Letters to the Editor

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Cardiac Abnormalities in Ischemic Cerebrovascular Disease

IAN R. STARKEY, MB, ChB, MRCP

RESPONSE BY: MASATO NISHIDE, M.D.

To the Editor:

The study reported by Nishide et al (Stroke 14,541–545, July–August 1983) is of interest in that atrial fibrillation and/or rheumatic heart disease (generally accepted as being associated with an increased risk of systemic thrombo-embolism) were found significantly more frequently in patients presenting with "ischemic cerebrovascular disease" than in the control subjects.

It is important to emphasize that the index cases in the reported case-control study were only those 350 patients with "ischemic cerebrovascular disease" (mainly completed stroke) who a) were admitted to the Division of Cerebrovascular Diseases of Hanwa Memorial Hospital, b) were admitted within 48 hours of the onset of symptoms and c) had a technically successful 2D echocardiogram performed. While it is impossible to overcome the inevitable problem of technically-unsuccessful echocardiography in a minority, one wonders how many patients in Japan who have a stroke are either not admitted to hospital or are admitted elsewhere than a specialist Department of Cerebrovascular Disease (at least initially after the onset of their symptoms) and whether, therefore, the patients investigated constitute a truly representative sample of all patients with ischemic cerebrovascular disease. Similarly, before deciding that the control group (350 sex- and age-matched hospital in-patients) truly represents the general population of Japan one would like to know exactly how the 350 were selected "in a blind manner" from 1000 eligible in-patients and it would also be nice to have some idea of the spectrum of disease in the control subjects. — a study which compared the prevalence (not "incidence"), by the way, as stated in the paper’s introductory paragraph of cardiac abnormalities in a group of patients with cerebrovascular disease with that in a control group consisting mainly of patients with heart disease would be a curious one indeed, while a control group consisting of, for instance, mainly surgical patients, might be expected to have a falsely-low prevalence of cardiac disease, the very presence of which might have precluded admission to hospital for consideration of surgical treatment. Without knowing the answers to these basic epidemiological questions, it would be dangerous to conclude, from these authors’ results alone, that a group of unselected subjects with stroke will necessarily have a higher prevalence of significant cardiac disease than the general population.

There are two more specific cardiological issues which also need clarification:

"Hypertrophic cardiomyopathy" (hereafter HCM) was found more commonly in stroke patients than in controls. Unfortunately the authors’ definition of HCM is ambiguous in that, while an end-diastolic interven-tricular septal thickness of greater than 1.5 cm is obligatory, it is not clear whether the additional criteria (such as systolic anterior motion of the anterior mitral leaflet, systolic semiclosure of the aortic valve, etc), "not sufficient for diagnosis in themselves" were nevertheless present in all the subjects labelled as having HCM. It is curious that, having mentioned that hypertension may be an etiological factor in the production of HCM in the elderly, the authors should assume that the greater prevalence of HCM in their patient group indicates that HCM is associated with an increased likelihood of cerebral embolism (would the authors be considering anticoagulant therapy in patients with this echocardiographic abnormality?) without at least discussing the other, and surely more likely, explanation, that hypertension is more common in stroke patients than in controls.

Finally, it is also unfortunate that the authors, who have in general been careful to define the echocardiographic abnormalities they describe, make no attempt to describe how they diagnosed the presence of an intracardiac thrombus, a notoriously difficult echocardiographic diagnosis, the limitations of which have been recently reviewed.1-2 This reaches crucial significance when we are told that 3 patients without evidence of structural cardiac disease or atrial fibrillation were found to have an intracardiac thrombus (unfortunately we are not told whether it is ventricular or atrial). While it is not possible, from the available data, to calculate the prevalence of intracardiac thrombs in patients with otherwise normal hearts, this finding would strengthen the argument that 2D echocardiography should be performed in all patients presenting with stroke, even if there is no clinical evidence of heart disease, a conclusion which has wide-ranging implications and differs from that reached in other echocardiographic studies of stroke patients.3-4-5

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RESPONSE

To the Editor:

The following is a response to I. R. Starkey’s letter:

To the Editor:

While our present material may not be perfectly representative of all stroke patients, we feel that it will be virtually impossible to obtain "ideal" material in the strictest sense of the word. Although both the exact number of stroke patients in Japan, and the percentage of those patients who are hospitalized are unknown, the distribution of the onset age of our patients with cerebral infarction was almost the same as that reported by K. Ueda, et al.1 Our 1,000 control cases were selected from inpatients of Hanwa Hospital, 80% were diagnosed as having trauma and/or gastrointestinal disease, while the remaining 20% were diagnosed as having diabetes mellitus, hypertension, ischemic heart disease, etc.2 DE studies were performed simultaneously on both the control group and the stroke patient group in the order of their admission into the hospital. We then selected 100 consecutive cases for the first age group 20 to 39 years old and 100 consecutive cases for the second age group 40 to 49 years old. A further 200 consecutive cases for each of the four age groups of every decade over 50 years of age were also selected.

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Finally, out of the 1,000 control patients, 350 were selected at random in numbers which corresponded to the number of actual ischemic cerebrovascular disease patients in each age group. This method of choosing a control group may be termed questionable, if it is considered to be the control group in a strict sense. As Dr. Starkey pointed out, the frequency of complicated cardiac disease varies according to the method by which the material is chosen. As the severity of ischemic cerebrovascular disease increases, the more frequently complications of cardiac disease will appear as mentioned in the "Discussion" section of our paper.

