocrinology clinic between May 2019 and March 2020 for a workup of obesity. Demographic data (sex, age), medical history, drugs they used and the laboratory data of the patients were evaluated from medical records.

Patients who have <18 years old have previously known or unknown thyroid dysfunction, taking thyroid-related medication, use drugs that affect thyroid functions and pituitary functions, have a previous history of head and neck radiation, history of pituitary dysfunction, bariatric surgery, pregnancy and chronic disease (DM, renal insufficiency, adrenal insufficiency, or any other systemic disease), were excluded from the study. Cushing's syndrome is also excluded.

Body measurements were performed on fasting patients wearing light underwear. Weight and height were measured to the nearest 0.10 kg and 0.10 cm, respectively, and BMI was expressed as body mass (kg)/height (m^2). Body mass index ≥ 30 kg/m^2 is used as obesity criteria which are defined by World Health Organization (WHO). Obesity is classified as class I (BMI;30.0-34.9 kg/m^2), class II (BMI; 35.0-39.9 kg/m^2) and class III obesity (BMI ≥40 kg/m^2).

All participants had taken fasting blood samples in the early morning in order to evaluate the thyroid function and pituitary function tests. Serum thyrotrophin (TSH), free triiodothyronine (fT3), and free thyroxine (fT4)

levels were measured by chemiluminescence methods. The normal ranges for TSH, fT3, and fT4 were 0.55–4.78 mU/L, 2.30–4.20 ng/L, and 0.89–1.76 ng/dl, respectively. Serum estrogen (E2), follicle-stimulating hormone (FSH), luteinizing hormone (LH), growth hormone (GH), insulin-like growth factor-I (IGF-I), total testosterone, cortisol, adrenocorticotrophic hormone (ACTH), were measured by chemiluminescent immunoassays (CLIA), free testosterone were measured by radioimmunoassay (RIA). Also, 24-hour urine-free cortisol levels and a 1 mg dexamethasone suppression test were performed.

Statistical analysis

All statistical analyses were performed with the SPSS 15.0 software package (SPSS Inc., Chicago, IL, USA). Descriptive analyses were presented using mean ± standard deviation (SD) for normally distributed variables, median and range (min-max) for non-normally distributed variables and as number of cases and (%) for nominal variables. The Chi-square test was used to investigate the difference between the groups regarding the categorical variables. The comparisons between groups were performed by the ANOVA for parametric variables and the Kruskal Wallis test for non-parametric variables to determine the best predictor(s). A p-value less than 0.05 was accepted as statistically significant.

Results

We retrospectively evaluated 192 patients with obesity. The mean age of the patients was 36.94±11.18 years. Total of the 192 patients, 44 (22.92%) were male, and 148 (77.08%) were female. The mean weight, height and BMI of the patients were 120.79±20.39 kg, 165.20±9.61 cm and 44.13±6.54, respectively. According to BMI classes, 12 (6.25%) patients were in class I, 38 (19.79%) patients were in class II and 142 (73.96%) patients were in class III obesity. According to the obesity classes, the number and percentage of female/male patients are shown in Table 1. There was no significant difference between the groups in terms of gender. The mean age of the patients was similar between the groups. No significant difference was found between the groups in hormonal parameters except IGF-I level (table 1). Also, in female patients, E2 levels were not different between the groups. Additionally, 1 mg dexamethasone suppression test was suppressed in all patients.

Table 1. Demographic data and the results of the patients according to the BMI classes

	Class I obesity (BMI; 30.0-34.9 kg/m²)	Class II obesity (BMI; 35.0-39.9 kg/m²)	Class III obesity (BMI ≥40 kg/m²)	p-value
Number of patients (n)/(%)	12 (6.25)	38 (19.79)	142 (73.96)	
Female/Male (number/percentage)	11 (91.67%) / 1 (8.33%)	25 (65.79%)/ 13 (34.21%)	112 (78.87%)/ 30 (%21.13)	0.108
Age (years)	36±13.20	38.34±11.75	36.64±10.90	0.680
Height (cm)	167.91±6.41	166.83±10.34	164.53±9.60	0.261
Weight (kg)	93.42±7.72	105.97±13.55	127.06±18.64	<0.001
BMI (kg/m²)	33.09±1.20	37.89±1.32	46.74±5.45	<0.001
fT3	3.21±0.46	3.32±0.57	3.28±0.49	0.593
fT4	1.06±0.11	1.18±0.11	1.18±0.29	0.050
TSH	2.45±1.26	2.02±0.84	2.26±0.87	0.363
LH (median; min-max)	4.35 (1.80-7.00)	4 (1.39-53.20)	5.40 (0.40-42.10)	0.081
FSH (median; min-max)	4.65 (2.60-9.60)	5.80 (1.90-122.20)	6.25 (1.20-82.20)	0.296
Total testosterone median (min-max)	24.00 (12-288)	22 (0.15-402.00)	33.00 (0.10-436)	0.318
Free testosterone median (min-max)	1.57 (0.94-16.21)	2.68 (0.76-15.05)	2.96 (0.43-15.83)	0.201
GH (median; min-max)	0.45 (0.05-1.20)	0.10 (0.05-5.20)	0.10 (4.50-114)	0.382
IGF-1 (median; min-max)	156 (126-184)	130 (53-981)	112 (15-981)	**0.034**
Cortisol	10.66±3.39	13.93±5.24	13.06±4.58	0.201
ACTH (median; min-max)	16.60 (6.30-39.60)	20.70 (6.70-84.40)	20.70 (4.50-114)	0.658
24-hour urine-free cortisol (median; min-max)	12.02 (8.94-21.22)	15.21 (4.47-159.14)	16.26 (3.08-95.30)	0.404

(BMI; body mass index, fT3; free triiodothyronine, fT4; free thyroxine, TSH; thyrotrophin, LH; luteinizing hormone, FSH; follicle stimulating hormone, GH; growth hormone, IGF-I; insulin-like growth factor-I, ACTH; adrenocorticotrophic hormone)

Discussion

GH and IGF-I have a crucial role in the regulation of metabolism and maintenance of body composition.[2] GH has both anabolic and catabolic effects on different tissues. It stimulates lipolysis in adipose tissue and protein

synthesis in muscle tissue. Therefore, reduced GH levels prone to weight gain, abdominal fat deposition and decreased muscle mass.[2] An inverse relationship was found between GH and BMI/visceral obesity regardless of age and gender.[4] In adult patients with obesity, GH secretion is blunted compared to lean individuals. It is found that both basal and stimulated GH levels have been reduced in patients with morbid obesity.[8] Studies related to IGF-I in obesity reported discordance results, but most of these studies showed decreased IGF-I levels.[9-12] These differences may be due to; methodological differences in measuring the IGF-I levels, diurnal variations of IGF-I and IGFBP-1, fasting or other hour-to-hour factors affecting the free IGF-I levels.[2] Another possible explanation may be the type of fat distribution since it has been demonstrated that visceral fat mass, rather than adiposity, is inversely correlated with IGF-I levels. In our study, we found that IGF-I levels decreased as the BMI classes increased.

There is a bilateral relationship between obesity and thyroid functions. While the thyroid gland is involved in the control of thermogenesis and appetite, its dysfunction is associated with secondary changes in body weight and composition.[13] Obesity is associated with modifications in the hypothalamus-pituitary-thyroid (HPT) axis, which leads to changes in thyroid functions.[2] The underlying mechanisms of these changes are not fully understood, and several hypotheses are suggested.[2] One of the most accepted explanations is that hyperthyrotropinaemia may be an adaptive response to increase thermogenesis and energy expenditure and minimize weight gain.[13] But, it has been suggested that if the increase in TSH levels was the main issue of this response, an increase in serum thyroid hormones would also be expected.[14] Furthermore, peripheral mechanisms can play a role in the changes in the HPT axis in obesity. In relation to that, Nannipieri et al. demonstrated that weight loss is associated with increased thyroid hormone receptors in subcutan fat tissue.[15] There is discordance between studies on thyroid hormone levels in patients with obesity. In the Danish DanThyr 1997–1998 population cohort, it is demonstrated that BMI is negatively correlated with fT4, but no correlation is found with total T3 and fT3 levels.[16] While later studies showed similar results,[17,18] other studies found opposite results or no relation.[19,20] Mele et al.,[14] showed that as the BMI class increased, there was an increase in TSH levels in women and a decrease in fT4 levels in men. In our study, we did not find any difference between fT3,fT4 and TSH levels and obesity classes. But fT4 levels were higher in class II and III obesity than class I obesity group (p=0.050).

There is a complex relationship between obesity and the hypothalamus-pituitary-adrenal axis (HPA). Steroid dysregulation in obesity may be due to a physiological increase in the HPA axis, changes in cortisol binding globulin (CBG), and increased activation of cortisol through the 11-hydroxy steroid dehydrogenase type 1.[4] Activation of the HPA axis in obesity leads to an increase in corticotropin-releasing hormone (CRH) and cortisol.[4] Most of the serum cortisol is bounded to CBG; only approximately 10% of cortisol is free and biologically active.[4] Hyperinsulinemia and obesity inhibit CBG and result in increased free cortisol levels.[4] But serum total cortisol levels are usually in normal ranges. This is probably due to the suppression of elevated

cortisol levels by negative feedback and, finally, inhibition of ACTH and CRH release. However, urine-free cortisol levels are often mildly elevated in these conditions.[4] When evaluating the obese patient, it is important not to miss Cushing syndrome (CS). Some conditions such as obesity, pregnancy, chronic alcoholism and severe depression are a spectrum of physiological to pathological states of hypercortisolemia and makes both the clinical and biochemical diagnosis more challenging.[4] In these conditions, investigations sometimes give false positive results, such as mildly elevated free urine cortisol levels and rarely a lack of cortisol suppression to dexamethasone.[21] In our study, there was no significant difference between BMI classes and cortisol and ACTH levels, as well as 24-hour urine-free cortisol. Also, the 1 mg dexamethasone suppression test was suppressed in all patients.

The effect of obesity on the gonadal axis shows a sexual dimorphism, usually accepted as hypogonadism in men, but hyperandrogenism in women affects fertility in both sexes.[2] Testosterone and estrogen have a crucial role in the maintenance of skeletal integrity, muscle mass, decreasing fat, as well as maintenance of sexual functions and several risk factors related to metabolic and cardiovascular diseases.[4] Obesity is a risk factor for hypogonadism by affecting the release of gonadotropin-releasing hormone (GnRH) and changing the luteinizing hormone pulse amplitude.[4,22] Adipose tissue worsens testosterone deficiency by increasing the aromatase enzyme, which converts the free testosterone to estrogen.[4,22] Also, as a result of negative feedback of a change in testosterone-estrogen ratio, decrease in the GnRH secretion from the hypothalamus, which later changes the LH amplitude and finally results in low testosterone levels.[22] It is often difficult to interpret the serum testosterone levels in patients with obesity. This is because of the multiple mechanisms, including; low total testosterone with normal free testosterone levels, low sex hormone binding globulin, and low free testosterone secondary to low GnRH levels.[4] In general, there is a negative correlation between BMI and free testosterone levels, and patients with obesity appear to have lower total testosterone levels compared with normal-weight men of similar age.[23] These biochemical parameters often improve with weight loss.[23] In women with obesity hyperandrogenism is common and is often associated with hyperinsulinemia and infertility similar to features seen in polycystic ovarian syndrome (PCOS). The aromatase enzyme found in adipose tissue increase the conversion of androgens to estrogen especially to estrone and result with endometrial hyperplasia and difficulty in fertility.[4] There was no significant difference was found between obesity classes and FSH, LH, total and free testosterone and E2 levels in our study.

