Subarachnoid Hemorrhage With Neurocardiogenic Stunning

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A well-recognized complication of acute neurologic injury from intracranial bleeding is cardiotoxicity with electrocardiographic changes and transient left ventricular dysfunction. The phenomenon, called neurocardiogenic stunning (NCS), occurs in 20% to 30% cases of patients with acute subarachnoid hemorrhage (SAH). In this article, we describe a patient with acute SAH complicated by NCS and use this case to highlight the pathogenesis, diagnostic challenges, and management dilemmas that arise in such patients. We also review conventional surgical and medical treatment and present new therapeutic options for this problem.
[Rev Cardiovasc Med. *2010;11(4):254-263 doi: 10.3909/ricm0544*]

Key words: Neurocardiogenic stunning • Left ventricular dysfunction • Subarachnoid hemorrhage • Stress-induced cardiomyopathy

In 1903, Cushing was the first to report changes in blood pressure and cardiac rhythm in patients with intracranial hemorrhage.[1] More than 40 years later, Byer and colleagues[2] described "electrocardiograms with large, upright T waves and long QT-intervals" in patients with subarachnoid hemorrhage (SAH). Autopsy studies in the 1960s confirmed pathologic evidence of myocardial necrosis in SAH cases, in both those with and without electrocardiographic (ECG) changes.[3] When these lesions, which simulated catecholamine release, were found to be similar to those found in animal models, the hypothesis that catecholamine overload is the major determinant of neurocardiogenic stunning (NCS) was secured.[4]

The intrinsic, automatic rhythm of the heart can be altered by the autonomic nervous system. The sympathetic nervous system supply to the heart leaves the spinal cord at the first 4 thoracic vertebrae, and supplies most of the muscle of the

heart. Stimulation via the cardiac β-1 receptors causes the heart rate and contractility to increase. The vagus nerve also supplies the atria, and stimulation causes bradycardia. There are nervous cardiac reflexes, including afferent nerves in the wall of the atria or aorta, that respond to stretch. When blood pressure is high, aortic receptors trigger a reflexive slowing of the heart to reduce cardiac output and blood pressure. Similarly, when blood pressure is low, heart rate increases (as occurs when a person goes into shock). Similar pressure receptors are found in the atria. When the atria distend as a result of pressure or volume overload, there is a reflex increase in the heart rate to augment forward output. When there is a sudden reduction in the pressure in the atria, the heart slows (Bainbridge reflex) and is the cause for the marked bradycardia sometimes seen during spinal anesthesia. Circulating catecholamines—epinephrine and norepinephrine—originate from 2 sources. Epinephrine is released by the adrenal medulla upon activation of preganglionic sympathetic nerves during times of stress (eg, emotional, physical). Norepinephrine is also released by the adrenal medulla (~20% total catecholamine release is norepinephrine). The primary source of circulating norepinephrine, however, is spillover from sympathetic nerves innervating blood vessels. Normally, most of the norepinephrine released by sympathetic nerves is taken back up by the nerves (some is also taken up by extraneuronal tissues such as the kidneys via locally produced renalase) where it is metabolized. A small amount of norepinephrine, however, diffuses into the central circulation. At times of high sympathetic nerve activation, the amount of norepinephrine entering the blood can increase dramatically, as occurs in instances of SAH with excessive stimulation of cardiac β-1 and postjunctional α-1 and α-2 adrenoceptors in peripheral arteries and veins. Overstimulation of this system can result in pathologic NCS with clinical presentations that can include ECG changes, arrhythmias, and ventricular dysfunction (Table 1). With current advances in cardiovascular imaging there is increasing recognition of this clinical entity.

The management of SAH can present a clinical dilemma, specifically in the case of severe NCS (which can present as syncope or heart failure), because traditional therapies to treat intracranial swelling (eg, permissive hypertension to maintain cerebral perfusion) may worsen left ventricular (LV) function. The following case report describes a patient who presented with complaints of abdominal pain, syncope, ECG changes, and LV dysfunction in the setting of a significant intracranial bleed. We describe the mechanisms for NCS, along with outcomes and treatment of this disorder.

Case Report

A 71-year-old woman was admitted to the emergency center for a brief syncopal episode that occurred 1 hour prior to admission.

