

Surgical Revascularization in Chronic Limb-threatening Ischemia in Diabetic Patients

Cristina Neagu¹, Alexandra Buzea², Alexandra Agache³, Dragoș Georgescu³, Traian Pătrașcu³

¹Diabetic Foot Compartment, "I. Cantacuzino" Clinical Hospital, Bucharest, Romania

²"C.C. Iliescu" Emergency Institute for Cardiovascular Disease, Bucharest, Romania

³1st General Surgery Clinique, "I. Cantacuzino" Clinical Hospital, Bucharest, Romania

Corresponding author:

Dragos Eugen Georgescu
Assistant Professor
General Surgery "Dr. I. Cantacuzino"
Clinical Hospital
5-7 Ion Movila str, district 2,
Bucharest Romania
E-mail: gfdragos@yahoo.com

Rezumat

Revascularizarea chirurgicală în ischemia cronică ce amenință viabilitatea membrului pelvin la pacienții diabetici

Diabetul zaharat este una din bolile cronice care a prezentat o creștere constantă a numărului de pacienți în ultimele decenii. După diagnosticul diabetului, evoluția către amputația membrului se face pas cu pas prin instalarea neuropatiei, apariția ulcerului, infectarea acestuia și existența arteriopatiei care, prin statusul ischemic al membrului, împiedică vindecarea. Prin refacerea fluxului arterial al membrului se rezolvă una dintre cauzele de apariție a leziunilor trofice, și anume ischemia.

Material și Metode: În cadrul Clinicii de Chirurgie a Spitalului Clinic Dr I Cantacuzino – Compartimentul Chirurgie Reparatrice a Piciorului Diabetic s-au efectuat primele revascularizări chirurgicale în urmă cu aproximativ 5 ani. În tot acest timp am depus eforturi constante pentru a scădea numărul de amputații majore prin diversificarea intervențiilor dedicate aproape în exclusivitate pacienților cu ulcer al piciorului diabetic.

Rezultate: Numărul amputațiilor majore a scăzut în urma intervențiilor de revascularizare și am obținut vindecarea completă a ulcerelor și o extremitate funcțională. Am avut 80 de pacienți în observație care au fost supuși intervențiilor de revascularizare, cu vârste cuprinse între 40 și 75 ani, 46 bărbați și 34 femei. Toți sunt diabetici cu ischemie critică și comorbidități variate: 24% hipertensiune arterială, 14% polineuropatie, 12% dislipidemie. Complicațiile apărute în primul an de urmărire postoperatorie au constat în 14 cazuri de tromboza de graft și doar 6 cazuri de amputații majore.

Received: 09.07.2018

Accepted: 18.09.2018

Concluzii: Înainte de a încerca orice tip de amputație, majoră sau minoră, după controlul infecției locale prin tratament, debridare excizională sau pansamente locale, și după evaluarea vasculară, este crucială restabilirea fluxului arterial.

Cuvinte cheie: diabet zaharat, picior diabetic, arteriopatie, ischemie critică, ischemie cronică ce amenință viabilitatea membrului, amputație

Abstract

Introduction: Diabetes mellitus is one of the chronic diseases that showed a steady increase in the number of patients in the last decades. After the diagnosis of diabetes mellitus, evolution towards limb amputation goes, step by step, through neuropathy, leg ulcers and infection appearance. The existence of diabetic arteriopathy prevents ulcer's healing due to the limb's ischemic status. By restoring arterial flow in the lower extremity, we solve the most important cause for diabetic foot ulcers, namely ischemia.

Material and Methods: In the Surgery Clinic of "Dr I Cantacuzino" Clinical Hospital, Surgical Repair of Diabetic Foot Compartment, the first revascularizations were made approx 5 years ago. During this time we have made constant efforts to lower the number of major amputations by diversifying the interventions dedicated almost exclusively to patients with ulcer of the diabetic foot.

