Serious Cardiac Arrhythmias After Stroke
Incidence, Time Course, and Predictors—A Systematic, Prospective Analysis

Bernd Kallmünzer, MD; Lorenz Breuer, MD; Nicolas Kahl; Tobias Bobinger, MD; Dorette Raaz-Schrauder, MD; Hagen Bernhard Huttner, MD; Stefan Schwab, MD; Martin Köhrmann, MD

Background and Purpose—Patients with acute cerebrovascular events are susceptible to serious cardiac arrhythmias, but data on the time course and the determinants of their onset are scarce.

Methods—The prospective Stroke-Arrhythmia-Monitoring-Database (SAMBA) assessed cardiac arrhythmias with need for urgent evaluation and treatment in 501 acute neurovascular patients during the first 72 hours after admission to a monitored stroke unit. Arrhythmias were systematically detected by structured processing of telemetric data. Time of arrhythmia onset and predisposing factors were investigated.

Results—Significant cardiac arrhythmias occurred in 25.1% of all patients. Incidence was highest during the first 24 hours after admission. Serious arrhythmic tachycardia (ventricular or supraventricular >130 beats/min) was more frequent than bradycardic arrhythmia (sinus-node dysfunction, bradycardhythmia, or atioventricular block °II and °III). Arrhythmias were independently associated with higher age and severer neurological deficits as measured by the National Institutes of Health Stroke Scale on admission.

Conclusions—The risk for significant cardiac arrhythmia after an acute cerebrovascular event is highest during the first 24 hours of care and declines with time during the first 3 days. Along with established vascular risk factors, the National Institutes of Health Stroke Scale may be considered for a stratified allocation of monitoring capabilities.

Clinical Trial Registration—URL: www.clinicaltrials.gov. Unique identifier: NCT01177748. (Stroke. 2012;43:2892-2897.)

Key Words: acute care ■ cardiac arrest ■ cardiac arrhythmia ■ stroke care ■ stroke units

Cardiac arrhythmias are highly prevalent during the acute phase of stroke and may harm patients by hemodynamic instability and sudden cardiac death.1,2 In addition to arrhythmias as a consequence of cardiac comorbidities, neurocardiological interactions and autonomic dysfunction may complicate the course of cerebrovascular disorders.3–5 Therefore, most stroke units are presently equipped with telemetric monitoring, which allows a timely diagnosis and initiation of emergency treatment in serious disturbances of heart rhythm and conduction.6 However, current guidelines do not give practical advice, in which cardiac monitoring of patients with stroke is of highest importance and how long it should be performed, because data on determinants and time course of arrhythmia onset in the acute phase are scarce.7–9 Although the resources for continuous monitoring on specialized wards are limited, the identification of high-risk patients and stratified allocation of monitoring capabilities is of particular clinical relevance. In this study, the time course and the predisposing factors of arrhythmia onset were systematically investigated during the first 72 hours of care.

Methods

Study Design and Patient Inclusion
This prospective observational trial was conducted during a 6-month period between May 2010 and December 2010 on consecutive patients with acute cerebral ischemia or hemorrhage admitted to our 14-bed dedicated stroke unit. The protocol was approved by the local ethics committee and registered with www.clinicaltrials.gov (NCT 01177748). Recently the results for the detection of atrial fibrillation were separately reported from this study.10 All patients with an acute cerebrovascular event admitted to our stroke unit were prospectively included in the study. Patients with stroke in need of mechanical ventilation are treated on our intensive care unit and were excluded from this analysis. The diagnosis of cerebral ischemia or hemorrhage was based on clinical findings and diagnostic imaging according to current guidelines.7,8,11 By routine, patients underwent a cardiovasc- cular diagnostic work-up and risk factor stratification including a baseline 12-lead electrocardiogram (ECG) and troponin I level on admission, echocardiography as well as extracranial and transcranial vascular ultrasound studies of the anterior and posterior circulation.

