Seasonal Variability and Meteorological Factors: Retrospective Study of the Incidence of Pulmonary Embolism From a Large United Kingdom Teaching Hospital

Kofi Nimako MBChB MRCP, Jan Poloniecki PhD,
Adrian Draper MD FRCP, and Tony Rahman MA DIC PhD FRCP

BACKGROUND: Seasonal variations in the incidence of pulmonary embolism (PE) have been reported. It has been suggested that changes in meteorological factors may explain this variation. Previous studies have provided inconsistent results, possibly as a result of a small number of observations, in some studies and confounding factors. OBJECTIVE: To investigate whether there is a seasonal variation in the incidence of idiopathic PE and to investigate its relationship with atmospheric pressure, humidity, and temperature. METHODS: A large retrospective study was conducted. All confirmed cases of PE at our institution over a 9-year period were included, except for those patients with a major risk factor for PE. Meteorological data were obtained from a local weather station. Days when there was at least one episode of PE (event day) were compared with days when there were no episodes of PE (non-event day). RESULTS: There were a total of 640 episodes of PE. There was a statistically significant lower percentage of event days in spring (13.8%), compared with the rest of the year (18.3%) ($P = .003$). The incidence of PE was related to decreased atmospheric pressure and increased temperature. For atmospheric pressure the relationship was most significant for the mean atmospheric pressure for the 2 days preceding clinical presentation with PE ($P = .02$). For temperature the relationship was most significant for the mean temperature for the 5 days preceding clinical presentation with PE ($P = .04$). CONCLUSIONS: The results confirm the presence of seasonal variations in episodes of idiopathic PE and an association between decreased atmospheric pressure and increased temperature. *Key words: pulmonary embolism; seasonal variability; meteorological factors; weather; atmospheric pressure; humidity and temperature.* [Respir Care 2012;57(8):1267–1272. © 2012 Daedalus Enterprises]

Introduction

Several investigators have suggested that seasonal variations occur in the incidence of fatal and non-fatal pulmonary embolism (PE).[1] The pathophysiological mechanisms underlying these observations remain controversial. One possible mechanism may be changes in meteorological factors that occur during the year that have a direct effect on thrombotic tendencies. Correlations with meteorological factors have been found with the incidence of other embolic diseases such as ischemic strokes and deep vein

Drs Nimako and Draper are affiliated with the Department of Respiratory Medicine; and Dr Rahman is affiliated with the Departments of Gastroenterology and Intensive Care Medicine, St George's Healthcare Trust, London, United Kingdom. Dr Poloniecki is affiliated with the Population Health Research Centre, St Georges University of London, United Kingdom.

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Correspondence: Kofi Nimako MBChB MRCP, Department of Respiratory Medicine, St George's Healthcare Trust, Blackshaw Road, London, United Kingdom SW17 0QT. E-mail: drkofi@yahoo.co.uk.

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thrombosis.[2] However, studies that have investigated relationships with meteorological factors and the incidence of PE have provided inconsistent results.[3-6] Many of the studies were based on only a small number of observations, and this may explain the inconsistent results.[3,4,6] These studies also included patients who had risk factors for PE (non-idiopathic PE), and therefore confounding factors may have influenced the results. Although risk factors for PE, such as surgery, cancer, and immobility, may not be directly implicated regarding the effect of meteorological factors, nonetheless they could be influenced indirectly.[6] We therefore undertook a large study of patients without risk factors for PE (idiopathic). In this retrospective study, we looked for seasonal variations in the incidence of idiopathic PE and a relationship with atmospheric pressure, humidity, or temperature.

QUICK LOOK

Current knowledge

Seasonal variations in the incidence of pulmonary embolism have been reported. The effects of atmospheric pressure, humidity, and temperature on the incidence of pulmonary embolism have not been determined.

What this paper contributes to our knowledge

This study confirms the seasonal variability in the incidence of pulmonary embolism, which occurs less often in the spring. Lower atmospheric pressure and higher temperature may be associated with higher incidence of pulmonary embolism.

