Aus der Klinik für Gefäßchirurgie und Phlebologie
Contilia Herz- und Gefäßzentrum

Elisabeth Krankenhaus Essen

Direktor: Prof. Dr. med. Johannes Hoffmann

Irrigation suction drainage and negative pressure wound therapy of lower extremity vascular graft infection in ileofemoral region: clinical and economical aspects

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Berichterstatter:	Prof. Dr. med. Johannes Hoffmann
Mittberichterstatter:	Priv.-Doz. Dr. med. Volker Ruppert
	Prof. Dr. med. Ulrich Hoffmann
Dekan:	Prof. Dr. med. dent. Reinhard Hickel

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Zusammenfassung Deutsch

Einleitung

Die ileofemorale arterielle Gefäßprotheseninfektion ist eine seltene Komplikation, die eine hohe Morbidität und Mortalität verursacht. Das führt meistens dazu, dass sich die klinischen Ergebnisse verschlechtern, die Lebensqualität leidet und die Krankenhauskosten steigen.

Die Risikofaktoren, die zu einer Gefäßinfektion im Ileofemoral-Bereich führen, können sehr unterschiedlich sein und durch vielerlei Faktoren bedingt sein. Die Modifikation von Risikofaktoren kann das klinische Ergebnis verbessern und kann ökonomisch sinnvoll sein .

Die Behandlung von Gefäßprotheseninfekten stellt auch heutzutage eine sehr große Herausforderung im Bereich der Gefäßchirurgie dar. Das Infektionsmanagement schließt mehrere Behandlungsmethoden ein. Dazu zählen u.a. die *chirurgische Behandlung mit Sanierung der Infektion* (Goldstandard), und im Anschluss die *Vacuum Assisted Closure Therapie* (VAC) oder eine kontinuierliche *Saug-Spül Drainage* (SSD) in Kombination mit einer Breitspektrum Antibiotika-Therapie.

Die *VAC Behandlung* spielt eine zunehmende Rolle in der Behandlung der Gefäßprotheseninfektion. Vor allem im letzten Jahrzehnt wurden gute klinische Ergebnisse für diese Therapie publiziert. Eine andere Methode ist die *SSD Therapie* für die Behandlung der Gefäßprotheseninfektion. Diese Therapiemethode ist im Vergleich zur *VAC Therapie* etwas wenig modern, jedoch wurden auch in der Vergangenheit gute Ergebnisse berichtet.

Hypothese

Diese Untersuchung besteht aus zwei Teilen: Teil 1 analysiert die verschiedenen Risikofaktoren, die einen Einfluss auf die Entwicklung der Gefäßprotheseninfektion nach der Operation haben können. In dieser Studie werden nicht nur traditionelle Risikofaktoren analysiert, sondern auch einigen spezifische Risikofaktoren wie Elektrolytstörungen, frühere orthopädische und unfallchirurgische Eingriffe im Bereich der Gefäßprotheseninfektion sowie die Auswirkungen von Chemotherapie und Bestrahlungstherapie. Die Auswirkungen dieser Risikofaktoren sind in bisherigen publizierten Veröffentlichungen nicht ausreichend dokumentiert.

Der zweite Teil dieser Studie umfasst die Analyse zweier Behandlungsmethoden bei Gefäßprotheseninfektion: Die *VAC Therapie* und *SSD Therapie*. Analysiert werden die klinischen Ergebnisse und wirtschaftliche Aspekte dieser beiden Behandlungsmethoden.

Material und Methoden

Insgesamt 57 Patienten mit *Gefäßprotheseninfektionen* im *Ileofemoral-Bereich* im Zeitraum zwischen 2007 und 2015 wurden in diese Studie miteinbezogen. Das *Contilia Herz und Gefäßzentrum Essen* führte insgesamt 6323 Operationen bei peripherer arterieller Verschlusskrankheit im Ileofemoral-Bereich in diesem Zeitraum durch.

Die Patienten stimmten bei Aufnahme der systematischen Erfassung von Daten zur Qualitätssicherung zu.

Die Patienten wurden retrospektiv in zwei Gruppen aufgeteilt: In die erste Gruppe wurden Patienten mit einer Gefäßprothesen-Infektion, die mit der *VAC Therapie* behandelt wurden, aufgenommen. Die zweite Gruppe schloss Patienten ein, die mit *SSD Therapie* therapiert wurden.

Die Akten der konsekutiven Patienten wurden retrospektiv analysiert, um mögliche Risikofaktoren und Ausschlusskriterien zu identifizieren. Zusätzlich wurden Entzündungsparameter, Transfusionsparameter, Aufenthaltsdauer auf der Intensivstation, Gesamtaufenthalt sowie Morbidität und Mortalität retrospektiv erfasst.

Bakteriologische Kulturen von tiefen Wundabstrichen sowie Antibiotika-Therapien wurden ebenfalls für jede Patientengruppe analysiert. Die Schwere der Gefäßprotheseninfektion bei allen beobachteten Patienten wurde nach *Szilagyi* klassifiziert.

Die *follow-up Zeit* nach der ersten gefäßchirurgischen Revision in dieser Studie betrug ein Jahr. Sobald die Patienten eine erneute Gefäßprotheseninfektion im Zeitraum dieses einen Jahres entwickelten, wurde eine detaillierte Analyse der Patientendaten für ein halbes Jahr nach der ersten Diagnose einer Gefäßprotheseninfektion durchgeführt.

Der ökonomische Aspekt wurde für beide Gruppen nach der ausgewählten Therapieoption abgewägt: *VAC Therapie* oder *SSD Therapie*. Die Materialkosten für jede Therapiemethode wurden sowohl pro Tag als auch als gesamte Behandlung für beide Gruppen berechnet.

Ergebnisse

In die Studie wurden insgesamt 57 Patienten eingeschlossen, 21 Patienten in die *SSD Therapie* Gruppe, 36 in die *VAC Therapie* Gruppe. Der Altersdurchschnitt lag bei 66,8 Jahren (von 34 bis 82) in der *SSD* Gruppe und 71,3 Jahren (von 55 bis 90) in der *VAC* Gruppe. In der *SSD* Gruppe waren 33,3% weibliche und 66,7% männliche Patienten, während in der *VAC* Gruppe 36,1% weiblich und 63,9% männlich waren. Die durchschnittliche Aufenthaltsdauer im Krankenhaus betrug 34 Tage für die *SSD* Gruppe und 38 Tage für die *VAC* Gruppe. Der Aufenthalt auf der Intensivstation betrug 5 Tage in der *SSD* Gruppe versus 4 Tage in der *VAC* Gruppe.

Die am häufigsten isolierten bakteriologischen Spezies aus dem Infektionsareal waren in beiden Gruppen *Staphylococcus aureus* sowie *Methicillin-resistenter Staphylococcus aureus*. Andere häufig auftretende Mikroorganismen enthalten *Escherichia coli* und *Pseudomonas aeruginosa*. Es gab keine Unterschiede in den isolierten Mikroorganismen zwischen beiden Gruppen.

Die Analyse der Risikofaktoren wie Diabetes, Elektrolytstörungen, Nikotinabusus oder Alkoholmissbrauch usw. zeigte keinen statistisch relevanten Unterschied zwischen den beiden Gruppen. Jedoch waren diese Faktoren bei vielen Patienten in beiden Gruppen vorhanden und spielten eine wichtige Rolle bei der Entwicklung der *vaskulären Implantatinfektion*.

Die Amputationsraten betrugen in der *SSD* Gruppe 33,3% (7/21) und in der *VAC* Gruppe 27,8% (10/36), die Mortalitätsraten 9,5% (2/21) und 8,3% (3/36) für die *SSD* Gruppe und die *VAC* Gruppe. Beide Parameter zeigten keine statistisch signifikanten Unterschiede zwischen den Gruppen ($p > 0,05$).

Die Initialkosten der SSD Therapie betrugen 20,50 €. Die Materialkosten pro Tag waren 4,36 €. In der *VAC* Gruppe kosteten die Behandlungen - je nach Wundbereich - von 276,08 € bis 293,44 €. Die Materialkosten für *VAC* Wechsel - die alle 4 Tage durchgeführt wurden - reichten von 73,32 € bis 84,60 €, je nach Wundbereich. Dies führte zu einem statistisch-signifikanten Unterschied ($p < 0,01$) zwischen den beide Gruppen.

Zusammenfassung

Gefäßprotheseninfektionen im *Ileofemoral*-Bereich sind schwere Komplikationen mit erheblichen klinischen und wirtschaftlichen Konsequenzen und beeinflussen die Lebensqualität der Patienten immens.

Die Risikofaktoren für eine Gefäßprotheseninfektion sind *Diabetes mellitus, Nikotinabusus* oder *Alkoholmissbrauch* und *Arteriosklerose*. Diese Risikofaktoren wurden nicht nur in beiden Patientengruppen sondern auch in der publizierten Literatur ausreichend dokumentiert. Durch die Studie wurden auch Elektrolytstörungen oder frühere chirurgische Operationen bzw. Manipulationen im *Ileofemoral*-Bereich als Risikofaktor charakterisiert und könnten kausal bei der Entwicklung der Gefäßprotheseninfektion sein. Weitere Studien sollten zukünftig folgen, um diese Risikofaktoren weiter detailliert zu analysieren.

Die VAC Therapie oder die SSD Therapie sind zu Therapie der ileofemorale Gefäßprotheseninfektion geeignet.

Obwohl beide Methoden in dieser Studie ähnliche klinische Ergebnisse zeigte, schien die SSD Therapie einen ökonomischen Vorteil im Vergleich zur VAC Therapie zu besitzen. Nachteil der SSD Therapie ist, dass diese nur angewandt werden kann, wenn der Patient kleinere Wundflächen hat. Patienten mit ausgeprägt infizierten Wundbereichen (> 80 cm^2) sollten nur mit der VAC Therapie behandelt werden.

Abstract

Introduction

Lower extremity vascular graft infection is a rare but potentially hazardous complication associated with long hospital stay, worsened clinical outcome, poor quality of life, and high hospital costs.

The risk factors leading to vascular graft infection are very specific and are mostly multifactorial. Reduction of risk factors can improve vascular graft surgery outcome and has an important impact on economics.

Vascular graft infection is one of the most challenging issues in vascular surgery. Graft infection management includes different treatment methods, such as graft surgery (gold standard), vacuum assisted closure therapy (VAC), and irrigation suction drainage (ISD), in combination with antibiotic therapy.

VAC therapy is playing an important role in vascular graft infection management, especially in the last 2 decades, with good results. ISD therapy is for vascular graft infection management alternative method; this elder technique, however, shows good clinical outcomes, as well.

Objectives

This study was divided into 2 parts – part 1 involved the analysis of different risk factors that may have an effect on the development of vascular graft infection after surgery. In this study, not only traditional risk factors but also several specific factors, such as electrolyte imbalance, previous orthopedic procedures on the ipsilateral site of the vascular graft, and the impact of chemotherapy and radiation therapy have been analyzed. The impact of some of these risk factors is not well documented in articles that have already been published.

The second part of this study involved analysis of 2 vascular graft infection management methods – vacuum assisted closure therapy and irrigation suction drainage therapy. The clinical outcomes of patients subjected to the 2 methods have been analyzed, as well as economical aspects.

Materials and Methods

57 patients with lower extremity vascular graft infections in the time period between 2007 and 2015 were included in the study. The Contilia Heart and Vascular surgery center performed

6323 lower extremity arterial graft operations overall during the respective time period. Patients were divided into 2 groups based on clinical management: in the first group, vacuum assisted drainage (VAC) therapy was used to manage vascular graft infections, while in the second group, irrigation suction drainage (ISD) therapy was used. The patients' clinical histories were analyzed retrospectively to identify possible risk factors for the development of vascular graft infection. Additionally, inflammatory parameters, transfusion parameters, length of stay in the intensive care unit (ICU), and total length of stay during the time of vascular graft infection management, as well as morbidity and mortality were analyzed. Bacteriological probes of wound swabs, as well as antibiotic therapies, were analyzed for each patient group retrospectively. Graft infections in all of these patients were classified according to Szilagyi's classification. The follow-up period after initial vascular graft surgery in this study was 1 year. If patients developed vascular graft infection, follow-up period after diagnosed infection was 6 months.

The economical aspect was analyzed for both groups according to the selected therapy option: ISD therapy or VAC therapy. The technical equipment costs for each therapy method were calculated and compared per day, as well as the total treatment costs for both groups.

Results

A total of 57 patients were included in this study. Of these, 21 patients were included in the ISD group, while 36 patients were included in the VAC group. Median age was 66.8 years (range, 34-82) in the ISD group vs. 71.3 (range, 55-90) in the VAC group. In the ISD group, 33.3% were female and 66.7% were male, while in the VAC group, 36.1% were female and 63.9% were male. Mean length of stay in the hospital was 34 days for the ISD group vs. 38 days for the VAC group. Mean duration of ICU stay was 5 days in the ISD group vs. 4 days in the VAC group.

The most commonly isolated bacteriological species from the surgical site infections were *Staphylococcus aureus* and Methicillin-resistant *Staphylococcus aureus*. Other common microorganisms included *Escherichia coli* and *Pseudomonas aeruginosa*. There were no differences in the isolated microorganisms between the groups (table 5).

Analysis of lower extremity risk factors showed no statistical difference between the groups with regard to vascular graft infection risk factors such as diabetes, electrolyte imbalance, smoking, alcohol abuse, etc. However, these factors were present in many patients in both

groups and are likely to play important roles in vascular graft infection development (table 12, 13, 23).

With regard to clinical outcomes, we reviewed the amputation rates and mortality rates of the patients in both groups. Amputation rates were 33.3% (7/21) and 27.8% (10/36), while mortality rates were 9.5% (2/21) and 8.3% (3/36) for the ISD group and the VAC group, respectively. Both parameters showed no statistically significant differences between groups ($p>0.05$).

The initial cost of the ISD therapy was 20.50 € and the technical material costs per day was 4.36 €. For the VAC group, depending on the wound area, the initial treatment costs ranged from 276.08 € to 293.44 €. The costs of changing of VAC materials, which was performed every 4 days, ranged from 73.32 € to 84.60 €, depending on the infected wound area. This caused a significant difference ($p<0.01$) in costs between the 2 groups.

Conclusions

Lower extremity graft infection is a serious complication of vascular graft surgery with significant economic implications and affects the patient's quality of life.

Majority of factors that increase the risk of developing vascular graft infection, such as diabetes mellitus, nicotine or alcohol abuse, and atherosclerosis, are present in our study patients, and have already been well-documented. The presence of electrolyte imbalance and previous orthopedic procedures in the vascular graft operative region were likewise noted in our study, and could have a role in the development of infection. Future studies, however, need to be done in order to prove this.

The management of vascular graft infection involved different options, such as VAC therapy or ISD therapy.

Although both methods showed similar clinical outcomes, ISD therapy appeared to be more advantageous than VAC therapy when analyzed in terms of economic. However, ISD therapy had some restrictions for use, depending on the infected wound area; specifically, it cannot be performed in large infected wound areas (>80 cm^2).

Content

Abbreviations

BMI	Body Mass Index
CRP	C-Reactive Protein
DHS	Dynamic Hip Screw
DRG	Diagnosis-Related Group System
GSV	Great Saphenous Vein
ICD-10	10th revision of the International Statistical Classification of Diseases and Related Health Problems
ICU	Intensive Care Unit
ISD	Irrigation Suction Drainage
MRSA	Methicillin-resistant Staphylococcus aureus
NaCl	Natrium Chloride
RBC	Red Blood Cell
PAD	Peripheral Vascular Disease
PTFE	Polytetrafluoroethylene Prosthesis
PU	Polyurethane Ether
VAC	Vacuum Assisted Closure Therapy
VRSA	Vancomycin-resistant Staphylococcus aureus

Introduction

Peripheral vascular graft infections are rare complications related to vascular graft surgery; complication rates vary from 1 up to 6 percent (70). Most vascular graft infections develop in patients with prosthetic graft implantation and seldom affect autologous vein grafts.

There is also a difference in vascular graft infection epidemiology, in terms of vascular graft localization. For example, aortic graft infection rates are lower, but at the same time, development of aortic prosthesis infection has more dramatic consequences compared to peripheral arterial graft infections. Peripheral vascular graft infections are uncommon and mostly develop in the ileofemoral region.

Another important issue in vascular graft infection risk factors represents the fact that prosthetic graft infection is more common after emergency procedures for ruptured aneurysms, and when prosthetic grafts have been implanted in the femoral region. The incidence of prosthetic graft infection following emergent surgical thoracic aortic procedures is significantly lower than after abdominal procedures or peripheral vascular interventions (95).

Another serious problem that makes studies about peripheral vascular graft infection difficult is that infection can develop a long time after vascular graft surgery, sometimes years after surgery.

Obviously, bacterial contamination is the main factor in the development of vascular graft infection. Bacterial contamination of the implant material and incorrect sterilization of operation instruments are rare but are important graft infection factors. Bacterial contamination may also occur via other routes, such as the hematogenous route or bacterial migration from subcutaneous tissue or skin flora. Lymphatic spread of infection is another particular route, mostly known to be associated with lower extremity vascular graft infection development; however, this remains to stay under discussion (31).

Infection at the beginning can be latent and usually does not have any symptoms; however, with time, it results in weakening of the vessel wall and disruption of the anastomosis. The inflammatory process results in the precipitation of aneurysmal dilatation, hemorrhage, and fistula formation. Vascular graft infection cannot only be associated with prosthesis erosion and life-threatening bleeding complications, but can also lead to serious septic complications with high mortality.

Until now there have not been many publications about this topic, there is still little available information with respect to optimal surgical and antimicrobial therapy approaches in the management of lower extremity vascular graft infection. In fact, most recommendations for treating lower extremity vascular graft infection are based mainly on small case series and expert opinion (28).

Classification of Vascular Graft Infections

Vascular graft infection is a general term. Conditions that fall under vascular infection include not only prosthesis infection, but also infection of tissues or skin in the area of the vascular graft. Vascular graft infection classification plays an important role in classifying the severity of peripheral vascular graft infection and is an important factor in developing specific management methods for infection according to the location of infection. Nowadays, the vascular community continues to use classification methods created 60 to 70 years ago. The two most common classifications are the Szilagyi classification (96) which is used in the analysis of this study, and the Samson classification (80). Not so well known is another classification method known as the Karl-Storck classification (Table A).

Table A

Groups	Szilagyi	Samson	Karl-Storck
I	infection involves only the dermis	infections extend no deeper than the dermis	superficial infection without involvement of the graft
II	infection extends into the subcutaneous tissue but does not invade the arterial implant	infections involve subcutaneous tissues but do not come into grossly observable direct contact with the graft	partial graft infection without involvement of the anastomosis
III	the arterial implant proper is involved in the infection	infections involve the body of the graft but not at an anastomosis	involvement of the anastomosis and suture line
IV		infections surround an exposed anastomosis but bacteraemia or anastomotic bleeding has not occurred	wound disruption and complete exposure of the graft/patch
V		infections involve a graft to artery anastomosis and are associated with septicaemia and/or bleeding at the time of presentation	all the above groups with concomitant septic bleeding/pseudoaneurysm
VI			all the above groups with graft thrombosis or septic emboli

Risk factors of Peripheral Vascular Graft Infections

Nicotine abuse

Nicotine abuse is a well-known risk factor of many diseases, such as cardiovascular diseases and oncological diseases. Patients with a history of nicotine abuse have a significantly increased risk of atherosclerosis, which results in peripheral arterial disease (PAD) or thromboangitis obliterans. There are many publications that report nicotine as one of the risk factors of (PAD) (108, 98). Nicotine affects the arterial wall directly. However indirect mechanisms increase in PAD development as well. Publications mostly show the negative effect of nicotine on the vascular graft after lower extremity vascular reconstructive surgery. Patients with a history of nicotine abuse undergoing peripheral vascular surgery suffer from a high number of postoperative complications, such as wound healing problems, postoperative lung infections, and lower extremity vascular graft infection. According to a study by Willigendale et al., it is important to clarify the status of tobacco use preoperatively because nicotine abuse puts the patients at higher risk for vascular complications, and the risk correlates with the daily amount of tobacco use preoperatively. In this study, they noted a 3 times greater risk of vascular graft failure in smokers compared to non-smokers undergoing vascular graft surgery (107). It is important to perform nicotine restriction if time allows, in order reducing these risks (98).

