

Vascular Graft Infection – A Single Centre Analysis

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Abstract

Though the frequency of vascular graft infections is very low, its consequences are too serious. The paper aims at the vascular graft infection causes analysis in a single centre. Results achievable by means of several approaches have been discussed and a possible way of lowering the vascular graft infection rate has been tested.

Material and methods: A population of 2812 patients having implanted an artificial vascular graft in 2000-2010 were prospectively followed up. Upon the analysis of risk factors, the control group of 653 patients operated on during 2011-2013 were followed up.

Results: Number of vascular graft infections was 28 (1,0%). Amputation rate was 19% (5 patients) and the overall mortality 14% (4 patients). Leading signs of the infection were local findings in 88%. All patients with the infection had two or more co-existing independent risk factors picked out by chi-square statistics. It was obesity, repeated interventions and emergency surgery ($p < 0,001$). Gender (men), co-existing infection, diabetes and too long bypass were also significant ($p < 0,01$). There was not MRSA infection at all. After adoption of risk factors reducing approach, there was not proven decreased infection occurrence in patients with implanted artificial grafts. However, during the control period, a higher share of autologous grafts and endovascular methods were used. Thus the overall infection rate was reduced from 0,43 to 0,31%.

Conclusion: The graft infection is not a matter of resistant bacteria, but the infection in general. An accumulation of more than two independent risk factors according to local situation should be avoided. As the infection treatment is very demanding with uncertain results, patient's wish should be taken into account as well. In all primaries, the use of the artificials ought to be minimized and endovascular procedures should be preferred, where appropriate. Emergency surgery should be avoided by in time indication to revascularization.

Keywords: Vascular graft; Infection; Prevention; Allograft; Surgery

Introduction

Vascular graft infection is a life-threatening complication with a very high risk of sepsis and major bleeding. Its incidence is reported to be around 1-5% [1]. The mortality of the aorto-iliac graft infections reaches 20-50% even in specialized centres. The MRSA infection has been reported to have higher mortality rates up to 56% in the supra-inguinal and 29% in the below the groin infections [2]. The reason for maintaining the incidence rate in spite of progress in antibiotic prophylaxis, new materials introduction and advances in surgical technique is not straightforward. A contribution is for sure brought about by the growing share of the elderly with co-morbidities and lower healing power. Longer mean survival after vascular surgery together with an earlier onset of arteriosclerosis means more often a need for some re-do procedure that is internally endowed with a higher infection risk as well. And at least, but not last, the over-treatment with broad-spectrum antibiotics makes the antibiotic prophylaxis less powerful and the following infection treatment more difficult due to poly-resistant bacterial stems selection.

There is still a problem with early diagnosis as there are no early signs of the infection there. Life threatening bleeding and/or sepsis are very often the first but late symptoms giving the vascular surgeon nearly no time for any time consuming diagnosing. PET CT seems to give the best results in the aorta-iliac region in recent years. But stained leucocytes plain gamma-ray imaging can be of some use as well.

As the treatment of graft infection is still unsatisfactory, and statistical evaluation of different modalities due to low infection appearance does not give significant results, this work aimed at the infection prevention together with the complication presentation and results of several treatment modalities in patients of our vascular

department. Upon picking out the relevant risk factors, a hypothesis to reduce the infection rate by the reduction of the number of risk factors was tested.

Material and Methods

A population of 2812 patients having implanted an artificial vascular graft within the period 2000-2010 were prospectively followed up. The shortest follow up period from the primary revascularization being 36 months well overtakes our median infection onset 11 months. Peri-operative prophylaxis of 1,0 g Cefazoline i.v. every 8 hour up to three single doses starting at the beginning of the surgery was administered to all of them. Parameters taken into account were sex, age, co-morbidity, leading symptoms of infection, laboratory data at admission, diagnostic modality, type of primary procedure, type of secondary procedure due to infection and result. Because of very low number of patients with vascular graft infection, only few parameters were statistically evaluated, and if, then by chi-squared method. As the analysis turned out to be statistically significant, no additional statistical methods needed to be engaged. Patients with artificial graft to the carotid artery were not included into this study as they did not

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develop any graft infection during the period. Our group of patients thus consisted of those with an aortic-iliac-femoral reconstruction.