Table 1
Overview of the Clinical Presentation and Diagnosis of Neurocardiogenic Stunning

Overview
Definition Acute myocardial dysfunction caused by intracranial pathology (including SAH)
Similar processes Takotsubo cardiomyopathy, stress cardiomyopathy, pheochromocytoma-associated cardiomyopathy, cocaine-induced cardiomyopathy
Presentation Headache, acute neurologic deficits, ECG changes, LV systolic dysfunction (ranging from asymptomatic to overt CHF), arrhythmias (benign to life threatening)
Diagnostic Testing
ECG QTc prolongation, T-wave inversion/flattening (referred to as *cerebral T waves*), diffuse ST-segment changes (elevation, inversion, or flattening)
Echocardiography Wide range of LV contractility patterns from global systolic dysfunction with apical sparing to apical ballooning Elevated cardiac biomarkers (troponin, CK-MB, BNP/NT-proBNP)
Prognosis 45% mortality within 30 days (mainly due to neurologic devastation), 20% to 30% rebleed at 1 month; thereafter, 3% per year; cardiac recovery is typical and occurs within days to weeks
Pearls
NCS is very common in patients with SAH
Close monitoring for arrhythmias is required
Anticoagulation, antithrombotic, and antiplatelet drugs should be avoided if possible
Patients may require circulatory support for cerebral perfusion

BNP, B-type natriuretic peptide; CHF, congestive heart failure; CK-MB, creatine kinase-MB; ECG, electrocardiogram; LV, left ventricular; NCS, neurocardiogenic stunning; NT-proBNP, *N*-terminal pro-BNP; SAH, subarachnoid hemorrhage.

Additionally, she reported having a dull, constant, nonlocalizing headache, epigastric pain, persistent vomiting, and diarrhea for the previous 48 hours. The patient did not recall the episode of syncope; however, it was witnessed by her husband. He stated that she "dropped suddenly" in the bedroom and was unconscious for several minutes. There was no trauma from the fall. There was no loss of bladder or bowel control, auras, tongue biting, postictal symptoms, or fatigue. The patient had never experienced a similar event before.

Her past medical history was notable for longstanding untreated hypertension. She did not take any prescribed medication and has smoked 1 pack of cigarettes per day for the past 53 years. On examination her blood pressure was 113/55 mm Hg, her pulse 57 beats/ min, and her respiratory rate was 14 breaths/min; she was afebrile and saturating 97% on 2 L of oxygen. She was in sinus rhythm on the telemetry monitor. Her physical examination was unremarkable; she was alert and oriented, in no distress, and the headache was nearly resolved. Her pupils were equal and extraocular movements were normal; results of a rapid neurologic examination were normal. Her serum chemistries and blood counts were within normal limits. Initial cardiac biomarker testing revealed a B-type natriuretic peptide (BNP) level of 729 pg/mL (normal ≤ 100 pg/mL), cardiac troponin I of 0.74 ng/mL (normal ≤ 0.20 ng/mL), total creatine kinase (CK) of 198 ng/mL (normal ≤ 150 ng/mL), CK-MB of 2.5 ng/mL (normal ≤ 5.0 ng/mL) with a CK–myoglobin index of 2.3% (normal ≤ 2.3), and myoglobin level of 122 ng/mL (normal ≤ 98 ng/mL).

The initial ECG showed prominent precordial T-wave inversion and a prolonged QT interval that were new when compared with a prior ECG (Figure 1). A 2-dimensional echocardiogram in

