MEDICINAL LEECHES FOR SURGICALLY UNCORRECTABLE VENOUS CONGESTION AFTER FREE FLAP BREAST RECONSTRUCTION

CHRISTOPHER J. PANNUCCI, M.D.,[†*] JONAS A. NELSON, M.D.,[†] CYNDI U. CHUNG, B.S., JOHN P. FISCHER, M.D., SUHAIL K. KANCHWALA, M.D., STEPHEN J. KOVACH, M.D., JOSEPH M. SERLETTI, M.D., and LIZA C. WU, M.D.

Background: Free tissue transfer is an accepted method for breast reconstruction. Surgically uncorrectable venous congestion is a rare but real occurrence after these procedures. Here, we report our experience with the management of surgically uncorrectable venous congestion after free flap breast reconstruction using medicinal leech therapy. *Methods:* We queried our prospectively maintained institutional database for all patients with venous congestion after free flap breast reconstruction since 2005. Chart review was performed for all patients having post-operative venous congestion. We compared patients with surgically correctable venous congestion and surgically uncorrectable venous congestion requiring medicinal leech therapy. *Results:* Twenty-three patients had post-operative venous congestion, and four of these patients were surgically uncorrectable requiring medicinal leech therapy. Patients who required leech therapy had lower hemoglobin nadirs, received more blood transfusions, and received a higher number of total units of red blood cells than patients who did not require leech therapy. Among four patients who required leech therapy, one flap was partially salvaged and three flaps were completely lost. Leech therapy was associated with higher total flap loss rates (75.0% vs. 42.1%) and longer length of stay (8.0 $\pm$ 3.6 days vs. 6.5 $\pm$ 2.1 days) when compared to non-leeched flaps. These differences were not statistically significant ($P = 0.32$ and $P = 0.43$, respectively). *Conclusions:* In patients with surgically uncorrectable venous congestion after free flap breast reconstruction, total flap loss is common despite leech therapy. When venous congestion cannot be corrected, total flap removal may be a better option than attempted salvage with leech therapy. © 2014 Wiley Periodicals, Inc. Microsurgery 00:000–000, 2014.

Leeches have been used for medicinal purposes for thousands of years.[1] Use of leeches for flaps with venous congestion was first reported in 1960 by Derganc and Zdravic. Their manuscript, published in the British Journal of Plastic Surgery, reported on salvage of a series of 20 tubed, walking-man type flaps using leech therapy.[2] However, leeches were not approved as a medical device by the United States Food and Drug Administration until 2004.[3]

Leeches ingest between 5 and 10 mL of blood per feeding, which can be ten times their own body weight. The leech mouth parts have three jaws, each of which contains 60–100 pairs of teeth. These jaws create the Y-shaped soft tissue defect consistently seen after leech detachment. Leech saliva contains hirudin, a thrombin inhibitor, and multiple other anticoagulants, anti-inflammatories, anesthetic, and vasodilator substances, the combination of which causes prolonged oozing from the bite site for up to 12 hours after the leech is detached. In the setting of venous congestion, blood withdrawl by leech is actually of secondary importance as the ongoing ooze is believed to be the principal mechanism for flap decongestion.[4]

Division of Plastic Surgery, University of Pennsylvania, Philadelphia, PA

*Correspondence to: Christopher Pannucci, MD MS; Division of Plastic Surgery, University of Pennsylvania, 3400 Spruce Street, 10 Penn Tower, Philadelphia, PA 19104, USA. E-mail: christopher.pannucci@uphs.upenn.edu

†C.J. Pannucci, J.A. Nelson contributed equally to this work.

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Leeches have been used to salvage many types of reconstructive procedures, including ear replantation,[5,6] lip replantation,[7] nasal skin avulsion,[8] penile replantation,[9] nipple congestion after elective breast surgery,[10] and head and neck reconstruction.[10–13] High salvage rates (>90%) of congested skin flaps and local flaps can be expected.[14] Replants survive over 70% of the time,[15] and finger and ear replants can reliably survive using bloodletting as the sole source of venous outflow.[5,16]

For congested free flaps, 30% total loss rates have been reported following leech application. This rate at least doubles for small reported subsets of transverse rectus abdominus myocutaneous (TRAM) and deep inferior epigastric perforator (DIEP) flaps, in which 60–100% total loss rates have been reported.[14,15] Although it appears that congested abdominal-based free tissue transfers fare poorly when compared to other tissues with venous congestion requiring leeches, a series of surgically uncorrectable venous congestion after free flap breast reconstruction has never been published. The purpose of this study was to critically examine the management of postoperative venous congestion with medicinal leeches to determine if there is a true role for this therapy in free flap breast reconstruction.