Obesity can lead to endocrine dysfunction involving the thyrotropic, gonadotropic, somatotropic, and corticotropic axis. In this study, we found that there was no difference in these functions according to obesity classes, except for the IGF-I level. Further studies are needed to investigate these functions in different classes of obesity.

Ethical Considerations: The present study was approved by the local ethics committee (Date: 22.02.2023, Number: 3328).

Conflict of Interest: The authors declare no conflict of interest.

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CONFRONTING THE DUAL CHALLENGE: THE IMPACT OF THE COVID-19 PANDEMIC ON THE MANAGEMENT OF ACUTE CORONARY SYNDROMES IN A LEADING TERTIARY HOSPITAL IN TURKEY

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Abstract

Objectives: In this study, we aimed to determine the impact of the SARS-CoV-2 pandemic (COVID-19) on the number, morbidity and mortality of acute myocardial infarction patients in Ankara Bilkent City Hospital, which has the largest patient capacity in the European region.

Materials and Methods: A total of 1173 patients who were hospitalized with the diagnosis of acute myocardial infarction in Ankara Bilkent City Hospital between December 2019 to July 2020 were included in this study. These patients were divided into two groups according to the admission date. In this study, in light of the measures taken with the onset of the COVID-19 pandemic in Turkey, the effect of the pandemic on hospital admissions, application types, number of patients, laboratory, echocardiography, and angiography parameters of patients diagnosed with acute myocardial infarction (AMI) was investigated.

Results: The month with the highest number of patients admitted to the emergency department was December, and the month with the lowest number was April. Compared to pre-COVID-19, an approximately 19% decrease was observed in hospital admissions after COVID-19. Also, medical treatment was more common than revascularization after the pandemic (73.43% vs. 26.56%, respectively, p <0.001). The frequency of non-culprit lesion intervention was significantly decreased after the COVID-19 pandemic compared to the time before the pandemic. (39.24% vs 60.75%, respectively, p= 0.002).

Conclusion: Coronavirus-19 pandemic reduced not only the admission of AMI patients to hospitals but also the frequency of revascularization and intervention in the non-culprit artery before discharge. All of these factors led to low ejection fraction and high troponin values in these patients.

Keywords: Acute myocardial infarction, covid-19 infection, pandemic, curfew, revascularization.

Introduction

The lack of effective and reliable treatment at the beginning of the COVID-19 pandemic caused a major crisis in the healthcare system. The increase in hospital admissions due to COVID-19 disease, coupled with the lack of effective treatment, resulted in almost all intensive care units being filled, thereby interrupting the treatment of other diseases.[1] As in many countries, practices such as curfew, reduced hospital admissions except in emergencies, and the postponement of elective procedures were implemented in Turkey. [2,3] The aim of this study is to investigate the modifications in the management of patients who presented with acute coronary syndrome to our tertiary care hospital during the pandemic period, in comparison to the pre-pandemic era. Specifically, the study seeks to analyze any changes in diagnostic, therapeutic and overall care procedures employed for this patient population and to identify the reasons behind such changes. By doing so, this research aims to shed light on the impact of the pandemic on healthcare delivery and contribute to the existing literature on acute coronary syndrome management during crisis situations.

Materials and Methods

The first case of the COVID-19 pandemic detected by the Ministry of Health in Turkey was on March 11, 2020.[4] In this study, the data of patients diagnosed with AMI as specified in the ICD code between December 1, 2019, and March 10, 2020, at Ankara Bilkent City Hospital were compared with patients diagnosed with the same code between March 11, 2020, and July 31, 2020, in the hospital data reporting system. Demographic data obtained from the system, mortality rates, length of hospital stay, whether revascularization was performed, the time of percutaneous interventions, the medical treatments, the comparison of thrombus load in terms of coronary artery disease during the procedure, mainly left ventricular ejection fraction (LVEF) levels in echocardiography performed at discharge were investigated in terms of how the pandemic affected the number of patients, mortality and morbidity. Hemogram (Symex K-1000, Kobe, Japan) and biochemistry parameters (Roche Diagnostic Modular Systems, Tokyo, Japan) for laboratory values were studied in the central biochemistry laboratory of our hospital. Echocardiographic examinations of the patients were evaluated by specialist cardiologist physicians in our hospital using the Philips Affiniti 50C, Release 3.0.3, 3000 Minuteman Road, Andover, MA 01810 USA model device. Imaging and evaluation were performed by specialist interventional cardiologists in our hospital with General Electric (GE) INNOVA IGS 620, Rye de la Miniere, France, and GE OPTIMA IGS 320 001, Milwaukee, Wisconsin, model devices used in the catheter laboratory in patients undergoing coronary angiography both during the working hours and the night shifts.

Statistical analysis

The Mann-Whitney U test was used to analyze continuous data, and the Chi-Square test was used for categorical data analysis. Missing data were excluded from the analysis process. All analyses were performed using the R program. Since the first COVID-19 case in Turkey was detected on March 11, March was divided into two periods for the analysis: March 1-10 and March 11-31. The aim of the study was to analyze the data recorded in the system, mainly regarding the differences in the number of patients who visited the hospital before and after the first COVID-19 case, the differences in the number of admitted patients, the differences in comorbidities, and whether there were differences in the procedures applied to the patients. The study also aimed to provide insights into what could be done in other waves of the pandemic or in other similar events.

Results

A total of 1173 people were included in the study, and Table 1 provides the sociodemographic characteristics and medical histories of the patients.

The month with the highest number of patients admitted to the emergency department was December, while the lowest month was April. In March, 145 patients were recorded, and 51 of these patients applied before the first COVID-19 case in Turkey. From December 2019 until the first COVID-19 case was reported, 627 patients presented to the emergency room, while from March 11, 2020, to July 2020, 506 patients came to the emergency room. Compared to the pre-COVID-19 period, there was an approximate 19% decrease in emergency room visits after COVID-19. Additionally, April, which followed the first COVID-19 case, was the month with the lowest number of patients. The decrease in the number of patients between December 2019 and July 2020 is shown linearly on the graph in Figure 1.

Table 1. The sociodemographic characteristics and medical histories of the patients

		Before COVID-19	After COVID-19		
		Median (25p-75p)	Median (25p-75p)	U	p
Age		61.0 (53.0-69.0)	60.0 (51.0-69.0)		0.119
		n (%)	n (%)	X^2	p
Gender	Male	467 (52.53)	422 (47.46)	1.260	0.260
	Female	160 (56.33)	124 (43.66)		
Coming from outside Ankara	No	63 (57.27)	47 (42.72)	1.600	0.210
	Yes	521 (50.92)	502 (49.07)		
History of DM	No	395 (51.76)	368 (48.23)	1.830	0.180
	Yes	215(55.98)	169 (44.01)		
History of HT	No	298 (49.58)	303 (50.41)	6.570	0.010
	Yes	312 (57.14)	234 (42.85)		
History of CVE	No	591 (53.48)	514 (46.51)	1.870	0.170
	Yes	17 (42.50)	23 (57.50)		
History of HL	No	471 (47.72)	516 (52.27)	84.770	<.001
	Yes	139 (86.87)	21 (13.12)		
History of CAD	No	380 (52.48)	344 (47.51)	0.470	0.490
	Yes	239 (54.56)	199 (45.43)		
Smoking	No	406 (50.68)	395 (49.31)	14.110	<.001
	Yes	193 (63.27)	112 (36.72)		
Blood type	0 RH +	111 (50.00)	111 (50.00)	2.520	0.930
	0 RH -	13 (48.14)	14 (51.85)		
	A RH +	168 (52.01)	155 (47.98)		
	A RH -	20 (62.50)	12 (37.50)		
	B RH +	58 (51.78)	54 (48.21)		
	B RH -	6 (54.54)	5 (45.45)		
	AB RH +	26 (46.42)	30 (53.57)		
	AB RH -	3 (50.00)	3 (50.00)		

(DM: Diabetes mellitus, HT: Hypertension, CVE: Cerebrovascular event, HL: Hyperlipidemia, CAD: Coronary artery disease)

Table 2 presents the proportion of patients who presented to the hospital by ambulance or from outside of Ankara, their diagnosis upon admission, LVEF values based on echocardiography and coronary angiography results, including thrombus and TIMI flow rates, and the revascularization status of the patients. The frequency of pre-COVID-19 LVEF being 35 and below (51.85%) and over 35 (53.37%) were higher than post-COVID-19, but this difference was not statistically significant (p=0.700). However, LVEF values were lower in April than in other months, particularly during the first months of the pandemic (Figure 2).
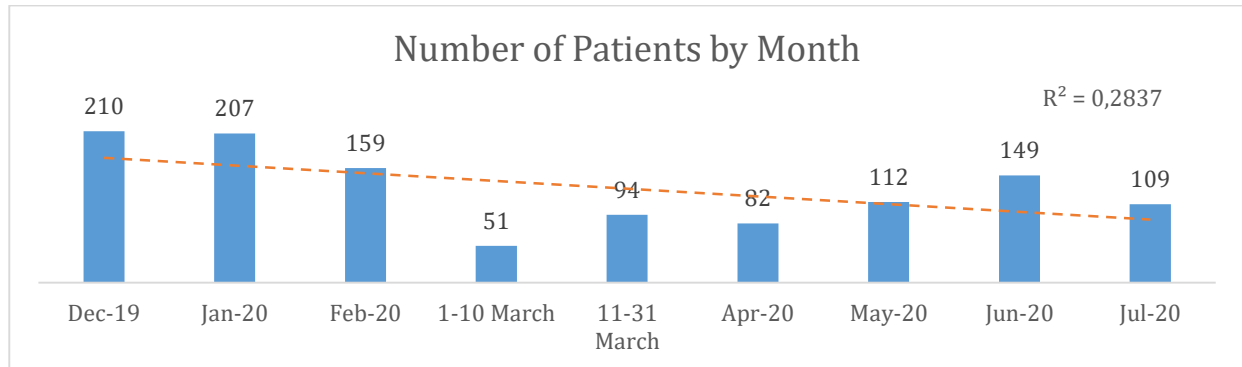
Figure 1. Distribution of the number of patients by months

