

# Comparative Effectiveness of Preventative Therapy for Venous Thromboembolism After Coronary Artery Bypass Graft Surgery

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**Background**—Controversy exists regarding the optimal preventative therapy for venous thromboembolism (VTE) after coronary artery bypass graft (CABG) surgery. We sought to compare the effectiveness and safety of the most commonly used regimens.

**Methods and Results**—We assembled a cohort of 92 699 patients who underwent CABG between 2004 and 2008, using the Premier database. Patients were categorized by method of VTE prevention initiated within 48 hours of surgery, including no preventative therapy (n=55 400), mechanical preventative therapy (n=21 162), subcutaneous unfractionated or low-molecular-weight heparin (n=10 718), subcutaneous fondaparinux (n=88), and concurrent mechanical-chemical therapy (n=5331). The incidence of VTE and major bleeding events within 6 weeks of CABG were compared, using multivariable and propensity score adjustment. The overall incidence of VTE for the entire cohort was 0.74%, and the incidence of major bleeding was 1.43%. VTE and bleeding events occurred with similar incidence in each of the patient categories (VTE: 0.70%, 0.79%, 0.81%, 1.14%, and 0.73%; major bleeding: 1.36%, 1.45%, 1.69%, 3.41%, 1.50%; no prevention, mechanical prevention, subcutaneous heparin, subcutaneous fondaparinux, concurrent mechanical-chemical prevention, respectively). Compared with receiving no prevention, the use of mechanical prevention or subcutaneous heparin did not significantly reduce the risk of VTE or change the risk of major bleeding ( $P=NS$ ).

**Conclusions**—Venous thromboembolism occurs infrequently after CABG. Compared with the use of no prevention, the administration of chemical or mechanical preventative therapies to CABG patients does not appreciably lower the risk of VTE. These data provide support for the common practice of administering no VTE preventative therapy after CABG, used for nearly 60% of patients within this cohort. (*Circ Cardiovasc Interv.* 2012;5:590-596.)

**Key Words:** CABG ■ venous thromboembolism ■ prevention ■ anticoagulants ■ comparative effectiveness

Postoperative venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolus (PE), remains an important health problem.<sup>1</sup> After cardiac surgery, VTE has been reported as a common cause of postoperative death,<sup>2-4</sup> and it is the fifth most common reason for hospital readmission after coronary artery bypass graft surgery (CABG).<sup>5</sup> Recent reports in the cardiac surgery literature have documented rates of clinically apparent VTE ranging from 0.5% to 1.3%,<sup>5-8</sup> although higher rates have been seen in studies using routine postoperative ultrasound surveillance.<sup>4,9,10</sup>

Several methods have been recommended for the prevention of VTE after cardiac surgery.<sup>1</sup> Chemical prophylaxis, including the use of subcutaneous unfractionated heparin or low-molecular-weight heparin (LMWH), is one of the most commonly used postoperative VTE preventative measures after noncardiac surgery, reducing the risk of DVT and PE by 40% to 70% in clinical trials.<sup>1,11,12</sup> Fondaparinux, a factor Xa inhibitor, is another option now available for chemical VTE prophylaxis, with favorable experience reported after orthopedic operations.<sup>13</sup> Mechanical preventative therapies, such as graduated compression thromboembolic deterrent (TED)

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stockings or intermittent pneumatic sequential compression devices (SCD), are also effective at reducing the incidence of perioperative VTE by preventing perioperative venous stasis and enhancing blood flow in the deep veins of the leg.<sup>14,15</sup>

VTE has traditionally been regarded as rare after CABG, possibly because of the large doses of heparin administered during cardiac operations. However, patients recovering from CABG often have a number of the common risk factors for postoperative VTE including obesity, hyperlipidemia, heart failure, older age, prolonged immobilization, and surgery on a lower limb (for harvesting of the saphenous vein).<sup>2,16-18</sup> Despite the extensive evidence supporting the use of VTE prophylaxis after noncardiac surgery, the value of post-CABG VTE prophylaxis remains unclear. This uncertainty was highlighted in the recent American College of Chest Physicians VTE preventative guidelines.<sup>1</sup> Given the lack of data, we evaluated the frequency with which VTE thromboprophylaxis is applied after CABG in contemporary cardiac surgical practice and sought to compare the effectiveness and safety of the most commonly used regimens.

