

An Effective Protocol for Perioperative Venous Thromboembolism Prophylaxis in DIEP Flap Breast Reconstruction: A Single Institution Retrospective Review

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Background: Deep inferior epigastric artery perforator (DIEP) free flap breast reconstruction is one of the most highly used procedures for autologous breast reconstruction. Many venous thromboembolism (VTE) risk assessment models have been proposed in breast reconstructive surgery, including the widely used Caprini score. However, a paucity of data suggests an effective standardized VTE protocol. The purpose of this study was to determine the rate of VTE in our DIEP flap patients who were treated with this protocol.

Methods: A retrospective single-center review of DIEP flap breast reconstruction from 2016 to 2021 was performed. Data were collected on 554 patients and 893 flaps including demographics, intraoperative and perioperative details, and postoperative course. Patients who were not treated with our standard protocol were excluded. Data were analyzed with $\alpha = 0.05$.

Results: The average age was 50.4 ± 9.9 years, and the total follow-up time was 16.9 ± 12.6 months. The average body mass index for the cohort was 30.1 ± 5.2 . During the 90 postoperative days, the mean length of hospital stay was 4.3 days. There were six cases of postoperative VTE: five patients presented with pulmonary embolism (0.9%) and one patient (0.2%) had deep venous thrombosis with an overall VTE prevalence of 1.1%. No specific single factor could be attributed to VTE occurrence.

Conclusions: Using our standardized VTE prophylaxis protocol, our institution was effective at keeping VTE rates low. Additional studies would be beneficial to determine optimal VTE prophylaxis protocols in higher-risk patients, such as those with known clotting disorders. (*Plast Reconstr Surg Glob Open* 2024; 12:e5688; doi: 10.1097/GOX.0000000000005688; Published online 21 March 2024.)

INTRODUCTION

Venous thromboembolism is a life- or limb-threatening condition that has been known to affect plastic surgery patients.¹ Since it was first introduced for breast surgery in 1994, the deep inferior epigastric perforator (DIEP) flap has remained the gold standard for autologous breast

reconstruction.² There have been multiple studies that have analyzed the VTE complications after pedicled transverse abdominus muscle (TRAM) flaps and microvascular breast reconstruction before the advent of the DIEP flap.³⁻⁵

Abdominal and sternal reconstruction VTE risks have previously been demonstrated in the literature with prophylaxis recommendations in numerous studies.⁶⁻⁸ The widely used Caprini risk assessment model (RAM)^{9,10} has become the preferred VTE model and is recommended by the American Society of Plastic Surgeons.¹¹ In fact, there have been multiple Caprini RAMs, including a 2005 and 2010, with one article finding the 2005 model having superior risk stratification.¹² Additionally, the Caprini RAM model fails to address the complexity of autologous breast reconstruction including surgical technique. One study analyzed the method of breast reconstruction performed and compared the VTE risks to various RAMs, including

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the Caprini RAM tool.³ This study showed that the method of reconstruction (TRAM, latissimus, implant) affected the patient's VTE risk.³ Huang et al¹³ used the Caprini RAM scoring for all of their patients along with a standard VTE prophylaxis in their DIEP population. Their prevalence rate of VTE was low (0.4%), and they found prolonged use (>1 week) of prophylactic anticoagulation may not be needed even when dictated by the Caprini model. There has been a growing consensus within the plastic surgery community for VTE prevention protocols that do not rely on Caprini recommendations. According to the Caprini model, all patients with scores 5 or greater should receive a minimum 1 week of postoperative prophylaxis.¹⁰ Most DIEP flap patients would fall into this range and would qualify for prolonged VTE prophylaxis.

Although numerous studies have been published identifying individual VTE risk factors,^{9,14,15} to date there have been minimal studies published identifying a standardized VTE prophylaxis protocol that is economical and effective. Autologous breast reconstruction patients represent a unique subset of patients in plastic surgery. These patients present with numerous risk factors that have been shown to increase VTE events, including a history of cancer, hormonal therapy, prolonged operative times, and multiple medical comorbidities.³ Historically, the prevalence of VTE in autologous breast reconstruction has been published in multiple studies, ranging between 2% and 4%.^{16,17}

The rationale for our study included using a standardized protocol established at our institution over a decade ago. Aspirin is particularly used in this protocol due to its low cost and proven effects on VTE prevention by affecting the formation of and adhesion to neutrophil extracellular traps that contribute to VTE.¹⁸

PATIENTS AND METHODS

This research protocol was approved via the University of Kansas Medical Center institutional review board (STUDY00147917). A retrospective chart review was performed on 554 patients (893 flaps) who underwent DIEP flap breast reconstruction between 2016 and 2021 at our institution. All patients received the standard VTE prophylaxis protocol in the form of:

1. Preoperative sequential compression devices and Aspirin 325 mg per rectum (for faster absorption).
2. Postoperative early ambulation and low-molecular-weight heparin subcutaneous administration postoperative day 1 (if no concern for postoperative bleed).
3. Enoxaparin 40 mg and daily sequential compression devices continued daily until hospital discharge (postoperative day 3).
4. Oral aspirin 81 mg daily administered 30 days postoperatively.

