RESEARCH LETTER

Variation in the incidence of pulmonary embolism and related mortality depending on the season and day of the week

Urszula Kosacka[1], Izabela E. Kiluk[1], Robert Milewski[2], Agnieszka M. Tycińska[1], Małgorzata Jasiewicz[1], Bożena Sobkowicz[1]

1 Department of Cardiology, Medical University of Bialystok, Białystok, Poland
2 Department of Statistics and Medical Informatics, Medical University of Bialystok, Białystok, Poland

Introduction Numerous studies have demonstrated that the occurrence of cardiovascular events shows seasonal and monthly variation, with the peak of hospital admissions and mortality during winter.[1,2]

Data regarding seasonal variation in the incidence of pulmonary embolism (PE) as well as seasonal variation in mortality among PE patients are not consistent.[3] However, several investigators reported more hospital admissions because of PE in winter.[4-6] Furthermore, the so called "weekend effect", leading to an increased mortality rate, has been observed in some cardiovascular diseases.[7,8] Patients admitted on weekends were less likely to undergo invasive diagnostic and therapeutic procedures, which resulted in higher mortality compared with patients admitted on weekdays. Similar observations were reported in patients with PE.[9]

The aim of our study was to assess seasonal and weekday/weekend variation in the incidence of PE and to determine whether any differences in mortality, if found, could be explained by the seasonal or weekday/weekend differences. To investigate the effect of weekend admissions on outcomes, we sought to compare the clinical characteristics of the patients as well as data on therapeutic procedures that had been used.

Patients and methods In this retrospective study, medical records of all consecutive patients with confirmed PE admitted to the Department of Cardiology at the Medical University of Bialystok in the years from 2004 to 2010 were reviewed and analyzed. We categorized admissions depending on the quarter of the year (winter: January–March; spring: April–June; summer: July–September; autumn: October–December) and days of the week. Weekend admissions were defined as those recorded between Friday midnight and Sunday midnight.

The diagnosis of PE was established mainly on the basis of multislice computed tomography angiography with contrast-agent enhancement. A minority of the patients were investigated using lung scanning or echocardiography.[10]

For the purpose of the current study, the following parameters were analyzed: time of hospitalization (day/month), demographic data, clinical features, risk factors for PE, treatment methods in PE and in-hospital mortality, additional tests performed within 24 hours from admission:

1 laboratory parameters: D-dimer and creatinine levels (estimated glomerular filtration rate [eGFR], calculated by the Modification of Diet in Renal Disease formula)

2 presence of tachycardia (>100 bpm) and supraventricular arrhythmias on admission electrocardiogram (ECG)

3 transthoracic echocardiography: right ventricular free wall contractility impairment, systolic pulmonary artery pressure, acceleration time of the pulmonary flow (ACT).

Data on long-term mortality (from all causes) were retrieved from the medical records and from a government registry of the local population (accessed, September 16, 2013).

A statistical analysis was performed using Statistica 10.0 (StatSoft, Inc., Tulsa, Oklahoma, United States) and IBM SPSS Statistics 21.0 (Predictive Solutions, United States). The following tests were used: the χ^2 test, Fisher exact test, Kolmogorov–Smirnov test with the Lilliefors correction, Shapiro–Wilk test, Mann–Whitney test, logistic regression, Cox proportional hazard model, Kaplan–Meier estimator, and log-rank test for

