DOI: 10.4149/BLL_2014_152

Bratisl Lek Listy 2014; 115 (12)
786 – 790

CLINICAL STUDY

Deceased elderly in-patients with pulmonary embolism

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Abstract: *Introduction:* Pulmonary embolism (PE) in the elderly is an immediate threat of life. Especially in old age clinical signs of PE are non-specific and could be both underestimated and overestimated. Aim of the study: The retrospective long-term study was aimed at conducting an analysis and comparison of pertinent influence of age, gender and immobility on occurrence of PE and sudden death.
Patients and method: Between 1995 and 2012 years we had altogether 12,746 elderly patients of an average age 80.6 ± 7.0 y (range 65–103 y) hospitalized at the Department of Geriatrics. All in-patients 65+ y were randomly admitted for internal hospitalization from the catchment area of Brno city (100,000 inhabitants). The subject of our interest was to study the documentation of deaths (including autopsy findings), which was caused by PE. Out of this number there were 8,540 women (66.3 %) and 4,206 men (33.7 %). Among all hospitalized patients PE in 700 cases (5.5 % of all admitted patients) was shown in a medical report. Among them there were 424 survivors (60.6 %; 134 men and 290 women).
Conclusion: The high occurrence of PE (particularly silent form) has crucial importance in the elderly mortality. Our recommendations would like to emphasize the need of no underestimation of this fact and to carry out preventive measures in all age groups (including the "oldest old" and frail persons) *(Tab. 3, Ref. 41)*. Text in PDF *www.elis.sk.*
Key words: pulmonary embolism (PE), advanced age, mortality, risk factors, immobility, prophylaxis.

Pulmonary embolism (PE) in the elderly is an immediate threat of life (1, 2). Especially in old age clinical signs of PE are non-specific and could be both underdiagnosed and overdiagnosed (3, 4).

Necropsy studies (5, 6) continued to show a high incidence of PE, which was considered the main cause of death in about 10 % of necropsies (7). Since the inpatient mortality in general hospitals is about 10%, it is estimated that about 1% of patients admitted to hospital die of PE (8). However, for every patient who dies of PE in a surgical ward, three die in nonsurgical wards (9).

The clinical non-recognition of venous thrombembolism prior to fatal PE implies that its detection and treatment cannot have a major impact on its mortality (1, 10); hence, identificaton of, and primary prophylaxis in, hospitalized patients (medical and surgical) at high absolute risk of DVT is required for its prevention (11).

The prospective study and following analysis of dates was aimed at conducting an analysis and comparison of pertinent influence of age, gender and immobility on occurrence of PE and sudden death. We analyzed the dates from medical reports (including certificate of inspection deceased and including autopsy reports).

Patients and methods

Between 1995 and 2012 years we had altogether 12,746 elderly patients of an average age 80.6 ± 7.0 y (range 65–103 y) hospitalized at the Department of Geriatrics. Out of this number there were 8,540 women (66.3 %) and 4,206 men (33.7 %). We divided the patient set into three different age subgroups (65–74 y; 75–84 y and ≥ 85 y; e.g. 21 %; 48 % and 31 % of all hospitalized patients) and compared the results among them. The number of deaths among all treated patients was 1,576 (12.6 %); 934 women (10.9 %) and 642 men (15.3 %). Mortality was increasing according to the age groups (see above): 9.8 %; 11.6 % and 15.3 %. Section was performed in 965 of the dead (61.2 %).

The division of the deceased patients shows into three different (above mentioned) age subgroups (65–74 y; 75–84 y and ≥ 85 y – i.e. 265; 708 and 603 persons in their age groups).

All the patients admitted at the geriatric department underwent complete intern examination, X-ray of lungs, ECG, basic biochemical and haematological analyses and occasionally also additional different examinations according to individual indication were performed. All in-patients 65+ y were randomly admitted for internal hospitalization from the catchment area of Brno city (120,000 inhabitants).

Among all hospitalized patients PE in 700 cases (5.5 % of all admitted patients) was shown in a medical report. Among them there were 424 survivors (60.6 %; 134 men and 290 women). 276 persons died in relation to PE.

