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Seasonal variation of pulmonary thromboembolism in Malatya, Turkey

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Abstract

Aim: Pulmonary thromboembolism (PTE) is a cause of high mortality and morbidity. The incidence of PTE increases over times. In the current study, we aimed to investigate the seasonal variation of PTE patients in Malatya, Turkey by using meteorological data.

Materials and Methods: Total of 207 PTE patients were included in the study. All meteorological data; atmospheric pressure, humidity, temperature changes and wind speed were recorded.

Results: In the current study, 113 (54.5%) patients were female and 94 (45.5%) patients were male. We diagnosed PTE most often in the autumn season. When the monthly distribution of patients was examined; the diagnosis was made most frequently (11.6%) in July and the least in February (4.3%). There was no statistically significant difference between the seasons and months in terms of the incidence of PTE ($p > 0.5$). The seasons pressure, temperature and humidity values were compared with each other, statistically significant difference was found ($p = 0.00$). There was a negative correlation between temperature and pressure and humidity. The frequency of PTE in patients without risk factors for PTE was examined by months. In these groups, PTE was most frequently diagnosed in May (11% n: 10) and least frequently diagnosed in July (2%, n: 3). There was no statistically significant difference between the seasons and months in terms of the incidence of patients with no risk factor for PTE ($p > 0.5$).

Introduction

Pulmonary embolism (PE) is defined as the obstruction of pulmonary arteries with different materials. Pulmonary thromboembolism (PTE) is a cause of high mortality and morbidity. The incidence of PTE has increased over times. Especially after the increased usage of spiral tomography in the clinic, the rate of diagnosis in the United States has increased, the incidence of the disease is 23-269/100,000 per year and the mortality rate is approximately 200,000 every year [1]. As a first study in the literature in 1940, De Takats reported a relationship between low atmospheric pressure and PTE and stated that the risk of PTE has been increasing in the spring season [2]. Afterwards, it is noteworthy that the studies that investigate the relationship between climate variability and PTE are increasing. There are two studies on this subject from two different regions in our country. When large scale studies are examined; all PTE patients with and without risk factors were included in the study. Risk factors of PTE such as primary hypercoagulation, malignancy, surgical operation or inactivity might occur at any time of the year. For this reason, it may be more accurate to include patients without risk factors while examining the distribution of PTE by season. In current study, we investigated the seasonal distribution of 207 PTE patients with or without risk factor of pulmonary embolism in Malatya City.

Materials and Methods

Between January 1, 2013 and December 31, 2015, 207 patients with PTE were included in the study. Hemoglobin, hematocrit, platelet and D-dimer values of 207 patients were recorded at the time of diagnosis. Lower extremity compression Doppler USG was performed in 159 patients to evaluate DVT. Spiral CT angiography was performed in 188 patients who were hemodynamically stable and has appropriate renal functions for imaging of the pulmonary artery truncus. Nineteen patients with renal insufficiency or unstable hemodynamics had undergone perfusion scintigraphy or bedside echocardiography (ECHO) .

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Multislice thorax CT which has 16 detectors had been used for PTE diagnosis (Siemens. The SOMATOM Spirit is a Multislice CT scanne). After the injection of the intravenous fluid, it obtains images with a cross-sectional range of 1mm at a speed of 14 mm/s.Radiological diagnostic criteria for PTE; partial filling defect, complete filling defect, peripheral vascular is considered as an increase in the attenuation around the trains.

We used Siemens Symbia S for ventilation/perfusion scintigraphy. PIOPED diagnostic criteria were used for the diagnosis of PTE. The result of high probability V/Q scintigraphy; it is highly diagnostic in patients with high and moderate clinical probability. In the absence of diagnostic (low-medium probability) scintigraphy, if the clinical scoring is low-probability and the lower extremity Doppler USG is negative for thrombosis, the diagnosis is excluded.

All meteorological data between 1th January 2013 and 31th December 2015, were obtained electronically with the permission of Regional Directorate of Meteorology, Malatya. Atmospheric pressure, humidity, temperature changes and wind speed were recorded accordingly.

