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Assessment of Endothelial Functions by Power Spectral Density of Hemodynamic Parameters in Skeletal Muscles

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Abstract: We assessed in 14 healthy volunteers and one septic patient low and very low frequency oscillations in hemodynamic parameters of muscles by studying their power spectra density exploiting time domain near-infrared and diffuse correlation spectroscopies.

1. Introduction

Endothelial functions are pivotal for our organism's regulatory processes, governing vasoregulation, homeostasis, and the barrier functions of blood vessels. However, various diseases, such as septic shock and acute respiratory distress syndrome, cause endothelial dysfunctions. In recent years, it has been demonstrated that combining near-infrared spectroscopy (NIRS) with vascular occlusion tests (VOT) can effectively discern the progression of these diseases. This integration could enable the evaluation of the severity of endothelial dysfunction through the reoxygenation rate after VOT [1,2].

As part of the VASCOVID (Horizon 2020 European project) project (https:\\vascovid.eu), we investigated an alternative approach to assess microvasculature functions. This method utilizes non-invasive and stationary diffuse optical (DO) monitoring of peripheral muscles, eliminating the requirement for additional uncomfortable interventions such as VOT. Building upon insights from laser Doppler flowmetry (LDF) and photopletismography (PPG) studies, we explored the feasibility of evaluating microvascular functions through the analysis of frequency spectra derived from hemodynamic parameters measured in microcirculatory system via DO. Indeed, from LDF studies, it has been demonstrated that blood flow oscillations are related to different physiological processes depending on their frequency [3]: components in the range [0.6 - 2.0] Hz are related to cardiac functions; components in the range [0.145 - 0.6] Hz are related to respiratory activity; components in the range I_3 = [0.052-0.145] Hz are related to myogenic activity; components in the range I_2 = [0.021 - 0.052] Hz (low frequency, LF), are related to neurogenic (sympathetic) activity; and very low frequency (VLF) components I_1 = [0.0095 - 0.021] Hz are related to the endothelial activity dependent on nitric oxide (NO). However, LDF and PPG are sensitive only to superficial tissues (i.e., skin), and they do not give insight on deep tissues as skeletal muscles.

In this work, we used a hybrid time domain NIRS (TD-NIRS) and diffuse correlation spectroscopy (DCS) device to measure the spectra of hemodynamic parameters during rest in four body areas: thenar eminence, plantar fascia, sternocleidomastoid, and forearm muscles (wrist flexor group). These muscles were selected to discern whether oscillations in DO measurements might be impacted by the proximity of major vessels (e.g., the sternocleidomastoid artery) and to identify if these oscillations are more pronounced in specific muscles, such as the distal muscles of the thenar eminence and plantar fascia. Furthermore, we compared the results obtained from healthy subjects with measurements taken from a septic patient in the intensive care unit (ICU).

2. Methods

Resting state measurements were performed on the four muscles sequentially, in a randomized order, and lasted 15 min for each position. The hybrid TD-NIRS and DCS device used in this study was previously developed in Politecnico di Milano and it enables concurrent measurements of hemoglobin concentration and blood flow, with an

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acquisition rate of 0.8 Hz (see [4] for more details) and a source detector separation of 2 cm and 1.5 cm for TD-NIRS and DCS modules, respectively.

A semi-infinite homogenous model for photon migration was used to retrieve the optical properties from TD-NIRS measurements at 670 nm and 830 nm, and by means of the Beer's law the oxygenated (HbO_2) and deoxygenated (HHb) haemoglobin concentrations were computed. The diffusion equation for the electric field autocorrelation function at 784 nm was exploited to retrieve the blood flow index (BFI). For each one of the 14 subjects and of the probe positions, the time traces were normalized by the 3rd order polynomial that best fitted the data; then the data were detrended to remove the continuous component. From the detrended data, the power spectral density (PSD) was computed at each frequency by means of the Welch algorithm, with Hamming windows of 300 s, with an overlap of 50%. Finally, we computed the average PSD and the standard error among all the volunteers for all the hemodynamic parameters.