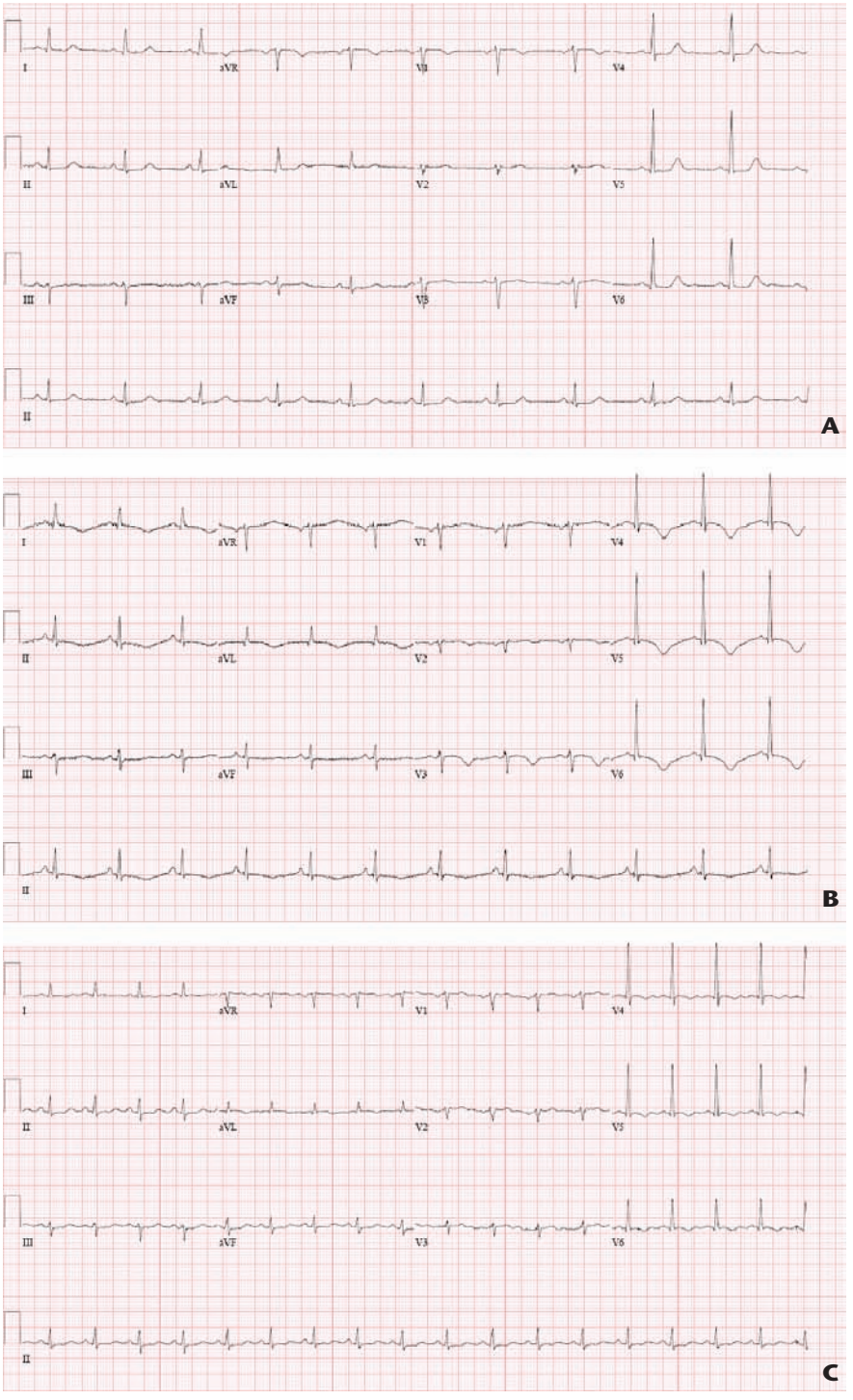


Figure 1. *Patient's initial 12-lead electrocardiograph (ECG).* **(A)** *18 months prior to presentation (normal; QT/QTc: 456/462 ms).* **(B)** *At the time of presentation with subarachnoid hemorrhage (diffuse inverted T waves prominent in leads V3-V6; QT/QTc: 504/551 ms).* **(C)** *ECG from hospital day 12, following treatment of subarachnoid hemorrhage and recovery of neurologic function (QT/QTc: 310/411 ms).*

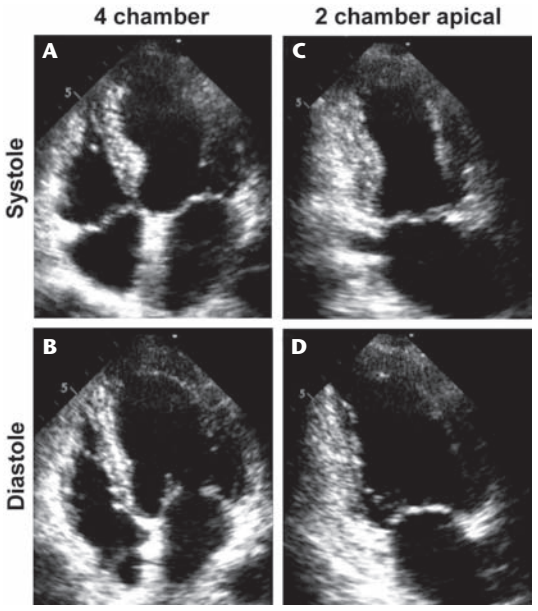


Figure 2. *Apical 4- and 2-chamber echocardiographic images in diastolic and systole of the patient obtained on admission.*

the emergency room revealed a dilated left ventricle with normal wall thickness, and profound mid and apical anterolateral akinesis with moderately depressed systolic function (Figure 2). With the history of epigastric pain, extensive anterior wall motion abnormality, and ECG changes, the emergency room physician activated the cardiac catheterization laboratory for a possible acute myocardial infarction (MI). There was concern that this patient had experienced a late-presentation MI and the loss of consciousness was a result of a malignant arrhythmia. Upon further discussion with the cardiologist, computed tomography (CT) of the head was performed and revealed a massive acute subarachnoid hemorrhage with bilateral temporal parietal extension and a developing communicating hydrocephalus without midline shift (Figure 3).

Cardiac catheterization was cancelled. The patient underwent cerebral angiography that demonstrated a 4-mm aneurysm arising at the junction of the left internal carotid artery and left posterior cerebral artery projecting posterolaterally (Figure 4).