Methods

Patients

St George's Hospital is a large teaching hospital in southwest London, United Kingdom. The records of all patients who had been referred to the Department of Radiology and Nuclear Medicine between January 2000 and October 2008 for either a computed tomography (CT) pulmonary angiogram or a ventilation and perfusion ($\dot{V}/\dot{Q}$) scan were reviewed. Patients with a known major risk factor for PE (surgical patients, obstetric patients, trauma/orthopedic patients, and oncology patients) were excluded from the analysis.[7] As immobility and hospitalization[7] is also a risk factor for PE, patients who were in hospital for more than 5 days before they had a CT pulmonary angiogram or $\dot{V}/\dot{Q}$ scan were also excluded. Although evidence suggests that immobility for 3 days increases risk of PE,[8] we chose 5 days because of the delay in obtaining a scan, which may be 48 hours, particularly on weekends. The study protocol was reviewed by the South West London Regional Ethics Committee 3 (previously known as the Wandsworth Regional Ethics Committee), who ruled that the study did not require a full submission to the research ethics committee.

Computed Tomography Pulmonary Angiography

From August 2007, CT angiography was obtained using a 64-slice scanner (GE Hi Speed CTi, GE Healthcare, United Kingdom) and 80–90 mL of iodinated contrast material. Prior to this, CT angiography was obtained with a single slice scanner (GE Lightspeed, GE Healthcare, United Kingdom), using 140 mL of iodinated contrast. A radiologist reported all scans. Patients were investigated by CT angiography as their initial investigation or following an intermediate or indeterminate $\dot{V}/\dot{Q}$ scan.

Ventilation/Perfusion Scan

All scans were reviewed by a radiologist and classified according to the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED)[9] criteria. Normal or low probability scans were classified as negative, while those with high probability were classified as positive. Patients with intermediate or indeterminate probability scans were subsequently investigated with CT pulmonary angiography.

Seasons

For each year, standard dates were used to define each season. Summer was defined as June 1 to August 31, autumn was defined as September 1 to November 30, winter was defined as December 1 to February 28/29 (depending on whether or not it was a leap year), and spring was defined as March 1 to May 31.

Meteorological Factors

Daily meteorological data for the same period (January 2000 to October 2008) were obtained from the British Atmospheric Data Centre; the meteorological data were recorded at a local weather station (the London Weather Centre). The weather station is situated in an area that is meteorologically representative of the area served by the hospital. The altitude of the weather center (22 m) is also similar to the altitude of the hospital and the surrounding area (21 m). The onset of the PE was defined as the day of presentation to the hospital. The unit of analysis was day. An event day was defined as a day in which 1 or more patients presented to the hospital with a subsequent diagnosis of PE. To help determine the timing of any biological influence of meteorological factors and clinical pre-

Table 1. Number of Event Days for Each Month

	2000	2001	2002	2003	2004	2005	2006	2007	2008
Jan	6	2	4	10	6	7	7	12	10
Feb	1	2	1	4	4	4	12	8	16
Mar	1	4	6	6	6	2	3	9	13
Apr	4	3	5	2	3	3	4	0	12
May	1	5	0	3	9	4	5	3	11
Jun	4	1	3	7	8	8	7	9	7
Jul	2	3	8	5	4	10	5	9	18
Aug	4	3	11	6	5	5	9	10	14
Sep	3	4	17	5	8	3	10	8	10
Oct	7	5	6	10	11	5	4	8	6
Nov	1	4	5	11	3	9	6	4	
Dec	3	4	3	3	6	9	4	7	

sentation of PE, meteorological data for the same day and the mean of the meteorological data for 2, 3, 4, 5, and 6 days preceding clinical presentation with PE were used for comparative purposes.

Statistical Analysis

The chi-square test was used to compare the percentage of event days for each season. The Student *t* test was used to compare meteorological factors on event days and non-event days. Multifactorial analysis was performed to assess the association of age and sex with the meteorological factors. Linear correlation (Pearson) or rank correlation (Spearman) was used to test for an association between age and the meteorological factors. Logistic regression was used to test for an association of sex ratio with the meteorological factors. For this study a 2-tailed P value of $< .05$ was regarded as indicating statistical significance.

