THE IMPACT OF ACUTE CARDIAC EVENTS ON LONG-TERM MORTALITY AFTER SUBARACHNOID HEMORRHAGE

Master Thesis in Medicine

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Abbreviations

AMI – Acute Myocardial Infarction
CIVA – Central Intensive Care Unit
CO – Cardiac Output
COPD – Chronic Obstructive Lung Disease
CT – Computed Tomography
CVD – Cardiovascular Disease
DCI – Delayed Cerebral Ischemia
EBI – Early Brain Injury
ECG – Electrocardiography
GCS – Glasgow Coma Scale,
HsTnT – High Sensitivity Troponin T, a biomarker indicating myocardial damage
ICP – Intracranial Pressure
IVH – Intraventricular Hemorrhage
LP – Lumbar Puncture
LVOTO – Left Ventricle Outflow Tract Obstruction
MF – Modified Fischer, a grading scale for estimating magnitude of SAH
NICU / ICU – Neurological Intensive Care Unit / Intensive Care Unit
NIVA – Neuro Intensive Care Unit
NT-proBNP – N-terminal Prohormon of Brain Natriuretic Peptide, a heart failure prohormone
PiCCO – Pulse index Continuous Cardiac Output
RLS – Reaction Grade Scale,
RWMA – Regional Wall Motion Abnormalities
SAH – Subarachnoid Hemorrhage
SIC – Stress-Induced Cardiomyopathy
WFNS – World Federation Neurosurgical Societies, a clinical grading scale of neurological symptoms
Abstract

INTRODUCTION. Acute cardiac events are common after subarachnoid hemorrhage (SAH) and are associated with an increased risk of poor outcome. However, the impact of cardiac events on long term mortality after SAH is barely studied.

OBJECTIVES. The aim was to evaluate the impact of acute cardiac events on long-term mortality after SAH. The hypothesis of this study was that these events are associated with an increased long-term mortality.

METHODS. This is a retrospective study. Medical records from all patients admitted to our NICU and general ICU from 2010 to 2015 with the diagnosis SAH were analyzed. Variables obtained were age, medical history, WFNS score, modified fisher grade, cerebral infarction during hospital admission, treatment, troponin release and NTproBNP levels, ECG, echocardiographic evaluation. Kaplan-Meier curves and Cox-regression were used in the statistical analyses.

RESULTS. A total of 708 patients were admitted with suspected/verified SAH during the study period. 118 patients did not fulfill SAH-diagnosis, 33 patients were not included due to long time to admission (>4 days) and in 28 patients no ECG/echo/cardiac biomarkers were obtained. Of the 529 patients analysed, 109 patients had died at the time mortality data was obtained (april 2016). In a univariate cox-regression model; WFNS grade 4-5, Fisher grade, age, history of hypertension, cardiovascular disease (CVD) or renal disease, levels of troponin and NTproBNP was significantly associated with a higher risk (hazard ratio) for death. A normal ECG was significantly associated with reduced mortality. Stress-Induced Cardiomyopathy was not significantly associated with an increased risk of death. In a multivariable cox-regression model, both troponin levels and NTproBNP levels were significantly associated with an increased risk of death when adjusting for WFNS grade 4-5,
age, history of CVD or renal disease and Fisher grade. However, these differences were only significant the first year after the hemorrhage.

CONCLUSIONS. Acute release of the cardiac biomarkers troponin and NTproBNP after SAH is an ominous clinical sign which is associated with an increased risk of death, especially the first year after the hemorrhage. Further research is needed to address whether measures to optimize cardiac treatment after SAH might improve outcome.
Introduction

Patients with a Subarachnoid Hemorrhage (SAH) are often affected by cardiac complications in the acute phase of the hemorrhage.[1] These cardiac events differ greatly in clinical significance; from subclinical electrocardiography (ECG) changes, troponin release to acute heart failure[2, 3]. Several studies have shown that cardiac events are associated with worse short term prognosis, but only a few have explored the impact of long term outcome[4].

Stressed Induced Cardiomyopathy

Overview

Stress-Induced Cardiomyopathy (SIC) is a relatively new diagnosis with the first scientific reports emerging in the early 90s from Sato et al in Japan. It is often referred to as Tako Tsubo Cardiomyopathy for its resemblances of a Tako Tsubo octopus trap used by Japanese fishermen in Hiroshima fishing market[5]. The condition presents itself as hypokinesia in the left ventricle of the heart, where the heart muscle form a balloon-like shape with little or no movement in affected regions. The condition is also known as Apical Ballooning Cardiomyopathy, Transient Apical Ballooning Syndrome, Broken Heart Syndrome and Stressed Induced Cardiomyopathy[6], which it will be named in this report.

Patients typically present with acute, angina-like chest pain, breathlessness and palpitations caused by arrhythmia or sinus tachycardia. In more severe cases the patient might experience pre-syncope or syncope due to ventricular tachyarrhythmia, cardiogenic chock or left ventricular outflow tract obstruction (LVOTO). Patients have described the chest pain as a wave of pressure emerging from the chest up to the neck and into the head. These symptoms are consistent with the catecholamine and hypertensive surge presented in SIC, frequently associated with anxiety and perspiration.[6]
The cause of the syndrome is still highly unknown but it has been shown to be strongly associated with catecholamine toxicity. The syndrome is usually preceded with a strong emotional or physical trigger prior to the debut, although there are reports that up to 33% of SIC-like diagnoses lack such a trigger prior the onset of symptoms[7]. Common emotional triggers are grief from losing a loved one, fear of public speaking, financial problems, arguing with a spouse or betrayal. Acute physical conditions such as asthma attacks, surgery, chemotherapy and stroke are examples of physical triggers. The symptoms of SIC mimic Acute Myocardial Infarctions (AMI) to a great extent and needs to be excluded when diagnosing a patient with SIC.[6]

Epidemiology
SIC is an uncommon condition. In a Nationwide Inpatient Study (NIS-USA) an estimated 0.02% of all acute hospitalized patients were diagnosed with SIC. The majority of these patients where post-menopausal women (90%)[6], which is confirmed by several other studies (a second NIS-USA study estimated an 89% and a German registry study estimated a 91% of patients being post-menopausal women)[8, 9]. The mean age of these patients where 66.9 years of age and almost 60% of all patients were 65 years or older. Risk factors for SIC include excessive use of alcohol, smoking, hyperlipidemia and a variety of anxiety states. [9]

