

Association of Acute Venous Thromboembolism With In-Hospital Outcomes of Coronary Artery Bypass Graft Surgery

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Background—While venous thromboembolism (VTE) prophylaxis is a strong recommendation after most surgeries, it is controversial in cardiac surgeries such as coronary artery bypass grafting (CABG), because of perceived low VTE incidence and increased bleeding risk. Prior studies may not have been adequately powered to study outcomes of VTE in this population. We sought to investigate the postoperative incidence and outcomes of CABG patients using a large national inpatient database.

Methods and Results—We utilized the 2013 to 2014 National Inpatient Sample to identify all patients >18 years of age who underwent CABG (without concomitant valvular procedures), and had VTE during the hospital stay. We then compared clinically relevant outcomes in patients with and without VTE. We identified 331 950 CABG procedures. Of these, 1.3% (n=4205) had VTE. Patients with VTE were more likely to be older (mean 67.2 ± 10.4 years versus 65.2 ± 10.4 years, $P < 0.001$). VTE was associated with higher incidence of inpatient mortality (6.8% versus 1.7%; adjusted odds ratio 1.92 [95% CI 1.40–2.65]; $P < 0.001$) and complications. VTE was also associated with higher cost (mean \pm SE \$81 995 \pm \$923 versus \$48 909 \pm \$55) and longer length of stay (mean \pm SE 17.06 \pm 0.16 days versus 8.52 \pm 0.01 days).

Conclusions—Our analysis of >330 000 CABG procedures suggests that while postoperative VTE after CABG is rare, it is associated with increased morbidity and mortality. Randomized controlled trials are needed to identify optimal strategies for VTE prophylaxis in these patients. (*J Am Heart Assoc.* 2019;8:e013246. DOI: 10.1161/JAHA.119.013246.)

Key Words: coronary artery bypass • coronary artery bypass graft surgery • venous thromboembolism • venous thrombosis

Venous thromboembolism (VTE) is a feared complication in patients undergoing surgical procedures and is associated with significant morbidity, mortality, and hospital

costs.^{1–3} As a result, pharmacological prophylaxis against VTE is strongly recommended in the perioperative period for most surgical patients, and is a benchmark used to evaluate quality of care.^{4,5}

However, for patients undergoing cardiac surgeries, including coronary artery bypass grafting (CABG), VTE prophylaxis is controversial. The incidence of perioperative VTE in CABG patients reported in the literature is low ($\approx 1\%$).^{6–8} Unfortunately, a majority of the current evidence regarding the incidence and outcomes of VTE, and optimal strategies for VTE prophylaxis in patients undergoing CABG, is from studies with limited sample sizes, and is of moderate-to-low quality as acknowledged by guidelines.^{9,10} Moreover, current evidence regarding benefit of prophylaxis versus bleeding complications is inconclusive.¹¹

Given the volume of patients undergoing CABG, and the significant adverse outcomes associated with perioperative VTE, we believe this issue needs further attention, and that a more robust understanding of the impact of VTE in the perioperative CABG period may help guide clinical management. In this study, we used a large national inpatient database to investigate the incidence and outcomes of perioperative VTE in patients undergoing CABG.

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Accompanying Tables S1 through S6 are available at <https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.013246>

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Clinical Perspective

What Is New?

- This is the largest study to investigate the incidence and outcomes of venous thromboembolism (VTE) in patients undergoing coronary artery bypass grafting (CABG).
- The incidence of VTE was low, but it was associated with increased morbidity and mortality, length of stay, and hospital costs in patients undergoing CABG.

What Are the Clinical Implications?

- Our results urge clinicians to acknowledge that while perioperative VTE after CABG is rare, it is associated with significant morbidity and mortality. Appropriately selected patients may benefit from VTE prophylaxis.
- However, further work is needed to identify optimal practices for VTE prophylaxis in patients undergoing cardiac surgeries, including the choice of pharmacologic agent for pharmacological prophylaxis.

