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Algorithm of Medical-Surgical Treatment in the Peripheral Arterial Disease of the Diabetic Patient

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ABSTRACT

Introduction: *We live in a society with a growing number of diabetics. That is why the number of diabetic patients with peripheral arterial disease is expanding, as is the number of cases of chronic ischemia, which threatens limb viability, or chronic limb-threatening ischemia (CLTI). The appearance of diabetic foot ulcers with an ischemic component represents the maximum risk of amputation in the absence of a firm and rapid revascularization intervention. In our study, we aim at early detection of patients who need infusion treatment immediately after surgical revascularization.*

Material and methods: *This is a six-year retrospective study of 115 patients with infrainguinal occlusive disease and CLTI. All subjects were classified according to the WIfI system before and after revascularization. We made a score based on the postoperative clinical evolution in the first three days in order to have an objective image of patients who received infusion treatment with PG E1.*

Results: *All patients included in our study had diabetes. They were divided into two groups, one comprising 86 patients who underwent exclusively surgical treatment, and the other comprising 29 patients, who received a combined surgical and medical treatment. We showed that subjects who had a low postoperative score and received infusion treatment had a higher rate of limb rescue in the first year.*

Conclusions: *In diabetic patients with infrainguinal occlusive disease who were treated in the Clinic, without the possibility of endovascular or hybrid interventions, the combination of infusion treatment with PG E1 after surgical revascularization led to a higher rate of limb rescue and healing of ischemic trophic lesions after one year.*

Keywords: diabetes mellitus, chronic ischemia threatening the lower limb, diabetic foot, revascularization, Alprostadil.

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INTRODUCTION

According to published WHO data, we are witnessing an increase in the global prevalence of diabetes among the population aged 18 and over, from 4.7% in 1980 to 8.5% in 2014 (1).

In this context, chronic ischemia that threatens the limb has become a global problem, and deterioration among patients with diabetes is constantly increasing. However, statistical data related to the treatment and evolution of patients suffering exclusively from diabetes are missing. Diabetics are a special category of patients, given that the complications are formidable and represent a major challenge for the vascular surgeon. Most of them show up for a vascular assessment only after the appearance of trophic lesions with loss of soft tissue, associating infection that can range from a minor one to sepsis. The therapeutic attitude towards these cases must be very carefully weighed, because ulcers are only the "visible part" of the iceberg. After the assessment, we usually find a variety of associated pathologies of the heart, kidneys, eyes, etc that need to be evaluated before revascularization surgery. Occasionally, patients have also a history of myocardial infarction, stroke or chronic kidney disease.

Peripheral arterial disease affects between 9-24% (2-4) of diabetic patients, and analogously, between 8-25% of them will develop diabetic foot ulcers (2, 5).

The appearance of trophic lesions in an ischemic lower limb is the most severe form of peripheral arterial disease and also a sign of severe ischemia (6).

The first revascularization intervention was performed in 2013, in "I. Juvara" General Surgery Clinic, Department of Diabetic Foot Repair Surgery of "I. Cantacuzino" Clinical Hospital, Bucharest, Romania. Having modest logistical resources, surgical infrainguinal or infrapopliteal revascularization were the only options of treatment for diabetic patients who approached the clinic. However, infrainguinal revascularization does not always lead to either rapid healing of ulcers or salvation of the lower limb from a major amputation. These evolutionary aspects, along with the need to add an adjuvant treatment, are both included in the present study.

MATERIAL AND METHODS

All patients included in our study had diabetes associated with leg ulcers and tissue loss, ranging from minimal to extensive gangrene or suppuration of the foot. Pstoperatively, they had a follow-up for at least one year, during which the healing of trophic lesions, patency of the bypass, need for an iterative bypass and minor or major amputations were all monitored. The types of bypass performed started from any infrainguinal level, with proximal, distal, pedicular or posterior tibial arthritis being the target artery of outflow.

This is a six-year retrospective study.

Depending on the immediate clinical evolution in the first 3-4 postoperative days, some patients received complementary infusion treatment with PG E1 (Alprostadil) (7). Based on observation sheets, we applied the WIfI Classification System: Amputation risk stratification based on Ulcer (Wound), Ischemia and infection severity (foot infection) (8).

What we have newly introduced in the evaluation of patients was the application of WIfI and postoperative classification after three to four days. This is considered similar to the pre- and postoperative TNM classification.