Clinical Subtypes
SIC is considered to be either primary or secondary. The primary variant is when the acute onset of cardiac symptoms is the main reason for a patient seeking medical care, usually at emergency medical facilities, primary care centers or acute cardiac facilities. These patients may or may not have an identifiably emotional trigger and may also have a variety of co-morbidities, although none of these being responsible for the sudden surge of catecholamines. Secondary SIC carries a substantial portion of the total number of cases. These patients are already hospitalized for other conditions such as medical, surgical, psychiatric, anaesthetic or
obstetric ones, and the sudden onset of catecholamine-oriented stress may be a complication of their primary condition or a specific treatment. In these cases, primary care should focus not only on SIC and its cardiac complications but also on the trigger. [6]

Patients of old age have considerably higher risk of suffering from both SIC and related complications to the syndrome. Only 10% of patients are <50 years of age. At the age of ≥75, patients have a higher risk of in hospital complications and mortality (6.8% vs 2.8%).[6]

Pathophysiology
The pathophysiology of SIC is still highly unknown and findings to this date suggest that the mechanism behind the syndrome is complex, reflecting integrated and systemic physiological responses to severe, acute stress, which triggers cardiovascular responses to a sudden surge in endogenous or exogenously administrated catecholamines. These catecholamines seem to play a central role in the SIC pathology, as the identified trigger is most often unexpected and sudden stress, leading to a sympathetic activation being present at the onset of symptoms. Exogenous administration of catecholamines as part of medical treatment may yield similar responses leading to SIC, but triggering a secondary SIC.[6] There are two major physiological paradigms to consider here. The first being the hypothalamic-pituitary-adrenal (HPA) axis and the cognitive centers of the brain, regulating the norepinephrine and epinephrine release as a response to a stress trigger. The second paradigm is the sympathetic activation and the response from the cardiovascular system, its coronary arteries, myocardium and peripheral blood vessels due to the sudden surge of catecholamines.[10, 11]

Studies have shown that serum catecholamine levels at the initial stage of SIC is significantly higher than resting levels in the same patient. The serum level was also higher in these patients with SIC compared to patients with acute heart failure caused by acute myocardial infarction (AMI).[6] These findings suggest an excessive epinephrine release and HPA increase in SIC patients. There has also been reports of SIC after administration of
sympathomimetic drugs such as Dobutamine.[12] SIC has also been induced in animal models by administration of beta-agonists. The syndrome has also been observed in numerous hyperadrenergic conditions such as sepsis, pheochromocytoma, SAH and brain death.[13-16] There are several hypotheses surrounding the exact mechanisms behind SIC. The first ones proposed microvascular dysfunction, a dissolved coronary artery or coronary artery spasm[17]. Since the LV hypokinesia in SIC usually extended beyond the area of which one coronary artery can supply, either several coronary arteries have to be affected at the same time or an abnormal anatomy of the coronary arteries have to be present, making these hypotheses less likely. [18]

In a recent conference of experts in the field, a summary of pathophysiological hypotheses was sub-divided into two groups; vascular and myocardial. Vascular hypothesis consisted of acute multivessel coronary spasm, aborted myocardial infarction with spontaneous recanalization and acute increased ventricular afterload. Myocardial causes were acute left ventricle out tract obstruction (LVOTO) and direct catecholamine-mediated myocardial stunning. There is no reason for these hypotheses to be mutually exclusive and studies have yielded conflicting results, indicating the pathophysiology of SIC might be a synergistic combinations of vascular and myocardial effects from the surge of catecholamines. [6] Catecholamine cardiotoxicity is well known and the first scientific reports on the matter originates from the 60’s[19].

**Diagnosis**

There are several diagnostic criteria proposed in diagnosing SIC, including the Japanese Takotsubo Cardiomyopathy Group, The Mayo Clinic, the Takotsubo Italian Network and the Gothenburg Group. The Heart Failure Association set a series of 7 diagnostic criterias for SIC in 2015[6]:

1. **Hypokinesia**
2. **Abnormal wall motion**
3. **Right ventricular involvement**
4. **Time course less than 1 week**
5. **Absence of obstructive coronary artery disease**
6. **Absence of other causes of cardiomyopathy**
7. **Recovery of systolic function within 8 weeks**
1. Transient regional wall motion abnormalities of LV or RV myocardium which are frequently, but not always, preceded by a stressful trigger (emotional or physical).

2. The regional wall motion abnormalities usually extend beyond a single epicardial vascular distribution, and often result in circumferential dysfunction of the ventricular segments involved.

3. The absence of culprit atherosclerotic coronary artery disease including acute plaque rupture, thrombus formation, and coronary dissection or other pathological conditions to explain the pattern of temporary LV dysfunction observed (e.g., hypertrophic cardiomyopathy, viral myocarditis.)

4. New and reversible electrocardiography (ECG) abnormalities (ST-elevation, ST-depression, LBBB, T-wave inversion and/or QTc prolongation) during the acute phase (3 months).

5. Significantly elevated serum natriuretic peptide (BNP or NT-proBNP) during the acute phase.

6. Positive but relatively small elevation in cardiac troponin measured with a conventional assay (i.e., disparity between the troponin level and the amount of dysfunctional myocardium present).

7. Recovery of ventricular systolic function on cardiac imaging at follow-up (3-6 months).

To differentiate SIC from AMI, guidance can be found in measuring elevated levels of hsTnT compared to time of symptom debut. It’s been demonstrated that in SIC, hsTnT is released shortly after onset of symptoms followed by a subsequent decline.[20] Whereas in myocardial infarction, peak levels are usually reached on day 2 or 3 after onset of symptoms. [21] The levels of hsTnT is however disproportionally low relative to the severeness of cardiac hypokinesia.[22]

**Treatment**

There are no randomized clinical trials that can support a specific recommendation of SIC-management. A general goal is to reach recovery of normal heart function. Current
recommendations are based on treatment of congestive heart failure which have no scientific evidence for SIC. These treatments are suboptimal and could be potentially harmful[6, 23].

