Increased Lower Extremity Venous Stasis May Contribute to Deep Venous Thrombosis Formation after Microsurgical Breast Reconstruction—An Ultrasonographic Study

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J Reconstr Microsurg 2017;33:173–178.

Abstract

Background Despite guideline-compliant prophylaxis, an increased rate of deep venous thrombosis (DVT) formation has been reported following autologous versus implant-based breast reconstruction. We hypothesized that tight abdominal fascia closure might decrease lower extremity venous return and promote venous stasis.

Methods An observational crossover study of patients who underwent autologous breast reconstruction using transverse rectus abdominis musculocutaneous/deep inferior epigastric artery perforator flaps was conducted. Ultrasonographic measurements of the left common femoral vein (CFV) and right internal jugular vein (IJV) were performed preoperatively, in the postanesthesia care unit, and on postoperative day (POD) 1. Parameters of interest included vessel diameter, circumference, area, and maximum flow velocity.

Results Eighteen patients with a mean age and body mass index of 52.7 years (range, 29–76 years) and 31.3 kg/m^2 (range, 21.9–43.4 kg/m^2) were included, respectively. A 29.8% increase in CFV diameter was observed on POD 1 ($p < 0.0001$). Similarly, a 24.3 and 69.9% increase in CFV circumference ($p = 0.0007$) and area ($p < 0.0001$) were noted, respectively. These correlated with a 28.4% decrease in maximum flow velocity in the CFV ($p = 0.0001$). Of note, none of these parameters displayed significant changes for the IJV, thus indicating that observed changes in the CFV were not the result of changes in perioperative fluid status.

Conclusion Postoperative changes observed in the CFV reflect increased lower extremity venous stasis after microsurgical breast reconstruction and may contribute to postoperative DVT formation.

Keywords
- plastic surgery
- breast reconstruction
- DVT

received
August 15, 2016
accepted after revision
October 8, 2016
published online
November 28, 2016

DOI http://dx.doi.org/10.1055/s-0036-1594297.
ISSN 0743-684X.

It has been established that higher long-term patient satisfaction as well as quality of life are associated with autologous versus implant-based breast reconstruction.[1–3] The most common donor site is the abdomen. Its soft tissue is unmatched not only with regard to quantity of tissue available but also in terms of tissue quality.[4] While superior reconstructive outcomes can be achieved with the use of autologous tissue, concerns regarding donor-site morbidity have resulted in the introduction of numerous technical modifications that aim to decrease donor-site morbidity.[5–8] To this end, it has been demonstrated that autologous breast reconstruction with the muscle-sparing transverse rectus abdominis musculocutaneous (MS-TRAM) flap and the deep inferior epigastric artery perforator (DIEP) flap is associated with a similar degree of insult to the abdominal wall.

In addition to donor-site morbidity, the incidence of postoperative medical complications after autologous breast reconstruction has increasingly become the focus of clinical investigation. An area of particular interest is the occurrence of postoperative deep venous thrombosis (DVT). Despite guideline-compliant prophylaxis, an increased rate of DVT formation has been reported following autologous versus implant-based breast reconstruction, with an even greater risk in the elderly.[9] These findings are particularly relevant in light of an increasing number of patients undergoing prophylactic bilateral mastectomy with immediate reconstruction. Interestingly, a higher rate of postoperative lower extremity DVT in patients undergoing bilateral (vs. unilateral) autologous breast reconstruction has been reported.[10] Factors contributing to this remain unknown. A variety of different causes have been discussed, however, including prolonged surgical duration, increased operative morbidity associated with bilateral reconstruction, and bilateral dissections close to the iliac vessels that may render these areas more thrombogenic as well as increased intra-abdominal pressure.[10–12]

The objective of this study was to shed light on contributing factors that facilitate the development of DVT formation in patients undergoing autologous breast reconstruction. This is in preparation for a larger study to investigate the role of these factors in venous thromboembolism (VTE) risk, and the role of mitigating these factors in VTE risk reduction. As described by Virchow, stasis of blood flow, hypercoagulability, and intimal damage all contribute to thrombus formation. We hypothesized that tight abdominal fascia closure might decrease lower extremity venous return and promote venous stasis.

Patients and Methods

An observational crossover study was conducted that included patients who underwent autologous breast reconstruction following mastectomy from October 2015 to January 2016. Institutional Review Board approval was obtained prior to enrolling patients in the study. Only patients who underwent breast reconstruction using abdominal tissue that required violation of the anterior rectus sheath, that is, MS-TRAM and DIEP flaps, were included in the study. Patients who underwent reconstruction with superficial inferior epigastric artery flaps and those with a history of chronic obstructive pulmonary disease, liver disease, DVT, and hypercoagulable state were excluded.