The differences in the occurrence of PE between genders were not statistically significant (Tab. 1). Highly statistically significant differences were between prevalence of PE among the deceased persons 65–74 y and the group ≥ 75 y ($\chi^2 = 10.005$; $p < 0.005$).

Moreover in advanced age typical multi-morbidity was connected with occurrence of geriatric giants (instability with falls, immobility, incontinence, intellectual and sensual impairments,

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Tab. 1. Occurrence of PE deceased in-patients according to age and gender.

	Female	Male	Statistical significance (χ^2 -test)
Age 65–74 y.	17 (13.8%)	29 (20.4%)	χ^2=2.002 p=NS
Age 75–84 y.	81 (20%)	52 (17.2%)	χ^2=0.847 p=NS
Age≥85 y.	62 (15.3%)	35 (17.7%)	χ^2=0.519 p=NS

Tab. 2. Occurrence of PE according to age subgroups and degree of mobility.

	65 – 74 y.	75 – 84 y.	85+ y.	∑
Confined to bed	67.3% (31)	57.1% (76)	60.8% (59)	166
Seat + shift chair – bed	10.9% (5)	24.8% (33)	20.6% (20)	58
Walking with an aid	15.2% (7)	12.8% (17)	13.4% (13)	37
Independent walking	6.5% (3)	5.3% (7)	5.1% (5)	15
∑ patients	46	133	97	276

dehydration etc.) that could be risky for development of PE. Pearson's correlation coefficient was for age and ADL-test –0.125 (p = NS); for age and cognitive functions (MMSE-test) –0.284 (p < 0.01); for age and falls –0.284 (p < 0.01); for age and continence –0.113 (p = NS); for age and obesity (BMI) –0.489 (p < 0.01).

All dates were collected in PC and statistically analyzed by the Microsoft Office Excell program (χ^2 -test; Student's t-test; Pearson's correlation coefficient).

Results

PE was present according to clinical signs and findings in 276 of deaths (17.5 %); among all obductions in 168 cases (17.4 %). Clinical summaries according to our results were mostly in agreement with section's observations. We confirmed the decreasing tendency among elderly people with PE action of LMWH prophylaxis (from about 24 % in first years of study to 10 % in last years).

2.1 % of admitted patients died in the department of geriatrics of PE.

We observed slightly decreasing tendency in the PE as the cause of death in years 1995–2011 (r = 0.241; p = NS).

Sudden death occurred in 142 cases (9 % of all deaths): PE as cause 83-times (30 % in set 276 persons with PE) and heart attack or failure 59-times among the others 1300 dead. Sudden death was present more frequently in the deceased with PE (χ^2=35.290; p < 0.005).

Silent PE as an incidental finding at autopsy was found in 213 cases of death of PE (77 % of them). It means that PE as an adventitious finding at autopsy form 13.5 %. Symptomatic PE represents 3.9 % of overall mortality.

Average age of the dead of PE was for women 82.5 ± 6.7 y and for men 80.0 ± 7.4 y. The occurrence of PE for female and male gender for each age periods as mentioned above was: A) 13.8 vs 20.4 %; B) 20 % vs 17.2 %; C) 15.3 vs 17.7 % (Tab. 1). The median of occurrence of PE was the age 82.5 y for female and 79.5 y for male. We did not find a statistical difference between both genders for all age subgroups.

Immobility seems to be a significant risk factor for both genders regardless of age. We compared separately the occurrence of PE between the groups: A) confined to bed versus other groups; B) confined to bed+ able to sit versus moving persons; C) particularly comparison of two most risky groups – confined to bed versus able sitting position (for all used (χ^2 –test; p < 0.001). The presence of mere immobility plays crucial role in both sets for the risk of death (mainly in relation to the frailty and FTT – "failure to thrive"). It was with PE in 81.2 % and among deceased without signs of PE in 83.7 % (χ^2 = 1.047; p = NS).

Table 2 shows the set according to mobility among the persons deceased of PE: 1. confined to bed; 2. able to sit; 3. moving with assistance of the second person, a permanent walking aid (crutch, stick, walker); 4. moving independently. Generally it was valuable that mobility worsened essentially with increasing age.