Risk stratification is essential for optimal treatment after diagnosing SIC. Risk factors are categorized into major risk factors (e.g age $\geq$ 75 years, Systolic BP $< 110$ mmHg, LVEF $< 35\%$, unexplained syncope, VT or VF) and minor risk factors (e.g age 70-75 years, LVEF 35-45%, ECG with QTc $\geq 500$ ms, pathological Q-waves, persistent ST-elevation). High risk is defined as the presence of at least one major or two minor risk factors and a clinical judgement is based on their severity.[6] A statement in European Journal of Heart Failure recommend that high risk patients should be monitored in a higher level hospital environment such as a coronary care unit or an intensive care unit. Lower risk cases of SIC where LVEF $> 45\%$ and no other complications are presented may be in consideration for an early discharge from hospital care. If LVEF is in the range of 35-45% and the patient has no other presented complications, beta-blockers and other heart failure medication may be of consideration.

Lower risk patients with SIC should be followed up within 3-6 months with a renewal of cardiac imaging to confirm recovery of RWMA as well as a review of the medication given as treatment for SIC.[6]

SIC has a negative effect on LVEF and tachycardia is seen as a compensation mechanism to maintain CO. Thus, inotropes are a controversial treatment as pulse frequency is already raised and the myocardium might be even more stressed with exogenous administrated catecholamines, such as inotropes. Cerebral perfusion pressure is important to maintain during SAH but can be challenging with a presence of acute heart failure in SIC. Cardiac output can be monitored with a PiCCO device.[20]
Complications

Most cases of SIC have good prognosis with rapid recovery of LV function and the syndrome is generally seen as relatively benign. In hospital mortality range from 2 to 5% and death is mainly caused by refractory cardiogenic shock or ventricular fibrillation. [24-26]

Most common complication is acute heart failure with an incidence of 12-45%. Mitral regurgitation, cardiogenic shock, arrhythmias, thrombus formation, pericardial effusion, ventricular wall rupture and right ventricular involvement are also known complications and need to be treated symptomatically. Thus, the importance of monitoring high risk patients is of utter importance. [6]

Cardiac Dysfunction in SAH

Cardiac dysfunction in the acute phase of SAH has been observed and known for a long period of time. The first publications were presented in 1903, a demonstration of increased blood pressure and arrhythmias after SAH[27]. It was first in the early 1990s that the first scientific descriptions of SIC were published. SIC was initially thought to be a separate condition from the cardiac events seen after SAH, and SAH was at first an exclusion criterion for the SIC-diagnosis. [28] As knowledge grew about this relatively unknown type of heart failure, SAH was accepted as a trigger.

Subarachnoid Hemorrhage

SAH is a cerebrovascular bleeding which in 80% of all cases is induced by an aneurysm rupture where blood flows into the subarachnoid space between the pia mater and the arachnoid membrane surrounding the brain. Non-aneurysmal bleedings include isolated prepontine SAH and generally have a good prognosis with low mortality. [29]

Acute symptoms include a particular harsh headache, often described as “thunder-clap headache”, neck pain, photophobia and nausea. Most common neurological findings are
impaired consciousness ranging from mild downiness and confusion to coma. Focal neurological deficits may present themselves as cranial nerve dysfunction such as diplopia, include hemiplegia.[20]

According to most studies, SAH carries an approximate of 51% mortality rate and on average one third of all patients need lifelong care after. The acute mortality is high, with 25% of all deaths occurring within the first 24 h and 10% before patients receives medical care. Most deaths occur within 2 weeks of onset of symptoms.[30] Poor neurological status on admission, age, magnitude of the hemorrhage are major factors correlating with poor outcome. Risk factors include hypertension, smoking, use of cocaine and alcoholism are major identifiable risk factors for SAH.[31]

SAH is rather rare type of cerebral hemorrhage and it accounts for approximately 5% of all strokes. However, the median age of onset is only 55 years of age with the high mortality rate, making the diagnosis account for as many loss-of life-years as patients with intracranial hemorrhage or ischemic stroke.[29]

WFNS is used as a clinical scale to grade the initial clinical features of the SAH bleeding. Several other scales are used but this one is the most commonly and preferably used since it is based on the Glasgow Come Scale (GCS).[32]

On hospital admission of a suspected SAH-patient, a computed tomography of the head is performed to confirm the diagnosis. If inconclusive, a lumbar puncture is performed after 6 hours of the CT to detect traces of blood in cerebrospinal fluid. Once diagnosis is established, a CT angiography or cerebral angography is performed to locate the aneurysm. About 15% of all patients are expected to have multiple aneurysms, so careful evaluation of all cerebral vessels needs to be undertaken.[29]
SAH should always be suspected in patients with the typical presentation such as the sudden onset of severe headache, nausea, neck pain, vomiting, syncope and photophobia. Retinal hemorrhage, a diminished level of consciousness, meningismus and focal neurological deficits should be evaluated during physical examination. [29]

**Treatment**

Evaluating the patient on emergency basis is of utter importance when treating patients with a SAH. Airway and cardiovascular function need to be maintained. Once initially stable, patient should be transferred to centers dedicated to neurocritical care. The main goal of treatment is to minimize the risk and damage of rebleeding, vasospasm and treating other neurological and medical complications. Early treatment of aneurysms is the main treatment in preventing rebleeding. Oral calcium antagonists are administrated as they have been proved to reduce the risk of poor outcome associated with ischemic complications such as vasospasm.[33]

The two main treatments for aneurysms consist of surgical clipping and endovascular coiling. Clinical trials suggest that early interventions yield better outcome than those who are treated later.[34] Securing a ruptured aneurysm have proven to be helpful in decreasing complications such as vasospasm.[35]

**Complications**

Brain damage is the major complication after a SAH and can be divided into early brain injury (EBI) and delayed cerebral ischemia (DCI).[36] The aneurysm ruptures in the onset of SAH, inducing an intracranial pressure (ICP) increase and as a response to this the Cushing reflex is activated, increasing blood pressure which further increases the ICP to the point where it is equivalent to the blood pressure. This happens within the first minute after the hemorrhage and ICP will then decrease unless intracranial hematoma or cerebrospinal fluid obstruction is present. During this process, cerebral perfusion level will drop resulting in a cerebral hypoperfusion which leads to an impaired level of consciousness. This hypoperfusion
leads to ischemic damages of the brain. A prolonged period of decreased cerebral perfusion is followed by poor neurological status on admission and worse prognosis of the patient. Intracerebral hemorrhage, cerebral inflammation and edema, impaired autoregulation, injury of the blood-brain-barrier and microcirculatory disturbances might further aggravate EBI. Hypoxia, re-bleeding and hydrocephalus are the most lethal complications in early EBI.[37]

