Vacuum-assisted wound closure versus alginate for the treatment of deep perivascular wound infections in the groin after vascular surgery

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Background: **Vacuum-assisted wound closure (VAC) therapy may heal wounds faster than conventional dressings after surgical debridement of perivascular groin infections after vascular surgery.**

Methods: **Patients with deep infected wounds (Szilagyi grade III) were surgically revised and left open for secondary healing, then randomized to either VAC or alginate (Sorbalgon) therapy, between February 2007 and November 2011. To test the hypothesis, it was calculated that 42 patients needed to be included (90% power, 5% level of significance). It was decided to perform an interim analysis after inclusion of 20 patients.**

Results: **Among 66 patients undergoing groin revision, 20 patients were included in this study. Patients were randomized to VAC (n = 10) or alginate (n = 10). The two groups were comparable in patient and wound characteristics. Time to full skin epithelialization was significantly shorter in the VAC group (median, 57 days) compared with the alginate group (median, 104 days; $P = .026$). The number of positive wound cultures of bacteria and C-reactive protein values decreased equally in both groups between surgical revision and day 21. One femur amputation was performed in each group as a consequence of the groin infection, one patient died during the in-hospital stay in the alginate group, and none died in the VAC group.**

Conclusions: **VAC achieves faster healing than alginate therapy after wound debridement for deep perivascular wound infections in the groin after vascular surgery. This finding does not allow further inclusion of patients from an ethical point of view, and this study was, therefore, stopped prematurely. (J Vasc Surg 2014;59:145-51.)**

Wound infection in the groin is a common problem after vascular surgery. Deep perivascular wound infection in the groin after arterial surgery is related to severe morbidity, long and costly hospital stay, leg amputation, and death.[1] Thus, a deep perivascular wound infection in the groin means great suffering for the patient. Vacuum-assisted wound closure (VAC) therapy is a form of negative pressure wound therapy (NPWT) that has been reported to have several beneficial effects on healing wounds such as creation of a moist wound-healing environment, drainage of superfluous fluid, reduction of tissue edema, cleansing deep wounds from bacteria, acceleration of the formation of vascularized granulation tissue, and faster approximation of wound edges.[2,3] VAC therapy of deep groin infection after vascular surgery has been reported to be a good treatment option in relation to a more aggressive surgical approach.[4-6] However, a higher level of evidence is warranted. In the current reports from The Cochrane Collaboration group[2] and the Swedish Council on Health Technology Assessment,[7] research with better quality was requested. The aim of this prospective randomized controlled study was to compare VAC vs the other best treatment (alginate wound dressing) in patients with deep perivascular groin infection after vascular surgery.

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METHODS

Study population and setting. This study was approved by the local ethics committee at Lund University (Dnr 616/2006). The study was planned and initiated before the formal requirement for the registration of interventional studies in a Clinical Trial Registry. The Vascular Center, Malmö-Lund, Skåne University Hospital, is a tertiary referral center for the southernmost part of Sweden with a primary catchment population of 800,000 inhabitants. Patients undergoing groin incisions for any vascular procedure were routinely given three prophylactic doses of the antibiotic dicloxacillin (Ekvacillin), where the first dose was administered at induction of anesthesia. Patients with deep perivascular groin infections (Szilagyi grade III)[1] were eligible for this study. Patients were prospectively enrolled, after written informed consent, between February 13, 2007 and November 24, 2011. Patients were monitored with wound cultures, blood sampling, and wound surface area measurement with Visitrak[8] (Smith-Nephew, Hull, UK) at one time point each week during the first 3 weeks and followed by personal nurses connected to the study until the wound was completely healed.