Atmospheric pressure unit is millibar (mb), humidity unit is %, temperature unit is C, wind speed unit is km/h. Atmospheric pressure, humidity, heat and wind speed data were calculated between the onset of symptoms and diagnosis. In case of the absence of the information about this period, the 3-day data before hospitalization was taken into account.

Data were analyzed using SPSS statistical software program (version 23, Inc, Chicago). The Mann-Whitney, Wilcoxon W, KI SQUARE, ANOVA , POST HOC tests were used. P value of 0.05 was considered significant. Ethical approval for this study was obtained from Inonu University Medical Faculty Ethics Committee.

Results

A total of 207 patients with PTE were included in the study. 113 patients were female (54.5%) and 94 were male (45.5%), and the mean age was 62.7 ± 15.5 years.

Demographic characteristics, risk factors and relationship with seasons are indicated in Table 1. In the analysis of distribution of PTE by season , PTE was mostly seen in the autumn (28% (n = 58)) and the least in the winter (19.3% (n = 40)) season. The distribution of PTE by season is indicated in Figure 1. When the gender of the patients diagnosed with PTE is analyzed by season; 24 men, 31 women in spring, 27 men, 27 women in summer, 27 men 31 women in autumn, 16 men 24 women were diagnosed in winter.

In the analysis of the monthly distribution of patients; the most common diagnosis was in July (11.6%) and the least in February (4.3%). The distribution of PTE by monthly is indicated in Figure 2. The climate characteristics of the Malatya Basin are different from the continental climate of Eastern Anatolia. The average annual temperature is 13.7 °C in Malatya. January is the coldest month of the year, the average temperature of January is -0.1 °C, the hottest month of July is the average 27.4 °C. Average temperature in Malatya province according to the seasons; It

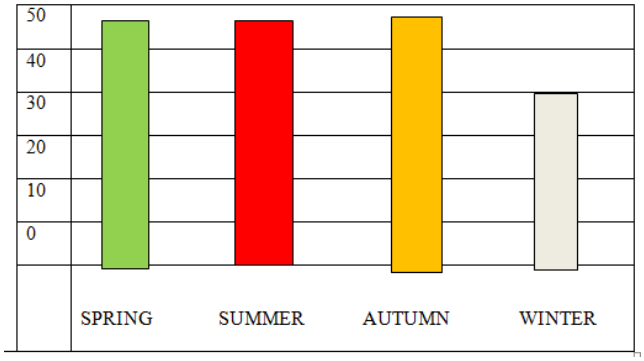

Figure 1. Seasonal distribution of patients. There was no statistically significant difference between the seasons in terms of the incidence of PTE (p> 0.5)

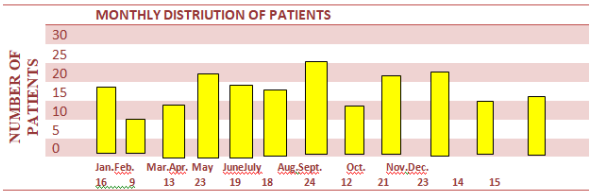

Figure 2. Monthly distribution of patients. There was no statistically significant difference between the months in terms of the incidence of PTE (p> 0.5).

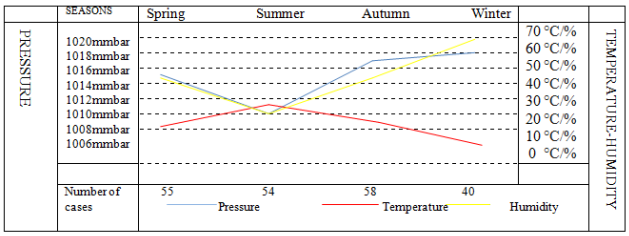

Figure 3. Relation of pressure, humidity and temperature with PTE according to seasons.

