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RESEARCH

FOLLOW UP RESULTS OF 65 YEARS OF AGE OR OLDER PATIENTS WITH PULMONARY EMBOLISM: RETROSPECTIVE EVALUATION OF 127 PATIENTS

ABSTRACT

Introduction: In recent years, with the increase in the elderly population, disease frequency has increased and the quality of life has decreased. The incidence of pulmonary embolism and the mortality rates are higher in the elderly population than the younger population. Thus, we aimed to demonstrate the follow up results of elderly patients with pulmonary embolism.

Materials and Method: The demographic data, the diagnosis and the treatment methods, the mortality rates and the factors contributing to mortality of 127 pulmonary embolism patients (women=51) aged 65 years or older were evaluated retrospectively. Chi-square test was used for statistical analysis.

Results: The mean age of the study population was 70.55±13.41 years, and the most frequent symptom was dyspnea (74.8%), the most frequent comorbidity was congestive heart failure (24.4%). Bed rest for more than 3 days (44.8%) was the prominent risk factor for pulmonary embolism. There was a significant relationship between proximal localization of pulmonary embolism with bed rest for more than 3 days ($p<0.01$) and comorbidities ($p=0.03$). Pulmonary embolism was the cause for early mortality and comorbidities were responsible for late mortality.

Conclusion: Clinicians should suspect pulmonary embolism in patients aged 65 years or older with complaints of dyspnea and chest pain. High rates of early mortality due to pulmonary embolism and frequent localization of pulmonary embolism in main pulmonary arteries indicate the importance of early diagnosis and treatment.

Key Words: Aged; Lung; Pulmonary Embolism.

ARAŞTIRMA

ALTMIŞBEŞ YAŞ VE ÜZERİ PULMONER EMBOLİLİ HASTALARIN İZLEM SONUÇLARI: 127 HASTANIN RETROSPEKTİF DEĞERLENDİRMESİ

ÖZ

Giriş: Günümüzde giderek artan yaşlanan nüfusta tedavi edilmesi gereken hastalık sıklığı da artmakta, yaşam kalitesi bozulmaktadır. Yaşlanan nüfustaki pulmoner emboli insidansı ve mortalite hızı genç nüfusa göre fazladır. Bu nedenle, bu çalışmada 65 yaş ve üzerindeki pulmoner embolisi olan hastaların takip sonuçlarının sunulması amaçlanmıştır.

Gereç ve Yöntem: Çalışmada, pulmoner emboli tanısı konulan 65 yaş ve üzeri 127 hastanın (kadın: 51) demografik verileri, tanı ve tedavi yöntemleri, mortalite oranları ve mortaliteye katkısı olan nedenleri geriye dönük olarak incelendi. Nitelik değişkenler arasındaki ilişki ki-kare testi ile değerlendirildi.

Bulgular: Yaş ortalaması 70.55±13.41 olan hastaların pulmoner emboli için en sık karşılaşılan yakınması nefes darlığı (%74.8), en sık eşlik eden hastalık konjestif kalp yetmezliği (%24.4) idi. Üç günden fazla yatak istirahati (%44.8) ön plandaki risk faktörüydü. Proksimal yerleşimli pulmoner emboli ile üç günden fazla yatak istirahati ($p<0.01$) ve birden fazla ek hastalık ($p=0.03$) arasında anlamlı ilişki bulundu. Hastaların erken mortalite oranları pulmoner emboli, geç mortalite oranları ise eşlik eden hastalıklar nedeniyleydi.

Sonuç: Nefes darlığı, göğüs ağrısı ile hastaneye başvuran 65 yaş ve üzeri hastalarda pulmoner emboliden şüphelenilmelidir. Pulmoner emboliye bağlı erken mortalite oranlarının fazla olması ve pulmoner embolinin sıklıkla ana pulmoner arterlerde yerleşmesi erken tanı ve tedavinin önemini göstermektedir.

Anahtar Sözcükler: Yaşlı; Akciğer; Pulmoner Emboli.

INTRODUCTION

Today, the number of people aged 60 years or older is 650 million and this number is expected to reach 1.2 billion in 2025 according to the data of World Health Organization (WHO) (1). In our country, the proportion of the elderly population was 5.6% in 2000 (2), and this number has increased to 7.3% in 2011 (3). The growth in the elderly population is accepted as the success of health politics and socioeconomic development. This leads to an increase in the number of elderly patients in clinics, thus thequality of life should be improved and the health related costs should be decreased.

