HAMIDIYE MEDICAL JOURNAL

The Official Journal of University of Health Sciences Turkey, Hamidiye Faculty of Medicine

E-ISSN: 2718-0956

August - 2021
Volume - 2
Issue - 2

ORIGINAL ARTICLES

galenos Publishing House

www.hamidiyemedj.com

hamidiye med j

HAMIDIYE MEDICAL JOURNAL

2021
Volume 2

Editorial Board

Publisher Contact
Address: Molla Gürani Mah. Kaçamak Sk. No: 21/1 34093 İstanbul, Turkey
Phone: +90 (212) 621 99 25 **Fax:** +90 (212) 621 99 27 **E-mail:** info@galenos.com.tr
Web: www.galenos.com.tr **Publisher Certificate Number:** 14521
Online Publication Date: August 2021 **E-ISSN:** 2718-0956
International periodical journal published three times in a year.

HAMIDIYE
MEDICAL JOURNAL

About Us

Hamidiye Medical Journal (Hamidiye Med J) is a peer-reviewed open-access international journal that publishes conducted in all fields of medicine, interesting case reports, and clinical images, invited reviews, editorials, letters, comments and letters to the Editor including reports on publication and research ethics. The journal is the official scientific publication of the Health Sciences University, Hamidiye Medical School, İstanbul, Turkey. It is published three times a year in April, July, and December. The language of the journal is English.

The journal is based on independent and unbiased double-blinded peer-reviewed principles. Only unpublished papers that are not under review for publication elsewhere can be submitted. Hamidiye Medical Journal does not accept multiple submissions and duplicate submission even though the previous one was published in a different language. The authors are responsible for the scientific content of the material to be published. Hamidiye Medical Journal reserves the right to request any research materials on which the paper is based.

Hamidiye Medical Journal encourages and enables academicians, researchers, specialists, and primary care physicians to publish their valuable research in all branches of medicine. The primary aim of the journal is to publish original articles with high scientific and ethical quality and serve as a good example of medical publications in the Turkey as well as in the World.

OPEN ACCESS POLICY

This journal provides immediate open access to its content on the principle that making research freely available to the public, supporting a greater global exchange of knowledge.

Open Access Policy is based on the rules of Budapest Open Access Initiative (BOAI) http://www.budapestopenaccessinitiative.org/. By "open access" to [peer-reviewed research literature], we mean its free availability on the public internet, permitting any users to read, download, copy, distribute, print, search, or link to the full texts of these articles, crawl them for indexing, pass them as data to software, or use them for any other lawful purpose, without financial, legal, or technical barriers other than those inseparable from gaining access to the internet itself. The only constraint on reproduction and distribution and the only role for copyright in this domain, is given to authors to retain control over the integrity of their work and the right to be properly acknowledged and cited.

Address for Correspondence

Selimiye Mah. Tıbbiye Cad. 34668 Üsküdar, İstanbul

Phone: +90 216 418 96 16

E-mail: tipfakultesi@sbu.edu.tr

Issuing Body

Galenos Yayınevi Tic. Ltd. Şti.

Molla Gürani Mah. Kaçamak Sok. No: 21, 34093, Fındıkzade, İstanbul, Turkiye

Phone: +90 212 621 99 25

Fax: +90 212 621 99 27

E-mail: info@galenos.com.tr

OPEN ACCESS

hamidiye med j

HAMIDIYE
MEDICAL JOURNAL

2021
Volume 2

Contents

ORIGINAL ARTICLES

CASE REPORT

ORIGINAL ARTICLE

DOI: 10.4274/hamidiyemedj.galenos.2021.57966

Hamidiye Med J 2021;2(2):50-56

Risk Factors for Pulmonary Embolism in Patients with Lung Cancer and Effects of Pulmonary Embolism on Prognosis

Akciğer Kanserli Hastalarda Pulmoner Emboli için Risk Faktörleri ve Pulmoner Embolinin Prognoza Etkileri

Aysu Ayrancı[1], Pınar Çimen[2], Nuran Katgı[2], Gülru Polat[2], Gülistan Karadeniz[2], Sami Deniz[2], Dursun Tatar[2]

[1]*Bakırçay University Çiğli Training and Research Hospital, Clinic of Pulmonology, İzmir, Turkey*

[2]*University of Health Sciences Turkey, Dr. Suat Seren Chest Diseases and Surgery Training and Research Hospital, Clinic of Pulmonology, İzmir, Turkey*

ABSTRACT

Background: Malignancy is an important risk factor for venous thromboembolism. Lung cancer is one of the frequently determined cancer associated with pulmonary embolism (PE). In our research, we compared lung cancer patients diagnosed with PE at the same period and lung cancer patients without PE. Besides, we investigated the risk factors that could predict PE in lung cancer patients, whether survival was different between patients who were diagnosed with PE incidentally and those who were diagnosed proactively.

Materials and Methods: The study's data came from lung cancer patients who were followed up between January 2012 and May 2017. A total of 235 patients with a thoracic angiographic computed tomography scan and/or ventilation/perfusion scintigraphy were included in the study. 109 patients with PE and 126 patients without a PE diagnosis were reported. Demographic information, lung cancer types and stages, time between lung cancer and PE, and survival were all recorded.

Results: The PE group's median age was 61 years (45-82 years), while the non-PE group's median age was 61 years (35-83 years). Adenocarcinoma was the most common histological form in the PE population, with higher leukocyte and C-reactive protein (CRP) levels and lower hemoglobin levels. The PE group had a mean survival time of 20.1±1.6 months, while the non-PE group had a mean survival time of 36.5±2.9 months. The mean survival time was significantly longer in the non-PE group (p<0.001).

Conclusion: Lung cancer patients with PE had a shorter survival. PE should be considered in patients with adenocarcinoma histology, leukocytosis, elevated CRP, anemia, and nutritional disorders.

Keywords: Lung cancer, prognosis, risk factors, pulmonary thromboembolism

ÖZ

Amaç: Malignite, venöz tromboembolizm için önemli risk faktörlerinden biridir. Akciğer kanseri, pulmoner emboli (PE) ile en sık ilişkili malignitelerden biridir. Çalışmamızda aynı dönemde PE tanısı almış akciğer kanseri hastaları ile PE'si olmayan akciğer kanseri hastalarını karşılaştırdık ve PE'nin sağkalım üzerindeki etkisini göstermeyi amaçladık. Ayrıca akciğer kanseri hastalarında PE'yi öngörebilecek risk faktörlerini ve tesadüfen PE tanısı alan hastalarda ve diğerlerinde sağkalımda bir fark olup olmadığını araştırdık.

Gereç ve Yöntemler: Çalışmadaki veriler Ocak 2012-Mayıs 2017 tarihleri arasında hastanemizde izlenen akciğer kanseri hastalarından elde edildi. Toraks anjiyo bilgisayarlı tomografi taraması ve/veya ventilasyon/perfüzyon sintigrafisi olan 235 hasta dahil edildi. Toraks anjiyo bilgisayarlı tomografi taraması ve ventilasyon/perfüzyon sintigrafisi ile yapılan incelemelerde PE tanısı alan 109, PE tanısı olmayan 126 hasta belirlendi. Demografik veriler, akciğer kanserinin tipleri ve evreleri, akciğer kanseri ile PE arasındaki süre ve sağkalım kaydedildi.

Bulgular: PE grubunun ortanca yaşı 61 (45-82) yıl ve PE olmayan grubun ortanca yaşı 61 yıl idi (35-83). PE grubunda en sık görülen histolojik tipin adenokarsinom olduğu, lökosit ve C-reaktif protein (CRP) değerlerinin daha yüksek, hemoglobin değerlerinin daha düşük olduğu görüldü. Akciğer kanseri tanısı konulduktan sonraki ortalama sağkalım süreleri karşılaştırıldığında; PE grubunun ortalama sağkalım süresi 20,1±1,6 ay ve PE olmayan grubun ortalama sağkalım süresi 36,5±2,9 aydı. Ortalama sağkalım süresi PE olmayan grupta anlamlı olarak daha uzundu (p<0,001).

Address for Correspondence: Aysu Ayrancı, Bakırçay University Çiğli Training and Research Hospital, Clinic of Pulmonology, İzmir, Turkey
E-mail: draysu87@gmail.com **ORCID ID:** orcid.org/0000-0002-8939-336X

Received: 03.02.2021 **Accepted:** 01.07.2021

ÖZ

Sonuç: Son olarak, PE'li akciğer kanseri hastalarının daha kısa hayatta kaldıklarını bulduk. Adenokarsinom histolojisi, lökositoz, yüksek CRP, anemi ve beslenme bozuklukları olan hastalarda, nefes darlığı ve göğüs ağrısı akciğer kanserine atfedilmeden önce PE de düşünülmelidir.

Anahtar Kelimeler: Akciğer kanseri, prognoz, risk faktörü, pulmoner tromboembolizm

Introduction

One of the most important risk factors for venous thromboembolism (VTE) is cancer, which raises the risk of VTE by 2-4 times. VTE composes of pulmonary embolism (PE) and deep vein thrombosis (DVT), and cancer patients are believed to have higher rate of VTE than the patients without cancer (1). The development of VTE in cancer patients is influenced by many factors. Thrombosis vulnerability is increased by elevated D-dimer, C-reactive protein (CRP), thrombosis history, and obesity (2,3). VTE is associated with a poor prognosis in cancer patients according to recent reports, and VTE is the second cause of death after all types of cancer (4,5,6). Lung cancer is one of the most frequently determined cancer associated with PE, and the risk of VTE is 20 times higher in lung cancer patients (7). PE is linked to an increase in patients' mortality rates. It has been shown in many clinical studies that PE is responsible for approximately 10% of deaths in lung cancer (8,9,10,11,12).

Respiratory symptoms are often associated with the underlying malignancy or disease progression in lung cancer patients. This may cause delay in the diagnosis of PE (13). Also, the widespread use of multi-detector computed tomography (CT) in the routine staging and follow-up period has caused an increase in the incidence of incidental PE (14). Although incidental PE cases have displayed different characteristics in comparative studies with symptomatic PE cases, similar approaches have been recommended according to the guidelines (15,16).

Therefore, early detection of PE is important, and starting early anticoagulation reduces the mortality rate up to 4 times (13). We compared lung cancer patients diagnosed with PE with lung cancer patients without PE during the same time span in order to demonstrate the impact of PE on survival. In addition, we assessed the risk factors that could predict PE in lung cancer patients, because survival was different between patients who were diagnosed with PE incidentally and those who were diagnosed proactively.

Material and Methods

Study Design

The data in this study were obtained from lung cancer patients who were followed up in a tertiary reference hospital for chest diseases between January 2012 and May 2017. The study was designed retrospectively and approval was obtained from the Local Ethics Committee of the our hospital (no: 49109414-806.02.02). Lung cancer patients diagnosed and/or followed up in our hospital over a 5-year period were analyzed using data obtained from the hospital information system. The medical histories of lung cancer patients were reviewed retrospectively. In this study, patients with thoracic angiographic CT and ventilation/perfusion (V/Q) scintigraphy were included in the study. The eighth tumor-node-metastasis (TNM) classification (17) was used to stage the patients with lung cancer, who were included in the study. PE was diagnosed with a CT scan as a strongly delineated pulmonary arterial filling defect present in at least two consecutive image parts and situated centrally inside the vessel or with extreme angles at the walls' interface (18). A diagnosis of PE was also made based on the results of a ventilation/perfusion (V/Q) scan that met the high likelihood criterion (19).

Clinical Data

The data of the patients were examined retrospectively and age, gender, body mass index, smoking status, additional diseases, lung cancer type, date of diagnosis, stage, treatments, date of PE detection, lung cancer stage at the time of PE detection, complaints, additional risk factors, DVT status, laboratory parameters, time between lung cancer and PE, and survival were recorded. The group in which PE was detected by thorax angiographic CT and V/Q scintigraphy was defined as the PE group. The group without PE was defined as the non-PE group. The patients in these two groups were matched for age, gender, histological type and stage. In addition, the patients in the PE group were divided into two as those with active complaints and those detected incidentally. The non-incidental group was investigated for the suspicion of PE and detected to have PE, and the incidental group included the cases in which PE was detected in the thoracic angiographic CT and/or V/Q scintigraphy performed for any reason during the follow-up. Their survival was recorded. Survival was evaluated as overall survival which was from the diagnosis.

Statistical Analysis

SPSS 18 was used to analyze the results (Statistical Package for the Social Sciences, Chicago, Illinois). Normal distributions with continuous variables and subgroups were used for both the sample size and the normal distribution analyses. The Kaplan-Meier method was used to measure intergroup survival, and the Mann-Whitney U test (non-parametric) was employed to compare these variables. In the multivariable analysis, variables with p<0.05 in the univariable analysis were included. To find independent risk factors for PE, researchers used multivariable stepwise logistic regression analysis. The hazard ratio and confidence interval for the 95 percent were determined. The type 1 error coefficient was set at alpha =0.05 for all statistical methods. In cases where the p value was less than 0.05, the difference between the groups was evaluated as statistically significant.

Results

The clinical data of 235 lung cancer patients were analyzed. One hundred-nine patients were classified as having PE. One hundred 26 patients without a diagnosis of PE were determined with CT and scintigraphy. Table 1 lists the characteristics of the patients. Two groups of patients were formed as the PE group and non-PE group. The PE group included 109 patients (male/female: 91/18) and the non-PE group included 126 (male/female: 108/18) patients. The PE group's median age was 61 years (45-82 years), while the non-PE group's median age was 61 years (35-83 years). A comorbid disorder was observed in 61.5% of patients in the PE group and 57.1% of patients in the non-PE group. The most common comorbidity in the PE group was hypertension (25.7%), while the most common comorbidity in the non-PE group was chronic obstructive pulmonary disease (COPD) (23%) (Table 1). White blood cell (WBC), pH and CRP were significantly higher, while hemoglobin (Hb), pressure of partial oxygen (pO_2), pressure of partial carbon dioxide (pCO_2), albumin and protein were significantly lower in the PE group when the cases were hospitalized. In the PE group, adenocarcinoma (56.9%) was the most prevalent histological type, whereas squamous cell carcinoma (46%) was the most common histological type in the non-PE group. The majority of lung cancer cases in both the PE group and non-PE group were in stage 3 and 4. The rate of patients who received chemotherapy was higher in the non-PE group compared to the other group (p<0.05).

When the time between a patient's diagnosis of lung cancer and the onset of PE is divided into months, the number of those who developed PE in 0-6 months after diagnosis was 40 (36.6%), the number of those who developed PE in 6-12 months was 25 (22.9%), and the number of those who developed PE after 12 months was 24 (22%). In the other 20 (18.3%) patients, PE and lung cancer were diagnosed at

Table 1. Characteristics of patients in the PE group and non-PE group

	PE group (n=109)	Non-PE group (n=126)	p
Age	61 (45,82)	61 (35,83)	0.572
Gender (male/female)	91/18	108/18	0.771
Smoking history (+/-)	98/11	106/20	0.417
BMI	25.9±3.5	26±5.1	0.962
Comorbidities			
DM	13 (12%)	13 (10.3%)	0.854
Hypertension	28 (25.7%)	20 (15.9%)	0.089
Cardiovascular disease	14 (12.8%)	16 (12.7%)	0.973
COPD	24 (22%)	29 (23%)	0.979
Other	3 (2.8%)	10 (8%)	0.058
Histologic types			
Squamous cell carcinoma	30 (27.5%)	58 (46%)	0.052
Adenocarcinoma	62 (56.9%)	45 (35.7%)	
Small cell carcinoma	16 (13.7%)	20 (15.9%)	
Mesothelioma	1 (0.9%)	2 (1.6%)	
Large cell carcinoma	0	1 (0.8%)	
Stage			
I	12 (11%)	15 (11.9%)	0.433
II	14 (12.8%)	26 (20.6%)	
III	45 (41.3%)	46 (36.5%)	
IV	38 (34.9%)	39 (30.2%)	
Chemotherapy treatment	86 (78.9%)	116 (92.1%)	0.007
Radiotherapy treatment	62 (56. 9%)	77 (61.1%)	0.511
Operation	25 (22.9%)	21 (16.7%)	0.297
Laboratory data			
WBC ($x10^9$/L)	11.2±4.4	9.4±3.9	0.0001
Hemoglobin (mg/dL)	11.8±1.5	13.1±1.7	0.0001
Platelet ($x10^9$/L)	291±145	303±112	0.136
PO_2 (mmHg)	69.4±16.6	87.4±18.9	0.0001
PCO_2 (mmHg)	31,9±6	39.1±7.9	0.0001
pH	7.47±0.05	7.41±0.04	0.0001
Protein (g/dL)	6.6±0.7	7±0.6	0.0001
Albumin (g/dL)	3.4±0.5	3.8±0.5	0.0001
CRP (mg/dL)	7.3±6.6	5.2±5.5	0.005

PE: Pulmonary embolism, BMI: Body mass index, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, WBC: White blood cell, pO_2: Partial pressure of oxygen, pCO_2: Partial pressure of carbon dioxide, CRP: C-reactive protein

the same time. In other words, 60 (54.9%) of the cases were diagnosed with PE in the first 6 months (Figure 1). When these periods-were evaluated together, the average time from the first-diagnosis of lung cancer to the development of pulmonary thromboembolism was calculated as 8.1±5.8 months.

In the PE group, 80 patients applied to the hospital with symptoms and the most common symptoms were dyspnea (68%) and chest pain (27.5%). Twenty-nine (26.6%) patients were diagnosed with PE incidentally during follow-up period for lung cancer. When the lower extremity venous Doppler ultrasonography reports of the PE group were examined, DVT was detected in 38 (34.9%) of the patients.

When comparing the PE group with the non-PE group, leukocyte count and CRP levels were significantly higher, while protein, albumin, Hb, and hematocrit levels were significantly lower. Furthermore, the PE group's pO_2 and pCO_2 levels were found to be substantially lower than in the other group (p<0.05) (Table 1).

In the multivariable analysis performed for the occurrence of PE in lung cancer; albumin cut-off ⩽3.5, hemoglobin cut-off ⩽13.6 and protein cut-off ⩽7.1, WBC cut-off> 10 and CRP cut-off> 4 were found to increase the risk of PE (Figure 2). It has been found that hypoalbuminemia, hypoproteinemia, anemia, leukocytosis and increased CRP level significantly increase the risk of developing PE in lung cancer [odds ratio (OR) value of 2.33, 2.79, 5.14, 2.86 and 2.84, respectively] (Table 2).

When comparing the mean survival period after a lung cancer diagnosis, the PE group had a mean survival period of 20.1±1.6 (16.8-23.4) months, while the non-PE group had a mean survival period of 36.5±2.9 (30.6-42.3) months. The non-PE group had a slightly longer average survival period (p<0.001) (Figure 3).

The mean survival period of coincidentally detected cases was 11.8±9.9 months, while the mean survival period of cases with active complaints was calculated as 7.2±8.3 months, when compared to other PE patients who were randomly determined (p<0.05) (Figure 4).