Results: The number of major amputations is lower after revascularisation and we have obtained complete ulcer's healing and a functional extremity. We have 80 patients in observation who underwent revascularisation surgery, ages between 40 and 75 years, 46 men and 34 women. All of them were diabetic patients with critical ischemia and various associated comorbidities: 24% arterial hypertension, 14% polineuropathy, 12% dyslipidemia. The complications occurred in the first year of follow-up were 14 cases of graft thrombosis and only 6 cases of major amputation.

Conclusions: Before tempting any type of amputation, major or minor, after local infection control by treatment, debridement or dressings, and after vascular evaluation, it is essential to restore arterial flow.

Key words: diabetes mellitus, diabetic foot, arteriopathy, critical limb ischemia, amputation

Introduction

Being an acute issue of contemporary society, diabetes mellitus, through its systemic complications, represents a huge challenge regarding treatment, for clinicians and surgeons alike.

Awareness of the problem and its effects are important steps for the management of the patient. The absence of glycaemia monitoring over a long period of time also resides in the lack of education as well as due to the poor media coverage of the risks associated with these high values.

We speak now about diabetes mellitus in epidemical parameters worldwide. In 2014,

according World Health Organisation, there were 422 million diabetic patients, compared with 108 million in 1980. The prevalence (age standardized) of diabetes almost doubled, from 4,7% to 8,5% in adult population (1). Late diagnosis of diabetes mellitus involves silent evolution with systemic adaptation to higher and higher glycaemic values, the occurrence of complications being faster in these cases. In this context, the diagnosis of peripheral arterial disease is often established when resting pain or trophic lesions occur.

The "diabetic foot" is a notion that includes ischemia, neuropathy and infection. These are the causes that lead to amputation and

usually they come in association.

That's where the vascular surgeon plays its major role in the diagnosis and management of peripheral artery disease in patients with diabetic foot ulcers.

Lower extremity amputation best exemplifies the impact of diabetes complications on the patient's quality of life. It is considered a medical failure although poor medical education and late addressability to the doctor are the causes.

The classical clinical symptomatology of arteriopathy does not enterly apply to diabetic patients, since the patient is denying intermittent claudication, often even resting pain, although the lesions have a specific arteriopathy appearance.

Because of this, the chances for a diabetic patient to develop trophic lesions of the lower limbs are much higher compared to a non-diabetic (2), their prognosis is worse than that of patients with frequent types of neoplasia (3), with a 50% mortality rate at 5 years for patients with major amputation (4).

Before tempting any type of amputation, major or minor, it is essential to restore the arterial flow in the lower extremity, unless general signs of infection are present.

Considering the Clinic's pattern of taking care almost exclusively diabetic patients, we will evaluate the results of surgical revascularization interventions from 2013 until the beginning of 2016 for diabetic foot ulcers.

Material and Method

We performed 80 surgical interventions of bypass and/or endarterectomy alone, since 2013 until 2016. There were 46 male patients and 34 female, ages 40 to 75. The selection was made exclusively for surgical revascularization, because in the Cantacuzino Clinical Hospital endovascular procedures are not available.

The study included only diabetic patients with foot ulcers, with varying degrees of neuropathy with or without extensive foot infection. We used classification in use until 2017, Fontaine and Rutherford for critical ischemia assessment.

Critical ischemia in the Fontaine classification is found in stage III and IV, and in the Rutherford classification in stages 4,5 and 6, and includes resting pain lasting for over 2 weeks that requires opioid analgesics and/or the presence of trophic lesions (5).

The patients wound appraisal was made according The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: Risk stratification based on Wound, Ischemia, and foot Infection (WIFI) (6). This System includes either ischemia or neuropathy alone as etiology factor for foot ulcers, with different grades for mixed ulcers between these two extremes.

The risk estimation of major amputation at 1 year falls within one of four classes: (6) Very low = clinical stage 1; Low = clinical stage 2; Moderate = clinical stage 3; High = clinical stage 4.

