Aortic Atheromas in Acute Ischemic Stroke Patients in Northern Israel

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Aim: There are currently no data on ethnic differences in aortic atherosclerosis in Arab and Jewish patients from northern Israel with acute ischemic stroke.

Methods: Data on demographic and risk factors alongside transesophageal echocardiography (TEE) data and treatment details for 509 patients with acute ischemic stroke were included in the study.

Results: The patients with aortic atheromas were older and had significantly more frequent vascular risk factors (hypertension, hyperlipidemia, and smoking), as well as vascular disease (ischemic heart disease, peripheral vascular disease, and carotid plaques). They were also treated with statins more often than those without aortic atheroma. Logistic regression analysis showed that age, smoking, ethnicity, and the presence of carotid plaques were independent predictors for aortic atheromas. Aortic plaques were found more frequently in Jewish patients than Arab patients (160 (41.9%) vs. 35 (27.3%); \( p=0.003 \)). This finding did not change after adjustment for age, sex, all vascular risk factors, and type of antithrombotic treatment. We did not find any difference between Arab and Jewish patients in the distribution of plaques by location or complexity before and after adjustment for age, sex, all vascular risk factors, or type of antithrombotic or lipid-lowering treatment.

Conclusions: Our findings emphasize the influence of ethnicity on the prevalence of aortic atheromas in acute ischemic stroke patients in northern Israel. The search for genetic, cultural, socioeconomic, and other factors explaining these ethnic differences should be the topic of future studies.


Key words: Aortic, Stroke, Ethnic, Israel

Introduction

One of the intriguing and unsolved issues in the etiology of acute ischemic stroke is the role of aortic atherosclerosis. There are extensive data in the literature exploring different aspects of aortic atherosclerosis in stroke patients. Whereas the question about the most appropriate treatment for those patients remains unanswered, there is no doubt that aortic atheromas are strongly associated with the appearance of the first as well as recurrent ischemic strokes and should be recognized as an important source of cardioembolism. Our study examines the influence of possible predictors, including the factor of ethnicity, on the prevalence of aortic atheromas, as detected by transesophageal echocardiography (TEE), in acute ischemic stroke patients in a bi-ethnic population of northern Israel.

Patients and Methods

This study is based on data from the computerized system used at Rambam Health Care Campus in Haifa, Israel, which contains all details about patients hospitalized since the end of 1999 as well as data from the Stroke Registry of the Department of Neurology. The collected data include demographic and risk factors, clinical status, work-up results, treatment regimens, and discharge details.

Data on 509 patients with acute ischemic stroke who underwent transesophageal echocardiography (TEE) as part of the work-up of patients with acute
ischemic stroke were used in the study. This means that the patients included in the study were non-consecutive stroke patients, but were consecutive patients undergoing TEE. The criteria for performing TEE were established by the joint cardio-neuro committee and included all patients 60 years old or younger, those above 60 with recurrent strokes, or those clinically or radiologically suspected as having an embolic stroke. All TEE studies were performed by senior cardiologists with a subspecialty in echocardiography including TEE. Examinations were performed using an Acuson Sequoia 512 machine (Siemens Medical Solutions, USA).

Ethnicity (Arab or Jewish) was established by place of birth and residence in addition to first and family names. Preliminary inter-observer agreement between four observers was employed for this method of classification of ethnicity in a bi-ethnic northern Israeli population evaluated in our laboratory, and agreement was found to be almost perfect, \( \kappa = 0.96 \), as assessed by Fleiss’ Kappa statistics.

Hypertension was defined as either systolic blood pressure \( \geq 140 \text{ mm Hg} \) or diastolic blood pressure \( \geq 90 \text{ mm Hg} \); the use of antihypertensive medication; or by a previously established diagnosis of hypertension (in most cases). In cases when hypertension was diagnosed for the first time we repeated measurements during hospitalization. Diabetes mellitus was defined as a recorded random blood glucose level \( \geq 200 \text{ mg/dL} \); the use of insulin or an oral hypoglycemic agent; or a previous diagnosis of diabetes mellitus. Hyperlipidemia was defined by the use of lipid-lowering medications; a fasting serum total cholesterol concentration of \( > 200 \text{ mg/dL} \), a low-density lipoprotein cholesterol concentration of \( > 140 \text{ mg/dL} \), a high-density lipoprotein cholesterol concentration of \( < 40 \text{ mg/dL} \), or a triglyceride concentration of \( > 150 \text{ mg/dL} \); or a previous diagnosis of hyperlipidemia. Atrial fibrillation was diagnosed by a physician who reviewed patients’ electrocardiograms; according to the medical records; or a previous medical diagnosis. Ischemic heart disease was defined as a history of myocardial infarction, angina pectoris, or signs of ischemia on the ECG or from the medical records. Peripheral vascular disease (PVD) was defined as a history of intermittent claudication, peripheral vascular surgery, or angioplasty or from a previous diagnosis.

The presence of carotid plaque was established by cervical duplex performed during hospitalization in our department as part of the work-up of acute stroke patients. Carotid plaque was defined as a focal structure that encroaches into the arterial lumen of at least 0.5 mm or 50% of the surrounding IMT value or demonstrates a thickness \( > 1.5 \text{ mm} \) as measured from the media-adventitia interface to the intima-lumen interface \[^{15}\].

TEE was performed according to standard practice guidelines, as previously described \[^{16, 17}\]. The thoracic aorta (ascending aorta, aortic arch, and descending thoracic aorta) was imaged in long- and short-axis views. Atherosclerotic plaques were defined as a focal structure encroaching into the arterial lumen.