Patients with a history of known clotting disorders were excluded from this study. Previous studies have shown benefits of VTE prophylaxis in high-risk patients.^{19,20} Our study included standard risk patients in order for our results to be more generalizable to the population. Patients with

Takeaways

Question: Is there an effective VTE protocol that keeps VTE prevalence low in a DIEP reconstruction patient population?

Findings: Over 554 patients were reviewed using the institution's standardized protocol, showing a low VTE prevalence rate of 1.1%.

Meaning: Risk stratification protocols are unnecessary in DIEP patient populations, and standardized protocols can be used to keep VTE rates low.

suspected VTE were assessed by venous Doppler ultrasound in the lower extremities and chest computerized tomography angiography. All patients with confirmed VTE were treated with anticoagulation regimens determined by consultation with internal medicine colleagues.

Patient records were reviewed, and data were collected including demographic information as well as preoperative and perioperative factors. Preoperative factors included age, body mass index (BMI), medical comorbidities, history of chemotherapy and/or radiation, hormonal therapy use, and smoking history. Perioperative factors included unilateral versus bilateral reconstruction, length of surgery, immediate versus delayed reconstruction, length of hospital stay, and VTE diagnosis. Both patients with malignancy and with genetic predisposition for malignancy were included in the study.

The primary method of breast reconstruction utilized was the DIEP flap for all patients. Each patient was treated with the standardized VTE prophylaxis protocol across all our institution's surgeons. Prophylactic dosing of enoxaparin was administered per BMI and was given until day of discharge (typically three days). Patients were examined for any evidence of VTE events including leg pain/edema, dyspnea, and hemodynamic instability. Diagnostic imaging was selectively utilized for each patient. Timing for diagnosis of VTE included up to 90 days after the operative procedure.

Fisher exact two-tailed test was used to determine the statistical significance for all categorical data variables. Continuous variables are presented as means and examined using analysis of variance. Data were collected using RedCap (University of Kansas Medical Center), and data were analyzed using Microsoft Excel (version 16.0, Microsoft Corporation, Redmond, Wash.). A value of $P < 0.05$ was considered statistically significant.

RESULTS

The average age at the time of DIEP flap reconstruction was 50.4 years old, and the average BMI was 30.1 kg per m² (Table 1). During the 90 postoperative days, the mean length of hospital stay was 4.3 days. Immediate breast reconstruction was performed in 12.6% of patients versus 87.4% for delayed reconstruction. A total of 82 (14.8%) patients did not have a primary malignancy diagnosis and surgery was performed prophylactically. Unilateral reconstruction was performed in 38.3% versus

Table 1. Demographics of Patient Population

Demographics	
N	554
Age	50.4±9.9
BMI	30.1±5.2
Medical history (%)	
Diabetes	46 (8.3)
Hypertension	152 (27.4)
Autoimmune disorder	34 (6)
CAD	4 (0.7)
Massive weight loss	19 (3.4)

61.2% for bilateral reconstruction. There were six cases of postoperative VTE: five patients presented with pulmonary embolism (0.9%), and one patient (0.2%) had deep venous thrombosis with an overall VTE prevalence of 1.1% (Table 2). All cases of VTE were patients with a malignancy diagnosis. The average age of patients who developed a VTE event was 48.1 years, and the average BMI was 34.3 (Table 3). The length of surgery for these patients was higher in the VTE group with an average time of 508 minutes. The mean length of stay was also higher in the VTE group at 5.6 days. No specific single factor could be attributed to VTE occurrence as no statistically significant data variables existed.

DISCUSSION

In this study, we evaluated the prevalence of venous thromboembolism (VTE) in patients who were not stratified by a RAM (standard risk population) and underwent breast reconstruction with DIEP flaps and were treated with our standard perioperative anticoagulation protocol. We have shown in our study that DIEP flap breast reconstruction has a low VTE prevalence rate of 1.1% using our institution's standardized protocol. Only six patients in our cohort experienced a VTE event, and although we were unable to determine a statistically significant risk factor, our rate of VTE occurrence is considerably lower than historically reported studies. Although our cohort included patients during the COVID-19 pandemic, no analysis was performed to associate outcomes with COVID-19 infection. Hamdi et al reported a 3.8% VTE rate after 106 free flaps that included 98 DIEP flaps, and Binder et al found 6.6% of VTE after

