Breast Reconstruction with Free Abdominal Flaps Is Associated with Persistent Lower Extremity Venous Stasis

Arash Momeni, M.D.
Sarah C. Sorice, M.D.
Alexander Y. Li, M.D., M.S.
Dung H. Nguyen, M.D.
Christopher Pannucci, M.D.

Palo Alto, Calif.; and Salt Lake City, Utah

Background: Previous work has demonstrated the occurrence of lower extremity venous stasis in the early postoperative period after breast reconstruction with free abdominal flaps. The authors investigated whether venous stasis persisted through the day of discharge, thus potentially exposing patients to an elevated risk of venous thromboembolism following discharge.

Methods: Patients who underwent breast reconstruction with free abdominal flaps were enrolled prospectively and underwent duplex ultrasound of the common femoral vein at the following time points: preoperatively, postoperative day 1, and day of discharge. Parameters of interest included common femoral vein diameter, area, and maximum flow velocity.

Results: Thirty patients with a mean age of 50.3 years (range, 29 to 70 years) underwent breast reconstruction with 52 free abdominal flaps. A significant increase in common femoral vein diameter (19.1 percent; $p < 0.01$) and area (46.8 percent; $p < 0.01$) correlated with a significant reduction in maximum flow velocity (−10.9 percent; $p = 0.03$) between baseline and postoperative day 1. These changes persisted through the day of discharge [common femoral vein diameter, 17.8 percent ($p < 0.01$); area, 46 percent ($p < 0.01$); and maximum flow velocity, −11.3 percent ($p = 0.01$)]. Venous parameters were not influenced by unilateral versus bilateral flap harvest ($p = 0.48$).

Conclusions: Postoperative lower extremity venous stasis following autologous breast reconstruction with free abdominal flaps seems to persist through the day of discharge. This finding may explain why patients remain at risk for venous thromboembolism after discharge. Although the authors' findings are at odds with current venous thromboembolism prophylaxis recommendations, additional studies are indicated to examine whether these findings translate into venous thromboembolism events. (*Plast. Reconstr. Surg.* 143: 1144e, 2019.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, IV.

Venous thromboembolism continues to be a major patient safety issue after surgical intervention. Significant morbidity and mortality is associated with the development of venous thromboembolism. With over 100,000 annual venous thromboembolism–related deaths in the United States, this disease entity represents the most common cause of preventable in-hospital death.[1,2] Furthermore, the associated economic burden is substantial, with annual costs to the U.S. health care system in excess of $7 billion.[3]

The importance of venous thromboembolism prevention has been recognized by organized plastic surgery. Significant resources have been invested into raising awareness and improving venous thromboembolism risk stratification and prophylaxis in patients undergoing plastic and reconstructive surgery. Initiatives such as

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the American Society of Plastic Surgeons Venous Thromboembolism Task Force, the Plastic Surgery Foundation–funded Venous Thromboembolism Prevention Study, and initiatives by the American Association of Plastic Surgeons reflect the significant emphasis placed on this particular area of clinical research.[2,4–6] Important questions, however, remain unanswered and include issues such as appropriate doses and duration of venous thromboembolism chemoprophylaxis. Furthermore, mechanisms underlying "breakthrough" venous thromboembolism events, defined as venous thromboembolism events despite guideline-compliant chemoprophylaxis, remain unknown. The Venous Thromboembolism Prevention Study demonstrated that despite daily enoxaparin prophylaxis, one patient in 25 with a Caprini score greater than 8 had a breakthrough venous thromboembolism event.[4] The occurrence of breakthrough venous thromboembolism events highlights the need for a more precise and individualized approach to venous thromboembolism prophylaxis.

Venous thromboembolism risk stratification and clinical research in other specialties have identified cancer patients as a particularly vulnerable patient population.[7,8] Of these, breast cancer patients represent the largest group treated by plastic surgeons. Symptomatic venous thromboembolism has been reported in up to 4 percent of patients undergoing autologous reconstruction using abdominal flaps.[9] An up to 20 percent rate of asymptomatic venous thromboembolism after autologous reconstruction has been reported.[10] In light of rising numbers of breast reconstruction in the United States, with more than 18,000 autologous reconstructions in 2013, a 35 percent increase in the number of annual breast reconstructions since 2000, and over 106,000 breast reconstructions in 2017 alone, the number of patients at risk for venous thromboembolism is alarmingly high.[11–13] It is important to note that an increased rate of deep venous thrombosis formation has been reported following autologous versus implant-based breast reconstruction despite guideline-compliant prophylaxis.[14] These findings are particularly relevant in light of an increasing number of patients undergoing prophylactic bilateral mastectomy with immediate reconstruction and the introduction of techniques that expand the indications for microsurgical breast reconstruction.[15,16] As such, it is of no surprise that the American Society of Plastic Surgeons Venous Thromboembolism Task Force identified "major breast reconstruction" as a procedure warranting additional prophylactic considerations.[2] Given the large number of patients at risk, particular emphasis on understanding the processes leading to venous thromboembolism development in this patient population is warranted.