Continuous Cardiac Monitoring
Continuous multimodal monitoring (Dräger, Infinity Series, Lübeck, Germany), included a 6-lead continuous ECG registration. Two traces
were displayed on digital screens positioned next to the patient and at a central control station. The system included an automated arrhythmia identification feature, which caused an acoustic alarm signal in case of suspected asystole, ventricular arrhythmia, tachycardia >120 beats/min, or bradycardia <40 beats/min. Because the system is susceptible to artifacts and dysfunction, the corresponding ECG strips are automatically saved and paper-printed. In case of suspected arrhythmia, a 12-lead ECG was conducted, evaluated by a cardiologist, and complemented by additional diagnostic measures as indicated by the clinician (eg, laboratory values, echocardiography, coronary angiography).

Processing of Telemetric ECG Data
The data from continuous cardiac telemetry were saved to a central hard disc and separately analyzed by a study investigator according to a structured algorithm as reported previously. In summary, a graphical 24-hour heart rate spectrum was generated and episodes with drops and boosts in heart rate, excesses of an upper or lower heart rate limit (120 beats/min and 40 beats/min, respectively), or changes in heart rate variation amplitude were evaluated. Furthermore, all episodes identified automatically by the system were analyzed and delimited from artifacts. Finally, a chronological beat-to-beat screening with focus on variations of RR intervals was performed and the time point of arrhythmia onset was determined. The results from the structured analysis were merged with the clinical data and all arrhythmias detected by either method were included provided that the criteria outlined subsequently were met.

Classification of Arrhythmia
This study focused on relevant cardiac arrhythmias, which require urgent evaluation and treatment in consent with current guidelines. This included all arrhythmic episodes causing symptoms (presyncope, syncope, circulatory arrest, dyspnea, acute heart failure) or meeting one of the following ECG criteria: (1) ventricular arrhythmia (ventricular fibrillation, ventricular flutter, sustained and nonsustained ventricular tachycardia, new-onset ventricular ectopy with couplets, and >300 premature ventricular beats/hour or ventricular bigeminus for >30 seconds (Figure 1, first rhythm strip)); (2) supraventricular tachycardia except sinus tachycardia with an excess of heart rate >130 beats/min and a duration >30 seconds (Figure 1, second rhythm strip)); (3) sinus arrest for >3 seconds or drop of heart rate <30 beats/min for >30 seconds as a consequence of sinuatrial block or asystole (Figure 1, third rhythm strip)); (4) as a consequence of second- or third-degree atrioventricular block (Figure 1, fourth rhythm strip)); or (5) in the context of atrial fibrillation (Figure 1, fifth rhythm strip)).
Arrhythmias meeting criteria of points (1) and (2) were summarized as “tachycardia,” whereas those under point (3) to point (5) were referred to “bradycardia.” All arrhythmias, which occurred during monitoring, were reported and patients with a history of cardiac arrhythmias were included.

Statistical Analysis
Data were processed using the PASW Statistics 18 (SPSS Inc) and the Office 2007 (Microsoft Corp) software packages. Normality of distribution was tested using the Shapiro-Wilk and Kolmogorov-Smirnov tests. Normally distributed data were summarized as means and SDs and compared using the Student t test. Other data were reported by median and interquartile ranges and the Mann-Whitney U test was used. Categorized variables were compared with the Pearson χ² test or Fisher exact test. The level of significance was set a priori at *P*≤0.05. An univariate logistic regression analysis was calculated to identify parameters that were associated with arrhythmia onset. All parameters that were significant or showed a trend in the univariate analysis (*P*<0.01) were included into a multivariable logistic regression model with significant arrhythmia as the dependent variable. To investigate the time course of arrhythmia onset, the time from admission was divided into 6 consecutive 12-hour intervals and the rate of arrhythmias per monitoring hour was calculated for each interval. In patients with sustained or recurrent episodes of the same arrhythmia, the time of onset of the first episode of each arrhythmia entity was counted for time course analysis.