Methods

Data Source

The data that support the findings of this study are available upon reasonable request. We obtained data from the 2013 to 2014 National Inpatient Sample (NIS) for this analysis. The NIS is the largest all-payer inpatient database in the United States. With about 8 million records per year, it includes a sample of >94% of discharges from all US hospitals, excluding federal facilities, and long-term acute care and rehabilitation facilities.¹² Discharge weights are provided to allow for production of national estimates. Given the de-identified nature of NIS data, our study was considered exempt from our institution's Institutional Review Board. All analyses in our study are weighted using provided discharge weights unless stated otherwise.

Study Design

We used the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes to identify all patients ≥ 18 years of age who underwent CABG during the study period (n=401 075). We also identified patients undergoing OPCAB (off-pump coronary artery bypass grafting) using relevant *ICD-9-CM* codes for cardiopulmonary bypass support during surgery. We excluded hospitalizations with concomitant valvular procedures (n=69 125). Patients with acute deep vein thrombosis (DVT) and/or pulmonary embolism (PE) were identified using their respective *ICD-9-CM* codes (see Tables S1 through S3 for list of *ICD-9-CM* codes used in this study).

We excluded patients with a diagnosis of thromboembolism of superficial veins.

Patients were divided into 2 groups: those with or without VTE. For baseline characteristics, we used patient-level characteristics such as age, sex, race, insurance status, and relevant comorbidities—history of prior VTE, alcohol abuse, malignancy (solid tumor and metastatic), anemias, heart failure, chronic pulmonary disease, coagulopathy, depression, diabetes mellitus, hypertension, liver disease, fluid and electrolyte disorders, neurological disorders, obesity, peripheral vascular disorders, chronic renal failure, valvular disease, smoking, and dyslipidemia. These comorbidities were identified using their respective *ICD-9-CM* codes (Table S2). Hospital-level characteristics included hospital bed size, location and teaching status, and region.

Outcomes

Our primary outcome of interest was all-cause in-hospital mortality. Secondary outcomes were incidence of acute kidney injury (AKI), AKI requiring dialysis (AKI-D), stroke, acute respiratory failure, bleeding, hospital costs, and length of stay. Complications were identified using their respective *ICD-9-CM* codes (Table S3).

Statistical Analysis

All statistical analyses were conducted using survey-specific techniques accounting for the stratified and multilevel nature of the data.¹³ Categorical data are provided as counts and percentages, and continuous data are provided as means with standard deviations or standard errors. Cost of stay was calculated by multiplying the total charges for stay by the provided cost-to-charge ratios. Because length of stay and cost were non-normally distributed, they were log-transformed for all analyses, and then back-transformed for reporting. Costs were inflation-adjusted for 2018 using Consumer Price Index data provided by the US Department of Labor.

All covariates had complete information except primary expected payer (0.2% missing) and race (6.5% missing). For primary expected payer, the missing values were replaced with the dominant category. For race, the missing value was treated as a separate category in regression models. This approach has been used by prior studies utilizing the NIS.^{14,15} Categorical variables were compared with the Pearson χ^2 test, while all continuous variables were compared with the Student *t* test. Complex-samples logistic or linear regression models adjusting for demographics, comorbidities, and hospital characteristics were used to compare in-hospital outcomes. In an additional analysis, we also studied outcomes among patients with PE (with or without DVT), and patients

with DVT only (without PE). Finally, we also assessed the influence of OPCAB on incidence of VTE, and on in-hospital mortality.

Unadjusted and adjusted odds ratios (aOR) are presented with 95% CIs. Statistical significance for *P* values was set at <0.05. All statistical analyses were done using the Statistical Package for Social Sciences version 25 (SPSS; IBM, Armonk, NY).

Results

During the study period, there were 331 950 weighted hospitalizations, of which 69 225 (20.9%) were OPCAB. Of the overall cohort, 1.3% (n=4205) had a concomitant diagnosis of VTE (0.4% [n=1205] with PE and 0.9% [n=2940] with only DVT [without PE]).

