Cardiac manifestations of subarachnoid hemorrhage

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Subarachnoid hemorrhage (SAH) is a devastating condition. It carries a high mortality rate, with 12% of patients dying before reaching the hospital. Aside from its neurological morbidities, SAH is associated with significant medical complications. Cardiac manifestations are common and can impact morbidity and mortality in SAH patients. This article will discuss the cardiac manifestations of SAH.

Keywords: aneurysmal subarachnoid hemorrhage • cardiac complications • cardiac manifestations of stroke • neurogenic stunned myocardium • tako-tsubo cardiomyopathy

Subarachnoid hemorrhage (SAH) is defined as acute extravasation of blood into the subarachnoid space and affects as many as 30,000 people annually in the USA [1]. The most common nontraumatic cause of SAH is rupture of saccular intracranial aneurysms. Aneurysmal SAH is associated with a 30-day mortality of 45%, with approximately 12% of patients dying before reaching medical attention [2,3]. The high morbidity and mortality associated with SAH is not limited to its neurological manifestations – medical complications are commonly encountered in patients with SAH. Physiological derangements associated with SAH are independent predictors of mortality and poor outcome [4].

Although the true incidence of cardiac manifestations in SAH has not been determined, it is probably seen in at least 50% of patients [5]. Studies over the years have demonstrated that cardiac disturbances in relation to SAH occur in a continuum with varying degrees of severity. The spectrum of severity spans from mild elevation in cardiac enzymes and ECG changes to overt clinical and echocardiographic pathology [6,7]. Markers for cardiac damage and dysfunction are associated with an increased mortality, poor outcome and delayed cerebral ischemia (DCI) after SAH [8]. The etiologic basis for SAH-associated cardiac changes is for the most part speculative. Genetic factors, specifically polymorphism of adrenoreceptors, may increase the risk of cardiac abnormalities after SAH [9]. Stress-induced cardiac injury has been well described and is seemingly associated with a sympathetic overdrive (‘fight or flight’) at times of emotional stress [10]. The same mechanism has been proposed to be responsible for cardiac abnormalities observed in patients with SAH – that is, catecholamine overstimulation of the myocardium during or shortly after the acute hemorrhage [11,12]. Elevated sympathetic tone causes a hyperdynamic cardiovascular status, which could ultimately lead to cardiac decompensation and failure [13,14]. Simultaneously, this pathologic state may be reflected as a variety of aberrant electrographic findings on the ECG. In this article, we will discuss various cardiac manifestations observed in patients with SAH.

Mild myocardial injury
To emphasize, myocardial injury associated with SAH varies in severity and could range from elevation of cardiac enzymes (CEs) with mild ECG changes to severe cardiomyopathy (CMO) with ventricular dysfunction and cardiogenic shock. Mild myocardial injury is usually manifested by an elevation in serum cardiac troponin I (cTn-I). These elevations occur in 20–68% of patients and are usually mild, not reaching the diagnostic threshold for myocardial infarction (MI) [15]. SAH patients presenting with more severe neurological symptoms based on their Hunt-Hess grades, those with more severe physiologic derangements or a history of cardiovascular disease are more likely to exhibit elevated cTn-I levels [15,16]. In fact, the degree of neurological injury as assessed by the Hunt-Hess grade is an independent predictor of myocardial injury after SAH [17]. Hunt-Hess is a five-point scale used to determine neurological disability in SAH and surgical risk.
Although there is a debate regarding the true prognostic value of elevated serum cTn-I in SAH, it does appear to be a powerful predictor for the occurrence of pulmonary and cardiac complications, especially in patients presenting with a high grade on the World Federation of Neurological Surgeons (WFNS) SAH clinical scale \[18\]. The WFNS scale is a five-point grading scale for the classification of the severity of SAH (the higher the grade, the more severe the neurological deficit). One study reported that the median time interval between the onset of SAH and peak cTn-I levels was 1.7 days and that the first measurement appeared to be the highest in most cases \[15\]. The same study demonstrated that peak cTn-I levels were predictive of an increased risk of hypotension requiring vasopressors, pulmonary edema, left ventricular (LV) dysfunction and DCI due to cerebral vasospasm. The overall results of studies looking at cTn-I elevations in SAH suggest that this marker is perhaps a more sensitive and specific indicator of myocardial injury than creatine kinase-MB (CK-MB; a sensitive and specific serological marker used in the diagnosis of myocardial infarction) \[19\]. Its levels and trends should therefore be monitored closely via serial measurements, especially in SAH patients with a prior history of cardiovascular disease and those presenting with severe neurological symptoms or significant physiological derangements.

