Subarachnoid Hemorrhage: Frequency and Severity of Cardiac Arrhythmias
A Survey of 70 Cases Studied in the Acute Phase

Alvaro Andreoli, Giuseppe di Pasquale, Giuseppe Pinelli, Paola Grazia, Francesco Tognetti, and Claudio Testa

The frequency and severity of cardiac arrhythmias were studied in 70 patients with spontaneous subarachnoid hemorrhage investigated prospectively with 24-hour Holter monitoring. Patients were <70 years old and without clinical and/or ECG signs of previous heart disease; Holter monitoring was initiated within 48 hours of subarachnoid hemorrhage. Arrhythmias were detected in 64 of the 70 patients (91%). Twenty-nine of the 70 patients (41%) showed serious cardiac arrhythmias; malignant ventricular arrhythmias, i.e., torsade de pointe and ventricular flutter or fibrillation, occurred in 3 cases. Serious ventricular arrhythmias were associated with QTc prolongation and hypokalemia. No correlation was found between the frequency and severity of cardiac arrhythmias and the neurologic condition, the site and extent of intracranial blood on computed tomography scan, or the location of ruptured malformation. The extremely high incidence of cardiac arrhythmias, sometimes serious, in the acute period after subarachnoid hemorrhage and the absence of clinical and radiologic predictors make systematic continuous ECG monitoring compulsory to improve the overall results of subarachnoid hemorrhage, irrespective of early or delayed surgical treatment. (Stroke 1987;18:558-564)

During the last decade there has been mounting awareness that amelioration and refinement of surgical techniques have not been accompanied by a proportional improvement in the overall outcome of subarachnoid hemorrhage (SAH) of aneurysmal origin.1-4 Therefore, neurosurgeons have progressively focused their attention and efforts on overall management rather than mere surgical treatment of this condition. Chief prognostic factors for the overall outcome of SAH are the direct effects of the initial bleeding and rebleeding, both of critical importance in the acute phase. Vasospasm, on the other hand, may heavily influence the subacute and delayed course of patients. Other complications of SAH in the acute phase are related to secondary cardiac disturbances, such as myocardial infarction, acute pulmonary edema, and cardiac arrhythmias. Myocardial infarction and pulmonary edema have received much attention in the literature.5-13 Conversely, although several investigators have demonstrated that patients with SAH are at risk for developing severe ventricular arrhythmias,14-27 information concerning the clinical significance of this disorder, namely, its frequency and severity, is scarce perhaps because of the paucity of continuous ECG studies performed in the early stage of SAH when cardiac arrhythmias are more likely to occur. This prospective study involved Holter monitoring performed in the acute phase to evaluate the frequency, time of appearance, type, and severity of cardiac arrhythmias in a series of patients affected by SAH.

Subjects and Methods
From May 1982 through December 1985, 210 patients suffering intracranial SAH were admitted to the First Division of Neurosurgery of the Bellaria Hospital in Bologna, Italy. Of these 210 patients, 110 (52%) were admitted within 48 hours of SAH. Seventy of these acute cases fulfilled the following requirements and were selected for the present study: 1) age <70 years and absence of previous heart disease; 2) ECG Holter monitoring initiated within 48 hours of SAH and technically adequate for at least 21 hours; 3) absence of angiographic vasospasm during Holter monitoring. There were 34 men and 36 women, aged 21-70 years (mean age, 52 years) (Figure 1).

Medical history was remarkable for systemic arterial hypertension in 22 cases. The neurologic status on admission was graded according to the Hunt-Hess scale28: 29 patients were Grades 1-2, 15 were Grade 3, and 26 were Grades 4-5. All patients underwent computed tomography (CT) scanning. A lumbar tap was occasionally performed after an unrevealing CT examination. The source of bleeding was determined in 66 cases by cerebral angiography, 1 patient had a postmortem diagnosis, and 3 patients were not investigated.

The cardiologic study protocol encompassed clinical evaluation, standard ECG, chest x-ray, and serum electrolyte profiles. All patients underwent continuous ECG Holter monitoring initiated within 48 hours of SAH. The recordings ranged from 21 to 26 hours (mean, 23 hours) and were performed using Avionics 445 A two-channel recorders in leads CM5 and CM6.
Tape recordings were analyzed with an Electrocardiocam scanner Avionics 660 B equipped with computer-assisted detection of arrhythmias. The QTc interval was measured using the Bazet formula from an average of 10 complexes of a standard ECG performed on the same day as Holter monitoring.

