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Contemporary Trends and Comparative Outcomes With Adjunctive Inferior Vena Cava Filter Placement in Patients Undergoing Catheter-Directed Thrombolysis for Deep Vein Thrombosis in the United States

Insights From the National Inpatient Sample

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ABSTRACT

OBJECTIVES The aim of this study was to investigate the contemporary trends and comparative effectiveness of adjunctive inferior vena cava filter (IVCF) placement in patients undergoing catheter-directed thrombolysis (CDT) for treatment of proximal lower extremity or caval deep vein thrombosis.

BACKGROUND CDT is being increasingly used in the management of proximal deep vein thrombosis. Although a significant number of patients treated with CDT undergo adjunctive IVCF placement, the benefit of this practice remains unknown.

METHODS The National Inpatient Sample database was used to identify all patients with proximal or caval deep vein thrombosis who underwent CDT (with and without adjunctive IVCF placement) in the United States between January 2005 and December 2013. A propensity score-matching algorithm was then used to derive 2 matched groups of patients (IVCF and no IVCF) for comparative outcomes (mortality and major and minor bleeding) and resource use analysis.

RESULTS Of the 7,119 patients treated with CDT, 2,421 (34%) received IVCFs. There was no significant difference in in-hospital mortality (0.7% vs 1.0%; $p = 0.20$), procedure-related hemorrhage (1.4% vs. 1.0%; $p = 0.23$), or intracranial hemorrhage (0.7% vs. 0.6%; $p = 0.70$) between the IVCF ($n = 2,259$) and no-IVCF ($n = 2,259$) groups, respectively. Patients undergoing IVCF placement had higher rates of hematoma (3.4% vs 2.1%; $p = 0.009$), higher in-hospital charges ($\$104,049 \pm 75,572$ vs. $\$92,881 \pm 80,194$; $p < 0.001$) and increased length of stay (7.3 ± 5.6 days vs. 6.9 ± 6.9 days; $p = 0.046$) compared with the no-IVCF group.

CONCLUSIONS This nationwide observational study suggests that one-third of all patients undergoing CDT receive IVCFs. IVCF use was not associated with a decrease in in-hospital mortality but was associated with higher inpatient charges and longer length of stay. (J Am Coll Cardiol Intv 2018;11:1390–7) © 2018 by the American College of Cardiology Foundation.

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Deep venous thrombosis (DVT) accounts for approximately 600,000 annual hospital visits in the United States, with an incidence ranging from 48 to 122 per 100,000 persons (1). Anatomically, DVT is often divided into proximal DVT, defined by an involvement of any vein above the crural level, and distal DVT, which involves the calf and/or distal veins (2). Proximal DVT has been shown to be associated with a higher risk for recurrent thromboembolic events and post-thrombotic syndrome (PTS), which results in marked quality of life impairment (3–5).

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Catheter-directed thrombolysis (CDT) is a fluoroscopically guided, minimally invasive procedure in which an infusion catheter is used to deliver thrombolytic agents directly into the venous thrombus. This technique, which can potentially re-establish blood flow through a newly occluded venous segment, was developed in an attempt to reduce the high incidence of PTS seen in patients treated with therapeutic anticoagulation alone. As a result of this perceived benefit, there has been a steady increase in CDT use in patients with proximal and caval DVT in the United States (6). Although smaller studies have suggested that CDT leads to a reduced incidence of PTS and an improvement in quality of life when used in acute DVT (7–14), the results of the recently published large randomized ATTRACT (Acute Venous Thrombosis: Thrombus Removal With Adjunctive Catheter-Directed Thrombolysis) trial suggest otherwise. In ATTRACT, patients with proximal DVT who underwent CDT had similar overall rates of PTS but increased incidence of major bleeding compared with patients treated with anticoagulation therapy alone (15).

Some operators elect to implant an inferior vena cava filter (IVCF) at the time of CDT in an attempt to prevent procedure-related clot migration and resultant pulmonary embolization (PE) (16). However, the frequency of developing symptomatic or fatal PE at the time of CDT is very low, and therefore the true benefit of this practice remains unclear (11). Furthermore, adjunctive use of IVCFs at the time of CDT increases procedural costs and subjects patients to complications related to IVCF implantation and subsequent retrieval (16,17). Current guidelines do not support the routine use of IVCFs at the time of CDT (18). The few studies performed to address this question were small and have shown conflicting results (16,19,20). We sought to investigate the contemporary trends, comparative effectiveness, and resource use of IVCF placement in patients undergoing CDT using a risk-adjusted propensity score-matching model.

