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ORIGINAL ARTICLE

INVESTIGATION OF THE FACTORS AFFECTING THE MORTALITY OF PATIENTS OVER 80 YEARS OF AGE DIAGNOSED WITH ACUTE PULMONARY THROMBOEMBOLISM

Abstract

Introduction: To investigate the factors affecting the 30-day mortality of patients over 80 years of age diagnosed with acute pulmonary thromboembolism.

Materials and method: This descriptive, retrospective, and single-center study reviewed the medical records of patients over 80 years of age who were admitted to the hospital with a diagnosis of acute pulmonary thromboembolism between January 1, 2008, and April 30, 2023. The factors associated with mortality in patients who had died were examined. The recorded values of factors considered to be the determinants of 30-day mortality were also determined.

Results: This study included 113 patients, with a mean age of 83.7 ± 2.7 years, and comprised of 68 (60.2%) females. During the one-month follow-up period, 30 patients (26.5%) died of acute pulmonary thromboembolism or related complications. No statistically significant difference in age and gender was observed between the exitus and non-exitus groups ($p > 0.05$). Moreover, no significant difference was observed between the two groups in terms of hypertension and diabetes ($p > 0.05$), whereas other comorbidities were statistically significantly higher in the exitus group ($p < 0.05$). In the linear regression analysis, heart failure ($p < 0.001$), D-dimer level ($p = 0.019$), partial arterial oxygen pressure ($p < 0.001$), systolic pulmonary artery pressure ($p < 0.001$), and recent history of major surgery ($p = 0.021$) were found to be factors that affected the mortality.

Conclusion: The presence of comorbidities, poor hemodynamic findings, poor oxygenation, high pulmonary artery pressure, and high D-dimer levels may be mortality indicators in acute pulmonary thromboembolism patients over 80 years of age.

Keywords: Pulmonary Embolism; Mortality; Ages.

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INTRODUCTION

Sudden blood flow interruption in the pulmonary artery and/or its branches is defined as acute pulmonary embolism. The condition that causes a sudden blood flow interruption is usually a thrombus originating from the lower extremity veins (1). The estimated annual incidence is 60–120 per 100,000 (1). Acute pulmonary thromboembolism (APT) is a cardiovascular disease that requires urgent diagnosis and could have a high mortality rate. The clinical presentation of patients with APT may range from asymptomatic to cardiogenic shock and sudden cardiac death (1–2). The most common presenting complaints include dyspnea, chest pain, syncope, hemoptysis, and an impaired general condition. APT can be observed in any age group; however, studies have revealed that its incidence increases with advancing age (2). The number of patients with APT is expected to increase due to prolonged life expectancy in the society and higher elderly patient population every year. The mortality rate of APT is much higher among elderly patients than in young patients and this increase is directly correlated with age (3). However, elderly patients may have a large number of comorbidities that may mimic these symptoms, thereby making the diagnosis difficult (3–4). After the diagnosis is made, high-risk patients should be identified and appropriate treatment should be initiated to prevent mortality and morbidity (1–2). To date, numerous laboratory as well as clinical parameters and scoring systems have been identified to diagnose high-risk patients. However, almost all these studies have been conducted in the normal patient population. No studies have specifically investigated the relationship of these parameters and scoring systems with short- and long-term mortality in elderly patients over 80 years of age. Therefore, this study aimed to investigate the factors affecting the 30-day mortality in patients over 80 years of age diagnosed with APT.

MATERIALS AND METHOD

The study was designed as a retrospective, single-center study. The records of patients with a diagnosis of APT and followed up at Baskent University Adana Dr. Turgut Noyan Training and Research Hospital between January 1, 2008, and April 30, 2023 were reviewed. Among these patients, patients aged ≥80 years and diagnosed with APT were included in the study.