Results

There were a total of 640 cases of idiopathic PE between January 2000 and August 2008. The majority of patients were female (female 348/640, 55.4%; male 292/640, 45.6%). The number of patients diagnosed following each modality was almost equal: 50.3% (322/640) were diagnosed following a high probability $\dot{V}/\dot{Q}$ scan, and 49.7% (318/640) were diagnosed following a CT pulmonary angiogram. The 640 cases of idiopathic PE occurred on 554 different days. Therefore there were 554 (17.17%) event days and 2,673 (82.3%) non-event days.

Relationship Between Episodes of Pulmonary Embolism and Seasons

Table 1 shows the number of event days for each month, and the Figure shows the average number of event days for each month for year ranges 2000–2002, 2003–2005, and 2006–2008. The percentage of event days for each of the seasons is detailed on Table 2. The chi-square test for the difference between the percentage of event days by season was statistically significant ($P = .01$). There was a statistically significant lower percentage of event days in spring (13.8%), compared to the rest of the year (18.3%) ($P = .003$).

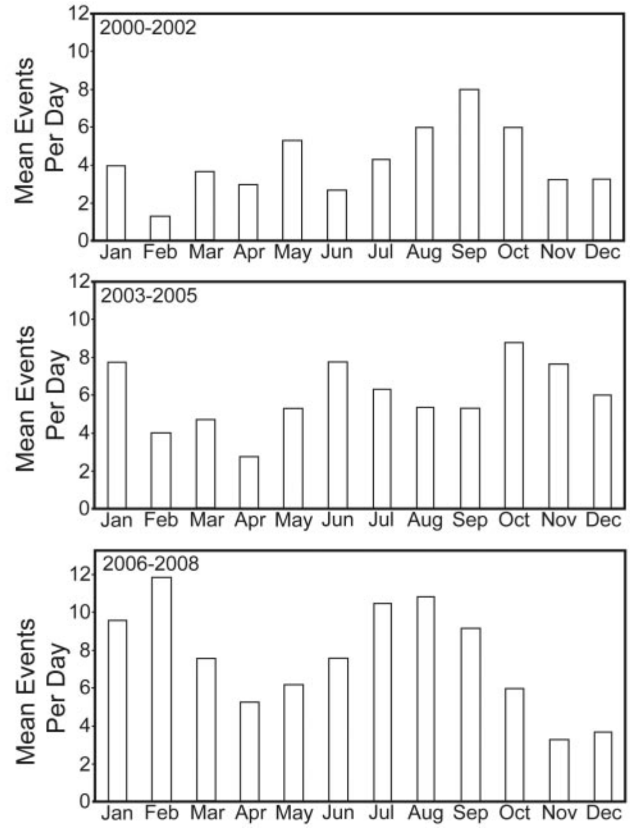

Figure. Average number of event days for each month for the year ranges 2000–2002, 2003–2005, and 2006–2008.

Table 2. Distribution of Event and Non-event Days According to Season

	Summer ($n = 828$)	Autumn ($n = 789$)	Winter ($n = 782$)	Spring ($n = 828$)
Number of event days	160	147	133	114
Percent of event days	19.3	18.6	17.0	13.8*
Number of non-event days	668	642	649	714
Percent of non-event days	80.7	81.4	83.0	86.2

* $P = .003$

Relationship Between the Incidence of Pulmonary Embolism and Meteorological Factors

Mean values for atmospheric pressure, humidity, and temperature on event days and non-event days are shown