ABBREVIATIONS AND ACRONYMS

CDT = catheter-directed thrombolysis

DVT = deep vein thrombosis

ICD-9-CM = International Classification of Diseases-9th Revision-Clinical Modification

IVCF = inferior vena cava filter

NIS = National Inpatient Sample

PE = pulmonary embolization

PTS = post-thrombotic syndrome

METHODS

STUDY DATA. The National Inpatient Sample (NIS) database was used to obtain study data. The NIS database is developed and maintained by the Agency for Healthcare Research and Quality, part of the Healthcare Cost and Utilization Project, which contains data from more than 7 million annual hospital discharges across the United States. The data in NIS are collected from approximately 1,050 hospitals across 45 states and represent a 20% stratified sample of all U.S. hospital discharges. The data can be further used to approximate the national estimates of all U.S. hospital discharges through the use of a weighting algorithm (21). Institutional Review Board approval was obtained for this study, and the requirement to obtain informed consent was waived.

STUDY POPULATION. International Classification of Diseases-9th Revision-Clinical Modification (ICD-9-CM) codes were used to identify all patients with principal discharge diagnoses of proximal DVT (ICD-9-CM code 453.41) or caval DVT (ICD-9-CM code 453.2) in the NIS database between January 2005 and December 2013. We then identified all patients who were treated with thrombolytic therapy (ICD-9-CM code 99.10) within this patient cohort. Given that systemic thrombolysis is rarely used for the treatment of lower extremity DVT, and patients with principal discharge diagnoses of PE (ICD-9-CM code 415.1) were not included in our study, we hypothesized that these patients received thrombolysis as part of CDT with or without mechanical thrombectomy. Patients treated with CDT were further stratified according to adjunctive IVCF placement (ICD-9-CM procedure

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code 38.7) into the IVCF group or no-IVCF group. We evaluated the contemporary trends in IVCF placement among patients treated with CDT. Patient selection flow diagram is shown in Online Figure 1.

We included all patients 18 years of age and older. Patients younger than 18 years and those in whom the age variable was missing were excluded from analysis. Furthermore, patients with isolated distal lower extremity DVT (ICD-9-CM code 453.42), pregnancy-related DVT (ICD-9-CM codes 671.3, 671.4, and 671.9), or unspecified lower extremity DVT (ICD-9-CM code 453.40) were not included.

COMPARATIVE OUTCOMES ANALYSIS. To adjust for the anticipated baseline differences in comorbidities and demographic characteristics between the IVCF and no-IVCF groups and to reduce the effect of selection and indication biases, we used propensity matching to derive 2 matched groups of patients (IVCF and no IVCF) that would be used for comparative outcomes and resource use analysis. Propensity matching was performed using a nearest-neighbor 1:1 variable ratio, parallel, balanced propensity score-matching method, which incorporated 56 clinical, hospital, and demographic covariates, including the Elixhauser comorbidity index (Online Table 1) (22). Because the ICD-9-CM code for PE (415.1) did not allow us to differentiate whether PE was diagnosed before CDT or was in fact a complication of the procedure, we decided to use PE as a matching variable. Doing so, made the incidence of PE (as either an initial diagnosis preceding CDT or an outcome of CDT) equal in both groups.

The primary endpoint of the study was in-hospital mortality. Secondary endpoints included blood transfusion rates, acute renal failure, cerebrovascular accident (ischemic and hemorrhagic), transient ischemic attacks, gastrointestinal bleeding, intracranial bleeding, procedure-related hematoma formation, procedure-related cardiac complications, angioplasty, venous stent placement rates, length of stay, and hospital charges.

SENSITIVITY ANALYSIS. Within the overall study cohort, we identified 185 patients (8.2%) whose IVCFs were placed in the days following CDT (Online Figure 2). To evaluate whether the outcomes of patients whose IVCFs were placed after the CDT procedure had any effect on the overall study results, we performed a separate analysis of only those patients whose IVCFs were placed either before or on the same day as CDT. We also evaluated the effect of matching for PE during our initial analysis by performing a secondary propensity-matched analysis in which PE was considered an outcome variable instead of a matching variable. Finally, a rule-out approach to sensitivity analysis was performed to determine whether any residual confounding (present after propensity matching) may have resulted in the significant differences in hospital charges and length of stay seen between the IVCF and no-IVCF groups (Online Figures 3 and 4) (23). Given the fact that residual confounding can still be present even after propensity matching, the rule-out approach gives us an idea about what the association of the unmeasured confounder would have to be with IVCF use (odds ratio between the exposure and confounder [OR_{EC}]) and the effect size (relative risk between confounder and outcome [RR_{CD}]) necessary to fully explain the observed outcomes (hospital charges and length of stay). Although this analysis does not directly eliminate the possibility of residual confounding, it essentially rules out the possibility that residual confounding would reach the necessary association and effect size to affect the observed results.