PATIENTS AND METHODS

Institutional Review Board approval was obtained from our institution prior to undertaking this study. The University of Pennsylvania's Division of Plastic Surgery prospectively maintains a database of free flap breast reconstruction patients (2005 to present). This database

Table 1. Demographic and Post-Operative Data for Four Patients with Surgically Uncorrectable Venous Congestion

#	Age	BMI	Flap type	Laterality	Summary	Leech protocol	POD of initiation	Days of therapy	# of leeches	# pRBC units	LOS (days)	Outcome
1	45.8	41.2	msfTRAM	Bilateral	Venous insufficiency	Every 4 hours	3	3	15	6	10	partial salvage
2	64.4	34.97	DIEP	Unilateral	Early venous thrombosis[a]	Every 2 hours	2	6	41	10	12	loss
3	58.3	41.6	msfTRAM	Bilateral	Venous insufficiency	Every 2 hours[b]	2	3	9	2	6	loss
4	46.8	28.3	SIEA	Bilateral	Late venous thrombosis	Every 6 hours	6	4	11	2	4	loss

POD, postoperative day; pRBC, packed red blood cells; LOS, length of stay in days; msfTRAM, muscle sparing free transverse rectus abdominus myocutaneous flap; DIEP, deep inferior epigastric perforator flap; SIEA, superficial inferior epigastric artery flap.
[a]*With continued venous congestion.*
[b]*This patient had a maximum of four leeches per day prescribed.*

was queried to identify patients with post-operative venous congestion or venous thrombosis. For identified patients, charts were reviewed retrospectively to examine surgical and non-surgical management of venous insufficiency. In addition, review of order histories, nursing notes and flow sheets, as well as pharmacy records identified frequency and duration of leech therapy, receipt of leech-specific antibiotics, and blood transfusions.

We compared patients in whom leeches were utilized for management of the venous insufficiency to those who were managed without the use of leeches. For this study, our outcomes of interest included days until return to the operating room (postoperative day, POD), need for blood transfusion (yes/no), total number of units transfused, hemoglobin nadir (g/dL), antibiotic regimen in the patients managed with leeches, partial flap loss, total flap loss, and total length of stay (days). Total flap loss was defined as complete failure of the free flap requiring debridement of the entire flap. Partial flap loss was defined as flap loss or atrophy up to 50% but not requiring immediate return to operating room. Flap salvage was defined as management of the venous insufficiency resulting in minimal to no change in volume of the reconstructed breast mound.

All data were entered into an Excel workbook (Microsoft Corporation, Redmond, WA). Statistical analyses included Fisher's Exact tests for categorical variables and the Wilcoxon Rank Sum test for continuous variables, given the small sample size and non-parametric nature of the data. All tests were two-tailed, and statistical significance was defined as $P < 0.05$. Analyses were performed using STATA IC 12.0 (StataCorp, College Station, TX).

RESULTS

We identified a total of 1,946 free flaps performed in 1,271 patients for breast reconstruction at our institution between March of 2005 and April of 2012. In total, 23 flaps (1.1%) experienced postoperative venous insufficiency. Of the 23 flaps, medicinal leeches were utilized in 4 (17.4%) patients (Tables 1 and 2).

In general, patients with post-operative flap venous insufficiency had high rates of obesity (39.1%), bilateral reconstruction (65.2%), and immediate reconstruction (78.3%). The majority of flaps were muscle-sparing free TRAM (msfTRAM) flaps (52.2%), although the overall distribution included DIEP flaps, superficial inferior epigastric (SIEA) flaps, gluteal artery perforator (GAP) flaps and transverse upper gracilis (TUG) flaps. Overall, 21 of 23 patients were taken back to the operating room for operative revision and or exploration. Two patients were treated medically.

