Use of Intra-aortic- Balloon Pump Counterpulsation in Patients with Symptomatic Vasospasm Following Subarachnoid Hemorrhage and Neurogenic Stress Cardiomyopathy

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Abstract

Introduction—Intra-aortic counterpulsation balloon pumps (IABPs) have been widely used to augment hemodynamics in critically ill patients with cardiogenic shock and have recently been proposed as a management strategy for subarachnoid hemorrhage (SAH) patients with neurogenic stress cardiomyopathy (NSC). Prior case series have described the use of IABP as a means to manage cardiogenic shock in this patient population; however, we sought to describe our experience with IABP as a means to wean vasopressor requirement while augmenting hemodynamics and maintaining pressures at goal.

Methods—Five patients were identified from a single center, prospective, observational cohort study that received an IABP for the management of ischemia related to cerebral vasospasm in the setting of NSC. We evaluated all cases for efficacy of IABP in reducing vasopressor requirement, and complications.

Results—Vasopressor requirements were reduced by a mean of 50% (range 25–65%) following IABPs placement within 24–48 h. There were no significant complications from IABPs. Out of the five patients, the outcome in three cases was favorable (mRS≤1). Two patients suffered delayed cerebral ischemia (DCI), one patient passed away due to severe sepsis, and one patient was left with severe disability. Only one patient required anticoagulation and that was for a preexisting deep venous thrombosis.

Conclusion—The use of IABPs may be beneficial as an adjunctive therapy in SAH patients with concomitant symptomatic vasospasm and NSC.

Keywords
Cardiomyopathy; cerebral vasospasm; intra-aortic balloon pump; subarachnoid hemorrhage

INTRODUCTION

Aneurysmal subarachnoid hemorrhage (aSAH) continues to be associated with high morbidity and mortality despite advances in neurocritical care [1–3]. Cerebral vasospasm after aSAH begins three days after ictus and peaks after seven to eight days. Radiographic vasospasm is recognized in 50–70% of patients with aSAH with 20–30% of patients developing clinical or symptomatic vasospasm which heralds a poorer prognosis [4–6]. Ten to 20% will experience permanent disability or die as a result of DCI [7]. Increasing intravascular volume with fluid augmentation, enhancing inotropic function, and raising vascular tone utilizing inotropic and vasopressors agents have become therapeutic keystones in the management of symptomatic vasospasm aiming to optimize mean arterial pressure (MAP), increase cerebral blood flow (CBF), and maintain cerebral perfusion pressure (CPP). Twenty to 30% of patients with SAH will also develop NSC [8–13] which may be present on admission or develop secondarily as a complication of management of symptomatic vasospasm with vasopressors [14,15,16]. NSC causes decreased cardiac output and hypotension. A review of the literature revealed a few case reports on the use of intra-aortic balloon counter pulsation pumps (IABP) in the management of patients...
with comorbid vasospasm and NSC [12,17–19]. In this paper, we describe five consecutive SAH patients with symptomatic vasospasm in whom IABPs was utilized to augment hemodynamics.

METHODS

The study was approved by the Columbia University Medical Center Institutional Review Board; in all cases written informed consent was obtained from the patient or a surrogate.

Study population

We retrospectively reviewed a single-center, prospectively maintained, observational database of patients with SAH and identified five patients that received an IABP for the management of ischemia related to cerebral vasospasm in the setting of NSC between May 2011 and April 2015. We evaluated all cases for complications and for efficacy in reducing vasopressor requirement.

Clinical management

Clinical management conformed to Neurocritical Care Society and American Heart Association guidelines [20,21]. All patients underwent electrocardiograms on admission. Cardiac troponin I testing was performed on admission and thereafter when clinically indicated. All patients received oral nimodipine and intravenous hydration with 0.9% saline with supplemental fluids as needed to maintain euvolemia. Hypertensive hypervolemic therapy was initiated for symptomatic vasospasm or when severe angiographic vasospasm was diagnosed in poor-grade patients by increasing systolic blood pressure (SBP) to 180 to 220 mmHg [10]. Patients who do not respond to volume augmentation receive pharmacologic cardiac support with inotropic and vasopressor agents and cardiac monitoring via pulse contour cardiac output (PiCCO®) [22] monitors or less frequently Swan-Ganz catheters. Patients who did not respond to medical therapy underwent neuroendovascular interventions to alleviate the symptomatic cerebral vasospasm. IABP was implanted in patients who developed concomitant NSC and symptomatic vasospasm when medical augmentation of cardiac function in isolation was deemed ineffective to reverse clinical symptoms and/or detrimental to the impaired cardiac function.

Data collection

Demographics, past medical history, baseline clinical status, imaging results, as well as treatment and complications during hospitalization were recorded prospectively. All data are adjudicated in a weekly meeting with the clinical providers that requires a consensus agreement of each data point.

