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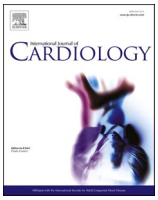

In-hospital and readmission outcomes of patients with cancer admitted for pulmonary embolism treated with or without catheter-based therapy

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ABSTRACT

Background: Cancer patients are at risk of pulmonary embolism (PE). Catheter-based therapies (CBT) are novel reperfusion options for PE though data in patients with cancer is lacking.
Study design and methods: Patients with intermediate- or high-risk PE were identified using the National Readmission Database (NRD) from 2017 to 2020. Primary outcome were in-hospital death and 90-day readmission. Secondary outcomes were in-hospital bleeding, 90-day readmission for venous thromboembolism (VTE)-related or right heart failure-related reasons and bleeding. Propensity scores were estimated using logistic regression and inverse-probability treatment weighting (IPTW) was utilized to compare outcomes between CBT and no CBT as well as CBT versus systemic thrombolysis.
Results: A total of 7785 patients were included (2511 with high-risk PE) of whom 1045 (13.4%) were managed with CBT. After IPTW, CBT was associated with lower rates of index hospitalization death (OR 0.89, 95% CI 0.83–0.96) and 90-day readmission (HR 0.75, 95% CI 0.69–0.81) but higher rates of in-hospital bleeding (OR 1.11, 95% CI 1.03–1.20) which was predominantly post-procedural bleeding. CBT was associated with lower risk of major bleeding (20.8% vs 24.8%; OR 0.80, 95% CI 0.68–0.94) compared with systemic thrombolysis.
Interpretation: Among patients with cancer with intermediate or high-risk PE, CBT was associated with lower in-hospital death and 90-day readmission. CBT was also associated with decreased risk of index hospitalization major bleeding compared with systemic thrombolysis. Prospective, randomized trials with inclusion of patients with cancer are needed to confirm these findings.

1. Introduction

Venous thromboembolism (VTE), including pulmonary embolism (PE) and deep vein thrombosis (DVT), are well-known complications in patients with cancer and impart a significant burden of morbidity and mortality [1–4]. Among patients with cancer, PE carries a high risk of mortality and imparts a four-fold increased risk in death [5]. Anticoagulation is the first-line therapy for PE with systemic thrombolytic therapy reserved for patients with hemodynamically unstable PE [6,7]. However, patients with cancer are at increased risk of bleeding from anticoagulation and system thrombolysis [8,9].

Catheter-based therapies (CBT), including catheter-directed thrombolysis (CDT) and percutaneous mechanical thrombectomy (MT), have been developed as reperfusion strategies for acute PE [10]. Guidelines recommend CBT for patients with high-risk PE (PE with hemodynamic instability or collapse including shock, cardiac arrest or requiring vasopressors) at high bleeding risk or with contraindications to systemic thrombolysis [11,12]. Single-arm studies and registries performed in intermediate-risk PE (those with right ventricular strain without hemodynamic compromise) have suggested a benefit in surrogate endpoints including right ventricular (RV) to left ventricular (LV) size ratio and mean pulmonary artery pressure (mPAP) [13–18]. In a prospective, non-randomized trial of high-risk PE, patients treated with MT had lower rates of in-hospital mortality compared with context arm (primarily systemic thrombolysis or anticoagulation) [19]. Another retrospective cohort study of patients with intermediate- and high-risk PE

Abbreviations: Catheter-based therapies, CBT; Catheter-directed thrombolysis, CDT; Mechanical thrombectomy, MT; Pulmonary embolism, PE; Venous thromboembolism, VTE.

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demonstrated an association between management with CBT and decrease in-hospital mortality and 90-day readmissions [20]. However, data on clinical outcomes among patients with cancer-associated PE managed with CBT are sparse. Additionally, patients with cancer are less likely to undergo invasive procedures for cardiovascular disorders including percutaneous coronary intervention (PCI) for acute myocardial infarction [21,22]. Therefore, we aimed to investigate in-hospital outcomes, including death and major bleeding, and 90-day readmissions in patients with cancer hospitalized with intermediate- or high-risk PE managed with versus without CBT.

2. Methods

2.1. Study design and population

We conducted a retrospective, observational cohort study using the National Readmission Database (NRD) from January 1, 2017 to December 31, 2020. The NRD is part of the Healthcare Cost and Utilization Project (HCUP) and is sponsored by the Agency for Healthcare Research and Quality (AHRQ). The NRD captures approximately 50% of hospitalizations in the United States and assigns unique identifiers to individual patients to track readmissions within a given calendar year. Patients with a primary diagnosis of PE were identified using International Classification of Diseases, tenth edition (ICD-10) codes (Supplemental Table 1). Among patients with multiple admissions for PE, the first admission in a given calendar year was considered the index PE hospitalization. Patients with concomitant diagnoses of cardiogenic shock, vasopressor use, or cardiac arrest were defined as high-risk PE. Intermediate-risk PE was defined as PE with cor pulmonale, type 2 myocardial infarction (MI, as a surrogate for cardiac biomarkers), or right heart failure (RHF, as a surrogate for right heart strain) without cardiogenic shock, vasopressor use, or cardiac arrest [20,23]. ICD-10 procedure codes were used to identify procedures including CBT, systemic thrombolysis, mechanical ventilation, and transfusion of blood products. Co-morbidities were also captured using ICD-10 codes (Supplemental Table 1). Cancer diagnoses and types were defined using ICD-10 codes (Supplemental Table 2). This study was deemed exempt by our Institutional Review Board given that the data used is publicly available and de-identified.

2.2. Outcomes

In-hospital and readmission outcomes were identified using ICD-10 codes (Supplemental Table 1). Primary outcomes were in-hospital death and 90-day all-cause readmission. Secondary, exploratory outcomes included 90-day VTE or RHF-related and bleeding-related readmissions, and index major bleeding (composite of gastrointestinal bleeding, intracranial bleeding, post-procedural bleeding and transfusion of blood products). VTE-related readmissions were defined as readmission with primary or secondary diagnosis of either DVT or PE, and RHF-related readmissions were defined as a readmission with primary or secondary diagnosis of RHF, cor pulmonale without mention of PE, or chronic thromboembolic pulmonary hypertension (CTEPH). Bleeding-related readmissions were defined as readmission with primary or secondary diagnosis of gastrointestinal (GI) bleeding, intracranial (IC) bleed, or procedure-related bleeding.

