Original article

Kardiologia Polska
2012; 70, 1: 15–22
ISSN 0022–9032

Acute pulmonary embolism: analysis of consecutive 353 patients hospitalised in a single centre. A 3-year experience

Andrzej Łabyk[1], Michał Ciurzyński[1], Krzysztof Jankowski[1], Maciej Kostrubiec[1], Barbara Lichodziejewska[1], Piotr Bienias[1], Justyna Pedowska-Włoszek[1], Szymon Pacho[1], Piotr Palczewski[2], Piotr Pruszczyk[1]

[1]Department of Internal Diseases and Cardiology, Medical University of Warsaw, Warsaw, Poland
[2]1st Department of Clinical Radiology, Medical University of Warsaw, Warsaw, Poland

Abstract

Background and aim: Despite significant progress on the diagnosis work-up of patients with suspented acute pulmonary embolism (APE), several therapeutic and prognostic issues have not yet been well established.

Methods: We analysed the clinical course of 353 consecutive patients (141 males, 212 females, mean age 64.7 ± 18.12 years) with APE confirmed by contrast-enhanced multidetector computed tomography who were diagnosed and treated in a reference hospital between 2007 and 2009.

Results: Among patients with APE, groups with high (HR), intermediate (IR) and low (LR) risk of early mortality were defined according to the recent European Society of Cardiology guidelines. High, intermediate and low risk groups included 23 patients (10 M, 13 F, age 70.13 ± 16.95 years), 146 patients (61 M, 85 F, age 65.77 ± 17.74 years), and 184 patients (70 M, 114 F, age 63.17 ± 18.45 years), respectively. Majority of patients (91.8%) were anticoagulated only with unfractionated or low-molecular-weight heparin, and thrombolysis was used in 24 patients, including 39.1% of HR patients, 8.9% of IR patients, and 1% of LR patients. In-hospital mortality rate was 7% overall (including 5.4% APE-related), 65.2% in HR (43.5% APE-related), 6.2% in IR (4.1% APE-related) and 2.2% in LR (1.63% APE-related). However, 4 of 9 high risk patients treated with thrombolysis died (mortality rate 44.4%), while mortality among HR patients not treated with thrombolysis reached 73.3%. Potential contraindications were taken into account before the decision to initiate thrombolysis. End-stage neoplasm or recent major surgery were considered contraindications for thrombolysis. Strong prognostic factors of overall in-hospital mortality included age (odd ratio [OR] 1.07, 95% confidence interval [CI] 1.02–1.12), heart rate (OR 1.04, 95% CI 1.02–1.06), and plasma creatinine level (OR 3.65, 95% CI 1.62–8.27), the latter also being a significant prognostic factor of mortality in low risk group (OR 3.9, 95% CI 1.6–9.8). NT-proBNP and troponin I plasma levels were also significant prognostic factors of in-hospital mortality (NT-proBNP: OR 5.91, 95% CI 2.38–14.65, $p < 0.05$; troponin I (cut-off value ≥ 0.1 μg/L): OR 2.77, 95% CI 0.97–7.93, $p = 0.056$). In the overall study population and also in non-high risk group, significant predictors of a combined endpoint (death, shock, intubation, catecholamines, and thrombolysis) were: age, heart rate, creatinine, troponin I, NT-proBNP, and tricuspid pressure gradient.

Conclusions: Despite adequate treatment there is a possibility of haemodynamic collapse and the need for thrombolysis in approximately 9% of intermediate risk APE patients. Not only age and compromised haemodynamic status but also plasma creatinine, NT-proBNP, and troponin I levels are prognostic factors of early in-hospital mortality in patients with APE. Due to high mortality rate among non-thrombolysed high risk patients, their therapy should be more aggressive and contraindications for thrombolysis should be less restrictive.

Key words: acute pulmonary embolism, treatment, thrombolysis, mortality

Kardiol Pol 2012; 70, 1: 15–22

Address for correspondence:
Prof. Piotr Pruszczyk, MD, PhD, Andrzej Łabyk, MD, Department of Internal Diseases and Cardiology, Medical University of Warsaw, ul. Lindleya 4, 02–005 Warszawa, Poland, tel: +48 22 502 11 44, +48 22 502 16 68, + 48 22 502 16 25, fax: +48 22 502 21 42, e-mail: endrjulab@tlen.pl
Received: 09.03.2011 **Accepted:** 24.08.2011

INTRODUCTION

Recent developments and current availability of imaging studies resulted in a significant progress in the diagnostic work-up in patients with suspected pulmonary embolism (PE). In 2008, the European Society of Cardiology (ESC) guidelines on the diagnosis and management of PE were published [1]. In this document, stratification of mortality risk due to PE based on clinical variables and markers of right ventricular (RV) overload and myocardial damage was clarified. Similar approach to mortality risk stratification was included in the American guidelines published in March 2011 [2]. In this study, we summarised our 3-year single centre experience in the diagnosis and treatment of PE, with particular regard to the use of ESC guidelines in clinical practice.

