Treatment of Right Heart Thromboemboli*

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Background: The presence of right heart thromboemboli complicating pulmonary thromboemboli carries with it an increased mortality rate compared to pulmonary thromboemboli alone, but little is known about the optimal management of this difficult clinical situation. This fact is highlighted in the case study of a patient with a 19-cm right atrial thrombus complicating bilateral pulmonary thromboemboli.

Study objectives: We sought to determine the effects of anticoagulation therapy, thrombolysis, and surgical embolectomy on mortality rate in patients with right heart thromboemboli.

Design: Retrospective analysis of all reported cases in the English language literature (1966 to 2000) of right heart thromboembolism in which age, sex, therapy, and outcome were reported.

Measurements and results: We analyzed 177 cases of right heart thromboembolism. Pulmonary thromboembolism was present in 98% of the cases. The patients were evenly divided by gender with an average age of 59.8 years (SD, 16.6 years) years. Dyspnea (54.2%), chest pain (22.6%), and syncope (17.5%) were the most common presenting symptoms. The treatments administered were none (9%), anticoagulation therapy (35.0%), surgical procedure (35.6%), or thrombolytic therapy (19.8%). The overall mortality rate was 27.1%. The mortality rate associated with no therapy, anticoagulation therapy, surgical embolectomy, and thrombolysis was 100.0%, 28.6%, 23.8%, and 11.3%, respectively. Using multivariate modeling with survival as the primary outcome, age and gender were not associated with mortality rate, but thrombolytic therapy was associated with an improved survival rate (p < 0.05) when compared either to anticoagulation therapy or surgery.

Conclusion: The presence of right heart thromboemboli may have diagnostic and therapeutic implications in pulmonary thromboembolism patients. A well-designed prospective, randomized trial is needed to determine the optimal treatment of right heart thromboemboli.

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Key words: heparin; pulmonary embolism; thrombectomy; thrombolytic therapy

Abbreviations: CI = confidence interval; OR = odds ratio; PFO = patent foramen ovale

Right heart thromboemboli represent mobilized deep venous thromboses that are lodged temporarily in the right atrium or ventricle. The increased use of two-dimensional echocardiography has led to increased detection of these thromboemboli, particularly in patients with suspected or confirmed pulmonary emboli. The presence of right heart thromboemboli appears to substantially increase the risk of mortality compared to the presence of pulmonary thromboemboli alone. Despite this, the optimal management of right heart thromboemboli remains unclear because there are no prospective randomized trials comparing anticoagulation therapy, thrombolytic therapy, and surgical removal.

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Therapeutic recommendations based on small numbers of consecutive patients or retrospective case series have failed to reach a consensus. Moreover, patient factors that are associated with an increased risk of mortality in this patient population are not well-defined.

Our interest in the clinical dilemma was stimulated by a patient with acute pulmonary thromboemboli in whom transthoracic echocardiography detected a right atrial thromboembolus. The role of transesophageal echocardiography and the choice of therapy in this patient were not clear-cut. The primary objective of the present study was to conduct a systematic review of all reported patients with...
right heart thromboemboli and to identify patient factors associated with mortality secondary to right heart thromboemboli.

**Case Presentation**

A 76-year-old man presented with a near-syncopal episode 10 days after undergoing resection of a meningioma. On arrival in the emergency department at an outside hospital, the patient was noted to have an initial BP of 71/46 mm Hg, a heart rate of 132 beats/min, a respiratory rate of 32 breaths/min, and oxygen saturation of 94% while breathing 100% oxygen. A physical examination was notable for the following: the presence of a healing craniotomy scar; a regular tachycardia without murmurs, rubs, or gallops; and a warm, swollen left lower extremity. The lungs were clear to auscultation, and the patient had no neurologic deficits. Arterial blood gas measurements while breathing 100% oxygen showed the following: pH, 7.48; PaO₂, 31 mm Hg; and PaCO₂, 68 mm Hg. The results of an initial ECG showed sinus tachycardia, bifascicular block, and ST-T-wave depression in leads II, III, aVF, and V₂ to V₆. A chest radiograph showed no abnormalities. A lower extremity venous Doppler ultrasound confirmed the presence of a deep venous thrombosis in the left lower extremity. A ventilation-perfusion lung scan revealed nearly absent perfusion of the right lung and grossly abnormal perfusion of the medial half of the left lung with normal ventilation, indicating a high probability of pulmonary embolism.