Early diagnosis and treatment are essential due to the severity of diseases and complications in the elderly population. The incidence of pulmonary embolism has increased in people aged 65 years or older, and it is a serious life threatening cardiovascular disease characterized by total or subtotal oclusion of pulmonary arterial system (4). Comorbidities in elderly patients increase the severity of PE (5). In the literature, PE incidence was found to be 50-60/100.000, 120/100.000, and 700/100.000 for patients younger than 65 years of age, for patients between 65-69 years of age and, for those older than 85 years of age respectively (6). Pulmonary embolism should be considered in differential diagnosis of elderly patients.

We aimed to present the demographic data, the relevant clinical and labaratory findings, the mortality rates and causes of PE in patients aged 65 years or older.

MATERIALS AND METHOD

Patients

One hundred twenty-seven patients (65-85 years of age, female/male: 51/76) admitted to the emergency service or the outpatient pulmonary diseases clinics of Diskapi Yildirim Beyazit Training and Research Hospital and Etlik Ihtisas Training and Research Hospital between January 2007-December 2011 with a diagnosis of PE according to computed tomography pulmonary angiography (BTPA) or/and ventilation/perfusion scintigraphy (V/Q scintigraphy) were included in the study. Patients hospitalized in other departments/clinics and patients with incomplete hospital records were excluded from the study. This study was approved by the Ethic Committe for Diskapi Yildirim Beyazit Training and Research Hospital. The study was planned according to Helsinki Declaration.

Risk factors for PE were defined as bed rest for more than 3 days in the last 4 weeks, malignancy, deep venous thrombosis (DVT), congestive heart failure, respiratory failure, end stage renal disease, obesity, cerebrovascular diseases, factor V Leiden mutation and protein S deficiency.

Risk factors related to the conditions were defined as lower extremity fracture, surgery within 4 weeks and major trauma. Early mortality was defined as death within first 30 days during hospitalization and/or after the discharge, and late mortality was defined as death after 30 days.

Variables

Demographic data, symptoms, comorbidities, physical examination and laboratory findings, arterial blood gas analysis results, posteroanterior chest x-rays, electrocardiography, echocardiography (ECHO), colored doppler ultrasonography (CDUS, Toshiba SSA, 270A, Tokyo, Japan) and CTPA and V/Q scintigraphy findings were evaluated retrospectively from patients' records. Patients were referred to another center for V/Q scintigraphy.

Serum D-dimer (Siemens BCS-XP, immunoturbidimetric method), creatinine (Siemens Advia 2400, enzyme kinetic method), protein S (Siemens BCS-XP, clotting method) levels were determined. Factor V Leiden gene mutation was analysed with polymerase chain reaction.

Echocardiographic evaluation was performed in left lateral position, with M-mode, 2-D and colored Doppler methods according to American Heart Society criteria (7). Right ventricular dysfunction was defined as right ventricular dilatation and hypokinesia according to echocardigraphic findings. Deep venous thrombosis was diagnosed via detection of thrombus with CDUS after detailed pyhsical examination.

Imaging Methods

All patients had posteroanterior chest x-rays. Spiral computed tomography with contrast material and and spiral CTPA were performed according to the PE protocol for patients with a clinical suspicion of PE (FOV: 35 cm, level thickness: 3 mm, pitch: 2 and i.v 120 ml contrast material) for evaluation of pulmonary arterial system and lung parenchyma. Embolism in pulmonary truncus, or main pulmonary artery, or lobar artery were classified as proximal localization and embolism in lobular-segmental and/or subsegmental arteries were classified as distal localization. Ventilation/Perfusion scintigraphy was performed in 31 patients with abnormal renal functions. Patients with high clinical suspicion and high

probability V/Q scintigraphy results for PE were enrolled to the study (8).

Treatment

All patients included in the study were treated according to the PE guidelines (4). Trombolytic treatment (Streptokinase 250.000 IU, bolus dose in 30 minutes then 100.000 IU/hr, infusion for 24 hours or recombinant tissue plasminogen activator (rt-PA) 100 mg intravenous administration for 2 hours), was administered only to 10 patients due to the risk of bleeding. Other patients received low molecular weight heparin (LMWH) as initial treatment. After 48-72 hours of hospitalisation oral anticoagulant drug (Warfarine sodium) was added to the treatment regimen. Anticoagulant drug dose was managed according to a target range of INR level between 2 and 3.