DCI is defined as cerebral ischemic events 48-72 h after the initial hemorrhage. Cerebral arterial vasospasm is a key component and is thought to be mediated by extravascular blood surrounding cerebral vessels. Microthrombi, microvascular constrictions, impaired autoregulation, endothelial injury and cortical spreading ischemia are also thought to be mechanisms of DCI. Feared complications at this stage of the hemorrhage is fever, inflammation, impaired hemodynamics and metabolic abnormalities.[20]

**Aim**

This study aims to evaluate the impact of acute cardiac events on long-term mortality after SAH, compared to patients who suffer from SAH without cardiac complications. Our hypothesis was that such events are associated with an increased long-term mortality.

**Material and method**

**Study Definition and Methodology**

This was a retrospective single center study. Medical records from Neurology Intensive Care Unit (NIVA) and Central Intensive Care Unit (CIVA) at Sahlgrenska University Hospital, Gothenburg, was collected on patients admitted between January 1st 2010 and December 31st 2015 using the ICD-10 diagnose code for Subarachnoid Hemorrhage. The study is part of a series of studies about Stress-Induced Cardiomyopathy by Jonatan Oras, MD and PhD. The inclusion criterion was hospital admission for suspected SAH in the mentioned period of time. The exclusion criteria were traumatic SAH, planned surgical/endovascular intervention of e g
cerebral arteriovenous malformation with SAH-complication, absence of heart parameters such as ECG, Echocardiography, hSTnT, NTproBNP, benign/prepontine hemorrhage and a history of acute myocardial infarction (AMI). Between 2010 and 2012, NTproBNP and hSTnT was not part of routine lab tests in suspected SAH-patients, although the tests were done sporadically.

For comparison of mortality between SAH-patients and the general population, an age and sex matched group were simulated using age/sex mortality data from the SCB for Västra Götalandsregionen, Matching 1 SAH patients to 10 non-SAH subjects.

Patients with confirmed or suspected SAH were rapidly transported to NIVA or in some cases CIVA for intensive care. After hospital admission, a non-contrast computed tomography (CT) scan was made to confirm SAH-diagnosis. If radiology was inconclusive or not showing signs of SAH, a lumbar punction (LP) was performed 6 hours after the CT-scan. Only a few patients were confirmed to suffer from SAH using LP and most of these patients were diagnosed with a benign/prepontine hemorrhage and were excluded from the study. After confirmation of SAH-diagnosis, a cerebral angiography or a CT angiography was performed to locate the source of bleeding. Surgical or endovascular treatment were performed rapidly, usually within 24 h of admission. A calcium channel-antagonist, Nimodipine, was administrated to all suspected SAH-patients after CT and/or LP, as a prophylactic treatment of vasospasm and delayed cerebral ischemia (DCI). In this acute stage of SAH, many patients also had indication for and received treatment with hypertension, hypervolemia and iatrogenic agents. If SAH was confirmed and no source of bleeding was found, a new cerebral angiography or CT angiography was performed within 1 week for re-evaluation.

In order to correctly confirm that the SAH study participants were accurately selected by the database search of ICD10-codes, each participant’s medical records where thoroughly reviewed.
Variables obtained for each SAH patient included in the study were: age, sex, time of admission, medical history, WFNS score, time to event (death or other factor making follow up not possible), endovascular/surgical intervention, modified Fisher grade, troponin release, NTproBNP levels, ECG and echocardiographic evaluation.

Variables explained

ECG on hospital admission was evaluated and assessed for ST-elevation, negative T-waves, other ST-T abnormalities, long QT or u-wave, left bundle branch block (LBBB) or right bundle branch block (RBBB). If the first ECG was inconclusive or wrongly performed, the next ECG to date was used, usually performed a few minutes after the first one.

Clinical grading of SAH was performed according to the World Federation of Neurosurgical Societies (WFNS) grading of SAH. This scale is based on the Glasgow Coma Scale (Table 1)

<table>
<thead>
<tr>
<th>WFNS</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>GCS 15</td>
</tr>
<tr>
<td>2</td>
<td>GCS 13-14</td>
</tr>
<tr>
<td>3</td>
<td>GCS 13-14 + motor deficits e.g. hemiplegia</td>
</tr>
<tr>
<td>4</td>
<td>GCS 7-12</td>
</tr>
<tr>
<td>5</td>
<td>GCS &lt;6</td>
</tr>
</tbody>
</table>

A neurological status was performed by a neurosurgeon, a neurologist or an anesthesiologist and a reaction level scale (RLS 85) was estimated. This corresponds to the motor component
of GCS. Verbal response and eye opening response was routinely evaluated and noted in the journal. WFNS score was dichotomized in the statistical analyses to WFNS 1-3 or WFNS 4-5.

CT-grading of SAH was estimated using Modified Fischer scale (MF) on admission CT. The scale primary focuses on distribution and amount of blood leaked in the subarachnoid space (Table 2). The scale primary predicts the risk of cerebral vasospasm.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Description of Fisher grade</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Modified Fisher Grade</strong></td>
<td><strong>Description</strong></td>
</tr>
<tr>
<td>1</td>
<td>No or minimal blood, no IVH</td>
</tr>
<tr>
<td>2</td>
<td>Minimal/localized blood, with IVH</td>
</tr>
<tr>
<td>3</td>
<td>Diffuse or focal thick blood, no IVH</td>
</tr>
<tr>
<td>4</td>
<td>Diffuse or focal thick blood, with IVH</td>
</tr>
</tbody>
</table>

Time to admission was estimated based on extracts from the patients’ medical records. Time of admission was always documented, and if time of onset of symptoms was unclear, an estimated time was used based on when the patient was last witnessed without symptoms. Due to the inaccuracy of this method, the time to admission was only used as an exclusion criterion. No analysis based on this data was performed.