2.3. Statistical analysis

Our primary analysis included all patients with cancer with intermediate- or high-risk PE. Secondary analyses included investigating outcomes among patients treated with CBT compared with systemic thrombolysis and MT compared with CDT. For our analyses comparing CBT to systemic thrombolysis and MT with CDT, patients who were treated with both were excluded. Propensity scores (PS) using a non-parsimonious multivariable logistic regression included age, sex, month of admission, year of admission, type of cancer, presence of metastatic cancer, primary brain tumor or metastatic brain tumor, Khorana high or intermediate risk cancer (stomach, pancreas, lung, lymphoma, gynecologic, bladder, testicular), smoking, hypertension, prior VTE, heart failure, diabetes, coronary artery disease (CAD), chronic kidney disease (CKD), liver disease, anemia, thrombocytopenia, long-term anticoagulation use, long-term antiplatelet use, malnutrition, prior stroke, home oxygen use, chronic lung disease, do-not resuscitate (DNR) status, palliative care, dementia, obesity, wheelchair-bound status, current or prior chemotherapy, prior irradiation, current or prior immunosuppression, chemotherapy-associated cytopenias, high-risk PE, cardiogenic shock, presence of other types of shock, DVT, respiratory failure during index hospitalization, mechanical ventilation, systemic thrombolysis use, hospital size and location, insurance and zip code median income. PS were used to perform inverse-probability treatment weighting (IPTW) analysis with 1/PS being assigned to patients treated with CBT and 1/(1-PS) for patients not treated with CBT [24]. Standardized mean difference (SMD) were calculated in order to assess for intergroup imbalances with variables being considered imbalanced if SMD was greater or equal to 0.10.

Given the increased risk of bleeding in patients with cancer who receive systemic thrombolysis, we compared the outcomes of patients with intermediate- or high-risk PE managed with CBT or systemic thrombolysis. Propensity scores were estimated in an identical fashion to our primary analysis and IPTW analysis was performed with 1/PS assigned to patients with systemic thrombolysis alone and 1/(1-PS) assigned for CBT alone.

Categorical outcomes were presented as frequency and percentages and comparisons between groups was performed using chi square tests before and after IPTW. IPTW logistic regression was used to estimate odds ratio (OR) and 95% confidence interval (CI) for in-hospital outcomes. Readmission outcomes were assessed using time-to-event analysis using Cox proportional hazards regression modeling to estimate hazards ratio (HR) before and after IPTW. Given time-to-event analyses only consider the first failure event after index hospitalization, we performed IPTW negative binomial regression to estimate incidence rate ratio (IRR) to estimate risk of recurrent all-cause, VTE or RHF-related, and bleeding-related readmissions using months left in the year after discharge as the exposure variable. Given the NRD does not track readmissions across calendar years, we excluded patients admitted after September for time-to-event analyses.

All tests were two-tailed and a p value of <0.05 was considered significant. Statistical analyses were performed using SPSS version 29.0 (IBM) and STATA version 15 (STATA).

3. Results

3.1. Baseline characteristics of patients with intermediate- or high-risk PE before and after IPTW

A total of 7785 patients were included (Supplemental Fig. 1), of whom 2511 (32.3%) had high-risk PE and 1045 (13.4%) were treated with CBT. Among the included patients, 4062 (52.2%) were female, 6589 (84.9%) had solid malignancy, 3766 (48.4%) had metastatic malignancy and 977 (12.5%) had primary or metastatic brain tumor. Of those treated with CBT, 635 (60.8%) were treated with CDT alone, 345 (33.0%) with MT alone, and 65 (6.2%) with both CDT and MT. Prior to IPTW, patients treated with CBT were younger (mean 66.5 vs 68.4 years, SMD = 0.157), less likely to have metastatic cancer (43.0% vs 49.2%, SMD = 0.125), have DNR status (16.8% vs 31.2%, SMD = 0.342), have encounter for palliative care (9.8% vs 20.3%, SMD = 0.297), and have high-risk PE (26.5% vs 33.1%, SMD = 0.145). After IPTW, all variables were balanced between groups, Table 1.

Outcomes of Patients with Intermediate- or High-Risk PE Treated with and without CBT.

Among patients with intermediate- or high-risk PE, 1804 (23.2%)

Table 1
Baseline unweighted and IPTW characteristics of patients with intermediate or high-risk pe treated with or without CBT.