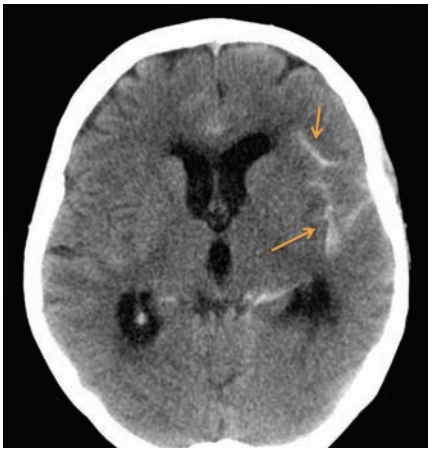
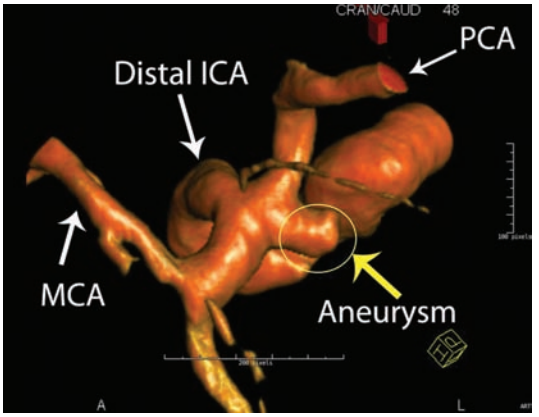


Figure 3. *Noncontrast computed tomography of the head demonstrating acute subarachnoid hemorrhage (arrows).*

Figure 4. *Three-dimensional reconstruction image of left cerebral angiography prior to intervention demonstrating the aneurysm (*yellow circle*), which projects posterolaterally at the junction of the distal left internal carotid artery (ICA), posterior cerebral artery (PCA), and middle cerebral artery (MCA).*



She underwent craniotomy, ventricular shunt placement, and aneurysm clipping. Following the surgery she was unable to be weaned off the ventilator and a follow-up head CT was without evidence of active bleeding. Repeat cerebral angiography confirmed cessation of bleeding and successful aneurysm clipping alongside the distal left internal carotid artery (Figure 5). Her neurologic impairment improved 48 hours later and she was extubated on the fourth postoperative day. The remainder of her hospital course was complicated by intermittent pyrexia, development of a deep vein thrombosis in the right common femoral vein, and a urinary tract infection. She was discharged to a subacute rehabilitation facility on hospital day 16. Follow-up ECG and echocardiogram within 3 weeks of discharge yielded normal results.

Clinical Manifestations

Significant cardiac dysfunction is not uncommon following neurologic injury. LV systolic dysfunction is evident in approximately 30% of patients within hours of acute intracranial bleeding and more than 75% of patients develop new ECG abnormalities.[5,6] The presentation can vary from asymptomatic to overt congestive heart failure with pulmonary edema

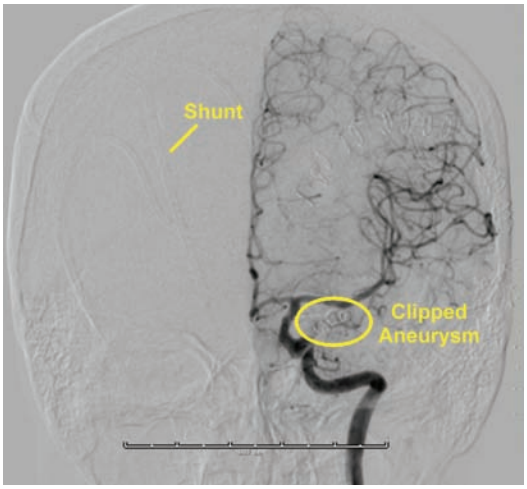


Figure 5. *Images from left cerebral angiography following craniotomy, aneurysm clipping, and ventricular shunt placement.*

(approximately 10% of SAH cases present with cardiogenic shock). Heart failure symptoms are more likely with worsening severity of SAH, ECG changes, increased cardiac markers of myocyte injury, and elevated BNP/*N*-terminal pro-BNP.[7] Additional clinical features are presented in Table 1.

Diagnostic Testing

Electrocardiography

Classic changes associated with SAH are QT interval prolongation, T-wave inversion, ST-segment elevation, and presence of U waves.[1] In one study of patients with SAH and LV dysfunction,[5] the presence of T-wave inversion and QTc prolongation had a sensitivity and specificity of 100% and 81%, respectively, for prediction of LV dysfunction. The study authors created an ECG score to predict severity of NCS in SAH and described strong correlations between score severity and subsequent in-hospital death.[6]