METHODS

Based on the review of medical records, we collected data on consecutive 353 patients hospitalised in our department with confirmed PE in 2007–2009.

Diagnosis of pulmonary embolism

Pulmonary embolism was mainly diagnosed using contrast-enhanced multidetector computed tomography (CT) (16-row GE LightSpeed Pro and 64-row Toshiba Aquilion systems) when thrombi were identified in segmental or more proximal branches of pulmonary arteries. In patients with underlying severe renal failure, lung perfusion scintigraphy was performed to avoid further deterioration of renal function. Lung perfusion scintigraphy was also performed in patients with high clinical probability of PE but a negative or nondiagnostic result of CT. In haemodynamically unstable patients, in whom performing CT was deemed unsafe, the diagnosis of acute PE (APE) was confirmed by transoesophageal echocardiography.

Risk stratification

In addition to clinical evaluation, echocardiographic examination (Philips IE33) was performed on admission to evaluate RV function. The RV overload was diagnosed when the following features were present: dilated hypokinetic RV, RV end-diastolic dimension to left ventricular end-diastolic dimension ratio in the apical four-chamber view above 0.9, tricuspid valve pressure gradient (TRPG) above 30 mm Hg with acceleration time (AcT) reduced below 80 ms and the presence of a biphasic pulmonary valve flow. Blood samples were collected to determine cardiac troponin I level (cTnI, Siemens Dimension RxL). Myocardial damage was diagnosed when cTnI level was ≥ 0.1 μg/L. In addition, NT-proBNP level (ECLIA, Roche Diagnostics) was measured in the majority of patients (n = 189). Echocardiographic and laboratory parameters were evaluated immediately upon hospital admission.

The study population was divided into groups with a high (HR), intermediate (IR) and low (LR) risk of early mortality due to APE according to the ESC guidelines from 2008. The HR group included haemodynamically unstable patients with systemic blood pressure below 90 mm Hg and evidence of peripheral tissue hypoperfusion. The IR group included normotensive patients with features of RV overload or biochemical evidence of myocardial damage. The LR group included normotensive patients without features of RV overload and with normal cTnI level. This risk stratification was based on the evaluation on admission.

In addition to PE severity, we evaluated the presence of concomitant conditions such as arterial hypertension, coronary artery disease, chronic obstructive pulmonary disease (COPD), diabetes, chronic kidney disease, previous stroke, and cancer. Lower limb venous ultrasonography was performed in nearly half of all patients.

Evaluation of the clinical course

We analysed the clinical course in all patients, including baseline variables such as age, heart rate, and blood pressure. The following endpoints were taken into account: systemic hypotension below 90 mm Hg, the need to use intravenous catecholamines in pressor doses, the need for intubation, treatment escalation, i.e. the use of thrombolysis in initially haemodynamically stable patients, and death. We evaluated in-hospital mortality and potential contributing factors. We also evaluated the rate and causes of bleeding complications defined as fatal bleeds and events requiring medical intervention such as red cell transfusion or surgical procedure.

Statistical analysis

Statistical analysis was performed using STATISTICA 2009 software. Results are expressed as mean values ± SD for normally distributed variables and median values and ranges for non-normally distributed variables. Student *t* test was used to compare groups of normally distributed variables, and Mann-Whitney (two-group comparisons) and Kruskal-Wallis (multiple group comparisons) tests were used for non-normally distributed variables. Categorical variables were compared using χ^2 test. Logistic regression analysis was used to determine predictors of mortality. Cut-off points of highest sensitivity and specificity were determined using receiver-operating characteristic (ROC) curves. A p value < 0.05 was considered statistically significant.

RESULTS

Diagnosis of pulmonary embolism

We analysed data collected in 353 patients in the mean age of 64.7 ± 18.12 (range 18–97) years. The PE was mainly confirmed by multidetector CT (in 242 patients). Lung perfusion scintigraphy confirmed the diagnosis in 29 patients, including 13 patients with concomitant chronic kidney disease. In 12 (3.5%) cases, lung scintigraphy was performed after CT yielded a non-diagnostic or negative result in a patient with a high clinical probability of APE. In 5 patients, the diagnosis of PE was confirmed by transoesophageal echocardiography.