Table 2. Hospital admission diagnosis and vascular disease status

		Before COVID-19	After COVID-19		
		n (%)	n (%)	X^2	p
Ambulance use	**No**	248 (53.91)	212 (46.08)	1.490	0.223
	Yes	336 (50.22)	333 (49.77)		
Diagnosis	**NSTEMI**	316 (53.28)	277 (46.71)	5.110	0.078
	STEMI	257 (51.72)	240 (48.28)		
	USAP	54 (65.06)	29 (34.93)		
Revascularization*	**0**	17 (26.56)	47 (73.43)	27.700	<.001
	1	500 (55.12)	407 (44.87)		
	2	88 (59.06)	61 (40.93)		
	3	15 (35.71)	27 (64.28)		
Non-culprit intervention	**No**	429 (50.64)	418 (49.35)	9.450	0.002
	Yes	192 (60.75)	124 (39.24)		
Slow flow	**No**	609 (53.00)	540 (47.00)	8.280	0.016
	Yes	11 (91.66)	1 (8.33)		
TIMI grade flow	**0**	96 (42.48)	130 (57.52)	13.800	0.069
	1	3 (50.00)	3 (50.00)		
	2	16 (61.53)	10 (38.46)		
	3	505 (55.86)	399 (44.13)		
Thrombus	**No**	548 (54.52)	457 (45.47)	4.410	0.036
	Yes	71 (45.51)	85 (54.48)		
Three vessel disease	**No**	577 (53.92)	493 (46.07)	1.760	0.185
	Yes	43 (46.73)	49 (53.26)		
LVEF	**35 and Below**	98 (51.85)	91 (48.14)	0.150	0.700
	Above 35	482 (53.37)	421 (46.62)		
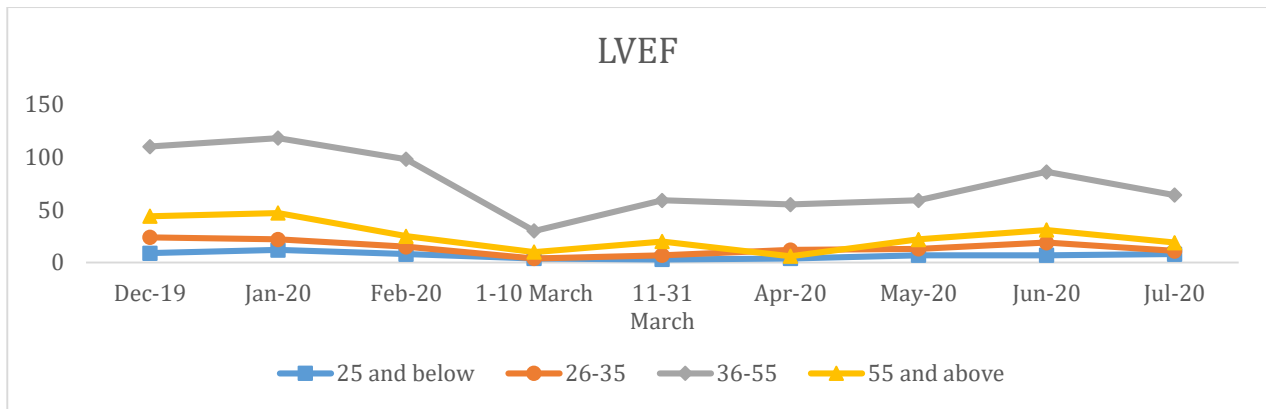
Figure 2. Distribution of LVEF values by months

Patients diagnosed with AMI who were admitted to the hospital were examined in four groups according to their revascularization status: Group 0: Patients who did not undergo coronary angiography, Group 1: Patients who underwent coronary angiography and stent placement, Group 2: Patients who underwent coronary angiography, and non-obstructive stenosis was detected, and Group 3: Patients who decided to have surgery after coronary angiography (Figure 3).

According to the results of the chi-square analysis, when patients were evaluated in terms of having the revascularization procedure or not, not having the procedure was more common after the COVID-19 pandemic, which was found to be statistically significant ($\chi2= 19.537$, p-value = <0.001) (Figure 4).

Table 3 presents the comparison of blood values of people who applied to the hospital in the pre and post-COVID-19 period.
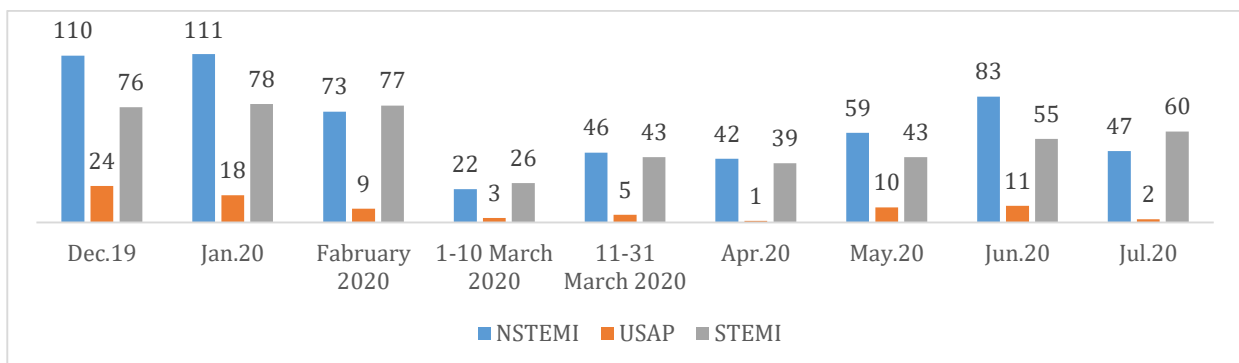
Figure 3. The number of NSTEMI and STEMI before and after pandemic

The patient groups who underwent coronary angiography were examined in three different groups as patients with medical follow-up, stent implantation, or operation decision. According to the results of the chi-square analysis, stent implantation was more common before the COVID-19 pandemic than after, and there was a significant relationship ($\chi2$= 7.304, p-value = 0.025). Also, the number of patients who were referred to the operation was higher after the COVID-19 pandemic (Figure 4).
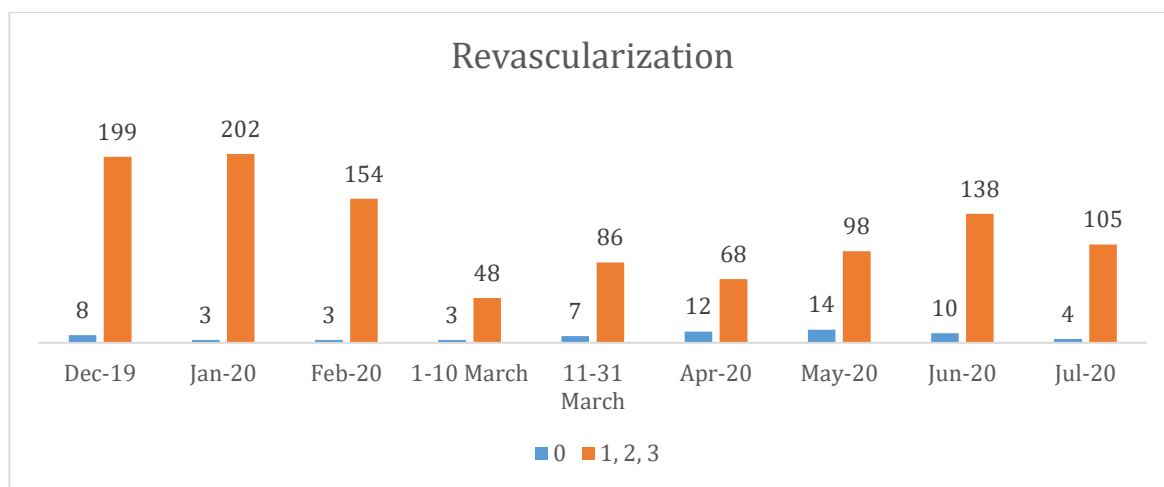
Figure 4. Distribution of the patients as two different groups as those who did not undergo revascularization (Group 0) and those who did (Groups 1-2-3), according to months

Table 3. Laboratory values at the time of admission to the hospital

	Before COVID-19 Median (25p-75p)	After COVID-19 Median (25p-75p)	p
Glucose	122 (99-171)	121 (99.8-177)	0.850
GFR	89 (70-100)	89 (67-102)	0.836
WBC	10 (8-13)	10 (8-12)	0.427
Neutrophil	7 (5-10)	7 (5-10)	0.983
Lymphocyte	2 (1-3)	2 (1-2)	0.041
Hemoglobin	14 (13-15)	14 (13-15)	0.065
Total cholesterol	174 (146-204)	182 (153-210)	0.018
LDL	112 (84-138)	118 (89-141)	0.360
HDL	34 (29-41)	34 (29-40)	0.793
Triglyceride	113 (74-172)	131 (84.3-198)	0.002
HS Troponin	1666 (85.3-12549)	2373 (198-14223)	0.057
Albumin	40 (34-43)	41 (37-44)	0.007
AST	34 (23-94)	43 (23-130)	0.011
ALT	23 (12-38.3)	27 (16-41)	0.020

(GFR: Glomerular filtration rate, WBC: White blood cell, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, AST: Aspartate aminotransferase, ALT: Alanine transaminase, HS Troponin: High sensitivity troponin)

Discussion

The results of our study indicate that the number of patients who presented to our hospital with the onset of the pandemic decreased by 50% compared to the previous month on a monthly basis. However, as the pandemic progressed, this decrease gradually declined, and the rate was 19% when compared to the three months before and after the pandemic. Reports from Austria, Italy, and the USA (California) also showed a decrease in hospital admissions for both STEMI and NSTEMI.[5-7] Similarly, studies conducted at the beginning of the pandemic in our country showed a higher decrease compared to previous years. [8-10] The history of hypertension and hyperlipidemia was higher in patients admitted to the hospital in the pre-COVID-19 period, which can be partly explained by the limitations of reaching the hospital that the pandemic brought for patients with accompanying comorbidities during this period. [11] In the medical histories of the patients regarding the risk of coronary artery disease, cigarette smoking significantly decreased after the COVID-19 period. Consistent with the literature, the reason for this situation may be the awareness that was created for the public about this issue after the pandemic.[12]

When examining the data of 1173 patients, it was observed that the revascularization rate of patients had decreased significantly after the COVID-19 pandemic. Additionally, thrombosed lesions in the coronary angiography findings of revascularized patients had increased statistically. Although the number of patients with three-vessel lesions was not statistically significant, a slight increase was observed after the pandemic. The reasons for this were thought to be related to the effect of the curfew and patients arriving late at the hospital due to the fear of contracting a COVID-19 infection while in the hospital. [13,14] After the pandemic, the incidence of slow flow was statistically less frequently observed. The analyses showed that patients underwent surgery more frequently after the pandemic, while stenting was performed less frequently. Based on these data, it can be said that more critical and thrombosed lesions were observed, resulting in an increase in patients with lesions with high SYNTAX scores after the pandemic. Thus, more patients underwent surgery, while stenting was performed less frequently. The frequency of thrombosed lesions increased statistically significantly after the pandemic. One of the reasons for this is patients who were infected with COVID-19 after the pandemic and were treated with a diagnosis of acute coronary syndrome. It is known in the literature that COVID-19 increases arterial and venous thromboembolism events due to the fact that it causes hypercoagulability, especially endothelial damage through the ACE-2 receptor. [15,16]

When comparing on a monthly basis, the highest number of patients with low LVEF was seen in April, which may have been due to the late admission of these patients at the beginning of the pandemic due to restrictions, hospitals being unprepared, and patients being reluctant to seek medical care. However, in the months following the onset of the pandemic, LVEF values started to be similar. During the pandemic, the frequency of intervention on non-culprit lesions was statistically lower. [17-19] This situation may have decreased after the

onset of the pandemic due to most doctors being assigned to different clinics, the risk of contracting COVID-19 during long procedures, the need to prevent transmission in the hospital, and the postponement of all elective procedures by the Ministry of Health. In the literature, it has been shown that the number of percutaneous coronary procedures performed during the COVID-19 pandemic in many countries has decreased. [20-22]

There was no change in the average duration of hospitalization of patients before or after the pandemic, but the duration of hospital stay was more stable before the pandemic. This situation can be explained by the fact that the hospitalization of some patients was prolonged due to the need for extra tests owing to similar symptoms that may have developed on the basis of MI, which could also be seen in COVID-19 infection. Additionally, some patients may have been discharged from the hospital earlier to reduce transmission. [23]

A statistically significant decrease was observed in lymphocyte counts after the COVID-19 pandemic (p=0.041). This may have been due to the fact that COVID-19-positive patients were also treated during the COVID-19 period, and lymphocyte deficiency could be observed in these patients. Additionally, low lymphocyte levels were indicative of a bad inflammatory process, and delayed medical applications may have contributed to the decrease.[24] Although no significant differences were observed in hemogram parameters other than lymphocyte values, troponin levels, liver function tests, and lipid levels of the patients were higher after the pandemic than before. This situation was primarily explained by the late arrival of patients. [11]

Pandemics are a persistent global concern that may recur if preventive measures are inadequate, as demonstrated by epidemiological studies. This study aimed to illustrate the potential repercussions of not intervening in high-mortality diseases, such as acute coronary syndrome, during ongoing and future pandemics due to insufficient protective measures. Our research recommends that patients with severe symptoms seek medical attention promptly, even during a pandemic, while also minimizing hospital occupancy rates.

