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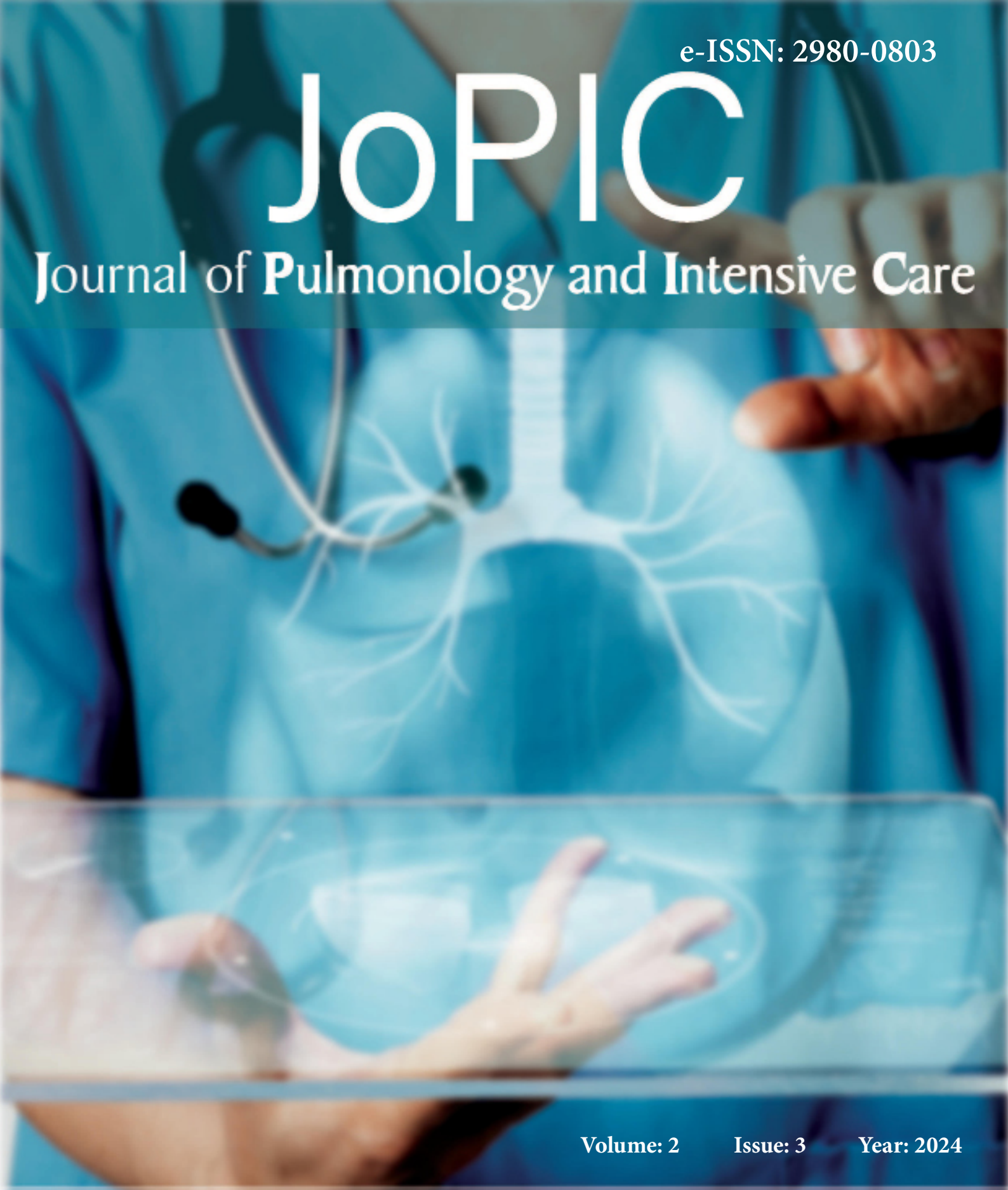

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The relationship between obstructive sleep apnea syndrome severity and vitamin D levels in sera

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ABSTRACT

Aims: Obstructive sleep apnea syndrome (OSAS) is a disorder characterized by complete or partial upper airway obstruction episodes and frequently decreased arterial oxygen saturation. Etiological factors and risk factors of OSAS are still investigated and studies in this topic continue. Until recently, researches were focused on the major effects of vitamin D on the bone metabolism and calcium homeostasis. Today; it has been found that vitamin D plays roles in many cells and tissues of human body additional to its functions in the musculoskeletal system. In our study, we aimed to examine vitamin D levels in patients who are diagnosed as OSAS and to investigate the relationship between OSAS and vitamin D deficiency.

Methods: 83 volunteers, who were suspected to have OSAS, were included in the study. They all underwent polysomnography (PSG) in the sleep disorders center in pulmonary department, between January 2015 – May 2015. Twenty cases with apnea hypopnea index (AHİ) <5/hour were evaluated as simple snoring/control group. Cases with AHİ >5/hour were diagnosed as OSAS; 22 patients were diagnosed as mild, 20 patients were diagnosed as moderate and 21 patients were diagnosed as severe OSAS. Blood samples of these patients were studied for the measurement of vitamin D 25(OH)D3, parathormone (PTH) , calcium (Ca), phosphor (P) levels and the samples were quickly delivered to biochemistry laboratory

Results: A statistically significant difference in vitamin D levels were observed ($p<0.05$) between the control and OSAS groups. However, no statistically significant difference was found in PTH, Ca, P levels among these groups ($p>0.05$). Vitamin D levels in the control group were significantly higher than the mild and the severe OSAS patients. No statistically significant difference was observed in PTH, Ca, P levels between these patients.

Conclusion: Our study indicates that there is a significant relationship between vitamin D deficiency and OSAS. This finding suggests that vitamin D deficiency may play a role in the OSAS physiopathology. There are few studies exists about the association between vitamin D deficiency and OSAS. In this regard, we think our study will contribute to the literature. Moreover; prospective, randomized, controlled studies with large series were needed.

Keywords: Obstructive sleep apnea syndrome, vitamin D, parathormone, calcium, phosphor

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is characterized by recurrent episodes of complete or partial upper airway obstruction during sleep and often a decrease in oxygen saturation in arterial blood.[1] It results in excessive daytime sleepiness, cognitive dysfunctions, and low quality of life.[2] Obesity is the leading risk factor in OSAS, and other risk factors are advanced age, male gender, ethnicity, family history, anatomical anomalies, and impaired respiratory control during sleep.[3,4]

Polysomnography (PSG) is the gold standard for the diagnosis and treatment of OSAS. According to the American Academy of sleeping diseases classification that uses the apnea-hypoapnea index (AHI), OSAS is divided into three categories as mild OSAS (AHI=5-15), moderate OSAS (AHI=15-30), and severe OSAS (AHI >30).[5]

Vitamin D is a fat-soluble vitamin. Unlike other vitamins, it is synthesized in the body and is also called a hormone. Also,

25-Hydroxycholecalciferol 25(OH)D3, which is the product of 25 hydroxylation, is the main circulating form of vitamin D and its levels in human plasma vary between 10-80 ng/ml (25-200 nmol/L). The most important parameter that shows the sufficiency of vitamin D is serum 25(OH)D3 level. Vitamin D and its metabolites have important clinical roles in calcium balance and bone metabolism.[6]

Studies conducted in recent years report that vitamin D has many more functions than its already known effects on calcium, phosphorus, and bone metabolism with its physiological effects on bones, intestines, kidneys, and parathyroid glands. It was reported that vitamin D deficiency plays roles in the development of autoimmune diseases, inflammatory bowel disease, rheumatoid arthritis, multiple sclerosis, diabetes, tonsillar hypertrophy, many cancers, and heart diseases. Also, vitamin D deficiency is reported to be at a high prevalence in patients with Chronic Obstructive Pulmonary Disease (COPD) in recent studies and is stated to cause susceptibility to lung infections.[7,8] It is also among the discussed topics that vitamin D deficiency might predispose individuals to OSAS by causing adenotonsillar hypertrophy, airway muscle weakness, and/or chronic rhinitis.[9] Myopathy and associated widespread muscle pain caused by vitamin D deficiency are also considered to disrupt sleep quality.[7] Based on previous studies, it is expected that as the OSAS severity increases, the calcium and phosphorus levels in the serum will decrease and the parathormone level will increase.

In the present study, the levels of 25(OH)D3, which is the serum form of vitamin D and which was proven to play roles in metabolism and the physiopathology of many diseases, were measured in patients diagnosed with OSAS. PTH, calcium, and phosphorus levels were also evaluated. The study also aimed to investigate whether there is a relationship between OSAS severity and vitamin D deficiency. We believe that the study will contribute to the literature because there are not enough studies on OSAS-vitamin D levels.

METHODS

The study was carried out with the permission of Ethics Committe of the Başkent University Faculty of Medicine (Date: 03.02.2015, Decision No: KA14/311). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The study was conducted within the scope of research project KA14/311 after the approval of the Ethics Committee of Başkent University Researches board between January 2015 and May 2015 with 83 volunteers who were hospitalized for one night at the Sleep Disorders Center of the Department of Chest Diseases and underwent PSG examinations with a preliminary diagnosis of OSAS.

Before the examinations, the identity data, gender, height, and body weight of the individuals were recorded by the technician on duty who would perform the examinations. The body mass index (BMI) of the patients was calculated. The patients were hospitalized at the sleep disorders center for one night and a polysomnographic examination was made with a polysomnography (PSG) device (astro-med grass-telefactor, RI, USA) and 2-channel EEG (C3A2 or C4A1), 2-channel EOG, ECG, EMG recordings (from chin and tibialis anterior muscle), oronasal airflow with thermistor and nasal cannula, thoracoabdominal movements, body position, oxygen saturation from fingertip with pulse oximeter measurements were made.

Patient Groups

The study included 83 cases whose polysomnographic examinations were scored manually, aged between 18 and 75, and did not meet exclusion criteria, considering their AHI values. Those with AHI <5/h were evaluated as the simple snoring/control group. Patients with AHI >5/h were considered OSAS and were grouped according to their stages as follows.

- AHI <5/hour: Simple snoring (20 cases)
- AHI=5-15/hour: Mild OSAS (22 cases)
- AHI=16-30/hour: Moderate OSAS (20 cases)
- AHI >30/hour: Severe OSAS (21 cases)

Exclusion Criteria

Among the patients who were diagnosed with OSAS by polysomnography, those with diseases or medication use known to affect vitamin D and calcium levels (parathyroid disease, sarcoidosis, chronic kidney disease, acute myocardial infarction, chronic liver disease, calcium and/or vitamin D use) were not included in the study.

Laboratory Examinations

Serum samples taken from the cases were quickly delivered to the laboratory without waiting for the study. A total of 25-hydrocholecalciferol, phosphorus, calcium, and parathormone were studied from serum samples and 25-hydroxycholecalciferol was studied with the chemiluminescent microparticle immunoassay (CMIA) method on the "abbott architect i2000" device and the reference value was taken as 9.4-52.4 ng/ml. Phosphorus was examined with the Phosphomolybdate method on the "abbott architect c8000" device and the reference value was taken as 2.3-4.7 mg/dl. Calcium was examined with the arsenazo III method on the "abbott architect c8000" device and the reference value was taken as 8.8-10 mg/dl. Parathormone was examined with the chemiluminescent enzyme immune method on the "intact PTH" device and the reference range was accepted as 15-68.3 pg/ml.

Statistical Analysis

Before the analyses, the suitability of the data to some assumptions was investigated. The "Kolmogorov Smirnov normality test" was used to analyze the suitability of normal distribution, and the "Levene test statistics" were used to test the suitability of the homogeneous variance assumption. In the analysis of the relevant data, the test to be applied was decided by considering whether the assumptions were met and the structure of the data. Descriptive statistics of continuous variables were given as mean ± standard deviation or median (minimum value-maximum value), and descriptive statistics of categorical variables were shown as number of patients and percentage (%). Blood parameters and sleep parameters between the control group and OSAS groups, the one way ANOVA test was used when the assumptions were met for continuous variables, and the Kruskall Wallis H test was used when the assumptions were not met in comparing demographic variables. For the

variables with a significant difference as a result of the one-way ANOVA test, the tukey test and tamhane test were used for pairwise comparisons between the groups, and for the variables with a significant difference as a result of Kruskall Wallis H-test, m Whitney U test was used for pairwise comparisons. Also, the Chi-square test was used to compare categorical variables between groups. The spearman correlation coefficient was used to investigate the relationship between continuous variables. Statistical analyses were performed by using the SPSS Statistics 20.0 statistical package program in the present study and the p values obtained in the test results were evaluated at the 95% confidence level and the α=0.05 significance level.

RESULTS

A total of 20 cases with AHI <5/hour, 22 cases with AHI=5-15/hour, 20 cases with AHI=16-30/hour, and 21 cases with AHI >30/hour were included in the study prospectively among those who underwent PSG. 83 cases were included. Although there were no statistically significant differences between the groups in terms of height and gender (p>0.05), there were significant differences between the groups in terms of age, weight, BMI, and neck circumference (p<0.05) (Table 1).

There were no statistically significant differences between the groups in terms of phosphorus, parathormone, and calcium values (p>0.05). However, a significant difference was detected in terms of vitamin D (p<0.05) (Table 2).

There were no statistically significant differences between the groups in terms of snoring, waking up breathless, nocturia, morning dry mouth, headache, and daytime sleepiness (p>0.05). No statistically significant differences were detected between the groups in terms of the epworth sleepiness scale (ESS), total sleep time, sleep adequacy, maximum SPO_2, minimum heart rate, and maximum heart rate (p>0.05). However, statistically significant differences were detected between the groups in terms of apnea-hypopnea index, apnea index, hypopnea index, arousal index, obstructive apnea count, hypopnea count, total O2 desaturation, oxygen desaturation index, average SPO_2, minimum SPO_2, and SPO_2 <90% residence time (p<0.05).

The values of the four groups were significantly different from each other in terms of apnea index, arousal index, obstructive apnea count, total O_2 desaturation, oxygen desaturation index, and SPO_2<90% stay-fold. Although the control group had the lowest value in terms of the variables, it was found that as the degree of apnea increased among the OSAS groups, other values also increased. Hypopnea index values and hypopnea numbers are similar and at the highest values in the severe and moderate OSAS groups. These parameters were lower in the mild OSAS group than in the severe and moderate OSAS groups and were lowest in the control group.

Average SPO_2 values were similar and highest in the control group and the mild OSAS group, lower in the moderate OSAS group, and lowest in the severe OSAS group. Minimum SPO_2 values were similar in the control group and mild OSAS group. The values of these groups were significantly higher than the severe OSAS group. The values of the control group were significantly higher than those of moderate OSAS. Also, minimum SPO_2 values of moderate and severe OSAS groups were similar. No statistically significant relationships were found between AHI and vitamin D (r=0.031, p=0.791) and PTH (r=0.046, p=0.697). There was no statistically significant relationship between vitamin D and phosphorus, calcium, ODI, SPO_2<90% hospital stay-fold (p >0.05)

Table 1. Patient characteristics in OSAS groups

	Simple snoring n:20	Mild OSAS n:22	Modarate OSAS n:20	Severe OSAS n:21	p
Gender F/M	3 (15 %) / (82 %)	3 (13.6 %) /19(86.4 %)	3 (15 %) /17 (85 %)	3 (14.3 %) /18 (85.7 %)	0.999
Age	40.1±8.4	44.4±11.3	51.1±12.6	50.9±12.4	0.005*
Height (cm)	173.7±7.3	172.7±8.0	173.8±9.5	171.8±8.2	0.857
Weight (kg)	82.3±12	87.2±12.2	90.2±13.7	98.1±15.4	0.0003*
BMI (kg/m²)	27.3±3.6	29.2±3.5	30.1±5.4	33.3±4.9	0*
Neck circumference (cm)	39.1±3.1	39.8±2.7	40.8±2.1	41.8±2.5	0.0009*

OSAS: Obstructive sleep apnea syndrome; BMI: Body mass index. , *p: < 0.05

Table 2. Distribution of laboratory parameters according to OSAS groups

	Simple snoring	Mild OSAS	Moderate OSAS	Severe OSAS	p
Vitamin D (ng/ml)	20.7±13.3	12.7±3.6	15.2±5.5	13.1±6.4	0.037*
Phosphorus (mg/dl)	3.1±0.6	3.5±0.8	3.5±0.6	3.6±0.5	0.115
Parathormone (pg/ml)	45.7±29.6	57.2±22.4	44.7±21.2	64.4±41.9	0.111
Calcium (mg/dl)	9.6±0.3	9.6±0.3	9.5±0.3	9.4±0.3	0.119

OSAS: Obstructive sleep apnea syndrome

DISCUSSION

Although there are many known causes in the pathophysiology of OSAS, its pathogenesis is still not fully elucidated. The factors contributing to OSAS vary from individual to individual, and its pathophysiology is quite complex. It is already known that males are at 2-3-fold higher risk of OSAS than women and similar rates were found in many studies in the literature4 because pharyngeal and supraglottic airway resistance in the upper respiratory tract is higher in men.[2,10,11] The male/female rate was 6/1 in the present study. According to the literature data, we attributed our higher male/female ratio to the fact that women are less likely to visit our clinic with OSAS symptoms such as snoring and apnea and that vitamin D preparations are frequently used in our society, especially in the postmenopausal period, because of their protective effect against osteoporosis, and these cases were thus excluded from the study.