The average hemoglobin nadir in patients with venous insufficiency was 7.3 $\pm$ 1.6 g/dL, and as such blood transfusions were utilized in 52% of patients, with the average number of units of red blood cells being 2.5 $\pm$ 3.6 units. 60% of patients with post-operative venous insufficiency lost at least a portion of their flap. 11 of 23 patients (47.8%) had total flap loss.

Medicinal leeches were used in four patients as an end treatment for surgically uncorrectable venous insufficiency. Patients in whom leeches were required had significantly higher body mass index than patients who did not require leech therapy (36.5 kg/m^2 vs. 28.5 kg/m^2, $P = 0.03$).

Initiation of leech therapy ranged from POD2 to POD6 and averaged 4 (range 3–6) days in duration. The average number of leeches utilized was 19 (range 15–41), with the most common protocol being two leeches every 2 hours. Antibiotic therapy to specifically cover *Aeromonas* (most commonly levaquin) was prescribed in 100% of patients.

When compared to patients who did not require leech therapy, patients undergoing leech therapy trended towards having lower postoperative hemoglobin nadirs (6.2 $\pm$ 0.7 g/dL vs. 7.5 $\pm$ 1.6 g/dL), and were more likely to receive blood transfusions (100% vs. 42.1%). Furthermore, they trended towards receiving a higher number of total units of red blood cells (5.0 units $\pm$ 3.8 units vs. 1.9 units $\pm$ 3.4 units). None of these differences were statistically significant ($P = 0.08$, $P = 0.10$, and $P = 0.07$, respectively).

Among the four patients who received leech therapy, one flap was partially salvaged. Three flaps were

Table 2. Comparison of Demographics Between Patients Who Did and Did Not Receive Leech Therapy

	No Leeches	Leeches	
Total *N*	19	4	
Flap type (*N*/%)			
TRAM	9 (47.4%)	3 (75.0%)	
DIEP	3 (15.8%)	1 (25.0%)	
SIEA	3 (15.8%)	0 (0%)	
GAP	2 (10.5%)	0 (0%)	
TUG	2 (10.5%)	0 (0%)	
			P value
Obesity (BMI $>$ 30) (*N*/%)	6 (31.6%)	3 (75.0%)	0.26
BMI (Mean $\pm$ SD)	28.5 $\pm$ 5.9	36.5 $\pm$ 6.3	0.03
Bilateral (*N*/%)	12 (63.2%)	3 (75.0%)	1
Immediate (*N*/%)	15 (78.9%)	3 (75.0%)	1

BMI, body mass index; TRAM, transverse rectus abdominus myocutaneous flap; DIEP, deep inferior epigastric perforator flap; SIEA, superficial inferior epigastric artery flap; GAP, gluteal artery perforator flap; TUG, transverse upper gracilis flap.

completely lost. Patients who required leeches were more likely to experience total flap loss when compared to patients who did not require leeches (75.0% vs. 42.1%). Patients who required leech therapy had prolonged hospitalizations when compared to patients who did not require leeches (8.0 $\pm$ 3.6 days vs. 6.5 $\pm$ 2.1 days) (Table 3). The differences in total flap loss and length of stay were not significantly different ($P = 0.32$ and $P = 0.43$, respectively). The patient listed as partial salvage had a viable skin island and flap at follow-up. She developed progressive volume loss within several months after surgery without firm areas of fat necrosis. The resultant asymmetry was planned to be fixed in the operating room, thus she was considered to be a partial flap salvage. Unfortunately, she then experienced a very early recurrence of inflammatory breast cancer requiring excision of mastectomy skin and part of the flap with split thickness skin grafting for ultimate coverage.

There were no leech-associated infections in any patient in this series.

In the 19 patients with surgically correctable venous insufficiency who were not treated with leeches, 8 flaps were salvaged (42.1%), and 3 experienced partial flap loss (15.8%). Of the salvaged flaps, five were noted to have fat necrosis with two noted to have significant volume loss. The majority of salvaged patients required significant revision.

