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In-hospital diagnostic strategies for acute pulmonary embolism — results of a single-center study based on the experience of a multi-profile clinical hospital

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Abstract

Introduction: *Acute pulmonary embolism (APE) is the most severe clinical presentation of venous thromboembolism (VTE) and inappropriate diagnostic strategies of APE lead to death or chronic thromboembolic pulmonary hypertension.*

Material and methods: *In prospective manner we followed patients admitted to a tertiary clinical center with APE proven with CT scan within the period of 24 months. We assessed diagnostic strategies of APE in different clinical departments of Polish multi-profile hospital and their association with prognosis.*

Results: *A total number of 178 patients with APE were enrolled in the study, of which 56 patients were diagnosed with APE in the emergency department (ED), 42 in cardiology departments, and 80 in other departments. No significant differences in diagnostic strategies between departments were found. Adherence to ESC guidelines was 56.1% and it was similar in compared departments ($p = 0.648$). The in-hospital mortality rate was 6.7%. In the 6 month follow-up period 18.1% of the studied died. Coronary artery disease ($p = 0.002$), cancer ($p = 0.032$), serious medical condition ($p = 0.047$), altered mental status ($p = 0.032$), CRP ($p = 0.006$), and hemoglobin ($p = 0.023$) were identified as predictors of clinical deterioration. Risk factors for in-hospital and 6-month mortality were congestive heart failure, serious medical condition, and systolic blood pressure ($p < 0.05$). Immobility over 3 days and cancer were also identified as predictors of death within 6 months ($p < 0.001$). There was no association between the type of the department, clinical deterioration, in-hospital, and 6-month mortality.*

Conclusion: *There is no difference in APE management and prognosis in different profile departments.*

Key words: 6-month mortality; guidelines adherence; in-hospital mortality; pulmonary embolism

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Introduction

Acute pulmonary embolism (APE) is the most severe clinical presentation of venous thromboembolism (VTE), which is the third cause of cardiovascular death [1]. The annual incidence of APE is estimated at around 80–180 cases per 100 000 people leading to death in 15% of patients in the first three months [2]. Because of nonspecific symptoms, which may suggest another condition, the diagnosis of PE might be challenging in real-life practice. Despite subsequent updates of the clinical guidelines and statements released by international societies dealing with VTE [3, 4], the diagnostic pathways in case of suspected APE in everyday practice are still burdened with numerous errors [5–7]. Undiagnosed APE leads to death, chronic thromboembolic pulmonary hypertension, disability, and worsening of quality of life.

The main objective of this study was to assess diagnostic strategies of APE in different clinical departments of a Polish multi-profile hospital and their association with prognosis.

Material and methods

We assessed the management of consecutive patients with diagnosed pulmonary embolism confirmed by imaging examination who were hospitalized in our center for more than 24 hours. The majority of the study group was included in the ZATPOL-2 registry. To be enrolled in the present study the subject had to have met the following criteria: age of at least 18 years and APE confirmed in computed tomography (CT). Chronic thromboembolic disease and APE without CT confirmation were the exclusion criteria. Recorded data included demographics, admission details, symptoms of APE, comorbidities, a serious medical condition defined as an illness or physical or mental condition that involves inpatient care in a hospital e.g severe pneumonia, VTE risk factors, bleeding risk factors, previous anticoagulation treatment, laboratory tests results, imaging tests results, in-hospital and home treatment, in-hospital deaths and clinical deterioration defined as the death of all-cause, use of vasopressors, respiratory failure, thrombolysis, embolectomy, bleeding complications.

The appropriateness of APE management was assessed according to the current guidelines [3, 4].

Our research was conducted in Central Research Hospital Ministry of Interior and Administration within 24 months.

The study protocol was approved by the ethical committee (44/PB/2013).

Statistical analysis

Categorical data were presented as counts and percentages. The chi-square test or Fischer's exact test were used to compare the distribution of categorical variables between groups. Continuous data were first tested for normality using Shapiro-Wilk test, then in descriptive statistics for normally distributed variables mean and standard deviation were reported; otherwise, median with the 25th and 75th percentiles (Q1 and Q3) were given. Normally distributed variables were compared between groups using t-Student test, otherwise Mann-Whitney test was used. Uni- and multivariable logistic regression models were used to identify risk factors of clinical deterioration, in-hospital, and 6-month mortality. In variables selection for the final multivariable logistic regression model, the backward stepwise regression elimination procedure with the minimization of the Akaike criterion was used. Odds ratio (OR) with 95% confidence intervals were calculated and Wald's test p value were reported. A p value < 0.05 was considered statistically significant. Two-sided tests were used. We did not use data imputation methods for missing data. Due to the small number of patients in non-cardiology departments, all patients from departments other than cardiology were combined into a non-cardiology group.