Medical history was obtained with focus on cardiac disease, cerebrovascular disease, hypertension, malignancy, renal disease, diabetes, COPD and other (e.g. rheumatoid arthritis).

Neurosurgical intervention, if performed, consist of ventricular drainage, endovascular coiling and/or surgical clipping of subarachnoid aneurysms. Other interventions consisted of craniotomy, lumbar drainage, intracranial pressure monitoring and ventriculoperitoneal shunt.
Levels of NTproBNP and hsTnT was obtained if taken during hospital admission. The peak levels within three days of onset of symptoms was used in the analysis. Samples obtained later than 3 days of onset of symptoms were excluded from the analysis.

Echocardiography was obtained if performed within 7 days of admission. Signs of hypokinesia or akinesia was documented by independent medical expertise, usually a cardiologist or a clinical physiologist. SIC was defined as transient RWMA without pre-existing cardiac disease.

**Outcome Variables and Predictors**

The primary outcome variable in this study was time to death, which was obtained from the hospital database connected to the Swedish Population Register. The primary predictors were the levels of cardiac biomarkers hsTnT and NTproBNP taken within three days of admission. The secondary predictors were SIC within a week of admission and ECG on admission. We adjusted for age, sex, WFNS score, modified fisher grade, medical history, treatment of aneurysm and cerebral infarction during hospital stay.

**Statistical Analysis**

All continuous variables were checked for normal distribution using histogram and Shapiro-Wilks test. Normal distributed variables are presented as mean ± standard deviation, non-normally distributed variables are presented as median (interquartile range). For comparison of means between two group with normally distributed variables, t-test was used. For comparison of medians between two groups with non-normally distributed variables, MannWhitney U test was used. For comparison of incidences between two groups with binary variables, Kaplan-Meier curves, uni- and multivariable Cox-regression hazard ratio were used in the survival analysis. In the multivariable analysis, variables with a p-value <0.10 in the univariable analysis were included in the multivariable analysis for adjusted analysis. In the
multivariable analysis, variables with a p-value <0.05 were considered significant. Software used was IBM SPSS ver 22.0. A p-value <0.05 was considered significant in the analyses.

Data Collection Procedure

Data collection was obtained through Melior, official platform for medical records used at Sahlgrenska University Hospital. Lab results was obtained through LabBest. Neurological imaging and independent evaluation by radiologists was obtained through WebAdapt.

Ethics

This study is approved by the local ethics committee in Gothenburg. Being a retrospective study of medical records, informed consent was not obtained. All patients where anonymized.

Results

Inclusion and patient characteristics

A total of 708 patients were admitted with suspected/verified SAH during the study period. 118 patients did not fulfill SAH-diagnosis, 33 patients were not included due to long time to admission (>4 days) and in 28 patients no ECG/echo/cardiac biomarkers were obtained. In the 529 patients analysed, 109 patients had died at the time mortality data was obtained (april 2016).

Out of the 529 patients included in the study protocol, 439 patients (83%) were admitted on day 1, 55 patients (10%) were admitted on day 2 and 35 patients (7%) were admitted on day 3 after onset of symptoms. Our primary predictors, levels of hsTnT were obtained in 428 patients (81%) and NTproBNP in 342 patients (65%). Secondary predictors; echo was performed on 237 patients (45%) and ECG in 457 patients (86%). Patients with WFNS 4-5 were more commonly examined with echocardiography (60% of patients with WFNS 4-5 vs 38% of patients with WFNS 1-3, p<0.001). This bias was not seen with the cardiac
biomarkers or ECG. A study flow chart of patient inclusion, exclusion and cardiac predictors obtained is shown in Figure 1.

A total of 32 patients (13%) had an echocardiographic ultrasound confirming SIC.

**Fig. 1** A brief protocol of number of patient inclusion, exclusion and variables obtained. $n =$ number of patients receiving the various tests.
<table>
<thead>
<tr>
<th>Category</th>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission data</td>
<td>Age, years</td>
<td>58 (49-67)</td>
</tr>
<tr>
<td></td>
<td>Female sex, N (%)</td>
<td>311 (59)</td>
</tr>
<tr>
<td></td>
<td>Hypertension, N (%)</td>
<td>186 (35)</td>
</tr>
<tr>
<td></td>
<td>Cardiac disease, N (%)</td>
<td>32 (6)</td>
</tr>
<tr>
<td></td>
<td>Cerebrovascular disease, N (%)</td>
<td>24 (5)</td>
</tr>
<tr>
<td></td>
<td>Previous SAH, N (%)</td>
<td>6 (1)</td>
</tr>
<tr>
<td></td>
<td>COPD, N (%)</td>
<td>15 (3)</td>
</tr>
<tr>
<td></td>
<td>Malignancy, N (%)</td>
<td>23 (4)</td>
</tr>
<tr>
<td></td>
<td>Diabetes, N (%)</td>
<td>18 (3)</td>
</tr>
<tr>
<td></td>
<td>Renal disease, N (%)</td>
<td>10 (2)</td>
</tr>
<tr>
<td>Medical history</td>
<td>Clinical SAH grade</td>
<td></td>
</tr>
<tr>
<td></td>
<td>WFNS 1, N (%)</td>
<td>245 (46)</td>
</tr>
<tr>
<td></td>
<td>WFNS 2, N (%)</td>
<td>109 (21)</td>
</tr>
<tr>
<td></td>
<td>WFNS 3, N (%)</td>
<td>15 (3)</td>
</tr>
<tr>
<td></td>
<td>WFNS 4, N (%)</td>
<td>90 (17)</td>
</tr>
<tr>
<td></td>
<td>WFNS 5, N (%)</td>
<td>65 (12)</td>
</tr>
<tr>
<td></td>
<td>Modified Fisher 1, N (%)</td>
<td>78 (15)</td>
</tr>
<tr>
<td></td>
<td>Modified Fisher 2, N (%)</td>
<td>94 (18)</td>
</tr>
<tr>
<td></td>
<td>Modified Fisher 3, N (%)</td>
<td>130 (25)</td>
</tr>
<tr>
<td></td>
<td>Modified Fisher 4, N (%)</td>
<td>223 (42)</td>
</tr>
<tr>
<td></td>
<td>Intracerebral hemorrhage, N (%)</td>
<td>70 (13)</td>
</tr>
<tr>
<td></td>
<td>Embolization, N (%)</td>
<td>284 (54)</td>
</tr>
<tr>
<td></td>
<td>Surgery, N (%)</td>
<td>130 (25)</td>
</tr>
<tr>
<td></td>
<td>Acute ventricular drainage, N (%)</td>
<td>210 (40)</td>
</tr>
<tr>
<td></td>
<td>Cerebral infarction, N (%)</td>
<td>192 (36)</td>
</tr>
</tbody>
</table>