One of the known risk factors regarding OSAS is age. It is most common between the ages of 40-65 and plateaus after the age of 65. The reason for this increase with age has not been fully elucidated, but it is considered that the effect of aging on body fat distribution, tissue elasticity, ventilation control, and pulmonary and cardiovascular functions plays roles, and increasing comorbidities in old age also increase the tendency to URI obstructions. The average age was similar in the control group and mild OSAS group in the present study, but significantly higher in the moderate and severe OSAS group when compared to the control group.

One of the known and most common risk factors for OSAS is obesity.[12] It is already known that the frequency of OSAS increases as BMI increases. In the OSAS study of Nieto et al.[13] conducted with 6132 cases, in which demographic characteristics and the presence of hypertension were questioned, it was found that BMI levels were correlated with AHI values, and as AHI increased, BMI also increased.

As it is already known, obesity is a major risk factor for OSAS and causes vitamin D deficiency. One of the reasons might be the decreased ability of obese individuals to go out because of their physical appearance and, as a result, the decrease in vitamin D synthesis. Another reason might be the increase in the active metabolite 1.25(OH)2D3, which acts on the liver with negative feedback and reduces the production of 25(OH)D3. Also, vitamin D, which is a fat-soluble molecule, accumulates in excess amounts in the fatty tissue in obese individuals, and thus its amount in circulation decreases.14 However, some studies examined the relationships of both OSAS and vitamin D deficiency with Type 2 diabetes mellitus and metabolic syndrome, separately from each other.

Neck circumference is also an important risk factor for OSAS. If the neck circumference is >43 cm in men and 38 cm in women, it increases the risk.[25] Neck circumference measurement shows the soft and fatty tissue in the URI. Fat tissue accumulates mostly in the lateral pharyngeal wall and lateral pharyngeal fat pads.[15] In hoffstein and mateika's study, neck circumference was found to be significantly higher in the OSAS group than in the control group (42.7 cm and 38.4 cm, respectively).[16] In another study conducted by Uyar et al.[17] in our country to examine the clinical profiles of patients with OSAS, they found the neck circumference to be 41 cm in the mild OSAS group, 42.8 cm in the moderate OSAS group, and 45.5 cm in the severe OSAS group. In the present study, the mean neck circumference showed a positive correlation with AHI values and was statistically significantly higher in the severe OSAS group than in the control group. In our study, patients diagnosed with OSAS had larger neck circumferences compared to the control group, which was consistent with literature data.Vitamin D regulates calcium and phosphorus metabolism and exerts this effect on the parathyroid glands, kidneys, bones, and intestines.[18,19] It also regulates bone mineralization and calcium homeostasis by showing a synergistic effect with PTH.[20] Until recently, the emphasis was placed on the major effects of vitamin D (especially on bone metabolism and calcium and phosphorus homeostasis). In our present day, after the discovery that vitamin D is present in many tissues and cells of the body, it is not understood that it has many functions other than the musculoskeletal system. Vitamin D receptors (VDR) are found in almost all tissues (i.e., heart, breast, skin, brain, pancreas, lymphocytes, etc.) except target organs such as bone, kidney, and intestine, which proves that vitamin D has many other functions besides its known functions. The main functions of these are the regulation of immune functions, cell profiling and differentiation, and hormone secretion.

Studies conducted on the functions of vitamin D continue today. The relationship between obstructive sleep apnea syndrome (OSAS) and vitamin D is a recently researched topic, and there are several studies on this subject.[21-25] Particular attention is being paid to whether vitamin D deficiency is involved in the etiology of OSAS and whether it contributes to the severity of OSAS.[21] In a previous review by McCarty et al.,[26] the relationship between vitamin D deficiency and sleep disorders was discussed, and it was reported that the deficiency of this vitamin might be involved in the etiology of OSAS and other sleep disorders through different mechanisms. It was also emphasized that vitamin D deficiency, which develops because of various reasons, causes bone pain secondary to bone demineralization. Bone pain causes sleep disruptions and insufficient sleep, causing daytime fatigue and physical inactivity in people, and prepares the ground for obesity in the future, indirectly creating a risk factor for OSAS. In the same review, it was also emphasized that myopathy caused by vitamin D deficiency was directly and indirectly involved in the physiopathogenesis of OSAS. It paves the way for obesity through similar mechanisms and constitutes a risk factor for OSAS by indirectly causing peripheral muscle pain. It directly causes weakness in the upper respiratory tract muscles as a result of myopathy and is involved in the etiology of OSAS. Recently, aside from the known effects of vitamin D, its functions in the immune system have also been emphasized. Studies report that vitamin D deficiency causes immune dysfunction. Immune system dysfunction causes tonsillar hypertrophy, which paves the way for upper airway obstruction and thus constitutes a risk factor for OSAS. It is already known that immune dysfunction causes upper respiratory tract infection, allergy, and systemic inflammation, which predisposes to chronic rhinitis in the future, which in turn constitutes a risk factor for OSAS.

There are few studies conducted in the literature examining the relationships between vitamin D and OSAS, which are summarized in Table 3. Some studies speculated that vitamin D deficiency is secondary to OSAS, and some studies argued that OSAS is secondary to vitamin D deficiency. Mete et al.[27] examined the relationships between OSAS and vitamin D deficiency and reported that vitamin D was significantly lower in the severe OSAS group than in the other groups. It has been argued that this finding might be because of several different mechanisms (one of which is associated with TNF-α, an inflammatory marker). TNF-α is observed at high levels throughout the day in OSAS, which is an inflammatory process. In a previous study that was conducted by Peterson et al.,[21] a negative correlation was found between serum vitamin D levels and TNF-α levels. On the other hand, decreased ability to go outside in patients with OSAS because of daytime sleepiness and therefore restricting sun exposure was shown to be a reason for vitamin D deficiency. It was also emphasized that hypoxemia caused by OSAS might also cause vitamin D deficiency. In the same study, parathormone,

Table 3. Polysomnography parameters in OSAS groups

	Simple snoring n:20	Mild OSAS n:22	Moderate OSAS n:20	Severe OSAS n:21	p
Epworth sleepiness scale	5.9±2.9	7.9±4.7	7.9±5.2	6.8±4.4	[a]0.406
Snore	20 (% 100)	21 (% 95.5)	20 (%100)	21 (%100)	[c]0.507
Waking up unable to breathe	9 (%45)	11 (% 50)	9 (%45)	17 (%81)	[c]056
Notruria	9 (%45)	8 (% 36.4)	9 (%45)	11 (%52.4)	[c]0.772
Morning mouth dryness	12 (%65)	14 (% 63.6)	9 (%45)	16 (%76.2)	[c]0.259
Headache	14 (% 70)	9 (%40.9)	10 (%50)	8 (%38.1)	[c]0.164
Daytime sleepiness	12 (% 60)	10 (%45.5)	10 (%50)	11 (%52.4)	[c]0.820
TST	344.8+55.6	332.8±52.6	328.1±40.2	313.6±73.8	[a]0.375
Sleep adequacy %	82.4±11.4	81.5±10.8	84.1±9.9	77.6±17.1	[a]0.404
AHI	1.1 0-4.9)	9.4 (5.4±14.3)	19.9 (15.2-29.1)	59.7 (32.9-109.1)	[b]0*
Apnea index	0 (0-06)	0.7 (0-3.1)	2.1 (0-8.16)	42.5 (1.1-105)	b0*
Hypopnea index	0.9 (0-4.7)	7.4 (4.2-13.5)	16.1 (5.2-25.8)	19.4 (2.8-64.7)	[b]0*
Arousal Index	6.8 (1.6-14.2)	11.8 (3.5-21.6)	16.4(4.5-28.8)	42.5 (1.1-101.2)	[b]0*
Obstructive apnea number	0 (0-3)	3 (0-13)	10.5 (0-69)	157 (6-353)	[b]0*
Hypopnea number	5.5 (0-25)	44 (19-88)	91.5 (29-140)	127 (12-395)	[b]0*
Total O_2 desaturation	5 (0-14)	25.5 (13-59)	67.5 (26-111)	219 (97-523	[b]0*
ODI	0.6 (0-2.1)	3.9 (2-8.6)	10.5 (4.1-17.8)	32.5 (15-76.3)	[b]0*
Average SPO_2	94.3±1.8	93.0±2.1	91.2±2.4	88.8±3.9	[b]0*
Minimum SPO_2	87.6±8.8	78.5±12.2	75.9±10.8	68.4±12.9	[b]0*
Maximum SPO_2	98.3±0.7	97.9±1.1	97.6±1.9	97.6±0.9	[a]0.199*
SPO_2 <90% stay time	0.22 (0-20.7)	3.8±(0-82.9)	18.3 (1-99.5)	64.6 (11.4-96.2)	[b]0*
Minimum heart rate	52±11	50.6±7.0	51.5±8.9	50.0±7.2	[a]0.886
Maximum heart rate	108.3±12.9	99.4±9.7	99.1±11.1	100.3±15.6	[a]0.68

OSAS: Obstructive sleep apnea syndrome TST: Total sleep duration; AHI: Apnea hypopnea index; ODI: Oxygen desaturation index. *p: < 0.05 , a: Anova, b: Kuruskall wallis H, c: Chi square test

phosphorus, and calcium levels were compared in the OSAS and control groups, and no significant differences were reported, as in our study. In another study conducted by Bozkurt et al.,[22] where vitamin D levels and glucose metabolism disorders in OSAS were compared, they showed that vitamin D levels decreased as AHI values increased. They found the vitamin D levels to be below 20 ng/ml in all groups, which they attributed to seasonal reasons because they conducted the study in the winter months. The adverse effects of vitamin D deficiency on glucose metabolism in OSAS were investigated in the present study. For this reason, it was argued that giving vitamin D to cases with OSAS might prevent abnormal glucose metabolism and inflammation. In a study by Barceló et al.,[23] where diabetes, obesity, hypertension, and metabolic syndrome components and vitamin D levels were compared in patients with OSAS, statistically significant relationships were found between obesity, hypertriglyceridemia, metabolic syndrome, and vitamin D deficiency. It was observed that vitamin D levels were lower in the severe OSAS group than in the other groups, but the difference was not statistically significant. They also argued that vitamin D deficiency might be a result of OSAS and that in obese individuals with OSAS, this fat-soluble vitamin might accumulate in adipose tissue and cause deficiency in serum emphasizing that obese individuals with OSAS go out less because of immobility and that vitamin D deficiency might occur because of reduced sunlight exposure. In the same study, it was also stated that parathormone increased as AHI values increased, and they considered that this was secondary to low vitamin D. In a previous study conducted by Erden et al.,[24] it was found that as AHI values increased in individuals with OSAS, vitamin D levels decreased, and vitamin D levels in the moderate and severe OSAS group were statistically and significantly lower than the control group. One of the known causes of vitamin D deficiency is old age, and in their study, they stated that the average age of the severe OSAS group was higher than in other groups, and they considered advanced age to be the cause of vitamin D deficiency. They also examined parathormone, calcium, and phosphorus levels and found the values to be similar between the groups, which is similar to our study. In a study by Gozal et al.,[25] vitamin D levels were compared in obese and normal-weight children with and without OSAS in the pediatric population. They found the lowest mean levels of vitamin D in children with OSAS who were obese. They also reported a negative correlation between AHI values and vitamin D and underlined that vitamin D deficiency causes an inflammatory process and increases inflammation in OSAS. They attributed the reason why vitamin D deficiency is more common in obese children to the relationship of both processes with insulin resistance. McCarty et al.[28] examined the relationship between EUS and vitamin D levels in 81 patients who applied to a sleep center with sleep problems and nonspecific pain. They found a negative correlation between vitamin D levels and EUS scores in individuals without vitamin D deficiency. When they divided the group with vitamin D deficiency into black and white races, they reported that EUS scores were higher in the black race, but they did not detect any correlations between EUS and vitamin D deficiency in both races. They also found lower vitamin D levels in black people and considered that this difference between races might be because of the difference in skin pigmentation, underlined that this was the first study in the literature examining the relationship between EUS and vitamin D deficiency, and stated that studies with larger study groups were needed. Liguori et al.[29] compared their patients who were diagnosed with OSAS with the control group and found that vitamin D was significantly higher in the control group. They applied CPAP treatment for 7 days to patients diagnosed with severe OSAS, and while post-treatment vitamin D levels were found to increase significantly in men, this increase was not detected in women. They considered that this difference between men and women might be because of the complex effects of sex hormones on vitamin D.

Snoring is among the most common symptoms that bring OSAS patients to the doctor. Snoring is observed in 70-95% of patients with obstructive sleep syndrome.[30] The most common symptom was snoring in our study. Snoring was detected as 100% in the control group, 95.5% in the mild

OSAS group, 100% in the moderate OSAS group, and 100% in the severe OSAS group.

Other symptoms of obstructive sleep apnea syndrome are daytime sleepiness, morning dry mouth, morning headache, waking up unable to breathe, and nocturia. We did not detect a statistically significant difference between the groups in these symptoms, which were questioned in our study. Total sleep time (TST) is the time spent asleep during a PSG recording, and it might decrease or remain normal in individuals with OSAS. The TST and sleep adequacy in the severe OSAS group were lower than the other groups in our study, but no statistically significant difference was found between the groups.

The lowest heart rate in ECG during sleep recording is called the minimum heart rate, and the highest heart rate is called the maximum heart rate. It is already known that bradyarrhythmias will occur during apnea as a result of increased parasympathetic activation in individuals with obstructive sleep apnea syndrome, and compensatory tachyarrhythmias will occur during the postapneic period. In a study conducted by Akdoğan to examine the heart rate variability in patients with OSAS, no statistically significant difference was detected between the minimum and maximum heart rates between the control group and patients with OSAS, and many other factors that affect the heart rate (age, gender, comorbidities, obesity, etc.) In our study, no statistically significant differences were found between the groups in terms of minimum and maximum heart rate.

It was found in the present study that as the OSAS severity increased, the apnea index, hypopnea index, arousal index, obstructive apnea number, hypopnea number, total oxygen desaturation, duration of saturation below 90%, and oxygen desaturation index increased. Also, in line with the literature data, it was found that as AHI values increased, minimum SPO_2, maximum SPO_2, and average SPO_2 values decreased.

Limitations

The factors limiting the study were that the total number of patients and the distribution between groups were lower compared to the literature because the study was conducted in a limited time. Another limiting factor was that the study was conducted between January and May, a period when sunlight is low in our country. Another limiting factor was that patients' daily vitamin D intake was not determined through diet. We would like to underline that in our literature review, we could not find a validated survey to show adequate vitamin D intake. For this reason, we are aware that we cannot fix this variable. The same limiting factor is seen in all studies. We believe that the cause of vitamin D deficiency in patients with OSAS will be revealed more clearly with future validated survey studies determining dietary vitamin D intake.