Limitations

The most significant limitation of the study was the unavailability of the patient's records from the onset of their symptoms until the balloon procedure was performed during angiography. As a result, factors such as the duration of processing after the pandemic, longer waiting times in the emergency room, and patients' delayed arrival at the hospital could not be directly evaluated. The study attributed findings such as lower LVEF values and higher rates of blood values associated with poor prognosis at the beginning of the pandemic to patients' late arrival, longer waiting times in the emergency department, and delayed processing. Additionally, the study was limited by the lack of data on mortality rates before and after the pandemic, which prevented the comparison of patients hospitalized with the diagnosis of acute coronary syndrome.

Ethical Considerations: Ethics committee approval was obtained from Ankara Yıldırım Beyazıt University Clinical Research Ethical Committee (Decision Date:07/10/2020, Decision Number:26379996/110)

Conflict of Interest: The authors declare no conflict of interest.

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A SCORING INDEX FOR PREDICTING THYROID MALIGNANCIES

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Abstract

Objectives: We evaluated ultrasonography (US) features of thyroid nodules ≤ 1 cm and > 1 cm and determined the features that might predict malignancy; we also aimed to develop a new scoring system considering US features to avoid unnecessary fine-needle aspiration biopsy (FNAB), particularly for sub-centimeter nodules.

Materials and Methods: We retrospectively evaluated 2233 nodules of 1118 patients who underwent thyroidectomy. US features predictive for malignant histopathology were evaluated by multivariate logistic regression analysis. A US index score was calculated for each nodule considering these features.

Results: 337 (15.11%) nodules were ≤1 cm, and 1896 (84.89%) were > 1 cm. In total, 173 (51.33%) of the ≤1 cm nodules were histopathologically benign, and 164 (48.67%) were malignant. Anteroposterior/transverse diameter (AP/T) ≥1, microcalcifications, macrocalcifications, and hypoechoic patterns were significantly more frequent in ≤1 cm malignant compared with benign nodules. Microcalcification, macrocalcification, hypoechoic and iso-hypoechoic patterns, and solid texture were significantly higher in the malignant than the benign group in > 1 cm nodules. The best cut-off of US index scores for discrimination of benign and malignant nodules were > 2 and > 4 for ≤1 cm and > 1 cm nodules, respectively.

Conclusion: Our US scoring system may help clinicians and surgeons to select nodules for FNAB more accurately, particularly those sub-centimeter in size.

Keywords: Sub-centimeter, supra-centimeter, thyroid nodule, ultrasonography features, ultrasonography scoring.

Introduction

Thyroid nodules are commonly seen among the adult population, especially in women.[1] The most important issue to be answered in a patient with a thyroid nodule is whether it is malignant or not because 5–13% of nodules harbor thyroid cancers.[2] Ultrasonography (US) is accepted to be a reliable and easily available diagnostic method with high sensitivity (90%) and specificity (85%) for this assessment in thyroid imaging.[3]

Several studies have made an effort to determine pathognomonic US features for malignancy, which leads to a risk stratification based on the following predictors: solid or mostly solid structure, hypoechogenicity, irregular margins, microcalcifications, a discontinuous halo, taller-than-wide (TTW) shape, intralesional flow on Doppler examinations, and a >20% size increase in 6 months.[4-6]

Furthermore, nodule size would be a predictor of malignancy.[7] In general, nodules >1 cm have the potential to be clinically significant cancers.[8] Despite all its positive qualities, diagnosis of malignancy cannot be determined solely by ultrasound features only.[9] To discriminate benign from malignant thyroid nodules, the least invasive preoperative modality is ultrasound-guided fine-needle aspiration biopsy (FNAB).[10] However, its diagnostic value in sub-centimeter thyroid nodules is controversial.

In the 2015 guidelines published by the American Thyroid Association (ATA), FNAB is not recommended for sub-centimeter nodules.[11] In contrast, other organizations and some authors have suggested that FNAB be performed on all nodules with suspicious US features independent of nodule size.[12,13] Recently, the thyroid imaging reporting and data system (TI-RADS) was developed for use in thyroid nodule risk stratification using various US features derived from the breast imaging reporting and data system.[4,14] But in some reports, it is reported that the clinical use is limited, and its practicality is challenging.[15] Therefore, it is important to determine the US features of thyroid nodules, particularly the sub-centimeter nodules. In this study, we evaluated US features in thyroid nodules ≤ 1 cm and > 1 cm and determined the features that might predict malignancy. We also aimed to develop a new scoring system considering US features to avoid or reduce unnecessary FNAB, particularly for sub-centimeter nodules.

Materials and Methods

Patients

We retrospectively evaluated patients who underwent thyroidectomy between January 2007 and December 2014 in our clinic. Patients < 16 years old and those with a history of thyroid surgery, percutaneous intervention, or radiotherapy to the head and neck were excluded from the study. Demographic data,

preoperative thyroid function, thyroid autoantibodies, US findings, and histopathological features were reviewed from medical records. Local ethical committee approval was obtained in accordance with the ethical standards of the Declaration of Helsinki.

Laboratory findings

Levels of thyroid-stimulating hormone (TSH), free triiodothyronine (fT3), free thyroxine (fT4), thyroid autoantibodies, thyroid peroxidase antibody (anti-TPO) and thyroglobulin antibody (anti-TG), and thyroglobulin were measured in all patients using a chemiluminescent method. The normal TSH, fT3, fT4, anti-Tg, and anti-TPO ranges were 0.40–4 µIU/mL, 1.57–4.71 pg/mL, 0.61–1.12 ng/dL, < 30 U/mL, and < 10 U/mL, respectively.

Conventional ultrasonography

All patients underwent preoperative US. The diameter (mm), nature, echogenicity, border regularity, microcalcifications and macrocalcifications, presence of a peripheral halo, and anteroposterior/transverse diameter ratio were evaluated. The echogenicity of the nodule was compared with that of the surrounding parenchyma and was classified as in our previous study;[16] hypoechoic, isoechoic, or iso-hypoechoic. The nature of the nodule was classified as solid (solid component > 50%), mixed (containing a cystic part), or pure cystic (almost cystic or very little solid), the same as our previous study.[16]

Ultrasonography-guided fine-needle aspiration biopsy

US-guided FNAB was performed by an experienced endocrinologist using a 23-gauge needle and 20 mL syringe. Written consent was obtained from all patients prior to FNAB. FNAB was performed for nodules > 1cm and those ≤ 1cm with suspicious US features (irregular border, hypoechoic nature, solid component, presence of microcalcifications, and taller-than-wide shape).[17]

Cytological and histopathological examinations

Material obtained by US-guided FNAB was evaluated according to the Bethesda system classification.[18] The cytology results were grouped as follows: 1) non-diagnostic, 2) benign, 3) atypia/follicular lesion of undetermined significance (AUS/FLUS), 4) follicular neoplasm/suspicious of follicular neoplasm, 5) suspicious for malignancy, and 6) malignant.[19,20]

Statistical analysis

The data analysis was performed using SPSS ver. 17.0 software (IBM Corp., Armonk, NY, USA). Continuous data are shown as means ± standard deviation or medians (range), and numbers and percentages were used for categorical variables. The χ^2 or Fisher's exact test was used to detect US differences between benign and malignant nodules, where appropriate. The diagnostic performance of the US features was evaluated by calculating the Sn, Sp, positive predictive value (PPV), negative predictive value (NPV), and accuracy.

The forward LR method of multiple binary logistic regression was used to develop the formula for recommending US-guided biopsy. Variables with a p-value < 0.25 in the univariate analysis were subjected to multivariate analysis, which included all variables of known clinical importance. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for each US characteristic. The least suspicious (lowest malignancy rate) feature was used as the reference if there were more than two subgroups of features, and the ORs of the other suspicious features were analyzed and compared. The diagnostic performance of the formula was evaluated by a receiver operating characteristic curve analysis. The best cut-off point for recommending biopsy and its corresponding diagnostic values were calculated. A p-value < 0.05 was considered significant.

Results

In total, 2,233 nodules from 1,118 patients were evaluated; 884 (79.10%) patients were female, and 234 (20.90%) were male. The mean age of the patients at diagnosis was 49.51±12.11 years (range 19–84 years). The anti-TPO positive rate was 24.32%, and the anti-TG positive rate was 24%.

337 (15.11%) nodules were ≤ 1 cm, and 1,896 (84.89%) were > 1 cm. FNAB was performed on 336 (15.20%) nodules ≤ 1 cm and on 1,872 (84.80%) > 1 cm. The cytological and histopathological results are shown in Table 1. The non-diagnostic results were similar between the ≤1 cm and >1 cm nodules, whereas the suspicious malignancy and malignant nodule categories were significantly more frequent among sub-centimeter nodules compared with those > 1 cm (p<0.001). Benign FNAB results were significantly more frequent in nodules > 1 cm (p<0.001). In total, 173 (51.33%) of the ≤ 1 cm nodules were histopathologically benign, and 164 (48.67%) were malignant. A total of 1,423 (75.10%) nodules > 1 cm were benign, and 473 (24.90%) were malignant (p<0.001) (Table 1)

A comparison of US features between benign and malignant nodules ≤1 cm and the diagnostic performance of these features for predicting the histopathological results are shown in Table 2. AP/T ≥ 1, microcalcifications, macrocalcifications, and a hypoechoic pattern were significantly more frequent, and the isoechoic pattern was significantly less frequent in the ≤ 1 cm malignant nodules compared with the benign nodules (Table 2).

