Postoperative Enoxaparin Prevents Symptomatic Venous Thromboembolism in High-Risk Plastic Surgery Patients

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Background: Venous thromboembolism is a major patient safety issue. The Plastic Surgery Foundation–sponsored Venous Thromboembolism Prevention Study examined whether postoperative enoxaparin prevents symptomatic venous thromboembolism in adult plastic surgery patients.

Methods: In 2009, four sites uniformly adopted a clinical protocol. Patients with a Caprini score of 3 or higher received postoperative enoxaparin prophylaxis for the duration of inpatient stay. Venous Thromboembolism Prevention Study historical control patients had an operation between 2006 and 2008 but received no chemoprophylaxis for 60 days after surgery. The primary study outcome was symptomatic 60-day venous thromboembolism.

Results: Three thousand three hundred thirty-four patients (1876 controls and 1458 enoxaparin patients) were included. Notable risk reduction was present in patients with a Caprini score greater than 8 (8.54 percent versus 4.07 percent; $p = 0.182$) and a Caprini score of 7 to 8 (2.55 percent versus 1.15 percent; $p = 0.230$) who received postoperative enoxaparin. Logistic regression was limited to highest risk patients (Caprini score ≥ 7) and demonstrated that length of stay greater than or equal to 4 days (adjusted odds ratio, 4.63; $p = 0.007$) and Caprini score greater than 8 (odds ratio, 2.71; $p = 0.027$) were independent predictors of venous thromboembolism. When controlling for length of stay and Caprini score, receipt of postoperative enoxaparin was protective against venous thromboembolism (odds ratio, 0.39; $p = 0.042$).

Conclusions: In high-risk plastic surgery patients, postoperative enoxaparin prophylaxis is protective against 60-day venous thromboembolism when controlling for baseline risk and length of stay. Hospitalization for 4 or more days is an independent risk factor for venous thromboembolism. (*Plast. Reconstr. Surg.* 128: 1093, 2011.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, III.

Venous thromboembolism encompasses deep venous thrombosis and pulmonary embolus and is a major source of morbidity and mortality among hospitalized patients. Symptomatic pulmonary embolus has a 10 percent mortality rate within the first hour. Among survivors of pulmonary embolus, many develop right ventricular dysfunction or chronic pulmonary hypertension.[1] Untreated, proximal deep venous thrombosis carries a 90-day pulmonary embolus risk of 50 percent. In addition, deep venous thrombosis is associated with a localized inflammatory process that can permanently damage venous valves, resulting in venous re-

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flux. This phenomenon, known as the postthrombotic syndrome, occurs in at least 10 percent of patients and causes a chronically swollen, infection-prone extremity that inhibits ambulation.[1] Development of postthrombotic syndrome is the major driver of poor quality of life after deep venous thrombosis.[2]

Venous thromboembolism has been identified as a major patient safety issue in surgical patients. In 2008, then–Surgeon General Steven K. Galson issued a "call to action" for deep venous thrombosis and pulmonary embolus. This document stressed the importance of ongoing efforts to promote venous thromboembolism awareness, risk stratification, and prevention.[3,4] Concomitantly, several articles were published that demonstrated that venous thromboembolism risk among plastic surgery patients was higher than previously thought.[5–8] Venous thromboembolism was thus identified as a major patient safety issue among plastic surgery patients. In response to growing concerns among the American Society of Plastic Surgeons membership, the Plastic Surgery Foundation's Research Oversight Committee identified venous thromboembolism risk stratification and prevention as its top patient safety research priority in 2008.[9]

The Venous Thromboembolism Prevention Study was funded in 2008 and was designed to address several critical questions in plastic surgery patients. Questions examined appropriate venous thromboembolism risk assessment and the effectiveness and safety of postoperative chemoprophylaxis. The Venous Thromboembolism Prevention Study Network has previously demonstrated that the Caprini risk-assessment model[10] can risk-stratify plastic surgery patients for 60-day venous thromboembolism events.[11] This article addresses the effectiveness of postoperative enoxaparin, a low-molecular-weight heparin, for prevention of 60-day, symptomatic venous thromboembolism events among adult plastic surgery patients. The safety profile of postoperative enoxaparin will be discussed in a separate article.