Clinical stage 5 corelates with an unsalvageable foot.

The particular characteristic of the diabetic patients is the presence of mixed foot ulcers caused by neuropathy and arteriopathy. All the patients presented infected mixed foot ulcers and for those with deep infection, SIRS or SEPSIS, a thorough debridement or small amputation was performed, followed by vascular assement and revascularization.

Infection control was based on susceptibility testing in all patients and the treatment with antibiotics followed an ascending pattern, whether single or multiple germs were present.

The management protocol of the diabetic patient with foot ulcer is complex and includes assessment of periferal artery disease using ankle-brachial index, arterial Doppler ultrasound or digital subtraction angiography.

Doppler ultrasound is the first-intention investigation in a diabetic patient. It includes B-mode echography, pulsed-wave, colour and power Doppler modalities to describe the arterial wall lesions and their severity, although it has limitations in diabetic arteriopathy. The calcified arterial walls creates a barrier for the ultrasound wave which prevents the attainment of valuable informations about the flow.

Nevertheless, the result depends on the

examiner knowledge in vascular surgery and his experience with this imaging technique, meaning good training is mandatory.

Arteriography remains “gold standard” in evaluating peripheral arterial disease in diabetic patients, especially when Doppler Ultrasound creates doubts about the existence or severity of arterial wall lesions (*Figs. 1, 2*).

Digital Subtraction Angiography completely

and precisely describes the arterial branches of the inferior limb, down to the tip of the toes, to establish the best therapeutic indication for a diabetic patient with foot ulcer and the chances of healing of a wound or postamputation. This diagnostic method can indicate the pedal runoff and guide the level of an eventual minor amputation (*Figs. 3, 4*).

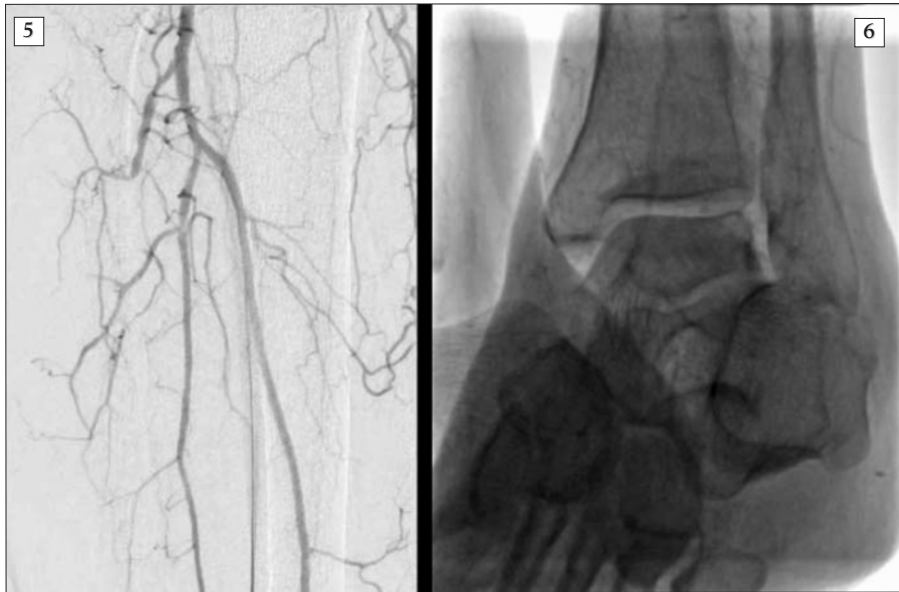
Infrapopliteal occlusive disease is charac-



Figures 1 and 2. Occlusion of superficial femoral artery, with a patent proximal popliteal artery (above the knee joint)



Figures 3 and 4. Patent calf arteries and evaluation of pedal arches



Figures 5 and 6. Lesions of the calf arteries; occlusion of the anterior tibial artery with reloading of the pedal artery

teristic to the diabetic patient with peripheral arterial disease, but association of proximal lesions with the distal ones usually leads to extensive trophic wounds, with significant inflammatory signs (*Figs. 5, 6*).

