ENDOTHELIAL FUNCTION IN YOUNG-ONSET CRYPTOGENIC ISCHEMIC STROKE: A PROSPECTIVE PILOT STUDY

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Introduction

Worldwide, approximately 1.3 million annual ischemic strokes (IS) occur prematurely in adults aged 18 to 49 years with an incidence of some 10 per 100 000 person-years in Caucasians¹, exhibiting also four- to ten-fold increased long-term mortality^{2,3}. Of these, up to 50% can be regarded as cryptogenic⁴, especially in youngest patients, often associated with conditions with poorly proven causality such as patent foramen ovale and common coagulopathies. We hypothesized that factors also leading endothelial dysfunction may be part of the cryptogenic IS pathogenesis.

Methods

In SECRETO study (NCT01934725) patients aged 18-49 years, hospitalized due to first-ever imaging-positive ischemic stroke of undetermined etiology, are enrolled and examined according to a standardized protocol. In this single-center pilot study, endothelial function was measured non-invasively from 115 patients with a peripheral arterial tonometry (EndoPAT®) both at baseline and at a 3-month control visit. Reactive Hyperemia Index (RHI) is the post-to-pre occlusion PAT signal ratio in the occluded side, normalized to the control side and further corrected for baseline vascular tone. Natural log transformation of RHI (lnRHI) was used to estimate endothelial function. Variables associated with lnRHI ($P < 0.2$) in bivariate comparison (preexisting hypertension, diabetes, lipid components, renal function [eGFR], waist-to-hip ratio) were entered into a linear regression analysis using the backward-stepwise approach adjusted for age and sex.

Figure. Endothelial function measurement with EndoPAT

(a) Diagram of the Endo-PAT set-up. (b) Representative traces from both the study and control arms showing the changes on the pulse amplitude after a 5-minute occlusion time (Figure from Itamar Medical).

Results

Mean lnRHI was 0.76 (SD ± 0.25) at baseline and 0.73 (SD ± 0.26) at 3-month visit ($p = 0.275$). Median delay from stroke-onset to lnRHI measurement was 9 days. At baseline, adjusted linear regression showed waist-to-hip ratio (beta -0.411; $p < 0.001$) and diabetes (beta -0.187; $p = 0.033$) to associate with a lower lnRHI (endothelial dysfunction). At 3-months, hypertension (beta -0.214; $p = 0.029$) and a high low-density lipoprotein cholesterol level (beta -0.230; $p = 0.020$) were associated with low lnRHI.

Conclusions

Endothelial dysfunction is associated with abdominal obesity, diabetes, hypertension, and hypercholesterolemia in young patients with new onset cryptogenic IS. Notably, factors associated with endothelial function were different immediately after an incident IS and 3 months after, suggesting this vascular event and its treatment may affect the patient risk profile related to endothelial function. Further analysis comparing endothelial function between patients and age- and sex-matches healthy controls will also be performed in SECRETO study in the near future to study the possible association of endothelial dysfunction with cryptogenic IS.

References

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