Cardiac Arrhythmias in Acute Stroke

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SUMMARY Cardiac arrhythmias were more frequent (P < 0.001) in 312 stroke patients admitted to an intensive care stroke unit, than in 92 patients admitted to the unit and subsequently found not to have strokes. This significant difference remained when a stroke subgroup and the non-stroke group were matched for age, sex and duration of stay in the unit (P < 0.005). Hypertension and hypertensive cardiac disease were more common in the stroke than in the non-stroke patients (P < 0.001).

These arrhythmias were rarely (2%) responsible for hemodynamic ischemic cerebrovascular lesions, but may have been associated with cerebral embolism in up to 17% of cases. The cardiac arrhythmias appeared to have little influence on the course of the subsequent recovery from stroke. Although these arrhythmias frequently reflect the high incidence of cardiac disease in stroke patients, in some cases they are secondary to the acute cerebrovascular lesion itself.

THE DETECTION of a cardiac arrhythmia in a patient with an acute cerebrovascular lesion prompts a search for a causal relationship. Any attempt to attribute focal cerebral ischemia to reduced cerebral perfusion is complicated by the alternative possibility of systemic arterial embolism, especially if the arrhythmia is acute in onset. Case reports attempting to relate cardiac arrhythmias to episodes of reduced cerebral perfusion are not convincing unless the alternative embolic etiology can be excluded.1,2

In patients with acute or recurrent cerebrovascular episodes where continuous cardiac monitoring or serial electrocardiography is available2,7 a high incidence of all types of cardiac arrhythmia is recorded. Nevertheless, the relationship between these arrhythmias and the cerebrovascular lesion remains uncertain. We have attempted to examine these relationships further by using the continuous observation facilities afforded by an intensive care stroke unit (ICSU).

Methods and Materials

Consecutive patients with a diagnosis of stroke were admitted to the ICSU where facilities for continuous observation and electrocardiographic (ECG) monitoring were available. In addition, standard 12-lead ECG's were recorded daily for the first 3 days.

Patients with consistently raised recumbent blood pressures above 160/90 were considered hypertensive. If there was also clinical, ECG or radiological evidence of cardiac hypertrophy they were classified as having hypertensive heart disease.

Patients with a history of angina, myocardial infarction or evidence of definite ischemic changes on ECG, as shown by ST depression in the absence of digitalis therapy, were classified as having ischemic heart disease.

The diagnosis of stroke was limited to parenchymal lesions of the brain due to cerebral ischemia or hemorrhage. Other cerebrovascular lesions such as subdural hematoma or subarachnoid hemorrhage were excluded. Diagnosis was aided by lumbar puncture unless contraindicated, EEG, brain scans, cerebral angiograms and in some cases computerized axial tomograms of the brain.

Cerebral embolism was diagnosed when a stroke occurred suddenly, sometimes accompanied by a seizure, and when a potential source of emboli could be demonstrated.

Results

Between January 1975 and January 1977, 92 of the 404 patients admitted to the Stroke Unit were found not to have strokes. This non-stroke group had a variety of illnesses including post-epileptic states, cerebral tumor, Ménière's disease and other conditions. Since the non-stroke patients were treated and observed in the same way as the stroke patients in the unit, they form a control group.

Age & Sex Factors

In the stroke group there were 171 males (mean age 70 ± 12 years, range 16–93) and 141 females (mean age 75 ± 9 years, range 46–95). In the non-stroke group there were 44 males (mean age 62 ± 19, range 16–95), and 48 females (mean age 68 ± 18, range 17–88). This age difference in the two groups was highly significant (P < 0.0005, Student's t-test). The stroke patients spent longer in the unit (mean stay 6.3 days) than the non-stroke cases (mean stay 3.2 days).

Incidence of Cardiac Disease

There was significantly more cardiac disease in the stroke group compared to the controls (P < 0.001, χ² test) (table 1). The increased incidence of hypertension in the stroke patient (174 cases, 56%) compared to the control group (35 cases, 38%) is reflected in the higher incidence of hypertensive heart disease (P < 0.001),

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although the incidence of ischemic heart disease is similar.