Table 1. Prevalence of concomitant diseases in the study population

Chronic obstructive pulmonary disease	29 (8%)
Ischaemic heart disease	82 (23.2%)
Remote myocardial infarction	19 (5.4%)
History of heart failure	51 (14.4%)
Arterial hypertension	126 (35.7%)
Diabetes	58 (16.4%)
History of renal failure	54 (15.3%)
Active malignancy	42 (11.9%)
History of malignancy	16 (4.5%)
Surgery	39 (11%)
Lower limb deep venous thrombosis	82 (23.2%)
History of venous thrombosis	35 (9.9%)
Stroke	10 (2.8%)
Trauma	25 (7%)
Contraception	5 (1.4%)
Pregnancy/peripartum period	2 (0.56%)

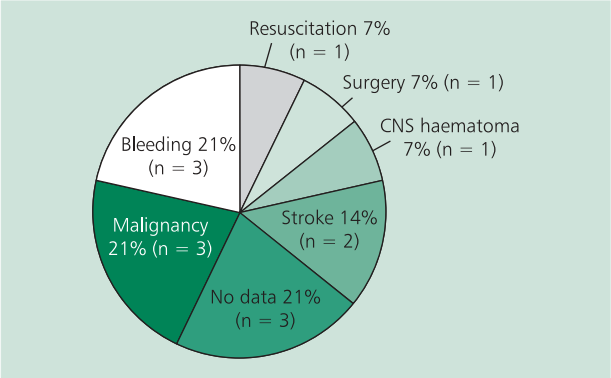

Figure 1. Reasons for not using thrombolytic treatment in patients from the high-risk group (n = 14); CNS — central nervous system

Clinical characteristics and concomitant conditions

The HR group constituted 6.5% (n = 23) of the overall study population (13 women [56.5%], age 70.13 ± 16.95 years), IR group — 41% of patients (n = 146, 85 women [58.2%], age 65.77 ± 17.74 years), and LR group — 52% of patients (n = 184, 114 women [62%], age 63.17 ± 18.45 years). The most common concomitant conditions included arterial hypertension (35.7%) and coronary artery disease (23.2%). Active or previous malignancy was found in 16.4% of patients, and 11% of patients underwent surgery within previous 30 days, while heart failure and COPD were noted less frequently (Table 1).

Lower limb venous ultrasonography was performed in 176 (49.9%) patients and confirmed deep venous thrombosis in 82 patients in this group.

In the overall study population, PE was considered idiopathic in 132 (37.4%) patients.

Clinical course

Thrombolytic treatment was used in 9 (39.1%) of 23 patients in HR group. In the remaining 14 patients this treatment was not initiated despite established indications due to perceived high risk of bleeding complications or advanced severe concomitant diseases such as disseminated malignancy. These patients were treated with heparin (Fig. 1).

Patients in LR group were treated with a full anticoagulant dose of low-molecular weight heparin (LMWH) adjusted to body weight. Only 8 patients in this group initially received intravenous treatment with unfractionated heparin (UFH) monitored with activated partial thromboplastin time. The indication for the use of UFH in this patient group was chronic kidney disease. Patients in IR group initially received anticoagulant treatment. Five patients in this group were recruited into the randomised PEITHO study that evaluated tenecteplase *vs* placebo in addition to intravenous UFH. In 13 (8.9%) patients in IR group with RV overload and/or elevated cTnI level, clinical deterioration with hypotension and increasing tachycardia was noted within several hours despite heparin treatment. These patients received intravenous thrombolytic treatment with alteplase (0.6 mg/kg body weight, up to 50 mg, in a 15-min bolus). In 1 patient with a mobile right atrial thrombus stuck in a patent foramen ovale, successful urgent embolectomy was performed with thrombus removal from the cardiac chambers and pulmonary arteries. Among LR patients, clinical deterioration despite therapy was observed in 4 (2.1%) patients, leading to thrombolysis in 2 (1%) cases; in the 2 remaining cases, thrombolysis was not initiated due to perceived high risk of bleeding complications or multiple concomitant diseases. These patients were also not considered candidates for cardiac surgical treatment.

Bleeding complications

Significant bleeding occurred in 16 (4.5%) patients, including fatal bleeding in 5 patients. The most common were central nervous system haemorrhages (2 patients), and the remaining cases included generalised massive bleeding and bleeding into a retroperitoneal (kidney) tumour. No significant differences in bleeding rates were noted between the study groups (Fig. 2).

Mortality

Overall in-hospital mortality was 7% (n = 28), including 5.4% due to APE (n = 19). In HR group, in-hospital mortality was 62.5% (n = 15), including 43.5% due to APE (n = 10). Causes of death related to APE included RV failure (6 patients) and recurrent embolism (4 patients). Other causes of death included myocardial infarction complicated with ventricular

