Background and Purpose. Forty percent of patients with a history of ischemic stroke or transient ischemic attack (TIA) have concomitant coronary artery disease. ST segment depression, detected by continuous electrocardiography, is associated with increased cardiac morbidity and mortality in patients with known coronary artery disease. While electrocardiographic changes have been associated with acute stroke, the etiology and significance of these changes remain unclear. In this pilot study we report the prevalence of ST segment depression and ventricular arrhythmias in patients with acute ischemic stroke or TIA monitored by continuous electrocardiography. Clinical predictors of ST segment depression and ventricular arrhythmia are also identified.

Methods. Consecutive patients presenting with acute ischemic stroke or TIA were enrolled within 72 hours of hospital admission and monitored by continuous electrocardiography for 48 hours. The electrocardiographic results were analyzed for periods of ST segment depression and ventricular arrhythmias.

Results. Of 51 patients with ischemic stroke or TIA, 15 (29%) had episodes of ST segment depression (95% confidence interval, 15% to 43%), and 18 (35%) had ventricular arrhythmias (95% confidence interval, 21% to 49%). In logistic regression analysis, increasing age ($P<.02$) and a left-sided neurological event ($P<.01$) were significant predictors of ST segment depression. Increasing numbers of atherosclerotic risk factors, a history of cardiac disease, and increasing or decreasing mean arterial pressure were not predictive of ST segment depression.

Conclusions. Patients with acute ischemic stroke or TIA have a 29% prevalence of ST segment depression within the first 5 days after their event. In comparison, the prevalence of ST depression is 2.5% to 8% in asymptomatic adults and 43% to 60% in patients with symptomatic coronary artery disease. The association of ST segment depression with left-sided neurological events suggests that the electrocardiographic changes are in part neurologically mediated. Further study is necessary to better define the brain-heart interaction and to determine whether ST segment depression in patients with ischemic stroke or TIA reflects underlying coronary artery disease. (Stroke. 1994;25:1820-1824.)

Key Words: cerebral ischemia, transient, coronary heart disease, electrocardiography

Cardiac death is the leading cause of mortality in patients who survive a stroke. The prevalence of significant coronary artery disease in stroke patients ranges from 21% to 60%. Even among patients without a history of heart disease, the prevalence of coronary artery disease is as high as 40%. ST segment depression detected by ambulatory electrocardiography predicts increased cardiac morbidity and mortality in patients with established coronary artery disease and has been associated with an increased rate of perioperative cardiac events in patients undergoing elective surgery for peripheral vascular disease. Continuous electrocardiographic (ECG) monitoring for ST segment depression in patients with a recent stroke or transient ischemic attack (TIA) may be an effective noninvasive method of identifying patients who would benefit most from further cardiac evaluation. If patients at highest risk for cardiac morbidity and mortality can be identified using continuous electrocardiography, appropriate pharmacological or mechanical interventions might improve outcome and reduce the high incidence of cardiac death in patients with cerebrovascular disease. This pilot study determined the prevalence of ST segment depression during continuous electrocardiography among patients with recent ischemic stroke or TIA.

Subjects and Methods. Patients admitted to the Acute Stroke Care Unit of Northwestern Memorial Hospital with recent ischemic stroke or TIA between November 1992 and December 1993 were evaluated for enrollment. Exclusion criteria included left bundle branch block, paced rhythm, or marked ST segment abnormalities on the admission ECG, such as left ventricular hypertrophy with strain pattern, which would interfere with interpretation of ECG results. Approximately 11 patients met the ECG exclusion criteria and were not enrolled. Eligible patients were enrolled within 72 hours of admission. The study was approved by the Institutional Review Board, and the protocol conformed with institutional guidelines for studies involving human subjects.

After giving informed consent, eligible patients were monitored by two-lead continuous electrocardiography (Q-Med) for approximately 48 hours. At the end of each 24-hour period
patients were interviewed for the occurrence of anginal symptoms, and their highest and lowest systolic and diastolic blood pressures were recorded. For most patients, blood pressure was recorded every 2 hours. A minority of patients underwent ECG monitoring after transfer from the Acute Stroke Care Unit to the general neurology service, where blood pressure was measured every 8 hours. Using the highest and lowest recorded systolic and diastolic blood pressures for each 24 hours of monitoring, peak and lowest mean arterial pressures were calculated for each patient.

