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Clot Burden and Comorbidity in Natural History of Untreated Pulmonary Thromboembolism

Autopsy Data in the Trial by Barritt And Jordan

To the Editor:

I read with interest the special report by Dalen (November 2002), who discussed the mortality of untreated pulmonary thromboembolism (PE). The only prospective randomized trial of anticoagulants vs placebo that showed benefit in acute PE was performed at the Bristol Royal Infirmary in 1957 and published shortly thereafter. Dalen quotes mortality of untreated PE as 38%.

In the study by Barritt and Jordan, 5 of 19 untreated patients died, which equates to 26% mortality, and it is unsure where the 38% quoted comes from. In addition, last year, an audit of the autopsy records of the participants enrolled in this landmark trial was conducted in order to ascertain the findings at death, as the original report was incomplete and has therefore been criticized. The findings are shown in Table 1. The audit, conducted within the Department of Pathology at the Bristol Royal Infirmary, illustrate two observations about the participants enrolled in the trial by Barritt and Jordan and who died with untreated PE: (1) coincidental morbidity and infection was likely to be contributory to their demise; and (2) a large amount of residual thrombus or clot burden was found both in the lung and in other venous sites with potential to embolize to the lung.

These observations should be kept in mind when deciding the cost/benefit ratio of anticoagulation in those patients identified to have small (subsegmental or less) PE with no source of potential thromboemboli and no continuing risk factors for venous thromboembolism. This difficult clinical question needs to be addressed especially in the light of rapidly improving imaging technology such as multidetector spiral CT angiography with which smaller PEs are detected.

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Table 1—Autopsy Findings of the Five Patients Who Died With PE Randomized to No Anticoagulation*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age, yr/sex</th>
<th>Underlying Diagnosis</th>
<th>Anatomic Site of Pulmonary Emboli</th>
<th>Source of Thromboemboli</th>
<th>Coincidental Infection</th>
<th>Noted</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>54/female</td>
<td>Extensive breast carcinoma</td>
<td>Left main branch</td>
<td>Right femoral DVT</td>
<td>Mixed organism empyema, bronchopneumonia and abscess</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>56/male</td>
<td>Post operation for intestinal obstruction (adhesions)</td>
<td>Main trunk</td>
<td>Left femoral DVT, hepatic vein thrombosis Bilateral popliteal DVT</td>
<td>Biliary tree sepsis</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>78/female</td>
<td>Post fractured ankle</td>
<td>Main trunk</td>
<td>Bilateral femoral DVT, right ventricular mural thrombus</td>
<td>Bronchopneumonia, fungal lung abscess Staphylococcus aureus lung abscess</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>57/male</td>
<td>Myocardial infarction</td>
<td>Left lobar</td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>41/male</td>
<td>Nephrotic syndrome secondary to primary amyloidosis</td>
<td>Both main branches</td>
<td>Left calf DVT, renal vein thrombosis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*From the study by Barritt and Jordan. DVT = deep vein thrombosis.

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To the Editor:

Dr. Iles is correct: the mortality of untreated pulmonary embolism (PE) in the small (but only) randomized clinical trial reported by
Barritt and Jordan\textsuperscript{1} was five deaths among 19 patients (26%), not 38% as shown in Table 1 in my article.\textsuperscript{2} I apologize for this error. Their findings,\textsuperscript{1} coupled with the other reports of the mortality of untreated PE,\textsuperscript{3–6} would indicate that the mortality of untreated PE is approximately 30%. Given the fact that the mortality of PE in patients treated with heparin and warfarin is <5%,\textsuperscript{7,8} it is unlikely that there will be additional randomized clinical trials comparing heparin to placebo in patients with PE, or additional reports of the mortality of untreated PE.

\textit{James E. Dalen, MD, MPH, Master FCCP}

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2 Dalen JE. Pulmonary embolism: what have we learned since Virchow? Treatment and prevention. Chest 2002; 122:1801–1817
6 Morrell MT, Truelove SC, Barr A. Pulmonary embolism. BMJ 1963; 2:830–835

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**Stair Climbing Test in Lung Resection Candidates With Low Predicted Postoperative FEV\textsubscript{1}**

\textit{To the Editor:}

We read with interest the article of Girish and colleagues (October 2003)\textsuperscript{1} on symptom-limited stair climbing test as an instrument to predict complications after thoracic and upper-abdominal surgery; however, we think the patients’ selection criteria used in their work are inappropriate and of little clinical use. The authors, in fact, excluded from lung resection those patients with a predicted postoperative FEV\textsubscript{1} (ppoFEV\textsubscript{1}) < 40% of predicted.

During the last 3 years, we used maximal stair climbing test on 307 patients for risk stratification before lung resection.\textsuperscript{2} Fifteen of these patients had a ppoFEV\textsubscript{1} < 40% of predicted. Nevertheless, they were submitted to lung resection (one segmentectomy, six lobectomies, eight pneumonectomies) for their good performance at the stair climbing test. Two patients climbed < 12 m, whereas the others climbed > 14 m, corresponding to our setting, approximately to three and four flights of stairs, respectively. Preoperative maximal oxygen uptake (VO\textsubscript{2}\textsubscript{max}) did not differ between patients with a ppoFEV\textsubscript{1} < 40% and those with a ppoFEV\textsubscript{1} ≥ 40% (26 mL/kg/min vs 25.9 mL/kg/min, respectively: \(p = 0.9\)). Only three patients acquired postoperative cardiopulmonary complications with no mortality, and the morbidity rate was not different from that of the patients with a ppoFEV\textsubscript{1} ≥ 40% (20% vs 17.5%, respectively; \(p = 0.8\)). All patients with a ppoFEV\textsubscript{1} < 40% were able to perform a postoperative exercise test before discharge, which did not show a different VO\textsubscript{2}\textsubscript{max} with respect to the patients with a ppoFEV\textsubscript{1} ≥ 40% (21.6 mL/kg/min vs 22.5 mL/kg/min, respectively; \(p = 0.4\)). We think that the stair climbing test is most useful in assessing the cardiorespiratory capacity of those patients traditionally considered at prohibitive risk for lung resection in order to minimize their improper exclusion from operation. Using this test allowed us to operate on an additional 15 patients who would have otherwise been denied surgery. Based on our results, we think that the practice of excluding patients from operation only for their low predicted postoperative pulmonary function without performing a preoperative exercise test is questionable. We currently exclude from operation only those patients with a ppoFEV\textsubscript{1} < 30% with an altitude climbed at the stair climbing test < 12 m.

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**Impact of Positive Microbiological Diagnosis on Management and Prognosis of Severe Community-Acquired Pneumonia**

\textit{To the Editor:}

In a recent study, Bello et al\textsuperscript{1} (January 2003) described their use of microbiological testing in 204 patients with severe community-acquired pneumonia (SCAP). Furthermore, they evaluated the impact of bacteriologic data on the management and prognosis of such patients, and compared etiologic agents according to whether patients underwent intubation or not.

The main results of this study were the following: a microbiological diagnosis of pneumonia was made in 71 intubated patients and in 46 nonintubated patients. Infections due to \textit{Legionella pneumophila} and \textit{Pseudomonas aeruginosa} infections were significantly more frequent in intubated than in nonintubated patients (15.1% vs 7.1% and 6.6% vs 1.0%, respectively). Positive microbiological test results led to antimicrobial treatment modifications in 85 patients; in 11 cases, modifications were justified because of the positive test.