Table 1. Histopathology and fine-needle aspiration biopsy results of the nodules according the nodule sizes

FNAB results	Nodule size		p
	≤ 1 cm n=336 (%)	> 1 cm n=1872 (%)	
Non-diagnostic	88 (26.20%)	482 (25.80%)	0.864
Benign	99 (29.41%)	887 (47.42%)	<0.001
AUS/FLUS	40 (11.90%)	237 (12.71%)	0.712
FN/SFN	6 (1.82%)	63 (3.30%)	0.320
Suspicious for malignancy	53 (15.81%)	103 (5.47%)	<0.001
Malignant	50 (14.86%)	100 (5.30%)	<0.001
Histopathology	≤ 1 cm n=337 (%)	> 1 cm n=1896 (%)	p
Benign	173 (51.33%)	1423 (75.10%)	<0.001
Malign	164 (48.67%)	473 (24.90%)	

(FNAB; fine-needle aspiration biopsy, AUS/FLUS; atypia/follicular lesion of undetermined significance, FN/SFN; follicular neoplasm/suspicious for follicular neoplasm)

Table 2. Comparison of ultrasonographic features between benign and malignant nodules and diagnostic performance of these features in the prediction of histopathological results according to the nodule sizes

Nodule Size	Variables	Benign (n=173) (%)	Malignant (n=164) (%)	p	Sn	Sp	PPV	NPV	Accuracy
≤1 cm	AP/T ratio								
	<1	138 (79.80%)	98 (64.12%)	0.002					
	≥1	35 (20.20%)	55 (35.88%)		35.91%	79.82%	61.10%	58.50%	59.20%
	Border regularity								
	Regular	49 (28.29%)	42 (25.60%)	0.575					
	Irregular	124 (71.71%)	122 (74.40%)		74.42%	28.30%	49.61%	53.80%	50.71%
	Presence of halo								
	Present	30 (17.30%)	19 (11.60%)	0.134	88.40%	17.31%	50.32%	61.20%	52.90%
	Absent	143 (82.70%)	145 (88.40%)						
	Microcalcification	33 (19.12%)	71 (43.31%)	<0.001	43.31%	80.91%	68.30%	60.11%	62.60%
	Macrocalcification	22 (12.74%)	41 (25.00%)	0.004	25.01%	87.30%	65.10%	55.10%	57.01%
	Echogenicity								
	Isoechoic	66 (38.22%)	32 (19.51%)	<0.001					
	Hypoechoic	30 (17.33%)	54 (32.91%)	<0.001	32.90%	82.70%	64.30%	56.51%	58.42%
	Isohypoechoic	77 (44.45%)	78 (47.58%)	0.574	47.61%	55.52%	50.31%	52.71%	51.60%
	Nodule texture								
	Cystic	3 (1.70%)	0 (0.00%)	0.248					
	Solid	170 (98. 30%)	163 (99.40%)	0.623	99.40%	1.71%	48.92%	75.03%	49.31%
	Mixed	0 (0.00%)	1 (0.60%)	0.487					

Nodule Size	Variables	Benign (n=1423) (%)	Malignant (n=473) (%)	p	Sn	Sp	PPV	NPV	Accuracy
> 1 cm	AP/T ratio								
	<1	1160 (82.31%)	366 (79.90%)	0.257					
	≥1	250 (17.69%)	92 (20.10%)		20.10%	82.31%	26.91%	76.00%	67.00%
	Border regularity								
	Regular	598 (42.00%)	195 (41.20%)	0.761					
	Irregular	825 (58.00%)	278 (58.80%)		58.81%	42.00%	25.21%	75.42%	46.21%
	Presence of halo								
	Present	441 (31.00%)	157 (33.21%)	0.372					
	Absent	982 (69.00%)	316 (66.79%)		66.81%	31.01%	24.31%	73.72%	40.01%
	Microcalcification	495 (34.81%)	221 (46.74%)	<0.001	46.72%	65.23%	30.93%	78.64%	60.62%
	Macrocalcification	344 (24.23%)	176 (37.26%)	<0.001	37.23%	75.81%	33.80 %	78.41%	66.20%
	Echogenicity								
	Isoechoic	801 (56.31%)	197 (41.60%)	<0.001					
	Hypoechoic	129 (9.11%)	85 (18.00%)	<0.001	17.81%	91.20%	40.20%	76.91%	72.92%
	Iso-hypoechoic	493 (34.58%)	191 (40.40%)	0.024	40.41%	65.41%	27.92%	76.71%	59.21%
	Nodule texture								
	Cystic	60 (4.18%)	7 (%1.51)	0.005					
	Solid	1350 (94. 91%)	462 (97.72%)	0.010	97.71%	5.10%	25.51%	86.91%	28.31%
	Mixed	13 (0.91%)	4 (0.77%)	1.000					

(Sn; sensitivity, Sp; specificity, PPV; positive predictive value, NPV; negative predictive value, AP/T ratio; anteroposteriortransvers ratio)

The US features of the benign and malignant > 1 cm nodules are compared and the diagnostic performance of these features is given in Table 2. Accordingly, microcalcifications, macrocalcifications, hypoechoic and iso-hypoechoic patterns, and solid nature were significantly more frequent in the malignant than in the benign group.

US features predictive of malignancy were evaluated by multivariate logistic regression analysis. The presence of microcalcifications, nodule echogenicity, AP/T ratio ≥ 1, and macrocalcifications were independent predictors of malignancy in nodules ≤ 1 cm (Table 3). Nodule echogenicity, macrocalcification, nodule texture, and microcalcifications were independent predictors for malignancy in nodules > 1 cm (Table 3).

Table 3. Predictive factors for malignancy according to the ultrasonographic features of the nodules ≤1 cm and >1 cm.

Nodules ≤1 cm	Odds ratio	95% Confidence interval		Wald	p
		Lower limit	Upper limit		
AP/T ratio ≥1	1.944	1.126	3.355	5.698	**0.017**
Microcalcification	3.308	1.915	5.713	18.410	**<0.001**
Macrocalcification	2.016	1.086	3.742	4.939	**0.026**
Isoechoic	1.000	-	-	-	-
Hypoechoic	2.732	1.398	5.339	8.638	**0.003**
Isohypoechoic	1.845	1.043	3.263	4.430	**0.035**
Nodules >1 cm	Odds ratio	95% Confidence interval		Wald	p
		Lower limit	Upper limit		
Microcalcification	1.370	1.065	1.763	6.002	**0.014**
Macrocalcification	1.781	1.366	2.323	18,163	**<0.001**
Isoechoic	1.000	-	-	-	-
Hypoechoic	3.507	2.402	5.120	42,217	**<0.001**
Isohypoechoic	1.488	1.174	1.887	10.764	**<0.001**
Cystic nodule	1.000	-	-	-	-
Solid nodule	4.487	1.881	10.702	11.457	**<0.001**
Mixed nodule	4.881	1.172	20.332	4.741	**0.029**

(AP/T ratio; anteroposteriortransvers ratio)

A US index score was calculated for each nodule considering the factors predicting malignancy. Table 4 shows the index score for each US factor separated into nodules ≤ 1 cm and those > 1 cm.

Table 4. Index scores related to ultrasonographic features of the nodules ≤ 1 cm and >1 cm that predict the malignancy

Ultrasonographic features	Ultrasonography index scores	
	Nodule size	
	≤1 cm	>1 cm
AP/T ratio		
<1	0	-
≥1	1	-
Microcalcification		
Absent	0	0
Present	1	1
Macrocalcification		
Absent	0	0
Present	1	1
Echogenicity		
Isoechoic	0	0
Isohypoechoic	1	1
Hypoechoic	2	2
Nodule texture		
Cystic	-	0
Mixed	-	1
Solid	-	2

(AP/T ratio; anteroposterior/transverse diameter ratio)

Accordingly, the mean index score for benign nodules was 2.091±1.190 and 3.041±1.060 in malignant nodules ≤1 cm (Table 5). The best cut-off value to discriminate benign and malignant nodules was > 2, with an Sn of 68.61%, Sp of 66.55%, PPV of 64.41%, and NPV of 70.61% in ≤ 1 cm nodules (Figure 1a). The mean index score for benign nodules was 3.971±1.460 and 4.951±1.701 in malignant nodules >1 cm (Table 5). The best US index score for predicting malignancy in nodules > 1 cm was > 4, with a Sn, Sp, PPV and NPV of 58.12%, 66.61%, 36.71%, and 82.71%, respectively (Figure 1b).

Table 5. Index scores related to US features that can predict malignancy in nodules ≤1 cm and >1 cm

	Nodule size	
	≤1 cm	>1 cm
Ultrasonographic index score		
Benign	2.091±1.190	3.971±1.460
Malignant	3.041±1.060	4.951±1.701
ROC analysis		
The area under the curve	0.722	0.665
95% Confidence interval	0.667-0.777	0.636-0.693
p-value	**<0.001**	**<0.001**
The best cut-off point	>2	>4
Sensitivity	68.612%	58.123%
Specificity	66.554%	66.610%
PPV	64.412%	36.711%
NPV	70.613%	82.712%

a) ROC curve of the nodules ≤1cm related with ultrasonographic index score *(ROC; receiver operating characteristic)*

b) ROC curve of the nodules >1cm related with ultrasonographic index score *(ROC; receiver operating characteristic)*
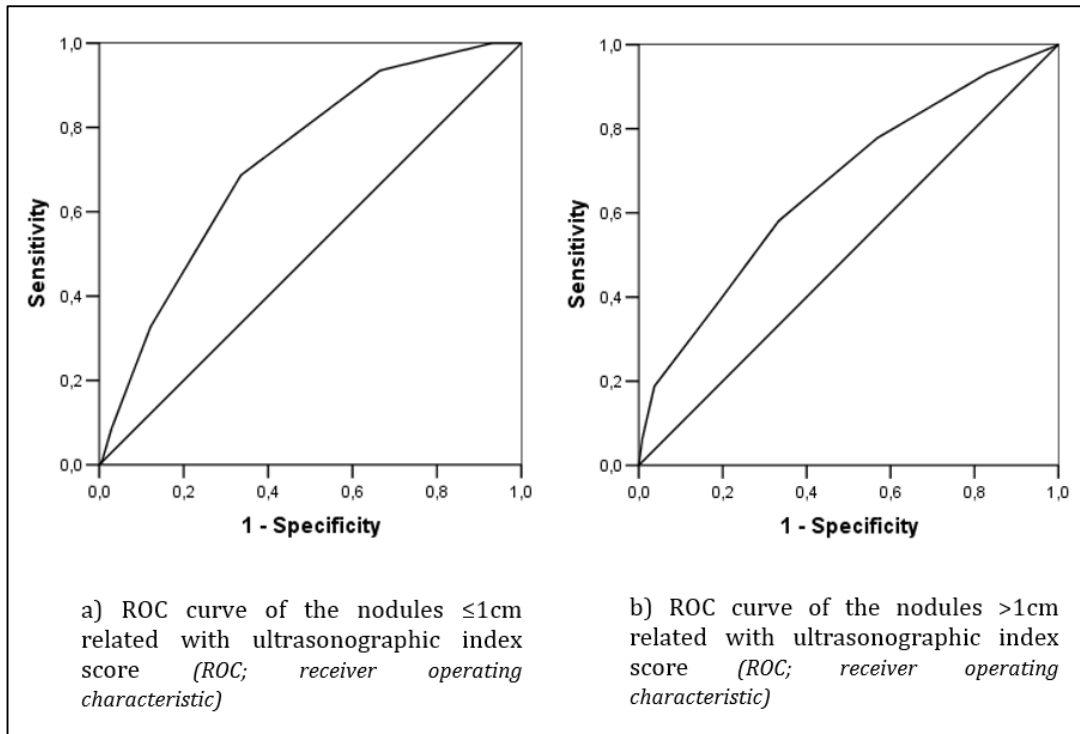
Figure 1. ROC curve of the nodules

Discussion

Fine needle aspiration biopsy is the primary method to define the malignancy risk of a thyroid nodule. However, it is not reasonable to perform FNAB for all thyroid nodules due to the relatively low malignancy rate. In addition, as the size of a nodule decreases, the rate of inadequate FNAB samples increases.[21]

There are conflicting reports relating to tumor size and thyroid malignancy. Retrospective studies suggested that with an increase in nodule size, there is no increase in the risk of malignancy.[7,22] It is reasonable to evaluate the malignancy risk of a thyroid nodule based on US findings or other clinical risk factors rather than size. Malignancy rates in sub-centimeter nodules were reported as 3–19% across studies.[23] Bo et al.[24] reported an overall malignancy rate of 16% in sub-centimeter thyroid nodules and 7.6% in ≥1 cm nodules based on FNAB results. The authors stated that they could not compare the two groups because FNAB was performed on supra-centimeter nodules regardless of US features, whereas it was performed only on sub-centimeter nodules with one or more suspicious US features.[24] Berker et al.[25] reported malignancy rates of 6% for sub-centimeter and 2.9% for supra-centimeter nodules. Whether FNAB is effective for sub-centimeter nodules is still controversial.[23,25] In our study, 48.67% of sub-centimeter nodules and 24.90% of supra-centimeter nodules were confirmed to be malignant by histopathology. Our higher rate of malignancy might have been due to the

appropriate selection of the nodules with suspicious US features, indicating them for biopsy or surgery due to our center's experience.