The Q-Med monitoring device includes a computer that was programmed to detect ST segment depression. ST segment depression was defined as depression of at least 1 mm measured 60 milliseconds after the J point and lasting at least 1 minute. Because the generally accepted measure of silent myocardial ischemia is ST segment depression, we did not include ST segment elevation as an outcome measure in our study. At the completion of monitoring, a printed copy of the computer-detected ST depression and ventricular arrhythmias was generated. These computer-detected events were then reviewed by our study cardiologist for verification of the outcomes of interest. The study cardiologist was blinded to patient characteristics. The ventricular arrhythmias included in our analysis were ventricular couplets or ventricular tachycardia. Ventricular tachycardia was defined as three or more consecutive premature ventricular contractions. Abnormal results were communicated to the patient's attending physician(s), and further cardiac workup or therapy was left to the discretion of the managing physician(s).

Pertinent medical history was obtained from the patient and medical record. Items recorded included age, cardiac history, number of atherosclerotic risk factors, use of cardiac medications, type of neurological event (stroke versus TIA), and side and location of the neurological event. The location of the neurological event was determined from the chart notes of the attending neurologist. The neurologist's assessment of the location was based on the patient's presenting symptoms as well as the results of neurological imaging studies. Cardiac history included previously diagnosed myocardial infarction, angina, or congestive heart failure. Atherosclerotic risk factors included hypertension, diabetes, hypercholesterolemia, and past or current smoking. Cardiac medication use was defined as outpatient treatment with a β-blocker, calcium channel blocker, nitrate, diuretic, or digoxin at the time of admission. This variable served as a marker for existing cardiac disease. Within 6 months after discharge, each patient's chart was reviewed for the occurrence of unstable angina, death, myocardial infarction, new arrhythmias, and subsequent stroke or TIA during the index hospitalization.

**Statistical Analysis**

Dependent variables were presence versus absence of ST depression and presence versus absence of ventricular arrhythmia. We performed $\chi^2$ tests of association for categorical variables and grouped $t$ tests for continuous variables. Independent variables included age, use of cardiac medications, number of risk factors for atherosclerosis, history of cardiac disease, type of neurological event (stroke versus TIA), side of event, and peak and lowest mean arterial pressures. All tests were two tailed. Logistic regression analysis was performed in two steps to identify clinical predictors of silent myocardial ischemia and ventricular arrhythmias. For the regression analysis, number of cardiac medications, number of cardiac diagnoses, and number of risk factors for atherosclerosis were entered into the model as continuous variables. An exploratory analysis first selected the four most predictive independent variables, which were subsequently reentered into a confirmatory logistic regression analysis.

**Results**

Fifty-five patients were enrolled between November 1992 and December 1993. Four patients were subsequently excluded because the cardiologist determined that they had baseline changes on continuous ECG results that interfered with ST segment analysis. Of the 51 remaining patients, 33 had ischemic strokes and 17 had TIAs. One patient presented with both a stroke and TIA. The mean length of monitoring time was 45 hours (range, 21 to 60 hours). The average monitor time was 44 hours for patients without ST segment depression and 48 hours for patients with ST segment depression. This difference was not statistically significant.

None of the patients had anginal symptoms during continuous electrocardiography. One patient died of infectious complications during the hospital stay. He did not have ST segment depression during ECG monitoring. Two patients had their hospital course altered by the results of their continuous monitoring. One patient underwent a workup for coronary artery disease because of ST segment depression and subsequently underwent three-vessel coronary artery bypass grafting. A second patient had a pacemaker placed because of 2- to 3-second pauses detected during continuous electrocardiography. No patients suffered a myocardial infarction, unstable angina, or cardiac death during their hospital stay.

Table 1 shows the characteristics of the study cohort. Eighty percent of the patients had at least one cardiac risk factor, and 22% had a history of angina, congestive heart failure, and/or a myocardial infarction. Fifty-five percent had a left-sided neurological event.

