

Research Article

Microcirculation Evaluation of Leg Ulcers - An Innovative Diagnostic Approach

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Abstract

Recent researches in the field of lower limb ulcers have focused on the persistent state of chronic inflammation the probable cause of delayed healing. The oximetry studies have also highlighted the hypoxia condition in the periwound territories. Using the LASCA method (Laser Speckle Contrast Analysis), which makes possible remote study of the ulcer bed, and transcutaneous oximetry was evaluated in 21 patients with lesions of the lower limbs of different origins the state of the microcirculation both of the bed that in the surrounding area the ulcerative lesion. The preliminary study allowed to highlight very low O₂ values (similar, if not worse than those found in subjects suffering from PAD) in the context of the ulcer and gradually decreasing values in the periwound site, suggesting the need to deepen the role of the microcirculation in the various evolutionary stages of the ulcerative lesion.

Keywords: Chronic inflammation; Laser Speckle Contrast Analysis (LASCA); Leg ulcers; Microcirculation; Perfusion Unit (PU); Region of Interest (ROI)

Introduction

In recent years, research into ulcers of the lower limbs has underlined the importance of chronic inflammation as the main cause of tissue repair delays [1,2]. Pathogenesis is still unclear, and many hypotheses have been proposed [3,4]. The data emerging from biochemical research have identified different molecules and enzymatic

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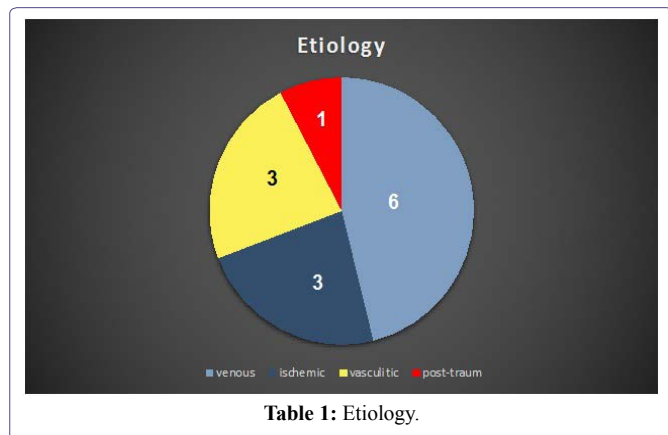
systems able to perpetuate the Chronicity of inflammation, and further acquisitions on cellularity (chemo-taxis, macrophages and monocytes) demonstrate their complex interconnection that makes it still difficult to univocally explain the processes involved respectively at the cellular level, intercellular and with the extracellular matrix [5-7]. Biofilms, ROS / NOS systems [8-13], microvesicles [14,15], metallo-proteases [3-5] and other factors have been examined and are sometimes held responsible for the transformation of the acute inflammatory state into chronic [14-20]. Only the presence of the infection in bio film form and the ability of the latter to modify the host's reaction appear to be able to provide a plausible explanation, but not all ulcers are infected and not all are found of biofilm [21,22]. Moreover, the research on the microcirculation has shown that at the level of the area surrounding the ulcer there is a hypoxia state that can cause suffering in the endothelial glycol-calyx [23-26]. Recent studies have demonstrated in vivo and in computational models that this structure is able to dialogue with endothelial cells and to release factors that can modify leukocyte populations (macrophages) inducing the development of pro-inflammatory populations [27-32].

Because of difficulty to obtain effective data in the bottom of the ulcer, Laser Speckle Contrast Analysis (LASCA) has been used to study capillary perfusion in this side [33-35]. LASCA is based on the concept that when a coherent light (as laser light) hits an object the scattered light will form a random interference pattern consisting in dark and brightness areas or speckle pattern. If the object is stationary the pattern will be clear, but with movement (as blood flow) speckle pattern will changes over time. By CCD camera is possible to capture these changes and depending on the degree of movement the level of blurring. The level of blurring is quantified by the speckle contrast and could be correlate with blood flow and blood perfusion measurement. Usually a helium-neon laser (633 nm) and CCD camera are employed for source and detector, respectively (Perimed AB) [36-40]. Aim of this research is the evaluation of skin circulation in vivo in patients affected of leg ulcers.

Methods

21 patients (13 males and 8 female average age 59, 6 ± 1, 4 yy) affected of leg ulcers were enrolled at Operative Unit of Angiology in Vittorio Emanuel Hospital Catania, Italy from September 2017 to January 2018 (Table 1).

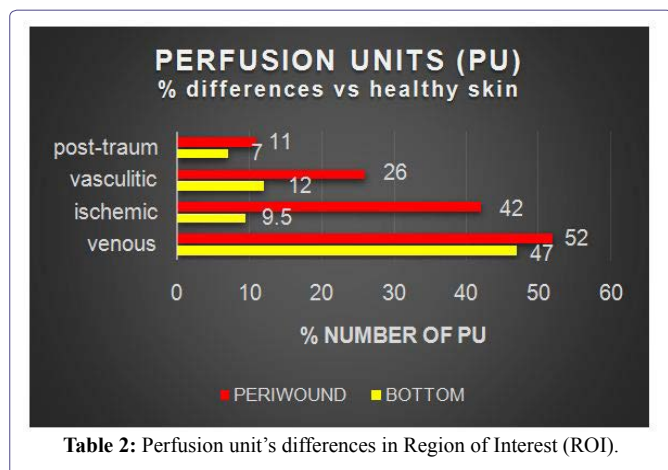
All patients underwent to clinical, instrumental and serological examination and during admittance period routinary anti-platelet therapy was administered. In venous patients affected of post-thrombotic syndrome antithrombotic therapy was administered (Acenocumarol or NAO) plus compressive therapy (high stiffness bandages) and topic application of silver sulphadiazine surfactant dressing directly on the wound [29-31]. Vasculitis patients were assessed by arterial and venous Eco Color Doppler and Serological Immunoassays. In post-traumatical cerno-arterial lesions were detected. Therapy was carried out with steroids, analgesics and local advanced dressings in vasculitic ulcers.



