Seminars in Vascular Surgery 28 (2015) 195–200

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# Application of autologous platelet-rich plasma to enhance wound healing after lower limb revascularization: A case series and literature review

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ARTICLE INFO

ABSTRACT

Dermal tissue loss in patients affected by critical limb ischemia represents a serious wound-healing problem, with high morbidity, prolonged hospital stay, and high patient care costs. Treatment of ischemic foot lesions requires limb revascularization by endovascular or open surgical intervention and individualized patient-specific wound care, including antibiotic therapy; devitalized/infected wound debridement; and advanced wound dressing. In selected patients, spinal cord stimulation, vacuum-assisted closure therapy, and bioengineered tissue or skin substitutes and growth factors have been shown to improve wound healing. In this study, we present our preliminary results on topical application of autologous platelet-rich plasma to enhance the process of wound healing after revascularization of lower limbs in patients affected by critical limb ischemia.

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## 1. Introduction

Critical limb ischemia (CLI) is a clinical syndrome in which patients with occlusive arterial disease of the legs experience chronic ischemic rest pain, ulcer, or gangrene [1,2].

Foot ulcers in patients with Rutherford stage 6 lesions represent a serious problem, with high levels of morbidity, long hospital stay, and high costs. Current methods of treatment are represented by endovascular and surgical revascularization [3,4] in association with specific antibiotic therapy

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http://dx.doi.org/10.1053/j.semvascsurg.2016.01.002
0895-7967/$ - see front matter © 2016 Elsevier Inc. All rights reserved.

**Table 1 – Demographic characteristics, comorbidities, Rutherford stage, preoperative eco–color–duplex parameters and the type of treatment.**

| Patient characteristics | Comorbidities | Rutherford stage | Ultrasound evaluation | Surgical/endovascular treatment | Outcomes |
|---|---|---|---|---|---|
| Patient 1<br>Sex, female<br>Age, 78 y | Hypertension<br>Myocardial ischemia<br>Dyslipidemia | 5, necrosis of the last two toes of the left foot | Superficial femoral artery stenosis<br>Occlusion of left peroneal and posterior tibial artery<br>Post-stenotic flow on the left anterior tibial artery (PSV = 20 cm/s) | Superficial femoral artery PTA<br>Anterior tibial artery PTA<br>Amputation of fourth and fifth toes of the foot | Anterior tibial artery PSV >40 cm/s |
| Patient 2<br>Sex, male<br>Age, 73 y | Hypertension<br>Dyslipidemia<br>Ex-smoker | 5, right heel necrosis | Post-stenotic flow on the posterior tibial artery (PSV=20 cm/s) | Posterior tibial artery PTA<br>Heel surgical debridement | Posterior tibial artery PSV >40 cm/s |
| Patient 3<br>Sex, male<br>Age, 76 y | Hypertension<br>Myocardial ischemia<br>Diabetes mellitus<br>Atrial fibrillation | 5, necrosis of the third toe of the right foot | Femoropopliteal occlusion<br>Post-occlusive flow on the retromalleolar posterior tibial artery (PSV = 10 cm/s) | Femoro-posterior tibial artery bypass using the great sap henous vein<br>Amputation of the third toe of the foot | Posterior tibial artery PSV >40 cm/s |

Abbreviations: PSV, peak systolic velocity; PTA, percutaneous transluminal angioplasty.

for infected lesions, repeated local debridement, advanced moist wound dressing [5,6], spinal cord stimulation [7-9], and vacuum-assisted closure therapy [10,11].

More recently, bioengineered tissue or skin substitutes [12] and growth factors [13,14] have been used to improve wound healing after revascularization of lower limbs.

In particular, autologous platelet-rich plasma (PRP) allows the application of large amounts of growth factors, which stimulate the production of collagen and extracellular matrix through minimum quantities of plasma.

Glycoprotein platelet-derived growth factor (PDGF) is the first growth factor to appear in the wound, starting the repair process of the connective tissue. Its most important specific activities include mitogenesis, angiogenesis, and macrophage activation [15,16]. Growth factors promote quick increase of the number of undifferentiated mesenchymal cells at the scar site during repair and healing time. Therefore, the PRP advantage is to accelerate the regenerative process through the quantity of growth factors present in the platelets. In the present study, we report our initial experience about autologous PRP application on foot ulcers to enhance wound healing after revascularization of lower limbs, and a literature review.

## 2. Materials and methods

Between April and July 2015, three patients affected by Rutherford stage 6 CLI were enrolled in the present study, consisting of PRP application on foot ulcers after revascularization of the lower limbs. Patients were included in the study if the wound had a mostly clean wound bed just before product application, without local and systemic clinical signs and symptoms of active infection. Exclusion criteria were malignancy in the wound bed, current use of chemotherapy and oral corticosteroid therapy, and history of malignant tumors with a disease-free interval of 3 years or less.

Demographic characteristics, comorbidities, Rutherford stage, preoperative eco–color–duplex parameters and type of treatment for all patients are listed in Table 1. Two patients with atherosclerosis of the tibial vessels were submitted to endovascular treatment through percutaneous transluminal angioplasty. One patient with femoropopliteal occlusion and tibial vessels disease required surgical revascularization of the lower limb (femoro-posterior tibial artery bypass using the great saphenous vein). No perioperative or postoperative complications occurred.

All patients underwent postoperative ultrasonography that showed improvement of the flow on the distal vessel revascularized and 3 days after revascularization they underwent surgical debridement of their foot lesion, minor amputation, or both, as reported in Table 1. No signs of systemic infection were recorded (eg, absence of fever or absence of leukocytosis) and wound culture test was negative in all cases.

### 2.1. PRP

The PRP solution was supplied by the Calabria Cord Blood Bank, Service of Immunohaematology and Transfusion Medicine of Reggio Calabria Hospital. Each patient was submitted to a venipuncture of approximately 90 mL distributed in

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