Then, a strategy to lower the vascular graft infection incidence and its clinical impact was adopted. A control group of 653 patients with an artificial graft implanted during 2011-2013 were followed up to evaluate its clinical impact.

Results

Twenty eight out of 2812 artificial vascular grafts got infected in 23 patients giving the infection incidence about 1,0%. The infection developed two-times in two patients. The number of prostheses implanted reached hardly 1/3 of all treated patients in our department as an autologous material is usually preferred. The mean interval from the primary graft implantation to the infection presentation was 11 months ranging from 13 days to 56 months. Symptoms leading to patients' readmission were mostly local in 22, i.e. 88%, cases including GIT bleeding (Table 1). The cultivated out bacterial spectrum shows Table 2. There was a higher portion of negative prostheses cultivations during first years. There was no negative cultivation in last two years. But when the cultivation negative the patients did not present any fever and leucocytes elevation. Two of them had elevated FW.

Local therapy in one case of the graft infection in the groin including its debridement, systemic antibiotics and local antiseptics turned out unsuccessful. The prosthesis had to be taken out because of recurring fistula formation. Graft removal only was used in four cases. One of these ended with the high amputation in thigh. The explantation together with a kind of plasty of the resulting vascular defect was used in eight cases. The autologous vein was used in six and a new artificial patch in two cases. One patient from this group had to undergo the high amputation thereafter. The infected graft removal followed by a new bypass reconstruction was done in twelve cases, mainly in aortic graft infections. The new reconstruction was done as a one stage procedure with the graft removal in nine cases. Three patients were revascularized later on. The autologous vein was used six times comprising four times the in-site placement. A prosthesis was used six times as well, but never in-site. Two patients after ex-site revascularization with prosthesis had to be amputated afterwards. Overall mortality rate was 16,0% (four patients). Three of them died of sepsis and one due to the myocardial infarction. The overall amputation rate was 20% (5 patients). The status of the patients after the graft removal, with or without any following revascularization, was the same or better than before the primary surgery in 14 patients (56%). It got worse, but it has never got critical in 2 patients (8%).

Decomposing the 2812 patients into two groups – with and without graft infection and comparing the groups according to primary surgery and gender we got data gathered in Table 3. They suggest that being a man and having peripheral bypass implanted are two independent risk factors for developing the infection (chi squared $p = 0,01$). From other relevant factors, these turned out to be independently significant: obesity (defined here as the BMI over 30), repeated interventions and emergency surgery ($p < 0,001$). Gender (man), co-existing infection, diabetes and below the knee or axillo-femoral bypass were also significant ($p < 0,01$).

There was not a MRSA infection at all. The major surgery showed no higher tendency to develop the graft infection. Figure 1 shows risk factors spectrum, and their frequency in the infected and non-infected groups.

Number of the independent risk factors, not taking into account

gender and prosthesis implantation, present at the time of primary surgery was higher than in the group without infection. The majority of our patients had two or more risk factors in the same time (Figure 1) Table 4. There is an inflection point close to two simultaneously presented risk factors with a steep acceleration of the graft infection risk.

We thus tried to decrease the number of simultaneously present risk factors. The actions taken were represented by the patient's body weight reduction, in time surgery prior stadium IV, good control of diabetes. But we failed to reduce the risk factors in the time of surgery

Out of 653 patients having any artificial bypass implanted during the second period, i.e. 2011-2013, eight got infected (1.2%). This number did not differ from the former period (chi-squared). Even the amputation rate and mortality failed to be statistically proven different.

Discussion

It is known that the more west we go geographically the higher frequency of MRSA infection can be found [3,4]. The reasons are not fully clear, though a connection with a liberal antibiotics policy and

Finding	Number of patients	% in the group of infected
Wet wound	16	57,0
Fever	9	32,0
Local resistance	7	25,0
Elevated FW	7	25,0
Elevated leucocytes	6	21,0
Elevated CRP	4	14,0
Bleeding	4	14,0
Pseudoaneurysm – pulsating resistance	3	11,0
Reconstruction closure	3	11,0
Local overall	25	89,0

Table 1: Leading symptoms of the graft infection.