In addition to its effects on the ECG, patients with intracranial bleeding are susceptible to a host of benign and malignant arrhythmias. The frequency of cardiac arrhythmias is present in 20% to 40% of patients with SAH-induced NCS.[8] In one observation of patients with SAH, sinus bradycardia was present in 23%, multifocal ventricular ectopy was present in 54%, asystolic intervals were present in 27%, and atrial fibrillation was present in 4%. In addition, patients with SAH are subject to metabolic and electrolyte dysregulation and thereby susceptible to rhythm disturbance native to those who are critically ill (eg, those with torsades de pointes). Ventricular arrhythmias are not uncommon and are reported in 14% of patients with SAH.[9] Interestingly, QTc prolongation did not increase the propensity for ventricular arrhythmia. Risks of ventricular arrhythmia included older age, slower heart rate, lack of angiotensin-converting enzyme inhibitors/angiotensin II receptor antagonists, and increased stroke severity. Among those presenting with out-of-hospital cardiac arrest, SAH with cardiac dysrhythmia is the underlying cause in approximately 4% to 10% of cases.[10] These arrests are commonly mistaken as primarily cardiovascular events and may be missed unless head imaging is performed.[11]

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Blood Biomarkers of Cardiac Injury and Dysfunction

Troponin I is elevated in 20% to 30% of patients with SAH and cardiac dysfunction,[7] and the rate of troponin I rise is prognostic of NCS severity in patients with SAH.[12] Likewise, BNP is strongly associated with both cardiac dysfunction and overall outcome.[8]

Echocardiography

The earliest LV contraction pattern to appear in acute SAH-induced NCS is diffuse hypokinesis of the LV with or without apical sparing. One study of 21 patients with SAH-induced NCS observed varied patterns of LV contraction that did not correlate with severity of SAH. In these 21 patients, there was severe LV hypokinesis with apical sparing in 14 patients, global LV hypokinesis affecting all wall segments in 9 patients, and mid-to-basilar LV dysfunction with mild apical hypokinesis in the remaining 5 patients.[13] The LV contraction pattern of NCS in SAH can be similar to other forms of stress cardiomyopathy such as takotsubo cardiomyopathy. One key characteristic of all

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stress-induced cardiomyopathies is regional wall motion abnormalities that extend across multiple coronary vascular territories.[14] However, the LV contraction pattern in NCS from SAH is often more subtle (ie, global hypokinesia) and most cases of SAH-induced NCS do not have severe apical dyskinesia with preserved function at the base (the apical ballooning pattern) that is pathognomonic of takotsubo cardiomyopathy.[14] Similar to other forms of stress cardiomyopathy, dramatic restoration of function and resolution of acute ventricular dilation can occur, although this depends on the inciting event and the diagnosis of SAH portends a dismal prognosis.[14]

Coronary Angiography

In the setting of an acute SAH with new-onset cardiomyopathy, cardiac catheterization should not be routinely performed because the cardiomyopathy is likely from NCS and primary treatment focus should be centered on the intracranial pathology.[13] In this setting, catheter-directed coronary angiography has low yield for demonstrating obstructive coronary artery disease. Furthermore, cardiac catheterization may delay treatment of SAH; it is often necessary to avoid antiplatelet or anticoagulant agents in SAH patients due to the risk of recurrent or worsened cerebral bleeding. Serial observation with echocardiography (or ECG monitoring) can be helpful to monitor trends in cardiac function. There are no data to guide cardiovascular practitioners on long-term follow-up testing of patients with treated (or resolved) SAH with NCS. However, repeat echocardiography or cardiac magnetic resonance imaging is suggested to evaluate LV recovery 4 to 12 weeks after hospital discharge.

Rarely, a concomitant acute coronary syndrome (ACS) may occur in patients with SAH. These patients will usually have presentation that is more typical of ACS. Concerning signs include markedly elevated and/or sustained cardiac troponin or CK-MB with a characteristic excursion over time, regional wall motion abnormalities in a single vascular territory on echocardiography, or ECG changes that do not fit the pattern of SAH.[15] Coronary angiography may be helpful; however, close coordination with neurology colleagues is needed to assess risk of recurrent subarachnoid bleeding and coordinate advanced therapy if needed. Temporizing measures such as coronary balloon angioplasty without stenting may be necessary. Finally, in some cases of severe SAH and NCS, placement of circulatory support devices may be useful.

In other types of stress cardiomyopathy included in the differential diagnosis, cardiac catheterization is indicated and may be required to fulfill diagnostic criteria.[16,17] As opposed to SAH with NCS, the clinical presentation of takotsubo cardiomyopathy is difficult to distinguish from ACS and patterns of LV dysfunction on echocardiography are not helpful. In one study, experienced echocardiographers were asked to distinguish takotsubo cardiomyopathy from acute anterior MI in 90 patients from the LV contraction pattern alone. In this study, 1 out of 4 cases were incorrectly labeled.[18]

The latest CT technology can provide imaging of an entire body in less than 6 seconds and may be useful in selected patients who present with both cardiac and neurologic symptoms. Coronary CT angiography is a noninvasive method to evaluate for obstructive coronary artery disease and may be useful when the diagnosis is not clear. In patients with embolic stroke, cardiac CT is useful for evaluation of a cardioembolic source and provides simultaneous assessment of coronary anatomy.[19] Further advances in cardiac CT (or cardiac magnetic resonance) allow precise assessment of LV function and myocardial perfusion data that may enable definitive diagnosis of stress cardiomyopathy versus acute coronary obstruction. Regardless, in patients with SAH, primary treatment of the cerebral dysfunction remains the priority and cardiac diagnosis and treatment are secondary and largely supportive.