An AP/T ratio ≥ 1 is a good predictor of malignancy in both supra and sub-centimeter thyroid nodules with high Sp.[23,26] Although solid nature is a weak indicator of malignancy in thyroid nodules in some studies, others have reported that it is a strong indicator.[25,27,28] Our study revealed that solid nature was significantly associated with malignancy in nodules > 1 cm but not in those ≤ 1cm. Berker et al.[25] found no significant association between solid nature and malignancy in sub-centimeter and supra-centimeter thyroid nodules.

The decrease in echogenicity indicates that the cells grow rapidly, and subsequently, follicles lose their normal alignment. This event is considered by some authors as representing an increased risk of malignancy.[9] Although some reports have revealed that a hypoechoic appearance of a thyroid nodule is significantly related to thyroid malignancy,[25] other studies did not confirm such a relationship.[29] Similar to previous studies reporting hypoechogenicity as a suspicious US feature,[25] hypoechoic patterns were significantly related to malignancy in both ≤1 cm and > 1 cm nodules in our study.

We also found a significant association between the presence of microcalcifications and macrocalcifications and malignancy in both groups. Berker et al.[25] observed a relationship between malignancy and microcalcifications only in sub-centimeter nodules and suggested that this association would have been significant in supra-centimeter nodules if their sample size had been larger.

Previous studies introduced different combinations of US features that are highly effective for differentiating benign and malignant thyroid nodules; however, different combinations of criteria were used in each study.[28] Papini et al. reported that irregular or blurred margins, intranodular vascular patterns, and microcalcifications were predictive of malignancy.[28] However, a single US feature seemed to be insufficient to differentially diagnose thyroid nodules. To define the malignancy risk, several reporting and data systems based on ultrasonographic features have been evaluated.[3] Horvath et al.[4] with a modified recommendation from Jin Kwak et al.[30] proposed the Thyroid Image Reporting and Data System (TI-RADS) in order to improve patient management and cost-effectiveness by avoiding unnecessary FNAB of thyroid nodules. However, its clinical use is limited, and it is difficult to apply in routine clinical practice.[3,15] Therefore, we developed a US scoring system based on the multivariate analysis considering US features predicting malignancy. The best cut-off score to discriminate benign and malignant nodules was > 2 for the ≤ 1 cm nodules and > 4 for > 1 cm nodules. Cheng et al. evaluated slightly different US featured predictive of malignancy in sub-centimeter thyroid nodules and revealed that irregular shape, hypoechogenicity, absence/incomplete capsule, calcifications, and AP/T ≥ 1 were strongly predictive of malignancy.[10] The mean US scores were 1.7±1.0 in the benign group and 3.4±1.1 in the malignant group. A cut-off score > 2 was predictive of malignant sub-centimeter nodules. Those authors

recommended FNAB for nodules with a US index score > 2. Zhang et al.[26] reported that echogenicity, marginal irregularity, and the height-to-width ratio were the US factors that best-predicted malignancy. They calculated a formula using these features and recommended FNAB for nodules with a predicted probability of ≥ 0.284 since such nodules had a high risk of malignancy. Pompili et al,[1] evaluated the total malignancy score (TMS) of 231 nodules in 231 consecutive patients. In the multivariate analysis, hypoechogenicity, a solid structure, the presence of microcalcifications, and the number of nodules were independent predictors of the final diagnosis. They found that 47 % of the nodules had a TMS <3, 18% had a TMS 3, and 35% had a TMS >3. The authors suggested that they could asses the risk of malignancy according to the TMS category, with no risk or negligible risk for a TMS <3, low risk for a TMS of 3, and medium or high risk for higher TMS values.

In our study, non-diagnostic FNAB results were similar in > 1 cm and ≤ 1 cm nodules which were consistent with Berker et al.[25] We also found higher suspicious for malignancy and malignancy FNAB results in nodules ≤ 1 cm compared with those > 1 cm. Our higher rate may be due to the fact that several small-sized suspicious thyroid nodules were referred to our tertiary hospital and the most suspicious nodules were selected for FNAB.

The major limitation of our study was that it was retrospective and from a single center. Second, although our clinicians are experienced in US, it is inevitable to have interobserver variability when assessing US features of thyroid nodules. Another limitation of our study was that nodule vascularization had not been evaluated in a considerable number of patients; thus, we did not include it in the analysis. Additionally, fewer sub-centimeter nodules were evaluated than larger nodules in our study.

In conclusion, as the clinical significance of small thyroid cancers is controversial, it is important to evaluate these nodules using the best strategy. Although many studies have assessed the risk of thyroid cancer attributable to certain US features and formulated a combination of US features to increase their predictive value for malignancy, the diagnostic accuracy of US remains limited. Ultrasonography scoring system may help clinicians and surgeons to select nodules for FNAB more accurately and prevent unnecessary sampling, particularly those sub-centimeter in size, and help to provide cost-effectiveness.

Ethical Considerations: The study has been approved by an Ethics Committee of the Faculty of Medicine of the local University (Date: 21.10.2015, Number: 208)

Conflict of Interest: The authors declare no conflict of interest.

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A CASE REPORT OF ACUTE APPENDICITIS PRESENTING WITH DIARRHEA

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Abstract

A 26-year-old female patient presented to the family medicine outpatient clinic with complaints of diarrhea, widespread abdominal pain, nausea, and vomiting, which had been going on for five days. In the first physical examination findings of the patient, there was widespread sensitivity in the abdomen, but there were no findings of defense or rebound. The patient was re-evaluated with the results of conducted tests, her abdominal examination was repeated, and rebound positivity was detected in the right lower quadrant. The patient was referred to the Emergency Department, and she was taken into operation by the general surgery team with the diagnosis of acute appendicitis. The most important factor in delaying the diagnosis of acute appendicitis is the presence of gastroenteritis. Cases of acute appendicitis presenting with diarrhea have been reported in the medical literature. Since acute pathologies should always be kept in mind in the differential diagnosis of patients who present to primary care with abdominal pain and diarrhea, it is deemed appropriate to present the case with literature.

Keywords: Appendicitis, enteritis, diarrhea, abdominal pain, abdomen, acute, appendix.

Introduction

Appendicitis is one of the most common causes of acute abdominal pain and one of the most common acute surgical conditions. Acute appendicitis is usually diagnosed based on clinical signs and symptoms. Right lower quadrant pain, abdominal rigidity, and periumbilical pain radiating to the right lower quadrant are confirmatory signs of acute appendicitis in adults.[1] There is no single sign, symptom, or diagnostic test that fully confirms the diagnosis.[2] The diagnostic accuracy of clinical evaluation for acute appendicitis is dependent on the experience of the examining Physician.[3] As an individual approach, laboratory tests such as the white blood cell (WBC) count and inflammatory biomarkers are useful. The recommended first-line approach consists of blood and urine tests for the etiology and ultrasonography in case of suspicion.[4] Diameter exceeding 6 mm in ultrasonography and loss of compression response of the appendix are diagnostically important.[1] There are various clinical scoring systems and the Alvarado scoring system is the most widely used one. It is particularly useful to rule out appendicitis and to select patients for further diagnostic investigations.[4]

In clinical practice, acute appendicitis can sometimes mimic acute gastroenteritis. Sometimes, diarrhea may be the first symptom, as enteric infections may cause appendicitis. [5] In this case study, a patient who presented to the Family Medicine outpatient clinic with complaints of abdominal pain and diarrhea and who was operated on with the diagnosis of acute appendicitis, will be presented. The patient in this manuscript has given verbal informed consent to the publication of their case details.

Case report

A 26-year-old female patient with a diagnosis of anxiety disorder, who is using sertraline 50 mg/day, presented to the family medicine outpatient clinic with complaints of diarrhea, diffuse abdominal pain, nausea, and vomiting, which had been going on for five days. The patient has no previous operation or accident history. She stated that she had been diagnosed with irritable bowel syndrome three years ago, but no treatment was started, and she has had no complaints for the past two years. In the patient's history, we see that she presented to an external center with the same complaints three days ago and that she was prescribed metronidazole 500 mg/day and metoclopramide 10 mg/day. The patient explained that her complaints did not regress despite the regular use of these medications. She stated that she had watery defecation every half hour and that there was no change in the color of her stool. She also stated that she had no appetite due to nausea, vomited the contents of her stomach after she ate, her stomach ache was widespread, she did not have a fever and did not have any problem with her urine. In the first physical examination findings of the patient, there was widespread sensitivity in the abdomen; there was no defense and no rebound, no costovertebral angle tenderness, the bowel sounds were hyperactive on auscultation, and skin turgor pressure was found to be normal.

Her body temperature was found to be 37.8 degrees, her blood pressure was 110/80 mmHg, and her pulse was 85/min. Other system examination findings were found to be normal. After the patient's blood, urine, stool tests, and blood results were seen, an abdominal X-ray was requested. Blood results showed WBC 9120/mm3, neutrophil rate 69.2%, C-reactive protein 0.0973 g/L (reference range: 0-0.005), and the total hCG to be negative. The microscopic analysis of the complete urinalysis was normal.

In the stool's microscopic examination, abundant leukocytes were seen in every area, but erythrocytes or parasite cysts and eggs were not seen. Giardia intestinalis rapid antigen test was negative, and there was no growth of Salmonella and Shigella spp in the stool culture. No acute pathology was detected in the standing abdominal X-ray of the patient. The patient's abdominal examination was repeated 3 hours after her first admission. The patient whose abdominal tenderness continued and who now developed rebound positivity in the right lower quadrant had a total Alvarado score that was calculated to be 6 points (Table 1). Her oral intake was stopped due to a possible operation, and she was referred to the Emergency Service.

Table 1. Alvarado Scoring System[4]

Feature	Score	Case Score
Migration of pain	1	0
Anorexia	1	1
Nausea	1	1
Tenderness in the right lower quadrant	2	2
Rebound Pain	1	1
Elevated temperature	1	1
Leukocytosis	2	0
The shift of white blood cell count to the left	1	0
Total	**10**	**6***

*Probable appendicitis, consider further imaging

Abdominal superficial tissue ultrasonography was performed, and "The Appendix diameter was measured as 6.2 mm, and the response to compression was lost. However, significant contamination or free fluid in the surrounding mesentery was not observed. The findings are suspicious for acute appendicitis," as stated in the report. The report for the abdominal and pelvis computerized tomography of the patient stated: "The appendix calibration was measured 7 mm in the right lower quadrant of the abdomen. There is no significant increase in density or fluid densities in the peri-appendicular fatty tissue around it. There was no significant free fluid or free air in the abdomen" (Figure 1). The patient was consulted by the General Surgery branch in the emergency department and was evaluated as having acute appendicitis with examination and findings, and the patient was taken to an emergency appendectomy operation. The pathology report of the appendectomy material after the

operation was compatible with acute appendicitis. Since the patient did not develop any additional pathologies in the postoperative period in the service, she was discharged with the necessary medical recommendations.