Correspondence to:
Izabela E. Kiluk, MD, Klinika Kardiologii, Uniwersytet Medyczny w Białymstoku, ul. M. Skłodowskiej-Curie 24A ,15-276 Białystok, Poland,
phone: +48-85-746-86-56,
fax: +48-85-746-86-04,
e-mail: izabela.kiluk@umb.edu.pl
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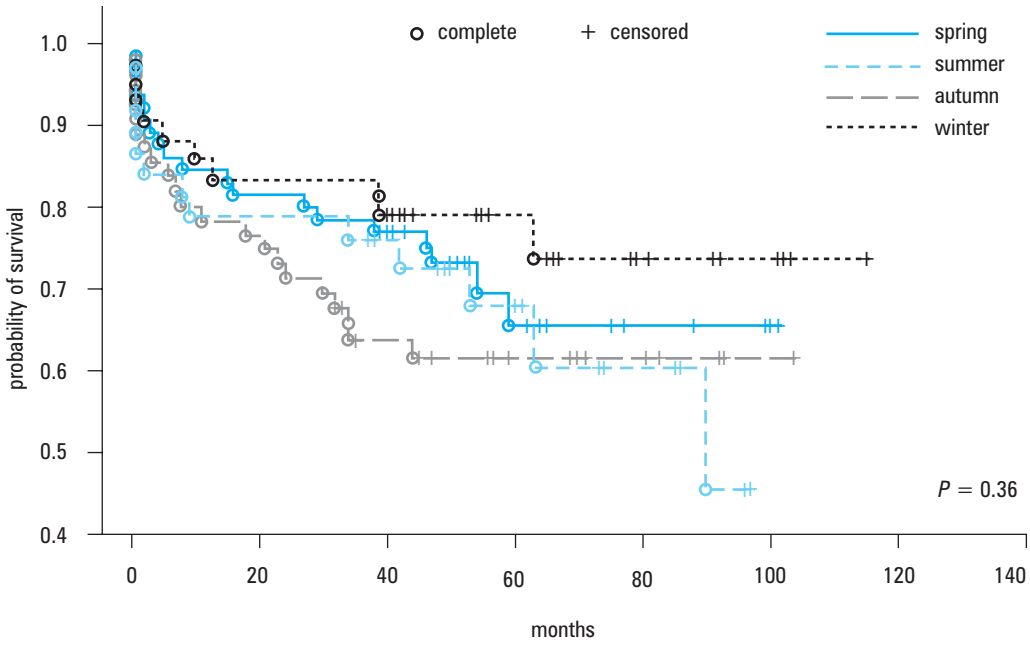

FIGURE Kaplan–Meier survival curves in patients with pulmonary embolism according to the seasons

2 groups and the χ^2 test for multiple groups. The Poisson regression was used to assess the relation between seasons and the number of admissions. A detailed description is available in Supplementary material online, *Statistical analysis*.

For all tests, a *P* value of less than 0.05 was considered statistically significant.

The study was approved by the institutional Review Board of the Medical University of Bialystok.

Results The study cohort included 238 patients admitted with a diagnosis of PE. The highest number of patients with PE was admitted to the hospital in spring (77 patients, 32.3%), followed by autumn (65 patients, 27.3%), and summer (49 patients, 20.7%), and the lowest number of admissions was noted in winter (47 patients, 19.7%). The number of admissions for PE in spring was significantly different from the number of admissions in summer ($P = 0.013$) and winter ($P = 0.0076$). No significant difference was found between the number of admissions for PE in spring and autumn ($P = 0.314$).

Weekdays/weekend admissions Weekends accounted for 17.6% of all admissions (42 patients). The proportion of hospitalizations on weekends was similar between the consecutive years (2004–2010) ($P = 0.784$).

The demographic and clinical characteristics and outcomes in patients admitted on weekends and weekdays were similar. The only differences were noted in admission ECG. In patients admitted on weekends, supraventricular arrhythmias were found more often ($P = 0.032$). Patients admitted on weekends and weekdays did not differ in terms of the length of the hospital stay and treatment used (Supplementary material online, *Tables S1 and S2*).

Mortality Overall, 25 in-hospital deaths (10.5%) and 63 deaths during follow-up (29.6%) were recorded, and 11 patients (5%) were lost to follow-up. No seasonal differences in early and late mortality rates were observed ($P = 0.404$). No differences in survival were noted between the 4 seasons ($P = 0.36$) (**FIGURE**). There were no differences in mortality (cumulative, in-hospital, and after discharge) between weekend and weekday admissions.

Among all the evaluated variables potentially associated with the prognosis, a significant independent correlation with in-hospital mortality was found in a multivariate analysis for malignancy (odds ratio [OR], 9.2; 95% confidence interval [CI], 1.42–59.72; $P = 0.02$), history of stroke (OR, 8.47; 95% CI, 1.28–56; $P = 0.027$), reduced eGFR (OR, 0.96; 95% CI, 0.92–1.00; $P = 0.038$), supraventricular arrhythmia on admission (OR, 6.76; 95% CI, 1.00–45.68; $P = 0.05$), and reduced ACT (<90 ms) on echocardiography (OR, 0.96; 95% CI, 0.93–1.00; $P = 0.041$). Long-term mortality was independently associated with age (hazard ratio [HR], 1.05; 95% CI, 1.02–1.08; $P = 0.001$), history of stroke (HR, 2.21; 95% CI, 1.02–4.78; $P = 0.044$), malignancy (HR, 3.99; 95% CI, 2.19–7.28; $P < 0.001$), and increased pulmonary artery systolic pressure (HR, 1.02; 95% CI, 1.00–1.03; $P = 0.05$).