Records of 1477 patients with an APT prediagnosis were accessed in the specified date range. The APT diagnosis could not be confirmed in 239 of these patients. Of the remaining 1238 patients, 1089 were excluded because they were under 80 years of age at the time of the event. The records of the remaining 149 patients were analyzed. However, 23, 11, and 2 patients were excluded because of incomplete file

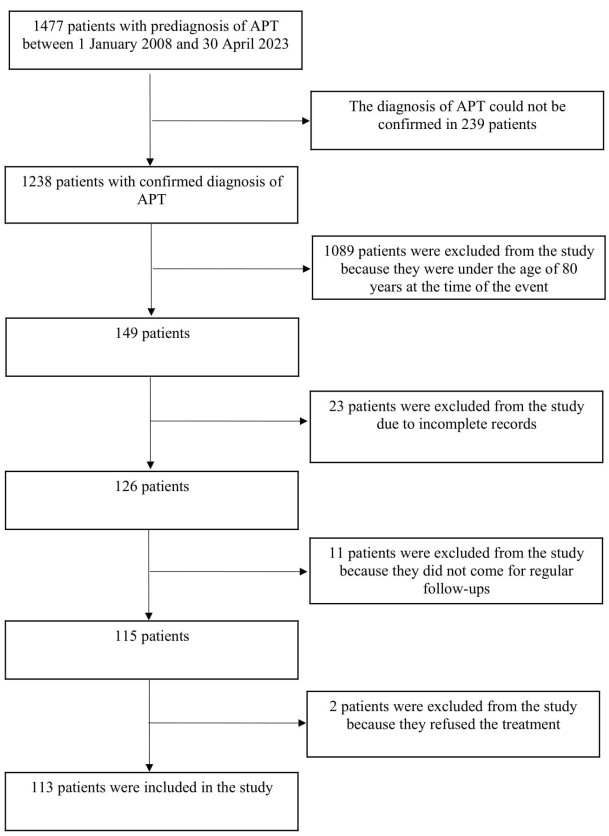

Figure 1. Study Design

records, because they did not attend regular follow-up visits, and because they refused treatment and left the hospital without permission, respectively. Finally, the remaining 113 patients were included in the study. The study design is depicted in Figure 1. Among all these patients, the APT diagnosis was confirmed only if thoracic computer tomography pulmonary angiography revealed filling defects in the main pulmonary artery and/or its branches.

The baseline demographic characteristics, vital signs, presenting complaints, comorbidity (diagnosed cancer, heart failure, chronic lung disease, chronic renal failure, or diabetes mellitus [DM]), the presence of deep vein thrombosis (DVT) by Doppler ultrasonography, and the recent history of major surgery were recorded. Partial arterial oxygen pressure (PaO_2) and oxygen saturation (SaO_2) in arterial blood gas, D-dimer, troponin positivity, hemoglobin, white blood cell (WBC) and platelet counts, and creatinine values were recorded. Echocardiographic evaluation was performed in accordance with the guidelines and ejection fraction (5). The estimated systolic pulmonary artery pressure (sPAP) and the presence or absence of right ventricular (RV) failure were evaluated based on the criteria in the guidelines. If RV failure was present, patients were classified into mild, moderate, and severe right heart failure based on the guidelines (5). An ejection fraction of <40% was considered to indicate heart failure. Further, chronic obstructive pulmonary disease (COPD), asthma, bronchiectasis, and pulmonary fibrosis diagnosed in accordance with the guidelines were considered to indicate a chronic lung disease.

Pulmonary embolism severity index (PESI) scores of all patients were calculated and recorded. In the PESI score, patient age and male gender were assigned 10 points; cancer was assigned 30 points; presence of heart failure or lung disease was assigned 10 points; pulse rate of ≥110 bpm was assigned 20 points; systolic blood pressure (SBP) of <100 mm Hg was assigned 30 points; respiratory rate of >30/min was assigned 20 points; body temperature of <36°C was assigned 20 points; mental status change was assigned 60 points; and SaO2 of <90% was assigned 20 points. All scores were summed. A total score of ≤65 was defined as class 1 (mild), 66–85 as class 2 (mild–moderate), 86–105 as class 3 (moderate), 106–125 as class 4 (moderate–heavy), and >125 as class 5 (severe) APT (1). At the 30-day follow-up, it was determined whether the patients were exitus due to APT or APT-related complications. It was also investigated whether laboratory and clinical values differed between the exitus as well as non-exitus patient groups, respectively. The recorded values that can be considered determinants of 30-day mortality were also evaluated.

