Electrocardiographic markers of abnormal left ventricular wall motion in acute subarachnoid hemorrhage

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A reversible and presumably neurogenic form of myocardial dysfunction may occur following subarachnoid hemorrhage (SAH), but the relationship of this finding to electrocardiographic abnormalities remains unclear. To clarify this issue, serial electrocardiograms (ECGs, mean 6.2 per patient) and echocardiograms (mean 3.4 days after SAH) were obtained in 57 SAH patients without preexisting cardiac disease. The goal was to determine which specific electrocardiographic changes, if any, reflect abnormal left ventricular wall motion in acute SAH.

Wall motion abnormalities were identified in five (8%) of 57 patients. Four of these affected patients experienced hypotension (systolic blood pressure < 100 mm Hg) and three exhibited pulmonary edema within 6 hours of SAH, compared to none of the 52 patients with normal wall motion (p < 0.0001). Patients with abnormal wall motion were more likely than patients with normal echocardiograms to have symmetrical T wave inversion (five of five vs. seven of 52, p < 0.001) and severe (≥ 500 msec) QTc segment prolongation (five of five vs. three of 52, p < 0.001) on serial ECGs. These associations maintained their significance with analysis limited to single ECGs performed on or near the day of echocardiography. Abnormal wall motion was also associated with borderline (2% to 5%) creatine kinase MB elevation (five of five vs. three of 52, p < 0.001) and poor neurological grade (p < 0.0001). Although no combination of findings on a single ECG resulted in 100% sensitivity for abnormal wall motion, the presence of either inverted T waves or severe QTc segment prolongation on serial ECGs was associated with 100% sensitivity and 81% specificity.

These results demonstrate an association between reduced left ventricular systolic function, mild creatine kinase MB elevation, and electrocardiographic repolarization abnormalities in acute SAH. Symmetrical T wave inversion and severe QTc segment prolongation best identified patients at risk for myocardial dysfunction and may serve as useful criteria for echocardiographic screening following SAH.

KEY WORDS • subarachnoid hemorrhage • electrocardiography • echocardiography • neurocardiology • myocardial dysfunction

The association of electrocardiographic abnormalities with injury to the central nervous system is well recognized. Although described in connection with a wide variety of disorders, neurogenic changes on electrocardiograms (ECGs) are particularly common following subarachnoid hemorrhage (SAH). Large clinical series indicate that 50% to 100% of patients experience at least one such abnormality during the acute stage of SAH. These abnormalities are usually transient, and include a vast array of findings, including peaked P waves, pathological Q waves, increased QRS voltages, ST segment elevation or depression, peaked or inverted T waves, prolonged QT intervals, large U waves, and rhythm disturbances. Although many of the electrocardiographic abnormalities associated with SAH are typical of those seen with myocardial ischemia from coronary artery disease, pathological studies have consistently failed to demonstrate this form of injury in affected subjects. However, in contrast to the belief that neurogenic changes on ECGs reflect purely electrical phenomena, affected patients frequently show evidence of structural cardiac damage. Increased levels of plasma myocardial enzymes and characteristic pathological lesions, known as contraction band necrosis or myofibrillar degeneration, are common findings in patients with SAH. More recently, echocardiographic studies have demonstrated reversible abnormalities of left ventricular wall motion in SAH pa-
ties on echocardiography. In these investigations, normal coronary arteries were demonstrated in all patients studied at autopsy or by coronary angiography, and in three subjects myocardial biopsy confirmed the presence of contraction band necrosis. Thus, in some patients, a reversible and presumably neurogenic form of myocardial injury characterized by reduced left ventricular systolic function may occur following SAH.

Hemodynamic instability and pulmonary edema occur frequently in SAH patients with wall motion abnormalities, supporting the notion that such injury may contribute to morbidity and mortality. Although electrocardiography may provide a rapid means of identifying patients with significant cardiac injury, the relationship between changes on ECGs and left ventricular dysfunction in SAH remains unclear. We conducted this study to determine which specific changes, if any, are associated with wall motion abnormalities in acute SAH, with the aim of developing electrocardiographic criteria for the identification of patients likely to demonstrate abnormalities on echocardiography.