All statistical analysis was performed by using R 3.4.0 (R Core Team (2017).

Results

Characteristics of the study group

Overall, 178 patients, median age 69.0 [IQR 57.0––80.8] years with CT— confirmed APE were enrolled in the study. Of these, 49% were women. APE was the main reason for hospitalization in 164 (92.1%) patients, while 7 (3.9%) subjects presented due to other causes, and 7 (3.9%) patients were admitted to the Department of Cardiac Surgery for surgical embolectomy procedure (Table 1).

Among 178 patients, 56 (31.5%) were diagnosed with APE in the emergency department (ED), 42 (23.6%) in cardiology units, and 80 (44.9%) subjects in other profile hospital wards. Subjects diagnosed in ED were more frequently with altered mental status and higher D-dimer plasma levels. Patients referred to cardiology units more often had dyspnea with exertion, substernal chest pain, syncope, tachycardia, hypoxemia, elevated troponin I serum level, and negative T wave in lead V_1–V_3 in ECG. Cough, fever, and elevated C-reactive protein (CRP) serum levels were found more frequently in a group diagnosed in other wards (Table 2).

Table 1. Patients hospitalized in different clinical departments

Department	Number (n)/ /percent (%)
All patients	178 (100)
Department of Allergology	26 (14.6)
Department of Gastric Surgery	3 (1.7)
Department of Vascular Surgery	1 (0.6)
Department Endocrinology	8 (4.5)
Department of Gastroenterology	3 (1.7)
Department of Hepatology	3 (1.7)
Department of Cardiac Surgery	7 (3.9)
Department of Invasive Cardiology	67 (37.6)
Department of Cardiology and Hypertension	20 (11.2)
Department of Nephrology	16 (9.0)
Department Neurology	2 (1.1)
Intensive Care Unit	2 (1.1)
Department of Oncology	7 (3.9)
Department of Orthopedics	2 (1.1)
Department of Rheumatology	10 (5.6)
Department of Urology	1 (0.6)

Diagnostic strategies in different clinical departments

The diagnostic process was similar in all departments with overall adherence to ESC guidelines rate of 56.1%. The diagnostic strategy was more likely to be appropriate in cardiology units (59.5%) than in ED (58.9%) and other wards (52.1%), however, the difference was not significant. In the group with the high probability of APE, hypotension, and shock, D-dimer measurement was the test most often used as the first stage of diagnostic management. It was performed in 100% of patients diagnosed in cardiology units, in 71.4% in ED, and in 50% in other wards. CT scan was the most common examination of the second stage performed in 66.7% of subjects undergoing the second test in cardiology units, 71.4% in ED, and in 60% in other wards. Similarly, in the group of a low and moderate probability of APE, most of the patients had D-dimer plasma level measured as the first examination (66.7% in cardiology units; 70.2% in ED and 64.2% in other wards, respectively) and CT scan as the second (65.7% in cardiology units vs. 75% in ED vs. 66.7% in other wards).

Factors associated with short-term and long-term prognosis

Of 56 patients diagnosed in ED, 80.4% were referred to cardiology units, whereas 19.6% to other wards. During the hospital observation, clinical deterioration occurred in 14 (16.1%) patients hospitalized in cardiology units and in 18 (19.8%) patients in other wards. Respiratory failure occurred in 3.9% of the subjects (2.3% in cardiology units vs. 5.5% in other wards). Bleeding complications were observed in 3.9% of the study cohort (3.4% in cardiology units, vs. 4.4% in other wards).Vasopressors were used in 7 (8%) patients in cardiology units vs. 10 (11%) in other hospital wards. Thrombolysis was administered only in 2 (2.3%) patients in cardiology units. Embolectomy was performed in 2 (2.3%) patients in cardiology units and 6 (6.6%) in other departments. The in-hospital mortality rate was 6.7% (12 cases). APE was found to be the cause of death in 9 (75%) subjects. The rest of the deaths were attributed to acute coronary syndrome, acute pancreatitis, and pneumonia. 6 patients died in cardiology units, as well as 6 patients died in other departments. In multivariable analysis, congestive heart failure, serious medical conditions, and lower systolic blood pressure were identified as factors associated with higher odds of in-hospital mortality (Table 3). Furthermore, significant predictors of clinical deterioration included ischemic heart disease, malignancy, serious medical condition, altered mental status, lower hemoglobin levels at admission, and higher CRP serum level at admission (Table 4).