Discussion Over the 7-year follow-up period, we found a seasonal variation in the incidence of PE with the highest admission rate in spring and the lowest in winter. We can hypothesize that the mechanism of such a seasonal pattern of PE occurrence may be due to the local characteristics of the Podlasie province, which is located in the northeast region of Poland with a harsh, continental climate. This region has the lowest population density in Poland (59 inhabitants per square kilometer), with as much as 40% of the population living in rural areas and a low number of hospitals. Snow cover lasts from November to March, and January is the coldest month of the

year with a temperature below –30°C. Perhaps the peak admission rate in spring may be related to a very long period of relative immobilization due to the cold weather. On the other hand, the lowest admission rates in winter months may be explained by difficulties in getting to a hospital from rural areas.

Multiple studies on seasonal variation in PE have been published and yielded inconsistent results.[3-5,11] This may be related to the fact that the studies were conducted in different parts of the world with different climates, among many other possible reasons.

Regarding the relationship between mortality and seasons, no seasonal peak in mortality rates among patients with PE was found in our study population. An analysis of data from the U.S. National Hospital Discharge Survey (including 184 201 patients who died due to PE) did not show any seasonal variation in the incidence of fatal PE.[12]

Data regarding the weekend effect in patients with PE are scarce.[9] In contrast to the previous studies, the present results do not show an effect of weekend admissions on mortality. The only significant difference between the groups was observed for ECG findings on admission. Patients admitted on weekends had supraventricular arrhythmias more often than those admitted on weekdays, which might indirectly indicate the severity of the clinical status.

How can we explain our findings? In most studies, national or regional databases were used, and data retrieved from such data sets were collected in different types of hospitals (ie, large university centers, high-volume hospitals, federal hospitals, or smaller local facilities). Our data are limited to a single university hospital in Białystok. The emergency department (ED) at the University Hospital in Bialystok is on duty 24/7 during the entire year serving annually about 53 000 patients. Our ED is adequately staffed (in terms of the proportion between junior and senior physicians and availability of consultants) with unrestricted access to diagnostic procedures such as computed tomography or ultrasonography throughout a week. Our health care system was standardized and unified between the ED and cardiology unit. Such quality of medical care may probably explain the lack of discrepancies between outcomes in PE patients treated on weekends or weekdays.

Study limitations Our study has several limitations. It was a retrospective analysis based on a limited number of patients (11 patients were lost to follow-up because they moved to a different address). However, our study lasted 7 years with a long-term follow-up, and patients came from the same geographical region. Finally, our findings are limited to a single university hospital, which may be considered a limitation but also an advantage (because of unified health care practices).

Conclusions In the study population, we confirmed seasonal variability in the occurrence of PE with the highest admission rate in spring and the lowest in winter. This variability had no effect on mortality. On the other hand, we did not demonstrate any weekend effect in patients with PE admitted to the Department of Cardiology in Bialystok. Weekend admissions for PE were not associated with increased mortality, worse clinical status, or a longer hospital stay.

Supplementary material online Supplementary material online is available with the online version of the paper at www.pamw.pl.

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Supplementary material online

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Statistical analysis Categorical variables were compared using the χ^2 test and the Fisher exact test. Normal variable distribution was evaluated by the Kolmogorov-Smirnov test with the Lilliefors correction and the Shapiro–Wilk test. Because of a nonnormal distribution of continuous variables, the Mann–Whitney test was used to assess differences between the 2 groups, and continuous variables are presented as median values with the 1st and the 3rd quartiles. Poisson regression was used to assess the relation between seasons and the number of admissions for PE. A multivariate logistic regression model was created. A Cox proportional hazard model was used to evaluate the effect of covariates on survival (long-term mortality). A univariate analysis was performed to identify variables that were significantly associated with mortality, and then a multivariate model was created. Survival was estimated using the Kaplan–Meier method. Differences between survival curves were evaluated by the log-rank test for the 2 groups and by the χ^2 test for multiple groups. For all tests, a *P* value of less than 0.05 was considered statistically significant.

Statistical analysis was performed using Statistica 10.0 (StatSoft, Inc., Tulsa, Oklahoma, United States) and IBM SPSS Statistics 21.0 (Predictive Solutions, United States).

The study was approved by the institutional Review Board of the Medical University of Bialystok.