Cardiovascular disease

Cardiovascular disease is one of the risk factors related to PAD, as well as to graft infection. Usually, valvular heart disease and coronary artery disease are associated with factors that cause peripheral arterial damage. High blood pressure damages coronary arteries and peripheral blood vessels, increasing PAD risk. According to current studies, approximately 35-55% of all patients with PAD have hypertension (25). Some studies report that patients with end-stage PAD tended to have hypertension that is either not diagnosed or poorly managed. Cardiovascular risk factors are predictive of the development of PAD requiring surgical intervention. This means that cardiovascular disease is an indirect risk factor for vascular graft infection, as it basically increases PAD risk (86).

Atherosclerosis

Atherosclerosis has a tremendous effect on the arterial wall. The effect of atherosclerosis includes thrombosis, endothelial dysfunction, lipid disturbances, platelet activation,

inflammation, oxidative stress in the arterial wall, vascular smooth cell activation, altered matrix metabolism and remodeling. All these factors are related to PAD development (27). Similar to cardiovascular disease, atherosclerosis is an indirect risk factor for vascular graft infection. There are reports that through time, atherosclerosis can have a negative impact on implanted vascular grafts by damaging them (105).

Another important effect of atherosclerosis was reported by Goran K et al. In his study, he reported that atherosclerosis reduce immune response. These changes can increase risk of decreased immune response in patients with PAD who undergo vascular graft surgery and increase risk of early vascular graft infection (41).

Cerebrovascular disease

Cerebrovascular disease and cardiovascular disease have more or less analogous mechanisms. Usually, cerebral stroke is caused by the same factors that cause peripheral or coronary artery damage. This parameter was analyzed as a risk factor for vascular graft infection in our study, as well as in many already published studies. It is considered as an etiological factor connected with cerebral blood vessel damage. The damage in cerebral blood vessels correlates with peripheral arterial damage, and it has been reported that changes in the cerebrovascular system can cause vascular graft damage, as well (21).

Diabetes mellitus

Diabetes (insulin and non-insulin dependent) is an important risk factor for PAD development. The gold standard nowadays is detection of glycosylated hemoglobin in diabetes patients. Selvin et al. have reported that increase in insulin dependent diabetes mellitus is related to increases the risk of PAD by about 25% (84). Over time, most diabetic patients develop neuropathy and microangiopathy, which is associated with arterial damage and PAD development.

Diabetes is associated with a decreased immunological response to infection that relates to the elevated vascular graft infection risk. Aside from a higher risk of vascular graft infection, there have also been reports that patients with diabetes mellitus have higher extremity amputation rates when compared with PAD patients without diabetes in the medical history. Mortality rates showed similar trends, indicating a 3 times higher mortality in patients with diabetes mellitus undergoing ileofemoral reconsturctions. (51).

There are some specific characteristics of arterial damage in diabetes patients. The PAD more frequently involves arteries anatomically distal to the knee when we compare with patients without diabetes mellitus (51, 40).

Diabetes is a well-known cause of surgical site infection as it is related with surgical wound healing problem and surgical site inflammation. There are studies which have analyzed tight glucose control preoperatively and perioperative, as well as postoperatively, in diabetic patients, in order to determine if glycemic control can reduce cardiovascular complications and surgical site complications, such as healing problems and infection development. However, these studies failed to show a decrease in surgical site wound complications, most likely owing to the deleterious effects of diabetes aside from hyperglycemia (93, 85).

Alcohol consumption

Alcohol has been extensively discussed as a risk factor for PAD and vascular graft infection. Most authors who have published studies about the impact of alcohol on the vascular system say that alcohol can have both positive and negative effects on the arterial wall. There are some studies, which report that alcohol in small doses reduces the risk of PAD, but moderate alcohol doses increase the PAD risk (103). Giles et al. reported that alcohol use in moderate doses is an important risk factor for PAD development (20).

As already mentioned, alcohol consumption has negative effects on the development of vascular graft prosthesis infection, serving as both a direct and indirect risk factor. Romeo et al. in his review article showed that the effect of high doses of alcohol consumption could directly suppress a wide range of immune responses and these results in an increased incidence of infection, which develops after peripheral vascular graft implantation. The consequences of alcohol abuse result in decreased immune response to the microorganisms that can colonize vascular grafts (79).

Obesity

Obesity is huge problem nowadays, and the trend has a tendency to rise, especially in high income countries. Obesity is a well-described risk factor for PAD development, and is likewise a direct risk factor for vascular graft infection.

Usually, obesity is associated with comorbidities, such as hypertension, dyslipidemia, and diabetes mellitus, which are themselves risk factors for PAD development and vascular graft infection (36). In addition, obesity is a predictive factor for surgical site infection in general

surgery and cardiac surgery, but there are also data about lower extremity vascular graft infection. Some studies found that obesity increases the risk of vascular graft infection, while other studies showed no statistically significant difference in the effect of obesity on vascular graft infection (36, 47, 67). Obesity has a positive effect on mortality rate after peripheral vascular graft infection. Thus, patients with normal or reduced body mass index (BMI) showed higher mortality compared to patients who are overweight (36). Kannel et al. found a correlation between elevated BMI and vascular graft infection. In this study, patients with increased BMI had slower progression of vascular graft infection (54). Other large epidemiological studies reveal the same results: that elevated BMI reduces vascular graft infection mortality and reduces PAD development as well as PAD progression (68, 26).

One of the negative effects of obesity is that patients who undergo vascular graft operations due to PAD have a higher incidence of wound hematoma, wound necrosis or seroma development. If these complications occurs patient requires revision operations, and the risk of vascular graft infection becomes higher (75).

Other risk factors

Other risk factors include those that can play a direct or indirect role on vascular graft infection development. These factors are not so commonly analyzed in previous studies. Such factors include kidney insufficiency and dialysis, electrolyte imbalance, foreign materials in the vascular graft implantation area, liver insufficiency, malnutrition, and lung diseases such as asthma and chronic obstructive bronchitis. Some of these factors definitely play a role as indirect factor for vascular graft infection, such as chronic obstructive bronchitis, which usually is a consequence of nicotine abuse. On the other hand, lung diseases such as asthma could increase the risk of vascular graft infection because of immunological mechanisms that lead to decreased immunity (97). Electrolyte imbalance is documented as a possible risk factor; however, only 1 study analyzes electrolyte changes and their correlation with vascular graft infection (38).

Vascular Graft Infection Pathophysiology

Vascular graft infection usually develops after bacterial contamination of the vascular graft. The vascular graft can be infected by some rare bacteria, such as mycobacterium, mycoplasma, or a fungal species (31, 27, 37)

Most contamination happens in the operation due to the patient's skin flora. There are several publications saying that soft tissue edema or injured skin structures in the operative area increase the risk of vascular graft infection development (83). Other possible infection routes, which are very rarely seen nowadays, include incompletely sterilized surgical instruments or vascular grafts. It has been reported that in emergency cases or in emergency reoperations, such as in cases of acute bleeding, the risk for an incompletely sterilized operative field will be higher and the risk for the occurrence of postoperative surgical site infection will also be greater (101). Yeager et al published another risk factor for possible postoperative infection. He reported that the risk for bacterial contamination increases with operation time and blood loss during the operation (109).

The infection can spread via the hematogenous route, whereby bacteria spread from other acute or chronic bacterial infections in the patient's body, such as urinary tract infections, or through dental procedures, or urological or endoscopic manipulations in the postoperative period. Usually, the hematogenous route is associated with late vascular graft infections.

The vascular graft implant develops infection through biofilm formation. A wide spectrum of microorganisms have been reported that can cause graft infections; however, the most common species isolated are Staphylococcus aureus and Streptococcus epidermidis (61).

Nowadays, many patients who undergo vascular graft implantation have significant amounts of mucin-producing coagulase-negative staphylococci on their skin, and at least 15% have methicillin-resistant (MRSA) strains preoperatively. This causes increasing vascular graft infection cases in which the MRSA strain has been isolated (55).

Pathogenically, mechanisms include bacterial invasion of the vascular graft or in perigraft tissues during the operation or in the early postoperative period. In the early postoperative period, the fluid-filled perigraft tissue environment is poorly perfused with blood and lymph, and for this reason, is isolated from the natural host defenses (23). In addition, the poorly vascularized perigraft area provides a good condition for bacteria to survive and proliferate. For this reason, even a very small amount of bacterial species can lead to possible prosthetic

graft infection. With time, the vascular graft material adapts to the patient's tissues; when the operated tissues have been better vascularized, the risk of development of prosthetic infection decreases.

Vascular Graft Infection Microbiology

There is a wide spectrum of pathogenic bacterial species, which are linked to vascular graft infection. The most common species include Staphylococcus aureus; however, the trend in the last decade is a decrease in vascular graft infection due to Staphylococcus aureus species due to perioperative antibiotic therapy. Nowadays, there are trends of increasing vascular graft infections due to normal skin flora and multi-resistant bacteriological strains (5).

On the other end of the spectrum is the situation with methicillin-resistant Staphylococcus aureus (MRSA). In the last decade, there have been many more reports about MRSA-induced vascular graft infection (8). Due to plasmid-mediated mutation of Staphylococcus aureus, the bacteria become resistant against beta-lactam antibiotics, as well as other antibiotic groups. As already mentioned, MRSA infection rates causing vascular graft infection have been increasing. The explanation could be that MRSA has now been often found in skin flora by population screening. PAD, in its end stage, when it requires ileofemoral graft implantation, leads to decreased immunity, which is very favorable for the MRSA species to cause graft infection. Another important point is that patients with end-stage PAD often have multiple diseases, which require prolonged hospital stay, resulting in a higher possibility to acquire MRSA infection (42). Kaebnick et al. have reported that in bacteriological analyses, more than half of early extracavitary vascular graft infections have shown that the most common microorganism was MRSA. Data is lacking with regard to the effect of MRSA infection on early mortality, infection recurrence or amputation rates, as compared to other bacteriological species (52).

Moreover, there are alarming trends that vancomycin-resistant Staphylococcus aureus (VRSA) will become the most common isolated pathogen in vascular graft infections based on bacteriological analysis in the next decade. The first VRSA has been isolated in 2002 from a dialysis shunt in a patient with multiple comorbidities, namely diabetes, foot ulcer, kidney dysfunction, and PAD. After this, VRSA has been isolated more and more often from infected vascular graft prostheses (92).

An interesting trend shows specific bacteriological species over time. In other words, there are differences in microorganisms that are isolated in an early vascular graft infection and in a late vascular graft infection. Early vascular graft infection is mostly caused by coagulase-positive Staphylococcus aureus, Escherichia coli, Proteus species, and Pseudomonas aeruginosa. Meanwhile, late infection, which develops after a few months or later, is mostly caused by Staphylococcus epidermidis or very rare fungal species (14, 33).

There are some studies, which have isolated specific microorganisms in cases of vascular graft infection, but in general, such cases are exclusions. For example, anaerobic bacterial species have been isolated from femoral graft infections. Usually, this affects patients with decreased immunological system response, such as patients with diabetes, leg ulcer, gangrene, or patients with a history of chemotherapy or radiation therapy (12). The previously mentioned fungal vascular graft infections show the same trend, and mostly affect patients with immunological deficits.

In many cases, the microbiological culture from the infected graft reveals two or more different microbiological species. Calliagro et al. in their study analyzed 42 patients with graft infections, and have seen that in 16 cases, both gram-positive and gram-negative species have been found (19).

Vascular Graft Infection Management

Vascular graft infection management is a challenge for all medical staff who take part in patient treatment. Infection management usually includes management of infected vascular graft hemorrhage, preservation of lower limb blood circulation, control of infection parameters, and sepsis prevention or early excessive treatment if septic symptoms develop. One of the most important ileofemoral vascular infection management methods includes lower limb revascularization via extra-anatomic pathways and excision and debridement of infected tissues (81, 35). Nowadays, there are tendencies to reduce aggressive surgical approaches, and instead proceed with more lenient surgical management and put more accent to proper antibacterial therapy, as well as to nutritional support. Other tendencies include methods such as rinse suction drainage or vacuum assisted drainage, which plays a more important role in vascular graft infection management (3, 10).

Surgical management of vascular graft infection

Surgery is one of mainstays in lower extremity vascular graft management. The important point in surgical management is the time when vascular graft infection is diagnosed.

Due to radiological diagnostic problems, there are still infections that are diagnosed late with septic symptoms, hemorrhage or hypovolemic shock. A combination of blood products and intravenous volume resuscitation, wide spectrum antibiotic therapy, and urgent surgical treatment is the only option in these cases. On the other hand, if infection is diagnosed early, it is possible to prepare the patient for surgery and reduce the manifestation of infection, which will improve clinical outcome.

Surgical management includes graft excision with or without revascularization, as it is the foreign body, which intensifies the infection. Graft excision can be followed by extra-anatomic revascularization or in situ replacement of the graft (Table B). Complete debridement of the infected vascular graft and debridement of the surrounding infected tissues is one of the techniques, but this is usually performed with some limitation if the surrounding infected tissue area is large (15).

Graft preservation as a surgical method has some limitations. It is indicated when infection involves autologous vein grafts, patches or infected prostheses which is made from polytetrafluoroethylene (PTFE) (18). Another condition when graft preservation can result in good clinical outcomes is that when patients do not have systemic septic symptoms, the infection develops in the early postoperative period (<4 months), infection is extracavitary, and no virulent microbiological species, such as MRSA or Pseudomonas aeruginosa or polymicrobial infection, have been found.

Graft preservation and local treatment can be applied to patients with segmental contamination and anastomoses must be spared. The local treatment includes surgical wound sterilization to reduce bacterial colonization in the wound, multiple infected tissue debridement, temporary placement of antibiotic-loaded beads, rotational muscle flap or fasciocutaneous flap coverage, and use of irrigation suction drainage or vacuum assisted closure therapy. In cases with septic symptoms, which develop as consequences of local therapy that have been used to treat vascular graft infection, it should be considered that treatment with vascular graft preservation typically results in failure, and graft excision with or without revascularization should follow (17). In cases wherein the surgeon decides to perform vascular graft excision without revascularization, the patient needs to have adequate collateral circulation in the extremity.

Extra-anatomic bypass and In situ revascularization

In situ revascularization is the main method of choice in patients with vascular graft infection and surrounding graft and tissue inflammation. In patients with septic symptoms, extra-anatomic bypass surgery can also be considered. This type of surgery can be done in more than one stage. The advantage for such an approach is that the patient can much better tolerate small surgeries, which are done in a stepwise manner, instead of a single large surgical procedure, with significant blood loss and other intraoperative complications. Abraham et al. in their study discovered that a stepwise extra-anatomical bypass approach not only reduced blood transfusion requirements, but also decreased mortality rates and lower extremity amputation rates (2). In the stepwise graft infection surgery, there are some concerns that infection can cross to the newly implanted graft from the infected vascular graft. However, studies are presently unable to confirm such concerns, and thus, the approach has been safely used in vascular graft infection patients (62).

In situ revascularization is one method that has been more and more popular nowadays. The advantages of in situ revascularization are a relatively short operation time and that it is technically easier to perform when compared with extra-anatomical bypass surgery. Moreover, in situ revascularization shows better clinical outcomes, reduced ICU days, reduced amputation rates, and lower mortality rates (71).

In situ revascularization has often been used for prosthetic grafts, arterial allografts or autologous venous grafts. The advantage of arterial allografts and autologous vein grafts is that they show better results with regard to reinfection rates, as compared to prosthesis implantation, as the patient's tissues have lower affinity to native tissues compared to foreign material.

In cases where the infection affects the aortofemoral region, the use of the great saphenous vein (GSV) or superficial veins from the lower extremity is possible. However, autologous vein preparation takes extra time and is associated with operation prolongation. Another problem is that the GSV or the superficial veins used in ileo-femoral or aorto-iliac reconstructions results in low patency rates, due to diameter mismatch (82).

The only disadvantage from this surgical method is that reinfection rates are potentially higher in patients with highly virulent microorganisms, such as Pseudomonas species or multiple microorganisms isolated from infected wounds. In such cases, in situ revascularization is not preferred.

Vacuum assisted wound closure

Vascular infection management in the ileofemoral region includes different treatment methods. The two important vascular infection management methods include operative treatment and antibiotic treatment. In the last decade, vacuum assisted wound closure therapy (VAC) has become more and more popular as a treatment method, with good results (11).

The VAC system, which can be used in cases of vascular graft infection, consists of inert reticulated open cell foam that needs to be adapted to the lower extremity wound. When the VAC foam is adapted to the wound, the VAC foam and the end of the wound need to be covered with a semi-occlusive film. Tubing needs to be attached to the VAC system via a small incision in the VAC foam, while the other end of the tubing system is attached to the VAC suction device. The suction device and configuration delivers negative pressure to the wound that can be administered in a continuous mode or in the intermittent mode (3).

The effect of negative wound pressure therapy in vascular graft infection can be described in the various actions on which this type of therapy has impact. First of all, it has been shown in some animal studies of chronic wound healing problems that with the VAC system, bacterial contamination in the wound becomes significantly lower and bacterial growth and colonization are reduced after a few days. At the same time, the VAC system has a positive effect on the wound due to increased perfusion. Increased perfusion and better circulation decreases bacterial contamination and hastens wound healing. Micro-deformation of the wound surface and suction of the exudate, which develops in the wound, improves healing (6, 64). These mechanisms of the VAC system can explain why negative pressure therapy is better than wet to moist dressings.

The effectiveness of VAC therapy versus standard dressings was shown in a study by Armstrong et al., who used this method in patients who underwent lower extremity amputations. One group of patients was treated with standard moist wound dressing, while the other group was managed with VAC therapy. The VAC group patients showed significantly lower hospital stay and a higher number of patients with completely healed wounds. The VAC group patients were also noted to have lower reoperation rates compared to standard moist wound dressing patients. In both groups, there were large numbers of patients who had amputation stump healing problems at the end of the study follow-up. The number of healing problems reached up to half of all patients included in the study. This indicates that there are some other unknown aspects affecting wound healing, and VAC therapy is not beneficial for all patients (7).

Irrigation suction drainage

Irrigation suction drainage (ISD) is one of the therapy options that have been used historically to treat surgical wound infection. There are publications in different surgical fields, including vascular surgery, which analyze ISD therapy use in complex surgical site infections. Most of the publications are in the cardiac surgery field, for which this kind of therapy was used to treat sternal wound infections, with good results (30). The use of this therapy can also be seen in orthopedic and trauma surgery, but nowadays, this method has been frequently replaced by VAC therapy (63). There are published data that VAC therapy shows better results compared to ISD therapy in reducing mortality and hospital stay (9). This type of therapy was used historically in vascular graft infection management with acceptable results, and many vascular surgery divisions are using this type of therapy nowadays. It should be noted that VAC therapy takes a more important role in vascular surgery, with good results, while ISD therapy, because of some restrictions such as wound area, remain to be the therapy of choice in lower extremity vascular graft infection.

Table B. Summary of vascular graft infection surgical management modified according to Thompson (99)

Treatment option	Manifestation	Extent of infection	Microbiology
Graft preservation/local therapy	Early infection, no sepsis	Not Dacron, graft body only, no anastomosis, segmental	Gram-positive, Staphylococcus species
Graft excision only	Graft thrombosis viable limb, adequate collaterals	Any	Any organism
Excision and ex situ bypass			
Simultaneous excision and revascularization	Unstable patient, hemorrhage, severe sepsis	Invasive infection	Any organism
Staged excision and revascularization	Stable patient, mild sepsis, no active hemorrhage	Invasive infection	Any organism
In situ replacement			
Prosthetic	No sepsis	Biofilm infection, segmental	Staphylococcus epidermidis, negative Gram stain
Autologous vein	No sepsis, severe occlusive disease	Invasive or biofilm, diffuse or segmental	Not Pseudomonas species

Objectives

The aim of this study is to include patients with lower extremity vascular graft infection, and to analyze risk factors, which could be associated with vascular graft infection. For all the patients included in the study, the vascular graft infection was managed either with the VAC system or the ISD system.