Clinical and radiological variables

The diagnosis of aSAH was established by admission computed tomography (CT) or by the presence of xanthochromia if the initial CT scan was nondiagnostic. All patients received a CTA and/or digital subtraction angiography (DSA) to determine the presence, size, and location of a ruptured aneurysm. The modified Fisher scale was used to characterize the risk of delayed cerebral ischemia. Delayed cerebral ischemia from cerebral vasospasm was defined as (1) clinical deterioration (i.e., a new focal deficit, decrease in level of consciousness, or both), and/or (2) a new infarct on CT that was not visible on the admission or immediate postoperative scan, when the cause was thought by the research team to be vasospasm [23].

Outcome assessment

The primary outcome measure was the effects of IABP on hemodynamics, pressor requirements, and short-term clinical response [5]. Secondary outcomes included the development of complications and functional outcome. All patients were also assessed for the development of IABP-related complications which included hematoma formation, limb ischemia, deep vein thrombosis, compartment syndrome, infection/sepsis, hemolytic anemia, or thrombocytopenia. Global outcome was assessed by in-person interview or telephone-structured interview at three months using the seven-point version of the modified Rankin Scale (mRS) rated from death to symptom-free full recovery (0) [24,25]. Poor outcome was defined as death or moderate-to-severe disability (unable to walk or tend to bodily needs, mRS score 4 to 6) [20,26,27].

RESULTS

Over a period between August 1996 and April 2015, a total of five patients were identified in our retrospectively review of a prospectively maintained, observational database of subarachnoid hemorrhage patients that received an IABP for the management of ischemia related to cerebral vasospasm in the setting of NSC.

All cases were evaluated for complications and for efficacy in reducing vasopressor requirement and in preventing DCI.

The mean age in our case series was 60 years and the median admission Hunt and Hess grade and modified Fisher grade was 3 and 3, respectively (Table 1). In all
our patients, there was a 10–15% drop in the ejection fraction (EF), with a mean admission EF of 50% (range 30–75%) and mean EF during the NSC of 30% (range 15–40%). The drop in ejection fraction was concomitant with increasing pressor requirements in the setting of symptomatic vasospasm. IABP was placed on average around day 8 and the mean duration of IABP requirement was 4 days (range 1–7 days) (Table 2).

Our cases required an initial augmentation rate of 1:1. Only one patient received anticoagulation and this case was the only one to develop an IABP-related complication. IABP placement permitted reduction in vasopressor requirements by a mean of 50% (range 25–65%) within 24–48 h (Table 3), and in four patients cardiac enzymes and function normalized. The outcome in three cases was favorable (mRS ≤1), and one patient was left with severe disability (Table 4).

All patients developed pulmonary effusions attributable to their compromised cardiac output in the setting of induced hypervolemia. One patient had developed an increased vasopressor requirement due to septic shock from pneumonia on post bleed day 3 (the IABP was placed on post-bleed day 8) and this patient subsequently passed away due to severe sepsis.

**DISCUSSION**

The brain–heart interaction is multifaceted, and an intact system is essential for normal cardiovascular and cerebrovascular function. Neurogenic stress cardiomyopathy (NSC) occurs during times of enhanced sympathetic tone and may be precipitated in part or entirely by excessive endogenous or exogenous catecholamine stimulation of the myocardium [28]. NSC is characterized by a severely reduced ejection fraction, mild elevations in troponin, and electrocardiographic abnormalities, including QTc prolongation and T wave and ST segment changes in the absence of obstructive CAD [12,28]. Echocardiographic abnormalities usually range from
regional or global wall motion abnormality and extend beyond a single coronary vascular territory [28].

Studies have shown that lesions affecting the ipsilateral insular cortex and amygdala may cause neurochemical derangements, resulting in an increase in synaptic norepinephrine levels leading to enhanced sympathetic outflow to the heart [14,15,16]. Over the past 10 years, several case reports described the efficacy of IABP in the management of concomitant cardiogenic shock and cerebral vasospasm following SAH. IABPs provided optimal hemodynamic support that resulted in neurological and cardiovascular improvement with eventual weaning of vasoactive medications [12,17–19]. In this paper, we describe our experience in utilizing IABP counterpulsation devices to augmented hemodynamics and wean the pharmacologic vasopressor requirements while managing symptomatic vasospasm secondary to SAH in patients who were admitted with normal cardiac function but subsequently progressed to NSC.

The exact etiology of NSC is unknown but the prevailing theory hypothesizes catecholamine-induced intracellular myocyte calcium overload causing myocardial stunning and microinfarction [15,29,30]. Acute left ventricular systolic dysfunction in association with aSAH has been reported to complicate the clinical course of SAH in 20–30% of cases, typically occurring within 72 h [13]. Female gender, poor neurological grade, and troponin elevation have been identified as independent predictors of NSC after SAH [11,28,31]. NSC has been associated with increased risk of SAH-associated cerebral vasospasm [11], and indeed, NSC in SAH may occur due to direct neurologic injury or as a complication of hemodynamic augmentation via exogenous catecholamines and catecholamine analogs (inotropes and vasopressors) [30] employed in the management of aSAH-induced vasospasm. In our case series, IABP allowed for adequate hemodynamic augmentation, and weaning of the vasopressors while maintaining adequate cerebral perfusion in patients with symptomatic vasospasm and NSC hence allowing for cardiac recovery.