### WHAT IS KNOWN

- Venous thromboembolism, including deep vein thrombosis and pulmonary embolus, remains an important health problem.
- After cardiac surgery, venous thromboembolism is a common cause of hospital readmission and postoperative death.
- Several methods are recommended for the prevention of venous thromboembolism after cardiac surgery, including chemical and mechanical prophylaxis, but controversy exists regarding the optimal strategy.

### WHAT THE STUDY ADDS

- Within a contemporary cohort of more than 90 000 patients who underwent coronary bypass, the rate of venous thromboembolism was relatively low (0.74%).
- Compared with the use of no prevention (used for nearly 60% of patients), the administration of chemical or mechanical preventative therapies did not appreciably lower the risk of venous thromboembolism after cardiac surgery.

## Methods

### Data

The study cohort was drawn from the Premier Perspective Comparative Database, a repository of hospital administrative data that includes approximately one-sixth of all hospitalizations in the United States. Premier data are audited, verified, and validated and are provided to hospitals for the purpose of tabulation and benchmarking against the performance of other institutions. This source contains a record of daily charges for all medications, procedures, and diagnostic tests during each patient's hospitalization, as well as patient and hospital characteristics, discharge diagnoses, and discharge status (including death). A number of studies have been performed using Premier data to evaluate population-based medication use and health outcomes.<sup>19-22</sup> This source is also used by the Food and Drug Administration (FDA),

as well as the Centers for Medicare and Medicaid Services Hospital Quality Incentive Demonstration to link hospital reimbursement to the quality of care and outcomes for selected procedures or conditions.<sup>21</sup>

For the purpose of this study, data from the Premier database were analyzed to measure in-hospital clinical outcomes and readmissions to Premier hospital facilities up to 6 weeks after the initial CABG hospitalization. The current study was approved by the institutional review board of the Brigham and Women's Hospital, Boston, MA.

### Cohort

We included all patients who underwent either on-pump or off-pump CABG (*International Classification of Disease-9* procedure 36.1x or 36.2x), including those recently admitted to hospital with a myocardial infarction, between January 1, 2004, and December 31, 2008. Patients were excluded if they underwent concurrent valve surgery at the time of CABG. To specifically focus on the efficacy and safety of VTE thromboprophylaxis, we also excluded patients who were treated in the hospital with warfarin before or within 48 hours after surgery and those who were treated with intravenous heparin within 48 hours after surgery. Patients who underwent CABG on the same day as hospital admission were excluded to allow for the accurate collection of demographic and comorbidity characteristics in the preoperative period. Finally, we excluded patients who developed early postoperative bleeding necessitating reopening (return to operating room) within 48 hours of surgery to reduce confounding and to better isolate outcomes associated with VTE thromboprophylaxis. Two days after surgery was considered the index date for the study analysis (ie, start of follow-up). Patients were followed for 6 weeks from the time of surgery, with follow-up terminating on February 11, 2009.