Because of the recent craniotomy, the patient initially was treated with the insertion of a filter in the inferior vena cava. A transthoracic echocardiogram revealed increased right ventricular size, a right ventricular systolic pressure estimated at 46 mm Hg, and a 1 × 4-cm right atrial mass prolapsing into the tricuspid valve (Fig 1, top, A). Systemic heparin therapy was administered, and the patient was transferred to the Johns Hopkins Hospital for further management. After a review of the transthoracic echocardiogram, the patient was taken urgently to surgery for the performance of a right atrial thrombectomy. Intraoperative transesophageal echocardiography revealed a large serpiginous right atrial mass that was approximately 10 cm in length (Fig 1, bottom, B) and thromboemboli in the main pulmonary arteries. A 19 × 1.2-cm thrombus was removed from the right atrium (Fig 2, top, A), large clots were removed from the right pulmonary artery (Fig 2, bottom, B) and the left pulmonary artery (Fig 2, bottom, C), and a patent foramen ovale (PFO) was repaired. Total bypass time was 26 min. The patient was discharged from the hospital in good condition, receiving warfarin anticoagulation therapy, 10 days following surgery.

**Materials and Methods**

A systematic search of the literature published from 1966 to 2000 (cutoff date, December 31, 1999) was undertaken using structured guidelines. The computerized search started with a broad MEDLINE search using the terms “right atria,” “right ventricle,” “right heart,” “embolus,” “thrombus,” “thromboemboli,” “thromboembolus,” and “echocardiography.” All citations were screened for the following eligibility criteria: studies with information on patient demographics; clinical presentation; diagnostic method; treatment; and outcome. Exclusionary criteria included studies on mural thrombus, catheter-related thrombi, pacemaker-related thrombi, tumor thrombi, or thrombi associated with surgical implants or anastomoses. Although the source of an embolus was not always identified in each study, we only accepted studies that were judged likely to represent thromboemboli. The electronic search noted above was supplemented by a search of the reference lists of eligible studies and relevant review articles. The authors of studies that lacked the necessary clinical data for the present review were contacted to obtain the missing information. Eighty-five studies were identified from the computerized search outlined above. Abstracts and bibliographies from these studies were reviewed to determine eligibility and to assess whether there were any additional studies of interest that were not identified in the computerized search. Ninety-five studies met the eligibility criteria, yielding a total of 177 patients (including the current case) with echocardiographically diagnosed right heart thromboemboli. Essential data elements that were sought for extraction for each patient included the following: age; gender; reported comorbidities; method of diagnosis (ie, transthoracic echocardiography, transesophageal echocardiography, or angiography); primary treatment (ie, no therapy, anticoagulation, thrombolytic therapy, or surgery); and outcome (ie, survival vs death). Therapeutic procedures such as catheter embolectomy were classified as surgical procedures.
Statistical Analysis

The data for continuous variables are presented as the mean ± SD. Two-tailed Student’s t tests were used to compare the mean values of continuous variables between the survivors and nonsurvivors. One-way analysis of variance was used to compare continuous variables between treatment groups. Significant F ratios were further examined by the least significance difference post hoc testing. χ² analysis and Fisher’s Exact Test were used to detect statistically significant differences in categorical variables between the two groups. For the purpose of the study objective, mortality was used as the primary outcome variable. Bivariate analyses were initially carried out to estimate the unadjusted odds ratios (ORs) and their 95% confidence intervals (CIs) for the association between mortality and predictor variables such as age, gender, and primary treatment method. To examine the independent effect of treatment on mortality from right heart thromboemboli, multivariate logistic regression analysis then was performed to control for possible confounding from other variables (eg, age or gender). Since the overall goal was to obtain the best-fitting logistic regression model for the outcome of mortality from right heart thromboemboli while minimizing the number of parameters, models were constructed with a stepwise addition or deletion of covariates. The results of a reduced model were compared to a larger model using the likelihood ratio test. The patients who received no therapy were excluded from analysis. All statistical tests were two-tailed, with significance at the 95% level.

Results

Of the 177 patients who were identified as having a right heart thromboembolus, there were 87 women (49.7%) and 88 men (50.3%). In two patients, the gender was not specified. The mean age of the sample was 59.8 ± 16.6 years. Women were generally older than men in the sample (62.8 vs 57.2 years, respectively; p < 0.02). Dyspnea, the most common symptom, was reported in 96 of the cases (54.2%). Chest pain and syncope were noted in 40 patients (22.6%) and 31 patients (17.5%), respectively. The initial diagnosis was made by transthoracic echocardiography in 147 patients (83.1%), whereas it was made by transesophageal echocardiography in 25 patients (14.1%). An initial diagnosis was made by M-mode echocardiography in four patients (2.2%).