In the 6-month follow-up period, death occurred in 30 (18.1%) patients. Within half a year from discharge, more than one-third of patients (36.9%) required re-hospitalization, and only one was diagnosed with recurrent PE.

In multivariate analysis congestive heart failure malignancy, immobility over 3 days, serious medical condition, and lower systolic blood pressure at presentation were identified as the factor for death within 6 months from diagnosis (Table 5). There was no association between type of the department and clinical deterioration, in-hospital, and 6-month mortality.

Discussion

Undiagnosed APE leads to death, chronic thromboembolic pulmonary hypertension, disability, and worsening quality of life. Currently, many EDs are overloaded and cardiology departments struggle with a too-small number of beds to meet patients' needs. The aim of this study was to show that hospitalization of a patient with APE in a non-cardiology unit did not worsen the prognosis.

Our data show that patients with symptoms typical for coronary artery disease (dyspnea, chest pain, syncope) were more often referred to cardiology departments, whereas subjects complaining of cough

Table 2. Characteristics of patients hospitalized in different clinical departments

Parameter	Clinical department			p-value
	Others	Cardiology	ED	
	Number (n)/percentage (%)			
Patients	80	42	56	
Age (years) (median [IQR])	66.5 [50.8–79.0]	72.5 [60.2–80.8]	68.5 [58.0–83.2]	0.358
Women	38 (47.5)	21 (50.0)	28 (50.0)	0.969
Men	42 (52.5)	21 (50.0)	28 (50.0)	
Dyspnea with exertion	45 (56.2)	37 (88.1)	38 (69.1)	0.002
Dyspnea at rest	31 (38.8)	22 (52.4)	23 (41.8)	0.345
Pleuritic chest pain	19 (23.8)	7 (16.7)	10 (18.2)	0.582
Substernal chest pain	5 (6.2)	10 (23.8)	3 (5.5)	0.007
Hemoptysis	11 (13.8)	2 (4.8)	3 (5.4)	0.160
Fever	18 (22.5)	2 (4.8)	7 (12.5)	0.028
Syncope	18 (22.8)	18 (42.9)	11 (19.6)	0.022
Tachycardia	31 (38.8)	23 (54.8)	17 (30.4)	0.049
Hypotension/shock	6 (7.5)	2 (4.8)	7 (12.5)	0.390
Cough	31 (38.8)	7 (16.7)	13 (23.2)	0.021
DVT symptoms	12 (15.0)	16 (38.1)	17 (30.9)	0.011
Coronary artery disease	15 (18.8)	11 (26.2)	11 (20.0)	0.618
Atrial fibrillation	11 (13.8)	9 (21.4)	11 (20.0)	0.481
Prior ischemic stroke	2 (2.5)	1 (2.4)	1 (1.8)	1.000
Prior hemorrhagic stroke	1 (1.2)	0 (0.0)	0 (0.0)	1.000
Chronic pulmonary disease	8 (10.0)	3 (7.1)	6 (10.9)	0.897
Cancer	17 (21.2)	8 (19.5)	9 (16.7)	0.805
Diabetes	20 (25.0)	11 (26.2)	10 (18.2)	0.567
Arterial hypertension	47 (58.8)	27 (64.3)	36 (65.5)	0.694
Prior major bleeding	3 (3.8)	1 (2.4)	4 (7.3)	0.581
Chronic liver disease	6 (7.5)	3 (7.1)	1 (1.8)	0.306
Orthopedics procedure within 3 months	5 (6.2)	1 (2.4)	5 (9.1)	0.444
Gynecologic procedure within 3 months	0 (0.0)	0 (0.0)	1 (1.8)	0.548
Surgical procedure within 3 months	8 (10.0)	2 (4.8)	3 (5.5)	0.607
Limb trauma with plaster	8 (10.0)	1 (2.4)	1 (1.8)	0.083
Lower limbs paralyses	2 (2.5)	2 (4.8)	3 (5.5)	0.615
Prior VTE	11 (13.8)	8 (19.0)	9 (16.1)	0.744
Family history of thrombophilia	2 (2.5)	1 (2.4)	2 (3.6)	1.000
Congestive heart failure class III/IV NYHA	8 (10.0)	2 (4.8)	2 (3.6)	0.374
Immobility > 3 days	10 (12.5)	3 (7.1)	9 (16.4)	0.394
Central line	3 (3.8)	0 (0.0)	0 (0.0)	0.329
Obesity	20 (25.0)	10 (23.8)	10 (18.2)	0.634
Long journey within 8 weeks	2 (2.5)	2 (4.8)	0 (0.0)	0.273
Serious medical condition	5 (6.2)	2 (4.8)	6 (10.9)	0.533
Mental disorders	7 (8.8)	0 (0.0)	8 (14.3)	0.028