CONCLUSION

In conclusion, in the present study in which the relationships between vitamin D and OSAS were examined, it was found that vitamin D levels were significantly lower in patients with OSAS than in the control group. We think that the study contributed to the few studies on this subject in the literature. However, we believe that larger series, prospective, randomized, controlled clinical studies are needed to better elucidate the mechanism of vitamin D deficiency on OSAS. We would also like to point out that controlled studies to investigate the success of vitamin D replacement therapy in patients with excessive daytime sleepiness might open a new page in the treatment of OSAS.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Ethics Committe of the Başkent University Faculty of Medicine (Date: 03.02.2015, Decision No: KA14/311).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

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

REFERENCES

1. Buysse DJ. International classification of sleep disorders, version 2: diagnostic coding manual. American Academy of Sleep Medicine, Rochester. 2005.
2. Silva GE, Goodwin JL, Vana KD, Quan SF. Obstructive sleep apnea and quality of life: comparison of the SAQLI, FOSQ, and SF-36 questionnaires. *Southwest J Pulm Crit Care*. 2016;13(3):137-149.
3. Al Lawati NM, Patel SR, Ayas NT. Epidemiology, risk factors, and consequences of obstructive sleep apnea and short sleep duration. *Prog Cardiovasc Dis*. 2009;51(4):285-293.
4. Young T, Skatrud J, Peppard PE. Risk factors for obstructive sleep apnea in adults. *JAMA*. 2004;29(16):6.
5. Iber C. Israel AS, Chesson AL, Quan SF. The AASM manual for the scoring of sleep and associated events. Rules, terminology and technical specifications. 1st ed: wenchester, Illıonis: American Academy of Sleep Medicine. 2007.
6. Yavuz D, Mete T, Yavuz R, Altunoğlu A. D Vitamini, kalsiyum, mineral metabolizması, D vitaminin iskelet dışı etkileri ve kronik böbrek yetmezliğinde nütrisyonel D vitamini kullanımı. *Ankara Med J*. 2014;14(4):162-171.
7. Skaaby T, Husemoen LLN, Thuesen BH, et al. Vitamin D status and chronic obstructive pulmonary disease: a prospective general population study. *PloS one*. 2014;9(3):90654.
8. Persson LJP, Aanerud M, Hiemstra PS, et al. Chronic obstructive pulmonary disease is associated with low levels of vitamin D. *PLoS One*. 2012;7(6):38934.
9. David E, McCarty M, Andrew L et al. The link between vitamin D metabolism and sleep medicine. *Sleep Med Rev*. 2014;18(4):311-319.
10. Jennum P. SjØl A. Epidemiology of snoring and obstructive sleep apnoea in a danish population, age 30–60. *J sleep Res*. 1992;1(4):240-244.
11. Çiftçi B. Bakmak ve görmek; uykuda solunum bozukluğu-hekim farkındalığı. *Solunum Hastalıkları Derg*. 2009;19(3):95-98.
12. Banno K, Kryger MH. Sleep apnea: clinical investigations in humans. *Sleep Med Rev*. 2007;8(4):400-426.
13. Nieto FJ, Young TB, Shahar E, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. *JAMA*. 2000;283(14):1829-1836.

14. Sözen T. D hormon: güncel gelişmeler. *Hacettepe Tıp Derg.* 2011;42(1): 14-27.
15. Köktürk O. Obstrüktif uyku apne sendromu fizyopatolojisi. Turk Toraks Derneği merkezi kurslar. *Turk Thorac J.* 2007;27(1)71-82.
16. Hoffstein V, Mateika S. Differences in abdominal and neck circumferences in patients with and without obstructive sleep apnoea. *Eur Respir J.* 1992;5(4):377-381.
17. Uyar M, Elbek O, Aydın N, et al. Clinical profiles of obstructive sleep apnea syndrome. Turk Thorac J. 2008;9(3):113.
18. Holick MF. McCollum award lecture, 1994: vitamin D-new horizons for the 21st century. *Am J Clin Nutr.* 1994;60(4):619-630.
19. Jameson JL, Weetman AP. Tiroid bezi hastalıkları. Harrison İç hastalıkları prensipleri (15. Edisyon). İstanbul: Nobel Matbaacılık. 2004;4(1):2060-2075.
20. Bordelon P, Ghetu MV, Langan R. Recognition and management of vitamin D deficiency. *Am Fam Physician*. 2009;15(80):841-846.
21. Mete T, Yalçın Y, Berker D, et al. Obstructive sleep apnea syndrome and its association with vitamin D deficiency. *J Endocrinol Invest*. 2013;36(9):681-685.
22. Bozkurt NC, Çakal E, Şahin M, et al. The relation of serum 25 hydroxyvitamin D levels with severity of obstructive sleep apnea and glucose metabolism abnormalities. *Endocrine*. 2012;41(3):518-525.
23. Barcelo A, Esquinas C, Pierola J, et al. Vitamin D status and parathyroid hormone levels in patients with obstructive sleep apnea. *Respiration*. 2013;86(4):295-301.
24. Erden ES, Genc S, Motor S, Investigation of serum bisphenol A, vitamin D, and parathyroid hormone levels in patients with obstructive sleep apnea syndrome. Endocrine. 2014;45(2):311-318.
25. Kheirandish Gozal L, Peris E, Gozal D. Vitamin D levels and obstructive sleep apnoea in children. Sleep Med. 2014;15(4):459-463.
26. Udwadia ZF, Doshi AV, Lonkar SG. Singh C.I. Prevalence of sleep disordered breathing and sleep apnea in middle-aged urban Indian men. *Am J Respir Crit Care Med*. 2004;169(2):168-173.
27. Peterson CA, Heffernan ME. Serum tumor necrosis factor-alpha concentrations are negatively correlated with serum 25 (OH) D concentrations in healthy women. *J Inflamm*. 2008;24(5):10.
28. McCarty DE, Reddy A, Keigley Q, et al. Vitamin D, race, and excessive daytime sleepiness. *J Clin Sleep Med*. 2012;8(6):693-697.
29. Liguori C, Romigi A, Izzi F, et al. Continuous positive airway pressure treatment increases serum vitamin D levels in male patients with obstructive sleep apnea. *J Clin Sleep Med*. 2015;15(11):603-607.
30. Schlosshan D, Elliott MW. Sleep. 3: Clinical presentation and diagnosis of the obstructive sleep apnoea hypopnoea syndrome. *Thorax*. 2004;59 (4):347-352.

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Frightening symptom hemoptysis: analysis of etiology, mortality, and treatment outcomes in a large cohort from the chest disease center in Turkiye

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ABSTRACT

Aims: Hemoptysis can indicate serious, potentially life-threatening conditions. The etiology varies by region and can include tuberculosis (TB) in developing countries and malignancies in developed regions.

Methods: This retrospective cohort study reviewed medical records of 400 hospitalized hemoptysis patients between June 2012 and March 2016. Data collected included patient demographics, comorbidities, hemoptysis volume, diagnostic tests, treatments, and outcomes. Survival rates and readmissions were tracked for 2-6 years post-discharge.

Results: Of the 400 patients, 88 (22%) were female and 312 (78%) were male. The leading causes of hemoptysis were bronchiectasis (14%), sequela of tuberculosis (TB sequelae; 19%), and malignancy (22.8%). The most common causes in male patients were lung cancer (27.2%) and TB sequelae (21.8%). Bronchiectasis accounted for 28.4% of cases in female patients, followed by drug-induced hemoptysis at 14.8%. The in-hospital mortality rate was 1% (n=4), with severe hemoptysis present in all four patients who died during admission for hemoptysis. The 2–6-year survival rate was 70.8% for women and 56.1% for men (p=0.005). The factors found to significantly worsen mortality risk were lung malignancy, age >65, diabetes, and chronic obstructive pulmonary disease (COPD).

Conclusion: Overall, lung cancer was found to be the leading cause of hemoptysis, with bronchiectasis being the leading cause in female patients and malignancy in male patients. Close monitoring of male patients is crucial due to higher mortality risk. Careful assessment of patients with hemoptysis having comorbidities such as diabetes and COPD is required due to the reduced survival rates associated with these conditions. Early detection and intervention for lung cancer are essential to optimize the prognosis of affected individuals.

Keywords: Hemoptysis, malignancy, survival rate

INTRODUCTION

Any instance of hemoptysis should be considered serious with prompt evaluation and treatment as it might indicate a life-threatening condition.[1] The etiology of hemoptysis and the percentage of cases attributable to each cause varies. Factors associated with these differences include the geographical region, the quantity of bleeding, and diagnostic techniques used.[2] Previous research has shown that hemoptysis is predominantly caused by tuberculosis (TB) and its effects in developing countries such as India.[3] However, in developed countries, hemoptysis is mostly caused by cancer. This may be due to the general increase in the prevalence of cancer, modern industrial lifestyle, higher use of tobacco products, and greater exposure to environmental toxins in these countries.[2,4]

The diagnosis of hemoptysis requires a comprehensive approach and includes recording the medical history, physical examination, laboratory tests, and the use of imaging modalities such as chest X-ray, computed tomography (CT), and bronchoscopy.[1] Use of some of these methods is contingent upon the resources of each health center, the proficiency of the treating clinician, and the stability of the patient's condition. Bronchoscopic procedures are crucial for patients who require airway control. Utilizing CT and bronchoscopy increases the likelihood of identifying the underlying cause of a patient's hemoptysis.[1,5] Hemoptysis management is determined by the severity of the bleeding and root cause.[6] It is crucial to prioritize the protection of the airway in patients

experiencing hemoptysis. Therefore, an interdisciplinary treatment approach is required. Antifibrinolytic medications are recommended for mild bleeding, while more severe cases may require therapies such as fiberoptic bronchoscopy (FOB) and local topical vasoconstrictive agents such as epinephrine or balloon blockers.[1,7] Moreover, bleeding can be mitigated by utilizing interventional techniques such as bronchial artery embolization (BAE), therapeutic bronchoscopic procedures, surgery, or a combination of these approaches.[6,7] Several studies have demonstrated that endobronchial treatment and BAE have a positive impact on patient survival.[8,9]

This study aimed to investigate various hemoptysis etiologies, evaluate the efficacy of current diagnostic testing methods, explore treatment options, and identify the factors that affect mortality risk. Our broader objective was to contribute to and enhance our current comprehension of the diverse hemoptysis etiologies and the therapeutic approaches to treatment. Our secondary objective was to identify differences between the sexes that might potentially contribute to the development of more personalized treatment plans. Timely identification and management of hemoptysis can substantially impact patient prognosis and life-threatening ramifications.

METHODS

The study was carried out with the permission of the İstanbul Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital Ethics Committee (Date: 21.06.2016 Decision No: 2016/26). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. In this. In this single-center retrospective cohort study, the medical records of 7.076 patients presenting to the emergency department with hemoptysis were comprehensively evaluated. From this group, a cohort of 452 patients hospitalized for hemoptysis between June 2012 and March 2016 was identified. Fifty-two patients were excluded from the study due to the absence of a postero-anterior chest X-ray or because they were under 18 or over 90 years old. As a result, the final sample consisted of 400 patients who were hospitalized with primary complaints of hemoptysis over a 4-year period. The study design is summarized in the flowchart shown in Figure 1.

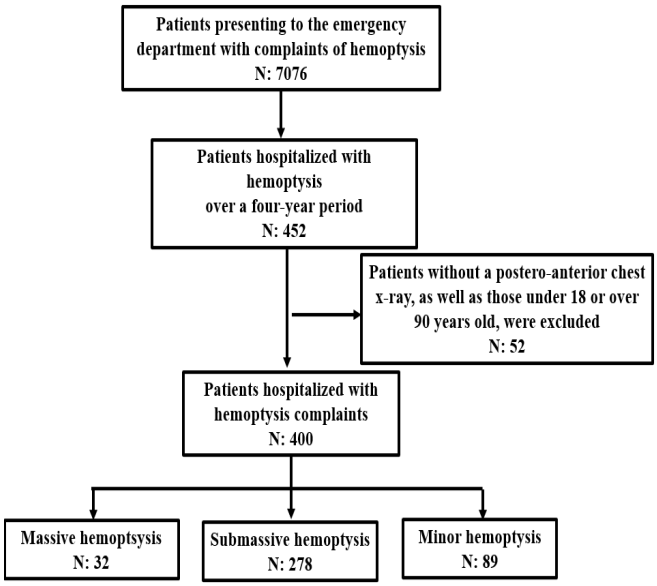

Figure 1. A flowchart presenting an overview of the study design is provided.

Participants' gender, age, medical histories, prescriptions, drug use (including anticoagulants, vitamin K antagonists, and platelet antiaggregant), test findings, history of hemoptysis, and treatment were all examined. Chest X-rays and, if available, chest CT scan results were documented. Hemoptysis was classified into three categories based on blood expectoration: minor (<50 ml/day), submissive (50–200 ml/day), and massive (>200 ml/day). For hemoptysis, patients received conservative treatment with antitussives, antibiotics, and tranexamic acid (TXA). In addition, the fundamental cause such as, tuberculosis was treated in accordance with the disease's care regimen. In other situations, supportive treatments such as airway protection, the placement of an endotracheal tube, and the administration of blood products were employed alongside invasive procedures such as endobronchial therapy with FOB or rigid bronchoscopy (RB), BAE, and surgery.

Patients diagnosed based on the findings of investigations and disease histories were documented. If a diagnosis could not be established by CT or diagnostic testing and the patient was taking anticoagulants or antiplatelets, the cause of hemoptysis was assumed to be drug-induced. All patients with unexplained hemoptysis and normal radiologic imaging were classified as having "cryptogenic hemoptysis." All in-hospital deaths from hemoptysis were recorded. The survival rates and frequency of hospital readmission for post discharge hemoptysis were tracked.

The patients were followed up for 2–6 years after they were discharged by analysis of their hospital registry records. The hospital's death notification system records for 2018 was used to determine the survival rates among our cohort. The endpoint for overall survival was death from all causes. During the follow-up period, any hospital readmissions due to post discharge hemoptysis we also documented. This data gathered shed light on the long-term prognoses of patients with hemoptysis.

Statistical Analysis

Was carried out using IBM SPSS Statistics for Windows version 23 (IBM Corp., Armonk, NY, USA). Categorical variables were examined using frequency distributions, while numerical variables were studied using descriptive statistics (mean, standard deviation, and median IQR). Categorical variables were compared using the chi-square and Fisher's exact tests. The Kaplan–Meier approach was used to determine survival rates. The log-rank test was used to identify the independent effects on overall survival. Cox regression was used to determine the effect of all covariates on overall survival. A p-value <0.05 was considered statistically significant.

RESULTS

Overall, 400 patients aged 18-90 years who were hospitalized for hemoptysis between June 2012 and March 2016 were included in this study. Of these patients, 312 (78%) were male and the mean age was 55.34±16.09 years (range 18-89). The most common comorbidities were hypertension (n=85, 21.3%) and chronic obstructive pulmonary disease (COPD) (n=65, 16.3%). Tuberculosis and malignancy were more prevalent in the male group (p <0.001, p=0.015), whereas asthma and bronchiectasis were more common in the female group (p=0.008, p=0.003) as etiologies of hemoptysis. A smoking

history was reported in 295 of the 400 (73.7%) patients, with a statistically higher prevalence in male patients than in female patients (n=203.65%; n=29.33%, respectively; p <0.001).

Of the total patients, 69.7% (n=278) presented with submissive hemoptysis, 22.3% (n=89) had minor hemoptysis, and 8% (n=32) had massive hemoptysis. Malignancy was the most common etiology in massive and minor hemoptysis groups, whereas TB sequela was the most common etiology in the submissive hemoptysis group. The most common histologic type of lung cancer was squamous cell carcinoma (27.4%). The demographic characteristics of the patients are shown in Table 1.

Malignancy was the most common cause of hemoptysis in the entire patient group (n=91, 22.8%), followed by TB sequela (n=76, 19%) and bronchiectasis (n=56, 14%). The etiologies of hemoptysis are shown in Table 2.

