Results of Graft Removal and Negative Pressure Wound Therapy in Management of Graft Infection

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Abstract

Graft infections are a challenging complication in lower extremity bypass surgery with poor outcome, even when treated with graft removal (Gr-R) as a gold standard therapy. The efficacy of negative pressure wound therapy (NPWT) for graft infections has been reported recently, but it is still controversial. The purpose of this study was to assess the efficacy of NPWT and Gr-R for treating graft infections. Twelve consecutive patients with graft infections from 2008 to 2014, treated with Gr-R or NPWT, were enrolled. Those procedures were assessed in complete wound healing, reinfection, amputation, and mortality rate. Five grafts were treated with Gr-R, and seven grafts with NPWT. The initial indications for bypass surgery were claudication, in five grafts treated with Gr-R and three grafts treated with NPWT, and critical limb ischemia in four grafts treated with NPWT. The median time until healing in Gr-R and NPWT was 12 and 59 days, with complete healing seen in 100 and 85.7%, respectively. The major amputation rate was 20 and 14.3%, and reinfection rate was 20 and 14.3%, respectively. There was no perioperative mortality. Gr-R did not show devastating outcome when applied for grafts without limb-threatening ischemia. NPWT showed a low level of invasiveness with excellent results, except for anastomosis site infections. To achieve optimal results, a tailored treatment strategy should be considered.

Keywords

- negative pressure wound therapy
- graft infection
- vascular surgery
- graft removal
- artificial graft
- complication
- infrainguinal bypass

A graft infection is reported to occur in 1 to 5% of patients who undergo lower extremity bypass surgery and often leads to a dreadful outcome, with the mortality rate reported to range from 10 to 20%.¹ Traditionally, graft removal (Gr-R) with or without revascularization has been the standard therapy for such an infection. However, because of high morbidity and mortality associated with that operation,² various graft preservation techniques have been utilized in an attempt to improve the outcome. Muscle flap coverage (MFC) with antibiotic administration following radical debridement showed a 75% initial success rate, although the reinfection rate was reported to be as high as 66%.^{3,4} Also, MFC may be overly invasive for high-risk patients with medical comorbidities. In this context, negative pressure wound therapy (NPWT), which is utilized for a variety of infectious wounds, has emerged as less invasive and a definitive therapy for graft infections following vascular surgery.^{5,6} However, the efficacy of NPWT and optimal

treatment strategy for graft infections remain unclear. Herein, we assessed the results of cases treated with NPWT and those with traditional Gr-R at our institute, to assess the optimal strategy for treating graft infections following lower extremity bypass surgery.

Materials and Methods

We retrospectively studied 12 consecutive patients with graft infections who underwent Gr-R or NPWT without MFC from 2008 to 2014 at our institute. Until 2011, graft infections were treated with Gr-R, while we began utilizing a preservation technique with NPWT from 2012. Patient demographics, initial indication for bypass surgery, type of graft materials for bypass, time to first presentation of graft infection, duration of NPWT, time to complete wound healing, and follow-up information (condition of infected wound, graft, limb, and overall health) were recorded.

In all cases, blood and wound cultures were obtained, and intravenous antibiotics were administered at least 2 weeks until the inflammation was completely relieved, and then followed by oral antibiotics intake for 3 to 6 months. The Gr-R procedure included radical debridement of infectious tissues and artificial grafts. Arteriotomy line after resection of an infected graft was closed using a vein patch. The wounds were directly closed unless debridement was unable to completely remove infectious tissues. The NPWT, with VAC system (KCI Medical, San Antonio, TX), were promptly initiated after radical debridement of infectious tissue and complete hemostasis was secured. NPWT was directly applied to the involved native arteries or grafts with a continuous negative pressure between 75 and 125 mm Hg. Initially, a lower negative pressure of 75 mm Hg was chosen to avoid a bleeding problem, then the negative pressure was gradually elevated to 125 mm Hg. The NPWT sponges were changed three times a week and minor bedside debridement was performed when needed during each dressing change. Duplex ultrasound, ankle-brachial index, and clinical examination findings were used to assess bypass graft patency. Patients were kept hospitalized until the wounds were completely covered with healthy granulation tissue, then all the patients were followed in our outpatient clinic until the wounds were completely epithelialized.

Statistical analysis was done with JMP (version 13.1, SAS Institute, NC). An unpaired *t*-test or Mann–Whitney U test was used to compare quantitative averages between two groups, and the χ^2 test was used to compare the proportion between the two groups. A *p*-value of < 0.05 was considered statistically significant.

Ethical Approval

All patients enrolled in this research have given their informed consent, which has been approve by our institutional committee on human research, and this protocol has been found acceptable by them.

