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Clinical characteristics and outcomes of neurogenic stress cadiomyopathy in aneurysmal subarachnoid hemorrhage

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ABSTRACT

Background: Aneurysmal subarachnoid hemorrhage (aSAH) is an often devastating form of stroke. Aside from the initial hemorrhage, cardiac complications can occur resulting in neurogenic stress cardiomyopathy (NCM), leading to impaired cardiac function. We investigated whether aSAH patients with NCM had poorer long term functional outcomes than patients without NCM. Mortality, vasospasm, and delayed ischemic complications were also evaluated.

Methods: A retrospective study of all patients admitted for aneurysmal subarachnoid hemorrhage (aSAH) from January 2006 to June 2011 ($n = 299$) was conducted. Those patients who underwent an echocardiogram were identified ($n = 120$) and were assigned to the NCM ($n = 49$) category based on echocardiographic findings defined by a depressed ejection fraction (EF%) along with a regional wall motion abnormality (RWMA) in a non-vascular pattern. Primary outcome measures included in-hospital mortality and functional outcomes as measured by the Modified Barthel Index (mBI) at 3 months and one year. Secondary analysis determined if there was an association between NCM, cerebral vasospasm and delayed cerebral ischemia.

Results: 16% of aSAH patients developed NCM. Mortality was higher ($p < .001$) in the NCM group ($n = 23$[46.9%]) than in the non-CM group ($n = 28$[11.2%]). Patients with NCM had poorer functional outcomes as measured by the mBI at both 3 months ($p = .002$) and 12 months ($p = .014$). The Hunt–Hess score was predictive of functional outcome as measured by the mBI at both 3 months ($p = .002$) as well as at 1 year ($p = .014$). NCM was associated with both death ($p = .047$ CI, 1.012–7.288) and vasospasm ($p = .008$ CI, 1.34–6.66) after correction for Hunt–Hess grade. Tobacco use ($p < .001$) and a history of diabetes mellitus ($p < .009$) were also associated with vasospasm. NCM was associated with higher in-hospital mortality ($p = .047$) in multivariate analysis.

Conclusion: NCM is seen in a substantial number of aSAH patients and when present, it is associated with higher mortality and poorer long-term functional outcomes. This finding may guide further prospective studies in order to determine if early recognition of NCM as well as optimization of cardiac output would improve mortality.

1. Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) is an often devastating form of hemorrhagic stroke with a mortality rate of up to 50% [1,2]. Most deaths occur within the first 2 days of onset with the majority related to the initial hemorrhage [3]. Delayed cerebral ischemia secondary to cerebral vasospasm can also occur in up 33% of patients leading to further morbidity and mortality [4]. The exact cause of vasospasm is unclear however, numerous comorbidities put patients at increased risk including the degree of intraventricular and cisternal hemorrhage, as well as aneurysm location [6].

Aside from the initial hemorrhage and associated cerebral injury, cardiac complications can also occur. ECG changes may be present in up to 96% of patients suffering aSAH with over 20% having positive cardiac enzymes [5–7]. In addition, RWMA can occur in 8–26% of patients [7–11]. The latter, often termed neurogenic stress cardiomyopathy (NCM), can lead to left ventricular (LV) dysfunction resulting in impaired cardiac output and pump

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failure. This potentially life-threatening condition further complicates the treatment of cerebral vasospasm which involves hyperdynamic therapy with both hypervolemia and induced hypertension.

Stress induced cardiomyopathy has been defined as a transient hypokinesis, akinesis, or dyskinesis of the LV basal or apical segments which extend beyond a single epicardial distribution in the absence of obstructive CAD, new EKG abnormalities and the absence of intracranial bleeding, such as seen in aSAH [12,13]. Generally this syndrome is seen in post-menopausal women and is self-limiting and carries a favorable prognosis with a mortality of less than 2% [12,14,15]. However, a similar process has been observed in a subset of patients suffering aSAH. The outcome from stress induced cardiomyopathy in this setting is less clear, as these patients have been excluded from most studies based on diagnostic criteria requiring the absence of intracranial hemorrhage [12]. Recently, it has been observed that the pathophysiologic process in both subgroups of patients is quite similar and likely overlap [16,17]. Importantly, the reduced LVEF, may have an added adverse effect in aSAH patients as it impairs the ability to treat cerebral vasospasm and associated ischemia [7,8].

In this study the incidence of NCM in patients with aSAH was determined. Both short term outcome, as measured by in-hospital mortality, and long term outcomes, as measured by the mBI at 3 and 12 months, were evaluated. Patients with severe LV dysfunction were included. The potential effects of NCM in patients with vasospasm, delayed cerebral ischemia (DCI), death, and functional outcomes were also assessed.

