Skin microcirculation in peripheral arterial obliterative disease

M. Rossi a,*, A. Carpi b

a Department of Internal Medicine, University of Pisa, Via Roma 67, 56100 Pisa, Italy
b Department of Reproduction and Ageing, University of Pisa, Pisa, Italy

Received 22 July 2004
Available online 25 August 2004

Abstract

The important role of microcirculation in the pathophysiology and symptoms of peripheral arterial obliterative disease (PAOD) has been progressively emphasized during the past twenty years, thanks to the use of different non-invasive methods, such as capillaroscopy, laser Doppler (LD) fluxmetry and transcutaneous measurement of oxygen tension (tcPO2). Basally, in the diseased leg of stage II PAOD patients, leg skin perfusion recorded by means of LD fluxmetry is quantitatively normal. However, spectral analysis of skin LD tracing shows an abnormal flowmotion, with increased amplitude of the flowmotion waves related to endothelial, neurogenic and myogenic activities, suggesting a relatively early skin microcirculatory adaptation in this PAOD stage. Following ischemia, an impaired total skin LD hyperemia and a reduced skin capillary nutritional blood flow at capillaroscopy, concomitantly with a reduced increase of flowmotion waves related to endothelial, myogenic and sympathetic activities, have been observed in the diseased leg of stage II PAOD patients. In critical limb ischemia (CLI), a more advanced cutaneous microcirculatory deterioration has been clarified, with a more severely impaired post-ischemic hyperemia, a reduced tcPO2 and a severely perturbed skin flowmotion in the diseased leg. This integrated skin microcirculatory diagnostic approach can be used for a better management of PAOD patients.

© 2004 Elsevier SAS. All rights reserved.

Keywords: Skin microcirculation; Leg atherosclerosis

1. Introduction

It is well known that an impairment in the leg skin microcirculation is one of the main features in advanced clinical stages of the peripheral arterial obliterative disease (PAOD), while an impairment of skeletal muscle microcirculation occurs in stage II PAOD patients during exercise. However, more recently, important changes of leg skin microcirculation have been shown also in stage II of PAOD, using different non invasive techniques, which have been available to investigate skin microcirculation in clinical settings. These techniques are allowing us to improve knowledge on the pathophysiology of leg skin microcirculation in all stages of PAOD and are enabling us to improve disease management in these patients.

This review, after describing the techniques used to study skin microcirculation and its physiology, intends to summarize the principal features of leg skin microcirculation in different stages of PAOD.

2. Techniques to study skin microcirculation

Capillaroscopy [1,2], laser Doppler (LD) fluxmetry [3] and transcutaneous measurement of oxygen tension (tcPO2) [4], are available for studying leg skin microcirculation in PAOD. Capillaroscopy allows the investigation of nailfold and skin capillaries morphology and density [1,2]. A sophisticated and computerized technique of capillaroscopy (videophotometric capillaroscopy) also permits to study non-invasively the blood flow in the nutritional skin capillaries [5,6]. By using different intravital fluorescent dyes, e.g. sodium fluorescein and indocyanine green, the microvascular dynamics, flow distribution and microvascular permeability can also be studied [7].

Laser Doppler fluxmetry allows continuous, non-invasive, real-time assessment of skin perfusion in a hemispheric illu-
3. Skin microcirculation physiology

The three main functions of skin microcirculation (skin tissue nutrition, heat exchange for thermoregulation and blood flow redistribution during stress) are guaranteed by its peculiar microvascular architecture and its high functional reserve [19]. Skin microvessels can be subdivided into thermoregulatory and nutritional vessels. Although the relative distribution of blood flow between the non-nutritional thermoregulatory vascular bed and the nutritional vessels varies considerably between different skin areas, nutritional capillaries usually carry less than 15% of total blood in the foot. Under extreme thermal stress, skin blood flow can account for up to 50% of the total cardiac output. Such a functional reserve is due to a fine control of cutaneous vascular resistance, capable of large dynamic changes in response to local, mechanical and humoral factors, as well as to the autonomic nervous signalling. A special feature of the cutaneous microvasculature is the presence of numerous arteriovenous (AV) anastomoses which are coils vessels with an average lumen of 35 µm, connecting arterioles and venules in the skin of the extremities. AV anastomoses, mainly present in the hands, feet, ears and the nail beds, allow the blood flow directly from the arterioles to the venules of the deep vascular plexus of the skin, bypassing the high-resistance arterioles and capillaries of the more superficial vascular plexus. Having a dense innervation and a thick layer of smooth muscle cells in their wall, AV anastomoses are involved in peripheral vasodilation in response to body heating and in vasoconstriction in response to cold [19].