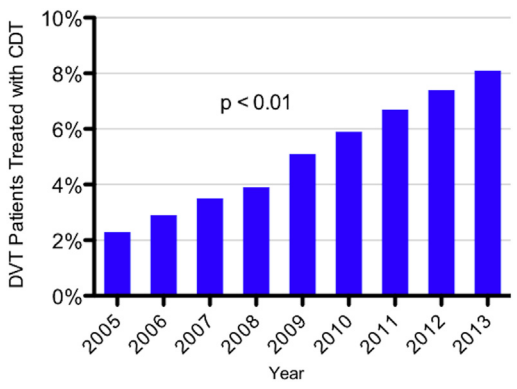
STATISTICAL ANALYSIS. The Cochrane-Armitage test was used to evaluate the trends of IVCF placement among patients treated with CDT. Descriptive summary statistics are presented as mean ± SD for continuous variables and as frequencies and percentages for categorical variables. Baseline characteristics and comparative outcomes were compared between the 2 groups using an independent-sample Student's *t*-test for continuous variables and the Pearson chi-square test for categorical variables. A p value of <0.05 was considered to indicate statistical significance. Multivariate logistic regression was used to estimate the race-adjusted odds ratios and 95% confidence intervals for the comparative outcomes analysis between the IVCF and no-IVCF groups. All statistical analyses were performed using SPSS version 22 (IBM, Armonk, New York) and SAS version 9.3 (SAS Institute, Cary, North Carolina).

Most categorical variables, including sex, hospital location, and teaching status, had <1% missing data and were imputed to the most common category. However, race had 12.2% missing data, and thus a dummy-variable adjustment method was used to preserve the full sample size (24). The comparative outcomes results were then adjusted for the race variable.

RESULTS

CHARACTERISTICS OF THE STUDY POPULATION. Between January 2005 and December 2013, a total of 138,049 patients with principal discharge diagnoses of proximal or caval DVT were identified in the NIS database, representing a national estimate of 663,417

FIGURE 1 Contemporary Trends in Catheter-Directed Thrombolysis Use in the United States (2005 to 2013)

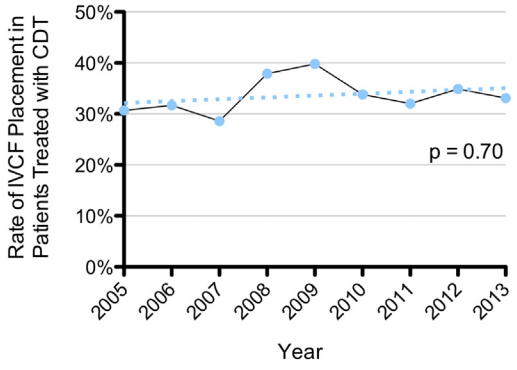


There was a significant increase in the use of catheter-directed thrombolysis (CDT) for treatment of proximal and caval deep vein thrombosis (DVT) during the study period.

DVT cases. Within this patient cohort, we identified 7,119 patients who underwent CDT (5.2%), and 2,421 of these patients (34%) underwent adjunctive IVCF placement. There was a steady increase in CDT use throughout the study period: from 2.3% in 2005 to 8.1% in 2013 ($p < 0.01$) (Figure 1), whereas the use of IVCFs in patients undergoing CDT remained unchanged (Figure 2).

Key unmatched baseline characteristics of the study patients are shown in Table 1. Among patients who underwent both CDT and IVCF placement, 74.6% (n = 1,685) had their IVCFs placed either on the same day as CDT or in the days before CDT (range 1 to 32 days before CDT). IVCFs were placed after CDT (range 1 to 30 days) in 8.2% of patients (n = 185) (Online Figure 2). Data on the timing of IVCF placement were missing for 17.2% of patients (n = 389).