Compared with patients without VTE, patients with VTE were slightly older (mean age 67.2±10.4 years versus 65.2±10.4 years, *P*<0.001), more likely to have a history of prior VTE (4.5% versus 1.8%, *P*<0.001), heart failure (6.9% versus 1.0%, *P*<0.001), coagulopathy (32.0% versus 17.8%, *P*<0.001), and renal failure (23.3% versus 15.6%, *P*<0.001). Baseline characteristics of the 2 groups are displayed in Table 1.

Independent predictors of VTE included the following: coagulopathy (aOR 1.71 [95% CI 1.46–2.01]; *P*<0.001), history of prior VTE (aOR 2.52 [95% CI 1.75–3.64]; *P*<0.001), heart failure (aOR 3.39 [95% CI 2.33–4.93]; *P*<0.001), obesity (aOR 1.33 [95% CI 1.12–1.57]; *P*=0.001), and chronic pulmonary disease (aOR 1.21 [95% CI 1.02–1.43]; *P*=0.03). Off-pump CABG was not an independent predictor of VTE (aOR 1.11 [95% CI 0.95–1.31], *P*=0.23) (Table 2).

Venous thromboembolism was associated with increased incidence of in-hospital mortality (6.8% versus 1.7%; aOR 1.92 [95% CI 1.40–2.65]; *P*<0.001), AKI (39.4% versus 16.3%; aOR 2.25 [95% CI 1.88–2.69]; *P*<0.001), AKI-D (3.9% versus 1.2%; aOR 1.66 [95% CI 1.07–2.55]; *P*=0.02), acute respiratory failure (45.1% versus 17.0%; aOR 2.71 [95% CI 2.33–3.15]; *P*<0.001), stroke (6.7% versus 1.8%; aOR 2.52 [95% CI 1.83–3.48]; *P*<0.001), and bleeding (18.2% versus 6.5%; aOR 2.22 [95% CI 1.85–2.67]; *P*<0.001). VTE was also associated with higher cost (mean±SE \$81 995±\$923 versus \$48 909±\$55) and longer length of stay (mean±SE 17.06±0.16 days versus 8.52±0.01 days) (Table 3). Our findings were similar for patients with PE or DVT-only (Table S4).

Off-pump CABG was not associated with in-hospital mortality in the overall cohort (aOR 1.16 [1.00–1.34], *P*=0.05) or in the VTE cohort (1.78 [0.90–3.53], *P*=0.08) (Table S5). In an analysis excluding all OPCAB cases, VTE continued to be associated with increased in-hospital mortality (5.9% versus 1.7%, aOR 1.87 [1.29–2.71]) (Table S6).

Discussion

Our study is the largest, nationally representative study to demonstrate that while VTE in patients undergoing CABG is infrequent, it is associated with higher in-hospital mortality and complications, longer length of stay, and higher average hospital costs.

VTE is a feared perioperative complication, and is associated with significant morbidity, mortality, prolonged hospital stays, and increased costs.^{1–3} While use of both mechanical and pharmacologic VTE prophylaxis is standard practice in most patients undergoing noncardiac surgery,^{4,5} pharmacologic VTE prophylaxis remains controversial for patients undergoing cardiac surgery, and protocols can differ considerably across institutions, even though patients undergoing cardiac surgeries have been found to be at increased risk of VTE compared with those undergoing general surgeries.^{6,16,17} Several reasons may explain the hesitance to use pharmacologic VTE prophylaxis in cardiac surgery patients. First, some believe that the incidence of perioperative VTE in cardiac surgery patients is relatively rare to be of clinical importance.¹⁸ There is a higher perceived risk of hemorrhagic complications such as pericardial effusions,^{19–21} and thus some clinicians prefer only mechanical prophylaxis alone over pharmacological agents. Some also believe that the generous amounts of intraoperative anticoagulation used during the procedure may persist in the perioperative period and offer protection.^{18,22}

However, prior work has found that patients undergoing cardiac surgery may be prothrombotic as early as postoperative day 1 persisting up to day 30.^{23–25} There is also evidence suggesting that pharmacological prophylaxis in these patients may be protective without significantly increasing the risk of clinically significant bleeding.²⁶ Fatal PE has been reported as being the cause of up to 20% of unexplained deaths after cardiac surgery,^{27,28} with as many as 50% being undiagnosed before death. Therefore, some advocate for early postprocedural initiation of pharmacological prophylaxis in patients who are not actively bleeding or those with multiple risk factors for VTE.^{9,16}