→

Parameter	Clinical department			p-value
	Others	Cardiology	ED	
	Number (n)/percentage (%)			
Low/moderate probability PE	78 (97.5)	41 (97.6)	56 (100.0)	0.607
High probability PE	2 (2.5)	1 (2.4)	0 (0.0)	
Hemoglobin (g/dL) (median [IQR])	12.8 [11.2–14.4]	13.0 [11.7–14.2]	13.2 [12.2–14.0]	0.529
D-dimer (μg/L) (median [IQR])	3984 [2346–8603]	5237 [4225–18926]	6676 [2885–18333]	0.020
CRP (mg/L) (median [IQR])	42.5 [17.5–82.7]	22.1 [7.9–40.2]	29.9 [6.2–64.1]	0.032
Troponin I (ng/dL) (median [IQR])	0.02 [0–0.12]	0.09 [0.01–0.37]	0.03 [0–0.14]	0.030
NT-proBNP (pg/mL) (median [IQR])	564 [289.5–8943]	1734 [623.8–3910.8]	530 [81–2622.0]	0.159
GFR (mL/min./1.73 m^2) (median [IQR])	69 [51.5–88]	65 [52.2–79.5]	75 [54.5–89.5]	0.463
Creatinine (mg/dL) (median [IQR])	0.95 [0.79–1.19]	0.95 [0.84–1.07]	0.92 [0.082–1.09]	0.818
Sinus rhythm	61 (89.7)	36 (85.7)	47 (85.5)	0.734
S1Q3T3 sign	7 (10.4)	10 (23.8)	10 (18.5)	0.169
Complete RBBB	7 (10.4)	9 (21.4)	3 (5.6)	0.070
Negative T wave V1–V3	13 (19.4)	18 (42.9)	13 (24.5)	0.024
Negative T wave V4–V6	7 (10.4)	7 (16.7)	5 (9.3)	0.527
Negative T wave II, III, aVF	11 (16.4)	5 (11.9)	6 (11.1)	0.656
Cardiac enlargement in chest X-ray	20 (36.4)	10 (40.0)	11 (42.3)	0.948
Pleural effusion	14 (25.9)	5 (20.0)	5 (19.2)	0.742
Elevated hemidiaphragm	4 (7.4)	3 (12.0)	2 (7.7)	0.815
Pulmonary artery enlargement	1 (1.9)	0 (0.0)	0 (0.0)	1.000
Atelectasis	8 (14.8)	1 (4.0)	2 (7.7)	0.340
Pulmonary parenchymal infiltrates	18 (33.3)	4 (16.0)	3 (11.5)	0.058
Pulmonary venous congestion	12 (22.2)	3 (12.0)	5 (19.2)	0.642
Normal chest X-ray	6 (11.1)	6 (24.0)	3 (12.0)	0.368

DVT — deep vein thrombosis; VTE — venous thromboembolism; NYHA — New York Heart Association; CRP — C-reactive protein; NT-proBNP — N-terminal pro hormone B type natriuretic peptide; GFR — glomerular filtration rate; RBBB — right bundle branch block