Table 3. Relationship of Meteorological Factors to Event and Non-event Days*

Days Prior to Admission	Atmospheric Pressure (mbar)	Temperature (°C)	Humidity (%)
Day of Admission			
Non-event day	1,015.2 (1,014.8–1,015.6)	12.4 (12.2–12.6)	70.2 (69.8–70.6)
Event day	1,014.5 (1,013.6–1,015.3)	12.8 (12.4–13.3)	70.1 (69.2–70.9)
Difference in the mean value	0.7 (−0.2 to 1.7)	−0.4 (−0.9 to 0.1)	0.15 (−0.8 to 1.1)
P	.12	.13	.75
2 Day Average			
Non-event day	1,015.0 (1,014.6–1,015.5)	12.4 (12.2–12.6)	70.2 (69.9–70.5)
Event day	1,013.5 (1,011.6–1,015.3)	12.8 (12.4–13.3)	70.0 (69.3–70.7)
Difference in the mean value	1.6 (0.3–2.8)	−0.4 (−0.9 to 0.0)	0.2 (−0.6 to 1.0)
P	.02	.07	.60
3 Day Average			
Non-event day	1,014.9 (1,014.4–1,015.4)	12.4 (12.2–12.6)	70.2 (69.9–70.5)
Event day	1,013.4 (1,011.3–1,015.5)	12.9 (12.4–13.3)	69.9 (69.2–70.6)
Difference in the mean value	1.5 (0.1–2.9)	−0.5 (−0.9 to 0.0)	0.3 (−0.5 to 1.0)
P	.04	.06	.47
4 Day Average			
Non-event day	1,014.7 (1,014.2–1,015.2)	12.4 (12.2–12.6)	70.1 (69.9–70.5)
Event day	1,013.3 (1,010.9–1,015.7)	12.9 (12.5–13.3)	70.0 (69.3–70.7)
Difference in the mean value	1.4 (−0.2 to 3.0)	−0.5 (−0.9 to 0.0)	0.2 (−0.5 to 0.9)
P	.08	.05	.63
5 Day Average			
Non-event day	1,014.6 (1,014.0–1,015.2)	12.4 (12.2–12.6)	70.2 (69.9–70.5)
Event day	1,013.0 (1,010.4–1,015.6)	12.9 (12.5–13.3)	69.9 (69.2–70.6)
Difference in the mean value	1.6 (−0.2 to 3.4)	−0.5 (−0.9 to 0.0)	0.3 (−0.4 to 1.0)
P	.08	.04	.46
6 Day Average			
Non-event day	1,014.4 (1,013.8–1,015.1)	12.4 (12.2–12.6)	70.2 (69.9–70.5)
Event day	1,012.8 (1,009.9–1,015.6)	12.9 (12.4–13.3)	69.9 (69.2–70.5)
Difference in the mean value	1.6 (−0.3 to 3.7)	−0.5 (−0.9 to 0.0)	0.3 (−0.4 to 1.0)
P	.09	.05	.34

* Results are expressed as differences in the mean (and 95% CI) values of meteorological factor on a non-event day and an event day.

in Table 3. There was no statistical difference between event days when compared to non-event days when the meteorological data for the day of presentation was used for comparative purposes. However, when considering short-term influences of meteorological factors, there was a significant relationship between incidence of PE and decreased atmospheric pressure and incidence of PE and increased temperature. No clear relationship was found between the incidence of PE and the immediate or short-term effect of humidity.

There was no linear correlation (Pearson) or rank correlation (Spearman) between age and the meteorological factors. Logistic regression was used to test for an association of sex ratio with the meteorological factors. There was no association between sex ratio and temperature, with and without adjustment for age ($P = .71$ and $P = .70$, respectively). There was no association between sex ratio and humidity, with or without adjustment for age ($P = .36$ and $P = .36$, respectively). For atmospheric pressure, however, there was a statistically significant association with and without adjustment for age ($P = .03$ and $P = .03$, respectively). The proportion of females was higher at lower pressure.

Discussion

The main finding from the present study is that a seasonal variation in the incidence of idiopathic PE exists and that meteorological factors may contribute to this variation. Our findings found a relationship between the incidence of PE and decreased atmospheric pressure and increased temperature. The associations were characterized by a delay between the influence of the meteorological factor and the clinical presentation with PE. Atmospheric pressure appears to have a more rapid influence than temperature. The relationship with atmospheric pressure was significant when the average value for the atmospheric pressure for the preceding 2 and 3 days was used, whereas the influence of temperature was significant only when the average temperature for the preceding 4, 5, and 6 days was used. The differences in meteorological factors on event days and non-event days were small. This makes the association valid and of interest for the everyday mechanism of PE, and not just for days of extreme weather. In addition, we found a significant association between sex ratio and atmospheric pressure. The proportion of females was higher at lower atmospheric pressure. This suggests that females may be more susceptible to the influence of low atmospheric pressure; however, this association will need to be confirmed in further studies.

