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Assessing blood flow, microvasculature, erythema and redness in hypertrophic scars: A cross sectional study showing different features that require precise definitions

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ABSTRACT

Background: In hypertrophic scar assessment, laser Doppler imaging (LDI), colorimetry and subjective assessment (POSAS) can be used to evaluate blood flow, erythema and redness, respectively. In addition, the microvasculature (i.e. presence of microvessels) can be determined by immunohistochemistry. These measurement techniques are frequently used in clinical practice and/or in research to evaluate treatment response and monitor scar development. However, until now it has not been tested to what extent the outcomes of these techniques are associated, whilst the outcome *terms* are frequently used interchangeably or replaced by the umbrella term 'vascularization'. This is confusing, as every technique seems to measure a specific feature. Therefore, we evaluated the correlations of the four measurement techniques.

Methods: We included 32 consecutive patients, aged ≥18 years, who underwent elective resection of a hypertrophic scar. Pre-operatively, we performed LDI (measuring blood flow), colorimetry (measuring erythema) and the POSAS (subjective redness) within the predefined scar area of interest (~1.5 cm). Subsequently, the scar was excised and the area of interest was sent for immunohistochemistry, to determine the presence of microvessels.

Results: Only a statistically significant correlation was found between erythema values (colorimetry) and subjective redness assessment (POSAS) ($r=0.403$, $p=0.030$). We found no correlations between the outcomes of LDI, immunohistochemistry and colorimetry.

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Conclusions: Blood flow, the presence of microvessels and erythema appear to be different hypertrophic scar features because they show an absence of correlation. Therefore, in the field of scar assessment, these outcome terms cannot be used interchangeably. In addition, we conclude that the term 'vascularization' does not seem appropriate to serve as an umbrella term. The use of precise definitions in research as well as in clinical practice is recommended.

1. Introduction

Surgical procedures, traumatic injuries and burns may cause hypertrophic scars [1]. These scars can have significant impact on patients' quality of life due to functional and cosmetic problems such as scar redness, increased thickness, pain, pruritus and contraction [2,3]. Hypertrophic scars result from a wide array of derailed wound healing processes [4,5]. Previous research suggests that new blood vessel formation, mainly apparent as angiogenic sprouting of pre-existing blood vessels, is an essential process in the development of hypertrophic scars [6]. Therefore, it has been hypothesized that several treatment regimens (e.g. laser, pressure garments and cryotherapy) work by destructing the microvasculature and/or reducing the blood flow [7–9]. This may result in hypoxia that would lead to fibroblast degeneration and collagen degradation, both enhancing shrinkage of the hypertrophic scar tissue.

When looking at hypertrophic scars in clinical practice, one could ask the question: which features make these scars so obvious and therefore problematic? Besides increased thickness, also the amount of redness appears to have a major impact on the judgement of scar quality by both clinicians and patients. But what are the underlying causes of scar redness and consequentially, how can this aberrant scar feature be assessed so that we can monitor the scars? Several measurement techniques are frequently used in clinical practice and in research to aid in the evaluation of scar development and treatment response [10–12]. For example, laser Doppler imaging (LDI), a non-invasive flow measurement technique, can be used to quantify and visualize blood flow in scars [13,14]. In a previous study, Oliveira et al. showed increased blood flow values in hypertrophic scars compared to normal skin [13]. Furthermore, color meters are used to measure erythema [15], which is often interpreted as an indirect measure of the microvasculature or blood flow.

Until now, it has never been tested to what extent the outcomes of frequently used measurement techniques are associated, whilst they all pursue to assess scar redness in a certain way. Therefore, we determined whether outcomes of the following measurement techniques are associated: colorimetry (measuring scar erythema), LDI (measuring blood flow values), immunohistochemical analysis (determining the presence of microvessels), and subjective assessment (measuring redness as perceived by observers). Moreover, in literature as well as in clinical practice, these four scar features are often used interchangeably and they are referred to as 'vascularization' or 'vascularity'. For the purpose of clarity, we also aimed to explore whether it is appropriate to gather these scar features under the umbrella term 'vascularization'.

2. Methods

2.1. Study design and patients

A cross-sectional multicenter study was performed between June 2013 and June 2015. We included 32 consecutive patients, aged ≥18 years, who underwent resection of a hypertrophic scar. Hypertrophic scars were defined as scars with a thickness score or vascularization score ≥3 as determined by the Patient and Observer Scar Assessment Scale (POSAS) [9,16]. Patients were recruited in three hospitals: the Red Cross Hospital in Beverwijk, the Netherlands, the Academic Hospital in Maastricht, the Netherlands and the University Hospital in Leuven, Belgium. The Medical Ethics Committee of the district Noord-Holland in the Netherlands approved the study protocol (reference number NH013.191) and agreed that this study was outside the scope of the Medical Research involving Human Subjects Act. However, in the light of the Declaration of Helsinki, written informed consent was obtained from all patients.

2.2. Measurement instruments

2.2.1. Laser Doppler imaging

To assess blood flow in the scar, the moorLDI2 Imaging System (Moor Instruments Ltd., Axminster, United Kingdom) was used. For product details and a thorough explanation on the working mechanism we refer to http://moorclinical.com. After completion of each LDI measurement, data were analyzed offline using moorLDI2 Research Software V6.0 [17]. The blood flow was automatically calculated and expressed in perfusion units (PU). In addition, adjacent healthy skin was measured to obtain a control blood flow value within each patient. The following LDI parameter settings were used: data unit: perfusion, bandwidth: 250 Hz–15 kHz, normalization: DC, scan speed: 4 ms/pixel, background threshold: 50 PU. In this way, the tissue depth probed by the moorLDI2 was approximately 2 mm, as confirmed by Moor Instruments.

2.2.2. Colorimetry

The most commonly used principles for measuring scar color are narrow-band reflectance spectrophotometry and tristimulus reflectance colorimetry. For this study, we only used narrow-band reflectance spectrophotometry values obtained in Beverwijk, the Netherlands (n=29), as measured by the DSM II ColorMeter (Cortex Technology, Hadsund, Denmark). The DSM II ColorMeter presents erythema and melanin index values, based on the differences in light absorption of red and green by hemoglobin and melanocytes, respectively [18,19]. This is achieved by two light-emitting diodes that illuminate a

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