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## Associations between serial pupillometer readings and intracranial pressure crises in neurocritical-care patients.

Antje Giede-Jeppe, et al. University of Erlangen

**Introduction**: Elevated intracranial pressure(ICP) and cerebral edema are common causes of mortality in neurocritical-care patients. Key monitoring techniques for ICP-elevation include neuroimaging and invasive ICP-measurement. Examination of the pupils is routinely performed to determine disturbances within cerebral physiology but shows high inter-rater variability. Portable infrared pupillometry is increasingly used in clinical routine, yet, it's benefit remains to be established in patients with elevated ICP. Aim of this study was to identify pupillary parameters associated with ICP-crisis in neurocritical-care patients.

**Methods**: We prospectively enrolled 39 critically-ill patients(subarachnoid hemorrhage/intracerebral hemorrhage/stroke) admitted to our neurointensive care unit(07/2016-11/2017) who required placement of external ventricular drains. We recorded serial pupillometer readings [i.e. maximum/minimum apertures(mm), constriction/dilation velocities(mm/sec.), latency period(sec.)] using a portable pupilometer (NeurOptics<sup>®</sup>) and corresponding ICP values every 3 hours after admission. Neurological Pupil index (NPi), an algorithm that compares various pupillary parameters to a normative model of pupil reaction to light, grades pupil-function on a scale of 0(nonreactive) to 5(normal). Receiver Operating Characteristic(ROC) Curve Analysis was performed to investigate associations between pupillary readings and ICP-crisis(ICP>20mmHg).

**Results:** In 39 patients (median age:58(51-68) years) 2414 serial pupillary assessments were available for analysis. In 14 of our patients 91 ICP-crises were detected. In these patients, median pupillometer readings differed between recordings during ICP-crises and recordings while ICP was <20mmHg for: NPi [3.8(3.6-4.1)C(Crisis)vs.NPi 4.3(3.9-4.6)];P<0.001, latency [0.25(0.22-0.28)(C)vs.0.24(0.22-0.27)];P<0.023, dilation-velocity[0.16(0.12-0.25)(C)vs.0.31(0.19-0.42];P<0.001, maximal constriction-velocity [0.73(0.51-1.21)(C)vs.1.29(0.92-1.67)];P<0.001, constriction-velocity [0.46(0.29-0.83)(C)vs.0.90(0.61-1.14)];P<0.001 and minimum pupil-size [2.1(2.0-2.4)(C)vs.2.0(1.8-2.3)];P<0.003. ROC analyses revealed a negative association between ICP-crisis and NPi ([AUC]0.285), maximal constriction-velocity ([AUC]0.307), constriction-velocity ([AUC]0.309). NPi<4.13 was associated with a 5.4fold higher rate of ICP-crisis compared to NPi>4.13 [NPi<4.13: 69/922(7.5%)vs. NPi>4.13: 22/1492 (1.5%);OR(95%CI):5.4(3.3-8.8); p<0.001].

**Conclusions**: Our data suggest an association between non-invasively detected changes in NPi, constriction-velocity or maximal constriction-velocity and ICP-crisis. However, clinical benefit of these parameters is subject to future studies.