Table 1. Demographic and clinical characteristics of patients with hemoptysis

Characteristic	n	%
Sex, male	312	78.0
Age in years (median ± SD)	55.34 ± 16.09	
Comorbidities		
Hypertension	85	21.3
COPD	65	16.3
Coronary artery disease	49	12.3
Diabetes mellitus	42	10.5
Tobacco use (current and former)	295	73.7
Male	203	65.0
Female	29	33.0
Tuberculosis history	103	25.8
Drug use		
Vitamin K antagonist	24	6.0
Acetylsalicylic acid	28	7.0
Others	10	2.5
More than one	6	1.5
Amount of bleeding		
Submassive	278	69.7
Massive	32	8.0
Minor	89	22.3
Recurrent hospitalization	101	25.3

COPD: Chronic obstructive pulmonary disease; SD: Standard deviation

Table 2. Hemoptysis etiologies

Etiological diagnosis	n	%
Malignancy	91	22.8
Tuberculosis sequela	76	19.0
Bronchiectasis	56	14.0
Drug-induced	43	10.8
Active tuberculosis	27	6.8
Pneumonia	17	4.3
Pulmonary embolism	10	2.5
Hemorrhagic diathesis	7	1.8
Anthracosis	5	1.3
Foreign body aspiration	4	1.0
Aspergilloma	2	0.5
Acute bronchitis	2	0.5
Sarcoidosis	2	0.5
Cryptogenic	63	15.7

The most common etiologies of hemoptysis in female patients were bronchiectasis (n=25, 28.4%), drug-induced etiologies (n=13, 14.8%), and TB sequela (n = 8, 9.1%). In male patients, malignancy (n = 85, 27.2%), TB sequelae (n=68, 21.8%), and bronchiectasis (n=31, 9.9%) were the most frequent causes of hemoptysis. Different etiologies according to sex are described in Table 3. Drug-induced hemoptysis was noted in 68 of the 400 (17%) patients, making it the second most common etiology in female patients (14.8%) and the fourth most common etiology in male patients (9.6%). Obvious cause of hemoptysis was not found in 63 patients (15.7%) (cryptogenic).n total, 25% of patients required rehospitalization, and the most common etiologies of hemoptysis in these cases were TB sequelae (n=31, 30.7%) and malignancy (n=24, 23.8%).

Table 3. Relationships between etiological diagnosis and sex in patients with hemoptysis

	Female		Male		
Diagnosis	**n**	**%**	**n**	**%**	**p***
Bronchiectasis	25	28.4%	31	9.9%	<0.001
Tuberculosis sequelae	8	9.1%	68	21.8%	0.007
Malignancy	6	6.8%	85	27.2%	<0.001
Acute bronchitis	2	2.3%	0	0.0%	0.008
Drug-induced	13	14.8%	30	9.6%	0.17
Active tuberculosis	5	5.7%	22	7.1%	0.65
Pneumonia	4	4.5%	13	4.2%	0.88
Pulmonary embolism	4	4.5%	6	1.9%	0.16
Hemorrhagic diathesis	2	2.3%	5	1.6%	0.67
Anthracosis	2	2.3%	3	1.0%	0.33
Foreign body aspiration	1	1.1%	3	1.0%	0.88
Aspergilloma	0	0.0%	2	0.6%	0.45
Sarcoidosis	1	1.1%	1	0.3%	0.34
Cryptogenic	17	19.3%	46	14.7%	0.30

The p-values for those etiological diagnoses significantly associated with sex are shown in bold.

All patients in our sample underwent a chest X-ray and 69.8% (n=279) exhibited radiologic abnormalities. Of the 400 patients, 334 also underwent a chest CT scan and radiologic abnormalities were detected in 79.2% of these individuals. Abnormal findings were identified in 65.7% of the 202 patients who underwent FOB, and 89.5% of the 19 patients who underwent RB. A confirmed diagnosis was made using chest X-rays in 64.5% of the patients, chest CT in 83.6%, FOB in 24.8%, RB in 52.6%, and a combination of FOB and chest CT in 84.7%. Diagnosis of the cause of their hemoptysis was made in 84.7% of the patients, with the highest rate of diagnostic success achieved using a combination of CT and bronchoscopy.

Medications were used to treat 88.8% of the patients (n=355), whereas 6.5% (n=26) underwent BAE, 1.7% received endobronchial treatment, and 1.3% (n=5) underwent surgery for bleeding control. BAE was performed in 34 patients, and the most common etiology of hemoptysis in this group was TB sequela (n=16, 47%). The BAE's success rate in stopping bleeding was 76.5%. The rate of bleeding recurrence was higher in patients with hemoptysis caused by TB sequelae (n=31, 30.7%) and malignancy (n=24, 23.8%). Eleven patients underwent surgery to treat hemoptysis. Lobectomy was performed in 2.0% (n=8), pneumonectomy in 0.5% (n=2) and lung wedge resection in 0.3% (n=1). Hemoptysis was controlled with surgical treatment in five patients (one malignancy, one anthracosis, two aspergilloma, and one foreign body aspiration).

In total, 1% of patients (n=4) died during hospitalization, all with massive hemoptysis. The 2-6 year overall survival rate was 70.8% (95% confidence interval (CI): 60-81.6) in women and 56.1% (95% CI: 50.2-62) in men (p=0.005) (Figure 2). In this patient population, the analysis also identified several risk

factors associated with mortality, including malignancy, age >65 years, COPD history, and diabetes history. The hazard ratios, *p*-values, and 95% CIs for all covariables are displayed in Table 4.

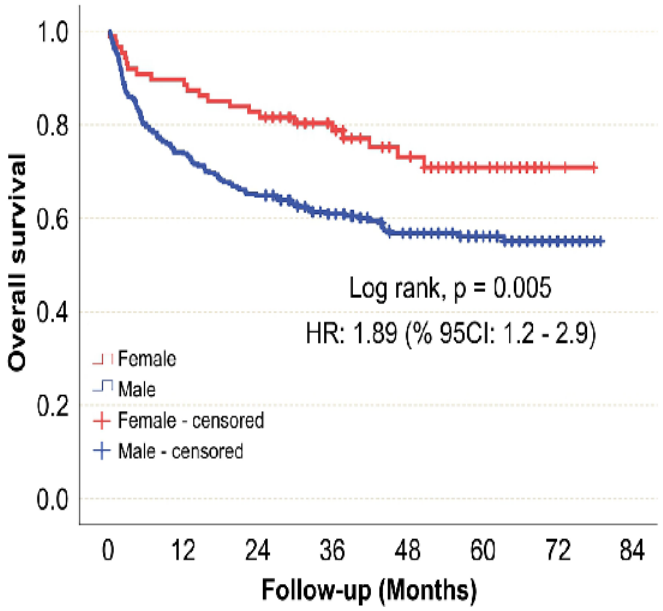

Figure 2. Cumulative hemoptysis survival rates of women and men calculated using the Kaplan Meier method. The patients were compared by sex using a log-rank test. The 2–6-year survival rates were 70.8% in women and 56.1% in men (p = 0.005)

Table 4. Results of a Cox regression mortality risk analysis of patients with hemoptysis based on age and comorbidities

Variable	p	Hazard ratio	95% CI Lower	95% CI Upper
Age >65 years	0.001	1.87	1.31	2.69
Pulmonary malignancy	<0.001	6.72	4.45	10.13
Diabetes mellitus	0.022	1.72	1.08	2.73
COPD	0.009	1.70	1.14	2.55
Bronchiectasis	0.57	0.82	0.43	1.60
Active tuberculosis	0.12	0.20	0.03	1.49
Atrial fibrillation	0.19	1.73	0.76	3.92
Hypertension	0.24	1.25	0.86	1.82
Chronic renal failure	0.97	1.02	0.36	2.86

The p-Values for those variables significantly associated with mortality are shown in bold.
CI: Confidence interval, COPD: Chronic obstructive pulmonary disease

DISCUSSION

The present study provides a comprehensive analysis of the etiologies, diagnostic modalities, treatment approaches, and prognostic factors associated with hemoptysis in a cohort of 400 patients. Given the extensive patient cohort involved, this study stands out in the literature. Our findings reveal that malignancy, particularly lung cancer, is the leading cause of hemoptysis, corroborating the trends observed in developed countries. This is contrasted with developing regions where tuberculosis and its sequelae remain predominant etiologies. Furthermore, the study highlights significant gender differences in the causes of hemoptysis, with bronchiectasis being more common in female patients and malignancy in male patients. The higher mortality rates observed in male patients underscore the need for heightened surveillance and prompt intervention, especially in those with comorbid conditions such as COPD, diabetes, and advanced age. These insights emphasize the importance of a tailored approach to managing hemoptysis, considering the underlying causes and individual patient characteristics to improve outcomes.

Malignancy was the leading cause of hemoptysis in our study. While some studies have ranked malignancy as the second, fourth, or fifth most frequent cause of hemoptysis, other studies, including the present study, have found it to be the leading cause.[2,4,10-13] Malignancy was the most common etiology in all participants, particularly in male patients and smokers. This highlights the importance of evaluating malignancy as a potential cause of hemoptysis in clinical settings, especially in these patients. This research revealed that squamous cell carcinoma was the most commonly occurring histologic type of lung cancer among patients with hemoptysis. Similarly, a 2018 study also identified squamous cell carcinoma as the predominant histologic type.[12] We attribute the increased prevalence of hemoptysis in patients with squamous cell carcinoma to the tumor's central location.

In this study, TB sequelae accounted for 19% of the etiologies among patients, which contrasts with some other studies that did not list this condition as a common cause.[4] However, two other studies reported that TB sequelae comprised 17.3% and 24% of the etiology.[11,14] The treatment of TB through direct observation has helped decrease the number of TB cases in Turkey, subsequently affecting the ratios of common etiologies in hemoptysis.[15] The increasing number of lung cancer cases in recent years is another influential factor that affects the hemoptysis etiology ratios.[16] We believe that due to the increasing number of cancer cases today, malignancies play a larger role in the etiology of hemoptysis. While tuberculosis-related hemoptysis cases have decreased due to the control of tuberculosis and advancements in treatment protocols, the incidence of lung cancer and other bronchopulmonary malignancies has increased due to modern lifestyles and environmental factors. In total, 25% of patients were hospitalized due to hemoptysis, with TB sequelae and malignancy being significant factors for recurrence. Therefore, close monitoring of these two patient groups for recurrence is necessary.

Bronchiectasis remains a prevalent health concern among women. This study identified bronchiectasis as the most common cause among women and the third most overall common cause. Sex-specific epidemiological, biological, and environmental variables influence the development of bronchiectasis, with a heavier disease burden in female patients.[17] A previous study found that 63.9% of those diagnosed with bronchiectasis are female, with postinfection illness being the predominant underlying cause.[18] Approximately 33% of the global population relies on solid fuels such as biomass and coal.[19] This has led to significant household air pollution, which poses substantial health risks, especially to women and children. The higher rate of bronchiectasis in female patients may be attributed to greater exposure to indoor air pollution compared to males. In male patients, we identified malignancy as the predominant cause, strongly associated with higher smoking rates. Therefore, it is crucial to conduct a detailed assessment to rule out cancer in patients with hemoptysis, particularly male patients with a history of smoking. Bronchiectasis should also be considered primarily in female patients who have been exposed to biomass or have a history of recurrent infections. Further research is warranted to investigate the differing factors underlying hemoptysis between the sexes.

Approximately 44% of our cases had diagnoses other than malignancy, bronchiectasis, and TB sequelae. In this study, cryptogenic hemoptysis occurred in 15.7% of the patients. Studies have reported varying rates of cryptogenic hemoptysis, ranging from 5.7%-50%.[20,21] While drug-induced hemoptysis is not commonly reported, it was the fourth most common etiology in this study, accounting for 10.8% of cases overall, and the second most common cause among female patients, accounting for 14.8%.[9,17] In recent years, the increased use of medications causing bleeding in cardiological treatments, coupled with inadequate monitoring of drug side effects in busy outpatient settings, may contribute to the rising incidence of drug-related hemoptysis. Given the potential challenges in early detection of drug side effects due to socio-cultural factors, clinicians should consider the possibility of drug-induced hemoptysis when evaluating patients presenting with this symptom.

In our study group, submissive hemoptysis was more prevalent than massive and minor hemoptysis, accounting for 69.7% of cases. This study observed massive hemoptysis in 8% of cases, with malignancy being the major cause. Similarly, malignancy was the most frequent cause in patients with minor hemoptysis. Since cancer may be a hidden cause of hemoptysis, a complete assessment is required regardless of the bleeding's intensity.[22] In this study, 30.2% of the patients presented with a normal chest X-ray; however, high-resolution chest CT detected bronchiectasis in 18.2%. Other studies have reported that 20%-40% of hemoptysis cases have normal chest X-ray findings, with bronchiectasis being the most common underlying pathology.[23,24]

In 88.8% of our patients, TXA and supportive treatment were effective to control bleeding. A study of a large cohort of patients with hemoptysis admitted to the emergency department found that the in-hospital mortality rate was significantly lower in patients receiving TXA compared with the control group, and was associated with a shorter hospital stay.[25] RB was performed on 19 patients in whom medical treatment failed to control bleeding. Among these patients, seven also received laser, argon plasma coagulation, and tumor debulking treatments. The number of patients who underwent surgery was small in our cohort. Five patients underwent surgical procedures including two with aspergilloma and one each with malignancy, anthracosis, and diesel fuel aspiration. Given the potential complications of surgery, it is advisable to opt for less invasive endobronchial therapy or BAE. A study found that BAE outperformed surgery in treating hemoptysis and recommended surgical treatment for patients not responding to BAE.[26] Surgical treatment should be considered when other treatments are not sufficient. BAE usage has grown since the study published by Remy et al.[27] in 1973. In our current study, the BAE treatment technique was administered to 34 patients (8.5%) through interventional radiology, and TB sequelae were diagnosed in 47% of these individuals. According to Tayal et al.,[28] 80% of patients undergoing BAE had TB sequelae. In our research, BAE effectively controlled bleeding in 76.5% of the patients. However, the bleeding recurrence rate was high in 61.8% of the patients (22/25) who reported recurrent bleeding, which was >57.7% stated by Fruchter et al.[29] Only one patient suffered from spinal ischemia, the most severe BAE consequence.

Hospitals' experience and capabilities, along with patient characteristics, can account for the varying mortality rates reported in different studies. Studies that only include patients with massive hemoptysis have often reported mortality rates as high as 30%–50%.[30,31] In a study of 8,240 patients with hemoptysis requiring hospitalization in the USA, the mortality rate during hospitalization was 4.5%, higher than that in the present study.[32] In this study, all patients who died (three with lung cancer and one with TB) had massive hemoptysis, resulting in a 1% mortality rate during hospitalization. The lower mortality rate in the present study can be attributed to the smaller number of patients with massive hemoptysis and the availability of an interventional pulmonology unit in our hospital. This study revealed a lower long-term overall survival rate among male patients. The 2–6-year survival rate was 70.8% for women and 56.1% for men. COPD, pulmonary malignancy, age >65 years, and a medical history of diabetes all affect survival rates. Other studies have also identified these risk factors, with malignancy being the most common factor influencing mortality.[33] Therefore, male patients with hemoptysis should receive close, long-term follow-up, especially if they also have a malignancy. This study has several limitations and strengths. The retrospective design and single-center setting may limit the generalizability of our findings. However, the large patient cohort enhances the study's robustness compared to other hemoptysis studies. We believe that this four-year dataset from our hospital, a reference center for chest diseases, provides valuable insights for future research. Nevertheless, prospective, multicenter studies are needed to confirm our findings and offer more comprehensive insights into the management of hemoptysis.

CONCLUSION

Our study, conducted at our leading chest disease center, sheds light on the etiologies, diagnostic approaches, treatment strategies, and prognostic factors associated with hemoptysis. Our findings underscore the importance of personalized management, taking into account individual patient characteristics and underlying causes, to improve outcomes. Clinicians should be mindful of the etiological factors, severity of hemoptysis, and risk factors influencing long-term survival rates. We believe this study offers valuable data for future research.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the İstanbul Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital Ethics Committee (Date: 21.06.2016, Decision No: 2016/26).