Materials and Methods

Study Population

From September 1991 to May 1993, we instituted a policy of routine echocardiographic screening of all patients with acute (≤ 6 days after onset) aneurysmal SAH admitted to the Columbia-Presbyterian Neurological Intensive Care Unit (neuro-ICU). During this period, 64 (85%) of 75 potentially eligible patients with SAH underwent echocardiography. Seven patients with a history of cardiac disease (four with coronary artery disease, two with valvular heart disease, and one with arrhythmia) were excluded from the present analysis, leaving a study sample of 57 patients. Nine potentially eligible patients were excluded due to logistical problems and two because of technically inadequate echocardiograms. Noneligible subjects included 31 patients admitted 7 days or more after SAH, 15 patients with nonaneurysmal SAH, and 20 patients admitted over a period of 9 weeks during which echocardiographic services for this purpose were not available.

Neurological status on admission was rated according to a modified Hunt and Hess scale (Grade I = mild headache, Grade V = deep coma). Subarachnoid hemorrhage was diagnosed by computed tomography or lumbar puncture in all subjects, and a protocol of urgent cerebral angiography and surgical clipping of the aneurysm followed by colloid volume expansion was adhered to unless the patient was either medically or neurologically unstable. Patients were evaluated daily for the following cardiopulmonary complications: 1) pulmonary edema, defined by the presence of characteristic diffuse infiltrates on chest x-ray films and reduced oxygenation requiring at least 40% supplemental oxygen; 2) hypertension, defined as a systolic blood pressure under 100 mm Hg requiring treatment with intravenous pressors; and 3) dysrythmia, defined as the new onset of atrial flutter or fibrillation, second or third degree atrioventricular block, or ventricular tachycardia or fibrillation. Noncardiac causes of pulmonary infiltrates, hypoxemia, or hypertension were rigorously excluded. All patients received phenytoin and nimodipine, and most were treated briefly with dexamethasone during the perioperative period.

Diagnostic Studies

A standard 12-lead ECG was obtained daily for 3 consecutive days on admission and approximately every other day thereafter. When available, ECGs obtained at other institutions prior to transfer were copied and reviewed, and all patients underwent continuous single-lead electrocardiographic monitoring while in the neuro-ICU. Blood samples for serum electrolyte, creatine kinase (CK), lactate dehydrogenase (LDH), and serum glutamic oxaloacetic transference (SGOT) levels were obtained daily for 3 consecutive days, and approximately every other day thereafter. Creatine kinase isozyme fractionation was performed using agarose gel electrophoresis on all values above normal range (0–50 U/L); CK-MB fractions between 2% and 5% are classified as borderline in our laboratory, with values above 5% considered diagnostic of myocardial infarction.

Echocardiograms and ECGs were interpreted separately by two cardiologists (D.S. and G.L.) blinded to the clinical status of the patients. The QTc intervals were calculated using the Bazett formula. Analyses were conducted on all ECGs obtained on or before SAH Day 14, and on single ECGs performed on or closest to the day of echocardiography, with preference given to ECGs that preceded the echocardiogram. The ECG abnormalities were classified and defined in accordance with established criteria as follows. 1) Rhythm: sinus tachycardia (> 100 bpm); sinus bradycardia (< 60 bpm); atrioventricular nodal rhythm; atrial premature contractions; ventricular premature contractions (VPCs); atrial fibrillation or flutter; ventricular tachycardia (≥ 3 consecutive VPCs) or fibrillation. 2) Impulse Conduction: long PR interval (> 0.20 seconds); short PR interval (< 0.12 seconds); right or left bundle branch block (QRS > 0.12 seconds); QTc segment prolongation (> 0.44 seconds); severe QTc segment prolongation (≥ 0.50 seconds). 3) QRS and ST-T Wave Morphology: Q or QS wave (> 0.04 seconds or amplitude ≥ 25% of R wave in same lead); ST segment elevation (≥ 0.1 mV with upward convexity); ST segment depression (≥ 0.1 mV, flat or downsloping); nonspecific ST segment (< 1 mm elevation or depression); peaked T wave (> 67% of R amplitude in same lead); flattened, isoelectric, or diphasic T wave; symmetrically inverted T wave (negative component ≥ 0.3 mV); asymmetrically inverted T wave (negative component ≥ 0.3 mV); U wave (> 0.1 mV). 4) Voltage Amplitude: right ventricular hypertrophy pattern (R/S ratio ≥ 1 in V1 and R ≥ 0.5 mV); left ventricular hypertrophy pattern (S in V1 and R in V5 ≥ 3.5 mV); peaked P wave (≥ 0.25 mV in II); left atrial enlargement pattern (≥ 0.1 mV negative and > 0.04 seconds in V1). For reference, standard electrocardiographic waves, segments, and intervals are diagrammed in Fig. 1.