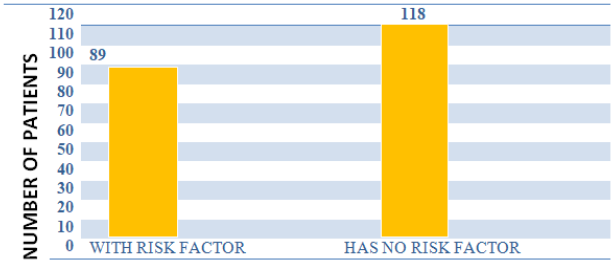

Figure 4. Risk factor of patients according to Virchow triad.

Table 1. Demographic characteristics of patients, risk factors and their relationship with seasons.

	Spring (n = 55)	Summer (n = 54)	Autumn (n = 58)	Winter (n= 40)
Woman/ man	31/24	27/27	31/27	24/16
Age	61.18 ± 15.38	63.67 ± 15.45	62.55 ± 16.22	62.75 ± 15.36
Age > 65	25	21	27	14
Hemoglobin (g / dl)	13.15 ± 2.11	12.03 ± 3.86	11.57 ± 4.53	12.00 ± 3.55
Hematocrit (%)	39.83 ± 6.63	37.58 ± 8.98	35.64 ± 13.84	37.25 ± 8.66
Platelets	236.500 ± 93.900	322.350 ± 45.946	± 217.530 118.470	231.830 ± 25390
Immobilization	10	7	7	4
Surgical	6	8	10	6
Pregnancy	1	0	0	0
Malignancy	10	7	7	4
Cardiovascular disease	1	1	6	0
COPD	1	2	0	0
Primary coagulopathy	3	2	1	2
No risk factors	24	18	25	22
Type of diagnosis				
CT angiography	50	50	50	38
ECHO / scintigraphy	5	4	8	2

Table 2. Hb, Htc and platelet levels in patients by seasons

SEASON	Patient (n)	Average age	Average Hb	Average HTC	Average PLT
Spring	55	61.2 (24-89)	13.1 (7.5-17.5)	39.8 (22.6-51.2)	236.5 (38-540)
Summer	54	63.7 (22-86)	12.0 (5,3-16,7)	37.6 (16.9-47.1)	322.4 (56-3432)
Autumn	58	62.6 (30-87)	11.6 (7.4 to 19.8)	35.6 (21.9-58.9)	217.5 (38-600)
Winter	40	64.0 (20-90)	12.0 (7.4 to 17.5)	37.3 (24.5-50.1)	231.8 (116-617)
Total	207	62.7	12,20	37.6	252.7

Table 3. Seasonal ranges of PTE patients without risk factors.

Seasons	Patient n (%)
Spring	24 (27)
Summer	18 (20)
Autumn	25 (28)
Winter	22 (25)
Total	89 (100)

Table 4. Monthly ranges of PTE patients without risk factors.

Months	Patient n (%)
January	9 (10)
February	5 (6)
March	7 (8)
April	7 (8)
May	10 (11)
June	9 (10)
July	2 (2)
August	7 (8)
September	8 (9)
October	8 (9)
November	9 (10)
December	8 (9)
Total	89

was measured as 12.3 °C in spring, 25.5 °C in summer, 14.4 °C in autumn and 1.3 °C in winter. However, this situation may change seasonally. In the Malatya province, the average wind speed was 10.6 km / h in the spring season, 12.5 km/h in the summer season, 8.6 km/h in the autumn season and 7.5 km/h in the winter season. Relative humidity rate in Malatya province was 60% in spring, 40% in summer, 58% in autumn and 74% in winter.

There was a statistically significant difference in the comparison of seasonal pressure, temperature and humidity values. ($p = 0.00$). There was a negative correlation between temperature and pressure and humidity. The seasonsal pressure, temperature and humidity values are indicated in Figure 3.

Patients with PTE were evaluated for age, Hb, Htc, thrombocyte count. In the examination of seasonal variation of

PTE patients by age; the mean age was the lowest in the spring (61.18 years, n = 55, 27%) and was the highest in the winter. (62.75 years, n = 40, 19%), ($p > 0.05$). Hb level was the lowest in the autumn and the highest in spring ($p > 0.05$). Platelet level was the lowest in the autumn and the highest in spring ($p > 0.05$). Laboratory parameters are indicated in Table 2.

