Clinical Neurology and Neurosurgery 128 (2015) 4–9

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Clinical outcomes after neurogenic stress induced cardiomyopathy in aneurysmal sub-arachnoid hemorrhage: A prospective cohort study

Kent J. Kilbourn[a,*], Gilbert Ching[b], David I. Silverman[b], Louise McCullough[c], Robert J. Brown[a,c]

[a] Hartford Hospital, Department of Neurosurgery, 80 Seymour Street, Hartford 06102, USA
[b] Hartford Hospital, Division of Cardiology, 80 Seymour Street, Hartford 06102, USA
[c] University of Connecticut Health Center, Department of Neurology, 263 Farmington Avenue, Farmington 06030, USA

ARTICLE INFO

Article history:
Received 21 June 2014
Received in revised form 1 September 2014
Accepted 26 October 2014
Available online 4 November 2014

Keywords:
Neurogenic stress cardiomyopathy
Aneurysmal subarachnoid hemorrhage
Tako-tsubo
Echocardiography

ABSTRACT

Introduction: Neurogenic stress cardiomyopathy (NCM) has been associated with poor outcomes in the setting of aneurysmal subarachnoid hemorrhage (aSAH). Much less is known regarding recovery of cardiac function. The aim of this prospective cohort study was to study the rate of early cardiac recovery after NCM and the potential effect of NCM on short term functional recovery. A secondary aim sought to determine whether certain biomarkers may be associated with the development of NCM.
Methods: Patients with confirmed aSAH between November 2012 and October 2013 were prospectively enrolled and received echocardiograms within 48 h of admission. Ejection fraction (%) and regional wall motion abnormality score index (RWMI) were noted. All patients with confirmed aSAH had a troponin and BNP level drawn on admission. Patients with confirmed NCM received a follow up echocardiogram 7–21 days after the initial echocardiogram. Clinical follow up at 3 months evaluated mortality, mRS and mBI scores.
Results: 63 patients with confirmed aSAH were enrolled. In this cohort 11 (17%) patients were confirmed to have NCM. The NCM group had higher in-hospital mortality [$n = 4(36.4\%)$] compared to the non-NCM group [$n = 5(9.6\%)$] ($p = .021$). At 3 months the development of NCM was associated with an unfavorable mRS ($p = 0.042$) and mBI ($p = 0.005$). Both an elevated BNP (>100 pg/mL) and elevated troponin (>0.3 mg/dL) were associated with the development of NCM. Follow-up echocardiograms were performed within 21 days of admission on 8 patients with NCM. An abnormal RWMI of 1.5 or higher was present in 5(71%) patients.
Conclusion: NCM is a frequent complication associated with aSAH. The onset of the disease occurs early in the course of aSAH and an elevated BNP and troponin may be associated with the onset of NCM. Cardiac function often remains impaired during the acute recovery phase potentially impeding resuscitation during this period. The routine use of short term follow-up echocardiography may be recommended.

1. Introduction

Cardiovascular complications are major contributors to morbidity after aneurysmal subarachnoid hemorrhage (aSAH). Regional wall motion abnormalities (RWMA) on echocardiography have been reported in up to 20% of patients after aSAH [1–6]. The injury pattern produced is commonly referred to as neurogenic stress cardiomyopathy (NCM) [1,7]. In the setting of aSAH, NCM is often used interchangeably with tako-tsubo cardiomyopathy (TTC) [8]. TTC was first described by the Japanese in the early 1990s and is a reversible cardiomyopathy usually seen in postmenopausal women who are subjected to an acute emotional stress [9]. TTC is also observed in the setting of acute medical illnesses such as sepsis. Other precipitants include intracranial bleeding, head trauma, ischemic stroke, pheochromocytoma, and administration of exogenous catecholaminergic agents such as inhaled beta-agonists and cocaine [10].

In patients suffering from NCM, the RWMA produced are often extensive enough to reduce left ventricular ejection fraction (LVEF). In addition to pulmonary edema and hypoxia, NCM can lead to decreased cardiac output and mean arterial pressure (MAP). Patients with NCM are at risk for fatal arrhythmias particularly those with SAH or right insular cortex lesions [10].

* Corresponding author at: 80 Seymour Street, JB 605, Hartford 06102, USA. Tel.: +1 860 545 1911; fax: +1 860 545 1911.
E-mail address: kent.kilbourn@hhchealth.org (K.J. Kilbourn).

http://dx.doi.org/10.1016/j.clineuro.2014.10.017
0303-8467/

Previous studies have shown that development of NCM predicts poor neurological outcome [1,11]. However, much less is known about these patients' cardiac outcomes, and if cardiac dysfunction persists and further complicates neurological recovery. It has been reported that patients with non-neurogenic stress cardiomyopathy have complete resolution of their cardiac abnormalities, and have all-cause mortality similar to that of the general population [12,13]. The aim of this prospective cohort study was to evaluate the rate of early recovery after the onset of NCM and to determine the effect of NCM on neurological outcome. We used echocardiography as the primary imaging modality by which to determine the incidence and follow the progression of NCM in these patients. Certain biomarkers were analyzed as possible predictors of the development of NCM.

2. Materials and methods

This study is a prospective, observational study carried out at Hartford Hospital in Hartford CT USA; a JCAHO designated Comprehensive Stroke Center. Hartford Hospital serves as a regional tertiary care facility, providing neurointerventional and neurosurgical services to catchment area of over 2 million people. Since 2001, the Stroke Center at Hartford Hospital (SCHH) has maintained a prospectively entered data registry which includes outcome measurements. aSAH was added in 2004. The study was conducted with the approval of the Institutional Review Board and a waiver of consent was granted for enrollment.