FIGURE 2 Contemporary Trends in Inferior Vena Cava Filter Placement Among Patients Undergoing Catheter-Directed Thrombolysis in the United States (2005 to 2013)



The rate of inferior vena cava filter (IVCF) placement remained stable in patients undergoing catheter-directed thrombolysis (CDT).

TABLE 1 Key Unmatched and Matched Baseline Clinical Characteristics of Patients Undergoing Catheter-Directed Thrombolysis With or Without Inferior Vena Cava Filter Placement for Proximal or Caval Deep Vein Thrombosis

	No IVCF	IVCF Group	p Value
Unmatched group	(n = 4,698)	(n = 2,421)	
Age (yrs)	53.5 ± 17.1	54.4 ± 17.2	0.036
Female	2,178 (46.4)	1,297 (53.6)	<0.001
Race			<0.001
Caucasian	3,078 (65.5)	1,677 (69.3)	
African American	493 (10.5)	188 (7.8)	
Other	405 (8.6)	267 (11.0)	
Unknown	722 (15.4)	289 (11.9)	
Caval involvement of DVT	830 (17.7)	227 (9.4)	<0.001
Active smoking	728 (15.5)	428 (17.7)	0.02
Hypercoagulable state	678 (14.4)	295 (12.2)	0.01
Chronic kidney disease	336 (7.2)	160 (6.6)	0.39
Coronary artery disease	455 (9.7)	252 (10.4)	0.33
Solid tumor without metastasis	163 (3.5)	95 (3.9)	0.33
Metastatic disease	261 (5.6)	122 (5.0)	0.36
All malignancies	856 (18.2)	434 (17.9)	0.76
History of VTE	748 (15.9)	226 (9.3)	<0.001
Annual CDT cases			0.143
0–5	3,061 (65.2)	1,535 (63.4)	
>5	1,637 (34.8)	886 (36.6)	
Matched group	(n = 2,259)	(n = 2,259)	
Age (yrs)	54.2 ± 16.9	54.3 ± 17.2	0.83
Female	1,214 (53.7)	1,191 (54.7)	0.52
Race			0.005
Caucasian	1,562 (69.1)	1,551 (68.7)	
African American	226 (10.0)	175 (7.7)	
Other	190 (8.4)	257 (11.4)	
Unknown	281 (12.4)	276 (12.2)	
Caval involvement of DVT	239 (10.6)	225 (10.0)	0.49
Active smoking	403 (17.8)	391 (17.3)	0.64
Hypercoagulable state	288 (12.7)	283 (12.5)	0.82
Chronic kidney disease	125 (5.5)	150 (6.6)	0.12
Coronary artery disease	209 (9.3)	232 (10.3)	0.25
Solid tumor without metastasis	92 (4.1)	86 (3.8)	0.65
Metastatic disease	112 (5.0)	115 (5.1)	0.84
All malignancies	414 (18.3)	403 (17.8)	0.67
Pulmonary embolism	544 (24.1)	540 (23.9)	0.89
History of VTE	232 (10.3)	225 (10.0)	0.73
Annual CDT cases			0.66
0–5	1,441 (63.8)	1,427 (63.2)	
>5	818 (36.2)	832 (36.8)	

Values are mean ± SD or n (%).
CDT = catheter-directed thrombolysis; DVT = deep vein thrombosis; IVCF = inferior vena cava filter; VTE = venous thromboembolism.

IN-HOSPITAL OUTCOMES OF IVCF PLACEMENT IN PATIENTS UNDERGOING CDT. The propensity score-matching algorithm yielded a total of 4,518 patients

TABLE 2 Matched Race-Adjusted Outcomes of Patients Undergoing Catheter-Directed Thrombolysis With or Without Inferior Vena Cava Filter Placement

