Institutional Outcomes of Leech Therapy for Venous Congestion in 87 Patients

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Abstract

Background We aimed to report the outcomes associated with leech therapy and to identify risk factors associated with reconstructive failure.

Methods We retrospectively reviewed cases of flap reconstruction or replanted appendages that required leech therapy over an 8-year period at the Duke University Medical Center. Using logistic regression, we assessed the association of risk factors with reconstructive failure.

Results The study cohort included 87 patients which correspond to 2.1% of 4,115 cases done during the study period. The most common flap recipient site was the lower extremity ($n = 33$, 37.9%) followed by the upper extremity ($n = 30$, 34.5%), head and neck ($n = 13$, 14.9%), and trunk ($n = 11$, 12.6%). Flap types were pedicled in 44 (50.5%) cases and free in 24 (27.5%) cases. Fifteen (17.2%) were digital replantation, and four (4.5%) were replanted appendages. The average duration of therapy was 4.6 days (range: 1–11). The overall leech therapy success rate was 60.9% (53/87) and accounted for cases without flap loss ($n = 45$, 51.7%) and with partial flap loss in which the original reconstructive goal was achieved without further reconstructive procedures ($n = 8$, 9.2%). Postoperative blood transfusion was administered in 32 (36.7%) cases, and infectious complications occurred in 7 cases in spite of the administration of prophylactic antibiotics (8%).

Conclusions This study represents the largest single-institution series evaluating the outcomes after leech therapy. Our data support the use of leeches as an adjunct for the management of venous congestion after reconstructive surgery. However, the morbidity associated with it should be considered, particularly the need for a blood transfusion.

Keywords
- leech therapy
- venous congestion
- *Hirudo medicinalis*
- medicinal leech

Venous congestion is a common complication that leads to tissue loss and reconstructive failure. Leech therapy for flap venous congestion has become popular among reconstructive surgeons given the physiological properties of the leech *Hirudo medicinalis*. The salivary gland of this leech contains the anticoagulant hirudin, platelet aggregation inhibitors, and highly specific proteases, all of which promote venous flow in the setting of congestion.[1–3] The first reference in modern literature of leech therapy for venous congestion after reconstructive surgery dates back to 1960. However, it

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was not until 2004 that the medicinal leech was approved by the Food and Drug Administration as a medical device in the United States.[4,5]

Leech therapy has been successfully used to alleviate venous congestion in a variety of compromised locoregional and free flaps after reconstruction of the trunk, head and neck, and extremities.[6–9] It has also been used to alleviate venous congestion after replantation of a variety of appendages such as the ear, nose, lip, and scalp as well as after digital replantation and ring avulsion injuries.[10–20] Nonetheless, leech therapy can be associated with significant complications, most commonly including *Aeromonas* infection and the need for blood transfusions.[21–26] Other complications that have been reported include leech bite scars, leech migration, psychosis, and prerenal azotemia.[27]

Although there are numerous case reports and small case series that describe the use of leech therapy, there is a paucity of large studies that objectively evaluate the effectiveness of this treatment. Furthermore, few studies describe the incidence of leech therapy in different types of flaps or accurately report its associated morbidities. The purpose of this study is to evaluate the outcomes after leech therapy in the largest reported single institutional series.

Methods

Institutional review board approval was obtained before performing this study. We retrospectively reviewed patients who underwent flap reconstruction or replantation of appendages between January 2006 and June 2014 at Duke University Medical Center (DUMC). The patient cohort was identified by querying the Duke Enterprise Data Unified Content Explorer (DEDUCE) for patients that underwent flap reconstruction or replantation of appendages and received medicinal leech therapy secondary to postoperative venous congestion. Demographic, operative, and postoperative data were obtained from the medical records. Each patient chart was reviewed to determine age, sex, race, body mass index (BMI), comorbidities, and American Society of Anesthesiologists (ASA) classification. The operative report was reviewed to determine if the surgical procedure was indicated after a traumatic or nontraumatic injury, type of flap used for reconstruction, total operative time, estimated blood loss, intraoperative blood transfusion, use of intraoperative vasoconstrictors, and intraoperative complications. Postoperative data included the length of leech therapy, anticoagulation regimen, antibiotic administration, postoperative blood transfusion, serum hemoglobin, and hematocrit before, and after leech therapy, hemoglobin value at the time of postoperative blood transfusion, reoperations, hospital length of stay, and postoperative length of stay.