### Covariates

We determined patient demographics and comorbidities by compiling hospital charge codes, diagnostic codes, procedure codes, and physician service claims during the index hospitalization. The following characteristics were identified: age, year of hospitalization, sex, race, marital status, length of hospital stay (before and after surgery), urgent or emergent hospital admission, previous CABG, previous percutaneous coronary intervention, presence of diabetes mellitus, congestive heart failure, obesity, chronic obstructive pulmonary disease, end-stage renal disease, number of CABG grafts performed, and the use of an internal mammary artery graft. We also determined the use of the following medications before surgery: angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, aldosterone agonists,  $\beta$ -blockers, calcium channel blockers, diuretics, aspirin, clopidogrel, dipyridamole, statins, fibrates, digoxin, and antiarrhythmic medications (amiodarone, dronedarone, sotalol, procainamide, propafenone). Hospitals were categorized both on geographic region as well as whether they were urban or rural. Hospitals accredited by the Association of American Medical Colleges were classified as teaching hospitals. All other hospitals were classified as nonteaching hospitals. The annualized volume of CABG patients treated by each hospital was estimated by dividing the total number of CABG patients for each hospital during the study time period by the number of years that each hospital performed 1 or more CABG operations. Hospitals were ranked in order of annualized volume and were then categorized into high-, medium-, and low-volume hospital tertiles.

### Exposure

We determined patient exposure to VTE preventative therapies within 48 hours after the day of surgery, and we classified patients on the basis of 5 VTE prevention strategies that were mutually exclusive and collectively exhaustive. Patients who were treated with TED stockings or SCDs in the postoperative period were classified as receiving mechanical preventative therapy. Patients who received subcutaneous VTE preventative doses of unfractionated heparin ( $\leq 15\ 000$  international units per day) or LMWH (enoxaparin  $\leq 40$  mg per day or dalteparin  $\leq 5000$  U per day) formed a second

category. Patients who received intravenous heparin or higher daily doses of subcutaneous LMWH (in keeping with VTE treatment rather than prevention) were specifically excluded from the cohort. A third category included patients who received subcutaneous fondaparinux (VTE prevention dose of 2.5 mg per day). The final 2 categories of patients included those who within 48 hours of surgery received concurrent mechanical and chemical (heparin, LMWH, or fondaparinux) preventative therapy and those who received no VTE prevention within 48 hours of surgery.

## Outcomes

The primary outcomes of this study were postoperative VTE and bleeding events within 6 weeks of surgery, starting 48 hours after surgery. Postoperative VTE was defined as a discharge diagnosis of DVT or PE during the index admission or a subsequent Premier hospital readmission, with an associated charge code for lower extremity venous imaging (ultrasound or venography) or pulmonary artery imaging (contrast computed tomography or ventilation/perfusion scan). The date of the imaging study was considered the date of VTE diagnosis. A postoperative bleeding event was defined as the transfusion of 3 or more units of packed red blood cells on a single day, any transfusion of platelets, fresh-frozen plasma or cryoprecipitate, and any upper or lower gastrointestinal endoscopy in the postoperative period.

## Statistical Analysis

We calculated crude incidence rates of VTE and bleeding for the 5 VTE prevention categories. To evaluate the comparative effectiveness and risks of the different preventive strategies, we used univariate and multivariable Cox modeling. Because the sample sizes and event rates were low in the fondaparinux and combined chemical and mechanical VTE prevention categories, these groups were excluded from our comparative analyses. In all analyses, patients were censored if they developed the outcome of interest, if they required redo-CABG more than 48 hours after the initial surgery, at the time of death, or at the end of the 6-week follow-up period if no outcome had occurred.

We used multivariable Cox proportional hazards models to adjust for potentially important differences between the patients. Factors of clinical relevance incorporated into the models were age, preoperative length of stay, sex, marital status, race, teaching hospital, urban hospital setting, hospital geographic location, the number of CABG grafts, the use of an internal mammary artery graft, year of surgery, urgent or emergent admission, hospital volume, preoperative medication use (angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, aldosterone agonists,  $\beta$ -blockers, calcium channel blockers, diuretics, aspirin, clopidogrel, dipyridamole, statins, fibrates, digoxin, and antiarrhythmic medications), previous CABG, previous percutaneous coronary intervention, presence of diabetes mellitus, chronic obstructive pulmonary disease, end-stage renal disease, the use of oxygen or telemetry before surgery, intensive care admission before surgery, and the performance of an echocardiogram before surgery. All of these factors were included in the models without variable selection. Hazard ratios (HR) are reported along with standard errors or 95% confidence intervals (CI). All analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC).