All eligible patients ages 18 years or greater admitted between November 2012 and October 2013 to the SCXX with aSAH were included the study (see Fig. 1). A diagnosis of aSAH was made by a non-contrast CAT scan of the head and confirmed by either conventional biplane cerebral angiogram or direct intraoperative observation. Exclusion criteria included; patients less than 18 years old; patients with prior LV systolic dysfunction; known heart failure; reduced EF on a prior echocardiogram; or ST segment elevation myocardial infarction (STEMI) from obstructive coronary artery disease diagnosed by cardiac angiogram if performed. Standard care for aSAH patients was provided for all enrollees. All patients were admitted to the neurosciences intensive care unit. Systolic blood pressure (SBP) was maintained less than 140 mmHg until the aneurysm was secured using intravenous labetalol and/or nicardipine infusion. A strategy of permissive hypertension was used once the aneurysm was secured. Hypotension (SBP <100 mmHg) was managed with intravenous fluids and vasopressors such as norepinephrine, neosynephrine, and vasopressin as needed. Patients with hydrocephalus were treated with external ventriculostomy drains. All patients received oral nimodopine and pravastatin within 24 h which were continued for 21 and 14 days, respectively. Patients were maintained euvolemic and intravenous fluids were adjusted to maintain a positive fluid balance.

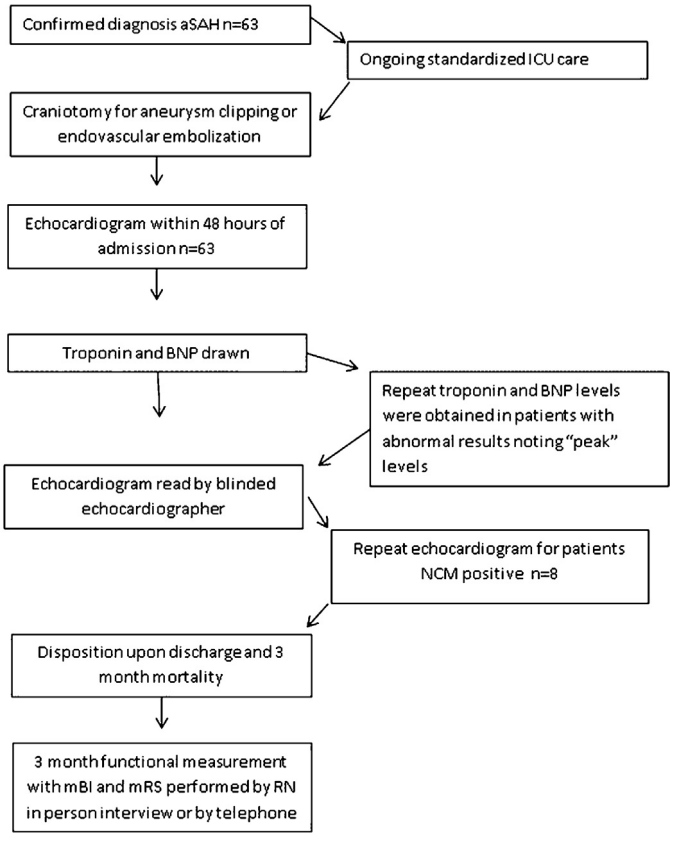

Fig. 1. Flowsheet depicting study protocol.

A baseline EKG, troponin, and serum B-type brain natriuretic peptide level (BNP) were obtained on all patients on admission. The biomarkers are part of an order set in our institution's electronic medical record system and specifically designated for patients with aSAH. An abnormal BNP, indicative of congestive heart failure, was defined as a serum level >100 pg/mL [14]. An abnormally elevated troponin at our institution is defined as >0.3 ng/dL [15,16]. Serial BNP and troponin levels were obtained with subsequent blood draws in patients with an initial abnormal level. Any evidence of cardiac ischemia including arrhythmias, EKG changes, or chest pain was investigated and managed as clinically indicated. Hemodynamic monitoring, including an arterial line, Flo-Trac (Edwards Lifesciences, Irvine CA), esophageal doppler monitor, or Swan-Ganz catheter were utilized as clinically indicated.

2.1. Echocardiography methodology

For consecutive patients enrolled in the study, a standard transthoracic echocardiogram was performed based on the recommendations and standards of the American Society of Echocardiography [17]. All echocardiograms were interpreted by a single physician who was blinded from the clinical information of the patients and performed within 48 h of admission. Follow-up echocardiograms were performed for patients with cardiomyopathy (defined as EF $\leq$55%) [18] within 21 days after admission. Chamber quantification was performed, including standard measurements of the LV wall thickness, LV mass, LV mass index, end-diastolic, end-systolic dimensions, left atrial diameter, and left atrial volume index. Simpson's method was performed for all patients to assess the left ventricular ejection fraction [17]. For patients with cardiomyopathy, LV wall abnormalities were assessed using the 16-segment model for LV segmentation according to the American Society of Echocardiography guidelines. Each of the 16 segments were assigned a score, where 1 = normal contractility or hyperkinesis, 2 = hypokinesis, 3 = akinesis, 4 = dyskinesis (paradoxical systolic motion), and 5 = aneurysmal. Regional wall-motion abnormality score index was derived by calculating the sum of all wall segment scores divided by the number of segments visualized. Therefore, a RWMA score of 1 is normal and >1 indicates the presence of wall motion abnormality. Patients with a wall motion abnormality but preserved EF% >55 would be classified as non-NCM, however, a patient without a regional wall motion abnormality but global hypokinesis would be positive for NCM.

Right ventricular function was evaluated by measuring the tricuspid annular systolic excursion. A tricuspid annular systolic excursion of less than 1.5 cm is associated with poor prognosis in a variety of cardiovascular diseases [19]. Pulmonary artery systolic pressure was also measured based on the velocity of the tricuspid regurgitation Doppler flow.