In 68% (141 cases) of stroke patients with concurrent cardiac disease, there was no apparent relationship between the cardiac and cerebrovascular lesions. In the remaining 63 cases there was a potential cardiac source of cerebral emboli. Thirty-six had chronic atrial fibrillation and 15 had paroxysmal atrial fibrillation. Four had probable mural embolism following recent myocardial infarction, and cerebral embolism occurred in 2 cases with ventricular aneurysm, 1 with a left atrial myxoma, 1 with the prolapsing mitral valve syndrome, and a further case with an aortic Starr-Edwards prosthesis. In each of 3 patients, an associated sick sinus syndrome (diagnosed only when both bradyarrhythmia and tachyarrhythmia were present) was associated with an acute cerebral embolic lesion.

Incidence of Cardiac Arrhythmias

Total Cardiac Arrhythmias

Two major groups of cardiac arrhythmias were evident solely on numerical grounds among the total number of cases studied. These were ectopic beats and atrial fibrillation, the third group comprising all other arrhythmias. Patients with cardiac arrhythmias were, therefore, divided into 3 groups:

1. Those with solely supraventricular or ventricular ectopic beats.
2. Cases with chronic or paroxysmal atrial fibrillation.
3. Those with other arrhythmias, including sick sinus syndrome, supraventricular and ventricular tachyarrhythmias.

There was a significantly increased incidence of the total number of cardiac arrhythmias in the stroke group compared to controls ($P < 0.001$, $x^2$ test) (table 2).

Since the age and sex incidence in the 2 groups was significantly different, patients in the control group were matched against the stroke group on the basis of age and sex. Eighty-two patients could be matched from each group and then their arrhythmias were evaluated. (Stroke subgroup mean age 69.6 ± 13.4 years, controls subgroup mean age 68.4 ± 14.9 years — not a significant difference). Fifty-four cases in this stroke subgroup had cardiac arrhythmias compared to 20 in the controls, still a highly significant difference ($P < 0.001$).

Since the stroke group spent longer in the unit than the controls their chance of arrhythmia detection was higher, so a further subgroup was matched. These patients from stroke and control groups had their cardiac arrhythmias recorded only for the first 3 days following admission. On this basis, and again matched for age and sex, 35 patients in each group were compared. Twenty-three patients in the stroke group had arrhythmias compared to 8 in the controls ($P < 0.005$). The incidence of arrhythmias was significantly increased in both the hemispheric infarction group ($P < 0.001$), and the hemispheric hemorrhage group of patients ($P < 0.05$).

Ectopic Beats

The commonest arrhythmias seen were supraventricular and ventricular ectopic beats. Since those occurring during the course of more serious arrhythmias are sometimes not recorded by intensive care unit

Table 1: Incidence of Heart Disease in Stroke and Control Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Total</th>
<th>Hyper.</th>
<th>Emb.</th>
<th>Other</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>312</td>
<td>128(41%)</td>
<td>48(15%)</td>
<td>9</td>
<td>204(65%)</td>
</tr>
<tr>
<td>Controls</td>
<td>92</td>
<td>20(22%)</td>
<td>16(17%)</td>
<td>3</td>
<td>39(42%)</td>
</tr>
</tbody>
</table>

*Difference from controls, $p < 0.001$.
†Difference from controls, $p < 0.005$.
•Difference from controls, $p < 0.05$.

Table 2: Type of Stroke Related to Group of Cardiac Arrhythmias

<table>
<thead>
<tr>
<th>Cerebral lesion</th>
<th>No.</th>
<th>Ectopic beats</th>
<th>Cardiac arrhythmias</th>
<th>Miscellaneous</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infarct:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemisphere</td>
<td>199</td>
<td>10</td>
<td>52†</td>
<td>10</td>
<td>112† (57%)</td>
</tr>
<tr>
<td>Brain stem</td>
<td>43</td>
<td>—</td>
<td>11</td>
<td>1</td>
<td>14 (32%)</td>
</tr>
<tr>
<td>TIAs:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemisphere</td>
<td>31</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td>3 (38%)</td>
</tr>
<tr>
<td>Brain stem</td>
<td>9</td>
<td>1</td>
<td>2</td>
<td>—</td>
<td>1 (44%)</td>
</tr>
<tr>
<td>Hemorrhage:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemisphere</td>
<td>24</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>10* (42%)</td>
</tr>
<tr>
<td>Brain stem</td>
<td>6</td>
<td>1</td>
<td>—</td>
<td>2</td>
<td>4 (67%)</td>
</tr>
<tr>
<td>Total</td>
<td>312</td>
<td>15</td>
<td>74†</td>
<td>15</td>
<td>155 (50%)</td>
</tr>
<tr>
<td>Controls</td>
<td>92</td>
<td>1</td>
<td>11</td>
<td>7</td>
<td>20 (22%)</td>
</tr>
</tbody>
</table>

