CLINICAL STUDY

A Survey of Submassive Pulmonary Embolism Treatment Preferences among Medical and Endovascular Physicians

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ABSTRACT

Purpose: To determine treatment preferences among endovascular and medical physicians who manage acute submassive pulmonary embolism (PE).

Materials and Methods: From July through August 2016, 83 sites across the United States were surveyed, and 60 completed the survey. Endovascular and medical physicians were asked to rate their predilection for catheter-directed thrombolysis (CDT) on a 5-point scale and for systemic thrombolysis (ST) as "yes" or "no" in seven case scenarios of submassive PE. A CDT score ≥ 4 was considered to represent a predilection for CDT. Mean scores were used to compare CDT preferences between physicians. Percentages of physicians who preferred CDT or ST were calculated. P values $< .05$ were considered statistically significant.

Results: Across all scenarios (numbered S1–S7) combined, endovascular physicians had a significantly higher CDT score (mean, 3.52) than medical physicians (mean, 3.01; $P < .0001$). Scenario-by-scenario analysis revealed that the mean CDT score was significantly higher for endovascular physicians (S1, 4.25; S2, 3.72; S3, 2.82; S4, 2.68; S5, 3.45; S6, 3.67; S7, 4.02) compared with medical physicians (S1, 3.62 [$P < .001$]; S2, 3.18 [$P < .001$]; S3, 2.45 [$P = .001$]; S4, 2.37 [$P = .011$]; S5, 2.97 [$P < .001$]; S6, 3.20 [$P < .001$]; S7, 3.53 [$P < .001$]). Overall, a significantly higher percentage of endovascular physicians (56.7%) indicated a predilection for CDT compared with medical physicians (37.9%; $P < .001$). Also, a significantly higher percentage of physicians, regardless of specialty, indicated a predilection for CDT (47.2%) than did for ST (5.3%; $P < .0001$).

Conclusions: Endovascular physicians exhibited a greater predilection for CDT to treat acute submassive PE compared with their medical colleagues. Endovascular and medical physicians seemed to more frequently choose CDT than ST.

ABBREVIATIONS

CDT = catheter-directed thrombolysis, CI = confidence interval, IVC = inferior vena cava, PE = pulmonary embolism, ST = systemic thrombolysis

Pulmonary embolism (PE) is the third leading cause of cardiovascular-related death in the United States, with a reported annual mortality of 100,000–180,000 patients (1–3). Immediate recognition and treatment with anticoagulation is essential. Some patients with massive and "submassive" PE may benefit from additional therapies beyond anticoagulation in view of their higher mortality risk than those with low risk PE (4–8).

There is uncertainty regarding the optimal therapy for patients with "intermediate-risk" or submassive PE, defined by right heart dysfunction without systemic hypotension (9–12). Submassive PE is associated with a higher rate of clinical deterioration and mortality than low-risk PE despite anticoagulation (11–16). One unanswered question is whether patients with submassive PE should be routinely considered for therapeutic escalation with thrombolytic agents, catheter-directed therapy, or surgical embolectomy to reduce these adverse outcomes (11). In particular, systemic thrombolysis (ST) has been extensively studied in this population. Recent meta-analyses (17,18) have demonstrated a small mortality benefit and a lower rate of clinical deterioration in patients with submassive PE treated with

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Figures E1 and E2 and Tables E1 and E2 are available online at *www.jvir.org*.

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ST. However, major and intracranial bleeding occur significantly more often in patients who receive ST compared with patients who receive anticoagulation alone (15,17,18). Therefore, anticoagulation alone is still considered the standard of care for most patients with submassive PE based on current evidence and guidelines (6,7,19).

In light of the limitations of anticoagulation and ST, catheter-directed thrombolysis (CDT) has garnered significant interest because of its potential to confer similar efficacy and a lower risk of bleeding compared with ST. CDT is performed by inserting a multiple-sidehole catheter directly into the thrombus and administering a low dose of fibrinolytic drug (typically 1–2 mg/h of recombinant tissue plasminogen activator infused over a period of 12–24 h) (20,21). However, there is scant literature on the clinical effectiveness and safety of CDT compared with ST and anticoagulation alone (11). Three prospective CDT trials (21–23) associated significant reductions in pulmonary artery pressures and improvements in right ventricular function and pulmonary blood flow with CDT. There were no fatal or intracranial bleeding events and few bleeding events that required therapy beyond transfusion (21–23). However, the data do not justify the routine performance of CDT for submassive PE.