Bacteria	Number of cases	Percentage from infected
<i>Staphylococcus aureus</i>	12	43,0
No microb bred	8	29,0
Staphylococcus coagulase negat.	8	29,0
Enterobacter, Klebsiela sp.	4	14,0
<i>Streptococcus pyogenes</i>	3	12,0
<i>Citrobacter freundii</i>	2	7,0
<i>Proteus vulgaris</i>	2	7,0
Diphtheroids	1	4,0
MRSA	0	0

Table 2: Microbial spectrum cultivated out of removed grafts.

	Infected Abs	Infected %	Non-infected %	Non-infected Abs
Number of reconstructions	28	100,0	100,0	2784
Men	22	76,0	67,0	1865
Women	6	24,0	33,0	919
Ao-F	9 (central 2, groin 7)	32,0	53,0	1476
F-P-C	12	44,0	27,0	752
F-F	6	21,0	9,0	251
Ax-F	1	4,0	1,0	27
Profundoplasty	0	0,0	10,0	281

Table 3: Incidence of the infection in relation to the type of primary reconstruction.

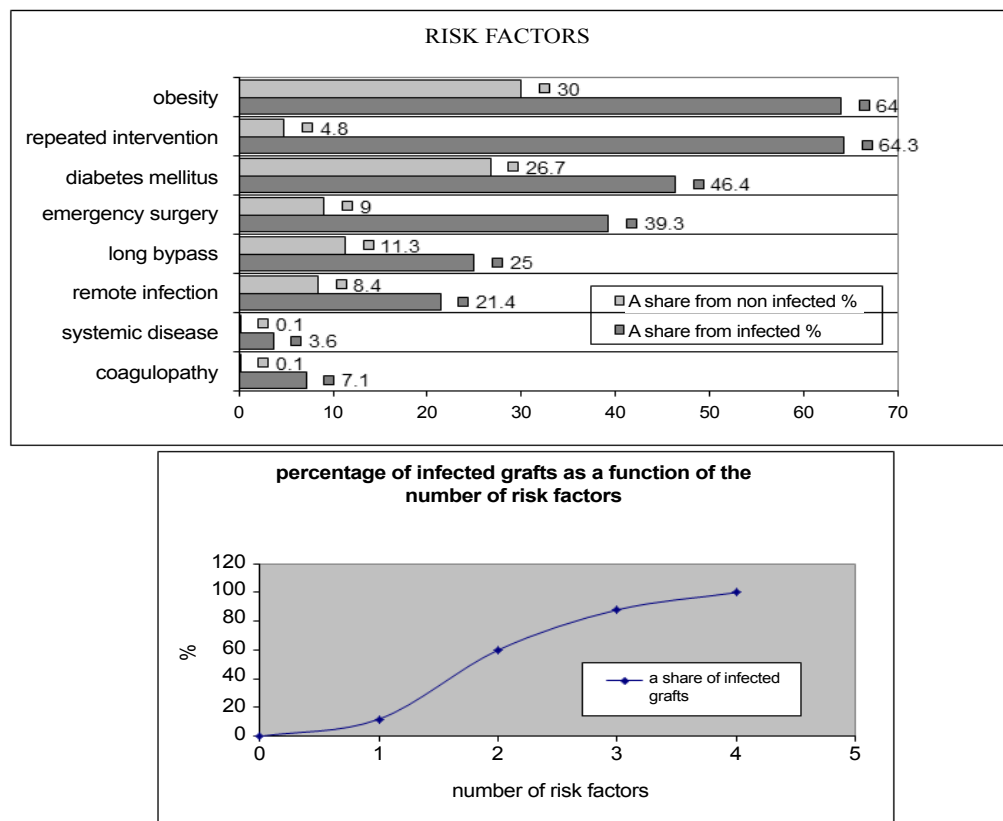


Figure 1: Percentage of infected grafts as a function of the number of risk factors.