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Pathophysiology

Catecholamine Surge

Coronary artery spasm, acute microvascular dysfunction, and acute thrombus with spontaneous reperfusion are largely disproven as causes of NCS.[8,20] Current theories for the pathophysiology are illustrated in Figure 6.

It is believed that SAH induces an intense sympathetic surge with catecholamine excess with direct and indirect effects on cardiac myocytes, resulting in the cardiac dysfunction in NCS. Supportive evidence exists for high catecholamine conditions (pheochromocytoma, cocaine use, and critical illness with sepsis inducing a similar cardiac dysfunction—stress cardiomyopathy).[21]

Similar to patients with stress cardiomyopathies, patients with SAH have an increase in plasma norepinephrine that appears rapidly and

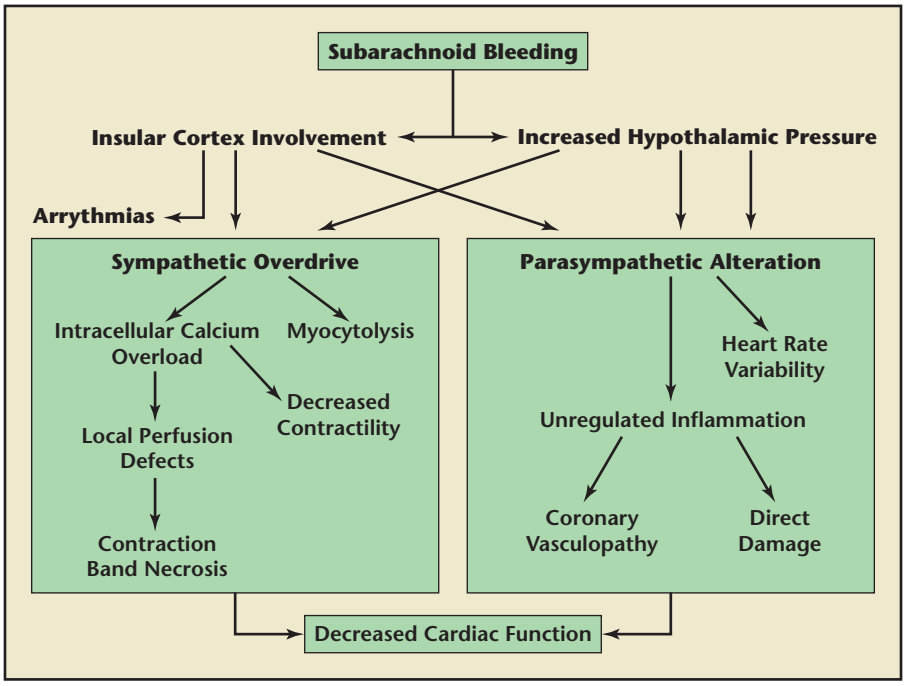

Figure 6. *Overview of the currently proposed theories of the pathophysiology of neurocardiogenic stunning.*

animal studies, the rate of rise and peak levels of noradrenalin, adrenaline, and 3-methoxy-4-hydroxyphenylglycol are positively correlated with degree of measurable cardiac biomarkers and LV dysfunction in SAH.[7,22] Arrhythmia scores were also higher in animals with an induced SAH procedure during sympathetic nerve stimulation and catecholamine infusion.[7]

Pathologically, myocytolysis was observed primarily proximal to the terminals of cardiac sympathetic nerves in samples from animal models with SAH.[22] Furthermore, increases in myocardial catecholamines led to an influx of calcium within myocytes, thereby causing a net reduction in myocardial contractility.[7] These same effects are present in both hypoxic and ischemic myocardium.[22]

β-*Receptor Polymorphisms and Catecholamine Cardiotoxicity*

With the evidence of catecholamine excess at least partially responsible for NCS, genetic polymorphisms of the adrenoceptors could explain the variable presentation of cardiac dysfunction in SAH patients. Specific genotypes for β-1, β-2, and α-adrenoceptors have been associated with an increased propensity to develop cardiac injury and dysfunction in SAH.[23] There is a 3- to 15-fold increased risk of developing cardiac dysfunction or troponin elevation in higher-risk alleles depending on the genotype.[23]