Table 3 analyzes the comparison between the deceased with and without PE according to the risk factors of PE and their presence in both sets. PE as a cause of death was present more frequently in patients with obesity (p < 0.005), stroke and trauma (p < 0.01), DVT (both p < 0.05). Tumors, heart failure and operation in the time of admission to the department are without statistically significant difference according to the presence PE. Conversely the occurrence of infection (mainly pulmonary and urinary) was highly statistically significant in the set without PE.

Pearson's coefficient of correlation between age and frequency of PE is for people to age 80 y r = 0.887; to age 85 y r = 0.759 and to 90 y r = 0.576 (for all p < 0.01).

Discussion

Half of the people, who have PE, have no symptoms. In our set we found silent PE in 213 cases of the deceased with PE (e.g.77 %). With increasing age the amount of people with silent PE is growing (3). This is, after myocard infarction and cerebrovascular events, the third most frequent cardiovascular cause of the death. Simultaneously it is one of the least often correctly diagnosed cardiovascular diseases (as in our set). In seniors the usage of standard diagnostic tools is often complicated by multi-morbidity, frailty and geriatric giants. Common is also concomitant presence of more risk factors (12, 13) of VTE as immobility, heart failure, tumors, etc. (see table 3 for our set). In such cases it is always necessary to approach to prophylactic measures.

The entities of deep venous thrombosis (DVT) and pulmonary embolism (PE) present a continuum of venous thromboembolic

Tab. 3. Analyzes of risk factors of PE according to the presence of PE.

	Infection	Tumors	Heart failure	Stroke	Obesity	DVT	Trauma	Operation
PE +	104 (37.7%)	77 (27.9%)	61 (22.2%)	87 (31.5%)	74 (27.7%)	8 (2.9%)	25 (9%)	38 (13.8%)
PE –	745 (57.3%)	366 (29.3%)	286 (22%)	522 (40.1%)	250 (19.2%)	15 (1.2%)	63 (4.8%)	202 (15.5%)
Statistical significance (χ^2 -test)	χ^2=35.290 p<0.005	χ^2=0.007 p=NS	χ^2=0.001 p=NS	χ^2=7.155 p<0.01	χ^2=9.175 p<0.005	χ^2=4.819 p<0.05	χ^2=7.660 p<0.01	χ^2=0.552 p=NS

disease (VTE), which is of crucial importance for elderly patients, and offer constant diagnostic and therapeutic challenges to physicians caring for patients of any age (3, 14). For multiple reasons, the incidence of both DVT and PE increases with age (9, 15). First, there is often a decrease in the leg muscle mass, setting the stage for stasis. There are increased thrombotic tendencies in the elderly (16), beginning around the age of 60, which may involve up to 20 % of those over age 85; these include impaired vascular wall fibrinolysis and hypercoagulable states. We found the same tendency in our set.

The diagnosis of venous thrombembolism (VTE) in the elderly is difficult, although the presentation is usually quite similar to that seen in younger patient groups. The most common presenting symptom of PE is some complaint of chest discomfort or pain, seen in approximately 35 % of patients in most series, usually without hemoptysis. Dyspnea and tachypnea occur frequently (17). We observed mentioned complaints in about 60 % of all people with PE, but in only 23 % among the deceased. Sometimes sudden-unexpected death could be the first manifestation of PE. Lucena (18) depicts this in approximately 25 % of analyzed patients. We found PE as the clinical cause for sudden death in 30 %.

Although circulatory collapse occurs in a relatively small proportion of the elderly, these latter patients are much more likely to have sustained massive pulmonary emboli and often have evidence of neurologic deficits and findings of pulmonary hypertension. Immobilization in medical ward (12, 19) is due to illness (e.g. infection, malignancy, heart failure, myocardial infarction, stroke, frailty, geriatric giants etc.). The cumulative risk of DVT and PE increases with the duration of immobility, suggesting a role for venous stasis in the inactive leg in the pathogenesis of DVT. We ascertained the positive relation between immobilization as basic risk factor in the elderly and geriatric giants in multimorbid frail persons.