30 DIEP flaps.^{21,22} These VTE events may not have been attributable to a specific risk factor due to the small number that occurred. This makes it difficult to draw any definitive conclusions regarding any associations. Although there was no statistically significant correlation, there were noticeable trends in risk factors among those who experienced a VTE event, including increased BMI, hormonal therapy, prolonged operative time, and bilateral reconstruction. Similar associations were noted by Moderrassi et al, who showed similar VTE rates as previously reported.²³

As pointed out by Moderrassi et al,²³ Guerra et al²⁴ reported a VTE rate of 0.8% in which they assessed 140 bilateral DIEP flap reconstructions.²⁴ They appropriately noted that their patients did not undergo systematic screening for VTE in the form of venous Doppler ultrasound or computed tomography angiography.^{23,24} Imaging, as in our study, was done only after the symptoms were apparent or if there was clinical suspicion. This raises an important point that the actual VTE rate is probably underestimated. Pannucci et al reported on the unreliability of clinical signs and this VTE underestimation.¹⁷ Lemaine et al performed systematic screening for VTE 5 days after DIEP or TRAM free flap reconstruction and found a higher VTE prevalence rate (3.4%) compared with those without systemic screening (0%).²⁵ Similarly in our study, VTE systematic screening in asymptomatic patients was not performed, which may have revealed a much higher VTE rate.

Pannucci et al have previously reported on the benefits and risks of prophylaxis for VTE prevention as well as the benefit of enoxaparin in high-risk patients.^{19,26} Of note, aspirin was not included in this protocol for 30 days postoperatively. In the systematic review and meta-analysis published, several recommendations are noted; however, in regard to autologous breast reconstruction, only the pedicled TRAM procedure is mentioned, and routine chemoprophylaxis is not recommended in nonrisk stratified patients.²⁶ Two questions arise; one, do RAMs prevent VTE events when utilized and followed? And two, does the method of autologous breast reconstruction influence the VTE risk? McKean et al²⁷ showed that patients with Caprini scores of more than 7 had significant symptomatic risk reduction with inpatient enoxaparin prophylaxis. However, our study shows that symptomatic VTE rates can remain low in a standard risk population without utilizing

Table 2. Patient Outcomes of Study Population

	Total	VTE	No VTE	P
No. patients (%)	554	6 (1.1)	548 (98.9)	n/a
Smokers ex, n (%)	152 (100)	0	152 (100)	0.06
Hospital length of stay, mean	4.3	5.6	4.1	0.6
Length of surgery (min), mean	478	508	490	0.73
Hematoma, n (%)	27	0 (0)	27 (4.9)	0.63
Neoadjuvant chemotherapy, n (%)	340 (61.4)	3 (50)	337 (61.5)	0.6
Neoadjuvant radiotherapy, n (%)	283 (51.1)	1 (16.7)	282 (51.4)	0.06
Perioperative hormone therapy, n (%)	249 (45)	4 (66.7)	245 (44.7)	0.82
Unilateral/bilateral DIEP, n (%)	215 (38.3)/339 (61.2)	2 (33.3)/4 (66.7)	213 (38.9)/335 (61.1)	0.95
Immediate/delayed reconstruction, n (%)	70 (12.6)/484 (87.4)	6 (100)/0	64 (11.7)/484 (88.3)	0.07

Table 3. VTE Patient Characteristics

Variable	Patient A	Patient B	Patient C	Patient D	Patient E	Patient F
Age	45	38	49	49	49	59
BMI	29.55	41.85	32.06	32.82	34.49	35.24
Smoking	/	/	/	/	/	/
Other comorbidities	/	Yes	/	/	/	/
Unilateral/bilateral	Bilateral	Bilateral	Unilateral	Bilateral	Bilateral	Unilateral
Immediate/delayed	Delayed	Delayed	Delayed	Delayed	Delayed	Delayed
Operating time (min)	712	508	493	470	495	370
Chemotherapy	/	/	Neo-adjuvant	Neo-adjuvant	Neo-adjuvant	Adjuvant
Radiotherapy	/	/	/	Yes	/	/
Hormonotherapy	Yes	Yes	No	Yes	Yes	/
Type of VTE	PE	PE	PE	DVT	PE	PE

Caprini scoring. Previous studies have shown the pedicled TRAM to have the highest VTE risk when compared with other methods and that current RAMs fail to stratify these risks.³ In our study, the Caprini score was not calculated for our study population, and risk stratification was not performed, as all patients were treated with the same standardized VTE prophylaxis protocol (unless history of blood clotting disorder). Caprini scoring would have been considered “high” in our study population with factors such as major surgery (> 45 minutes), malignancy, BMI of more than 25, and age 41–60 years attributable to the majority of our patients. However, our VTE prevalence rate remained quite low at 1.1% despite not utilizing a RAM. Additionally, these recommendations fail to address microvascular free tissue transfer with DIEP flaps specifically, which remains the gold standard today. This further strengthens the argument that there is no consensus on VTE prophylaxis recommendations within the plastic surgery community on one of the most utilized methods of autologous breast reconstruction. Our study presents a potential protocol that can be implemented to keep VTE rates low without using a RAM.