Anticoagulant treatment was continued for 6 months.

Statistical Analysis

Statistical Product and Services Solutions (SPSS) for Windows version 13.0 (SPSS Inc, Chicago, IL, USA) was used in this retrospective study for the statistical analysis. Chi-square test was performed for the analysis of variables. Statistical significance level was $p<0.05$.

Results

Demographic Data of Patients and Risk Factors

Mean age of 127 patients recruited to the study was 70.55±13.41 (65-85 years) and 51(40.1%) of them was female. Demographic data and risk factors are outlined in Table 1.

Clinical and Laboratory Findings

Patients' symptoms, clinical and laboratory findings, anteroposterior chest x-rays, and echocardiographic assesments are demonstrated in Table 2. Most frequent symptom was dyspnea (74.8%), most frequent sign was tachypnea (74%).

Cardiomegaly (35.4%) and atelectasis (29.9%) were frequent findings in posteroanterior chest x-rays. According to echocardiographic assesments, 62.2% of the patients had right ventricular systolic dysfuntion. Serum creatinine levels were high in 78.7% of the patients. Serum D-dimer level was within the normal range in 40 patients with PE (31.5%). Also, 24.4% of patients was diagnosed with V/Q scintigraphy due to abnormal creatinine levels.

Table 1— Demographic Data of Patients with Pulmonary Embolism And Risk Factors

Variables	n	%
Age (65-85 years)		
(Mean age±Standart deviation)	70.55±13.41	
Female/Male	51/76	
Bed rest more than 3 days	57	44.8
Congestive Heart Failure	31	24.4
Deep Venous Thrombosis	29	22.8
Chronic respiratory failure	25	19.6
Fracture of lower extremity	21	16.5
Obesity	19	14.9
Chronic renal failure	17	13.3
Cerebrovascular disease	16	12.5
Surgery	15	11.8
Malignancy	13	10.2
Major trauma	7	5.5
Factor V Leiden deficiency	1	0.7

Localization of Pulmonary Embolism

Pulmonary embolism in pulmonary truncus was detected only in 6 patients (4.7%). Right inferior lobar artery (34.6%) and left inferior lobar artery (24.4%) were frequent localizations. Localizations of PE are shown in Table 3 according to CTPA.

Variables Related to Localization of Pulmonary Embolism in Pulmonary Arteries

Relations between PE localization and age, DVT, serum creatinine levels, bed rest for more than 3 days and comorbidites are demonstrated in table 4. There was no significant relation between localization of PE and DVT and serum creatinine levels.

Proximal localization was significantly more frequent in patients with bed rest for more than 3 days ($p<0.01$) and with comorbidities ($p=0.03$).

Mortality Rates

Early and late mortality rates were evaluated and are shown in table 2. Total mortality of 127 patients was 22%, and 8.6% was classified as early, while 13.4% was classified as late mortality. The most frequent cause of early mortality was PE and the most ferquent cause of late mortality was presence of comorbidites. Early and late mortality rates are outlined in Figure 1.

Table 2— Clinical Data and Mortality of Patients with Pulmonary Embolism

Symptoms	n	%
Dyspnea	95	74.8
Chest pain	91	71.6
Cough	52	40.9
Hemoptysis	33	16.5
Syncope	19	14.9
Signs		
Tachypnea (≥20/min)	94	74
Tachycardia (>100/min)	80	62.9
DVT findings	29	22.8
Fever (38.5 °C)	20	15.7
Cyanosis	15	11.8
Chest x-ray		
Normal	26	20.4
Cardiomegaly	45	35.4
Atelectasis	38	29.9
Infiltration	31	24.4
Pleural effusion	19	14.9
Echocardiography		
Right ventricle systolic dysfunction (+)	79	62.2
Right ventricle systolic dysfunction (-)	48	37.8
Laboratory results		
Serum creatinine (0.6-1.27 mg/dl)		
<1	27	21.3
1-2	69	54.3
>2	31	24.4
Serum D-dimer level (<500µg/mL)		
500-1500	40	31.5
1500-4500	55	43.4
>4500	32	25.1
Diagnostic Method		
V/Q scintigraphy	31	24.4
CTPA	96	75.6
Mortality		
Early mortality	11	8.6
After rt-PA use	1	0.7
Pulmonary embolism	6	4.7
Comorbidities more than one	2	1.6
Malignancy	2	1.6
Late mortality	17	13.4
After rt-PA use	—	—
Pulmonary embolism	—	—
Comorbidities more than one	15	11.8
Malignancy	2	1.6

DVT: Deep venous thrombosis, V/Q Scintigrahy: Ventilasyon/perfüzyon scintigraphy, CTPA: Computed tomography pulmonary angiography, rt-PA: Tissue plasminogen activator.