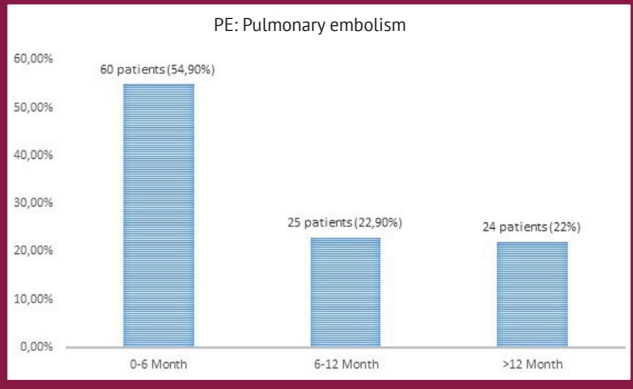

Figure 1. Time to PE diagnosis

Discussion

Patients with PE were found to have a slightly shorter life expectancy rate than those without PE. Adenocarcinoma was found to be the most common histological type in the

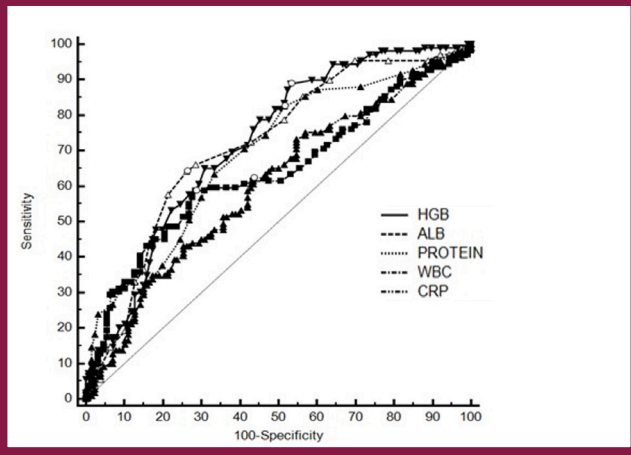

Figure 2. Risk factors for PE in patients with lung cancer by ROC analysis

PE: Pulmonary embolism, HGB: Hemoglobin, ALB: Albumin, WBC: White blood cell, CRP: C-reactive protein

Table 2. Risk factors for PE in patients with lung cancer by roc analysis

Factor	Cut-off	Sensitivity	Specifity	OR	AUC	p
Albumin (g/dL)	⩽3.5	64.2%	56.3%	2.33	0.71 (0.65-0.77)	<0.0001
Hb (mg/dL)	⩽13.6	88.9%	46.8%	5.14	0.72 (0.66-0.78)	<0.0001
Protein (g/dL)	⩽7.1	82.5%	48.4%	2.79	0.69 (0.62-0.75)	<0.0001
WBC (mg/dL)	>10	58.7%	71.4%	2.86	0.63 (0.57-0.69)	0.0002
CRP (mg/dL)	>4	62.3%	56.3%	2.84	0.60 (0.54-0.66)	0.0045

PE: Pulmonary embolism, OR: Odds ratio, AUC: Area under the curve, Hb: Hemoglobin, WBC: White blood cell, CRP: C-reactive protein

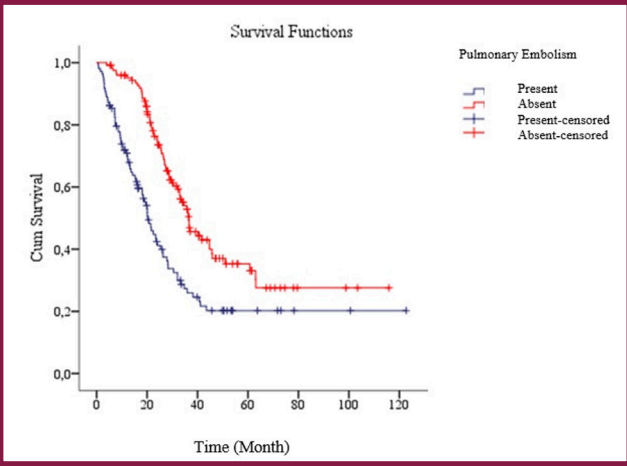

Figure 3. Comparison of life cycle between groups

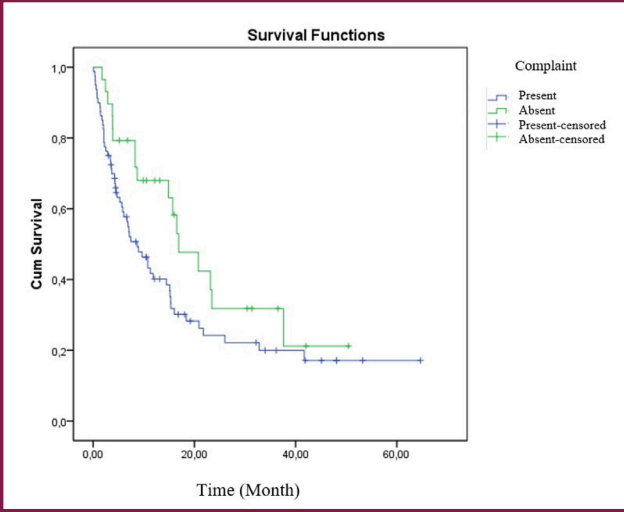

Figure 4. Survival curve of incidental and non-incidental PE patients

PE cases; PE mostly occurred within the first 6 months of cancer diagnosis; peripheral blood leukocyte and CRP values were higher; Hb, hematocrit, protein and albumin values were lower and this group consisted of patients who did not receive chemotherapy. PE was found to be 2.3 percent in this study.

Anemia, leukocytosis, increased CRP, hypoalbuminemia and hypoproteinemia were found to be risk factors for PE in lung cancer in this study.

In the study of Sorenson et al. (20), in cancer cases with VTE, the risk of death in a year was found to be three times higher than in cases without VTE. A cohort analysis comparing the survival of cancer cases with and without VTE showed that cases with VTE had a higher mortality rate (21). In another study, in which Ma and Wen (22) compared 30 cases with PE and 60 cases without PE, survival was shorter in the PE group.

Another research showed that PE was a weak prognostic factor in lung cancer cases, with cancer cases who had VTE leading to a lower life expectancy compared to those who did not (20). In our study, the mean survival time in the PE group was found to be 16 months shorter than in the non-PE group.

Anemia and leukocytosis in lung cancer patients have been studied as risk factors that may lead to the development of PE (10,22,23,24). In this study, it was found that when the hemoglobin was less than 13.6 mg/dL, the risk of PE increased by 5.1-fold and the leukocyte was more than >10x10μ/L, the risk of PE increased by 2.8-fold.

VTE, which involves DVT and PE, is thought to affect anywhere in 4% - 28% of cancer patients, depending on the type and stage of the tumor. Lung cancer is the sixth most common cause of PE, according to estimations (25). Despite this, there is little knowledge about the association between PE and lung cancer (8,11,26,27). In our study, the incidence of PE was found to be 2.3%, which is a lower rate in the incidence compared to the literature. One reason for the low incidence was because we considered it as the incidence of PE while they evaluated the incidence as VTE in the other studies. And the second one, there were probably many patients with asymptomatic VTE that were not detected and not all lung cancer patients remaining were screened for VTE.

Khorana et al. (28) found being a woman and over 65 years of age as risk factors for VTE, while Mehic et al. (29) found that the rate of VTE was three times more in men than in women. In their studies by Chew et al. (30), they did not show any difference between the two genders in terms of VTE. In our study, no significant difference was observed between the two groups in terms of age and sex.

PE appears to be associated with lung cancer not only by stage but also by histological type. Adenocarcinoma is thought to be the most thrombogenic tumor, making the cases more vulnerable to VTE (7,8). Blom et al. (7) found that the risk of VTE was 20 times greater in non-small cell lung cancer cases than the majority, and that there was an elevated risk of VTE in adenocarcinoma cases compared to cases with squamous cell cancer. In another study, 8,014 cases with lung cancer were evaluated, and adenocarcinoma was found to be the most common histological type associated with PE (13). In our study, the rate of adenocarcinoma was higher in the PE group.

As in many studies, in a retrospective research, it was stated that VTE was detected more frequently in patients

receiving chemotherapy for lung cancer than those who did not (31). However, in our research, the rate of receiving chemotherapy was significantly lower in the patients in the PE group. The reason for this is that chemotherapy was not applied due to the poor performance in our study.

In a large cohort research conducted by Blom et al. (32) in 2006, it was reported that the riskiest period for VTE was the onset period immediately after the diagnosis, and the risk later changed according to the presence of metastasis. In the study of Lee et al. (8) it is stated that PE can occur in a wide range from 3-4 months to 10 years after the diagnosis of lung cancer. There are also studies reporting that the incidence of VTE occurring in the first 6 months after lung cancer diagnosis is approximately 4 times higher than that occurring later (7,33). PE developed in more than half of our patients (54.9%) within the first 6 months in accordance with the literature.

Due to the advances in multi-detector CT technique and its increasing use in routine staging and monitoring of cancer patients, the frequency of detection of incidental PE has increased (34). In our study, where 4,842 lung cancer patients were scanned for 5 years, 29 out of 109 cases were detected incidentally. In a review of lung cancer cases conducted by Shinagare et al. (15) no substantial difference in survival was found between the two groups. In another retrospective research conducted in 2014, patients with asymptomatic PE were reported to have a better prognosis than the other group (31). In this report, when the mean survival time of the cases was evaluated, it was seen that there was a statistically significantly better life span in the incidental group compared to the other group. It was thought that this situation was as a result of the timely initiation of anticoagulant therapy in cases with incidental PE.

Study Limitations

This study has some limitations. Firstly, it was a retrospective research and it did not include all the cases diagnosed with lung cancer that had a VTE event. The clinical information of some patients was not available and some patients were followed up in another hospital after lung cancer diagnosis.

Conclusion

Accompanying PE in lung cancer shortens the survival. Because the PE occurred more in patients with adenocarcinoma histology, leukocytosis, elevated CRP, anemia, and nutritional disorders, PE should be considered in these patients.

Ethics

Ethics Committee Approval: The study was designed retrospectively and approval was obtained from the Local Ethics Committee of the University of Health Sciences Turkey, Dr. Suat Seren Chest Diseases and Surgery Training and Research Hospital (no: 49109414-806.02.02).

Informed Consent: The study was designed retrospectively.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.A., P.Ç., N.K., S.D., D.T., Concept: A.A., P.Ç., N.K., G.P., G.K., S.D., D.T., Design: A.A., P.Ç., G.P., G.K., D.T., Data Collection or Processing: A.A., N.K., S.D., Analysis or Interpretation: A.A., P.Ç., N.K., G.P., G.K., S.D., D.T., Literature Search: A.A., G.P., G.K., D.T., Writing: A.A., P.Ç., G.P., G.K., D.T.

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

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

REFERENCES

1. Heit JA, O'Fallon WM, Petterson TM, Lohse CM, Silverstein MD, Mohr DN, et al. Relative impact of risk factors for deep vein thrombosis and pulmonary embolism: a population based study. Arch Intern Med. 2002;162:1245-1248. [CrossRef]
2. Falanga A, Marchetti M, Vignoli A. Coagulation and cancer: Biological and clinical aspects. J Thromb Haemost. 2013;11:223-233. [CrossRef]
3. Khorana AA, Francis CW, Culakova E, Lyman GH. Risk factors for chemotherapy associated venous thromboembolism in a prospective observational study. Cancer. 2005;104:2822-2829. [CrossRef]
4. Abdol RNB, Jones G, Bhandari M, Berndt MC, Metharom P. Cancer-associated thrombosis: an overview of mechanisms, risk factors, and treatment. Cancers (Basel). 2018;10:380. [CrossRef]
5. Astruc N, Ianotto JC, Metges JP, Lacut K, Delluc A. External validation of the modified Ottawa score for risk stratification of recurrent cancer-associated thrombosis. Eur J Intern Med. 2016;36:e11-e12. [CrossRef]
6. Ay C, Unal UK. Epidemiology and risk factors for venous thromboembolism in lung cancer. Curr Opin Oncol. 2016;28:145-149. [CrossRef]
7. Blom JW, Osanto S, Rosendaal FR. The risk of a venous thrombotic event in lung cancer patients: higher risk for adenocarcinoma than squamous cell carcinoma. J Thromb Haemost. 2004;2:1760-1765. [CrossRef]
8. Lee JW, Cha SI, Jung CY, Choi WI, Jeon KN, Yoo SS, et al. Clinical course of pulmonary embolism in lung cancer patients. Respiration. 2009;78:42-48. [CrossRef]
9. Xu X, Yang H, Qiao L, Tan Z, Jin J, Jin Y, et al. Clinical characteristic and outcomes of lung cancer patients with venous thromboembolism. Zhonghua Yi Xue Za Zhi. 2014;94:2045-2049. [CrossRef]
10. Sun W, Wang H, Wen Z, Ma N, Xiao Y, Ma L, et al. Clinical characteristics of lung cancer complicated with pulmonary embolism. Zhonghua Jie He Hu Xi Za Zhi. 2016;39:198-202.
11. Chuang YM, Yu CJ. Clinical characteristics and outcomes of lung cancer with pulmonary embolism. Oncology. 2009;77:100-106. [CrossRef]
12. Nichols L, Saunders R, Knollmann FD. Causes of death of patients with lung cancer. Arch Pathol Lab Med. 2012;136:1552-1557. [CrossRef]

13. Sun JM, Kim TS, Lee J, Park YH, Ahn JS, Kim H, et al. Unsuspected pulmonary emboli in lung cancer patients: the impact on survival and the significance of anticoagulation therapy. Lung Cancer. 2010;69:330-336. [CrossRef]
14. Silverstein MD, Heit JA, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ, et al. Trends in the incidence of deep vein thrombosis and pulmonary embolism: a 25 year population based study. Arch Intern Med 1998;158:585-593. [CrossRef]
15. Shinagare AB, Okajima Y, Oxnard GR, Dipiro PJ, Johnson BE, Hatabu H, et al. Unsuspected pulmonary embolism in lung cancer patients: comparison of clinical characteristics and outcome with suspected pulmonary embolism. Lung Cancer. 2012;78:161-166. [CrossRef]
16. Tiseo M, Bersanelli M, Barili MP, Bartolotti M, De Luca G, Gelsomino F, et al. Asymptomatic pulmonary embolism in lung cancer: Prevalence and analysis of clinical and radiological characteristics in 141 outpatients. Tumori. 2012;98:594-600. [CrossRef]
17. Goldstraw P, Chansky K, Crowley J, Rami Porta R, Asamura H, Eberhardt WEE, et al. The IASLC lung cancer staging project: Proposals for revision of the TNM stage groupings in the forthcoming (eighth) edition of the TNM Classification for lung cancer. J Thorac Oncol. 2016;11:39-51. [CrossRef]
18. Gladish GW, Choe DH, Marom EM, Sabloff BS, Broemeling LD, Munden RF. Incidental pulmonary emboli in oncology patients: prevalence, CT evaluation, and natural history. Radiology. 2006;240:246-255. [CrossRef]
19. The PIOPED Investigators. Value of the ventilation/ perfusion scan in acute pulmonary embolism. Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). JAMA. 1990;263:2753-2759. [CrossRef]
20. Sorensen HT, Mellemkjær L, Olsen JH, Baron JA. Prognosis of Cancers Associated with Venous Thromboembolism. N Engl J Med. 2000;343:1846-1850. [CrossRef]
21. Chew HK, Wun T, Harvey D, Zhou H, White RH. Incidence of venous thromboembolism and its effect on survival among patients with common cancers. Arch Intern Med. 2006;166:458-464. [CrossRef]
22. Ma L, Wen Z. Risk factors and prognosis of pulmonary embolism in patients with lung cancer. Medicine (Baltimore) 2017;96:e6638. doi: 10.1097/MD.0000000000006638. [CrossRef]
23. Li N, Wang Y. Clinical features in 23 lung cancer patients complicated with pulmonary thromboembolism. Zhongguo Fei Ai Za Zhi. 2014;17:254-259. [CrossRef]
24. Zhang Y, Yang Y, Chen W, Guo L, Liang L, Zhai Z, et al. Prevalence and associations of VTE in patients with newly diagnosed lung cancer. Chest. 2014;146:650-658. [CrossRef]
25. Shinagare AB, Guo M, Hatabu H, Krajewski KM, Andriole K, Van Den Abbeele AD, et al. Incidence of pulmonary embolism in oncologic outpatients at a tertiary cancer center. Cancer. 2011;117:3860-3866. [CrossRef]
26. Sakuragi T, Sakao Y, Furukawa K, Rikitake K, Ohtsubo S, Okazaki Y, et al. Successful management of acute pulmonary embolism after surgery for lung cancer. Eur J Cardio thoracic Surg. 2003;24:580-587. [CrossRef]
27. Shao L, Wang ZH, Zuo JY. Clinical analysis of 23 lung cancer patients accompanied by pulmonary embolism. Ai Zheng. 2009;28:416-419. [CrossRef]
28. Khorana AA, Francis CW, Culakova E, Kuderer NM, Lyman GH. Frequency, risk factors, and trends for venous thromboembolism among hospitalized cancer patients. Cancer. 2007;110:2339-2346. [CrossRef]
29. Mehic B, Zutic H, Mehic A. Profile of venous thromboembolism at the patients with non small cell lung carcinoma. HealthMED. 2009;3:3-7. [CrossRef]
30. Chew HK, Davies AM, Wun T, Harvey D, Zhou H, White RH. The incidence of venous thromboembolism among patients with primary lung cancer. J Thromb Haemost. 2008;6:601-608. [CrossRef]
31. Alexander M, Kirsa S, Wolfe R, MacManus M, Ball D, Solomon B, et al. Thromboembolism in lung cancer An area of urgent unmet need. Lung Cancer. 2014;84:275-280. [CrossRef]
32. Blom JW, Vanderschoot JPM, Oostindiër MJ, Osanto S, van der Meer FJM, Rosendaal FR. Incidence of venous thrombosis in a large cohort of 66,329 cancer patients: results of a record linkage study. J Thromb Haemost. 2006;4:529-535. [CrossRef]
33. Blom JW, Doggen CJM, Osanto S, Rosendaal FR. Malignancies, prothrombotic mutations, and the risk of venous thrombosis. J Am Med Assoc. 2005;293:715-722. [CrossRef]
34. Gosselin M V, Rubin GD, Leung AN, Huang J, Rizk NW. Unsuspected pulmonary embolism: prospective detection on routine helical CT scans. Radiology. 1998;208:209-215. [CrossRef]

ORIGINAL ARTICLE

DOI: 10.4274/hamidiyemedj.galenos.2021.07379

Hamidiye Med J 2021;2(2):57-63

Is There Any Difference in the Predictive Findings for VUR in Different Age Groups? Evaluation of VCUG and USG Examinations in 539 Children with Febrile Urinary Tract Infection

Farklı Yaş Gruplarında VUR için Prediktif Bulgularda Fark Var Mıdır? Ateşli İdrar Yolu Enfeksiyonu Olan 539 Çocuğun USG ve VCUG Muayenelerinin Değerlendirilmesi

Doğuş Güney[1], Gökhan Demirtaş[2], Süleyman Arif Bostancı[1], Hüseyin Tuğrul Tiryaki[2]

[1]*Ankara City Hospital, Children's Hospital, Clinic of Pediatric Surgery, Ankara, Turkey*

[2]*Ankara City Hospital, Children's Hospital, Clinic of Pediatric Urology, Ankara, Turkey*

ABSTRACT

Background: The clinical presentation and the course of vesicoureteral reflux (VUR) vary according to age. All guidelines for the evaluation of urinary tract infections (UTIs) focus on infants under 2 years of age. To determine which factors might predict the presence of VUR among different age groups, we retrospectively reviewed the factors including patient characteristics and renal bladder ultrasonography (RBUS) and findings obtained from voiding cystourethrography (VCUG) examinations in a children's hospital.

Materials and Methods: RBUS and VCUG reports of 539 patients performed for febrile UTI in 2016 were reviewed. The associations between RBUS findings and abnormalities found in VCUG findings were investigated. The predictive findings of RBUS for VUR were evaluated among three age groups (0-2 y, 2-5y, and >5 years).

Results: In total, 368 girls (68.3%) and 171 boys (31.7%) with a mean age of 6.29+4.18 years were evaluated. RBUS results were abnormal in 78.5% of patients. VUR was reported in 284 (52.7%) patients who underwent a VCUG. A significant result in the multivariate analysis of patients at 0-2 years of age was that RBUS renal parenchymal thinning was a predictor of VUR. Patients over 5 years of age were found to have a higher risk of VUR when patients had moderate to severe hydronephrosis accompanying parenchymal thinning.

Conclusion: In children younger than 2 years, thinned parenchymal thickness helped predict the findings for VUR. Predicting the presence of VUR made no significant difference among the RBUS findings in children at the age of 2-5 years. Thinned parenchymal and moderate to severe hydronephrosis were significantly correlated with the presence of reflux for children older than 5 years.