	Unweighted				Inverse-Probability Treatment Weighting		
	All Patients $N = 7785$	No CBT $N = 6740$	CBT $N = 1045$	SMD	No CBT	CBT	SMD
Age, years (SD)	68.1 (12.0)	68.4 (12.0)	66.5 (11.5)	0.157	68.1 (12.1)	67.6 (11.2)	0.048
Female Sex, N (%)	4062 (52.2)	3526 (52.3)	536 (51.3)	0.020	52.2%	53.2%	0.020
CBT Type, N (%)				N/A			N/A
CDT Alone	635 (8.2)	0	635 (60.8)		0	57.4%	
MT Alone	345 (4.4)	0	345 (33.0)		0	35.9%	
Both MT and CDT	65 (0.8)	0	65 (6.2)		0	6.7%	
Cancer Characteristics, N (%)							
Solid Cancer	6589 (84.6)	5721 (84.9)	868 (83.1)	0.049	84.6%	85.7%	0.031
Hematologic Cancer	1351 (17.4)	1161 (17.2)	190 (18.2)	0.026	17.3%	16.5%	0.021
Brain Tumor or Metastasis	977 (12.5)	883 (13.1)	94 (9.0)	0.131	12.6%	13.8%	0.035
Metastatic Cancer	3766 (48.4)	3317 (49.2)	449 (43.0)	0.125	48.4%	51.0%	0.052
Khorana High or Intermediate Risk	3730 (47.9)	3299 (48.9)	431 (41.2)	0.155	48.0%	49.0%	0.020
Co-Morbidities, N (%)							
Hypertension	4853 (62.3)	4212 (62.5)	641 (61.3)	0.025	62.3%	61.6%	0.014
Prior VTE	885 (11.4)	753 (11.2)	132 (12.6)	0.043	11.4%	12.5%	0.034
Heart Failure	2208 (28.4)	1929 (28.6)	279 (26.7)	0.042	28.4%	29.2%	0.018
Diabetes Mellitus	2033 (26.1)	1750 (26.0)	283 (27.1)	0.025	26.1%	25.0%	0.025
AF	1440 (18.5)	1277 (18.9)	163 (15.6)	0.087	18.5%	18.7%	0.005
CAD	2953 (37.9)	2601 (38.6)	352 (33.7)	0.102	37.9%	36.3%	0.033
Smoking	2869 (36.9)	2508 (37.2)	361 (34.5)	0.056	36.9%	36.2%	0.015
PAD	279 (3.6)	250 (3.7)	29 (2.8)	0.051	3.6%	3.1%	0.028
CKD	1159 (14.9)	1029 (15.3)	130 (12.4)	0.084	14.9%	13.2%	0.049
Chronic Lung Disease	1888 (24.3)	1680 (24.9)	208 (19.9)	0.120	24.3%	23.8%	0.012
Home Oxygen	428 (5.5)	390 (5.8)	38 (3.6)	0.104	5.5%	5.5%	< 0.001
Prior Stroke	377 (4.8)	330 (4.9)	47 (4.5)	0.019	4.8%	4.0%	0.039
Liver Disease	726 (9.3)	627 (9.3)	99 (9.5)	0.007	9.3%	10.0%	0.024
Anemia	2938 (37.7)	2478 (36.8)	460 (44.0)	0.147	37.7%	38.3%	0.012
Thrombocytopenia	1053 (13.5)	893 (13.2)	160 (15.3)	0.060	13.5%	14.2%	0.020
Long-term Anticoagulation	981 (12.6)	858 (12.7)	123 (11.8)	0.060	12.6%	13.4%	0.024
Long-Term Antiplatelet	975 (12.5)	844 (12.5)	131 (12.5)	< 0.001	12.5%	11.6%	0.028
DNR Status	2281 (29.3)	2105 (31.2)	176 (16.8)	0.342	29.3%	29.5%	0.004
Palliative Care	1473 (18.9)	1371 (20.3)	102 (9.8)	0.297	18.9%	19.4%	0.013
Dementia	333 (4.3)	308 (4.6)	25 (2.4)	0.120	4.3%	4.1%	0.010
Malnutrition	1287 (16.5)	1127 (16.7)	160 (15.3)	0.038	16.5%	16.3%	0.005
Wheelchair-Bound	125 (1.6)	114 (1.7)	11 (1.1)	0.051	1.6%	1.6%	< 0.001
Obesity	1410 (18.1)	1154 (17.1)	256 (24.5)	0.183	18.1%	18.3%	0.005
Current or Prior Chemotherapy	842 (10.8)	721 (10.7)	121 (11.6)	0.029	10.8%	11.7%	0.028
Prior Irradiation	795 (10.2)	677 (10.0)	118 (11.3)	0.042	10.2%	10.7%	0.016
Chemotherapy-Associated Cytopenias	483 (6.2)	410 (6.1)	73 (7.0)	0.036	6.2%	6.7%	0.020
Current or Prior Immunosuppression	222 (2.9)	196 (2.9)	26 (2.5)	0.025	2.9%	3.5%	0.034
Hospitalization Characteristics, N (%)							
High-Risk PE	2511 (32.3)	2234 (33.1)	277 (26.5)	0.145	32.3%	34.2%	0.040
DVT	3698 (47.5)	3076 (45.6)	622 (59.5)	0.281	47.5%	48.6%	0.022
Respiratory Failure	4423 (56.8)	3808 (56.5)	615 (58.9)	0.049	56.8%	58.0%	0.024
Mechanical Ventilation	1528 (19.6)	1373 (20.4)	155 (14.8)	0.147	19.7%	21.9%	0.054
Systemic Thrombolysis	919 (11.8)	838 (12.4)	81 (7.8)	0.153	11.8%	13.9%	0.063
Large or Medium Hospital	6688 (85.9)	5757 (85.4)	931 (89.1)	0.111	85.9%	86.1%	0.006
Urban Teaching Hospital	6129 (78.7)	5295 (78.6)	834 (79.8)	0.030	78.8%	79.3%	0.012
Medicare	4881 (62.7)	4268 (63.3)	613 (58.7)	0.094	62.7%	60.6%	0.043
Medicaid	628 (8.1)	552 (8.2)	76 (7.3)	0.034	8.1%	8.2%	0.004
Private Insurance	1955 (25.1)	1647 (24.4)	308 (29.5)	0.115	25.1%	26.9%	0.041
Lowest Quartile Zip Code for Income	1858 (23.9)	1604 (23.8)	254 (24.3)	0.012	23.9%	23.6%	0.007

AF, atrial fibrillation; CAD, coronary artery disease; CBT, catheter based therapy; CDT, catheter-directed thrombolysis; CKD, chronic kidney disease; DNR, do-not-resuscitate; DVT, deep vein thrombosis; ECMO, extracorporeal membrane oxygenation; IPTW, inverse probability treatment weighting; MI, myocardial infarction; MT, mechanical thrombectomy; PAD, peripheral arterial disease; PE, pulmonary embolism; SD, standard deviation; SMD, standard mean difference; VTE, venous thromboembolism.

and 1442 (18.5%) had index hospitalization death and major bleeding, respectively. Additionally, 419 (5.4%) experienced GI, 122 (1.6%) IC and 654 (8.4%) post-procedure bleeding. Among 4402 of patients with intermediate- or high-risk PE who survived the index hospitalization, 1205 (27.4%) were readmitted for any reason, 266 (6.0%) for VTE or RHF, and 97 (2.2%) for major bleeding at 90 days, Supplemental Table 3. After IPTW, patients with CBT had lower rates of in-hospital death (21.7% vs 23.7%; OR 0.89, 95% CI 0.83–0.96) and 90-day all-cause readmission (22.2% vs 28.4%; HR 0.75, 95% CI 0.69–0.81), Table 2. Patients treated with CBT also had lower rates VTE or RHF readmission (3.6% vs 6.4%; HR 0.56, 95% CI 0.46–0.68) though with higher rates of index hospitalization major bleeding (20.1% vs 18.5%; OR 1.11, 95 CI 1.03–1.20) which was predominantly post-procedure bleeding (12.2% vs 8.0%; OR 1.60, 95% CI 1.44–1.78), Supplemental Table 4.

Prior to IPTW, a total of 714 readmissions occurred in 246 (23.5%) patients managed with CBT and 1623 readmissions occurred in 4730 (24.0%) patients without CBT. Additionally, 54 VTE or RHF-related readmissions occurred in 48 (4.6%) patients with CBT and 389 occurred in 346 (5.6%) patients without CBT, and 33 bleeding-related readmissions occurred in 28 (2.7%) patients with CBT and 172 bleeding-related readmissions occurred in 146 (2.2%) patients without CBT. After IPTW negative binomial regression, CBT was associated with lower rates of all-cause recurrent readmissions (IRR 0.91, 95% CI

Table 2
Cox Proportional Hazards and Negative Binomial Regression Models for Risk of Outcomes of Patients Managed with CBT Compared with No CBT.