*Age parameter is presented as median (interquartile range) of all patients included. All values are presented as n (%)SAH; Subarachnoid hemorrhage, WFNS; World federation of neurosurgeon grading of SAH, COPD; Chronic obstructive pulmonary disease*
Patient characteristics are presented in Table 3. Median age of patients in this study were 58 years. A total of 311 patients (59%) were female, 186 patients (35%) had a history of hypertension and 32 patients (6%) had a history of cardiac disease. A total of 155 patients (29%) had WFNS grade 4-5, 233 patients (42%) had Modified Fisher grade 4 on admission CT and 192 patients (36%) had cerebral infarction between onset of SAH and hospital discharge or death. A total of 210 patients received treatment with acute ventricular drainage (40%), 284 patients (54%) received aneurysmal treatment by intravascular embolization and 130 patients (25%) through open surgery by clipping.

Cardiac variables

Median level of hsTnT was 13ng/l and median level of NTproBNP was 785ng/l (Table 4). Levels of hsTnT was higher in patients with history of hypertension or cardiac disease, WFNS 4-5, modified Fisher grade 4 or intracerebral hemorrhage. Levels of NTproBNP was higher in women, patients with history of hypertension, cardiac disease or cerebrovascular disease, patients with WFNS 4-5, modified Fisher grade 4 or intracerebral hemorrhage. SIC was more common in women (88% of SIC patients, p<0.001), patients with WFNS 4-5 (69% of SIC patients, p<0.001) while patients with history of hypertension had a lower incidence of SIC (16% of SIC patients, p=0.026). Patients with SIC had higher levels of hsTnT (median 17ng/l vs 437ng/l, p<0.001) and NTproBNP (median 1075ng/l vs 7245ng/l). Patients with SIC also had lower ejection fraction (median 51% vs 65%). An abnormal ECG was more common in patients with history of cardiac disease or cerebrovascular disease. WFNS or modified Fisher grade did not have an impact on having abnormal ECG.

60% of all patients performing an echo had WFNS 4-5 on admission. Many patients with hsTnT-leakage and ECG-pathologies did not obtain an echo
hsTnT and NTproBNP are presented as median (interquartile range). The other variables are presented as n (%). SIC; Stress-induced cardiomyopathy

Survival

Overall mortality was 21% (109 of 529 patients) during the study period. A history of cardiac, cerebrovascular or renal disease was all associated with increased risk of death and was merged to one group, avoiding too small groups in the analysis. Patients with higher age, history of hypertension, cardiac-, cerebrovascular-, or renal disease had a higher risk of death. Furthermore, patients with admission status WFNS 4-5, intracerebral hemorrhage, modified Fisher grade 4 or cerebral infarction during hospital stay had a higher risk of death (Table 5).

Table 4. Summary of cardiac variables in the population

<table>
<thead>
<tr>
<th>Category</th>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biomarkers</td>
<td>Peak hsTnT, ng/l</td>
<td>13 (6-54)</td>
</tr>
<tr>
<td></td>
<td>Peak NTproBNP, ng/l</td>
<td>785 (368-1750)</td>
</tr>
<tr>
<td>Echocardiography</td>
<td>SIC, N (%)</td>
<td>32 (13)</td>
</tr>
<tr>
<td></td>
<td>Non-SIC, N(%)</td>
<td>205 (87)</td>
</tr>
<tr>
<td>Electrocardiography</td>
<td>Normal, N (%)</td>
<td>215 (47)</td>
</tr>
<tr>
<td></td>
<td>ST elevations, N (%)</td>
<td>10 (2)</td>
</tr>
<tr>
<td></td>
<td>Negative T-wave , N (%)</td>
<td>20 (4)</td>
</tr>
<tr>
<td></td>
<td>Long QT/u-wave, N (%)</td>
<td>39 (9)</td>
</tr>
<tr>
<td></td>
<td>Other ST-T segment abnormalities, N (%)</td>
<td>124 (27)</td>
</tr>
<tr>
<td></td>
<td>RBBB/LBBB, N (%)</td>
<td>22 (5)</td>
</tr>
<tr>
<td></td>
<td>Other (Q-wave, poor R-wave progression), N (%)</td>
<td>27 (6)</td>
</tr>
</tbody>
</table>
In a multivariable analysis, age, history of cardiovascular or renal disease, WFNS 4-5 and cerebral infarction were independently associated with a higher risk of death (Table 5).

Of the cardiac variables, peak levels of hsTnT and NTproBNP were associated with an increased risk of death. Having a normal ECG was associated with a lower risk of death, this was the strongest variable associated with risk of death of the ECG variables. SIC was not significantly associated with an increased risk of death (Table 6). Ejection fraction was associated with an increased risk of death. Peak levels of hsTnT and NTproBNP were significantly associated with an increased risk of death also when adjusting for age, history of cardiovascular or renal disease, WFNS 4-5 and cerebral infarction. A normal ECG or ejection fraction was not significantly associated with lower risk of death when adjusting for these variables (Table 6).

Kaplan Meier curves for WFNS 4-5, hsTnT and NTproBNP (divided by upper quartile or lower three quartiles), SIC and normal ECG are shown in Figure 2B-2E. Except for having an abnormal ECG, the differences in mortality observed in these groups were only significant the first year after the hemorrhage. Furthermore, comparing the whole SAH-population with age/sex matched controls; SAH-patients had the same mortality as controls one year after the hemorrhage (Figure 2A).
Fig 2. Kaplan Meier curves of survival. hsTnT (2C) and NTproBNP (2D) are divided by upper quartile or lower three quartiles. One year after the hemorrhage, mortality was the same in SAH-survivors as in the general population (A). WFNS 4-5 (B), hsTnT (C) and NTproBNP
(D) were also associated with an increased risk of death, but only the first year after the hemorrhage. Stress-induced cardiomyopathy was not associated with an increased risk of death (E). An abnormal ECG were associated with an increased risk of death, also later than one year after the hemorrhage.

