Negative-pressure wound therapy for deep groin vascular infections

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SUMMARY

Introduction Infection of synthetic graft in the groin is a rare but devastating complication. When it occurs, several possibilities of treatment are available. Extra-anatomic reconstruction and *in-situ* implantation of new, infection resistant grafts are associated with high mortality and morbidity. Therefore, more conservative approach is needed in some cases. Negative-pressure wound therapy is one of the options in treating such patients.

Objective The aim of this study was to assess the outcome for deep groin vascular graft infection treated with negative-pressure wound therapy.

Methods Seventeen patients (19 wounds), treated for Szilagyi grade III groin infections between October 2011 and June 2014, were enrolled into this observational study.

Results Majority of the wounds (11/19) were healed by secondary intention, and the rest of the wounds (8/19) were healed by primary intention after initial negative-pressure wound therapy and graft substitution with silver-coated prostheses or autologous artery/vein implantation. No early mortality was observed. Minor bleeding was observed in one patient. Reinfection was noted in three wounds. Only one graft occlusion was noted. Late mortality was observed in three patients.

Conclusion Negative-pressure wound therapy seems to be safe for groin vascular graft infections and comfortable for both patient and surgeon. However, the rate of persistent infection is high. This technique, in our opinion, can be used as a "bridge" from initial wound debridement to definitive wound management, when good local conditions are achieved for graft substitution, either with new synthetic graft with antimicrobial properties or autologous artery/vein. In selected cases of deep groin infections it can be used as the only therapeutic approach in wound treatment.

Keywords: groin infection; synthetic graft infection; negative-pressure wound therapy

INTRODUCTION

Majority of reconstructions in the field of arterial vascular surgery are associated with synthetic graft implantation. Among different complications that accompany their use, one of the most devastating is graft infection. It can occur in up to 5% of patients [1].

When diagnosed, several possibilities for treatment are available. The traditional treatment consists of the graft excision and extra-anatomic reconstruction, which is a definitive solution, although there are some circumstances when these reconstructions are not feasible, such as the occlusion of the popliteal artery, which does not allow transobturator bypass for groin infection. Also, more infection-resistant conduits can be utilized for *in-situ* reconstruction, such as autologous veins or arteries. Although not intended for use in an infected area, synthetic grafts with antimicrobial properties such as silver-coated and rifampicin-soaked prostheses could be an option when dealing with this devastating complication. All these procedures are associated with high morbidity and mortality [2]. In these settings patients are exposed to stress from surgery and other possible complications associated with it. Furthermore, reinfection rate is significant, and amounts to 18.5% for *in-situ* silver-coated grafts in infrainguinal localization [3]. Because of this, various graft preservation techniques have been increasingly utilized in an attempt to improve outcome [4, 5].

Argenta and Morykwas [6] as well as Morykwas et al. [7] studied negative-pressure wound therapy in plastic and reconstructive surgery, as well as in the treatment of mediastinitis after sternotomy for heart surgery. Now, it has emerged as a new therapeutic approach in dealing with infected wounds, including perivascular and arterial graft infections. Today, negative-pressure wound therapy has become routine in many hospitals worldwide. However, there are a limited number of papers dealing with Szilagyi grade III infections treated in this manner.

Negative-pressure wound therapy creates a moist wound-healing environment; it drains excessive fluid from the wound, reduces tissue edema, cleans deep wounds from bacteria, accelerates the formation of granulation tissue and induces faster approximation of wound edges [8, 9].

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Graft preservation may be an option when the anastomosis is intact – only a small part of the graft is exposed, the patient has no systemic signs of sepsis, the graft is patent, and the causative microorganism is not *Pseudomonas aeruginosa* [5]. It is reasonable to assume that in these circumstances even a clinically healed infection is transformed into a low-grade state, which can be reactivated during the course of time.

OBJECTIVE

The aim of the present study was to assess early and short-term results obtained for deep groin vascular graft infection treated with negative-pressure therapy, as well as to compare treatment outcome between patients with early and late graft infections.

METHODS

All patients with Szilagyi grade III infections in the groin who were treated at our institution from October 2011 to June 2014 were included in this observational prospective study with a retrospective analysis of the primary operation. Patients treated with extra-anatomic bypass or who underwent major amputation for vital indications were excluded.

Patient demographics, type of previous intervention, type of graft materials used in the second procedures performed, duration of negative-pressure wound therapy, early and short-term morbidity and mortality, complications of negative-pressure therapy, reinfection, type of wound healing, causative microorganisms, graft patency, and follow-up information (the condition of the groin, graft, ipsilateral limb, and overall health) were recorded.