Cardiomyopathy

The most severe form of cardiac injury in SAH is neurogenic stunned myocardium (NSM) \[20\]. The elevated sympathetic tone causes a transient calcium overload with decreased responsiveness of contractile filaments to this cation, ultimately leading to myocardial depression \[21\]. Involvement of oxygen-derived free radicals has also been proposed \[14\]. Histopathologically, this form of myocardial injury is characterized by subendocardial contraction band necrosis \[22\]. Echocardiographic studies have shown abnormalities of LV contractility and wall motion that are usually reversible \[23\]. These echocardiographic wall motion abnormalities are associated with impaired LV function, which may, in some cases, severely compromise cardiac output (CO), leading to cardiogenic shock \[13\].

Neurogenic stunned myocardium associated with SAH has been compared with an entity described in cardiology literature: takotsubo cardiomyopathy (TC). Initially reported in the 1990s by the Japanese in postmenopausal women, this type of CMO appears to be precipitated by acute emotional stress and is consequently sometimes referred to as ‘the broken heart syndrome’ \[24–26\]. A unique feature of TC is the presence of wall-motion abnormalities on echocardiogram in face of patent epicardial arteries as demonstrated by coronary angiography \[24,25\]. Furthermore, echocardiography typically shows aberrant motion involving the cardiac apex (60% of cases), occasionally with a characteristic ‘ballooning’ \[10\]. The most favored hypothesis regarding the pathophysiology of TC is epicardial coronary spasm \[27\].

Neurogenic stunned myocardium occurs in approximately 20–30% of patients with SAH \[28\]. Predictors of LV dysfunction in SAH patients are peak CK-MB levels above 2%, poor neurological grade and female gender \[13\]. Severely impaired LV performance can precipitate cerebral vasospasm and DCI via its effect on cerebral blood flow (CBF) \[8\]. Reduced CO will lead to a drop in mean arterial pressure, causing a reduction in CBF. Thus, optimal heart function is critical in preventing progression of neurological dysfunction and promoting recovery in patients with SAH.

Fortunately, NSM is reversible, although full recovery may take several weeks \[23\]. In experimental canine models, NSM was reversible within 48 h \[29\]. One study reported that, among a cohort of SAH patients who suffered NSM, the mean ejection fraction was 38% initially and 55% at recovery \[30\]. However, the dilemma occurs when hypervolemic/hemodilutional/hypertensive therapy (‘triple-H’) is required to overcome and treat symptomatic cerebral vasospasm in patients with compromised LV function owing to NSM. The use of inotropes, such as dobutamine or milrinone, with an aim to optimize CO has been shown to be effective in this clinical scenario \[33,32\]. In severe cases where CO is refractory to inotropic formulations or when the patient develops complications with triple-H therapy (such as pulmonary edema and fluid overload), implementation of intra-aortic balloon pump may be necessary \[33,34\].

ECG findings

Electrocardiograph changes are quite common in SAH patients, especially in the first 72 h of presentation \[35\]. During the acute stage, 50–100% of patients with SAH will exhibit ECG changes with various morphological patterns \[36–38\]. The most common ECG changes in patients with SAH are STsegment alterations (15–51%), changes in T waves (12–92%), prominent U waves (4–47%), and QTc prolongation (11–66%) \[7,39\]. These ECG abnormalities are usually seen in patients with severe neurological injury and are not independently predictive of mortality \[38\]. A study of 106 patients with SAH and ECG changes showed that ST depression was related to the Acute Physiology and Chronic Health Evaluation II score (APACHE II score; which is used to classify severity of disease in the intensive care unit), Hunt-Hess scale, and the WFNS score, but not to the development of cerebral vasospasm or increased intracranial pressure \[40\]. Moreover, by multivariate analysis, this study determined that ECG alterations are not independently related to neurological outcome. As for the relationship between these electrographic findings and LV function, it can be said that although ECG findings in patients with SAH and TC are similar, those in SAH are mostly not related to LV dysfunction \[41\].

