Retinal vessel analysis

Retinal vessels are readily accessible for analysis, and vessel diameter is a robust determinant of retinal blood flow. Inspection and photographic documentation of retinal vessel configuration is part of routine ophthalmological practice using commercially available fundus cameras. The “Dynamic Vessel Analyzer” (DVA, Imedos Systems UG, Jena, Germany–use for research only) is a modification of a high end fundus camera (FF450, Carl Zeiss GmbH, Jena, Germany) with tailored hardware and software modules, allowing static and dynamic retinal vessel analysis (RVA, IMEDOS, Jena, Germany). In addition to dimensional analysis, a flicker light stimulation can induce caliber changes of retinal vessels, an index for autoregulatory quality [1)].

Retinal vessel analysis has been employed in several cross-sectional and interventional clinical studies in ophthalmology and other specialities, including cardiology, neurology, neurosurgery, nephrology, gynaecology, sports medicine, diabetology, hypertensiology and others. Static retinal vessel analysis is an inexpensive, reproducible, non-invasive technique, which can be used to make a prognostic statement on the vascular health of an individual patient. Dynamic retinal vessel analysis possesses a broader spectrum of diagnostic applications than the static procedure, as it examines changes in vessel diameter continuously over time. The use of several different methodological modalities for retinal vessel analysis together with their relevant quantitative biomarkers represents a promising approach for the evaluation of vascular diseases and cerebro- or cardiovascular morbidity and mortality. Interdisciplinary clinical application of these vascular biomarkers is becoming increasingly important in ophthalmology and other specialities [2)].

Impairment of neurovascular coupling (NVC) was reported in the context of subarachnoid hemorrhage and may correlate with disease severity and outcome. However, previous techniques to evaluate NVC required invasive procedures. Retinal vessels may represent an alternative option for non-invasive assessment of NVC.

A prototype of an adapted retinal vessel analyzer was used to assess retinal vessel diameter in mice. Dynamic vessel analysis (DVA) included an application of monochromatic flicker light impulses in predefined frequencies for evaluating NVC. All retinae were harvested after DVA and electroretinograms were performed.

A total of 104 retinal scans were conducted in 21 male mice (90 scans). Quantitative arterial recordings were feasible only in a minority of animals, showing an emphasized reaction to flicker light impulses (8 mice; 14 scans). A characteristic venous response to flicker light, however, could observed in the majority of animals. Repeated measurements resulted in a significant decrease of baseline venous diameter (7 mice; 7 scans, $p < 0.05$). Ex-vivo electroretinograms, performed after in-vivo DVA, demonstrated a significant reduction of transretinal signaling in animals with repeated DVA ($n = 6$, $p < 0.001$).

To the best of our knowledge, this is the first non-invasive study assessing murine retinal vessel response to flicker light with characteristic changes in NVC. The imaging system can be used for basic research and enables the investigation of retinal vessel dimension and function in control mice and genetically modified animals [3)].

Impaired cerebral autoregulation and neurovascular coupling (NVC) contribute to delayed cerebral ischemia after subarachnoid hemorrhage (SAH). Retinal vessel analysis (RVA) allows non-invasive assessment of vessel dimension and NVC hereby demonstrating a predictive value in the context of various neurovascular diseases. Using RVA as a translational approach, we aimed to assess the retinal vessels in patients with SAH. RVA was performed prospectively in 24 patients with acute SAH (group A: day 5-14), in 11 patients 3 months after ictus (group B: day 90 ± 35), and in 35 age-matched healthy controls (group C). Data was acquired using a Retinal Vessel Analyzer (Imedos Systems UG, Jena) for examination of retinal vessel dimension and NVC using flicker-light excitation. Diameter of retinal vessels-central retinal arteriolar and venular equivalent-was significantly reduced in the acute phase ($p < 0.001$) with gradual improvement in group B ($p < 0.05$). Arterial NVC of group A was significantly impaired with diminished dilatation ($p < 0.001$) and reduced area under the curve ($p < 0.01$) when compared to group C. Group B showed persistent prolonged latency of arterial dilation ($p < 0.05$). Venous NVC was significantly delayed after SAH compared to group C (A $p < 0.001$; B $p < 0.05$). To our knowledge, this is the first clinical study to document retinal vasoconstriction and impairment of NVC in patients with SAH. Using non-invasive RVA as a translational approach, characteristic patterns of compromise were detected for the arterial and venous compartment of the neurovascular unit in a time-dependent fashion. Recruitment will continue to facilitate a correlation analysis with clinical course and outcome [4)].

In a prospective pilot study, we performed RVA in six patients awake and cooperative with SAH in the acute phase (day 2-14) and eight patients at the time of follow-up (mean 4.6±1.7months after SAH), and included 33 age-matched healthy controls. Data was acquired using a manoeuvrable Dynamic Vessel Analyzer (Imedos Systems UG, Jena) for examination of retinal vessel dimension and neurovascular coupling.

Image quality was satisfactory in the majority of cases (93.3%). In the acute phase after SAH, retinal arteries were significantly dilated when compared to the control group (124.2±4.3MU vs 110.9±11.4MU, $p<0.01$), a difference that persisted to a lesser extent in the later stage of the disease (122.7±17.2MU, $p<0.05$). Testing for neurovascular coupling showed a trend towards impaired primary vasodilation and secondary vasoconstriction ($p = 0.08$, $p = 0.09$ resp.) initially and partial recovery at the time of follow-up, indicating a relative improvement in a time-dependent fashion.

RVA is technically feasible in patients with SAH and can detect fluctuations in vessel diameter and autoregulation even in less severely affected patients. Preliminary data suggests potential for RVA as a new and non-invasive tool for advanced SAH monitoring, but clinical relevance and prognostic value will have to be determined in a larger cohort [5)].

1)
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