Unfortunately, the best strategy for prophylaxis (or choice of pharmacological agent) remains unclear, with current evidence limited to small observational studies or randomized controlled trials. This lack of consensus regarding optimal prophylactic strategies is evident in conflicting guidelines.^{9–11} The European Association for Cardiothoracic Surgery recommends pharmacologic prophylaxis from the first perioperative day,⁹ while the American College of Chest Physicians (ACCP) deems cardiac surgery patients to be at moderate risk for VTE but high risk for bleeding, and currently recommends mechanical over pharmacologic prophylaxis for patients undergoing cardiac surgery (Grade 2C) and the addition of pharmacological agents (Grade 2C) if patients have a

Table 1. Baseline Characteristics of Study Population

Characteristic	No VTE (n=327 745)	VTE (n=4205)	P Value
Age, y	65.2±10.4	67.2±10.4	<0.001
Female	82 660 (25.2%)	1280 (30.4%)	<0.001
Race			
White	240 775 (73.5%)	2960 (70.4%)	0.05
Black	21 455 (6.5%)	440 (10.5%)	<0.001
Hispanic	22 745 (6.9%)	245 (5.8%)	0.21
Other	21 605 (6.6%)	265 (6.3%)	0.74
Missing	21 165 (6.5%)	295 (7.0%)	0.56
Insurance			
Medicare	184 800 (56.4%)	2720 (64.7%)	<0.001
Medicaid	22 875 (7.0%)	340 (8.1%)	0.22
Private	105 060 (32.1%)	935 (22.2%)	<0.001
Self/uninsured	15 010 (4.6%)	210 (5.0%)	0.56
OPCAB	68 245 (20.8)	980 (23.3%)	0.09
Comorbidities			
Prior VTE	5840 (1.8%)	190 (4.5%)	<0.001
Alcohol abuse	11 660 (3.6%)	210 (5.0%)	<0.001
Deficiency anemias	54 985 (17.7%)	880 (20.9%)	<0.001
Chronic blood loss anemia	3760 (1.1%)	50 (1.2%)	0.80
Heart failure	3145 (1.0%)	290 (6.9%)	<0.001
Chronic pulmonary disease	72 305 (22.1%)	1145 (27.2%)	<0.001
Coagulopathy	58 460 (17.8%)	1345 (32.0%)	<0.001
Depression	25 225 (7.7%)	310 (7.4%)	0.43
Diabetes mellitus (without complications)	119 605 (36.5%)	1335 (31.7%)	<0.001
Diabetes mellitus (with complications)	31 200 (9.5%)	490 (11.7%)	0.04
Hypertension	266 290 (81.2%)	3025 (71.9%)	<0.001
Hypothyroidism	33 810 (10.3%)	410 (9.8%)	0.23
Liver disease	5510 (1.7%)	85 (2.0%)	0.09
Fluid and electrolyte disorders	104 885 (32.0%)	2230 (53.0%)	<0.001
Other neurological disorders	12 870 (3.9%)	230 (5.5%)	<0.001
Obesity	80 920 (24.7%)	1160 (27.6%)	<0.001
Peripheral vascular disorders	49 155 (15.0%)	940 (22.4%)	<0.001
Renal failure	51 275 (15.6%)	980 (23.3%)	<0.001
Solid tumor (without metastasis)	3230 (1.0%)	15 (0.4%)	<0.001
Metastatic cancer	545 (0.2%)	15 (0.4%)	0.003
Valvular disease	1075 (0.3%)	115 (2.7%)	<0.001
Smoking	68 190 (20.8%)	700 (16.6%)	<0.001
Dyslipidemia	251 245 (76.7%)	2555 (60.8%)	<0.001
Bed size of hospital			
Small	29 295 (8.9%)	40 (5.7%)	<0.001
Medium	77 975 (23.8%)	885 (21.0%)	<0.001
Large	220 475 (67.3%)	3080 (73.2%)	<0.001