We added four more clinical parameters: sleep quality, degree of pain relief, distal pulse recurrence and local bleeding for patients with minor amputations prior to surgery.

We made a score from all seven parameters, with a minimum of 1 and a maximum of 13.

Population included in the study

A total of 115 patients were selected. The mandatory eligibility requirement was that they had diabetes with infrainguinal occlusive disease and stage III or IV Fontaine critical ischemia. Subsequently, patients were stratified according to the WIfI classification and were included in the 3 and 4 clinical stages. Patients with occlusive aorto-iliac disease and those with heart failure class III and IV NYHA were excluded due to logistical limitations of the Clinic.

Revascularizations were performed between 2013-2018, and patients were followed for at least one year postoperatively.

Study strategy

Patients were divided into two groups, one who underwent exclusively surgical treatment, and

the other who received additional infusion treatment with Alprostadil postoperatively. Retrospectively, based on clinical and minimally invasive evaluation by IGB, they were WIfI restadialized at 48-72 hours postoperatively and quantified on a numerical scale by four other parameters: pain, sleep quality, presence of distal pulse at the posterior and/or pedial tibial artery and appearance of local bleeding at the level of abutments from minor amputations.

The the score was put together as follows:

- the increase in IGB by 0.6 was noted with four points: 0.5 scored with three points, 0.4 with two points, and 0.1-0.3 one point;
- the presence of pain: unchanged=0 points; intense=1 point; improved=2 points; no pain=3 points;
- sleep quality: did not sleep=0 points; good=1 point; very good=2 points;
- presence of pulse: absent distal=0 points; present in the tibial or foot artery=1 point; present in the posterior tibial artery and foot=2 points;
- local bleeding: absent=0 points; present=1 point; abundant=2 points.

Group characteristics

In both groups, males predominated (over 60%). Given that the age of 55 is a critical threshold for both sexes, the majority of our subjects were aged 55 years and older. Importantly, older age was more frequent among female patients, most of them being between 75 and 84 years old in group 1 and 65 to 74 in group 2.

Men display a more severe form of arterial disease at a younger age (Figure 1).

Patient comorbidities are also among the most important characteristics of the studied groups: smoking, ischemic coronary heart disease, dyslipidemia, obesity, hypertension, chronic renal failure, and heart failure.

Thus, in both groups, the percentage of smokers is significantly higher in men comparatively to women (49.12-50.00% male smokers, compared to 17.24-27.27% female smokers).

Ischemic coronary heart disease is frequently found in both groups, without significant gender variations (27.27-35.09%).

Dyslipidemia also does not show significant variations between the two sexes, but it has a higher percentage of impairment compared to other comorbidities (68.97-81.82%).

RESULTS

The evolution of WIfI score between preoperative and postoperative stage in both groups is a favorable one, with a decrease of amputation risk (Figure 2).

However, a higher percentage of cases in the second group had a constant postoperative evolution and therefore, an unchanged risk of amputation after one year. These patients are the ones who have benefited the most from the infusion treatment with Alprostadil.

We have also statistically interpreted the evolution of WIfI classification according to the decrease or increase of risk levels in the postoperative phase compared to the preoperative one (Figure 3).