Two-dimensional color-flow Doppler transthoracic echocardiograms were performed in the neuro-ICU (Sonos 1000 apparatus; Hewlett-Packard Imaging Systems Division, Andover, MA). All initial studies were performed within 3 days of admission, and most patients underwent a repeat examination 4 to 6 days after the first study. Standard parasternal long axis, short axis, and apical two- and four-chamber views were obtained for analysis of left ventricular function. Echocardiograms were reviewed using a standardized Cardioscan evaluation form. Wall motion was classified as normal,
**Electrocardiographic in subarachnoid hemorrhage**

**TABLE 1**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Neurological Grade†</th>
<th>Aneurysm Site</th>
<th>Pulmonary Edema</th>
<th>Hypothesis</th>
<th>Infarction From Vasospasm</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57, F</td>
<td>V</td>
<td>unknown</td>
<td>yes</td>
<td>yes</td>
<td>bilat MCA</td>
<td>none</td>
<td>died</td>
</tr>
<tr>
<td>2</td>
<td>60, F</td>
<td>IV</td>
<td>rt PCoA</td>
<td>no</td>
<td>no</td>
<td>none</td>
<td>dependent, lt hemiparesis</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>54, F</td>
<td>V</td>
<td>lt PCoA</td>
<td>no</td>
<td>yes</td>
<td>lt MCA</td>
<td>vegetative</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>41, F</td>
<td>III</td>
<td>lt ophthalmic</td>
<td>yes</td>
<td>yes</td>
<td>lt MCA</td>
<td>dependent, rt hemiparesis</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>48, F</td>
<td>III</td>
<td>lt VA/basilar</td>
<td>yes</td>
<td>yes</td>
<td>none</td>
<td>normal</td>
<td></td>
</tr>
</tbody>
</table>

* MCA = middle cerebral artery; PCoA = posterior communicating artery; VA = vertebral artery. See text for definitions.
† Grade according to Hunt and Hess, as modified.38

Results

Left ventricular wall motion abnormalities were detected in five (8%) of the 57 patients in this series; the clinical features of these five patients are presented in Table 1. Computerized tomography revealed diffuse SAH in the basal cisterns in all five patients, parenchymal hemorrhage in the right temporal lobe of Case 1 and left temporal lobe of Case 2, and intraventricular hemorrhage requiring emergency ventriculostomy in Cases 3 and 4. Within 6 hours of onset of SAH, four of these patients experienced sudden hypotension (systolic blood pressure < 100 mm Hg) requiring treatment with intravenous pressor agents, and three exhibited pulmonary edema associated with severe hypoxemia (PO2 ≤ 120 mm Hg on 100% inspired oxygen via endotracheal tube). In contrast, none of the 52 patients with normal echocardiograms experienced hypotension or pulmonary edema (p < 0.0001, Fisher’s exact test). None of the affected patients complained of chest pain, and no patient in the study developed significant dysrhythmias. Echocardiography was performed prior to surgery in the three patients with wall motion abnormalities (Cases 2, 4, and 5) who underwent clip ligation of their aneurysm. Coronary angiography performed 10 days after SAH in Case 5 was normal except for mild stenosis of the middle right coronary artery (50%) and moderate stenosis of the second diagonal branch of the left anterior descending artery (70%). The clinical features of Cases 1, 4, and 5 have been described in detail elsewhere.23

The distribution and time course of the wall motion abnormalities in Cases 1 to 5 are shown in Table 2. In all five patients, ejection fractions were initially moderately or severely reduced and, in four, regional hypokinesia or akinnesia extended beyond the territory of a single coronary artery. Serial echocardiography was performed in four patients and showed progressive recovery of function in all involved segments, with concurrent normalization of the ejection fraction 14 to 44 days after SAH. Apical thrombus was detected in two patients, and in one patient developed between studies performed on Day 1 and Day 4 after SAH.