Keywords: Vesicoureteral reflux, renal bladder ultrasonography, voiding cystourethrography

ÖZ

Amaç: Vezikoüreteral reflünün (VUR) klinik prezentasyonu ve seyri yaşa göre değişim göstermektedir. İdrar yolu enfeksiyonlarının (İYE) değerlendirilmesi için yapılmış tüm kılavuzlar 2 yaş altındaki çocuklar üzerinde yoğunlaşmaktadır. Değişik yaş grupları arasında VUR düşündürecek faktörleri tespit etmek amacıyla bir çocuk hastanesindeki hasta özellikleri, üriner ultrason (RBUS) ve voiding sistoürerografi (VCUG) bulguları dahil olmak üzere retrospektif olarak değerlendirildi.

Gereç ve Yöntemler: 2016'da ateşli İYE nedeniyle 539 hastaya yapılmış olan RBUS ve VCUG raporları değerlendirildi. RBUS bulguları ve anormal VCUG bulguları arasındaki ilişki araştırıldı. RBUS'de görülen, VUR düşündürecek bulgular üç yaş grubu arasında değerlendirildi (0-2 yaş, 2-5 yaş, ve >5 yaş).

Bulgular: Ortalama yaşı 6,29+4,18 yıl olan toplamda 386 kız ve 171 erkek değerlendirildi. Sıfır-iki yaş arası hastalarda yapılan çok değişkenli analizde, RBUS'de böbrekte parankimal incelme görülmesi VUR açısından anlamlı olarak sonuçlandı. Orta-ileri derece hidronefroza eşlik eden parankimal incelmesi olan 5 yaş ve üzeri hastalarda VUR riskinin daha yüksek olduğu görüldü.

Sonuç: Parankim kalınlığının incelmesi 2 yaş altındaki hastalarda VUR düşünülmesinde yardımcı olmuştur. İki-beş yaş arası çocuklarda VUR düşünülmesi RBUS bulguları arasında anlamlı değişiklik oluşturmamıştır. Beş yaştan büyük çocuklarda VUR varlığı ile incelmiş parankim ve orta-ileri derece hidronefroz varlığı arasında anlamlı ilişki olduğu görülmüştür.

Anahtar Kelimeler: Vezikoüreteral reflü, üriner sistem ultrason, voiding sistoüretrografi

Address for Correspondence: Hüseyin Tuğrul Tiryaki, Ankara City Hospital, Children's Hospital, Clinic of Pediatric Urology, Ankara, Turkey
Phone: +90 532 372 80 15 E-mail: httiryaki@hotmail.com **ORCID ID:** orcid.org/0000-0002-9544-1137
Received: 19.02.2021 **Accepted:** 20.04.2021

Introduction

Vesicoureteral reflux (VUR) is a common condition in children. The incidence of VUR is 0.4-1.8% in children and 25-40% of those children have acute pyelonephritis (1,2,3,4). Voiding cystourethrography (VCUG), the most common fluoroscopic study method used for children, is the gold standard for the diagnosis of VUR (5,6). VCUG is an invasive procedure that carries the risk of radiation exposure and iatrogenic urinary tract infections (UTI), and requires urethral catheterization, which can be stressful for children and their families (7,8,9). Therefore, the indication must be evaluated very carefully.

There is no consensus on imaging studies to be performed on a child with febrile UTI in different guidelines (10). The European Society of Pediatric Urology (ESPU) guidelines recommended renal and bladder ultrasonography (RBUS) in all children with febrile UTIs (11). VCUG or dimercaptosuccinic acid (DMSA) scanning (the bottom-up or the top-down approach) is advised in all patients with febrile UTI and aged <1 year. The American Academy of Pediatrics (AAP) guidelines (12) recommend children between the ages of 2 and 24 months who present an initial febrile UTI should have an RBUS. Only if there are abnormalities on the RBUS or after a second febrile UTI, patients should be considered for a VCUG.

The clinical presentation and course of VUR vary by age. A biphasic age distribution occurs when children are diagnosed with VUR based on their presentation. The first group is recognized following an investigation of antenatal hydronephrosis, predominantly in males. The second group is diagnosed later, after a UTI, and is predominantly female (13,14). In guidelines, when and how to investigate the presence of VUR in children with a febrile UTI is defined depending on the age and gender of the patient (10,11,12). However, there are no studies evaluating whether diagnostic RBUS and VCUG investigations differ according to age group in the literature. The aim of this study was to investigate whether US and VCUG examinations of different age groups differed in revealing the presence of VUR.

Material and Methods

Permission from the Ethics Committee (number 2018-128) was obtained from the Ankara City Hospital, Child Health and Diseases, Hematology and Oncology Training and Research Hospital. We retrospectively evaluated the medical records of 539 children who underwent VCUG and RBUS investigation for febrile UTI between January 1, 2016, and December 31, 2016. Consent form was obtained from the patients' families. The VCUG and RBUS reports were received from hospital records. VCUG and RBUS that were performed for other indications such as antenatal hydronephrosis, neurogenic bladder etc. were not included.

The cases in all age groups with febrile UTI in our hospital were investigated with RBUS. We included children with confirmed febrile UTIs, with positive urinalysis and culture results. The cases with recurrent UTIs and first febrile UTI cases with RBUS findings including hydronephrosis, ureter dilation, increased parenchymal echogenicity, and decreased parenchymal thickness underwent VCUG evaluation. Children with a single UTI did not undergo VCUG if they had a normal RBUS.

The UTI was considered certain if there was any growth of a single uropathogen in a suprapubic aspiration or if there was the growth of a single uropathogen in 100,000 colony-forming units per milliliter (CFU/mL) in one or more samples of clean-catch urine or bag specimen with urinalysis results consistent with UTI (positive leukocyte esterase test, nitrite test, or microscopic analysis positive for leukocytes or bacteria). The term "febrile" was determined to be 38.0 °C. The criteria for "recurrent UTI" were fulfilled if the child had another culture-confirmed UTI between the first febrile UTI and the VCUG.

The RBUS was performed at the time of diagnosis of UTI, while VCUG was performed 4 weeks after the infection resolved.

The RBUS findings included hydronephrosis, ureter dilation, parenchymal echogenicity, and parenchymal thickness. In this study, echogenicity of kidney was classified as either normal or increased. Dilation was graded based on the report provided by the radiologist staff on duty; grades expressed the Society for Fetal Urology scale (15). Ureter morphology was categorized as "dilated" or "not dilated" without diameter data.

The diagnosis and grade of VUR was identified through VCUG on the basis of international reflux classification (16). Children with grade 1 to 3 reflux were stratified as having low-grade reflux, while those with grade 4 to 5 reflux as having high-grade reflux.

Patients were divided into three groups according to ages (0-2 years; 2-5 years; >5 years). Predictive findings detected in RBUS for VCUG indication were compared in different age groups.

Statistical Analysis

Descriptive continuous variables were presented as mean, standard deviation, and minimum and maximum values, and categorical values were defined as percentages. Continuous variables from the two groups were compared using the Mann-Whitney U test, and groups of more than two were compared using the Kruskal-Wallis variance

analysis. Nominal variables of two or more groups were compared using either the chi-square test or the Fisher's Exact test. RBUS performance on VUR diagnosis was tested using diagnostic accuracy criterion (sensitivity, specificity, positive predictive value, and negative predictive value). We analyzed the relationship between ultrasonography and cystourethrography using generalized estimating equations to take into account that the two kidneys from the same patient could not be considered independent. This method is seen as an extension of the general linear models developed for the dependent data. In this method, general linear models are adapted to the marginal distributions of repetitive dependent variables. Statistical analyses were performed using SPSS, version 12.0 of the program (Chicago Inc., 2006), and $p<0.05$ was accepted as significant.

Results

In our children hospital, 671 VCUG examinations were performed in 2016. The indications for VCUG were febrile UTI (n=539, 80.3%), neurogenic conditions (n=50, 7.5%), antenatal hydronephrosis (n=36, 5.4%), voiding disorders (n=33, 4.9%), and others (trauma-anotomic abnormalities) (n=13, 1.9%).

Patient Characteristics

Only cases with febrile UTI were included in the study. There were 368 females (68.3%) and 171 males (31.7%), totally 539 cases with a mean age of 6.29±4.18 years (range: 0.08-18 years). Thirty-six of the cases also have a diagnosis of antenatal hydronephrosis in addition to UTI. group 1 consisted of 124 infants aged <2 years (23%); group 2 consisted of 122 children aged 2 to 5 years (22.6%); and group 3 consisted of 293 children older than 5 years (54.4%). The ratio of female patients was significantly higher in the group of children older than 5 years compared to the other age groups (74.1% in the group of children older than 5 years old, 60.6% in the group of children aged 2-5 years, and 62.1% in the group of children younger than 2 years, $p<0.001$). Demographics and imaging results are shown in Table 1.

Abnormalities such as hydronephrosis, ureter dilation, parenchymal dilation, parenchymal thinning, or increased echogenicity were noted in 423 (78.5%) cases on RBUS. One hundred sixteen (21.5%) of patients had entirely normal RBUS findings. Pathological bladder findings were detected in 167 patients (30.9%). VCUG was performed to patients who had abnormal findings in the RBUS in the first febrile urinary tract infection, or who had normal RBUS and recurrent febrile urinary tract. VCUG findings were pathologic in 284 (52.7%) patients and normal in 255 (47.3%) patients.

Table 1. Patients demographics and imaging findings in 539 cases

Gender male female total 0-2 years 47 (37.9%) 77 (62.1%) 124; 23% 2-5 years 48 (39.4%) 74 (60.6%) 122; 22.6% > 5years 76 (25.9%) 217 (74.1%) 293; 54.4% Total 171 (31.7%) 368 (68.3%) 539; 100%		
Findings of ultrasonography investigation		
Ultrasonography findings	**n**	**%**
Normal (recurrent fUTI)	116	21.5
Abnormal (first fUTI)	423	78.5
Total	539	100
VCUG findings	**n**	**%**
VUR		
No	255	47.3
Yes	284	52.7
Laterization of VUR		
Right	84	29.6
Left	89	31.3
Bilateral	111	39.1
Total	284	100
VUR grades		
Grade 1	34	11.9
Grade 2	60	21.1
Grade 3	97	34.2
Grade 4	63	22.2
Grade 5	30	10.6

fUTI: Febrile urinary tract infection, VCUG: Voiding cystourethrogram, VUR: Vesicoureteral reflux, p-value <0.05

Factors That Indicate the Existence of VUR

The sensitivity and specificity of the RBUS to identify VUR were 80.2% and 24.4%, respectively. False positivity [95% confidence interval (CI)] was 54.5%, and the false negative rate (95% CI) was 52.4%. Univariate analysis results comparing the non-refluxing group with the refluxing group are listed in Table 2. Age and gender had no significant effect on VUR. The refluxing group had significantly higher numbers of patients with hyronephrosis, thinned parenchyma, and increased echogenicity.

The results of univariate and multivariate analyses, designed with a generalized linear model distinguishing the non-refluxing group from the refluxing group for all three age groups, are shown in Tables 3 and 4. In children younger than 2 years, a significant variable which predicted the presence of reflux was thinned parenchyma. No significant difference in predicting the presence of reflux was found among the RBUS findings in children aged 2-5 years. Thinned parenchyma and moderate to severe hydronephrosis were significantly correlated with the presence of reflux for the children older than 5 years.

Table 2. Statistical analysis results between the non- refluxing and refluxing groups

Variables	VUR (-)		VUR (+)		
	N, (M/F)	%	N, (M/F)	%	p
Age groups					
Younger than 2 years	59 (M26/F33)	46.7	65 (M21/F44)	53.3	0.654
2-5 years	50 (M14/F36)	34.6	72 (M34/F38)	65.4	
Older than 5 years	147 (M31/F116)	29.4	156 (M45/F111)	70.6	
Hydronephrosis					
No	97	34.5	184	65.5	**0.044**
Mild	66	41.7	92	58.3	
Moderate-severe	21	21	79	79	
Parenchyma					
Normal	145	39.8	219	60.2	**0.000**
Thinned	39	22.3	136	77.7	
Ureter					
Not dilated	154	35.1	284	64.9	0.235
Dilated	30	29.7	71	70.3	
Echogenicity					
Normal	145	36.1	257	63.9	**0.004**
Increased	39	28.5	98	71.5	

VUR: Vesicoureteral reflux, p-value <0.05, N: Number of patient, M: Male, F: Female

Table 3. Generalized estimating equations analysis results of age groups for the prediction of VUR

p		<2 years		2-5 years		>5 years	
		OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	
Gender	Female Male	0.053	1.756 (0.992- 3.109)	0.415	0.789 (0.447- 1.394)	0.215	0.779 (0.524- 1.157)
Hydronephrosis	No Mild Moderate- severe	0.067	0.552 (0.292- 1.043)	0.661	0.824 (0.346- 1.960)	**0.008**	0.488 (0.287- 0.831)
Parenchymal thickness	Normal Thinned	**0.003**	0.481 (0.296- 0.784)	0.237	0.700 (0.387- 1.265)	**0.004**	0.583 (0.403- 0.844)
Ureter	Not dilated Dilated	0.155	0.603 (0.300- 1.212)	0.181	0.557 (0.236- 1.313)	0.795	0.924 (0.509- 1.677)
Parenchymal Echogenicity	Normal Increased	0.355	0.549 (0.154- 1.958)	0.111	0.381 (0.116- 1.247)	0.375	0.663 (0.268- 1.643)

VUR: Vesicoureteral reflux, p-value <0.05, OR: Odds ratio, CI: Confidence interval

In cases with increased renal echogenicity, it was observed that the likelihood of VUR increased significantly. In patients under 2 years of age, the RBUS examination revealed that those who had renal parenchymal thinning were twice as likely to have VUR. In patients over 5 years of age, the risk of VUR was 2.27 times higher in patients with moderate and severe hydronephrosis than in patients without hydronephrosis. In patients with parenchymal thinning, the risk of VUR was 2.7 times higher than those without thinning.

Table 4. Predictors of VUR based on RBUS for age groups

Age groups	Parameter	p	Odds ratio	95% CI
0-2	Parenchymal thickness, normal	0.029	0.498	0.266- 0.931
Over 5 years	Parenchymal thickness, normal	0.029	0.63	0.415- 0.954
	No hyrdonephrosis	0.048	0.557	0.312- 0.994

VUR: Vesicoureteral reflux, p-value <0.05, CI: Confidence interval

It was noted that the presence of antenatal diagnosis (p=0,041) and the increase in bladder wall thickness (p=0.032) in RBUS were significant findings for VUR. It was observed that antenatal diagnosis alone increased the probability of VUR 2.2 times, and elevated bladder wall thickness increased the probability of VUR 1.51 times.

The incidence of high grade (grade 4-5) VUR was significantly correlated with the presence of hydronephrosis [Odds ratio (OR)=1.44, 95% CI (1.04-2.0), p=0.027], decreased parenchymal thinning [OR=1.487,95% CI (1.14-1.92), p=0.003], ureteral dilatation [OR=1.58, 95% CI (1.07-2.339, p=0.02], and an increased grade of parenchymal echogenicity [OR=1.89,95% CI (1.10-3.24), p=0.02].

No statistically significant difference was found between the patients who had a first febrile urinary tract infection and those who had recurrent febrile ITUs in terms of age, gender and the presence of VUR (Table 5).

Discussion

There is a controversy on the precise indications for VCUG after a first febrile UTI. Children under two years of age were carefully evaluated for UTIs, especially since their symptoms were not specific and the chances of renal damage were high. All guidelines provide recommendations on how to evaluate UTIs, especially in children under 2 years of age (10). The AAP (12) guidelines recommend VCUG after abnormal renal ultrasound or 2 febrile urinary tract infections. The ESPU guidelines (11) advise VCUG or DMSA for all children with UTI. With new advancement in fluoroscopy, the radiation exposure with variable rate pulsatile fluoroscopy is reported 10 times less than that of the traditional continuous fluoroscopic units and 5 times less than that of a DMSA scan (17). Because anatomical details can be seen better and VUR grading can be done in our hospital, VCUG evaluation is preferred to DMSA after RBUS investigation. The study presents data to determine which factors might predict the presence of VUR among three age groups (0-2 y, 2-5 y, and >5 years). In our study, according to the evaluations, observing thinned parenchyma in children under the age of 2 years and over 5 years was predictive of VUR. RBUS examination is not a predictor in patients aged 2-5 years; therefore, the evaluation of patients aged 2-5 years must be performed more carefully.

In the evaluation of VUR in children, significant attention has been given to the assessment of hydronephrosis shown with RBUS and cortical scars shown with renal scintigraphy. There is no information about predictive findings for VUR on USG for different age groups in the literature. Although patients with normal RBUS may have a high-grade VUR, a significant correlation between the severity of hydronephrosis and reflux grade has been shown before (18). In our study, the frequency of VUR increased significantly in patients with moderate to severe hydronephrosis. However, little attention has been given to renal parenchymal thickness or echogenicity detected through RBUS. Renal parenchymal thinning was another predictive factor for the risk of VUR in patients. In the children older than five years, who were investigated due to a UTI, because of the late presentation of reflux nephropathy, the presence of hydronephrosis and parenchymal thinning detected on ultrasonography significantly increased the risk of VUR. Although increased renal parenchymal echogenicity is a common renal ultrasonography finding in patients with recurrent UTI (19) and first febrile UTI (20), echogenicity of the kidney is not noted as a predictive factor for VUR in children in other studies. Our findings on echogenicity of the kidney is contributed as a new scientific finding on this issue.

The predictors of high-grade VUR detected on RBUS included dilated ureter, moderate to severe hydronephrosis, parenchymal thinning, and increased echogenicity.

Table 5. Number of patients per group, age, sex, the absence or presence of VUR and first febrile UTI or recurrent febrile UTI

VUR +		Male		Female		Total
		VUR +	VUR -	VUR +	VUR -	
First febrile UTI	0-2 years	18 45%	22 55%	36 59%	25 41%	101 23.9%
	2-5 years	29 69%	13 31%	28 50%	28 50%	98 23.2%
	<5 years	36 57%	27 43%	79 49%	82 51%	224 52.9%
	Total	83 57%	62 43%	143 51%	135 49%	423 79%
Recurrent febrile UTI urinary infection	0-2 years	3 42%	4 58%	6 37.5%	10 62.5%	23 19.8%
	2-5 years	5 83%	1 17%	9 50%	9 50%	24 20.7%
	<5 years	7 53.8%	6 46.2%	29 51.7%	27 48.3%	69 59.5%
	Total	15 57%	11 43%	44 48%	46 52%	116 21%

UTI: Urinary tract infection, VUR: vesicoureteral reflux

Considering all of the variables, pathologic findings detected by RBUS seem to increase the possibility of encountering higher grade VURs in VCUG, and increased renal echogenicity suggests the highest diagnostic accuracy for high-grade VUR with odds ratio of 1.9, followed by dilated ureter, parenchymal thinning, and presence of hydronephrosis. Here, we present the first study that evaluates renal parenchymal thickness and renal echogenicity detected on RBUS as predictors of VUR in patients who experienced VCUG. Parenchymal thinning was a predictive finding for children under 2 years of age as well as in children over 5 years of age. Especially in children older than 5 years, if the parenchymal thinning was detected using ultrasonography, the probability of reflux should be considered.

In this study, no significant difference is detected when comparing gender and presence of VUR in all age groups between the patients who had a first febrile urinary tract infection and the patients who had recurrent febrile urinary tract infections.

Study Limitations

The major limitation of our study is its retrospective nature. Also, the data are from a single referral children's hospital. We also included VCUG examinations performed only in one year. Finally, we did not evaluate renal scintigraphy findings, although this would provide more information about renal functions and scars. The strength of our work can be defined as increased statistical power according to the large number of participants.

Conclusions

In conclusion, abnormal RBUS findings, such as hydronephrosis, parenchymal thinning, and increased echogenicity, have a higher probability of VUR, and these findings can be affected by the age of the child patient. In children younger than 2 years, thinned renal parenchyme predicted findings for VUR. There was no significant difference in predicting the presence of VUR among the RBUS findings in children at 2-5 years of age. Thinned parenchymal and moderate to severe hydronephrosis were significantly correlated with the presence of reflux for the children older than 5 years. High-grade VUR was 1.9 times higher in renal echogenicity with dilated ureter, parenchymal thinning, and presence of hydronephrosis. The results of our study show that all ultrasonographic findings need to be taken into account when evaluating a child with the suspicion of reflux to avoid unnecessarily performing invasive VCUGs.

