# Cryopreserved Venous Allografts in Supra-inguinal Reconstructions: A Single Centre Experience

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> **WHAT THIS PAPER ADDS**
> The current study introduces arterial reconstructions with cryopreserved femoral and vena caval vein allografts as a novel technique in the supra-inguinal setting with a low rate of re-infections and acceptable number of graft re-interventions on mid term analysis.

**Objective:** This study introduces a novel technique for supra-inguinal arterial reconstructions with cryopreserved femoral vein and caval allografts with a low re-infection rate and an acceptable graft re-intervention rate on early mid term analysis.
**Methods:** Patients treated from February 2012 to March 2018 with cryopreserved venous allograft reconstructions owing to infection in the supra-inguinal area were reviewed retrospectively. The primary end points were re-infection and the treatment related mortality rate. Secondary end points were 30 and 90 day and overall mortality and graft re-intervention rate.
**Results:** Of the 23 patients treated with cryopreserved venous allografts for infection in aorto-iliac area, 21 (91%) patients underwent reconstruction with cryopreserved femoral veins and two (9%) with vena cava. Indications for treatment were aortic graft infections ($n = 12$ [52%]), mycotic aneurysms ($n = 5$ [22%]), femorofemoral prosthetic infections ($n = 3$ [13%]), anastomotic pseudo-aneurysms ($n = 2$ [9%]), and aortic thrombosis with intestinal spillage ($n = 1$ [4%]). In hospital and 90 day mortality were 9% ($n = 2$); overall treatment related mortality during the median follow up of 15 months was 13% ($n = 3$). During the follow up, two allografts were re-operated on owing to anastomotic dilatation and one because of re-infection, resulting in a re-intervention rate of 13% ($n = 3$). None of the grafts was lost and there were no amputations. At the end of follow up 17 patients (74%) were alive. Kaplan—Meier estimation for survival was 76% (95% confidence interval [CI] 57%—95%) at one year and 70% (95% CI 49%—91%) at two years.
**Conclusion:** Cryopreserved venous allografts appear to be an infection resistant and reasonably safe reconstruction material in the aorto-iliac axis based upon the early mid term analysis from a single centre experience. Further research is needed to compare their performance with other biological reconstruction material.

## INTRODUCTION

Aortic graft infection (AGI) and primary aorto-iliac infections are a major challenge in vascular surgery. Mycotic aneurysms can be treated by an endovascular stent graft, while acknowledging a considerable risk of re-infection; however, AGI requires a prosthetic graft explant with concomitant lower limb revascularisation.[1—3] While *in situ* reconstruction with prosthetic material is feasible for non-invasive,

primarily opportunistic (e.g., low virulence) bacteria, septic infections should be treated with biological material such as autologous femoral veins (FVs) or cryopreserved allografts.[4—9] Occasionally, post-thrombotic changes and small calibre autologous veins can make them unsuitable for reconstructions, or frail patients cannot tolerate excessive surgical trauma. The downsides of cryopreserved arterial allografts are late degeneration and thrombotic occlusions.[7,9,10] The knowledge of cryopreserved venous allograft (CVA) durability is mostly based on small calibre saphenous vein grafts, which have poor patency in lower limb reconstructions.[11,12] Cryopreserved FVs have been successfully employed in haemodialysis access surgery; however,

information on their durability and infection resistance in the supra-inguinal setting is based on case series only.[13,14]

The aims of current study were to evaluate infection resistance and early mid term durability of large CVAs for supra-inguinal arterial reconstruction. Primary outcome measures were re-infection and graft related mortality during follow up. Secondary outcome measures were 30 day, 90 day, and overall mortality, as well as graft re-intervention rate.

## MATERIALS AND METHODS

Autologous FVs are the preferred vascular reconstruction material of Helsinki University Hospital (HUH) for primary vascular infection or prosthetic graft infection in the aorto-iliac axis, but after the Helsinki University Children's Hospital Homograft Bank started to cryopreserve vascular grafts in 2012, selected cases can be treated with allografts. Cryopreserved allografts have been used when the autologous FV has been post-thrombotic, owing to the patients' poor general condition, in the presence of advanced peripheral arterial disease, emergencies, or if a need for biological graft is revealed during surgery.