Our findings of a seasonal variation in PE are consistent with a number of similar studies. Most of these have found an increased incidence of PE or venous thromboembolism in the autumn and winter months.[10-13] Consistent with our findings, Manfredini et al,[13] in a large multicenter Italian study (2,119 subjects), found that venous thromboembolism were less frequent in spring. However, contrary to our findings, Meral et al[3] found a peak in the incidence of PE in the spring months. However, this was a small study (91 patients) that took place at high altitude (1,800 m) with very different weather conditions to our own.

The finding of a relationship between decreased atmospheric pressure and the incidence of PE is consistent with other studies.[3-5] Interestingly, Oztuna et al[4] found a relationship using the average atmospheric pressure for the preceding 3 days, and Scott et al,[5] using a lag model, found that the incidence of PE was related to a decrease in atmospheric pressure during the 3 days preceding the PE.

Our data support only a relationship between atmospheric pressure and idiopathic PE, and do not provide evidence of a causal relationship. However, it has been proposed by Murayama[14] that atmospheric pressure may have a direct effect on thrombotic tendencies, by inducing platelet aggregation. Our finding of an association between increased temperature and incidence of idiopathic PE is more controversial, since it would be assumed that cooler weather would increase the risk of PE. Oztuna et al[4] have demonstrated that mild cooling can produce an increase of blood viscosity, and Mavri et al[15] found that a procoagulant profile developed in venous blood during winter months. In addition, as a consequence of cold weather it is clear that people live a more sedentary lifestyle that could further increase thrombotic tendencies. However, it is also true that on hotter days and during the holiday period people are more likely to travel in cars for longer distances. Dehydration is more likely to be a problem in the hotter months, due to perspiration, and this may lead to an increase in blood viscosity and PE.

Our findings add to the growing evidence supporting a seasonal variation in PE and the potential influence of meteorological factors. However, controversy still exists, mainly as a result of conflicting results. Some investigators have found no seasonal variation in PE or venous thromboembolism[6,16] and others have found no relationship between atmospheric pressure and temperature and the incidence of PE.[6] We found no relationship between humidity and the incidence of PE, whereas other investigators have reported an association.[4] The inconsistent results suggest that the influence of meteorological factors is not as important as better known risk factors for PE. There is also likely to be interplay between the different meteorological factors. Furthermore, the seasonal variation in PE is likely to be influenced by a number of factors, and not just meteorological factors. For example, there may also be other important risk factors such as the prothrombotic changes related to seasonal factors such as acute respiratory-tract infections. The incidence of respiratory-tract infections vary during the year, and they are known to induce an exaggerated inflammatory response in older adults with an associated increase in fibrinogen.[17] Seasonal variability in PE could also be explained by seasonal variations in human behavior and mobility.

Potential limitations should be considered when interpreting the results of the present study. The study was retrospective, and this may raise concern over the possibility of missed cases. In addition, the number of event days increased through the study period (see Fig. 1). It is likely that this is a result of a lower threshold for investigating patients for PE.[18] It is therefore possible that a number of cases were missed during the early study period. However, it is unlikely that any missed cases would have altered the seasonal variations demonstrated, since any missed cases would have been spread equally throughout the seasons. A further limitation of our study is that, although our hospital is only 10 km from the weather station, it serves a population of 1.3 million people across a large area of southwest London, and it is therefore conceivable that some patients may have lived a lot farther than 10 km from the weather station. Consequently, the meteorological factors that they were exposed to would have been different from that recorded at the weather station. It was our intention to study the seasonal variability and the influence of meteorological factors on idiopathic PE, so we excluded patients with major risk factors for PE. However, we did not exclude patients with minor risk factors for PE, such as cardiorespiratory disease, neurological disability, estrogen therapy, obesity, and thrombotic disorders.[7] It is therefore possible that our cohort included patients with non-idiopathic PE.

Conclusions

This study containing the largest United Kingdom cohort of patients presenting with idiopathic PE from a single hospital confirms the seasonal variability in the incidence of PE. Episodes were found to occur less often in spring. The study found an association between decreased atmospheric pressure and increased temperature and the risk of PE.

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