	No IVCF Group	IVCF Group	OR (95% CI)	p Value
Death	23 (1.0)	15 (0.7)	0.67 (0.34–1.26)	0.20
Blood transfusion	237 (10.5)	255 (11.3)	1.09 (0.90–1.31)	0.37
GI bleeding	44 (1.9)	32 (1.4)	0.73 (0.46–1.15)	0.17
Intracranial hemorrhage	13 (0.6)	15 (0.7)	1.16 (0.55–2.45)	0.70
Hematoma	47 (2.1)	76 (3.4)	1.63 (1.13–2.36)	0.009
Procedure-related hemorrhage	23 (1.0)	32 (1.4)	1.40 (0.81–2.39)	0.23
Length of stay (days)	6.0 (3.0–9.0)	6.0 (4.0–9.0)	–	<0.001
Charges ($)	92,881 ± 80,194	104,049 ± 75,572	–	<0.001
Peripheral angioplasty	1329 (58.8)	1394 (61.7)	1.13 (1.001–1.27)	0.048
Peripheral stent	634 (28.1)	673 (29.8)	1.09 (0.96–1.24)	0.20
Procedure-related renal failure	8 (0.4)	4 (0.2)	0.50 (0.15–1.65)	0.25
Acute renal failure	188 (8.3)	195 (8.6)	1.04 (0.84–1.28)	0.71
Transient ischemic attack	2 (0.1)	1 (0.04)	0.50 (0.045–5.49)	0.57
Embolic stroke	2 (0.1)	2 (0.1)	1.01 (0.14–7.20)	0.99
Procedure-related cardiac complications	5 (0.2)	5 (0.2)	1.01 (0.29–3.51)	0.98

Values are n (%), mean ± SD, or median (interquartile range).
CI = confidence interval; GI = gastrointestinal; OR = odds ratio; other abbreviations as in Table 1.

(2,259 patients receiving adjunctive IVCFs and 2,259 patients without IVCF placement) who were included in the comparative outcomes analysis (C statistic = 0.67). Propensity matching resulted into 2 groups of patients whose baseline characteristics were well matched for all variables except race (Table 1).

Matched race-adjusted in-hospital outcomes are shown in Table 2. There were no significant differences in in-hospital mortality (0.7% vs 1.0%; p = 0.20), gastrointestinal bleeding (1.4% vs. 1.9%; p = 0.17), procedure-related hemorrhage (1.4% vs. 1.0%; p = 0.23), intracranial hemorrhage (0.7% vs. 0.6%; p = 0.70), and blood transfusion rates (11.3% vs. 10.5%; p = 0.37) between the IVCF and no-IVCF groups, respectively. Patients undergoing IVCF placement had higher rates of hematoma formation (3.4% vs 2.1%; p = 0.009), increased length of stay (7.3 ± 5.6 days vs. 6.9 ± 6.9 days; p = 0.048), and higher in-hospital charges ($104,049 ± 75,572 vs. $92,881 ± 80,194; p < 0.001) compared with the no-IVCF group. Patients in the IVCF group were also significantly more likely to have venous angioplasty compared with the no-IVCF group (61.7% vs. 58.8%; p = 0.048) despite similar rates of venous stent placement (29.8% vs. 28.1%; p = 0.20), respectively.

SENSITIVITY ANALYSIS. Given that 8.2% of patients had IVCFs placed after CDT, we performed a separate analysis of only those patients whose IVCFs were placed either before or on the day of CDT (Online Table 2). Patients in whom the timing of IVCF placement was unknown were also excluded from this sensitivity analysis. In this patient cohort, similar to the initial analysis, IVCF placement did not improve in-hospital mortality. There were also no differences in the rates of blood transfusion, gastrointestinal bleeding, intracranial hemorrhage, stroke or transient ischemic attack, and renal failure between the IVCF and no-IVCF groups. The rates of hematoma formation, peripheral angioplasty, and venous stent placement, as well as hospital charges, were higher in the IVCF group. This sensitivity analysis revealed that inclusion of patients whose IVCF placement was performed after CDT did not significantly alter the main results of the study.

A second sensitivity analysis was performed to evaluate the effect of matching for PE during the initial evaluation (Online Table 3). Sensitivity analysis revealed that even when PE was considered as an outcome variable, the overall results were similar to the initial propensity-matched analysis in which the PE variable was matched.

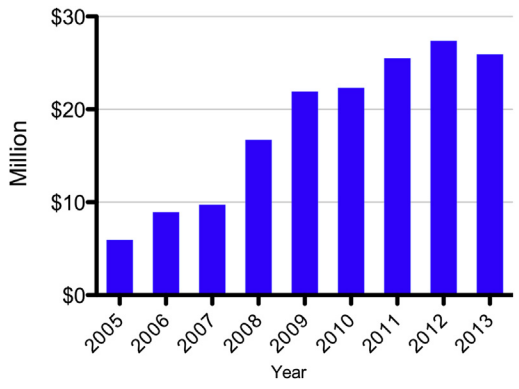
Using the rule-out approach for the hospital charge endpoint (Online Figure 3), we estimated that for an unmeasured confounder to fully explain our estimates in increased charges seen in the IVCF group, the confounder had to have a 3 times higher association with the IVCF than the no-IVCF group and would itself have to result in an 8-fold charge increase. The rule-out approach for the length-of-stay endpoint (Online Figure 4) revealed that for an unmeasured confounder to fully explain our estimates in longer lengths of stay in the IVCF group, the confounder had to have a 2 times higher association with the IVCF than the no-IVCF group and would by itself have to result in a 3-fold length-of-stay increase.