Informed Consent

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

Referee Evaluation Process
Externally peer-reviewed.

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

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

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

REFERENCES

1. Kathuria H, Hollingsworth HM, Vilvendhan R, Reardon C. Management of life-threatening hemoptysis. *J Intens Care*. 2020;5(8)23.
2. Mondoni M, Carlucci P, Job S, et al. Observational, multicenter study on the epidemiology of hemoptysis. *Int J Cardiovasc Imaging*. 2018;51(1):1701813.
3. Munjal SK, Natarajan S, Vinay V, Meenakshisundaram A. Clinical profile of patients hospitalized with hemoptysis. *J Family Med Prim Care*. 2022;11(11):7267-7271.
4. Quigley N, Gagnon S, Fortin M. A etiology, diagnosis and treatment of moderate-to-severe hemoptysis in a North American academic center. *ERJ Open Res*. 2020;6(4): 00204-2020.
5. Davoodi M, Kordi M, Gharibvand MM, Shoushtari MH, Borsi H, Bahadoram M. Hemoptysis: comparison of diagnostic accuracy of multi detector CT scan and bronchoscopy. *Glob J Health Sci*. 2015;7(3): 373-377.
6. O'Gurek D, Choi HY. Hemoptysis: evaluation and management. *Am Fam Physician*. 2022;105(2):144-151.
7. Davidson K, Shojaee S. Managing massive hemoptysis. *Chest*. 2020;157 (1):77-88.
8. Fartoukh M, Demoule A, Sanchez O, et al. Randomized trial of first-line bronchial artery embolization for non-severe hemoptysis of mild abundance. *BMJ Open Respir Res*. 2021;8(1):000949.
9. Avasarala SK, Rickman OB. Endobronchial therapies for diagnosis, staging, and treatment of lung cancer. *Surg Clin North Am*. 2022;102 (3):393-412.
10. Özgül MA, Turna A, Yıldız P, et al. Risk factors and recurrence patterns in 203 patients with hemoptysis. *Tuberk Toraks*. 2006;54(3):243-248.
11. Abal AT, Nair PC, Cherian J. Hemoptysis: a etiology, evaluation and outcome: a prospective study in a third-world country. *Respir Med*. 2001; 95(7):548-552.
12. Arooj P, Bredin E, Henry MT, et al. Bronchoscopy in the investigation of outpatients with hemoptysis at a lung cancer clinic. *Respir Med*. 2018;139 (1):1-5.
13. Fidan A, Özdoğan S, Oruç O, Salepçi B, Öcal Z, Çağlayan B. Hemoptysis: a retrospective analysis of 108 cases. *Respir Med*. 2002;96(9):677-680.
14. Kumar A, Gupta AK, Gautam AK, et al. Not all hemoptysis is tuberculosis think of other etiologies. A lesson from a chest clinic in a rural tertiary care center in central India. *Int J Environ Res Public Health*. 2016;5(8):1662.
15. Yıldırım Z, Turkkani MH, Bozkurt H, et al. Effects of the health transformation programme on tuberculosis burden in Turkiye. *Respir Med*. 2013;107(12):2029-2037.
16. Bade BC, Dela Cruz CS. Lung Cancer 2020: epidemiology, etiology, and prevention. *Clin Chest Med*. 2020;41(1):1-24.
17. Vidaillac C, Yong VFL, Jaggi TK, Soh MM, Choti SH. Gender differences in bronchiectasis: a real issue? *Breathe*. 2018;14(2):108-121.
18. Martinez García MA, Villa C, Dobarganes Y, et al. RIBRON: the Spanish online bronchiectasis registry. Characterization of the first 1912 patients. RIBRON: el registro español informatizado de bronquiectasias. Caracterización de los primeros 1.912 pacientes. *Archivos de Bronconeumologia*. 2021;57(1):28-35.
19. Gordon SB, Bruce NG, Grigg J, et al. Respiratory risks from household air pollution in low and middle income countries. *Lancet*. 2014;2(10):823-860.
20. Park JE, Seo JA, Cha JG, et al. Association between high blood pressure in the emergency department and cryptogenic hemoptysis. *J Clin Med*. 2022;11(18): 5302.
21. Ittrich H, Bockhorn M, Klose H, Simon MD. The diagnosis and treatment of hemoptysis. *Dtsch Arztebl Int*. 2017;114(21):371-381.
22. Uzun O, Atasoy Y, Fındık S, Atıcı AG, Erkan L. A prospective evaluation of hemoptysis cases in a tertiary referral hospital. *Clin Respir J*. 2010;4(3): 131-138.
23. Revel MP, Fournier LS, Hennebique AS, et al. Can CT replace bronchoscopy in the detection of the site and cause of bleeding in patients with large or massive hemoptysis? *Am J Roentgenol*. 2002;179(5):1217-1224.
24. Ünsal E, Köksal D, Çimen F, et al. Analysis of patients with hemoptysis in a reference hospital for chest diseases. *Tuberk Toraks*. 2006;54(1):34-42.
25. Kinoshita T, Ohbe H, Matsui H, Fushimi K, Ogura H, Yasunaga H. Effect of tranexamic acid on mortality in patients with hemoptysis: a nationwide study. *Crit Care*. 2019;23(1):347.
26. Parrot A, Khalil A, Roques S, et al. Management of severe hemoptysis: experience in a specialized center. *Rev Pneumol Clin* . 2007;63(3):202-210.
27. Rémy J, Arnaud A, Fardou H, Giraud R, Voisin C. Treatment of hemoptysis by embolization of bronchial arteries. *Radiolog*. 1977;122(1):33-37.
28. Tayal M, Chauhan U, Sharma P, Dev R, Dua R, Kumar S. Bronchial artery embolization. What further we can offer? *Wideochir Inne Tech Maloinwazyjne*. 2020;15(3):478-487.
29. Fruchter O, Schneer S, Rusanov V, Belenky A, Kramer MR. Bronchial artery embolization for massive hemoptysis: long-term follow-up. *Asian Cardiovasc Thorac Ann*. 2015;23(1):55-60.
30. Conlan AA, Hurwitz SS, Krige L, Nicolaou N, Pool R. Massive hemoptysis. Review of 123 cases. *J Thorac Cardiovasc Surg*. 1983;85(1):120-124.
31. Gourin A, Garzon AA. Operative treatment of massive hemoptysis. *Ann Thorac Surg*. 1974;18(1):52-60.
32. Lim RK, Tremblay A, Lu S, Somayaji R. Evaluating hemoptysis hospitalizations among patients with bronchiectasis in the United States: a population-based cohort study. *BMC Pulm Med*. 2021;21(1):392.
33. Lee BR, Yu JY, Ban HJ, et al. Analysis of patients with hemoptysis in a tertiary referral hospital. *Tuberc Respir Dis*. 2012;73(2):107-114.

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The evaluation of pneumoconiosis by risk factors gender and age groups in Turkiye, in 1990-2021: incidence, prevalence, deaths, and disability-adjusted life years

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ABSTRACT

Aims: The aim of this study was to evaluate the incidence and prevalence of pneumoconiosis, pneumoconiosis-related disability-adjusted life years (DALY) score, deaths and risk factors by gender and year in Turkiye.

Methods: In this study, the estimation data prepared by the Institute for health metrics and evaluation (IHME) for Turkiye in the global burden of disease study covering the years 1990-2021 were used. Descriptive statistics are given as mean and standard deviation. Comparisons according to gender were made with Independent Samples t test. The relationships between numerical variables were analyzed by pearson correlation coefficient (r).

Results: A total of 1755 pneumoconiosis-related deaths occurred in Turkiye between 1990 and 2021. Of the deaths, 687 (39%) were due to silicosis, 489 (28%) to coal worker pneumoconiosis, 451 (26%) to asbestosis and 128 (7%) to other pneumoconiosis. Of those who died, 1619 (92%) were men. The DALY score, incidence and prevalence are also higher in men. The most common risk factor affecting men is silica exposure, while for women it is asbestos exposure. After 2016, incidence and prevalence are decreasing.

Conclusion: Pneumoconiosis is more fatal in men and in the 65-80 age group. The effects of the disease vary across countries and even regions within the same country. It is important to take these differences into account in future research on pneumoconiosis. Regulation of working environments in sectors known to cause the disease will both ensure that people are less affected by an important occupational disease and prevent loss of workforce.

Keywords: Pneumoconiosis, asbestosis, silicosis, coal worker pneumoconiosis, risk factors

INTRODUCTION

Pneumoconiosis is the general name of fibrosis and other tissue reactions that develop due to the accumulation of substances such as dust, fibers or smoke in the lungs, which are often caused by exposure to industrial working environment.[1] It is one of the most common occupational diseases in the world and carries great social and economic burdens as specific treatment methods for pneumoconiosis are currently lacking.[2] The most common factors causing pneumoconiosis are asbestos fibers, crystalline silica and coal dust.[3] The three most common types of pneumoconiosis are asbestosis, silicosis and coal worker pneumoconiosis, although the first two are much more common.[4]

Silica exposure occurs in many workplaces such as mining and quarries, construction, glass, iron and steel, tire and plastic production, agricultural chemicals and automobile repair.[1,5,6] Asbestos exposure occurs frequently in workplaces such as asbestos cement production, ceiling covering, wall covering, fireproof fabric, brake and clutch linings, gasket making, ship building and repair.[1,5,6]

In addition to the duration and total amount of exposure to asbestos, silica, smoke, gas, etc. in these work environments, smoking, exposure to cigarette smoke, age and gender (more fatal in men) may increase the likelihood of developing the disease and the severity of the disease.[7,8] Factors such as regular ventilation in the workplace, taking the necessary precautions in the work environment and regular examinations are among the protective factors against pneumoconiosis.[6]

The aim of this study was to evaluate the incidence and prevalence of pneumoconiosis, pneumoconiosis-related disability-adjusted life years (DALY) score, deaths and risk factors by gender and year in Turkiye. The aim of the study is to evaluate the changes in the factors associated with pneumoconiosis over the years. The secondary goal of the study is to evaluate the changes in the factors associated with pneumoconiosis over the years.

METHODS

In the global burden of disease study conducted by the IHME-(healthdata.org) to cover the years 1990-2021, estimation data prepared for Turkiye were used.[9] The acquisition and estimation of data within the scope of the global burden of disease study is carried out by IHME.[10] Since secondary data were utilized, the study did not require Ethics Committee approval. Within the scope of the study, the number of deaths due to pneumoconiosis, DALY (Disability-adjusted life year) score, incidence and prevalence were analyzed according to risk factors, gender and years. Risk factors were occupational exposure to asbestos, occupational exposure to silica, and occupational particulate matter, gases, and fumes (PMGF) as shared by IHME.

In this study, estimated data calculated in the Global Burden of Disease Study conducted by IHME were used. The limitation of the study is that analyses were based on estimated data rather than real data.

Statistical Analysis

Descriptive statistics are given as mean and standard deviation. Comparisons according to gender were made with independent samples t test. The relationships between numerical variables were analyzed with Pearson correlation coefficient (r). Excel (Microsoft 365 Apps for enterprise) and IBM SPSS Statistics 27.0.1.0 programs were used for statistical analysis, calculations, and graphic design.

RESULTS

In this study, the number of deaths due to pneumoconiosis, DALY scores and risk factors, and the incidence and prevalence of pneumoconiosis were evaluated by gender between 1990 and 2021 in Turkiye due to estimated data on IHME. In this study, the number of deaths due to pneumoconiosis, DALY scores and risk factors, and the incidence and prevalence of pneumoconiosis were evaluated by gender between 1990 and 2021.9 A total of 1755 pneumoconiosis-related deaths occurred in Turkiye between 1990 and 2021. Of the deaths, 687 (39%) were due to silicosis, 489 (28%) to coal worker pneumoconiosis, 451 (26%) to asbestosis and 128 (7%) to other pneumoconiosis. Of those who died, 1619 (92%) were men. In Figure 1 above, the total number of deaths, total DALYs, incidence and prevalence numbers due to pneumoconiosis are presented by sex and year. It is seen that each variable analyzed has increased over the years and is higher in men. Although the incidence and prevalence are higher in men, the values for both sexes are quite close to each other. Figure 2 above presents the total number of deaths, total DALYs, incidence and prevalence of pneumoconiosis by sex and age. The total number of deaths and total DALY scores are highest in men between 65 and 75 years of age, with a gradual decline at higher ages. Incidence is higher in women between 25-40 years of age and prevalence is higher in women between 35-45 years of age, and higher in men at other ages.

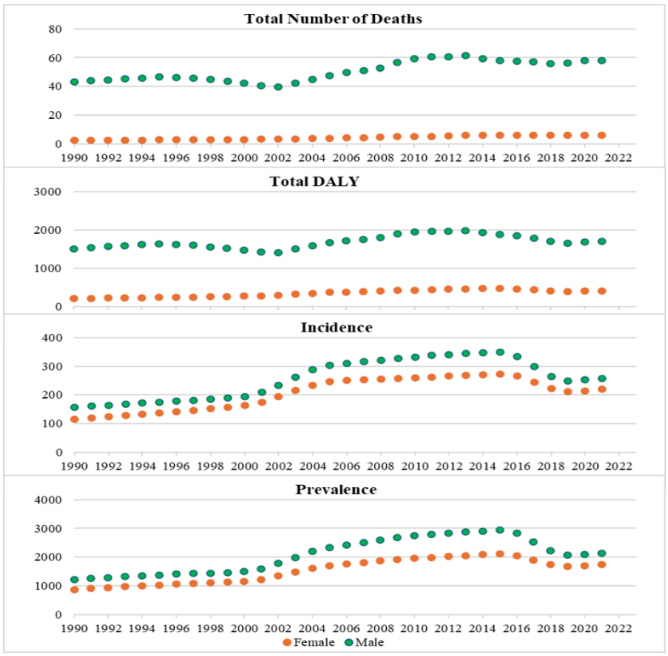

Figure 1. Number of Pneumoconiosis-related deaths, DALY, Incidence and Prevalance by gender and year.

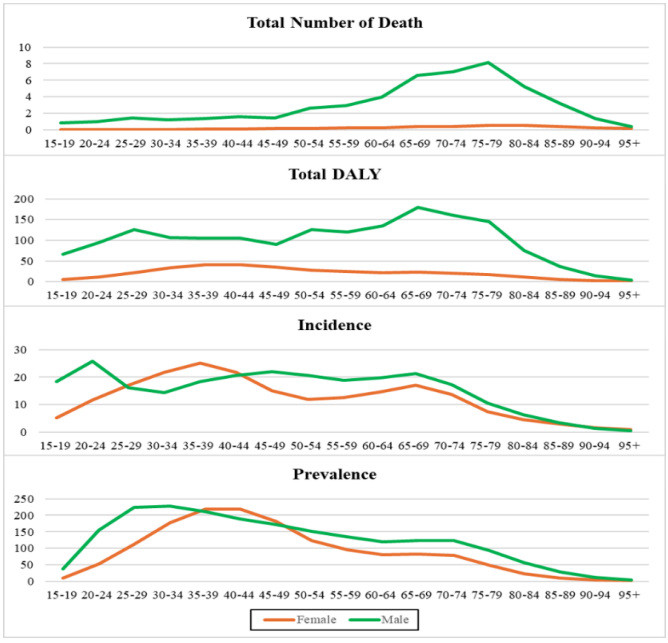

Figure 2. Number of Pneumoconiosis-related deaths, DALY, Incidence and Prevalance by gender and age group.

The difference between men and women shown in Figure 1 and Figure 2 was statistically analyzed for all age groups and all years (Table 1). It was observed that males had higher mean values in terms of number of deaths, DALYs, incidence and prevalence and this difference was found to be statistically significant ($p<0.001$). Table 2 below shows the percentage of deaths by risk factors by sex and age. Accordingly, for both men and in general, silica exposure (responsible for 40.3%-82.4% of deaths from pneumoconiosis) was found to be the risk factor causing the highest number of deaths for those aged 50 years and younger. In women, PMGF (36.8%-50.5%) was found in the 55-80 age range and asbestos exposure

was found to be the effective risk factor in other age groups, although this varied according to age. The difference between the percentages of silica, asbestos exposure and PMGF in men and women was analyzed by t-test and a significant difference was found (p<0.001).