DISCUSSION

This examination of medicinal leech therapy in autologous breast reconstruction draws from a high volume center, in which nearly 2,000 breast-free flaps have been performed since 2005. Overall, 23 patients were identified who experienced post-operative venous insufficiency. Among those 23 patients, only 4 required leech therapy. However, even with these small numbers of events, the outcomes we report are similar to others:[14] breast reconstruction patients with surgically uncorrectable venous congestion who require leech therapy generally did poorly. In our series, three of four patients experienced total flap loss. Each of the patients required an additional operative procedure for flap debridement, and on average these patients had 1.5 days longer hospital stays. The observed phenomenon likely is related to the sheer mass of tissue needing to be drained. Unlike an ear, lip, or finger replantation, free flaps for breast reconstruction commonly weigh between 500 and 1,000 g. These flaps likely do poorly because adequate flap drainage with leech therapy alone is difficult.

We appreciate that this article reports on a relatively small number of patients. However, it is worth noting that in our experience of nearly 2,000 free flap breast reconstructions, we have seen this problem in only four flaps. For many surgeons, this complication may only be seen once in a career. In cases where personal experience cannot be used to guide practice, individual surgeons may turn to the literature to review the experience of others. It is in this light that we believe our experience and management strategy with this problem is particularly useful.

In our experience, if venous congestion or insufficiency is noted, operative exploration is performed in an expedited fashion. Only two patients with very late venous thromboses were not operatively explored.[17] If a thrombosis or venous outflow problem is noted, and it is believed to be early in the evolution of the process, we proceed to the operating room for attempted salvage, as a thrombotic event or technical issue is considered to be the cause. However, in situations where a thrombotic even is believed to be late in evolution, a decision is made between exploration and debridement of the flap. Studies have demonstrated that early detection and expedited return to the operating room are associated with better outcomes.[18,19] Later thrombotic events, however, may result in higher rates of failure.[20] In each case where leech therapy was applied, the patient was explored in the operating room in an attempt to correct the venous insufficiency. The insufficiency was ultimately determined to be uncorrectable, even with anastomotic revision. Given this finding, the leech therapy was initiated.

Based on this experience and examination, we have now altered our practice patterns. Specifically, for cases of surgically uncorrectable venous insufficiency involving the entire flap (as opposed to a segmental area), we no longer send patients back to the floor with a congested flap and a plan for leech therapy. The flap is removed at the same operative procedure in which venous outflow cannot be established, and a second reconstructive procedure may be undertaken at that time. We have adopted a policy to no longer utilize medicinal leech therapy for

Table 3. Comparison of Outcomes Between Patients Who Did and Did Not Receive Leech Therapy

	No Leeches	Leeches	*P* value
POD of return to OR (mean ± SD, range)	5.0 ± 5.6 (0–21)	13.5 ± 13.9 (1–27)	0.41
LOS (mean ± SD, range)	6.5 ± 2.1 (4–12)	8.0 ± 3.6 (4–12)	0.43
hgb nadir (mean ± SD)	7.5 ± 1.6	6.2 ± 0.7	0.08
Transfusion (*n*, %)	8 (42.1%)	4 (100.0%)	0.1
# of transfused units (mean ± SD)	1.9 ± 3.4	5.0 ± 3.8	0.07
Any loss (*n*, %)	10 (52.6%)	4 (100.0%)	0.13
Total loss (*n*, %)	8 (42.1%)	3 (75.0%)	0.32
Partial loss (*n*, %)	2 (10.5%)	1 (25.0%)	0.25

POD, postoperative day; OR, operating room; LOS, length of stay; hgb, hemoglobin.

autologous breast reconstruction given the mass of tissue which needs to be drained.