DISCUSSION

This is the first nationwide observational study to evaluate contemporary trends and comparative outcomes of adjunctive IVCF placement in patients undergoing CDT for treatment of proximal or caval DVT. The major findings of our study are as follows: 1) although the use of CDT for treatment of proximal and caval DVT continues to increase in the United States, the use of adjunctive IVCF placement has remained steady at about 30%; 2) IVCF use was not associated with any in-hospital mortality benefit; and 3) there was an increased incidence of hematoma formation and resource use in patients undergoing IVCF placement.

The rate of CDT use in the treatment of proximal and caval DVT was previously reported to be 5.9% in 2010 in the United States (6). In the present

FIGURE 3 Incremental Cost of Inferior Vena Cava Filter Placement in Patients Treated With Catheter-Directed Thrombolysis (2005 to 2013)



The incremental cost associated with the use of inferior vena cava filters at the time of catheter-directed thrombolysis is substantial.

study, we note a continued increase in CDT use up to 8% in 2013. A prior study that specifically evaluated patients with inferior vena caval thrombosis observed a 35% rate of CDT use (25). Given the recent publication of the ATTRACT trial (15), which showed similar overall rates of PTS and an increased incidence of major bleeding among patients with proximal DVT treated with CDT, the rate of CDT may be expected to decrease over the coming years.

Limited data exist on the effectiveness of IVCF use in patients undergoing CDT for the treatment of proximal DVT. Despite this, our study suggests that IVCFs are used in one-third of all patients undergoing CDT in the United States. Multiple small prior studies have reported successful entrapment of clots by IVCFs during and immediately after CDT (26–28). However, the clinical impact of clot embolization in these patients has not been well established (29). The majority of PE events were asymptomatic and did not lead to any long-term complications during the 3-year follow-up period.

We did not observe any in-hospital mortality benefit in patients treated with adjunctive IVCF placement. Sharifi et al. (19) previously showed that IVCF placement during percutaneous endovenous intervention reduced the risk for iatrogenic PE but did not confer a survival benefit. In contrast, Protack et al. (16) did not observe any PE or mortality events during treatment with CDT regardless of IVCF placement. Therefore, although IVCFs may be effective in capturing thrombus during CDT (27,28), the low frequency of symptomatic and hemodynamically significant PEs in this setting argues against routine IVCF placement before CDT (9,16,30).

Although we did not observe any significant differences in the rates of cerebrovascular or gastrointestinal bleeding, we did find an increased rate of procedure-related hematoma formation in the IVCF group compared with the no-IVCF group (3.4% vs. 2.1%). We believe that the higher incidence of procedure-related hematoma formation in the IVCF group is due to the concomitant use of thrombolytic agents plus an additional venous access site for IVCF implantation.

In our analysis, placement of an IVCF at the time of CDT resulted in significantly increased health care costs ($104,049 vs. $92,881) and a prolonged length of stay (7.3 days vs. 6.9 days) compared with the no-IVCF group, respectively. Given the increasing rates of CDT use in the United States over the course of the study period, the overall weighted incremental hospitalization costs associated with IVCF placement increased from $5.9 million in 2005 to $25.3 million in 2013 (**Figure 3**). The increased upfront resource use evidence in our study warrants a review of the cost-effectiveness of IVCF placement to better inform the development of future guidelines.

STUDY LIMITATIONS. First, the timing of incident PE was unknown relative to CDT. Thus, PE may have been present before or be the result of CDT. Nevertheless, sensitivity analysis revealed that matching for the PE variable did not have any significant impact on the hard endpoint of mortality, which was similar between the IVCF and no-IVCF groups regardless of whether the PE variable was matched for or not. Therefore, although our study is unable to provide data regarding post-CDT PE events, lack of mortality benefit in the IVCF group is an important finding. Furthermore, prior studies that specifically evaluated the use of prophylactic IVCF placement for prevention of clinically significant PE in patients undergoing CDT failed to show an incremental benefit with IVCF use (16,19). Second, the effect of unmeasured confounding variables is unknown. However, our rigorous propensity score matching markedly reduced this effect, as reflected by our sensitivity analysis. Third, the comparative outcomes of IVCF placement in patients with iliofemoral DVT versus femoropopliteal DVT could not be assessed in our study. Fourth, our study data are subject to the limitations of the claims-based databases. However, because the discharge diagnoses codes for proximal or caval DVT have been shown to have >95%

sensitivity and specificity (31), we believe that our outcomes are reliable. Finally, the NIS does not provide survival information beyond the inpatient hospital stay. Thus, post-hospitalization outcomes are unknown, and our observations need to be confirmed in other datasets with longer term follow-up.