All of the reconstruction procedures in this study were complicated by postoperative venous congestion. Additional complications were categorized as thrombotic, wound related, infectious, hemorrhagic, or other complications. Thrombotic complications included venous or arterial thrombosis; wound-related problems included necrosis, dehiscence, seroma, and edema; infectious complications included documented instances of cellulitis or the presence of an abscess requiring surgical drainage, and hemorrhagic complications included postoperative bleeding requiring reexploration for hemostasis.

After reconstruction, total flap salvage, partial flap loss, or total flap loss were evaluated. Total savage included those flaps or appendages in which no tissue was lost postoperatively. Partial flap loss included those flaps or appendages where a portion of the tissue was lost, yet a portion of the originally transplanted tissue remained. Total flap loss was defined as the complete loss of a flap or appendage that could not be salvaged. The success of leech therapy was defined as complete survival of the tissue or partial survival of the tissue without the need for additional reconstructive procedures (other than debridement of the nonviable tissue and local wound care) to achieve the initial reconstructive goal. Failure or leech therapy was defined as total flap loss or partial flap loss requiring additional reconstructive procedures (for instance, skin grafting, biological dressing or additional flaps) to achieve the initial reconstructive goal.

Statistical Methods

Continuous variables were summarized as mean; standard deviation, median, and interquartile range and nonparametric Kruskal–Wallis rank sum tests were used to compare continuous variables between patient groups formed by flap type or surgical outcomes. Categorical variables were summarized as frequency and percentage, and chi-square test or Fisher's exact tests were performed to examine the association of categorical variables and patient groups. For analyses related to leech therapy success and flap type, we excluded the four patients with native tissue flap because we were unable to combine this group of a small number of patients with other flap type groups. Multivariable logistic regression was conducted to evaluate potential risk factors associated with leech therapy success. Age, BMI category, diabetes, flap type, indication for reconstruction, postoperative packed red blood cells (PRBCs) transfusion, and ASA classification were considered for inclusion in the model. Variables that were not significant predictors after adjustment for other covariates ($p < 0.1$) were removed in a backward selection process. Regression diagnostic checks were assessed, and the C-index (or area under the receiver operating characteristic curve) was presented as a measure of model goodness of fit. Data processing and statistical analysis were conducted using R 3.2.1 (R Core Team, Vienna, Austria, 2015).

Results

A total of 4,115 patients were identified in the inpatient institutional database. These cases were performed by the plastic surgery, orthopedic surgery, and otolaryngology services. During the study period, leech therapy was used in 2.1% of identified cases (87/4,115). The baseline characteristics of the study population are shown in ►**Table 1**. The most common flap recipient site was the lower extremity ($n = 33$, 37.9%) followed by the upper extremity ($n = 30$, 34.5%), head and neck ($n = 13$, 14.9%), and trunk ($n = 11$, 12.6%). Flap types were pedicled in 44 (50.5%) cases and free

Table 1 Demographic characteristics of cohort

Demographic characteristics ($N = 87$)	Mean (SD) or *n* (%)
Age	49.7 (18.1)
Gender	
Female	34 (39.1%)
Male	53 (60.9%)
Race	
Caucasian	71 (81.6%)
African American	11 (12.6%)
Others	5 (5.7%)
Body mass index	28.4 (6.4)
Cancer	22 (25.3%)
Cardiovascular disease	6 (6.9%)
Hypertension	28 (32.2%)
Diabetes	13 (14.9%)
ASA class	
1	9 (10.3%)
2	34 (39.1%)
3	38 (43.7%)
4	2 (2.3%)

Abbreviations: ASA, American Society of Anesthesiologist; SD, standard deviation.