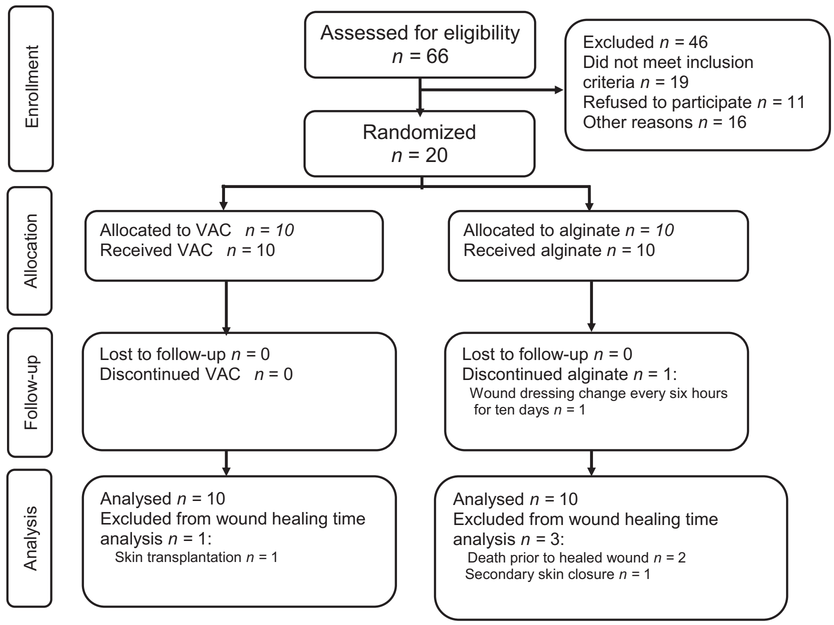

Fig 1. CONSORT (CONsolidated Standards Of Reporting Trials) diagram. Patients with deep perivascular groin infections after vascular surgery throughout the study period *VAC*, Vacuum-assisted wound closure.

Randomization. In this randomized study, VAC therapy was compared with alginate. During the study period, two different alginate dressings were available: Sorbalgon (Hartmann ScandiCare AB, Anderstorp, Sweden) or Melgisorb (Mölnlycke Health Care AB, Götenburg, Sweden) wound dressings with a high absorptive capacity. Randomization was performed by C. M. after surgical debridement, where each patient withdrew a marked note, "VAC" or "alginate," from an envelope.

Dressings. Alginate was at the time considered to be the "best other treatment" choice. Alginate is a dressing composed of calcium and alga, with a high absorptive capacity. When the dressing is soaked with wound fluid and blood, a gel is formed, aiming to retain the superfluous fluid and bacteria within the wound to prevent soggy damage of the surrounding skin. All patients with deep groin infections first underwent careful wound revision, removal of all necrotic subcutaneous or skin tissue with scissors or ladle, and drainage of all infected wound cavities followed by irrigation with saline, under either regional or general anesthesia. Wound cultures adjacent to the graft or native arteries were obtained. After adequate hemostasis, Aquacel Hydrofiber (ConvaTec, Bromma, Sweden) was applied to fill the wound cavity before an outer wound dressing with absorptive capacity, Sterilet Ontex (Selefa Trade AB, Spånga, Sweden), was used to reinforce the inner dressing. In case of randomization to VAC, VAC therapy was started the day after the surgical revision, and a polyurethane sponge was applied with a continuous topical negative pressure of 125 mm Hg. Changes of VAC dressings were performed three times per week. Visible graft material and native arteries were covered routinely with a nonadhesive silicon-based dressing (Mepitel, Mölnlycke Health Care AB) to minimize any possible trauma to the vascular anastomosis or arterial reconstruction, which hypothetically could be generated by VAC therapy. In case of randomization to alginate, dressings were changed as often as clinically indicated. The patients were treated in-hospital as long as any graft material or native artery was visible. As soon as the arterial reconstruction was covered with granulation tissue, in an otherwise fit patient, wound treatment could be continued at home. The wound was followed up by nurses connected to the study until full skin epithelialization. Local complications were documented from the day of wound debridement and revision to the end of follow-up, April 2, 2012.

Definitions. Hypertension was defined if the patient previously had been diagnosed with hypertension or was taking antihypertensive medication. Cerebrovascular disease was considered if there was a history of stroke (cerebral bleeding or infarction) or transient ischemic attack. Ischemic heart disease was considered if there was a history of myocardial infarction, angina pectoris, coronary artery bypass graft, or percutaneous coronary angioplasty. Diabetes mellitus was noted if the patient had antidiabetic treatment with diet, oral hypoglycemic agents, or insulin. Smoking included both current and former tobacco smokers. Anemia was defined as hemoglobin <134 g/L in men and <117 g/L in women. Renal insufficiency was defined as creatinine >90 μmol/L in women and >105 μmol/L in men. Failure to wound treatment was defined as a nonhealed wound in the groin after 4 months, visible graft material or femoral artery after 1 month of treatment, or amputation or death as a consequence of the groin infection.