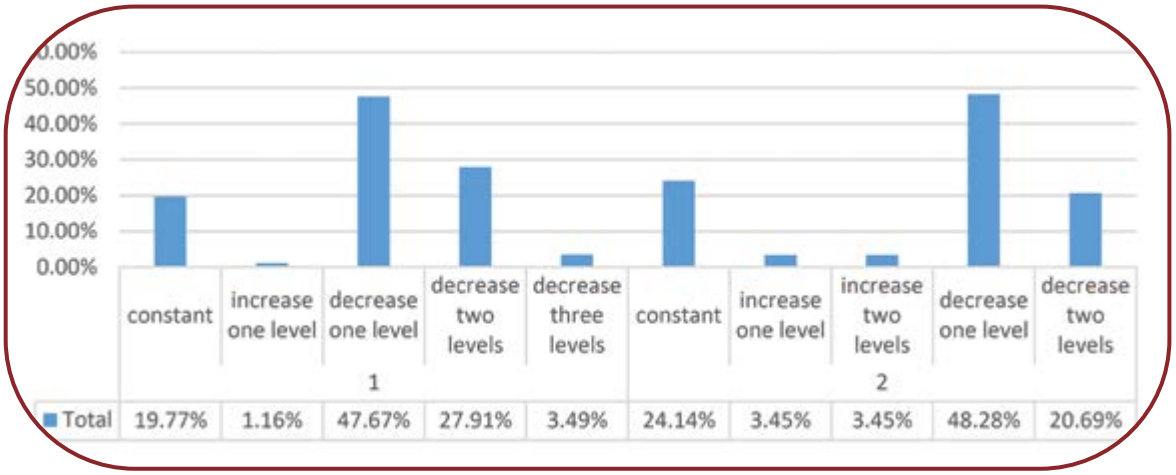

FIGURE 1. Patient distribution according to group, gender and age

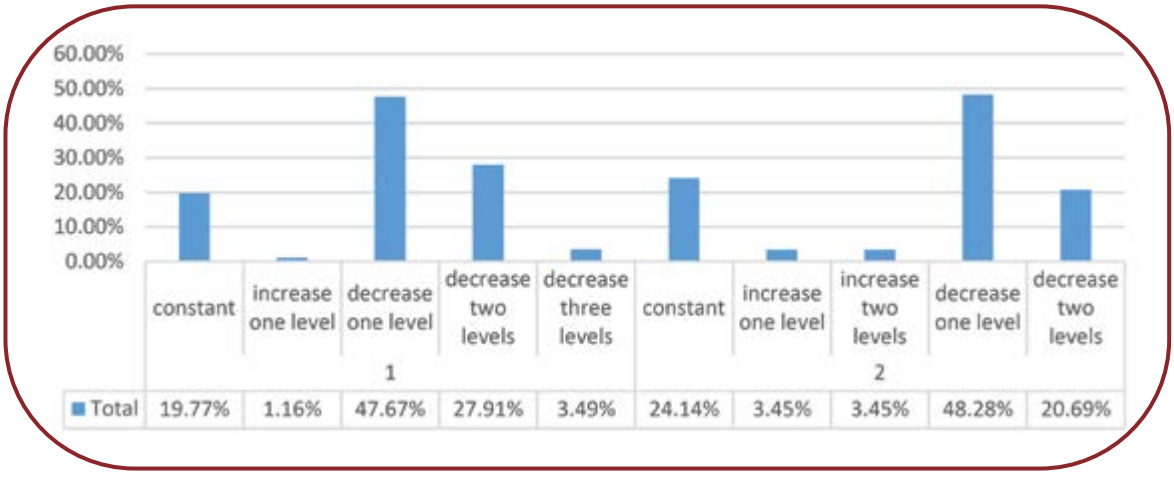

FIGURE 2. Evolution of WIfI level between preoperative and postoperative stage

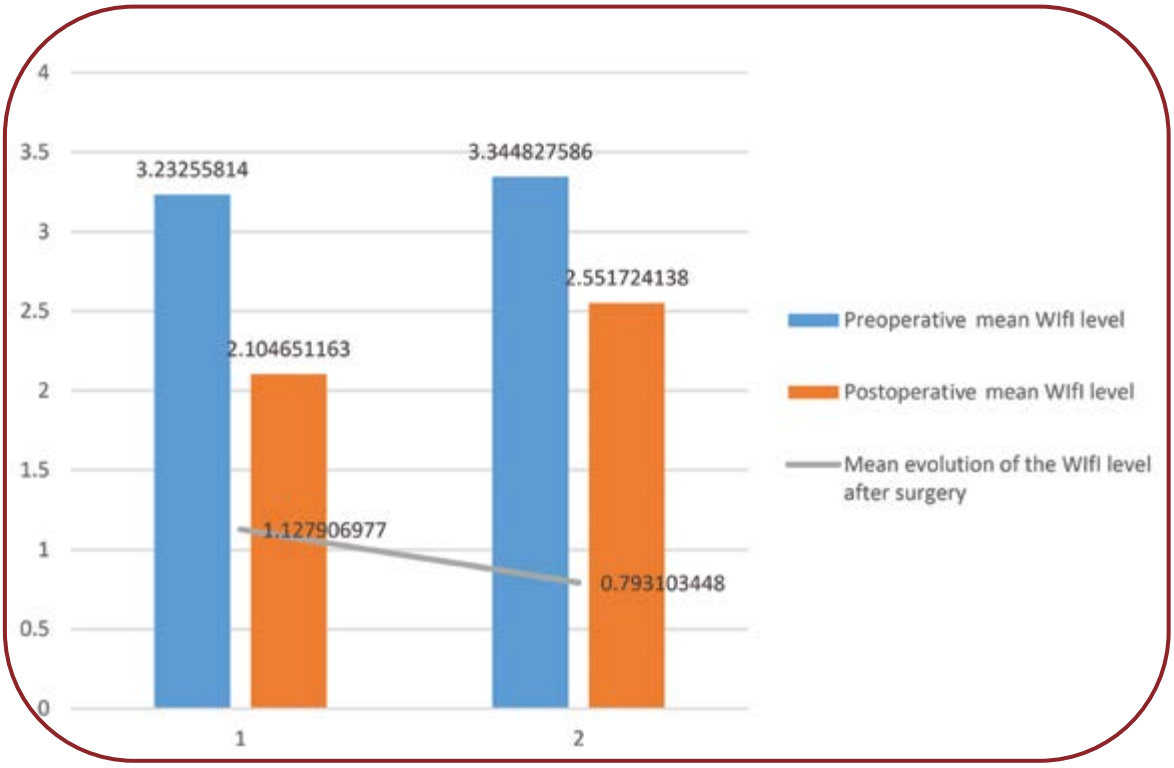

FIGURE 3. Average preoperative and postoperative WIfI level and its evolution

The postoperative situation improved in both groups, but significantly more in the first group, which is due to a more severe initial impairment in group 2 than group 1.

The score completes the postoperative WIfI assessment, a higher score signifying a very good clinical evolution of the revascularized lower limb and an improved general condition of patients. We asked ourselves if there were any connections between this score and the application of infusion treatment, and the statistical answer was affirmative.

Patients in group 2 had a much lower score than those from group 1, even if both groups spanned over the entire range of scores (Figure 4). The explanation is that post-vascular clinical outcomes were much better in the first group than group 2.

This is much better displayed in Figure 5 with grouped scores.