	Unweighted	IPTW
In-Hospital Outcomes	OR (95% CI)	OR (95% CI)
Death	0.45 (0.38–0.55)	0.89 (0.83–0.96)
Major Bleeding [a]	1.11 (0.94–1.31)	1.11 (1.03–1.20)
Gastrointestinal Bleeding	0.89 (0.66–1.20)	0.89 (0.77–1.02)
Intracranial Bleeding	0.70 (0.38–1.28)	0.95 (0.73–1.22)
Post-Procedural Bleeding	1.69 (1.37–2.07)	1.60 (1.44–1.78)
Transfusion	0.93 (0.74–1.16)	0.90 (0.81–1.01)
90-Day Readmissions	HR (95% CI)	HR (95% CI)
Any Readmission	0.70 (0.59–0.84)	0.75 (0.69–0.81)
Recurrent Readmissions	IRR (95% CI)	IRR (95% CI)
Any readmission	0.99 (0.83–1.17)	0.91 (0.84–0.99)

CI, confidence interval; HR, hazard ratio; IRR, incidence rate ratio; IPTW, inverse-probability treatment weighting; OR, odds ratio; RHF, right heart failure; VTE, venous thromboembolism.
[a] Composite of index hospitalization gastrointestinal, intracranial, or post-procedural bleeding or transfusion of blood products.

0.84–0.99) and VTE or RHF recurrent readmission (IRR 0.65, 95% CI 0.55–0.77) but not bleeding readmission (IRR 1.15, 95% CI 0.91–1.44), Table 2. Cumulative incidence curves after IPTW of all-cause, VTE or RHF, and bleeding 90-day readmission are shown in Fig. 1.

3.2. Baseline characteristics and outcomes of patients treated with cbt and systemic thrombolysis

A total of 1802 patients were treated with either systemic thrombolysis (838; 46.5%) or CBT (964; 53.5%). Prior to IPTW, patients treated with CBT were more likely to have primary brain tumor or metastasis to brain (9.3% vs 3.8%, SMD = 0.224) and less likely to have high-risk PE (25.2% vs 57.4%, SMD = 0.692), cardiac arrest (5.9% vs 26.3%, SMD = 0.578), cardiogenic shock (18.7% vs 35.3%, SMD = 0.381) and need mechanical ventilation (13.4% vs 37.8%, SMD = 0.582). After IPTW, variables were well balanced between groups (Table 3).

After IPTW, there was no difference in in-hospital death (20.2% vs 21.7%; OR 0.92 95% CI 0.78–1.08), 90-day all-cause (20.9% vs 24.1%; HR 0.86, 95% CI 0.72–1.03) and VTE or RHF related readmissions (4.2% vs 4.6%; HR 1.12, 95% CI 0.75–1.68) between patients treated with CBT and systemic thrombolysis (Supplemental Table 3). Additionally, there was an association between lower risk of major bleeding (20.8% vs 24.8%; OR 0.80, 95% CI 0.68–0.94), including intracranial bleeding (1.0% vs 2.5%; OR 0.54, 95% CI 0.32–0.94) during index hospitalization among patients managed with CBT compared with systemic thrombolysis. However, there was an increase in 90-day bleeding-related readmissions with CBT when compared with systemic thrombolysis (2.5% vs 0.9%; HR 2.75, 95% CI 1.31–5.77), Supplemental Table 5. Moreover, 42.4% of the bleeding readmissions in the CBT group were due to post-procedure bleeding compared with 15.4% of the bleeding readmissions in the systemic thrombolysis group. After IPTW negative binomial regression, there no difference in rates of all-cause (IRR 1.08, 95% CI 0.91–1.27), VTE or RHF (IRR 1.05, 95% CI 0.74–1.51), and bleeding related (IRR 1.41, 95% CI 0.89–2.23) recurrent readmissions.

3.3. Baseline characteristics and outcomes of patients treated with CDT and MT

Among patients managed with CBT, 959 patients were managed with either CDT (623; 65.0%) or MT (336; 35%). Prior to IPTW, patients managed with MT had higher rates of solid cancer (88.4% vs 79.9%, SMD = 0.234), primary brain tumor or metastasis to brain (19.6% vs 3.7%, SMD = 0.512), metastatic cancer (47.9% vs 39.5%, SMD = 0.170), high-risk PE (36.3% vs 18.9%, SMD = 0.397), cardiac arrest (10.1% vs 5.3%, SMD = 0.181), cardiogenic shock (26.8% vs 13.5%, SMD = 0.336), and receive systemic thrombolysis (14.0% vs 4.5%, SMD = 0.332). After IPTW, variables were well-balanced between groups, Table 4.

After IPTW, there was no difference in index hospitalization death (12.4% vs 14.7%; OR 0.83, 95% CI 0.51–1.35) or major bleeding (21.6% vs 18.7%; OR 1.20, 95% CI 0.78–1.83) between patients managed with MT alone compared with CDT alone, Supplemental Table 3. There was also no difference in all-cause (20.7% vs 22.7%; HR 0.90, 95% CI 0.73–1.09), VTE or RHF related (7.5% vs 3.3%; HR 1.34, 95% CI 0.84–2.13), and bleeding related readmission (3.1% vs 2.9%; HR 0.77, 95% CI 0.44–1.36). After IPTW negative binomial regression, there was no association between CBT and rates of all-cause (IRR 0.86, 95% CI 0.70–1.07) and bleeding related recurrent readmission (IRR 0.75, 95% CI 0.41–1.37), however there was an associated with increased rates of VTE or RHF related recurrent readmission (IRR 1.63, 95% CI 1.10–2.42). Logistic, Cox proportional hazards, and negative binomial regression modeling outcomes of CBT versus systemic thrombolysis and CDT versus MT are shown in Table 5. Cumulative incidence curves after IPTW of all-cause, VTE or RHF related, and bleeding related 90-day readmission in patients treated with systemic thrombolysis compared with CBT and MT versus CDT are shown in Fig. 2.

4. Discussion

In this retrospective, observational cohort study, among patients with cancer and intermediate- or high-risk PE, management with CBT was associated with lower risk of in-hospital death and 90-day readmission. Additionally, CBT was also associated with decreased risk of VTE or RHF-related readmission at the expense of increased risk of index hospitalization major bleeding primarily driven by post-procedural