As shown in Table 1, 35 patients (19.8%) received anticoagulation therapy, 63 patients (35.6%) underwent a surgical procedure, and 62 patients (35.0%) were treated with thrombolytic therapy. Sixteen patients (9.0%) received no therapy. Excluding the no-therapy group from analysis, the average age of the patients who were treated with anticoagulation was significantly greater than the surgically treated patients (age, 65.7 ± 14 vs 56.6 ± 18.4 years, respectively; p < 0.05). The average age of the thrombolysis group (60.5 ± 15.6 years) was not different from that of patients treated either with anticoagulation therapy or surgery. The overall mortality rate in the study sample was 27.1% (48 of 177 patients). The mortality rates in patients who received anticoagulation therapy, surgical embolectomy, and thrombolysis are shown in Table 1.

Table 1—Effect of Treatment on Mortality in Right Heart Thromboembolism

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Patients</th>
<th>Age, yr</th>
<th>Mortality, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heparin</td>
<td>35 (19.8)</td>
<td>65.7 ± 14.0</td>
<td>28.6%</td>
</tr>
<tr>
<td>Surgery</td>
<td>63 (35.6)</td>
<td>56.6 ± 18.4</td>
<td>23.8%</td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>62 (35.0)</td>
<td>60.5 ± 15.6</td>
<td>11.3%</td>
</tr>
</tbody>
</table>

*Values given as No. (%) or mean ± SD, unless otherwise indicated. †p < 0.05 vs surgery.
sis were 28.6%, 23.8%, and 11.3%, respectively. Patients receiving no therapy had a 100% mortality rate.

To determine the independent effect of treatment on mortality from right heart thromboemboli, multivariate logistic regression models were constructed to adjust for confounding variables (Table 2). In the multivariate modeling, patients who received no therapy were not included because there were no survivors in that group. For the remaining patient sample (n = 160), age was not significantly associated with mortality from right heart thromboemboli (model 1). The OR for an increase in age of 1 year was 1.02 (95% CI, 0.99 to 1.04). The addition of gender as a variable to the model including age did not change the log likelihood of the model (model 2), indicating that gender also was not associated with mortality. However, treatment was significantly predictive of mortality from right heart thromboemboli. Using anticoagulation as the reference group, patients who received thrombolysis were noted to have an OR for mortality of 0.33 (95% CI, 0.11 to 0.98), indicating a protective effect for thrombosis compared to anticoagulation therapy (model 3). The OR for mortality in the surgical group was 0.86 (95% CI, 0.32 to 2.29) compared to anticoagulation therapy, but the effect was not statistically significant. To determine whether thrombolytic therapy was superior to surgery, we conducted subgroup analyses in which mortality was compared between these two treatments (model 4). In the sample of 123 patients who underwent surgery or received thrombolytics, surgery was associated with an increased risk of mortality (OR, 2.83; 95% CI, 1.04 to 7.69).

To assess the potential influence of reporting bias on our results, we compared mortality within the subgroup of patients reported in the consecutive series for which treatment and outcome data were available. 2,3,95,100–102 In that analysis, anticoagulation therapy was associated with a mortality rate of 37.5% (6 of 16 patients), whereas surgery and thrombolytic therapy had mortality rates of 29% (9 of 31 patients) and 15% (6 of 30 patients), respectively. χ² analysis revealed a trend toward an improved mortality rate in the thrombolytic therapy group compared to anticoagulation therapy alone (p < 0.08).

**Discussion**

Right heart thromboemboli represent embolized deep venous thromboses that are temporarily lodged in the right atrium or ventricle and are often referred to as “emboli in transit.” They present a distinctive appearance on two-dimensional transthoracic and transesophageal echocardiography. Since the initial case report by Covarrubias and colleagues, 31 many authors 1,6,51,103 have described right heart thrombi as highly mobile, coiled, or serpiginous masses moving within the right atrium or ventricle. These often prolapse into the tricuspid or pulmonic valve during the cardiac cycle. A point of attachment often is unseen or is visualized as a thin stalk. The echocardiographic appearance of thromboemboli is distinct from those of mural thrombi, which show less motion during the cardiac cycle, a broad-based attachment to the heart wall, and occasional focal calcification. Thromboemboli are difficult to distinguish from myxomas, although some authors 51 have suggested that differences in acoustic density allow for discrimination.