PATIENTS AND METHODS

Study Inclusion and Exclusion Criteria

In 2008, the Venous Thromboembolism Prevention Study was funded by the Plastic Surgery Foundation. The Venous Thromboembolism Prevention Study Network consisted of four tertiary care hospitals, including the University of Pittsburgh (Pittsburgh, Pa.), the University of Texas Southwestern (Dallas, Texas), Regions Hospital (St. Paul, Minn.), and the University of Michigan (Ann Arbor, Mich.). Over a 6-month period after funding, Venous Thromboembolism Prevention Study Network members refined and mutually agreed on the study's clinical protocol. The protocol was based on an extensive review of the surgical literature and was designed to reflect evidence-based "best practice" for venous thromboembolism prophylaxis. Studies from the general surgery and surgical subspecialty literature were extrapolated to the plastic surgery patient population where appropriate. Between March of 2009 and September of 2009, the study protocol was implemented at each site. Data acquisition concluded on December 31, 2010. All data were acquired retrospectively.

Each Venous Thromboembolism Prevention Study site implemented an identical clinical protocol to risk-stratify and subsequently provide postoperative chemoprophylaxis to adult (age 18 years or older) plastic surgery patients. Preoperative risk stratification was performed using the Caprini risk-assessment model (Fig. 1).[10] Eligibility requirements for the clinical protocol included adult patients at moderate to high risk for venous thromboembolism (Caprini score ≥ 3), operation under general anesthesia, and postoperative admission to the hospital for at least an overnight stay. Eligible patients received a standard venous thromboembolism chemoprophylaxis regimen of postoperative enoxaparin (40 mg subcutaneously once daily or 30 mg subcutaneously twice daily for patients with a body mass index >40). Subcutaneous enoxaparin administration was initiated 6 to 8 hours after surgery and continued for the duration of inpatient stay. Timing of medication initiation and duration of enoxaparin prophylaxis was confirmed using inpatient pharmacy records.

Patients who received any preoperative heparin product were excluded. Patients who received any nonaspirin anticoagulant medication after surgery [including but not limited to intravenous heparin, subcutaneous unfractionated heparin, nonenoxaparin low-molecular-weight heparins, or Coumadin (Bristol-Myers Squibb, New York, N.Y.)] were excluded, except when these medications were used to treat a newly diagnosed venous thromboembolism. Patients who received a single bolus of intravenous heparin during microsurgical procedures were not excluded. Patients who received a nonprotocol enoxaparin dosage, who had enoxaparin initiated more than 6 to 8 hours after surgery, or who had gaps in their daily postoperative enoxaparin regimen were excluded. Postoperative aspirin administration was allowable