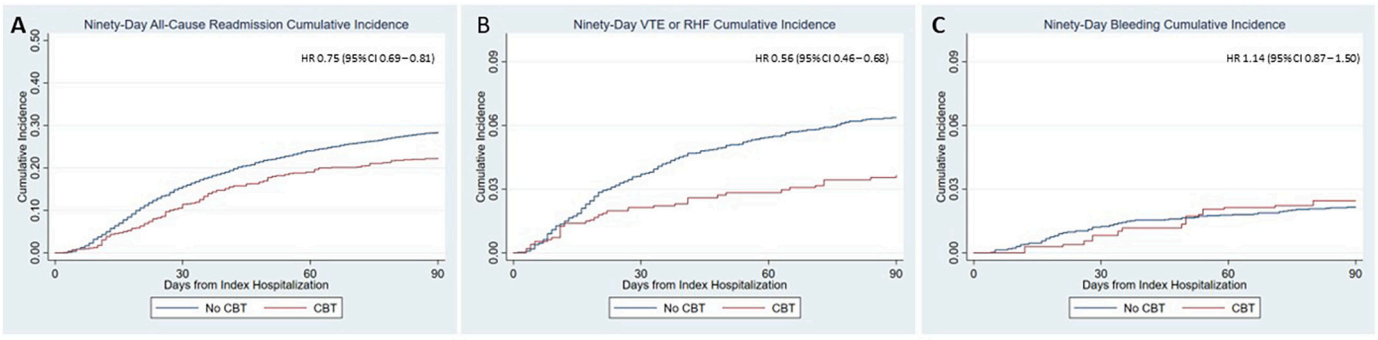

Fig. 1. Cumulative Incidence Curve of Readmission Outcomes After IPTW of Patients with Intermediate- or High-Risk PE Treated with versus without CBT.
Cumulative incidence curves of 90-day all-cause (A), VTE or RHF-related (B), and bleeding (C) readmissions among patients with cancer and intermediate- or high-risk PE treated with versus without CBT after inverse-probability treatment weighting.

Table 3
Baseline Unweighted and IPTW Characteristics of Patients with Intermediate or High-Risk PE Treated with CBT Compared with Systemic Thrombolysis.

	Unweighted				Inverse-Probability Treatment Weighting		
	All Patients $N = 1802$	Systemic Thrombolysis $N = 838$	CBT $N = 964$	SMD	Systemic Thrombolysis	CBT	SMD
Age, years (SD)	66.3 (11.6)	65.9 (11.9)	66.8 (11.3)	0.076	66.5 (11.5)	66.4 (11.3)	0.004
Female Sex, N (%)	951 (52.8)	450 (53.7)	501 (52.0)	0.034	53.0%	52.8%	0.004
Cancer Characteristics, N (%)							
Solid Cancer	1474 (81.8)	672 (80.2)	802 (83.2)	0.078	82.2%	82.6%	0.011
Hematologic Cancer	362 (20.1)	187 (22.3)	175 (18.2)	0.102	19.8%	19.4%	0.010
Brain Tumor or Metastasis	122 (6.8)	32 (3.8)	90 (9.3)	0.224	8.0%	7.0%	0.038
Metastatic Cancer	748 (41.5)	340 (40.6)	408 (42.3)	0.035	41.9%	42.3%	0.008
Khorana High or Intermediate Risk	774 (43.0)	377 (45.0)	397 (41.2)	0.077	42.9%	44.0%	0.022
Co-Morbidities, N (%)							
Hypertension	1120 (62.2)	527 (62.9)	593 (61.5)	0.029	63.3%	63.3%	< 0.001
Prior VTE	210 (11.7)	88 (10.5)	122 (12.7)	0.069	12.1%	11.8%	0.009
CHF	476 (26.4)	224 (26.7)	252 (26.1)	0.014	27.7%	28.5%	0.018
DM	499 (27.7)	243 (29.0)	256 (26.6)	0.054	27.5%	26.7%	0.018
AF	298 (16.5)	149 (17.8)	149 (15.5)	0.062	15.4%	15.8%	0.011
CAD	578 (32.1)	248 (29.6)	330 (34.2)	0.099	32.2%	32.6%	0.009
Smoking	601 (33.4)	262 (31.3)	339 (35.2)	0.083	34.0%	34.0%	< 0.001
PAD	58 (3.2)	31 (3.7)	27 (2.8)	0.051	3.0%	3.1%	0.006
CKD	232 (12.9)	112 (13.4)	120 (12.4)	0.030	13.0%	13.2%	0.006
Chronic Lung Disease	355 (19.7)	162 (19.3)	193 (20.0)	0.018	19.8%	20.3%	0.012
Home Oxygen	57 (3.2)	24 (2.9)	33 (3.4)	0.029	2.9%	3.0%	0.006
Prior Stroke	79 (4.4)	34 (4.1)	45 (4.7)	0.029	4.9%	4.4%	0.024
Liver Disease	221 (12.3)	134 (16.0)	87 (9.0)	0.213	12.3%	12.6%	0.009
Anemia	769 (42.7)	346 (41.3)	423 (43.9)	0.053	42.5%	43.1%	0.012
Thrombocytopenia	279 (15.5)	129 (15.4)	150 (15.6)	0.006	15.4%	15.3%	0.003
Long-term Anticoagulation	195 (10.8)	84 (10.0)	111 (11.5)	0.048	11.5%	11.0%	0.016
Long-Term Antiplatelet	222 (12.3)	102 (12.2)	120 (12.4)	0.006	12.1%	11.7%	0.012
DNR Status	381 (21.1)	220 (26.3)	161 (16.7)	0.235	21.6%	21.3%	0.007
Palliative Care	246 (13.7)	152 (18.1)	94 (9.8)	0.241	14.2%	13.9%	0.009
Dementia	43 (2.4)	20 (2.4)	23 (2.4)	< 0.001	2.5%	2.4%	0.006
Malnutrition	265 (14.7)	120 (14.3)	145 (15.0)	0.020	13.5%	14.9%	0.040
Wheelchair-Bound	24 (1.3)	14 (1.7)	10 (1.0)	0.061	1.2%	1.3%	0.009
Obesity	428 (23.8)	191 (22.8)	237 (24.6)	0.042	24.5%	24.6%	0.002
Current or Prior Chemotherapy	216 (12.0)	105 (12.5)	111 (11.5)	0.031	12.1%	12.0%	0.003
Prior Irradiation	190 (10.5)	78 (9.3)	112 (11.6)	0.075	9.3%	10.0%	0.024
Chemotherapy-Associated Cytopenias	115 (6.4)	48 (5.7)	67 (7.0)	0.053	6.9%	6.6%	0.012
Current or Prior Immunosuppression	40 (2.2)	16 (1.9)	24 (2.5)	0.041	2.1%	2.4%	0.020
Hospitalization Characteristics, N (%)							
High-Risk PE	724 (40.2)	481 (57.4)	243 (25.2)	0.692	39.5%	39.1%	0.008
Cardiac Arrest	277 (15.4)	220 (26.3)	57 (5.9)	0.578	15.1%	13.8%	0.037
Cardiogenic Shock	476 (26.4)	296 (35.3)	180 (18.7)	0.381	26.0%	26.1%	0.002
Other Shock	358 (19.9)	233 (27.8)	125 (13.0)	0.374	19.5%	19.4%	0.003
DVT	987 (54.8)	408 (48.7)	579 (60.1)	0.230	55.4%	56.3%	0.018
Respiratory Failure	1123 (62.3)	565 (67.4)	558 (57.9)	0.197	63.9%	62.6%	0.027
Mechanical Ventilation	446 (24.8)	317 (37.8)	129 (13.4)	0.582	24.0%	22.7%	0.031
Large or Medium Hospital	1623 (90.1)	763 (91.1)	860 (89.2)	0.064	89.7%	89.6%	0.003
Urban Teaching Hospital	1476 (81.9)	705 (84.1)	771 (80.0)	0.107	82.1%	82.0%	0.003
Medicare	1056 (58.6)	482 (57.5)	574 (59.5)	0.041	58.7%	59.5%	0.016
Medicaid	138 (7.7)	69 (8.2)	69 (7.2)	0.038	7.2%	7.4%	0.008
Private Insurance	527 (29.2)	252 (30.1)	275 (28.5)	0.035	28.7%	28.5%	0.004
Lowest Quartile Zip Code for Income	427 (23.7)	197 (23.5)	230 (23.9)	0.009	23.5%	24.2%	0.016