Based on the Homograft Bank's registry, all patients treated with CVAs for supra-inguinal reconstruction at HUH from February 2012 to March 2018 were identified and patients treated for infectious reasons in supra-inguinal region were included in the study. Data were collected retrospectively from a computerised database and manually from patients' charts.

### Pre-operative details

The collected data included demographic parameters (age, sex, smoking), comorbidities (diabetes, coronary disease, hypertension, heart failure, chronic obstructive pulmonary disease, cerebrovascular disease, renal insufficiency), indication for operation, urgency, information on arterial rupture, and bacterial cultures (if available). All patients had pre-operative contrast enhanced computed tomography (CT) and/or magnetic resonance imaging done to confirm the diagnosis and make a surgical plan.

Patients with an infection were evaluated pre-operatively by a surgeon, an anaesthetist, and an internist, whether in the emergency department or electively, to assess the risk of surgery. If trauma from autologous vein harvest was judged to be excessive, allografts were preferred. FVs were scanned with duplex ultrasound and suitability for reconstruction assessed. ABI and toe pressure were measured and if at a critical level, or if there was awareness of long arterial occlusions at the superficial femoral and/or popliteal level, autologous vein harvest was denied owing to the possibility of wound healing problems. The diagnosis of infection was made based on symptoms (fever, abdominal/back/groin pain, prosthetic material exposed in the wound, or graft cutaneous fistula), elevated infection markers and/or positive bacterial culture, and suspicion of infection in radiological studies (saccular, rapidly growing aneurysm with soft tissue oedema or surrounding gas, liquid/oedema/

gas around prosthetic graft, intestinal communication). The diagnosis was confirmed intra-operatively with findings such as arterial rupture in grossly infected tissue, mycotic aneurysm or purulent discharge around the aorto-iliac graft, or failure of graft incorporation with the presence of fluid. Antimicrobial therapy was determined by an infectious disease specialist and started based on bacterial culture, or empirically, with cefuroxime and vancomycin. When a mycotic aneurysm was diagnosed with unclear bacteriology, salmonella was also covered.

### Allograft management and operative details

Allografts were harvested from multi-organ donors by certified vascular surgeons and placed into transportation liquid Medium199. Only macroscopically good quality, large calibre veins with a diameter >6 mm were acquired. In the Homograft Bank, allografts were transferred to antibiotic decontamination medium for a minimum of 24 h. Prior to cryopreservation, cryoprotectant was added and allografts were packed into hermetically sealed double bags in 10% dimethyl sulfoxide solution. Cryopreservation in the Homograft Bank is temperature controlled and allografts are stored in nitrogen vapour at −180 °C for up to five years.

The thawing process was initiated by lifting the allograft package from the nitrogen vapour into a 37 °C water bath for 30 min. Cryoprotectant was washed out in three different containers of saline for 5 min each time.

Pre-operative preparation of the allografts included resection of excessive perigraft tissue and double ligation of the side branches. When the proximal suture line was attenuated by valve pockets, the area was excised to secure a durable anastomosis. Venous grafts were everted, and valves excised under direct vision to avoid possible reasons for stenotic lesions. If a pantaloon-shaped graft was necessary, the proximal ends of the grafts were split and sutured together with a continuous polypropylene suture to match the aortic diameter. One vena cava was used as a tube for aorto-aortic reconstruction and in another case a few centimetres of iliac veins were included to create an aortic bifurcation. Aortic anastomoses were reinforced with a piece of autologous tensor fascia lata.[5] Intraperitoneal grafts were covered with omentum if technically possible.