CONCLUSIONS

The results of this large national observational study suggest that there is no mortality benefit with adjunctive IVCF use at the time of CDT. However, IVCF use was associated with an increase in procedure-related hematoma formation, in-hospital costs, and length of stay. On the basis of these results, we believe that IVCFs should not be routinely placed in patients undergoing CDT. Additional well-designed, randomized controlled trials are encouraged to elucidate the implications of IVCF placement in patients undergoing CDT.

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PERSPECTIVES

WHAT IS KNOWN? DVT is a common disorder that has the potential to cause life-threatening PE. CDT is being increasingly used for patients with proximal or caval DVT. Some operators elect to place an adjunctive IVCF at the time of CDT in an attempt to reduce the risk for iatrogenic PE.

WHAT IS NEW? Our study is the first to evaluate national trends and outcomes of adjunctive IVCF use at the time of CDT. In a large sample of U.S. patients with proximal or caval DVT, IVCFs were placed in one-third of all patients treated with CDT. IVCF placement did not improve in-hospital mortality but was associated with higher bleeding rates, increased length of stay, and higher in-hospital charges compared with patients not undergoing IVCF implantation.

WHAT IS NEXT? A randomized controlled trial is needed to specifically evaluate the use of adjunctive IVCF placement at the time of CDT. Until that time, routine use of IVCFs at the time of CDT for treatment of proximal or caval DVT is not indicated.

REFERENCES

1. Kiernan TJ, Cepeda B, Kiernan GD, Yan BP. Current status of pharmacological thrombolytic therapy and mechanical thrombectomy for the treatment of acute deep venous thrombosis. Cardiovasc Hematol Agents Med Chemi 2009;7:12–8.

2. Jenkins JS, Michael P. Deep venous thrombosis: an interventionalist's approach. Ochsner J 2014;14:633–40.

3. Hansson PO, Sorbo J, Eriksson H. Recurrent venous thromboembolism after deep vein thrombosis: incidence and risk factors. Arch Intern Med 2000;160:769–74.

4. Kahn SR, Hirsch A, Shrier I. Effect of post-thrombotic syndrome on health-related quality of life after deep venous thrombosis. Arch Intern Med 2002;162:1144–8.

5. Stain M, Schönauer V, Minar E, et al. The post-thrombotic syndrome: risk factors and impact on the course of thrombotic disease. J Thromb Haemost 2005;3:2671–6.

6. Bashir R, Zack CJ, Zhao H, Comerota AJ, Bove AA. Comparative outcomes of catheter-directed thrombolysis plus anticoagulation vs anticoagulation alone to treat lower-extremity proximal deep vein thrombosis. JAMA Intern Med 2014;174:1494–501.

7. Comerota AJ. Quality-of-life improvement using thrombolytic therapy for iliofemoral deep venous thrombosis. Rev Cardiovasc Med 2002;3 Suppl 2:S61–7.

8. AbuRahma AF, Perkins SE, Wulu JT, Ng HK. Iliofemoral deep vein thrombosis: conventional therapy versus lysis and percutaneous transluminal angioplasty and stenting. Ann Surg 2001;233:752–60.

9. Broholm R, Sillesen H, Damsgaard MT, et al. Postthrombotic syndrome and quality of life in patients with iliofemoral venous thrombosis treated with catheter-directed thrombolysis. J Vasc Surg 2011;54 Suppl:18S–25S.

10. Meissner MH, Gloviczki P, Comerota AJ, et al. Early thrombus removal strategies for acute deep venous thrombosis: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. J Vasc Surg 2012;55:1449–62.

11. Mewissen MW, Seabrook GR, Meissner MH, Cynamon J, Labropoulos N, Haughton SH. Catheter-directed thrombolysis for lower extremity deep venous thrombosis: report of a national multicenter registry. Radiology 1999;211:39–49.