Table1. Number of death, DALY, incidence, prevalence: by gender (all years, all ages).

	Female		Male		Female- Male
	Mean	SD	Mean	SD	
Death	4.270	1.413	50.589	7.093	t=36.226; p<0.001
DALY	342.509	90.098	1687.348	169.744	t=39.587; p<0.001
Incidence	205.494	55.126	256.428	69.103	t=-3.259; p=0.002
Prevelance	1531.090	425.577	2067.204	604.647	t=-4.102; p<0.001

Number: Number of deaths in the population, DALY: Disability-adjusted life years

Table 2. Percent of deaths caused by risk factors by gender (all years, all ages)

Age Group	Female			Male			Both		
	Asbest* (%)	Silica ** (%)	PMGF *** (%)	Asbest (%)	Silica (%)	PMGF (%)	Asbest (%)	Silica (%)	PMGF (%)
15-19	0.742	0.021	0.236	0.235	0.427	0.338	0.265	0.403	0.332
20-24	0.399	0.086	0.512	0.108	0.660	0.233	0.102	0.677	0.221
25-29	0.480	0.166	0.353	0.162	0.753	0.086	0.126	0.824	0.051
30-34	0.439	0.163	0.396	0.245	0.571	0.184	0.207	0.656	0.139
35-39	0.357	0.177	0.466	0.148	0.477	0.375	0.082	0.578	0.340
40-44	0.402	0.228	0.371	0.283	0.467	0.251	0.201	0.631	0.169
45-49	0.495	0.217	0.286	0.314	0.430	0.255	0.180	0.600	0.219
50-54	0.508	0.225	0.265	0.410	0.321	0.269	0.213	0.506	0.281
55-59	0.328	0.170	0.502	0.336	0.179	0.486	0.236	0.309	0.455
60-64	0.304	0.191	0.505	0.334	0.169	0.496	0.229	0.313	0.459
65-69	0.367	0.264	0.368	0.458	0.181	0.360	0.185	0.430	0.385
70-74	0.325	0.225	0.450	0.416	0.120	0.460	0.262	0.321	0.417
75-79	0.300	0.230	0.469	0.365	0.118	0.515	0.291	0.313	0.395
80-84	0.386	0.264	0.350	0.624	0.100	0.273	0.243	0.357	0.400
85-89	0.408	0.322	0.269	0.549	0.105	0.346	0.364	0.414	0.220
90-94	0.412	0.299	0.289	0.615	0.070	0.315	0.350	0.382	0.268
95+	0.448	0.212	0.338	0.600	0.065	0.332	0.378	0.283	0.338
All Ages	0.259	0.387	0.353	0.543	0.044	0.412	0.229	0.425	0.346

Percent: Proportion of deaths from a specific cause compared to deaths from all causes
*Occupational exposure to asbestos
**Occupational exposure to silica
***Occupational particulate matter, gases, and fumes

The number of deaths due to risk factors was analyzed and significant associations were found in all age groups (p<0.001). All associations were strong to very strong (Table 3).

Table 3. Relationships between the number of deaths caused by risk factors by gender (all years, all ages).

	Asbest*-Silica**		Asbest- PMGF***		Silica- PMGF	
	r	p	r	p	r	p
15-19	0.953	<0.001	0.959	<0.001	0.986	<0.001
20-24	0.924	<0.001	0.947	<0.001	0.987	<0.001
25-29	0.939	<0.001	0.910	<0.001	0.902	<0.001
30-34	0.946	<0.001	0.945	<0.001	0.951	<0.001
35-39	0.639	<0.001	0.683	<0.001	0.985	<0.001
40-44	0.936	<0.001	0.952	<0.001	0.961	<0.001
45-49	0.757	<0.001	0.833	<0.001	0.973	<0.001
50-54	0.898	<0.001	0.901	<0.001	0.990	<0.001
55-59	0.928	<0.001	0.965	<0.001	0.983	<0.001
60-64	0.916	<0.001	0.942	<0.001	0.987	<0.001
65-69	0.901	<0.001	0.944	<0.001	0.981	<0.001
70-74	0.943	<0.001	0.969	<0.001	0.985	<0.001
75-79	0.962	<0.001	0.986	<0.001	0.968	<0.001
80-84	0.908	<0.001	0.945	<0.001	0.983	<0.001
85-89	0.954	<0.001	0.960	<0.001	0.931	<0.001
90-94	0.929	<0.001	0.993	<0.001	0.937	<0.001
95+	0.796	<0.001	0.976	<0.001	0.883	<0.001
All Ages	0.886	<0.001	0.958	<0.001	0.970	<0.001

*Occupational exposure to asbestos
**Occupational exposure to silica
***Occupational particulate matter, gases, and fumes

Table 4 above shows the comparison of the number of deaths and mean DALY scores by gender for all age groups. The number of deaths and DALY scores due to risk factors were higher in men and this difference was statistically significant (p<0.001). The most significant difference occurred in silica for both number of deaths (t=58.509; p<0.001) and DALY score (t=60.187; p<0.001).

Table 4. Comparison of the number of deaths due to risk factors and mean DALY scores by gender (all years, all ages)

Mean		Female		Male		Female-Male
		SD	Mean	SD		
Death Number	Asbest*	2.353	0.766	11.726	3.230	t=15.975; p<0.001
	Silica**	0.145	0.050	21.304	2.045	t=58.509; p<0.001
	PMGF***	1.772	0.617	17.500	2.539	t=34.057; p<0.001
DALY Scores	Asbest	174.258	48.278	336.820	73.738	t=10.434; p<0.001
	Silica	24.555	4.653	828.904	75.456	t=60.187; p<0.001
	PMGF	143.645	38.016	520.128	58.072	t=30.683; p<0.001

*Occupational exposure to asbestos
**Occupational exposure to silica
***Occupational particulate matter, gases, and fumes
PMGF: Particulate matter, gases, and fumes

DISCUSSION

In a study conducted by Zhao et al.[11] in China, it was found that pneumoconiosis affects young adults aged 24-44 years and men more frequently and that the most common type is silicosis. In a study investigating silicosis cases in the UK, it was found that 93% of cases were caused by silica exposure, men were more affected and cases were most common among workers in metal manufacturing (21%) and quarries.[12] In this study, total deaths, total DALYs, incidence and prevalence were higher in men. However, both incidence and prevalence values are quite close to each other in men and women. In some age ranges, they are even higher in women. It is thought that this may be due to regional factors or the fact that women are more involved in working life in Turkiye (2014:30.3%; 2023:35.8%).[13] In addition, from 2014 to 2023, the number of women working in mining and quarrying, manufacturing, electricity, gas, steam, water supply and sewerage and construction sectors, which are known to directly affect pneumoconiosis, increases.[13]

In a study conducted in the USA, it was found that the highest prevalence of pneumonoconiosis was in the age group over 75 years and in men, approximately 70.0%-72.5% asbestosis was seen, and the prevalence increased by 3-10% annually between 2002-2009, and decreased significantly by 3%-5% between 2009-2019.[14] In this study, silica was found to be the most effective cause of death in men and asbestos and PMGF in women. The prevalence was found to be similar in men and women and was quite high in the age range of 20-50 years. Moreover, incidence and prevalence increased between 2000 and 2016 and decreased after 2016. It is thought that this may be due to changes in working environments.

A study conducted in Jiangsu, China found that between 1956 and 2021, the DALY score due to pneumoconiosis gradually decreased and the highest DALY score occurred due to silica.[15] Another study for China as a whole found that the DALY score increased by 20.8% between 1990 and 2019.[16] In this study, it was observed that the DALY score due to pneumoconiosis in Turkiye did not change significantly over the years and mostly affected the 65-80 age group.

The study's strength is that it examines the incidence, prevalence, death and DALY statistics due to pneumoconiosis between 1990 and 2021 by gender and age. It is thought that the study will make a significant contribution to the literature

by examining the disease burden over a long period. The use of estimated data published by IHME is a limitation of the study.

CONCLUSION

The increase in the prevalence of pneumoconiosis and the number of deaths in Turkiye over the years can be explained by the increase in the number of workers in sectors known to cause pneumoconiosis. While the number of deaths in men is significantly higher, the fact that there is no significant difference between the sexes in terms of prevalence and incidence can be considered as an indication that men experience the disease much more severely.

Studies show that the number of deaths, DALYs, incidence and prevalence of pneumoconiosis can vary significantly from country to country, even in different regions of the same country. Therefore, regional factors should be taken into account in interventions to prevent pneumoconiosis. In addition, gender differences should be investigated in more detail and policy recommendations should be developed. Regulation of working environments in sectors known to cause the disease will both ensure that people are less affected by an important occupational disease and prevent loss of workforce.

ETHICAL DECLARATIONS

Ethics Committee Approval

Since secondary data were utilized, the study did not require Ethics Committee approval.

Informed Consent

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

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

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

REFERENCES

1. TC. Sağlık Bakanlığı. Pnömokonyozlarda sağlık gözetimi, klinik tanı, kayıt, bildirim ve izlem protokolü. *2021;1190(1):128.*
2. Li Y, Cheng Z, Fan H, Hao C, Yao W. Epigenetic changes and functions in pneumoconiosis. *Oxid Med Cell Longev.* 2022;20(22):2523066. doi: 10.1155/2022/2523066
3. Chong S, Lee KS, Chung MJ, Han J, Kwon OJ, Kim TS. Pneumoconiosis: comparison of imaging and pathologic findings. *Radiographics*. 2006; 26(1):59-77. doi:10.1148/rg.261055070
4. Nguyen JA, Salmi D. Educational case: pneumoconiosis. *Acad Pathol.* 2021;11(8):237428952 11013530. doi:10.1177/23742895211013530
5. Demir C, Demir AU, Evcik E. Çalışma yaşamında pnömokonyoz. 2022. Çalışma ve Sosyal Güvenlik Bakanlığı, İş Sağlığı ve Güvenliği Genel Müdürlüğü ISBN: 978-625-8097-00-9.
6. Bell JL, Mazurek JM. Trends in pneumoconiosis deaths - United States, 1999-2018. *MMWR Morb Mortal Wkly Rep.* 2020;69(23):693-698. doi: 10.15585/mmwr.mm6923a1
7. Su X, Kong X, Yu X, Zhang X. Incidence and influencing factors of occupational pneumoconiosis: a systematic review and meta-analysis. *BMJ Open*. 2023;13(3):1-12. doi:10.1136/bmj open-2022-065114
8. Chen J, Ye S, Mao L, Xie W, Nie H, Su M. Characteristics and factors associated with morbidity of migrant workers with pneumoconiosis: a cross-sectional study. *BMJ Open*. 2022;12(11):064596. doi:10.1136/ bmjopen-2022-064596
9. Roth GJ. Global burden of disease collaborative network. global burden of disease study 2017 (GBD 2017) results. Seattle, United States: institute for health metrics and evaluation (IHME). *Lancet*. 2018;392(1): 1736-1788.
10. IHME. Global burden of disease (GBD). Accessed. 2024. https://www.healthdata.org/research-analysis/about-gbd
11. Zhao JQ, Li JG, Zhao CX. Prevalence of pneumoconiosis among young adults aged 24-44 years in a heavily industrialized province of China. *J Occup Health*. 2019;61(1):73-81. doi:10.1002/1348-9585.12029
12. Barber CM, Fishwick D, Carder M, van Tongeren M. Epidemiology of silicosis: reports from the SWORD scheme in the UK from 1996 to 2017. *Occup Environ Med*. 2019;76(1):17-21. doi:10.1136/oemed-2018-105337
13. TÜİK. Turkiye istatistik kurumu merkezi dağıtım sistemi, accessed. 2024. https://biruni.tuik.gov.tr/medas/?kn=95&locale=tr
14. Kurth L, Casey ML, Mazurek JM, Blackley DJ. Pneumoconiosis incidence and prevalence among US medicare beneficiaries, 1999-2019. *Am J Ind Med*. 2023;66(10):831-841. doi:10.1002/ajim.23519
15. Duan Z, Zhou L, Wang T, Han L, Zhang J. Survival and disease burden analysis of occupational pneumoconiosis from 1956 to 2021 in jiangsu province. *J Occup Environ Med*. 2023;65(5):407-412. doi:10.1097Jom. 0000000000002795
16. Li J, Yin P, Wang H, et al. The burden of pneumoconiosis in China: an analysis from the Global burden of disease study 2019. *BMC Public Health*. 2022;22(1):1114. doi:10.1186/s12889-022-13541-x

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Case Report

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CRRT Experience in a patient diagnosed with anthracofibrosis in intensive care : a case report

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ABSTRACT

Bronchial anthracofibrosis is characterized by dark pigmentation (anthracosis) in the bronchial mucosa, often accompanied by bronchial stenosis or obstruction due to fibrosis in the same area. Diagnosis is typically established via bronchoscopy in patients who do not fully respond to treatment, exhibit radiological abnormalities, and have obstructive lung disease. Anthracofibrosis is mostly observed in conjunction with tuberculosis but can also frequently accompany pneumonia, necessitating close monitoring. In the intensive care unit (ICU), continuous renal replacement therapy (CRRT) is commonly used for critically ill patients with acute kidney injury (AKI) secondary to sepsis. It is particularly preferred in patients with acute renal failure (ARF) who have hemodynamic instability and are on inotropic agents. We present a case of a 78-year-old male admitted to the ICU due to pneumonia secondary to sepsis, septic shock, and AKI. During his ICU stay, frequent airway obstructions necessitated bronchoscopy, revealing a diagnosis of anthracofibrosis. CRRT was initiated due to hypotension and anuria under inotropic support. However, the patient exhibited disseminated intravascular coagulation (DIC) due to sepsis, along with intrabronchial hemorrhages and clot formations, resulting in airway obstruction and increased airway pressure. These complications hindered prolonged CRRT due to increased hemodynamic instability.

This case report aims to highlight the impact of increased airway pressure on CRRT in patients with obstructive lung diseases like anthracofibrosis. In such cases, the potential for increased hemodynamic instability should be considered, and measures to reduce airway pressure should be implemented.

Keywords: Anthracosis, airway pressure, septic shock, continuous renal replacement therapy

INTRODUCTION

Bronchial anthracofibrosis is characterized by dark pigmentation (anthracosis) in the bronchial mucosa, often accompanied by bronchial stenosis or fibrosis-related obstruction in the same area.[1] Diagnosis is commonly established through bronchoscopy in patients with obstructive lung diseases who exhibit radiological abnormalities and do not fully respond to treatment.[2] While the main cause of anthracosis/anthracofibrosis remains unknown, it is thought that exposure to biomass, genetics, chronic inflammatory reactions, air pollution, domestic pollution, and prolonged contact with chronic infections like tuberculosis play roles in the development of the disease.[3,4] While a review of the literature on anthracofibrosis shows it predominantly appears in conjunction with tuberculosis[1,5,6] it can also frequently coincide with pneumonia, necessitating close monitoring.[7,8]

In the intensive care unit (ICU), the incidence of Acute Kidney Injury (AKI) due to sepsis ranges from 15-20%, with CRRT (Continuous renal replacement therapy) being a frequently used treatment modality for critically ill patients.[9] Compared to intermittent hemodialysis, CRRT is preferred for its lesser hemodynamic instability and ability to be administered without anticoagulants or with alternative anticoagulation protocols in patients with bleeding disorders.[10]

Increased airway pressure in obstructive lung diseases can lead to hemodynamic disturbances.[11] In the case of septic shock, hemodynamic disturbance occurs, which leads to impaired tissue perfusion.[12] Although CRRT is a preferred dialysis method in hemodynamic disorders, its use is limited in severely hypotensive patients. Hypoxia and vasopressor use are independent risk factors for early mortality during CRRT.[13] This case report aims to draw attention to the hemodynamic disturbances resulting from airway obstruction in a patient with anthracofibrosis, emphasizing the challenges this poses for critical applications such as CRRT.