The technique involves creating a bypass with autologous vein or prosthetic material between two regions of the artery, that evades the occluded area. What significantly burdens the surgeon's work are the wall calcifications. Sometimes is very difficult to find a segment with good quality of the arterial wall (*Figs. 7, 8*).

The autologous material is preferably the ipsilateral internal saphenous vein. If the vein has already been used for a coronary by-pass

or if it does not meet the required criteria, it is possible to use the contralateral internal saphenous vein, external saphenous vein or the cephalic vein.

These last two variants are used less frequently, since synthetic prostheses successfully replace the autologous material. However, in below the knee bypass, syntetic grafts is not recomanded. The benefits of using the inversed saphenous vein are multiple, but for the diabetic patient with foot ulcer the most important is a lower risk of bypass infection. The selection of patients was made taking in consideration the patients comorbidities and the anaesthetic-surgical risk. Patients with high risk were addressed to endovascular



Figures 7 and 8. Proximal anastomosis between the common femoral artery and the popliteal artery



Figures 9 and 10. Distal bypass on the pedal artery.

revascularization. If there is a high risk for open surgery or great extent of trophic lesions with SIRS or SEPSIS associated, then major amputation is required. Typical revascularization interventions for the diabetic patient with infrapopliteal arterial disease are distal bypasses that target the pedal artery or the posterior tibial artery as outflow vessels. Above the knee inflow lesions in these cases are minimal, thus the location for proximal anastomosis is chosen as distal as possible, preferably the distal popliteal artery (*Figs. 9, 10*).

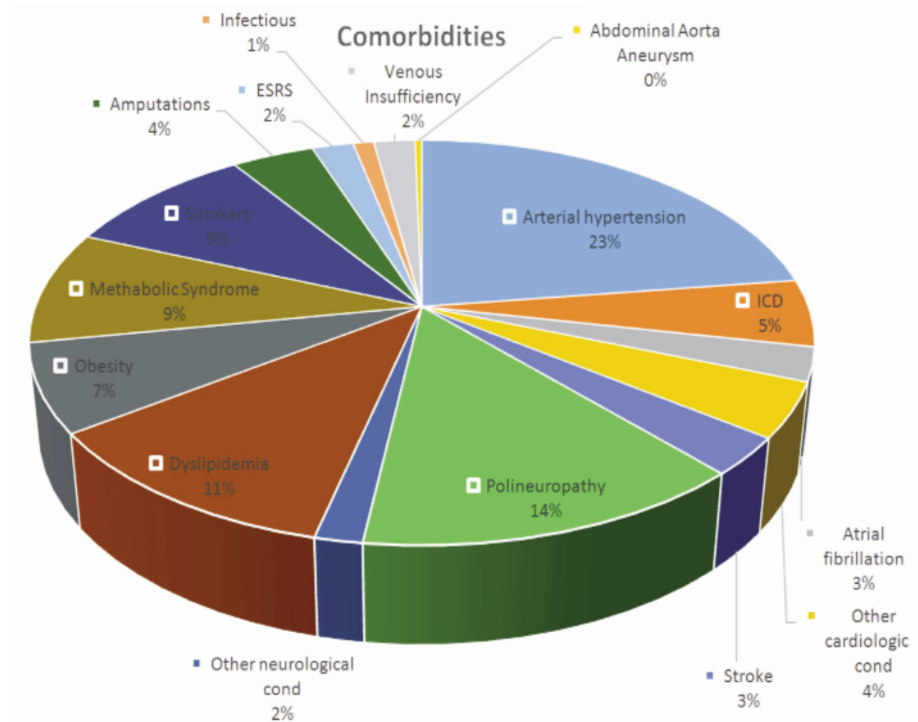
For a complete diagnosis of the vascular bed in the foot and the choice of the recipient vessel we only used arteriography as first intention. We have complied with ESC/ESVS 2017 guidelines for the material used for the grafting and have only used the reversed great saphenous