Fifteen patients (29%) had ST segment depression during continuous electrocardiography. Ninety-five patients had either couplets or ventricular tachycardia during continuous ECG monitoring (95% confidence interval, 15% to 43%). Table 1 shows the characteristics of patients with and without ST segment depression. Patients with ST segment depression were 6.7 years older than patients without ST segment depression ($P<.06$). Compared with patients without ST segment depression, patients with ST segment depression were neither more likely to have cardiac risk factors nor have a history of cardiac disease. Patients with ST segment depression were significantly more likely to have a left-sided neurological event ($P<.02$). Table 2 shows the results of logistic regression analysis, in which independent predictors of ST depression were identified. Increasing age ($P<.02$) and a left-sided neurological event ($P<.01$) were significant predictors of ST segment depression. A history of cardiac disease, atherosclerotic risk factors, use of cardiac medications, and increasing or decreasing mean arterial pressure were not predictive of ST depression.

Eighteen patients (35%) had either couplets or ventricular tachycardia during continuous monitoring (95% confidence interval, 21% to 49%). As shown in Table 3, patients with a ventricular arrhythmia were 5 years younger than patients without arrhythmia, but the difference was not significant. In logistic regression analysis, there were no significant clinical predictors of ventricular arrhythmias (Table 4).

**Discussion**

Although prior studies have shown that 13% to 19% of patients with ischemic stroke have new ST segment...
depression on 12-lead ECG, we know of only one other study that prospectively used continuous monitoring to document the prevalence of ST depression in patients with acute stroke or TIA. This study, by Lavy et al, found a 19% incidence of new ST segment depression in 43 patients with ischemic stroke by obtaining ECGs both sequentially and when ST segment changes were observed during telemetry in an intensive care unit. However, this prior study used one-lead electrocardiography rather than two-lead and relied on continuous naked eye observation of a telemetry monitor by medical students or nursing staff for detection of ST segment changes. Our methods are likely to be more sensitive in detecting and quantifying ST segment depression. Using a continuous ECG monitoring device programmed to detect and record episodes of 1-mm ST depression, we found that 29% of patients admitted for an ischemic neurological event had transient ST segment depression. In support of neurologically mediated ECG changes, our data showed that 80% of patients with ST segment depression had a left hemispheric event. Among patients with a left-sided neurological event, 43% had ST segment depression. In contrast, 13% of patients with a right-sided event had ST segment depression.

ST segment depression in this patient population is likely to be mediated by both cardiac and neurological mechanisms. Support for a cardiac etiology includes the following: 21% to 60% of patients with cerebrovascular disease have concomitant coronary artery disease. After acute stroke or TIA, catecholamine levels and systemic blood pressure are often high. In patients with coexistent coronary artery disease, these stresses might induce myocardial ischemia, manifest by asymptomatic ST segment depression.

Evidence for neurologically mediated ECG changes comes from autopsy studies showing an absence of coronary atherosclerosis in some patients with ECG changes after stroke or subarachnoid hemorrhage. Instead, myocytolysis, a pathological finding of swollen myocytes, interstitial hemorrhage, and myofibrillary degeneration, has been documented in cardiac muscle of patients with ECG changes after stroke or subarachnoid hemorrhage. Myocytolysis is found in the setting of increased serum catecholamine levels. In laboratory animals, microscopic changes of myocytolysis have been shown to occasionally center around nerve endings within the heart.

Our results did not show that patients with ST segment depression were more likely to have known cardiac disease or greater numbers of atherosclerotic risk factors. However, our study does not rule out coronary artery disease as a mediator of ST segment depression in this patient population. In support of neurologically mediated ECG changes, our data showed that 80% of patients with ST segment depression had a left hemispheric event. Among patients with a left-sided neurological event, 43% had ST segment depression. In contrast, 13% of patients with a right-sided event had ST segment depression.

Data to support lateralization of neurologically mediated ECG changes come from animal studies and often implicate the insular cortex. The insular cortex lies below the frontoparietal and temporal opercula and is supplied by the middle cerebral artery.