Statistical methods. Data management and statistical analysis were performed using the SPSS for Windows, v. 20.0 (SPSS Inc, Chicago, Ill). Differences in proportions were analyzed with the χ^2 test or Fisher exact test. Continuous variables were expressed in median and range, and group difference analyzed with the Mann-Whitney *U* test. Based on a previous study[4] where median complete wound healing time was 55 days in 27 groins, we hypothesized that wound healing time with alginate wound treatment would be 30 days longer. To be able to show that VAC treatment is superior to alginate treatment, with a 90% power and 5% level of significance, we needed to include 42 patients in this randomized study, 21 in each group.[9] Flow of the eligible patients of the study was expressed with a CONSORT (CONsolidated Standards Of Reporting Trials) diagram.[10] It was decided to perform an interim analysis at the planning stages of the study after inclusion of 20 patients because of the previous positive experience and expected superiority with VAC treatment, and in case of a superior healing advantage with VAC treatment, the study would be stopped prematurely for ethical reasons. *P* values of $<.05$ were considered significant.

RESULTS

Patients with deep perivascular groin infections after vascular surgery. There were 66 patients assessed for eligibility (Fig 1). Nineteen patients did not meet the inclusion criteria. They are simultaneous VAC therapy of other wounds (n = 8), inability to comply with the study protocol during follow-up (n = 6), and inability to comprehend the study information (n = 5). Eleven patients refused to participate. The surgeon chose the method in six patients and four patients chose to be treated with VAC therapy. In sixteen patients, the surgeons were unaware of the study. Hence, 46 patients were excluded and 20 patients were randomized to either VAC therapy (Fig 2, *A*) or alginate (Fig 2, *B*). The 46 excluded patients were treated with VAC therapy.

Characteristics of the randomized patients. The indications for vascular or endovascular surgery were peripheral arterial occlusive disease (VAC group [n = 7]; alginate group [n = 6]), abdominal aortic aneurysm (n = 2 for both groups), coronary artery disease (alginate group [n = 2]), and renal artery disease (VAC group [n = 1]). The following primary operative procedures were performed: common femoral endarterectomy (VAC group [n = 1]; alginate group [n = 3]), common femoral endarterectomy and stenting of iliac artery (VAC group [n = 3]), interposition graft in the common femoral artery (n = 1 for both groups), common femoral artery embolectomy (alginate group [n = 1]), endovascular infrainguinal artery recanalization (n = 1 for both groups), local intra-arterial thrombolysis (VAC [n = 1]), endovascular aneurysm repair (n = 2 for both groups), coronary artery angiography (alginate group [n = 2]), and inadvertent femoral artery catheterization attempting femoral venous access for hemodialysis (VAC group [n = 1]). Characteristics of the randomized patient are shown in Tables I and II. There was a trend that body mass index was higher (Table I) and that the wound was deeper after surgical debridement (Table II) among patients randomized to alginate.