Peri-operatively the infection diagnosis was confirmed by infected exudate or gross intestinal spillage in the operating area and additional tissue and/or prosthetic graft samples were taken. Other data collected intra-operatively included type of vascular reconstruction and concomitant procedures, graft material used, blood type (ABO) match, supra-renal cross clamp, presence of aorto-enteric erosion/fistula (AEF), blood loss, and operation time.

### Post-operative details

Post-operative data included length of stay in the intensive care unit and in hospital and post-operative complications (cardiac, respiratory, gastro-intestinal, cerebrovascular and renal complications, re-operations due to graft bleeding or thrombosis, ischaemia, amputation, death, or other

reasons). During follow up, data on post-operative antithrombotic/anticoagulant medication, antimicrobial therapy, and major amputations were collected. Clinical follow up was organised one month after discharge and with radiological studies at six months and one year. Thereafter, yearly radiological follow up with CT angiography or magnetic resonance angiography for intraperitoneal grafts, and triplex ultrasound for extraperitoneal grafts, was recommended. Graft related complications (stenosis, thrombosis, aneurysm development, rupture) and need for re-interventions defined graft durability. Graft re-infection was defined as graft rupture in a septic patient, recurrent AEF, or isolation of micro-organisms from the ruptured graft. Furthermore, dates and causes of death were extracted from the case records and Cause of Death Registry of Statistics Finland.

### Statistical analysis

Statistical analysis was performed using SPSS 22 software (IBM, Armonk, NY, USA). Continuous variables are expressed as median (range). Univariable analysis was done using Fisher's exact test and the Kurskal—Wallis test to analyse the risk factors (age, smoking status, diabetes, hypertension, coronary disease, heart failure, chronic obstructive pulmonary disease, cerebrovascular disease, renal insufficiency, positive blood culture, emergency operation, arterial rupture, suprarenal aortic clamp location, operation time and blood loss, and presence of AEF) associated with 30 day, treatment related, and overall mortality. Cox regression analysis was done to evaluate the association between graft thrombosis and ABO match. All tests were two tailed and $p < .05$ was considered statistically significant. Multivariable analysis was precluded by the small number of patients. Survival was calculated using the Kaplan—Meier method.

Owing to the retrospective nature of the study, permission from the ethical committee was not required. The hospital study board granted clinical approval.

### RESULTS

Based on the Homograft Bank registry, 24 patients were treated for arterial supra-inguinal infection with CVAs. One iliac artery was reconstructed with allografts after abdominal gunshot injury but was later covered with a stent graft owing to additional iliac artery rupture and therefore excluded.

Fifteen men (65%) and eight women (35%), with a median age of 69 years (range 24—87 years), were included in the study. Patient comorbidities and demographic details are given in Table 1. The most common indication for operation was AGI in 12 (52%) patients and mycotic aneurysm in five (22%). The cryopreserved FV allografts were used in 21 (91%) patients and vena cava allografts in two (9%). Indications for operation and peri-operative details are shown in Table 2.

**Table 1. Patient comorbidities and demographics (n = 23)**

| Male, n (%) | 15 (65) |
|---|---|
| Age, years, median (range) | 69 (24−87) |
| *Pre-operative conditions, n (%)* | |
| Hypertension | 20 (87) |
| Coronary heart disease | 10 (43) |
| Diabetes mellitus | 9 (39) |
| Chronic obstructive pulmonary disease | 9 (39) |
| Cerebrovascular disease | 6 (26) |
| Renal insufficiency | 5 (22) |
| Cardiac insufficiency | 3 (13) |
| Smoking | 11 (48) |

### Post-operative complications

Post-operative complications necessitating re-operation occurred in 10 (43%) patients of which one was due to graft re-infection and subsequent rupture. This patient had operation site *Candida* infection, which was not covered initially with antifungal medication. After a few attempts to suture the bleeding sites, both pantaloon graft limbs were re-reconstructed with a new CVA and the patient treated with fluconazole. The patient continued to have systemic