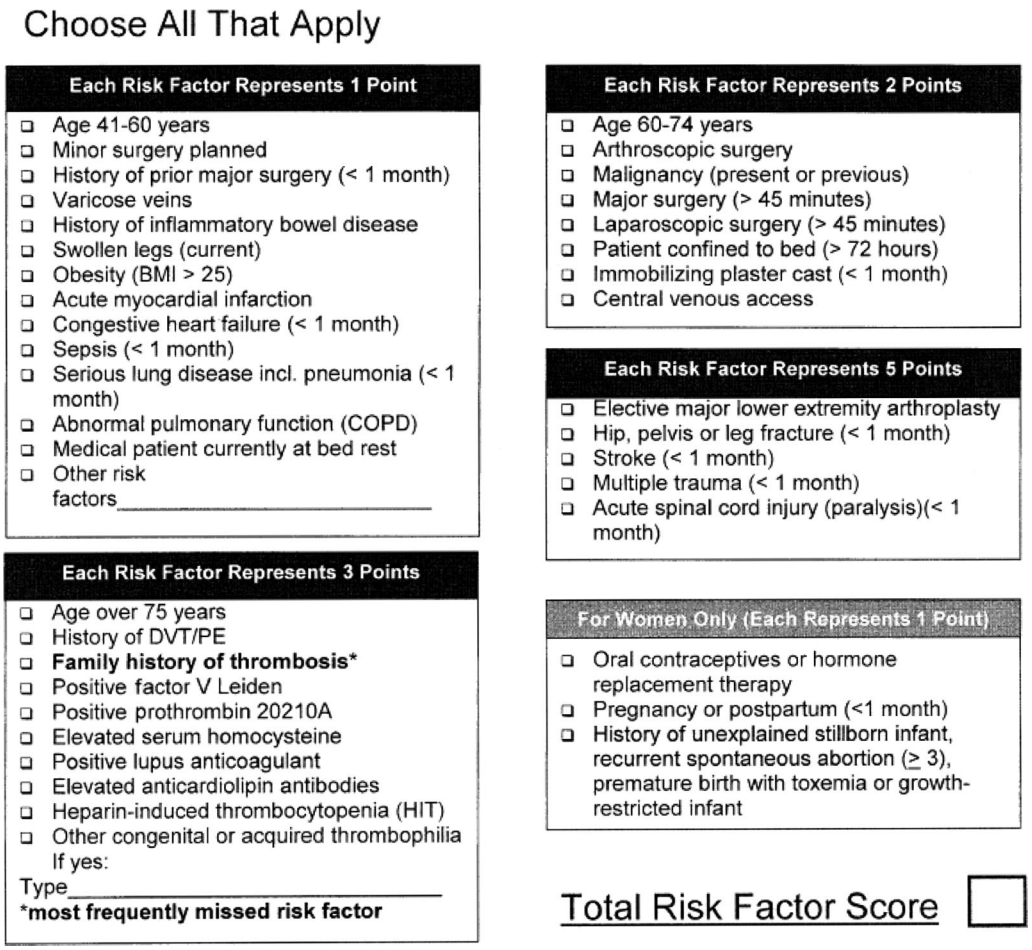

Fig. 1. The Caprini risk-assessment model. (Reprinted from Caprini JA. Thrombosis risk assessment as a guide to quality patient care. *Dis Mon*. 2005;51:70–78. Used with permission.)

and was tracked as a separate independent variable. Patients who were prescribed postdischarge prophylaxis with any nonaspirin anticoagulant medication were excluded. Use of perioperative and postoperative sequential compression devices was the standard of care at all four Venous Thromboembolism Prevention Study sites.

Initial in-progress review of Venous Thromboembolism Prevention Study data indicated that the majority of lower extremity trauma reconstruction patients had multiple operations, including débridement and/or bony fixation, before plastic surgery consultation. The vast majority of these patients received prophylactic-dose anticoagulation before definitive reconstruction by plastic surgery. Receipt of preoperative anticoagulation would represent a notable confounder for our clinical question. To avoid confounding, all patients who had lower extremity reconstruction after acute traumatic injury were excluded from the Venous Thromboembolism Prevention Study.

At each Venous Thromboembolism Prevention Study site, historical control patients were identified using medical record review for cases performed between 2006 and 2008. Historical control eligibility criteria were identical to those for patients in the clinical protocol group with one exception. Control patients did not receive unfractionated heparin, low-molecular-weight heparin, Coumadin, or other means of prophylactic or therapeutic anticoagulation for 60 days after surgery. This included the patient's inpatient stay and postdischarge course. Receipt of aspirin did not exclude patients from being historical controls.

Independent Variables

Medical record review was performed by physician-led teams at each Venous Thromboembolism Prevention Study site. Before chart review, each team leader was required to participate in a standardized training session. Training was ad-

ministered by Venous Thromboembolism Prevention Study coordinators and included focused educational sessions on Venous Thromboembolism Prevention Study eligibility criteria and outcomes of interest, the Caprini risk-assessment model, and proper use of the Web-based data collection system (see below). Retrospective chart review was performed for all patients to identify venous thromboembolism risk factors according to the 2005 version of the Caprini risk-assessment model. An aggregate Caprini score that reflected risk factors present before (e.g., age, body mass index, medical comorbidities, or personal/family history of venous thromboembolism) and during (e.g., total operative time or insertion of central venous line) hospitalization was generated. We collected several additional independent variables that were not included in the Caprini score. These included the year in which the procedure was performed, Venous Thromboembolism Prevention Study site, patient sex, whether multiple operations were performed during the initial hospitalization, surgical procedure type and location, enoxaparin administration according to protocol, administration of aspirin, and length of hospitalization.

Dependent Variables

Dependent variables included symptomatic deep venous thrombosis or symptomatic pulmonary embolus. All deep venous thrombosis or pulmonary embolus events required confirmation using an objective image method, such as venous duplex ultrasound, venography, ventilation-perfusion scan, or computed tomography. Autopsy-proven deep venous thrombosis or pulmonary embolus were considered as postoperative events only if the pathologist's report indicated that venous thromboembolism was the cause of or a major contributor to death. Medical record review was performed for 60 days after surgery to identify deep venous thrombosis or pulmonary embolus events. Patients whose medical records lacked 60 days of follow-up were excluded. A composite venous thromboembolism variable, encompassing patients with either deep venous thrombosis or pulmonary embolus, was created.