Table 3— Localization of Pulmonary Embolism in Computed Tomography Pulmonary Angiography

Localization	n	%
Pulmonary truncus	6	4.7
Right main pulmonary artery	10	7.8
Left main pulmonary artery	6	4.7
Right inferior lobar artery	44	34.6
Left inferior lobar artery	31	24.4
Right superior lobar artery	11	8.6
Left superior lobar artery	7	5.5
Segment level in right pulmonary artery	18	14.1
Segment level in left pulmonary artery	11	8.6
Subsegment level in right superior lobar artery	9	7
Subsegment level in left superior lobar artery	4	3.1
Subsegment level in right inferior lobar artery	9	7
Subsegment level in left inferior lobar artery	8	6.2

Discussion

In previous studies, the increase in the incidence of PE with age and the difficulties in the diagnosis of PE have been demonstrated (9,10). Furthermore, the mortality rate of PE is shown to be higher in patients aged 65 years or older when compared to the younger patients. Pulmonary embolism ranked third among hospital related mortality causes in the elderly population (11). In general, specificity of symptoms and clinical findings in PE is low. In patients aged 65 years or older admitted to the hospital with complaints of dyspnea and chest pain, clinicans should consider PE for the differential diagnosis. In our study, consistent with the literature (12-

Table 4— Relationship Between Localization of Pulmonary Embolism and Variables

Değişkenler	Proximal Localization PE n(%)	Distal Localization PE n(%)	p*
DVT (+) (n: 29)	17	12	0.8
Serum creatinine (0.6-1.27 mg/dl) level			0.07
<1 (n: 27)	17	10	
1-2 (n: 69)	51	18	
>2 (n: 31)	17	14	
Bed rest more than 3 days (n: 87)	73	14	<0.01
Comorbidities more than 1 (n: 101)	80	21	0.03

PE: Pulmomary embolism, DVT: Deep venous thrombosis.
*Chi-square test was used, p<0.05 was accepted as significant for relations.

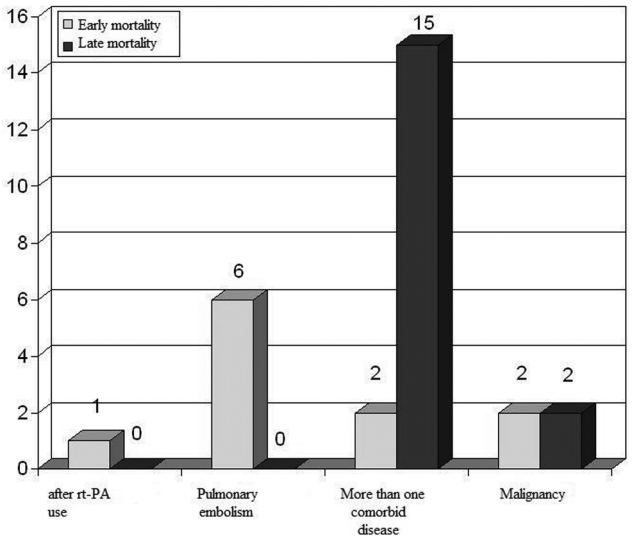

Figure 1

14), dyspnea (74.8%), chest pain (71.6%), tachypnea (74%), tachycardia (62.9%) were common symptoms and clinical findings. Moreover, tachypnea and tachycardia may be observed in other comorbidities (e.g. cardiovascular diseases). Chest pain incidence can decrease together with the decrease in visseral pain perception in some elderly patients. In these cases, PE can not be diagnosed (15). Thus, clinicians should be careful in the diagnosis of PE in elderly patients.