We previously hypothesized that postoperative lower extremity deep venous system stasis is a procedure-specific key contributing factor to postoperative venous thromboembolism risk following autologous breast reconstruction with free abdominal flaps. In a prospective pilot study of patients who underwent autologous breast reconstruction with free muscle-sparing transverse rectus abdominis musculocutaneous (TRAM) and deep inferior epigastric artery perforator (DIEP) flaps, we detected abnormal vascular dimensions and flow patterns in the lower extremity deep venous system postoperatively.[17] The duration of these venous abnormalities, however, is unknown. Given this uncertainly, we felt it prudent to prospectively investigate whether patients would display unfavorable deep venous system characteristics at the time of discharge.

PATIENTS AND METHODS

Institutional review board approval was obtained before patient enrollment. Adult (older than 18 years) female patients who were scheduled to undergo postmastectomy autologous breast reconstruction at Stanford University Medical Center were enrolled prospectively in the study. Only patients who underwent breast reconstruction with free abdominal flaps that required incision of the anterior rectus sheath (i.e., muscle-sparing TRAM and DIEP flaps) were included. Exclusion criteria included reconstruction using superficial inferior epigastric artery flaps, donor-sites other than the abdomen, chronic obstructive pulmonary disease, and liver disease.

As reported previously,[17] ultrasonographic measurements were performed using a SonoSite S-Series (SonoSite, Inc., Bothell, Wash.) with a multifrequency (13 to 6 MHz), high-definition linear transducer. All examinations were performed at the left common femoral vein 1 cm distal to the saphenofemoral junction. Parameters of interest included vessel diameter (in centimeters), cross-sectional area (in centimeters squared), and maximum flow velocity (in centimeters per second). Measurements were taken at three time points: (1) preoperatively, (2) postoperative day 1, and (3) day of discharge (Fig. 1). We limited our examinations to the common femoral vein given our previously reported findings that changes in

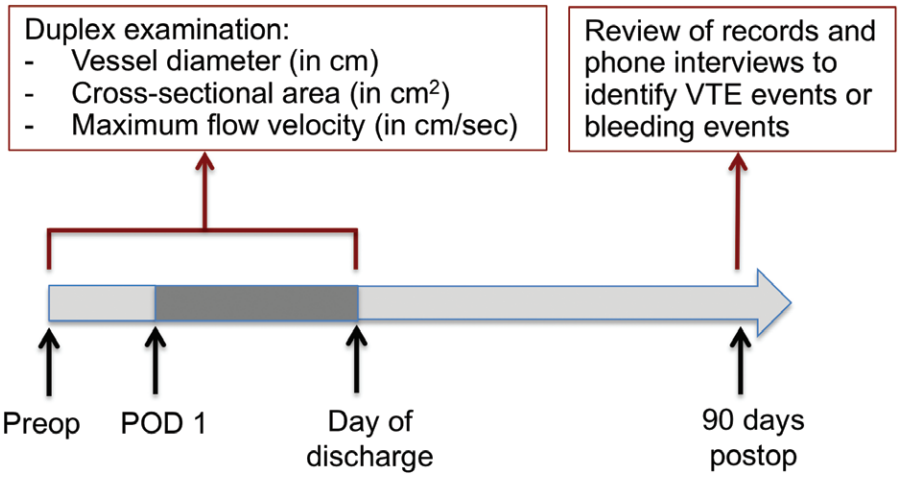

Fig. 1. Study workflow. *VTE*, venous thromboembolism; *POD*, postoperative day.

common femoral vein parameters are most likely a direct consequence of the constricting effect of abdominal wall closure rather than changes in intravenous volume status.[17] Of note, all examinations were performed with the patient in the same position (i.e., Fowler position). Sequential compression devices were removed temporarily during measurements. All patients received venous thromboembolism chemoprophylaxis for the duration of their hospitalization (i.e., sequential compression devices and daily subcutaneous administration of 40 mg of enoxaparin). No chemoprophylaxis was administered after discharge. Patients were contacted at 90 days postoperatively to inquire about postoperative venous thromboembolism or bleeding events (Fig. 1).

