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Safety of DIEP Flap Reconstruction in Patients with Factor V Leiden: A Retrospective Cohort Study

Anamika Veeramani, BS
Justin C. McCarty, DO, MPH
Brittany L. Vieira, MD
Sarah Karinja, MD
Andrea L. Pusic, MD, MHS
Matthew J. Carty, MD
Jessica Erdmann-Sager, MD

Background: Factor V Leiden (FVL) is the most common inherited thrombophilia in White people. Thrombotic complications resulting from free flap breast reconstruction in FVL patients have been studied to a limited degree. We evaluated whether patients heterozygous for a FVL mutation undergoing deep inferior epigastric perforator flap reconstruction had increased risk of micro- or macrovascular thrombotic complications compared with patients without a diagnosed thrombophilia.

Methods: We performed a retrospective cohort study of deep inferior epigastric perforator flap reconstructions at Brigham and Women's Hospital (1/2015–12/2020) comparing patients diagnosed as FVL heterozygotes compared with matched controls without a diagnosed thrombophilia. Patients were matched using coarsened exact matching algorithm based on clinical characteristics. The primary outcomes were micro- (return to OR for flap compromise, flap loss) and macrovascular (venous thromboembolism) complications.

Results: A total of 506 patients (812 flaps) were included in this study. Eleven patients (17 flaps) were FVL heterozygotes. After matching, 10 patients (16 flaps) with FVL were matched to 55 patients (94 flaps). The return to OR for flap compromise was 0% in the FVL cohort compared with 5% (n = 5/94, 3/94 flaps lost, $P = 1.00$) in the matched controls (1.9%, n = 15/795 in unmatched controls, 0.6%, n = 5/795 loss rate). There were zero venous thromboembolism events among FVL patients compared with 2% of controls (n = 1/55).

Conclusions: FVL heterozygosity did not increase the risk of micro- or macrovascular complications in patients undergoing deep inferior epigastric perforator flap breast reconstruction. This study supports the safety of microvascular reconstruction in this group of patients when appropriate venous thromboembolism prophylaxis is given. *(Plast Reconstr Surg Glob Open 2022;10:e4244; doi: 10.1097/GOX.0000000000004244; Published online 25 April 2022.)*

INTRODUCTION

Factor V Leiden (FVL) is the most common inherited thrombophilia in White people, at 3%–8% of the population.[1,2] Certain subgroups have an even higher prevalence of FVL polymorphisms, which have been found in 14.4% of persons of Lebanese descent and 21.8% of individuals of Jordanian descent.[3] In addition, other groups, such as African Americans, not traditionally associated with FVL mutations still are diagnosed with it at a rate of approximately 1%.[2] The prevalent FVL mutation is a single point mutation in the gene encoding factor V resulting in activated protein C resistance and subsequent increases in thrombin.[4] Individuals heterozygous for FVL have a three- to seven-fold increased risk of venous thromboembolism (VTE), and an 80-fold increased risk if homozygous for FVL. FVL is found to be primarily associated with venous thrombosis rather than with arterial thrombosis.[5]

Thrombophilias including FVL have significant implications for patients undergoing microsurgical procedures. First, thombophilias may confer an increased risk of microvascular thromboses, leading to an increased flap loss rate.[6] Second, as microsurgical cases tend to be longer in duration, the incidence of postoperative VTE after microsurgical reconstructions could be higher in thrombophilic populations. Establishing accurate rates of flap loss and postoperative VTE in thrombophilic patients is

From the Division of Plastic and Reconstructive Surgery, Brigham and Women's Hospital, Boston, Mass.

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Drs. Veeramani and McCarty contributed equally to this work.

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necessary in order to provide informed consent for these cases.