In parallel to the literature, bed rest for more than 3 days were frequent risk factors in our PE patients. In the elderly population, daily routine movements are slow due to aging and comorbidities (16). Therefore the number of bedridden patients is high in the population aged 65 years or older. There were PE patients on bed rest for more than 3 days (44.8%) and comorbidities (79.5%) in our study. Significant correlations between proximal localization of PE with bed rest for more than 3 days ($p<0.01$) and comorbidities such as congestive heart failure, chronic respiratory failure ($p=0.03$) were found. Genetic predispositions are important in the pathogenesis of PE (4). Incidence of PE increases with malignancies and surgical procedures. Fifteen patients (11.8%) had surgery before the diagnosis of PE, 13 (10.2%) patients had malignancy and Factor V Leiden mutation was detected in one patient (0.7%) in our study.

Common findings in posteroanterior chest x-rays were defined as cardiomegaly, pulmonary edema, atelectasis, pleural effusion, elevation of hemidiagraphma in the literature (17,18). In our study, 26 patients had normal chest x-ray findings. Cardiomegaly (35.4%), and atelectasis (29.9%) were frequent abnormal findings in chest x-rays.

Echocardiography is commonly used in the diagnosis and management of PE in recent years. Right ventricular systolic dysfunction is seen in 40% of PE patients (5). Presence of previous cor pulmonale will increase this ratio. In our study, 62.2% patients had right ventricular systolic dysfunction in echocardiographic assessments.

In previous studies, reliability of serum D-dimer level has been low especially in hospitalized, elderly patients with comorbidities. Thus, low serum D-dimer level should not be used in patients with high clinical probability (19). Diagnostic imaging methods should be used especially in patients with high clinical probability and normal serum D-dimer level (20). In our study, 40 (31.5%) patients had normal serum D-dimer level. In these patients, PE was diagnosed with high clinical probability and imaging methods.

There are studies demonstrating the increase in serum creatinine level as a poor prognostic factor (21). In our study although an increase in serum creatinine levels was observed in 70.8% of subjects, there was no significant correlation with PE localization and mortality rates. Pulmonary embolism incidence in lobar arteries and segmenter levels was high in previous studies (20,21). Consistent with the literature, PE incidence was high in proximal level in our study.

Higher PE incidence in lobar arteries and segmenter levels has been demonstrated in previous studies (22,23). In a study by de Monye, et al. (22), 7.7% of 487 patients had PE in pulmonary truncus, 14.6% of 487 patients had PE in right and left pulmonary arteries, 28.5% of 487 patients had PE in lobar arteries, 26.9% of 487 patients had PE in segmenter arteries, and 22.3% of 487 patients had PE in subsegmenter arteries. In another study (23), PE incidence was 58% in segmenter and larger arteries and 42% in subsegmenter and smaller arteries. In our study PE incidence was higher in the proximal level.

Renal functions of elderly patients are generally impaired or within upper limits. Contrast materials used in CTPA can cause acute renal failure. Therefore diagnostic tools for elderly patients should be selected carefully. We used V/Q scintigraphy for diagnosis in 24.4% of patients due to renal failure in our study.

An important side effect of thrombolytic and anticoagulant drugs is bleeding especially in the elderly patients. Thrombolytic therapy was used in 10 patients with hemodynamic instability. Early mortality due to bleeding was seen in

only one patient after thrombolytic therapy. Other patients received LMWH as initial therapy.

The treatment was continued with Warfarin. However, in case of problems in patients' cooperation as in neurologic disorders and bleeding, Warfarin treatment should be discontinued (5). In our study, no hemorrhagic complication during LMWH and Warfarin use was detected and LMWH treatment was continued in 7 patients with neurologic disorders.

Especially in PE patients aged 65 years and older, mortality is high in the first hours. Thus, early diagnosis and treatment of PE is very important for prognosis. Bulbul, et al. found the mortality rate of PE as 9.6% and a high mortality in patients with hypotension and/or comorbidities (24). Particularly, in elderly patients with cardiopulmonary diseases, PE poses a higher risk for hemodynamic instability and increase in mortality (5). In concordance with other studies (12,25), we found that early mortality was due to PE and late mortality was due to cardiovascular diseases.

In conclusion, PE incidence is increasing in the elderly population. Proximal localization effects the prognosis especially in immobile PE patients with comorbidities. Moreover, the duration of hospitalization, health related costs, and mortality rates may increase in these patients. Thus, patients aged 65 years or older should be followed regularly for existing comorbidities, risk factors and additional problems like PE.

Limitations of the Study

Data was obtained from patients records retrospectively. Patients with inadequate data were excluded from the study. Patients with possible PE deceased before the diagnosis were also excluded from the study.

Conflict of Interests

All authors have no conflict of interests.

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