Additional analysis was performed with a high-dimensional propensity score that was developed using a previously validated multistep algorithm.<sup>23</sup> This algorithm generates covariates on the basis of the individual charge codes recorded for a patient and then estimates a propensity score that includes all of the investigator-specified covariates plus 400 empirically created covariates that are most likely to confound the exposure and outcome under study. We adjusted for deciles of the resulting propensity score in a Cox proportional hazards model.

Moreover, the estimated risk of a VTE or bleeding event was determined for each treatment group from the Cox proportional hazard models, using a set of reference covariate values and a specified time point of 7 days of follow-up.<sup>24</sup> For the reference covariates, mean values were applied for continuous variables and the most prevalent category was used for categorical variables. This

provided an approximate absolute risk for an "average patient" in each treatment group. To compare VTE prevention strategies, the estimated risk difference was calculated as the difference between any of the 2 prevention groups.

Further, we performed secondary analysis to compare the VTE outcomes of patients undergoing either on-pump CABG (81.0%) or off-pump surgery without cardiopulmonary bypass (19.0%), as well as endoscopic (47.5%) or open saphenous vein harvesting (52.5%). We also assessed the impact of intraoperative heparin dose on the incidence of VTE by classifying patients into 3 equal tertiles, based on increasing doses of heparin on the day of surgery. Finally, we compared VTE prevention strategies for the excluded group of patients who underwent surgery on the first-day of hospitalization. Because complete demographic and comorbidity characteristics were not available for these first-day patients, we performed Cox modeling for VTE and bleeding events using a modification of the Elixhauser comorbid adjustment technique<sup>25,26</sup> (online-only Data Supplement Appendix).

## Results

### Patient Cohort

Our cohort consisted of 92 699 patients who underwent CABG between 2004 and 2008. The mean age of the cohort was  $65.1 \pm 11.1$  years, and 70.5% of patients were male. The majority of patients were cared for at teaching hospitals (57.9%). Patients were classified into 5 categories, based on VTE prevention strategy initiated within 48 hours of surgery, including no preventative therapy (n=55 400), mechanical preventative therapy (n=21 162), subcutaneous unfractionated or LMWH (n=10 718), subcutaneous fondaparinux (n=88), and concurrent mechanical and chemical preventative therapy (n=5331). Table 1 describes the characteristics of patients in each of the 5 groups. Compared with the other groups, patients who received either heparin or fondaparinux had higher rates of diabetes mellitus, more commonly had surgery at an urban hospital, and had the highest usage rates of  $\beta$ -blockers before surgery. All of these patient characteristics were included in the multivariable analysis. The mean follow-up time for the patient cohort was  $64.0 \pm 63.0$  days after the date of CABG.

### VTE Events and the Impact of Preventative Therapy

The overall incidence of VTE for the entire cohort was 0.74%. The VTE incidence was similar in each of the 5 patient groups (Table 2), varying from 0.70% (no prevention) to 1.14% (fondaparinux).

Compared with the use of no prevention, the use of mechanical prevention did not significantly reduce the risk of VTE in unadjusted analysis (unadjusted HR, 1.12; 95% CI, 0.93, 1.34). With multivariable adjustment (Table 3), there was no decrease in the risk of VTE with mechanical preventive therapy compared with the use of no prevention (propensity-adjusted HR, 1.14; 95% CI, 0.90, 1.43). The corresponding estimated absolute risk difference was small (0.02%) and nonsignificant.