Arrhythmias were categorized as 1) life-threatening ventricular arrhythmias, i.e., torsade de pointe, ventricular flutter, ventricular fibrillation; 2) serious ventricular tachyarrhythmias, i.e., ventricular premature complexes (VPC) as defined in Lown Classes 4 and 5; Class 4, successive VPCs with couplets or salvos; Class 5, ventricular tachycardia or early diastolic VPCs; 3) supraventricular tachyarrhythmias, i.e., episodes of paroxysmal atrial fibrillation or supraventricular tachycardia; 4) bradyarrhythmias, i.e., sinoatrial block, sinus arrest lasting a minimum of 4 seconds, second-degree atioventricular block, atioventricular dissociation, idioventricular rhythm; 5) nonsignificant arrhythmias, i.e., sporadic supraventricular complexes, VPCs as defined in Lown Classes 1, 2, or 3 (Class 1, VPCs < 30/hr; Class 2, VPCs > 30/hr; Class 3, multiform VPCs), sinus bradycardia, sinus tachycardia, sinus arrhythmia, wandering pacemaker. Arrhythmias of Groups 1–4 were considered serious.

No clinical or CT evidence of rebleeding emerged during Holter monitoring. Four patients, deeply comatose as a consequence of the initial bleeding, died during the recording. Early intracranial surgery for aneurysm clipping was accomplished during Holter monitoring in 12 cases.

The $\chi^2$ test with Yates' correction was used to correlate ventricular arrhythmias with both the QTc interval duration and the serum potassium level.

Results

Cardiac arrhythmias were detected in 64 of the 70 patients (91%), and serious cardiac arrhythmias occurred in 29 (41%). No significant difference existed between the sexes. A higher frequency of severe cardiac arrhythmias was observed in patients older than 61 years; however, the level of significance was not reached (Figure 1).

The timing of Holter monitoring proved of some importance. Serious rhythm disorders more frequently occurred when the examination was initiated within 24 hours of SAH. Moreover, all 3 cases of life-threatening ventricular arrhythmia were recorded in Holter examinations initiated within 24 hours (Table 1). These "malignant" arrhythmias consisted of torsade de pointe-type, atypical ventricular tachycardia associated with episodes of ventricular flutter in 1 case, and degenerated to ventricular fibrillation with asystole in another. The last patient, awake and without extensive cerebral damage, survived with cardiopulmonary resuscitation. The remaining 2 cases were in critical clinical condition and died.

The roles of hypokalemia (< 3.9 mEq/l) and QTc

<table>
<thead>
<tr>
<th>Arrhythmias</th>
<th>Holter monitoring initiated within</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0–24 hrs of SAH (n = 47)</td>
<td>24–48 hrs of SAH (n = 23)</td>
</tr>
<tr>
<td>1. Life-threatening VA</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>2. Serious ventricular tachyarrhythmias</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>3. Supraventricular tachyarrhythmias</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>4. Bradyarrhythmias</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>5. Variable association of 2, 3, and 4 above</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>21 (45%)</td>
<td>8 (35%)</td>
</tr>
</tbody>
</table>

SAH, subarachnoid hemorrhage; VA, ventricular arrhythmia.
interval prolongation (> 440 msec) were investigated in relation to the occurrence of ventricular tachyarrhythmias. A mild to severe hypokalemia was observed in 36 of the 70 patients (51%). A slightly lower serum potassium concentration was found in those cases with serious ventricular tachyarrhythmias (3.8 ± 0.52 mEq/l) compared with the remaining patients (3.91 ± 0.47), but the difference was not significant. Nevertheless, a marked hypokalemia (3.3 ± 0 mEq/l; p < 0.05) was observed in those 3 patients with life-threatening ventricular arrhythmias (Figure 2). A prolonged QTc interval was present in 29 cases (41%), but no significant difference was found between the patients with ventricular tachyarrhythmias (474 ± 74 msec) and those without (452 ± 66 msec). However, a significantly longer QTc interval (p < 0.01) was observed in the 3 cases with malignant ventricular arrhythmias (587 ± 64 msec) (Figure 3).

