Arterial Stiffness and Stroke in Sickle Cell Disease

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Background and Purpose—Large vessels are also affected in sickle cell disease. The aim of this study was to assess several parameters in adult patients with sickle cell disease compared with control subjects and in patients with sickle cell disease with stroke.

Methods—Carotid arterial stiffness, intima-media thickness, and transcranial Doppler ultrasonography were measured.

Results—Arterial stiffness and transcranial Doppler velocity were significantly increased in 49 patients with sickle cell disease compared with 47 control subjects ($P<0.05$) and especially in patients with stroke ($P<0.05$).

Conclusions—These data suggest that transcranial Doppler and arterial stiffness might be associated to stroke in adult patients with sickle cell disease. (Stroke. 2012;43:00-00.)

Key Words: arterial stiffness ▪ sickle cell disease ▪ stroke

Sickle cell disease (SCD) is a disease of the microcirculation, although several theories also suggest involvement of large vessels. Because there are some common pathophysiological features between atheroma and SCD vasculopathy, the authors performed this study to assess carotid arterial stiffness (AS), intima-media thickness, and transcranial Doppler ultrasonography (TCD) in patients with SCD. We further evaluated whether these parameters were associated to stroke in patients with SCD.

Patients and Methods

Our patient population consisted of 49 patients with SCD matched for cardiovascular risk factors with 47 healthy subjects with the same ethnic origin admitted for post-traumatic disease. All subjects gave their written informed consent before entering the study in accordance with the Declaration of Helsinki. Eligibility criteria included all forms of SCD with patients at least 18 years of age.

Exclusion criteria were smoking, diabetes, hypercholesterolemia, pregnancy, hypertension, the use of cardiovascular drugs, SCD crisis or infection during the month before inclusion, and blood transfusion within the preceding 3 months.

All participants underwent clinical examination, had medical histories and treatments recorded, biological screening, and had, at the time of the clinical event and during the study, transthoracic Doppler echocardiography; carotid intima-media thickness, AS, and TCD velocity measurements.

Biological screening consisted of full blood cell count, hemoglobin electrophoresis, hemoglobin S, lactate dehydrogenase, haptoglobin, ferritin, fibrinogen, C-reactive protein, erythrocyte sedimentation rate, cholesterol, triglycerides, liver tests, erythropoietin, brain natriuretic peptide levels, fasting blood glucose, and creatinine.

Measurements of carotid intima-media thickness (Doppler B echography), AS using Peterson elastic modulus (Doppler M echography), and TCD (ultrasound system; Hitachi, Toshiba) were performed as described previously.1–4 Systolic, diastolic, time-averaged mean velocity of maximum blood flow and mean blood flow velocities were measured.

Comparisons between numeric data were performed using the Newman–Keul test or Student $t$ test for unpaired or paired data. Correlations were evaluated by linear regression analyses. A $P$ value 0.05 was considered statistically significant.

Results

Data from 47 sickle cell homozygous patients were completely recorded. The patients’ mean age was 27 years (range, 18–39 years) with a male to female ratio of 3:1.

Comparative demographical, biological, and echographical parameters of the patients with SCD and control subjects revealed that patients had elevated AS and TCD velocity ($P<0.05$) and lower blood pressure and cholesterol ($P<0.05$). Multiple stepwise regression analyses were performed (adjustments for age, height, heart rate, hemoglobin level, cholesterol). It revealed that AS was independently and positively associated with age and diastolic blood pressure ($R^2=0.63, F=15.56, P<0.001$) and TCD with age ($R^2=0.61, F=15.24, P<0.001$).

Ten (21%) patients with SCD had stroke. In patients with suggestive symptoms, stroke was diagnosed by a CT scan and confirmed by cerebral MRI. In 19% of the patients, silent stroke was exclusively detected by MRI. Both AS and TCD were significantly increased in patients with stroke versus patients without ($P<0.005$; TCD 138±25 cm/s versus 111±19 cm/s).
Patients with stroke had, at the time of the clinical event and during the study, increased TCD in 40% of the cases and elevated AS in 90%.

In patients with SCD without stroke, TCD velocities were elevated in 23% of cases and AS in 8.8%. No differences in treatment were observed among all these patients.

**Discussion**

Our study suggests that patients with SCD present an increased vascular rigidity and TCD velocity of large vessels as compared with control subjects.

TCD provides a noninvasive method of predicting stroke risk in children with SCD.

It has been investigated if the same velocity criteria are available in adults with SCD, because there are some limitations for TCD related to anatomic changes.

Some data suggest the usefulness of TCD in all patients with SCD to detect stroke risk.

It has been reported that TCD velocities in adults present a different pattern and a higher incidence of brain imaging abnormalities when compared with children.

However, TCD velocities in adults are lower than in children, and velocity criteria used in children are not useful.

Increased AS represents a marker of cardiovascular mortality. Some reports have observed a decreased AS in patients with SCD. Because stiffness is influenced by arterial pressure, we have expected that this parameter would be lower in our cohort (with lower blood pressure compared with control subjects); however, we found the opposite.

These data are consistent with reports that found that aortic strain, distensibility, and AS were elevated in adult SCD. Increased AS and endothelial dysfunction were detected by Aessopos et al; and some data suggest that endothelial-dependent vasodilation is altered from early childhood.

Our data strengthen the hypothesis of the similarities between atherosclerosis and SCD vasculopathy.

In our study, TCD was altered in 40% and AS in 90% of patients with SCD with stroke at the time of diagnosis and during the study.

Moreover, patients with SCD without stroke had an increased TCD in 23% and AS in 8.8% of cases.

Our data suggest that carotid AS is increased in patients with SCD compared with control subjects and further increased in patients with SCD with stroke.

These data cannot be formal, the retrospective nature of this study and the small sample size represent the major limitation of this study. Moreover, intracranial blood velocities can vary widely in normal subjects, and some of our patients had previous stroke and chronic therapy, which could modify AS.

A prospective study is required to evaluate if arterial rigidity should be included in the screening of cardiovascular risk in patients with SCD to identify high risk for patients with stroke.

**Disclosures**

None.

**References**


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