The use of heparin or LMWH for VTE prevention did not significantly reduce the risk of VTE compared with the use of no prevention (Table 3), either in unadjusted (unadjusted HR, 1.15; 95% CI, 0.91, 1.45) or adjusted analysis (propensity-adjusted HR, 0.89; 95% CI, 0.68, 1.16). The corresponding

**Table 1. Patient Characteristics**

Characteristic	No Prevention (n=55 400)	TED or SCD (n=21 162)	Heparin or LMWH (n=10 718)	Fondaparinux (n=88)	Chemical and Mechanical (n=5331)
<b>Patient characteristics</b>					
Age, y, mean±SD	65.37±11.11	64.98±11.01	65.53±11.08	63.14±10.37	64.63±11.05
Male sex	39 218 (70.8%)	15 118 (71.4%)	7324 (68.3%)	61 (69.3%)	3630 (68.1%)
White race	40 424 (73.0%)	15 928 (75.3%)	7733 (72.1%)	77 (87.5%)	3962 (74.3%)
Urgent or emergent	39 601 (71.5%)	14 897 (70.4%)	7255 (67.7%)	60 (68.2%)	3925 (73.6%)
Preoperative length of stay, d, mean±SD	4.33±2.84	4.52±2.99	4.56±3.17	4.52±3.36	4.65±3.02
Chronic obstructive pulmonary disease	7676 (13.9%)	2899 (13.7%)	1797 (16.8%)	16 (18.2%)	887 (16.6%)
Diabetes mellitus	16 416 (29.6%)	6675 (31.5%)	3776 (35.2%)	61 (69.3%)	1837 (34.5%)
Congestive heart failure	11 914 (21.5%)	4846 (22.9%)	3020 (28.2%)	21 (23.9%)	1273 (23.9%)
Obesity	8587 (15.5%)	3389 (16.0%)	1781 (16.6%)	30 (34.1%)	986 (18.5%)
End-stage renal disease	1784 (3.2%)	642 (3.0%)	536 (5.0%)	7 (8.0%)	217 (4.1%)
Previous percutaneous coronary intervention	2464 (4.4%)	987 (4.7%)	577 (5.4%)	3 (3.4%)	275 (5.2%)
Previous coronary artery bypass graft surgery	988 (1.8%)	290 (1.4%)	167 (1.6%)	0 (0.0%)	90 (1.7%)
<b>Preoperative medications</b>					
Angiotensin-converting enzyme inhibitor	21 617 (39.0%)	8791 (41.5%)	4490 (41.9%)	33 (37.5%)	2347 (44.0%)
Angiotensin receptor blocker	5719 (10.3%)	2178 (10.3%)	1162 (10.8%)	11 (12.5%)	568 (10.7%)
Dipyridamole	621 (1.1%)	316 (1.5%)	177 (1.7%)	0 (0.0%)	99 (1.9%)
Aldosterone agonist	1325 (2.4%)	532 (2.5%)	335 (3.1%)	0 (0.0%)	173 (3.2%)
Aspirin	34 131 (61.6%)	12 620 (59.6%)	6976 (65.1%)	77 (87.5%)	3702 (69.4%)
β-Blocker	42 003 (75.8%)	16 188 (76.5%)	8504 (79.3%)	77 (87.5%)	4196 (78.7%)
Calcium channel blocker	10 835 (19.6%)	4242 (20.0%)	2340 (21.8%)	30 (34.1%)	1116 (20.9%)
Clopidogrel	8863 (16.0%)	3440 (16.3%)	2137 (19.9%)	23 (26.1%)	1235 (23.2%)
Digoxin	1957 (3.5%)	790 (3.7%)	530 (4.9%)	2 (2.3%)	272 (5.1%)
Fibrate	2097 (3.8%)	865 (4.1%)	452 (4.2%)	7 (8.0%)	271 (5.1%)
Diuretic	10 759 (19.4%)	4158 (19.6%)	2557 (23.9%)	17 (19.3%)	1182 (22.2%)
Statin	35 397 (63.9%)	13 872 (65.6%)	6969 (65.0%)	73 (83.0%)	3509 (65.8%)
Antiarrhythmic medication	5339 (9.6%)	3940 (18.6%)	976 (9.1%)	8 (9.1%)	429 (8.0%)
<b>Hospital characteristics</b>					
Teaching hospital	32 903 (59.4%)	12 290 (58.1%)	5195 (48.5%)	69 (78.4%)	3206 (60.1%)
Urban hospital	51 056 (92.2%)	18 569 (87.7%)	10 207 (95.2%)	88 (100.0%)	4981 (93.4%)
High-volume center	37 514 (67.7%)	12 976 (61.3%)	6213 (58.0%)	72 (81.8%)	3645 (68.4%)
<b>Surgery characteristics</b>					
No. of grafts, mean±SD	3.33±1.05	3.36±1.05	3.34±1.06	3.27±1.01	3.35±1.05
Mammary graft	48 900 (88.3%)	18 574 (87.8%)	9259 (86.4%)	73 (83.0%)	4694 (88.1%)
Postoperative length of stay, d, mean±SD	7.10±6.89	7.79±6.67	8.07±8.33	7.09±5.19	8.00±7.10