Results

Patient Characteristics

► **Table 1** shows the patient characteristics. The median age of those who underwent Gr-R was 64 years (range: 58–80), while that of those who underwent NPWT was 80 years (range: 69–89). As compared with the Gr-R group, the NPWT group showed relatively high rates of comorbidities, such as diabetes mellitus (*n* = 6; 86%), ischemic heart disease (*n* = 3; 43%), and cerebrovascular disease (*n* = 5; 71%). Primary indications for bypass surgery were claudication (Gr-R: *n* = 5, 100%; NPWT: *n* = 3, 43%) and critical limb ischemia (Gr-R: *n* = 0, 0%; NPWT: *n* = 4, 57%).

Microbiology

Microbiologic cultures were positive in 11 of the 12 cases (► **Table 2**) and 3 grafts had mixed bacteriology results. *Staphylococcus aureus* was most common in the Gr-R, while *Staphylococcus epidermidis* was most common in NPWT. One graft was infected with *Escherichia coli* septicemia and two

Table 1 Patient characteristics

	Gr-R, N = 5	NPWT, N = 7	p
Age, median (range)	64 (58–80)	80 (69–89)	0.02
Male gender	4 (80.0%)	4 (57.1%)	0.58
Comorbidities			
Hypertension	5 (100%)	7 (100%)	1.00
Dyslipidemia	3 (60.0%)	5 (71.4%)	1.00
Diabetes mellitus	0 (0%)	6 (86%)	0.001
Ischemic heart disease	0 (0%)	3 (42.9%)	0.20
Cerebrovascular disease	2 (40.0%)	5 (71.4%)	0.56
Primary indication for bypass			
Claudication	5 (100%)	3 (43%)	0.08
Critical limb ischemia	0 (0%)	4 (57%)	

Abbreviations: Gr-R, graft removal; NPWT, negative pressure wound therapy.

Table 2 Microbiology findings of cultured wound samples obtained during primary debridement

	Gr-R	NPWT
Skin flora		
Methicillin-sensitive <i>Staphylococcus aureus</i>	2	1
Methicillin-resistant <i>Staphylococcus aureus</i>	1	1
<i>Staphylococcus epidermidis</i>	0	4
Intestinal flora		
<i>Escherichia coli</i>	2	2
<i>Proteus vulgaris</i>	0	1
Unknown	1	0

Abbreviations: Gr-R, graft removal; NPWT, negative pressure wound therapy.
Note: Values shown represent number of grafts.

with *Pseudomonas aeruginosa* septicemia in the Gr-R group, while two grafts were infected with Methicillin-resistant *Staphylococcus aureus* septicemia in the NPWT group. In cases infected with Gram-positive organisms, major amputation was not required and no reinfection occurred, while in cases infected with Gram-negative organisms, major amputations were performed in two cases and reinfection occurred in two cases (► **Table 3**).

Treatment

Of all the 12 cases, 5 patients were managed with Gr-R and 7 with NPWT. Their clinical data are shown in ► **Table 3**.

Gr-R Group

All grafts had Szilagy grade III infections. Four grafts were polytetrafluoroethylene (PTFE) and one was Dacron. One

Table 3 Clinical data for 12 patients with infected grafts treated with Gr-R or NPWT

Patient No.	Initial bypass surgery	Graft type	Szilagyi grade	Microbiology	NPWT duration (d)	Wound closure (d)	Outcome
Gr-R							
1	Femorofemoral	ePTFE	III	Unknown	—	8	Healed
2	Iliofemoral	ePTFE	III	MSSA	—	26	Healed
3	Axillofemoral	ePTFE	III	MSSA	—	10	Healed
4	Femoropopliteal	ePTFE	III	MRSA <i>E. coli</i>	—	58	Healed
5	Aorta-femoral	Dacron	III	<i>E. coli</i>		73	Major amputation Reinfection 5 mo later
NPWT							
6	Femorofemoral	ePTFE	III	<i>P. vulgaris</i>	11	Failure	Major amputation
7	Femoral patch	Vein	III	MRSA <i>E. coli</i>	43	150	Healed
8	Femoropopliteal	ePTFE	II	<i>S. epidermidis</i>	20	40	Healed
9	Femoropopliteal	ePTFE	II	MSSA <i>E. coli</i>	56	60	Reinfection 4 mo later
10	Axillofemoral	Dacron	III	<i>S. epidermidis</i>	46	53	Healed
11	Axillofemoral	ePTFE	III	<i>S. epidermidis</i>	45	58	Healed
12	Femoropopliteal	ePTFE	III	<i>S. epidermidis</i>	55	180	Healed

Abbreviations: *E. coli*, *Escherichia coli*; ePTFE, expanded polytetrafluoroethylene; Gr-R, graft removal; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; NPWT, negative pressure wound therapy; *P. vulgaris*, *Proteus vulgaris*; *S. epidermidis*, *Staphylococcus epidermidis*.

patient (patient 1) required subsequent revascularization for severely worsened claudication, while the other three (patient 2–4) showed ankle-brachial index deterioration to the prebypass level, but did not require revascularization because their symptoms were well controlled conservatively. Four patients were treated by total Gr-R (patient 1–4), while one by partial Gr-R (patient 5). All wounds with total Gr-R were directly closed, while patient 5 treated with partial Gr-R was treated in combination with NPWT.