Diseases that are the predisposing factor for PTE; COPD, immobilization, postoperative PTE, malignancy, hereditary thrombophilia, pregnancy, vasculitis, inflammatory bowel diseases, heart and hematological diseases were evaluated. The number of patients who has comorbid disease was 118 (57%) and the number of patients without any comorbid disease was 89 (43%). Comorbidities are indicated in Figure 4.

In the distribution analysis of PTE patients without a predisposing factor, it was observed that most patients were diagnosed in the autumn season (n: 25 (28%)) and at least the patient was diagnosed in the summer season (n: 18 (20%)). The relation of PTE incidence with seasons was analyzed by chi-square test ($p > 0.05$). The distribution analysis of PTE patients without a predisposing factor according to the seasons are indicated in Table 3.

The incidence of PTE patients without risk factors was examined by monthly. The frequency of PTE was highest in May (n:10, 11%)) and the lowest in July (n:2, 3%)). The relationship between PTE incidence and months was analyzed by chi-square test ($p > 0.05$).

5 patients were diagnosed with recurrent PTE during the follow-up period. Three of these patients had Deep Vein Thrombosis (DVT). Three of the cases has been developed Chronic thromboembolic pulmonary hypertension (CTEPH) (1.5%). DVT was detected in 80 (51%) of 159 patients who had underwent lower extremity doppler USG with a prediagnosis of DVT. One patient had isolated arterial thrombus and one patient had upper extremity venous thrombus. One patient was diagnosed with arterial and venous thrombus. Of the 80 patients who were diagnosed with DVT, 42 (52%) had right lower extremity, 12 (15%) had bilateral lower extremity and 23 (33%) had left lower extremity DVT.

We diagnosed PTE most often in the autumn season. When the monthly distribution of patients was examined; the diagnosis was made most frequently in July. There was no statistically significant difference between the seasons and months in terms of the incidence of PTE.

Discussion

In this study, we aimed to demonstrate the relationship between the prevalence of PTE and atmospheric pressure, climate, temperature, humidity and wind speed. We observed that the frequency of PTE increased in autumn (n = 58, 28%), ($p > 0.05$). There was no significant correlation between PTE prevalence and temperature, humidity, and atmospheric pressure ($p > 0.05$).We also found that the presence or absence of risk factors for PTE had no effect on the relationship between PTE and climate or atmospheric variables.

For the first time in 1940, De Takats reported a relationship between low atmospheric pressure and PTE and stated that the risk of PTE increased in spring [2]. Later, there is an increasing number of studies investigating whether there is a relationship between climate variability and PTE. When Boulay et al. retrospectively evaluated 62,237 patients diagnosed with PTE and 65,081 patients diagnosed with DVT according to ICD codes in all hospitals in France between 2010 and 2011. Both PTE and DVT patients were observed to increase especially in winter and decrease in summer. They reported that the difference was statistically significant [3]. Christensen et al. reported that 25% (n = 38.110) of the 152,548 PTE patients were diagnosed in the summer months and 26% (n = 39.769) were diagnosed in the winter months. They found a statistically significant relationship [5]. Sharma et al. reported that the incidence of PTE in autumn and winter increased 2.9 times compared to spring and summer [6].

All of the above-mentioned studies have reported an increase in the incidence of PTE, especially during the cold season. Biliora et al. reported that cold weather caused an increase in the incidence of PTE in winter with a negative effect on protein C and S.[7]. In the current study, we observed that the incidence of PTE increased in hot seasons (spring and summer).