Among the 19 cases with HCM (hypertrophic cardiomyopathy) in the patient group in our study, systolic anterior motion of the anterior mitral leaflet was found in 11 cases, systolic semiclosure of AV in 8 cases, and HCM was confirmed by autopsy in 3 of the patients who died in the acute stage. As discussed in our paper, aging and hypertension have now been recognized as causes of HCM, and HCM is considered to be etiologically different in younger and older patients. Although it was not mentioned in the "Results" section of our paper, a history of hypertension was evident in 170 (or 49%) of the 350 cases in the patient group, and 136 (or 39%) of the 350 cases in the control group. No significant differences were found despite the tendency for hypertension to be more frequent in the patient group. Judging from this, the factor which causes ischemic cerebrovascular disease can be considered to be more closely related to structural changes of the heart than to hypertension itself.

As indicated by Dr. Starkey, a diagnosis of intracardiac thrombus is difficult. Furthermore, there are limitations concerning the size of thrombus which can be detected, depending on the type of instrument which is used. The diagnosis was made according to the results detected by 2DE regardless of the findings by M-mode. Although 2DE has been recognized as the most reliable instrument so far in diagnosing intracardiac thrombi, left atrography and/or left ventriculography were performed simultaneously as often as possible in order to reconfirm the diagnosis obtained by 2DE. The diagnostic capability of 2DE was confirmed when 11 dead cases in the acute stage were confirmed by autopsy to have had thrombi which were detected by 2DE.

In our present study, intracardiac thrombi were found in the left atrium in all 3 cases without structural cardiac disease or atrial fibrillation. In 2 of the 3 cases thrombi projected out of the left atrium, while in the third case a thrombus measuring 2 cm in diameter was attached to the posterior wall of the left atrium. Left atrography was performed in 2 of the above cases and revealed the presence of thrombi in both cases. All 3 of these cases were diagnosed by heart monitor as not having had any significant arrhythmia for 48 hours and the function of hemostasis was normal. Even while the significance of the above 3 cases remains unexplained, we believe the number of similar cases detected in the future will increase as the number of case studies by 2DE increases.

References

Federal Funding for Research in Stroke

To the Editor:

In a recent paper (Toole J.F., Toole W.W.: Federal funding for research in stroke and trauma: a clinical investigator's viewpoint. Stroke 15: 168-171, 1984) a footnote on page 169 states "The investment in stroke research by the American Heart Association was $499,763 in 1981-82." It would be of interest to know how this figure was derived, particularly because opinions about what constitutes "stroke research" may vary.

I have reviewed "Program Awards for Cardiovascular Research 1982-1983" published by the American Heart Association. Assuming a narrow definition for stroke research (studies of the pathophysiology of the cerebral circulation) at the time of publication the AHA was funding seven Established Investigators for approximately $250,000, three Clinician-Scientists for approximately $125,000, and five Grants-in-Aid for approximately $130,000. The total is quite close to the Tooles' figure for (apparently) one year earlier.

However, these figures far underestimate the case for support of stroke research by the AHA. In addition to funds allocated by the national organization, the Affiliates of the AHA support research locally. Also, funds are awarded for studies that would be included in a somewhat broader definition for stroke research: regulation and neural control of the circulation, functions of neurotransmitters: techniques for measurement of blood flow and for imaging; mechanisms of clotting and platelet activity: influences of risk factors: mechanisms of hypertension and atherosclerosis; functions of endothelium and smooth muscle; and studies of the neuromuscular junction, among others.

Nonetheless, some investigators or administrators may feel that the AHA should provide even more support for stroke research, in view of the total research budget of the AHA, the importance of the problem, and the size of the Stroke Council in relation to the other Scientific Councils of the AHA. Perhaps this is correct. However, as the representative of the Stroke Council to the Research Committee of the AHA I have not detected any explicit or implicit bias against funding stroke research. There are no categorical allocations or quotas for funding.

Rather, each application competes on its own merits. Funding for stroke research is limited by the relatively small numbers of applications that meet the specific published criteria for the research programs of the AHA, and by the relatively small numbers of applicants who are neither overqualified nor underqualified for support within AHA guidelines.

I would be pleased to discuss this matter in detail with anyone who wishes additional information.

Arthur G. Waltz, M.D.
San Francisco, California

To the Editor:

Dr. Waltz is correct in stating that support by the American Heart Association for all categories related to stroke exceeds the amount allocated from its central office — total funds invested by the AHA in stroke research, education, and prevention would also include those supplied by its Affiliates. However, it is our suspicion that support for stroke programs by the Affiliates is a very small proportion of the $30,000,000 AHA annual budget. An accounting would clarify the matter.

One of the main themes of our article was to suggest that heightened public awareness and visibility of the hazard of stroke are needed. The American Heart Association is very effective in educating the public about prudent diet, heart disease, and hypertension, but its commitments in the field of stroke are all but invisible, despite 20 years of effort on the part of many dedicated physicians and laymen to increase the commitment of the entire AHA in this effort.

Furthermore, it is our observation that lay action groups are the most effective means for increasing federal funding for research and that the AHA has provided this for the NHLBI, but a similar group within AHA which highlights the needs of the stroke field for NINCHS has yet to be achieved.

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http://stroke.ahajournals.org/content/15/6/1081.citation

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