### Table 5. Cox survival regression of medical history and admission variables,

<table>
<thead>
<tr>
<th></th>
<th>Bivariable regression</th>
<th></th>
<th></th>
<th></th>
<th>Multivariable regression</th>
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<tbody>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
<td>Sig</td>
<td>HR</td>
<td>95% CI</td>
<td>Sig</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.06</td>
<td>1.04 - 1.07</td>
<td>&lt;0.001</td>
<td>1.05</td>
<td>1.03 - 1.07</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Female sex</td>
<td>1.35</td>
<td>0.93 - 1.97</td>
<td>0.114</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.75</td>
<td>1.19 - 2.56</td>
<td>0.004</td>
<td>1.04</td>
<td>0.70 - 1.56</td>
<td>0.832</td>
<td></td>
</tr>
<tr>
<td>Cardiac or renal disease</td>
<td>2.64</td>
<td>1.66 - 4.18</td>
<td>&lt;0.001</td>
<td>1.70</td>
<td>1.06 - 2.74</td>
<td>0.029</td>
<td></td>
</tr>
<tr>
<td>Previous SAH</td>
<td>1.74</td>
<td>0.43 - 7.05</td>
<td>0.438</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>1.23</td>
<td>0.45 - 3.33</td>
<td>0.688</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignancy</td>
<td>1.81</td>
<td>0.88 - 3.72</td>
<td>0.107</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.85</td>
<td>0.81 - 4.22</td>
<td>0.142</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1.14</td>
<td>0.58 - 2.26</td>
<td>0.701</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WFNS 4-5</td>
<td>4.23</td>
<td>2.89 - 6.19</td>
<td>&lt;0.001</td>
<td>3.26</td>
<td>2.13 - 4.98</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Intracerebral hemorrhage</td>
<td>2.19</td>
<td>1.40 - 3.43</td>
<td>0.001</td>
<td>0.90</td>
<td>0.55 - 1.48</td>
<td>0.688</td>
<td></td>
</tr>
<tr>
<td>Modified Fisher grade 4</td>
<td>2.36</td>
<td>1.61 - 3.47</td>
<td>&lt;0.001</td>
<td>1.30</td>
<td>0.87 - 1.96</td>
<td>0.206</td>
<td></td>
</tr>
<tr>
<td>Cerebral infarction</td>
<td>2.93</td>
<td>2.00 - 4.30</td>
<td>&lt;0.001</td>
<td>1.87</td>
<td>1.24 - 2.83</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>Embolisation vs surgery</td>
<td>0.81</td>
<td>0.56 - 1.18</td>
<td>0.268</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Non-cardiac Variables Cox Regression. HR; Hazard Ratio.*

### Table 6. Cox survival regression of cardiac variables

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted</th>
<th></th>
<th></th>
<th>Adjusted</th>
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<th></th>
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<tbody>
<tr>
<td></td>
<td>HR</td>
<td>95% CI</td>
<td>Sig</td>
<td>HR</td>
<td>95% CI</td>
<td>Sig</td>
</tr>
<tr>
<td>Peak hsTnT, per 100ng/l</td>
<td>1.17</td>
<td>1.11 - 1.24</td>
<td>&lt;0.001</td>
<td>1.08</td>
<td>1.02 - 1.15</td>
<td>0.014</td>
</tr>
<tr>
<td>Peak NTproBNP, per 1000ng/l</td>
<td>1.09</td>
<td>1.06 - 1.11</td>
<td>&lt;0.001</td>
<td>1.05</td>
<td>1.02 - 1.08</td>
<td>0.001</td>
</tr>
<tr>
<td>Normal ECG</td>
<td>0.53</td>
<td>0.35 - 0.80</td>
<td>0.003</td>
<td>0.70</td>
<td>0.46 - 1.08</td>
<td>0.107</td>
</tr>
<tr>
<td>Stress induced cardiomyopathy</td>
<td>1.68</td>
<td>0.87 - 3.24</td>
<td>0.124</td>
<td>1.26</td>
<td>0.63 - 2.52</td>
<td>0.507</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>0.97</td>
<td>0.94 - 0.99</td>
<td>0.032</td>
<td>0.97</td>
<td>0.94 - 1.01</td>
<td>0.117</td>
</tr>
</tbody>
</table>

In the adjusted analysis, cardiac variables were adjusted for age, history of cardiovascular or renal disease, WFNS 4-5 and cerebral infarction. HR; Hazard Ratio.
Discussion

In this retrospective study, the aim was to evaluate whether acute cardiac events after SAH were associated with an increased long-term mortality. Cardiac biomarkers hsTnT and NTproBNP were both independently associated with increased risk of death while SIC and having abnormal ECG were not. However, these differences were only significant the first year after the hemorrhage.

In this study, patients with a higher age, medical history of a cardiovascular or renal disease, poor neurological status on admission and cerebral infarction during hospital stay were independently associated with an increased risk of death. Both hsTnT and NTproBNP were associated with an increased risk of death also when adjusting for these non-cardiac variables strongly associated with an increased mortality. This suggests that myocardial damage, as measured with troponin release, has an additive role in the risk of dying after SAH (Figure 3). Since NTproBNP, a biomarker of cardiac dysfunction, and ejection fraction was associated with an increased risk of death; an impaired cardiac function might contribute to or be the mediator to a poor prognosis. However, the increased risk of death was only significant the first year after the hemorrhage so release of cardiac biomarkers did not affect long-term mortality. Our hypothesis was that cardiac events would increase the risk of death since it increases the risk of cerebral damage and a cardiac insult is associated with a higher risk of death in other patient groups. However, either our hypothesis was false or all patients with a cardiac event died in the acute phase of the disease. Surprisingly, SIC was not associated with an increased risk of death. This was unexpected since SIC is shown to be associated with increased mortality in other settings. Having an abnormal ECG on admission was associated with an increased risk of long-term mortality in the univariable analysis. However, some patients might have had an abnormal ECG due to diagnosed or undiagnosed chronic cardiac disease upon admission and ECG-abnormalities were not significant in the adjusted analysis.
Interestingly, we also found that SAH-survivors had the same mortality one year after the hemorrhage as the general population.