Table 2 Outcomes based on flap type

	Total salvage *n* (%)	Partial salvage *n* (%)	Total loss *n* (%)	Successful *n* (%)
Locoregional flap	26 (59.1)	11 (25)	7 (15.9)	31 (70.4)
Gluteal	1	–	–	1
Dorsalis pedis	1	–	–	1
External oblique	–	1	–	1
FDMA	–	1	1	1
Fillet flap	–	–	1	–
Forehead	2	–	–	2
Groin	1	–	–	1
Lateral arm	–	1	–	1
Latissimus dorsi	1	–	2	1
Pectoralis major	–	1	–	1
Propeller	4	1	–	4
Radial forearm	1	1	1	1
Sartorius	1	–	–	1
Scalp	–	–	1	–
Sural	13	4	–	−14
Tensor fascia latae	–	1	–	–
Trapezius	1	–	–	1
Rectus abdominis	–	−1	1	–
Free flap	10 (41.7)	10 (41.7)	4 (16.7)	12 (50)
Anterolateral thigh	3	4	3	3
Fibula	1	1	–	1
Lateral arm	–	1	–	–
Latissimus dorsi	–	1	–	1
Submental	1	–	–	1
Radial forearm	2	1	–	2
Rectus abdominis	3	2	1	4
Native tissue	1 (25)	2 (50)	1 (25)	2 (50)
Cheek	–	1	–	–
Ear replant	1	1	–	2
Scalp replant	–	–	1	–
Replantation	8 (53.3)	0 (0)	7 (46.7)	8 (53.3)
Digit	8	–	5	8
Thumb	–	–	2	–

Abbreviation: FDMA, first dorsal metacarpal artery.

in 24 (27.5%) cases. There were 15 (17.2%) cases of replanted digits and four (4.5%) cases of replanted appendages. The specific types of flaps are shown in ►**Table 2**. The most common indication for reconstruction was a nonhealing wound ($n = 35$, 40.2%), followed by trauma ($n = 36$, 41.4%) and neoplasm resection ($n = 16$, 18.4%).

All cases included in the study were complicated with venous congestion requiring leech therapy. Due to limitations in the documentation, we could only determine the exact amount of leeches used for 14 patients. The mean number of leeches used for this group was 24.8 (range: 2–77). Overall, the average duration of leech therapy was 4.6 (range: 1–11) days, and there were no significant differences among patients that underwent locoregional flaps, free flaps, or appendage replantation. The mean postoperative length of stay was 12.1 (range: 1–72) days, and there were no significant differences among patients that underwent locoregional flaps, free flaps, or appendage replantation.

The overall success rate following leech therapy was 60.9% (53/87) and accounted for cases without flap loss ($n = 45$, 51.7%) and with partial flap loss without the need for additional reconstructive procedures ($n = 8$, 9.2%). The overall leech therapy failure rate was 39.1% and accounted for cases with a total flap or replant loss ($n = 19$, 21.8%) and partial flap loss with the need for additional reconstructive procedures to achieve the initial reconstructive goal ($n = 15$, 17.2%).

Specifically for locoregional and free flaps, the success rate for leech therapy was 70.45% (31/44) and 50% (12/24), respectively. There was no significant difference in leech therapy outcomes between locoregional and free flaps ($p = 0.095$, chi-square test). Leech therapy was successful in 53.3% (8/15) of patients that underwent digital replantation. There was no significant association between type of reconstruction (excluding native tissue replantation) and reconstructive failure ($p = 0.217$, Fisher's exact test). Additional outcomes based on flap type are shown in ►**Table 3**.

In 50 cases (57.5%), one or more additional postoperative complications occurred. No patient died within 30 days of the initial reconstruction. Subjects that underwent free flap reconstruction were significantly more likely than locoregional flaps

Table 3 Outcomes by flap type

	Free flap $n = 24$	Native tissue $n = 4$	Pedicled $n = 44$	Replantation $n = 15$	Total $n = 87$	p Value[a]
Days of leech therapy						0.072
Mean (SD)	4.5 (2.6)	6.5 (2.4)	4.1 (2.1)	5.7 (3)	4.6 (2.5)	
PRBC unit transfused						0.073
Mean (SD)	2.2 (3.1)	0.3 (0.6)	1 (1.5)	1 (3.9)	1.3 (2.6)	
Donor site complication						0.38
Yes	2 (8.3%)	0 (0.0%)	1 (2.3%)	0 (0.0%)	3 (3.4%)	
Recipient site complication						0.046
Yes	19 (79.2%)	3 (75.0%)	21 (47.7%)	7 (46.7%)	50 (57.5%)	
Resurgery						0.019
Yes	19 (79.2%)	3 (75.0%)	19 (43.2%)	7 (46.7%)	48 (55.2%)	
Hospital length of stay						0.16
Mean (SD)	15.8 (16.4)	20.8 (17.3)	16.3 (14.5)	9.3 (7)	15.2 (14.3)	
PLOS						0.083
Mean (SD)	14.5 (14.8)	20.8 (17.3)	11 (11.9)	9.5 (7)	12.1 (12.4)	

Abbreviations: PLOS, postoperative length of stay; SD, standard deviation.
[a]p Values were calculated based on Fisher's exact test or Kruskal–Wallis test as appropriate.

to experience additional postoperative complications (complication after free flap: 19/24 [79.2%] vs. complication after locoregional flap: 21/44 [47.7%]; $p = 0.019$, Fisher's exact test).

