Chapter 9

Comparison of risk profile and clinical outcome of patients after acute pulmonary embolism in university and non-university hospitals

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Abstract

Background

Current knowledge on diagnostic management and treatment of patients with acute pulmonary embolism (PE) is partly derived from outcome studies including patients from university hospitals alone. It is debatable whether these data are applicable to patients in non-university hospitals. The aim of this study was to compare baseline characteristics and clinical outcome of patients with PE treated in university hospitals versus patients treated in non-university hospitals.

Methods

Post-hoc analysis on data derived from Christopher study, a prospective multicenter management study.

Results

A total of 399 (59%) patients with PE presented to a university hospital and 275 (41%) to a non-university teaching hospital. The characteristics of patients from the university and non-university hospitals were different with respect to female ratio (46% vs. 56%, Odds Ratio [OR] 0.65, 95% confidence interval [CI] 0.47-0.88), outpatient ratio (73% vs. 84%, OR 0.53, 95%CI 0.36-0.79), presence of immobilization (37% vs. 23%, OR 2.0, 95%CI 1.4-2.8) and the presence of active malignancy (19% vs. 12%, OR 1.6, 95%CI 1.1-2.5). Risk on venous thromboembolic recurrence (3.3% vs. 2.6% OR 1.3, 95%CI 0.50-3.3) and mortality (9.0% vs 6.9% OR 1.3, 95%CI 0.75-2.4) were higher for patients in university than in non-university hospitals. Bleedings occurred twice more often in patients from university hospitals (4.3% vs 2.2% OR 2.0, 95%CI 0.77-5.1).

Conclusion

Physicians should be aware of differences in patient characteristics and outcome between university and non-university hospitals when interpreting results from large clinical trials and applying these to their everyday medical practice.

Introduction

Current knowledge regarding diagnostic management and treatment of patients with acute pulmonary embolism (PE) is mainly derived from large outcome studies including patients from university and non-university hospitals or university hospitals alone.[1-4] A common perception of university hospitals is that they treat more severely ill patients than non-university hospitals.[5] Therefore, it must be debated whether data on the diagnostic management and treatment of patients with acute PE derived from university hospitals are relevant and applicable to everyday patient care in non-university hospitals, and vice-versa. We hypothesized that patients from university hospitals would be a population with more comorbidity than in non-university hospitals. Accordingly, we investigated differences between baseline risk factors predicting adverse clinical outcome (e.g. higher age, immobilization, cancer and cardiopulmonary comorbidity) in patients with established acute PE in university and non-university hospitals. In addition, the clinical outcome of these patient groups was compared.

Methods

We performed a post-hoc analysis on data obtained from a large multicenter prospective cohort follow-up study.[2] In this study, executed from November 2002 until September 2004, consecutive hemodynamic stable patients with computed tomography proven acute PE were followed for a period of 3 months to document the occurrence of recurrent symptomatic venous thromboembolic events. All patients were treated according to the previously followed guidelines.[6] Furthermore, all patients were treated as inpatients and hemodynamically instable patients were excluded from the study. Therefore, no patient was treated with fibrinolytic drugs or vena cava filter. Secondary endpoints were all-cause mortality and bleeding complications. Follow-up consisted of a hospital visit or telephone interview with the patient after 3 months. Patients were instructed to contact the study center immediately in case of complaints suggestive of PE, deep vein thrombosis (DVT) or bleeding. In case of clinically suspected DVT, PE or bleeding objective tests were performed to confirm the diagnosis. Symptomatic recurrent VTE was considered to have occurred if recurrent PE or DVT were documented objectively, or if there was a death in which PE could not be confidently ruled out as a contributing cause. The objective criterion for the diagnosis of recurrent PE was a new intraluminal filling defect on spiral CT or pulmonary angiography, cut-off of contrast material in a vessel > 2.5 mm in diameter on pulmonary angiography, a new perfusion defect involving at least 75% of a segment, with corresponding normal ventilation (*i.e.* a high probability lung scan), a new non-diagnostic lung scan accompanied by documentation of DVT by ultrasonography or venography, or confirmation of a new PE at autopsy. The objective criterion of a new DVT was a new, non-compressible venous segment or a substantial increase (≥ 4 mm) in

the diameter of the thrombus during full compression in a previously abnormal segment on ultrasonography or a new intraluminal filling defect on venography. Mortality was defined as death due to recurrent PE (fatal PE), fatal bleeding, cancer, or another established diagnosis. Information about the cause of death was obtained from autopsy reports or from a clinical report. Hemorrhagic complications were the composite of major bleeding and clinically relevant bleeding. Major bleeding was defined as fatal bleeding, and/or symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, or intramuscular with compartment syndrome, and/or bleeding causing a fall in hemoglobin level of ≥ 20 g/L (1.24 mmol/L), or leading to transfusion of ≥ 2 U of whole blood or red cells. Bleeding was considered clinically relevant when the episode did not qualify as a major bleeding but included one of the following: epistaxis requiring intervention, formation of a large hematoma visible on the skin or spontaneous macroscopic hematuria.[7] All patients were treated with therapeutic doses of unfractionated or low molecular weight heparin followed by vitamin K antagonist for a period of at least 6 months. Patients diagnosed as outpatients as well as inpatients were eligible. The study was executed in 12 hospitals in the Netherlands, of which five were university hospitals. Non-university hospitals differed in size from 330 to 1386 patient beds and university hospitals from 715 to 1100 patient beds. All participating centers had comparable services including emergency units, intensive care units and 24-hour access to a CT scan. A total of 673 patients with acute PE completed 3 months follow-up with one patient lost to follow-up (0.15%).