Unless contraindicated for medical reasons, surgical exploration with examination of the venous anastamosis is the initial management strategy for congested flaps. Surgical exploration can identify problems with the pedicle orientation (such as a twist or kink) or the anastamosis itself, and provides the opportunity for thrombectomy, tPA injection, venous anastamosis revision, superficial-to-deep bypass, vein grafting, or venous supercharging.[21,22]

Several authors advocate for routine anastamosis of a second outflow vein[23,24] to minimize the chance of venous congestion. Double venous drainage may act as an insurance policy. One study of dual venous anastamosis which used implantable Doppler probes showed that five of 291 anastamoses between the deep inferior epigastric vein and the internal mammary vein thrombosed. However, the single vein thrombosis had no clinical effect on the flap itself,[24] which spared the patient a second operative procedure. Flaps with double vein anastamosis were less likely to have a return to the operating room for clinically significant venous congestion (0.3% vs. 4.9% and 0% vs. 2.6% in two large series).[23,24] Dual vein anastamosis may decrease risk for fat necrosis in DIEP flaps.[23] Anastamosis of a second vein did not significantly increase operative time.[24]

Leech use is not a benign intervention. Complications can be categorized into three groups: complications related to the leech itself, complications related to infections transmitted by the leech, and complications secondary to blood transfusion requirements.

Although most leeches attach to the site where they are applied and affect the local environment, tunneling of leech into flap through the bite wound,[25] or migration into an adjacent body cavity such as the oral cavity, rectum, or vagina[26] can occur. Such an event would require additional procedures to remove the organism.

Regarding infections inoculated by the leech, a large systematic review demonstrated an overall infection rate of 14%. The most predominant bacteria in oral flora of medicinal leeches is *Aeromonas hydrophila*.[27] Infection is known to be associated with decreased survival of flap or replant.[15,28] For patients who developed infection, the flap or replant loss rate was 63%. For patients without infection, the flap or replant loss rate was 12%.[28] Prophylactic antibiotics are known to reduce the observed infection rate by over 50%.[15] The antibiotic of choice is typically regarded as Ciprofloxacin, a fluoroquinolone.

Fluoroquinolone-resistant *Aeromonas*, in addition to other bacterial species (including *Proteus* and *Morganella*), have been identified in leech-associated infections.[15,29] These infections can require extended course of intravenous antibiotics via central venous access.[29] Sepsis from *Aeromonas* infection has been reported after replantation.[30] If leeches are utilized, appropriate antibiotic coverage is mandatory. All patients in our cohort were administered appropriate prophylactic antibiotic therapy at the time of leech therapy initiation.

Blood transfusions are common when leech therapy is used. A large systematic review showed that 50% of patients receiving leech therapy also require blood transfusion.[28] Among those receiving blood, transfusion requirements range from two to 29 units.[5,7,12–15] For an individual patient, use of 350 leeches and transfusions of 29 units have been reported.[13] Our results demonstrate that all patients who underwent leech therapy were transfused, in a range from two to 10 units of packed red blood cells. Transfusions are certainly not without complication, ranging from transfusion reactions to bacterial or viral infection transmission. Our group has recently examined the utilization of transfusions in autologous breast reconstruction and noted higher rates of complications when transfusions were utilized.[31]

In addition to blood transfusion and infection, leech therapy is associated with other downstream complications. In a series of eight surgically uncorrectable venous obstructions after free flap head and neck reconstruction, Chepeha et al.[12] report patient stays in the ICU ranging from 5 to 14 days. 62.5% of patients developed ICU psychosis and 50% developed prerenal azotemia.

Our study is limited by the relatively rare nature of the event we chose to study. Furthermore, it is a retrospective study and may be prone to observer bias, recording bias and selection bias overall. All results and conclusions

should be examined in this light. As noted above, we report on a very small number of patients (four) with surgically uncorrectable venous congestion after free flap breast reconstruction. These patients were drawn from an extensive experience of nearly 2,000 free flap breast reconstructions performed since 2005. While some may argue that drawing conclusions based on four patients is inappropriate, it is worth noting that many surgeons may see this problem only once in a career. If and when this occurs, published data on even a small number of patients will be helpful to guide patient-level decisions.

CONCLUSIONS

Venous congestion after free-flap breast reconstruction is a relatively rare event, occurring in 1.1% of free flaps for breast reconstruction. Surgically uncorrectable venous congestion is even more uncommon, with an observed rate of 0.2%. Patients with surgically uncorrectable venous congestion fare poorly and can expect to lose most or all of their reconstruction, even if leech therapy is utilized. When surgically uncorrectable venous congestion after free flap breast reconstruction is identified, surgeons should consider total flap removal instead of leech therapy.

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