Some microsurgeons believe that it is safe to proceed with microsurgical reconstruction in the setting of FVL heterozygosity; however, supporting data are scarce. The largest series to date on free tissue transfer in hypercoagulable patients was published by Wang et al in 2012.[6] In this series of 41 patients (58 flaps) with all types of hypercoagulable conditions, a flap loss rate of 15.5% was found, which was a significant increase from an institutional baseline flap loss rate of 1.8%. However, only two patients (who underwent two flaps) in their series had an FVL mutation, and neither experienced any flap complications.[6] More recently in 2021, Liu et al presented a similar study of hypercoagulable patients undergoing free flap breast reconstruction (FFBR).[7] Their study included 19 patients with a hypercoagulable disorder, seven of whom had FVL heterozygosity. They found an overall thrombotic complication rate of 47.4% with one instance of flap loss; however, this study did not specify complication rates by hypercoagulable disorder. Both of the above case series added significantly to the literature; however, they were not limited to FVL nor did they present a matched control group.

Studies exclusively examining heterozygous FVL patients have been limited to case reports.[8,9] In 2011, Khansa et al described two cases of flap loss in patients with FVL heterozygosity who underwent FFBR.[8] In 2018, Zavlin et al described two cases of successful DIEP flap reconstruction in patients with FVL heterozygosity.[10] These small studies have made it difficult to generalize about the safety—or lack thereof—of FFBR in FVL patients.

In the current study, we compared patients heterozygous for a FVL mutation to matched controls as well as to a larger unmatched cohort to evaluate whether FVL increases risk for thrombotic complications or flap loss following deep inferior epigastric artery perforator (DIEP) flap reconstruction relative to patients without a FVL diagnosis. The primary outcome was the rate of intraoperative or postoperative microvascular thrombosis and postoperative VTE. Secondary outcomes were the rate of 30-day major and minor complications. We hypothesized that preoperative diagnosis of FVL would not significantly increase micro- or macrovascular complications when appropriate prophylactic measures were utilized.

Takeaways

Question: Are DIEP flaps safe in patients who are heterozygous for factor V Leiden mutations?

Findings: In this retrospective cohort, we examined whether thromboses, flap loss, and/or venous thromboembolism were more common in patients who were heterozygous for factor V Leiden mutations compared with those who do not carry that diagnosis. We found no significant difference in microvascular complications, such as thromboses and flap loss, or macrovascular complications, such as deep venous thrombosis or pulmonary embolus.

Meaning: Our data support the performance of DIEP flaps in patients who are heterozygous for factor V Leiden.

METHODS

Study Design

This was a retrospective, single-institution cohort study of female patients undergoing microsurgical DIEP flap breast reconstruction comparing patients with a diagnosis of FVL heterozygous mutation with those without an identified mutation. The primary outcome was microvascular flap complications and macrovascular complications. Secondary outcomes included any major or minor complications. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies.[11] The study was approved by the Mass General Brigham Institutional Review Board (Protocol number 2020P002326), and all research was conducted according to the guidelines described in the Declaration of Helsinki.

Setting and Participants

Patients who underwent FFBR at Brigham and Women's Hospital, Boston, Massachusetts between January 2015 and December 2020. Patients were seen at regular intervals in the postoperative period after discharge from the hospital, typically 1 week and 3 months postdischarge, and then as needed. Patient data were recorded in a HIPAA-compliant REDCap database.[12] Inclusion criterion for the exposure group included all patients with a pre- or postoperative diagnosis of FVL heterozygous mutation who underwent DIEP flap breast reconstruction. Exclusion criterion for the exposure group was performance of a nonDIEP breast free flap such as muscle-sparing free TRAM flaps, free TRAM flaps, and thigh and buttock flaps. Free flaps were limited to DIEPs in order to homogenize the cohort. These patients were not excluded if the planned operation was a DIEP flap but intraoperative conversion to a different operation occurred due to intraoperative thrombotic complications. Patients in the control group were excluded if they had any hypercoagulable diagnoses.

In all cases, arterial anastomoses were hand-sewn with 8-0 Nylon sutures. Venous anastomoses were performed with the Synovis coupler (Synovis Micro Companies Alliance, Inc.). All patients received our standard perioperative anticoagulation protocol for microsurgical breast reconstruction, which consists of subcutaneous heparin 5,000 units administered in the preoperative holding area and postoperatively three times daily while inpatient. Our standard protocol also includes sequential compression devices intra- and postoperatively as well as aspirin 121.5 mg daily postoperatively for 30 days.