Results

Baseline Characteristics
Five hundred one patients (median age, 72 years; interquartile range, 60.5–80) were included, of whom 46.5% were women. Ninety-two percent had acute cerebral ischemia (Table 1). In all other patients, the diagnosis was intracerebral hemorrhage. The participants were awake and breathing spontaneously at the time of inclusion. The median National Institutes of Health Stroke Scale (NIHSS) on admission was 3 (interquartile range, 1–7). A structural heart disease was present in 36.5% (coronary artery disease 54.1%, hypertensive heart disease 29.0%, valvular heart disease 10.4%, others 6.6%). A total of 30.3% of all patients were on medication with antiarhythmic effects (Class I: none; Class II: 142, Class III: 5, Class IV: 5). Fifty-seven patients (11.3%) had pre-existing functional dependence (modified Rankin Scale score ≥3).

Detection of Serious Arrhythmias
The patients received median effective monitoring for 73 hours (interquartile range, 60–84 hours). Times without connection to the system, for example, during examinations, radiological scans, or physical therapy, were not counted. In all other patients, the diagnosis was intracerebral hemorrhage. The participants were awake and breathing spontaneously at the time of inclusion. The median National Institutes of Health Stroke Scale (NIHSS) on admission was 3 (interquartile range, 1–7). A structural heart disease was present in 36.5% (coronary artery disease 54.1%, hypertensive heart disease 29.0%, valvular heart disease 10.4%, others 6.6%). A total of 30.3% of all patients were on medication with antiarhythmic effects (Class I: none; Class II: 142, Class III: 5, Class IV: 5). Fifty-seven patients (11.3%) had pre-existing functional dependence (modified Rankin Scale score ≥3).

Detection of Cardiac Arrhythmia
The patients received median effective monitoring for 73 hours (interquartile range, 60–84 hours). Times without connection to the system, for example, during examinations, radiological scans, or physical therapy, were not counted. In summary, 139 serious events of arrhythmia were detected in 126 patients (25.1%; Table 2). Twenty-four percent of all episodes were associated with obvious clinical symptoms (eg, hemodynamic instability). Eighty-four patients had significant tachycardia, 30 from bradycardia and 12 patients from both. Tachycardiac arrhythmias were statistically more frequent than bradycardias *P*<0.001. Nonnormo-frequent atrial fibrillation was the most common entity and was responsible for 68.7% of all supraventricular tachycardia. One case was classified as atrial flutter with intermittant 1:2 atrioventricular conduction, 15 cases as focal atrial tachycardia, and 10 cases were undetermined supraventricular tachycardias. Six patients had ventricular tachycardia, which were self-terminating within

<table>
<thead>
<tr>
<th><strong>Table 1. Baseline Characteristics</strong></th>
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<tbody>
<tr>
<td><strong>Significant Arrhythmias</strong></td>
</tr>
<tr>
<td>Sex, male</td>
</tr>
<tr>
<td>Age, y (median, IQR)</td>
</tr>
<tr>
<td>Cerebral ischemia</td>
</tr>
<tr>
<td>Intracerebral hemorrhage</td>
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<tr>
<td>NIHSS on admission (IQR)</td>
</tr>
<tr>
<td>Arterial hypertension</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td>Smoking</td>
</tr>
<tr>
<td>Carotid intima-media thickness &gt;1.0 mm (n=467)</td>
</tr>
<tr>
<td>Systolic blood pressure on admission, mm Hg, mean±SD</td>
</tr>
<tr>
<td>Prestroke mRS (IQR)</td>
</tr>
<tr>
<td>Structural heart disease</td>
</tr>
<tr>
<td>TropinonI &gt;0.04 ng/mL on admission (n=419)</td>
</tr>
<tr>
<td>HbA1c (%)</td>
</tr>
</tbody>
</table>

IQR indicates interquartile range; NIHSS, National Institutes of Health Stroke Scale; mRSS, modified Rankin Scale.