TED indicates thromboembolic deterrent stockings; SCD, sequential compression devices; and LMWH, low-molecular-weight heparin.

absolute risk difference was also small (0.01%) and nonsignificant.

### Bleeding Events and the Impact of Preventative Therapy

The overall incidence of bleeding events for the entire cohort was 1.43%. The bleeding event rate in each of the 5 patient groups (Table 2) varied from 1.36% (no prevention) to 3.41% (fondaparinux).

Compared with the use of no prevention, the use of heparin or LMWH did not significantly increase the risk of bleeding events (Table 4), either in unadjusted (unadjusted HR, 0.95; 95% CI, 0.80, 1.11) or adjusted analysis (propensity-adjusted HR, 1.04; 95% CI, 0.87, 1.24). The corresponding estimated absolute risk difference was small (0.02%) and nonsignificant.

Similarly, there was no significant bleeding risk associated with the use of mechanical preventative therapy compared

**Table 2. Venous Thromboembolism and Bleeding Events According to Postoperative Preventative Strategy**

Preventative Therapy	VTE Events, n (%)	Bleeding Events, n (%)
No prevention (n=55 400)	390 (0.70%)	751 (1.36%)
TED or SCD (n=21 162)	167 (0.79%)	306 (1.45%)
Heparin or LMWH (n=10 718)	87 (0.81%)	181 (1.69%)
Fondaparinux (n=88)	1 (1.14%)	3 (3.41%)
Chemical and mechanical (n=5331)	39 (0.73%)	80 (1.50%)
Total (n=92 699)	684 (0.74%)	1321 (1.43%)

VTE indicates venous thromboembolism; TED, thromboembolic deterrent stockings; SCD, sequential compression devices; and LMWH, low-molecular-weight heparin.

with the use of no prevention (propensity-adjusted HR, 0.95; 95% CI, 0.81, 1.11). The corresponding absolute risk difference was small (0.18%) and nonsignificant.

### Secondary Analysis

The use of cardiopulmonary bypass did not affect the incidence of VTE after surgery (0.78% versus 0.73%, off-pump versus on-pump,  $P=0.43$ ). Endoscopic saphenous vein harvesting also did not significantly affect the incidence of VTE events (0.74% versus 0.74%, endoscopic versus open,  $P=0.99$ ). Moreover, there was no significant relationship between the dose of heparin administered at the time of surgery and the incidence of postoperative VTE ( $P=0.11$ ). Finally, the analysis focused on excluded patients who had undergone surgery on the first day of hospitalization yielded results that are generally similar to the main findings of the study and are featured in the online-only Data Supplement Appendix.