*Difference from controls, $p < 0.001$.
†Difference from controls, $p < 0.005$ (both types ectopic beats).
*Difference from controls, $p < 0.05$.
TIAs = Transient ischemic attack; SVPB = Supraventricular ectopic beats; VPB = Ventricular ectopic beats; PAF = Paroxysmal atrial fibrillation, observed only on cardiac monitor; CAF = Chronic atrial fibrillation, established or consistent atrial fibrillation.
staff, the overall incidence of ectopic beats is probably slightly underestimated.

The incidence of all types of ectopic beats was significantly increased in the stroke group (table 2), and especially in the hemispheric infarct patients, whereas there was no difference from controls when cases with brain stem infarctions were compared.

**Atrial Fibrillation**

There was no significant difference in the incidence of chronic or paroxysmal atrial fibrillation between the stroke and control group. However, there was a significant difference ($P < 0.01$) when the hemispheric infarct groups only were compared. This relationship may indicate a cardiac source of emboli at least in some cases.

**Miscellaneous Arrhythmias**

In the 15 patients with miscellaneous cardiac arrhythmias there were 8 cases of sick sinus syndrome (bradycardia-tachycardia syndrome), 2 with paroxysmal atrial flutter, and 1 case respectively of paroxysmal atrial tachycardia, paroxysmal junctional tachycardia, and idioventricular rhythm in those patients with cerebral ischemic lesions. In addition, one patient with hemispheric hemorrhage had paroxysmal atrial tachycardia.

In this group of miscellaneous arrhythmias, 6 patients may have had their cerebral ischemic lesions on a cardiac hemodynamic basis which represents 2% of 282 cerebral ischemic lesions. They were all elderly (mean age 77 years), and five had sick sinus syndrome, the sixth having an idioventricular rhythm. Prolonged periods of asystole were observed in all these cases. All had associated confusional states or syncopal episodes prior to their acute ischemic cerebrovascular lesions. None had cerebral angiography, though 2 patients had carotid bruises. In 1 patient, TIA's were accompanied by episodes of asystole on the cardiac monitor. The insertion of a cardiac pacemaker in this patient was followed by the abrupt cessation of further neurological episodes.

Apart from these possible hemodynamic episodes, the arrhythmias appeared to have little effect on the course of the stroke. If all 45 patients with atrial fibrillation and the remaining 3 cases of sick sinus syndrome could be considered potential candidates for cerebral embolism, then up to 17% of the ischemic stroke group (282 cases) may have had embolic strokes.

**Effect of Raised Intracranial Pressure**

In the cerebral hemorrhage group, a pattern of cardiac arrhythmias was commonly seen in patients with terminal raised intracranial pressure ("coning"). This consisted of progressive bradycardia to a point of nodal escape followed by idioventricular rhythm and finally cardiac arrest. These "terminal" arrhythmias were, therefore, not included in the analysis.

<table>
<thead>
<tr>
<th>Location</th>
<th>Ischemic strokes</th>
<th>Hemorrhagic strokes</th>
<th>All strokes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemisphere</td>
<td>123/230† (53%)</td>
<td>10/24 (42%)</td>
<td>133/254*</td>
</tr>
<tr>
<td>Brain stem</td>
<td>18/52† (35%)</td>
<td>4/6 (67%)</td>
<td>22/58*</td>
</tr>
</tbody>
</table>

*Difference, $p < 0.05$. †Difference, $p < 0.02$.

**Relationship of Cardiac Arrhythmia to Site of Cerebral Lesion**

Cerebral hemispheric lesions were associated with significantly more cardiac arrhythmias than those of brain stem location ($P < 0.05, \chi^2$ test) (table 3). This increased incidence in hemispheric lesions was more striking if only those patients with ischemic strokes were compared ($P < 0.02$). The corresponding figures for hemorrhagic strokes are too small to be meaningful.