The first objective was to compare both methods (VAC versus ISD) retrospectively to see if there is any significant difference in clinical outcome between the 2 methods.

The second objective was to analyze treatment costs and economic benefits between the 2 methods and to find out which method is more cost effective.

Materials and Methods

Patients with lower extremity vascular graft infection that developed after vascular graft implantation in the ileofemoral region consecutively were included in this study. This is a retrospective study, and includes patients in a 9-year time period, from year 2006 up to year 2015. The follow-up period after primary ileofemoral vascular graft surgery was 1 year. In this time period, the patient history was analyzed for development of graft infection. If there was no infection diagnosed in the first year after operation, no future follow-up was done.

If infection was diagnosed in the first year after initial operation, the patient's medical history was analyzed in detail. The aim was to find possible preoperative risk factors, which could play roles in vascular graft infection development. We analyzed acute management after vascular graft infection was diagnosed, and follow-up after diagnosis of infection was 6 months.

From 2006 up to 2015, Contilia Heart and Vascular Surgical Centre did 6232 lower extremity vascular reconstruction operations. We used a clinical diagnosis-related group (DRG) system to find patients with lower extremity vascular graft infection. From the ICD-10 (10th revision of the International Statistical Classification of Diseases and Related Health Problems) diagnostic coding system, we used the following codes to determine which patients have been diagnosed with vascular graft infection after the initial operation:

T82.7 - Infection and inflammatory reaction due to other cardiac and vascular devices, implants and grafts

T82.8 - Other specified complications of cardiac and vascular prosthetic devices, implants and grafts

T82.9 - Unspecified complication of cardiac and vascular prosthetic device, implant and graft

These codes and subcodes were used to filter the patient list and to identify patients with possible vascular graft infection. After filtration of the aforementioned codes and subcodes, the patient list included 1209 patients. The large patient count can be explained by patients who had infections in other localizations, as well as patients with vascular graft thrombosis, bleeding after initial operation, and aneurysm formation.

Eight out of 1209 patients developed infections of the lower extremity vascular graft. These patients already had external vascular reconstructions in another hospital or their vascular graft infection was already treated in other hospital. These patients were excluded from our study.

First of all, because the full medical histories of these patients are unavailable, and secondly, our goal was to analyze initial management after ileofemoral graft infection diagnosis.

We did the analysis of all 1201 patients. We looked through the patients' charts to determine the lower extremity vascular graft initial operation. After the initial operation date was found, we looked through patient charts in the 1-year period to find information about vascular graft infection.

The time period 1 year after initial surgery was chosen because our goal was to standardize patient follow-up. As our study began in the year 2016, the patients who were included in the year 2015 were able to complete the minimum follow-up time.

After the 1201 patients' clinical histories were analyzed, we found 67 patients who were primarily included in our study. After primary analysis, we did a detailed patient clinical history analysis according to the following parameters. The rest 1134 patients did not correspond to our study criteria. Twenty-seven from 1134 patients had aortic infection, which not involved ileofemoral region. For this reason, they were not included in the study.

We made a list of possible infection risk parameters based on literature review. We did a MEDLINE search with following criteria: "lower extremity vascular graft infection", "vascular graft infection risk factors", "femoral graft infection", "ileofemoral vascular graft infection".

We excluded all non-English language publications, and all publications, which did not include peripheral lower extremity vascular graft infection. Publications with information about risk factors for vascular graft infection were included in our study to create our databases. From our Medline initial search, we found 1352 publications which, after looking through publication abstracts, were narrowed down to 26 publications that contained information about possible risk factors for lower extremity vascular graft infection. Based on these 26 publications, we made a risk factor database for peripheral vascular graft infection. Additionally, we included some data in our database, which could have an effect on infection development but has been rarely analyzed, such as electrolyte imbalance.

In our database, we listed many possible risk factors, which include well-known risk factors such as atherosclerosis, and alcohol and nicotine consumption, as well as not well-published possible risk factors that have a negative effect on immunity, and as a result, can increase the risk of vascular graft infection. Such risk factors include other infections, renal insufficiency,

and orthopedic procedures with foreign material implantation on the ipsilateral side of the vascular bypass graft.

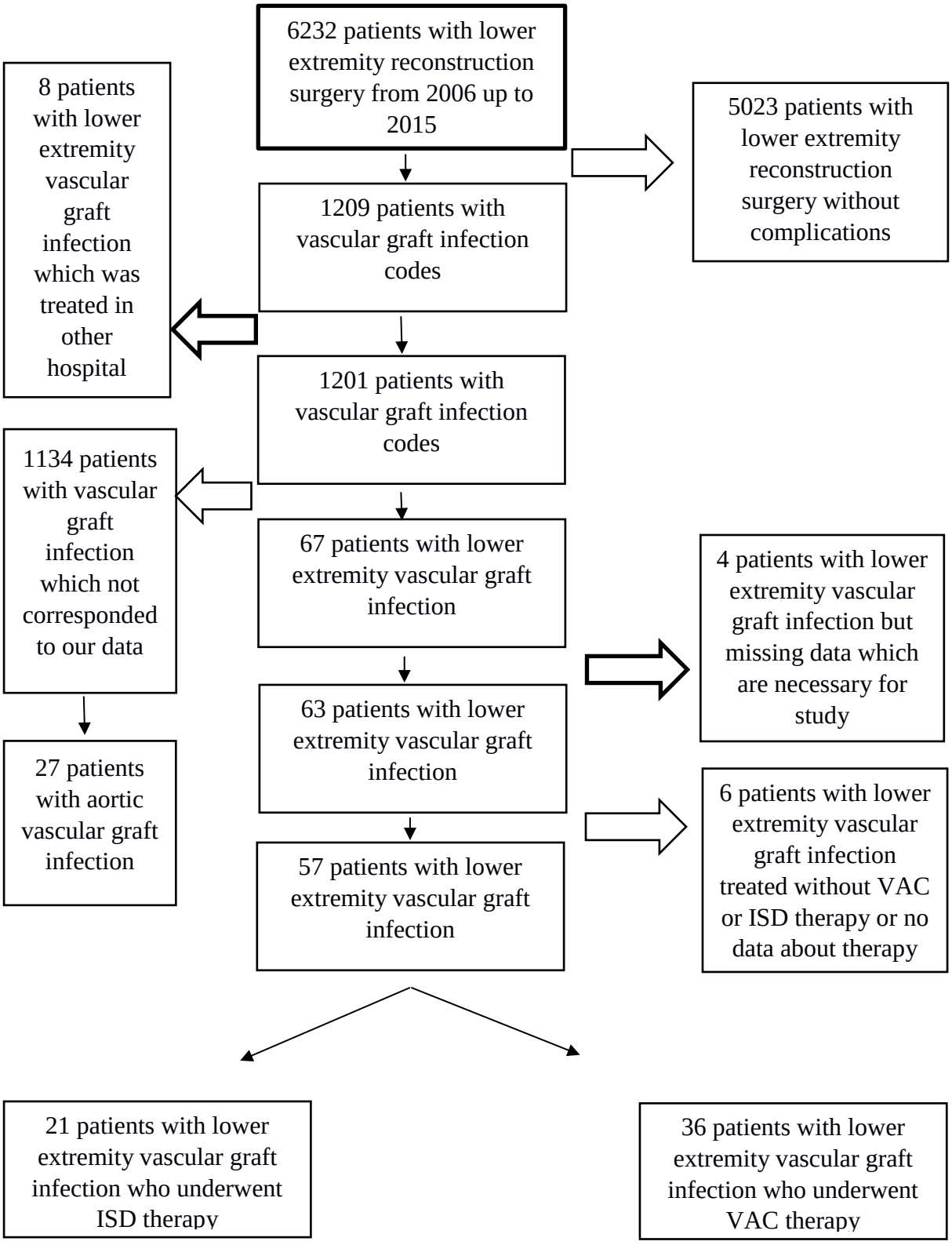
After analysis of the patients' histories, we found 4 patients with missing information that is necessary for our study. These patients were thus excluded from the study.

The next important step was to find information about vascular graft infection management methods. Aside from information about reoperations, it was important for us to gather information about vascular graft infection treatment with VAC therapy or irrigation suction drainage (ISD) therapy.

Since one important aim of this study was to analyze the economic benefit of the 2 management methods, we looked through the patients' medical histories to determine which of the methods was used in the treatment process and additionally analyzed costs related to respective treatment. Of the 63 remaining subjects, 6 patients had no recorded information regarding the use of VAC therapy or ISD therapy in the patient history. For this reason, we excluded these patients from our study.

Finally, 57 patients corresponded to all our criteria and were included in the study. From these patients, medical histories were collected, as well as data about possible risk factors, and information about intensive care unit (ICU) stay and hospital stay until discharge. Information about the initial operation and reoperation, was included for all 57 patients (Table C).

Table C: Study population



The infection grade was classified according to the Szilagyi classification. The patients were classified in to 2 groups, according to which type of management – therapy (VAC or ISD) was applied.

Owing to the fact that there are no specific criteria for vascular graft infection diagnostic, the patients with suspected clinical symptoms such as local pain, swelling, warmth or redness of the vascular graft wound, fever, or laboratory findings such as leukocytosis or increased infection markers with clinical correlate, as well as radiological imaging - computer tomography scan - were used as a criteria for vascular graft infection diagnosis and treatment initiation.

For each patient diagnosed with vascular graft infection, bacteriological identification of the bacterial species causing the infection was done. In cases where there were different bacteriological species isolated from the infected wound, all pathogens were documented in our database. All 57 patients who were included in the study had bacteriological species isolated from the infected wound.

Therapy with ISD or VAC was initiated when the patient had an ileofemoral vascular graft infection. This therapy was combined with surgery on the infected area and antibiotic management. The method utilized – whether ISD or VAC – was dependent on the decision of the surgeon. There were no specific internal standards in our division as to when ISD therapy or VAC therapy is preferred. Usually it was decision from vascular surgeon on duty which of methods have been preferred. The only contraindication to the ISD therapy was a large wound area when wound closure was not possible or a known suspected allergic reaction to the ISD components. In such cases, VAC therapy was preferred.

The surgical intervention is known as the gold standard procedure for a vascular graft infection. The patients with diagnosed ileofemoral vascular graft infection underwent revision surgery in our Vascular Surgery Center. According to the grade of infection, patients underwent infected wound debridement, if infection involved dermis or subcutaneous tissues, or total infected vascular graft explanation with autogenous vein *in situ* replacement of infection with vascular graft involvement. Another option which was performed on infection with prosthesis involvement was extra-anatomical bypass with autogenous vein reconstruction (see Table D).

Table D. Ileofemoral vascular graft infection management regarding the infection grade.

	Irrigation drainage therapy Number of patients	Vacuum- assisted closure therapy Number of patients
Dermis and soft tissues debridement of vascular graft infection	14	22
Debridement of soft tissues with infected vascular graft explantation and *in situ* reconstruction	6	11
Debridement of soft tissues with infected vascular graft explantation and extra-anatomical autogenous vein reconstruction	1	3

Our clinical division has made internal guidelines for the use of ISD therapy. Thus, we have a standardized therapy approach for all ISD patients with vascular graft infection.

ISD therapy was initially applied in the operation theater. If the patient is able to tolerate it, we perform the ISD application under local anesthesia. We used 1% mepivacaine to infiltrate the wound tissues. Our therapeutic concept includes taking bacteriological swabs for microbiology prior to irrigation of the infected wound. After swabbing, wound disinfection with liquid iodine was performed, followed by wound debridement of necrotic tissues if necessary. After the wound is irrigated, 2 drainages were placed in the wound. Usually, the first drainage size is 12 Fr or 14 Fr, while the second drainage size is either a 16 Fr or 18 Fr. After drainage has been placed onto the wound, the wound was closed with surgical subcutaneous and cutaneous sutures. We normally use interrupted surgical sutures. After wound closure, we placed sterile dressing and connected the first drainage to 1 L of Natrium Chloride 0.9% (NaCl) bottle admixed with 60 ml of liquid iodine (Betaisodona® liquid). The second drainage was then

connected to a normal drainage bag. After this procedure, the patient can be moved from the operation theater to the vascular surgery ward or in severe cases when ISD was combined with infected vascular graft surgery, to the ICU. The infusion rate of the NaCl and iodine bottle is 1 L in 24 hours. After 24 hours, the bottle was changed to a new one. The therapy time is 5 days. On day 6, we use only 1 L of NaCl 0.9% infusion. On day 7, we evacuate the drainage from the wound. Wound dressing changes were done daily. According to the protocol, the nurse will check the volume of the second drainage bottle twice a day to ensure that the irrigation suction system works and is not blocked. In the case of blocks or clotted drainage, we used a 50 ml NaCl 0.9% infusion pump syringe, which the nurse connects to the drainage in order to irrigate the system.

The VAC system is another method of vascular graft infection management that we are using. The first procedure is VAC installation, which was performed in the operation theater. Change of VAC foam was likewise done in the operation theater. The initial VAC system installation was routinely combined with a debridement of necrotic wound tissue. Culture swabs were taken for microbiology before wound irrigation with saline liquid. After the microbiology has been taken, the necrotic wound tissues were surgically removed and adequate hemostasis achieved. Prior to application of the drape, we prepare the peri-wound skin, ensuring that the skin is dry and there are no sign of infected tissue. Skin densification around the surgical wound was done to clear the skin of perspiration, oil or body fluids that will make the skin moist. After the wound is prepared, the sterile open-cell foam dressing is placed into the wound cavity. The foam can be adapted to the wound by cutting it into the wound form. We used black foam, which is made from polyurethane ether (PU). The black foam has larger pores, is lighter, easily collapsible, and hydrophobic, with a pore size of 400 to 600 nm. After the foam is placed over the wound, we embedded in the foam a fenestrated evacuation tube, which was connected to a computer-controlled vacuum pump that contains a fluid collection canister. At the end of the procedure, the wound and peri-wound skin was sealed with an adhesive drape. We used double-layered drapes, which are especially commercially designed for VAC therapy. The main point is that by applying the drape, we cover the following wound area: the foam and tubing, and at least 3 to 5 centimeters of surrounding healthy tissue. This ensures a seal. Our internal standards included changing the foam and drape every 72 to 96 hours. By changing the foam regularly, we were able to evaluate the wound condition and adherence to the wound bed was prevented. In cases of tissue adhesion, we used sterile NaCl 0.9% liquid to loosen the foam for removal from the wound bed and the peri-wound skin. Our standard included VAC system changes

under local anesthesia using 1% lidocaine solution. In cases where patients are unable to tolerate local anesthesia only, systemic pain reduction by the anesthesia team with remifentanil infusion was done. In worst cases, general anesthesia was applied for VAC system changes.

The last step of VAC system installation included application of negative pressure on the surgical wound. We used the VAC pump option with continuous pressure normally in the range of 50 up to 100 mmHg. The pressure was set to continuous for the first 48 hours and was elevated as required thereafter. Continuous suction modus was routinely used in wound healing process.

As our study included the economic benefits of VAC versus ISD therapy, we contacted our hospital finance department to find out the treatment prices for each of the therapy options. To make it simple, we noted only the costs, which are related to VAC drainage or ISD drainage therapy. That means we did not include costs, which are constant for both patient groups, such as hospital costs including ICU days, operation costs, personal costs, radiological microbiological investigation, etc. We presumed that these costs are equal for both patient groups. For this reason, we did our calculation based on the materials and medication costs, which were explicit only for VAC or ISD drainage therapy. We did not include anesthesia costs, as our primary standards included VAC and ISD system changes under local anesthesia. For the ISD system, there was no need to change the system itself, and only the bottle of irrigation liquid must be changed. Usually, ISD drainage evacuation can be done without anesthesia or under local anesthesia.

The VAC or ISD drainage system set up was done in the operation theater. The irrigation liquid change was normally done in the ward. The VAC system change was done in the operation theater. We did not include operation time for both procedures because we could not specify the exact time needed for ISD or VAC system installation, as in addition to these system installations, there was usually wound revision, or in some cases, vascular graft explantation performed at the same time. In addition, for many patients in both groups, this type of therapy was associated with wound debridement, as well as manipulation of the vascular graft, which required general anesthesia.

Statistical analysis

Patients with vascular graft infections were identified using diagnosis-related group system (DRG), which was used in our hospital. For the patients' medical history analysis, we used the Meierhofer AG (MCC) program, where all the patients' medical charts have been saved electronically. The patient data was collected in Microsoft Excel 2010. For statistical analysis, we used the statistical analysis program IBM SPSS 22.0 version. We used descriptive statistical methods to analyze the basic features of our data. For the group population analysis, we used mean values and standard deviation. For categorical variables, we used the Chi square test and Fisher's exact test. The level of significance was set at $p< 0.05$. The independent t-test, also called the two sample t-test or student's t-test, was used to determine whether there was a statistically significant difference between the means in the 2 unrelated groups. For the survival rates, we used Kaplan-Meier curves, which graphically showed survival rates in both patient groups. The medical treatment costs, which included VAC therapy and ISD therapy, were figured out through our finance department using the DRG system program.

Results

The objectives of our study were to analyze possible risk factors for vascular graft infection, to compare vascular graft infection management options (VAC therapy versus ISD therapy), and to determine differences between the 2 methods and analyze the clinical outcome for each patient group. The second objective was to analyze both management methods in terms of costs, in order to find out which is the more cost-effective method.

VAC versus ISD Group population characteristics

In our study, we included 57 patients, who were divided into 2 groups: the ISD group included a total of 21 patients (7 female – 33%, 14 male – 66%), while the VAC group included 36 patients (13 female – 36%, 23 male – 63%) (Figure 1). The mean age in the ISD group was 66.7 years versus 71.3 years in the VAC group (Table 1). In the ISD group, mean height and weight were 166 cm and 86.2 kg in females, and 175.2 cm and 84.2 kg in males. The mean body mass index in the ISD group was 31.2 for females and 27.3 for males. In the VAC group, the mean height and weight were 161.6 cm and 71.9 kg in females, and 173.9 cm and 76.6 kg in males. The mean body mass index in the VAC group was 27.4 for females and 25.2 for males (Table 2). Based on the population characteristics, we did not find any statistical difference between the 2 groups ($p>0.05$).

Szilagyi classification

All patients included in the study were classified according to the Szilagyi classification. Grade I infection according to the Szilagyi classification was noted in 6 patients in the ISD group versus 8 patients in the VAC group. Grade II infection was seen in 8 patients in the ISD group versus 14 patients in the VAC group. Grade III infection was seen in 7 patients in the ISD group versus 14 patients in the VAC group (Table 3). There was no statistically significant difference between the 2 groups.

Vascular graft localization

In this study, we analyzed the anatomical locations of the infected vascular grafts in both groups. Ileofemoral bypass was performed in 8/21 patients in the ISD group versus 12/36 patients in the VAC group. Femoropopliteal bypass was performed in 7/21 patients in the ISD group versus 13/36 patients in the VAC group. Much fewer were patients who underwent ileopopliteal bypass, which included 2/21 and 5/36 patients in the ISD and the VAC groups, respectively. Patients who underwent aortobifemoral bypass were 3/21 in the ISD group and

5/36 in the VAC group. Only 1 patient in each group underwent axillofemoral bypass (Figure 2).

Additionally, we analyzed if patients already underwent previous ipsilateral bypass in the operative region. In case with a history of previous ipsilateral bypass operation, the procedure is more challenging and operation time is longer, which correlates with graft infection development. Ipsilateral vascular bypass was performed in 4/21 patients in the ISD group and 10/36 patients in the VAC group (Figure 3). There was no statistically significant difference between the 2 groups ($p>0.05$) with regard to this.

