

Trends in catheter-directed thrombolysis and systemic thrombolysis for the treatment of pulmonary embolism



Pulmonary embolism (PE) is the third leading cardiovascular cause of death after myocardial infarction and stroke in the United States, accounting for nearly 100,000 deaths each year.¹⁻³ Catheter-directed thrombolysis (CDT) and systemic thrombolysis (ST) are both used to treat intermediate- and high-risk PEs, although evidence supporting the safety and efficacy of CDT is sparse. National trends in the utilization of CDT and ST have not been well described, in part because of the limitations of publicly available administrative data sets. In this report, we aim to describe contemporary trends in the utilization of CDT and ST in a cohort of patients with acute PE selected from a comprehensive commercial insurance claims database.

Methods

From a large private-payer administrative claims database (Optum Clinformatics Data Mart), we identified PE hospitalizations which occurred between January 1, 2004, and December 31, 2014 (Figure 1). We examined the primary and secondary diagnosis fields of hospitalization files for PE *International Statistical Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes (415.1X, 634.6X, 635.6X, 636.6X, 637.6X, 638.6, and 673.2X). To identify patients who received CDT, we searched physician claims associated with each PE hospitalization for Current Procedural Terminology codes 37201 and 37211, indicating transcatheter thrombolytic infusion. We identified patients receiving ST by locating claims with the ICD-9-CM procedural code 99.10, corresponding to thrombolytic agent infusion. Because CDT and ST can commonly be used to treat other conditions, any patient with a primary ICD-9-CM diagnosis code for stroke (433.X, 434.X) or deep venous thrombosis (453.4X) with a Current Procedural Terminology code for lower extremity venography (75820 and 75822) was excluded. Given the extreme rarity of coincident diagnoses of acute myocardial infarction and PE (<.003% [n = 7] in our cohort) and the implausibility that patients would truly exhibit both diagnoses, we did not exclude patients with a diagnosis code for acute myocardial infarction. The nonparametric Mann-Kendall test for trend was used to assess for a statistically significant change in the use of CDT and ST over time. The study protocol was deemed exempt by the University of Pennsylvania Institutional Review Board, and the need for informed consent was waived as all data

were deidentified. The study was supported by intramural funding from the University of Pennsylvania Cardiovascular Outcomes, Quality, and Evaluative Research Center as well as by extramural funding from National Institutes of Health grant 4T32HL007843-20 provided to Dr Adusumalli. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper, and its final contents.