The diagnosis of graft infection was established by interview, clinical examination, wound cultures, elevated white blood cell count ($>10 \times 10^9$/l), and multi-slice computed tomography to determine the extent of infection.

Broad-spectrum antibiotics were given initially and changed, accordingly, when appropriate wound cultures were obtained. Debridement of all wounds was performed prior to the start of negative-pressure wound therapy. In some patients, due to graft occlusion, new silver-coated grafts were inserted in the groin, as well as in patients who underwent lymphostasis. However, due to persistent infection, few patients underwent autologous vein/arterial graft insertion in order to achieve wound healing. Usually, two days after surgery negative-pressure wound therapy was started, when hemostasis was achieved. Vacuum therapy and wound dressing was performed in the manner suggested by the manufacturer (KCI Medical, San Antonio, TX, USA) with continuous negative pressure of 125 mmHg. Vaseline gauze was used to cover grafts and native arteries to avoid direct contact with the polyurethane sponge. The sponges were changed three times a week. All the patients were treated in hospital, and during the course they received adequate antibiotic treatment, which continued after their discharge with oral therapy for one month at the most.

Follow-up examination was performed after one, three, and six months thereafter. Clinical examination and ankle-brachial index determination were performed.

Statistical analysis

Results are presented as number (%) for categorical data. Student's t-test and Fisher's exact test were used for analysis. For the difference between age, a bootstrapping method was used, and for the duration and costs, exact tests were performed. A two-sided $p < 0.05$ was considered significant. All the data were analyzed using SPSS 20.0 (IBM Corp, Armonk, NY, USA).

RESULTS

Mean age of patients was 63.1 ± 10.7 years (range 42–85 years). Thirteen patients were male and four were female. Four patients were classified according to American Society of Anesthesiology (ASA) as IV, and 13 of them as ASA III stage. In all 17 patients, infection involved previously implanted synthetic grafts (and all of them were Dacron grafts), and was confined to the groin. Part of the anastomosis was exposed in 5/19 wounds after initial debridement. Diabetes mellitus was present in 70.6% of patients, and five (29.4%) patients had fever without signs of sepsis. In total, 19 wounds were treated with negative-pressure wound therapy. Type of previous surgery is shown in Table 1.

In 12 patients infection was early (up to one month after the initial surgery, 15.58 ± 7.07 days), and in five patients it was late (after one month from the initial surgery performed, 8.40 ± 3.91 months). In all the patients multislice computed tomography was performed, and in all of them examination showed perigraft fluid, with collection confined only to the groin. Causative microorganisms are shown in Table 2.

Five patients had polymicrobial infection, and in one patient the wound swab was sterile.

Mean duration of negative-pressure wound therapy was 45 days (5–100 days), and costs ranged from €150 to €4,000, with average value of €1,100.

Majority of wounds (11/19) healed by secondary intention with granulation tissue covering exposed graft over time. Rest of wounds (8/19) healed by primary intention after initial negative-pressure wound therapy. Table 3 shows type of surgery performed in infected groin wounds.

No early mortality, up to 30 days, was observed. Complications during their hospital stay were recorded in six patients. Three of them had lymphatic cyst, one patient developed acute coronary syndrome and percutaneous coronary intervention was performed. One patient suffered ischemic stroke, and one had epistaxis and an epileptic seizure. Complications of negative-pressure wound therapy were noted in only one wound (1/19) and consisted of minor bleeding from wound edge. No other complications were observed.

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Table 1. Type of surgery previously performed in the study patients

Type of surgery	Number of patients
Aortobifemoral bypass	11
Iliacofemoral bypass	3
Femoropopliteal bypass	2
Femorofemoral cross-over bypass	1

Table 2. Microorganisms cultured from infected wounds

Microorganism	Number of patients
Vancomycin resistant enterococcus	2
Klebsiella enterobacter	3
Staphylococcus epidermidis	1
MSSA	2
Proteus vulgaris	2
Enterococcus	2
Staphylococcus species	2
Escherichia coli	1
Enterobacter	1
Proteus mirabilis	1
Acinetobacter	1

MSSA – methicillin-sensitive *Staphylococcus aureus*

Table 3. Grafts used for the reconstruction of groin blood vessels

Type of surgery performed	Number of wounds
Graft preservation	7
Silver graft implantation	6
Autologous vein/artery implantation	6

Persistent infection was observed in six patients (six wounds) and all of them had virulent microorganisms isolated from the wounds (vancomycin-resistant enterococcus, *Klebsiella*, *Staphylococcus aureus*, *Escherichia coli*, *Enterobacter*, *Proteus mirabilis* and *vulgaris*).