Variables

The primary exposure of interest was the diagnosis of FVL heterozygous mutation, which could have been made pre- or postoperatively. During preoperative consultations in our practice, patients are queried for a personal or family history of VTE, and/or a history of two or

more miscarriages. Any patient whose history indicates an increased risk of arterial or venous thromboses is sent for a hypercoagulable workup, and then referred to hematology as deemed necessary based on the results of testing and clinical history.

Patient demographic and clinical variables were prospectively obtained from the electronic medical record. Patient demographic and clinical variables included age, body mass index (BMI), patient comorbidities, prior history of smoking (no active smokers undergo free flap reconstruction at our institution), and prior radiation therapy to the recipient site. Operative variables of interest include unilateral or bilateral reconstruction, flap weight, and immediate or delayed timing of reconstruction.

Outcomes

The primary outcomes of interest were microvascular and macrovascular complications. Microvascular complications were defined as need for intraoperative revision of the arterial or venous anastomosis and return to the operating room for flap compromise. Status of the flap following revision or return to the OR was defined as salvaged, partially salvaged, or lost. Macrovascular complications included the postoperative diagnosis of a deep venous thrombosis (DVT) and/or a pulmonary embolism (PE), confirmed by duplex ultrasound for DVT and CTA for PE. Additional details were obtained specifically regarding the clinical management of each patient in the FVL group, including whether hematology consultation was obtained, whether medications that increase risk of VTE were held preoperatively, and what anticoagulation regimen was recommended and used.

Secondary outcomes included 30-day major and minor complication rates. Major complications included return to OR for hematoma or requirement of blood transfusion, infection requiring readmission for IV antibiotics or reoperation, DVT or PE, pneumothorax, return to OR for flap compromise, and readmission. Minor complications included mastectomy skin flap necrosis, abdominal skin flap or umbilical necrosis or partial dehiscence, seroma, and infection treated with oral antibiotics alone.

Statistical Analysis

A matched analysis using coarsened exact matching was performed as a method of causal inference.[13] The FVL mutation exposure group was matched between one and five control patients, using the coarsened exact matching algorithm to a control group of patients without a FVL mutation, based on age at performance of reconstruction in 10-year increments, BMI categorized as underweight (<18.5), normal weight (18.6–24.9), overweight (25.0–29.9), obese (30.0–34.9), and morbidly obese (>35.0), one or more comorbid conditions, smoking history, preoperative radiation therapy to the recipient site, unilateral or bilateral breast reconstruction, and whether the operation was immediate or delayed breast reconstruction. The reason for selection of coarsened exact matching is that it has optimal statistical properties when assessing rare outcomes and can reduce imbalance, estimate error, bias, and model dependence.[13,14] Additionally, the selection of this matching algorithm rather than a traditional parsimonious regression analysis was because of the expectation for rare outcomes in the primary outcome of interest, thus limiting the ability to adjust for confounders without overfitting of the model.

Statistical analysis was then performed between the matched exposure and control groups using appropriate statistical tests. Additional tests were performed based on the number of flaps in each group to account for bilateral reconstructive cases. Fisher exact test was used for assessing categorical variables. A two-sample t-test or Wilcoxon rank-sum test was used to assess continuous variables based on the normality of the data. There were no missing data in the variables of interest in this study. Statistical significance was defined using a two-sided α of 0.05 and/or 95% confidence intervals. Stata software version 16.1 (StataCorp) was used for all statistical analysis.

RESULTS

Patient Demographics

During the study time period, 11 patients with FVL mutation underwent 17 DIEP flaps (five unilateral and six bilateral) for an incidence of FVL within the study pool of 2.2% (n = 11/506). Two additional patients with FVL mutation underwent FFBR but were excluded as they underwent non-DIEP flap reconstruction. An estimated 13 patients with a thrombophilia other than FVL were excluded from the control group. The FVL patients were matched to a control group using the coarsened exact matching algorithm from a remaining pool of 495 patients meeting inclusion criterion who underwent a total of 795 (195 unilateral and 300 bilateral) FFBRs. After matching, 10 patients with FVL were successfully matched to 55 patients (Table 1). One of the FVL patients could not be appropriately matched and so was excluded. There was good balance between patient characteristics after matching with the mean (SD) age of the matched cohort 51.1 (6.8) years (FVL 51.6 (5.8) versus 51.4 (6.7); $P = 0.92$). The median [Interquartile range (IQR)] overall BMI was 27.9 kg/m^2 (26.5–30). Eleven of 16 (69%) flaps in the FVL group were performed immediately ($P = 0.77$) compared with 72% (n = 68/94) in the matched control group. Flap recipient sites were previously radiated 38% (n = 6/16) of the time in the FVL group and 35% (n = 33/94) in the matched control group ($P = 1.00$). Mean flap weights were similar between the FVL (666.5 g) and control group (652.5 g, $P = 0.91$) in the full cohort as well as in the matched FVL group (668 g) and matched control group (653 g, $P = 0.67$).