The incidence of right heart thromboemboli is unknown. Nearly 100% of detected cases are associated with the presence of proven pulmonary embolism, but this may represent selection bias in diagnosis. The majority of right heart thromboemboli are located in the right atrium. Echocardiographic studies in patients with pulmonary embolism show an incidence of right heart thromboembolism between 3% and 23%, with a combined incidence of 9% across several large series studying consecutive patients. 2,3,100–102 However, these studies most likely underestimated the true incidence of right heart thromboemboli in this patient population because

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**Table 2—Logistic Regression Models for Mortality From Right Heart Thromboemboli**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.02 (0.99–1.04)</td>
<td>1.02 (0.99–1.04)</td>
<td>1.02 (0.99–1.04)</td>
<td>1.02 (0.99–1.04)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1.00†</td>
<td>1.00†</td>
<td>1.00†</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.00 (0.45–2.20)</td>
<td>0.96 (0.42–2.16)</td>
<td>0.96 (0.42–2.16)</td>
<td></td>
</tr>
<tr>
<td>Primary treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticoagulation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>0.33 (0.11–0.98)</td>
<td>1.00†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>0.86 (0.32–2.29)</td>
<td>2.83 (1.04–7.69)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Values given as OR (95% CI).
†Reference value.
transhilar echocardiography was used as the predominant screening test. When compared to transeosophageal echocardiography, transthoracic studies show a 50 to 60% sensitivity for the detection of right heart thrombi and, as demonstrated in our patient presentation, also may underestimate the clot size. Thus, the true incidence of right heart thromboemboli in patients suspected of pulmonary emboli may approach 20%. Autopsy studies have found right heart thrombi in 3 to 12% of patients with pulmonary emboli, but routine autopsy examination often fails to identify right heart thromboemboli due to the shortcomings of the standard dissection technique (G. Hutchins, MD; personal communication; April 26, 1999). Moreover, the postmortem incidence may be lower than the antemortem incidence because the cause of death in many cases may result from a further embolism of the right heart thrombus into the pulmonary arteries.

The antemortem detection of a right heart thromboembolism may have both diagnostic and therapeutic implications. For example, the presence of a right heart thromboembolism confirms the diagnosis of thromboembolic disease and thus may avoid the additional risks associated with pulmonary artery catheterization and IV contrast administration. In addition, the potential to dislodge a right atrial thrombus could influence the decision to place catheters through the right atrium for other purposes such as the measurement of pulmonary capillary wedge pressure or the transjugular placement of inferior vena cava filters. Echocardiography may be particularly helpful in patients with either suspected or confirmed massive pulmonary emboli (eg, systemic hypotension, severe hypoxemia, occlusion of > 50% of the pulmonary arterial system, or right ventricular overload on transthoracic echocardiography) given the increased incidence of right heart thromboembolism in this patient subgroup. Of note, transeosophageal echocardiography detected central pulmonary emboli with an 80% sensitivity and 100% specificity in patients with suspected massive pulmonary emboli, suggesting that it may be diagnostically useful in this situation even if a right heart thromboembolus is absent. Echocardiography also provides the ability to detect the presence of a right-to-left shunt through a PFO. The combination of a right atrial clot and a PFO could lead to the paradoxical embolization of the arterial circulation, thus increasing the urgency for prompt therapy. Moreover, as in our patient, the preoperative diagnosis of a PFO ensures surgical correction if a surgical embolectomy of the right heart thromboembolus is undertaken.