CASE

A 78-year-old male presented to the emergency room with complaints of shortness of breath and altered consciousness. He was admitted to the ICU with diagnoses of pneumonia, sepsis, respiratory failure, and AKI. Thoracic (computed tomography) CT imaging showed findings consistent with infiltrative pneumonia, while brain CT and diffusion MRI (magnetic resonance imaging). revealed no abnormalities. Blood tests confirmed AKI and sepsis (Table). The patient's history included diabetes mellitus, hypertension, and a past cerebrovascular event. Initially, the patient received oxygen support via a reservoir mask but was electively intubated on the second day due to worsening respiratory distress and tachypnea, and switched to SIMV-VC mode. The cultures taken on the first day showed no growth, and the patient's cultures were sent again on the second day due to the development of fever.

The cultures taken on the first day showed no growth, but repeat cultures on the second day revealed fever development. Noradrenaline infusion was initiated due to hypotension. Fluid replacement therapy was administered based on hemodynamic monitoring. The patient was started on piperacillin/tazobactam and clarithromycin. Despite initial urine output of 1800cc and an intake and output (I&O) balance of 420, urine output decreased to 220cc on the second day, prompting a loop diuretic infusion. As the patient became anuric and remained on noradrenaline, CRRT was initiated but had to be terminated after 48 hours due to low venous return pressure alarms. Following the initiation of CRRT, the patient's urine output increased. During this period, the mechanical ventilator alarmed twice due to increased pressure and blockage in the endotracheal tube, necessitating its replacement. Clots were observed within the intubation tube. A fiberoptic bronchoscopy (FOB) was performed after the third blockage, revealing organized clots completely occluding the lumen from the mid-trachea downward. These clots could not be cleared via FOB and were subsequently removed using rigid bronchoscopy with basket and forceps biopsies. The clots extended distally into both main bronchi up to the segmental orifices, which were thoroughly cleaned. Attempts to recommence CRRT for the oliguric patient on high-dose inotropic support were unsuccessful, as it was terminated after two hours due to low-pressure alarms. The patient, who had melena during the night observations, had oral intake stopped, and a proton pump inhibitor infusion was administered. The melena continued for 2 days. Laboratory results (Table 1) and clinical findings suggested the presence of disseminated intravascular coagulation (DIC) secondary to sepsis.

Given the recurrence of clotting and hemorrhagic elements in the intubation tube and persistent pressure alarms on the mechanical ventilator, another FOB was conducted. This examination revealed anthracotic plaques covering all lobes and segments, with bronchi and segments obstructed by fibrin plugs, leading to a diagnosis of bronchial anthracofibrosis. During this period, the patient's blood culture grew methicillin-resistant staphylococcus Aureus (MRSA), and urine culture grew non-albicans Candida, necessitating a switch to tigecycline, fluconazole, and imipenem. Subsequent cultures showed no growth.

Table . Laboratory findings observed during the patient's intensive care admission

Blood values	Admission values	Post-first CRRT values	Post-first CRRT values	Post-fOB values	Post-IHD values
Leukocyte (K/ ul)	9.9	8.8	16.1	10.7	2.6
Hemoglobin (g/dl)	15.6	13.9	11.3	8.5	8.0
Platelets (cell x10⁹/L)	137.000	120.000	151.000	78.000	36.000
Urea (mg/dl)	134	268	99	404	252
Creatinine (mg/dl)	2.92	8.21	2.89	7.6	5.44
GFR (ml/dk)	21.3	6.2	21.5	6.7	10.0
Lactate (mmol/L)	4	3.5	2	1.8	3.8
CRP (mg/L)	401	261	247	127	179
PCT (ng/ml)	92.36	55.89	25.6	10.8	3.43
D-dimer (ng/ml)	25.290	35.200	14.280	31.600	14.810
aPTT (s)	34.2	32.8	37.4	31.2	42.4
PT (s)	16.8	18.2	16.4	21.4	19.9
INR	1.48	1.62	1.44	1.97	1.73

CRRT: Continuous renal replacement therapy, FOB: Fiberoptic bronchoscopy, IHD: Intermittent hemodialysis, GFR: Glomerular filtration rate, CRP: C-reactive protein, PCT: Procalcitonin, aPTT: Activated partial thromboplastin time, PT: Prothrombin time, INR: International normalized ratio

The patient's third CRRT attempt lasted seven hours before being terminated due to similar complications. Consequently, the patient underwent hemodialysis without heparin for two hours, during which one unit of erythrocyte suspension was transfused. CRRT or intermittent hemodialysis could not be continued due to the patient's hemodynamic instability while anuric and receiving high-dose inotropic support.

The patient's hemodynamic status and overall condition progressively deteriorated, culminating in cardiac arrest on the 20th day of ICU admission. Resuscitation efforts were unsuccessful, and the patient was pronounced deceased.

DISCUSSION

Anthracofibrosis is characterized as an obstructive lung disease marked by black pigmentation, known as anthracosis, and fibrosis in the bronchial mucosa, resulting in a narrowing that can obstruct the bronchial lumen. Increased airway pressure may also be observed due to airway obstruction.[2] In our patient, the mechanical ventilator frequently alarmed due to increased airway pressure. Despite changing the endotracheal tube, high airway pressure persisted, prompting a bronchoscopy that confirmed the diagnosis of anthracofibrosis. Bronchoscopy revealed fibrin plugs and clots, which were removed in an attempt to reduce airway pressure. Hyperinflation in patients with airway obstruction can disrupt venous return, potentially leading to hypotension and hemodynamic collapse.[14]

Hypotension is a significant risk factor for in-hospital mortality and can frequently occur in patients undergoing CRRT.[15] An increase in airway pressure in patients undergoing CRRT has been found to be an independent risk factor for mortality.[16] Our patient also had a sepsis and septic shock secondary to pneumonia. The patient was hypotensive due to both high airway pressure and septic shock. CRRT was applied due to the patient receiving inotropic support, being anuric, and exhibiting signs of fluid overload.

During CRRT, pressure alarms can occur due to various reasons, including blockages, hematomas in the vein, circuit obstruction or kinking, venous stenosis, high coagulation states, and hypotension. In our case, upon encountering a pressure alarm during CRRT, the central dialysis catheter's location was adjusted, ensuring smooth blood inflow and

outflow with no blockage in the CRRT line. The pressure alarm was attributed to hypotension caused by septic shock, DIC, and increased airway pressure. DIC is a systemic process causing both thrombosis and bleeding, and it is a frequent and serious complication of sepsis and septic shock, associated with high mortality and morbidity.[17] In our patient's follow-ups, DIC developed due to sepsis, leading to both gastrointestinal and intrabronchial bleedings. The resulting intrabronchial bleedings and clots also caused airway obstruction and increased airway pressure, in addition to anthracofibrosis.

The CRRT circuit can lead to the consumption of clotting factors and can increase the risk of clotting due to high pressure and turbulence in the connections. While systemic anticoagulation is often deemed sufficient to prevent the clotting of the recurring CRRT circuit in most cases, additional anticoagulant might need to be added in some situations.[18] Thrombocytopenia is commonly seen in patients undergoing CRRT, and it has been found that mortality is higher in patients who are thrombocytopenic and undergoing CRRT9.[19,20] In our case, even though the heparin dose was adjusted according to the aPTT value, most of the time, there was no need for heparin due to thrombocytopenia and increased aPTT resulting from DIC.

This study has limitations, it is based on a single case. Additionally, the patient's anamnesis lacked data regarding the etiology of anthracofibrosis, making it difficult to ascertain the exact cause of anthracofibrosis development. It is suspected that pneumonia may have been a contributing factor.

CONCLUSION

In cases of obstructive lung diseases such as anthracofibrosis, which do not respond to bronchodilators, it is crucial to recognize that increased airway pressure can significantly exacerbate hemodynamic instability in critically ill patients. Measures should be taken to reduce airway pressure to mitigate these effects.

ETHICAL DECLARATIONS

Informed Consent
The patient signed and free and informed consent form.

Referee Evaluation Process
Externally peer-reviewed.

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

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

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REFERENCES

1. Bekci TT, Maden E, Emre L. Bronchial anthracofibrosis case with endobronchial tuberculosis. *Int J Med Sci*. 2011;8(1):84-87.
2. Kim YJ, Jung CY, Shin HW, Lee BK. Biomass smoke induced bronchial an- thracofibrosis: presenting features and clinical course. *Respir Med*. 2009;103(5):757-765.
3. Jamaati H, Sharifi A, Mirenayat MS, et al. What do we know about anthracofibrosis? A literature review. *Tanaffos*. 2017;16(3):175-189.
4. Yılmazel Uçar E, Araz Ö, Akgün M, et al. Bronşiyal antrakozis-antrakofibrozis: potansiyel nedenler ve klinik özellikler. *Eurasian J Pulmonol*. 2014;16(1):17-20.
5. Wynn GJ, Turkington PM, O'Driscoll BR. Anthracofibrosis, bronchial stenosis with overlying anthracotic mucosa: possibly a new occupational lung disorder: a series of seven cases from one UK hospital. *Chest*. 2008; 134(5):1069-1073.
6. Hemmati SH, Shahriar M, Molaei NA. What causes anthracofibrosis? Either tuberculosis or smoke. Pakistan J Med Sci. 2008;24(3):395.
7. Lee HS, Maeng JH, Park PG, et al. Clinical features of simple bronchial anthracofibrosis which is not associated with tuberculosis. *Tuberc Respir Dis*. 2002;53(5):510-518.
8. Rangelov K, Sethi S. The first described case of occupational anthracofibrosis in the USA. *Case Rep Pulmonol. 2014;14(23):460594.*
9. Cho AY, Yoon HJ, Lee KY, Sun IO. Clinical characteristics of sepsis-induced acute kidney injury in patients undergoing continuous renal replacement therapy. *Renal fail*. 2018;40(1):403-409.
10. Morabito S, Pistolesi V, Cibelli L, Pierucci A. Continuous renal replacement therapies (CRRT) will remain the most widely adopted dialysis modality in the critically ill. *G Ital Nefrol*. 2009;26(1):13-21.
11. Güven M. Mekanik ventilasyon uygulamaları. 11. Ulusal İç Hastalıkları Kongresi, 30 Eylül-4 Ekim 2009, Antalya, Kongre Kitapçığı. 52-56.
12. Yıldız F, Karakoç E. Sepsiste hemodinamik destek. *Arşiv Kaynak Tarama Derg*. 2014;23(2):157-167.
13. Prasad B, Urbanski M, Ferguson TW, Karreman E, Tangri N. Early mortality on continuous renal replacement therapy (CRRT): the prairie CRRT study. *Can J Kidney Health Dis*. 2016;36(3):124.
14. Gladwin MT, Pierson DJ. Mechanical ventilation of the patient with severe chronic obstructive pulmonary disease. *Intensive Care Med*. 1998;24:898–910.
15. Shawwa K, Kompotiatis P, Jentzer JC, et al. Hypotension within one-hour from starting CRRT is associated with in-hospital mortality. *J Crit Care*. 2019;54(1):7-13.
16. Flores FX, Brophy PD, Symons JM, et al. Continuous renal replacement therapy (CRRT) after stem cell transplantation. A report from the prospective pediatric CRRT registry group. *Pediatric Nephrology*. 2008; 23:625-630.
17. Tagami T, Matsui H, Horiguchi H, et al. Antithrombin and mortality in severe pneumonia patients with sepsis-associated disseminated intravascular coagulation: an observational nationwide study. *J Thromb Haemost*. 2014;12(9):1470-1479.
18. Foti L, Villa G, Romagnoli S, Ricci Z. Acute kidney injury and extracorporeal membrane oxygenation: review on multiple organ support options. *Int J Nephrol Renovasc Dis*. 2021;13(14):321-29.
19. Guru PK, Singh TD, Akhoundi A, Kashani KB. Association of thrombocytopenia and mortality in critically ill patients on continuous renal replacement therapy. *Nephron*. 2016;133(3):175-182.
20. Wu B, Gong D, Xu B, et al. Decreased platelet count in patients receiving continuous veno-venous hemofiltration: a single-center retrospective study. *PLoS One*. 2014;9(5):97286.

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Case Report

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Combined paravertebral and erector spinae plane block in non-intubated video-assisted thoracoscopic wedge resection: a case report

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ABSTRACT

Thoracic surgery is often performed under general anesthesia, with intubation required. Less invasive surgical and anesthesiology approaches, such as a combination of video-assisted thoracic surgery (VATS) and regional nerve blocks, have been utilized to facilitate early recovery. In this case report, a patient undergoing VATS will be presented using thoracic paravertebral block (TPVB) and erector spinae plane blocks (ESPB) as the primary anesthesia approach. A twenty-eight-year-old male patient with no known comorbidity had been evaluated for VATS to undergo wedge resection of the right middle lobe due to non-resolving repeated pneumothorax. As the patient had bullous lung presence at the contralateral side as well, invasive ventilation was deemed risky, and, as an alternative approach, real-time ultrasound-guide TPV and ESPB block were performed with intravenous midazolam 2 mg and fentanyl 50 mcg utilized to prevent anxiety and pain control. A total of 20 ml bupivacaine and 10 mL 2% lidocaine were used for nerve blocks and for maintenance of sedation; 2 mg midazolam, 50 mg ketamine, 50 mcg fentanyl, and 150 mg propofol were used within 90 minutes of operation. After VATS, the patient was admitted to the surgical intensive care unit, and no complication was observed post-operatively, with a successful transfer to the ward afterward. Maintenance of an unproblematic perioperative period is as paramount as the surgery itself. A combination of protocols, with the limitation of post-operative opioid usage by sedation and less invasive surgical methods, such as non-intubated VATS being presented in this case report, allows an earlier recovery period and less complication by preserving lung function. TPV and ESPB, in this case, granted exclusion of intubation, less invasive to thoracic epidural anesthesia, and control of possible complications due to an already bullous lung.

Keywords: Thoracic paravertebral block, erector spinae plane block, video-assisted thoracic surgery, non-intubated video-assisted thoracoscopic surgery, NIVATS

INTRODUCTION

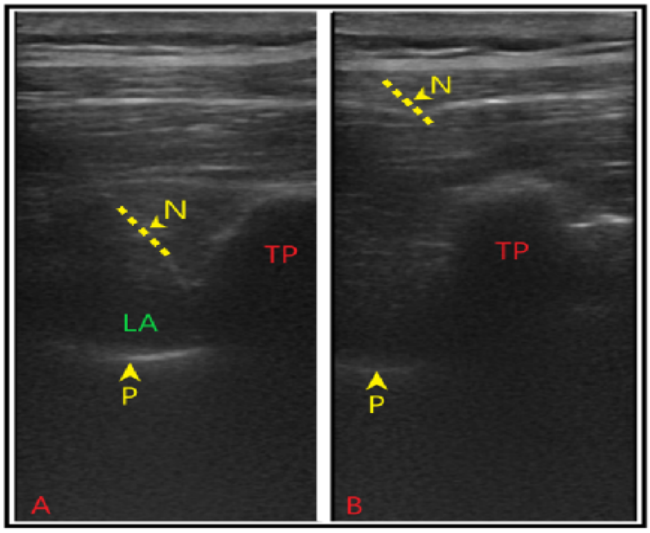
In thoracic surgery, many procedures are performed under general anesthesia and with a double-lumen tube (DLT) intubation. These requirements necessitate the use of neuromuscular blockage and maintenance of anesthesia with intravenous and/or volatile agents. Utilization of these agents, in turn, may cause complications such as a delay in post-operative recovery.[1] Enhanced recovery after surgery (ERAS) protocols have recently been widely accepted in thoracic surgeries.[2] Video-assisted thoracic surgery (VATS) procedures using regional or thoracic nerve blocks are increasingly used in non-intubated patients. These practices also significantly increase compliance with ERAS protocols. This approach allows the exclusion of neuromuscular blockage and the requirement for DLT while allowing an optimal surgical procedure and reducing any post-operative complication rate that may be related to these invasive modalities.[3] This reduction in post-operative risk is significant in pulmonary complications, which, due to the nature of the procedure, is relatively higher than other non-thoracic operations. Performing these blocks as the sole method of anesthesia is also a topic that has become increasingly accepted in recent years.