Web-Based Data Collection

The American Society of Plastic Surgeons launched the Tracking Operations and Outcomes for Plastic Surgeons in 2002 to provide a Health Insurance Portability and Accountability Act–compliant, secure, and confidential data repository.[12] The existing Tracking Operations and Outcomes for Plastic Surgeons platform was modified for Venous Thromboembolism Prevention Study purposes. Sites were provided with individualized log-in and password information. Upload of deidentified data to the modified Tracking Operations and Outcomes for Plastic Surgeons site was performed by physician-led teams at each Venous Thromboembolism Prevention Study site. Deidentified data were stored on a secure data server and were provided to study personnel for analysis on request.

Statistical Analysis

The Stata 11 statistical package (StataCorp LP, College Station, Texas) was used to perform all statistical analyses. Bivariate statistics were generated using the two-tailed t test, chi-square test, Fisher's exact test, or Wilcoxon rank sum test as appropriate. Descriptive statistics that examined deep venous thrombosis, pulmonary embolus, and venous thromboembolism incidence were generated and were stratified by various risk factors. Patients were stratified by Caprini score at accepted and published levels (Caprini scores of 3 to 4, 5 to 6, 7 to 8, and >8).[11,13,14] Caprini score was treated as an ordinal variable that provided an estimate of baseline venous thromboembolism risk.[11] Risk-stratified analyses were performed, including simple stratified analyses and multivariable logistic regression. To avoid colinearity, variables used in Caprini score generation were not used as independent variables in the logistic regression model. A value of $p < 0.05$ was considered significant.

Expected Risk Reduction and Sample Size Calculation

Our pilot data included 634 adult plastic surgery patients with a Caprini score greater than or equal to 3 who received no chemoprophylaxis after surgery. The 60-day incidence of symptomatic venous thromboembolism among these patients was 2.52 percent. Prior research[15,16] supports a 50 percent reduction in symptomatic venous thromboembolism using postoperative, inpatient low-molecular weight heparin chemoprophylaxis. Thus, we hypothesized that our postoperative enoxaparin chemoprophylaxis protocol would decrease the incidence of symptomatic venous thromboembolism from 2.52 percent to 1.26 percent.

Sample size calculation was performed for the primary study endpoint, specifically, an expected reduction in symptomatic venous thromboembo-

lism from 2.52 percent to 1.26 percent. Our assumptions included $\alpha = 0.05$, $\beta = 0.20$, power of 0.80, and n_1:n_2 of 1:1. With these assumptions, the Venous Thromboembolism Prevention Study would have 80 percent power to detect the expected difference if 1988 patients were included in each cohort. Our initial study design included 1988 patients in each of the historical control and intervention groups (approximately 500 patients per study cohort per study site). Before initiating this study, each Venous Thromboembolism Prevention Study site received institutional review board approval.

RESULTS

Complete data were present for 3334 patients who met eligibility criteria. This included 1876 historical control patients and 1458 intervention patients. When compared with historical controls, intervention patients had significantly increased age, higher body mass index, longer operative time, longer length of hospitalization, and higher Caprini score (Table 1).

We have previously shown that increased Caprini score correlates with increased 60-day venous thromboembolism events in a nonlinear fashion.[11] Stratified analysis was performed to examine the composition of historical control and intervention cohorts. The intervention cohort consisted of a notably higher risk patient population (Fig. 2).

Stratified analysis demonstrated that venous thromboembolism risk reduction was most apparent among high-risk and highest risk patients (those with a Caprini score ≥7) who received postoperative enoxaparin (Fig. 3). Minimal risk reduction was seen in the Caprini score 3 to 4 and Caprini score 5 to 6 groups. When postoperative enoxaparin was provided, notable risk reduction was present for patients with a Caprini score of 7 to 8 (2.55 percent versus 1.15 percent; $p = 0.230$) and a Caprini score greater than 8 (8.54 percent versus 4.07 percent; $p = 0.182$). In patients with a Caprini score of 7 to 8 and greater than 8, the observed absolute risk reductions of 1.40 percent and 4.47 percent correspond to a number needed to treat of 71.4 and 22.4, respectively, to prevent one venous thromboembolism event.

Table 1. Demographics Comparing Historical Control and Intervention Groups

	Historical Controls	Postoperative Enoxaparin	*p*
No.	1876	1458	
Mean age, yr	48.7	50.3	0.002
Mean BMI	29.0	30.0	<0.001
BMI ≥30	34.2%	41.2%	<0.001
Female sex	63.2	68.7	0.001
Median Caprini score	4	5	<0.001
Mean operative time, hr	3.1	3.8	<0.001
Multiple operations during hospitalization	13.1%	13.4%	0.780
Postoperative aspirin use	8.6%	7.8%	0.357
Mean length of stay, days	3.1	3.8	<0.001

BMI, body mass index.