Clinical characteristics of the entire study group of 57 patients are summarized in Table 3. Compared to those with normal echocardiograms, patients with abnormal wall motion had worse Hunt and Hess scores on admission (p ≤ 0.0001), but did not differ with respect to age, sex, or history of hypertension. Peak preoperative CK, LDH, and SGOT levels were significantly higher in patients with abnormal wall motion than in those with normal echocardiograms. The mean day on which peak CK levels occurred was similar in the two groups (in most patients, on SAH Day 1 or 2). Borderline elevation of the CK-MB isoenzyme fraction (range 2.0%–4.4%) occurred in all five patients with abnormal wall motion, compared to only three of 52 patients with normal echocardiograms (p < 0.001). In almost all patients, CK-MB fractions peaked on SAH Day 1 or 2.

Electrocardiographic abnormalities occurred in 56 (98%) of 57 patients in the study cohort, and are summarized in Table 4. The most frequent findings on serial ECGs were flattened or diphasic T waves (70%), QTc prolongation (≥ 440 msec) (67%), sinus bradycardia (44%), U waves (35%), sinus tachycardia (23%), symmetrically inverted T waves (21%), left ventricular hypertrophy (19%), ventricular premature complexes (14%), and peaked P waves (9%). Univariate statistical analysis revealed significant associations between abnormal wall motion and the presence of either symmetric T wave inversion or severe QTc prolongation (≥ 500 msec) on serial ECGs. With analysis limited to single ECGs performed on (50 cases) or near (seven cases) the day of echocardiography, only symmetric T wave inversion remained highly associated (p < 0.001) with abnormal wall motion. However, mean maximal QTc was significantly increased in patients with abnormal wall motion. Normal wall motion...
Myocardial Dysfunction in Acute SAH

Abnormal wall motion occurred in five (9%) of the 57 patients with SAH and no history of cardiac disease in our study. Three prior echocardiographic studies in SAH patients, reported a similar cumulative frequency of abnormal wall motion (9%, 17 of 184 cases). Wall motion abnormalities in our study were significantly associated with poor neurological grade, elevated total CK levels, and borderline (2%–5%) CK-MB elevation. Similarly, all three prior studies noted an association between abnormal wall motion and poor neurological grade, and both studies in which CK-MB was measured found elevated levels in affected patients.

In contrast, prior investigations have yielded conflicting data concerning the relationship between changes on ECGs and left ventricular dysfunction. Pollick, analyzed ECGs obtained on the first 3 hospital days in 13 SAH patients with no history of heart disease. Inverted T waves were found in all four patients with wall motion abnormalities as opposed to one of nine patients with normal echocardiograms (p < 0.01), but QTc intervals did not differ between the two groups. Sato, et al., found wall motion abnormalities in nine of 130 SAH patients, but did not exclude subjects with preexisting cardiac disease. Eight patients exhibited severe QTc prolongation (≥ 500 msec), eight had ST segment elevation or depression on their admission ECG, and seven later developed inverted T waves. Although abnormalities were found on the ECGs of 90 of 121 patients with normal echocardiograms, they were not described in detail. Davies, et al., detected echocardiographic abnormalities in four of 41 SAH patients with no history of heart disease, and found no relationship between changes on ECGs and abnormal wall motion. However, these investigators analyzed only one ECG per patient (obtained an average of 7.9 days range 1–30) after SAH, and performed echocardiography an average of 2.8 days after electrocardiography. Thus, acute and quickly resolving electrocardiographic changes and echocardiographic abnormalities may have been missed in some subjects.

More recently, Kono, et al., reported a series of 12 patients in whom coronary angiography and left ventriculography were performed acutely following SAH. Apical wall motion was significantly reduced in seven patients with ST segment elevation compared to those with normal ST segments, and echocardiographic evidence of

Discussion

Our study confirms prior reports indicating that a reversible and presumably neurogenic form of cardiac injury characterized by left ventricular systolic dysfunction may occur following SAH. We also found that two specific electrocardiographic changes, symmetrical T wave inversion and severe QTc prolongation (≥ 500 msec), are highly associated with this form of cardiac injury. These abnormalities may serve as useful markers of possible left ventricular dysfunction in acute SAH, and may aid in the identification of patients who require echocardiographic screening.