*P*<0.05.

30 seconds in all cases. Three of them experienced recurrent episodes. Bradyarrhythmias with atrial fibrillation was the most frequent condition among significant bradycardia. Apart from that, 8 patients had sinus-node dysfunction, 10 patients had atrioventricular conduction disturbances *II*, and one patient from intermittent complete atrioventricular block. Patients with arrhythmias were found to be significantly older (median, 79 versus 70 years; Table 1) and to suffer more frequently from arterial hypertension and pre-existing disabilities as scored on the modified Rankin Scale. Furthermore, clinical deficits on the NIHSS were more severe and cardiac comorbidities more frequent among patients with arrhythmias.

<table>
<thead>
<tr>
<th><strong>Table 2. Detection of Cardiac Arrhythmia</strong></th>
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<tbody>
<tr>
<td><strong>Arrhythmia</strong></td>
</tr>
<tr>
<td>Tachycardia</td>
</tr>
<tr>
<td>Sustained VT</td>
</tr>
<tr>
<td>Nonsustained VT</td>
</tr>
<tr>
<td>Ventricular ectopy</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>Atrial flutter</td>
</tr>
<tr>
<td>Focal atrial tachycardia</td>
</tr>
<tr>
<td>Undetermined SVT</td>
</tr>
<tr>
<td>Bradycardia</td>
</tr>
<tr>
<td>Asystole/SA block</td>
</tr>
<tr>
<td>AV block <em>II</em></td>
</tr>
<tr>
<td>AV block <em>III</em></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
</tr>
</tbody>
</table>

VT indicates ventricular tachycardia; SVT, supraventricular tachycardia; SA, sinusatrial; AV, atrioventricular.
Once detected, all arrhythmias were immediately evaluated for therapeutic consequences. Whenever indicated, patients were started on oral anticoagulants. In addition, detection of arrhythmia led to direct antiarrhythmic treatment in 77.7% of all cases. One patient with primary asystole was successfully resuscitated and transferred to the intensive care unit. Eleven patients underwent implantation of a permanent cardiac pacemaker system. Two patients were treated with implantable cardioverter–defibrillator devices after diagnostic coronary angiography. Apart from that, 92 patients were treated by initiation or modification of antiarrhythmic pharmacotherapy. Treatment of tachycardia was successfully established by pharmacological heart rate control in all cases; emergency cardioversion was not necessary in any patient (Table 3).

### Time Course of Arrhythmia Onset

Figure 2 shows the time profile of arrhythmia onset. Both brady- and tachyarrhythmia showed the highest incidence during the first hours after admission to the stroke unit. Afterward the rate of arrhythmia declined and remained on a lower level. A total of 52.2% of all detected arrhythmias occurred within 12 hours and 74.4% within 24 hours after admission.

### Predictors of Cardiac Arrhythmias

The univariate logistic regression analysis revealed that the following factors were significantly associated or showed a trend toward association with arrhythmia onset: age (years; OR, 1.061; 95% CI, 1.040–1.082; \( P < 0.001 \)), NIHSS on admission (score; OR, 1.077; CI, 1.042–1.112; \( P < 0.001 \)), arterial hypertension (OR, 2.93; CI, 1.504–5.682; \( P < 0.002 \)), hyperlipidemia (OR, 0.677; CI, 0.449–1.018; \( P = 0.061 \)), systolic blood pressure on admission (mm Hg; OR, 1.009; CI, 1.001–1.016; \( P = 0.027 \)), and presence of a structural heart disease (OR, 1.706; CI, 1.131–2.571; \( P = 0.011 \)). These factors were included into a multivariable logistic regression model. The results are shown in Table 3.