Length of stay is a marker of illness severity and is not included in the Caprini score. Longer lengths of stay were associated with increased rates of venous thromboembolism on bivariate analysis. Among historical controls, patients who stayed greater than or equal to 7 days (4.35 percent versus 0.64 percent; $p < 0.001$) and patients who stayed 4 to 6 days (1.12 percent versus 0.64 percent; $p = 0.411$) were more likely to have postoperative venous thromboembolism when compared with those who stayed for 1 to 3 days. Among intervention patients, those who stayed greater than or equal to 7 days (3.87 percent versus 0.38 percent; $p < 0.001$) and those who stayed 4 to 6 days (0.82 percent versus 0.38 percent; $p = 0.336$) were more likely to experience postoperative venous thromboembolism when compared with patients with a length of stay of 1 to 3 days (Fig. 4).

Logistic regression analysis was limited to the high-risk and highest risk patient subgroups (Caprini score ≥7). Venous thromboembolism was the dependent variable of interest. Independent variables included length of stay (dichotomized to length of stay ≥4 or <4 days), stratified Caprini score, and receipt of postoperative enoxaparin. Logistic regression demonstrated that length of stay greater than or equal to 4 days (adjusted odds ratio, 4.63; $p = 0.007$) and Caprini score greater than 8 (adjusted odds ratio, 2.71; $p = 0.027$) were each independent predictors of venous thromboembolism. When controlling for length of stay and Caprini score, receipt of postoperative enoxaparin was protective against venous thromboembolism (adjusted odds ratio, 0.39; $p = 0.042$) (Table 2).

For both control and intervention groups, there were no significant differences in reported rates of venous thromboembolism by site. Frequencies of individual Caprini score risk factors in patients with and without venous thromboembolism are provided in Table 3. Frequencies of venous thromboembolism stratified by procedure type are listed in Table 4.

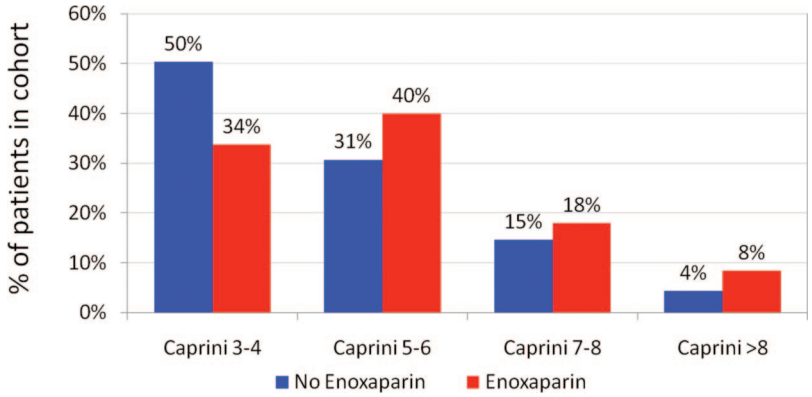

Fig. 2. Composition of cohorts stratified by Caprini score.

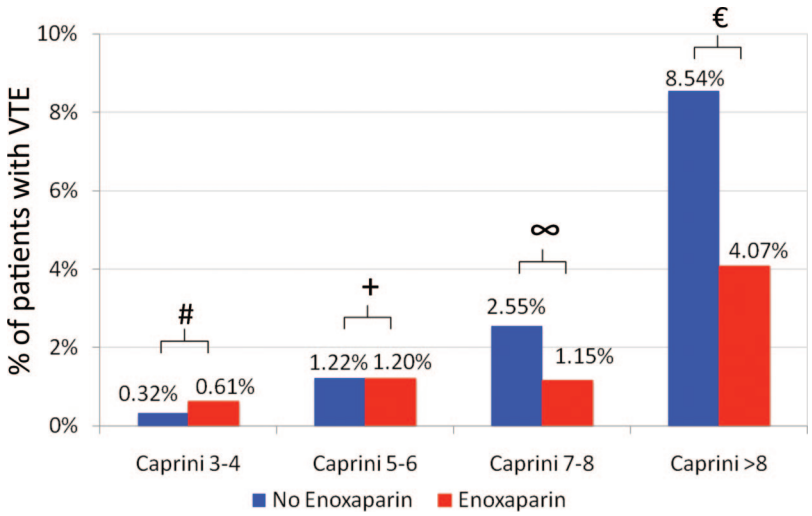

Fig. 3. Rates of venous thromboembolism stratified by Caprini score and receipt of postoperative enoxaparin (#$p = 0.414$; +$p = 0.982$; ∞$p = 0.230$; €$p = 0.182$).