Ethics

Ethics Committee Approval: Permission from the Ethics Committee (number 2018-128) was obtained from the Ankara City Hospital, Child Health and Diseases, Hematology and Oncology Training and Research Hospital.

Informed Consent: Consent form was obtained from the patients' families.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.T.T., D.G., S.A.B., G.D., Concept: D.G., H.T.T., Design: H.T.T., G.D., Data Collection or Processing: G.D., Analysis or Interpretation: S.A.B., Literature Search: D.G., G.D., Writing: D.G., H.T.T.

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

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

References

1. Gleeson FV, Gordon I. Imaging in urinary tract infection. Arch Dis Child. 1991;66:1282-1283. [Crossref]
2. Smellie JM, Normand IC. Clinical features and signifi¬cance of urinary tract infection in children. Proc R Soc Med. 1966;59:415-416. [Crossref]
3. Savage DC, Wilson MI, McHardy M, Dewar DA, Fee WM. Covert bacteriuria of childhood. A clinical and epidemiological study. Arch Dis Child. 1973;48:8-20. [Crossref]
4. Wein AJ, Schoenberg HW. A review of 402 girls with recurrent urinary tract infection. J Urol. 1972;107:329-331. [Crossref]
5. Domina JG, Sanchez R, Meesa IR, Christodoulou E. Evaluation of pediatric VCUG at an academic children's hospital: Is the radiographic scout image necessary? Pediatr Radiol. 2015;45:855-861. [Crossref]
6. Schneider K, Krüger-Stollfuss I, Ernst G Kohn MM. Paediatric fluoroscopy: a survey of children's hospitals in Europe. Part I. Staffing, frequency of fluoroscopic procedures and investigation technique. Pediatr Radiol. 2001;31:238-246. [Crossref]
7. Rachmiel M, Aladjem M, Starinsky R, Strauss S, Villa Y, Goldman M. Symptomatic urinary tract infections following voiding cystourethrography. Pediatr Nephrol. 2005;20:1449-1452. [Crossref]
8. Lachenmyer LL, Anderson JJ, Clayton DB, Thomas JC, Pope JC, Adams MC, et al. Analysis of an intervention to reduce parental anxiety prior to voiding cystourethrogram. J Pediatr Urol. 2013;9:1223-1228. [Crossref]
9. Perisinakis K, Raissaki M, Damilakis J, Stratakis J, Neratzoulakis J, Gourtsoyiannis N. Fluoroscopy-controlled voiding cystourethrography in infants and children: Are the radiation risk strivial? Eur Radiol. 2006;16:846-851. [Crossref]
10. Okarska-Napierała M, Wasilewska A, Kuchar E. Urinary tract infection in children: Diagnosis, treatment, imaging Comparison of current guidelines. J Pediatr Urol. 2017;13:567-573. [Crossref]
11. Stein R, Dogan HS, Hoebeke P, Kocvara R, Nijman RJ, Radmayr C, et al. European Association of Urology and European Society for Pediatric Urology. Urinary tract infections in children: EAU/ESPU guidelines. Eur Urol. 2015;67:546-558. [Crossref]
12. Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management, Roberts KB. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. Pediatrics. 2011;128:595-610. [Crossref]
13. Vallee J, Vallee M, Greenfield S, Wan J, Springate J. Contemporary incidence of morbidity related to vesicoureteral reflux. Urology. 1999;53:812-815. [Crossref]

14. Leslie B, Moore K, Salle JL, Khoury AE, Cook A, Braga LHP, et al. Outcome of antibiotic prophylaxis discontinuation in patients with persistent vesicoureteral reflux initially presenting with febrile urinary tract infection: time to event analysis. J Urol. 2010;184:1093-1098. [Crossref]
15. Fernbach SK, Maizels M, Conway JJ. Ultrasound grading of hydronephrosis: introduction to the system used by the Society for Fetal Urology. Pediatr Radiol. 1993;23:478-480. [Crossref]
16. Lebowitz RL, Olbing H, Parkkulainen KV, Smellie JM, Tamminen-Möbius TE. International system of radiographic grading of vesicoureteric reflux. International Reflux Study in Children. Pediatr Radiol. 1985;15:105-109. [Crossref]
17. Ward VL, Strauss KJ, Barnewolt CE, Zurakowski D, Venkatakrishnan V, Frederic H, et al. Pediatric radiation exposure and effective dose reduction during voiding cystourethrography. Radiology. 2008:249:1002-1009. [Crossref]
18. Kovanlikaya A, Kazam J, Dunning A, Poppas D, Johnson V, Medina C, et al. The role of ultrasonography in predicting vesicoureteral reflux. Urology. 2014;84:1205-1210. [Crossref]
19. Doğan G, İpek H. Comparison of Primary and Recurrent Urinary Tract Infections in Children Cureus 2020;17:e7019. doi: 10.7759/cureus.7019. [Crossref]
20. Nickavar A, Safaeian B, Abhari MB. Radiologic and clinical evaluation of children with first febrile urinary tract infection Int J Pediatr Adolesc Med. 2015;2:24-28. [Crossref]

ORIGINAL ARTICLE

DOI: 10.4274/hamidiyemedj.galenos.2021.02411

Hamidiye Med J 2021;2(2):64-69

Does the Cannulated Screw Tension Band Improve Quadriceps Muscle Strength, Atrophy, Implant Irritation and Functional Results in Patella Fractures Compared to the Kirschner Wire Tension Band?

Kanüllü Vida Gergi Bandı, Kirschner Teli Gergi Bandına Göre Patella Kırıklarında Kuadriseps Kas Gücünü, Atrofiyi, İmplant İritasyonunu ve Fonksiyonel Sonuçları İyileştirir Mi?

Cafer Özgür Hançerli[1], Necati Doğan[2], Gürkan Çalışkan[1], İdris Aykut[1], Deniz Gulabi[1], Cemil Ertürk[1]

[1]*University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital, Clinic of Orthopaedics and Traumatology, İstanbul, Turkey*

[2]*University of Health Sciences Turkey, İstanbul Başakşehir Çam and Sakura City Hospital, Clinic of Orthopaedics and Traumatology, İstanbul, Turkey*

ABSTRACT

Background: We aimed to evaluate the effects of the cannulated screw tension band and Kirschner (K) wire tension band methods on quadriceps muscle strength and atrophy, implant irritation and functional results in the treatment of patella fractures.

Materials and Methods: In this study, 70 patients with a diagnosis of patella fracture, who were operated in our clinic between January 2015 and May 2019, were retrospectively evaluated. Patients were operated in two separate groups: in group 1, 21 patients were fitted with a cannulated screw tension band, and in group 2, 49 patients were treated by the K wire tension band method. The Lysholm score was used for clinical evaluation. The loss of extensor muscle strength in the patients was measured with an analogue dynamometer.

Results: There was no difference in the effect of two different techniques, age, gender, and fracture type on the duration of fracture union in the surgical treatment of patella fractures ($p>0.05$). Clinically, there was no difference in Lysholm score between the two groups ($p>0.05$). Knee extensor muscle strength decreased in both groups compared to the healthy side ($p<0.05$), and the two groups were similar ($p>0.05$). We found that the thigh diameter was decreased compared to the healthy side in patients who underwent surgery for patella fracture ($p=0.001$). There was no difference in thigh diameter difference between the two groups ($p>0.05$).

Conclusion: With the two different techniques, quadriceps muscle strength, atrophy and clinical results were similar. In the K-wire tension band method, more implant removal was required due to irritation.

Keywords: Cannulated screw tension band, Kirschner wire tension band, muscle strength loss, patella fracture

ÖZ

Amaç: Patella kırıklarının tedavisinde kanüllü vida gergi bandı ve Kirschner (K) teli gergi bandı yöntemlerinin kuadriseps kas gücü ve atrofisi, implant iritasyonu ve fonksiyonel sonuçlar üzerindeki etkilerini değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Bu çalışmada Ocak 2015-Mayıs 2019 tarihleri arasında kliniğimizde patella kırığı tanısı alan 70 hasta retrospektif olarak değerlendirildi. Hastalar iki ayrı grupta ameliyat edildi: Grup 1'de 21 hastaya kanüllü vida gergi bandı uygulandı ve grup 2'de 49 hasta K tel gergi bandı yöntemi ile tedavi edildi. Lysholm skoru klinik değerlendirme için kullanıldı. Hastalarda ekstansör kas gücü kaybı analog dinamometre ile ölçüldü.

Bulgular: Patella kırıklarının cerrahi tedavisinde iki farklı tekniğin, yaş, cinsiyet ve kırık tipinin kırığın kaynama süresi üzerine etkisinde fark yoktu ($p>0,05$). Klinik olarak Lysholm skorunda iki grup arasında fark yoktu ($p>0,05$). Her iki grupta diz ekstansör kas gücü sağlıklı tarafa göre azaldı ($p<0,05$) ve iki grup benzerdi ($p>0,05$). Patella kırığı nedeniyle ameliyat edilen hastalarda uyluk çapının sağlıklı tarafa göre azaldığını saptadık ($p=0,001$). İki grup arasında uyluk çapı açısından fark yoktu ($p>0,05$).

Address for Correspondence: Cafer Özgür Hançerli, University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital, Clinic of Orthopaedics and Traumatology, İstanbul, Turkey

Phone: +905335773159 E-mail: cozgurhancerli@yahoo.com.tr **ORCID ID:** orcid.org/0000-0002-4518-1998

Received: 10.03.2021 **Accepted:** 12.07.2021

ÖZ

Sonuç: Kuadriseps kas gücü, atrofi ve klinik sonuçlar iki farklı teknikle benzerdi. K-teli gergi bandı yönteminde tahriş nedeniyle daha fazla implant çıkarılması gerekiyordu.

Anahtar Kelimeler: Kanüllü vida gergi band, Kirschner tel gergi bandı, kas gücü kaybı, patella kırığı

Introduction

Patella fractures are among the fractures, whose frequency is increasing with the increase of traffic accidents and occupational accidents, and they constitute approximately 1% of all fractures (1). The main task of the patella is to contribute to knee extension by increasing the strength of the quadriceps muscle (2). The most common type of fracture is a transverse fracture, which is indirectly traumatic. The accepted indications for surgery are the absence of active knee extension and more than 2 mm of displacement between the parts and stepping inside the joint (1,3). Inadequate treatment after patella fractures leads to decreased knee extension strength, loss of range of motion in the knee joint, and patellafemoral and tibia femoral arthritis (4).

Different methods used in the surgical treatment of patella fractures continue to be interesting (5). Many methods have been defined in the treatment, and predictable union rates have been achieved with these treatment methods. The most classical method in treatment is the tension band method, which is applied together with Kirschner (K) wires, which converts the tensile forces into compression forces in the fracture line (6). Although tension band with K-wires is the most commonly used method in the surgical treatment of patella fractures, problems such as implant irritation (7,8), loss of quadriceps muscle strength (7,8,9) and quadriceps atrophy (10) have been reported to occur due to K-wires. Therefore, a solution was sought with tension bands passing through the cannulated screw as an alternative to the tension band made with K-wires (9,11).

Current studies show that there is less skin and quadriceps muscle trauma with tension bands passing through the cannulated screw (12). On the other hand, studies comparing these two methods in terms of quadriceps muscle weakness, quadriceps atrophy and clinical results are quite limited (13). For this reason, in this study, we wanted to retrospectively compare the results of cases with the cannulated screw tension band method and the K-wire tension band method.

Material and Methods

Patients admitted to our hospital with a diagnosis of displaced patella fracture between January 2015 and May 2019 were evaluated retrospectively. Approval for this study was obtained from the University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital, Ethics Committee for this study (KAEK/2018.12.78). Exclusion criteria were as follows: patients whose records could not be accessed, those with a history of septic arthritis, osteomyelitis or poliomyelitis in their lower extremities, or a history of concurrent or previous lower extremity fractures, patients who had undergone more than one operation, who did not accept surgical treatment or who were operated in another hospital, patients who did not accept surgery and patients who had fracture type AO, type A or type B, old fractures, and open or pathological fractures.

Of the 70 patients included in the study, 21 patients (group 1) were treated by applying an anterior 8-shaped tension band (9,12) with self-compressing fully threaded headless screws and cerclage wires passing through screw holes (Figure 1 a, b, c, d), and 49 patients (group 2) were treated with 2 K-wires (5,6) and the 8-shaped anterior

Figure 1. Cannulated screw tension band 1a. Before surgery A.P. radiography, 1b. Preoperative lateral radiography, 1c. Postoperative A.P. radiography, 1d. Postoperative lateral radiography

tension band method (5,6) applied around the K-wires (Figure 2 a, b, c, d).

Figure 2. K-wire tension band 2a. Before surgery A.P. radiography, 2b. Preoperative lateral radiography, 2c. Postoperative A.P. radiography, 2d. Postoperative lateral radiography

A long leg plaster splint was applied to the patients in both groups after surgery for approximately two weeks. In the second week, the splints were removed, joint movements were initiated by allowing 90 degrees of flexion with the angle-adjusted knee brace. Physical therapy was applied to the patients in various centers in the sixth postoperative week.

At the final check, the range of motion of the joint and the intact side and the operated side thigh diameters of all patients were measured in the standing and lying positions from the mid-thigh, and quadriceps muscle strength was measured on both sides (13). Quadriceps muscle strength was measured by a specialist physiotherapist using an analogue dynamometer, by asking the patients to perform forced extension while the knee was flexed at 90 degrees. Before the measurement, the patients were given warm-up exercises for 10 minutes and the measurement was explained. Three separate measurements were made to both lower extremities and the average of these measurements was taken. The difference of quadriceps strength on the operated side compared to the healthy side was expressed as percentage decrease by calculating with the formula (healthy side muscle strength - operated side muscle strength)/healthy side muscle strength. Patients with implant irritation were removed, and their final control was clinically evaluated after removal.

Short form-36 (SF-36), Knee Injury and Osteoarthritis Outcome score (KOOS) and Lysholm scoring systems are frequently used to determine the health status of patients with patella fractures (5). With the SF-36, results are affected by environmental factors, as it evaluates the physical function of the patient as well as the emotional state and social functions. KOOS, on the other hand, is a test for knee osteoarthritis. This is why we chose to use the Lysholm test, which only includes questions about knee problem (11). The Lysholm knee score is a knee scoring scale that asks whether patients have disruption while walking, whether they use support, whether there is a locking in the knee, knee joint stability, the character of the knee pain, swelling, and whether they have problems while climbing stairs or crouching.

The most reliable method for measuring muscle strength is the biodex dynamometer (14). However, measuring muscle strength with this method is expensive and requires special training, whereas measurement of quadriceps muscle strength with an analogue dynamometer is an easy and inexpensive method. The reliability of this method was shown in the study (14). Measurements made with an analogue dynamometer are generally used after knee ligament injuries and the reconstruction of these injuries. The disadvantage of the method is the difficulty of patient compliance. We also used an analogue dynamometer to measure quadriceps muscle strength in our patients.

Statistical Analysis

Statistical Package for the Social Sciences 22 was used for statistical analysis. The data obtained by counting were expressed as a percentage and the data obtained by measurement as a ratio and mean ± standard deviation. Evaluation of whether the data obtained from the measurements were suitable for normal distribution was performed with the Kolmogorow-Smirnov test. The t-test or Mann-Whitney U test was used for the comparison of groups. Categorical data were analyzed using the chi-square tests. A p value of less than 0.05 was considered statistically significant.

Results

The demographic data of the patients are shown in Table 1. The two groups were similar in terms of gender, age, side, type of fracture and duration of union (p>0.05).

Table 1. Demographic data of the patients

	Grup I (n=21)	Grup II (n=49)	p
Gender (male/female)	15/6	40/9	**0.08**
Fracture side (right/left)	4/17	18/31	0.577
Age	41.3	39.3	0.302
Dominant side (right/left)	17/4	41/8	0.593
Fracture type (C1/C2/C3)	10/7/4	30/13/6	**0.399**
Fracture union(day)	51.7	58.5	0.950
Follow-up time (month)	35.7	29.9	**0.451**

When a comparison was made with the healthy side in the quadriceps muscle strength measurement performed with an analogue dynamometer, there was a 33.5% decrease in group 1 and a 34.4% decrease in group 2. The difference was significant in terms of reduction in muscle strength ($p<0.05$). When all patients were evaluated, a 34.1±21.9% (0-80) loss of strength on the fracture side was found. There was no significant difference in muscle strength loss in patients with screws and K-wires ($p>0.05$). There was an average of 1.5 cm (group 1: 1.66 cm, group 2: 1.44 cm) difference in thigh diameter in the operated patients, but there was no significant difference between the two groups ($p>0.05$). Implants had to be removed in 22 patients due to irritation. The implants of one (4.7%) patient in group 1 and 21 (42.8%) patients in group 2 were removed. There was a significant difference between the two groups ($p<0.001$). Implant removal procedures were performed after an average of 9.2 months (3-21 months). There was no statistically significant difference in the measurement of quadriceps muscle strength in group 2 patients with implants compared to patients without implants ($p<0.05$) Table 2.

The Lysholm knee score was 89.95±4.4 (81-99) in group 1 and 91.1±6.6 (78-100) in group 2. There was no significant difference between the groups ($p>0.05$).

The range of motion of the joint was evaluated as "complete" in all patients, except for a limitation of 30 degrees of flexion in one patient to whom a tension band was applied. No implant-related infection was encountered in the patients. Heterotopic ossification (two patients in the lower pole of the patella and one patient in the upper pole) was detected in the last follow-up of three of our patients.

Table 2. Clinical results of both techniques

	Grup I (n=21)	Grup II (n=49)	p
Loss of muscle strength (%)	33.5	34.4	**0.944**
The decrease in thigh diameter (cm)	1.66	1.44	0.631
Lysholm score	89.95	91.1	0.617
Implant removal	1	21	0.001

Discussion

The main results of this study were, first, that there was no difference between the two groups in terms of quadriceps muscle strength and thigh diameter, but in both groups, the operated side quadriceps strength and thigh diameter were significantly weakened compared to the non-operated side. Second, implant irritation was more in the tension band with K-wire. Therefore, the need for implant removal was greater with the tension band with K-wire. Third, both groups were similar in clinical and radiological healing. Finally, the tension band with K-wire was similar in quadriceps muscle strength in the subgroups with and without implants.

Many treatment methods are used in the surgical treatment of patella fractures. Although the K-wire tension band is the preferred method, methods such as cannula screw, arthroscopy-assisted cannula screw, cannula screw tension band, screw-plate and non-absorbable suture osteosynthesis are used. Partial or total patellectomy can be applied in fractures where fixation is not possible. However, the search for the best treatment method continues. The most important reason for the search for treatment methods is that the K-wire tension band causes implant irritation. The cannula screw and tension band method, on the other hand, has become a preferred method with less implant irritation and less need for implant removal. K-wire tension band and/or circumferential sutures continue to be the current treatment method for multi-part fractures and fractures where the broken pieces are too small to apply screws (AO C3-1, C3-2, C3-3).

A decrease in extensor muscle strength after patella fracture is a frequently encountered situation (13). This decrease in extensor muscle strength may be the inevitable consequence of an injured extensor mechanism. However, patients' avoidance of the injured extremity may also be the cause of weakness. In the measurements we made, we found that approximately 80% of the patients had a decrease in muscle strength. Results of extensor muscle strength measurement with an analogue dynamometer, which we applied an average of 31.6 months after surgery, were significantly lower, regardless of the complaints of the patients (13,15). Quadriceps atrophy is a common condition after patella fracture (10). The decrease in thigh diameter on the operated side was significant in the measurements we made in the patients, but the decrease in thigh diameter was not different between the two groups.