Abbreviations defined in Table 1.

bleeding. Our study also suggests that CBT was associated with decreased index hospitalization major bleeding when compared with systemic thrombolysis. There was no significant difference in index hospitalization death or major bleeding and 90-day readmissions between patients managed with either CDT or MT.

Pulmonary embolism is common among patients with cancer and can be a potentially life-threatening complication that warrants urgent intervention [25]. Patients with cancer are often excluded from interventional device trials and therefore data are sparse with regards to outcomes of CBT in patients with PE and cancer [26]. Among the general population, large randomized trials examining the efficacy and safety of CBT for the treatment of PE are lacking. However small single-armed trials and registry studies have suggested hemodynamic improvement with CBT and multiple randomized clinical trials are currently underway including PEERLESS (NCT05111613), HI-PEITHO (NCT04790370), STORM-PE (NCT05684796), and PE-TRACT (NCT05591118) [13–17,27]. However, these trials exclude patients with cancer and therefore randomized data investigating the efficacy and safety of CBT in patients with cancer, particularly those with metastatic cancer (which make up almost 50% of our cohort), will be lacking for the foreseeable future. Though case reports have described successful use of CBT in cancer-associated PE, data on outcomes are sparse [28,29]. A prior study of patients with cancer admitted with intermediate- or high-risk PE found an association between CBT and lower in-hospital mortality similar to our study [30]. However, this prior study did not evaluate readmissions or potential short- and intermediate-term outcomes. Notably our study suggests an association between lower risk of 90-day VTE or RHF readmission after index PE hospitalization among those managed with CBT which may allude to a potential short- or intermediate-term benefit post-hospitalization in this patient population. This hypothesis will need to be confirmed in prospective, randomized studies. However, there was an association with increased risk

Table 4
Baseline Unweighted and IPTW Characteristics of Patients with Intermediate or High-Risk PE Treated with CDT Compared with MT.

	Unweighted				Inverse-Probability Treatment Weighting		
	All Patients $N = 959$	CDT $N = 623$	MT $N = 336$	SMD	CDT	MT	SMD
Age, years (SD)	66.4 (11.5)	66.3 (11.8)	66.6 (11.0)	0.026	66.1 (11.9)	66.2 (11.0)	0.003
Female Sex, N (%)	501 (52.2)	325 (52.2)	176 (52.4)	0.004	53.3%	50.4%	0.058
Cancer Characteristics, N (%)							
Solid Cancer	795 (82.9)	498 (79.9)	297 (88.4)	0.234	83.7%	85.2%	0.041
Hematologic Cancer	173 (18.0)	130 (20.9)	43 (12.8)	0.218	17.0%	15.4%	0.043
Brain Tumor or Metastasis	89 (9.3)	23 (3.7)	66 (19.6)	0.512	12.0%	9.6%	0.077
Metastatic Cancer	407 (42.4)	246 (39.5)	161 (47.9)	0.170	41.1%	43.7%	0.053
Khorana High or Intermediate Risk	401 (41.8)	247 (39.6)	154 (45.8)	0.126	40.5%	46.1%	0.113
Co-Morbidities, N (%)							
Hypertension	584 (60.9)	387 (62.1)	197 (58.6)	0.072	59.7%	59.4%	0.006
Prior VTE	125 (13.0)	80 (12.8)	45 (13.4)	0.018	14.1%	13.7%	0.012
CHF	246 (25.7)	145 (23.3)	101 (30.1)	0.154	25.9%	23.6%	0.053
DM	256 (26.7)	163 (26.2)	93 (27.7)	0.034	28.7%	25.8%	0.065
AF	149 (15.5)	94 (15.1)	55 (16.4)	0.036	16.3%	16.0%	0.008
CAD	324 (33.8)	209 (33.5)	115 (34.2)	0.015	31.5%	34.2%	0.058
Smoking	335 (34.9)	223 (35.8)	112 (33.3)	0.053	33.3%	33.0%	0.006
PAD	23 (2.4)	11 (1.8)	12 (3.6)	0.111	1.9%	2.0%	0.007
CKD	117 (12.2)	74 (11.9)	43 (12.8)	0.027	13.9%	11.9%	0.060
Chronic Lung Disease	195 (20.3)	129 (20.7)	66 (19.6)	0.027	18.1%	18.5%	0.010
Home Oxygen	35 (3.6)	21 (3.4)	14 (4.2)	0.042	3.2%	3.5%	0.017
Prior Stroke	43 (4.5)	31 (5.0)	12 (3.6)	0.069	4.1%	4.6%	0.025
Liver Disease	83 (8.7)	51 (8.2)	32 (9.5)	0.046	8.5%	10.2%	0.058
Anemia	417 (43.5)	254 (40.8)	163 (48.5)	0.155	45.6%	41.1%	0.091
Thrombocytopenia	144 (15.0)	93 (14.9)	51 (15.2)	0.008	16.0%	18.5%	0.066
Long-term Anticoagulation	116 (12.1)	74 (11.9)	42 (12.5)	0.018	11.4%	11.9%	0.016
Long-Term Antiplatelet	122 (12.7)	94 (15.1)	28 (8.3)	0.213	11.9%	12.7%	0.024
DNR Status	155 (16.2)	96 (15.4)	59 (17.6)	0.059	17.8%	17.3%	0.013
Palliative Care	89 (9.3)	53 (8.5)	36 (10.7)	0.075	9.9%	8.3%	0.056
Dementia	21 (2.2)	14 (2.2)	7 (2.1)	0.007	2.0%	1.9%	0.007
Malnutrition	139 (14.5)	92 (14.8)	47 (14.0)	0.023	14.7%	12.5%	0.064
Wheelchair-Bound	11 (1.1)	6 (1.0)	5 (1.5)	0.045	1.2%	1.2%	< 0.001
Obesity	235 (24.5)	167 (26.8)	68 (20.2)	0.156	25.0%	24.0%	0.023
Current or Prior Chemotherapy	115 (12.0)	76 (12.2)	39 (11.6)	0.019	13.0%	12.0%	0.030
Prior Irradiation	111 (11.6)	65 (10.4)	46 (13.7)	0.101	12.6%	10.7%	0.059
Chemotherapy-Associated Cytopenias	66 (6.9)	41 (6.6)	25 (7.4)	0.031	6.5%	7.4%	0.035
Current or Prior Immunosuppression	23 (2.4)	11 (1.8)	12 (3.6)	0.111	2.3%	2.0%	0.021
Hospitalization Characteristics, N (%)							
High-Risk PE	240 (25.0)	118 (18.9)	122 (36.3)	0.397	27.2%	25.7%	0.034
Cardiac Arrest	67 (7.0)	33 (5.3)	34 (10.1)	0.181	7.3%	6.4%	0.036
Cardiogenic Shock	174 (18.1)	84 (13.5)	90 (26.8)	0.336	19.0%	19.1%	0.003
Other Shock	115 (12.0)	54 (8.7)	61 (18.2)	0.281	12.2%	12.5%	0.009
DVT	568 (59.2)	368 (59.1)	200 (59.5)	0.008	58.3%	57.9%	0.008
Respiratory Failure	555 (57.9)	348 (55.9)	207 (61.6)	0.116	57.8%	54.1%	0.075
Mechanical Ventilation	139 (14.5)	78 (12.5)	61 (18.2)	0.159	15.4%	13.7%	0.048
Systemic Thrombolysis	75 (7.8)	28 (4.5)	47 (14.0)	0.332	9.0%	8.7%	0.011
Large or Medium Hospital	865 (90.2)	560 (89.9)	305 (90.8)	0.030	90.9%	88.4%	0.082
Urban Teaching Hospital	765 (79.8)	489 (78.5)	276 (82.1)	0.091	79.6%	79.4%	0.005
Medicare	559 (58.3)	363 (58.3)	196 (58.3)	< 0.001	57.1%	53.9%	0.064
Medicaid	72 (7.5)	44 (7.1)	28 (8.3)	0.045	7.4%	8.0%	0.023
Private Insurance	283 (29.5)	184 (29.5)	99 (29.5)	< 0.001	30.8%	32.3%	0.032
Lowest Quartile Zip Code for Income	244 (25.4)	163 (26.2)	81 (24.1)	0.048	25.5%	23.7%	0.042