DISCUSSION

We report the results of the Venous Thromboembolism Prevention Study, a multicenter, retrospective cohort study that examined whether postoperative enoxaparin decreases symptomatic, 60-day venous thromboembolism events in adult plastic and reconstructive surgery patients. Our results indicate that several factors are independently associated with venous thromboembolism. These include elevated Caprini score and length of stay greater than or equal to 4 days. In addition, when controlling for Caprini score and length of stay, receipt of postoperative enoxaparin was protective against 60-day venous thromboembolism events in high-risk patients (patients with a Caprini score ≥7).

As Hayward et al. note, risk should be considered at the individual level, not at the aggregate trial or population level.[17] Summary results from a study reflect only the arithmetic mean, which can be misleading when the population consists largely of low-risk patients. In addition, different risk-to-benefit ratios may exist for patients at variable levels of baseline risk. Multivariable risk-stratified analysis is thus preferred to identify clinically important subgroups that may receive improved benefit or excess harm from an intervention.[17–19] Risk-stratified analyses were presented throughout this article.

Between 1 and 7 percent of surgeons have personally experienced a venous thromboembolism–related patient death after high-risk plastic surgery.[20–22] Plastic surgeons' self-reported practice patterns indicate a disparity between clinical understanding and clinical practice. The majority of surgeons can identify patients at high risk for postoperative venous thromboembolism. However, examination of

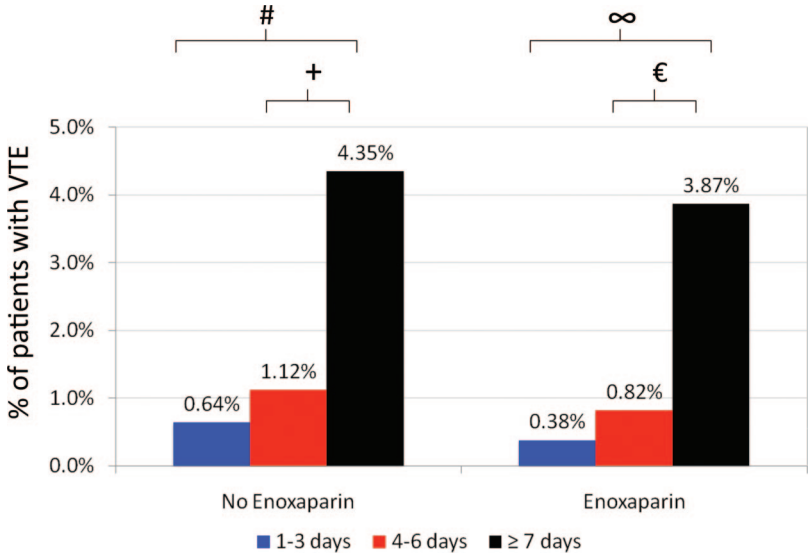

Fig. 4. Rates of venous thromboembolism stratified by length of stay and receipt of postoperative enoxaparin (#$p < 0.001$; +$p = 0.411$; ∞$p < 0.001$; €$p = 0.336$).

Table 2. Adjusted Odds for Venous Thromboembolism from a Multivariable Logistic Regression Model

	Adjusted Odds Ratio (95% CI)	*p*
Length of stay		
1–3 days	Reference	—
≥4 days	4.63 (1.52–14.17)	0.007
Caprini score		
7–8	Reference	—
>8	2.71 (1.12–6.52)	0.027
Group		
Historical control	Reference	—
Postoperative enoxaparin	0.39 (0.16–0.97)	0.042

CI, confidence interval.

their self-reported practice patterns indicates that a substantial proportion of surgeons (>50 percent) provide inadequate levels of venous thromboembolism prophylaxis for high-risk patients.[20,22] In addition, surgeons recognize modifiable venous thromboembolism risk factors (such as oral contraceptive use) but may fail to modify those factors before surgery.[23]

"Never event" is a poor descriptor for venous thromboembolism, as it implies that all events are potentially preventable.[24] Breakthrough venous thromboembolism events routinely occur in the face of rigorous protocols and criterion-standard prophylaxis, as has been reported in the plastic surgery,[25,26] orthopedic surgery,[27–29] and general surgery[30–32] literature. We observed multiple breakthrough events in the Venous Thromboembolism Prevention Study enoxaparin group, although the distinct causes of these events remain unclear. Unrecognized hypercoagulability has been identified as a major contributor to venous thromboembolism risk.[33–36] Venous Thromboembolism Prevention Study data support the belief that a prior personal history of venous thromboembolism is an important risk factor as well (Table 3).