The yield of volume expansion and induced hypertension is often limited by the severely diminished cardiac output in these patients. Recently, less conventional tools have been recruited to the neurointensivist’s armamentarium. The IABP is designed to increase coronary perfusion, by utilizing the counterpulsation technique, hence augmenting diastolic pressure, reducing LV afterload, LV wall tension, and oxygen demand and providing hemodynamic augmentation in critically ill patients with cardiogenic shock [23,24]. Depending upon the patient’s hemodynamic status, the balloon may be programmed to assist every beat (1:1) or less often (1:2, 1:4, or 1:8). With hemodynamic improvement, the device can be “weaned” to less frequent cycling before complete removal.

Animal studies on cerebral blood flow (CBF) supported the ability of IABP to raise CBF in the setting of cerebral vasospasm and vascular dysregulation following aneurysmal SAH [32]. Further studies looking into the prophylactic use of IABP in patients with SAH prior to the development of radiographic or clinical vasospasm or NSC showed that IABPs enhanced mean CBF over the course of treatment, but neurological deficits developed regardless [33]. In a randomized controlled trial looking at the prophylactic use of IABP in high-risk SAH patients prior to the development of vasospasm or NSC, there was neither a statistically significant difference in outcome nor any no long-term complications secondary to IABP. Additionally CBF was not different between groups and the trial did not show clinical bene-

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<td>Centrum semiovale infarcts attributed to vasospasm.</td>
<td>Refractory vasospasm NSC</td>
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fit following SAH in patients with normal cardiac function [34].

With regards to safety, IABPs do not appear to be associated with any significant complication risk as evidenced by the largest trial involving the IABP was the intra-aortic balloon pump in cardiogenic shock II (IABP-SHOCK II) trial [35]. Although there was no significant difference in the primary outcome of 30-day mortality between IABP and controls, the IABP group and the control group did not differ significantly with respect to the rates of major bleeding (3.3% and 4.4%, respectively; \( P=0.51 \)), peripheral ischemic complications (4.3% and 3.4%, \( P=0.53 \)), sepsis (15.7% and 20.5%, \( P=0.15 \)), or stroke (0.7% and 1.7%, \( P=0.28 \)) [19]. Although the evidence is sparse, conventionally unfractionated heparin infusions are recommended to prevent catheter-related thrombotic events. A recent review paper analyzing the evidence regarding anticoagulation in patients requiring IABP showed that there was no significant difference in the risk of limb ischemia; however, incidence of bleeding was significantly increased in the heparinized group [36]. Therefore, when IABPs are indicated in patients admitted to the neurologic intensive care unit (ICU), risks and benefits of heparinization should be weighed in each case rather than being an automatic response to the use of an IABP [36]. In our institution, we have avoided anticoagulation when the IABP is set at 1:1 beat augmentation. Some advocate for a sheath-less technique with patients requiring IABP yet have a contraindication to anticoagulation as this technique entails an exceedingly low complication rate [37].

The primary limitation of our study is that it includes a small number of patients, the lack of randomization, and that we were unable to obtain coronary catheterization; however, in all our cases, IABP placement enabled rapid de-escalation of high vasopressor doses, and in three patients, we subsequently saw the normalization of cardiac enzymes and reversal of the myocardial dysfunction over time. Despite the fact that we cannot draw out any large scale conclusions, in a select few patients good outcomes can be achieved with the aid of IABP in patients with SAH and those patients may be able to have an acceptable quality of life.

CONCLUSION

Management of symptomatic vasospasm in a patient with SAH and NSC is challenging. Despite the limited evidence available, IABPs may be effective and safely used in patients with concomitant symptomatic cerebral vasospasm with a compromised myocardium who become intolerant to aggressive pharmacologic hemodynamic augmentation. Further research is necessary to establish decisively the efficacy of this adjunctive intervention in SAH.

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COMPETING INTERESTS STATEMENT

There are no competing interests.

CONTRIBUTORSHIP STATEMENT

Fawaz Al-Mufti, Nicholas Morris A, Shouri Lahiri, William Roth, Iona Machado, Sachin Agarwal, Soojin Park involved in the acquisition of data, analysis and interpretation, draft of the manuscript, critical revision of the manuscript for important intellectual content. Jens Wicscht involved in the Critical revision of the manuscript for important intellectual content. Drafting of the manuscript and critical revision of the manuscript for important intellectual content are done by Philip M Meyers, E Sander Connolly. Jan Claassen involved in the acquisition of data, analysis and interpretation, draft of the manuscript, critical revision of the manuscript for important intellectual content, study supervision.

DATA SHARING STATEMENT

There is no additional unpublished data from the study.

REFERENCES