**Table 2. Indications for operation and peri-operative details (n = 23)**

| *Indication for operation* | |
|---|---|
| Aortic graft infection | 12 (52) |
| Mycotic aneurysms − infrarenal/visceral | 3/2 (13/9) |
| Femorofemoral prosthetic infection | 3 (13) |
| Infected pseudo-aneurysm | 2 (9) |
| Large intestinal spillage in situation requiring emergency aortic reconstruction | 1 (4) |
| Emergency operation | 8 (35) |
| Rupture | 5 (22) |
| *Type of grafts used* | |
| Femoral vein | 21 (91) |
| Vena cava | 2 (9) |
| *Type of surgical reconstruction* | |
| Y shaped graft | 16 (70) |
| Iliofemoral reconstruction | 3 (13) |
| Crossover | 2 (9) |
| Axillobifemoral/partial | 1/1 (4/4) |
| *Concomitant procedures* | |
| Femoropopliteal bypass, bilateral | 1 (4) |
| Femoral endarterectomy, bilateral | 1 (4) |
| Bypass to/re-implantation of visceral arteries | 3 (13) |
| Thrombectomy of visceral arteries | 1 (4) |
| Temporary visceral perfusion bypass | 2 (9) |
| Duodenal/intestinal resection | 3 (13) |
| Cholecystectomy | 1 (4) |
| Omentoplasty | 10 (43) |
| Sartorius myoplasty | 13 (57) |
| Vastus lateralis myoplasty | 1 (4) |
| Aorto-enteric fistula | 2 (9) |
| Suprarenal clamp | 6 (26) |
| Median (range) operation time, min | 451 (164−620) |
| Median (range) blood loss, mL | 3800 (100−10 600) |
| ABO match | 11 (48) |

Data are *n* (%) unless otherwise indicated. ABO = blood types.

candidiasis and the new rupture was treated again with a new cryovein. Thereafter, grafts remained intact. The most common medical complications were respiratory complications (*n* = 6 [26%]) and renal insufficiency (*n* = 3 [13%]). Post-operative complications are listed in Table 3.

### Microbiology

A positive bacterial culture was isolated from 70% (*n* = 16) of patients, of whom 17% (*n* = 4) had polymicrobial growth. The most commonly isolated pathogen was *Staphylococcus aureus* (*n* = 5 [22%]) followed by *Streptococcus* species (*n* = 3 [13%]) (Table 4). Post-operative antimicrobial medication was assigned based on the susceptibility of isolated strains or continued empirically based on clinical suspicion. The duration of medication was assigned individually and based on isolated pathogens, severity of infection, concomitant infections, and post-operative disease course. The median time of post-operative antimicrobial medication was 12 weeks (range 3–85 weeks); at the end of follow up, two patients were still taking antibiotics owing to the short follow up time.

### Antithrombotic medication

During the early post-operative period patients were treated routinely with low molecular weight heparin and

**Table 3.** Post-operative complications and hospital stay (*n* = 23)

| | |
|---|---|
| *Surgical complications* | 10 (43) |
| Re-operation for haemorrhage | 4 (17) |
| Graft rupture | 1 (4) |
| Broken thread | 1 (4) |
| Rupture of infra-inguinal bypass | 1 (4) |
| Gastro-intestinal bleeding | 1 (4) |
| Re-operation for ischaemia | 1 (4) |
| Infra-inguinal bypass thrombosis | 1 (4) |
| Gastro-intestinal and thoracic complications | 3 (13) |
| Intestinal necrosis | 3 (13) |
| VATS (haemothorax, empyema) | 1 (4) |
| Other | |
| Wound complications | 3 (13) |
| Open abdomen treatment | 2 (9) |
| *Medical complications* | 9 (39) |
| Respiratory complications | 6 (26) |
| Severe renal dysfunction | 3 (13) |
| New onset dialysis, temporary/permanent | 2/1 (9/4) |
| Cardiac complications | 2 (9) |
| Gastro-intestinal complications | 1 (4) |
| Acute stroke | 1 (4) |
| Other | |
| Wound infection | 4 (17) |
| Delirium | 2 (9) |
| Rhabdomyolysis | 1 (4) |
| HIT | 1 (4) |
| Median (range) length of stay in ICU, d | 2 (0–35) |
| Median (range) length of stay in tertiary referral hospital, d | 22 (4–90) |

Data are *n* (%) unless otherwise indicated. VATS = video assisted thoracoscopy; HIT = heparin induced thrombocytopenia; ICU = intensive care unit.