The most effective therapy for patients with right heart thromboemboli remains unknown. This issue is critical because the presence of a right heart thromboembolus complicating a pulmonary thromboembolism appears to carry a poor prognosis. Chartier et al reported a mortality rate of 45% in the most recent series of consecutive patients (n = 38) with right heart thromboembolism. All of these deaths occurred within the first 24 h of hospitalization, underscoring the need to rapidly diagnose and treat right heart thromboembolism. We found that the overall mortality rate in patients with right heart thromboemboli that has been reported in the English literature was 28%, with mortality rates in untreated patients of 100%. In contrast, the inhospital mortality rate for acute pulmonary embolism (treated predominantly with heparin therapy) was reported to be 2.5%. It is not clear whether the right heart thromboembolism itself contributes to the worse outcome or simply serves as a marker for the presence of massive pulmonary thromboembolism. In either case, the increased mortality associated with the presence of right heart thromboemboli has triggered an ongoing debate about the optimal therapy for this condition. Existing published reports differ in their recommendations for treatment by advocating surgical removal, the administration of thrombolytic agents, or anticoagulation therapy with heparin. The last analysis of all published patients with right heart thromboembolism (n = 119) found similar mortality rates for surgery, thrombolysis, and heparin anticoagulation therapy (38%, 38%, and 30%, respectively) and thus concluded that heparin therapy was the treatment of choice. The authors did not report the number of patients in each treatment group, however, so it is not clear whether all three treatments were reasonably represented. Unfortunately, there are no prospective trials to definitively answer this question or to assess other risk factors that may be related to mortality. Therefore, we attempted to collect all patients with right heart thromboembolism reported in the English language literature in which information regarding age, sex, treatment, and outcome were provided. Recognizing the limitations inherent in this type of data set, our results suggest that thrombolytic therapy was associated with a reduction in mortality compared to anticoagulation or surgical therapy. Taken at face value, this result is not surprising. Nearly all patients with right heart thromboembolism had coexisting massive bilateral pulmonary emboli. Thus, anticoagulation therapy alone could be hazardous given the presence of a floating thrombus in the right heart that could embolize a severely compromised pulmonary circulation. Surgical embolectomy has its own set of potential complications including an inherent delay of at least hours, general anesthesia, cardiopulmonary bypass, and the inability to remove coexisting...
pulmonary thromboemboli beyond the central pulmonary arteries. One of the major advantages of the surgical approach is the ability to simultaneously repair a PFO, thus reducing the risk of a subsequent paradoxical embolism. The percutaneous catheter-directed retrieval of clots is a promising possibility, but only four cases have been reported to date.\textsuperscript{44,45} In contrast, thrombolytic therapy can be administered quickly and results in the simultaneous thrombolysis of cardiac and pulmonary arterial thromboemboli as well as a thrombus in the femoral venous circulation. The major complication of thrombolytic therapy is significant bleeding, which occurs in as many as 22% of patients.\textsuperscript{110} Thus, as in our patient, it is important to screen patients carefully for contraindications to thrombolysis.

There are several alternative explanations for the apparent effect of thrombolytic therapy on mortality, given the limitations of the available data. Nonrandomized data suffer from the possibility of selection bias. For example, patients treated with anticoagulation therapy may have had coexisting conditions that prevented consideration either of thrombolytic therapy or surgical intervention and, thus, resulted in an increased mortality rate that was not directly related to the choice of thromboembolism treatment. Similarly, coexisting conditions in patients undergoing surgical therapy may have precluded the use of thrombolytic therapy and may have contributed to an enhanced mortality rate in the surgical group. Finally, a reporting bias may have affected the mortality rate in one or more of the groups because of a tendency to report only favorable or unfavorable outcomes. Unfortunately, there was insufficient information to allow an analysis of coexisting conditions or reasons for treatment choice in the majority of cases. Inasmuch as age correlates with coexisting conditions, the significantly older age in the heparin-treated patients compared to those treated with surgery suggests that some of the patients treated with heparin may have been considered to be too sick to tolerate cardiopulmonary bypass, thus introducing selection bias into this comparison. The multivariate logistic regression model was used to control for any potential effect of age on treatment outcome. In contrast, the age of the patients treated with thrombolytic therapy was not different from that of the other groups despite the significant protective effect of thrombolysis on mortality compared to the other two treatments. To address the possibility of a reporting bias, we compared mortality rates in patients who were reported in the consecutive series.\textsuperscript{2,3,5,100–102} Although the number of patients derived from these studies was small, the trend (\(p < 0.08\)) toward a decreased mortality rate following thrombolytic therapy suggests that reporting bias may not have been the major explanation for our results in the larger data set. Despite these potential limitations, our study examines the mortality associated with right heart thromboembolism in the largest sample of patients currently reported in the literature. At most, these data can be used only to suggest the possibility that thrombolytic therapy is the treatment of choice in this clinical setting. A well-designed prospective randomized trial is needed to provide guidance for the treatment of right heart thromboembolism. The suggestion by our analysis that one of the available forms of therapy for this dangerous condition may reduce the associated mortality rate underscores the need for such data.

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