Factor V Leiden Cohort Specific Characteristics

Table 2 outlines in greater detail the relevant clinical histories of each patient in the FVL cohort. None of these patients had a personal history of VTE, and three patients (27%) had a first-degree relative with prior VTE. One patient (9.1%) had an additional hypercoagulability diagnosis, anticardiolipin antibody syndrome. Five patients (45%) were referred for hematology consultation preoperatively and received recommendations for

Table 1. Baseline Characteristics of Patients Undergoing Free Flap Breast Reconstruction

	Patient Level					
	Full Cohort (n = 506)			Coarsened Exact Matched Cohort (n = 65)		
Characteristic	Control (n = 495)	Factor V Leiden (n = 11)	*P*	Control (n = 55)	Factor V Leiden (n = 10)	*P*
Age (y), mean (SD)	49.9 (8.9)	50.8 (6.1)	0.74	51.4 (6.7)	51.6 (5.8)	0.92
BMI, median (IQR)	28.45 (25.8–31.6)	26.1 (25.3–29)	0.15	28.2 (26.6–29.6)	26.7 (25.8–29)	0.17
Hypertension	89 (18.0%)	3 (27.3%)	0.43	5 (9%)	3 (30%)	0.098
Diabetes mellitus	24 (4.8%)	1 (9.1%)	0.43	3 (5%)	1 (10%)	0.50
Former smoker*	103 (20.9%)	1 (10.0%)	0.70	11 (20%)	1 (11%)	1.00
Laterality			0.76			0.48
Unilateral	195 (39.4%)	5 (45.5%)		16 (29%)	4 (40%)	
Bilateral	300 (60.6%)	6 (54.5%)		39 (71%)	6 (60%)	
Overall operative time (min)	540 (426.5–633.5)	540 (415–608)	0.94	561.5 (463.5–630)	545 (461–608)	0.96
Hospital length of stay (d), median (IQR)	5 (4–5)	4 (4–5)	0.18	5 (4–5)	4 (4–5)	0.22
	Microsurgical Free Flap Level					
	Full Cohort (n = 812)			Coarsened Exact Matched Cohort (n = 110)		
Characteristic	Control (n = 795)	Factor V Leiden (n = 17)	*P*	Control (n = 94)	Factor V Leiden (n = 16)	*P*
Timing of reconstruction			0.086			0.77
Immediate	454 (57.1%)	6 (35.3%)		26 (28%)	5 (31%)	
Delayed	341 (42.9%)	11 (64.7%)		68 (72%)	11 (69%)	
Prior radiation to recipient site	397 (49.9%)	6 (35.3%)	0.33	33 (35%)	6 (38%)	1.00
Flap weight in grams, median (IQR)	652.5 (505–820)	666.5 (527.5–762.5)	0.91	653 (549–774)	668 (530–765)	0.67

*No active smokers underwent microsurgical breast reconstruction during the study period.

perioperative anticoagulation (Table 3). Three of four patients (75%) who were taking prothrombotic medications that increase the risk of VTE (tamoxifen, letrozole, and hormone replacement therapy) were instructed to discontinue those medications prior to surgery.

The majority of our FVL group (82%) received our standard protocol plus at least 17 days of LMWH postoperatively (Table 3). In addition, hematology recommended that one of these eight patients receive an aspirin one day prior to surgery. Two patients in the FVL cohort received our standard protocol with no extended anticoagulation.