**Table 4.** Microorganisms cultured (*n* = 23)

| | *n* (%) |
|---|---|
| Positive bacterial growth | 16 (70) |
| Monomicrobial growth | 12 (52) |
| Polymicrobial growth | 4 (17) |
| *Staphylococcus aureus* | 5 (22) |
| *Escherichia coli* | 3 (13) |
| *Streptococcus spp.* | 3 (13) |
| *Coagulase negative Staphylococcus strains (incl. S. epidermidis)* | 2 (9) |
| *Pseudomonas* | 2 (9) |
| *Staphylococcus lugdunensis* | 2 (9) |
| *Prevotella* | 2 (9) |
| *Candida albicans* | 1 (4) |
| *Enterococcus faecalis* | 1 (4) |
| *Enterobacter cloacae* | 1 (4) |
| *Arcanobacterium bernardiae* | 1 (4) |
| *Diphtheroid* | 1 (4) |

spp = species.

with at least one antiplatelet medicine (unless contra-indicated, *n* = 4 [17%]). After the post-operative period four (17%) patients continued with dual antiplatelet treatment (DAPT), seven (30%) patients were anticoagulated, and 10 (43%) continued with single antiplatelet medicine. Primary indications for DAPT or anticoagulation were not linked to allograft reconstruction.

### Primary outcomes

The graft re-infection rate during the median follow up of 15 months was 4% (*n* = 1). The only re-infection occurred in the early post-operative period due to untreated *Candida* infection (see more details in "Post-operative complications").

Overall the treatment related mortality was 13% (*n* = 3). In addition to two septic patients who died in the early post-operative period, one patient with aortobifemoral and femorofemoral graft infection died seven months later. Owing to advanced cardiac disease, the patient underwent only subtotal graft resection and died as a result of preserved infected aortic graft stump blow out with a functioning axillobifemoral bypass made of cryopreserved veins. All treatment related reasons for death are in Table 5.

### Secondary outcomes

Thirty day, 90 day, and in hospital mortality were 9% (*n* = 2). At the end of a median follow up of 15 months (range 3–62 months), overall survival was 17 (74%).

None of the grafts occluded during follow up. Two anastomotic aneurysms appeared, one after partial resection of an infected prosthetic graft, which was treated with prosthetic interposition, and the other in anastomosis with native artery that was treated with a covered stent. Altogether, three patients underwent a secondary procedure; thus, the freedom from graft re-interventions during the follow up was 87%. The limb salvage rate was 100%.

**Table 5.** In hospital and treatment related mortality

| Age, y | Indication for operation | Urgent operation | Indication for allograft | Allograft used | Arterial reconstruction and concomitant reconstruction | Microbiology | Post-operative complications | Cause of death | Post-operative day of death |
|---|---|---|---|---|---|---|---|---|---|
| 70 | AGI, groin abscess | No | High risk patient | FV | Aortobifemoral bypass and sartorius myoplasty | *Streptococcus pneumoniae* | Intestinal necrosis, open abdomen, pneumonia, delirium | Intestinal necrosis, peritonitis | 21 |
| 60 | Acute aortic thrombosis with AKI and peritonitis | Yes | High risk patient, emergency | FV | Aortobi-iliac reconstruction, SMA, renal artery and coeliac trunk thrombectomy, stenting of SMA, cholecystectomy, intestinal resection | Intestinal spillage | Intestinal necrosis, open abdomen, AKI with dialysis | Intestinal necrosis, peritonitis | 23 |
| 64 | AGI and femorofemoral bypass infection | No | High risk patient | FV | Subtotal aortic and total crossover graft resection, axillobifemoral bypass, bilateral femoral endarterectomy and sartorius myoplasty | *Escherichia coli* | Myocardial infarction, *Clostridium* infection | Aortic prosthesis stump infection and rupture | 210 |

Patients who died within 30 days are presented on lighter background. AGI = aortic graft infection; AKI = acute kidney injury; FV = femoral vein; SMA = superior mesenteric artery.