Study exclusion criteria

Patients whose APT diagnosis could not be confirmed by computed tomography, whose file records could not be accessed, who did not undergo echocardiographic evaluation in their hospitalization records, who left the hospital voluntarily after admission, who were noncompliant and refused treatment, who were under 80 years of age, who did not attend regular follow-up within 30 days post-discharge, who were noncompliant and refused treatment post-discharge, and who had missing records of the abovementioned clinical or laboratory values were not included in the study.

Statistical analyses

SPSS computer program (Windows; SPSS, Inc., Chicago, Illinois, USA) was used to all statistical analyses. Kolmogorov-Smirnov test was used to evaluate whether the continuous variables conformed to the normal distribution. The values were expressed as mean ± standard deviation if they display the normal distribution, and as median and interquartile range [IQR] if they do not display the normal distribution. Proportion was used to

display categorical data. Chi-square test was used to compare categorical data. Unpaired t test was used to compare continuous variables that display the normal distribution while Mann–Whitney U-test was used to compare continuous variables that did not display the normal distribution. Standard multiple linear regression analysis was performed to identify independent predictors of mortality.

RESULTS

The study included 113 patients. The mean age was 83.7±2.7 years and 68 (60.2%) of the patients were females. At the 1-month follow-up period, 30 patients (26.5%) died of APT or APT-related complications. The most common comorbidity was hypertension in 60.2% (68) of patients. No patients had end-stage renal failure or liver failure. The median PESI score was 104 (IQR = 29.5), and 23 (20.4%) of the patients were classified in the high-risk group based on the PESI score; no patient was classified in the low-risk group. Echocardiography revealed normal RV function in 61 (54%) patients, whereas 4 (3.5%) patients had severe RV failure. The most common presenting complaint was dyspnea in 94.6% (107) of patients. Further, two patients (1.7%) presented with cardiogenic shock. The baseline demographic, clinical, and laboratory data of the patients are summarized in Table 1. No statistically significant difference in age and gender was observed between the exitus and non-exitus groups (p>0.05). No significant difference in comorbidity such as hypertension and DM was observed between the two groups (p > 0.05), whereas other comorbidities were statistically significantly different between the two groups (p < 0.05). Similarly, in terms of laboratory values, the creatinine, hemoglobin, WBC, and platelet counts were similar between the two groups (p < 0.05). The comparison of laboratory, clinical, and demographic characteristics of patients with and without exitus is summarized in Table 2. According

Table 1. Baseline clinical, demographic, and laboratory values of the study population

Age, years	83.7 ± 2.7
Female gender n (%)	68 (60.2)
SBP <100 mm Hg n (%)	10 (8.8)
Heart rate ≥110 bpm n (%)	32 (28.3)
Respiratory rate >30	10 (8.8)
Active cancer n (%)	17 (15)
Deep venous thrombosis n (%)	45 (39.8)
Major surgery n (%)	14 (12.3)
Hypertension n (%)	68 (60.2)
Diabetes mellitus n (%)	23 (20.4)
Coronary artery disease n (%)	35 (31)
Smoking n (%)	12 (10.6)
Heart failure n (%)	16 (14.2)
Chronic lung disease n (%)	25 (22.1)
Temperature <36°C n (%)	9 (7.9)
Altered mental status n (%)	5 (4.4)
Arterial oxygen saturation <90 n (%)	46 (40.7)
Positive Troponin n (%)	92 (81.4)
PESI points	104 (IQR = 29.5)
PESI groups	
Low risk n (%)	0 (0)
Intermediate–low risk n (%)	24 (21.2)
Intermediate risk n (%)	36 (31.9)
Intermediate–high risk n (%)	30 (26.5)
High risk n (%)	23 (20.4)
D-dimer (µg/L)	8170 (IQR = 4550)
Ejection fraction (%)	53.1 ± 8.1
sPAP (mm Hg)	33 ± 11.7
Right ventricle functions	
Normal n (%)	61 (54)
Mild depressed n (%)	33 (29.2)
Moderate depressed n (%)	15 (13.3)
Severe depressed n (%)	4 (3.5)
Creatinine (mg/dL)	0.9 ± 0.5
Hemoglobin (gr/dL)	13.8 ± 1.5
WBC (/mm^3)	7525 ± 2293
Platelets (100/mm^3)	274 (IQR = 86)
Dyspnea n (%)	107 (94.6)
Chest pain n (%)	65 (57.5)
Cough n (%)	47 (41.5)
Syncope n (%)	19 (16.8)
Fatigue n (%)	15 (13.2)
Vomiting n (%)	11 (9.7)
Cardiogenic shock n (%)	2 (1.7)

