



Precise quantification of extravascular fluid and oedema severity in heart failure

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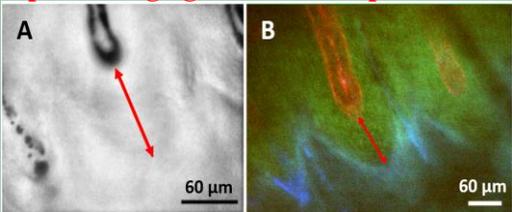
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Background & Purpose

Heart failure is a serious medical problem. It covers between two and for percent of the population in European countries. Early diagnosis of heart failure (HF) severity and prediction of acute decompensating is complicated due to the absence of specific symptoms and objective measurable criteria.

Here we present a new indicator of the HF severity based on the soft tissue optical imaging in nail-fold capillaries.



Comparison of the perivascular zone (PZ) linear size, obtained *in vivo* for the same capillary in the (A) white light reflection and (B) multiphoton imaging modes using the Nikon A1R MP system. PZ borders correspond to the border of viable epidermis, and the size of the PZ is similar in both modes

The study protocol was approved by the Ethics Committee of the Medical Research and Educational Center, Lomonosov Moscow State University.

Materials & Methods

We enrolled in the study 129 adults, including 79 patients with NYHA I-III functional classes of HF, and 50 healthy volunteers without history or risk factors for cardiovascular disease. All patients with HF underwent a standard clinical and laboratory examination including comprehensive

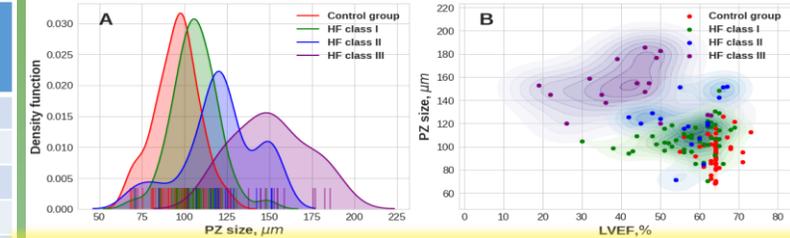
Measurement of the perivascular zone (PZ) linear size



Microvascular measurements were performed between 9 and 11 a.m. following a minimum of 12 hours overnight fasting in a quiet temperature-controlled room, in the seated position and the left hand at heart level using a digital capillaroscope Kapillaroskan-1 (AET, Russia). High magnification resolution video recordings from each subject were captured for quantitative analysis with custom software that allows measurement of the PZ.

Results

	Groups to compare	F ₁ -score %	Sensitivity %	Specificity %
PZ size	Control vs. HF I	69 ± 14	70 ± 16	65 ± 12
	HF I vs. HF II	69 ± 22	75 ± 13	72 ± 14
	HF II vs. HF III	71 ± 24	75 ± 25	77 ± 20
LVEF	Control vs. HF I	71 ± 10	57 ± 11	88 ± 8
	HF I vs. HF II	37 ± 26	32 ± 21	53 ± 20
	HF II vs. HF III	72 ± 28	82 ± 15	83 ± 15
PZ size and LVEF	Control vs. HF I	76 ± 12	75 ± 9	78 ± 9
	HF I vs. HF II	71 ± 17	75 ± 13	70 ± 14
	HF II vs. HF III	72 ± 21	82 ± 15	85 ± 20



A) Distribution of subjects in the control and HF groups by the PZ size. B) Bivariate density distribution of patients in the control and HF groups by LVEF and PZ size. Kernel density estimation is presented as the solid line or contour levels, rug plot presented as vertical bars

Table presents the highest F1-scores, sensitivities and specificities for classification carried out with one and two variables. the PZ size proved to be the best in terms of both specificity and selectivity, while LVEF exhibited the highest specificity but low sensitivity. It was also revealed that the use of three or more parameters for classification of HS functional class does not increase the sensitivity

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Conclusions

Linear PZ size has shown high sensitivity and specificity in identifying patients with different NYHA heart failure classes. The significance of this parameter, determined by several methods of statistical analysis, exceeded that for all other parameters, including LVEF. In addition, the use of two or more parameters did not lead to a significant increase in predictive power.

The results of *in vivo* multiphoton tomography of nail folds combined with fluorescence imaging of life expectancy indicate that PZ size is determined by the accumulation of interstitial fluid in the epidermis. Therefore, we propose a new quantitative and highly sensitive non-invasive index of HF and its severity. This approach is of interest for the early diagnosis and monitoring of interstitial fluid retention.