Abbreviations defined in Table 1.

of index hospitalization bleeding among patients managed with CBT that was predominantly driven by post-procedural bleeding.

Patients with cancer are at increased risk of bleeding with anticoagulation and systemic thrombolysis [8,9]. Systemic thrombolysis is indicated for PE with hemodynamic compromise though the risk of bleeding, especially among patients with cancer, is a concern. Studies have described lower use of systemic thrombolysis among patients with cancer and VTE [9,31]. In one meta-analysis of patients with PE, CDT was associated with lower risk of in-hospital mortality and bleeding compared with systemic thrombolysis [32]. Other studies using administrative databases have also shown treatment with CDT to be associated with decreased in-hospital mortality and bleeding compared with systemic thrombolysis [33–35]. These studies suggest that CBT may offer a safer alternative to systemic thrombolysis among patients with cancer and PE, who are at high risk of bleeding. Prior to our study, there are limited data on bleeding and outcomes of patients with cancer treated with CBT compared with systemic thrombolysis. Our study suggests that though there was no statistically significant association between CBT and index hospitalization death, there was an association with decreased risk of index hospitalization major bleeding including decreased intracranial hemorrhage compared with systemic thrombolysis. These results are similar to a recent meta-analysis of patients without cancer with acute PE which showed a decreased risk of intracranial bleed among patients treated with CDT compared with systemic thrombolysis [36]. However, in our study there was an increased risk of 90-day readmission for bleeding among patients with CBT that was largely driven by post-procedural bleeding. These results suggest that CBT may be safe in patients with cancer and intermediate- or high-risk PE though clinicians should be mindful of post-procedural bleeding and complications in this population.

Catheter-based therapies include both CDT and MT and data on head-to-head comparisons of the two modalities are currently lacking

Table 5
Cox Proportional Hazards and Negative Binomial Regression Models for Risk of Outcomes.

	Risk of CBT versus Systemic Thrombolysis		Risk of MT versus CDT	
	Unweighted	IPTW	Unweighted	IPTW
In-Hospital Outcomes	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Death	0.29 (0.23–0.37)	0.92 (0.78–1.08)	1.52 (1.04–2.23)	0.83 (0.51–1.35)
Major Bleeding [a]	0.63 (0.50–0.78)	0.80 (0.68–0.94)	2.12 (1.53–2.94)	1.20 (0.78–1.83)
Gastrointestinal Bleeding	0.68 (0.46–1.00)	0.91 (0.69–1.20)	1.51 (0.83–2.77)	0.94 (0.62–1.43)
Intracranial Bleeding	0.41 (0.19–0.87)	0.54 (0.32–0.94)	3.77 (1.13–12.63)	2.27 (0.82–6.29)
Post-Procedural Bleeding	0.91 (0.69–1.21)	1.10 (0.90–1.35)	1.74 (1.18–2.57)	1.15 (0.88–1.50)
Transfusion	0.50 (0.37–0.66)	0.63 (0.52–0.77)	1.69 (1.07–2.65)	1.26 (0.92–1.72)
90-Day Readmissions	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Any Readmission	0.89 (0.69–1.15)	0.86 (0.72–1.03)	0.94 (0.70–1.25)	0.90 (0.73–1.09)
Recurrent Readmissions	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)
Any Readmission	1.27 (1.01–1.61)	1.08 (0.91–1.27)	1.16 (0.84–1.59)	0.86 (0.70–1.07)

Abbreviations defined in Table 2.
[a] Composite of index hospitalization gastrointestinal, intracranial, or post-procedural bleeding or transfusion of blood products.

though prospective, randomized, trials are currently underway. Although CDT in theory minimizes systemic thrombolysis administration via local delivery of thrombolytic agents, there is a concern of some systemic exposure. Indeed, in a meta-analysis, CDT was associated with decreased mortality than anticoagulation alone but higher major bleeding and a non-statistically significant trend towards increased intracranial hemorrhage [36]. In a nationwide study of the NRD of patients with high-risk PE, in-hospital death, intracranial bleeding and non-intracranial bleeding outcomes were similar between MT and CDT [37]. However, patients with cancer are at increased risk of bleeding, particularly intracranial bleeding, due to metastatic disease [38]. Our study found no association between in-hospital death and intracranial bleeding among patients with MT compared with CDT. There was also no difference in 90-day readmission outcomes, including VTE or RHF readmissions. However, there was an association between MT and total readmissions for VTE or RHF after IPTW negative binomial regression. Given that patients with MT had higher risk factors for bleeding and interruptions in anticoagulation post-hospitalization may explain these findings. However, given that medication use data, including post-hospitalization, is unavailable in the NRD, further studies are needed to test this hypothesis.

