

Short- and long-term outcomes after aneurysmal subarachnoid hemorrhage

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligens försvaras i M106 K Isaksson, Medicinargatan 16, den 6:e oktober, klockan 09.00

av Sandra Bjerkne Wenneberg

Fakultetsopponent:

Professor Michelle Chew

Institutionen för biomedicinska och kliniska vetenskaper, Linköpings Universitet, Linköping, Sverige

Avhandlingen baseras på följande delarbeten

I. Bjerkne Wenneberg S, Löwhagen Hendén PM, Oras J, Naredi S, Block L, Ljungqvist J, Odenstedt Hergès H. Heart rate variability monitoring for the detection of delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage. *Acta Anaesthesiol Scand.* 2020; 64:945–952

II. Bjerkne Wenneberg S, Odenstedt Hergès H, Svedin P, Mallard C, Karlsson T, Adiels M, Naredi S, Block L. Association between inflammatory response and outcome after subarachnoid haemorrhage. *Acta Neurol Scand.* 2021; 143:195–205

III. Wenneberg S. B., Block, L., Sörbo, A., Naredi, S., Oras, J., Hendén, P. L., Ljungqvist, J., Liljencrantz, J. & Hergès, H. O. Long-term outcomes after aneurysmal subarachnoid hemorrhage: A prospective observational cohort study. *Acta Neurol Scand.* 2022; 146(5):525-536

IV. Bjerkne Wenneberg S, Block L, Oras J, Löwhagen Hendén P, Liljencrantz J, Odenstedt Hergès H. Mental fatigue after aneurysmal subarachnoid hemorrhage. A prospective 5-year follow-up study. Manuscript. 2023.

**SAHLGRENKA AKADEMIN
INSTITUTIONEN FÖR KLINISKA VETENSKAPER**



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Sandra Bjerkne Wenneberg

Avdelningen för anesthesiologi och intensivvård, institutionen för kliniska vetenskaper, Sahlgrenska akademien, Göteborgs universitet, Sverige, 2023

Abstract

Aneurysmal subarachnoid hemorrhage (aSAH) is a sudden and devastating event with significant morbidity and mortality. The development of delayed cerebral ischemia (DCI) is a major contributor to the observed high morbidity. Prompt detection of these injuries remains a considerable challenge. This dissertation explores two approaches: heart rate variability (HRV) analysis and inflammatory biomarker evaluation. As an increasing number of patients survive the acute phase, it is crucial to understand the long-term post-SAHA complications and sequelae experienced by patients.

HRV data and blood samples for inflammatory biomarkers were collected from patients during the acute phase. Correlations between these parameters and the development of DCI and overall outcome were investigated. Follow-up assessments at 1-, 3-, and 5 years post-hemorrhage were conducted via telephone interviews and self-assessment questionnaires.

In study I, altered HRV patterns indicating increased sympathetic activation were observed for the patient cohort, particularly those who developed DCI. However, the predictive value of HRV for DCI onset was limited. Patients who did not survive beyond the first year exhibited reduced HRV compared with survivors. Study II investigated the potential of five inflammatory biomarkers (TNF- α , IL-6, IL-1Ra, ICAM-1, and CRP) in peripheral blood to predict DCI. No clear association was found between elevated levels of biomarkers and DCI development. However, patients with unfavorable outcomes had higher biomarker levels during the acute phase. Studies III and IV revealed that cognitive impairments, especially mental fatigue persisted several years after the initial hemorrhage. Although many patients improved, approximately half continued to experience mental fatigue after 5 years. Further research is needed to refine prediction methods for the development of DCI. Follow-up assessments should extend several years after an aSAH and include broad assessment instruments focusing on cognitive outcomes, particularly mental fatigue.

Keywords: Aneurysmal subarachnoid hemorrhage, Delayed cerebral ischemia, Biomarker, Inflammation, Heart rate variability, Long-term outcome, Self-assessment, Cognitive impairments, Mental fatigue