Microvascular and Macrovascular Complications

The rates of micro- and macrovascular thrombotic complications are presented in Table 4. None of the flaps (n = 0/17) in the FVL patients or the matched FVL group (n = 0/16) had an intraoperative thrombosis, whereas in the matched control group 2% (n = 2/94) underwent intraoperative revision of an anastomosis (*P* = 1.00). No patients in the FVL cohort developed postoperative thromboses that required re-exploration and resulted in salvage, whereas five (5%) of the matched control group did (*P* = 1.00), which was a higher rate of flap compromise than the unmatched controls (1.9%, n = 15/795). The postoperative flap loss rate in the FVL cohort was zero and three of the five flaps re-operated on in the matched control group were lost (*P* = 1.00). This rate of flap loss was also higher than that seen in the unmatched control group, where only five flaps out of 795 were lost (0.6%). No patients in the FVL cohort experienced VTE in the immediate 30-day postoperative period, whereas one patient (2%) of the matched control group did (*P* = 1.00) and three patients (0.6%) of the unmatched control group did (*P* = 1.00).

Overall Major and Minor Complications

Table 5 outlines major and minor complications in the FVL and control groups, and these are presented on

Table 2. Detailed Clinical Information for Patients in the FVL Cohort

Case	Age (y)	BMI (kg/m²)	Tobacco Use	Personal History of DVT/PE	Family History of VTE	Additional Hypercoagulability Diagnosis	Preoperative Radiation	Timing of FVL Diagnosis
1	57	26.11	Prior	No	Yes	No	BCT	<1 mo preoperative
2	49	27.3	Never	No	Yes	No	BCT	<1 mo preoperative
3	40	26.1	Prior	No	No	Anticardiolipin antibody syndrome	None	<1 mo preoperative
4	46	21.5	Never	No	No	No	None	>1 y preoperative
5	52	26.6	Never	No	No	No	None	>1 y preoperative
6	60	25.3	Prior	No	No	No	None	>1 y postop
7	55	30.5	Prior	No	No	No	None	<1 mo postoperative
8	55	30.7	Never	No	No	No	None	<1 mo preoperative
9	43	24.5	Never	No	Yes	No	BCT	<1 mo preoperative
10	53	29.0	Never	No	No	No	BCT	<1 mo preoperative
11	49	26.4	Never	No	No	No	BCT	>1 y preoperative

Table 3. FVL Cohort Anticoagulation Protocols and VTE Outcomes

Case	Preoperative Hematology Evaluation	Hypercoagulable Medications Held	Preoperative Anticoagulation	Postoperative Anticoagulation	Postoperative VTE
1	No	N/A	Standard*	Standard† + 28d LMWH	None
2	Yes	N/A	Standard	Standard + 28d LMWH	None
3	No	Yes‡	Standard	Standard + 28d LMWH	None
4	Yes	Yes§	Standard	Standard + 28d LMWH	None
5	Yes	N/A	Standard	Standard + 28d LMWH	None
6	No	N/A	Standard	Standard	None
7	No	No¶	Standard	Standard	None
8	No	N/A	Standard	Standard + 28d LMWH	None
9	Yes	N/A	121.5 mg ASA 1 day preoperative + Standard	Standard + 30d LMWH	None
10	No	Yes‖	Standard	Standard + 17d LMWH	None
11	Yes	N/A	Standard	Standard + 28d LMWH	None

*Standard Preoperative Anticoagulation Protocol: 5000 units subcutaneous heparin (SQH) immediately preoperatively, with pneumatic compression boots during surgery.
†Standard postoperative anticoagulation protocol: 121.5 mg daily aspirin for 30 days after surgery.
‡Held tamoxifen for 3 weeks prior to surgery.
§Stopped hormone replacement therapy (estrogen patch and progesterone) prior to surgery.
¶Tamoxifen was not held prior to surgery.
‖Held letrozole for 2 weeks prior to surgery.

a per patient rather than a per flap basis. The major complication rate was not significantly higher in the control group than in the FVL group (13% versus 0%, $P = 0.58$). Minor complications also were not significantly different between the control and FVL groups (35% versus 40%, $P = 0.73$). Most minor complications were mastectomy skin necrosis, abdominal necrosis, or umbilical necrosis, which were managed conservatively.