We likewise noted information about any additional foreign material in the area of operation, as it can be a risk factor in elevating vascular graft infection risk. Majority of the patients (16/21 in the ISD group, 21/36 in the VAC group) did not have any additional material in the operative area at the time of initial operation. Meanwhile, there were 4/21 patients in the ISD group and 12/36 patients in the VAC group who had ipsilateral hip prosthesis. One patient in each group had osteosynthesis with a plate in the operative area, and 2 patients in the VAC group had hip osteosynthesis with dynamic hip screw (DHS fixation) (Figure 4).

Amputation rates

The amputation rates were calculated in both groups. Vascular graft infection resulting in lower extremity amputation occurred in 7/21 patients in the ISD group versus 10/36 patients in the VAC group. The p-value did not show statistical significance between the 2 groups (Table 4).

Hospital stay

We analyzed the length of hospital stay for both patients groups after vascular graft infection was diagnosed. We did explicit analysis of ICU days and normal vascular surgery ward days. In the ISD group, the mean hospital stay duration was 34.2 days versus 37.7 days for the VAC group. The mean ICU stay after ISD therapy was 4.9 days and 4.1 days after VAC therapy. There was no statistically significant difference seen between the 2 groups in the length of ICU or ward stay (Table 5).

Additionally, we did analysis of the time period of the VAC and ISD therapies. The mean ISD therapy duration was 7.2 days (from 7 days up to 8 days), while mean VAC therapy duration was 14.8 days (from 7 days up to 24 days) (Table 6). This was a statistically significant difference between the 2 groups ($p<0.01$).

Bacteriology

There are different bacteriological species isolated from the infected wounds. One of the most common species in both groups was methicillin-resistant Staphylococcus aureus (MRSA). In the VAC group, there were 15 patients with isolated MRSA infection versus 3 patients in the ISD group, this shows statistically significant difference between groups ($p<0.05$). The most common bacteriological species isolated in the ISD group was Staphylococcus aureus, which was found in 7 patients versus 9 patients in the VAC group. The other bacteriological species were isolated only for 1 to 3 patients, and can be seen on Table 7.

Antibiotic therapy

We analyzed antibiotic therapy preoperatively and intraoperatively during the initial operation, as well as antibiotic therapy during ISD or VAC initiation. We were able to find out antibiotic therapy using patient charts and anesthesiology protocols.

In the ISD group, 3 patients were already being given antibiotics before the initial operation versus 4 patients in the VAC group. The 2 patients in the ISD group who were being given antibiotics preoperatively had other active infections, elevated infection parameters or immunosuppressed conditions. In the VAC group, we were not able to find such correlation (Table 8).

During vascular bypass graft operation, all patients perioperatively received a single intravenous shot of antibiotic. In the ISD group, 20 patients received Cefuroxime and 1 patient received Sulbactam/Ampicillin because of open peritoneum (peritoneal incision during preparation). In the VAC group, the tendency was similar, with 33 patients receiving Cefuroxime, 1 patient receiving Sulbactam/Ampicillin because of open peritoneum, and 2 patients receiving Clindamycin because of allergic reaction to Penicillin (Table 9).

The antibiotic therapy given upon initiation of the ISD or VAC therapy was decided according to the patient's bacteriological results or antibiogram, or if there was no information about bacteriological status, broad-spectrum antibiotic therapy was initiated. Cefuroxime was continued as antibiotic in 10/21 patients in the ISD group versus 16/36 patients in the VAC group. Vancomycin was given to 5/21 patients in the ISD group versus 14/36 patients in the ISD group, because of MRSA in bacteriology results, or according to the patient's clinical history when bacteriology was not available. Detailed antibiotic therapy is shown in Table 10.

Clinical outcome

The clinical outcome showed no statistical difference between the 2 groups. There were 4/21 patients in the ISD group who were transferred directly to a rehabilitation clinic versus 12/36 patients in the VAC group. In the ISD group, there was 1 patient who was transferred to another hospital due to non-medical reasons. In the ISD group, 14/21 patients were discharged from hospital versus 21/36 patients in VAC group. The mortality rate was 2/21 patients in the ISD group versus 3/36 patients in the VAC group. Detailed information is shown in Figure 5.

Blood transfusion

The blood transfusion rates between the 2 groups show no statistical difference. We analyzed blood transfusion requirements during the operation and in the first 48 hours after surgery. During the operation, the average transfused amount was 0.76 units in the ISD group compared to 0.58 units in the VAC group.

After ISD or VAC therapy was initiated, an average of 2.14 units of blood versus 1.67 units were transfused within the first 48 hours (Table 11). It must be noted that VAC and ISD therapy initiation was often combined with revision operation.

In the ISD group, 13/21 patients required blood transfusion during the operation or within 48 hours after surgery, compared to 24/36 patients in the VAC group (Table 12).

Risk factors for vascular graft infection

We did analysis of possible vascular graft risk factors for patients with vascular graft infection. The risk factors included in our analysis must have already been present before the initial vascular graft infection. We looked at both groups to see how many of the patients had certain risk factors and analyzed them to see if there were differences in certain risk parameters between the 2 groups.

The risk factors which we analyzed included non-insulin dependent diabetes mellitus and insulin dependent diabetes mellitus, which was present in 9/21 patients in the ISD group and in 14/36 patients in the VAC group. There was likewise no statistically significant difference ($p>0.05$) between the groups if the parameter used was diabetes in general, i.e. a combination of insulin dependent and non-insulin dependent diabetes mellitus.

Renal insufficiency was diagnosed for 5/21 patients in the ISD group and 6/36 in VAC group. From those patients, 3 patients in the ISD group and 2 patients in the VAC group had terminal renal insufficiency, which required dialysis therapy.

Liver failure rate was low and was diagnosed in 2 patients in the ISD group and in 1 patient in the VAC group.

Alcohol and nicotine abuses were 2 factors, which played important roles in vascular graft infection development. According to our data, 8/21 patients had histories of alcohol abuse in the ISD group and 11/36 in the VAC group. There was no difference between the groups. Meanwhile, nicotine abuse history was positive for 15/21 patients in the ISD group and 24/36 patients in the VAC group.

The respiratory diseases we analyzed included 2 common respiratory illnesses - bronchial asthma and chronic obstructive bronchitis. The other pathological conditions related to the lungs were rare and involved only a few patients; we opted not to do analysis of these conditions. Bronchial asthma was present in only 1 case in the VAC group, while chronic obstructive bronchitis was present in 10/21 patients in the ISD group and in 16/36 patients in the VAC group.

Cerebrovascular disease is 1 of the additional parameters, which we analyzed to get a general impression about risk factors. Cerebrovascular disease was diagnosed in 7/21 patients in the ISD group versus 11/36 in the VAC group.

Urinary tract infection was rarely present, with only 2 patients in the ISD group and 1 patient in the VAC group with this condition.

In the all of analyzed risk factor parameters, there was no statistically significant difference between the 2 groups. The summary of risk factors is shown on Table 13.

Diabetic foot ulceration is one of the factors related to vascular graft infection. In this study, the number of patients who presented with foot ulcers was very small. We analyzed diabetic foot ulceration according to the Wagner-Meggitt classification (50). All patients had grade 0 up to grade 2 diabetic foot, according to Warner-Meggitt. No patients had grade 3 up to grade 5 ulcers in either group. Diabetic foot ulceration was diagnosed in 7 patients in the ISD group versus 3 patients in the VAC group. Because of the small number of patients, we did not do explicit analysis for each diabetic foot grade. There was no statistical difference between the groups (Figure 6).

Immunosuppression or immunosuppressive medications prolong the healing process and are important risk factors for wound infection. In both analyzed groups, there were only 2 patients who were immunosuppressed at the time of initial operation or when ISD or VAC therapy was began. Both patients who had vascular graft infection and immunosuppression were in the VAC group. One female patient had a history of the chemotherapy for invasive breast carcinoma. This patient presented with acute occlusion of the femoral artery, and for this reason, underwent vascular graft operation. The other patient had the same history of acute ileofemoral occlusion, but the patient was on radiation therapy due to oropharyngeal carcinoma. No patients in the ISD group had immunosuppression.

For endocrine disorders, we analyzed 2 conditions, which play roles in vascular graft infection – hypercholesterolemia and hypolipoproteinemia.

Hypercholesterolemia was a common disorder in both groups, and was diagnosed for 11/21 patients in the ISD group and 19/36 patients in the VAC group. Almost identical results were seen for hypolipoproteinemia, with 10/21 patients in the ISD group and 19/36 patients in the VAC group having this condition. There was no statistical difference between the groups (Figure 7a and Figure 7b).

The other endocrine disorder we analyzed was malnutrition. It has been described as a risk factor for vascular graft infection development and prolonged healing process. The number of patients with malnutrition was small – 1/21 patients in the ISD group versus 4/36 patients in the VAC group. We did not find any statistical difference between the groups with regard to malnutrition.

Operation time

We also did analysis of the operation time. As most of the operations involved combined surgical management, which included revision operation and VAC or ISD therapy initiation at the same time, we decided to analyze common operation time. The operation time ranged from 70 up to 320 minutes, with an average operation time of 167 minutes in the ISD group. For the VAC group, operation duration ranged from 56 up to 280 minutes, with an average time of 155 minutes, with no statistically significant difference between the groups (Table 14a).

The operation time for VAC system change every 72 hours was also analyzed. The operation duration ranged from 25 up to 105 minutes, with an average of 54 minutes (Table 14b).

Laboratory results

Laboratory parameters included serum sodium and potassium levels at the time of initial operation. The hypothesis was that electrolyte imbalance can play a role in vascular graft infection development. The other parameters we analyzed at 3 time points included levels of hemoglobin, leucocytes, and C-reactive protein. The 3 time points included before the initial vascular graft surgery, before the initiation of the VAC or ISD therapy, and before discharge from clinic, or in cases of death, the last available laboratory parameters.

Before vascular graft operation, 15/21 patients in the ISD group had normal sodium levels versus 27/36 patients in the VAC group. Hyponatremia was present in 6/21 patients in the ISD group and 9/36 patients in VAC group (Table 15). The mean sodium level in the ISD group was 138 mmol/L (minimum 131 mmol/L up to maximum 145 mmol/L). In the VAC group, mean sodium level was 137 mmol/L (minimum 128 mmol/L up to maximum 144 mmol/L).

Potassium levels before vascular graft operation in the ISD group were normal for 19/21 patients; 1 patient presented with hyperkalemia and another patient presented with hypokalemia. In the VAC group, 33/36 patients presented with normal potassium levels, while 3/36 patients presented with hyperkalemia (Table 16). The mean potassium level in the ISD group was 4.4 mmol/L (minimum 3.4 mmol/L up to maximum 5.6 mmol/L) versus 4.3 mmol/L (minimum 3.6 mmol/L up to maximum 5.7 mmol/L) in the VAC group.

Total leucocyte level (normal range from 4.4 x 10^9/L up to 11.3 x 10^9/L) was analyzed initially before vascular graft surgery, with a mean level of 10.98 x 10^9/L (range from 3.97 x 10^9/L up to 31.35 x 10^9/L) in the ISD group versus 9.41 x 10^9/L (range from 4.00 x 10^9/L up to 16.40 x 10^9/L) in the VAC group.

The total mean leucocyte level at the time of ISD or VAC therapy initiation was 19.14 x 10^9/L (range from 10.75 x 10^9/L up to 34.98 x 10^9/L) in the ISD group versus 17.01 x 10^9/L (range from 7.24 x 10^9/L up to 30.47 x 10^9/L) in the VAC group.

The mean total leucocyte level at the time of discharge from clinic in the ISD group was 10.37 x 10^9/L (range from 5.18 x 10^9/L up to 24.00 x 10^9/L) versus 10.37 x 10^9/L (range from 4.35 x 10^9/L up to 21.10 x 10^9/L) in the VAC group (Table 17).

The hemoglobin level (normal range from 11.1 g/dl up to 16.4 g/dl) was analyzed initially before vascular graft surgery, with a mean level of 12.8 g/dl (range from 8.8 g/dl up to 16.7 g/dl) in the ISD group versus 11.8 g/dl (range from 7.0 g/dl up to 17.4 g/dl) in the VAC group.

The hemoglobin level at the time of ISD or VAC therapy initiation was 8.5 g/dl (range from 6.1 g/dl up to 11.5 g/dl) in the ISD group versus 8.4 g/dl (range from 6.5 g/dl up to 12.5 g/dl) in the VAC group.

The mean hemoglobin level at the time of discharge from clinic was 10.8 g/dl (range from 7.4 g/dl up to 14.1 g/dl) in the ISD group versus 10.5 g/dl (range from 8.0 g/dl up to 13.7 g/dl) in the VAC group (Table 18).

The C-reactive protein (CRP) levels (normal range is <1.0 mg/dL) were analyzed before vascular graft surgery, with a mean level of 6.8 mg/dL (range from 0.1 mg/dL up to 33.6 mg/dL) in the ISD group versus 2.4 mg/dL (range from 0.1 mg/dL up to 27.7 mg/dL) in the VAC group.

The CRP levels at the time of ISD or VAC therapy initiation was 21.7 mg/dL (range from 9.4 mg/dL up to 44.9 mg/dL) in the ISD group versus 22.0 mg/dL (range from 1.2 mg/dL up to 47.0 mg/dL) in the VAC group.

The mean CRP levels at the time of discharge from clinic in the ISD group was 4.4 mg/dL (range from 0.2 mg/dL up to 31.5 mg/dL) versus 3.7 mg/dL (range from 0.1 mg/dL up to 21.4 mg/dL) in the VAC group (Table 19).

Patients with multiple infections

The presence of another infection, whether chronic or acute, usually decreases immunity and can be one of the risk factors for vascular graft infection development. We checked if the patient has another infection present at the time when ISD or VAC therapy was initiated. In both groups, there were 4 patients who had another infection present when ISD or VAC therapy began. We did not perform detailed analysis of infection status because of the small number of patients. The most common infection was respiratory airway infection or chronic respiratory airway infection exacerbation, which was present in 2 patients in the ISD group versus 3 patients in the VAC group. two patients in the ISD group had urinary tract infection versus 1 patient in the VAC group (Table 20).

VAC versus ISD therapy failure

Our analysis included initial ISD or VAC therapy failure. Therapy failure was defined as the use of other additional vascular graft infection management methods, as well as repeat VAC therapy, or in case of ISD failure, initiation of VAC therapy. In cases of failure, we no longer analyzed the effect of subsequent VAC therapies or other management methods. In both groups,

there were 3 patients who did not experience any beneficial effect from the initial VAC therapy or ISD therapy. In fact, in the ISD group, 2/3 patients with therapy failure died at the end of the therapy, while in the VAC group, 3/3 patients with initial therapy failure died. One patient who developed ISD failure was subsequently managed with VAC therapy.

VAC versus ISD economical aspect

We analyzed the ISD and VAC therapy costs after therapy initiation. Calculation of material costs were done for 2 periods – 1 week after beginning therapy, and a 3-week period.

Because VAC therapy duration can last up to 3 weeks, we calculated costs for a maximum 3-week time period, to show the economical difference between both therapy costs.

The therapy costs were based on material costs for a 1-week period for the ISD therapy and for a maximum of 3 weeks for the VAC therapy.

In the ISD group, the initial material equipment and costs were 20.50 € per patient. The used material and material costs are summarized in Table 21. Daily material costs without personal costs were 4.36 € (day 2 to day 5). The material costs on day 6 included only NaCl irrigation, and on day 7, drainage was removed. Total costs of the ISD therapy was 38.83 €.

The initial VAC therapy costs depended on the surgical wound area. Based on surgical wound area, 3 calculations were done - for small surgical wounds with a size of 10 cm x 8 cm x 3 cm, medium wounds 20 cm x 12.5 cm x 3 cm, and large wounds 25 cm x 15 cm x 3 cm. The therapy initiation of small wounds costs 276.08 €, medium wounds 287.91 €, and large wounds 293.44 € (Table 22).

The Contilia vascular division standard included VAC system changes every 3 to 4 days. As the VAC system can be used for up to 21 days, the calculations were performed for a 1-week and 3-week time period. The material costs for VAC system change for small wounds were 73.32 €, medium wounds 79.06 €, and large wounds 84.60 € (Table 23). At the end of the therapy, the wound was closed; the material costs for wound closure was 13.99 € (Table 24).

The costs between the groups for lower extremity infected vascular graft therapy showed a statistically significant difference ($p<0.05$). For a 1-week period, the difference between the ISD and VAC therapies were 324.56 € for small wounds, 342.13 € for medium wounds, and 353.02 € for large wounds (Table 25 and Figure 8).

Moreover, if VAC therapy was continued for 21 days, the material costs for the VAC therapy increased dramatically in comparison with the ISD therapy. If the patient's VAC therapy was done for 3 weeks, the material costs reached 729.99 € for small wounds up to 815.03 € for large wounds (Table 26 and Figure 9). Patients need to add hospital stay costs, personal costs, and VAC system change costs, as well. That all results in a much more expensive therapy cost if VAC therapy is used. However, VAC therapy may be performed for patients with more serious vascular graft infections with larger operative wounds, and management of such patients per se costs more than management of patients with not so serious vascular graft infections.

Discussion

Lower extremity vascular graft infections are not very common. The management of an infected vascular graft can be very challenging, and usually requires multiple management methods and a multidisciplinary approach, which requires large expenses.

Lower extremity vascular graft infection rates are 1% up to 5%, based on different studies (22, 49). Our department results were very similar: from 6232 patients who underwent lower extremity vascular graft surgery, 67 patients developed vascular graft infection, which is 1.07%. The downside is that we reviewed the patient's histories only for a 12-month period; thus, it is theoretically possible that there are cases of late vascular graft infection that we missed.

Different classification methods have been used to classify vascular graft infection grade. The two most popular classification methods are the Szilagyi and Samson classification. The Szilagyi classification is not as detailed when compared with the Samson classification, which analyzes the infected area in a more detailed manner, with conventional treatment for Samson classification grades 1 and 2, and surgical treatment for Samson grades 3 and 4 (80).

Krejči et al. in their study analyzed patients with inguinal vascular graft infection, and to classify patients, they used the Szilagyi classification. In their study, 75% of all patients were Szilagyi grades I and II and 25% of patients were Szilagyi grade III (57). One other study from Dosluoglu et al. showed Szilagyi grade III in 46% of all cases and Grade II and I in 54% of cases (32). This shows how broad the variety of vascular graft infection is. In our study, Szilagyi grades I and II were seen in 66.7% of patients in the ISD group 61.1% of patients in the VAC group. Grade III infection was noted in 33.3% of the ISD group and 38.9% of the VAC group. These corresponds to average results compared to other studies.

Amputation rates in lower extremity vascular graft infections differs a lot in the published studies. The reason for that is its multifactorial nature, which influences amputation rates. Sousa et al. analyzed 18 patients who developed vascular graft infection after femoropopliteal bypass surgery in the time period from 2007 up to 2012. In the study, amputation rates were as high as 55% (91). Another study done by Acosta et al. analyzed amputation rates using different management aspects - patients with vascular graft infections who underwent VAC therapy as a treatment method. In the 7-year period, they included 37 patients with lower extremity vascular graft infections, with a follow-up time of 15 months. All patients underwent VAC

therapy and resulted in amputation rates of 33% (3). In other studies, amputation rates depended on the time after initial graft operation, and on infection development and management options; all these aspects resulted in amputation rates, which ranged from 18 up to 53% (13, 94).

Our amputation rates showed similar results. In the VAC group, amputations rates reached 27.8%, while in the ISD group, it was 33.3%. The study of Acosta et al. and our study clearly showed the benefit of VAC or ISD therapy in vascular graft infection management.

Our study population had a mortality of 5/57 patients. The 2 patients who underwent ISD therapy management died at the end of therapy. One patient who underwent ISD therapy had therapy failure and was switched to VAC therapy. The 3 patients in the VAC group died during the therapy period or at the end of therapy, which showed similar results to the study of Svensson, with a 66% mortality in failure cases. Overall mortality in our study was approximately 10% in all included patients, which correlates with other published studies.

There were 14/21 patients in the ISD group and 21/36 patients in the VAC group who were discharged from hospital after successful treatment. These patients were evaluated in outpatient department, however follow up period differs a lot, and we could not exclude situation that some of patients continuing they follow up in other hospitals.