### Discussion

Controversy exists regarding the need for routine VTE prophylaxis after CABG.<sup>1</sup> In this observational study of 92 699 patients who underwent CABG between 2004 and 2008, we observed that nearly 60% of CABG patients received no postoperative VTE prophylaxis and that the overall incidence of VTE was <1%. The use of mechanical prevention or chemical prevention did not significantly reduce the risk of VTE or increase the risk of major bleeding compared with no therapy. These data provide support for the common practice of administering no VTE preventative therapy after CABG.

Strong evidence is available to support the use of VTE prevention after noncardiac surgery. In use for nearly 40 years, numerous studies have documented the benefits of subcutaneous heparin for VTE prophylaxis, particularly after general and orthopedic surgery, with meta-analyses estimating a reduction in postoperative DVT and PE by 40% to 70%.<sup>1,11</sup> More recent experience has also been favorable with the use of LMWH<sup>12</sup> and the factor Xa inhibitor fondaparinux for postoperative chemical VTE prophylaxis.<sup>13</sup> Alternatively, mechanical preventative therapies such as TED stockings or SCDs may be used for the reduction of perioperative VTE. Compared with anticoagulant-based prophylaxis, mechanical strategies promote blood flow in the deep veins of the legs and are recommended as preventative therapy for patients believed to be at high risk for bleeding complications.<sup>1,14,15</sup>

Despite the data available to support the use of VTE preventative strategies after noncardiac surgery, very few studies have evaluated the impact of VTE prophylaxis after cardiac operations. To our knowledge, only 2 trials have prospectively assessed VTE thromboprophylaxis after CABG. In a study published in 1995, Goldhaber et al<sup>27</sup> evaluated the optimal mechanical strategy for VTE prevention after CABG, randomly assigning 344 patients to receive either TED stockings alone or the combination of TED stockings plus SCDs after surgery. Screening ultrasound before discharge detected asymptomatic DVT in 19% of patients assigned to the combined therapy and in 22% of those assigned to TED stockings alone, but this difference was not statistically significant.<sup>27</sup> In the second randomized trial (published in 1996), Ramos et al<sup>17</sup> compared the administration of twice-daily subcutaneous unfractionated heparin alone with the combination of subcutaneous heparin plus SCDs in 2551 patients who underwent cardiac surgery (>90% CABG) between 1984 and 1994. Although limited by its unblinded design and prolonged duration, this trial reported that the addition of SCDs to heparin therapy significantly decreased the incidence of symptomatic PE from 4% to 1.5% (relative risk reduction, 62%; 95% CI, 47%, 71%;  $P<0.001$ ). Nevertheless, this study was performed in an earlier era, before the routine administration of postoperative antiplatelet therapy<sup>28</sup> and the aggressive use of physical therapy and rehabilitation after CABG.<sup>29</sup> Moreover, there was no placebo arm in the study, and the incidence of PE was relatively high in this trial. Studies performed in more recent years have estimated the combined risk of post-CABG DVT

**Table 3. Risk of Venous Thromboembolism With Preventative Therapy Compared With the Use of No Prevention**

	Unadjusted HR (95% CI)	Adjusted HR (95% CI)*	Adjusted HR (95% CI) plus propensity score†	Estimated Risk Difference (95% CI)‡
TED or SCD	1.12 (0.93, 1.34)	1.16 (0.96, 1.39)	1.14 (0.90, 1.43)	0.02% (−0.06%, 0.11%)
Heparin or LMWH	1.15 (0.91, 1.45)	1.07 (0.84, 1.35)	0.89 (0.68, 1.16)	0.01% (−0.07%, 0.09%)

HR indicates hazard ratio; CI, confidence interval; TED, thromboembolic deterrent stockings; SCD, sequential compression devices; and LMWH, low-molecular-weight heparin.

\*Multivariable adjustment.

†Multivariable adjustment with high-dimensional propensity score.

‡Estimates of absolute risk difference determined from Cox proportional hazard models using reference covariate values.