Continued

Table 1. Continued

Characteristic	No VTE (n=327 745)	VTE (n=4205)	P Value
Hospital location and teaching status			
Rural	11 625 (3.5%)	105 (2.2%)	<0.001
Urban nonteaching	90 620 (27.6%)	1030 (24.5%)	<0.001
Urban teaching	225 500 (68.8%)	3070 (73.0%)	<0.001
Region			
Northeast	52 355 (16.0%)	585 (13.9%)	<0.001
Midwest	77 065 (23.5%)	975 (23.2%)	0.62
South	145 095 (44.3%)	2035 (48.4%)	<0.001
West	53 230 (16.2%)	610 (14.5%)	0.002

Variables are mean±SD or n (%). OPCAB indicates off-pump coronary artery bypass grafting; VTE, venous thromboembolism.

prolonged hospital stay because of nonhemorrhagic surgical complications.¹⁰ Unfortunately, although mechanical prophylaxis alone is generally preferred, poor patient tolerance and compliance may reduce the efficacy of this method.

The incidence of perioperative VTE observed in our study is consistent with previous findings in patients undergoing CABG.^{6,7,18} However, this is likely an underestimate, since diagnosis of VTE post cardiac surgery can be challenging as the signs and symptoms associated with DVT and PE (such as tachycardia, chest pain, leg erythema, and edema) can also be attributable to surgery. Moreover, some patients may also have asymptomatic VTE that would be otherwise undiagnosed. Viana et al found rates of postoperative DVT and PE (diagnosed utilizing computed tomographic pulmonary angiography and lower extremity venous compressive ultrasound) to be as high as 20%, in their prospective, observational, single-center study of 100 patients undergoing elective CABG.²⁹

Cardiac surgery patients often have several risk factors for perioperative VTE, and the risk factors associated with VTE in our study (Table 2) have been identified by others as well.^{30,31}

Table 2. Predictors of VTE During Hospitalization

Risk Factor	Adjusted OR [95% CI]*	P Value
Coagulopathy	1.71 [1.46–2.01]	<0.001
Prior VTE	2.52 [1.75–3.64]	<0.001
Heart failure	3.39 [2.33–4.93]	<0.001
Obesity	1.33 [1.12–1.57]	0.001
Age	1.01 [1.001–1.020]	0.02
Chronic pulmonary disease	1.21 [1.02–1.43]	0.03
OPCAB	1.11 [0.95–1.31]	0.23

OPCAB indicates off-pump coronary artery bypass grafting; OR, odds ratio; VTE, venous thromboembolism.

*Adjusted for age, race, sex, insurance status, hospital characteristics, and all comorbidities listed in Table 1.

It has also been postulated that OPCAB may be associated with increased thromboembolism compared with on-pump CABG.²⁵ We found that OPCAB was not associated with increased incidence of VTE in our population, nor was it associated with increased in-hospital mortality. Furthermore, VTE continued to be associated with increased mortality despite exclusion of OPCAB cases from our analysis (Table S6), further suggesting that VTE has an effect on mortality independent of OPCAB.

Our results urge clinicians to acknowledge that while VTE may be rare after CABG, it is still a real threat and is associated with increased morbidity and mortality. We did note a higher incidence of bleeding in the VTE group, which may be because of the use of therapeutic anticoagulation after diagnosis. Unfortunately, it is difficult to identify with certainty which patients are at risk for bleeding. However, as prior work has shown, some patients may not be at increased risk of bleeding and may benefit from earlier initiation of pharmacologic prophylaxis. Our results highlight a need for large randomized control trials to evaluate optimal prophylactic practices in patients undergoing CABG.