Figure 1. The image of the appendix section (arrow) on the abdominal and computerized pelvis tomography of the patient

Discussion

An accurate and efficient diagnosis of acute appendicitis can reduce morbidity and mortality from perforation and other complications.[6] There is no single sign, symptom, or diagnostic test that fully confirms the diagnosis of appendicitis.[2] Early symptoms and physical examination findings of appendicitis are often unclear. For these reasons, delay in the diagnosis of acute appendicitis is common but missed or delayed diagnosis of appendicitis can lead to serious complications such as perforation. Therefore, in the presence of suspected acute appendicitis, it is important to follow the patient and repeat the physical examination at regular intervals. Some limited evidence suggests that repeated laboratory evaluation may increase sensitivity in detecting appendicitis, especially in patients who present earlier.[3]

In clinical practice, acute appendicitis can sometimes mimic acute gastroenteritis, and diarrhea may be the first symptom, as sometimes enteric infections may cause appendicitis.[5] Differentiating acute appendicitis and acute gastroenteritis in the presence of diarrhea poses a challenge for clinicians at an early stage.[7] Cases of acute appendicitis presenting with diarrhea have been reported in the literature.[2,7-9] Although sometimes the laboratory findings are the same, careful analysis of the history and physical examination help distinguish acute appendicitis from enteritis. Peritoneal irritation findings such as increased sensitivity around the McBurney point, defense, and rebound are more common in acute appendicitis than enteritis.[7]

What is expected from the primary care physician is to carefully evaluate the patients who come with abdominal pain, to start the treatment of the patients who can be treated in primary care immediately, to refer the patient to a higher center under appropriate conditions without wasting time, even if a cause such as acute abdomen that requires further examination and treatment is considered. Patients whose diagnosis has not been clarified should be followed up and re-evaluated with a physical examination at regular intervals.[10] In our case study, although the patient's inflammatory abdominal pain was compatible with acute appendicitis, the fact that physical examination findings suggestive of acute appendicitis were absent in the first examination of the patient but became evident in the follow-up examination, which shows the importance of following up the patients whose diagnoses are not clear.

In conclusion, in the presence of diarrhea, the differential diagnosis of acute appendicitis from enteritis is difficult, and this delays timely intervention. In addition, the early signs of acute appendicitis are unclear, and close follow-up and repetition of physical examination at regular intervals in patients with suspected acute appendicitis are important in diagnosis.

Ethical Considerations: An informed consent taken from the patient.

Conflict of Interest: The authors declare no conflict of interest.

*This case was presented as a poster presentation at the Ankahed 10th Ankara Family Medicine Congress on 16-18 September 2022.

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FROM TRAUMA TO POST-TRAUMATIC STRESS DISORDER: IDENTIFICATION OF THE RISK FACTORS

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Abstract

People encounter various traumatic events throughout their lives. However, most people can cope with these stressful life events in different ways without experiencing any long-term mental problems. Post-Traumatic Stress Disorder (PTSD) is a chronic and important psychiatric disorder that develops in a small number of people as a result of short or long-term exposure to one or more traumatic events and affects the life of an individual. For this reason, it is important to identify people at risk for the development of PTSD and to apply appropriate intervention methods for these people to prevent the disability caused by PTSD. In this review article, the factors that lead to the risk of developing PTSD in individuals exposed to trauma are discussed in light of current information in the literature.

Keywords: Psychological trauma, post-traumatic stress disorder, risk factors.

Introduction

Trauma is described as single or multiple events or series of events that have lasting negative effects on an individual's physical, mental, or social state that is physically or emotionally harmful or threatening.[1] Trauma is defined in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), directly or indirectly, as an actual or intimidating encounter with death, serious injury, or sexual assault.[2]

Studies investigating the frequency of exposure to a traumatic situation show that trauma exposure is quite common. The literature has shown that the frequency of experiencing a traumatic event throughout life is 17-83% and varies according to demographic characteristics.[3,4] It is stated that exposure to more than one traumatic event is not uncommon, and 34% of men and 25% of women have been exposed to two or more traumas.[5]

Many different psychiatric disorders such as depression, anxiety disorder, alcohol and substance use disorder, and trauma-related disorders may occur in individuals exposed to trauma. [6] Some of these people may have post-traumatic stress disorder (PTSD).

PTSD, which is one of the trauma-related disorders, is a psychiatric disorder characterized by re-experiencing the event, negative changes in cognitions and affect, dissociative symptoms, avoidance from the reminders of the trauma, and hyperarousal symptoms resulting from direct or indirect exposure to a traumatic event.[2] Although the lifetime risk of PTSD is reported to be approximately 8%, the frequency of PTSD can vary significantly between different demographic groups, as in the incidence of trauma.[7]

Although quite high trauma exposure rates have been reported in the literature, not every trauma results in trauma-related psychiatric disorders. Trauma is a necessary, but not sufficient factor for the development of PTSD. For this reason, it is very important to identify the groups at high risk for PTSD and to offer appropriate psychosocial support and follow-up plan to these groups. This article aimed to review the factors that lead to the risk of developing PTSD in individuals exposed to trauma in light of current information in the literature.

Risk Factors for the Development of PTSD

There are many research and review studies examining the risk factors in the etiology of PTSD. When these studies are examined, the risk factors that predispose to the development of PTSD can be grouped under three main headings as pre-traumatic risk factors, trauma-related risk factors, and post-traumatic risk factors, as shown in Figure 1.

Pre-Traumatic Risk Factors

Gender, sexual orientation, intellectual capacity, personality traits, presence of a history of previous trauma or psychiatric illness, and some genetic factors have been shown as pre-traumatic risk factors for the development of PTSD.

Gender and Sexual Orientation

It has been shown that the probability of encountering a life-long traumatic event is higher in men than in women. However, studies have reported that women are almost twice as likely as men to have a lifetime diagnosis of PTSD. It has been revealed that this difference is maintained, although it decreases when the trauma type is controlled.[8]
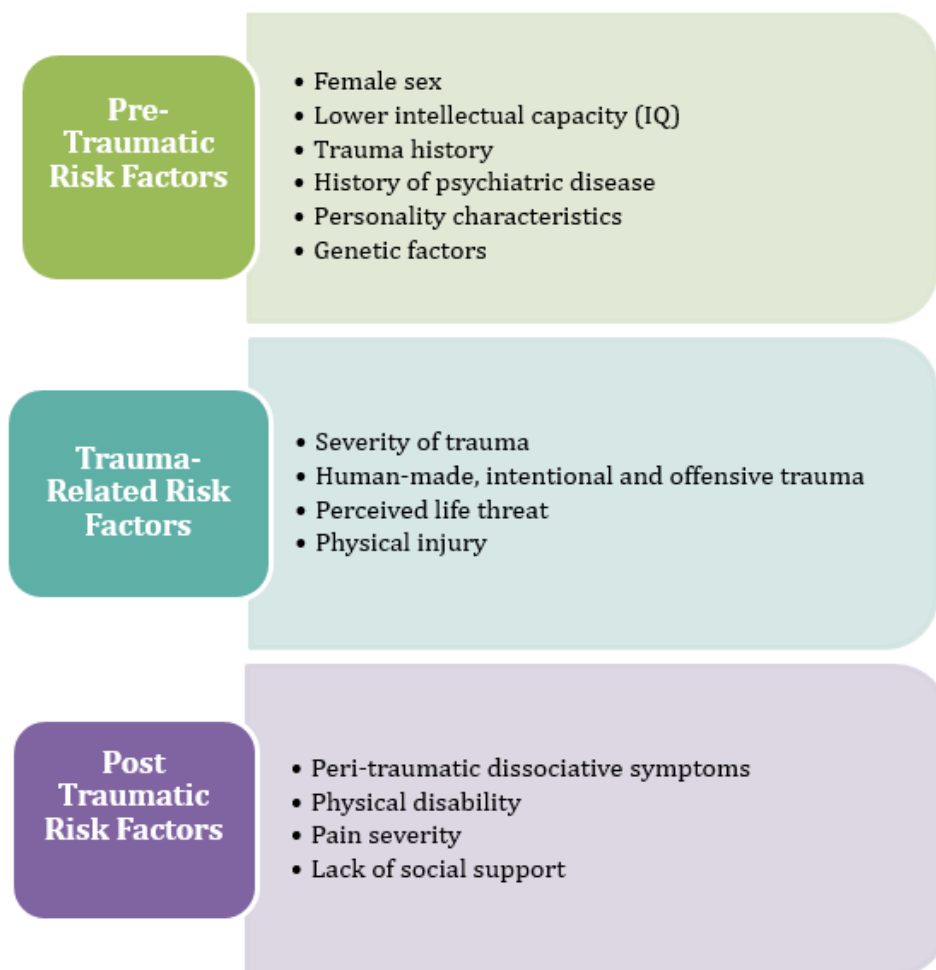

Pre-Traumatic Risk Factors
- Female sex
- Lower intellectual capacity (IQ)
- Trauma history
- History of psychiatric disease
- Personality characteristics
- Genetic factors

Trauma-Related Risk Factors
- Severity of trauma
- Human-made, intentional and offensive trauma
- Perceived life threat
- Physical injury

Post Traumatic Risk Factors
- Peri-traumatic dissociative symptoms
- Physical disability
- Pain severity
- Lack of social support

Figure 1. Classification of risk factors for the development of post-traumatic stress disorder

The studies searching for the reasons for this difference suggested that risky trauma exposures such as sexual assault for the formation of PTSD may be more common in women.[9] However, it was stated that the fact that this difference was preserved even after controlling for the trauma type could be due to gender differences in trauma-related cognitions, emotional reactivity, emotion regulation, and coping strategies.[10] More frequent dissociative symptoms in women and hyper-arousal symptoms in men could be related to these differences.[11]

In addition, the fact that social support is more inadequate for women in many cases, more frequent history of childhood trauma in women, and cultural factors on gender roles and gender are thought to contribute to women being a risky group for PTSD.[11,12]

In addition to gender, it has been stated that sexual identity and orientation may also be risk factors for the development of PTSD. Compared to heterosexual people, it has been shown that the rates of exposure to trauma are increased among homosexual, bisexual, and transgender people and they are more likely to be diagnosed with PTSD.[13]

Intellectual Capacity

It has been shown that there is a relationship between intellectual disability and the risk of violence, abuse and/or neglect.[14] Research on trauma-related stress responses has shown that intelligence affects how an individual processes the traumatic experiences. It has been also shown that high cognitive capacity is protective against developing PTSD. For this reason, it was emphasized that cognitive deficits increase the risk of PTSD. Moreover, the diagnosis of PTSD may be missed if adequate psychiatric evaluation is not performed due to cognitive limitations. In review studies, it has been reported that the incidence of PTSD in these individuals is approximately 10%. In addition to that, it has been stated that the trauma itself negatively affects intellectual skills and may further impair their quality of life.[15]

Previous Trauma History

When individuals with a diagnosis of PTSD were evaluated, it was observed that there was often a history of exposure to trauma before the trauma that caused PTSD. Prior exposure to traumatic events has been associated with greater vulnerability to the PTSD effects of subsequent trauma.[16] It has been emphasized that the effects of trauma are cumulative and therefore, a later trauma that appears may have a greater impact on the individual than a trauma that occurred many years ago.

