Stress-Induced Cardiomyopathy -
Clinical and Experimental Studies

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Sahlgrenska Akademin vid Göteborgs Universitet kommer att offentligen förvaras i Hjärtats Aula, Sahlgrenska Universitetssjukhuset, Göteborg, fredagen den 13 november 2015, kl 13.00.

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Avhandlingen baseras på följande delarbeten:


Abstract

Background: Stress-induced cardiomyopathy (SIC) is an acute cardiac condition with akinesia in the left ventricle (LV) that can be severe. A stress-trigger, physical or emotional, is usually identified preceding onset of symptoms and catecholamine overstimulation is involved in the pathogenesis of SIC. The akinesia seen in SIC is reversible and the short term prognosis is therefore considered to be very good. However, recent data suggest that the long term prognosis is equivalent to patients suffering from myocardial infarction. Physical triggers and critical illness are the major triggers of SIC and especially patients with subarachnoid hemorrhage (SAH) frequently develop SIC. Patients with SIC after SAH have an increased risk of secondary cerebral infarction and have a worse short-term prognosis.

Aim: The aim was to evaluate if the biomarkers of myocardial injury (hsTnT) and cardiac dysfunction (NT-proBNP) could be used for identification of patients with SIC after SAH and if patients with increased levels of hsTnT and NT-proBNP had an increased risk of poor long-term prognosis (Paper I, II). In an experimental animal model of SIC, the aim was to evaluate cardioprotective properties of different anesthetics (Paper III, IV).

Methods: The first study (Paper I) was retrospective. Data was collected from all patients admitted to the NICU, Sahlgrenska University Hospital, during almost five years. Patients with an echocardiography performed and the biomarkers hsTnT or NT-proBNP were obtained were included in the analysis. The second study (Paper II) was prospective. All consecutive patients admitted to the NICU, Sahlgrenska University Hospital, during two years were enrolled in the study. hsTnT and NT-proBNP were taken on admission and the three following days and clinical data were obtained. Follow-up was performed one year after onset of symptoms. In Paper III and IV, SIC was induced with an intraperitoneal bolus of isoprenaline in Sprague Dawley rats. Different anesthetics were applied prior to induction of SIC. Vital parameters were measured and small animal echocardiography was performed. A proteomic analysis was performed for assessment of cardioprotective pathways.

Results: Patients with SIC after SAH could be identified with the cardiac biomarkers hsTnT and NT-proBNP (Paper I). Increased levels of hsTnT were independently associated with a higher risk of poor long-term outcome when adjusted for age, neurological status on admission and cerebral infarction. Increased levels of hsTnT and NT-proBNP was associated with a higher risk of delayed cerebral infarction (Paper II). In the experimental studies, isoflurane had a cardioprotective dose-response effect while propofol and ketamine were not cardioprotective. The cardioprotective mechanism was not mediated through anesthesia per se, by reducing myocardial oxygen demand or by activating the mKATp-channels described in anesthetic preconditioning. In a proteomic analysis, we found that isoflurane attenuated virtually all the pathogenic pathways induced in SIC. Isoflurane seem to act by competitive inhibition the intracellular beta-receptor signalling pathway.

Conclusion: Patients with increased levels of hsTnT or NT-proBNP have a higher risk of delayed cerebral infarction and poor long-term prognosis. These patients should be examined with echocardiography for detection of SIC and cardiac output should be monitored to optimize hemodynamics, ensuring cerebral perfusion. Although many aspects are to be considered, isoflurane sedation might be beneficial in patients suffering from SAH.

Keywords: stress-induced cardiomyopathy, tako-tsubo, subarachnoid hemorrhage, isoflurane, outcome, cerebral infarction, hsTnT, NT-proBNP, proteomics, bioinformatics

ISBN: 978-91-628-9615-7 (e-published)
https://hdl.handle.net/2077/39562