2. Methods

This study is a secondary statistical analysis of existing data from the Hartford Hospital Stroke Center. Data of patients admitted for subarachnoid hemorrhage (SAH) from January 2006 to June 2011 was analyzed. The Stroke Center at Hartford Hospital (SCHH) is certified by the Joint Commission of Accreditation of Healthcare Organizations (JCAHO) as a Primary Stroke Center and serves as a tertiary referral center. The study was conducted with the approval of the Institutional Review Board.

The main objective of this study was to determine if NCM is related to in hospital mortality or poorer functional outcomes. Additionally, secondary analyses were performed in order to determine if there was an association among patients with NCM and the prevalence of vasospasm and DCI. Data collection was initiated through the Institution's Stroke Database, a patient registry maintained by the Stroke Center and the HealthCare Research Institute and collected by a trained registered nurse. Data elements were confirmed or clarified through review of electronic and physical patient charts. Long-term outcomes were measured using 3-month and 12-month Modified Barthel Index (mBI) scores. The mBI (a scale of 0–20 with 20 being normal and 0 for total functional dependence) was obtained by telephone interview at 3 months and 1 year after stroke by a stroke center nurse and data coordinator [18]. The mBI is a reliable and valid measure of functional independence and serves as a useful tool to assess intervention outcomes [18]. Mild to no disability is indicated by a mBI of 15 or above [19].

A total of 611 patients were identified as having SAH during the time period examined time period and comprised the initial study population. Included were those patients with a diagnosis of aneurysmal subarachnoid hemorrhage with (1) a CT scan and a cerebral angiogram, (2) a positive lumbar puncture with laboratory evidence of xanthochromia and a cerebral angiogram. The following exclusion criteria were then applied; pre-existing coronary artery disease; a known diagnosis of cardiomyopathy including prior pacemaker or automatic implantable cardiac defibrillator; ETOH abuse; prior documented arrhythmia; and non-aneurysmal subarachnoid hemorrhage. This yielded 299 patients that were included in the final analysis, 49 of whom were positive for NCM (see Fig. 1).

2.1. Clinical protocol

The 299 charts were then extracted and those with evidence of a depressed EF%, regional wall motion abnormality (RWMA), or elevated troponin were identified.

An echocardiogram was indicated in patients with (1) cardiac dysrhythmia or evidence of cardiac ischemia on 12 lead EKG; (2) an elevated troponin (>0.3 ng/mL); (3) chest pain. An abnormal echocardiogram was identified as, (1) mild with RWMA and an

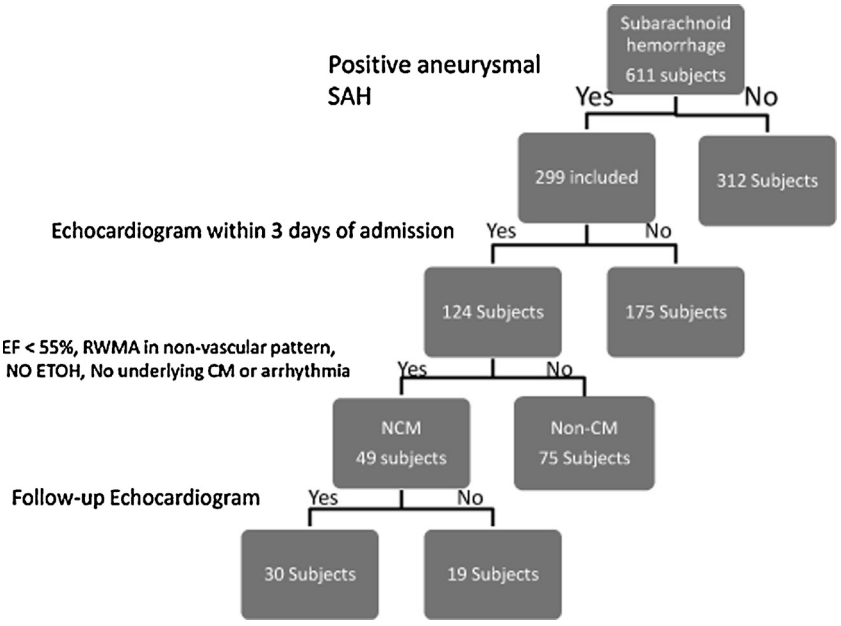

Fig. 1. Flowchart representing inclusion/exclusion criteria.