In thoracic surgery, thoracic paravertebral block (TPVB) and erector spinae plane blocks (ESPB) have been shown to provide analgesia and adequate anesthesia with minimal sedation.[4–6] Among additional methods that could be utilized in thoracic wall blocks, which can be applied with a single needle insertion, are thoracic epidural anesthesia (TEA) and serratus anterior plane block (SAPB). The combination of ESPB and TPVB is a relatively new method that was validated in its safety and effectiveness.[7] Similarly, the combination of both methods was found superior to either ESPB and TPVB alone, which varied within studies, as one study found the combination superior to ESPB but not TPVB, while the other stated the combination was superior to TPVB but similar to ESPB.[8,9] In this case, we will discuss a patient who underwent VATS under TPVB and ESPB block as the primary anesthesia approach.

CASE

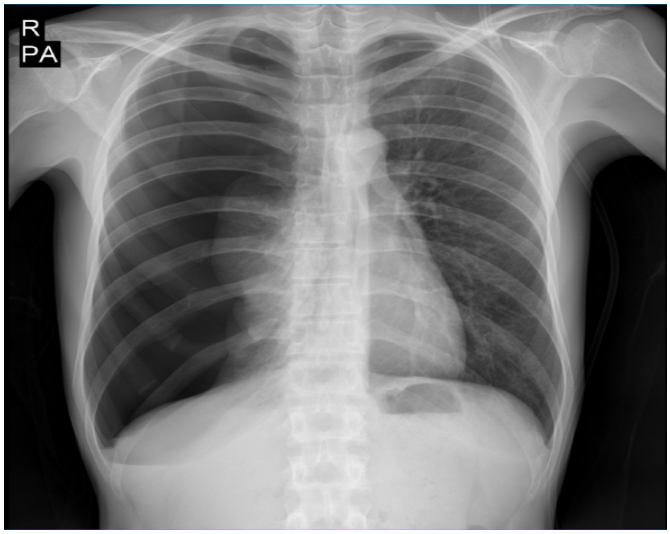
A twenty-eight-year-old male patient with no known comorbidity had been admitted to the thoracic surgery ward due to a right-side pneumothorax requiring a chest tube. Medical history revealed that he had a repeated right pneumothorax history; thus, further investigation was performed. Bullous lung formation was observed in the bilateral lungs in the requested computed chest tomography. During follow-up, the right lung was deemed non-expanding, and wedge resection for the right middle lobe by VATS was planned.

As the patient's left lung was bullous as well, avoidance of invasive ventilation was considered, and a regional approach with sedo-analgesia was preferred, and the patient's written and verbal approval was received. The procedure was performed by an experienced performer who was also certified in ultrasonography. After standard American Society Of Anesthesiologists (ASA) monitorization, real-time ultrasound-guided TPVB and ESPB block were utilized to visualize the fifth and sixth thoracic vertebral transverse processes. The hypothesis was that TPVB and ESPB would provide adequate analgesia, and the purpose would be to avoid invasive ventilation under this regimen. Midazolam 2 mg and fentanyl 50 mcg were administered intravenously prior to block application to prevent pain and anxiety. TPVB was then performed by injection of local anesthetic in the paravertebral space at T5 level (10 ml 0.5% bupivacaine,5 ml 2% lidocaine), followed by ESPB performed between erector spinae muscle and thoracic transverse process at the same level (10 ml %0.5 bupivacaine, 5 ml 2% lidocaine) (Figure 1). Before local anesthesia injection, all block applications were initially checked in hydrodissection with saline. After 15 minutes of waiting for blocks to settle, a pin prick test was used to evaluate the dermatomal area examination and confirm an adequate block. The operation started after a Ramsay Sedation Score of 3 was reached. The surgeon and the operating team were experienced with the procedure and NIVATS application.

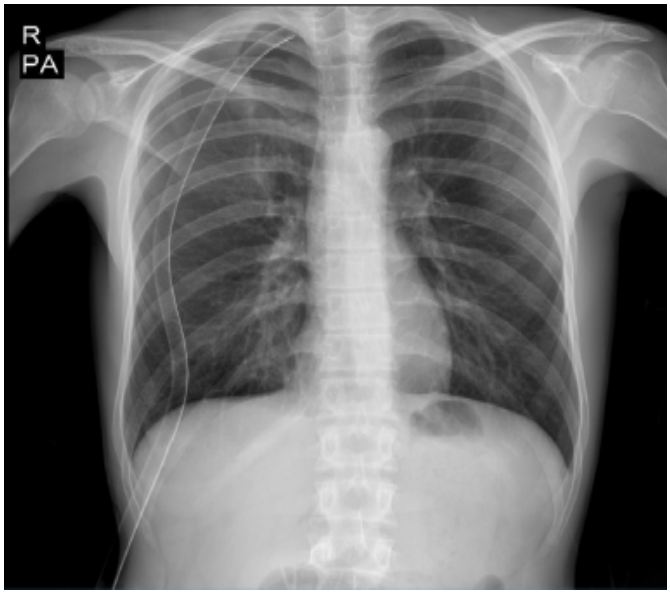


N: Needle (yellow dotted line), TP: Transverse process, LA: Local anesthesia, P: Pleural Line.
Figure 1. Ultrasound-guided thoracic paravertebral and erector spinae block

For maintenance sedation, 2 mg midazolam, 50 mg ketamine, 50 mcg fentanyl, and 150 mg propofol were used within 90 minutes. After VATS were performed with uniport, the patient was uneventfully admitted to the surgical intensive care unit. A singular postoperative drain was inserted. (Figure 2-3) The total surgery duration was 90 minutes. Oral intake was resumed after four hours, and the patient did not report post-operative pain while under surveillance with Numerical Rating Scale (NRS). The postoperative NRS above four required additional analgesia, with analgesia performed under the guidance of an anesthesiologist by a pain management nurse. No post-operative complication was observed, and the patient was transferred to the ward. Total hospitalization duration was, including intensive care stay, with postoperative day being counted as 0, 4 days.



*In the preoperative chest x-ray, an evident pneumothorax on the right side can be seen, with all structures relocated to the right hilus
Figure 2. Preoperative chest X-ray



*After chest tube insertion, an adequate response to pneumothorax is present after the end of surgical intervention.
Figure 3. Post-operative Chest X-ray

DISCUSSION

Maintaining an unproblematic perioperative period is as paramount as the surgery itself. Under ideal conditions, this practice may allow for earlier hospital discharge while reducing overall mortality and complications from underlying comorbidities. An increased preference for ERAS protocols

has been utilized to facilitate this benefit.[2] Combining all these approaches grants what may be called a golden key to a successful surgery. Limitation of post-operative opioid requirement after invasive procedures is essential, especially in thoracic surgeries, which often have a high incidence of pulmonary complications. Alternative anesthesia methods have been utilized, along with less invasive surgical techniques for this purpose, with non-intubated VATS being one option preferred.[10]

Such methods limit complications arising from general anesthesia usage, neuromuscular blockage requirement, and intubation-related issues, ranging from sore throat to possible esophageal intubation. The preference for VATS also does not require mandatory lung isolation methods, which limits possible physiological and mechanical issues caused by these methods.[10]

In this case, the patient was young and did not have any severe comorbidities; however, the presence of bilateral bullous lung and the requirement of positive pressure ventilation could have led to catastrophic consequences. Under TPVB and ESPB, VATS could be performed without intubation, and the mentioned complications were limited. Patient comfort was another parameter, as earlier hospital discharge reduced the need for sedation, and better overall pain management was provided. These benefits were also evident in intensive care unit requirements being less required in the mentioned patients, further supporting the claim of better overall care and patient comfort. Early oral intake was also allowed in these patients, which lessened possible post-operative nausea and vomiting. The minimally invasive nature of VATS also contributes to overall safety and allows regional anesthesia with sedation to be used as the sole method of anesthesia.[11,12]

Another topic of interest was choosing the optimal block method. Thoracic epidural anesthesia (TEA) had been the preferred method for non-intubated patients; however, considering its invasive nature and possible risk of epidural hematoma, abscess, urinary retention, and similar complications, it was considered somewhat limited in terms of having a role in ERAS protocols.[13] Additionally, current ERAS guidelines state that inadequate evidence is available to recommend a routine non-intubated approach for patients. However, it also states that the methods show promise and further studies are required. Combined approaches such as the one presented in this case are relatively more straightforward for the operator and patient while allowing better control of side effects. Considering both block procedures were performed under a single needle injection, failure to maintain a neural blockage was considered limited, as one failed block could have been compensated by the other. The combination of blocks, in general, provided a lower block failure and allowed more effective analgesia to be provided.

Control of pulmonary symptoms was another benefit of limited intervention to otherwise stable pulmonary systems. Preservation of lung function, along with the mentioned benefits of earlier hospital discharge and lower complication rates, have also been reported in thoracic surgery series.[14,15] There have also been case reports stating that patients who had otherwise been unfit for the thoracic intervention were able to undergo procedures with minimally invasive methods and non-intubation approaches. A study evaluated 16 patients going under NIVATS with a combination of ESPB and TPVB had similar results presented in our case report, with adequate safety profiles presented.[16]

CONCLUSION

It can be stated that VATS and non-intubated approaches reduce many complications, especially those that could be attributed to the pulmonary system. Further prospective studies, especially regarding thoracic ERAS protocols, would illuminate the safety of these approaches.

ETHICAL DECLARATIONS

Informed Consent

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

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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Author Contributions

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

REFERENCES

1. Moningi S, Patki A, Padhy N, Ramachandran G. Enhanced recovery after surgery: An anesthesiologist's perspective. *J Anaesthesiol Clin Pharmacol*. 2019;35(1):5-13.
2. Dinic VD, Stojanovic MD, Markovic D, et al. Enhanced recovery in thoracic surgery: a review. *Front Med*. 2018;5(1):5-14.
3. Pincus E. Regional anesthesia: an overview. *AORN J*. 2019;110(3):263-272.
4. Moorthy A, Eochagáin A, Dempsey E, et al. Postoperative recovery with continuous erector spinae plane block or video-assisted paravertebral block after minimally invasive thoracic surgery: a prospective, randomized controlled trial. *Br J Anaesth*. 2023;130(1):137-147. doi: 10.1016/j.bja.2022.07.051
5. Komatsu T, Kino A, Inoue M, et al. Paravertebral block for video-assisted thoracoscopic surgery: analgesic effectiveness and role in fast-track surgery. *Int J Surg*. 2014;12(9):936-939. doi: 10.1016/j.ijsu.2014.07.272
6. Liu L, Xin N, Zhang L, et al. Effects of ultrasound-guided erector spinae plane block on postoperative analgesia and plasma cytokine levels after uniportal VATS: a prospective randomized controlled trial. *J Anesth*. 2021;35(1):3-9. doi: 10.1007/s00540-020-02848-x
7. Zengin M, Alagöz A, Sazak H, et al. Comparison of efficacy of erector spinae plane block, thoracic paravertebral block, and erector spinae plane block and thoracic paravertebral block combination for acute pain after video-assisted thoracoscopic surgery: a randomized controlled study. *Minerva Anestesiol*. 2023;89(3):138-148.
8. Zengin M, Baldemir R, Ulger G, Sazak H, Alagoz A. Postoperative analgesic efficacy of thoracic paravertebralb and erectors plane block combination in video-assisted thoracic surgery. *Cureus*. 2021;13(6):15614.

9. Fu Z, Zhang Y, Zhou Y, et al. A comparison of paravertebral block, erector spinae plane block and the combination of erector spinae plane block and paravertebral block for post-operative analgesia after video-assisted thoracoscopic surgery: a randomised controlled trial. *J Minim Access Surg*. 2022;18(2):241.
10. Wen Y, Liang H, Qiu G, et al. Non-intubated spontaneous ventilation in video-assisted thoracoscopic surgery: ameta-analysis *Eur J Cardiothorac Surg*. 2020;57(3):428-437. doi.org/10.1093/ejcts/ezz279
11. Kao MC, Lan CH, Huang CJ. Anesthesia for awake video-assisted thoracic surgery. *Acta Anaesthesiol Taiwan*. 2012;50(3):126-130.
12. Lin J, Liao Y, Gong C, et al. Regional analgesia in video-assisted thoracic surgery: a bayesian network meta-analysis. *Front Med*. 2022; 9(6):842332.
13. Freise H, Van Aken HK. Risks and benefits of thoracic epidural anesthesia. *Br J Anaesth*. 2011;107(6):859-868. doi.org/10.1093/bja/aer339
14. Mudannayake R, Martinez G, Bello I, Gimenez-Milà M. Non-intubated thoracic surgery: a physiological approach. *Arch Bronconeumol*. 2023;59(11):699-701.
15. Tacconi F, Pompeo E. Non-intubated video-assisted thoracic surgery:w does evidence stand? *J Thorac Dis*. 2016;8(4):364-375.
16. Alagoz A, Findik G, Sazak H, et al. Non-intubated video-assisted thoracoscopic surgery under combination of erector spinae plane block and thoracic paravertebral block. *BMC Anesthesiol*. 2022;22(1):99.

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Letter to Editor

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Awareness and management of slipping rib syndrome

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Dear Editor,

Slipping Rib Syndrome (SRS) is a clinical condition resulting from the instability of the costochondral junction, typically involving the lower ribs (8th, 9th, and 10th ribs). This syndrome leads to severe and often intermittent chest pain due to the entrapment of intercostal nerves. SRS, first described by Cyrix in 1919, is characterized by abnormal mobility of the lower ribs.[1]

Diagnosing SRS is often challenging as the symptoms can mimic many other causes of chest pain. Typical clinical features include sharp pain in the lower rib area that worsens with movement, tenderness on palpation, and pain provoked by the Hooking maneuver. On physical examination, pain elicited by palpation of the affected ribs is a specific sign of SRS.

Recent literature reviews have highlighted significant advances in the diagnosis and treatment of SRS. Mekhail et al.[2] have shown that ultrasound can confirm the diagnosis of SRS due to its non-invasive natüre. Additionally, Romano et al.[3] noted that surgical intervention in SRS provides excellent pain relief and proposed that reduced thickness of the rectus abdominis muscle could be a new diagnostic sign of the syndrome.

Treatment options vary depending on the severity and duration of the patient's symptoms. Gress et al.[4] reported that intercostal nerve blocks could provide both diagnostic confirmation and symptomatic relief in SRS. This method is particularly useful for patients who are not candidates for surgical treatment. Botulinum toxin injections can also be used in some cases to alleviate pain.

Surgical treatment is considered when conservative methods are inadequate. One of the most common surgical procedures is the excision of the affected costal cartilage. This procedure relieves pain by removing the cartilage causing nerve entrapment. Madeka et al.[5] highlighted the success and safety of minimally invasive rib fixation and costal cartilage excision as alternative techniques in SRS treatment. These methods are preferred due to their less invasive nature and faster recovery times.

CONCLUSION

Improving the clinical diagnosis and treatment methods for SRS requires further research and awareness. This syndrome can significantly impact patients' quality of life, and early diagnosis and appropriate treatment can markedly enhance their well-being.

ETHICAL DECLARATIONS

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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Author Contributions

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

REFERENCES

1. Cyriax E. On various conditions that may simulate the referred pains of visceral disease, and a consideration of these from the point of view of cause and effect. *Practitioner.* 1919;102:(1)314-322.
2. Mekhail FG, Montgomery JR, Spicer PJ. Slipping rib syndrome presentation in a young woman. *Radiol Case Rep.* 2022;17(11):4376-4378.
3. Romano R, Gavezzoli D, Gallazzi MS, Benvenuti MR. A new sign of the slipping rib syndrome? *Interact Cardiovasc Thorac Surg.* 2022;34(2):331-332.
4. Gress K, Charipova K, Kassem H, et al. A Comprehensive review of slipping rib syndrome: treatment and management. *Psychopharmacology Bull.* 2020;50(4):189-196.
5. Madeka I, Alaparthi S, Moreta M, et al. A review of slipping rib syndrome: diagnostic and treatment updates to a rare and challenging problem. *J Clin Med.* 2023;12(24):7671.