There are several important limitations to our study. First, our results are reliant on accurate *ICD-9-CM* coding, and some cases of superficial vein thromboses may have been misclassified as DVT. We attempted to mitigate this by excluding codes for superficial vein thrombosis from the DVT group. Second, since the NIS does not contain information on the type of VTE prophylaxis used in patients, there may have been patients who received mechanical and/or pharmacologic VTE prophylaxis in our study. Hence, we were not able to ascertain the influence of prophylaxis strategy on incidence and outcomes of VTE, including bleeding. Third, we could not identify the method used to diagnose VTE (imaging, clinical symptoms, or both), because this information is not available in the NIS. Fourth, because the NIS does not contain information on the temporal relationship between CABG and

Table 3. In-Hospital Outcomes in Patients Undergoing CABG With and Without VTE

Outcome	No VTE	VTE	P Value
In-hospital mortality			
Incidence, %	1.7	6.8	
Unadjusted OR [95% CI]	Ref	4.14 [3.14–5.45]	<0.001
Adjusted OR [95% CI]*	Ref	1.92 [1.40–2.65]	<0.001
AKI			
Incidence, %	16.3	39.4	...
Unadjusted OR [95% CI]	Ref	3.34 [2.90–3.85]	<0.001
Adjusted OR [95% CI]*	Ref	2.25 [1.88–2.69]	<0.001
AKI-D			
Incidence, %	1.2	3.9	...
Unadjusted OR [95% CI]	Ref	3.48 [2.41–5.01]	<0.001
Adjusted OR [95% CI]*	Ref	1.66 [1.07–2.55]	0.02
Acute respiratory failure			
Incidence, %	17.0	45.1	...
Unadjusted OR [95% CI]	Ref	4.00 [3.49–4.60]	<0.001
Adjusted OR [95% CI]*	Ref	2.71 [2.33–3.15]	<0.001
Stroke			
Incidence, %	1.8	6.7	...
Unadjusted OR [95% CI]	Ref	3.96 [2.98–5.26]	<0.001
Adjusted OR [95% CI]*	Ref	2.52 [1.83–3.48]	<0.001
Bleeding			
Incidence, %	6.5	18.2	...
Unadjusted OR [95% CI]	Ref	3.21 [2.69–3.82]	<0.001
Adjusted OR [95% CI]*	Ref	2.22 [1.85–2.67]	<0.001
Length of stay			
Days±SE	8.52±0.01	17.06±0.16	...
Unadjusted parameter estimate [†]	Ref	2.00 [1.92–2.09]	<0.001
Adjusted parameter estimate* [†]	Ref	1.69 [1.64–1.76]	<0.001
Average hospital costs			
Mean±SE, \$	48 909±55	81 995±923	...
Unadjusted parameter estimate [†]	Ref	1.68 [1.59–1.77]	<0.001
Adjusted parameter estimate* [†]	Ref	1.46 [1.39–1.53]	<0.001

AKI indicates acute kidney injury; AKI-D, AKI requiring dialysis; CABG, coronary artery bypass grafting; OR, odds ratio; VTE, venous thromboembolism.

*Adjusted for age, race, sex, insurance status, hospital characteristics, and all comorbidities listed in Table 1.

[†]Parameter estimates represent the antilog of the β regression coefficients obtained from the log-transformed regression models.

incidence of VTE, it is possible that some patients may have had acute VTE before CABG during the same hospitalization, and we were not able to exclude these patients from our analysis. Moreover, because the NIS is an inpatient-only database, it does not contain any information on VTE events that may have occurred after discharge. Lastly, given the retrospective observational nature of our study, and the lack of granular information in the NIS, we were only able to show

an association of VTE with increased mortality, and were unable to identify whether any deaths were directly attributable to VTE.

Conclusions

In our study of >330 000 CABG procedures, we found that while the incidence of perioperative VTE is low, it is

associated with increased in-hospital morbidity and mortality, prolonged length of stay, and increased hospital costs. Unlike most surgeries for which it is strongly recommended, perioperative VTE prophylaxis in cardiac surgery patients remains controversial, and large randomized controlled trials are needed to evaluate optimal prophylaxis strategies.

Disclosures

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SUPPLEMENTAL MATERIAL

Table S1. International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) codes used to identify study population.