The association between adrenoceptor genotype and risk for cardiac involvement provides insight into the pathophysiology of NCS. The high-risk β-1 adrenoceptor allele of *β-1AR 1165C>G* encodes an arginine versus a glycine at amino acid 389, which leads to an increase in adenyl cyclase activity.[23] This results in increased cardiac sensitivity to catecholamines and susceptibility to congestive heart failure. α-2-adrenoceptors regulate the release of norepinephrine from cardiac sympathetic nerves. In the high-risk allele, a 4-amino acid deletion results in loss of function of a key inhibitory feedback mechanism, thereby causing increased release of presynaptic norepinephrine in these individuals.[23] The high-risk allele in β-2 adrenoreceptors has been known to be associated with an increased risk of adverse cardiovascular events in the elderly by unknown mechanisms.[23]

Vagal Activity and Inflammation

A new mechanism has been recently proposed to describe changes within the sympathetic and parasympathetic nervous system in the setting of inflammation; this may partly explain cardiac dysfunction of NCS and other stress cardiomyopathies.[24] Preliminary findings describe a vagal role in modulating systemic inflammation through acetylcholine receptors ("neuroinflammatory reflex") that can suppress inflammation.[25] The cardiac inflammation seen in SAH could be enhanced through changes in the parasympathetic system and exacerbated by concurrent sympathetic denervation of the heart in patients with SAH.[20]

The impact of inflammation on NCS has been studied in the setting of cardiac transplantation (when the donor heart originated in a patient who expired from intracranial hemorrhage [ICH]). In one study, biopsies were obtained from patients 1 week after transplantation and intravascular ultrasound was performed over the course of 1 year in 40 donor patients who died of intracerebral hemorrhage (n = 20) and trauma (n = 20).[26] Myocardial biopsies of ICH donor hearts demonstrated increased expression of matrix metalloproteinases associated with inflammation. Also, at 1-year follow-up, the ICH donor hearts had higher rates of fibrosis and coronary vasculopathy.[27] In addition, there was an increase in messenger RNA expression of angiotensin II type 1

receptor (which is upregulated in acute inflammation) in ICH donor heart and splenic lymphocytes, indicating increased inflammation systemically prior to transplantation, presumably from the ICH event.[27]

Relationship With Takotsubo Cardiomyopathy

Stress cardiomyopathy, presents as a reversible cardiac dysfunction after a period of acute severe distress. The Mayo criteria for the diagnosis of takotsubo cardiomyopathy are provided in Table 2.[16,17] The pathologic mechanisms in takotsubo cardiomyopathy are similar to those of SAH with NCS and are believed to be secondary to direct and indirect effects of catecholamines. Wittstein and colleagues[28] demonstrated that catecholamine levels were 2- to 3-fold higher than normal in patients with LV apical ballooning versus actual MI. In patients with takotsubo cardiomyopathy, calcium overload due to catecholamine excess is expected in cardiomyocytes, leading to contractile dysfunction, similar to NCS.[29] The hallmark of takotsubo cardiomyopathy is reversal of dysfunction; it also has a lower mortality rate than SAH with NCS (in the range of 0% to 8%).[16] The relatively poor outcome in SAH with NCS is attributable to neurologic devastation that is not present in the setting of takotsubo cardiomyopathy.

Table 2
Modified Mayo Criteria for the Diagnosis of Takotsubo Cardiomyopathy

1. Transient hypokinesis, akinesis, or dyskinesis in the left ventricular midsegments with or without apical involvement
2. Regional wall motion abnormalities beyond single vascular territory in the presence of a stress trigger; absence of coronary disease or angiographic evidence of plaque
3. New electrocardiographic abnormalities or modest elevation of cardiac troponin
4. Absence of pheochromocytoma, myocarditis, or intracranial bleeding

in SAH and its propensity for arrhythmias.

Many therapies for SAH are cardioinhibitory and these effects are thought to be potentiated in patients with NCS.[8] Specific strategies of SAH therapy to improve cerebral blood flow include permissive hypertension, hemodilution, and hypervolemia. Permissive hypertension increases wall stress and myocardial oxygen demand, thus worsening NCS. Hemodilution lowers oxygen delivery to the myocardium, predisposing patients to ischemia and arrhythmias. Hypervolemia can cause increased filling pressures and can lead to pulmonary edema, which has been reported in up to 17% of patients.[30] Despite these complications, SAH therapy should not be completely withheld in most cases, due to the grave consequences of untreated cerebral vasospasm and worsening neurologic injury. In extreme cases of SAH with cardiovascular collapse, the patient may benefit from the placement of an intra-aortic balloon pump for both systemic and central nervous system perfusion.[8]