IQR—interquartile range; PESI—pulmonary embolism severity index; SBP—systolic blood pressure; sPAP—systolic pulmonary artery pressure; WBC—white blood cell

Table 2. Comparison of baseline clinical, demographic, and laboratory values between the with exitus and without exitus groups

	Exitus (n = 30)	No exitus (n = 83)	p
Female gender n (%)	17 (56.7)	51 (61.4)	0.647
Age (years)	83.3 ± 2.2	83.9 ± 2.9	0.273
Active cancer n (%)	11 (36.7)	6 (7.2)	<0.001
Heart failure n (%)	10 (33.3)	6 (7.2)	<0.001
Chronic lung disease n (%)	13 (43.3)	12 (14.5)	0.001
Hypertension n (%)	17 (56.7)	51 (61.4)	0.647
Diabetes mellitus n (%)	5 (16.7)	18 (21.7)	0.558
Smoking n (%)	7 (23.3)	5 (6)	0.008
Coronary artery disease n (%)	15 (50)	20 (24.1)	0.009
Deep venous thrombosis n (%)	18 (60)	27 (32.5)	0.008
Major surgery n (%)	8 (26.7)	6 (7.2)	0.006
Saturation (%)	83.1 ± 5.3	91.9 ± 3	<0.001
PESI point	140.5 (IQR = 75.5)	93 (IQR = 25)	<0.001
D-dimer (µg/L)	10040 (IQR = 3675)	7890 (IQR = 5450)	0.001
Systolic blood pressure (mm Hg)	108.1 ± 17.5	134.8 ± 16.8	<0.001
Oxygen (mm Hg)	71.8 ± 4.7	82.6 ± 8.1	<0.001
sPAP (mm Hg)	46 ± 13.8	28.3 ± 6	<0.001
Creatinine (mg/dL)	1.1 ± 0.7	0.9 ± 0.4	0.129
Hemoglobin (gr/dL)	14.2 ± 1.2	13.7 ± 1.5	0.1
WBC (/mm^3)	7232 ± 2250	7631 ± 2313	0.417
Platelets (100/mm^3)	272 (IQR = 70.7)	274 (IQR = 88)	0.876

IQR—interquartile range; PESI—pulmonary embolism severity index; sPAP—systolic pulmonary artery pressure; WBC—white blood cell

Table 3. Multiple linear regression analysis of mortality with clinical variables

	Beta coefficient	p	95% confidence interval	
			Lower	Upper
Age	-0.058	0.364	-0.029	0.011
Gender	0.048	0.458	-0.071	0.157
Active cancer	0.137	0.155	-0.065	0.403
Heart failure	0.231	<0.001	0.134	0.451
Chronic lung disease	-0.002	0.980	-0.149	0.146
PESI score	-0.127	0.370	-0.004	0.002
D-dimer	0.201	0.019	0.000	0.000
Arterial oxygen pressure	-0.305	<0.001	-0.024	-0.007
sPAP	0.584	<0.001	0.014	0.030
Positive troponin	0.121	0.075	-0.014	0.290
Diabetes mellitus	0.036	0.569	-0.098	0.178
Hypertension	-0.062	0.328	-0.169	0.057
Smoking	-0.78	0.304	-0.327	0.103
Coronary artery disease	0.086	0.230	-0.053	0.218
Deep venous thrombosis	-0.28	0.680	-0.149	0.098
Major surgery	0.198	0.021	0.042	0.489

PESI—pulmonary embolism severity index; sPAP—systolic pulmonary artery pressure

to the linear regression analysis, heart failure ($p < 0.001$), D-dimer level ($p = 0.019$), PaO2 ($p < 0.001$), sPAP value ($p < 0.001$), and a recent history of major surgery ($p = 0.021$) were found to be factors that influenced mortality. All regression analysis results are summarized in Table 3.