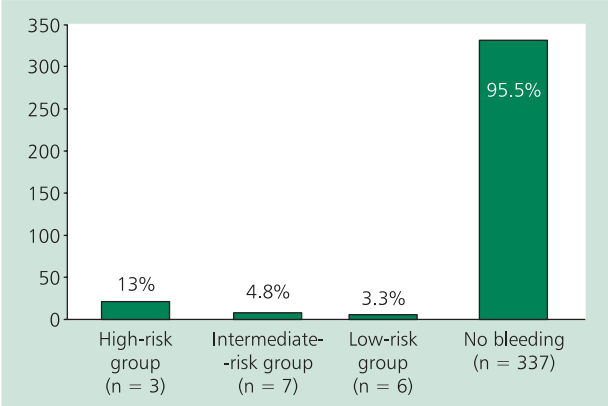

Figure 2. Bleeding rates — total n = 16 (4.5%)

Table 3. Risk factors for mortality in the study population (n = 353)

	OR	95% CI	P
Age [years]	1.07	1.02–1.12	< 0.05
Heart rate [bpm]	1.04	1.02–1.06	< 0.05
SBP [mm Hg]	1.01	0.99–1.34	NS
DBP [mm Hg]	1.02	0.99–1.05	NS
Creatinine [mg/dL]	3.65	1.62–8.27	< 0.05
NT-proBNP [pg/mL]	5.91	2.38–14.65	< 0.05
cTnI [μg/L]	2.77	0.97–7.93	0.056
TRPG [mm Hg]	1.01	0.98–1.05	NS
Acceleration time [ms]	0.99	0.97–1.02	NS

OR — odds ratio; CI — confidence interval; rest abbreviations as in Table 2

fibrillation, severe generalised bleeding in 2 patients following thrombolytic treatment, and terminal disseminated malignancy in the remaining patients. Overall in-hospital mortality in HR patients who received thrombolytic treatment was 44.4% (n = 4) compared to 73.3% (n = 11) in HR patients who did not receive thrombolytic treatment.

In-hospital mortality in IR group was 6.2% (n = 9), including 4.1% due to APE (n = 6). Death was caused by recurrent embolism in 2 patients, and by irreversible RV failure in the remaining 4 patients. Other causes of death included 1 case of intracerebral bleeding and 2 cases of terminal disseminated malignancy. Among 13 patients in this group who received thrombolytic treatment, 1 patient died due to bleeding.

In-hospital mortality in LR group was 2.2% (n = 4), including 1.6% (n = 3) due to APE. One patient in this group died due to irreversible RV failure, and 2 patients died due to recurrent embolism. In these 2 cases, thrombolysis was not initiated due to high bleeding risk. One patient receiving anticoagulant treatment died due to acute haemorrhagic stroke. Of note, no significant complications of thrombolytic therapy were observed in the 2 patients in LR group who received such treatment due to haemodynamic deterioration.

Risk factors for mortality

Patients who died were significantly older, and had significantly higher median heart rate and median serum creatinine, cTnI and NT-proBNP levels (Table 2). Significant risk factors for mortality in the overall study population included age (odds ratio [OR] 1.07, 95% confidence interval [CI] 1.02–1.12), heart rate (OR 1.04, 95% CI 1.02–1.06), creatinine level (OR 3.65, 95% CI 1.62–8.27), and logarithmically transformed NT-proBNP level (ln[NT-proBNP], OR 5.91, 95% CI 2.38–14.65) (Table 3). Analysis performed separately in the three risk groups showed that only creatinine level was a significant predictor of mortality in LR group (OR 3.9, 95% CI 1.6–9.8). In our analysis, cTnI level (cut-off value ≥ 0.1 μg/L) was border-

Table 2. Comparison of selected clinical, laboratory, and echocardiographic parameters between patients who died and patients who survived

	Overall study population (n = 353)	Death (n = 28)	Survivors (n = 325)	P
Age [years]	70 (18–97)	76.5 (43–97)	69 (18–95)	< 0.05
Heart rate [bpm]	90 (54–160)	105 (70–160)	90 (54–160)	< 0.05
SBP [mm Hg]	130 (60–180)	115 (60–180)	130 (60–180)	NS
DBP [mm Hg]	80 (30–120)	70 (40–110)	80 (30–120)	NS
Creatinine [mg/dL]	1.0 (0.41–5.02)	1.42 (0.6–5.02)	1.0 (0.41–4.3)	< 0.05
NT-proBNP [pg/mL]	2047.5 (16.3–60958)	9865 (618–60958)	1543 (16–33340)	< 0.05
cTnI [μg/L]	0.05 (0.00–18.5)	0.26 (0.08–3.2)	0.04 (0.00–18.2)	< 0.05
TRPG [mm Hg]	35 (4–86)	40 (23–59)	35 (4–86)	NS
Acceleration time [ms]	70 (23–170)	70 (45–150)	71 (23–170)	NS

Data are presented as median values and ranges; SBP — systolic blood pressure; DBP — diastolic blood pressure; cTnI — cardiac troponin I level; TRPG — tricuspid valve pressure gradient