**Table 4. Risk of Bleeding With Preventative Therapy Compared With the Use of No Prevention**

	Unadjusted HR (95% CI)	Adjusted HR (95% CI)*	Adjusted HR (95% CI) Plus Propensity Score†	Estimated Risk Difference (95% CI)‡
TED or SCD	0.88 (0.77, 1.00)	0.90 (0.79, 1.03)	0.95 (0.81, 1.11)	-0.18% (-0.81%, 0.44%)
Heparin or LMWH	0.95 (0.80, 1.11)	1.01 (0.86, 1.19)	1.04 (0.87, 1.24)	0.02% (-0.67%, 0.72%)

HR indicates hazard ratio; CI, confidence interval; TED, thromboembolic deterrent stockings; SCD, sequential compression devices; and LMWH, low-molecular-weight heparin.

\*Multivariable adjustment.

†Multivariable adjustment with high-dimensional propensity score.

‡Estimates of absolute risk difference determined from Cox proportional hazard models using reference covariate values.

and PE to be closer to 1%,<sup>5-8</sup> similar to the findings of the current study.

In a summary of the literature, the recent American College of Chest Physicians VTE preventative guidelines acknowledged that uncertainty exists regarding the need for routine thromboprophylaxis after CABG.<sup>1</sup> Our analysis confirms this premise, principally because VTE events are fairly uncommon after CABG. Marginal differences were seen in our comparison of the 5 prevention strategies, raising the question of whether VTE prophylaxis has any clear benefits in this patient population. Of note, several reviews on the subject have proposed that new clinical trials should be performed to identify the optimal approach for post-CABG VTE prevention.<sup>1,4,30</sup> Given the low event rate, however, we believe it will be difficult if not impossible to conduct adequately powered trials to prospectively compare different VTE prevention strategies after CABG.

Our results should be interpreted in the context of several limitations. First, we used administrative data collected from the Premier Database. These data do not contain detailed clinical information such as the reasons for physicians' choices regarding VTE prophylaxis strategies. Moreover, this dataset only contains information pertaining to hospital admissions to facilities participating in Premier. Therefore, it is possible that our analysis underestimated the incidence of post-CABG VTE, since we could not capture the data for an unknown but probably small number of patients who could have been readmitted for late VTE events to facilities outside of the network of Premier hospitals. Although our study was observational in nature, we attempted to control for confounding by excluding patients who had early perioperative bleeding complications (reopening), and we performed adjustment using multivariable and high-dimensional propensity score analysis. Despite applying these sophisticated statistical techniques, however, it remains possible that unmeasured or unknown confounders influenced the results.

Patients who underwent CABG on the same day as hospital admission were excluded from the study to ensure the accurate collection of demographic and comorbidity characteristics in the preoperative period (online-only Data Supplement Appendix). Therefore, our results may not necessarily be generalizable to all CABG patients and those with different demographic or clinical characteristics. Further, for the purpose of completeness, we included patients in this study who were treated with fondaparinux or the combination of chemical and mechanical therapy. Although the bleeding risk appeared higher in the fondaparinux group (3.4%), this was

probably a reflection of small sample size. Ultimately, because the sample size and event rates were low in the fondaparinux and combined chemical and mechanical groups, these strategies were excluded from the comparative analysis. Overall, the results of this study suggest a lack of benefit associated with VTE prevention strategies after CABG. Nevertheless, we acknowledge that aggressive VTE prophylaxis may be appropriate for CABG patients who are nonambulatory and exhibiting a slow recovery during a complicated and lengthy postoperative course.<sup>1,4</sup>

In summary, VTE occurs relatively infrequently after CABG. Compared with the use of no prevention, the routine administration of chemical or mechanical preventative therapies to CABG patients does not appreciably lower the risk of VTE. These data provide support for the common practice of administering no VTE preventative therapy after CABG, used for nearly 60% of patients within this cohort.

## Disclosures

None.

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