### Statistical analysis

Kaplan—Meier estimations of survival and freedom from graft re-interventions at one year were 76% (95% confidence interval [CI] 57%—95%) and 90% (95% CI 76%—100%), respectively; at two years the estimates were 70% (95% CI 49%—91%) and 90% (76%—100%), respectively (Fig. 1). Univariable analysis revealed no risk factors significantly associated with 30 day or treatment related mortality; however, heart failure (hazard ratio [HR] 6.9, 95% CI 1.37—34.52; $p$ = .019) was associated with overall total mortality. ABO mismatch was not associated with graft complications (HR 1.53, 95% CI 0.12—18.94; $p$ = .743).
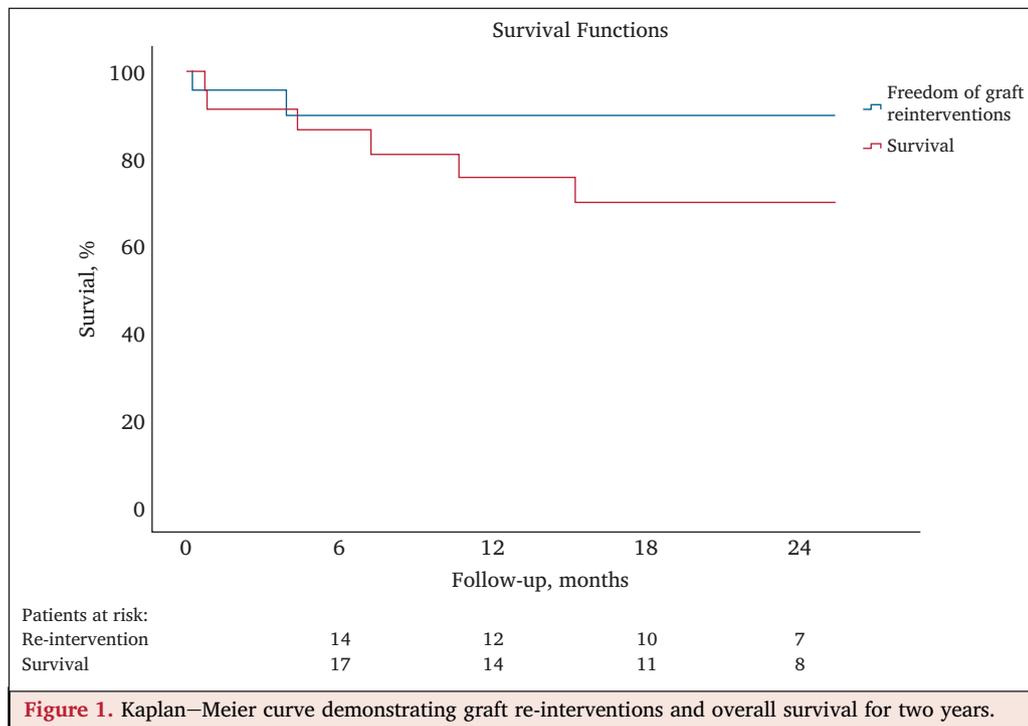
### DISCUSSION

The current report from HUH on CVAs implanted for suprainguinal vascular infections shows good infection resistance and graft durability in the early mid term analysis, with a moderate amount of non-lethal graft aneurysmal complications and no thrombotic occlusions.