12. Sharifi M, Mehdipour M, Bay C, Smith G, Sharifi J. Endovenous therapy for deep venous thrombosis: the TORPEDO trial. Catheter Cardiovasc Interv 2010;76:316–25.

13. Singh H, Masuda EM. Comparing short-term outcomes of femoral-popliteal and iliofemoral deep venous thrombosis: early lysis and development of reflux. Ann Vasc Surg 2005;19:74–9.

14. Haig Y, Enden T, Grotta O, et al. Post-thrombotic syndrome after catheter-directed thrombolysis for deep vein thrombosis (CaVenT): 5-year follow-up results of an open-label, randomized trial. Lancet Haematol 2016;3:e64–71.

15. Vedantham S, Goldhaber SA, Julian JA, et al., for the ATTRACT Trial Investigators. Pharmacomechanical catheter-directed thrombolysis for deep-vein thrombosis. N Engl J Med 2017;377:2240–52.

16. Protack CD, Bakken AM, Patel N, Saad WE, Waldman DL, Davies MG. Long-term outcomes of catheter directed thrombolysis for lower extremity deep venous thrombosis without prophylactic inferior vena cava filter placement. J Vasc Surg 2007;45:992–7.

17. Grossman C, McPherson S. Safety and efficacy of catheter-directed thrombolysis for iliofemoral venous thrombosis. AJR Am J Roentgenol 1999;172:667–72.

18. DeYoung E, Minocha J. Inferior vena cava filters: guidelines, best practice, and expanding indications. Semin Intervent Radiol 2016;33:65–70.

19. Sharifi M, Bay C, Skrocki L, Lawson D, Mazdeh S. Role of IVC filters in endovenous therapy for deep venous thrombosis: the FILTER-PEVI (Filter Implantation to Lower Thromboembolic Risk in Percutaneous Endovenous Intervention) trial. Cardiovasc Interv Radiol 2012;35:1408–13.

20. Herrera S, Comerota AJ. Embolization during treatment of deep venous thrombosis: incidence, importance, and prevention. Techn Vasc Interv Radiol 2011;14:58–64.

21. Overview of the Nationwide Inpatient Sample (NIS): Healthcare Cost and Utilization Project (HCUP). Available at: http://www.hcup-us.ahrq.gov/nisoverview.jsp. Accessed October 20, 2017.

22. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. Med Care 1998;36:8–27.

23. Schneeweiss S. Sensitivity analysis and external adjustment for unmeasured confounders in epidemiologic database studies of therapeutics. Pharmacoepidemiol Drug Safety 2006;15:291–303.

24. Cohen J. Applied multiple regression/correlation analysis for the behavioral sciences, Vol. 18. Hillsdale, NJ: Lawrence Erlbaum, 1983.

25. Alkhouli M, Zack CJ, Zhao H, Shafi I, Bashir R. Comparative outcomes of catheter-directed thrombolysis plus anticoagulation versus anticoagulation alone in the treatment of inferior vena caval thrombosis. Circ Cardiovasc Interv 2015;8:e001882.

26. Kölbel T, Alhadad A, Acosta S, Lindh M, Ivancev K, Gottsäter A. Thrombus embolization into IVC filters during catheter-directed thrombolysis for proximal deep venous thrombosis. J Endovasc Ther 2008;15:605–13.

27. Yamagami T, Kato T, Hirota T, Yoshimatsu R, Matsumoto T, Nishimura T. Prophylactic implantation of inferior vena cava filter during interventional radiological treatment for deep venous thrombosis of the lower extremity. Br J Radiol 2006;79:584–91.

28. Yamagami T, Nishimura T. Prophylactic implantation of inferior vena cava filter during endovascular therapies for deep venous thrombosis of the lower extremities. Ann Vasc Dis 2011;4:19–23.

29. García-Fuster MJ, Fabia MJ, Furió E, et al. Should we look for silent pulmonary embolism in patients with deep venous thrombosis? BMC Cardiovasc Dis 2014;14:178.

30. Kölbel T, Lindh M, Holst J, et al. Extensive acute deep vein thrombosis of the iliocaval segment: midterm results of thrombolysis and stent placement. J Vasc Interv Radiol 2007;18:243–50.

31. White RH, Garcia M, Sadeghi B, et al. Evaluation of the predictive value of ICD-9-CM coded administrative data for venous thromboembolism in the United States. Thromb Res 2010;126:61–7.

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APPENDIX For supplemental tables and figures, please see the online version of this paper.