Additional parameters recorded included age (in years), body mass index (in kilograms per meter squared), ethnicity, medical history, prior abdominal surgery, American Society of Anesthesiologists classification, smoking history, laterality of reconstruction, and timing of reconstruction. Intraoperative parameters of interest included the type of flap (muscle-sparing TRAM versus DIEP flap), width of fascia excision (in centimeters), type of fascia closure (primary closure with or without inlay mesh versus bridging mesh), intraoperative fluid administration (in milliliters), and duration of surgery (in minutes). Study data were collected and managed using Research Electronic Data Capture (REDCap) electronic data capture tools.[18] [Research Electronic Data Capture tools are hosted at the Stanford Center for Clinical Informatics. Research Electronic Data Capture is a secure, Web-based application designed to support data capture for research studies, providing (1) an intuitive interface for validated data entry; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for importing data from external sources.]

Statistical Analysis

Data were collated and analyzed using R version 3.2.4 (R Core Team 2013). Univariate analysis was performed to compare demographic variables between unilateral versus bilateral treatment groups by means of the Fisher's exact test. Continuous variables were compared by means of *t* test. Changes in measures of vessel dynamics at time points of postoperative day 1 and day of discharge versus preoperative baseline were then compared using a paired *t* test. A multivariate linear regression was used to model changes in vessel dynamics against collected clinical variables, notably age, body mass index, American Society of Anesthesiologists class, width of fascial excision, fluid status, and case duration. Statistical significance was defined as $p < 0.05$.

RESULTS

Thirty patients with a mean age of 50.3 ± 10.0 years (range, 29 to 70 years) and mean body mass index of 29.2 ± 4.9 kg/m² (range, 21.8 to 39.2 kg/m²) were enrolled prospectively in this study. The majority of patients were Caucasian (n = 18), followed by Hispanic (n = 7) and Asian (n = 5). Table 1 lists patient demographics and medical comorbidities. Nineteen patients (63.3 percent) had previous abdominal procedures, the most common being cesarean delivery [n = 11 (36.7 percent)]. None of the patients were active smokers; 27 (90 percent) had never smoked and three (10 percent) had quit more than 6 months before

Table 1. Patient Demographics and Medical Comorbidities of Study Subjects*

Characteristic	Value
No. of patients	30
No. of breasts/flaps	52
Age at the time of surgery, yr	
Mean ± SD	50.3 ± 10.0
Range	29–70
BMI, kg/m^2	
Mean ± SD	29.2 ± 4.9
Range	21.8–39.2
Medical comorbidities	
Hypertension	3 (10)
Arrhythmia	2 (6.7)
Hyperlipidemia	5 (16.7)
Asthma/chronic obstructive pulmonary disease	3 (10)
Obstructive sleep apnea	1 (3.3)
Diabetes mellitus	2 (6.7)
Anxiety	3 (10)
Depression	3 (10)
Neoadjuvant treatment	
Chemotherapy	7 (23.3)
Radiotherapy	0
ASA classification	
1	3
2	19
3	8

BMI, body mass index; ASA, American Society of Anesthesiologists.
*Note that several subjects had >1 comorbidity.

surgery. The majority of patients were American Society of Anesthesiologists class 2 [n = 19 (63.3 percent)], followed by American Society of Anesthesiologists class 3 [n = 8 (26.7 percent)] and American Society of Anesthesiologists class 1 [n = 3 (10 percent)]. The median Caprini score was 7 (range, 5 to 12). Seven patients (23.3 percent) had a history of neoadjuvant chemotherapy, and none had undergone neoadjuvant radiotherapy (Table 1).

A total of 52 breast reconstructions were performed with free abdominal flaps. The majority of patients underwent immediate [n = 25 (83.3 percent)] and bilateral reconstruction [n = 22 (73.3 percent)]. Free muscle-sparing TRAM flaps were most commonly performed [44 flaps (84.6 percent)], with the remaining eight flaps (15.4 percent) being DIEP flaps. The mean width of fascial excision was 1.7 cm and 2.4 cm in unilateral and bilateral reconstructions, respectively (p = 0.48). Primary fascial closure was achieved in all patients. Furthermore, inlay polypropylene mesh was used in all cases. No flap loss was noted.

Duplex examination of the common femoral vein demonstrated a significant increase in common femoral vein diameter (19.1 percent; $p < 0.01$) and area (46.8 percent; $p < 0.01$) between baseline and postoperative day 1. This structural change correlated with a significant reduction in maximum flow velocity (–10.9 percent; p = 0.03) between baseline and postoperative day 1. Importantly, these changes persisted until the day of discharge. A significant increase in common femoral vein diameter (17.8 percent; $p < 0.01$) and area (46 percent; $p < 0.01$) correlated with a significant reduction in maximum flow velocity (–11.3 percent; $p < 0.01$) between baseline and day of discharge. No significant changes were noted between postoperative day 1 and day of discharge (Fig. 2). Venous parameters were not influenced by unilateral versus bilateral flap harvest ($p = 0.48$). Of note, multivariate linear regression identified prolonged case duration to be significantly associated with an increase in common femoral vein diameter ($p < 0.01$) and area ($p < 0.01$) but not with maximum flow velocity ($p = 0.86$).