Reinfection occurred in three groin wounds (three patients) in total. These patients had *Enterococcus* and *Staphylococcus epidermidis* isolated from their wounds. The same pathogens were isolated when primary graft infection was treated in those patients. Only one graft occlusion was noted during the follow-up period. Table 4 summarizes abovementioned data and shows that no statistically significant difference was observed when comparison was performed between outcome of early and late graft infections.

Late mortality was observed in 3/17 patients who were admitted to hospital several months after negative-pressure wound therapy due to reinfection and sepsis. Cause of death was multiple organ failure in all three cases.

Also, no statistically significant difference was observed when comparison between early and late infection outcome was performed regarding age, duration of negative-pressure therapy, and costs. Table 5 summarizes these data.

Eventually, all wounds healed (100%). Seven grafts were preserved (36.8%), and in 12 (63.2%) cases we had to substitute infected grafts with silver coated grafts (six cases) and autologous artery/vein (also six cases). In four

Table 4. Outcome of negative-pressure therapy of early and late synthetic graft infection ($p < 0.05$ is considered significant)

Parameter		Infection				p value
		Early		Late		
		N	%	N	%	
Gender	Male	9	75	4	80	1.000
	Female	3	25	1	20	
Early mortality (up to 30 days)	No	12	100	5	100	-
	Yes	0	0	0	0	
Early morbidity (up to 30 days)	No	7	58.3	4	80	0.600
	Yes	5	41.7	1	20	
Complications of negative-pressure therapy	No	12	100	4	80	0.294
	Yes	0	0	1	20	
Persistent infection (up to 30 days)	No	8	66.7	3	60	1.000
	Yes	4	33.3	2	40	
Reinfection	No	10	90.9	2	50	0.154
	Yes	1	9.1	2	50	
Graft patency	No	1	8.3	0	0	1.000
	Yes	11	91.7	5	100	

Table 5. Analysis of age, duration, and costs of negative-pressure therapy ($p < 0.05$ is considered significant)

Parameter	Infection	N	Mean	SD	Med.	Min.	Max.	p-value
Age (years)	Early	12	64.17	11.496	61.50	42	85	0.549
	Late	5	60.60	9.236	63.00	50	71	
	Total	17	63.12	10.723	62.00	42	85	
Duration of negative-pressure therapy (days)	Early	12	47.42	29.623	45.00	9	100	0.574
	Late	5	38.00	30.943	45.00	5	80	
	Total	17	44.65	29.364	45.00	5	100	
Cost of negative-pressure therapy (euros)	Early	11	1,000	1,100	450	150	3,700	0.583
	Late	5	1,300	1,400	1,000	200	3,800	
	Total	16	1,100	1,200	650	150	3,800	

N – number of patients; Mean – mean value; SD – standard deviation; Med. – median value; Min. – minimum value; Max. – maximum value

cases when silver-coated graft was implanted, wound dehiscence (probably caused by inadequate debridement) occurred and negative-pressure therapy continued with graft preservation. In other two cases of silver graft implantation, the wound was closed after graft substitution in the usual manner and eventually healed *per primam,* in six cases due to persistent infection (the probable cause of such high rate of persistent infection is more virulent pathogens and overall poor health condition of these patients). In these six cases, all wounds healed *per primam intentionem* after infected grafts were substituted with autologous artery/vein.

DISCUSSION

The use of negative-pressure wound therapy in vascular surgery started with pioneer works of Demaria et al. [10] and Giovannini et al. [11], who were the first authors that applied this technique on exposed blood vessels. They successfully treated two patients with groin infections. After that, several publications have appeared with good early and midterm results regarding this technique [5, 8,12]. Overall mortality in these series was reported to be 0% up to 18 months of follow-up. However, Dosluoglu et al. [5] reported 27% of mortality during follow-up of 33 months. Mayer et al. [13] also found a high rate of long-term mortality (41%). This could be explained by a longer follow-up period in his study.

Overall mortality in our series was 18%. No early death was noted, and all of them were observed in the follow-up period and were related to reinfection. Similar results were obtained by Mayer et al. [13], who reported 30-day and one-year mortality to be 0% and 16%, respectively.