In patient 5, due to the sustained acute limb ischemia with motor function deficit and groin site graft infection on admission, which occurred after abrupt graft occlusion, major amputation with the level of ex-articulation being the hip joint was required. The infected graft in the groin was partially resected, and then the graft stump was completely covered with granulation tissue after applying NPWT for 27 days and complete epithelialization was secured on post-operative day 73. Unfortunately, after stopping the antibiotics when the graft was completely covered with healthy granulation tissue, infection recurred 5 months later as a minor fistula formation, which was successfully treated with open drainage and antibiotics medication.

NPWT Group

Of the seven infected grafts in NPWT, two were Szilagyi grade II and five grade III. Among those with Szilagyi III, three grafts were PTFEs, one a Dacron graft, and one a vein graft patch.

The medical conditions of some patients in this group were very poor with a higher incidence of critical limb ischemia. In patient 9, postoperative heart failure occurred which required intensive care with mechanical ventilation, while patient 6, 7, and 9 required temporary hemodialysis for acute renal failure immediately after mere debridement.

Patient 6 ended in above-knee amputation 11 days after the initiation of NPWT due to massive bleeding from the anastomosis site, which seemed to have been deteriorated by the infection. The causative bacteria were *Proteus vulgaris*, followed by methicillin-resistant *Staphylococcus aureus septicemia*. Patient 9 suffered infection recurrence 4 months later from the complete wound epithelialization, which was successfully treated again with NPWT preserving the graft. The overall graft preservation rate was 87.5%.

Outcomes

The outcomes of Gr-R and NPWT are shown in ►Table 4. In those groups, the median time to complete wound healing was 12 (range: 8–73) and 59 days (40–180), respectively, infection recurrence rate was 20 and 14%, respectively, and 30-day amputation rate was 20 and 14%, respectively. Regarding the time to complete wound healing, the time in Gr-R was relatively short ($p = 0.08$), but there was no statistically significant difference partially due to the small number of cases. The 30-day major amputation rate ($p = 1.00$) and infection recurrence rate ($p = 1.00$) were equivalent in both groups. There were no 30-day mortalities in both groups.

Table 4 Outcomes of Gr-R and NPWT for infected grafts

	Gr-R	NPWT	<i>p</i>
Time to wound closure, median d (range)	12 (8–73)	59 (40–180)	0.08
Follow-up period, median mo (range)	43 (5–67)	8 (0.1–27)	0.18
Completely healed wounds	5 (100%)	6 (85%)	1.00
Recurrence of infection	1 (20%)	1 (14%)	1.00
Major amputation within 30 d	1 (20%)	1 (14%)	1.00
Mortality within 30 d	0 (0%)	0 (0%)	1.00

Abbreviations: Gr-R, graft removal; NPWT, negative pressure wound therapy.

Discussion

A graft infection following vascular surgery is a devastating complication with substantial threat to life and the limb. Even with the Gr-R, which is the gold standard therapy, morbidity and mortality are still high; mortality rates ranging from 9 to 36% and major amputation rates ranging from 9 to 52%.^{1–3,7} Therefore, alternative strategies have been pursued to achieve better outcomes. In this study, we assessed both the traditional Gr-R method and a NPWT graft preservation technique for graft infections.

In our series, NPWT showed good results comparable with previous reports with regard to amputation (14%) and mortality (0%) rates, while Gr-R also showed more favorable results than previous reports (20 and 0%, respectively). These may be attributed to the relatively good medical condition of our cases in the Gr-R group with a lower rate of comorbidities, without limb-threatening ischemia. We think that Gr-R is still applicable with acceptable results for patients without significant comorbidities.