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Management

Management strategies are highlighted in Table 3. Definitive surgical and/or vascular treatment is needed to stop aneurysmal bleeding and reduce intracranial hypertension if present. This commonly involves craniotomy, surgical clipping of the aneurysm, and cerebral shunting with temporary intracranial pressure monitoring. Careful avoidance of drugs that can lengthen the QT interval is important because of the high incidence of QTc prolongation

Table 3
Outline of Management Strategies for SAH Complicated With NCS

- Stabilization of life-threatening arrhythmias
- Correct electrolyte/acid-base abnormalities
- Avoid QTc-prolonging drugs
- Surgical clipping/endovascular approach for aneurysmal bleeding have equivalent outcomes
- Permissive hypertension, hypervolemia, and hemodilution are used to preserve cerebral perfusion and overcome cerebral vasospasm (these therapies worsen cardiac function)
- Patients with cardiovascular collapse may benefit from mechanical support devices (eg, balloon pump)
- Nimodipine improves neurologic outcomes (unknown mechanism)
- Avoid agents that worsen bleeding

Data from Bederson JB et al.[38] and Kassell NF et al.[39]

Treating Cardiac Dysfunction

Agents that block sympathetic activity may be cardioprotective in SAH patients. One study showed normalization of ECG changes after administration of 80 mg of propranolol.[31] A randomized, controlled trial comparing 80 mg of propranolol and 20 mg of phentolamine with placebo showed no mortality benefit; however, upon autopsy of deceased patients, those who received placebo all showed necrotic myocardial lesions, compared with none in the propranolol-treated group.[32]

High-risk adrenoceptor genotypes could potentially benefit from adrenergic blockade in the setting of NCS.[22] Future genetic stratification of patients according to adrenoreceptor polymorphisms may be useful in treating stress cardiomyopathies. With calcium overload playing a possible role in necrosis, calcium blockers could be considered mechanistically; however, there are no published studies supporting their use in SAH with NCS.[8]

Although the exact mechanism of the neuroinflammatory reflex has yet to be described, it has been shown that impaired heart variability—implying an altered parasympathetic tone in the heart—portends a higher morbidity and mortality.[33] If the parasympathetic system is, in fact, playing a role in NCS, therapies could be developed to modulate it. For instance, it was shown previously in endotoxic animals that vagus nerve stimulation resulted in lower cardiac tumor necrosis factor levels and the attenuation of the development of systemic shock.[25] CNI-1493 (an inhibitor of phosphorylation of p38 mitogen-activated protein kinase) activated the cholinergic anti-inflammatory pathway centrally and, when administered into cerebral ventricles, suppressed serum TNF in endotoxemic rats and protected against the development of endotoxin-induced shock.[34,35] The role of an α-7 subunit of the nicotinic acetylcholine receptor has been identified in vagus nerve–induced cholinergic signaling[25,36] and could also be a future therapeutic target.[35] Melanocortin adrenocortin-stimulating hormone-(1–24) improved survival and improved cardiovascular and respiratory function of rats with acute hemorrhagic shock.[37] Direct electrical stimulation of the vagus nerve is a current therapeutic approach to treat intractable seizures and may also be useful in SAH with NCS.[24]

Outcomes

In a population-based study the 30-day mortality rate of all SAH patients was 45%, with most mortality occurring within the first 1 to 2 days as a result of neurologic devastation.[23,38] The risk for recurrent subarachnoid bleeding is 20% to 30% in the first month and then 3% per year.[38]

Although obvious dangers exist with decreased LV function (resulting in hypotension or decreased oxygenation) in the setting of cerebral vasospasm, an important feature of this etiology of LV dysfunction is the potential for improvement and possibly complete recovery.[7]

Conclusions

Specific ECG changes, echocardiographic findings, and elevated cardiac biomarkers suggest SAH with NCS. Sympathetic overload with catecholamine toxicity, susceptibility of adrenergic receptor genotypes, and parasympathetic changes in the neuroinflammatory reflex are all putative mechanisms of myocyte injury. Although cardiac dysfunction is common in SAH, the main contributor to morbidity and mortality is the intracranial pathology and thus in most cases preservation of cerebral perfusion takes precedence. ■

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Main Points

- Neurocardiogenic stunning (NCS) in patients with subarachnoid hemorrhage (SAH) is associated with elevated cardiac biomarkers, specific electrocardiographic changes, and transthoracic echocardiography findings.
- There are multiple factors thought to contribute to NCS pathology including sympathetic overdrive, differences in adrenergic receptor genotypes, and parasympathetic changes in the neuroinflammatory process.
- NCS patients require close monitoring and therapy for arrhythmias and could potentially require cardiac support.
- Avoid anticoagulation, antithrombotic, or antiplatelet therapy for NCS-induced cardiac dysfunction with the active SAH.
- There is no routine evidence-based treatment at this time.

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