No correlation was found between frequency and severity of cardiac rhythm disorders and neurologic condition (Table 2) or the site and extent of intracranial blood collection on CT scan (Table 3). The source of bleeding was also not significant. Serious arrhythmias were randomly distributed in the 3 groups: 1) intracranial aneurysms, 2) cerebral arteriovenous malformations (AVMs), and 3) SAH of unknown origin. The location of the vascular malformation was also unrelated to cardiac arrhythmias (Table 4).

Of the 70 patients, 32 with intracranial aneurysm and 1 with cerebral AVM were operated on. Twelve had intracranial surgery within 48 hours of bleeding, during Holter monitoring. Two of these 12 patients had emergency surgery for a life-threatening intracerebral hematoma and died; no arrhythmias were detected in them either during or after surgery. The remaining 10 patients were treated according to "early" surgery pro-

FIGURE 2. Correlation between ventricular arrhythmias (VA) and serum potassium concentration in 70 SAH patients studied acutely.

FIGURE 3. Correlation between ventricular arrhythmias (VA) and QTc duration in 70 SAH patients studied acutely.
remarked that the death rate for SAH patients before acute mortality in some circumstances. It has been proposed that the aggressive diagnostic and therapeutic maneuvers carried out in the acute phase of SAH, particularly when an early surgery protocol is planned (early angiographic study and intracranial surgery, intraoperative hypotension, high-dose mannitol, induced hypervolemia, etc.) may not allow an adequate evaluation of the cardiac condition and, at the same time, may themselves be detrimental.

For these reasons, an early cardiologic assessment including continuous ECG monitoring may be beneficial to SAH patients irrespective of the protocol (early or delayed surgery) instituted to diagnose the cardiac rhythm disorders early. The role of ECG Holter recording in SAH has already been stressed in the literature. Estanol et al. reported some type of arrhythmias in all of the 15 patients admitted within 24 hours of intracranial aneurysm rupture who received ECG monitoring for at least 5 days; 20% of these cases showed life-threatening arrhythmias. Sen and coworkers studied 8 patients with SAH and found significant ventricular arrhythmias, especially in association with vasospasm and/or rebleeding. Prolonged ECG monitoring (averaging 120 hours) was performed in the “acute” phase, but the time interval was not specified.

Our prospective study confirms the early appearance of arrhythmias in the overwhelming majority (91%) of patients with SAH from different sources. Serious rhythm abnormalities affected 41% of our cases and were more frequently detected during the first 24 hours after SAH. Malignant ventricular arrhythmias were strictly limited to the first day after the bleeding. It can be speculated that severe arrhythmias are responsible for the death of some patients either before a definitive diagnosis of SAH is made or early after admission to the neurosurgical unit. A systematic application of Holter monitoring should shed light on this subject.

One may wonder whether cardiac rhythm disorders are secondary to severe cerebral damage or, conversely, are an independent factor which may condition the prognosis. The experiences of Parizel and Estanol and Marin seem to favor the latter assumption.

### Table 2. Distribution of Cardiac Arrhythmias in 70 SAH Patients in Relation to the Clinical Grade According to the Hunt-Hess Scale

<table>
<thead>
<tr>
<th>Arrhythmias</th>
<th>Hunt-Hess Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-2</td>
</tr>
<tr>
<td>1. Life-threatening VA</td>
<td>1</td>
</tr>
<tr>
<td>2. Serious ventricular tachyarrhythmias</td>
<td>3</td>
</tr>
<tr>
<td>3. Supraventricular tachyarrhythmias</td>
<td>3</td>
</tr>
<tr>
<td>4. Bradyarrhythmias</td>
<td>4</td>
</tr>
<tr>
<td>5. Variable association of 2, 3, and 4</td>
<td>2</td>
</tr>
<tr>
<td>6. Absent or nonsignificant</td>
<td>16</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>29</td>
</tr>
</tbody>
</table>

SAH, subarachnoid hemorrhage; VA, ventricular arrhythmia.

tocol. In these 10 cases, Holter monitoring was normal in 3 (2 died, 1 had a good result); in the other 7 patients, serious cardiac arrhythmias were detected during and/or shortly after surgery. In particular, bradyarrhythmias were demonstrated in 4 cases (1 death, 3 good results), serious ventricular tachyarrhythmia in 1 case (good result), and supraventricular tachyarrhythmia in another case (good result). The last patient had combined tachyarrhythmias and bradyarrhythmias (good result).