Overall amputation and reinfection rates were 0–5% reported in previously mentioned publications. Although we found no amputations in our study, the rate of reinfection was much higher, but acceptable in our opinion, and during the follow-up we found 16% (3/19 wounds) of reinfection in previously healed wounds. Persistent infection was observed in 31% (6/19 wounds), and those patients were treated with autologous artery/vein *in-situ* insertion, after the removal of the infected synthetic graft.

Regarding causative pathogens, Calligaro et al. [14] reported 40% of limb salvage when involved microorganism was *Pseudomonas,* which is reported to be very aggressive. In our series we had no *Pseudomonas* infection. However, Mayer et al. [13] found no association between *Pseudomonas* infection and the need for graft excision. In their opinion, patients presenting with *Pseudomonas* infection are not poorer candidates for any type of graft preservation technique.

In our study, only one (1/19 wounds, 5%) complication of negative-pressure wound therapy occurred, and it presented as minor bleeding from wound edge. Mayer et al. [13] reported also one (2%), but serious bleeding due to inadequate previous resection of infected artery. Svensson et al. [15] reported bleeding complications in two patients (2/33 wounds, 6%). Authors of that study also reported the median total cost per patient for the negative-pressure therapy to be about €1,300 [15]. In our study, the average cost of such therapy was €1,100 per patient.

All the patients in our study experienced complete wound healing. Majority of wounds (11/19, 58%) healed by secondary intention with granulation tissue covering exposed graft over time. The rest of the wounds (8/19, 42%) healed by primary intention after the initial wound debridement and negative-pressure therapy. After that, graft substitution with autologous artery/vein or silver-coated grafts was performed and the wounds were closed in the usual manner.

CONCLUSION

Negative-pressure wound therapy seems to be safe for groin vascular graft infections with no early mortality, virtually no complications of its use, and excellent patency rate of 95%.

Comfortable for both patient and surgeon, this approach emerges as a new and promising therapeutic option in these difficult patients. However, high rate of persistent infection which we found mandates careful selection of patients for this approach. This technique, in our opinion, can be used as a "bridge" from initial wound debridement to definitive wound management, when good local conditions are achieved for graft substitution, either with a new synthetic graft with antimicrobial properties or autologous artery/vein. In selected cases of deep groin infections, this technique can be used as the only therapeutic approach in wound treatment.

The limitation of this study is the small number of patients and short follow-up period of average 10.0 ± 5.8 months (range of 1–24 months). Also, there was no comparative group in the study. Therefore, no statistically significant differences were observed when comparing outcome of early and late synthetic graft infections. Despite this fact, we observed better results in patients with shorter duration of infection caused by less virulent microorganisms, in whom negative-pressure wound therapy was commenced early. New studies with larger number of subjects are needed to clarify the role and establish the algorithm for negative-pressure wound therapy in the field of vascular surgery.

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Терапија негативним притиском у лечењу инфекције графта у препони

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КРАТАК САДРЖАЈ

Увод Инфекција синтетског графта у препони је ретка али озбиљна компликација. Може се лечити на више начина. Екстраанатомски бајпас и *in situ* имплантација новог, на инфекцију отпорног графта су повезани са значајним морбидитетом и морталитетом. Због тога је у неким случајевима потребан конзервативнији приступ у лечењу. Терапија негативним притиском је једна од могућности у лечењу тих болесника.

Циљ рада Циљ рада је био да се прикажу резултати лечења инфекције синтетског графта у препони употребом негативног притиска.

Методе рада У ову опсервациону студију је укључено 17 болесника (19 рана) који су лечени због инфекције графта у препони (*Szilagyi* III) између октобра 2011. и јуна 2014. године.

Резултати Већина рана (11/19) зарастала је *per secundam*, док су остале ране зарасле *per primam* после иницијалне примене терапије негативним притиском, а онда је следила замена инфициране протезе силвер графтом или аутологном артеријом/веном. Није забележен ниједан рани смртни случај. Мање крварење је забележено код једног болесника. Реинфекција је настала код три болесника. Забележена је једна оклузија графта. Касни морталитет је регистрован код три болесника.

Закључак Примена терапије негативним притиском је, чини се, безбедна код инфекције графта у препони и подобан метод и за болесника и за хирурга. Ипак, учесталост перзистентне инфекције је висока. По нашем мишљењу, ова техника може бити употребљена као „премошћење“ од иницијалног дебридмана до дефинитивног збрињавања ране, када постоје добри локални услови за супституцију графта било новом протезом са антимикробним својствима или аутологном артеријом/веном. Код селектованих случајева инфекције графта у препони може бити коришћена као једини начин лечења.

Кључне речи: препонска инфекција; инфекција синтетског графта; терапија негативним притиском

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