**Discussion**

Previous studies in patients with acute cerebrovascular lesions have demonstrated a high incidence of cardiac arrhythmias and other ECG abnormalities. The reduced cardiac output resulting from these arrhythmias was considered as contributing to the cerebral lesion by reducing cerebral blood flow.

In an intensive care study of acute stroke patients Lavy et al. found 29 out of 43 cases (67%) with cerebral ischemia had either ischemic changes on ECG or cardiac arrhythmias. These abnormalities were transient in 25 cases and permanent in 4 and since they appeared at the onset of the stroke were not considered to represent previous cardiac disease. The authors concluded that disturbed cardiac function in stroke may lead to further cerebral hemodynamic damage.

Ambulatory ECG monitoring reveals an even higher incidence of arrhythmias. In one study 74% of 130 out-patients complaining of syncope and dizziness were found to have cardiac arrhythmias but none had focal cerebral symptoms. Walter et al., investigating 39 patients with cerebral ischemia, found that 10 had significant arrhythmias on ambulatory ECG monitoring and 8 of these were in cases with diffuse cerebral symptoms. The remaining 2 patients who were described as having transient ischemic attacks had symptoms equally well explained on the basis of global ischemia. In the study of McHenry et al. 6 of 10 patients with cerebral ischemic symptoms had cardiac arrhythmias and 8 had angiographic proof of significant cerebrovascular disease. The arrhythmias ranged from ventricular ectopics to intraventricular conduction defects and it was suggested that these cardiac abnormalities could account for the neurological event.

In an attempt to test the role of hypotension in transient cerebral ischemia, Kendell and Marshall used a tilt table to induce hypotension in 37 patients with a
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previous history of TIAs. Focal ischemic symptoms preceded global ischemic symptoms in only 1 case, in whom angiography had demonstrated carotid siphon disease.

Corday and Irving10 induced arrhythmias in dogs by open manipulation of the heart and produced a decrease in carotid artery flow as well as reducing mean arterial blood pressure to 50–60 mm Hg. They concluded that since carotid artery flow fell there was a decrease in the cerebral blood flow though they did not measure it directly. However, the significance of autoregulation of the cerebral blood flow was not appreciated until 195911 when it was realized that the cerebral blood flow is largely independent of mean arterial blood pressure until it falls to about 50% of the normal level. Further, during carotid artery clamping at endarterectomy reduced carotid artery blood flow bears little relationship to cerebral blood flow until it becomes seriously impaired.12,13 In the light of present knowledge, it is unlikely that the experiments of Corday and Irving produced any appreciable change in cerebral blood flow and probably not enough to induce focal ischemic lesions.

Reed et al.14 divided 290 patients requiring pacemakers into 3 groups; first a neurologically asymptomatic group, secondly those with generalized neurological symptoms, and thirdly a group of patients with focal ischemic symptoms. Only 4 patients had focal deficits and in only 2 of these could symptoms be attributed to their particular episode of cardiac dysfunction. One of these 4 patients had symptoms of global cerebral ischemia during pacemaker failure and not the focal symptoms originally experienced. The vast majority of their patients (81%) had generalized symptoms such as syncope or "gray outs". They concluded that transient focal cerebral ischemia rarely occurred secondary to reduced cardiac output from cardiac arrhythmias.

In only 6 patients in our series might the neurological lesion be attributed to a cardiac arrhythmia on a hemodynamic basis, suggesting that the hypotensive episode occurred in the presence of a stenotic cerebral arterial lesion. Unfortunately, since none of these 6 patients underwent cerebral angiography, this impression remains unconfirmed. Such a mechanism is easier to demonstrate in patients with reversible transient focal episodes than in those where the stroke is complete and irreversible. Five of these patients had sick sinus syndrome and since previous studies15,16 have attributed a major role to systemic embolism in patients with this syndrome, an embolic etiology cannot be excluded.

An alternative explanation for the high frequency of cardiac arrhythmias observed in stroke patients is that underlying systemic atherosclerosis is common to both cardiac and cerebral blood vessels. Hindfelt and Nilson17 found ECG abnormalities in patients with infratentorial infarctions and later investigated ischemic strokes in young adults and noted similar cardiographic changes. These authors concluded that there was no direct relationship between these changes and the cerebral lesions, but that they represented coincidental basic vascular disease. The significantly increased incidence of cardiac disease in stroke patients noted by us, as well as by other authors,5 presumably explains some of the arrhythmias that we have documented here.