The use of chemoprophylaxis in autologous reconstruction varies regarding dosage and duration. Pannucci et al reported that a “one size fits all approach” may not be adequate in preventing VTE events due to the pharmacodynamics of enoxaparin and under-dosing that may occur.²⁸ When considering chemoprophylaxis, real-time Factor Xa levels and enoxaparin dose adjustments lead to higher risk reduction versus standard 40 mg of enoxaparin.²⁸ The duration of chemoprophylaxis has been shown to vary where McKean et al recommend patients receive extended LMWH postdischarge, completing a total of 14 days of treatment.²⁹ In our study, 40 mg of enoxaparin is initiated on a postoperative day 1 until discharge. Additionally, patients are placed on 81 mg of aspirin daily for 30 days postoperatively. Multiple studies have shown the benefit of chemoprophylaxis in high-risk patients.^{20,27,30} We purposefully did not include high-risk patients (those with known clotting disorders) in our study population. These patients were typically sent to our hematology/oncology colleagues for individualized anticoagulative therapy. Our study was designed to assess the VTE prevalence among nonhigh-risk patients using our standardized prophylaxis protocol. Numerous studies offer practical guidelines and

recommendations for the prevention of VTE in plastic surgery patients.^{31–33} However, these studies all fail to provide standardized methods for VTE prophylaxis in patients undergoing autologous breast reconstruction with DIEP flaps. An argument can be made that prolonged chemoprophylaxis may not be required.

Huang et al¹³ reported an overall VTE rate of 0.4% in their DIEP flap population over a period of 10 years. Our study complements their findings and further validates the argument that Caprini RAM should not be utilized for DIEP flap patients. Although our findings were similar, we did note some key differences. Our VTE rate was calculated over a 90-day postoperative period (compared with 60 days). One of our study patients had a VTE event outside of 60 days and therefore increased our overall prevalence rate when compared with the Huang study. Two additional key differences were our study did not routinely score any of the participants according to Caprini and our use of aspirin. At our institution, we administer rectal aspirin (325 mg) preoperatively and continue oral aspirin for a total of 30 days postoperatively. In the Huang et al¹³ study, before 2015 one dose of rectal aspirin and oral aspirin were administered until the day of discharge, and after 2015 only one dose of rectal aspirin postoperatively in the PACU was given. The use of aspirin to prevent VTE has been well documented¹⁸ and has been shown to affect the formation of and adhesion to the neutrophil extracellular traps that contribute to VTE. Aspirin is low cost compared with other prophylactic modalities (ie, LMWH, DOACs), and this benefit cannot be overstated. Both our study, along with Huang et al¹³ embolden the argument that the Caprini model needs to be re-evaluated and may not be necessary for DIEP patient populations.

Despite having 554 patients, there are some study limitations. Although we report the symptomatic VTE rate, the actual VTE rate may be under-reported as we did not conduct systematic screening. As was mentioned previously, conducting preoperative screening along with postoperative surveillance may be beneficial in future studies to capture the true VTE rates. An additional limitation was the retrospective nature of our study as well as only including a single institution. Future studies that examine prospective data should be carried out to further our understanding of proper VTE prophylaxis in plastic surgery patients. The aim of these studies would also include determining

optimal timing, dosing, and duration of chemoprophylaxis as well as their use in high-risk patient populations. Our study failed to identify any attributable risk factors to VTE occurrence, and we may benefit from future studies that further characterize both patient and operative risk factors that can contribute to VTE risk.

CONCLUSIONS

The DIEP flap remains the gold standard for autologous breast reconstruction. To date, there has been no consensus on perioperative prophylactic anticoagulation in DIEP flap patients. Our study reports low VTE prevalence rates with an effective and economical prophylactic regimen (using aspirin) without utilizing a RAM. This low VTE rate can be attributed to our institution's standardized VTE prophylaxis protocol and further solidifies recent findings that blanket Caprini recommendations do not apply to DIEP patient populations. Future prospective studies to determine optimal VTE prophylaxis in high-risk patients would be beneficial as well as multi-institutional studies. Further, screening of asymptomatic patients in future studies would be advantageous to delineate more accurate VTE rates.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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