During the follow-up period, one patient (3.3 percent) who had undergone bilateral immediate breast reconstruction developed a pulmonary embolus on postoperative day 10 and was successfully treated with therapeutic enoxaparin. The remaining study subjects did not report any venous thromboembolism or bleeding events at the 90-day follow-up.

DISCUSSION

Despite national initiatives to raise awareness and the introduction of best practices to facilitate venous thromboembolism chemoprophylaxis, venous thromboembolism continues to be a public health burden. Patients with breast cancer who choose to undergo autologous reconstruction represent a population that is at a particularly high risk for developing postoperative venous thromboembolism.[19] Importantly, they remain at risk for up to 13 weeks postoperatively.[20] This observation is not surprising when considering the population being treated, which is characterized by established risk factors for postoperative venous thromboembolism, including female sex, cancer diagnosis, and prolonged surgery. Surgical duration has been demonstrated to be directly associated with an increased risk for venous thromboembolism.[21] This observation is of particular interest in light of the fact that prolonged case duration was associated with an increase in common femoral vein diameter and area in the present study.

The venous thromboembolism risk derived from the aforementioned factors is further increased by the very nature of the donor site (i.e., the abdomen). Considering that among patients who undergo outpatient aesthetic surgery

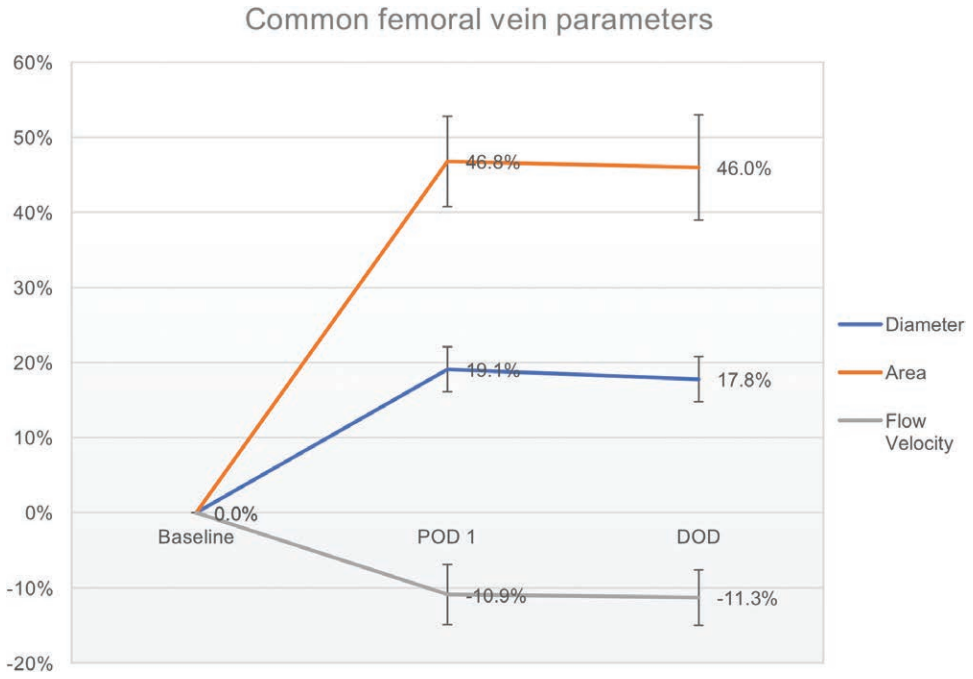

Fig. 2. Changes in common femoral vein diameter, cross-sectional area, and maximum flow velocity over time. Note the persistence of changes from baseline through the day of discharge. *POD*, postoperative day; *DOD*, day of discharge. Standard errors per measurement are depicted.

procedures those who undergo abdominoplasty represent 58 percent of all cases of postoperative venous thromboembolism highlights the fact that surgical alteration of the abdominal wall appears to have an impact on the postoperative venous thromboembolism risk.[22] Finally, the median Caprini score of 7 in this study reflects the susceptibility of this patient population to postoperative venous thromboembolism. Importantly, the benefit of venous thromboembolism chemoprophylaxis in this high-risk patient population was recently demonstrated.[23]