Although the search for the best surgical method to be applied in patella fractures continues, the K-wire tension band method is the most common method (16). The most common complication of K-wire tension band application is anterior knee pain due to implant irritation. Although symptomatic

implant removal is not seen as a serious complication, it causes an unplanned second operation and increases costs (12). In the literature, the proportion of patients requiring implant removal due to anterior knee pain is around 36.8%. In our series, this rate was 42.8%. In addition, the absence of a significant difference in the decrease in quadriceps muscle strength of patients with and without implants, in patients to whom we applied a tension band with K-wires, suggests that the loss of muscle strength may be associated with the injury to the extensor mechanism due to trauma rather than the method used (13).

Common complications after patella fracture surgery are implant irritation, joint stiffness, loss of reduction, osteoarthrosis, infection, and non-union. Joint stiffness is the most common complication in patella fractures, regardless of the treatment method. Immobilization lasting longer than six weeks results in joint stiffness (17). In our patients, there was no difference between the two methods in terms of joint stiffness. It has been reported that 0-20% loss of fixation occurs in patella fractures treated with surgery (17,18). In our series, a patient in whom we applied a tension band K-wire developed fixation loss in the first month, and then revision was performed with the screw tension band method. Osteoarthrosis may occur as a result of joint damage at the time of injury. It has been shown radiographically that there is a greater incidence of patellofemoral arthrosis when compared to the contralateral extremity years after fracture healing (19). In our cases, patellofemoral osteoarthrosis was present in three of our patients to whom K-wire tension bands were applied. The reason for the low rate of osteoarthrosis may be the short follow-up period. Infection can be seen in 3-30% of patellar fractures treated with surgery (17,18). In our series, we did not have any patients who developed infection. Nonunion after surgical treatment of patella fractures is a rare complication. In our series, all patients had adequate union. In a meta-analysis report, it was emphasized that there was no difference in the surgical success rate, operation time, fracture healing time, and the number of infections between cannulated screw and K-wire tension tape in the treatment of patellar fracture, but cannulated screw tension tape was superior to K wire tension tape in reducing the incidence of complications (5).

In recent years, many biomechanical studies have been performed in the treatment of patellar fractures, both in cadavers and in artificial bone models (20,21,22). In these studies, the cannulated screw tension band method has been accepted as the most powerful biomechanical fixation method (23). Since these studies were carried out under laboratory conditions, their effects on fracture healing are controversial. On the other hand, similar results have been reported in terms of clinical results related to both methods (12). The results were similar in the Lysholm knee scoring of group 1 and group 2 patients at the final check. This finding is compatible with the literature (5). On the other hand, although fewer patients were treated with the cannulated screw in our study than with K-wire, the union times were similar. Likewise, we obtained clinically similar results in both groups (12).

Study Limitations

This study had some limitations. First, it was a single-center and retrospective study. Second, the patient group in which the cannulated screw tension band was applied was significantly smaller than the patient group in which the K-wire tension band was applied.

In this study, a comparison was made between the cannulated screw and K-wire tension band methods in patellar fractures regarding clinical and radiological improvement and quadriceps muscle strength. Although a greater need for implant removal was determined in the K-wire tension band method due to irritation, quadriceps muscle strength and atrophy were similar in the subgroups with and without implants, although they were weaker compared to the healthy leg.

Conclusion

We think that it would be more meaningful to focus on physical therapy protocols to increase muscle strength after treatment in patella fractures rather than on the choice of treatment method.

Ethics

Ethics Committee Approval: Approval was obtained from the University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital, Ethics Committee for this study (KAEK/2018.12.78).

Informed Consent: Patients admitted to our hospital with a diagnosis of displaced patella fracture between January 2015 and May 2019 were evaluated retrospectively.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: C.Ö.H., N.D., G.Ç., D.G., C.E., Concept: C.Ö.H., N.D., C.E., Design: C.Ö.H., N.D., G.Ç., İ.A., D.G., C.E., Data Collection or Processing: C.Ö.H., N.D., G.Ç., D.G., C.E., Analysis or Interpretation: C.Ö.H., N.D., Literature Search: C.Ö.H., N.D., C.E., Writing: C.Ö.H., N.D., G.Ç., İ.A., D.G., C.E.

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

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

References

1. Boström A. Fracture of the patella. A study of 422 patellar fractures. Acta Orthop Scand Suppl. 1972;143:1-80. [Crossref]
2. Muralidhar BM, Madhusudan H, Mohan M. Study of patellar fractures treated by modified tension band wiring–a prospective study. Int J Orthop Sci. 2017;3:864-871. [Crossref]
3. Melvin JS, Mehta S. Patellar fractures in adults. J Am Acad Orthop Surg. 2011;19:198-207. [Crossref]
4. Vedel JO, Vistrup S, Larsen P, Elsoe R. Altered long-term health-related quality of life in patients following patella fractures: a long-term follow-up study of 49 patients. Eur J Trauma Emerg Surg. 2018;44:707-716. [Crossref]
5. Zhang Y, Xu Z, Zhong W, Liu F, Tang J. Efficacy of K-wire tension band fixation compared with other alternatives for patella fractures: a meta-analysis. J Orthop Surg Res. 2018;13:226. [Crossref]
6. Blum L, Hake M. Orif patella fracture with a tension band construct. J Orthop Trauma. 2017;31(Suppl 3):S8-S9. [Crossref]
7. Tian Y, Zhou F, Ji H, Zhang Z, Guo Y. Cannulated screw and cable are superior to modified tension band in the treatment of transverse patella fractures. Clin Orthop Relat Res. 2011;469:3429-3435. [Crossref]
8. Kim MB, Lee YH, Shin WC, Baek GH. Locked tension band wiring using ring pins for patellar fractures: a method of minimising implant migration. Arch Orthop Trauma Surg. 2014;134:1537-1543. [Crossref]
9. Malik M, Halwai MA. Open reduction and internal fixation of patellar fractures with tension band wiring through cannulated screws. J Knee Surg. 2014;27:377-382. [Crossref]
10. Vatansever M, Kuyurtay F, Sadioğlu M. Surgical management of patellar fractures. Acta Orthop Traumatol Turc. 1996;30:290-293. [Crossref]
11. Lin T, Liu J, Xiao B, Fu D, Yang S. Comparison of the outcomes of cannulated screws vs. modified tension band wiring fixation techniques in the management of mildly displaced patellar fractures. BMC Musculoskelet Disord. 2015;16:282. [Crossref]
12. Hoshino CM, Tran W, Tiberi JV, Black MH, Li BH, Gold SM, et al. Complications following tension-band fixation of patellar fractures with cannulated screws compared with Kirschner wires. J Bone Joint Surg Am. 2013;95:653-659. [Crossref]
13. LeBrun CT, Langford JR, Sagi HC. Functional outcomes after operatively treated patella fractures. J Orthop Trauma. 2012;26:422-426. [Crossref]
14. Almeida GPL, Albano TR, Melo AKP. Hand-held dynamometer identifies asymmetries in torque of the quadriceps muscle after anterior cruciate ligament reconstruction. Knee Surg Sports Traumatol Arthrosc. 2019;27:2494-2501. [Crossref]
15. Carpenter JE, Kasman RA, Patel N, Lee ML, Goldstein SA. Biomechanical evaluation of current patella fracture fixation techniques. J Orthop Trauma. 1997;11:351-356. [Crossref]
16. Henrichsen JL, Wilhem SK, Siljander MP, Kalma JJ, Karadsheh MS. Treatment of patella fractures. Orthopedics. 2018;41:e747-e755. doi: 10.3928/01477447-20181010-08. [Crossref]
17. Böstman O, Kiviluoto O, Nirhamo J. Comminuted displaced fractures of the patella. Injury. 1981;13:196-202. [Crossref]
18. Smith ST, Cramer KE, Karges DE, Watson JT, Moed BR. Early complications in the operative treatment of patella fractures. J Orthop Trauma. 1997;11:183-187. [Crossref]
19. Sorensen KH. The late prognosis after fracture of the patella. Acta Orthop Scand. 1964;34:198-212. [Crossref]
20. Baydar ML, Atay T, Gürbüz Ö, Baykal BY, Burç H, Kırdemir V, et al. Compressive screwing of transverse patella fractures provides better resistance to traction than tension band. Eur J Orthop Surg Traumatol. 2011;21:105-110. [Crossref]
21. Wurm S, Augat P, Bühren V. Biomechanical assessment of locked plating for the fixation of patella fractures. J Orthop Trauma. 2015;29:e305-e308. [Crossref]
22. Martin JM, Applin DT, McGrady LM, Wang M, Schmeling GJ. Biomechanical comparison of tension band fixation of patella transverse fracture: headless screws versus headed screws. J Orthop Trauma. 2019;33:e240-e245. [Crossref]
23. Burvant JG, Thomas KA, Alexander R, Harris MB. Evaluation of methods of internal fixation of transverse patella fractures: a biomechanical study. J Orthop Trauma. 1994;8:147-153. [Crossref]

ORIGINAL ARTICLE

DOI: 10.4274/hamidiyemedj.galenos.2021.96268

Hamidiye Med J 2021;2(2):70-76

The Relationship Between Myocardial Performance Index and Renal Resistive Index in Resistant Hypertension

Dirençli Hipertansiyonda Miyokard Performans İndeksi ile Renal Rezistif İndeks Arasındaki İlişki

Cafer Panç[1], İsmail Gürbak[1], Arda Güler[1], Çağdaş Topel[2], Mehmet Ertürk[1]

[1]*University of Health Sciences Turkey, Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital, Clinic of Cardiology, İstanbul, Turkey*

[2]*University of Health Sciences Turkey, Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital, Clinic of Radiology, İstanbul, Turkey*

ABSTRACT

Background: Renal resistive index (RRI), an index measured in renal arteries, is related to cardiac structural changes. Myocardial performance index (MPI), a valuable method to show subclinical myocardial dysfunction, contributes to risk assessment due to detecting the early stages of diastolic and systolic dysfunctions. We aimed to examine the relationship between RRI and MPI in resistant hypertension (RHT).

Materials and Methods: One hundred and twenty-six patients who were admitted to our outpatient clinic were enrolled in this single-center, cross-sectional prospective study. All patients underwent echocardiography and renal Doppler ultrasound. Two groups were created according to the presence of subclinical left ventricle (LV) dysfunction: patients with lower MPI group (MPI<0.5, n=50) and patients with higher MPI group (MPI≥0.5, n=76).

Results: Higher MPI group was associated with higher LV end-diastolic diameter, LV mass index, left atrium diameter, LV end-systolic diameter, posterior wall diameter, E velocity, interventricular septum diameter, and RRI. In multivariable logistic regression analysis, age [odds ratio (OR): 1.070, 95% confidence interval (CI): 1.016-1.126, p=0.010], left atrium diameter (OR: 1.111, 95% CI: 1.027-1.202, p=0.008) and RRI (OR: 6.404, 95% CI: 2.767-19.899, p<0.025) were associated with subclinical LV dysfunction. RRI showed a good positive correlation with MPI (r=0.527, p<0.001).

Conclusion: Our study suggests that increased RRI is associated with subclinical LV dysfunction assessed by increased MPI in patients with RHT.

Keywords: Resistant hypertension, myocardial performance index, renal resistive index

ÖZ

Amaç: Doppler ultrason ile değerlendirilen renal rezistif indeks (RRI), hipertansif hastalarda yapısal kardiyak değişiklikler ile ilişkilidir. Doku Doppler ekokardiyografi ile elde edilen miyokardiyal performans indeksi (MPI) sistolik ve diyastolik fonksiyonları aynı anda gösterir. Çalışmanın amacı dirençli hipertansiyonu (RHT) olan hastalarda RRI ve MPI arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntemler: Bu prospektif çalışma, dirençli hipertansiyonu olan 126 poliklinik hastasını (%59,5 kadın, ortalama yaş 58±9 yıl) kapsamaktadır. Tüm hastalara ekokardiyografi ve renal Doppler ultrason yapıldı. Hastalar subklinik sol ventrikül (SV) disfonksiyonunun varlığına göre iki gruba ayrıldı: Düşük MPI grubu (MPI<0,5, n=50) ve yüksek MPI grubu (MPI≥0,5, n=76).

Bulgular: Yüksek MPI grubu, daha yüksek SV diyastolik çapı, SV sistolik çapı, interventriküler septum çapı, arka duvar çapı, SV kitle indeksi, sol atriyum çapı, E hızı ve RRI ile ilişkili olarak bulundu. Çok değişkenli lojistik regresyon analizinde, yaş [olasılık oranı (OR): 1.070, %95 güven aralığı (CI): 1.016-1.126, p=0,010], sol atrium çapı (OR: 1.111, %95 CI: 1.027-1.202, p=0,008) ve RRI (OR: 6.404, %95 CI: 2.767-19.899, p<0,025) subklinik SV disfonksiyonu ile ilişkili olarak bulundu. Korelasyon analizinde, RRI, MPI ile iyi bir pozitif korelasyon gösterdi (r=0,527, p<0,001).

Sonuç: Çalışmamız, artmış RRI'nin RHT'li hastalarda artmış MPI ile değerlendirilen subklinik LV disfonksiyonu ile ilişkili olduğunu düşündürmektedir.

Anahtar Kelimeler: Dirençli hipertansiyon, miyokardiyal performans indeksi, renal rezistif indeks

Address for Correspondence: Cafer Panç, University of Health Sciences Turkey, Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital, Clinic of Cardiology, İstanbul, Turkey

Phone: +90 505 718 40 86 E-mail: caferpanc@gmail.com **ORCID ID:** orcid.org/0000-0003-3692-1170 **Received:** 22.03.2021 **Accepted:** 18.06.2021

Introduction

Resistant hypertension (RHT) is the inability to keep blood pressure under control despite using three or more drugs (one of which is a diuretic) at the maximum tolerable dose (1). Observational studies show that the prevalence of RHT is around 10-20% in the hypertensive population (2,3). In RHT, constant high blood pressure values increase cardiovascular risk considerably. In extensive cross-sectional studies, RHT was strongly associated with more cardiovascular events than the other hypertensive patients (4,5). Although many factors cause RHT, renal diseases are among the most common reasons.

Renal resistive index (RRI) is an index measured in renal arteries and particularly useful in demonstrating the microvascular and macrovascular interaction between the arterial system and the kidney. High resistive values (>0.7) are associated with more adverse cardiovascular events and renal failure progression (6). It reflects central arterial hemodynamics and left ventricle systolic and diastolic function (7,8). Increased arterial stiffness in RHT leads to increased renal arterial circulation pressure and renal vascular resistance (9). Pulse wave velocity (PWV) was positively correlated with RRI, and PWV was an independent predictor of RRI in a cross-sectional study in hypertensive patients (10). Moreover, arterial stiffness was detected as a cause of subclinical myocardial dysfunction in another study (11). Myocardial performance index (MPI), a valuable method to show subclinical myocardial dysfunction, makes a significant contribution to risk assessment due to detecting the early stages of diastolic and systolic dysfunctions (12).

The relationship between the MPI and RRI is still unknown in RHT patients. We aimed to examine the relationship between RRI and MPI in RHT.

Material and Methods

One hundred and twenty-six patients who were admitted to our outpatient clinic were enrolled in this single-center, cross-sectional prospective study. We collected patients' medical history, prescribed drugs, and active smoking status in the initial examination. Echocardiography and renal Doppler ultrasound were performed within one week of the initial examination.

We excluded patients with chronic kidney disease (eGFR <30 mL/min/1.73 m^2), renal artery stenosis, nephrectomy, coronary disease, severe valvular disease, atrial fibrillation, pulmonary hypertension, heart failure (left ventricular EF <55%), acute or chronic infectious or inflammatory disease, malignancy, pregnancy, and chronic liver disease. We conducted the study in accordance with the Helsinki Declaration. We took a Mehmet Akif Ersoy Cardiovascular Surgery Training and Research Hospital local ethics committee approval for the study and written informed consent from all the participants.

Patients whose blood pressure remained above 140/90 despite using at least three antihypertensive drugs, one of which was a diuretic, or who used >4 antihypertensive drug classes in the last month, regardless of blood pressure, were accepted as RHT.

Echocardiography

All participants underwent echocardiography by a single experienced operator who did not know the patients' clinical status. According to the current guidelines, the examination was performed using a Philips Epiq 7C echocardiography device (13). We recorded tissue Doppler images at a speed of 100 mm/s from the lateral mitral annulus. Isovolumetric contraction time (IVCT) was measured from the time from the end of the A' wave to the beginning of the S' wave. Isovolumetric relaxation time (IVRT) was measured from the time from the end of the S' wave and the beginning of the E' wave. Ejection time (ET) was found by subtracting IVCT and IVRT from total non-filling time (Figure 1). The MPI value was calculated with the formula below.

Myocardial performance index = (isovolumetric contraction time + isovolumetric relaxation time)/ejection time (14).

We considered MPI≥0.5 as abnormal and defined it as subclinical LV dysfunction (15,16,17).

Renal Ultrasound and Doppler Examination

All participants underwent ultrasonographic examination using Doppler sonography by a single experienced operator

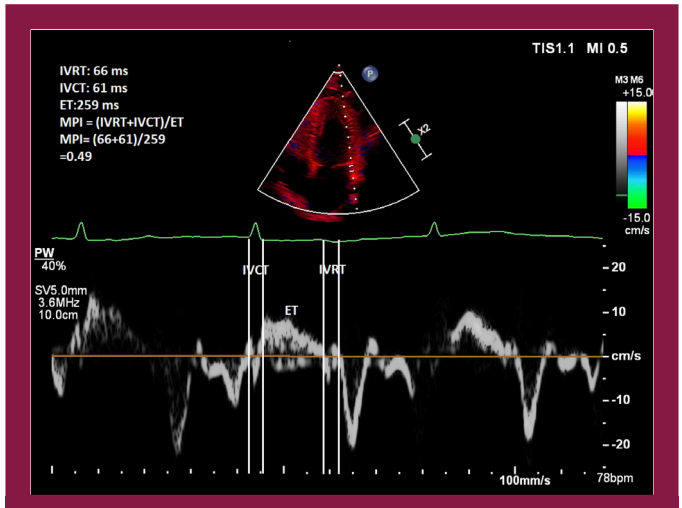

Figure 1: Computation of myocardial performance index
MPI: Myocardial performance index, IVRT: Isovolumetric relaxation time, IVCT: Isovolumetric contraction time, ET: Ejection time

who did not know the patients' clinical data. Firstly, we assessed both kidneys for any structural pathology. After that, Doppler parameters, including peak systolic velocity (Vmax) and minimum diastolic velocity (Vmin) from interlobar arteries of both kidneys, were obtained. We calculated RRI by the following formula: Renal resistive index = (Vmax-Vmin)/Vmax. RRIs were calculated by taking the average of both kidneys.

Statistical Analyses

We did statistical analyses with SPSS (version 21.0 IBM, USA). We considered $p<0.05$ as statistically significant. We detected the distribution of the variables with the Kolmogorov-Smirnov test. We presented quantitative variables with normal distribution as mean ± standard deviation and non-normal distribution as median (25^{th} to 75^{th} percentile). We expressed categorical variables as numbers (%). The Student's t-test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables were used to compare quantitative variables. The Pearson chi-square and Fisher Exact tests were performed for categorical variables. We performed logistic regression analysis to detect the independent predictors of subclinical myocardial dysfunction. Variables with $p<0.10$ in univariable analysis were included for the multivariable logistic regression analysis with backward selection model. Correlation between MPI and RRI was assessed using the Pearson correlation analysis.

Results

We included one hundred and twenty-six outpatients with RHT. Patients were divided into two groups according to subclinical LV dysfunction: Patients with MPI<0.5 (lower MPI group, n=50) and patients with MPI≥0.5 (higher MPI group, n=76). The higher MPI group was significantly older than the lower MPI group (60.6±8.8 vs. 54.9±8.2, $p<0.001$). Both groups were balanced in gender, diabetes mellitus, hyperlipidemia, smoking, body mass index, and biochemical parameters. The higher MPI group was associated with higher left ventricle end-systolic diameter (LVESd), interventricular septum diameter (IVSd), posterior wall diameter, left ventricle end-diastolic diameter (LVEDd), left ventricle mass index (LVMI), E velocity, left atrium diameter (LAd) and RRI [0.711±0.042 vs. 0.652±0.050, $p=0.008$, (Figure 2)]. Also, the higher MPI group had a lower left ventricle ejection fraction. Baseline clinical, laboratory, and echocardiographic parameters of the patients were shown in Table 1. In multivariable logistic regression analysis, age [odds ratio (OR): 1.070, 95% confidence interval (CI): 1.016-1.126, $p=0.010$], LAd (OR: 1.111, 95% CI: 1.027-1.202, $p=0.008$) and RRI (OR: 6.404, 95% CI: 2.767-19.899, $p<0.025$) were independent predictors of subclinical left ventricle dysfunction (Table 2). In correlation analysis, RRI showed a good positive correlation with MPI ($r=0.527$, $p<0.001$) (Figure 3).