Cryopreserved arterial allografts are a commonly used reconstruction material in the aorto-iliac position when a biological graft is needed. Improvements in cryopreservation techniques have enhanced their durability, but based on the latest reports, the rate of graft related complications varies from 19% to 55%.[1,7,9,15,16] There are fewer aneurysmal degenerations (0%—4%) and pseudo-aneurysms (0%—4%), with the exception of a recent report from France where graft aneurysms were a late complication in 22% of cases. However, frequently lethal graft ruptures (4%—24%) and thrombotic occlusions (4%—7%) remain a problem.[7,9,10,15]

Early cryopreserved arterial or venous graft rupture may occur as a result of re-infection or morphological changes in the allograft wall.[17,18] Despite antimicrobial treatment, continuing sepsis or fungal infection may result in any biological graft re-infection and subsequent rupture.[5,6,10,13] There was one early rupture in the current cohort with *Candida albicans* cultured from the explanted graft.[19,20] The literature reports arterial allograft ruptures due to *Candida* infection as a complication in renal transplant and access surgery.[13,21] Thus, a possible correlation between *Candida* predilection to a somewhat altered endothelium and immunosuppression may put cryopreserved grafts at risk.[19,21] *Candida* can be transmitted with a contaminated graft during organ procurement, but, more frequently, systemic fungal infection is a recipient borne complication of bacterial sepsis due to a reduction in host resistance or a local contaminant, in the case of aorto-enteric complications.[8,21,22] Therefore, constant evaluation of infection parameters, a high clinical suspicion of fungal infection, and a multidisciplinary team approach is advised in the care of these complicated patients.[10] Of note, methicillin resistant *S. aureus* (MRSA) was not represented in the current cohort. Owing to the small number of patients and the low incidence of MRSA in Nordic countries, cryopreserved FV allograft resistance to MRSA remains unknown.[23]

The wall integrity of cryopreserved allografts is disturbed with rushed freezing or thawing, aggressive handling, and robust vascular clamps.[24] Arteries, with more densely packed cells in tissue, might be more prone to cryopreservation induced mechanical stress than veins, with cells in more loosely packed tissue.[25,26] Owing to the risk of structural graft complications, any cryopreserved conduit must be handled with care and its aorto-iliac anastomoses created tension free and circumferentially reinforced.[5,10] Aortic anastomoses were reinforced with patients' own tensor fascia lata in the current cohort; nevertheless, two anastomotic dilatations developed in the iliac area which lacked external support, which should be addressed in future procedures.

**Figure 1.** Kaplan−Meier curve demonstrating graft re-interventions and overall survival for two years.

Acute thrombosis is a known complication with arterial allografts, as well as great saphenous vein allografts, in the infrainguinal setting.[7,9,12,15,27] Current cryopreservation methods aim to preserve endothelium for its antithrombogenic properties; however, a disadvantage of endothelial cells is immunogenicity due to their presentation of major histocompatibility complex classes I and II.[12,27,28] Immunological reaction may be responsible for graft destruction and thrombosis causing fragmentation of elastin, cellular accumulation, capillary ingrowth, endothelial thickening, and fibrotic stenosis as presented in morphological studies.[28,29] No occlusions among vein grafts were seen in the present study. When cryopreserved conduits were introduced at 2012 in HUH, both, arterial and venous allografts were used. After experiencing two acute occlusions of arterial grafts and atherosclerotic degeneration in infrainguinal bypasses (unpublished data), it was decided to implant venous grafts only (see details in Supplementary Material). Different behaviours may result from structural or immunological differences between the two types of conduit, since the cryopreservation and thawing protocols were the same.

Two CVAs studied histologically in the authors' clinic prior to implantation revealed no endothelium in the conduit's lumen, only in small adventitial vessels. However, no thrombotic complications occurred among vein recipients. Lack of endothelium results in a lesser immunological reaction and therefore in better patency. Furthermore, large calibre and high volume flow in the supra-inguinal setting make FV allografts independent of endothelial function. Aavik et al.[30] reported significantly better patency of fresh great saphenous vein allografts in the aortic position compared with small calibre saphenous veins in the infrainguinal position. The authors emphasised the large calibre (8−9 mm) and indicated that preservation in cold saline resulted in denudation of endothelial cells.[30] Moreover, based on the current cohort, single antiplatelet treatment appears sufficient for long term antithrombotic medication after combination with low molecular weight heparin in the early post-operative period.