Cardiac events after SAH are extensively studied. Several studies have shown an increased risk of poor functional outcome and an increased risk of short-term death [1, 38, 39]. However, the impact of cardiac events on long-term outcome is barely studied. To our knowledge, there are only two studies assessing the impact of cardiac events on long-term outcome. One of these studies, by Zaroff et al[4], was a register study and found that myonecrosis after SAH was associated with an increased long-term mortality and an increased risk of long-term cardiac events. However, this study did not adjust for other important variables of mortality such as WFNS score and age. The other study, by Bihorac et al [40], found that SIC was not associated with increased risk of mortality, as found in the present study.

The overall long-term mortality of SAH patients are sparsely studied. One study by from Finland published in 2015 showed that SAH-patients carries a 17% increased mortality after 20 years of ictus. [41] An American study published in 2009 estimated that standard mortality rate for SAH patients were 1.7 with a mean follow up time of 8.1 years.[42] Both these studies underline that long-term mortality data on SAH patients is scarce.

To our surprise, we found in our study that the mortality was the same as in controls one year after the hemorrhage. Both studies referred to above have an inclusion from the 1980s. A review article [43] from 2013 suggested that the prognosis of SAH-patients is getting better. Our study is one of the first studies to validate the long-term mortality of SAH-patients is actually being improved over time.

What is the possible relationship between myocardial damage and dysfunction and an increased risk of death? It is plausible that a decreased cardiac output contributes to a poor
perfusion pressure, especially since cerebral autoregulation is damaged after a SAH[44].

Endogenous catecholamines are also shown to increase cerebral oxygen demand in a damaged blood-brain barrier, which is found after SAH[45, 46]. This combination might be fatal in these patients. Another explanation might be that patients with troponin release suffer from a more serious brain injury in conjunction with the bleeding. When the aneurysm ruptures, blood enters the subarachnoid space and increases ICP rapidly, reaching a plateau at the same level as mean arterial pressure after approximately one minute after the bleeding[47, 48]. This increase in ICP leads to a decreased cerebral blood flow, ultimately leading to a cerebral hypoperfusion and the patient become unconscious[37, 49]. This might by physiological as it facilitates clotting of the ruptured aneurysm and ICP gradually normalizes within minutes in survivors[48]. However, the rapid rise in ICP and/or global cerebral ischemia initiates the Cushing reflex with an instant activation of the sympathetic nervous system and this activation might be more severe with more ischemia. Since we believe that sympathetic overstimulation is crucial for cardiac damage and SIC after SAH this might only reflect a more severe brain damage that could be used in addition to the clinical grading of SAH.

**Strengths and Weaknesses**

The main limitation of this study is that it is a retrospective single center study. However, all patients admitted with suspected SAH were consecutively included from the beginning of the study. The follow up time of patients and outcome was up to 6 years which may be considered as a weakness. However, the mortality was increased only the first year after hemorrhage in patients with biomarker release and compared to an age and sex-matched control group. The first 2 years of the study period, cardiac biomarkers were not taken on routine, making a possible bias for patients being more ill to receive these tests.

Echocardiography was not performed on routine during any period of time during the study period, which may contribute a bias towards critically ill patients. This bias was supported by
our data, 60% of patients performing an echocardiography was either WFNS 4 or 5. In addition, many patients with hsTnT-leakage and ECG-pathologies did not obtain an echocardiography. One might argue that many sub-clinical SIC pathologies might have gone undetected through this study, as many patients had who had TnT leakage did not obtain an echo. A previous study has shown moderate hsTnT-increase in SAH patients with SIC, with a peak value on hospital admission in 90% of patients. [20]

Conclusion and Clinical Implications

Acute cardiac events after Subarachnoid Hemorrhage is common and may lead to impaired cardiac function. Studies show that such events have an increased mortality and that cardiac biomarkers hsTnT and NTproBNP identify high-risk patients that could benefit from intensive hemodynamic monitoring with hemodynamic optimization.

We found that peak hsTnT and NTproBNP in the acute phase of subarachnoid hemorrhage is independently associated with an increased mortality up to 1 year after onset of symptoms. Further research is needed to address whether measures to optimize cardiac treatment after SAH might improve outcome.

Stressed-induced Cardiomyopathy was not significantly associated with increased mortality in patients with SAH this study. However, the main test to indicate this condition being echocardiography is not taken on routine on these patients making a bias for more ill patients. Evaluating how SIC impacts on long-term mortality has proven to be challenging as previous studies are scarce and yield conflicting results.[4, 40]

Populärvetenskaplig sammanfattning på svenska

Subarachnoidalblödning är en fruktad form av hjärnblödning och karakteriseras av en plötslig kraftig huvudvärk ofta beskriven som en åskknall. En vanlig komplikation i samband med
detta är en påverkan på hjärtat som kallas för stressinducerad kardiomyopati, vilket innebär att delar av hjärtväggen rör sig mindre eller inte alls. Det är inte helt säkert hur detta sker men det finns starka kopplingar till ökad cirkulation av catecholaminer så som adrenalin i samband insjuknandet. I denna studie har man undersökt hur hjärt påverkan i den akuta fasen av subarachnoidalblödning påverkar långtidsöverlevnaden genom att samla in data från journalsystem som används inom sjukvården. Genom att använda statistiska överlevnadsanalyser har man visat att hjärtmarkörerna hsTnT och NTproBNP är oberoende associerade till ökad risk för död upp till 1 år efter insjuknande. Man kunde inte se att stressinducerad kardiomyopati var associerat med ökad risk för död. Dock så görs ej testet för att påvisa denna hjärt påverkan rutinmässigt vid insjuknande av en subarachnoidalblödning och det finns risk att många patienter som hade en hjärt påverkan likt denna inte noterades. Det är viktigt att framtida forskning inriktar sig på att utvärdera betydelsen av hsTnT och NTproBNP i samband med subarachnoidalblödning för att optimera hjärtbehandling i samband med detta insjuknande.

Acknowledgements

This study was part of the examination project for EN in Master of science in Medicine at Sahlgrenska University Hospital and in a part of a series of studies in Stressed-Induced Cardiomyopathy lead by JO.

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