DISCUSSION

The results of our study revealed that the 30-day mortality rate of patients over 80 years of age with an APT is 26.5%. The comorbidity rate was significantly higher in the exitus group. The presence of comorbidity, high PESI score at presentation, poor hemodynamic findings, poor oxygenation, high sPAP, and high D-dimer levels may be indicators of mortality in patients over 80 years of age.

The incidence and prevalence of APT and DVT were found to increase with age. The APT mortality was rather variable depending on the patient group investigated and ranged between 1% and 60% (6–7). A few studies that aimed to determine which patients are at higher risk have been conducted mostly in the young patient population. In a retrospective study by El Ghoul et al. with 100 patients, hypotension, the presence of cancer, RV dysfunction on echocardiography, and severe hypoxemia were found as predictors of in-hospital mortality (8). They obtained similar results to those of our study. Another study conducted by Friz et al. revealed that patients over 80 years of age had a 30-day mortality of 18.9% and a 90-day mortality of 29.7%. According to the results of the same study, the negative predictive value of the PESI score was found to be 94.1% as an indicator of the 30-day mortality and 88.2% as an indicator of the 90-day mortality. In conclusion, that study concluded that better risk scoring systems are required for the elderly patient group (9). In our study, the mortality rate was found to be 26.5%. This rate is compatible with the findings in related literature. In another study conducted by Gupta et al., with 183 patients (mean age 63 years in this study), the presence of cancer, age, WBC count, the presence of DM, the presence of liver disease, female gender, and the presence of massive APT at baseline were found to be independent predictors of long-term mortality (mean, 4.1 years) (10). Another study conducted by Keller et al., with 129 patients, demonstrated age as an independent risk factor for mortality and mortality that increases with increasing age (11). In all mortality studies, identifying high-risk patients is extremely important in terms of preventing mortality.

Further, poor hemodynamic findings, impaired RV function, and elevated sPAP are expected to be associated with mortality. Ammari et al., with 32 patients with submassive APT, revealed that high brain natriuretic peptide (BNP) level, impaired function, and high RV pulmonary artery pressure may be indicators of mortality (12). Moreover, acute RV dilatation and RV failure that develop in acute APT decrease the cardiac output in the left ventricle. The resulting hypotension causes organ hypoperfusion and increases mortality (13). The effects of these hemodynamic mechanisms in the young patient population are well known. Considering that the elderly patient population has lower cardiac reserve, it is likely to be affected more by this hemodynamic disturbance.

D-dimer is a fibrin formation and degradation biomarker. A high D-dimer level is associated with recurrent DVT, APT risk, and mortality (14). Since an increased D-dimer level indicates high thrombus burden, it is expected to be associated with mortality. Our study is consistent with the literature in this respect.

The effects of DM on the mortality rate of APT is unclear. In a large-scale study by Schmitt et al. (1,174,196 pulmonary embolism patients, 53.8% aged ≥70 years, 53.5% women, and among these, 219,550 [18.7%] patients with DM were included), mortality was reportedly higher in patients with DM compared to those without DM in patients with APT.

In this study, DM was reported as an independent risk factor for in-hospital mortality (15). In another large-scale registry study, DM was not found to be an independent risk factor for mortality (16). It must be noted that these studies were conducted in a normal patient population.

Study Limitations

One of the greatest limitations of this study is that it was conducted retrospectively with file records. Further, the small number of patients and lack of a standardized treatment strategy in patients included in the study is additional important limitations. In future research, the findings need to be supported by multicenter studies with a large number of patients and standardized treatment protocols.

CONCLUSION

Patients aged >80 years with APT had a high mortality rate. A high number of comorbidities, poor hemodynamic findings at presentation, RV failure, high sPAP, poor oxygenation, and high D-dimer levels may be associated with mortality.

Conflict of Interest: None declared

Ethical Approval: All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration. This study was approved by Baskent University Institutional Review Board (Project no: KA 23/294) and supported by Baskent University Research Fund.