### Table 1. Clinical Characteristics Associated With ST Segment Depression in Patients With Acute Ischemic Stroke or Transient Ischemic Attack

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Patients (n=51)</th>
<th>ST Segment Depression</th>
<th>Univariate P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean age, y</td>
<td>Present (n=15)</td>
<td>Absent (n=36)</td>
</tr>
<tr>
<td>Mean age, y</td>
<td>65.4</td>
<td>70.1</td>
<td>63.4</td>
</tr>
<tr>
<td>Peak MAP, mm Hg*</td>
<td>123</td>
<td>123</td>
<td>122</td>
</tr>
<tr>
<td>Lowest MAP, mm Hg**</td>
<td>86</td>
<td>88</td>
<td>86</td>
</tr>
<tr>
<td>Cardiac history</td>
<td>11 (22%)</td>
<td>2 (13%)</td>
<td>9 (25%)</td>
</tr>
<tr>
<td>Atherosclerotic risk factors</td>
<td>41 (80%)</td>
<td>12 (60%)</td>
<td>29 (81%)</td>
</tr>
<tr>
<td>Use of cardiac medications</td>
<td>20 (39%)</td>
<td>6 (40%)</td>
<td>14 (39%)</td>
</tr>
<tr>
<td>Stroke†</td>
<td>33 (65%)</td>
<td>10 (67%)</td>
<td>23 (64%)</td>
</tr>
<tr>
<td>TIA</td>
<td>17 (33%)</td>
<td>4 (27%)</td>
<td>13 (36%)</td>
</tr>
<tr>
<td>Left-sided neurological event</td>
<td>28 (55%)</td>
<td>12 (80%)†</td>
<td>16 (44%)</td>
</tr>
</tbody>
</table>

MAP indicates mean arterial pressure; TIA, transient ischemic attack.

*Peak and lowest MAPs were calculated from the highest and lowest recorded systolic and diastolic pressures during monitoring.
†One patient had both a stroke and a TIA.
‡For one patient with a TIA manifest as gait unsteadiness the side of the event could not be definitively determined.

### Table 2. Clinical Predictors of ST Segment Depression on Continuous Electrocardiography in Patients With Ischemic Stroke or Transient Ischemic Attack: Results of Two-Step Logistic Regression

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increasing age</td>
<td>1.09/y</td>
<td>&lt;.02</td>
</tr>
<tr>
<td>History of cardiac disease</td>
<td>0.344</td>
<td>.22</td>
</tr>
<tr>
<td>Presence of cardiac risk factors</td>
<td>0.784</td>
<td>.50</td>
</tr>
<tr>
<td>Left-sided neurological event</td>
<td>3.2</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>
area of chronotropic control has been identified within the rat insular cortex. Insular stimulation in the rat has been shown to induce norepinephrine-mediated tachycardia via nerves ending in cardiac muscle. In the cat, ligation of the left middle cerebral artery resulted in increased catecholamine levels compared with sham-operated controls when blood supply to the insular cortex was affected. Other studies in the rat, however, showed that infarction of the right insular cortex was associated with increased arterial blood pressure and norepinephrine levels. In epileptic humans undergoing temporal lobectomy, intraoperative stimulation of the right insular cortex caused increased heart rate and pressor responses. In another study of epileptic humans, tachycardia followed inactivation of the left hemisphere but not the right hemisphere using intracarotid amobarbital injections. Areas surrounding the insular cortex may exert tonic inhibition of sympathetic impulses from the insular cortex. Infarction of these areas could conceivably result in increased catecholamine levels accompanied by cardiac and ECG changes.

Interestingly, the relation between a left-sided neurological event and ST segment depression was even stronger when the patients with TIA were excluded from the logistic regression analysis (relative risk, 5.3). Since most of the patients with a diagnosis of TIA were asymptomatic during most or all of their time period of monitoring, any neurologically mediated stimulus causing ST depression may have been absent during monitoring of the patients with TIA. However, it is also possible that the mediators released by an acute ischemic neurological event remain present after the neurological manifestations of the event have subsided. These mediators may continue stimulating coronary vasospasm after the patient has returned to baseline neurologically.