There are a wide spectrum of a microbiological species, which induce vascular graft infections, which means that broad-spectrum antibiotic therapy needs to be initiated in cases of infection, if the agent is not known. Calligaro et al. in their study analyzed 141 patients with lower extremity vascular graft infection. As in this retrospective study, patients were collected from over a 15-year period, and analyzed microbiological variability for early and late vascular graft infections. The most frequently isolated bacteria were Staphylococcus aureus and Pseudomonas aeruginosa. Other common bacteriological species included Staphylococcus epidermidis, Streptococcus faecalis, Proteus species, and Escherichia coli (16). Another study done by Siracuse et al. analyzed 19 patients in series in a 10-year period. The most common isolated bacteria included Staphylococcus epidermidis (37%), Staphylococcus aureus (26%), Enterococcus species (10%), and MRSA (5%) (84).

There is an increasing tendency for MRSA to induce vascular graft infection, especially in the last decade. Herrera et al. reported that the most common bacteriological species isolated from graft infection included Staphylococcus epidermidis, Pseudomonas aeruginosa, Escherichia coli, and MRSA (44).

In our study, we had equal tendencies. In the VAC group, the most common isolated bacteria was MRSA, Staphylococcus aureus, and Enterococcus faecalis. In the ISD group, the 2 most common isolates were Staphylococcus aureus and MRSA. Pseudomonas aeruginosa was isolated in 2.8% of cases in the VAC group and in 9.7% of all cases in the ISD group.

Basically, our study showed that MRSA is continuing to become a more frequently isolated organism from infected vascular graft wounds. The frequency of other bacteria showed the same kind of results as the literature.

Antibiotic therapy is always a widely debated topic, especially in the last decade, because of rising resistance against antibiotics. Before the initial operation, all patients were given a single shot of the antibiotic Cefuroxime, or in the case of penicillin allergy, Clindamycin. Cefazolin is another antibiotic of choice because Staphylococcus aureus and Streptococcus epidermidis are common infectious agents (53). In the study by Hasselgren et al., they analyzed the effect of Cefuroxime. Significantly reduced surgical site infection was shown compared to the placebo group (43).

In cases of vascular graft infection development, escalation of antibiotic therapy is usually done. Our aim was to give antibiotics according to the bacteriological results and antibiogram; however, results from the laboratory were not always readily available. In most of the cases, the commonly used antibiotic was Cefuroxime, used in 44.4% of the VAC group and 47.6% of the ISD group. This antibiotic was used as a single shot antibiotic for the initial operation, as its antibiotic spectrum covers most of the common bacterial species causing vascular graft infections. The second most common antibiotic in both groups is Vancomycin, used in 38.9% of the VAC group and 23.8% of the ISD group, which correlated with the bacteriological results from our study – 14.3% MRSA isolates in the ISD group and 41.7% MRSA isolates in the VAC group ($p<0.05$). This is the only statistically significant difference between groups in bacteriological analysis. After diagnosis of vascular graft infection, Vancomycin was given to patients with specific risk factors, such as long hospital stay prior to operation or MRSA infection in other locations.

Erb et al. reported a series of 10 patients with peripheral vascular graft infection. Empirical antibiotic therapy included administration of Amoxicillin clavulanate in 70% of all cases, and Ceftriaxone in 20% of cases. In this study, Vancomycin was not used as empiric therapy (34). A Penicillin group antibiotic, especially Piperacillin/tazobactam, which covers anaerobes and Bacteroides fragilis, is recommended as the therapy of choice for these patients (78). There

have been controversial discussions about the use of carbapenem antibiotic in cases of vascular graft infections, because of the rising number of carbapenemase-producing Enterobacteriaceae (69). Hodgkiss-Harlow et al. did analysis of surgical site infection in aortic surgery. They reported an increase in number of MRSA infection in the last decade. In this study, similar to our study, their preferred primary antibiotic is a first or second generation cephalosporin. Additionally, they suggested coverage of MRSA in case of infection develops. In our institution, for most cases, we used Vancomycin or Linezolid to cover for MRSA; others, such as Hodgkiss-Harlow et al., prefer Daptomycin as the antibiotic of choice, because it produces rapid, concentration-dependent bactericidal activity to all Gram-positive bacteria, including MRSA, and controversially, shows better results in penetrating bacteria biofilms and killing bacteria in stationary-phase growth compared to Vancomycin and Linezolid (46).

Red blood cell (RBC) transfusions were analyzed in 2 aspects: during VAC or ISD therapy initiation, and within 48 hours after the VAC or ISD therapy was initiated. The RBC transfusions during the operation were associated with bleeding when VAC or ISD therapy initiation was combined with large infected wound debridement and surgery on the infected vascular graft. However, many patients who receive RBC transfusions already had a low hemoglobin level initially. This can be explained by many factors, with one of the main factor being infection or septic complications after initial vascular graft surgery, which is associated with lower hemoglobin levels. The other factors for anemia are initial vascular graft surgery and its association with loss of blood, volume therapy, and the systemic inflammatory response.

There are not many studies that analyze RBC transfusions in the setting of VAC or ISD therapy initiation. Moreover, there are no studies available that analyze RBC transfusion rates specific for lower extremity vascular graft infection management with VAC or ISD therapy. There are some general studies from cardiac surgery that report controversial opinions, stating that VAC therapy is associated with higher hemolysis and resulting in larger RBC transfusions postoperatively (24). On the other hand, other studies report that there are no differences with regard to hemolysis in patients with VAC drainage or ISD therapy (58).

The study from O'Keeffe et al. is one of the few studies that analyze RBC transfusions in lower extremity vascular surgery. Unfortunately, this study reported about primary operations, and not about transfusion management related to vascular graft infection reoperation using VAC or ISD therapy. They reported on the correlation between RBC transfusion and increased morbidity and mortality postoperatively. Moreover, in the cases of low hemoglobin level of 7

g/dl but with no active bleeding, there has been no evidence that RBC transfusion will give patients the benefit of faster recovery (73). In our study, before initial vascular graft operation, mean hemoglobin level was 12.8 g/dl and 11.8 g/dl in the ISD and VAC groups, respectively. The average hemoglobin level at the time of VAC or ISD therapy initiation was 8.5 g/dl. Our division hospital anesthesia team usually begins RBC transfusion if hemoglobin level is ≤8 g/dl. The hemoglobin decrease during the operation or postoperatively was obviously multifactorial; one of main reasons is intraoperative volume therapy and hemodilution. The persistent anemia preoperatively before revision operation in combination with VAC or ISD therapy explains why high blood transfusion rates are over 60% in both groups.

Previous vascular graft bypass operations and future revision operations or vascular graft bypass reoperation definitely is challenging, because of surgical difficulties and increased operation time, which is associated with increased risk of vascular graft infection. In our study, 14/57 patients already had a previous vascular graft bypass operation. These patients had longer operation times, which correlates with longer exposure of the open surgical wound to the environment, possible hypothermia during the procedure, and inadequate dosage of antibiotics. These are important factors that increase the risk of vascular graft infection development (38).

As mentioned, we analyzed the patient's clinical histories to find out possible infection risk factors. As this topic has been widely discussed in many publications, we analyzed some well-known risk factors and added several extra factors, which could possibly have influence in vascular graft infection development.

There are some publications that say that the risk for vascular graft infection increases if a patient has had previous surgery with implantation of foreign material in the vascular graft operation site. In our study, we did not find any statistically significant correlation between both groups related to previous surgery with implantation of foreign material. However according to the study population 20/57 patients who had foreign material implanted, developed vascular graft infections (29, 100).

Endocrine disorders, such as hypercholesterolemia and hypolipoproteinemia, usually have a negative effect, not only to the normal vascular system, but also to implanted vascular grafts. Walton et al. in 1986 reported about lipid deposition in the vascular graft, which resulted in graft stenosis and calcification, and vascular graft aneurysm formation (106). The other study which showed the negative effects of hypercholesterolemia and hypolipoproteinemia is the study of Abbruzzese et al., where they analyzed the benefit of statin therapy in patients after

inguinal vascular graft operation. This study included 172 patients who underwent vascular graft surgery, and the subjects were divided in to 2 groups. The group given statin therapy showed 3.2 times better graft preservation compared to the control group (1). This confirms the harmful effect of hypercholesterolemia and hypolipoproteinemia on vascular graft walls.

In our study, patients in both groups with confirmed diagnosis of hypercholesterolemia and/or hypolipoproteinemia were already started on statin therapy before or after surgical vascular graft implantation. Our study showed that hypercholesterolemia was diagnosed before initial vascular graft surgery in 47.6% of the ISD group and in 52.8% of the VAC group. Hypolipoproteinemia was diagnosed in 52.4% of patients in the ISD group and 52.8% of patients in the VAC group. These results were better than those of the study by Hirsch et al. They report that hypercholesterolemia was present in more than 60% of all patients with PAD; however, it should be mentioned that their study analyzed PAD patients, not those who underwent vascular graft surgery specifically (45).

Hospital lengths of stay differ depending on the treatment options used to treat vascular graft infection. The length of hospital stay does not differ from data published in other studies. In previous studies, hospital length of stay varies depending on the infection grade, other comorbidities, and the isolated bacteriological species. For this reason, the hospital stay varies, from a median of 45 days up to 85 days (32). Most of the patients' average length of hospital stay was 51 days (10, 102). Our study shows lower than average hospital lengths of stay, with an average of 34.2 hospital days in the ISD group and 37.7 days in the VAC group. This is comparable with other studies that used VAC therapy for vascular graft infection treatment. The analysis of ISD therapy and its impact on the length of hospital stay was not possible, as there are no studies, which analyzed length of hospital stay using ISD therapy for inguinal vascular graft infections.

The VAC therapy duration was 14.8 days. This was similar to other studies, with average VAC therapy duration of 16 days up to 21 days (10, 102).

Vascular graft infection factors are multivariable, and in many cases, the presence of multiple factors can increase the risk of infection development. However, there are some risk factors that are more frequently seen in patients with vascular graft infections.

It is important to point out that risk factors need to be separated into 2 categories – the risk factors for PAD development, and the risk factors for vascular graft infection, which develops after the operation. It is also necessary to mention that there are some of risk factors, which can

affect PAD development, as well as play a role in vascular graft infection development. Such factors include atherosclerosis and hypercholesterolemia, diabetes mellitus, and immunosuppression, which prolongs the healing process and decreases immune response to bacterial colonization. Other risk factors that have an influence on vascular graft infection development after surgical intervention are operation length, perioperative antibiotic therapy, operation field disinfection, and the size of the operation field (83).

Diabetes mellitus is a very common disorder that damages the blood vessel wall and also has an effect on vascular graft infection development, not only in the short term, but also in the long run. Our study showed that 9/21 (42%) patients in the ISD group and 14/36 (38%) patients in the VAC group had diabetes. Other studies that have analyzed vascular graft risk factors have shown similar results. The study of Siracuse et al. showed that diabetes mellitus was diagnosed in 230/460 patients who received lower extremity vascular graft operations for PAD (90). Another study by Mirzaie et al. which analyzed aortofemoral vascular graft infection showed that diabetes mellitus before initial vascular graft operation was diagnosed in 45.4% male patients and 18.1% of female patients. This study showed a difference in gender, which can be explained by the small number of patients included in the study (11 patients) (65). Diabetes mellitus plays an important role on the development of vascular graft infection, as confirmed by the study of Koutsoumbelis et al., where they analyzed and confirmed that diabetes mellitus has a negative effect on a patient's immunity, increasing the risk for surgical site infection development, as well as increasing the time for surgical wound healing (56).

Another factor that plays an important role is renal insufficiency. There are no clear pathophysiological mechanisms on how renal insufficiency can affect PAD development, and in the case of surgery, how renal insufficiency increases the risk of infection. One hypothesis is that renal insufficiency has a negative effect on the cardiovascular system, with atherosclerosis formation and vascular remodeling. The association with atherosclerosis is well-documented as one of the main risk factors for PAD. Another mechanism that could have a negative effect include increased inflammation biomarker production by patients with renal insufficiency. Biomarkers, such as C-reactive protein or interleukin-6, play a role in atherosclerosis development and development of PAD. Future detailed studies need to be done in order to understand the effect of renal insufficiency on vascular graft infection development after surgery (4, 48, 74).

The previously mentioned study of Siracuse et al. also showed that 16% of patients who develop vascular graft infection have renal insufficiency. From the epidemiological point of view, our study has similar epidemiology, with 23% of patients having renal insufficiency in the ISD group and 16% in the VAC group (90).

Alcohol and nicotine abuse are very well-known risk factors for atherosclerotic changes in blood vessels and are indirect factors for vascular graft infection. In our study, 71% in the ISD group and 66% in the VAC group had documented nicotine abuse at the time of initial vascular graft surgery. The study by Siracuse et al. showed that 38% of patients had a history of nicotine use or active nicotine abuse (90). Another study done by Hallihan et al. showed 92 (54%) from 170 patients who underwent lower extremity vascular graft surgery had a history of nicotine abuse (39). These 2 studies showed that nicotine abuse, as well as alcohol abuse, varies a lot in different studies. According to most of the studies, nicotine has a negative effect not only on the cardiovascular system, but also on the implanted vascular graft. This can be seen in the review study by Willigendael et al., where they analyzed 29 studies that included information about the effect of nicotine on vascular graft failure after operation. The study showed significant differences between smokers and non-smokers who underwent vascular graft surgery (107).

As already mentioned, the same relationship is seen with alcohol consumption and graft infection. Alcohol in low dosages can actually reduce cardiovascular risk; however, if alcohol is used in higher dosages, it has a negative effect on the cardiovascular system, and in case of vascular graft surgery, on the vascular graft. Singh et al. did a retrospective study for an 8-year period, where they included 14788 patients who underwent lower extremity vascular graft surgery. The patient's characteristics revealed that 11.6% of all patients had alcohol consumption in the history (87). In our study, 38% of all patients in the ISD group and 30% of all patients in the VAC group had alcohol consumption in their history. Another study done by Antonios et al. analyzed patients who underwent vascular graft surgery and had postoperative vascular graft failure. This study showed that alcohol consumption was seen in 11.9% of the vascular graft failure group and 6.9% in the control group (5). The mentioned study confirms that alcohol use increases the risk of vascular graft infection development when compared with the control group. The differences seen with regard to alcohol consumption between studies can be explained by the fact that there is no definite criteria for alcohol consumption and different authors use different interpretations of the term. In general, alcohol consumption

refers to high dose of alcohol use daily; however, the amount of alcohol used varies between studies.

Interestingly, cerebrovascular disease may be a risk factor for vascular graft infection development. Cerebrovascular diseases, such as ischemic strokes, are usually connected with development of atherosclerosis. The damaged vascular system due to atherosclerosis is a risk factor for PAD. In the results, if the cause for atherosclerosis, which includes the cerebrovascular system, are not reduced or liquidated, then the risk for vascular graft infection development becomes higher. The study by Hallihan et al. showed that cerebrovascular disease was diagnosed in 11% of patients who underwent lower extremity vascular graft surgery (39). In comparison with our study, cerebrovascular disease was documented for 7/21 (33%) patients in the ISD group versus 11/36 (30%) patients in the VAC group.

ISD therapy as a successful vascular graft infection management method has already been described in 1980, when Popovsky et al. did an analysis of management methods for preserving infected grafts (77). ISD therapy was widely used in the past in cardiothoracic surgery for mediastinal infection and chronic sternal infection, but even in these studies, they failed to analyze the economic aspects of this treatment (72).

ISD therapy can be used to manage not only chronic infections, but also acute surgical wound infections, as well. In cases of infected wounds, depending on the irrigation volume, it has also been associated with acceptable results (88).

One of the explanations why ISD therapy as a management method is not analyzed from the economical aspect is because of its obviously low material costs, as there are no modern technologies involved.

Thus, ISD can be used for small wounds that can be closed in a surgical manner. The material costs and personal costs for ISD therapy will be cheaper than those for VAC therapy, which uses commercially available and expensive VAC devices.

Our study reports on the differences in the costs of negative wound pressure therapy, as well as in the outcomes of different devices used for surgical site infection treatment. In our department, we are using vacuum assisted devices (VAC®), which is one of most popular, and according to the study by Law et al., is cheaper compared to other negative wound pressure therapy devices (59).

We did calculations of graft infection management using the VAC or the ISD for a 1-week period and a 3-week period. Basically, the calculation analysis was done for a 1-week period, as the ISD therapy duration in our division is 1 week. VAC therapy can be done for a longer period of time, which will increase management costs. For this reason, we also did a 3-week cost analysis, to show the VAC treatment cost in this period. The 3-week period was used because our results showed that maximal VAC therapy duration was 24 days. In addition, subsequent VAC therapy management in our study patients was possible; however, we did not analyze these anymore.

ISD therapy was used only once in vascular graft infection complex therapy management. If the therapy results were ineffective, we switched to other management methods, which included VAC therapy.

Unfortunately, VAC therapy failure in vascular graft infection management has been reported. Svensson et al. in their study reported about 33 vascular graft infections that were managed with VAC therapy. Six infected wounds or 18% of the infected vascular grafts that were managed with VAC therapy were unsuccessful. Of those 6, 4 patients died at the end of therapy (94). Another study done by Berger et al. showed VAC therapy success rate to be 82% of managed cases, which is more or less similar to the results of Svensson et al. It must be mentioned that in the study of Berger et al., the study population showed 100% survival for a follow-up time of 380 days (10).

Our study revealed that 3 patients in the ISD group and 3 patients in the VAC group encountered therapy failure. This resulted in an 8.3% treatment failure rate for the VAC group and a 14.2% failure rate in the ISD group. Our study showed better outcomes than those mentioned previously; we believe that there is a multifactorial influence that is important in VAC failure, specifically the combination of the bacteriological species causing infection, the stage of infection, antibiotic therapy, and other comorbidities.

The treatment cost analysis plays a very important role especially in the last few decades, where medical treatment costs have risen tremendously. Because of its multidisciplinary approach, long hospital stay and operative management, the cost of vascular graft infection treatment are very high. At the same time, not many studies analyze the economical aspect of vascular graft infection management. Many studies generally state that graft infection management is very expensive, without including the specific treatment cost analysis (76, 89).

VAC therapy can be applied in chronic surgical wound infection treatment. There are many studies analyzing the economic aspects of VAC therapy in different surgical fields. For example, an interesting study published by Mokhtari et al. included 38 patients who underwent coronary artery bypass surgery and developed deep sternal infection after initial operation, which was managed with VAC therapy. The coronary artery bypass operation costs were 17574 USD, and in the case of infection, the treatment costs rise to an average of 26 670 USD. In severe infection cases, these costs reached up to 60 546 USD. Those results showed how tremendously high the costs can be if surgical site infection develops postoperatively (66).

VAC therapy is an expensive infected wound treatment method. However, in spite of its high costs, VAC therapy shows benefit in faster management of infected wounds, which results in lower treatment costs when compared with other infection management methods. This is shown in the study of Vuerstaek et. al, where they stated that VAC treatment reduced hospital costs because patients with infected wounds treated with VAC were discharged 29 days after admission, in comparison to 45 days in patients whose wound was managed in another way (104).

Svensson et al. analyzed the VAC therapy costs in patients with lower extremity vascular graft infection. From the 33 patients who were included in the study and were managed with VAC therapy, the median VAC therapy treatment costs were 1 299 € (from 210 € up to 7 416 €), with overall median treatment costs of 26 022 €. The average duration of VAC treatment was 20 days (from 3 up to 119 days).

In our study, we analyzed the period of up to the 3 weeks; this means that in day 21, our treatment costs, depending on the surgical wound area, can reach 815 €. Minimal VAC therapy treatment costs 276 €, which is more or less equal to the results of the study of Svensson et al. Our study did not include costs that were linked to the patient's stay in the ICU or vascular surgery ward, as well as revision operation costs, which are more or less equal for both groups.

Overall, there are few information available about the economical aspect of ISD therapy. Although this therapy method is well-known historically, there are no publications that looked at the economical aspect of this therapy method until now.