Ultrasonographic measurements were performed using a SonoSite S-Series (SonoSite, Inc., Bothell, WA) with a multifrequency (13–6 MHz), high-definition linear transducer. All examinations were performed at the left common femoral vein (CFV), 1 cm distal to the saphenofemoral junction, and the right internal jugular vein (IJV). Parameters recorded included vessel diameter (in cm), circumference (in cm), area (in cm^2), and maximum flow velocity (in cm/s). Measurements were taken at three time points: (1) in the preoperative holding area prior to surgery, (2) in the postanesthesia care unit (PACU), and (3) on postoperative day (POD) 1. Of note, all measurements were taken with the patient in the same position, that is, Fowler position, and without sequential compression devices (SCDs).

Additional parameters recorded for each study subject included age, body mass index (BMI), ethnicity, past medical history, prior abdominal surgery, location of abdominal scars, American Society of Anesthesiologists (ASA) classification, smoking history, history of chemotherapy, history of radiotherapy, laterality of reconstruction, and timing of reconstruction.

Intraoperative parameters of interest included type of flap (MS-TRAM vs. DIEP flap), width of fascia excision (in cm), type of fascia closure (primary closure vs. underlay bridging mesh), width of bridged segment (in cm), intravenous fluid (IVF) administration (in mL), estimated blood loss (in mL), urine output (in mL), and duration of surgery (in minute). Furthermore, in addition to the ultrasound measurements on POD 1, the following parameters were recorded: total IVF administration (in mL), urine output (in mL), and drain output (in mL).

Of note, all patients received VTE prophylaxis consisting of subcutaneous heparin (5,000 units every 8 hours beginning preoperatively on the day of surgery and continued until the day of discharge) as well as SCDs until ambulatory. Also, patients were mobilized on POD 1.

Statistical Analysis

Shapiro–Wilk analyses were employed to determine the distribution of IVFs given intraoperatively and to guide further testing decisions. Two-tailed paired *t*-tests and Wilcoxon signed-rank tests were used to compare the vascular changes in the right IJV and the left CFV in the various subgroups. Statistical analysis was done using Stata/IC 13.1 (College Station, TX).

Results

In this study, 18 patients with a mean age and BMI of 52.7 years (range, 29–76 years) and 31.3 kg/m^2 (range, 21.9–43.4 kg/m^2) were included, respectively. The majority of patients were Caucasians (13 patients) followed by African Americans (3 patients), Hispanic (1 patient), and Asian (1 patient). ►**Table 1** displays the medical comorbidities of the study subjects. Nine patients (50%) had previous abdominal procedures, with a Pfannenstiel scar being the most common ($N = 6$ [33.3%]). None of the patients were active smokers. The majority of patients were ASA class 2 ($N = 11$ [61.1%]), followed by ASA class 3 ($N = 6$ [33.3%]) and ASA class 1 ($N = 1$ [5.6%]).

Table 1 Patient comorbidities

Past medical history	*N* (%)
Hypertension	5 (27.8)
Hyperlipidemia	5 (27.8)
Asthma	2 (11.1)
Obstructive sleep apnea	2 (11.1)
Noninsulin dependent diabetes mellitus	1 (5.6)
Thyroid disorder	2 (11.1)
Rheumatologic disorder	5 (27.8)
Depression	3 (16.7)
Anxiety	1 (5.6)

Note: Numerous study subjects had > 1 comorbidity.

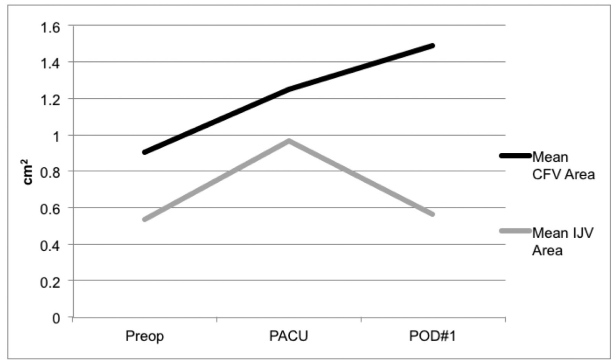

Fig. 2 Changes in vessel area. A significant increase in mean CFV area is noted over time ($p < 0.0001$). CFV, common femoral vein; IJV, internal jugular vein; PACU, postanesthesia care unit; POD, postoperative day; Preop, preoperative.