DISCUSSION

In this single-institution study, DIEP flap breast reconstruction was not associated with higher rates of micro- or macrovascular complications in patients heterozygous for FVL compared with either matched or unmatched control groups. Over a 5-year period, 17 DIEP flaps were performed on 11 patients who were heterozygous for FVL, and none of those patients experienced intraoperative thromboses, postoperative thromboses, or flap loss. Higher rates of intraoperative thromboses, postoperative thromboses, and flap loss were found in the control group but did not reach statistical significance and were within the range of expected outcomes in the literature.[15,16] There were no significant differences in postoperative VTE in the FVL group compared with the matched or unmatched control groups. Major and minor complications were not significantly different between the two groups. Our findings suggest that patients with FVL heterozygosity undergoing DIEP flap breast reconstruction likely have similar risks for micro- or macrovascular thrombotic complications as patients without the mutation, provided that standard VTE prophylaxis regimen is extended into the postoperative period.

Cardiac, transplant, and orthopedic surgery have more systematically evaluated thrombotic events in this patient population.[17–19] These studies identified higher rates of thrombotic complications in FVL heterozygotes, including arterial thromboses and VTE. In renal transplantations,

Table 4. Microvascular Complications on a per Flap Basis and Macrovascular Complications per Patient Basis

	Microsurgical Free Flap Level					
	Full Cohort (n = 812)			Coarsened Exact Matched Cohort (n = 110)		
Characteristic	Control (n = 795)	Factor V Leiden (n = 17)	*P*	Control (n = 94)	Factor V Leiden (n = 16)	*P*
Revision of anastomosis intraoperatively	30 (3.8%)	0 (0.0%)	1.00	2 (2%)	0 (0%)	1.00
Artery	21 (2.6%)	0 (0.0%)		2 (2%)	0 (0%)	
Vein	4 (0.5%)	0 (0.0%)		0 (0%)	0 (0%)	
Artery and vein	5 (0.6%)	0 (0.0%)		0 (0%)	0 (0%)	
Status of flap after intraoperative revision						
Flap salvaged	30 (100%)	n/a		2 (100%)	n/a	
Flap partially salvaged	0 (0.0%)	n/a		0 (0.0%)	n/a	
Flap lost	0 (0.0%)	n/a		0 (0.0%)	n/a	
Return to OR for flap compromise	15 (1.9%)	0 (0.0%)	1.00	5 (5%)	0 (0%)	1.00
Status of flap after re-exploration						
Flap salvaged	9 (1.1%)	0 (0.0%)		2 (2%)	0 (0%)	
Flap partially salvaged	1 (0.1%)	0 (0.0%)		0 (0.0%)	0 (0.0%)	
Flap lost	5 (0.6%)	0 (0.0%)		3 (3%)	0 (0%)	
	Macrovascular Patient Level					
	Full Cohort (n = 506)			Coarsened Exact Matched Cohort (n = 65)		
Characteristic	Control (n = 495)	Factor V Leiden (n = 11)	*P*	Control (n = 55)	Factor V Leiden (n = 10)	*P*
Venous thromboembolism within 30 d	3 (0.6%)	0 (0.0%)	1.00	1 (2%)	0 (0%)	1.00

Table 5. Major and Minor 30-day Complications

	Patient Level					
	Full Cohort (n = 506)			Coarsened Exact Matched Cohort (n = 65)		
Characteristic	Control (n = 495)	Factor V Leiden (n = 11)	*P*	Control (n = 55)	Factor V Leiden (n = 10)	*P*
Major complication	58 (11.7%)	0 (0.0%)	0.62	7 (13%)	0 (0%)	0.58
Flap compromise with return to OR	15 (1.9%)	0 (0.0%)	1.00	5 (5%)	0 (0%)	1.00
Pulmonary embolism within 30 d	3 (0.6%)	0 (0.0%)	1	1 (2%)	0 (0%)	.00
Hematoma requiring return to OR	24 (4.8%)	0 (0.0%)	1	2 (4%)	0 (0%)	.00
Infection requiring return to OR	3 (0.6%)	0 (0.0%)	1	1 (2%)	0 (0%)	.00
Readmission for infection and IV antibiotics	6 (1.2%)	0 (0.0%)	1	0 (0%)	0 (0%)	
Pneumothorax requiring chest tube placement	7 (1.4%)	0 (0.0%)	1	1 (2%)	0 (0%)	.00
Readmission for medical issues	8 (1.6%)	0 (0.0%)	1	0 (0%)	0 (0%)	
Minor complication	112 (22.6%)	4 (36.4%)	0.28	19 (35%)	4 (40%)	.73
Mastectomy skin flap necrosis	50 (10.1%)	3 (27.3%)	0.098	7 (13%)	3 (30%)	.18
Abdominal skin necrosis	67 (13.5%)	1 (9.1%)	1	13 (24%)	1 (10%)	.68
Seroma requiring tap/drain placement	18 (3.6%)	2 (18.2%)	0.066	2 (4%)	2 (20%)	.11
Infection/cellulitis managed with oral antibiotics	10 (2.0%)	1 (9.1%)	0.22	1 (2%)	1 (10%)	.29