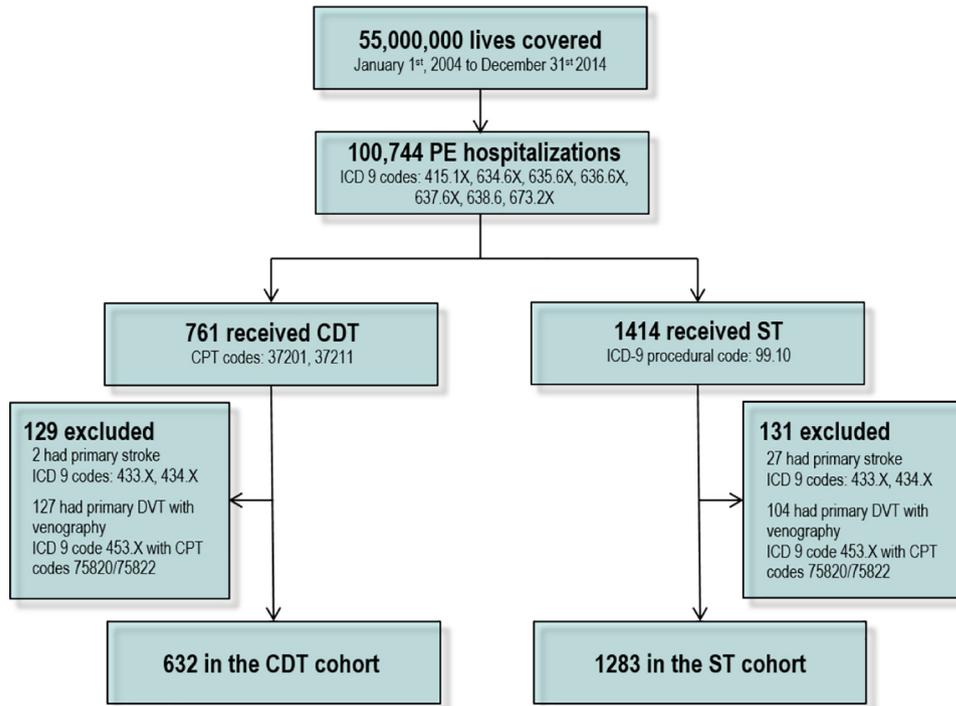
Results

We identified 100,744 admissions for PE from 2004 to 2014, with a mean (SD) patient age of 57.4 (16.2) years old. During this time, the number of PE hospitalizations per year increased from 3,225 to 13,096 ($P < .001$), although the total number of covered lives in the OptumInsight database remained stable. Twenty-five percent of this cohort had critical care billing codes, indicating that physicians perceived them to have a high probability of imminent, life-threatening deterioration in condition. Fifty-nine percent of patients had a coincident (nonprimary) diagnosis of deep vein thrombosis. A total of 1,915 patients (1.9%) received either CDT (n = 632) or ST (n = 1283), whereas 7.7% of patients with critical care billing received either form of thrombolysis. The annual number of patients receiving CDT increased from 39 in 2004 to 115 in 2014 ($P = .001$), whereas the annual number of patients receiving ST increased from 40 in 2004 to 215 in 2014 ($P < .001$) (Figure 2).

Discussion

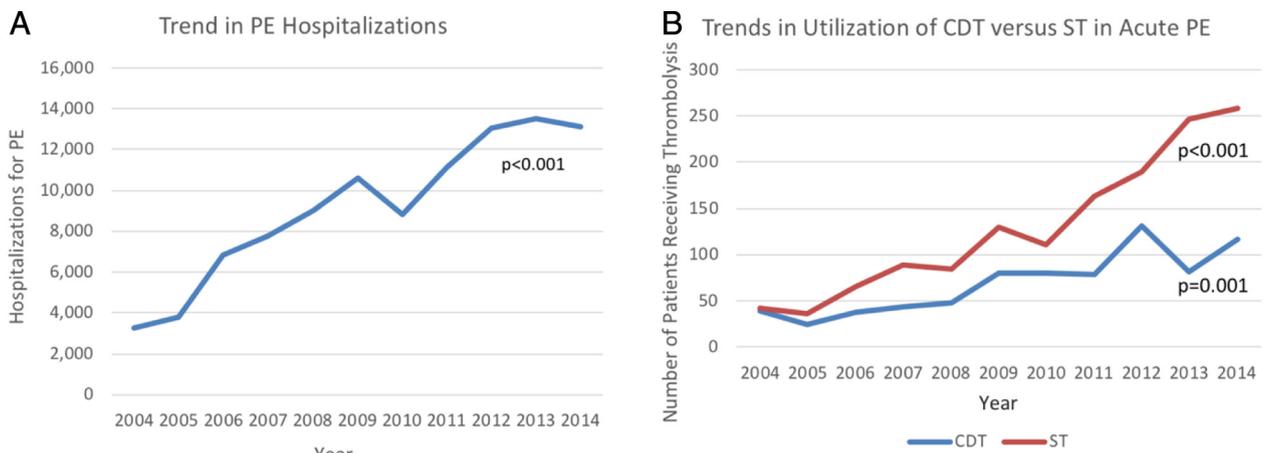
Our analysis reveals there was an increase in the number of PE patients treated with either ST or CDT from 2004 to 2014, although the absolute number of patients receiving each invasive therapy and the average annual percentage increase in treated patients were low. Although this cohort of patients is primarily younger than 65 and therefore was more likely to be appropriate candidates for aggressive PE treatment than older patients, the use of ST and CDT was infrequent (<2%). Prior studies have reported that the percentage of hospitalized PE patients with potentially life-threatening PEs ranges between 10% and 30%,^{4,5} and therefore, the infrequent use of CDT/ST in this study was unexpected. The low rate of utilization of CDT and ST has several potential explanations, including the lack of a rigorous evidence base to guide clinicians in selecting appropriate patients for these therapies. Despite over a decade of clinical use of ST and CDT, there have been a lack of studies, aside from the recent PEITHO randomized clinical trial,^{6,7} which clarify the most appropriate clinical scenarios for these therapies. We believe the trends identified by our study illustrate the need for rigorous, multicenter comparative effectiveness evaluations of ST and CDT using observational cohorts or appropriately powered randomized clinical trials to fully optimize the use of these therapies in patients with PE.

Figure 1



Cohort generation methodology.

Figure 2



A, Trend in PE hospitalizations from 2004 to 2014. B, Trends in utilization of CDT versus ST in the management of patients with acute PE from 2004 to 2014.

Am Heart J 2019;83–8.
0002-8703
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<https://doi.org/10.1016/j.ahj.2018.09.013>

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