Ten (55.6%) and 4 (22.2%) patients had a history of neo-adjuvant chemo- and radiotherapy, respectively. A total of 28 flaps were transferred for the purpose of unilateral ($N = 8$ [44.4%]) and bilateral ($N = 10$ [55.6%]) reconstruction. The most common flap was the MS-2 TRAM flap ($N = 22$ [78.6%]), followed by the DIEP flap ($N = 4$ [14.3%]) and MS-1 TRAM flap ($N = 2$ [7.1%]). Primary fascia closure was obtained in 11 patients (61.1%) with the mean width of fascia excision being 1.8 and 2.4 cm in unilateral and bilateral flap harvests, respectively. Bridged-mesh repair of the anterior rectus sheath was performed in the remaining seven patients (38.9%). Immediate reconstruction was performed in the majority of cases ($N = 13$ [72.2%]), whereas the remaining 5 (27.8%) patients underwent delayed reconstruction.

Duplex examination of the IJV demonstrated a temporary increase in vessel diameter in the PACU followed by a return to preoperative dimensions by POD 1 ($p = 0.75$). In contrast, the CFV diameter increased progressively, demonstrating a 29.8% increase on POD 1 ($p < 0.0001$) (►**Fig. 1**). Similar observations were made when assessing vessel circumference and area. While the mean IJV circumference returned to preoperative dimensions on POD 1 ($p = 0.93$), a 24.3% increase in CFV circumference was noted on POD 1 ($p = 0.0007$). Even more pronounced was the difference in vessel area. While the IJV area returned to preoperative dimensions on POD 1 ($p = 0.65$), a 69.9% increase was noted in CFV area on POD 1 ($p < 0.0001$) (►**Fig. 2**).

In addition to vascular dimensions, flow velocity was measured to better assess the functional changes. Changes in flow velocity correlated with changes in vessel dimension, in as much as a temporary decrease in maximum flow velocity in the IJV in the PACU was followed by a trend toward returning to preoperative values while a progressive decrease of maximum flow velocity was noted in the CFV, with a 28.4% decrease being noted on POD 1 ($p = 0.0001$) (►**Fig. 3**).

Interestingly, the technique of fascia repair appeared to influence flow velocity as bridged-mesh repair of the anterior rectus sheath correlated with a trend toward recovery of flow velocity on POD 1 ($p = 0.08$), whereas a progressive decrease in flow velocity was noted following primary fascia closure ($p = 0.0002$) (►**Fig. 4**).

Fluid status, including IVF administration, urine output, and drain output, did not appear to exert an effect on the outcomes of interest (data not shown).

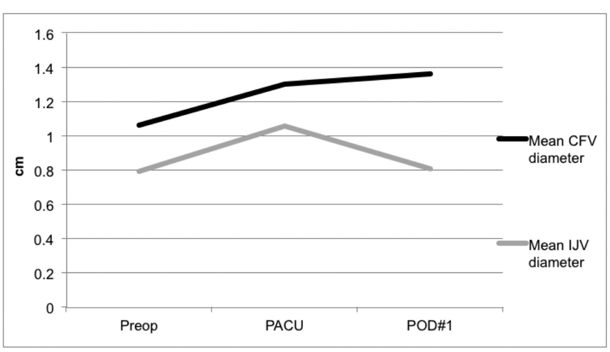

Fig. 1 Changes in vessel diameter. A significant increase in mean CFV diameter is noted over time ($p < 0.0001$). CFV, common femoral vein; IJV, internal jugular vein; PACU, postanesthesia care unit; POD, postoperative day; Preop, preoperative.

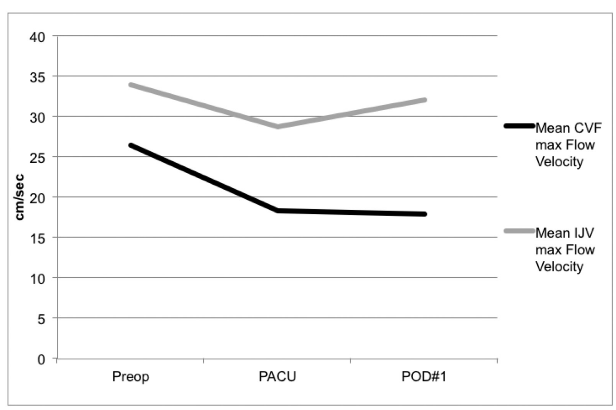

Fig. 3 Changes in maximum flow velocity. A significant decrease in mean maximum CFV flow velocity is noted over time ($p = 0.0001$). CFV, common femoral vein; IJV, internal jugular vein; PACU, postanesthesia care unit; POD, postoperative day; Preop, preoperative.