On the other hand, many patients with graft infections are not good candidates for Gr-R in real world due to their high risk comorbidities: Nearly half of our cases, treated with NPWT, did not tolerate mere debridement under general anesthesia, though additional revascularization after Gr-R would be often required due to the recurrent ischemic symptoms. In this regard, graft preservation techniques may be superior to Gr-R in some situations. Of graft preservation techniques previously reported, MFC is a well-accepted technique, but its high reinfection rate and invasiveness are troublesome. In these circumstances, NPWT is increasingly applied to treat graft infections as a less invasive and curative technique.^{3,4,8,9} Theoretically, the effects of NPWT include a reduction of bacterial content in wounds, increasing blood flow, promoting granulation tissue formation, and creating an optimal environment to combat infection.^{8,10–12} Although published findings are limited, high graft preservation, low reinfection, and low amputation rates have been reported.^{5,6,12,13} In our series, NPWT resulted in a

comparably good graft preservation rate of 87.5% and low amputation rate of 14%. Anastomotic site infection may be a contraindication to NPWT. One case (patient 6) in the NPWT group had an anastomosis site infection with virulent bacteria, which led to major bleeding and ultimately a major amputation. Previous reports also noted major bleeding complication in NPWT, especially when a graft anastomosis was fully exposed.^{5,6} Svensson et al speculated that this complication might be caused by the residual infection at the suture line and the suture deterioration hastened by NPWT.^{5,6} Thus, in cases of infection directly involving the anastomotic line, graft preservation would be difficult and prompt revascularization followed by Gr-R will be the priority.

As for infection recurrence, previous reports have shown encouraging data of low recurrence rates of 0 to 20% in NPWT cases, even after a long-term follow-up.^{10,12} Our study also noted a relatively low reinfection rate of 14.3%. However, in one case (graft 9), insufficient debridement might be the cause of infection recurrence. Although the graft infection was initially assessed as Szilagyi grade II, when recurrence occurred, computed tomography revealed perigraft fluid collection and inflammation, indicating a grade III infection, implying that radical debridement may be a prerequisite to avoid infection recurrence in NPWT, the same as when performing a muscle flap technique.¹⁴ In another patient, who underwent Gr-R combined with NPWT (graft 5), though complete epithelialization was established, virulent *E. coli* reinfection occurred and induced a skin fistula 5 months later. In consideration of several reports showing successful avoidance of infection recurrence caused by virulent Gram-negative bacteria with NPWT followed by long-term antibiotics administration for nearly 6 months,^{5,8,10} those in combination seem to play an important role in preventing reinfection in cases with virulent bacteria. However, the efficacy of NPWT combined with antibiotics remains unclear and an appropriate duration of antibiotics therapy must be analyzed in the future.¹⁰

In a few cases in NPWT, a long period of time was necessary to achieve complete wound healing, probably due to poorly controlled diabetes mellitus, poor nutritional status, and large infected cavities. We speculate that the most important factor might be the tissue blood perfusion. In patients with poor tissue perfusion, while NPWT accelerates wound healing by tissue perfusion augmentation, the wound healing process may be extremely slowed with the intrinsic poor perfusion status after NPWT application. For such patients, we speculate that MFC or skin graft following NPWT will shorten the time needed for complete wound healing. MFC alone may be insufficient to treat a graft infection due to the high rate of reinfection,^{3,4} while NPWT can offset this weakness by reducing infected cavity size and bacterial content.^{8,10,12} Theoretically, muscle flap with a rich capillary network accelerates granulation tissue proliferation and can help to foster wound healing even under the intrinsic poor perfusion status.³ Although the timing of MFC for patients with a poor medical condition should be carefully considered because of the high level of

invasiveness, it may shorten hospital stay, and relieve patient pain and exhaustion. Verma et al reported the efficacy of NPWT in conjunction with antibiotics administration and use of a Sartorius muscle flap to facilitate rapid conversion of a large infected cavity to a manageable lesion in an average of 16 days.¹⁵

Good results were achieved with NPWT for treating infected grafts in our series in spite of some cases of amputation, prolonged wound healing, and infection recurrence. Further evaluation of this treatment modality may be necessary to determine optimal indications for this treatment. This may include tissue blood perfusion testing and more appropriate antibiotic therapy for specific bacterial infections.

Our study has several limitations. It is retrospective in nature and the considerable difference in demographics and extremely small number of cases, make the direct comparison of the two therapies nearly impossible. However, we believe that this study at least showed the effectiveness of NPWT and Gr-R for applicable patients. Further studies should be conducted to clarify the most appropriate indications for each therapy.

Conclusion

In the treatment of graft infections, the results of Gr-R were acceptable when applied for cases without limb-threatening ischemia and poor medical conditions. In contrast, NPWT was quite effective in graft preservation with low reinfection and amputation rates, though anastomosis site infection was refractory to NPWT. To achieve optimal results, a tailored treatment strategy must be considered.

Authors' Contributions

Study conception: K.M.

Writing: K.M.

Critical review and revision: All authors.

Final approval of the article: All authors.

Accountability for all aspects of the work: All authors.

Conflict of Interest

The authors have no conflicts of interest to declare with respect to authorship and/or publication of this article.

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