One explanted CVA owing to anastomotic dilatation was histologically investigated. We identified elastin fragmentation, but no inflammatory infiltrate, supporting the hypothesis of diminished immunogenicity. The main cause of graft complications in venous allografts in the current cohort appeared to be mechanical injury from cryopreservation and handling, which could be addressed with improved freezing and thawing protocols in the future.[25] ABO mismatch has been discussed as a possible reason for immunological reaction and subsequent complications; nevertheless, in case of arterial allografts, no supporting evidence exists.[31] Cryopreserved saphenous vein patency might be improved by ABO matching.[11,12,32] The present study showed no correlation between ABO mismatch and graft complications; furthermore, two occluded arterial grafts were ABO matched (see Supplementary Material).

Re-infections are the reason why biological materials were included in the treatment of infection in vascular beds. Rifampicin-soaked grafts and silver grafts have been used successfully in low virulence bacterial infections; however, implanting prosthetic material in highly virulent bacterial infections, such as Gram-negative bacteria or *S. aureus*, increases the re-infection rate to >20%.[2,4,33] Moreover, soaking in rifampicin may promote the emergence of rifampicin resistant staphylococci, undermining the

further use of potent antimicrobial agent.[34] Autologous FV grafts, cryopreserved conduits, and self made xenopericardial tubes (XPTs) present similar re-infection rates of 0%−6% in the aorto-iliac setting.[5−7,9,35,36] XPTs are excellent for short interpositions, but reconstructing an aorto-bifemoral bypass is a technical challenge and evidence for overall long term graft durability is currently lacking. Autologous FVs are immunologically excellent and durable, presenting with an acceptable amount of non-lethal stenosis as late complications. In the mid term analysis, the results of two types of veins are comparable; however, the present advantage of autologous grafts are the long term durability results.[5,6] Nevertheless, if autologous veins are unavailable or patients present with a prohibitive risk of vein harvest, cryopreserved allografts are an excellent alternative for supra-inguinal reconstruction. Total biological reconstruction also spares patients from lifelong antimicrobial treatment and subsequent complications without undermining the outcome.[4−6,9,35] The median length of post-operative antimicrobial treatment in current cohort was twelve weeks and none of the patients continued suppressive treatment permanently.

The present literature does not provide valid evidence for the preference of one treatment method over the others for vascular infections in the supra-inguinal area. Therefore, centres managing these complex patients must have access and the necessary skills to provide a treatment method tailored individually, based on severity of disease, the patient's condition, and life expectancy. Currently, the preferred reconstruction material at HUH remain autologous FVs. CVAs are used for aorto-iliac bypass if autologous material is not available. XPT or cryopreserved aortic allografts are alternatives for very short aorto-aortic interposition, due to their appropriate calibre.

The current study has several limitations. The small number of patients and lack of comparison between reconstruction with CVA and other treatment methods for vascular infections in the supra-inguinal area are the main limitations. Mixed indications for arterial bypass make the cohort heterogenic and conclusions hard to draw. Owing to the retrospective nature of the study, the possibility of a selection bias exists and the small number of patients limited any statistical analysis. Furthermore, as a result of the relatively short follow up, the long term durability of CVA cannot be evaluated and a considered approach is recommended until further research is done.

## CONCLUSION

In grossly contaminated conditions, biological grafts should be considered for patients fit for open surgery. Cryopreserved FV allografts appear to be infection resistant and show reasonable durability in early mid term analysis with few aneurysmal dilatations and no thrombotic complications. Further research is needed to provide data on long term durability and compare their performance with other biological grafts used for aorto-iliac reconstructions.

## APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2019.06.024.

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