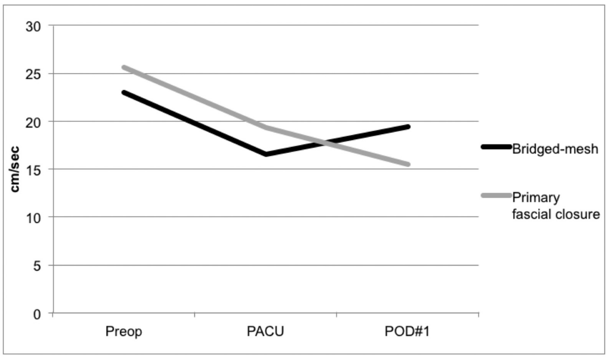

Fig. 4 Changes in maximum flow velocity. While a progressive decrease in mean maximum CFV flow velocity is noted in patients undergoing primary fascial closure over time ($p = 0.0001$). CFV, common femoral vein; PACU, postanesthesia care unit; POD, postoperative day; Preop, preoperative.

Of note, a 76-year-old patient who underwent unilateral breast reconstruction with a MS-2 TRAM flap was diagnosed with pulmonary embolism (PE) on POD 4. She had undergone minimal fascia excision (0.5 cm) followed by primary fascia closure. Postoperative vascular imaging had revealed a 37.5% increase in CFV area and a 38.3% decrease in maximum flow velocity on POD 1. Guideline-compliant treatment of PE was initiated, which was followed by an otherwise unremarkable postoperative recovery.

Discussion

Symptomatic VTE has been reported in patients undergoing autologous breast reconstruction using abdominal flaps in up to 4% of cases.[13] More importantly, a substantially larger number of patients is estimated to develop asymptomatic VTE after autologous breast reconstruction, with rates of up to 20% being reported.[14] In light of rising numbers of breast reconstruction in the United States, with more than 18,000 autologous procedures reported in 2013 alone, the number of patients at risk for developing VTE is alarmingly high.[15,16]

Of the various reconstructive modalities, autologous breast reconstruction using abdominal tissue has been identified as being associated with the highest risk of developing postoperative VTE.[17] A recent retrospective analysis comparing outcomes after pedicled TRAM flap, pedicled latissimus dorsi flap, and implant-based reconstruction concluded that "the major factor leading to VTE appears to be the method of reconstruction rather than individual patient factors."[17] Symptomatic VTE was reported in 6% of patients in the pedicled TRAM group (vs. none in the other groups). A variety of reasons for the increased VTE rate in this patient population were discussed, including decreased postoperative mobility secondary to pain, decreased venous return secondary to abdominal wall closure, as well as placement in the modified beach chair position.[17]

The issue of abdominal wall plication (as seen in abdominoplasty) or fascia closure (following TRAM flap harvest) being associated with decreased venous return secondary to increased intra-abdominal pressure has previously been discussed.[11,12,18,19] In fact, a recently presented study of healthy female volunteers who were placed in abdominal compression garments displayed vascular changes in the CFV paralleling the findings of this study, that is, increased venous stasis and decreased flow velocity.[20]

Losken et al presented their experience with 77 patients who underwent breast reconstruction with pedicled TRAM flaps of which 12.9% experienced at least one episode of elevated intra-abdominal pressure (defined as $\geq$ 20 mm Hg). The authors concluded that "a transient component of abdominal compartment syndrome does exist after TRAM flap breast reconstruction."[11] Interestingly, two patients (2.6%) in their series developed postoperative VTE, both of which had elevated intra-abdominal pressure. The authors, therefore, speculated that increased intra-abdominal pressure might impair venous flow, thus, contributing to the development of venous thrombosis.[11] Vascular imaging, however, was not routinely performed in their study.

In a follow-up study comparing intra-abdominal pressure measurements of the previously reported 77 pedicled TRAM patients with 29 consecutive patients undergoing breast reconstruction with free MS-TRAM flaps, Losken et al reported significantly lower intra-abdominal pressures in the latter group.[12] Interestingly, intra-abdominal pressures in the free TRAM group resembled values following tension-free mesh closure of pedicled TRAM flap donor sites, which had been found to have no significant differences in intra-abdominal pressure when compared with controls in the authors' original study.[11,12]

This latter finding is particularly noteworthy as it highlights the importance of vascular imaging to determine the functional effects on lower extremity venous drainage instead of relying on surrogate diagnostic studies, such as intra-abdominal pressure measurement. Based on the findings of Losken et al,[12] one would have to assume that free MS-TRAM-based reconstruction would not be associated with decreased venous return. As seen in the present study, however, a significant decrease in lower extremity venous drainage was noted postoperatively following either free MS-TRAM or DIEP flap-based reconstruction. We do agree with Losken et al,[11] however, that bridged-mesh closure appears to have a protective effect in that the initial decrease in flow velocity in the CFV in the PACU was followed by a trend toward recovery of flow velocity by POD 1, whereas a progressive and significant decrease in flow velocity was noted following primary fascia closure.