We observed more cardiac arrhythmias in patients with lesions in the cerebral hemisphere than in those with lesions in the brain stem. This may represent a primary neurogenic effect or the release of neurotransmitter substances into the systemic circulation through the damaged blood brain barrier. Cardiac arrhythmias produced by experimental cerebral ischemia can be prevented by autonomic blockade.18 The well documented cases of cardiac arrhythmias and ECG changes secondary to intracranial hemorrhage20 may be explained by the finding of significantly elevated levels of plasma catecholamines.21

In a serial analysis of serum creatine phosphokinase (CPK) in 224 patients with acute cerebrovascular lesions22 elevated levels were found in 5% of cases. ECG changes in some of these patients also suggested myocardial damage unsuspected at the time. CPK-MB isoenzyme levels were assayed in a further 64 cases and found to be elevated in 17%. These observations suggest that clinically undetected myocardial lesions occur in association with the acute cerebrovascular lesion and may be responsible for some of the arrhythmias observed.

Acknowledgment

We thank Dr. Fred Demanuele, Biostatistics, Sunnybrook Medical Centre, for statistical advice.

References

Xenon-133 Inhalation Method for Regional Cerebral Blood Flow Measurements: Normal Values and Test-Retest Results

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EDWARD BASS, M.D., F.R.C.P., DAVID A. STUMP, PH.D.,
RODNEY WILLIAMS, M.S., RICHARD WITCOFSKI, PH.D.,
GEORGE HOWARD, M.S., AND JAMES F. TOOLE, M.D.

SUMMARY The purpose of this investigation is to determine the normal values for regional cerebral blood flow (rCBF) as determined by the xenon inhalation method of Obrist. Normal values for all rCBF parameters were measured in 15 healthy individuals. Our data are compared with the normal data obtained by other investigators. In addition, test-retest rCBF measurements were performed to determine the reproducibility of the method. Our results show that the method is highly reproducible when carried out in serial studies over a short period of time.

ONE METHOD for determining the pathophysiologic alterations in cerebral vascular disease is by regional cerebral blood flow (rCBF) measurements. These can be done in a serial manner to follow the natural history of the regional blood flow disturbance or to determine the effect of therapy in patients with transient ischemic attacks and acute strokes. A great deal of work has been performed using the invasive carotid injection method to measure regional cerebral blood flow. At the present time there is available a non-invasive method to measure regional cerebral blood flow. This was originally described by Mallett and Veall1-2 and was subsequently modified by Obrist and his colleagues.3-4 Data on normal values using this method have been reported by Obrist et al.,6 Corbett and Eidelman,6 and by Meyer et al.7 Normal values as well as test-retest results were described by Blauenstein and his associates.8 The background of the xenon-inhalation method has been discussed by Merory et al.9 and Meyer et al.7 10 The purpose of this paper is to report the results of regional cerebral blood flow measurements by the xenon inhalation method in normal individuals and to test the reproducibility of the method by serial measurements.

Methods

The equipment and methods used consisted of a 16-channel Harshaw TASC-5 system with the PDP-11-05 computer along with the computer program described by Obrist. Seven regions were measured over each side of the head. The studies were performed by having the subject breathe 8 millicuries of xenon-133 per liter for a period of 1 minute from a 10 liter Radx Ventl-Con Spirometer. The xenon in air was administered via a Bennett Benefit mask No. 5253 containing a port for withdrawal of continuous samples for radioisotopic analysis of the air curve and for an estimation of carbon dioxide levels. End-tidal air sampling was taken directly from the mouthpiece over a 2 inch scintillation probe in the shielded Ventl-Con to obtain the air curve for xenon. End-tidal air was pulled over the air probe at a rate of 1.5 liters per second and took less than 2 seconds to reach the air probe from the mouthpiece. The probes were Harshaw type M12 SHA1/3/4-x consisting of a 0.5 X 0.5 inch NaI (T1) crystal fitted with a 1 inch lead and stainless steel collimator with an 0.5 inch internal diameter.

Probes were placed in fixed positions mounted on a modified motorcycle helmet as suggested by Meyer et
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