	Infected Abs	Infected %	Non-infected %	Non-infected Abs
coagulopathy	2	8,0	0,1	2
Systemic autoimmune disorder	1	4,0	0,1	3
Co-existing infection	5	20,0	8,6	206
Long bypass (Ax-F, F-C from groin)	7	28,0	12,1	289
Emergency surgery	9	36,0	9,8	233
Diabetes mellitus	11	44,0	29,7	710
Repeated (incl DSA) intervention	14	56,0	5,3	126
Obesity	16	64,0	17,6	421

Table 4: Pre-existing risk factors before primary surgery (coagulopathy is meant as a serious clinically manifest, not hidden, obesity – BMI over 30).

advanced cultivation techniques might be expected. However, MRSA stem did not appeared in our series at all. During the first years, there was a noteworthy share of negative bacteriological cultures amongst our patients. As methods of sample collection, transportation to the laboratory and cultivation have been improving, now we get a higher share of positive cultivates today. Some rare bacterial stems can be now detected. It has been proven statistically even in our thoraco-surgical patients recently. Thus one can argue, whether the increased share of MRSA and other atypical bacteria or G-negative bacteria in these patients might be ascribed to improving the cultivation quality rather than really changing the microbiological spectrum. No one reports increased incidence of vascular graft infections, only a shift to more resistant bacteria. It seems like if it had not been MRSA it would have been another pathogen. The death related to the MRSA infection is reported slightly higher [5], though. The prevention of graft contamination during the surgery and early afterwards seems to be the key component of success. All actions taken against the MRSA should be taken simply against the infection in general, comprising patients

selection and surgery timing and technique. This approach can reduce the risk factors number. Other ways to decrease the infection rate are barrier nursing regime, proper ATB prophylaxis, and possible use of shielded artificial grafts (rifampicin, teicoplanin, silver, gel sealing). One has to have in mind, that the risky space for bacteria settlement is not only the prosthesis itself, but rather the thin (thick in case of huge haematoma) space between the prosthesis and the very body.

According to our results, the leading symptoms of vascular graft infection are the local ones. So when there is a suspicion for the graft infection, it is usually sufficient to check the local status. Only one case of bypass closure due to infection was recorded amongst our patients, however. The finding can be (but need not be) supported by blood chemistry and sedimentation, and by the ultrasound picture of free fluid round the prosthesis that, however, might not be present. Blood cultivations can give results strongly dependent on the time and way of collection, time and way of specimen transportation, and cultivation skills aside from the very pathogen. When still in doubt, mainly in

aortic location, the most sensitive tool seems to be PET-CT evaluation. But this examination is usually out of reach of the vast majority of vascular units. CT angiography, DSA or stained lymphocytes plain gamma-ray imaging can give a kind of information as well. Excluding other sources of infection in unclear cases is a must. If there is still an overall deterioration of the patient's status pointing to some localised infection round the graft, it ought to be proceeded with surgery even without proven graft infection, because it is for sure there.

When the infection is proven we have many choices, none of them being the right one [6]. In that, the Szilagy's classification should be replaced with the Samson's one. Because if there is no involvement of an anastomosis (Szilagy III, Samson III), we have some time to play with radical local debridement, dressing with antiseptics, and at the end maybe vascularized muscle flap transfer [7,8]. And all of that under appropriate antibiotic shield according to proven cultivations. On the other hand, the whole procedure must be much more urgent and intensive in anastomotic infections due to high risk of sudden bleeding to death (Szilagy still grade III, but Samson IV). Then we can do away with the graft only with a direct suture of the vascular defect, or with a kind of "plasty" either with homologous vein or sometimes even the original prosthesis remnants in unaffected anastomosis [9] and wait. However, the situation often requires an early revascularization. Or, we can simply amputate the ischemic extremity. Though cruel this solution may seem, it is actually the safest and the shortest way to recovery and life sparing in some cases. The needed revascularization can be done in the same procedure or it can be postponed after healing out the infection. In-site early revascularization is loaded with higher infection risk than primary reconstruction and then ex-site reconstructions as well. As a graft, preferably homologous material or shielded artificial graft or allograft can be used. Safenous vein having been used already or insufficient, cephalic vein in peripheral or superficial femoral vein in aortic localisations can be used [10].