Venous thromboembolism represents a financial burden for patients and payers. The mean cost of hospitalization for an index deep venous thrombosis event is over $20,000.[37] Previous work has shown that enoxaparin is a cost-effective method of venous thromboembolism prevention.[38–40] In July of 2010, the U.S. Food and Drug Administration approved production of enoxaparin in generic form, which should result in substantially decreased costs to patients.[41]

For a complete overview of venous thromboembolism in plastic surgery, we refer readers to two excellent reviews that have recently been published by Miszkiewicz and colleagues[42] and Venturi and colleagues.[43] These reviews built on the foundation of several outstanding reviews and consensus statements published previously.[44–46]

Limitations

Figure 2 demonstrates that our intervention group consisted of a patient population at higher baseline risk for venous thromboembolism. This may have been attributable to two factors. First, an increasing proportion of plastic and reconstructive surgery is being performed in the outpatient setting. Young, healthy pa-

Table 3. Frequency of Individual Caprini Risk-Assessment Model Risk Factors in Patients with and without Postoperative Venous Thromboembolism

	Without VTE (%)	With VTE (%)	*p*
No.	3292	42	
Risk factor			
One-point risk factors			
Age 41–59 years	1789 (54.3)	19 (45.2)	0.239
Minor surgery planned	164 (5.0)	5 (11.9)	0.042
Major surgery within 30 days	434 (13.2)	18 (42.9)	<0.001
Varicose veins	32 (1.0)	0 (0)	0.521
History of IBD	23 (0.7)	0 (0)	0.587
Swollen legs (current)	106 (3.2)	2 (1.3)	0.575
BMI >25	2426 (73.7)	37 (88.1)	0.035
Acute myocardial infarction <3 months	2 (0.1)	3 (7.1)	<0.001
Congestive heart failure <1 months	21 (0.6)	3 (7.1)	<0.001
Sepsis <1 month	15 (0.5)	0 (0)	0.661
Serious lung disease (including pneumonia) <1 month	15 (0.5)	0 (0)	0.661
Chronic obstructive pulmonary disease	68 (2.1)	4 (9.5)	0.001
Two-point risk factors			
Age 60–74 years	531 (16.1)	11 (6.2)	0.079
Arthroscopic surgery	5 (0.2)	0 (0)	0.800
Malignancy (present or previous)	1224 (37.2)	13 (31.0)	0.406
Major surgery >45 minutes	3105 (94.3)	38 (90.5)	0.287
Laparoscopic surgery >45 minutes	6 (0.2)	0 (0)	0.782
Central venous access	286 (8.7)	13 (31.0)	<0.001
Three-point risk factors	149 (4.5)	3 (7.1)	0.419
Age ≥75 years	109 (3.3)	5 (11.9)	0.002
History of DVT/PE	34 (1.0)	1 (2.4)	0.394
Family history of DVT/PE	8 (0.2)	0 (0)	0.749
Factor V Leiden–positive	1 (0.03)	0 (0)	0.910
Prothrombin 20210A–positive	3 (0.1)	0 (0)	0.845
Lupus anticoagulant–positive	3 (0.1)	0 (0)	0.845
Heparin-induced thrombocytopenia	0 (0)	0 (0)	—
Elevated serum homocysteine	0 (0)	0 (0)	—
Elevated anticardiolipin antibodies	7 (0.2)	0 (0)	0.765
Other congenital or inherited thrombophilia	3 (0.1)	0 (0)	0.845
Polycythemia vera			
Five-point risk factors			
Elective major lower extremity arthroplasty	18 (0.6)	0 (0)	0.631
Hip, pelvis, or leg fracture <1 mo	13 (0.4)	0 (0)	0.683
Stroke <1 month	1 (0.03)	0 (0)	0.910
Multiple trauma <1 mon	73 (2.2)	3 (7.1)	0.034
Acute spinal cord injury or paralysis <1 month	3 (0.1)	0 (0)	0.845
Female patients only			
No.	2168	20	
One-point risk factors			
Oral contraceptives	154 (7.1)	2 (10.0)	0.616
Pregnancy or postpartum (<1 month)	4 (0.2)	0 (0)	—
History of unexplained stillborn infant recurrent spontaneous abortion (≥3), premature birth with toxemia or growth-restricted infant	6 (0.3)	0 (0)	—