Table 4. Factors predicting the occurrence of a combined endpoint (all-cause in-hospital deaths, need for intubation, shock, need to use catecholamines, and need to use thrombolysis) in the overall study population (n = 353) and in non-high-risk group (IR + LR; n = 330)

	Study population (n = 353)			IR + LR (n = 330)		
	OR	95% CI	P	OR	95% CI	P
Age [years]	1.02	1.00–1.03	< 0.05	1.02	0.99–1.04	NS
Heart rate [bpm]	1.03	1.02–1.04	< 0.05	1.02	1.00–1.04	< 0.05
SBP [mm Hg]	0.98	0.97–0.99	NS	1.00	0.98–1.02	NS
DBP [mm Hg]	0.98	0.96–1.00	NS	1.00	0.98–1.03	NS
Creatinine [mg/dL]	2.02	1.28–3.18	< 0.05	1.66	1.01–2.70	< 0.05
NT-proBNP [pg/mL]	4.15	2.26–7.61	< 0.05	4.18	2.00–8.70	< 0.05
cTnI [μg/L]	3.95	1.79–8.66	< 0.05	3.16	1.25–7.99	< 0.05
TRPG [mm Hg]	1.03	1.00–1.05	< 0.05	1.04	1.01–1.07	< 0.05
Acceleration time [ms]	0.97	0.96–0.99	NS	0.98	0.96–0.99	NS

Abbreviations as in Table 2

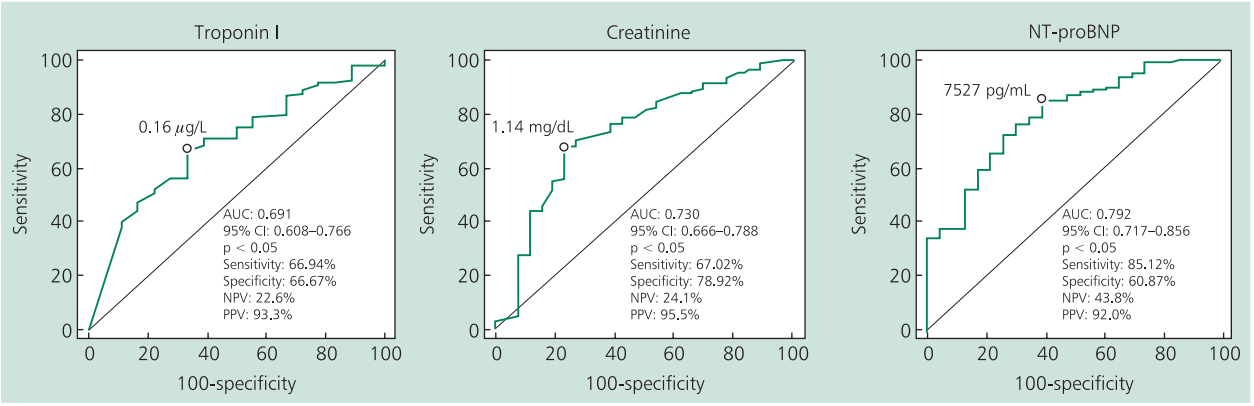

Figure 3. New cut-off biomarker levels determined using ROC curves; AUC — area under curve; CI — confidence interval; NPV — negative predictive value; PPV — positive predictive value

line significant risk factor for mortality despite a significant difference in median cTnI level between patients who died and those who survived.

In an additional analysis including non-high-risk patients (IR and LR groups combined), ln[NT-proBNP] and ln[creatinine] were significant predictors of mortality risk (OR 6.47, 95% CI 1.79–23.29, and OR 2.5, 95% CI 1.38–1.4, respectively). In addition, ln[NT-proBNP], cTnI and creatinine levels were significant predictors of the combined endpoint including all-cause in-hospital deaths, the need for intubation, shock, the need to use intravenous catecholamines in pressor doses, and thrombolysis (OR 4.15, 95% CI 2.26–7.61, OR 3.95, 95% CI 1.79–8.66, and OR 2.02, 95% CI 1.28––3.18, respectively). Significant predictors of the combined endpoint also included age, heart rate and TRPG. Apart from age, the same variables were predictors of the combined endpoint among non-high-risk patients (Table 4).

Using ROC curves, we determined new cut-off levels of the biomarkers examined in our study population that offered optimal sensitivity and specificity for predicting mortality (Fig. 3). An analysis of in-hospital mortality using these new cut-off biomarker levels also showed that creatinine, cTnI, and NT-proBNP levels were significant predictors of in-hospital deaths (Table 5).