In patients affected of PAD iloprostev. Infusion was administered daily for a week. In each patient pO₂, pCO₂, Laser doppler and Laser Speckle Contrast Analysis (LASCA) (Peri Cam PSI System, Perimed Italy) on three Regions Of Interest (ROI) corresponding to the bottom of the wound, periwound area and peripheral area of skin as healthy skin were studied.

Results

Data show increase of Perfusion Units (PU) in periwound areas in allulcers. In venous and vasculitic PU were greater respectively 52, 3 and 26% than healthy control. Also ischemic ulcers, even poorly, showed the same trend (Table 2).



In this last group iloprost infusion have reduced PU in perilesional areas and increased PU in the bottom of ulcer. No significant changes were present in vasculitic ulcers after iloprost administration (Figure 1). Local administration of SSD (Surfactant Silver Sulphadiazine) Gel-Dressing was followed by reduction of PUs both in the bottom and periwound areas. Data analysis at basal time high lights a greater amount of PU sin periwound areas (ROI) than in the bottom and check areas.

After SSD-dressing administration a decreased number of PU sin periwound and an increase in bottom area have been observed (Figure 2). Despite the limited number of cases examined, the preliminary data review implies a number of considerations:

- Imaging by means of laser speckle allows the observation of the ulcer bed in real time and the changes that occur after the administration of vaso active substances.
- There is a correlation between PUs and oximetric data.
- Especially in vasculitis patients, even the presence of chronic inflammation of the skin, oxymetry values tend to be hypoxic.
- After the administration of drugs, achronic inflammation in periwound area persists.
- Data of Laser-doppler show the presence of vasomotion before and after the administration of SSD-dressing and of iloprost.

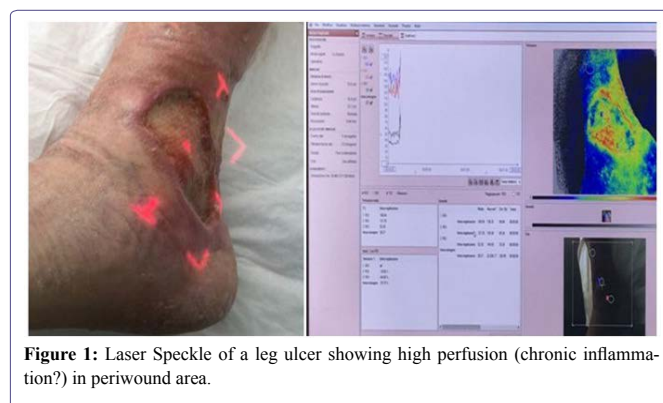


Figure 1: Laser Speckle of a leg ulcer showing high perfusion (chronic inflammation?) in periwound area.

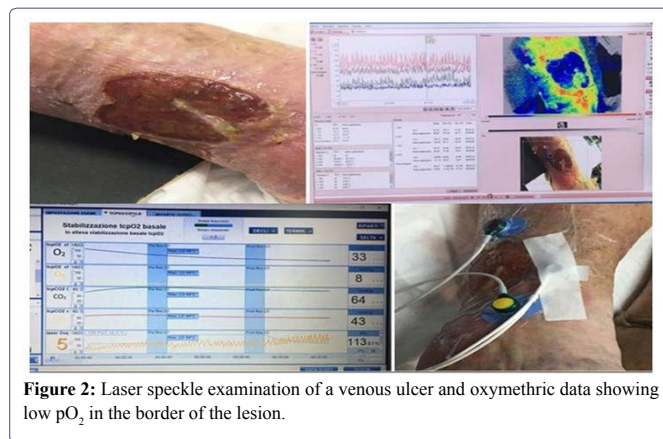


Figure 2: Laser speckle examination of a venous ulcer and oxymetric data showing low pO₂ in the border of the lesion.

This could be interpreted as the primary cause of the chronicity of the lesion and the presence of elevated levels of MMPs in the exudates and ulcer tissue confirm the state of chronic inflammation.

Even the administration of the SSD-Gel dressing (a transparent gel and which does not alter their fraction of the laser light) LASCA is able to determine (especially in the bottom of the ulcer) the same PUs alterations observed after infusion of iloprost, but it is not yet clear whether this information is related to anti-inflammatory and antibacterial properties of the dressing or its own vasoactive properties.

Conclusion

Data analysis high lights confirm the presence of a chronic inflammation in all the ulcers. The alteration of skin microcirculation is more evident in periwound areas, while in the bottom number of

PU is poor. After the local application of topical SSD dressing, PU numbers in the bottom are increased. These data suggest a direct correlation between iloprost infusion and capillary bed vasodilatation. The effect of SSD dressing could be explained by its direct anti-inflammatory and antiseptic properties they could be responsible of the micro-environment changes in the bottom of ulcer. The persistence of a ring area surrounding the ulcer (presence of chronic inflammation) could be explained as there all cause of delay in healing. These data are not significant from a statistical point of view, but open up new diagnostic horizons in the field of wound care. This new method together with O₂ oxymetry and Laser-doppler, allows evaluating in vivo and in real time the microcirculation directly in the bottom of ulcer helping to verify the effectiveness of both systemic and local-therapy in this area.

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