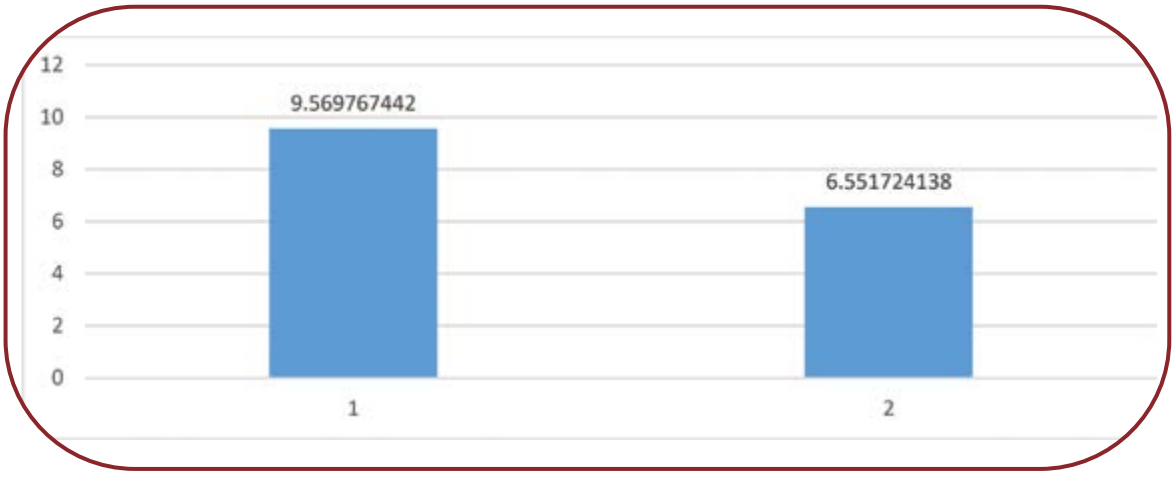

FIGURE 4. The average score of the two groups

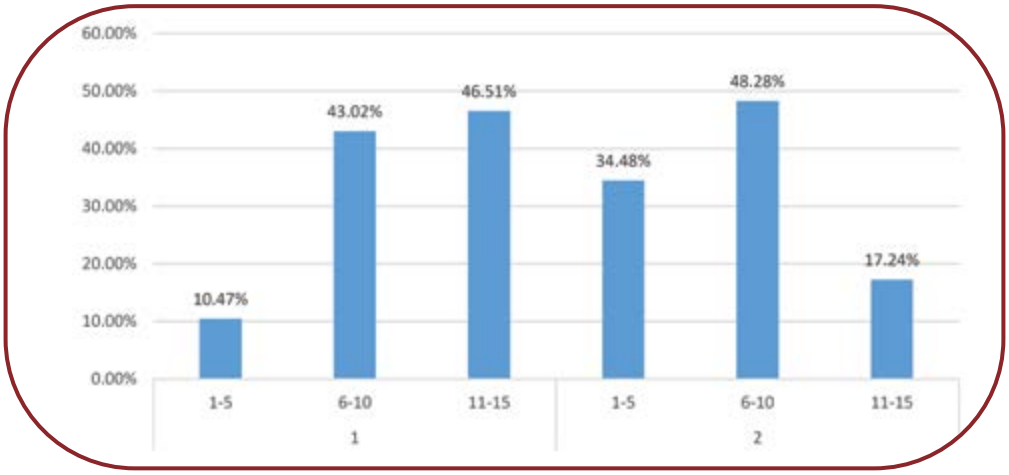

FIGURE 5. Patient distribution by score in the two groups

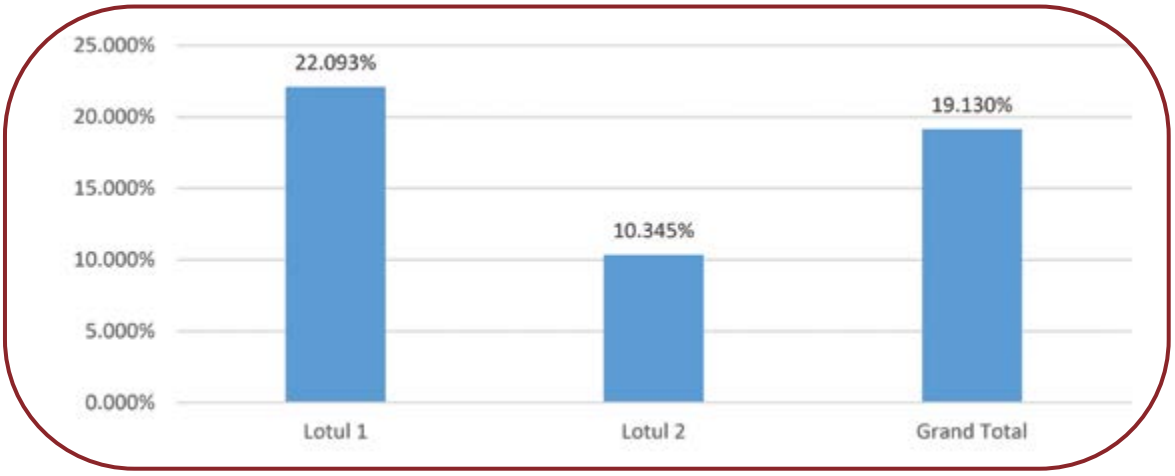

FIGURE 6. The rate of major amputations in the number of patients

We have also calculated the statistical correlation between group and score and we obtained a negative value of (-0.428112032). The interpretation is that there is an inverse statistical correlation (negative value) between the score and group number (a lower score points to group 2, a