VTE, venous thromboembolism; IBD, inflammatory bowel disease; BMI, body mass index; DVT, deep venous thrombosis; PE, pulmonary embolus.

tients are preferentially selected for day-case surgery. This may account for the decreased proportion of low-risk patients in our more recent cohort. In addition, this finding may be explained by a surgeon-level bias in provision of postoperative chemoprophylaxis. In the period during which our historical controls were collected (2006 to 2008), some surgeons may have identified high-risk patients and provided them with chemoprophylaxis. By definition, these patients were not eligible for inclusion in the historical control cohort. Given that a selection bias was clearly present between our two cohorts, a risk-stratified analysis was most appropriate.

Table 4 reports the observed rates of venous thromboembolism stratified by procedure type. Because of a paucity of outcome events in each subgroup, we cannot provide a subgroup analysis of rates of venous thromboembolism stratified by both procedure type and receipt of enoxaparin.

We believe that length of stay is an important marker of illness severity (e.g., sicker patients have

Table 4. Rate of Venous Thromboembolism Stratified by Procedure Type

Procedure Type	No. of Patients	Rate of VTE (No. of Patients)
Upper extremity reconstruction	494	1.21% (6)
Postmastectomy breast reconstruction (implant or autologous tissue)	846	0.71% (6)
Breast reduction	302	0.66% (2)
Cosmetic breast surgery	39	0
Body contouring (non-postbariatric)	153	0
Body contouring (postbariatric)	229	0
Nontrauma lower extremity reconstruction	263	0.76% (2)
Head and neck reconstruction	421	1.66% (7)
Chest/abdominal wall/back reconstruction	301	3.99% (12)
Burn reconstruction	31	3.23% (1)
Decubitus ulcers (débridement or reconstruction)	232	2.16% (5)
Facial cosmetic surgery	70	0
Microsurgery/free tissue transfer	218	2.29% (5)
Genitourinary reconstruction	58	1.72% (1)

VTE, venous thromboembolism.

longer hospitalizations) and, as a result, have incorporated this variable into our multivariable risk model. However, given our study protocol, length of stay could also be viewed as a marker of duration of intervention (e.g., postoperative enoxaparin was provided for the duration of inpatient stay). We have attempted to control for these factors by using length of stay as an independent variable in a logistic regression model. The model results demonstrate that length of stay greater than or equal to 4 days is an independent risk factor for venous thromboembolism. In addition, when controlling for length of stay, receipt of postoperative enoxaparin is protective against venous thromboembolism (odds ratio, 0.39; $p = 0.042$).

A recent review article on venous thromboembolism in plastic surgery patients, co-written by leaders from plastic and vascular surgery, recommends that patients with ongoing venous thromboembolism risk factors receive 7 days of postoperative chemoprophylaxis. In addition, they recommend that cancer patients receive 28 days of postoperative chemoprophylaxis.[43] These recommendations are not based on data from the plastic surgery literature; instead, they are extrapolated from randomized controlled trials conducted in abdominal and pelvic cancer patients.[30–32] The optimal duration of chemoprophylaxis in plastic surgery patients remains unknown. Future trials should randomize plastic surgery patients at equal baseline risk to different durations of chemoprophylaxis to examine this important issue.

Studies published after the Venous Thromboembolism Prevention Study protocol was designed and implemented indicated that venous thromboembolism risk may remain elevated for up to 90 days after surgery.[47] As Venous Thromboembolism Prevention Study follow-up was limited to 60 days after surgery, late venous thromboembolism events may not be included in our data. Similarly, screening studies have shown that high-risk plastic surgery patients have rates of asymptomatic venous thromboembolism between 3.4 and 16.7 percent.[25,48] These rates are similar to rates of asymptomatic venous thromboembolism reported in other high-risk populations.[27–32,49–53] The Venous Thromboembolism Prevention Study reports the 60-day rate of symptomatic venous thromboembolism, which likely underestimates the true rate of venous thromboembolism after plastic and reconstructive surgery.

CONCLUSIONS

In high-risk plastic surgery patients (Caprini score ≥7), receipt of postoperative, prophylactic dose enoxaparin is protective against 60-day venous thromboembolism events when controlling for baseline risk and length of stay. Length of stay greater than or equal to 4 days is also an independent risk factor for venous thromboembolism. Optimal duration of prophylaxis remains an important topic for further research.

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