FVL heterozygosity increased the risk of renal vein thrombosis, predisposing to early graft loss; however, routine thrombophilia screening and appropriate anticoagulation regimens mitigated this effect.[19,20] Similar findings were reported in cardiac surgery (including coronary artery bypass grafting, aortic valve reconstruction, and pulmonary thromboendarterectomy), wherein both venous and arterial thromboses of grafts were observed at a higher incidence in patients with FVL heterozygosity; in patients with this mutation who received perioperative anticoagulation with coumadin, no thromboembolic events were observed.[18] In a prospective study evaluating 1600 patients from 12 European counties undergoing total hip or knee surgery wherein all patients were screened for FVL mutations and prothrombin gene mutations, the investigators found a nonsignificant trend toward increased risk of VTE in FVL patients.[17] These studies from other surgical specialties generally conclude that the best course of action to protect these patients from VTE includes a robust screening and perioperative anticoagulation protocol, with consultation of hematology if appropriate. Our findings support a similar approach for DIEP flap reconstruction.

Upon initial evaluation for breast reconstruction, our patients are queried for prior history of VTE, family history of VTE, and a history of two or more miscarriages. Other studies have additionally recommended asking about a personal history of varicose veins.[21] Appropriate laboratory screening for thrombophilias can then be performed. Referral to hematology is then considered, especially if the patient is found to have more than one thrombophilia, or if the patient has had prior thrombotic events. The most common recommendation from hematology for patients with FVL heterozygosity is for our standard protocol plus a 28-day course of subcutaneous enoxaparin injection. Patients may also be counseled to improve modifiable factors such as smoking cessation, weight loss, and medication cessation.[22–24]

The results of this study must be viewed within the context of the study design. The fact that not all patients in our cohort were tested for FVL mutations makes it likely that there were additional patients with undiagnosed FVL mutations who underwent free flap breast reconstruction in the control group. The prevalence of FVL in our study of 2% supports this notion; however, as unexplained thrombosis in our practice intraoperatively or postoperatively results in hypercoagulability testing, it is likely that the thrombotic risk would not be higher if all patients were tested universally. No patients who were homozygous for FVL were included in our study because we deem them to be of prohibitive risk for free tissue transfer. Additional limitations of the present study include a small sample size and the rarity of thrombotic complications, which results in outcomes being less likely to achieve statistical significance. This was the reasoning for the choice of coarsened exact matching to reduce bias in the results; however, as there were no thrombotic complications in the FVL group, performing this same study with a larger population would be of interest.

CONCLUSIONS

Given the prevalence of DIEP flap reconstruction[25] and the prevalence of FVL heterozygosity, practicing microsurgeons are likely to encounter a scenario where FFBR is potentially indicated in FVL heterozygotes. In this cohort study, DIEP flap reconstruction in patients heterozygous for FVL mutations was not associated with higher microvascular and VTE rates compared with a control group. DIEP flap reconstruction is reasonable to consider in this patient population, especially when a standardized peri- and postoperative anticoagulation protocol is followed.

Jessica Erdmann-Sager, MD
Division of Plastic and Reconstructive Surgery
Brigham and Women's Hospital
75 Francis St.
Boston, MA 02215
E-mail: jerdmannsager@bwh.harvard.edu

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