Our study has limitations that should be considered when interpreting our results. Given data in the NRD are gathered from administrative ICD-10 codes, granular details including vital signs, and laboratory values are unavailable. Data on medication administration during and after hospitalization, including anticoagulation, are not available and therefore may represent unmeasured confounding. Additionally, cancer-specific characteristics including cancer staging, prior or current treatment, and extent of cancer at the time of admission are unavailable. The NRD also does not record race or ethnicity, which limits analysis on the impact of race or ethnicity on outcomes and are a source of potential confounding. The classification of intermediate- and high-risk PE are based on ICD-10 codes, however given that laboratory and imaging findings of right ventricular strain are unavailable, it is possible that some patients may not have been classified accurately or that some patients may not have been included in our analysis who otherwise would have been if those variables were available. Additionally, it is possible that patients initially presented with intermediate-risk PE and then developed high-risk features during their hospitalization and therefore classified as high-risk. This may have led to an overrepresentation of high-risk patients in our study. Nonetheless, high-

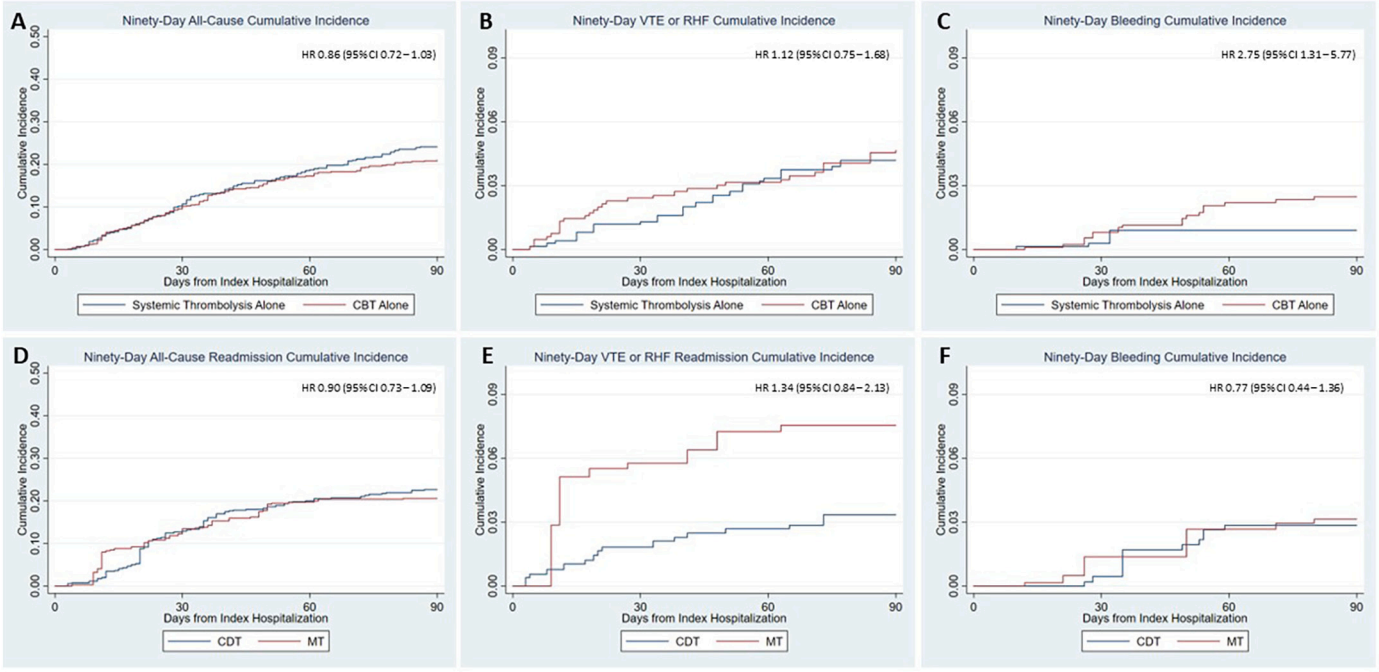

Fig. 2. Cumulative Incidence of 90-Day Readmission Outcomes of Secondary Analyses.
Cumulative incidence curves depicting 90-day all-cause (A), VTE or RHF-related (B), and bleeding-related readmissions (C) among patients treated with CBT or systemic thrombolysis. Kaplan-Meier cumulative incidence curves depicting 90-day all-cause (D), VTE or RHF-related (E), and bleeding-related readmissions (F) among patients treated with CDT or MT.

risk PE in our study had increased in-hospital mortality compared with intermediate-risk PE consistent with what would be expected for those cohorts. Given the procedure data in the NRD is captured via ICD-10 codes, data on specific CBT devices and techniques are unavailable and merit further investigation in more granular datasets. Additionally, while we attempted to account for frailty using a validated risk score, all patient factors influencing decision for CBT treatment are not captured in the NRD, and therefore our current analysis cannot rule out unmeasured confounders despite statistical adjustments.

5. Conclusions

Our study suggests that among patients with cancer hospitalized with intermediate- or high-risk PE, treatment with CBT was associated with a reduced risk of in-hospital death, and 90-day all-cause and VTE or RHF-related readmissions. Moreover, treatment with CBT was associated with a lower risk of major bleeding, including intracranial bleeding, compared with systemic thrombolysis while no difference in outcomes was evident between MT and CDT groups. Given the burden of PE in patients with cancer, it is important this patient population is included in prospective studies and clinical trials of CBT in PE and such trials are necessary to confirm our findings.

5.1. Impact on daily practice

Catheter-based therapies are increasingly used for reperfusion in patients with acute PE. Patients with cancer are at high risk of PE though invasive interventions are often deferred in this patient population. This study suggests that CBT is associated with reduced risk of death and readmissions among patients with cancer and intermediate- or high-risk PE though inclusion of cancer patients in prospective clinical trials is needed to confirm these findings.

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CRediT authorship contribution statement

Orly Leiva: Conceptualization, Formal analysis, Investigation, Methodology, Software, Writing – original draft, Writing – review & editing. **Eric H. Yang:** Writing – review & editing. **Rachel P. Rosovsky:** Conceptualization, Writing – review & editing. **Carlos Alviar:** Investigation, Writing – review & editing. **Sripal Bangalore:** Conceptualization, Investigation, Methodology, Project administration, Resources, Supervision, Writing – review & editing.

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