The major diagnostic strategy (20) required is one of constant suspicion and concern and a consideration that, in any older hospitalized patient who is "failing to thrive," to ask whether this could be due to pulmonary embolism, because both the symptoms and standard laboratory findings are nonspecific (21) and the diagnosis is too often made postmortem. The classic triad of hemoptysis, pleuritic chest pain, and clinically apparent thrombophlebitis is infrequently seen, in less than 10 % of elderly patients with VTE and suspicion of PE carry out at least any basic and complementary examinations e.g. as clinical pretest probability (22–24), X-ray, ECG, D-dimer levels (25, 28) etc. to be started effective therapeutic measures as soon as possible (29). Salaun (30) emphasizes as non-invasive diagnostics for PE combining of clinical assessment, D-dimer, ultrasonography and lung scan.

That is a medical emergency because a large embolism, or sometimes many repeated smaller ones, can be fatal in a short time. When the heart is continually overworked, it may enlarge, and it may eventually fail to perform. A large PE can cause heart or lung failure. This seems to be especially important in advanced age where coronary heart disease (heart failure too) has growing tendency. Fortunately chances of surviving a PE increase when a physician can diagnose and treat the patient quickly.

Low-molecular-weight heparin (LMWH) in therapeutical doses in symptomatic and in prophylactic doses in asymptomatic cases with coincident risk factors we used practically in all cases in our study as other authors (31, 32).

Prophylaxis reduces the incidence of fatal pulmonary emboli by two thirds in hospitalized patients at risk of developing venous clots. Prophylaxis against PE is of paramount importance because VTE is difficult to detect and poses an excessive medical and economic burden (33).

Donzé (34) proposes for evaluation of severity PE index with 11 prognostic variables (age, male sex, comorbid illnesses, cancer, heart failure, altered mental status, chronic lung disease etc.) to stratify patients into five classes. Overall mortality in his study was 6.5 %.

Autopsy studies in the United Kingdom (5) and Sweden (6, 9) continued to show a high incidence of PE, which was considered the main cause of death in about 10 % of necropsies. Since the inpatient mortality in general hospitals is about 10 %, it is estimated that about 1% of patients admitted to hospital die PE. In our set 2.1 % was valuable for all admitted in-patients. However, for every patient who dies of PE in a surgical ward, three die in nonsurgical wards. This is not only a common problem but a serious one: the in-hospital mortality of elderly patients over the age of 65 with documented pulmonary embolism was 21 % in the Prospective Investigation of Pulmonary Embolism Diagnosis Study (35), and the 1-year mortality was 39 % (36). Recent data suggest these numbers may be even higher (37). Volschan (19) presents overall mortality 14.1% and as independent death risks emphasizes age > 65 y; bed rest >72 h; chronic cor pulmonale; sinus tachycardia and tachypnoe. We found the overall mortality for PE 17.6 % in our patient set > 65 y with decreasing tendency among elderly people with PE action of LMWH prophylaxis.

Surprising are the studies from recent decades showing decrease of overall mortality of PE (7, 38) to the range 2.1–3.4 %. Cohen (39) depicted in his study decrease of prevalence of PE mortality during 25 years period from 6.1 % to 2.1 %. These changes are explained with newly used tromboprophylaxis, early mobilization and changes in hospital practice. These numbers are considerably lower than the above mentioned dates, but we studied mostly old-old people. Majority of patients who die of PE do not have a pre-mortem diagnosis VTE and many have life-threatening diseases. Therefore an autopsy represents irreplaceable gold standard for confirmation of diagnosis. Simpson (40) indicates that no unequivocal evidence exists linking any single treatment for acute, severe PE with a significant reduction in mortality.

The clinical non-recognition of VTE prior to fatal PE implies that its detection and treatment cannot have a major impact on its mortality; hence, identificaton and primary prophylaxis of hospitalized in-patients (medical and surgical) at high absolute risk of DVT is required for its prevention (41).

The high occurrence of PE (particularly its silent form) has crucial importance in the elderly mortality. Our recommendations would like to emphasize the need of no underestimation of this fact and to carry out preventive measures in all age groups (including the "oldest old" and frail persons).

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Received May 23, 2013.
Accepted April 15, 2014.