vein (7). After restoring arterial flow, diabetic neuropathy remains the main pathology of the diabetic foot, especially if a distal pulse is obtained. Neuropathy is a hindrance to healing ulcers, many of which need adjuvant methods of local treatment (special dressings, negative pressure therapy), minor amputations, debridement of necrotic tissue that remains after revascularization, cutaneous plasties or orthopaedic interventions (*Figs. 11, 12, 13, 14*).

As a result of these successive procedures, the limb must be functional and be able to be fitted with customized footwear. Unloading of weight from the affected areas by means of orthotics leads to a much faster healing of minor amputation stumps. Infection control is done with maximum antibiotic therapy, which does not meet the criteria in diabetic patients.



Figures 11-14. Use of negative pressure after popliteal-pedal by-pass and minor amputations; results

Figure 15. Comorbidities

Results

We performed 80 surgical interventions of bypass and/or endarterectomy alone, since 2013 until 2016. There were 46 male patients and 34 female, ages 40 to 75. In the 46-65 age cluster there were more male patients, while patients over 71 were mostly female. Diabetic patients have a higher risk of perioperative events because of their comorbidities (*Fig. 15*). According comorbidities arterial hypertension, dyslipidaemia and neuropathy were most frequently associated with diabetes.

Smoking, associated with diabetes, determines more severe arterial lesions, with occlusions of the iliac, common femoral and superficial femoral artery. In our group the percentage of smokers was about 35%. Using the WiFi risk stratification system there were 63 patients in clinical stage 3 meaning a moderate risk of amputation at 1 year and 17 patients in clinical stage 2 with a low risk of amputation. The Wound grading of this Classification System divides our patients as following: 26 cases with grade 1, 42 cases with grade 2 and 12 cases with grade 3. The type of

occlusive disease for which surgery was performed was preponderant infra-inguinal, 93%, and the stage of the disease according to Leriche-Fontaine classification was critical ischemia (stages III and IV), with trophic lesions – 80%. We had 69 interventions for femuro-popliteal disease. In 73% inversed saphenous vein was used, 16% colagenated Dacron® and 11% PTFE graft. For infra-popliteal disease we performed 5 distal bypasses only with inversed great saphenous vein. The pedal or posterior tibial artery were the targeted outflow artery (*Fig. 16*).

There were also 6 endarterectomy procedures with enlargement plasty, representing 7,5%, involving the common femoral, profound femoral or superficial femoral arteries. Early complications after surgery occurred in 23 cases such as graft thrombosis - 61%, infection – 13%, not necessary leading to major amputation (*Fig. 17*).

The results up to one year are encouraging. The rate of success at 6 months was approximately 80%. Of the 20% of complications, 43% were major amputations (6 cases), the rest of patients having healed lesions and a function-