Other complications associated with leech therapy included the need for postoperative blood transfusion in 32 (36.7%) cases. Patients received an average of 3.3 (range: 1–15) units of PRBC. The average hemoglobin value at the time of blood transfusion was 7.4 (range: 6.7–7.9) g/dL. Before leech therapy, the average hemoglobin, and hematocrit levels were 10.8 (range: 6.3–17) g/dL and 32% (range: 20–48%), respectively. Following leech therapy, the average hemoglobin, and hematocrit levels were 9.8 (range: 6–15.6) g/dL and 29.7% (range: 8.7–43%), respectively. There was no significant difference between locoregional and free flaps regarding the need for postoperative PRBC (transfusion after free flap 11/24 [45.8%] vs. transfusion after locoregional flap 19/44 [43.2%]; $p = 1$, chi-square test). Postoperative PRBC was less frequently required in subjects that underwent digital replantation ($n = 1/15$, 6.7%) than other groups ($p = 0.018$, Fisher's exact test). Infectious complications occurred in seven cases (8%) in spite of the administration of prophylactic antibiotics. The majority of patients received ciprofloxacin. However, three patients received Zosyn (Wyeth-Pfizer) and one received gentamicin. There were no documented cases of *Aeromonas hydrophilia* following leech therapy.

A total of 48 (66.7%) patients required a reoperation most commonly classified as debridement ($n = 31/48$, 64.6%), revision amputation ($n = 7/48$, 14.6%), or microvascular revision ($n = 9/48$, 18.8%). Other reasons for reoperation included three (6.3%) patients who required flap revision (flap debulking and repositioning), two (4.2%) who required a hematoma evacuation and two (4.2%) who underwent incision and drainage. Subjects in the free flap group were significantly more likely than subjects in the locoregional flap group to undergo a reoperation (reoperation after free flap: 19/24 [79.2%] vs. reoperation after locoregional flap: 19/44 [43.2%]; $p = 0.005$, Fisher's exact test).

Among the 23 patients with partial flap loss, 22 (95.7%) of them underwent an average of 2.1 (range: 1–6) reoperations. Also, among the 19 patients with total flap loss, 18 (94.7%) of them underwent an average of 1.6 (range: 1–4) reoperations. Out of 45 patient with no flap loss, only 8 (17.7%) of them underwent a reoperation.

After considering all potential risk factors, results of the logistic regression analyses indicated that traumatic cases (nontraumatic 18/56 [32.1%] vs. traumatic 16/31 [51.62%]) were marginally associated with increased odds of reconstructive failure after leech therapy. Specifically, the odds of reconstructive failure for patients with a history of trauma as an indication for reconstruction over the odds of reconstructive failure for patients with no history of trauma was 2.25 (odds ratio: 2.25, 95% confidence interval: 0.92, 5.62, $p = 0.077$).

Discussion

The use of leeches to relieve venous congestion is an accepted therapeutic tool, yet their use remains relatively uncommon given that other conventional and effective strategies are often attempted first.[28] In our series, leeches were used in only 87 (2.1%) of all reconstruction procedures. To our knowledge, this represents the largest clinical series from a single institution in which outcomes following leech therapy are evaluated.

Overall, leech therapy avoided total flap or appendage loss secondary to venous congestion in 61% of cases. The success of therapy in our series is lower than that reported by Whitaker et al in a recent systematic multicenter review of

277 reported cases of locoregional flaps, free tissue transfers, and replanted appendages, in which the leech therapy success rate was 77.9%.[27] Of note, in their systematic review, the authors defined the success of therapy as survival of the tissue or flap even in the setting of partial flap loss but without specifying whether the original reconstructive goal was achieved or not in this group. For instance, partial loss of a critical portion of a transverse rectus abdominis muscle (TRAM) flap for breast reconstruction may constitute a reconstructive failure. Similarly, partial loss of a flap intended to cover hardware with resultant exposure of such represents reconstructive failure despite a partial salvage of the flap itself. For this reason, in our series, we considered a successful therapy only when no flap was lost or when the original reconstructive goal was achieved in spite of the amount of tissue lost.