The fine-tuning of skin microvascular resistance and blood flow distribution is obtained through the dynamic oscillations of the diameter of the arterioles, i.e. vasomotion [20,21]. At a given time, not all skin microvascular units are open and perfused. The functional recruitment of previously inactive units represents a further mechanism for increasing capillary perfusion during exercise or passive thermal stress [22]. Different control mechanisms modulate diameter of arterioles, which results in blood flow oscillations, the so-called flowmotion [20,21].

Power spectral analysis of human skin Laser Doppler perfusion signals has detected five frequency components of skin flowmotion [16]: the band 0.6–1.8 Hz due to transmission to cutaneous microcirculation of the haemodynamic modifications synchronous with heart activity [23], the band 0.2–0.6 Hz consistent with respiration [24], the band 0.02–0.06 Hz associated to sympathetic activity [25], the band 0.06–0.2 Hz related to myogenic activity of the vessel walls [16] and the band 0.007–0.02 Hz more specifically related to the activity of vascular endothelium [16].

4. Leg skin microcirculation in stage II PAOD

A quantitatively normal baseline leg skin perfusion has been observed at LD fluxmetry in the diseased leg of stage II PAOD patients [3]. In spite of this finding, spectral analysis of skin LD tracing showed an abnormal flowmotion pattern in the diseased leg of these patients, with an abnormally increased amplitude of the flowmotion waves related to endothelial function, neurogenic and myogenic activities. This suggests a compensatory mechanism, which maintains a normal leg skin perfusion in these patients.

Skin post-ischemic hyperemia, a method used to explore the skin microcirculatory adaptation to vascular disease [12–15], showed a blunted or delayed response in stage II PAOD patients [3,12,13], with a positive relationship between the time from release to peak-flux and the severity of PAOD [13,14]. This is in line with the observation of an impaired hyperemic response in skin capillaries blood flow nutritional after 1 min of arterial occlusion in these patients using videophotometric capillaryscopy [6]. Moreover, flow-
motion waves related to endothelial, myogenic and sympathetic activities did not increase during skin post-ischemic hyperemia. These data suggest that the compensatory mechanisms, which maintain the normal leg skin perfusion in baseline conditions, are exhausted during post-ischemic hyperemia, with consequent delayed or blunted skin hyperemic response.

Another finding of impaired skin microcirculation in these patients is a blunted hyperemic response to iontophoresic delivery of ACh and SNP, suggesting an endothelium and a smooth muscle dysfunction, respectively [12,17]. Patients with PAOD frequently show co-morbidity, such as arterial hypertension, diabetes mellitus and hypercholesterolemia, which can negatively affect endothelial and smooth muscle cell function [17,26].

Moreover, the skin vascular bed is considered a good “window”, reflecting other vascular beds of the body [11]. This makes the assessment of skin microcirculation a very useful tool in studying microcirculation in different pathological conditions, in which also other vascular beds can be involved.

A reduction of skin hyperemic response to ACh iontophoresis delivery at the peak of claudication was observed in stage II PAOD patients, in spite of a preserved response to SNP, suggesting that exhaustive intermittent claudication is associated with a further impairment of skin endothelial dysfunction [17]. This event can represent the cutaneous manifestation of a more extensive endothelial vascular impairment, associated with exercise-induced lower limb ischemia [27], and suggests not to exceed the threshold of claudication during rehabilitation program of stage II PAOD patients [17].