Inclusion criteria	
CABG	36.1x
Acute deep vein thrombosis	451.11, 451.19, 451.83, 451.81, 453.40, 453.41, 453.42, 453.82, 453.84, 453.85, 453.86, 453.87, 453.89, 453.2
Pulmonary embolism	415.1, 415.11, 415.13, 415.19
Exclusion criteria	
SAVR	35.21, 35.22
Aortic root procedures	38.44, 38.45
Tricuspid valve procedures	35.14, 35.27, 35.28
Pulmonic valve procedures	35.13, 35.25, 35.26
Mitral valve procedures	35.12, 35.23, 35.24

CABG: coronary artery bypass grafting; SAVR: surgical aortic valve replacement

Table S2. International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) or Clinical Classification Software (CCS) codes used to identify comorbidities.

Comorbidity	
Hyperlipidemia	CCS 53
Prior history of VTE (including chronic VTE)	V12.51, 453.7X, , 453.5X
Smoking	305.1-305.13
CPB use	39.61, 39.66

CCS: Clinical Classification Software; CPB: cardiopulmonary bypass; VTE: venous thromboembolism.

All other comorbidities in Table 1 were identified using the Elixhauser comorbidities included with the NIS.

Table S3. International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) codes used to identify in-hospital complications.

In-hospital complication	
Stroke	997.01, 997.02, 431, 433.x1, 434.x1, 344.6x
Acute Respiratory Failure	518.81 , 518.82, 518.84, 799.1, 786.09, 518.4, 518.51
AKI	584.5, 584.6, 584.7, 584.8, 584.9
AKI-D	584.x + 39.95
Bleeding	430, 431, 432.x, 336, 362.43, 362.81, 363.61, 363.62, 363.72, 364.41, 3736.32, 377.42, 379.23; 423.0 + 37.0; 923.x + 729.71, 924.x + 729.72, 922.2-9 + 729.73; 456.0, 456.20, 530.7, 530.82, 531.00, 531.01, 531.20, 531.21, 531.40, 531.41, 31.60, 531.61, 532.00, 532.01, 532.20, 532.21, 532.40, 532.41, 532.60, 532.61, 533.00, 533.01, 533.20, 533.21, 533.40, 533.41, 533.60, 533.61, 534.00, 534.01, 534.20, 534.21, 534.40, 534.41, 534.60, 534.61, 569.3, 578.0, 578.1, 578.9, 568.81, 599.70, 599.71, 719.1x, 784.7, 784.8, 459, 998.11, 998.12, 285.1 + 998.00, 998.09, 785.50, 785.59, 276.52 + 00.17 + 99.0x

AKI: acute kidney injury; AKI-D: AKI requiring dialysis

Table S4. Multivariable analysis of in-hospital outcomes, in PE and DVT-only groups.

Outcome	No PE	PE	P value	No DVT	DVT-only	P value
In-hospital mortality						
Incidence (%)	1.8	10.0		1.8	5.6	
Unadjusted OR [95% CI]	Ref	6.17 [4.04-9.42]	<0.001	Ref	3.32[2.33-4.75]	<0.001
Adjusted OR [95% CI] *	Ref	3.46 [2.07 - 5.78]	<0.001	Ref	1.43 [0.96-2.13]	0.08
AKI						
Incidence (%)	16.5	33.2		16.3	41.8	
Unadjusted OR [95% CI]	Ref	2.51 [1.93-3.27]	<0.001	Ref	3.68[3.11-4.36]	<0.001
Adjusted OR [95% CI] *	Ref	1.83 [1.34-2.50]	<0.001	Ref	2.43 [1.95-3.02]	<0.001
AKI-D						
Incidence (%)	1.2	2.9		1.2	4.3	