Conclusions

Lower extremity vascular graft infection is a rare but serious condition, which is associated with a long hospital stay, increased mortality, and has a negative effect on the patient's life quality. Moreover, vascular graft infection management is linked to high treatment costs.

Risk factors, which can increase the likelihood of vascular graft infection development, are multifactorial. Risk factors with a negative effect on the implanted vascular graft include nicotine and alcohol abuse, which are important factors for atherosclerotic changes in the vascular system. Other important factor include diabetes mellitus, which is not only associated with atherosclerotic changes, but is also linked to decreased immunity and surgical wound healing. The data confirms the same risk factors that have been analyzed in other studies of lower extremity vascular graft infections.

Our data analysis showed that not only traditional well-known risk factors play roles in vascular graft infection development, but other factors, such as the presence of hip prosthesis, osteosynthesis with plate or screws, and malnutrition or electrolyte imbalance, may result in infection, as well. Future prospective studies with larger patient and control groups need to be performed to confirm this.

The treatment for vascular graft infection includes different options; in the last two decades, one promising treatment method has become popular: the VAC therapy. Another modified therapy option includes ISD therapy.

Both therapy options have good results in lower extremity vascular graft infection treatment. The differences between therapy results have not been seen and in the most cases, both therapies show successful results, in combination with antibiotic therapy and, if necessary, surgical treatment.

VAC therapy compared with ISD therapy showed no statistical difference in hospital stay.\. Nonsignificant difference between groups in the hospital days are linked to different maximal therapy time in the ISD and the VAC groups.

The amputation rates between the groups showed that amputation rates are higher in the VAC group when compared with the ISD group but without any statistical significance. The same results are seen in the mortality rates, which were slightly higher in the VAC group. For this parameter, no statistical significance between the groups were seen, as well.

ISD therapy is more cost-effective in comparison to VAC therapy and showed major benefits in the economical aspect when both treatment costs were analyzed. Moreover, ISD therapy is simple to apply and requires minimal equipment to be performed when compare with VAC therapy, which requires more technological skills from the surgeon.

The treatment period time is shorter in the ISD therapy group compare to the VAC therapy group.

The negative aspect of ISD therapy is its limitation for vascular graft infections. Specifically, this type of therapy can be used only for relative small wounds where wound closure is possible. For vascular graft infections combined with surgical tissue infections that require wound tissue debridement resulting in large wound areas with no options to close the wound, ISD therapy cannot be performed. Other negative aspect include allergically reaction on iodine. In such case, the VAC therapy is superior to the ISD therapy, because of iodine containing disinfection liquid used in wound drainage.