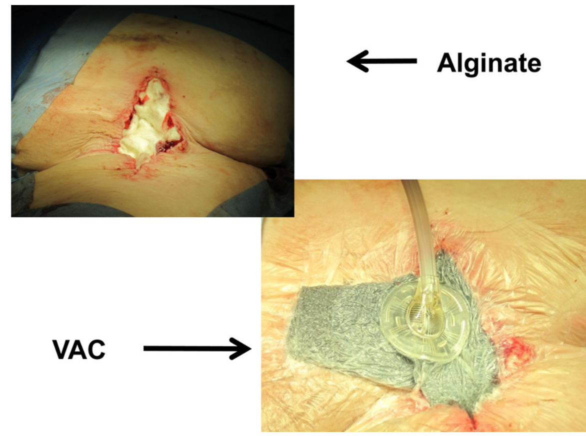

Fig 2. The two modalities of wound dressing treatment are exemplified in the same patient who had undergone surgical revision of a deep perivascular wound infection in the left groin after vascular surgery. Vacuum-assisted wound closure (*VAC*) therapy application: The black sponge is placed within the wound cavity. An occlusive self-adhesive film is then placed above the adjacent skin and a second black sponge is placed above the skin-protective film and connected with the first placed sponge. A semipermeable self-adhesive film covers the two sponges. A cut creating a circular hole, approximately 3 cm in diameter, in the occlusive film is made, and the suction device is finally attached and the VAC device activated at 125 mm Hg of continuous negative pressure. Note the location of the suction device between the two sponges and the need of a second sponge bridging to the first sponge to safely be able to place the suction device without risking suction lesions in the skin. Alginate application: The dressings fill the entire wound cavity, and the wound is then covered by an outer absorptive dressing.

Microbiology. The rate of wound infection with *Staphylococcus aureus* or intestinal flora was the same in the two groups (Table II). Infection with bacteria pertaining to the intestinal flora was the most common cause (Table III). Clearances of bacteria from the wounds were equally slow in both groups (Table III).

According to the wound culture results and testing of bacterial resistance, 11 patients (seven patients in VAC and four in alginate group) received antibiotics tested to be not sensitive to the specific bacteria cultured for a time of 1-32 days (4-32 days and 1-17 days, respectively). The median number of positive wound cultures during wound treatment was 4.5 (range, 2-6) and 6 (range, 1-13) for the VAC and alginate groups, respectively ($P = .32$).

Wound healing. Time to full skin epithelialization was significantly shorter in the VAC (median, 57 days) compared with the alginate (median, 104 days) group ($P = .026$) (Table IV). One patient in the alginate group had a sustained high frequency of daily dressing changes and change of patient clothes and bed linens, leading to an

Table I. Characteristics of the randomized patients

	VAC (n = 10)	*Alginate (n =10)*	P *value*
Sex (M/F)	8/2	5/5	.35
Age, years	71 (60-81)	73 (66-84)	.66
Comorbidities			
Ischemic heart diseases	5 (50)	8 (80)	.35
Diabetes mellitus	4 (40)	7 (70)	.37
Cerebrovascular diseases	2 (20)	2 (20)	1.0
Any previous vascular surgery	5 (50)	8 (80)	.35
BMI[a]	26 (22.3-37.3)	31.5 (23.9-39.8)	.095

BMI, Body mass index; *VAC,* vacuum-assisted wound closure.
[a]Weight (kg)/length^2 (m^2).
Continuous data are presented as median (range) and categoric data as number (%).

Table II. Surgical- and wound-related factors

	VAC (n = 10)	*Alginate (n = 10)*	P *value*
Laboratory test just prior to the surgical revision			
C-reactive protein, mg/L	150 (4-473)	128 (9-370)	.80
Leukocytes, $\times 10^9$/L	9.3 (6.2-13.5)	11.0 (7.0-14.8)	.14
Anesthesia			
Regional/general	2/8	4/6	.63
Surgical factors			
Multiple previous groin incisions	5 (50)	7 (70)	.65
Reoperation for bleeding	5 (50)	4 (40)	1.0
Synthetic graft infection	4 (40)	4 (40)	1.0
Time of index procedure to randomization, days	16 (12-170)	16 (8-110)	.44
Wounds and microbiology after surgical revision			
Positive culture			
Staphylococcus aureus	3 (30)	0 (0)	.21
Intestinal flora	9 (90)	7 (70)	.58
Wound surface area, cm^2	13 (7.6-37.6)	20.5 (4.6-44.5)	.58
Wound depth, cm	4 (2.3-8.5)	6 (2.5-13.5)	.089

VAC, Vacuum-assisted wound closure.
Continuous data are presented as median (range) and categoric data as number (%).

unethical study situation, and it was determined by the study investigators to cross over to VAC therapy after 10 days of alginate treatment. Wound treatment time was significantly shorter outside hospital in the VAC group compared with the alginate group ($P = .034$). There were no differences in wound surface area after surgical debridement to 21 days of treatment between the two groups (Table IV). Reduction of C-reactive protein was the same in the two groups (Table V).