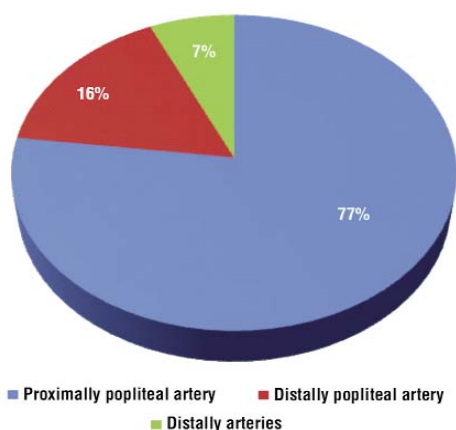


Figure 16. Targeted artery for outflow

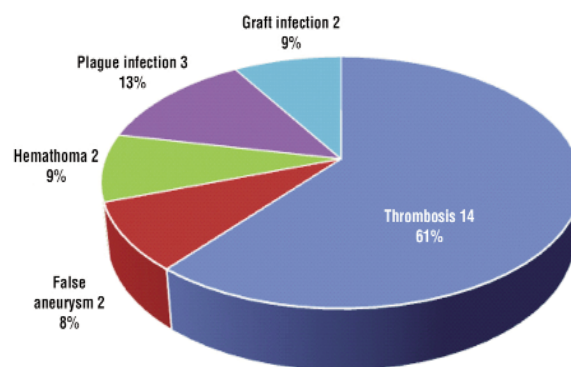


Figure 17. Early bypass complications

al lower limb, even with a thrombosed bypass (Fig. 18).

All 6 cases of major amputation that occurred in the first year belonged within Grade 3 Wound Classification System and clinical stage 3 of the WiFi Classification. Our results fit in the literature with a low rate of amputations after revascularisation surgery.

Discussions

Major amputations have a restrained indication today and their number decreased, probably by facilitating the accessibility of patients to vascular surgery, especially in developed countries. They are considered a failure of health services and represent the final step in treating patients with chronic limb-threatening ischemia. Necrosis or extensive gangrene, immobilized patients or patients with severe comorbidities remain among the indications for per primam amputations. In the case of terminal patients, it is recommended to abstain from a traumatic gesture that does not bring any benefit. Secondary amputations are indicated in case of a thrombosed bypass without possibility of revascularization or in case the trophic lesions progress despite a functional bypass (7).

Referring to the existing literature, a review on the efficiency of revascularization of the diabetic foot with ulcer from 2013 and its update from 2016, which take into account

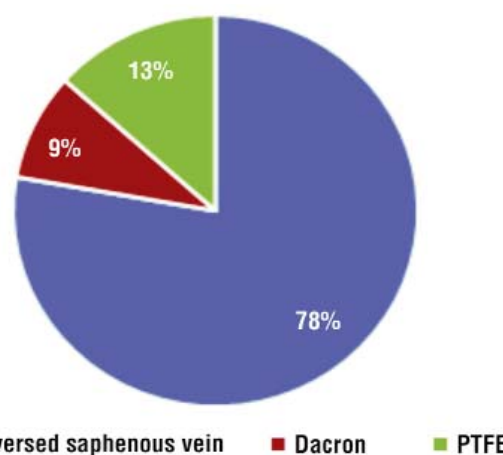


Figure 18. Patency at one year depending on the material use

articles published between 1980 and 2014, with 56 eligible articles, concluded that there was no significant difference between the results obtained by the two methods of revascularization, surgical and interventional. Healing of the diabetic foot ulcers was ~60% in the first year, and the limb saving rate was slightly higher by surgical techniques, 85% compared to 78% interventional. Total survival rate was 50% at 5 years (8). The BASIL study conducted in 2010 compares the results of angioplasty vs by-pass, amputation rates and survival for the two methods. No significant difference was established, but the advantage of endovascular techniques was established in patients with higher anaesthetic-

surgical risk and much better results than prosthetic by-passes (9). Diabetic patients with peripheral artery disease have a peculiar evolution compared with general population or patients with arteriopathy alone, therefore there is a very high variability of the results obtained after revascularization.

Revascularization should be of first intention in critical ischemia of the diabetic foot, but it is not guarantor of healing of trophic lesions or rescue of the limb. The presence of arterial disease related to diabetes is the most important risk factor in the failure in healing trophic lesions, and there is no investigation that can predict the evolution on trophic ulcers. Often, we use adjuvant treatment methods such as local dressings or negative pressure that helps to debride, hydrate or granulate, depending on the phase they are in. A rigorous therapeutic protocol of diabetic foot ulcers is very difficult to establish, with unpredictable events even after revascularization, as there are many cases that do not benefit from restoration of arterial flow and yet do not reach major amputation. But the natural order of therapeutic indications should not endanger the patient's life, then save the limb and then its functionality.