Although the mechanism of venous thromboembolism development in this population remains incompletely understood, we previously hypothesized that lower extremity venous stasis is a key contributing factor to postoperative venous thromboembolism formation. This is likely a function of abdominal wall plication (following abdominoplasty) or fascia closure (following muscle-sparing TRAM or DIEP flap harvest). The potential impact of these maneuvers on decreased venous return secondary to an increase in intraabdominal pressure has been discussed by others.[24–27] In a study of 77 patients who underwent autologous breast reconstruction with pedicled TRAM flaps with a 2.6 percent rate of postoperative venous thromboembolism, Losken et al. concluded that following TRAM flap harvest a "transient component of abdominal compartment syndrome does exist."[24] Pannucci et al. demonstrated in a case of a pedicled TRAM flap transfer a 14 percent increase in femoral vein diameter along with a decrease in flow volume in the femoral vein postoperatively.[26] In a pilot study, we were able to demonstrate that abdominal flap harvest would indeed result in lower extremity venous stasis in the early postoperative period (i.e., on postoperative day 1).[17] Furthermore, we demonstrated that these vascular changes were independent of intravenous fluid status but rather the result of abdominal constriction.[17]

Venous stasis, a cornerstone of the Virchow triad, is undoubtedly a risk factor for thrombus formation. In fact, it has been demonstrated that venous stasis and vessel dilation can cause intimal microtears, leading to exposure of subendothelial collagen, and thus serving as initiation sites for thrombus formation.[28] What is unknown to date is the duration of these unfavorable vascular changes and to what extent these changes impact the development of distinct venous thromboembolism events in plastic surgery patients undergoing breast reconstruction.

We hypothesized that abnormal venous flow patterns persist beyond the duration of hospitalization, thus potentially being a contributing factor to the sustained risk for venous thromboembolism

postoperatively. This is supported by the observation that the majority of events occur after hospital discharge.[20] Our study findings demonstrate that, indeed, unfavorable changes in the lower extremity venous system persist through the day of discharge. This is an important observation, as the duration of chemical venous thromboembolism prophylaxis is limited to the duration of hospitalization only. This is noteworthy, as the advent of enhanced recovery after surgery protocols has resulted in a significant decrease in the length of hospital stay.[29] Thus, patients who undergo microsurgical breast reconstruction consequently are provided an even shorter period of venous thromboembolism chemoprophylaxis. This, in turn, could result in an undesired increase in the number of postdischarge venous thromboembolism events as enhanced recovery after surgery protocols are more widely implemented.

Some have proposed extended postoperative venous thromboembolism chemoprophylaxis following breast reconstruction. However, prophylaxis beyond discharge is currently not standard of care after microsurgical breast reconstruction.[14] In contrast to other high-risk patient groups in which this practice has been shown to significantly reduce venous thromboembolism events, the same has not yet been demonstrated in patients undergoing breast reconstruction.[30,31] We hope that our study findings along with the knowledge that the majority of venous thromboembolism events following autologous breast reconstruction with free abdominal flaps occur after discharge will initiate further research to investigate the issue of extended-duration venous thromboembolism chemoprophylaxis in this patient population.

It is noteworthy that unilateral versus bilateral flap harvest did not appear to impact postoperative venous parameters. Although counterintuitive at first glance, an explanation for this observation is provided by virtue of insignificant differences in the width of fascial excision at the time of flap harvest. The lack of difference is possibly related to surgeon bias (i.e., more liberal fascial harvest in unilateral cases knowing that the contralateral anterior rectus sheath is left unaltered versus bilateral cases, where the risk for abdominal wall morbidity is greater, thus resulting in greater attention being paid to fascial preservation).

Limitations of the present study include the fact that we did not investigate the effect of lower extremity venous changes on postoperative venous thromboembolism events. The study would have been underpowered to address this objective. Thus, the clinical impact of our observations (i.e., to what degree lower extremity venous stasis translates into distinct postoperative venous thromboembolism events) remains to be determined. Certainly, further research to ascertain to what extent these changes translate into distinct venous thromboembolism events is needed.

CONCLUSIONS

Postoperative changes in the lower extremity venous system consistent with venous stasis persist for the duration of hospital stay following autologous breast reconstruction with free abdominal flaps. These alterations may be a contributing factor for the development of postoperative venous thromboembolism events. Further research is indicated to determine the clinical importance of these observations.

Arash Momeni, M.D.
Division of Plastic and Reconstructive Surgery
Stanford University Medical Center
770 Welch Road, Suite 400
Palo Alto, Calif. 04304
amomeni@stanford.edu

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