Amputation and mortality. Five patients underwent amputation during a median follow-up period of 14 months (range, 2.2-51). Three patients in the VAC group underwent amputation; one transfemoral amputation was performed as a consequence of the groin infection, and two patients underwent transfemoral amputation because of worsening of the critical limb ischemia. Two patients in the alginate group underwent amputation; one transfemoral amputation was performed as a consequence of the groin infection and one patient underwent minor amputation (metatarsal) because of worsening of the critical limb ischemia. One patient died during in-hospital stay in the alginate group and none died in the VAC group (Table IV). Two and five patients in the VAC group and the alginate group, respectively, had died by the end of follow-up ($P = .35$).

Analysis of the nonrandomized patients. There was no difference in the frequency of failed wound treatment between the nonrandomized (17/46; 37%) and the randomized (6/20; 30%) patients ($P = .59$). The median wound healing time for the nonrandomized patients was 64 days (n = 31; $P = .30$ vs VAC in the randomized group).

DISCUSSION

The present prospective randomized controlled study showed that the wound healing rate was twice as fast with VAC therapy compared with alginate therapy for perivascular deep groin infections after vascular surgery. Even though the number of patients available for statistical analysis was reduced to one-half in relation to the estimated number needed in the sample size calculation, it was, nevertheless, possible to show that VAC therapy was superior to alginate in terms of a faster wound healing. The median wound healing time in the VAC group was

Table III. Microbiology: Results of the wound cultures obtained at primary surgical debridement

Bacteria	*VAC (n = 10)*	*Alginate (n =10)*
Intestinal flora		
Enterococcus faecalis	4	5
Proteus mirabilis	1	3
Escherichia coli	2	
Enterobacter cloacae	2	
Klebsiella oxytoca	1	
Enterococcus faecium		1
Pseudomonas aeruginosa		1
Serratia marcescens	1	
Morganella morganii		1
Bacteroides fragilis		1
Anaerobic bacteriae	1	1
Skin flora		
Staphylococcus aureus	3	
Staphylococcus epidermidis	1	
Staphylococcus species		1
Negative	1	2
Summary of types of bacteria	16	14
Days from start of study	*Number of patients with positive cultures*	*Number of patients with positive cultures*
0 (surgical debridement)	9	8
7	8	7
14	9	7
21	8	6

VAC, Vacuum-assisted wound closure.
The sum of the number of types of bacteria is more than the number of wounds; there was growth of more than one type of bacteria in some wounds.

57 days, comparable with the results obtained in a previous study[5] and also with the nonrandomized patients that were eligible for this study. It is difficult to tell if alginate therapy was the best choice as the best comparative wound treatment option in the control group, but it is hard to see that any other passive wound treatment would have performed much better. It is likely that the main result of this study would have remained valid regardless of control group. In a recent randomized clinical trial including 24 patients, NPWT resulted in two times faster wound healing than treatment with sodium hypochlorite in patients with difficult-to-heal wounds.[11]

The two groups were comparable in terms of age, sex, and comorbidities. There was a trend that body mass index was higher, and the wound was deeper after surgical debridement in the alginate group. Since obese patients often have multiple skin folds near the groin, wound dressings might be difficult to apply, and disturbances of fluid leakage to the surrounding skin and secondary skin damage might be a relatively greater problem among these patients, leading to a somewhat impaired wound healing.[12,13] It seems advantageous to have a foam dressing applied in the groin connected to a VAC machine that drains the exudate continuously away from the wound edges, especially in the obese. On the other hand, a higher proportion of patients in the alginate group received proper antibiotic treatment. The level of importance of each of these factors for healing of deep perivascular wound infections in the groin is unclear.

The mechanism of action for accelerating wound healing in VAC therapy has been attributed to various factors. In contrast to Pinocy et al,[14] who found that VAC therapy rapidly cleared the groin wounds from positive smears with total elimination of bacteria with 14 days of VAC therapy, the present study showed a much slower reduction of the number of positive smears in both groups without differences between groups. Again, a more appropriate antibiotic regime after wound debridement might have had an influence of the reduction of the amount of bacteria at the different time points in both groups. There is, however, no scientific support, so far, that VAC therapy promotes bacterial clearance from the wound.[3] Furthermore, there was no difference in reduction of C-reactive protein in relation to time between the two groups.