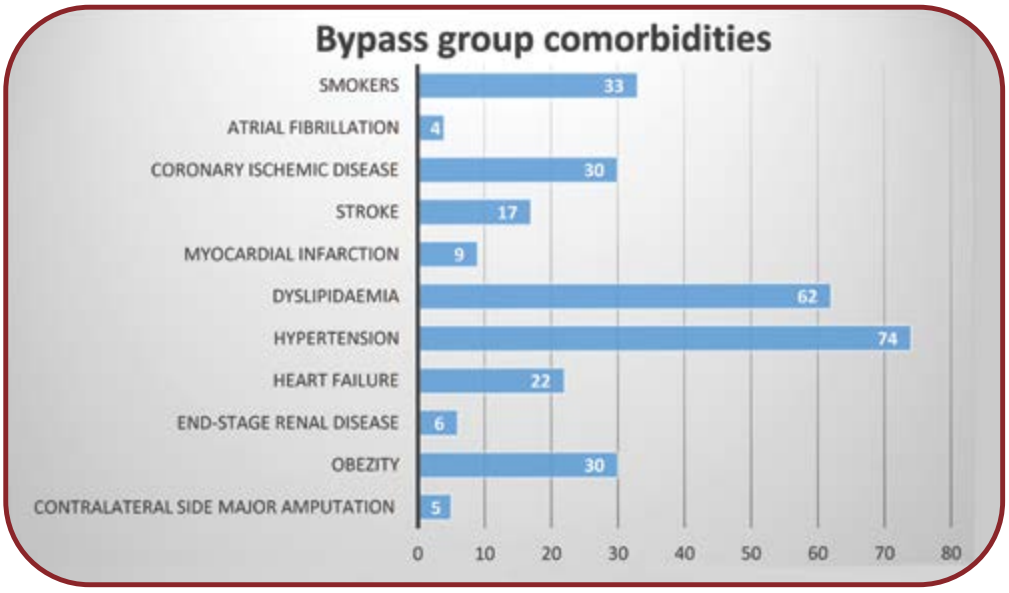

FIGURE 7. Bypass group comorbidities

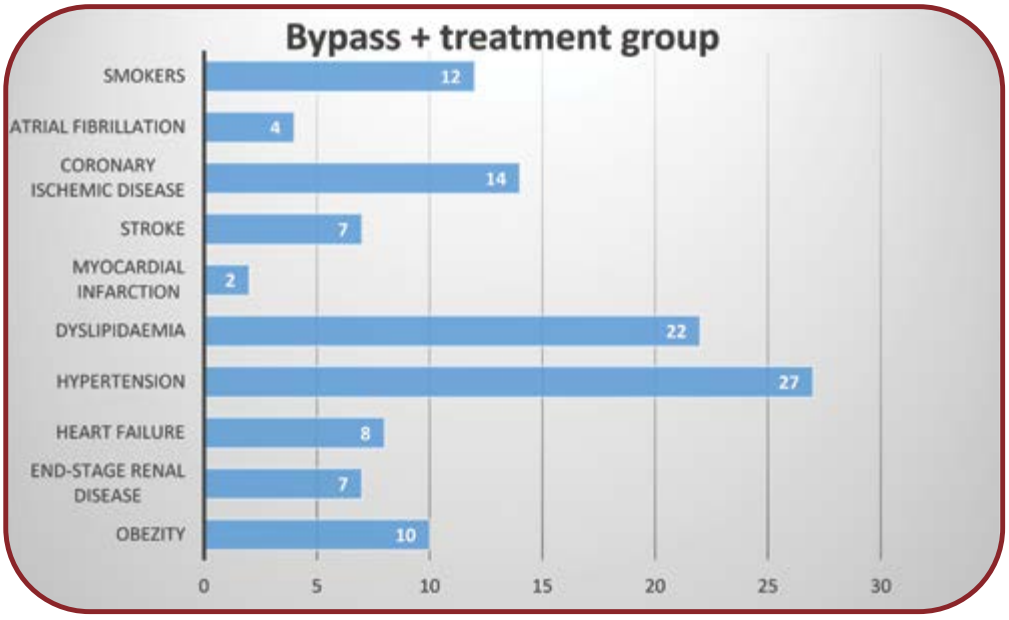

FIGURE 8. Bypass + treatment group

higher score points to group 1), but it cannot be said that automatically a low score belongs to group 2 and a high score to group 1.

Regarding the number of amputations, there is an important difference between the two groups, but overall, their rate is reported in the literature (9) (Figure 6).

This study is dedicated to diabetic patients with infrainguinal occlusive disease and chronic ischemia that threatens the lower limb. There are patients with both type I and type II diabetes, insulin-requiring or treated with oral antidiabetics. All patients were investigated by arterial Doppler ultrasound and/or lower limb arteriography. Patients eligible for open surgery were selected, for which anesthesia-surgical risk assessment was performed and for whom we followed the pre-established preoperative protocol. There were patients with numerous comorbidities, of which the most common were hypertension and dyslipidemia (Figures 7 and 8).

The idea to supplement the postoperative treatment with Alprostadil came after we observed the steady or very slow evolution of minor postamputation wounds or excisional debridements. This situation occurred in patients with

more a extensive deterioration of the leg trunks, so with a poor receptor ground, and not necessarily with interventions prior to extensive revascularization.