DISCUSSION

According to both European and American guidelines, patients at high risk of early mortality should receive intensive, i.e. thrombolytic treatment, and remaining patients can be treated with LMWH or UFH. In our study, the group with a high mortality risk due to APE included 6.5% of patients. Mortality in this group was higher than reported in European guidelines but was very similar to data reported in observational studies [3–6]. Of note, thrombolytic therapy was rarely

Table 5. Biomarkers as significant predictors of mortality — new cut-off levels determined using ROC curves

	Cut-off value	Odds ratio	95% confidence interval	P
Creatinine [mg/dL]	1.14 mg/dL	6.61	2.52–17.38	< 0.05
NT-proBNP [pg/mL]	7527 pg/mL	8.35	3.14–22.22	< 0.05
cTnI [μg/L]	0.16 μg/L	3.64	1.27–10.45	< 0.05

used in this group, as this treatment was employed in only about 40% of patients. The reason for this was high perceived risk of bleeding complications following thrombolytic treatment, mainly in patients with disseminated malignancies or after recent major surgical procedures. Although in some studies thrombolytic treatment was used in 48% of patients with APE with high risk of early mortality, this proportion was reduced to 28.7% when patients with contraindications for thrombolysis were taken into account [7]. However, we believe that thrombolysis remains underused in patients with high risk APE. In our study population, the decision to withhold thrombolytic therapy was most commonly related to the presence of disseminated malignancy (21%), active bleeding (21%) or recent stroke (14%). In addition, 1 patient underwent recent major surgery, 1 patient had central nervous system haematoma, and 1 patient after traumatic cardiopulmonary resuscitation had multiple medical comorbidities. Potential alternative treatment with shock patients in whom thrombolysis cannot be safely used is percutaneous fragmentation of thrombi located in pulmonary arteries. Such an approach is particularly recommended in the current American guidelines [2]. Another option is surgical embolectomy, but patients with active malignancies or multiple medical comorbidities are not good candidates for such treatment. In our study, pulmonary embolectomy was performed in 1 patient with intermediate risk APE in whom echocardiography revealed a mobile right atrial thrombus stuck in a patent foramen ovale.

Some patients in our study received thrombolytic therapy despite significant contraindications to such treatment, for example a patient treated on the second postoperative day after stent-graft implantation due to abdominal aortic aneurysm. The patient suffered no bleeding complications and was discharged home in a good clinical condition. We understand that the decision to initiate intensive treatment is difficult, particularly in severely ill patients. However, two reports of successful use of full or reduced doses of thrombolytic drugs in patients with perceived absolute contraindications to thrombolysis and our own experience suggest it may be justified to attempt thrombolytic treatment in such patients with high risk APE [8, 9]. In view of relatively few bleeding events noted in our study, it seems that contraindications to thrombolysis might be less restrictive. Regardless of the controversies related to the use of thrombolytic treatment in patients after recent surgical procedures, studies show that fatal APE is more common in patients with no history of surgical treatment [10]. Percutaneous embolectomy is a potential therapeutic option in this patient group. With 24-h availability of cardiac catheterisation services and the current guidelines emphasising the role of such treatment, percutaneous embolectomy should be more widely employed.

Risk stratification was performed based on the clinical evaluation on admission, so thrombolytic treatment could be used in IR and LR patients if clinical deterioration (i.e. hypotension) occurred during further hospitalisation. Both European and American guidelines emphasize the role of estimating both the likelihood of PE and the risk of early mortality due to PE, which is crucial for the selection of appropriate treatment. Based on easily obtainable clinical variables (blood pressure, evidence of shock), it is possible to identify patients who require aggressive treatment, i.e. thrombolysis. If there is no evidence of haemodynamic instability, further stratification of early mortality risk is performed using easily obtainable parameters, such as serum cTnI level measurement or evaluation of RV overload in the echocardiographic examination. According to guidelines, anticoagulation can be withheld until confirmation of PE only in patients with low clinical probability of the disease. This emphasizes the importance of initial, simple clinical evaluation of the risk of early mortality due to PE.

Re-evaluation of the indications for thrombolytic treatment in APE seems justified, particularly in the context of ongoing studies related to the role of thrombolysis, such as the PEITHO trial (tenecteplase *vs* placebo). Results of this study may show that there is a group of APE patients with a moderate risk of early mortality who would benefit from thrombolytic treatment. This would significantly increase the number of potential candidates for thrombolysis, also directing clinician attention to contraindications to such intensive treatment. Of note, clinical deterioration necessitating the use of thrombolysis occurred despite initial heparin treatment in 13 patients in IR group (8.9%) and in 2 LR patients in our study, i.e. overall in 4.5% of patients who were initially in a haemodynamically stable condition. Cardiac troponin I level was elevated in 9 of these 15 patients. This indicates the need for close monitoring of IR patients in the initial treatment period to identify relatively frequent occurrences of clinical deterioration and the need for rapid treatment escalation. Thus, it may also be warranted to develop additional methods of risk stratification that would identify

"very low risk" patients in whom very good outcomes may be expected.