A case report of a pedicled TRAM flap in which vascular and bladder pressure changes were determined demonstrated a 14% increase in femoral vein diameter postoperatively, along with a decrease of flow volume in the femoral vein, reaching a nadir of 36% of baseline value in POD 2.[18] Although similar trends are seen in the present study, that is, postoperative increase in vessel diameter and decrease in flow velocity, a major difference between the present study and the previously published case report is the choice of reconstruction and its potential impact on intra-abdominal pressure. Pannucci et al used a pedicled TRAM flap with excision of up to 4 cm wide segment of fascia with additional contralateral fascia plication.[18] In contrast, all patients in the present study underwent free tissue transfer with minimal fascia excision. The mean width of fascia excision (even after bilateral reconstruction in patients with primary fascia closure) was less than 2.5 cm. Furthermore, contralateral fascia plication was not performed, due to the minimal amount of fascia excision in unilateral reconstructions. In light of the increased amount of fascia excision with pedicled TRAM flap harvest, it is not surprising that patients undergoing breast reconstruction utilizing this approach have the highest reported rate of VTE.[21]

Although our results support the hypothesis that tight fascia closure might decrease venous return and promote venous stasis, other variables, such as amount of IVF administration, could conceivably be responsible for changes in vessel diameter. To control for this variable, simultaneous measurements of the IJV were performed. Although the temporary increase in IJV diameter, circumference, and area in the PACU was most likely related to intraoperative IVF administration, these parameters in addition to flow velocity normalized by POD 1. In contrast, evidence of venous stasis worsened in the CFV. As such, changes in intravascular volume are not accountable for changes seen in the CFV on POD 1. The increase in diameter, circumference, and area of the CFV along with the decrease in flow velocity is, hence, most likely a direct consequence of the constricting effect following abdominal wall closure. This is, furthermore, supported by the fact that the technique of fascia closure impacted venous flow velocity in a significant manner, as patients following bridged-mesh repair demonstrated a trend toward recovery of flow velocity on POD 1, whereas a progressive decrease in flow velocity was noted in patients after primary fascia closure.

In light of our findings, we believe that tightening of the abdominal fascia secondary to closure of the anterior rectus sheath results in unfavorable changes in lower extremity drainage patterns and, thus, might represent a contributing factor to the development of VTE in patients undergoing microsurgical autologous breast reconstruction. This risk is perhaps, furthermore, increased by the fact that patients are routinely placed in the Fowler position postoperatively, a position known to independently worsen venous stasis.[20] Hence, surgeons face a dilemma, as an incision in the anterior rectus sheath for flap harvest has to be made, the fascia has to be closed, and the patient has to be placed in the Fowler position to facilitate wound closure. One has to, therefore, balance the risk of VTE with the risk of abdominal hernia and bulge formation. A recent study reported the rate of surgically repaired abdominal hernia following free TRAM and DIEP flap to be 5.7 and 1.8%, respectively.[22] Given that primary fascia closure, whenever possible, is preferable,[23] solutions to mitigate the risk of VTE might include (1) limiting the amount of fascia excision at the time of flap harvest, (2) prolonging the duration of chemoprophylaxis, and (3) bridging-mesh closure of the abdominal wall as a last resort.

Numerous questions remain unanswered and should be the focus of future investigations. It deserves mentioning that the objective of this study was not to examine VTE risk reduction, and it would have been substantially underpowered to do so, given the incidence of VTE after microsurgical breast reconstruction.

Future studies should establish the duration of abnormal venous drainage patterns as this might influence the duration of VTE chemoprophylaxis. Furthermore, as bridged-mesh repair seems to have a protective effect, determining the maximum width of fascia excision beyond which a bridged-mesh technique should be employed appears prudent. Finally, future research should investigate the mechanism by which venous stasis, as seen following abdominal wall plication, contributes to the formation of lower extremity DVT.

In conclusion, postoperative changes observed in the CFV reflect increased lower extremity venous stasis after microsurgical breast reconstruction and may contribute to postoperative DVT formation.

Funding
None.

Conflict of Interest
None declared.

Ethical Approval
The Internal Review Board of the University of Pennsylvania approved this study.

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