Staut et al. observed that fibrinogen levels increased by approximately 23%, especially in cold weather, and increased risk of VTE due to decreased physical activity and increase respiratory infections [8]. In this case, an increase in the incidence of VTE can be expected in people living in geographic regions with cold climates. In particular, the study conducted in Denmark, one of the Northern European countries with high socioeconomic status, diagnosed 152,548 patients in 30 years. Therefore, 5,000 patients diagnosed with embolism annually in Denmark. Since 1980, the population of Denmark has increased by only 300,000 and the annual incidence of PTE in Denmark, which was 5,123,000 in 2010, is around 1/1000. This is the expected value for the incidence of PTE [1]. When the literature is analyzed, we observed that the incidence of PTE is similar in most countries. In the light of this information, we thought that the incidence of PTE was independent of geography and climate.

Riberio et al. reported that the incidence of PTE in spring was less, but not statistically significant [9] whereas Tromsö, Milan and Leiden found that the decrease in the incidence of PTE in spring was significant. Seasonal variability of embolism could not be explained because the incidence of embolism in cold seasons (autumn and winter) was lower than in warm seasons (spring and summer) [10].

In addition to some studies showing that the incidence of PTE is related to the seasons, there are also some studies indicating that there is no difference. The most noteworthy of these studies is the study conducted by Stein et al in the USA between 1979 and 1999 with 2,475,000 PTE and 5,767,000 DVT patients. According to this very large series of studies, the incidence of PTE and DVT is not related to seasons and months, as in our study [11]. Bilora et al. did not show a significant relationship between the prevalence of non-massive PTE or DVT and the seasons [12]. Similarly, Scott et al. reported that there is no relationship between PTE development and season and baro-

metric pressure [13]. These results are consistent with the study we conducted in our clinic.

When comprehensive studies are examined; we observed that all PTE patients with and without risk factors were included in the study. Risk factors such as primary hypercoagulation, malignancy, surgical operation, inactivity may occur for PTE anytime of the year. The patient may be operated at any season or may have a disease that may cause immobilization, such as fracture or cerebrovascular event. Therefore, when examining the seasonal distribution of PTE, it may be a more accurate approach to evaluate PTE patients without risk factors.

When the literature is examined, there is no study investigating the seasonal variability of PTE in patients without risk factors. In the current study, 89 (43%) patients were diagnosed with PTE without predisposing factors for embolism. Although the number of PTE patients without risk factors is limited, this study is the first article investigating the seasonal variability of PTE in patients without risk factors. There was no statistically significant difference in the seasonal distribution of patients without risk factors. In addition, there was no statistically significant difference in the distribution of these patients by months.

Doppler USG was performed in 159 patients to evaluate DVT. If DVT diagnosis cannot be made with ultrasonography, we evaluated with serial ultrasonographic imaging (5.,7,14. Days). In the current study DVT was detected in 80 (51%) of 159 patients. In the literature, we have observed that very few studies have been investigated on the prevalence of DVT in patients with PTE. Several reports have shown a relatively high prevalence of concomitant DVT, ranging from 10% to 93% in various studies with differing methodologies [14].

The literature on the anatomical distribution of the lower extremity deep vein thrombosis was examined. Ouriel et al. in their study, they observed that the left to right DVT ratio was 1.32: 1 in total [15]. In the current study, we observed that the right to left DVT ratio was 1.57:1 in total. There are few studies investigating the anatomical distribution of deep vein thrombosis in VTE patients.

Chronic thromboembolic pulmonary hypertension (CTEPH) is a complication of pulmonary embolism and a major cause of chronic pulmonary hypertension leading to right heart failure and death. The incidence of CTEPH after symptomatic acute pulmonary embolism is reported to incidence 3.4% (95% CI 2.1−4.4%) [16]. In the current study, the incidence of CTEPH was 1.5%

Conclusion

Venous thromboembolism (VTE) is a systemic and potentially fatal disease. We did not find difference in the incidence of PTE between seasons and months ($p > 0.5$). This result was similar for patients without risk factors for PTE. Therefore, PTE patients can be diagnosed at any time. Frequency of PTE and DVT association is high and doppler USG should be performed these patients. Even in patients receiving appropriate treatment for acute pulmonary embolism, a significant proportion of patients may experience incomplete resolution, which puts them at risk of developing CTEPH.

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