Fatal pulmonary embolism in hospitalised medical patients

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Abstract
This study aimed to determine the frequency of fatal pulmonary emboli in hospitalised medical patients by a retrospective necropsy review and prospective non-interventional patient follow up study. The main outcome measure, necropsy proven fatal pulmonary embolism, was determined from 400 consecutive necropsies and 200 consecutive medical inpatient episodes. Fatal pulmonary embolism was recorded in 29 of 400 necropsies; 17 were medical patients. Thirty one of 200 consecutive medical patients died. Fourteen necropsies were performed and revealed pulmonary embolism as the cause of death in five patients. The incidence of necropsy proven fatal pulmonary embolism was therefore 2.5% (95% confidence intervals 0.8% to 5.7%). Therefore, one in 40 medical patients had pulmonary embolism recorded as the cause of death at necropsy. As the necropsy rate was only 45% the incidence of fatal pulmonary embolism may be greater. There is, therefore, a need to perform more large prospective studies to confirm the incidence of fatal pulmonary embolism in medical patients and to identify risk factors and effective antithrombotic prophylaxis.

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Keywords: necropsy; pulmonary embolism; antithrombotic prophylaxis

In necropsy studies conducted before the widespread adoption of thromboembolic prophylaxis, fatal pulmonary embolism was found more often in medical than in surgical patients. We conducted an initial retrospective review of necropsy records and then a prospective follow up of medical patients to calculate the frequency of fatal pulmonary embolism. We also attempted to identify simple clinical risk factors that might be used to recognise high risk patients in future interventional studies.

Methods
NECROPSY STUDY
The necropsy records of 400 consecutive examinations performed in Addenbrooke's hospital were reviewed. The number of fatal and non-fatal pulmonary emboli were recorded and whether patients were medical or surgical. The case records of medical patients with pulmonary embolism were then examined. Patients with more than one medical problem were categorised as having “multiple medical problems” and severe immobility was recorded when the patient was bed bound. The time in hospital before death and the nature of death were recorded. The resuscitation plan and the record of thromboembolic prophylaxis were identified from the patient notes.

FOLLOW UP STUDY
Two hundred consecutive medical patients were followed prospectively for the duration of hospitalisation. Thromboembolic prophylaxis was recorded by an observer independent of the clinical team caring for the patient. Primary end points of the study were death and necropsy proven fatal pulmonary embolism. In addition the number of pulmonary emboli diagnosed and treated successfully were recorded.

Results
NECROPSY STUDY
Fatal pulmonary embolism had been recorded in 29 of the 400 autopsies (7.25%, 95% confidence intervals (CI) 4.9% to 10.2%). There were an additional 16 non-fatal pulmonary emboli giving a total of 45 pulmonary emboli in 400 autopsies (11.25%, 95% CI 8.2% to 14.3%). Twenty four patients with pulmonary emboli were medical patients, with 10 surgical and 11 coroner’s cases. Seventeen of the 24 medical patients were thought to have died of the pulmonary embolus compared with four of the 10 surgical patients. The clinical case notes of 21 of the 24 medical patients were available (table 1).

FOLLOW UP STUDY
Follow up information was available on all 200 patients. Twenty eight received prophylactic low dose heparin and 10 had graded pressure stockings applied. Thirty one of the patients died (15.5%). Fourteen necropsies were performed and revealed fatal pulmonary embolism in five. The incidence of necropsy proven fatal pulmonary embolism was therefore 2.5% (95% CI 0.8% to 5.7%). The necropsy rate was
Table 1 Clinical details of medical patients with pulmonary emboli identified from autopsy records

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 males, 11 females</td>
<td>Median age 78 years (range 45 to 92)</td>
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<tr>
<td>5/21 younger than 65 years</td>
<td>17/21 had multiple medical problems</td>
</tr>
<tr>
<td>15/17 living more than 48 hours had severe immobility</td>
<td>19/21 did not have DVT or PE suspected in life</td>
</tr>
<tr>
<td>8/21 died without warning</td>
<td>7/21 died after &quot;collapsing&quot;</td>
</tr>
<tr>
<td>13 received no prophylaxis, 9 of these were &quot;for resuscitation&quot;</td>
<td>Average inpatient stay before death 19 days (range 1 to 66)</td>
</tr>
</tbody>
</table>

DVT, deep vein thrombosis; PE, pulmonary embolism.

only 45% so an approximation of the total frequency of fatal pulmonary embolism was 5.5%. Thus one in 20 medical inpatients may die of pulmonary embolism. Two further episodes of pulmonary embolism were diagnosed and treated.

Discussion

The risk of deep vein thrombosis and pulmonary embolism in surgical patients and prevention by mechanical and pharmacological intervention is established. However, few studies have defined the frequency or clinical importance of venous thromboembolism in medical patients. In previous necropsy studies, fatal pulmonary embolism was found more often in medical than in surgical patients and this was also the case in our study. Furthermore, we found that pulmonary emboli in medical patients were more often considered fatal. Two-thirds of necropsy proven pulmonary emboli occurred in medical patients and 71% of these were considered to be the cause of death. In order to determine an approximate frequency of fatal pulmonary embolus in medical patients, we prospectively recruited consecutive medical patients, 15.5% of whom died. Where necropsy was performed, pulmonary embolism was considered to be the cause of death in one-third of patients. Therefore, approximately 5%, or one in 20, medical patients may die of pulmonary embolism during hospital admission. Larger prospective follow up studies are required to define the frequency more accurately.

While the median age of patients who died of pulmonary embolism was 78 years, the age range was wide. The youngest patient was 45 years old. Some patients may have terminal disease and prophylaxis may be inappropriate; however, the majority of patients in our necropsy study was considered to be for resuscitation, and therefore prevention of death from pulmonary embolism would have been appropriate. Most of the patients who died of pulmonary embolism had multiple medical problems and severe immobility, and were therefore identifiable as high-risk patients.

Thromboembolic prophylaxis could be targeted at these patients although further study is required to determine the proportion of all patients who would be considered to be at high risk. While randomised studies of prophylactic heparin in medical patients have shown a reduction in asymptomatic calf vein thrombosis, a reduction in fatal pulmonary embolism has not yet been demonstrated. A single large study found that overall mortality in patients receiving unfractionated heparin, 5000 units subcutaneously, twice daily, was 7.8% compared with 10.9% in controls, but the randomisation in this study was unconventional. It is tempting to assume that effective thromboembolic prophylaxis in surgical patients will also be effective in medical patients. However, in contrast to medical patients prophylaxis can be initiated in surgical patients before the thrombogenic stimulus of surgery. In medical patients the stimulus is chronic and is usually present before admission to hospital. In surgical patients the risk of clinically significant venous thromboembolism following surgery may be quite short (weeks), whereas in medical patients the illness and the precipitating factors for thromboembolism may be prolonged. The assumption that graded pressure stockings or short term low dose heparin will be effective in medical patients cannot be made. There is, therefore, an urgent need to perform large prospective randomised studies to identify effective antithrombotic prophylaxis for high risk medical patients.

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