In our series, leech therapy was most commonly used for locoregional flaps (50.6%). When venous congestion complicates this type of flaps, we typically consider other methods of relieving venous congestion such as suture removal or surgical delay.[28,29] When these primary interventions are not an option or effective, leech therapy is indicated (►**Fig. 1**).[28,29] For this cohort, the overall success rate of therapy was 70.4%. Nearly two-thirds (59.1%) of all locoregional flaps were performed in the lower extremity, and of those, the reverse sural flap was the most common (65.4%). The increased incidence of leech therapy in the locoregional flap group may be explained by the fact that the sural flap has a higher incidence of venous congestion compared with other pedicled flaps.[30]

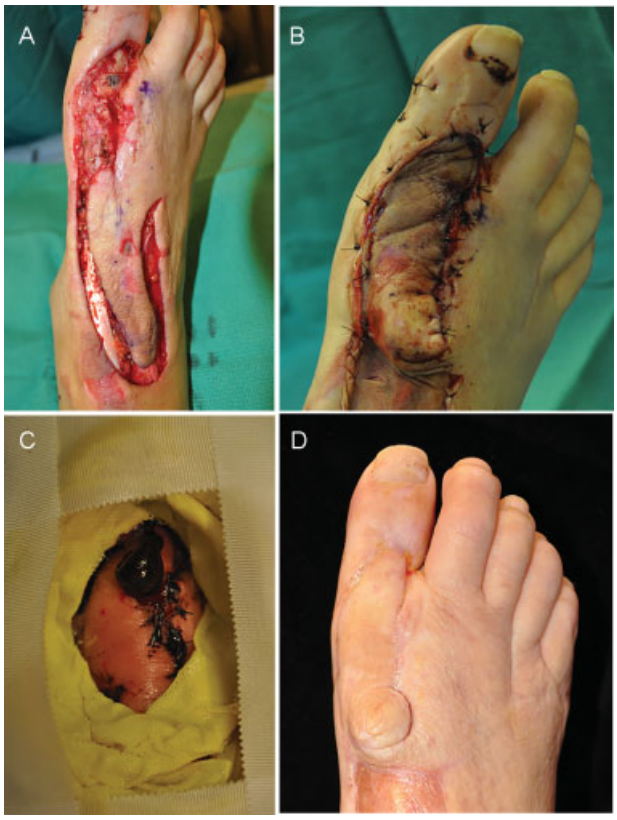

Fig. 1 (**A**) A 55-year-old female patient with an exposed bone following the first-toe arthrodesis. To cover the defect a reverse first dorsal metacarpal artery flap has been elevated, (**B**) in the operating room there is venous congestion of the flap, (**C**) flap undergoing leech therapy, (**D**) final result after complete flap survival.

Leeches were used to relieve venous congestion after free flap reconstruction in 24 (27.5%) cases. In contrast to locoregional flaps, venous congestion of free flaps in the early postoperative period is typically due to venous thrombosis.[31] If venous congestion is identified after a free flap, it is our practice to perform an emergent exploration to reestablish venous outflow through means of revision of the anastomosis, creation of an additional venous anastomosis, thrombectomy, or revision of the flap to relieve a mechanical obstruction before considering leech therapy.[26,32] We recognize that a prompt diagnosis and intervention provides the best chance of salvage in a compromised free flap. However, in certain circumstances, the venous obstruction may not be surgically correctable due to lack of alternate recipient venous access or microcirculatory problems within the flap. For these complicated cases, leeches can be used as an adjunct therapy in an attempt to salvage the compromised flap.[28,32] In the systematic review done by Whitaker et al, free flaps were the most common flaps that required leech therapy.[27] In this cohort, the authors report a success rate of therapy of 82.4%. However, they did not characterize the type and location of the free tissue transfers included their analysis. In our series of 24 free flaps, the success rate of leech therapy was 50%, which is similar to that reported in other smaller series of free flaps.[7,28] In this group, out of the six patients that underwent free TRAM breast reconstruction, three were completely salvaged, two were partially salvaged, and only one was completely lost. Nguyen et al reported their outcomes in five cases of free flap breast reconstruction in which two were completely salvaged, and three were completely lost.[28] Similarly, Pannucci et al reported their outcomes in four cases of free flap breast reconstruction in which only one flap was partially salvaged, and three flaps were completely lost.[32] In their study, the authors caution against the use of leech therapy in patients with surgically uncorrectable venous congestion after free flap breast reconstruction given that total flap loss was common in spite of leech therapy and led to the longer length of stay compared with nonleeched flaps. However, the small study size precluded any meaningful inferences, and the decision to attempt salvage with leech therapy in these challenging cases should be made on an individual basis.