In support of our finding that increasing age is associated with ST segment depression, studies in aged rats show that increasing age is associated with increased catecholamine levels, ECG changes, and mortality after middle cerebral artery occlusion. We found a 35% prevalence of ventricular couplets or tachycardia in our patient cohort. Eight percent had ventricular tachycardia. Luxon et al found a 12% prevalence of ventricular couplets or tachycardia among 60 patients with a TIA monitored with continuous electrocardiography. Rem et al showed that 4% of patients with acute stroke or TIA had ventricular tachycardia. An association between ventricular arrhythmias and left-sided neurological events might be expected if left-sided neurological events result in increased catecholamine levels as described above. However, in a patient population with a high prevalence of coronary artery disease, ST segment depression may be stimulated at a lower level of catecholamines than ventricular arrhythmias.

As a pilot study intended to ascertain the prevalence of ST segment depression in patients with ischemic stroke or TIA, our study has several shortcomings, including a limited number of patients and lack of a simultaneous control group. Although previous data suggest that catecholamines are likely to mediate ECG changes in patients with neurological disease, we did not measure catecholamine levels in our patients. Patients with coronary artery disease and asymptomatic ST depression on continuous electrocardiography

### Table 3. Clinical Characteristics Associated With Ventricular Arrhythmia In Patients With Acute Ischemic Stroke or Transient Ischemic Attack

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Patients (n=51)</th>
<th>Present (n=18)</th>
<th>Absent (n=33)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y</td>
<td>65.4</td>
<td>62</td>
<td>67</td>
<td>.16</td>
</tr>
<tr>
<td>Peak MAP, mm Hg*</td>
<td>123</td>
<td>117</td>
<td>126</td>
<td>.12</td>
</tr>
<tr>
<td>Lowest MAP, mm Hg</td>
<td>86</td>
<td>87</td>
<td>86</td>
<td>.65</td>
</tr>
<tr>
<td>Cardiac history</td>
<td>11 (22%)</td>
<td>4 (22%)</td>
<td>7 (21%)</td>
<td>.93</td>
</tr>
<tr>
<td>Cardiac risk factors</td>
<td>41 (80%)</td>
<td>13 (72%)</td>
<td>28 (85%)</td>
<td>.28</td>
</tr>
<tr>
<td>Use of cardiac medications</td>
<td>20 (39%)</td>
<td>7 (39%)</td>
<td>13 (39%)</td>
<td>.97</td>
</tr>
<tr>
<td>Stroke†</td>
<td>33 (65%)</td>
<td>12 (67%)</td>
<td>22 (67%)</td>
<td>1.0</td>
</tr>
<tr>
<td>TIA</td>
<td>17 (33%)</td>
<td>6 (33%)</td>
<td>12 (36%)</td>
<td>.94</td>
</tr>
<tr>
<td>Left-sided neurological event</td>
<td>28 (55%)</td>
<td>12 (67%)</td>
<td>16 (50%)†</td>
<td>.25</td>
</tr>
</tbody>
</table>

MAP indicates mean arterial pressure; TIA, transient ischemic attack.

†One patient had both a stroke and a TIA.
‡For one patient with a TIA manifest as gait unsteadiness the side of the event could not be definitively determined.

### Table 4. Results of Two-Step Logistic Regression Analysis of Clinical Predictors of Ventricular Arrhythmia

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.98</td>
<td>.40</td>
</tr>
<tr>
<td>Left-sided neurological event</td>
<td>1.4</td>
<td>.29</td>
</tr>
<tr>
<td>Increasing MAP</td>
<td>0.96</td>
<td>.11</td>
</tr>
<tr>
<td>Use of cardiac medications</td>
<td>1.51</td>
<td>.38</td>
</tr>
</tbody>
</table>

MAP indicates mean arterial pressure.
have increased cardiac morbidity and mortality. Likewise, new 12-lead ECG changes after stroke or TIA predict a poorer prognosis. A recent randomized clinical trial showed a decrease in cardiac morbidity and mortality when patients with coronary artery disease and Holter monitor-detected asymptomatic ST segment depression were treated with β-blockers. Further study is necessary to determine the relation between coronary artery disease, ECG changes, neurological influences, and cardiac morbidity and mortality in patients with cerebrovascular disease. Because the majority of patients who survive a stroke ultimately succumb to cardiac disease, the ability of continuous electrocardiography to identify patients at highest risk for cardiac death deserves further investigation.

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