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Figures

Figure 1

Gender Characteristics of VAC vs. ISD Group

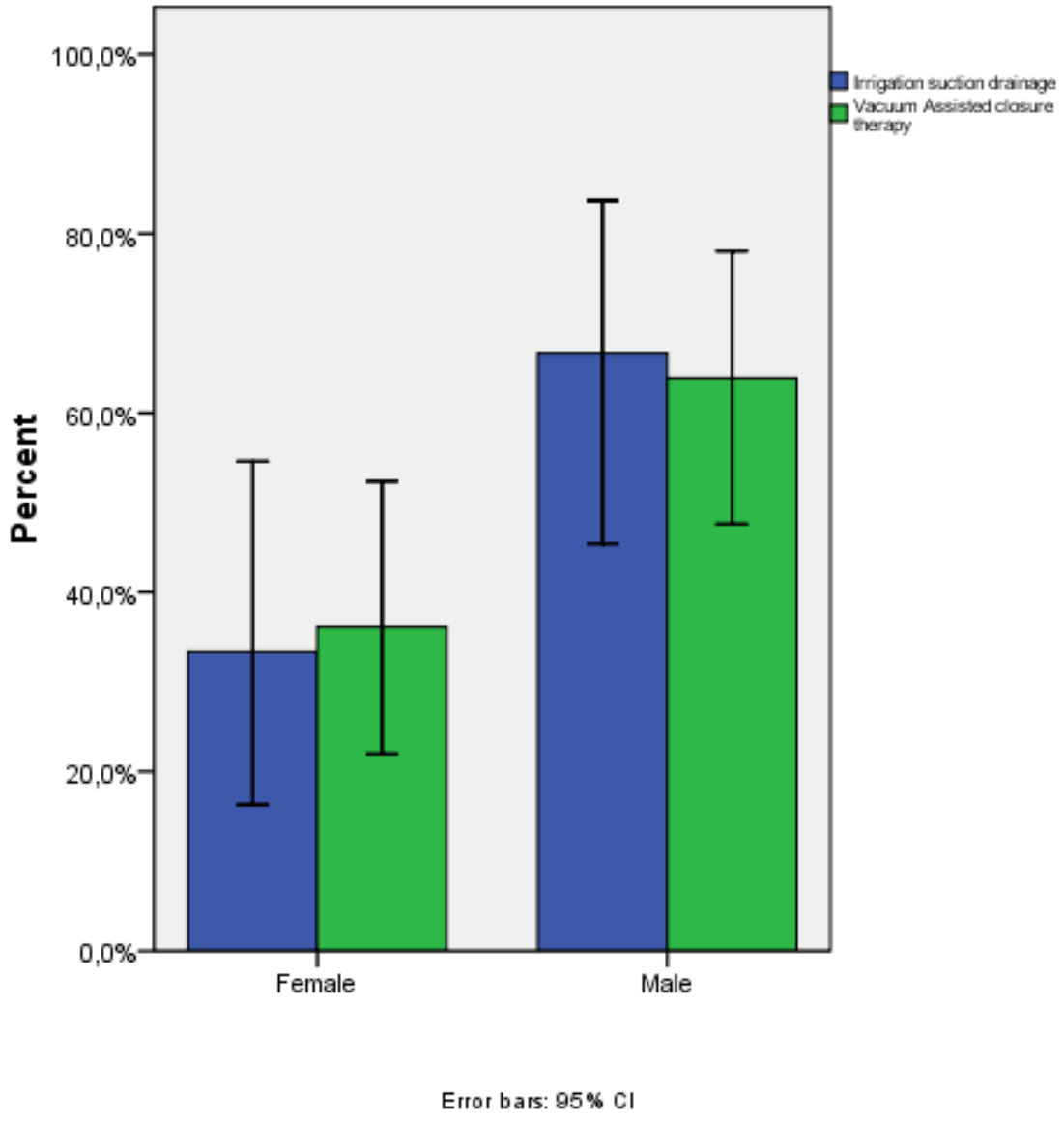


Figure 2

Anatomical Location of Infection in VAC vs. ISD Group

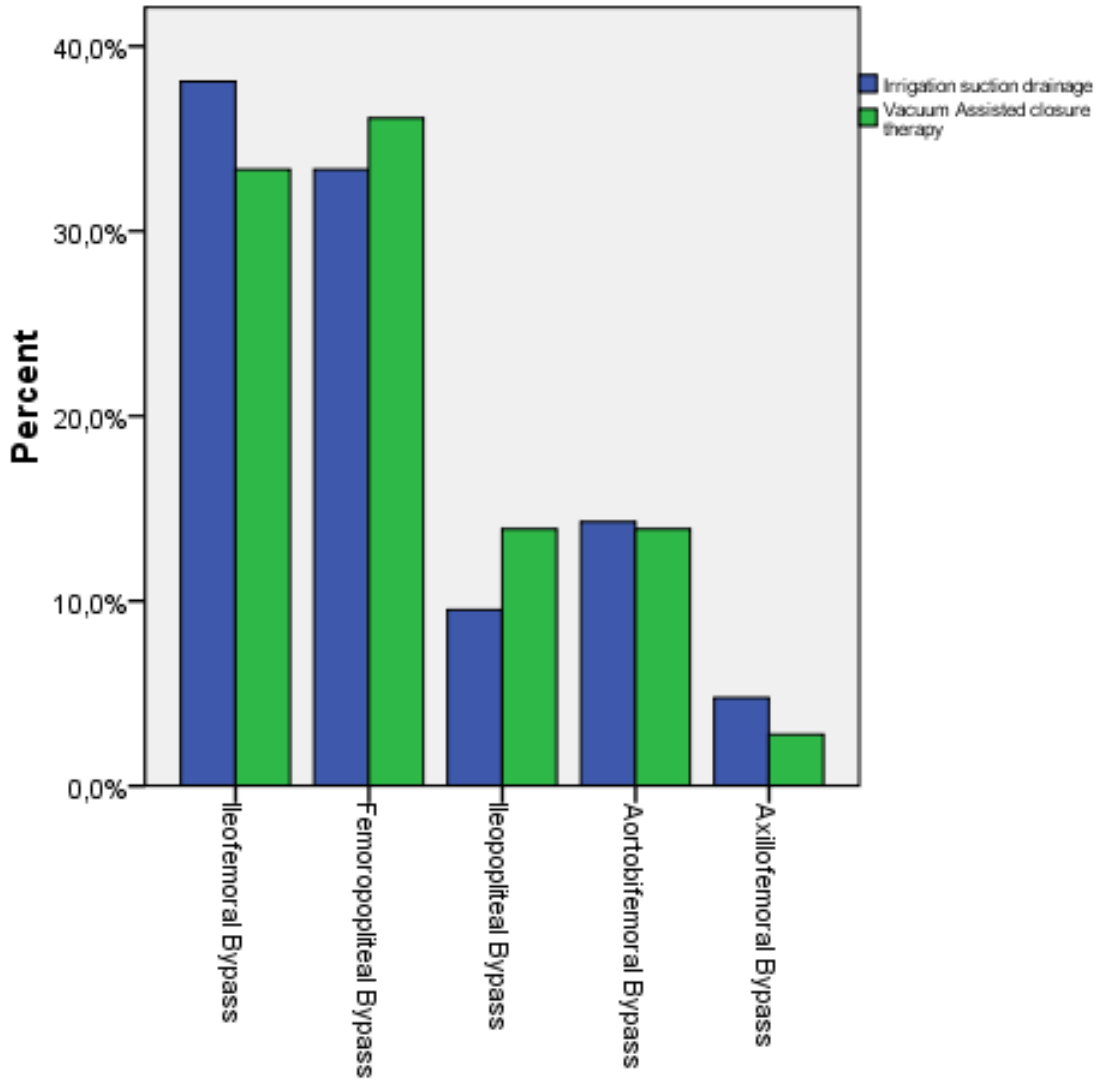


Figure 3

Previous Ipsilateral Vascular Bypass Graft Surgery in VAC vs ISD Group

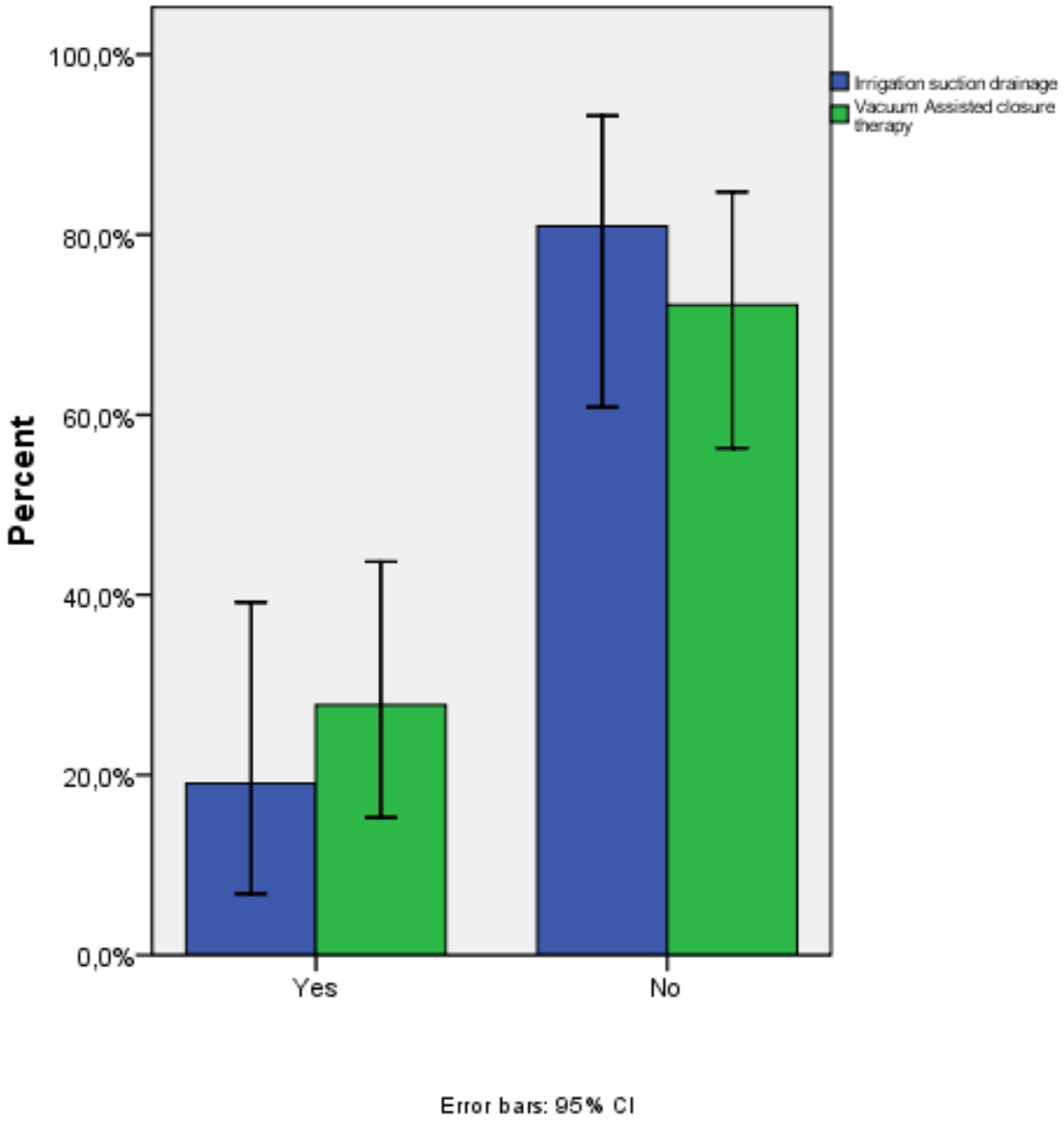


Figure 4

Foreign Material in the Ipsilateral Site

of Vascular Graft in VAC vs. ISD Group

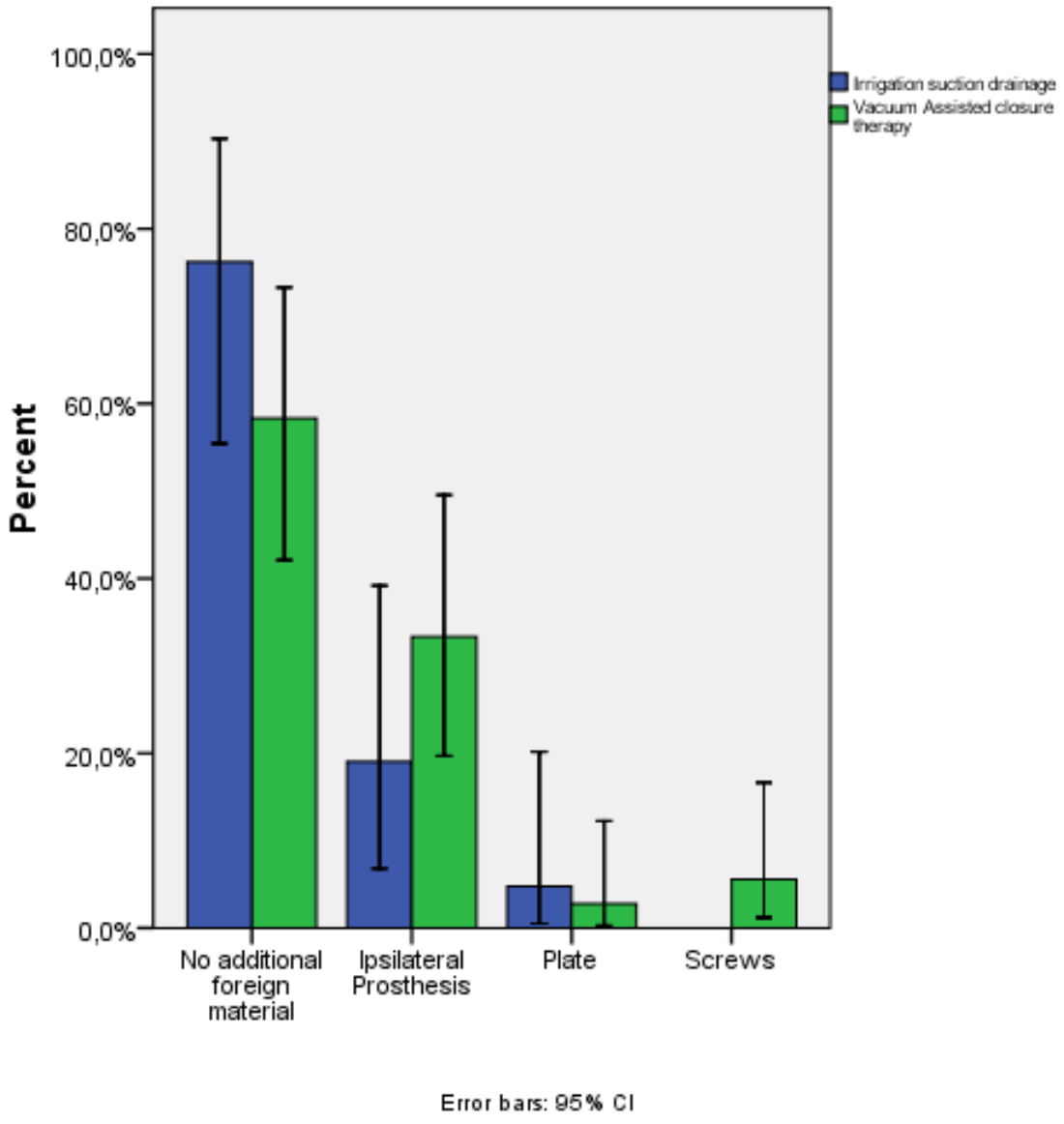


Figure 5

Clinical Outcomes of VAC vs. ISD Group

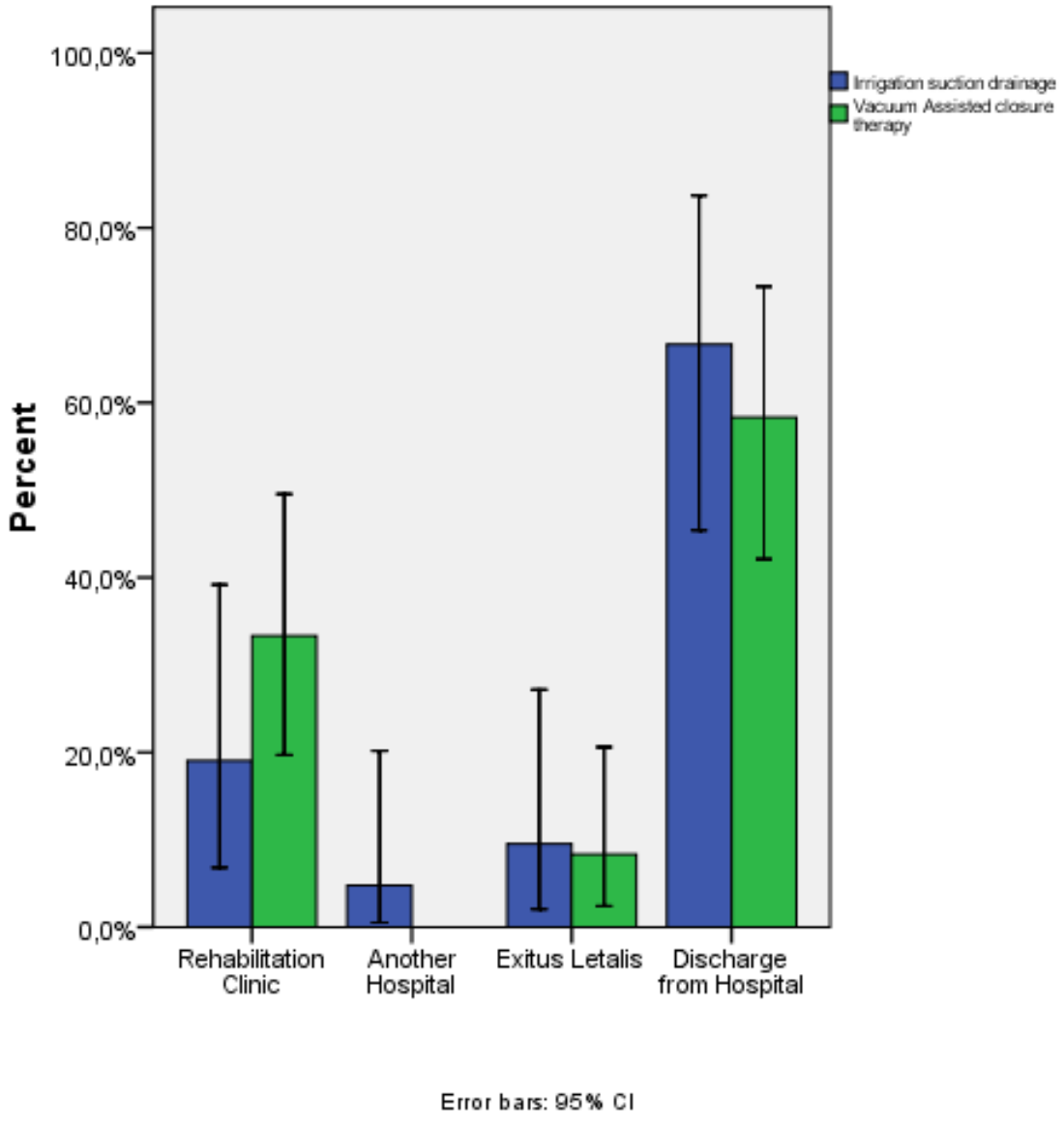


Figure 6

Diabetic Foot in VAC vs. ISD Group

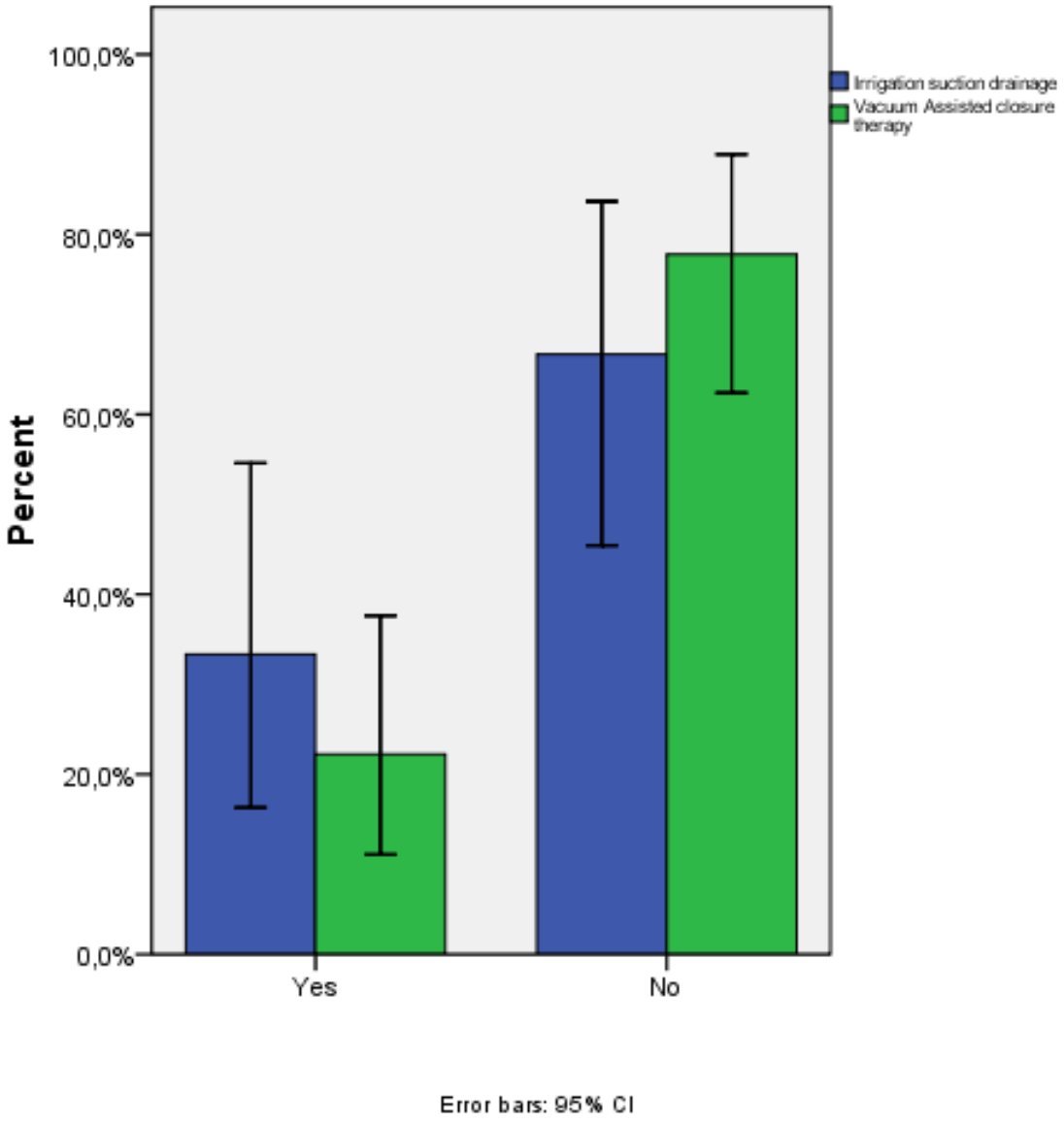


Figure 7a

Endocrine Disorders in VAC vs. ISD Group

Hypolipoproteinemia

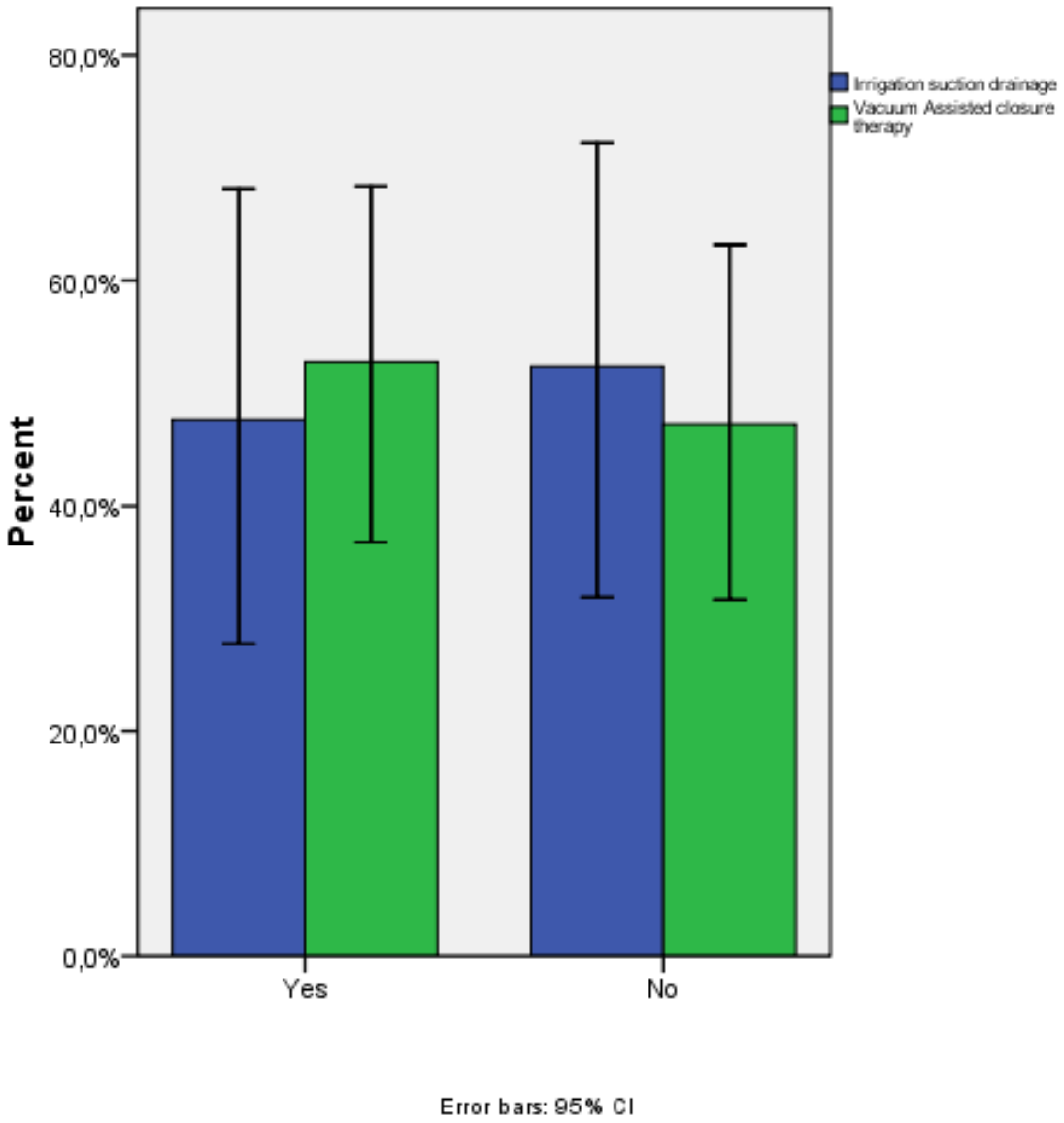


Figure 7b

Endocrine Disorders in VAC vs. ISD Group

Hypercholesterinemia

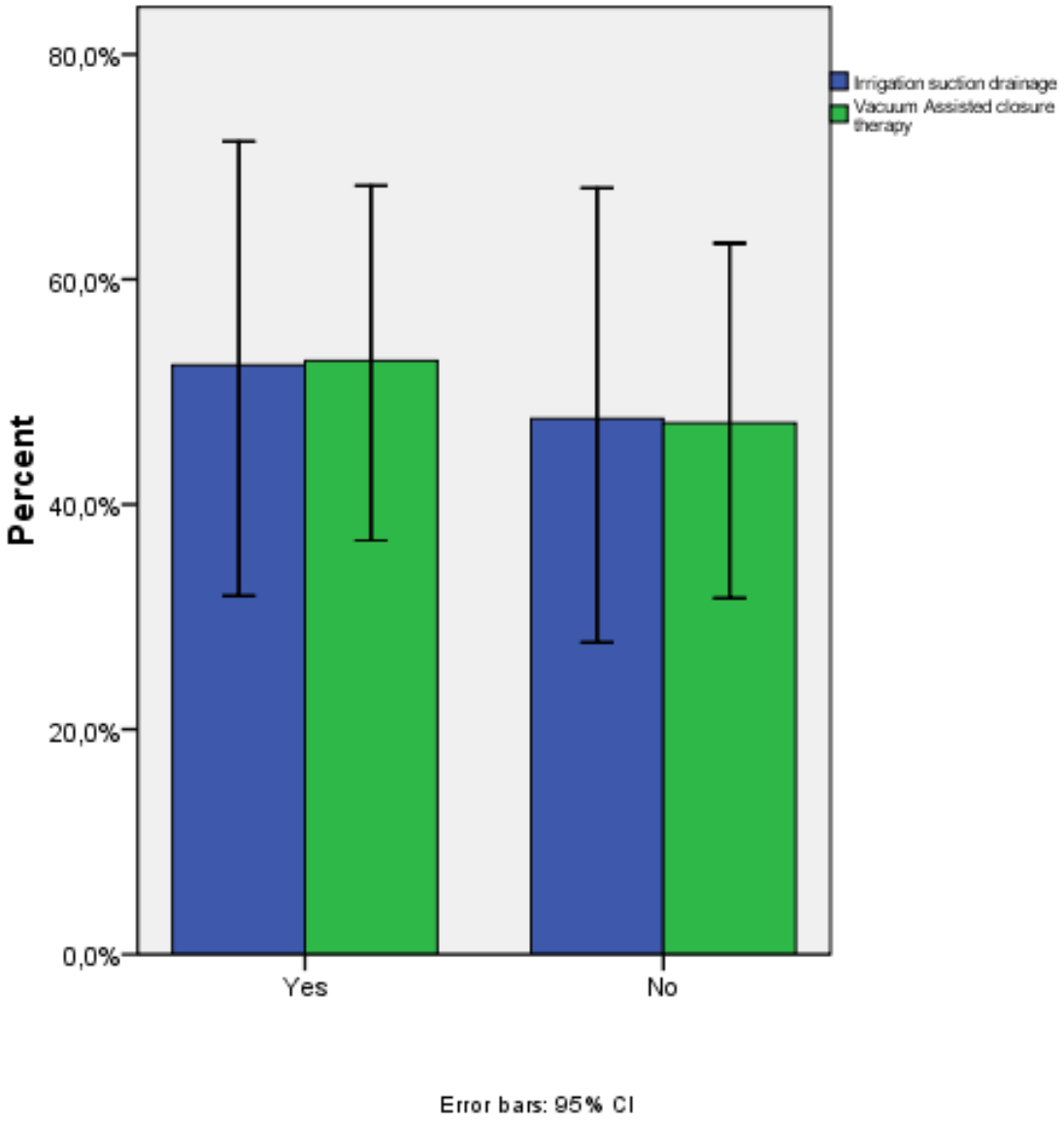


Figure 8

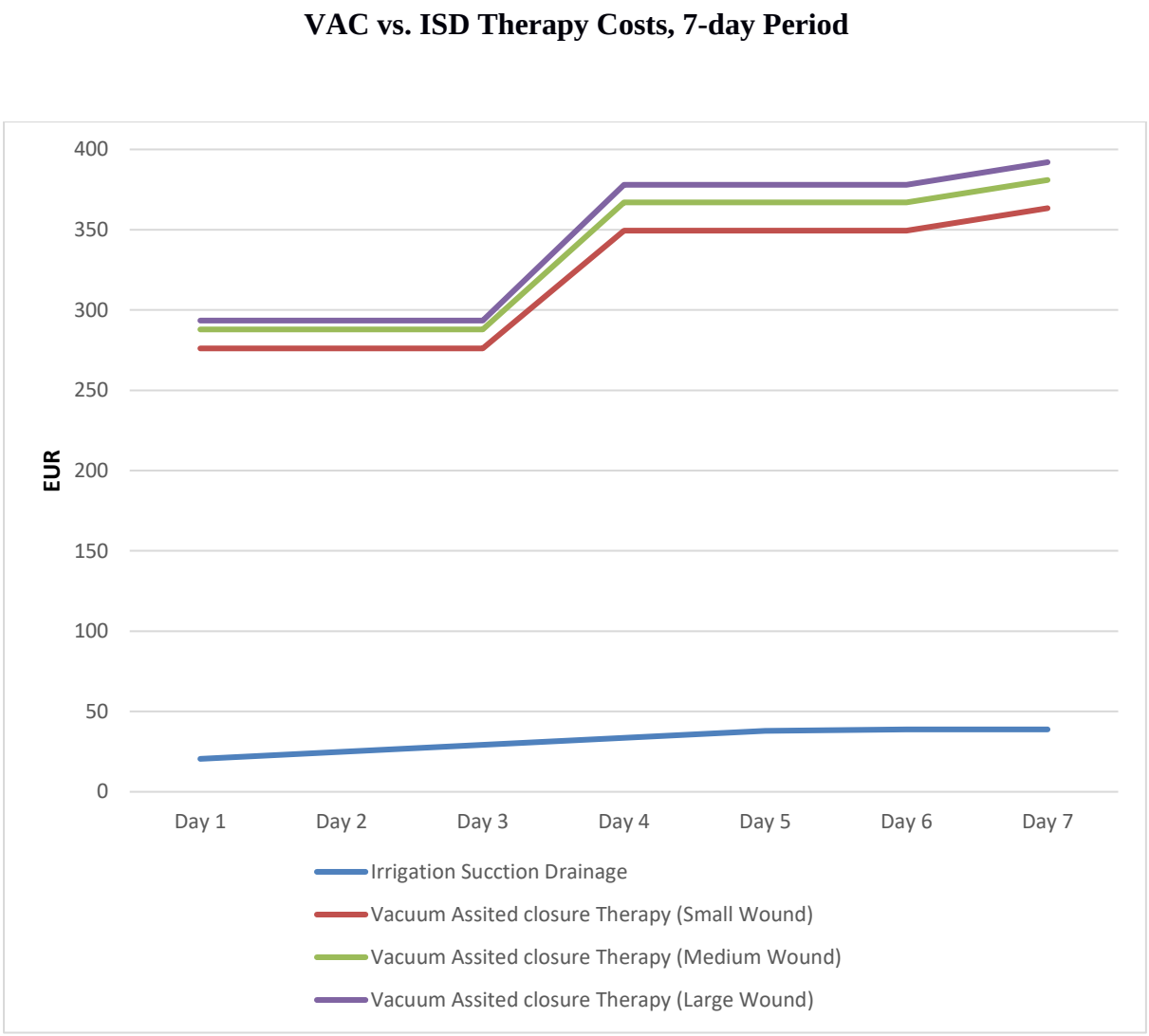
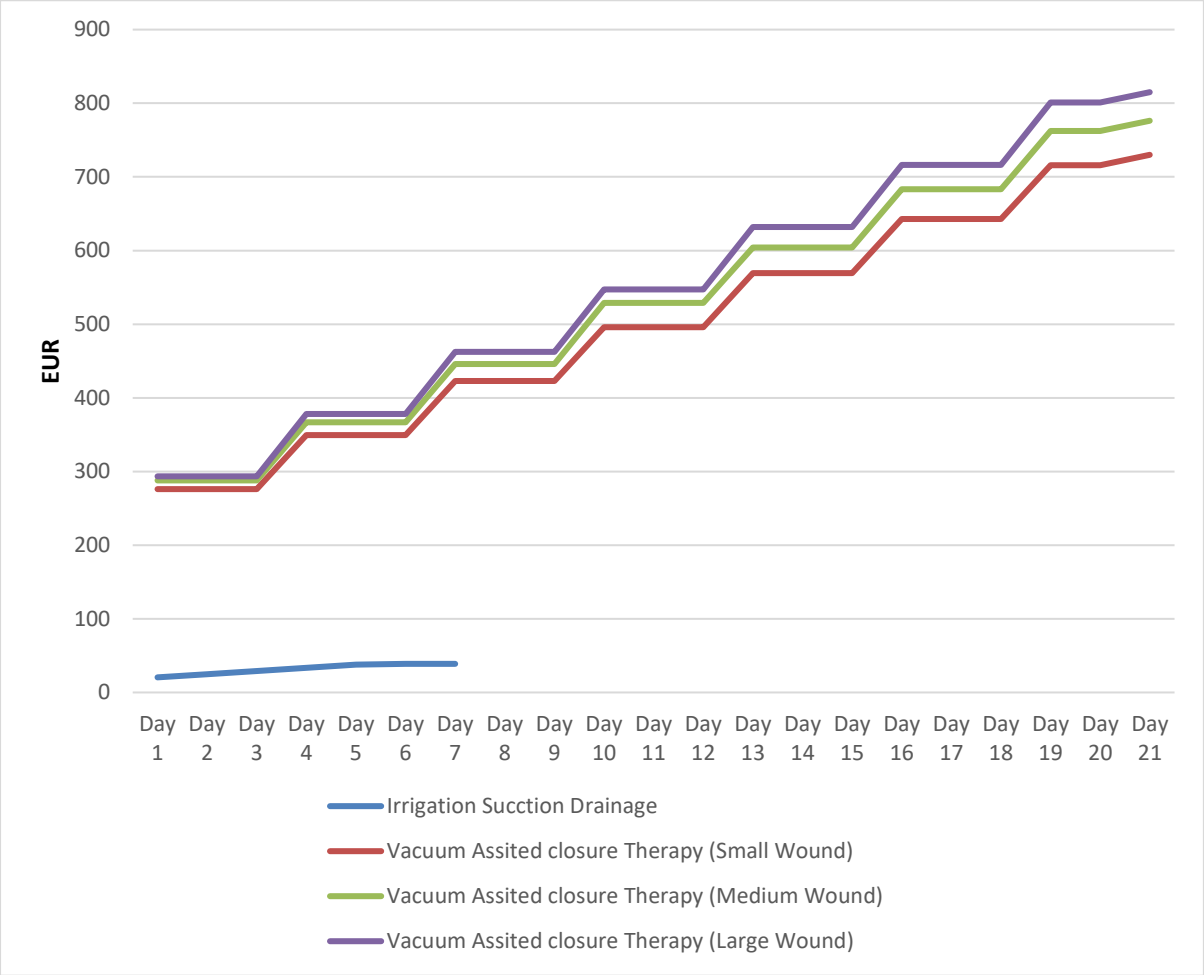