The most important predictors of early mortality due to PE that were identified in our study are consistent with previous findings [11, 12]. Of note, serum creatinine level was found to be a significant predictor of mortality risk both in the overall study population and in non-high risk and low risk groups. As already mentioned, clinical evaluation combined with echocardiographic and laboratory parameters allows risk stratification and selection of appropriate treatment. Heart rate monitoring and determination of creatinine, cTn I, and NT-proBNP levels are crucial in patients with PE, particularly those at non-high risk of early mortality, allowing identification of patients who are at risk of clinical deterioration and death despite being haemodynamically stable on admission. In our study, creatinine and NT-proBNP levels were independent predictors of total mortality. Although cTnI level was significantly higher in patients who died than in those who survived, it was not identified as an independent predictor of total mortality. In contrast, it was a significant predictor of a complicated clinical course, as reflected by a combined endpoint that included not only deaths but also thrombolysis, shock and the use of pressor doses of catecholamines. Of note, elevated troponin level was a major factor taken into account when decisions were made to initiate thrombolytic treatment. This may explain why cTnI level was only of borderline significance ($p = 0.56$) in predicting mortality in the study population.

Limitations of the study

An obvious limitation of our analysis was its retrospective nature. Although retrospective design of the study had a major effect on the results of statistical analyses, our findings are comparable to those reported by other authors and indicate that problems we discussed above are common and require further active international cooperation in an attempt to optimise the management of patients with APE.

CONCLUSIONS

Not only age and compromised haemodynamic status but also plasma creatinine, NT-proBNP, and troponin I levels are prognostic factors in patients with APE. Due to high mortality rate among non-thrombolysed HR patients, therapy in this group should be more aggressive and contraindications for thrombolysis should be less restrictive. Despite anticoagulation, haemodynamic deterioration requiring thrombolytic therapy may occur in about one in 10 IR patients with APE.

Conflict of interest: *none declared*

References

1. Guidelines on the diagnosis and management of acute pulmonary embolism. The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). Eur Heart J, 2008; 29: 2276–2315.
2. Jaff MR, McMurtry MS, Archer SL et al. Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension: a scientific statement from the American Heart Association. Circulation, 2011; 123: 1788–1830.
3. Laporte S, Mismetti P, Décousus H et al.; RIETE Investigators. Clinical predictors for fatal pulmonary embolism in 15,520 patients with venous thromboembolism: findings from the Registro Informatizado de la Enfermedad TromboEmbolica venosa (RIETE) Registry. Circulation, 2008; 117: 1711–1716.
4. Goldhaber SZ, Visani L, De Rosa M. Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER). Lancet, 1999; 353: 1386–1389.
5. Kucher N, Rossi E, De Rosa M et al. Massive pulmonary embolism. Circulation, 2006; 113: 577–582.
6. Agnelli G, Becattini C, Kirschstein T. Thrombolysis vs heparin in the treatment of pulmonary embolism: a clinical outcome-based meta-analysis. Arch Intern Med, 2002; 162: 2537–2541.
7. Kasper W, Konstantinides S, Geibel A et al. Management strategies and determinants of outcome in acute major pulmonary embolism: results of a multicenter registry. J Am Coll Cardiol, 1997; 30: 1165–1171.
8. Bulpa P, Carbutti G, Osselaer JC et al. Low-dose urokinase in massive pulmonary embolism when standard thrombolysis is contraindicated. Chest, 2009; 136: 1141–1143.
9. Han S, Chaya C, Hoo GW. Thrombolytic therapy for massive pulmonary embolism in a patient with a known intracranial tumor. J Intensive Care Med, 2006; 21: 240–245.
10. Alikhan R, Peters F, Wilmott R et al. Fatal pulmonary embolism in hospitalised patients: a necropsy review. J Clin Pathol, 2004; 57: 1254–127.
11. Pruszczyk P, Bochowicz A, Torbicki A et al. Cardiac troponin T monitoring identifies high-risk group of normotensive patients with acute pulmonary embolism. Chest, 2003; 123: 1947–1952.
12. Kostrubiec M, Łabyk A, Pedowska-Włoszek J et al. Assessment of renal dysfunction improves troponin-based short-term prognosis in patients with acute symptomatic pulmonary embolism. J Thromb Haemost, 2010; 8: 651–658.

Ostra zatorowość płucna: analiza kolejnych 353 pacjentów hospitalizowanych w jednym ośrodku. Doświadczenie 3-letnie

Andrzej Łabyk[1], Michał Ciurzyński[1], Krzysztof Jankowski[1], Maciej Kostrubiec[1], Barbara Lichodziejewska[1], Piotr Bienias[1], Justyna Pedowska-Włoszek[1], Szymon Pacho[1], Piotr Palczewski[2], Piotr Pruszczyk[1]

[1]Klinika Chorób Wewnętrznych i Kardiologii, Warszawski Uniwersytet Medyczny, Warszawa
[2]I Zakład Radiologii Klinicznej, Warszawski Uniwersytet Medyczny, Warszawa

Streszczenie

Wstęp i cel: Celem pracy była charakterystyka grupy i wczesnych wyników leczenia pacjentów z ostrą zatorowością płucną (OZP), hospitalizowanych w jednym ośrodku.