Discussion

Our study's main findings are as follows: 1) We found a significant correlation between RRI and MPI in patients with RHT, 2) We observed that patients with high MPI value, which is considered as LV subclinical dysfunction, were older and echocardiographic parameters associated with systolic function and diastolic dysfunction such as LV mass index, E value, and E/A were more impaired in this group, 3) According to regression analysis, we found that RRI was associated with subclinical LV dysfunction in this group of patients.

HT is a significant disease with a close relationship with cardiovascular, neurological, and renal poor outcomes. Although most hypertension cases can be treated with medications, approximately 10-20% of these patients are resistant to treatment (1). In a small study with 86 patients, it was found that RHT patients had a 2-fold increase in cardiovascular risk than controlled HT patients (18). In another study, Sahinarslan et al. (4) showed that cardiovascular and renal damage was higher in RHT in a study including 205,750 patients. These findings are significant as the number of patients with RHT is expected to increase because of the increasing risk factors such as diabetes and obesity. End-organ damage develops faster in RHT patients and increases morbidity and mortality. In the first two years of follow-up, there were significant excess risks of these adverse outcomes, particularly MACE, cardiovascular mortality, and stroke incidence in a randomized controlled study by Cardoso and Salles (19). In a study by Gaudieri et al. (20), the coronary vascular function was shown to be more impaired in patients with RHT, as demonstrated by myocardial perfusion reserve. Another end-organ injury that increases the risk of mortality with cardiac end-organ damage is renal function. There is a two-way relationship between renal functions and treatment resistance in patients with RHT. While the most common cause of RHT is kidney diseases, RHT also increases worse renal outcomes (21). Viazzi et al. (22) showed that the presence of RHT was related to impairment in renal function in hypertensive and diabetic patients with normal renal function. Considering all, both cardiac and renal involvement frequently occur in patients with RHT and simple methods showing these two end-organ damages may be important in risk classification.

MPI is an important parameter that can show systolic and diastolic functions simultaneously (23). In addition to being an early and robust predictor of left ventricular injury in the adult population, it has been associated with poor outcomes in many diseases (24,25,26). It is an essential parameter for

Table 1. Baseline features of patients

	Lower MPI (n=50)	Higher MPI (n=76)	Total (n=126)	p
Age (years)	54.9±8.2	60.6±8.8	58.4±9.0	**<0.001**
Female gender, n (%)	33 (66)	42 (55)	75 (59.5)	0.230
Body mass index (kg/m²)	30.8±4.3	31.3±4.9	31.1±4.6	0.610
Diabetes mellitus, n (%)	13 (26)	18 (23.7)	33 (23.4)	0.564
Hyperlipidemia, n (%)	22 (44)	40 (52.6)	62 (49.2)	0.343
Smoking, n (%)	12 (24)	14 (18.4)	26 (20.6)	0.449
Biochemical parameters				
-Hemoglobin (g/dL)	13.2±1.5	13.6±1.6	13.5±1.6	0.145
-Total cholesterol (mg/dL)	204±40	202±43	205±42	0.789
-HDL-c (mg/dL)	51±16	49±12	50±14	0.329
-LDL-c (mg/dL)	123±38	120±37	123±38	0.733
-Triglyceride (mg/dL)	149±66	157±73	154±69	0.544
-Creatinine (mg/dL)	0.75 (0.66-0.8)	0.80 (0.6-0.9)	0.8 (0.6-0.9)	0.524
-Glucose (mg/dL)	97 (88-109)	95 (88-104)	97 (88-109)	0.966
Echocardiographic parameters				
-LV ejection fraction (%)	61 (60-63)	60 (60-62)	60 (60-62)	**0.012**
-LVEDd (mm)	45.32±3.90	47.23±4.70	46.3±4.42	**0.019**
-LVESd (mm)	28.98±3.74	30.47±4.03	29.78±3.93	**0.039**
-IVSd (mm)	11 (10-12)	12 (11-13)	12 (11-12)	**<0.001**
-PWd (mm)	10 (9-11)	10 (10-11)	10 (9-11)	**0.004**
-LVMI (g/m²)	94.21±23.49	105.47±25.70	100.5±25.9	**0.014**
-LAd (mm)	31.3±5.1	35.3±5.6	33.4±5.7	**<0.001**
-E velocity (cm/sn)	60.6±14.0	68.9±14.6	65.6±14.9	**0.002**
-A velocity (cm/sn)	77.2±13.2	80.6±18.6	79.3±16.7	0.258
-E/A ratio	0.81±0.23	0.88±0.27	0.85±0.26	0.106
-E' velocity (cm/s)	7.9 (6.2-9)	7.1 (6.2-10)	7.9 (6.2-9)	0.100
-A' velocity (cm/s)	11 (9-14)	10 (8.7-12.4)	8 (6-10.4)	0.250
-S' (cm/s)	9 (7.6-10)	8 (7-10)	8.1 (7-10)	0.117
-E to E' ratio	8.58±2.77	8.73±2.64	8.6±2.6	0.774
RRI	0.652±0.050	0.711±0.042	0.677±0.039	**0.008**

IVSd: Interventricular septum diameter, LAd: Left atrium diameter, LVEDd: Left ventricle end-diastolic diameter, LVESd: Left ventricle end-systolic diameter, LVMI: Left ventricular mass index, PWd: Posterior wall diameter, RRI: Renal resistive index, MPI: Myocardial performance index, HDL: High-density lipoprotein, LDL: Low-density lipoprotein

detecting left ventricular diastolic dysfunction by early stages and its association with hemodynamic changes is caused by the heart's impaired relaxation. MPI increases not only in diastolic dysfunction but also in systolic insufficiency caused by decreased pumping power (27). In our study, in parallel with these data, impaired diastolic dysfunction and systolic dysfunction were correlated with high MPI values. Ejection fraction, the most basic systolic function parameter, was lower in patients with high MPI values. In RHT patients, myocardial involvement and diastolic and systolic dysfunction are comorbid consequences that create significant end-organ damage. We hypothesize a relationship between MPI, which indicates this myocardial involvement, and renal functions, which is another crucial end-organ damage of RHT.

RRI, initially measured only in renal diseases, has gained importance as a risk factor by being evaluated in patients with cardiovascular diseases (28). Although the pathophysiological link between RRI and cardiovascular outcomes is not yet clearly understood, studies have concluded that this index is associated with renal function, renal atherosclerosis, tubulointerstitial damage, and an indicator of systemic arterial atherosclerosis (29). Tedesco et al. (30) showed that high RRI

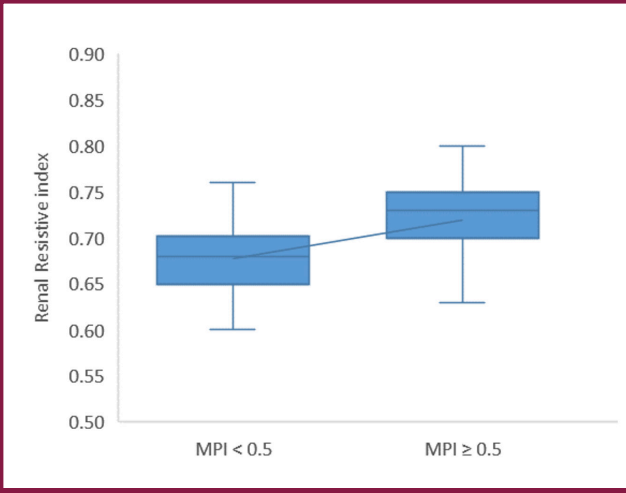

Figure 2. Comparison of renal resistive index values according to the cut-off value of MPI
MPI: Myocardial performance index

levels were associated with systemic hemodynamic changes and cardiovascular parameters in hypertensive patients. In another study, high RRI values were related to carotid and coronary artery damage (29). A study conducted by Quisi et al. (31) showed a significant association between RRI and MPI in the general population. In a study, the association of renal hemodynamics with RHT was examined. They found that patients with RHT had greater levels of the renal resistive index. Also, the RRI was an independent predictor of RHT after adjusting for clinical features (32). It can be concluded that high RRI values are associated with hypertension-related end-organ damage in the heart. Similar to these studies' results, it has been shown that high RRI values in RHT patients correlate with MPI, which is associated with impaired myocardial function in our study.

Study Limitations

First, it was conducted in a single center, and because of that, the results cannot be generalized to the total population. Second, the sample size was small; hence, further prospective

Table 2. Univariable and multivariable logistic regression analysis with backward model selection to predict independent predictors of subclinical left ventricle dysfunction

Variables	Univariable		Multivariable analysis with backward model selection	
	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p
Age	1.081 (1.033-1.131)	**0.005**	1.070 (1.016-1.126)	**0.010**
Female gender	1.571 (0.750-2.292)	0.231	-	-
Diabetes Mellitus	0.883 (0.387-2.014)	0.768	-	-
Hyperlipidemia	1.414 (0.690-2.897)	0.344	-	-
Smoking	0.715 (0.299-1.707)	0.450	-	-
Body mass index	1.020 (0.945-1.102)	0.607	-	-
LV ejection fraction	0.767 (0.623-0.943)	**0.012**	-	-
LVEDd	1.104 (1.015-1.202)	**0.021**	-	-
LVESd	1.103 (1.004-1.211)	**0.041**	-	-
LAd	1.146 (1.064-1.234)	**<0.001**	1.111 (1.027-1.202)	**0.008**
LVMI	1.020 (1.003-1.036)	**0.017**	-	-
E/A	3.538 (0.743-16.833)	0.112	-	-
E' velocity	1.220 (1.007-1.477)	**0.042**	-	-
A' velocity	0.987 (0.955-1.020)	0.439	-	-
Glucose	1.011 (0.994-1.029)	0.200	-	-
Creatinine	2.587 (0.353-18.947)	0.349	-	-
Hemoglobin	1.189 (0.943-1.483)	0.148	-	-
Total cholesterol	0.999 (0.990-1.007)	0.787	-	-
HDL-c	0.988 (0.964-1.012)	0.326	-	-
LDL-c	0.998 (0.989-1.008)	0.730	-	-
Triglyceride	1.002 (0.996-1.007)	0.541	-	-
RRI	6.769 (1.886-24.293)	**0.008**	6.404 (2.767-19.899)	**0.025**

IVSd: Interventricular septum diameter, LAd: Left atrium diameter, LVEDd: Left ventricle end-diastolic diameter, LVESd: Left ventricle end-systolic diameter, LVMI: Left ventricular mass index, PWd: Posterior wall diameter, RRI: Renal resistive index, HDL: High-density lipoprotein, LDL: Low-density lipoprotein

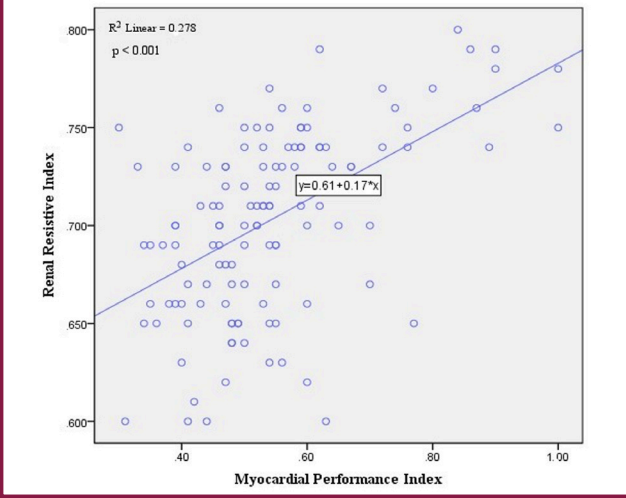

Figure 3. Association between the renal resistive index and the myocardial performance index

studies with larger cohorts may be needed to confirm the results. Finally, antihypertensive drugs can affect RRI values, and we did not evaluate the effects of the drugs.

Conclusion

Our study suggests that increased RRI is associated with subclinical LV dysfunction assessed by increased MPI in patients with RHT. In RHT, RRI assessment could play an integral role in evaluating both cardiovascular and renal damage and guiding treatment. We need future more extensive prospective studies to elucidate better the associations found in this study.

Ethics

Ethics Committee Approval: The study were approved by the Mehmet Akif Ersoy Cardiovascular Surgery Training and Research Hospital of Local Ethics Committee (Protocol number: 2020-75).

Informed Consent: Written informed consent from all the participants.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: C.P., Ç.T., Concept: C.P., İ.G., M.E., Design: C.P., İ.G., Data Collection or Processing: C.P., A.G., Analysis or Interpretation: C.P., Ç.T., Literature Search: C.P., İ.G., A.G., Writing: C.P., A.G., M.E.,

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

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

References

1. Williams B, Mancia G, Spiering W, Rosei EA, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J 2018;39:3021-104. [Crossref]
2. Noubiap JJ, Nansseu JR, Nyaga UF, Sime PS, Francis I, Bigna JJ. Global prevalence of resistant hypertension: a meta-analysis of data from 3.2 million patients. Heart. 2019;105:98-105.
3. Yakovlevitch M, Black HR. Resistant hypertension in a tertiary care clinic. Arch Intern Med. 1991;151:1786-1792. [Crossref]
4. Sahinarslan A, Gazi E, Aktoz M, Ozkan C, Ulusal Okyay G, Ucar Elalmis, et al. Consensus paper on the evaluation and treatment of resistant hypertension by the Turkish Society of Cardiology. Anatol J Cardiol. 2020;24:137-152. [Crossref]
5. Sim JJ, Bhandari SK, Shi J, Reynolds K, Calhoun DA, Kalantar-Zadeh K et al. Comparative risk of renal, cardiovascular, and mortality outcomes in controlled, uncontrolled resistant, and nonresistant hypertension. Kidney Int. 2015;88:622-632.
6. Doi Y, Iwashima Y, Yoshihara F, Kamide K, Hayashi S, Kubota Y, et al. Renal resistive index and cardiovascular and renal outcomes in essential hypertension. Hypertension. 2012;60:770-777. [Crossref]
7. Kuznetsova T, Cauwenberghs N, Knez J, Knez J, Thijs L, Liu YP, et al. Doppler indexes of left ventricular systolic and diastolic flow and central pulse pressure in relation to renal resistive index. Am J Hypertens. 2015;28:535-545. [Crossref]
8. Hashimoto J, Ito S. Central pulse pressure and aortic stiffness determine renal hemodynamics: pathophysiological implication for microalbuminuria in hypertension. Hypertension. 2011;58:839-846. [Crossref]
9. Safar ME, London GM, Plante GE. Arterial stiffness and kidney function. Hypertension. 2004;43:163-168. [Crossref]
10. Calabia J, Torguet P, Garcia I, Martin N, Mate G, Marin A, et al. The relationship between renal resistive index, arterial stiffness, and atherosclerotic burden: the link between macrocirculation and microcirculation. J Clin Hypertens (Greenwich). 2014;16:186-191. [Crossref]
11. Gur M, Yilmaz R, Demirbag R, Yildiz A, Ozdogru I, Bas MM, et al. Relationship between myocardial performance index and aortic distensibility in patients with essential hypertension. Int J Clin Pract. 2008;62:138-142. [Crossref]
12. Ulucay A, Tatli E. Myocardial performance index. Anadolu Kardiyol Derg. 2008;8:143-148. [Crossref]
13. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2015;16:233-270. [Crossref]
14. Tei C, Ling LH, Hodge DO, Bailey KR, Oh JK, Rodeheffer RJ, et al. New index of combined systolic and diastolic myocardial performance: a simple and reproducible measure of cardiac function--a study in normals and dilated cardiomyopathy. J Cardiol. 1995;26:357-366. [Crossref]
15. Akyuz AR, Turan T, Gurbak I, Korkmaz L, Agac MT, Celik S. The relationship between presystolic wave and subclinical left ventricular dysfunction in asymptomatic hypertensive patients. Blood Press Monit. 2016;21:277-281. [Crossref]
16. Gurbak I, Yildiz I, Panc C. Relation between aortic knob width and subclinical left ventricular dysfunction in hypertensive patients. Clin Exp Hypertens. 2018;40:589-594. [Crossref]
17. Armstrong WF, Ryan T. Feigenbaum's echocardiography. 7th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins Health; 2010. [Crossref]
18. Redon J, Campos C, Narciso ML, Rodicio JL, Pascual JM, Ruilope LM.

Prognostic value of ambulatory blood pressure monitoring in refractory hypertension: a prospective study. Hypertension. 1998;31:712-718. [Crossref]

19. Cardoso CRL, Salles GF. Refractory hypertension and risks of adverse cardiovascular events and mortality in patients with resistant hypertension: a prospective cohort study. J Am Heart Assoc. 2020;9:e017634. doi: 10.1161/JAHA.120.017634 [Crossref]
20. Gaudieri V, Acampa W, Rozza F, Fillaus JA, Greco BA, Forman JP, et al. Coronary vascular function in patients with resistant hypertension and normal myocardial perfusion: a propensity score analysis. Eur Heart J Cardiovasc Imaging. 2019;20:949-958. [Crossref]
21. Braam B, Taler SJ, Rahman M, Fillaus JA, Greco BA, Forman JP, et al. Recognition and Management of Resistant Hypertension. Clin J Am Soc Nephrol 2017;12:524-535. [Crossref]
22. Viazzi F, Piscitelli P, Ceriello A, Fioretto P, Giorda C, Guida P, et al; AMD-Annals Study Group. Resistant hypertension, time-updated blood pressure values and renal outcome in type 2 diabetes mellitus. J Am Heart Assoc. 2017;6:e006745. doi: 10.1161/JAHA.117.006745. [Crossref]
23. Tei C, Nishimura RA, Seward JB, Tajik AJ. Noninvasive Doppler-derived myocardial performance index: correlation with simultaneous measurements of cardiac catheterization measurements. J Am Soc Echocardiogr. 1997;10:169-178. [Crossref]
24. Tei C, Dujardin KS, Hodge DO, Kyle RA, Tajik AJ, Seward JB. Doppler index combining systolic and diastolic myocardial performance: clinical value in cardiac amyloidosis. J Am Coll Cardiol. 1996;28:658-664. [Crossref]
25. Harjai KJ, Scott L, Vivekananthan K, Nunez E, Edupuganti R. The Tei index: a new prognostic index for patients with symptomatic heart failure. J Am Soc Echocardiogr. 2002;15:864-868. [Crossref]
26. Galiuto L. Value of the myocardial performance index in myocardial infarction. Heart. 2005;91:565-567. [Crossref]
27. LaCorte JC, Cabreriza SE, Rabkin DG, Printz BF, Coku L, Weinberg A, et al. Correlation of the Tei index with invasive measurements of ventricular function in a porcine model. J Am Soc Echocardiogr. 2003;16:442-447. [Crossref]
28. Di Nicolo P, Granata A. Renal Resistive Index: not only kidney. Clin Exp Nephrol. 2017;21:359-366. [Crossref]
29. Raff U, Schmidt BM, Schwab J, Schwarz TK, Achenbach S, Bär I, et al. Renal resistive index in addition to low-grade albuminuria complements screening for target organ damage in therapy-resistant hypertension. J Hypertens. 2010;28:608-614. [Crossref]
30. Tedesco MA, Natale F, Mocerino R, Tassinario G, Calabro R. Renal resistive index and cardiovascular organ damage in a large population of hypertensive patients. J Hum Hypertens. 2007;21:291-296. [Crossref]
31. Quisi A, Harbalioglu H, Ozel MA, Alici G, Genc O, Kurt IH. The association between the renal resistive index and the myocardial performance index in the general population. Echocardiography. 2020;37:1399-1405. [Crossref]
32. Kintis K, Tsioufis C, Kasiakogias A, Dimitriadis K, Konstantinidis D, Andrikou E, et al. Noninvasive assessment of haemodynamics in resistant hypertension: the role of the renal resistive index. J Hypertens. 2017;35:578-584. [Crossref]

ORIGINAL ARTICLE

DOI: 10.4274/hamidiyemedj.galenos.2021.14622

Hamidiye Med J 2021;2(2):77-82

Evaluation of Low Back Pain and Its Effects in Health Employees

Sağlık Çalışanlarında Bel Ağrısı ve Etkilerinin Değerlendirilmesi

İlknur Demir, Güzin Zeren Öztürk

University of Health Sciences Turkey, Şişli Hamidiye Etfal Training and Research Hospital, Clinic of Family Medicine, İstanbul, Turkey

ABSTRACT

Background: It is reported that more than 80% of the world's population experience low back pain at any time in their lives. Low back pain is a common cause of morbidity among health employees. Health employees are a high-risk group in terms of low back pain due to difficult physical workload and ergonomic problems. The aim of our study was to evaluate low back pain and its effects in health employees.