### Therapeutic Consequences

Once detected, all arrhythmias were immediately evaluated for therapeutic consequences. Whenever indicated, patients were started on oral anticoagulants. In addition, detection of arrhythmia led to direct antiarrhythmic treatment in 77.7% of all cases. One patient with primary asystole was successfully resuscitated and transferred to the intensive care unit. Eleven patients underwent implantation of a permanent cardiac pacemaker system. Two patients were treated with implantable cardioverter–defibrillator devices after diagnostic coronary angiography. Apart from that, 92 patients were treated by initiation or modification of antiarrhythmic pharmacotherapy. Treatment of tachycardia was successfully established by pharmacological heart rate control in all cases; emergency cardioversion was not necessary in any patient (Table 3).

### Table 3. Therapeutic Consequences of Detected Arrhythmias

<table>
<thead>
<tr>
<th>Arrhythmia Type</th>
<th>CPR</th>
<th>PM/ICD</th>
<th>Angiography</th>
<th>Pharmacotherapy*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventricular tachycardia/ectopy (n=13)</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Supraventricular tachycardia (n=83)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>66</td>
</tr>
<tr>
<td>Asystolia/SA block (n=8)</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>AV block °II and °III (n=11)</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Bradycardiac AF (n=24)</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>11</td>
</tr>
</tbody>
</table>

CPR indicates cardiopulmonary resuscitation; PM, pacemaker; ICD, implantable cardioverter–defibrillator; AV, atrioventricular; AF, atrial fibrillation.

*Initiation or modification of treatment.

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**Figure 2.** Time profile of arrhythmia onset in 501 patients within 72 hours after admission. The number of detected arrhythmias per monitoring hour is separately shown for bradycardiac arrhythmia (A) and tachycardiac arrhythmia (B).
in Table 4. Only age and NIHSS scores on admission were independent predictors of arrhythmia onset within the first 72 hours after admission to the stroke unit.

Discussion

Cardiac arrhythmias are a frequent and potentially fatal complication of acute cerebrovascular diseases. This study investigated the incidence, time profile, and predictors of arrhythmias in 501 prospectively included patients. Every fourth participant had arrhythmias with need for urgent evaluation. Rhythmologic consequences arose in 77.7% of cases. The highest risk for arrhythmia onset was evident within the first 24 hours after admission, during which 74% of all events occurred. Higher age and a more severe neurologic deficit were independent predictors of arrhythmia onset.

Time Course of Arrhythmia Onset During the Acute Phase of Stroke

It may be general consensus that patients with acute ischemic stroke should have cardiac monitoring for at least the first 24 hours after the event to screen for significant arrhythmia and sudden cardiac death. However, data on the time profile of arrhythmia onset during the acute phase are scarce. Modification of cardiac autonomic tone after stroke can occur with temporal latency and therefore suggests the risk of cardiac complications beyond the first 24 hours. Consistently, the peak of serious cardiac adverse events including cardiac death, myocardial infarction, and cardiac failure was reported to occur between Day 2 and Day 3. In the present study, monitoring was performed for a median of 73 hours. Within this period we found a markedly decline of arrhythmia incidence with time, whereas the greatest risk was evident during the first 24 hours. These data therefore support the current conventions in cardiac monitoring, which is most effective during the first 24 hours but should liberally be expanded, especially in patients with a significant risk profile.

Incidence of Serious Tachycardia and Bradycardia

The main corpus of data on arrhythmia in acute stroke arises from studies that were carried out >3 decades ago. The incidence rate of arrhythmias was reported in these studies with a remarkable high fluctuation, ranging from 31% to 87% of all patients. A number of factors may be responsible for the reported discrepancies: conflicting definition of arrhythmias as well as different techniques, duration, and different evaluation of cardiac monitoring. In some studies, the diagnosis of stroke was established clinically in absence of CT scanning, because modern imaging techniques have not been generally available yet. In addition, sinus tachycardia or isolated premature ventricular or supraventricular beats were reported as significant arrhythmia. However, recommendations on the treatment of asymptomatic premature beats have meanwhile been modified and urgent therapeutic intervention is no longer indicated in the majority of cases. Sinus tachycardia may occur as a physiological chronotropic effect during physiotherapy in many patients with stroke. Therefore, these conditions are not classified as serious and they were in contrast to some previous studies excluded from the present investigation.