3. Results and discussion

The PSD of BFI was significantly higher (more than 2 order of magnitude) compared to those of hemoglobin concentrations, indicating the presence of stronger oscillatory components in the recorded DCS signal than in the TD-NIRS signal. Moreover, differences were observed in the PSD of BFI measured in different body areas: distal muscles (thenar eminence and plantar fascia) showed significantly higher spectral power at LF and VLF (Figure 1a), suggesting that these frequency bands in the BFI signal could be suitable biomarkers to evaluate endothelial functions. Finally, we compared the PSD measured on the thenar eminence of a septic patient in ICU with the ones of healthy volunteers (Figure 1b): the septic patient showed lower spectra at VLF, suggesting a different endothelial behavior.

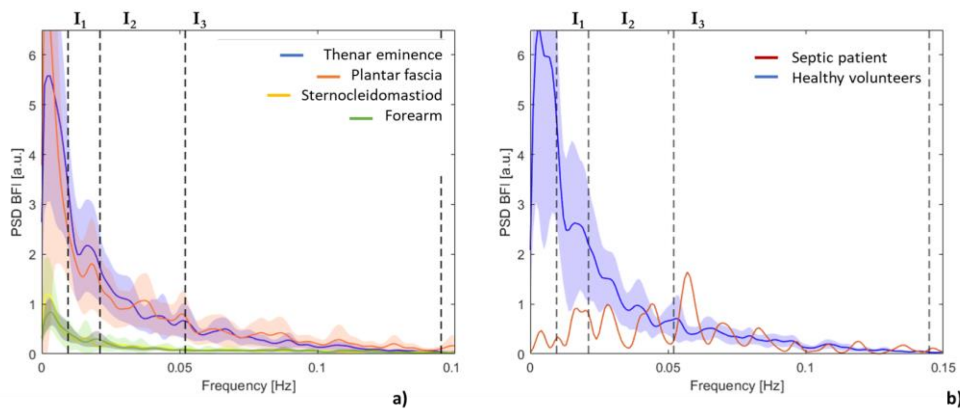

Figure 1: Panel a): PSD of BFI averaged among all the participants, in different muscles. Lines are the average values, while shadows are the corresponding standard errors. Panel b): comparison of the PSD of BFI measured on healthy volunteers and on a septic patient (yellow line), on the thenar eminence.

4. Conclusions

We tested the possibility to noninvasively assess LF and VLF spontaneous oscillations of microvasculature by resting state measurements of skeletal muscles hemodynamics via DO methods. Frequency analysis showed that TD-NIRS and DCS techniques are both suitable to detect LF and VLF oscillations, with a larger PSD in the case of BFI with respect to the hemoglobin concentrations. This study marks a significant step toward assessing endothelial hemodynamic activity in skeletal muscles through DO technologies, eliminating the need for additional interventions. Our promising case study involving a septic patient suggests potential applications for monitoring endothelial impairments in resting state conditions, considering the well-established damage to the microvascular endothelium in sepsis. Moving forward, we aim to expand our research by involving a larger cohort of healthy volunteers and ICU patients.

[1] Niezen, C.K., Massari, D., Vos, J.J. et al. The use of a vascular occlusion test combined with near-infrared spectroscopy in perioperative care: a systematic review. J Clin Monit Comput 36, 933–946 (2022). https://doi.org/10.1007/s10877-021-00779-w

[2] J. Creteur, T. Carollo, G. Soldati, G. Buchele, D. De Backer, and J. L. Vincent, "The prognostic value of muscle StO2 in septic patients," Intensive Care Med. 33, 1549–56 (2007)

[3] A. Stefanovska and M. Bračič, "Physics of the human cardiovascular system," Contemp. Phys. 40, 31–55 (1999).

[4] C. Amendola, M. Lacerenza, M. Buttafava, A. Tosi, L. Spinelli, D. Contini, and A. Torricelli, "A compact multi-distance dcs and time domain nirs hybrid system for hemodynamic and metabolic measurements," Sensors (Switzerland) 21, 870 (2021)