Approximately 4–8% of SAH patients will have malignant arrhythmias that include ventricular tachycardia (VT), torsade de pointe and asystole \[20,35\]. Incidence figures as high as 91% for general and 41% for life-threatening arrhythmias have been reported \[42\]. In their study group, Frontera et al. reported that atrial fibrillation and flutter were the most common arrhythmias \[43\]. The investigators further related an association of arrhythmias with an increased risk of cardiovascular co-morbidity, prolonged hospital stay, and poor outcome or death after SAH (after adjusting for other predictors). Predictors for the development of arrhythmia after SAH are increasing age, severity of neurological symptoms,
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An observational period of 8.5 years involving 765 out-of-hospital medications to lower blood pressure and subsequently reduce CBF.

Rhythmia in SAH must be weighed against the potential for these immediate causes in 27 individuals (4%).

Survival without neurological damage from SAH following OHCA is quite rare.

Subarachnoid hemorrhage can also lead to cardiac arrest. Over an observational period of 8.5 years involving 765 out-of-hospital cardiac arrests (OHCAs), spontaneous SAH was identified as the immediate cause in 27 individuals (4%). Asystole or pulseless electric activity was the initial cardiac rhythm in the majority of these patients and only one survived, but with significant neurological deficit. Survival without neurological damage from SAH following OHCA is quite rare.

Conclusion
Aneurysmal SAH is associated with a high rate of morbidity and mortality, not only from the neurologic ictus and sequelae, but also from the related systemic pathophysiology, most importantly, cardiac manifestations.

The associated cardiac disturbances range from incidental and subtle, as in mild myocardial injury and enzyme release, to catastrophic and life-threatening cardiac dysrhythmias, failure and shock. These disturbances, despite their severity, are usually transient, and awareness of them can help guide the management of these patients through the period of DCI.

Likewise, their presence and severity may be able to contribute to more accurate prediction of morbidity and mortality. As continued research elucidates the etiology of the cardiac disturbances associated with SAH, our understanding of the normal physiologic connections between the brain and the cardiovascular system can be expected to expand as well, ultimately resulting in better optimization of treatment for different subsets of neurologic injury.

Expert commentary & five-year view
Cardiac complications are commonly observed in patients with acute SAH. Patients may present with arrhythmias, acute coronary ischemic syndromes and acute left ventricular dysfunction, which can vary from mild abnormalities to cardiogenic shock and pulmonary edema. The underlying cardiac injury appears to be mediated by a massive increase in sympathetic tone. When managed carefully, cardiac complications are usually reversible, and even patients with severe left ventricular dysfunction may recover fully within a few weeks of the acute event. Given the high frequency of cardiac complications, routine cardiac enzyme measurement, with a low threshold for echocardiographic evaluation, may help to identify those patients at greater risk. Most major complications and death are related to brain injury, the prevention of which should be the major focus of therapy in patients with SAH.

More investigation, especially in the form of prospective studies, is certainly needed to better identify which patients are at greatest risk, and to develop better strategies for prevention. Perhaps early intervention with medical therapy could minimize cardiac complications. Prospective registries and clinical trials may help elucidate ways to prevent cardiac events and refine hemodynamic management strategies.

Financial & competing interests disclosure
The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

Key issues

- Cardiac manifestations are common in patients with subarachnoid hemorrhage (SAH).
- The spectrum of myocardial injury associated with SAH varies in severity and could range from mild elevation of cardiac enzymes or ECG changes to severe cardiomyopathy and cardiogenic shock.
- Cardiac injury related to SAH is postulated to be a result of overstimulation of the systemic sympathetic tone.
- Fortunately, when managed carefully, cardiac complications are usually reversible.

References
Papers of special note have been highlighted as:
** of considerable interest


** Review of the most recent guidelines in the management of subarachnoid hemorrhage (SAH).


** Useful review on the cardiac manifestations of SAH.


More in-depth review of ECG abnormalities in SAH.