### Discussion

The unsatisfactory overall results of delayed surgery protocols for ruptured intracranial aneurysms account for the renewed interest in early surgery protocols. As a consequence, early diagnosis of SAH and prompt referral of patients to neurosurgical care units are increasingly recommended. This may explain the enhanced attention to some clinical symptoms observed in patients admitted on an emergency basis. Among the problems complicating the acute care of SAH patients, cardiac arrhythmias were recognized almost two decades ago, but only a few reports on long-term ECG monitoring have emphasized their frequency and importance. The results of a previous study by our institution on 52 consecutive patients with SAH showed that significant cardiac arrhythmias (complex VPCs, ventricular tachycardia, sinus arrests) were prevalent in a group of 31 patients studied with Holter monitoring within 48 hours of SAH. Significant cardiac arrhythmias were rare in a later stage. Fifty-two percent of our SAH patients were referred to our department within 48 hours of bleeding. The present investigation was therefore undertaken to assess the frequency, severity, and possible prognostic implication of arrhythmias in the acute phase of SAH.

Two points must be outlined: 1) arrhythmias are supposedly responsible for clinical deterioration or acute mortality in some circumstances. It has been remarked that the death rate for SAH patients before arriving at a hospital appears to be about 15% and 2) the aggressive diagnostic and therapeutic maneuvers carried out in the acute phase of SAH, particularly when an early surgery protocol is planned (early angiographic study and intracranial surgery, intraoperative hypotension, high-dose mannitol, induced hypervolemia, etc.) may not allow an adequate evaluation of the cardiac condition and, at the same time, may themselves be detrimental.

For these reasons, an early cardiologic assessment including continuous ECG monitoring may be beneficial to SAH patients irrespective of the protocol (early or delayed surgery) instituted to diagnose the cardiac rhythm disorders early. The role of ECG Holter recording in SAH has already been stressed in the literature. Estanol et al. reported some type of arrhythmias in all of the 15 patients admitted within 24 hours of intracranial aneurysm rupture who received ECG monitoring for at least 5 days; 20% of these cases showed life-threatening arrhythmias. Sen and coworkers studied 8 patients with SAH and found significant ventricular arrhythmias, especially in association with vasospasm and/or rebleeding. Prolonged ECG monitoring (averaging 120 hours) was performed in the “acute” phase, but the time interval was not specified.

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### Table 3. Distribution of Cardiac Arrhythmias in 70 SAH Patients in Relation to the CT Findings

<table>
<thead>
<tr>
<th>CT findings</th>
<th>SAH</th>
<th>+</th>
<th>SAH</th>
<th>+</th>
<th>IVH</th>
<th>+</th>
<th>ICH</th>
<th>+</th>
<th>ICH</th>
<th>Normal</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrhythmias</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Life-threatening VA</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Serious ventricular tachyarrhythmias</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Supraventricular tachyarrhythmias</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Bradyarrhythmias</td>
<td>5</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Variable association of 2, 3, and 4 above</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Absent or nonsignificant</td>
<td>16</td>
<td>8</td>
<td>10</td>
<td>3</td>
<td>4</td>
<td>41</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>30</td>
<td>13</td>
<td>18</td>
<td>4</td>
<td>5</td>
<td>70</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

SAH, subarachnoid hemorrhage; CT, computed tomography; IVH, intraventricular hemorrhage; ICH, intracerebral hemorrhage; VA, ventricular arrhythmia.
tion. The spontaneous or pharmacologically induced reversion to a normal sinus rhythm in the cases described by these authors and the subsequent improvement of the neurologic condition are demonstrative. Our experience, of torsade de pointe associated with ventricular fibrillation in a patient in good neurologic condition who showed cardiorespiratory arrest during Holter monitoring but who survived with cardiopulmonary resuscitation, indicates that prompt recognition and treatment of the cardiac disorders play an important role in the patients’ survival.