Complex plaques were defined as protruding \( (> 4 \text{ mm thick}) \) plaques, ulcerated plaques (by visual assessment in cases when irregular crater within the plaque), or plaques with mobile debris, and simple plaques were defined in the absence of these complex features. In the current analysis, aortic atherosclerosis was defined as the presence of plaque of any degree in any aortic segment.

### Statistical Analysis

Initial basic comparisons between patients with and without aortic atheromas consisted of t-tests for continuous data and chi-square tests for categorical data. In order to control for the combined influence of multiple risk factors, multivariate logistic regression analyses were conducted. As a consequence of these analyses, the significant influence of ethnicity on the prevalence of aortic atheroma was further evaluated separately by individual risk factors, again using t-tests and chi-square analyses as appropriate. We also examined the influence of ethnicity on different characteristics of aortic plaque, such as thickness, ulceration, and complexity. JMP and SAS (SAS Institute, Cary, NC, USA) were used for statistical analyses.

### Results

Of the 509 patients with acute ischemic stroke that were included in the study, patients with aortic atheromas were older and had significantly more frequent vascular risk factors (hypertension, hyperlipidemia, and smoking) as well as vascular disease (ischemic heart disease, peripheral vascular disease, and carotid plaques). They were also treated with statins more often than those without aortic atheroma (Table 1). Logistic regression analysis of possible predictors of aortic atheroma showed that age, smoking, Jewish ethnicity, and the presence of carotid plaques were independent predictors of aortic atheromas (Table 2).

There were 381 (74.9%) of Jewish and 128 Arab patients. The Arab patients were younger than the Jewish patients and had a higher frequency of diabetes mellitus. There was no difference in the distribution
of other vascular risk factors or the frequency of coronary, peripheral, or carotid vascular disease between the Arab and Jewish patients (Table 3). Aortic plaques were found more frequently in Jewish patients than in Arab patients (160 (41.9%) vs. 35 (27.3%); \( p = 0.003 \)). This finding did not change after adjustment for age, sex, all vascular risk factors, or type of antithrombotic or lipid-lowering treatment. We did not find any difference between Arab and Jewish patients in the distribution of plaques by location or complexity (thickness, ulcerations, or mobile debris) before and after adjustment for age, sex, all vascular risk factors, or type of antithrombotic or anticoagulant treatment (Table 4).
Discussion

In the present study, we examined the possible predictors of aortic atheromas in acute ischemic stroke patients in northern Israel. We found that age, smoking, presence of carotid plaques, and Jewish ethnicity were independently associated with the presence of aortic plaques. Evidence regarding the independent influence of the first three factors on aortic atherosclerosis can be found in the literature. Age is a well-known predictor of the development of atherosclerosis on the whole and aortic atherosclerosis in part. Smoking is independently connected with both the development and progression of aortic atherosclerosis. According to our data, there is no correlation between other routine vascular risk factors and aortic atheromas. The correlation between the presence of carotid and aortic atheromas is known from the literature. Our data also confirmed this connection, demonstrating that double lesions - carotid and aortic - are frequent in stroke patients.

The most interesting finding of our study was undoubtedly the independent influence of ethnicity on the prevalence of aortic atheromas in stroke patients. Racial and ethnic differences in stroke have been the subject of strong and constantly growing interest in recent years, particularly in regard to the influence of ethnicity on the etiology, clinical picture, and outcome of ischemic stroke. Available data on the influence of ethnicity on aortic atherosclerosis in acute stroke patients are extremely limited. We found very few studies in the literature devoted to this important topic, all of which were focused on differences in the US population. Di Tullio et al. did not find significant differences in the frequency of aortic atheromas by ethnic group. Di Tullio et al. also performed TEE in 152 elderly patients with stroke and in 152 matched control patients. The authors found that complex atheromas are more frequent in stroke patients.
were twice as frequent in white patients with stroke as in black or Hispanic patients. Gupta et al. 38 who retrospectively examined the clinical data and TEE of 1553 ischemic stroke patients, found that whites had significantly greater plaque prevalence and plaque burden, even though they had significantly less hypertension and diabetes mellitus than their black counterparts. Similar results were found by Ward et al. 39, who evaluated 318 patients referred for TEE after unexplained stroke or transient ischemic attack. African-Americans were found to have fewer complex aortic atheromas than Caucasian patients, both before and after adjustment for vascular risk factors. Other studies investigating different populations can be found in the literature.40,41.

The results of these studies emphasize the importance of ethnicity in the prevalence of aortic plaques, which in turn are associated with ischemic stroke. Our study showed significant differences in the prevalence of aortic atheromas between the Arab and Jewish populations in northern Israel. Despite the higher occurrence of diabetes in Arab patients, while other routine vascular risk factors were equally distributed, aortic plaques were found more frequently in Jewish patients with ischemic stroke. Statistical adjustments were made for possible confounding factors, but this did not change our main result.

There are some limitations in our study. First, the TEE protocol was not pre-specified. Second, the sample size of subgroups was insufficient to establish a possible association of ethnicity with thicker and more complicated plaques. Third, both Jewish and Arab ethnic groups in northern Israel could be additionally divided into subgroups (e.g., Ashkenazi vs. Sephardic Jews and Muslim vs. Christian Arabs), with possible differences in genetic, socioeconomic, and cultural backgrounds. Another limitation of the study was the inability to perform sub-typing of patients by the etiology of ischemic stroke by TOAST classification. TOAST requires a workup including cervical ultrasound or CTA for evaluation of extra- and intra-cranial vessels. Such workup was not completed for all patients included in the study.

In conclusion, the results of our study emphasize the importance of ethnicity as a factor influencing the prevalence of aortic atheromas in acute ischemic stroke patients. The search for genetic, cultural, socioeconomic, and other factors explaining these ethnic differences, as well as the exploration of aortic atherosclerosis in other ethnic populations, should be the topic of future studies.

References

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