Allograft implantation has a demanding management. The department should be backed by a transplantation team, tissue bank, and nor the law requirements are always easy to be met. When using cryopreserved grafts, no immuno-suppression is recommended [11]. However, one can argue whether it is not needed because a higher graft insufficiency rate was reported. Thus the extra-anatomical axillo-femoral bypass has been reported to have better long time results [12]. It can be related to cryopreservation damage and lack of immuno-suppression either. Because it seems that a-cellular collagen matrix matters most in allografts with cells causing the problems, the more careful flushing out the cells from allografts rather than preserving their vitality could be a solution.

On the other hand, to avoid this extra-anatomical reconstruction and to allow for two-in-one procedure, the cryopreserved allograft is a useful method for bridging to another prosthesis reconstruction. The living donor allografts are reported to have better long-time results. But they require life-long (maybe, no one knows) immuno-suppression. Though the blood levels of from example Cyclosporine A, are nearly ten times lower than in other organ transplantation (960 mg/l vs. 100-500 mg/l), it brings about another risk factor for the infection burst, and possible future tumour development, although it is not really a matter of concern in elderly [13].

Because the treatment has success rate and time consumption heavily dependent of procedure undertaken, with no certain results, the surgeon should know all these ways, and the patient's opinion should be weighed as well.

An extra-anatomical reconstruction followed by the infected graft removal is not used in our department. This is considered to be an independent risk factor for new infection flaring up. We rather wait what happens after infected graft removal with postponed new revascularization. At least few hours or more give the patient time to decrease blood bacteria levels that can settle the new prosthesis, or stabilize patient in sepsis with improved tissue microcirculation. According to our experiences, only local treatment without graft removal is highly unreliable method that can be used only when anastomosis stays unaffected. In-site artificial graft implantation in one session ought to be avoided, even when new "bacteria resistant" silver or teicoplanin or triclosan or rifampicin -bonded gel sealed dacron prostheses are used. They are intended for use when there is a high risk of prosthesis contamination during its implantation because of many risk factors or infection of other localisation present (it comprises ex-site one-time procedures for previous graft infection), or in immuno-compromised patients [14-16]. Although some report good results with in-site bypass grafting in infected aortic aneurysms [17] or infected aortic grafts in low-virulence bacterial strains [18], it should be borne in mind that the results are compared in symptomatic patients with very high risk of immediate death.

Our limb salvage rates and mortality rates are fully comparable with other reported in the literature. Though we had no MRSA cultivated out, the problems to be faced were very similar to other groups independent of the bacterial stem. It is the good infection prevention that is for sure the best "treatment modality" of infected vascular grafts. Some factors cannot be influenced mainly in emergency revascularization. Many, however, are medical staff and/or patient dependent a great deal. It can be seen upon our results compared with the literature that lowering the number of independent risk factors may have high impact on the infection incidence. The majority of our patients with infection had 2 and more independent risk factors present at the time of surgery (Table 5), aside of artificial prosthesis implantation. The most striking difference between the groups with and without graft infection seemed to be the repeated intervention (comprising graft puncture during angiography in our two infected cases), obesity and emergency surgery. Gender (men), co-existing infection, diabetes and too long bypass were also significant ($p < 0,01$, chi squared).

We were not able to decrease the risk factors and even the graft infection frequency in our control period. There are many problems connected with the actions taken against the infection. For example, the majority of our patients with peripheral bypasses does not occupy ICU. So it is sometimes difficult to maintain the desired normal blood glucose level. For more, many of our patients are often coming for surgery with not well compensated diabetes. This may be the reason, aside of the deteriorated microcirculation by the diabetic micro-angiopathy and leucocytes malfunction, for the diabetic patients to develop infection. The length of the bypass connected with the infection development can be ascribed either to the large surface the graft represents or rather the prolonged operation time. The break point between the above and below the knee bypasses is somewhere below 2 hours, as we always try to harvest the autologous vein at first. The prosthesis comes as a

Number of factors	Number of patients	Percentage
0	0	0,0
1	3	12,0
2	12	48,0
3	7	28,0
4	3	12,0

Table 5: Number of co-existing risk factor at the time of primary surgery.

second choice method done for the limb salvage. Then it can be argued whether there would be a higher share of limbs spared with higher infection risk than limb loss if the prostheses were not implanted. When dealing with the axillo-femoral bypass, it usually represents at least the second visit to the groin after some preceding surgery thus combining the risk factors of long surgery and repeated procedure. The risk factors may vary surgical department by surgical department. So it is necessary that every surgeon picks out his own potential risk factors to focus on. However, some common recommendations can be stated up on the discussion.