REFERENCES

1. Freund Y, Cohen-Aubart F, Bloom B. Acute Pulmonary Embolism: A Review. JAMA. 2022; 328 (13): 1336-1345. (DOI: 10.1001/jama.2022.16815).
2. Konstantinides SV, Meyer G, Becattini C, et al. The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). Eur Respir J. 2019; 54 (3): 1901647. (DOI: 10.1183/13993003.01647-2019).
3. Ozyurt S, Gumus A, Yilmaz Kara B, et al. Changing clinical characteristics of pulmonary thromboembolism in the elderly. Turkish Journal of Geriatrics. 2018; 21 (2): 166-172. (DOI: 10.31086/tjgeri.2018240417).
4. Tuncay E, Kanmaz Dilek Z, Aras G, et al. The validity of the spesi score in mortality prediction at four-year follow-up of patients with pulmonary embolism and aged over 65 years. Turkish Journal of Geriatrics. 2021; 24(4): 585-598. (DOI:10.31086/tjgeri.2021.256)
5. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015; 28(1): 1-39.e14. (DOI: 10.1016/j.echo.2014.10.003).
6. Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012; 141(2 Suppl): e419S-e496S. (DOI: 10.1378/chest.11-2301).
7. Becattini C, Agnelli G. Acute pulmonary embolism: risk stratification in the emergency department. Intern Emerg Med. 2007; 2(2): 119-129. (DOI: 10.1007/s11739-007-0033-y).
8. El Ghoul J, Bendayekh A, Fki W, et al. Facteurs de risque de mortalité hospitalière au cours de l'embolie pulmonaire en milieu de pneumologie [Risk factors for hospital mortality during pulmonary embolism]. Ann Cardiol Angeiol (Paris). 2020; 69(1): 7-11. French. (DOI: 10.1016/j.ancard.2020.01.001).
9. Polo Friz H, Molteni M, Del Sorbo D, et al. Mortality at 30 and 90 days in elderly patients with pulmonary embolism: a retrospective cohort study. Intern Emerg Med. 2015; 10(4): 431-436. (DOI: 10.1007/s11739-014-1179-z).
10. Gupta R, Ammari Z, Dasa O, et al. Long-term mortality after massive, submassive, and low-risk pulmonary embolism. Vasc Med. 2020; 25(2): 141-149. (DOI: 10.1177/1358863X19886374).

11. Keller K, Beule J, Coldewey M, Geyer M, Balzer JO, Dippold W. The risk factor age in normotensive patients with pulmonary embolism: Effectiveness of age in predicting submassive pulmonary embolism, cardiac injury, right ventricular dysfunction and elevated systolic pulmonary artery pressure in normotensive pulmonary embolism patients. Exp Gerontol. 2015; 69: 116-121. (DOI: 10.1016/j.exger.2015.05.007).

12. Ammari Z, Al-Sarie M, Ea A, et al. Predictors of reduced cardiac index in patients with acute submassive pulmonary embolism. Catheter Cardiovasc Interv. 2021; 97(2): 292-298. (doı: 10.1002/ccd.29269).

13. Bowers T, Goldstein JA. Hemodynamic compromise in pulmonary embolism: "A tale of two ventricles". Catheter Cardiovasc Interv. 2021; 97(2): 299-300. (DOI: 10.1002/ccd.29497).

14. Halaby R, Popma CJ, Cohen A, et al. D-Dimer elevation and adverse outcomes. J Thromb Thrombolysis. 2015; 39(1): 55-9. (DOI: 10.1007/s11239-014-1101-6).

15. Schmitt VH, Hobohm L, Sivanathan V, et al. Diabetes mellitus and its impact on mortality rate and outcome in pulmonary embolism. J Diabetes Investig. 2022; 13(4): 725-737. (DOI: 10.1111/jdi.13710).

16. de Miguel-Díez J, López-de-Andrés A, Jiménez-Trujillo et al. RIETE Investigators. Mortality after pulmonary embolism in patients with diabetes. Findings from the RIETE registry. Eur J Intern Med. 2019; 59: 46-52. (DOI: 10.1016/j.ejim.2018.08.001).