Table S1 Demographic and clinical characteristic as well as treatment and outcomes of patients admitted for pulmonary embolism at weekends and on weekdays

Characteristics	**Weekend**	**Weekdays**	***P* value**
overall, n (%)	42 (17.6)	196 (82.4)	
age, y	71 (52–79)	66 (52–76)	0.3
male sex, n (%)	21 (50)	87 (44.4)	0.3
clinical symptoms on admission, n (%)			
dyspnea	34 (87.2)	157 (86.3)	0.6
chest pain	13 (33.3)	49 (26.8)	0.3
syncope	7 (17.9)	31 (16.9)	0.5
cough	2 (5.1)	11 (6)	0.6
hemoptysis	1 (2.4)	6 (3.1)	0.6
comorbidities and addictions, n (%)			
hypertension	21 (50)	103 (52.6)	0.5
atrial fibrillation	9 (21.4)	32 (16.3)	0.3
history of nicotine addiction	5 (15.6)	5 (15.6)	0.1
stroke	6 (14.3)	19 (19.7)	0.3
active nicotine use	4 (12.5)	19 (15)	0.5
diabetes	5 (11.9)	31 (15.8)	0.4
hyperlipidemia	5 (11.9)	26 (13.3)	0.5
history of coronary artery disease	5 (11.9)	24 (12.2)	0.6
mental retardation or dementia	4 (9.5)	18 (9.2)	0.6
acute coronary syndrome	3 (7.1)	4 (2)	0.1
thyroid diseases	3 (7.1)	12 (6.1)	0.5
the most important predisposing factors for PE, n (%)			

deep venous thrombosis overall	19 (45.2)	78 (38.8)	0.3
obesity (BMI >30 kg/m^2)	11 (40.7)	63 (45.3)	0.4
overweight (BMI 25–30 kg/m^2)	6 (22.2)	23 (16.5)	0.3
immobilization	6 (14.3)	39 (19.9)	0.3
malignancy	5 (11.9)	31 (15.8)	0.4
pregnancy and the postpartum period	1 (2.4)	4 (2)	0.6
endocarditis	0 (0)	2 (1)	0.7
treatment			
unfractionated heparin	24 (57.1)	117 (59.7)	0.4
low molecular-weight heparin	21 (50)	95 (48.9)	0.5
acenocoumarol	20 (47.6)	71 (36.2)	0.1
fibrinolysis (rtPA/streptokinase)	7/0 (16.7)	21/1 (10.7)	0.2
warfarin	6 (14.3)	34 (17.3)	0.4
by Peitho study protocol	4 (9.5)	7 (3.6)	0.1
by Amplify study protocol	3 (7.1)	5 (2.6)	0.2
by Cassiopea study protocol	2 (4.8)	23 (11.7)	0.1
hemorrhagic complications	2 (4.8)	10 (5.1)	0.6
length of the hospital stay, days	10 (7–12)	10 (7–13)	0.7
in-hospital mortality	3 (7.1)	22 (11.2)	0.3
long-term mortality	12 (31.6)	51 (29.3)	0.8

Data are presented as median (interquartile range) or number (percentage) of patients.

P <0.05

Abbreviations: BMI, body mass index; PE, pulmonary embolism

Table S2 Comparison of laboratory, electrocardiographic, and echocardiographic parameters.

Additional parameters	**Weekend**	**Weekdays**	***P* value**
laboratory parameters			
troponin I, ng/ml	0.1 (0.03–0.42)	0.07 (0.01–0.54)	0.6
D-dimer, ug/dl	6.13 (3.36–19.93)	5.58 (3.04–14.81)	0.6
serum creatinine, mg/dl	1.03 (0.8–1.3)	1 (0.8–1.25)	0.9
eGFR, ml/min/1.73 m^2	66 (51–93)	73 (50–89)	0.8
electrocardiographic sings			
tachycardia, >100/min	8 (19.5)	64 (33.2)	0.059
supraventricular arrhythmias	8 (19)	15 (7.8)	0.032
echocardiographic signs			
impairment of the right ventricle	27(67.5)	117 (64.3)	0.4
VmaxTR, m/s	3.1 (2.9–3.6)	3 (2.7–3.5)	0.3
PASP, mmHg	51.5 (45–64)	49 (40–64)	0.7
ACT, ms	55 (50–78.5)	65 (50–85)	0.5
right-sided cardiac thrombus	5 (12.5 %)	16 (9 %)	0.3

Data are presented as median (interquartile range) or number (percentage) of patients.

P <0.05

Abbreviations: ACT, acceleration time of right ventricular ejection; eGFR, estimated glomerular filtration rate; PASP, pulmonary artery systolic pressure; VmaxTR, maximum velocity of tricuspid regurgitation