Materials and Methods: The study was conducted in April 2017 at Şişli Hamidiye Etfal Research and Training Hospital. The questionnaire form designed by the researcher and the Oswetry Scale were applied to the participants by face to face inquiry method. The statistical program SPSS was used to analyze data.

Results: Of the participants, 39.16% (n=103) had low back pain. Participants were divided into two groups as those with and without back pain. Age, gender, mean body mass index (BMI), BMI classification, educational status, smoking status and working time in the profession were found to be statistically significant between the two groups ($p<0.005$). The mean Oswestry Scale score of individuals with low back pain was 19.38±11.17. Participants were divided into two groups according to their level of exposure as mild (0-40%) and severe (≥40%), and related factors were examined. A significant relationship was found with the mean BMI, BMI classification and profession ($p<0.005$).

Conclusion: Two-fifths of the healthcare professionals had low back pain. During the periodic examinations of healthcare personnel, low back pain should be questioned. These groups should be examined in more detail and exercise recommendations should be made for smoking cessation, weight loss and muscle strengthening, since they are common in women, those with high school or lower education, those who spend a longer time in the profession, and those who are smokers, overweight and obese.

Keywords: Low back pain, hospital personel, risk factors

ÖZ

Amaç: Dünya nüfusunun %80'inden fazlası hayatlarının herhangi bir anında bel ağrısı bildirmektedir. Bel ağrısı, sağlık çalışanlarında yaygın bir morbidite nedenidir. Sağlık çalışanları, zorlu fiziksel iş yükleri, ergonomik sorunları nedeni ile bel ağrısı açısından yüksek riskli bir gruptadırlar. Bu çalışmada, sağlık çalışanlarında bel ağrısı ve etkilerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Çalışma 2017 Nisan ayında Şişli Hamidiye Etfal Eğitim ve Araştırma Hastanesi çalışanlarına yapılmıştır. Katılımcılara tarafımızca hazırlanan anket formu ve Oswetry Skalası yüz yüze sorgulama yöntemi ile uygulanmıştır. İstatistiksel analizde SPSS programı kullanılmıştır.

Bulgular: Katılımcılardan bel ağrısı olanların oranı %39,16 (n=103) idi. Katılımcılar bel ağrısı olan ve olmayan olarak iki gruba ayrılmıştır. Yaş, cinsiyet, beden kitle indeksi (BKI) ortalaması, BKI sınıflama, eğitim durumu, sigara içme durumu ve meslekteki çalışma süresi açısından her iki grup arasında istatistiksel anlamlı fark bulunmuştur ($p<0.005$). Bel ağrısı olan bireylerin Oswestry Skalası puan ortalaması 19,38±11,17 idi. Katılımcılar etkilenim düzeyine göre hafif etkilenim (%0-40) ve ciddi etkilenim (≥%40) olarak gruplara ayrılarak ilişkili faktörler incelenmiştir. Ortalama BKI, BKI sınıflama, meslek ile anlamlı ilişki saptanmıştır ($p<0.005$).

Sonuç: Sağlık çalışanlarının beşte ikisinde bel ağrısı saptanmıştır. Sağlık personellerinin periyodik muayeneleri esnasında bel ağrısı sorgulanmalıdır. Kadın cinsiyette, lise ve altı eğitim düzeyine sahiplerde, meslekte daha uzun süre geçirenlerde, sigara içenlerde, fazla kilolu ve obezlerde sık olması sebebiyle bu gruplar daha ayrıntılı incelenmeli ve sigara bırakma, kilo verme ve kas güçlendirmesi için yapılabilecek egzersiz önerilerinde bulunulmalıdır.

Anahtar Kelimeler: Bel ağrısı, hastane personeli, risk faktörleri

Address for Correspondence: İlknur Demir, University of Health Sciences Turkey, Şişli Hamidiye Etfal Training and Research Hospital, Clinic of Family Medicine, İstanbul, Turkey
Phone: +90 212 373 50 00 E-mail: ilknurdemir25@gmail.com **ORCID ID:** orcid.org/0000-0003-0055-7186
Received: 07.05.2021 **Accepted:** 11.06.2021

Introduction

Low back pain is located in the lumbar region between the last costal rib and the gluteal curve (1). It is reported that more than 80% of the world's population experience low back pain at any time in their lives (2,3). However, as most low back pain resolves within the first two weeks without any treatment, individuals with low back pain lasting longer than 2 weeks and/or requiring treatment are affected by low back pain as a result of functional incapacity (4,5).

Epidemiological studies show that there are a variety of risk factors affecting the incidence and prevalence of low back pain. Personal risk factors for low back pain may be listed as age, gender, occupation, body mass index (BMI), family history, smoking, alcohol intake and physical activity levels (6). A person's occupation and working conditions may cause the occurrence of low back pain.

Low back pain is a common cause of morbidity among health employees (2). Health employees constitute a high-risk group in terms of low back pain due to difficult physical workload (long working hours, shift work, being on call, etc.) and ergonomic problems (transferring patients, repositioning patients, frequent bending, lifting heavy loads, pulling and pushing, remaining in the same position for long periods, repeated movements) (7,8,9).

The aim of our study was to evaluate low back pain and its effects in health employees.

Material and Methods

Research Population and Sample

The research was a single-center descriptive study. The study was performed with employees in Şişli Hamidiye Etfal Training and Research Hospital from April 01, 2017 to April 30, 2017. At the time of the study, the hospital employed a total of 2,318 people, with 694 doctors, 790 nurses (nurses, midwives, emergency medicine technicians), and 834 other personnel (data entry, security, cleaning). Layered sampling was applied with 95% confidence interval and the sample size was calculated as 263 people (doctors: 79, nurses: 89, others: 95). Participants were included in the study after obtaining verbal consent.

Those with congenital hip dislocation, spine fracture history, known psychiatric or neurologic disease increasing low back pain risk, different length legs for any reason or inflammatory low back pain were not included in the study. Ethics committee permission was granted by Şişli Hamidiye Etfal Research and Training Hospital Ethics Committee (date: 07 March 2017, decision number: 1436).

Data Collection Tools

Socio-demographic data for participants, BMI calculations and the presence of low back pain were questioned. Individuals with low back pain lasting longer than 2 weeks and/or requiring treatment were assessed as having low back pain, and participants were divided into two groups as those with and without low back pain. Moreover, relevant factors were evaluated.

Oswestry Scale

Participants with low back pain were applied the Oswestry Scale (OS) to determine effect levels. This scale was published by Fairbank and Pynsent (10) with the aim of assessing functional capacity of individuals. Turkish validity and reliability were examined by Yakut et al. (11) and the scale was prepared for use by Akbay (12). The OS comprises ten subgroups (pain intensity, self-care, lifting-carrying, walking, sitting, standing, sleep, traveling and social life). Points vary from 0 to 50 and the patient score is assessed with the formula: Total score = (points received by participant/maximum possible points) x 100. Levels of effect increase as total score increases.

Accordingly, results are grouped as;

- 0-20% low back pain does not cause a significant problem in the patient's life.
- 20-40% low back pain mildly restricts the patient's daily life.
- 40-60% low back pain significantly restricts the patient's daily life.
- 60-80% low back pain fully restricts the patient's daily life.
- 80-100% bedridden.

Participants in the study were divided into two groups as those with mild level of effects (0-40%) and those with serious effects (≥40%), and associated factors were investigated.

Statistical Analysis

The SPSS 20.0 program was used in the study. Descriptive statistics were given as number and percentage for categoric variables and as mean, standard deviation, minimum and maximum for numerical variables. Numerical variables were compared in two independent groups with the Student's t-test when normal distribution conditions were present and with the Mann-Whitney U test when normal distribution conditions were not present. Rates in independent groups were compared with the chi-square analysis. Values of $p<0.05$ were accepted as statistically significant.

Results

The ages of the 263 people participating in the study varied from 20 to 65 years, with the mean age of 33.89±9.04

years. Of participants, 58.55% were women (n=154) and 41.45% were men (n=109). Participants comprised higher rates of married individuals (51.33%, n=135). The mean BMI of participants was 38±4.12 (15.62-45.72) and 9.3% were obese (n=22). There were 145 participants who did not smoke (55.13%). For all participants, the mean working duration in their profession was 9.16±7.91 years (1-36).

Among the participants, 39.16% had low back pain (n=103). Participants were divided into two groups as those with and without low back pain, and relevant factors were investigated (Table 1). Accordingly, there were statistically significant differences found between the two groups in terms of age, gender, mean BMI, BMI classification, educational status, smoking habit and professional working duration (p=0.002, p=0.049, p=0,001, p<0.001, p=0.019, p=0.003, and p=0.007, respectively). As age, weight, mean BMI, and professional working duration increased, the experience of low back pain increased. Additionally, educational level lower than high school, smoking rate and the rate of being female gender were significantly higher.

The mean OS points of individuals with low back pain were 19.38±11.17 (1-48). The effect status according to OS is given in Figure 1, with most people (31.09%, n=32) experiencing mild limitation of daily life. Investigation of related factors when participants were divided into two groups according to mild effect (0-40%) and severe effect (≥40%) is shown in Table 2. There were significant associations identified for mean BMI, BMI classification and profession (p=0.013, p=0.017, and p=0.029, respectively).

Discussion

Health employees were identified to experience low back pain in any period of life at rates of 46.30-84% in the

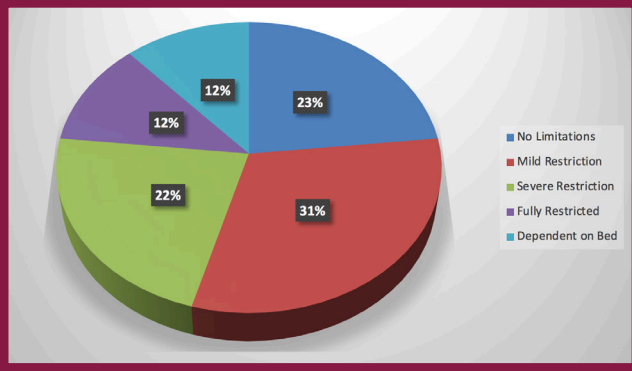

Figure 1. Affected states according to the Oswestry Scale

Table 1. Participants' low back pain status and evaluation of related factors

		With low back pain (n=103)		Without low back pain (n=160)		
		n	%	n	%	p
Gender	Female	68	44.20	86	55.80	0.049
	Male	35	32.10	74	67.90	
Age (years) Mean ± SD		35.95±9.51		32.56±8.49		0.002
Weight (kg) Mean ± SD		71.50±13.96		68.51±14.22		0.106
Height (cm) Mean ± SD		167.35±8.77		169.43±8.65		0.086
BMI (kg/m^2) Mean ± SD		25.40±4.26		23.72±3.91		0.001
BMI classification	Normal and underweight	46	29.67	109	70.32	<0.001
	Overweight and obese	57	52.77	51	47.22	
Marital status	Married	57	42.22	78	57.77	0.297
	Single	46	35.93	82	64.06	
Education status	Under high school	26	54.16	22	45.83	0.019
	High school and over	77	35.81	138	64.18	
Smoking status	Smoking	57	49.13	59	50.86	0.003
	Non-smoking	46	31.29	101	68.70	
Occupation	Physician	25	31.64	54	68.35	0.207
	Nurse	40	44.94	49	55.05	
	Other staff	38	40	57	60	
Working time in the occupation mean ± SD		10.78±8.07		8.07±7.65		0.007

BMI: Body mass index, SD: Standart deviation, kg: Kilogramme, cm: Centimeter

Table 2. Evaluation of the affected participants with low back pain and related factors

		Those with mild level of effects (0%-40%) (n=56)		Those with serious effects (≥40%) (n=47)		
		n	%	n	%	p
Gender	Female	34	50	34	50	0.215
	Male	22	62.9	13	37.1	
Age (years) Mean ± SD		35.39±9.72		36.62±9.33		0.466
Weight (kg) Mean ± SD		70.89±16.02		72.23±11.14		0.222
Height (cm) Mean ± SD		168.95±9.27		165.45±7.82		0.056
BMI (kg/m^2) Mean ± SD		24.69±4.43		26.25±3.92		0.013
BMI classification	Normal and underweight	31	55.4	15	44.6	0.017
	Overweight and obese	25	31.9	32	56.1	
Marital status	Married	27	48.2	30	63.8	0.112
	Single	29	51.8	17	36.2	
Education status	Under high school	10	38.5	16	61.5	0.060
	High school and over	46	59.7	31	40.3	
Smoking status	Smoking	32	56.1	25	43.9	0.688
	Non-smoking	24	52.2	22	47.8	
Occupation	Physician	19	76	6	24	0.029
	Nurse	21	52.5	19	47.5	
	Other staff	16	42.1	22	57.9	
Working time in the occupation mean ± SD		10.21±8.58		11.47±7.30		0.130

BMI: Body mass index, SD: Standart deviation, kg: Kilogramme, cm: Centimeter

literature (9,13,14,15,16,17,18,19). The rate in our study was 39.16%, which may be due to the fact that our study only questioned individuals with low back pain lasting more than 2 weeks and/or requiring treatment and not in any period of life.

In the literature, low back pain can be observed in any age group, though it is stated to be higher in the group with active working life aged from 20 to 55 years (9,20). In the study, the mean age of individuals with low back pain was compatible with this age group and higher than those without low back pain. The identification of low back pain at significantly higher rates in the female gender is consistent with the literature; women may be exposed to higher rates than men due to lifelong hormonal variations (pregnancy, menopause, etc.) (9,13,21). The observation of higher rates of low back pain in those with educational level of high school or lower may be due to increased awareness of the use of body mechanisms and protective precautions as a part of healthy life and movement in accordance with this in those with increased educational level (20).

In our study, experience of low back pain with longer duration in the profession was statistically significant. As the duration of working in a profession increases, this may cause increased duration of exposure to risk factors involved in the profession. In fact, Arasan et al. (15) found lifelong and point prevalence of low back pain was increased duration of employment in a profession. Deksisa Abebe et al. (22) observed that health employees working longer than 12 years had higher prevalence of low back pain compared to those employed for durations less than 12 years.

Health employees are reported to smoke at different rates from 13.9 to 46.3% (13,14,23). In this study, the smoking rate was 38%. In the literature, just as there are studies showing a correlation between smoking and low back pain (21,23,24,25), there are studies showing no correlation (15,20,26). Studies proposing no effect of smoking on low back pain give reasons such as nicotine's analgesic effect and depression-reducing effects of nicotine; studies stating that there is an association indicate that smoking increases the risk of low back pain incidence due to disrupting nutrition of the vertebral disk, making the disk more susceptible to external factors, and reducing blood perfusion in the spine and muscles due to vasoconstriction caused by nicotine in cigarettes (23). In

our study, a significant association was identified between smoking and experience of low back pain and there is a need for advanced research about this topic.

A meta-analysis revealed a significant correlation between BMI and low back pain (27). In the study, low back pain had significantly higher rates in overweight and obese participants and the mean BMI of the group with low back pain was identified to be higher. Due to the additional weight carried by overweight and obese individuals, they may have weak back and abdominal muscles (28). This situation increases stress in the musculo-skeletal system (28,29). Additionally, obesity causes higher compressive forces on the lumbar spine during a variety of movements, which may cause increased mechanical load on the spine (22,28,29).

In the study, most health employees with low back pain had mild degree of restriction of daily life activities according to the mean OS; however, a considerable portion (9.60%) was bedridden. A study by Güzel and Altındağ (30) found 41.7% of participants had no limitation, while 5.5% had severe restriction. Solak Kabataş et al. (31) identified the rate of 40.0% for mild effect and the rate of 3.3% for severe effect. This situation illustrates that low back pain may affect health employees to different degrees and at a variety of rates; in fact, the reality is that it may cause severe functional incapacity leading to being bedridden. In terms of profession, other personnel being more affected may be due to the excess of bodily labor.

In the study, those severely affected by low back pain had higher mean BMI; the rate of severe effect among overweight and obese participants was identified to be significantly high. Obesity on its own is related to increased production of cytokines and acute phase reactants and activation of proinflammatory pathways, which may lead to delayed healing in this situation (32,33).

Conclusion

In conclusion, two out of five health employees were identified to have low back pain. Low back pain was observed more frequently in those who had female gender, education level of high school or lower, and longer duration in their profession, who smoked, and who were overweight or obese. It was revealed that being overweight and obese and working as other health personnel caused severe degree of effect of low back pain.

In light of these results, it may be concluded that it is necessary to inquire about low back pain during periodic examinations of health personnel. We think it is necessary to investigate groups who have female gender, high school or lower educational level, longer period in the profession, who are smokers, and those who are overweight and obese in more detail due to higher incidence and to recommend quitting smoking, losing weight and exercises for muscle strengthening.

Ethics

Ethics Committee Approval: Ethics committee permission was granted by Şişli Hamidiye Etfal Training and Research Hospital Ethics Committee (date: 07 March 2017, decision number: 1436).

Informed Consent: Participants were included in the study after obtaining verbal consent.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: İ.D., G.Z.Ö., Concept: İ.D., G.Z.Ö., Design: İ.D., G.Z.Ö., Data Collection or Processing: İ.D., Analysis or Interpretation: İ.D., G.Z.Ö., Literature Search: İ.D., G.Z.Ö., Writing: İ.D., G.Z.Ö.