For an objective evaluation of the postoperative evolution, we have included several parameters besides those from the WifI classification. The use of WIfI classification and post-vascularization was considered beneficial by us. This classification has the same structure as the TNM classification and therefore, it seems appropriate to use it both before and after surgery. The optimal restadialization interval was found to be three days postoperatively.

The difference between the number of amputations in the two groups, which was almost double in group 1, probably comes from the inequality in the number of patients. However, it may suggest a much better outcome in patients with combination infusion therapy, even if their initial condition is more deteriorated than in group 1.

In the first group, we had a higher number of leg amputations, which were performed in the first month postoperatively, and a higher number of thigh amputations, which were performed after more than six months. Major amputations occurred mostly in moderate and high risk patients with clinical stages 3 and 4 WIfI. There were four amputations in the very low and low risk groups (clinical stages 1 and 2), which were imposed by the spread of the infection.

In the second group, the higher frequency of thigh amputations was maintained at over six months postoperatively. Also, three of the four amputations occurred in low-risk patients, due to the spread of the infection.

This phenomenon, that is present in both groups, is due to diabetic neuropathy.

There is an obvious usefulness of the score designed by us, as patients in group 2 have a lower average score than those in group 1; so, it is recommended that patients with a postoperative score lower than 9 benefit from infusion treatment with Alprostadil.

DISCUSSIONS

In practice, especially in diabetic patients, rescuing the lower limb with trophic lesions depends on several factors, with ischemia being just one of them. The classification systems that were imagined and implemented until 2014 failed to adequately assess the extent of ulcer and the severity of infection. Stratification of amputation risk and the benefit of lower limb revascularization were the main objectives of WIfI classification (Wound, Ischemia, foot Infection) (10). At the same time, this new classification changed the definition of critical ischemia of the lower limb. It has been used since 1954, when it was included as the last stage in the Fontaine classification and it applies exclusively to arteriopathic patients (10). The advantage of the WIfI classification is that it includes chronic occlusive arterial disease through the degree of ischemia, also addressing diabetic foot lesions: necrosis, ulcer, infection or gangrene and quantifies their extent and systemic impact. The 64 possible combinations fall into four risk groups of amputation after one year, also estimating the benefit of revascularization (very low, low, moderate and very high). In all cases, an attempt is made to stop the infectious outbreak, either through antibiotic treatment alone, or through minor amputations (transphalangeal, radius, transmetatarsal forefoot, Lisfranc or Chopart) (5, 8, 10).

In the literature, WIfI classification is used for reassessment at one month postoperatively. Given the similaritiy to the TNM classification, we tried a new approach to WIfI staging, using it in the first days after surgery.

In the first 48-72 hours after the restoration of the arterial flow of a lower limb, we noticed an improvement of patient's general condition and quality of sleep, associated with pain amelioration or even disappearance. In situations where these newly introduced parameters did not improve, with patients retaining a degree of residual ischemia, we used additional treatment with infusion Alprostadil.

Although there are not many studies on its exclusively use in diabetic patients and ESPECIAL randomized multicenter trial did not prove a clear benefit of the Alprostadil (7) treatment, we introduced it as a life-saving solution for residual ischemia. We believe that combining sustained exercise and a recovery program is a very important aspect of the treatment, which is applicable to all patients.

The literature also reports that the rate of major postrevascular amputations ranges between 10 and 15%, with about 63% of operations being

performed in the first year and a maximum in the first six months (11).

The presence of ulcers and gangrene with varying degrees of spread was the most important predictor, as in our case.

CONCLUSIONS

The overall amputation rate of 19% overlaps with data from the specialised literature, which encourages us to continue to develop revascularization interventions in an open way in "I. Juvara" Surgery Clinic of the "I. Cantacuzino" Clinical Hospital.

The implementation of the scoring system that we have configured will help us obtain the healing of abutments of minor amputations and save the limb from a major amputation.

The score is easy to calculate based on clinical parameters, most of them self-provided by patients, who are the most objective in evaluating their own postoperative evolution.

A study aiming to explore the evolution of patients in which revascularization is not possible, who have chronic ischemia threatening the lower limb and trophic lesions, receive treatment with Alprostadil and follow a recovery program should be considered. ❑

Conflicts of interest: none declared.
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