In response to a Research Consensus Panel's recommendation to address this data gap (12), an application for a randomized trial of CDT was submitted to the National Heart, Lung, and Blood Institute. As part of this application, a survey was sent to potential clinical trial sites across the United States to assess practice patterns among medical and endovascular physicians who manage submassive PE. The purpose of the present study is to report treatment tendencies in regard to the use of CDT.

MATERIALS AND METHODS

Study Design and Outcomes

From July through August 2016, a link to an electronic survey (via *surveymonkey.com*) entitled "Pulmonary Embolism—Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis (PE-TRACT) Study Site Questionnaire" was sent to 83 sites across the United States that had participated in previous venous thromboembolism trials and/or were part of the Pulmonary Embolism Response Team Consortium (*http://pertconsortium.org*). The survey was closed on September 1, 2016, and results were analyzed. The 60-item online questionnaire collected sites' demographic data, research capabilities, and practice preferences regarding submassive PE. Seven case scenarios of submassive PE were presented; the clinical scenarios included variable age presentations, medical histories, and clinical symptoms and signs (**Table 1**). The sites' primary investigators, as well as their endovascular and medical colleagues, ranked their predilection for CDT on a scale of 1–5. Scores of 4 ("probably yes") and 5 ("always") indicated a predilection for CDT whereas a score of 3 ("possibly") was considered equivocal. A score of 1 ("never") or 2 ("most likely not") was considered a predilection for anticoagulation alone. Respondents also indicated whether they would consider ST and/or recommend placement of an inferior vena cava (IVC) filter for each scenario ("yes" or "no").

Demographic Data

Of 63 respondents to the survey (75.9%), 3 submitted partial responses and were excluded from the analysis, resulting in a total of 60 sites with complete responses across 26 US states (**Fig E1** [available online at *www.jvir.org*]). Principal investigators from each site were interventional radiologists (26 of 60; 43.3%), interventional cardiologists (20 of 60; 33.3%), vascular surgeons (5 of 60; 8.3%), pulmonologists (4 of 60; 6.7%), general cardiologists (3 of 60; 5.0%), and emergency physicians (2 of 60; 3.3%). The majority of respondents (54 of 60; 90%) practiced in an academic center: 33 (55.0%) in a university hospital and 21 (35.0%) in a community hospital with an academic affiliation. Twenty-six sites (43.3%) reported data from one affiliate hospital in addition to the primary hospital, and 12 sites (20%) reported data from a second affiliate hospital. The total number of registered hospital beds across all sites (including affiliate hospitals) was 20,405 (mean, 603.8 per site; median, 499.5; range, 125–2,247). Respondents estimated 25–1,800 PE diagnoses per year. In terms of annual PE diagnoses, most sites reported 100–200 (17 of 60 sites; 28.3%) or $>$ 400 (17 of 60 sites; 28.3%; **Table E1** [available online at *www.jvir.org*]).

The majority of endovascular coinvestigators (20 of 60; 33.3%) performed $\leq$ 10 CDT procedures per year, 14 (23.3%) reported performing 11–20, 14 (23.3%) reported performing 21–30, and 12 (20%) reported performing $>$ 30.

Statistical Analysis

Because the numbers derived from Likert scales represent ordinal responses, and the nonnormal distributions of response data can result in a mean score that is not a helpful measure of the data's central tendency (24,25), the mean scores with 95% confidence intervals (CIs) were used only to compare CDT preferences between endovascular and medical physicians, whereas the median scores were used to measure the central tendency (24,25). For the purpose of the analysis, the CDT scores were converted into a binary outcome: a score $\geq$ 4 was considered to represent a predilection for CDT. By definition, absence of a predilection for CDT (ie, score $\leq$ 2) implied a predilection for anticoagulation alone.

To account for site-specific biases toward or against CDT, physicians' data from the same site were analyzed as pairs by using an exact paired-sample McNemar test. Logistic regression was used to compare the physicians in terms of overall predilection over all scenarios. All statistical tests were conducted at the two-sided 5% significance level by using SAS software (version 9.3; SAS, Cary, North Carolina). P values $<$ .05 indicated statistically significant findings.