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TABLE 2

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Day of Echo†</th>
<th>Base‡</th>
<th>Mid LV‡</th>
<th>Apex‡</th>
<th>Ejection Fraction§</th>
<th>Thrombus</th>
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<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>0 0 0 0 0 0</td>
<td>1 1 0 1 1</td>
<td>2 2 2 2</td>
<td>severely reduced</td>
<td>absent</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>0 0 0 0 0 0</td>
<td>1 1 1 1 1</td>
<td>1 1 1 1</td>
<td>moderately reduced</td>
<td>absent</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>0 0 0 0 0 0</td>
<td>0 0 0 0 0</td>
<td>0 0 0 0</td>
<td>mildly reduced</td>
<td>absent</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>0 0 0 0 0 0</td>
<td>1 1 1 1 1</td>
<td>1 1 1 1</td>
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<td>absent</td>
</tr>
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<tr>
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<td></td>
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<tr>
<td>8</td>
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<td>1 0 0 0</td>
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<td>absent</td>
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<tr>
<td>9</td>
<td>0 0 0 0 0 0 0</td>
<td>0 0 0 0 0</td>
<td>1 1 1 1</td>
<td>mildly reduced</td>
<td>absent</td>
<td></td>
</tr>
<tr>
<td>10</td>
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<tr>
<td>13</td>
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<td>normal</td>
<td>absent</td>
<td></td>
</tr>
</tbody>
</table>

* LV = left ventricle; A = anterior; L = lateral; IP = inferoposterior; AS = anterior septum; PS = posterior septum; S = septum.
† Echo = echocardiography. Day 0 refers to calendar day of onset of subarachnoid hemorrhage.
‡ 0 = normal; 1 = hypokinetic; 2 = akinetic.
§ Severely reduced = < 30%; moderately reduced = 30%–40%; mildly reduced = 40%–50%.
Electrocardiography in subarachnoid hemorrhage

**TABLE 3**

Clinical characteristics of subarachnoid hemorrhage patients with and without abnormal left ventricular wall motion

<table>
<thead>
<tr>
<th>Factor</th>
<th>Total Group</th>
<th>Normal</th>
<th>Wall Motion Abnormality</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of cases</td>
<td>57</td>
<td>52</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>mean age (yrs)</td>
<td>50 ± 12</td>
<td>50 ± 12</td>
<td>54 ± 8</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>women</td>
<td>38 (67%)</td>
<td>33 (63%)</td>
<td>5 (100%)</td>
<td>0.158</td>
</tr>
<tr>
<td>neurological grade†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>9 (16%)</td>
<td>9 (17%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>18 (32%)</td>
<td>18 (35%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>20 (35%)</td>
<td>18 (35%)</td>
<td>2 (40%)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>8 (14%)</td>
<td>7 (13%)</td>
<td>1 (20%)</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>2 (4%)</td>
<td>0 (0%)</td>
<td>2 (40%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>history of hypertension</td>
<td>26 (46%)</td>
<td>23 (44%)</td>
<td>3 (60%)</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>mean day of surgery (range)‡</td>
<td>2.6 ± 1.9 (0–10)</td>
<td>2.6 ± 1.9</td>
<td>5.7 ± 4.5</td>
<td>0.014</td>
</tr>
<tr>
<td>mean day of echocardiography (range)</td>
<td>3.4 ± 1.8 (1–9)</td>
<td>3.6 ± 1.8</td>
<td>2.0 ± 1.4</td>
<td>0.061</td>
</tr>
<tr>
<td>mean day of first ECG (range)</td>
<td>1.0 ± 1.3 (0–6)</td>
<td>1.1 ± 1.4</td>
<td>0.2 ± 0.5</td>
<td>0.167</td>
</tr>
<tr>
<td>mean total of ECGs studied (range)</td>
<td>6.2 ± 2.1 (1–11)</td>
<td>5.9 ± 2.0</td>
<td>8.4 ± 2.1</td>
<td>0.011</td>
</tr>
<tr>
<td>any CK–MB level ≥ 1%</td>
<td>26 (46%)</td>
<td>21 (40%)</td>
<td>5 (100%)</td>
<td>0.016</td>
</tr>
<tr>
<td>any CK–MB level ≥ 2%</td>
<td>8 (14%)</td>
<td>6 (10%)</td>
<td>5 (100%)</td>
<td>&gt;0.001</td>
</tr>
<tr>
<td>mean day of peak preop CK level (range)‡</td>
<td>1.6 ± 1.4 (0–6)</td>
<td>1.7 ± 1.5</td>
<td>1.4 ± 0.9</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td>mean peak preop CK level (U/L) (range)</td>
<td>241 ± 371 (18–2335)</td>
<td>205 ± 267</td>
<td>612 ± 911</td>
<td>0.018</td>
</tr>
<tr>
<td>mean peak preop LDH level (U/L) (range)</td>
<td>255 ± 109 (128–821)</td>
<td>232 ± 54</td>
<td>492 ± 223</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>mean peak preop SGOT level (U/L) (range)</td>
<td>33 ± 27 (7–193)</td>
<td>28 ± 13</td>
<td>79 ± 68</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* ECG = electrocardiogram; CK = creatine kinase; LDH = lactate dehydrogenase; SGOT = serum glutamic oxaloacetic transaminase. Day 0 refers to calendar day of onset of subarachnoid hemorrhage. Means presented as ± standard deviation.
† Grade according to Hunt and Hess, as modified. 38
‡ Surgery not performed in one patient with normal echocardiogram and two patients with abnormal wall motion.