VAC vs. ISD Therapy Costs, 7-day Period
400
350
300
250
200
150
100
50
0
EUR
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Day 7
Irrigation Sucction Drainage
Vacuum Assited closure Therapy (Small Wound)
Vacuum Assited closure Therapy (Medium Wound)
Vacuum Assited closure Therapy (Large Wound)

Figure 9

VAC vs. ISD Therapy Costs, 21-day Period



Tables

Table 1

Age in VAC Group vs. ISD Group

		N	Minimum	Maximum	Mean	Std. Deviation
Irrigation suction drainage	Age, years	21	34	82	66.7	11.38
Vacuum assisted closure therapy	Age, years	36	55	90	71.3	9.91

Table 2

Patient Characteristics

Gender			Number of patients	Minimum	Maximum	Mean	Std. Deviation
Female	Irrigation suction drainage	Height (cm)	7	164	172	166.00	3.21
		Weight (kg)	7	68	120	86.29	16.99
		BMI (kg/m^2)	7	25.3	42.0	31.28	5.824
	Vacuum assisted closure therapy	Height (cm)	13	154	174	161.62	6.39
		Weight (kg)	13	55	98	71.92	14.81
		BMI (kg/m^2)	13	22.0	36.4	27.41	4.82
Male	Irrigation suction drainage	Height (cm)	14	168	183	175.29	4.44
		Weight (kg)	14	63	118	84.29	16.37
		BMI (kg/m^2)	14	21.0	37.2	27.38	4.91
	Vacuum assisted closure therapy	Height (cm)	23	165	181	173.91	4.42
		Weight (kg)	23	50	95	76.61	11.86
		BMI (kg/m^2)	23	18.4	30.4	25.27	3.46

* BMI – body mass index

Table 3

Szilagyi Classification in VAC vs. ISD Group

			Patients	Percent
Irrigation suction drainage	Grade	1	6	28.6
		2	8	38.1
		3	7	33.3
		Total number of patients	21	100
Vacuum assisted closure therapy	Grade	1	8	22.2
		2	14	38.9
		3	14	38.9
		Total number of patients	36	

Table 4

Amputation Rates in VAC vs. ISD Group

			Patients	Percent
Irrigation suction drainage		Yes	7	33.3
		No	14	66.7
		Total number of patients	21	100
.Vacuum assisted closure therapy		Yes	10	27.8
		No	26	72.2
		Total number of patients	36	

Table 5

Hospital Stay (Days) in VAC vs. ISD Group

		Number of patients	Minimum	Maximum	Mean	Std. Deviation
Irrigation suction drainage	Hospital ward stay (Days)	21	9	87	34.19	23.46
	ICU (Days)	21	0	19	4.86	6.382
Vacuum assisted closure therapy	Hospital ward stay (Days)	36	10	126	37.72	26.263
	ICU (Days)	36	0	33	4.14	6.37

* ICU – intensive care unit

Table 6

Average Therapy Days in VAC vs. ISD Group

	Number of patients	Mean therapy days	Std. Deviation	Std. Error Mean
Irrigation suction drainage	21	7.23	0.43	0.09
Vacuum assisted closure therapy	36	14.88	5.53	0.92

		t-test for Equality of Means					
		F	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference
Therapy days	Equal variances assumed	33.055	-6.301	55	0.001	-7.65079	1.21415
	Equal variances not assumed		-8.252	35.743	0.001	-7.65079	0.92710

Table 7

Bacteriological Characteristic in VAC vs. ISD Group

			Number of patients	Percent
Irrigation suction drainage		Klebsiella Pneumoniae	1	4.8
		Proteus Mirabilis	1	4.8
		Staphylococcus Lugdunensis	2	9.5
		Pseudomonas Aeruginosa	2	9.5
		Escherichia Coli	2	9.5
		Streptococcus Agalactiae	2	9.5
		MRSA	3	14.3
		Enterococcus Faecalis	1	4.8
		Staphylococcus Aureus	7	33.3
		Total Number of Patients	21	100
Vacuum assisted closure therapy		Peptostreptococcus Species	1	2.8
		Proteus Mirabilis	1	2.8
		Staphylococcus Lugdunensis	1	2.8
		Pseudomonas Aeruginosa	1	2.8
		Escherichia Coli	3	8.3
		MRSA	15	41.7
		Enterococcus Faecalis	3	8.3
		Staphylococcus Aureus	9	25
		Staphylococcus Epidermidis	1	2.8
		Clostridium Difficile	1	2.8
		Total Number of Patients	36	

* MRSA – Methicillin-resistant Staphylococcus aureus

Table 8

Antibiotic Therapy at least 24 hours before first vascular graft surgery in VAC vs. ISD Group

		Number of patients	Percent
Irrigation suction drainage	Yes	3	14.3
	No	18	85.7
Vacuum assisted closure therapy	Yes	4	11.1
	No	32	88.9

Table 9

Intraioperative Initial Antibiotic Therapy in VAC vs. ISD Group

		Number of patients	Percent
Irrigation suction drainage	Cefuroxim	20	95.2
	Unacid	1	4.8
Vacuum assisted closure therapy	Cefuroxim	33	91.7
	Unacid	1	2.8
	Clindamycin	2	5.6

Table 10

Intraoperative Antibiotic Therapy at VAC or ISD Therapy Initiation

		Number of patients	Percent
Irrigation suction drainage	Cefuroxim	10	47.6
	Vancomycin	5	23.8
	Linezolid	1	4.8
	Ciprofloxaci	3	14.3
	Cefadroxil	1	4.8
	Moxifloxacin	1	4.8
Vacuum assisted closure therapy	Cefuroxim	16	44.4
	Clindamycin	1	2.8
	Vancomycin	14	38.9
	Linezolid	2	5.6
	Cefazolin	1	2.8
	Piperacillin/Tazobactam	2	5.6

Table 11

Blood Transfusion Units in VAC vs. ISD Group

		Number of Patients	Minimum	Maximum	Mean	Std. Deviation
Irrigation suction drainage	Amount of blood units transfusion in operation time	21	0	4	0.76	1.17
	Amount of blood units transfusion in the first 48 hours after revision surgery	21	0	6	2.14	2.22
Vacuum assisted closure therapy	Amount of blood units transfusion in operation time	36	0	2	0.58	0.90
	Amount of blood units transfusion in first 48 hours after revision surgery	36	0	6	1.67	1.69

Table 12

Blood Transfusion Characteristics in VAC vs. ISD Group

			Frequency	Percent
Irrigation suction drainage		Yes	13	61.9
		No	8	38.1
		Total number of patients	21	100
Vacuum assisted closure therapy		Yes	24	66.7
		No	12	33.3
		Total number of patients	36	

Table 13

Vascular Graft Risk Factors Summary, VAC vs. ISD Group

		Irrigation suction drainage	Percentage	Vacuum assisted closure therapy	Percent
Insulin-dependent diabetes mellitus	Yes	6	28.6	9	25
	No	15	71.4	27	75
Non-insulin dependent diabetes mellitus	Yes	3	14.3	5	13.9
	No	18	85.7	31	86.1
Renal insufficiency	Yes	5	23.8	6	16.7
	No	16	76.2	30	83.3
Dialysis	Yes	3	14.3	2	5.6
	No	18	85.7	34	94.4
Liver failure	Yes	2	9.5	1	2.8
	No	19	90.5	35	97.2
Alcohol	Yes	8	38.1	11	30.6
	No	13	61.9	25	69.4
Smoking	Yes	15	71.4	24	66.7
	No	6	28.6	12	33.3
Respiratory disease	No	11	52.4	19	52.8
	Chronic Bronchitis	10	47.6	16	44.4
	Asthma	0	0	1	2.8
Cerebrovascular disease	Yes	7	33.3	11	30.6
	No	14	66.7	25	69.4
Urinary tract infection	Yes	2	9.5	1	2.8
	No	19	90.5	35	97.2
Malnutrition	Yes	1	4.8	4	11.1
	No	20	95.2	32	88.9

Chemotherapy	Yes	0	0	1	2.8
	No	21	100	35	97.2
Radiation therapy	Yes	0	0	1	2.8
	No	21	100	35	97.2
Immunosuppression	Yes	0	0	2	5.6
	No	21	100	34	94.4

Table 14a

First Revision Operation Time in VAC vs. ISD Group

		Number of patients	Minimum	Maximum	Mean	Std. Deviation
Irrigation suction drainage	Length of operation, min	21	70	320	167	73.22
Vacuum assisted closure therapy	Length of operation, min	36	56	280	156	56.29

Table 14b

Operation Time of VAC System Change

		Number of patients	Minimum	Maximum	Mean	Std. Deviation
Vacuum assisted closure therapy	Length of operation, min	36	25	105	54.3333	17.35

Table 15

Sodium Levels Before Initial Vascular Graft Surgery in VAC vs. ISD Group

		Number of patients	Percent
Irrigation suction drainage	Normonatremia	15	71.4
	Hyponatremia	6	28.6
Vacuum assisted closure therapy	Normonatremia	27	75
	Hyponatremia	9	25

Table 16

Potassium Level Before Initial Vascular Graft Surgery in VAC vs. ISD Group

		Number of patients	Percent
Irrigation suction drainage	Normokalemia	19	90.5
	Hyperkalemia	1	4.8
	Hypokalemia	1	4.8
Vacuum assisted closure therapy	Normokalemia	33	91.7
	Hyperkalemia	3	8.3

Table 17

Leucocyte Levels (10^9/l) in VAC vs ISD Group

		Minimum	Maximum	Mean	Std. Deviation
Irrigation suction drainage	Leucocytes before initial operation	3.97	31.35	10.98	6.19
	Leucocytes before VAC or ISD therapy begin	10.75	34.98	19.14	5.96
	Leucocytes before discharge from clinic	5.18	24.00	10.37	4.74
Vacuum assisted closure therapy	Leucocytes before initial operation	4.00	16.40	9.41	2.80
	Leucocytes before VAC or ISD therapy begin	7.24	30.47	17.01	4.54
	Leucocytes before discharge from clinic	4.35	21.10	10.37	3.01

Table 18

Haemoglobin Levels (g/dl) in VAC vs. ISD Group

		Minimum	Maximum	Mean	Std. Deviation
Irrigation suction drainage	Haemoglobin before initial operation	8.8	16.7	12.81	2.23
	Haemoglobin before VAC or ISD therapy begin	6.1	11.5	8.50	1.70
	Haemoglobin before discharge from clinic	7.4	14.1	10.81	2.06
Vacuum assisted closure therapy	Haemoglobin before initial operation	7.0	17.4	11.85	2.36
	Haemoglobin before VAC and ISD therapy begin	6.5	12.5	8.45	1.48
	Haemoglobin before discharge from clinic	8.0	13.7	10.58	1.42

Table 19

C reactive protein levels (mg/dl) in VAC vs. ISD group

		Minimum	Maximum	Mean	Std. Deviation
Irrigation suction drainage	C Reactive Protein before initial operation	0.1	33.6	6.80	11.27
	C Reactive Protein before VAC or ISD therapy begin	9.4	44.9	21.77	9.64
	C Reactive Protein before discharge form clinic	0.2	31.5	4.49	7.06
Vacuum Assisted closure therapy	C Reactive Protein before initial operation	0.1	27.7	2.45	5.80
	C Reactive Protein before VAC or ISD therapy	1.2	47.0	22.03	10.98
	C Reactive Protein before discharge form clinic	0.1	21.4	3.74	4.86

Table 20

Infection at the time of Initial Vascular Graft Surgery in VAC vs. ISD Group

		Number of patients	Percent
Irrigation suction drainage	Yes	4	19
	No	17	81
Vacuum assisted closure therapy	Yes	4	11.1
	No	32	88.9

Table 21

ISD Therapy Costs

ISD initial therapy material costs	
	€
NaCl 0,9% 1000ml Ecotainer Spül 3570160	0.83
Vicryl viol gefl 2-0 6x45 V1226H	3.44
Vicryl viol gefl 2-0 6x45 V1226H	3.44
Prolene blau 3-0 120 2XSH EH7584H	3.14
Prolene blau 3-0 120 2XSH EH7584H	3.14
Urindrainages. m. Hahn 2L steril 690212	1.49
Urindrainages. m. Hahn 2L steril 690212	1.49
Betaisodonna Lösung 120 ml	3.53
Sum	**20.50**
ISD therapy material daily costs	
NaCl 0,9% 1000ml Ecotainer Spül 3570160	0.83
Betaisodonna Lösung 120 ml	3.53
Sum	**4.36**

Table 22

VAC Therapy Initial Costs According to Wound Area

Initial VAC therapy material costs (small wound)	
Antimikrobielle Gaze-Rolle Kerlix 11,4cm	7.14
Cutimed Sorbact Wundf. 17x28cm 7269300	3.55
PICO 10x20cm Einmalunterdr.-System/Verb.	165.41
Renasys Gelstreifen 10x7cm 66801082	4.76
Renasys GO 300 ml Kanister 66800914	23.21
Renasys GO Tragegurt 66800163	20.23
Renasys Port-Kit 66800799	20.47
Renasys Y-Konnektor 66800971	5.53
Schaumst.-Kit, klein 10x8 x3cm 66800794	25.79
Transp. NPWT Folie,groß 20x30 66800394	6.08
Sum	**276.08**

Initial VAC therapy material costs (medium wound)	
Ant+A22:B47imikrobielle Gaze-Rolle Kerlix 11,4cm	7.14
Cutimed Sorbact Wundf. 17x28cm 7269300	3.55
PICO 10x30cm Einmalunterdr.-System/Verb.	165.41
Renasys Gelstreifen 10x7cm 66801082	4.76
Renasys GO 300 ml Kanister 66800914	23.21
Renasys GO Tragegurt 66800163	20.23
Renasys Port-Kit 66800799	20.47
Renasys Y-Konnektor 66800971	5.53
Schaumst.-Kit,mittel 20x12,5x3 66800795	31.54
Transp. NPWT Folie,groß 20x30 66800394	6.08
Sum	**287.91**

Initial VAC therapy material costs (large wound)	
Antimikrobielle Gaze-Rolle Kerlix 11,4cm	7.14
Cutimed Sorbact Wundf. 17x28cm 7269300	3.55
PICO 10x40cm Einmalunterdr.-System/Verb.	165.41
Renasys Gelstreifen 10x7cm 66801082	4.76
Renasys GO 300 ml Kanister 66800914	23.21
Renasys GO Tragegurt 66800163	20.23
Renasys Port-Kit 66800799	20.47
Renasys Y-Konnektor 66800971	5.53
Schaumst.-Kit, groß 25x15 x3 66800796	37.07
Transp. NPWT Folie,groß 20x30 66800394	6.08
Sum	**293.44**

Table 23

VAC Change Costs According to Wound Area

VAC change therapy material costs (small wound)	
Antimikrobielle Gaze-Rolle Kerlix 11,4cm	7.14
Cutimed Sorbact Wundf. 17x28cm 7269300	3.55
Renasys Gelstreifen 10x7cm 66801082	4.76
Renasys Port-Kit 66800799	20.47
Renasys Y-Konnektor 66800971	5.53
Schaumst.-Kit, klein 10x8 x3cm 66800794	25.79
Transp. NPWT Folie,groß 20x30 66800394	6.08
Sum	**73.32**

VAC change therapy material costs (medium wound)	
Antimikrobielle Gaze-Rolle Kerlix 11,4cm	7.14
Cutimed Sorbact Wundf. 17x28cm 7269300	3.55
Renasys Gelstreifen 10x7cm 66801082	4.76
Renasys Port-Kit 66800799	20.47
Renasys Y-Konnektor 66800971	5.53
Schaumst.-Kit,mittel 20x12,5x3 66800795	31.54
Transp. NPWT Folie,groß 20x30 66800394	6.08
Sum	**79.06**

VAC change therapy material costs (large wound)	
Antimikrobielle Gaze-Rolle Kerlix 11,4cm	7.14
Cutimed Sorbact Wundf. 17x28cm 7269300	3.55
Renasys Gelstreifen 10x7cm 66801082	4.76
Renasys Port-Kit 66800799	20.47
Renasys Y-Konnektor 66800971	5.53
Schaumst.-Kit, groß 25x15 x3 66800796	37.07
Transp. NPWT Folie,groß 20x30 66800394	6.08
Sum	**84.60**

Table 24

VAC Therapy Costs by End of VAC Therapy

Vacuum assisted closure (Wound Closure end therapy)	
NaCl 0,9% 1000ml Ecotainer Spül 3570160	0.83
Vicryl viol gefl 2-0 6x45 V1226H	3.44
Vicryl viol gefl 2-0 6x45 V1226H	3.44
Prolene blau 3-0 120 2XSH EH7584H	3.14
Prolene blau 3-0 120 2XSH EH7584H	3.14
Sum	**13.99**

Table 25

VAC vs. ISD Therapy Costs, 7-day Period

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Irrigation suction drainage	20.5	24.86	29.22	33.58	37.94	38.83	38.83
Vacuum assisted closure therapy (Small wound)	276.08	276.08	276.08	349.4	349.4	349.4	363.39
Vacuum assisted closure therapy (Medium wound)	287.91	287.91	287.91	366.97	366.97	366.97	380.96
Vacuum assisted closure therapy (Large wound)	293.44	293.44	293.44	378.04	378.04	378.04	392.03

Table 26

VAC vs. ISD Therapy Costs, 21-day Period

	Day 1	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**	**Day 7**
Irrigation suction Drainage	20.5	24.86	29.22	33.58	37.94	38.83	38.83
Vacuum assisted closure Therapy (Small wound)	276.08	276.08	276.08	349.4	349.4	349.4	422.72
Vacuum assisted closure Therapy (Medium wound)	287.91	287.91	287.91	366.97	366.97	366.97	446.03
Vacuum assisted closure Therapy (Large wound)	293.44	293.44	293.44	378.04	378.04	378.04	462.64
	Day 8	**Day 9**	**Day 10**	**Day 11**	**Day 12**	**Day 13**	**Day 14**
Irrigation suction drainage							
Vacuum assisted closure therapy (Small wound)	422.72	422.72	496.04	496.04	496.04	569.36	569.36
Vacuum assisted closure therapy (Medium wound)	446.03	446.03	529.09	529.09	529.09	604.15	604.15
Vacuum assisted closure therapy (Large wound)	462.64	462.64	547.24	547.24	547.24	631.84	631.84
	Day 15	**Day 16**	**Day 17**	**Day 18**	**Day 19**	**Day 20**	**Day 21**
Irrigation suction drainage							
Vacuum assisted closure therapy (Small wound)	569.36	642.68	642.68	642.68	716	716	729.99
Vacuum assisted closure therapy (Medium wound)	604.15	683.21	683.21	683.21	762.27	762.27	776.26
Vacuum assisted closure therapy (Large wound)	631.84	716.44	716.44	716.44	801.04	801.04	815.03

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Eidesstattliche Versicherung

Bokums Kristaps

Name, Vorname

Ich erkläre hiermit an Eides statt,

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