Infection prevention

1. Proper patients selection. Malnutrition, though considered as a risk factor in general surgery, has not been proven in randomised trials to influence infection rate [19]. It is necessary to reliably compensate all known co-morbidities well ahead the surgery.
2. Appropriate type of revascularization procedure. The best way to avoid infection is to get rid of artificial grafts use or minimize their usage, mainly in patients with two and more risk factors presented. Endovascular procedures should be preferred, where appropriate. Emergency surgery should be avoided by proper patients dispensarisation schemes and in time revascularization.
3. Good prophylaxis given on time (with the first skin cut) and with the right agent upon the ATB centre consultation is a must. Single dose prophylaxis seems to give the best results [20-22]. Pre-operative hospital stay should be minimized. Operating field should be shaved only if necessary right before the surgery avoiding any cuts into the skin.
4. Gentle surgical technique is compulsory with no excess of electro-cautery, no excess in tissue trauma by hooks. Compression or distraction interferes with the good microcirculation. Even minor bleeding from tissues must be reliably treated. Duration of surgery should be minimized (below 2 hours) and hospital stay of a patient ought to be as short as possible.
5. Maintenance of appropriate tissue conditions is needed. During the surgery and thereafter, proper glycaemia levels (fully normal) and tissue oxygenation must be maintained. This means, besides other things, stable blood circulation without any centralisation. The body core temperature must not fall below 35,6°C during the surgery [23].
6. Any diagnostic puncture of an artificial reconstruction should be avoided. And if necessary, then under a good prophylaxis.
7. If the usage of an artificial graft is unavoidable than do use shielded (silver, teicoplanin, rifampicin bonded) prostheses in patients operated on in emergency or with more than two risk factors present.

Infection treatment

1. Does the infection require an emergency surgery - bleeding or sepsis?
 - a. Do the shortest procedure to save the very life and possibly the limb affected.
 - b. Operate according to damage control surgery

- c. If an allograft is intended, the cryopreserved one is usually accessible.
2. It is possible to postpone the surgery?
 - a. There is a time to rethink the best strategy
 - b. Freshly harvested allograft can be used in the aorto-iliac region.
3. Does the infected bypass takeout mean the state before the surgery?
 - a. Just remove the bypass infected and postpone the revascularization until necessary.
4. Is it the very anastomosis that is affected?
 - a. Always take out the bypass. The risk of the bleeding is too high.
5. High degree damage of soft tissues by the infection?
 - a. Never revascularize in-site in the same time
6. Is the in-site reconstruction the only way?
 - a. Never use an artificial graft in-site. Even the shielded dacron prostheses are not intended for that use (see leaflets).

We failed to show, that the last recommendations would lead to a drop down of the graft infections. The straightforward explanation might be the small number of infected cases. However, a deeper analysis was conducted. In the field of infection prevention there was a failure to decrease the number of emergency surgery. Many factors including GP's attitude and patients behaviour could not be influenced. However, a portion of patients revascularized by means of autologous material or endovascular way increased significantly. Thus, actually, the infection rate overall has dropped down from 0.43% to 0,31%, though statistically insignificant due to low numbers. The portion of patients with diabetes was also higher in the later period group.

Regarding the results of the infection treatment, again there was no statistically significant difference at the first sight. However, the results in the later period were achieved with the mean hospitalisation stay cut by half (Mann-Whitney test, $p < 0.05$) and with less procedures and readmissions.

Conclusion

In spite of very low frequency of vascular graft infections, their number can be further lowered. When treated individually and properly, if not the clinical results, than the cost-effectiveness is very likely to get improved.

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