Outcome	No PE	PE	P value	No DVT	DVT-only	P value
Unadjusted OR [95% CI]	Ref	2.48 [1.17-5.27]	<0.001	Ref	3.76[2.46-5.74]	<0.001
Adjusted OR [95% CI] *	Ref	1.89 [0.80-4.47]	0.14	Ref	1.52 [0.92 – 2.53]	0.12
Acute Respiratory Failure						
Incidence (%)	17.3	45.2				
Unadjusted OR [95% CI]	Ref	3.96 [3.10-5.05]	<0.001	Ref	4.03 [3.43-4.73]	<0.001
Adjusted OR [95% CI] *	Ref	2.93 [2.26-3.80]	<0.001	Ref	2.63 [2.20- 3.14]	<0.001
Stroke						
Incidence (%)	1.8	2.5	1.8	8.5		
Unadjusted OR [95% CI]	Ref	1.37 [0.61-3.08]	0.52	Ref	5.15 [3.80-6.98]	<0.001
Adjusted OR [95% CI] *	Ref	0.97 [0.42 – 2.21]	0.94	Ref	3.18 [2.25 – 4.50]	<0.001

Outcome	No PE	PE	P value	No DVT	DVT-only	P value
Bleeding						
Incidence (%)	6.6	19.1	6.5	17.7		
Unadjusted OR [95% CI]	Ref	3.34 [2.38-4.70]	<0.001	Ref	3.07 [2.47 – 3.78]	<0.001
Adjusted OR [95% CI] *	Ref	2.49 [1.74-3.56]	<0.001	Ref	2.06 [1.65 – 2.58]	<0.001
Length of stay						
Days ± SE	8.58 ± 0.01	17.09 ± 0.31		8.55 ± 0.01	16.80 ± 0.10	
Unadjusted parameter estimate†	Ref	1.99[1.84-2.15]	<0.001	Ref	2.01 [1.92-2.11]	<0.001
Adjusted parameter estimate*†	Ref	1.77[1.64-1.90]	<0.001	Ref	1.67[1.60-1.75]	<0.001
Average hospital cost						

Outcome	No PE	PE	P value	No DVT	DVT-only	P value
Mean \pm SE (\$)	46,073 \pm 52	74,563 \pm 1528	-	45,936 \pm 52	78,401 \pm 1068	-
Unadjusted parameter estimate [†]	Ref	1.62 [1.49-1.77]	<0.001	Ref	1.71[1.60-1.82]	<0.001
Adjusted parameter estimate ^{*†}	Ref	1.47[1.35-1.60]	<0.001	Ref	1.46 [1.38-1.55]	<0.001

PE: pulmonary embolism; DVT: deep vein thrombosis; AKI: acute kidney injury; AKI-D: AKI requiring dialysis; OR: odds ratio; SE: standard error

*Adjusted for age, race, sex, insurance status, hospital characteristics, and all comorbidities listed in Table 1.

[†]Parameter estimates represent the antilog of the β regression coefficients obtained from the log-transformed regression models.

Table S5. Association of OPCAB with in-hospital mortality.

Mortality	Unadjusted OR [95% CI]	Adjusted OR [95% CI]	P value [‡]
Overall mortality*	1.25 [1.09 – 1.44]	1.16 [1.00 – 1.34]	0.05
In VTE group †	1.72 [0.96 – 3.07]	1.78 [0.90 – 3.53]	0.10
In non-VTE group †	1.23 [1.06 – 1.41]	1.15 [0.99 – 1.33]	0.08

OPCAB: off-pump coronary artery bypass grafting; OR: odds ratio; VTE: venous thromboembolism.

*Adjusted for age, race, sex, insurance status, VTE status, hospital characteristics, and all comorbidities listed in Table 1.

† Adjusted for age, race, sex, insurance status, hospital characteristics, and all comorbidities listed in Table 1.

‡ P values provided for adjusted analyses.

Table S6. In-hospital mortality in patients undergoing CABG with and without VTE (excluding OPCAB cases).

	No VTE	VTE	P value
Incidence of in-hospital mortality (%)	1.7	5.9	-
Unadjusted OR [95% CI]	Ref	3.73 [2.67 – 5.21]	<0.001
Adjusted OR [95% CI]*	Ref	1.87 [1.29 – 2.71]	0.001

CABG: coronary artery bypass grafting; OPCAB: off-pump coronary artery bypass grafting; OR: odds ratio; VTE: venous thromboembolism.

*Adjusted for age, race, sex, insurance status, hospital characteristics and all comorbidities listed in Table 1.