improvement was noted in all but one patient who died early in the clinical course. In all seven patients, coronary angiography performed while the ECG showed ST segment elevation revealed no evidence of stenosis or vasospasm. Although the authors emphasized the association of ST elevation with myocardial dysfunction in their study population, other abnormalities detected by serial electrocardiography were not systematically analyzed.

**Significance of ECG Changes in SAH**

We performed this analysis to further clarify the relationship between changes on ECGs and left ventricular dysfunction in patients with acute SAH. Specifically, we tested the hypothesis that, of the multitude of specific electrocardiographic changes encountered in SAH, one or more are closely associated with abnormal wall motion. We excluded patients with known cardiac disease to avoid findings on ECGs or echocardiograms related to non-neurogenic mechanisms. Multiple ECGs (mean 6.2 per patient) were analyzed in a blinded fashion, with the first ECG obtained an average of 1.0 days (range 0–6) after SAH. Fifty-six (98%) of the 57 patients had at least one abnormal ECG. Similarly, Brouwers, et al.,3 found at least one abnormality in all 61 SAH patients studied serially (mean 6.0 ECGs per patient), whereas lower rates (40%–89%) have been reported in studies analyzing fewer ECGs.2,27,31,32,41

The main finding of our study is the association of two specific electrocardiographic abnormalities, namely symmetrical T wave inversion and severe QTc prolongation (≥ 500 msec), with abnormal left ventricular wall motion in acute SAH. Although these associations maintained their significance with analysis limited to single ECGs, the sensitivity of these findings for contractile dysfunction was maximum (100%) with serial electrocardiography. This result almost certainly reflects the well-known transient and evolving nature of neurogenic changes on ECGs,33,44 and underscores the importance of serial electrocardiographic monitoring in SAH.

Our results suggest that not all neurogenic ECG changes are alike, in that some are more likely than others to be associated with myocardial damage. Because T wave inversion and severe QTc prolongation occurred in patients with normal as well as abnormal wall motion in our study, we consider these to be markers of possible left ventricular dysfunction rather than a result of this form of injury. Hypothalamic28 and cardiac nerve 22,36,37,46 stimulation produce T wave inversion and QT prolongation in animals, indicating that these findings reflect intense sympathetic activation of the myocardium. The association of T wave changes and QTc prolongation with acute neurological injury in humans has been confirmed by Rudehill and coworkers,31 who found these abnormalities (as well as U waves and ectopic beats) significantly more often in patients with SAH than in subjects with brain tumors.

**Mechanism of Neurogenic Cardiac Injury**

Although left ventricular wall motion abnormalities are usually attributed to ischemia or infarction from coronary artery disease, contraction band necrosis is the likely pathological substrate of cardiac injury in our patients. Four of five affected patients developed widespread areas of hypokinesis or akinesis which extended beyond the territory of a single coronary artery, in association with peak

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CK-MB levels smaller than anticipated (range 2.0%–4.4%) given the extent of left ventricular dysfunction. Hypokinesis consistently involved the apex (Table 2), in agreement with the findings of Kono, et al.20 In the four patients studied serially, all affected segments progressively normalized over a period of weeks. An identical distribution of wall motion abnormality and pattern of recovery has been described in previous echocardiographic studies in patients with SAH.30,34 Contraction band necrosis involves the left ventricle in a similar diffuse pattern, with multifocal microscopic lesions that primarily involve the endocardium,11,15 and is rarely found if the patient survives longer than 2 weeks, presumably because the changes are reversible.19 In contrast to coagulation necrosis from cerebral ischemia or hypoxia, our experience and that of others indicates that this form of injury can also contribute to complications related to surgery or hypertensive, hypervolemic therapy for symptomatic vasospasm.