Conclusion

A national medical educational program will really facilitate the access to patients' health services, first step being the family doctor. When the diagnosis of diabetic mellitus is set, a short clinical exam of the vascular status must be done, and, if needed, the patient should be addressed to a vascular surgeon. The diagnosis of the arterial occlusive disease, its stage, time and opportunity for additional investigations will be established.

Late presentation to a doctor, after the apparition of the diabetic foot ulcers, increases the risk of amputation. Before tempting any type of amputation, major or minor, after local infection control by treatment, debridement or dressings, and after vascular evaluation, it is essential to restore arterial flow hemodynamics. The type of revascularization is decided from

case to case, endovascular or surgical. In the Cantacuzino Clinical Hospital only surgical revascularization is possible for the moment. Bypass is indicated, to be done using autologous material as much as possible, especially the ones targeting the foot arteries. The length should not outrun the occlusion and it should preserve the capital of permeable arteries.

After revascularization, the neuropathy will dictate, in most cases, the evolution of the trophic lesions, infection and the need for amputation. In these cases we frequently use the negative pressure to obtain complete healing of the minor amputations stumps.

The rate of major amputation (under or above the knee) was almost 7% in the first 6 months, patients presenting for periodic follow-ups, very few being lost from observation.

Diabetic patients have a higher cardiovascular risk than the general population and require an aggressive management of risk factors such as smoking, arterial hypertension or dyslipidemia with antiplatelet and lipid lowering agents..

The results we obtained are encouraging and motivate our activity to prevent major amputations.

Conflict of interest

All author declare that they have no conflict of interest.

References

1. WorldHealth Organisation: Global Report on Diabetes 2016, <http://www.who.int/diabetes/globalreport/en/>
2. Neagu C, Patrascu T. Surgical revascularization in chronic and critical ischemia of diabetic foot. 4th International Conference on Interdisciplinary Management of Diabetes Mellitus and its complications. Surgical Crossroads with Diabetes Mellitus. Interdiab. Ed Niculescu; 2018. p. 194-204.
3. Armstrong DG, Wrobel J, Robbins JM. Guest Editorial: are diabetes-related wounds and amputations worse than cancer? *Int Wound J.* 2007;4(4):286-7.
4. Forsythe RO, Hinchliffe RJ. Management of critical limb ischemia in the patient with diabetes. *J Cardiovasc Surg (Torino).* 2016; 57(2):273-81. Epub 2015 Dec 2.
5. Rutherford RB, Baker JD, Ernst C, Johnston KW, Porter JM, Ahn S, et al. Recommended standards for reports dealing with lower extremity ischemia: revised version. *J Vasc Surg.* 1997;26(3):517-38.
6. Mills JL, Conte MS, Armstrong DG, Pomposelli FB, Schanzler A, Sidaway AN, et al. The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: risk stratification

- based on wound, ischemia, and foot infection (WIFI). *J Vasc Surg.* 2014;59(1):220-34.e1-2.
7. Aboyans V, Ricco JB, Bartelink MEL, Björck M, Brodmann M, Cohnert T, et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries Endorsed by: the European Stroke Organization (ESO) The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). *Eur Heart J.* 2018; 39(9):763-816.
 8. Hinchliffe RJ, Brownrigg JR, Andros G, Apelqvist J, Boyko EJ, FitrIDGE R, et al. Effectiveness of revascularization of the ulcerated foot in patients with diabetes and peripheral artery disease: a systematic review. *Diabetes Metab Res Rev.* 2016;32 Suppl 1:136-44.
 9. Bradbury AW, Adam DJ, Bell J, Forbes JF, Fowkes GR, Gillespie I, Vaughan Ruckley C, Raab GM. Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial: Analysis of amputation free and overall survival by treatment received. *J. Vasc. Surg.* 2010; 51(5 Supplement):18S-31S.