Videophotometric capillaroscopy is particularly useful in stage II PAOD diabetic patients who are susceptible to develop foot ulcer despite of apparently adequate baseline skin perfusion in their extremities. The capillary blood flow results severely reduced during reactive hyperaemia in stage II PAOD diabetic patients, while total skin perfusion investigated by LD fluxmetry is normal in these patients during the same test [28]. These findings indicate that sufficient blood reaches the investigated area, but does not enter into the skin capillaries [28], contributing to the higher risk of chronic foot ulcers in diabetic patients with PAOD.

5. Leg skin microcirculation in critical limb ischemia

Values of skin perfusion below normal values have been recorded only at level of toe pulp in PAOD patients with critical limb ischemia (CLI) [29]. A severely altered pattern of skin flowmotion, with reduced prevalence of slow waves and increased prevalence of fast waves, has been recorded in patients with critical limb ischemia at the diseased leg [30,31]. This finding is consistent with the exhaustion of the compensatory mechanisms of skin perfusion basally active in stage II PAOD patients, concurring to the skin microcirculatory nutrition defect, which characterizes this disease stage.

A cutaneous microvascular remodeling, with reduced capillary density, has also been recently demonstrated in PAOD patients with leg ulceration [32], contributing to the advanced skin microcirculatory impairment.

With regard to normal subjects or stage II PAOD patients, patients with CLI show an increased skin LD flux during leg dependency [33,34]. This suggests that the normal postural vasoconstriction response, that limits the increase of capillary pressure, is compromised in patients with CLI. This favors capillary hypertension and filtration of fluid in excess [33]. The resulting edema, commonly observed in patients with CLI, can compress nutritive capillaries and increase oxygen diffusion distance, further contributing to the impairment of tissue nutrition. Furthermore, peak capillary flow velocity after occlusion can be increasingly compromised [6], by perturbed vasomotion and perfusion pressure reduction.

In the past, transcutaneous measurement of oxygen tension has been used for predicting limb loss in patients with critical limb ischemia [35,36] and different cut-off of TcpO2 have been suggested: 10 mmHg [35] or 20 mmHg [36]. However, recent data have shown that TcpO2 is a more accurate predictor of future limb amputation in patients with non-reconstructible CLI, when associated with findings of skin microcirculation obtained by other investigations such as capillaroscopy and LD fluxmetry [37]. Patients classified with “poor” leg skin microcirculation, according to a combination of a capillary density lower than 20/mm², absent reactive hyperemia in LD tracing and TcpO2 lower than 10 mmHg at the diseased leg, required amputation in a follow-up period as long as 36 months. In the groups with “good” leg skin microcirculation (capillary density of 20/mm² or more, presence of reactive hyperemia in LD tracing and TcpO2 of 30 mmHg or more) nonsurgical treatment was sufficient for limb salvage. On the other hand, the ankle blood pressure, which is related to the degree of macrovascular disease, showed a poor predictive value for the occurrence of amputation [37].

Table 1 summarizes the principal results of the above reported techniques in different stages of PAOD.

6. Conclusion

The role of skin microcirculation in the pathophysiology and symptoms of PAOD has been elucidated thanks to an integrated approach of different morphological and microhaemodynamic techniques.

Haemodynamic changes in skin microcirculation have also been found in stage II PAOD patients, both in baseline conditions and during different stress tests, suggesting a
relatively early microcirculatory adaptation. A more advanced cutaneous microcirculatory deterioration has been confirmed and further clarified in critical limb ischemia. This skin microcirculatory diagnostic approach can be used for a better management of PAOD patients.

 Moreover, the skin vascular bed, more and more appears a good “window” for investigating the general microcirculatory involvement in systemic vascular diseases.

References


Anvar M, Khiabani H, Kroese A, Stranden E. Patterns of skin flow-motion in the lower limbs of patients with chronic critical limb ischaemia (CLI) and oedema. Eur J Vasc Endovasc Surg 2000;20:536–44.