**Clinical Implications**

Cardiac injury associated with abnormal wall motion in SAH cases may affect outcome adversely in a number of ways. Affected patients frequently experience pulmonary edema or hemodynamic instability in the acute setting,25,30,34,35 which may lead to secondary brain injury from cerebral ischemia or hypoxia. Our experience and that of others indicates that this form of injury can also be thrombogenic, and can serve as a source of cerebral embolism.30 Potentially fatal ventricular arrhythmias, although infrequent, have been associated with severe QTc prolongation and hypokalemia.10 Finally, reduced left ventricular hemodynamic performance, which has been associated with CK-MB release in SAH patients,26 may contribute to complications related to surgery or hypertensive, hypervolemic therapy for symptomatic vasospasm.

Because affected patients may benefit from cardiac rhythm and invasive hemodynamic monitoring,25 it is important to diagnose wall motion abnormalities following an autopsy study was identified as the cause of apical septal hypokinesis in a patient with SAH.36 Regardless of the precise mechanism, however, it is clear that coronary artery disease was not required to produce the pattern of myocardial injury observed in our patients. Prior studies have reported normal coronary arteries in all patients with wall motion abnormalities after SAH who were studied by angiography or at autopsy.22,25,30,34,45 Similarly, the distribution of luminal stenosis on coronary angiography in our Case 5 was insufficient to explain the extent of wall motion abnormality demonstrated by echocardiography.

**TABLE 4**

Electrocardiographic abnormalities in 57 patients with subarachnoid hemorrhage*  

<table>
<thead>
<tr>
<th>Factor</th>
<th>All ECGs</th>
<th>Single ECG†</th>
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<tbody>
<tr>
<td>no. of cases</td>
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<tr>
<td>rhythm</td>
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* Electrocardiographic abnormalities not listed in the table were not identified in the study population. For categories & definitions of abnormalities, see text. ECG = electrocardiogram; WMA = wall motion abnormality. Means presented as ± standard deviation.
† Single ECG obtained on (50 cases) or near (seven cases) the day of echocardiography.
Acute SAH

- Perform daily ECGs
- Measure CK-MB

Yes

- Echocardiogram
- Invasive hemodynamic monitoring
- Consider delayed surgery

No

Symmetric T wave inversion or severe QTc prolongation on ECG?

Yes

Perform Echocardiogram

No

Wall motion abnormality?

Yes

- Proceed with early surgery & standard management
- Invasive hemodynamic monitoring for surgery and/or volume expansion

No

Fig. 2. Suggested clinical algorithm for the detection of left ventricular dysfunction in patients with acute subarachnoid hemorrhage (SAH). Refer to text for details. ECG = electrocardiogram; CK = creatine kinase. * = Q waves, ST segment elevation, or other abnormalities diagnostic of acute ischemia.

SAH. A suggested clinical algorithm for the detection of left ventricular dysfunction in cases of acute SAH is presented in Fig. 2. Our findings suggest that T wave inversion and severe QTc prolongation are sensitive markers of this form of injury and, in addition to obvious ischemic changes (such as Q waves or ST segment elevation), should be considered indications for echocardiography. Borderline (2%–5%) CK-MB elevation appears to be an equally valuable indicator of potential left ventricular dysfunction, but the usefulness of this test is limited by the time required to perform the assay. We do not consider the presence of abnormal wall motion to be an absolute contraindication to early surgery in patients who are hemodynamically stable, but advocate invasive hemodynamic monitoring during both the peri- and postoperative period. Further research is required to confirm the relationship between T wave inversion, QTc prolongation, and abnormal wall motion found in our study, to ascertain maximally sensitive and specific electrocardiographic criteria for echocardiographic screening, and to determine the optimal treatment of cardiac injury in patients with acute SAH.

Acknowledgments

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References


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