Table 3. Multivariable analysis for in-hospital mortality in study group

Parameter	Odds ratio (95%CI)	p-value
Coronary artery disease	0.27 (0.01–4.23)	0.386
Atrial fibrillation	2.07 (0.07–46.18)	0.629
Congestive heart failure (NYHA III/IV)	142.09 (3.42–29705.65)	0.021
Immobility > 3 days	27.39 (1.33–2217.19)	0.053
Central line	127.79 (0.87–459544.46)	0.114
Serious medical condition	175.19 (7.35–27269.27)	0.007
Systolic blood pressure (mmHg)	0.91 (0.81–0.99)	0.048
D-dimer	0.99 (0.93–1.05)	0.671

and fever suggesting pneumonia, were more often hospitalized in other profile wards. In the IPER registry patients admitted to the cardiology department were more frequently hemodynamically unstable or with prior VTE episodes. Meanwhile, subjects with a history of immobility over 3 days were more often referred to internal medicine departments [8].

The current study shows that the overall adherence of diagnostic strategies to ESC recommendations was 56.1%, which supports results from previous research [8, 9]. Surprisingly, we found no significant difference

Table 4. Multivariable analysis for clinical deterioration in study population

Parameter	Odds ratio (95%CI)	p-value
Coronary artery disease	16.38 (3.17–115.68)	0.002
Cancer	7.44 (1.25–52.61)	0.032
Chronic liver disease	1.04 (0.06–12.34)	0.977
Serious medical condition	19.62 (1.39–642.04)	0.047
Altered mental status	17.59 (1.49–439.94)	0.032
Hemoglobin	0.63 (0.413–0.92)	0.023
CRP	1.15 (1.01–1.03)	0.006
RV/LV	9.73 (0.16–1013.58)	0.305
AcT (ms)	0.97 (0.93–1.00)	0.092

CRP — C-reactive protein; RV/LV — right ventricle/left ventricle ratio; AcT — right ventricular outflow Doppler acceleration time

Table 5. Multivariable analysis for 6-month mortality in study cohort

Parameter	Odds ratio (95%CI)	p-value
Cancer	20.40 (6.45–76.72)	< 0.001
Congestive heart failure	21.93 (3.99–132.63)	< 0.001
Immobility > 3 days	10.42 (2.85–42.08)	0.001
Serious medical condition	17.24 (3.44–103.16)	0.001
Systolic blood pressure (mmHg)	0.97 (0.95–0.99)	0.004
Hemoglobin (g/dL)	0.79 (0.591–1.05)	0.106

between clinical departments as far as compliance to guidelines is concerned.

The clinical deterioration risk factors identified in our patients extend previous literature. We found that ischemic heart disease, malignancy, serious medical condition, alerted mental status, lower hemoglobin and CRP serum level were associated with poor in-hospital outcomes. In the previously mentioned IPER registry immobility over 4 days before admission, hemodynamic instability, and cardiovascular disease were found to be related to the poor clinical course [8].

The overall in-hospital mortality in our research was 6.7%, which is similar to that observed in the IPER registry (6.7%) and SWIVTER registry (6.6%) [10]. In the IPER registry predictors of poor prognosis were age over 75 years, immobility over 3 days, and hemodynamic instability [8]. Meanwhile, in our research risk factors of in-hospital deaths were congestive heart failure, serious medical condition, immobility over 3 days, and low systolic blood pressure at admission.

In the 6 months follow-up period mortality rate was 18.1%. The risk factors of death in half a year in our study were congestive heart failure, malignancy, immobility over 3 days, serious medical condition, and lower systolic blood pressure at admission was also associated with poor prognosis. In SWTCO65+ study 6-month mortality rate was 13.6%. It was found that patients with higher high-sensitivity troponin T serum levels had a higher risk of death within 6 months [11].

To the best of our knowledge, this is the first study comparing diagnostic strategies in different clinical departments.

Limitations of the study

The main limitation of our research is that it was a single-center study. Our research was based on the registry, so the treatment was not standardized, which could affect mortality and clinical deterioration.

Conclusion

Summing up, we found that adherence to ESC guidelines was comparable between hospital departments and there was no direct relation between type of department, clinical deterioration, in-hospital, and 6-month mortality.

Conflict of interest

None.

List of abbreviations:

APE — acute pulmonary embolism; CT — computed tomography; ED — emergency department; ESC

— European Society of Cardiology; VTE — venous thromboembolism.

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