The relationship between previous trauma and PTSD varies according to the type of current traumatic experience. It has been reported that having a previous trauma history is more strongly associated with PTSD

when the current traumatic experience includes interpersonal violence such as assault, rape, or domestic violence rather than war or accident.[17]

Studies have shown that a history of childhood trauma increases the risk of trauma-related PTSD in adulthood.[18] The incidence of PTSD is reported higher in individuals who have experienced emotional neglect or sexual abuse, especially in their childhood period.[19]

In contrast to these findings, it is also observed that some people have developed effective coping strategies for their previous traumatic experiences or that they can cope with the new trauma more easily because they have learned to adapt to the consequences of the trauma. It has been stated that this condition, called post-traumatic growth, could be protective for people.[20]

History of Psychiatric Disease

A history of mental disorders such as pre-traumatic mood disorder, anxiety disorders, or conduct disorder is associated with developing PTSD.[21] Some studies have demonstrated that the risk of later PTSD increases with the presence of one or more psychiatric disorders, such as depression, anxiety disorder, and somatoform disorder before trauma exposure, particularly in women.[22]

From a psychosocial perspective, it is thought that the socioeconomic conditions or interpersonal relationships of individuals with pre-existing psychiatric disorders predispose them to experience a traumatic event. Additionally, it is emphasized that the presence of mental illnesses can make it difficult to cope with the trauma encountered by an individual and therefore pave the way for the development of PTSD.[22]

Personality Characteristics

Studies in the literature have suggested that temperament characteristics are associated with exposure to trauma and the risk of developing PTSD. Neurotic personality traits are associated with higher rates of PTSD.[23] Temperament characteristics such as avoidant and hostile attitudes are also shown to be correlated with the risk of developing PTSD.[24]

Research has identified certain temperamental characteristics that are associated with an increased risk of developing PTSD. Specifically, individuals with low levels of self-directedness and cooperativeness, which reflect underdeveloped executive functions, are more vulnerable to developing PTSD[25]. Additionally, factors such as low psychological resilience, high levels of harm avoidance behaviors, difficulties in regulating negative emotions, and specific cognitive schemas, including feelings of defectiveness, lack of self-control, self-sacrifice,

unrelenting standards, fear of abandonment, enmeshment, and vulnerability, have been found to be associated with an elevated risk of PTSD.[26,27]

These findings highlight the complex interplay between individual temperament, cognitive processes, and the development of PTSD. Temperamental traits that indicate deficits in executive functions, along with maladaptive cognitive schemas and difficulties in emotion regulation, contribute to an increased susceptibility to experiencing and coping with traumatic events.

Genetic Factors

It has been suggested that the differences in resilience and PTSD risk in individuals who have experienced similar trauma may be due to the basic variables in biological processes determined by multiple genetic and epigenetic factors. High heritability rates have been reported in studies on genetic factors associated with the development of PTSD.

Genetic connectivity and twin studies on the etiopathogenesis of PTSD indicate a high heritability ranging from 13-69%. It has also been shown that the risk of exposure to certain types of trauma may have an important genetic component. The contribution of genetic factors is found higher in high-risk traumas such as sexual and physical neglect or abuse in childhood compared to other traumas.[28]

In PTSD-related candidate gene association studies, more than 25 genes have been identified as involved in neurotransmitter systems and stress signaling pathways. In particular, single nucleotide polymorphisms (SNPs) that are claimed to be effective at receptor levels and transporter mechanisms have been identified in dopaminergic and serotonergic pathways associated with stress response.[29] It has also been shown that genetic variants in the glucocorticoid receptor and binding proteins that affect the hypothalamus-pituitary-adrenal (HPA) axis, which is one of the main regulators of the biological response to stress, are associated with the risk of PTSD.[29] Moreover, it is suggested that genetic changes in different signaling pathways such as some neurotrophic factors, ApoE, catecholamines, and endogenous opioids may predispose to the development of PTSD.[30]

It has been stated that exposure to trauma may cause epigenetic changes, causing changes in the genetic opening, and this may pose a risk for psychiatric disorders such as PTSD. In animal studies, DNA methylation and histone modifications that may affect neurogenesis, neuron plasticity, and HPA pathway have been shown to cause PTSD clinic.[31,32] In studies investigating the effects of early traumatic life events on DNA methylation in the hippocampus tissue, epigenetic changes are reported more prominently in genes that affect neuronal plasticity specifically.[33] It has been reported that these epigenetic mechanisms, which have an important role

in synaptic plasticity, may be responsible for traumatic memory and the formation of intrusive and repetitive memories, which are prominent symptoms of PTSD.[29]

Trauma-Related Risk Factors

When the trauma-related risk factors for the development of PTSD are examined, the severity of the trauma, the type of traumatic experience, and the severity of the perceived threat to life are found to be associated with the risk of developing PTSD.

Severity of Trauma

Conditions such as direct exposure to trauma, physical injury as a result of trauma, or loss of loved ones, which show the objective severity of the traumatic event, are generally associated with the development of PTSD.[34]

It is shown that direct exposure to trauma, such as experiencing trauma directly or witnessing a traumatic event experienced by others, has a more severe impact on the person than indirect trauma exposure, such as hearing about an event from others or learning through the media. When the traumas that are directly exposed are examined, experiencing the trauma directly has a more devastating effect than witnessing the trauma experienced by others. On the other hand, it has been shown that the closeness and emotional relationship of the person with the person witnessed changes the way of perceiving the severity of the trauma.[35]

It has been reported that physical injury to a person after a traumatic event may be a predictor for the development of PTSD. About half of the people who were seriously injured in car accidents, fires, stabbings, gunshots, or other incidents have been shown to have PTSD and/or alcohol use problems one year after discharge from trauma surgery units.[36]

Type of Trauma

Studies have shown that exposure to human-mediated intentional and offensive trauma is an important risk factor for the development of PTSD. It is found that the traumatic event is more likely to result in PTSD than many other types of trauma, especially in individuals who have been sexually assaulted. Factors such as being attacked by a stranger, being threatened, being exposed to an event in a safe place, having a history of childhood sexual abuse, and not receiving adequate social support after sexual assault further increase the risk of developing PTSD.[37]

Domestic and partner violence is also quite common and could be traumatic. Although women are more frequently reported to be exposed to domestic and partner violence than men, there is no significant difference

reported between the genders in terms of PTSD symptoms. Moderate to severe PTSD symptoms were reported as a result of partner-related traumatic events in 24% of women and 20% of men.[38] Although physical, sexual, and psychological violence and abuse from partners are all significantly associated with PTSD, psychological violence has been reported to have the strongest association with developing PTSD.[39]

The lifetime risk of experiencing PTSD for soldiers and armed personnel participating in wars or conflicts is reported up to 35%. Particularly, it has been shown that factors such as participating in a violent and long-term conflict, witnessing injured or dying people, physical disability, and inadequate post-conflict social support increase the risk of PTSD.[40]

Trauma resulting from political violence and conflicts, which are common, especially among refugee groups, is widespread throughout the world and is one of the important types of trauma for the development of PTSD. In these groups, exposure to violence in early childhood, being in ethnic or religious minority groups, exposure to physical torture, and multiple trauma experiences were found to be more closely associated with PTSD risk.[41]

Natural disasters have a significant impact on a large number of people within a short period of time. Events such as earthquakes, floods, and tornadoes not only cause physical destruction but also contribute to psychological trauma. The presence of community members or outsiders in the affected areas can create a sense of chaos, adding to the stress experienced by individuals. The disruption of daily routines and the loss of familiar surroundings further exacerbate the traumatic experiences. Additionally, human-made mistakes and oversights that contribute to the severity of the disaster can increase the trauma experienced by individuals.[1] Knowing that the disaster could have been prevented or mitigated can evoke feelings of anger, helplessness and increased the severity of traumatic experience.

Financial and life-threatening risks are also prevalent during natural disasters. The loss of property, limited access to basic necessities, and displacement from homes add to the distress and uncertainty individuals face. In crowded shelters, privacy may be compromised, further impacting psychological well-being. Furthermore, media coverage of the disaster and the repetitive exposure to images of devastation can be distressing and can retraumatize individuals. The prolonged time required to restore daily routines, activities, and services, such as schools reopening, resuming work, or having access to basic supplies, can complicate the recovery process and increase the risk of developing PTSD.[1]

Perceived Life Threat

What the events mean to the individual and what kind of life-threat perception they create are as important as the type and severity of the trauma. There are studies suggesting that the perceived fear of death during a traumatic event is related to PTSD.

Traumas in which a person is intensely worried about their life are associated with an increased risk of PTSD. In a large sample study, it was shown that when a threat to life is perceived, the probability of developing PTSD is 1.6 times higher and it stands out more than other risk factors.[42] Perceived fear of death or threat to life is an independent factor that increases the risk of PTSD in different types of trauma, such as domestic violence, war experiences, sexual assault, or physical illness.[43, 44]

Post Traumatic Risk Factors

Considering the post-traumatic period, it has been revealed that hospitalizations, chronic pain, physical disability, dissociative symptoms, and inadequacies in social support could be risk factors for the development of PTSD.

Dissociative Symptoms

Studies in the literature have revealed that dissociative symptoms experienced during and after trauma are an important risk factor for PTSD. In many meta-analyses, it has been reported that peritraumatic dissociative symptoms predict the development of PTSD.[17,45] Not only in retrospective studies, but also in prospectively designed studies, it has been shown that peritraumatic dissociative symptoms are strongly associated with PTSD, and it has been emphasized that this is not the result of a recall error in remote memory shadowed by PTSD.[46] Some studies have suggested that the relationship between peritraumatic dissociative symptoms and PTSD is relatively weak.[47] It has been stated that one reason why some studies have found a stronger association between peritraumatic dissociation and PTSD than others may be because this association is significantly stronger in women than in men.

Research suggests that individuals with high anxiety sensitivity are more likely to experience heightened peritraumatic dissociative experiences. These peritraumatic dissociative symptoms can serve as markers for an increased risk of developing PTSD in the future[48]. Furthermore, studies have indicated that the persistence of dissociative symptoms following a traumatic event may have a stronger association with the risk of developing PTSD than the peritraumatic dissociation itself. This suggests that individuals who continue to experience dissociative symptoms after the trauma may be particularly vulnerable to developing PTSD.[49]

Physical Disability and Pain

Numerous studies have shown that a high heart rate (>95/min) at first admission to the emergency department is a risk factor for PTSD in people with physical injury.[50] While no relationship was found between length of stay in hospital and PTSD, it was stated that the history of intensive care hospitalization may have a moderate relationship with PTSD.[51]

PTSD has been associated with pain severity in patients with severe physical injury.[52] There is evidence for a two-way interaction between pain and PTSD. It has been suggested that chronic pain may be a reminder of the traumatic event that triggers re-experiencing, while PTSD symptoms such as insomnia may lower the pain threshold.[53] The level of physical disability and loss of daily functioning are associated with an increased risk of PTSD.[54,55] It has also been stated that there may be a relationship between mild traumatic brain injury and the development of PTSD.[56]

Social Support

Studies have revealed that social support after trauma is a protective factor for the development of PTSD.[17] Numerous studies have demonstrated that inadequacy in social assistance and support from the environment is one of the most consistent risk factors for PTSD. Lack of social support is more strongly associated with the development of PTSD in women than in men.[57] Contrararly, it has been shown that adequate social services, which can support adequate living conditions in the post-traumatic period, reduces post-traumatic symptoms in the long term.[58]

In addition to the positive and protective nature of social support, it is also reported that negative social criticism and reactions may increase the risk of PTSD. In some studies, the effect of negative social reactions is found higher than positive forms of support in adjusting to and explaining trauma.[59] Although positive reactions to trauma have a weak protective role against the development of psychopathologies such as PTSD, it is emphasized that negative social reactions may be predictive for many psychiatric disorders, including PTSD.[60]

Conclusion

The risk of experiencing PTSD for individuals who have been traumatized varies depending on different personal, event-related, and environmental factors. It is the prevention of traumatic experiences that will definitively prevent the risk of developing PTSD. However, in cases where trauma is exposed, evaluation of individuals in terms of risk factors is important for rapid support and intervention. Therefore, information about the individual's life history, personality traits, methods of coping with stress, and trauma experience should be discussed in detail. The meaning of the trauma experience for the person and how it creates a threat perception should also be examined. Different institutions and interdisciplinary cooperation should be established to provide medical, psychological, economic, and social support that can help people maintain their physical and social functionality in the post-traumatic period.

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