Patients after acute stroke have an increased risk for sudden cardiac death. In these cases, ventricular fibrillation or pulseless ventricular tachycardia are the leading causes of cardiac arrest. Several prospective trials have documented improved survival with prophylactic implantable cardioverter–defibrillator therapy in high-risk patients with cardiac diseases and ventricular arrhythmia. In the present study, 2.6% of patients with ventricular arrhythmia were identified. Although the episodes were self-terminating in all cases, telemetry monitoring detected 2 patients who required treatment by cardioverter–defibrillator implantation.

Inconsistency is seen with previous reports on bradyarrhythmias; although Norris and colleagues detected not one single case of atrioventricular block II or III in 312 patients with acute stroke. Rem and coworkers reported these conditions in 3.2% of individuals using 48-hour cardiac monitoring. However, bradycardia including intermittent atrioventricular blocks may easily be missed by telemetric monitoring, for example, during unattended time periods or as a consequence of insufficient experience on arrhythmia discrimination among the stroke unit personal. In our cohort, telemetric monitoring was combined with a structured reading algorithm for the ECG data and significant bradyarrhythmias were identified in 8.4% of all participants. The comparably high detection rate suggests that a structured reading algorithm is able to improve the sensitivity of conventional telemetric monitoring and should constantly supplement treatment on specialized stroke units.

Predictors of Cardiac Arrhythmia After Stroke

The analysis of risk factors in the present study revealed that arrhythmias occurred more frequently among patients with pre-existing cardiac comorbidities and established vascular risk factors, including higher age, arterial hypertension, and diabetes mellitus. In addition, differences were also found in the degree of neurological deficits: patients with arrhythmia were clinically affected more severely, reflected by a median NIHSS score of 5.5 versus 2 in patients without arrhythmias. A number of potential confounding factors may be involved in this association, including relationships among stroke severity, cardiac diseases, and vascular risk factors. However, after adjustment for these cofactors, the NIHSS score was still an independent predictor of arrhythmia onset. Previous investigations found that the NIHSS
also correlates with the impairment of cardiovascular autonomic control, indicated by a loss of overall autonomic modulation, lower parasympathetic tone, impaired baroreflex sensitivity, and a shift toward sympathetic dominance with higher NIHSS scores. In addition, it was repeatedly noted that both cardiovascular and neurological causes may account for sudden death after ischemic stroke. Therefore, the NIHSS score on admission may be used for risk-stratified allocation of monitoring capabilities beyond the first 24 hours of care.

Limitations
Limitations of the present study are the single-center design with a restricted number of arrhythmia cases. However, currently this study is among the largest systematic and prospective analyses on cardiac arrhythmias during the acute phase of stroke. Our study cohort represents a classical population on a stroke unit and patients in need of mechanical ventilation were not included in this analysis. Ongoing studies will investigate incidence, time profile, and predictors of cardiac arrhythmias in patients with stroke during neurointensive care. In addition, data were focused on telemetric monitoring in the very early phase after stroke onset. Although our results suggest that most arrhythmias in the acute phase occur within the first 24 hours, future studies should additionally cover the subacute phase of stroke to gain more information on cardiovascular destabilization, arrhythmias, and sudden cardiac death after discharge from the stroke unit.

Conclusions
Systematic analysis of telemetric monitoring in patients with acute stroke is highly effective for detecting severe cardiac arrhythmias. Most events occur within the first 24 hours after stroke unit admission but may be encountered later. Older age as well as stroke severity are independent predictors of cardiac arrhythmias and may be used as factors for risk-stratified allocation of prolonged monitoring after stroke.

Disclosures
None.

References
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