Results

The baseline characteristics of the included patients are shown in Table 1. A total of 399 (59%) patients attended a university hospital and 275 (41%) a non-university teaching hospital. The characteristics of patients from the university and non-university hospitals were different with respect to female ratio (46% vs. 56%, Odds Ratio [OR] 0.65, 95% confidence interval [CI] 0.47-0.88), outpatient ratio (73% vs. 84%, OR 0.53, 95% CI 0.36-0.79), presence of immobilization (37% vs. 23%, OR 2.0, 95% CI 1.4-2.8) and the presence of active malignancy (19% vs. 12%, OR 1.6, 95% CI 1.1-2.5). The rates of adverse clinical events are presented in Table 2. Overall 55 patients died; of these, 11 patients died because of fatal recurrent PE and two died because of fatal hemorrhage. The cause of death in the remaining patients was mainly malignancy or cardiovascular disease. The time of death ranged from 1 to 90 days, with a median of 22 days. Risk of venous thromboembolic recurrence (3.3% vs. 2.6% OR 1.3, 95% CI 0.50-3.3) and mortality (9.0% vs. 6.9% OR 1.3, 95% CI 0.75-2.4) was higher for patients in university than in non-university hospitals. Furthermore, bleeding occurred in 23 patients, and was fatal in two of these. Both fatal bleeding events occurred out of hospital, while seven of the eight non-fatal major bleedings occurred in the hospital and 7 of 13 clinically relevant

Table 1. Baseline characteristics

Characteristics	University hospital (n=399)	Non-university teaching hospital (n=275)	OR
Age (years)	56± 18	59±18	NS
Female gender	183 (46)	156 (56)	0.65 (0.47-0.88)
Duration of complaints (days)	5.9±11	6.4±10	NS
Outpatients	294 (73)	231 (84)	0.53 (0.36-0.79)
Risk factors for VTE			
Paralysis	23 (5.8)	15 (5.5)	NS
Immobilization	151 (37)	65 (23)	2.0 (1.4-2.8)
Recent surgery	33 (8.3)	34 (12)	NS
History of VTE	69 (17)	48 (17)	NS
Heart failure	26 (6.5)	14 (5.1)	NS
COPD	34 (8.5)	28 (10)	NS
Active malignancy	89 (19)	41 (12)	1.6 (1.1-2.5)
Clinical findings			
Hemoptysis	37 (9.3)	19 (6.9)	NS
Tachycardia	143 (35)	104 (37)	NS

Categorical data are displayed as No (%). Numerical data are displayed as means ± standard deviation. VTE= venous thromboembolism, COPD = chronic obstructive pulmonary disease, OR = Odds Ratio

Table 2. Adverse clinical outcome in a three months follow-up period

	University hospital (n=399)	Non-university teaching hospital (n=274)
Total recurrences	13 (3.3)	7 (2.6)
Fatal recurrent PE	6 (1.5)	5 (1.8)
Non-fatal recurrent PE	2 (0.5)	1 (0.4)
Non-fatal recurrent DVT	5 (1.3)	1 (0.4)
All bleeding complications	17 (4.3)	6 (2.2)
Fatal bleeding	1 (0.3)	1 (0.4)
Major bleeding	7 (1.8)	1 (0.4)
Clinically relevant bleeding	9 (2.3)	4 (1.5)
All cause mortality	36 (9.0)	19 (6.9)

Data are displayed as No (%).
PE = pulmonary embolism, DVT = deep vein thrombosis

bleedings occurred in the hospital. Hemorrhagic complications occurred twice more often in patients from university hospitals (4.3% vs. 2.2% OR 2.0, 95% CI 0.77-5.1). These bleeding complications were strongly associated with the baseline presence of active malignancy (OR 3.4, 95% CI 1.5-7.9).

Discussion

Our data demonstrate that patients with acute PE presenting to university hospitals are different from patients presenting to non-university hospitals regarding gender, proportion of outpatients and malignancy. Especially the latter two are established risk factors for adverse events and mortality in the first 3 months following acute PE.[8] To our best knowledge, there were no different characteristics between the hospitals other than being a university hospital, which could have biased these study observations. According to our hypothesis we identified differences in baseline characteristics and observed a higher rate of adverse clinical events in patients from university hospitals than in patients from non-university hospitals. Of note, we found a significant association between bleeding and malignant comorbidity. This association has been described previously and thus underlines the validity of our study results.[9] Of note, correlations between additional patient demographics were not studied. A limitation of our study is that although we have performed a post hoc analysis of a reasonable large patient cohort, the study might have included too few patients to detect a significant difference between the patient cohorts.

In summary, we have identified important differences in demographics, comorbidity and clinical outcome between patients diagnosed with PE in university and in non-university hospitals. Physicians should be aware of these differences when interpreting results from large clinical trials and applying these to their everyday medical practice.

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