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

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

References

1. Cargnin ZA, Schneider DG, Vargas MAO, Machado RR. Non-specific low back pain and its relation to the nursing work process. Rev Lat Am Enfermagem. 2019;27:e3172. doi: 10.1590/1518-8345.2915.3172. [Crossref]
2. Sanjoy SS, Ahsan GU, Nabi H, Joy ZF, Hossain A. Occupational factors and low back pain: a cross-sectional study of Bangladeshi female nurses. BMC Res Notes. 2017;10:173. [Crossref]
3. Illés ST. A derékfájás: mikor és mit tegyünk? [Low back pain: when and what to do]. Orv Hetil. 2015;156:1315-1320. (Hungarian) [Crossref]
4. Akyüz GD. Bel Ağrılarında Tanı, Ayırıcı Tanı ve Baş Etme Stratejileri. Uluslararası Katılımlı Türk Romatoloji Kongresi, Antalya, Türkiye. 2019;133. [Crossref]
5. Oğuz S, Kaptan H. Low back pain in working life. Turkish Med Assoc Occup Heal Saf Mag. 2005;45-48. [Crossref]
6. Şimşek Ş, Yağci N, Şenol H. Prevalence of and risk factors for low back pain among healthcare workers in Denizli. Pain. 2017;29:71-78. [Crossref]
7. Kostanoğlu A, Şüheda Gözaydınoğlu TMK. Investıgatıon Of Nonspecıfıc Low Back Paın In Hospıtal And Home Health Care Professıonals. acta medica nicomedia. 2020;3(1):1-19. [Crossref]
8. Ando S, Ono Y, Shimaoka M, Hiruta S, Hattori Y, Hori F, et al. Associations of self estimated workloads with musculoskeletal symptoms among hospital nurses. Occup Environ Med. 2000;57:211-216. [Crossref]
9. Awosan KJ, Yikawe SS, Oche OM, Oboirien M. Prevalence, perception and correlates of low back pain among healthcare workers in tertiary health institutions in Sokoto, Nigeria. Ghana Med J. 2017;51:164-174. [Crossref]
10. Fairbank JC, Pynsent PB. The Oswestry disability index. Spine (Phila Pa 1976). 2000;25:2940-2953.
11. Yakut E, Düger T, Öksüz Ç, Yörükan S, Üreten K, Turan D, et al. Validation of the Turkish version of the oswestry disability index for patients with low back pain. Spine (Phila Pa 1976). 2004;29:581-585. [Crossref]
12. Akbay A. Oswestry Scale. Last Accessed Date: 02.01.2021. Available from: http://www.spinetr.com/Uploads/files/skor/Oswestry.pdf [Crossref]
13. Leblebicioğlu H, Bayraktar D, Khorshtd L, Sarıtaş N. Functional Deficiency Related Low Back Pain Among Nurses Working in a State Hospital and the Associated Factors. Int Ref J Nurs Res. 2018;0:61-81. [Crossref]

14. Terzi R, Altin F. The prevalence of low back pain in hospital staff and its relationship with chronic fatigue syndrome and occupational factors. Pain. 2015;27:149-154. [Crossref]
15. Arasan F. Determination of the prevalence of low back pain among nurses working in a university hospital Abstract. Cerrahpaşa Tıp Derg. 2009;40:136-143. [Crossref]
16. Airaksinen O, Brox JI, Cedraschi C, Hildebrandt J, Klaber-Moffett J, Kovacs F, et al; COST B13 Working Group on Guidelines for Chronic Low Back Pain. Chapter 4. European guidelines for the management of chronic nonspecific low back pain. Eur Spine J. 2006 Mar;15 Suppl 2(Suppl 2):S192-300. doi: 10.1007/s00586-006-1072-1. [Crossref]
17. Shieh SH, Sung FC, Su CH, Tsai Y, Hsieh VC. Increased low back pain risk in nurses with high workload for patient care: a questionnaire survey. Taiwan J Obstet Gynecol. 2016;55:525-529. [Crossref]
18. Trinkoff AM, Lipscomb JA, Geiger-Brown J, Brady B. Musculoskeletal problems of the neck, shoulder, and back and functional consequences in nurses. Am J Ind Med. 2002;41:170-178. [Crossref]
19. Cunningham C, Flynn T, Blake C. Low back pain and occupation among Irish health service workers. Occup Med (Lond). 2006;56:447-454. [Crossref]
20. Yılmaz E, Özkan S. Determination of the Prevalence of Low Back Pain Among Nurses Working in Hospitals. Turk J Phys Med Rehab. 2008;54:8-12. [Crossref]
21. Altinel L, Köse KC, Ergan V, Işik C, Aksoy Y, Ozdemir A, et al. [The prevalence of low back pain and risk factors among adult population in Afyon region, Turkey]. Acta Orthop Traumatol Turc. 2008;42:328-333. (Turkish) [Crossref]
22. Deksisa Abebe A. Prevalence of low back pain and associated risk factors among Adama Hospital Medical College Staff, Ethiopia. Eur J Prev Med. 2015;3:188-192. [Crossref]
23. Urgan U, Hamzaoğlu O. Examination of the frequency of low back pain and the factors affecting low back pain among the assistants working at Kocaeli University Faculty of Medicine. Occup Heal Saf J. 2016;16:49-56. [Crossref]
24. Esen ES, Toprak D. Evaluation of the Prevalence and Associated Factors of Low Back Pain. Ankara Med J. 2018;4:460-469. [Crossref]
25. Ayvat PÜ, Aydin ON, Oğurlu M. Risk factors associated with lower back pain in the Polyclinic of Algology. Pain. 2012;24:165-170. [Crossref]
26. Albayrak İ, Nilay Ş, Karahan AY, Hatice U, Üniversitesi S, Meram T, et al. The relation of smoking with the low back pain. Gen Med J. 2010;20:55-59. [Crossref]
27. Shiri R, Karppinen J, Leino-Arjas P, Solovieva S, Viikari-Juntura E. The association between obesity and low back pain: a meta-analysis. Am J Epidemiol. 2010;171:135-154. [Crossref]
28. Hu HY, Chou YJ, Chou P, Chen LK, Huang N. Association between obesity and injury among Taiwanese adults. Int J Obes (Lond). 2009;33:878-884. [Crossref]
29. Alnaami I, Awadalla NJ, Alkhairy M, Alburidy S, Alqarni A, Algarni A, et al. Prevalence and factors associated with low back pain among health care workers in southwestern Saudi Arabia. BMC Musculoskelet Disord. 2019;20:56. [Crossref]
30. Güzel HÇ. Altındağ Ö. Relationship between low back pain, neck pain, psychical situation and quality of life and the burnout syndrome in hospital workers. Cumhur Üniv Sağ Bil Enst Derg. 2021;1:36-45. [Crossref]
31. Solak Kabataş M, Kocuk M, Küçükler Ö. Evaluation of frequency and factors affecting low back pain in health care workers. Fırat Üniversitesi Sağlık Bilim Tıp Derg. 2012;2:65-72. [Crossref]
32. Tilg H, Moschen AR. Adipocytokines: mediators linking adipose tissue, inflammation and immunity. Nat Rev Immunol. 2006;6:772-783. [Crossref]
33. Demirci Ş, Gün C. Adipose tissue and some proteins released from adipose tissue. MAKÜ Sag Bil Enst Derg. 2017;5:155-179. [Crossref]

CASE REPORT

DOI: 10.4274/hamidiyemedj.galenos.2021.69775

Hamidiye Med J 2021;2(2):83-85

Idiopathic Pneumatosis Cystoides Intestinalis in A 35-Year-Old Man Who was Diagnosed Incidentally

Rastlantısal Olarak İdiyopatik Pnömatozis Sistoides İntestinalis Tanısı Konulan 35 Yaşındaki Hasta

İrfan Küçük[1], Yusuf Yazgan[1], Mustafa Kaplan[2], Alpaslan Tanoğlu[1]

[1]*University of Health Sciences Turkey, Sultan 2. Abdulhamid Han Training and Research Hospital, Clinic of Gastroenterology, İstanbul, Turkey*

[2]*University of Health Sciences Turkey, Sultan 2. Abdulhamid Han Training and Research Hospital, Clinic of Internal Medicine, İstanbul, Turkey*

ABSTRACT

Signs and symptoms of pneumatosis cystoides intestinalis (PCI) vary depending on the localization of cystic lesions in the gastrointestinal tract. Since PCI is not a frequent disease, diagnosis is usually made incidentally. PCI mostly occurs as a result of various clinical conditions. Principally, treatment is managed according to the cause. It is usually benign and rarely causes serious complications. In this case report, we introduce a 35-year-old man who was admitted to the hospital with non-specific symptoms.

Keywords: Idiopathic, pneumatosis cystoides intestinalis, incidentally

ÖZ

Pnömatozis cystoides intestinalis'in (PCI) belirti ve semptomları, gastrointestinal sistemdeki kistik lezyonların lokalizasyonuna göre değişir. PCI sık görülen bir hastalık olmadığından tanı genellikle tesadüfen konur. PCI çoğunlukla çeşitli klinik durumların bir sonucu olarak ortaya çıkar. Prensip olarak tedavi, nedene göre yönetilir. Genellikle iyi bir seyri vardır, PCI nadiren ciddi komplikasyonlara yol açar. Bu olgu sunumunda, hastaneye non-spesifik semptomlarla başvuran 35 yaşında bir erkek hastayı sunuyoruz.

Anahtar Kelimeler: İdiyopatik, pnömatozis sistoides intestinal, rastlantısal

Introduction

Pneumatosis cystoides intestinalis (PCI) is a very uncommon entity. This clinical picture may be diagnosed incidentally in radiologic or endoscopic examinations performed for different clinical indications. Usually, submucosal, intramucosal or subserosal layers of gut are occupied with single or multiple cysts full of air bubbles. There are very few reports of PCI occurring in the duodenum and rectum. Although the etiopathogenesis of PCI is not known precisely, it is thought to arise due to inflammation, physical damage of the intestinal mucosa, malnutrition, dysbacteriosis in which the balance of beneficial-harmful bacteria is impaired, gastrointestinal dysmotility and immune dysfunction (1,2,3). It may cause intra-abdominal free air. In 85% of the cases, PCI is associated with another pathology. Clinical findings are generally not clear but rarely PCI presents with serious clinical conditions like bleeding or perforation. In this study, we present a 35-year-old man incidentally diagnosed as PCI.

Case Report

A 35-year-old patient complaining moderate to severe abdominal pain with flatulence and epigastric pain was admitted to gastroenterology department of our institution. He did not have any chronic disease, any medication, any illicit or over-the-counter drug usage. He was suffering from abdominal pain and intermittent constipation for six years. The patient especially reported that abdominal discomfort was proportional to the amount of food intake. Physical examination was normal except epigastric sensitivity and abdominal distension with palpation. Biochemical laboratory tests were all normal.

Upper gastrointestinal endoscopy revealed hyperemic antral gastropathy. Five bubble-like and grape shaped submucosal cystic polypoid lesions in the distal part of descending colon were reported in colonoscopy. They were 10-30 mm in diameter and resembling like lipomatous polyps or gastric fundal varices (Figure 1). There were also

Address for Correspondence: Mustafa Kaplan, University of Health Sciences Turkey, Sultan 2. Abdulhamid Han Training and Research Hospital, Clinic of Internal Medicine, İstanbul, Turkey Phone: +90 533 567 28 71 E-mail: dr_mustafakaplan@yahoo.com **ORCID ID:** orcid.org/0000-0002-0354-4762

Received: 21.05.2021 **Accepted:** 25.06.2021

two distinct polyps with a diameter of 10 mm below and above this area. Smooth and bluish colored polypoid mucosa differing from adjacent non-polypoid tissue was noteworthy (Figure 1). The patient's history, laboratory results and physical findings were not consistent with portal hypertension and there was no pillow sign indicating a lipomatous polyp.

The bubble-like appearance made us think to use a sclerotherapy needle to test whether these subepithelial lesions contained gaseous material. Polyps suddenly became deflated when punctured and the mucosa turned to normal color like adjacent area. White epithelial ring surrounded the deflated polypoid region (Figure 2). This sign also strengthened our diagnosis of submucosal PCI. Later, we deflated the other ones with sclerotherapy needle. In the upper parts of the descending colon, the other whitish epithelial rings indicating the spontaneous explosion of these submucosal cystic polyps also were noted. In addition, written consent was obtained from the patient.

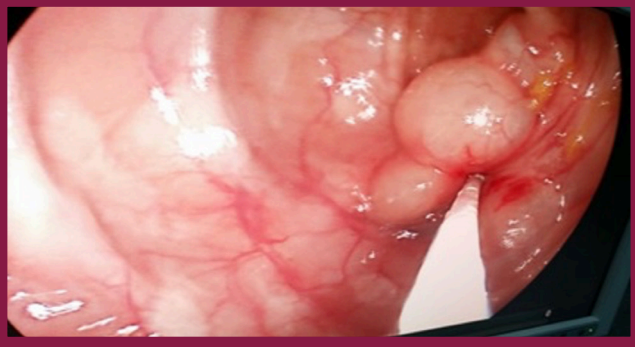

Figure 1. Deflating of the gas filled cystisc lesions in colonoscopy

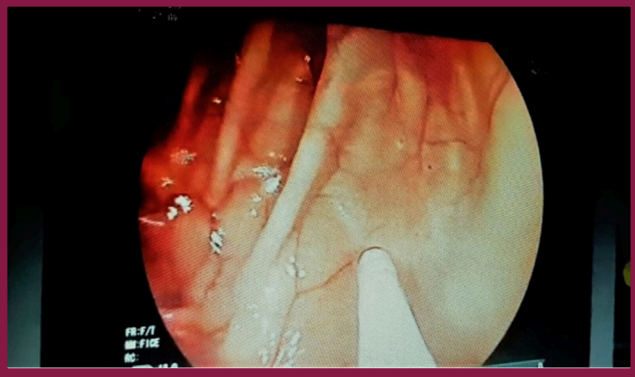

Figure 2. Appearance of the cystic lesion after deflation. Whitish and rim like epithelial ring surrounded the deflated cyst

Discussion

PCI is typically explained as being gas-filled cysts in the intestinal submucosa and/or subserosa. PCI is a rarely seen condition and formerly reported with the incidence of 0.03%. PCI may be encountered in all age groups (1,2,3). Since it coincides with other clinical scenarios and some cases have vague symptoms, determining the exact incidence is very difficult. First description in literature was made by Olmsted and Madewell (4) in the 18th century and then subcategorized by Koss (5). It is predominant in males between the ages of 30 and 50 years.

PCI may present with different clinical conditions. It usually associates with severe clinical entities and may lead to complications including acute abdominal pain, gastrointestinal bleeding, perforation, pneumoperitoneum, and volvulus (6,7). Nevertheless, it may present with benign situations as in this case. Prognosis usually correlates with the underlying disease.

Because of the wide spectrum of clinical settings and sometimes having silent clinical picture, PCI can be underdiagnosed. The exact pathophysiology of PCI is not entirely explained. This gray zone is probably multifactorial. PCI may be idiopathic (15%) or secondary (85%) to a lot of gastrointestinal and non-gastrointestinal problems (8). Secondary gastrointestinal conditions are intestinal ischemia, infarction and perforation, inflammatory bowel diseases, AIDS enteropathy, peptic ulcer disease, Coronavirus disease-2019 tuberculosis, and C. difficile infections. Secondary non-gastrointestinal disease may include chronic obstructive pulmonary disease, cystic fibrosis, diabetes mellitus, anti-diabetic medications like acarbose or voglibose, scleroderma, lymphoproliferative disorders and bone marrow or solid organ transplantation (8). During infancy, most causes are secondary to necrotizing enterocolitis. Our patient did not have any comorbidity.

Mechanical, bacterial, and biochemical explanations have been put forward to explain the exact pathogenesis of PCI. In line with the mechanical theory, gas enters into the intestinal wall from either the luminal surface through breaks in the mucosa or through the serosal surface by tracking along mesenteric blood vessels (9). In bacterial theory, PCI has been reproduced experimentally by injecting the gas-forming bacillus *Clostridium perfringens* into the bowel wall of rats. Further supporting the bacterial theory is that PCI may resolve following treatment with antibiotics (10). Finally, elemental diets have been reported to improve PCI presumably by removing substrate for the production of gas by bacteria (11). Our patient also noted that his abdominal discomfort was proportional to the amount of food intake and this situation may be supportive of bacterial theory of

PCI. Food content way also induce gas forming bacteria in the intestinal tract. Biochemical theory depends on the idea that luminal bacteria produce large amounts of hydrogen gas through the fermentation of mainly carbohydrates and other kind of foods, and hydrogen gas invades mucosal layers. All pathogenetic factors may contribute to the formation of PCI.

PCI can locate in any part of the gastrointestinal tract except the stomach. The small bowel is the most affected region and the colon is the second one. In some cases, both regions may become affected. The cysts may involve all three layers (mucosa, submucosa, subserosa). Subserosal cysts are more commonly seen in small intestinal pneumatosis while submucosal cysts are more commonly seen in colonic pneumatosis as in this case (12). There was not any evidence of small intestinal pneumatosis in plain abdominal X-ray (Figure 3). Endoscopic procedure may report bubble-like pattern, grape or beaded circular forms, linear or cobblestone gas formation and irregular forms. The bubble-like lesions need to be differentiate from intestinal polyps (1,2). Our case had bubble-like and grape patterns. Symptoms may vary depending on the region affected. In a series of 919 patients, small intestinal disease associated symptoms were vomiting, abdominal pain, abdominal distention, weight loss, and diarrhea. In patients with colonic pneumatosis, most frequent symptoms were diarrhea, hematochezia, abdominal pain, distention and prolonged constipation. Other symptoms were flatulence, loss of appetite, and tenesmus, which were reported in our case (12).

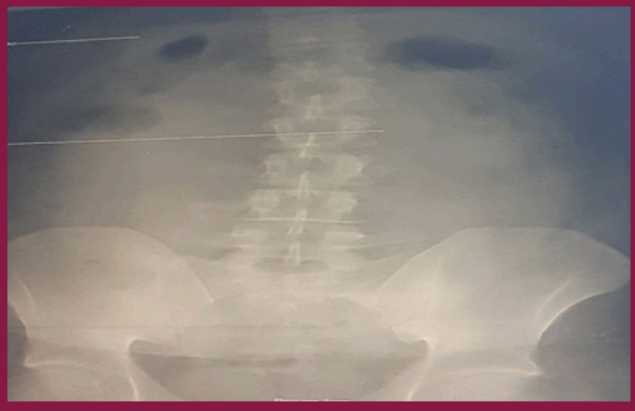

Figure 3. X-ray graphy of the abdomen after colonoscopy

Conclusion

Besides non-specific gastrointestinal symptoms, life-threatening conditions may accompany PCI at presentation. This clinicopathological entity should be taken into consideration in clinical practice.

Ethics

Informed Consent: Written consent was obtained from the patient.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: İ.K., Y.Y., M.K., A.T., Concept: İ.K., Y.Y., M.K., A.T., Design: İ.K., Y.Y., M.K., A.T., Data Collection or Processing: İ.K., Y.Y., M.K., A.T., Analysis or Interpretation: İ.K., Y.Y., M.K., A.T., Literature Search: İ.K., Y.Y., M.K., A.T., Writing: İ.K., Y.Y., M.K., A.T.

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

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

References

1. Heng Y, Schuffler MD, Haggitt RC, Rohrmann CA. Pneumatosis intestinalis: a review. Am J Gastroenterol. 1995;90:1747-1758. [Crossref]
2. Wang YJ, Wang YM, Zheng YM, Jiang HQ, Zhang J. Pneumatosis cystoides intestinalis: six case reports and a review of the literature. BMC Gastroenterol. 2018;18:100. [Crossref]
3. St Peter SD, Abbas MA, Kelly KA. The spectrum of pneumatosis intestinalis. Arch Surg. 2003;138:68-75. [Crossref]
4. Olmsted WW, Madewell JE. Pneumatosis cystoides intestinalis: a pathophysiologic explanation of the roentgenographic signs. Gastrointest Radiol. 1976;1:177-181. [Crossref]
5. Koss LG. Abdominal gas cysts (pneumatosis cystoides intestinorum hominis); an analysis with a report of a case and a critical review of the literature. AMA Arch Pathol. 1952;53:523-549. [Crossref]
6. Nusret A, Seyfettin YAH, Hayrettin Y, Nurullah B. Pnömatozis sistoides intestinalis: olgu sunumu. T Klin J Med Sci. 2002;22:63-66. [Crossref]
7. Kopp AF, Gronewaller E, Laniado M. Pneumatosis cystoides intestinalis with pneumoperitoneum and pneumoretroperitoneum following chemotherapy. Abdom Imaging. 1997;22:395-397. [Crossref]
8. Knechtle SJ, Davidoff AM, Rice RP. Pneumatosis intestinalis. Surgical management and clinical outcome. Ann Surg. 1990;212:160-165. [Crossref]
9. Pieterse AS, Leong AS, Rowland R. The mucosal changes and pathogenesis of pneumatosis cystoides intestinalis. Hum Pathol. 1985;16:683-688. [Crossref]
10. Ellis BW. Symptomatic treatment of primary pneumatosis coli with metronidazole. Br Med J. 1980;280:763-764. [Crossref]
11. Van der Linden W, Marsell R. Pneumatosis cystoides coli associated with high H2 excretion. Treatment with an elemental diet. Scand J Gastroenterol. 1979;14:173-174. [Crossref]
12. Jamart J. Pneumatosis cystoides intestinalis. A statistical study of 919 cases. Acta Hepatogastroenterol (Stuttg). 1979;26:419-422. [Crossref]