Clinical condition does not seem to influence the appearance and severity of cardiac arrhythmias. In our series serious rhythm disorders occurred in alert as well as in comatose patients. Conversely, Sen et al discovered significant ventricular arrhythmias only in patients with a complicated clinical course, i.e., cerebral vasospasm, rebleeding, or both.

Besides the possible role of a short time interval from bleeding, we also found some relation with QTc interval prolongation and low serum potassium level. A prolonged QTc interval is frequently observed in patients with SAH, and serious ventricular arrhythmias have been reported in association with this ECG abnormality. Other authors have described hypothalamic lesions in SAH patients who developed arrhythmias. These disorders were also obtained experimentally by stimulating the posterior hypothalamus and the midbrain. The location of the ruptured vascular malformation was also of no significance in our cases, while a higher incidence of arrhythmias in patients with aneurysms of the anterior part of the circle of Willis has been suggested.

Considering the poor reliability of clinical and radiologic data to predict which SAH patients are at risk for cardiac arrhythmias, we advise prolonged ECG monitoring in all cases during the acute stage of SAH. Patients in this phase are more at risk for developing arrhythmias and, at the same time, are potential candidates for the aggressive treatment of an early surgery protocol. In our small series undergoing surgery within 24 hours of SAH, 7 of 10 patients exhibited serious cardiac arrhythmias during or shortly after the operation. This finding seems noteworthy to us although its role in the ultimate outcome remains unclear; in fact, only 1 of 7 patients with arrhythmias died compared with 2 of 3 without arrhythmias.

A final remark relates to the prophylaxis and therapy of post-SAH arrhythmias. Only anecdotal cases treated pharmacologically have been reported, and prophylaxis with autonomic blockers has been recommended. However, indiscriminate administration of β-blockers, as suggested by experimental data, may be harmful due to the frequent occurrence of bradyarrhythmias. As a result of our study, we recommend particular surveillance of those patients with significant QTc prolongation, along with the prompt correction of electrolyte disturbances and timely treatment with antiarrhythmic drugs or temporary pacing.

Authoritative studies have shown that cardiac diseases do not contribute significantly to the morbidity and mortality of SAH patients. However, the importance of cardiac arrhythmias in this condition is not established because the majority of cases have neither

Table 4. Distribution of Cardiac Arrhythmias in 70 SAH Patients in Relation to the Source of Bleeding

<table>
<thead>
<tr>
<th>Arrhythmias</th>
<th>Source of bleeding</th>
<th>Unknown investigated</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Life-threatening VA</td>
<td>ACoA</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2. Serious ventricular tachyarrhythmias</td>
<td>PCoA</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>3. Supraventricular tachyarrhythmias</td>
<td>MCA</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>4. Bradyarrhythmias</td>
<td>VB</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>5. Variable association of 2, 3, and 4</td>
<td>AVM</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>6. Absent or nonsignificant</td>
<td></td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>28</td>
<td>12</td>
</tr>
</tbody>
</table>

SAH, subarachnoid hemorrhage; VA, ventricular arrhythmia. Source of bleeding: AVM, arteriovenous malformation; ACoA, anterior communicating artery; PCoA, posterior communicating artery; MCA, middle cerebral artery; VB, vertebrobasilar system.
routine cardiac monitoring nor specific cardiologic treatment in the very early phase. This comprehensive cardiologic approach could be a further step toward the improvement of overall management of SAH irrespective of the protocol (early or delayed surgery) adopted by the neurosurgeon.

References


49. Hunt D, Gore I: Myocardial lesions following experimental
48. Smith M, Ray CI: Cardiac arrhythmias, increased intracranial pressure and the autonomic nervous system. Chest 1972; 61(suppl):125–133
50. Weidler DJ, Das SK, Sodeman TM. Cardiac arrhythmias secondary to acute cerebral ischemia: Prevention by autonomic blockade (abstract). Circulation 1976;102(suppl 2):53


Key Words • Holter monitoring • cardiac arrhythmias • subarachnoid hemorrhage • cerebral aneurysm
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