Although all six patients that underwent head and neck free flaps in our study were either completely or partially salvaged, the success rate of leech therapy was 50%. Chepeha et al reported similar results in eight patients that developed venous obstruction not considered salvageable by conventional surgical or thrombolytic therapy.[26] In their series, five patients were completely salvaged, and three patients were partially salvaged. Of note, these patients received an average of 215 leeches for an average of 9.6 days and received an average of 13 units of PRBC. The authors attribute their success to the aggressive leech therapy salvage protocol used. However, due to substantial morbidity including prolonged hospitalization, intensive care unit psychosis, prerenal azotemia,

and large transfusion requirements, the authors advocate the judicious application of their protocol.

In cases of digital replantation complicated by venous congestion, leech therapy can be very valuable, especially when a venous anastomosis is not feasible.[33] In our series of 15 digital replantations requiring leech therapy, 53.3% of the replantations were salvaged, and 46.6% were lost. Foucher and Norris reported a salvage rate of 65.5% in 58 cases of digital replantation treated with leech therapy.[27,33] Of note, the authors reported a similar salvage rate of 60.6% in 33 replantation cases where a venous repair could not be performed. In our series, a venous anastomosis could not be performed in eight cases, and the salvage rate was not significantly different compared with those in which a venous anastomosis was performed.

The morbidity associated with leech therapy is largely due to blood loss and the need for blood transfusion. It is estimated that the average blood meal volume for the medicinal leech is 2.5 to 5 mL.[29,34] However, most of the bleeding associated with leech therapy is derived from the oozing that occurs after leech detachment which can reach 50 mL over 6 hours and last 48 to 72 hours.[29,34] Thus, the likelihood of needing a blood transfusion increases with the duration of leech therapy. In our study, the average duration of leech therapy was 4.6 days, and a postoperative blood transfusion was required in 36.7% of cases. These patients received an average of 3.3 units of PRBC. Our rate of transfusion is lower compared with the rate of 49.75% reported by Whitaker et al in their analysis of 52 articles that reported the use of blood transfusion.[27] It should be noted that in these complex reconstructive cases, in addition to the hemorrhagic effects caused by the leech, the majority of patients receive concomitant anticoagulation for either therapeutic or prophylactic reason. Therefore, it is likely that the synergistic pharmacological combination, rather than the leech therapy alone contributes to the amount of reported blood transfusions. At present, leech therapy protocols should include having a current type and screen before leeching and close monitoring of hemoglobin and hematocrit levels.

Our incidence of infectious complications was 8% in spite of the administration of antimicrobial prophylaxis against *Aeromonas* species. According to some reports, the infection rates can be as high as 36.2%, which emphasizes the importance of providing adequate antimicrobial prophylaxis.[35] Recent microbiological and clinical studies on the susceptibility of *Aeromonas* strains have demonstrated that strains are susceptible to fluoroquinolones, sulfamethoxazole/trimethoprim, aminosides, and third generation cephalosporins, but resistant to amoxicillin/clavulanic acid and second generation cephalosporins.[36,37]

Our study is not without limitations. First, the retrospective nature of the study and the limitations in documentation precluded us from accurately estimating the amount of leeches used per patients, except 14 subjects which is a limited sample of the total cohort. Furthermore, although an aim of the study was to identify risk factors associated with reconstructive failure in patients undergoing leech therapy, we could not identify any significant associations likely due to the limited data available regarding potential risk factors and the size of the cohort.

Conclusion

To our knowledge, this study represents the largest single-institution series evaluating the outcomes after leech therapy. Our data support the use of leeches as an adjunct for the management of venous congestion when traditional methods to relieve venous congestion have failed. Also, it is important that patients undergoing leech therapy are appropriately educated about the potential risks associated with this treatment.

Note
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