Although not analyzed in the present study, edema reduction and control of fluid leakage might be those critical factors that make VAC superior to alginate therapy in terms of wound healing. The leakage may sometimes be significant, with an initial drainage of more than 500 mL of exudates per day. In fact, one patient had to abandon alginate therapy after 10 days of treatment because of a sustained high frequency of daily dressing changes and change of patient clothes and bed linens, leading to an unethical study situation. Another useful clinical implication for the closed VAC therapy system may be that leakage of infected fluid is prevented from transmission to other patients.

There are several methods for measuring wound volume, which would have been the most appropriate way to follow wound healing. The validity and reproducibility of all these methods has been questioned, especially simple and cost-effective methods for routine clinical use.[15] Consequently, it was not possible to establish a feasible bedside method for measuring volume of the wound cavity in the groin. Therefore, wound surface area together with wound depth were measured as separate variables during the first 3 weeks, and it was not possible to show that early wound contraction,[16] in terms of wound surface area reduction, was a mechanism for a faster wound healing in the VAC group. Instead, wound treatment time after hospital discharge to complete skin epithelialization was found to be much shorter in the VAC group. There is evidence, however, that NPWT achieves faster reduction of wound volume than conventional dressings in the early stages of wound healing as well.[10]

Only 20 patients were included during a long, 4.5-year study period, which implies that there were difficulties in enrollment of patients. The CONSORT diagram (Fig 1) indicates that some patients did not meet the inclusion criteria, whereas 16 patients were not included due to logistic problems or due to surgeons' preference of treatment without considering randomization of a potential study candidate. Both surgeons and patients were probably

Table IV. Wound healing

	VAC (n = 10)	*Alginate (n = 10)*	P *value*
Time to full skin epithelialization, days	57 (25-115) n = 9	104 (57-175) n = 7	.026
Wound treatment in-hospital stay, days	13 (5-93)	20 (6-76)	.79
Wound treatment outside hospital, days	42 (18-81)	79 (32-171)	.034
Failure to wound treatment[a]	1 (10)	5 (50)	.14
Amputation or death following groin infection	1 (10)	1 (10)	1.0
Time (days from start of study)	*Wound surface area, cm²*	*Wound surface area, cm²*	
0 (after surgical debridement)	18.8 (7.6-37.6)	22.3 (4.6-44.5; n = 10)	.58
7	12.0 (1.3-44.9)	16.6 (5.9-53.8; n = 10)	.48
14	7.5 (0.6-92.5)	10.8 (2.0-33.8; n = 9)	.36
21	3.5 (0-92.5)	6.5 (2.7-26.3; n = 9)	.24

[a]Failure to wound treatment = nonhealed wounds in the groin after 4 months, visible graft material or femoral artery after 1 month of treatment, or amputation or death as a consequence of the groin infection.
Continuous data are presented as median (range) and categoric data as number (%).

Table V. Reduction of C-reactive protein (*CRP*) during treatment

	CRP, mg/L, median		
Time, days	*VAC (n =10)*	*Alginate (n = 10)*	P *value*
0 (before surgical debridement)	149	128	.76
7	11	20	.68
14	7	13	.46
21	6	9	.81

VAC, Vacuum-assisted wound closure.

more reluctant to use the other treatment than VAC therapy at the end compared with the start of study. However, it is notably difficult to recruit a high proportion of randomized patients in clinical trials in surgery among those eligible.[17] Since the results after VAC therapy for perivascular groin infections was perceived as very good,[5] accepted by clinicians as the gold standard for treatment, and preferred by the personnel staff, the ratio of randomized patients must be considered as reasonable.

CONCLUSIONS

VAC therapy induced faster wound healing than alginate therapy in patients with deep perivascular wound infections in the groin after vascular surgery. This finding does not allow further inclusion of patients from an ethical point of view, and this study was, therefore, stopped prematurely.

AUTHOR CONTRIBUTIONS

Conception and design: CM, SA
Analysis and interpretation: CM, SA
Data collection: CM, CW, SA
Writing the article: CM, SA, CWH
Critical revision of the article: CM, SA, CWH, CW
Final approval of the article: CM, SA, CWH, CW
Statistical analysis: CM, SA
Obtained funding: SA
Overall responsibility: SA

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