Metody: Przeanalizowano dane 353 kolejnych pacjentów, 141 mężczyzn i 212 kobiet (średni wiek 64,7 ± 18,12 roku) z OZP, leczonych w ośrodku referencyjnym w latach 2007–2009.

Wyniki: Pacjentów podzielono na grupy: wysokiego (WR), pośredniego (PR) i niskiego (NR) ryzyka zgonu z powodu OZP, zgodnie z aktualnymi wytycznymi Europejskiego Towarzystwa Kardiologicznego. Grupa WR objęła 23 pacjentów (10 M, 13 K, wiek 70,1 ± 16,9 roku), grupa PR — 146 pacjentów (61 M, 85 K, wiek 65,77 ± 17,74 roku), a grupa NR — 184 chorych (70 M, 114 K, wiek 63,17 ± 18,4 roku). Większość (91,8%) chorych była leczona heparynami (niefrakcjonowaną lub drobnocząsteczkową). Trombolizę zastosowano u 24 pacjentów: 39,1% z grupy WR, 8,9% z grupy PR i 1% z grupy NR. Całkowita śmiertelność wewnątrzszpitalna wyniosła 7% (z powodu OZP 5,4%), w grupie WR — 65,2% (OZP 43,5%), w grupie PR — 6,2% (OZP 4,1%), w grupie NR — 2,2% (OZP 1,6%). Czterech z 9 pacjentów WR, którzy otrzymali leki trombolityczne, zmarło (śmiertelność 44,4%), natomiast śmiertelność u chorych z grupy WR nieleczonych trombolitycznie wyniosła 73,3%. Decyzję o rozpoczęciu terapii trombolitycznej oparto na wynikach analizy przeciwwskazań. U 13 (8,9%) pacjentów z grupy PR mimo początkowego zastosowania heparyn wystąpiło pogorszenie stanu klinicznego z koniecznością wdrożenia leczenia trombolitycznego. Istotnymi czynnikami prognostycznymi śmiertelności całkowitej były: wiek [OR 1,07 (95% CI 1,02–1,12) na 1 rok życia], częstotliwość rytmu serca [OR 1,04 (95% CI 1,02–1,06) na 1 uderzenie/min], stężenie kreatyniny [OR 3,65 (95% CI 1,62–8,27)]. Stężenia NT-proBNP i troponiny I okazały się również czynnikami prognostycznymi zgonu w badanej grupie: OR dla ln NT-proBNP — 5,91 (95% CI 2,38–14,65), $p < 0,05$; OR dla troponiny I — 2,77 (95% CI 0,97–7,93), $p = 0,056$. Zarówno w całej grupie, jak i u początkowo stabilnych hemodynamicznie pacjentów predyktorami połączonego punktu końcowego obejmującego zgon, wystąpienie wstrząsu, konieczność intubacji, zastosowania katecholamin lub eskalacji leczenia w postaci trombolizy były: wiek, czynność serca, stężenie kreatyniny, troponiny I, NT-proBNP w surowicy i gradient ciśnień przez zastawkę trójdzielną.

Wnioski: U ok. 9% chorych z OZP pośredniego ryzyka mimo leczenia przeciwzakrzepowego może dojść do pogorszenia stanu i konieczności zastosowania trombolizy. Nie tylko wiek i stan hemodynamiczny, ale również stężenia kreatyniny, NT-proBNP i troponiny I wpływają na rokowanie u pacjentów z OZP. Ze względu na wysoki odsetek zgonów u osób wysokiego ryzyka nieleczonych trombolitycznie terapia w tej grupie powinna być bardziej intensywna, a przeciwwskazania do niej mniej restrykcyjne.

Słowa kluczowe: ostra zatorowość płucna, leczenie, tromboliza, śmiertelność

Kardiol Pol 2012; 70, 1: 15–22

Adres do korespondencji:
prof. dr hab. n. med. Piotr Pruszczyk, lek. Andrzej Łabyk, Klinika Chorób Wewnętrznych i Kardiologii, Warszawski Uniwersytet Medyczny, ul. Lindleya 4, 02–005 Warszawa, tel: +48 22 502 11 44, +48 22 502 16 68, + 48 22 502 16 25, faks: +48 22 502 21 42, e-mail: endrjulab@tlen.pl
Praca wpłynęła: 09.03.2011 r. **Zaakceptowana do druku:** 24.08.2011 r.