

CARDIAC SOURCES OF EMBOLISM IN IRANIAN STROKE PATIENTS

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Abstract

INTRODUCTION: Rheumatic valvular disease is a common complication of rheumatic fever in children in developing countries. Later in life, rheumatic valvular disease becomes an important modifiable risk factor of stroke. The incidence of rheumatic valvular disease and its complications are unknown in Iran.

METHODS: This is a prospective study of 302 consecutive patients admitted to a tertiary care hospital in Iran, with a diagnosis of non-hemorrhagic stroke between June 2005 and June 2006. All patients underwent diagnostic workup to determine stroke etiology according to clinical indications. Diagnosis and classification of stroke was made based on the PIC criteria.

RESULTS: Among 302 stroke patients (mean age: 66.78±14.36 years), 60 (20%) (mean age: 65.61±17.48 years) had cardiac sources of embolism (CSE). Rheumatic mitral stenosis was present in 28 (46.6%) of these patients. Atrial fibrillation was documented in 19 patients (67.8%) with rheumatic valvular disease. The remaining 32 patients (53.3%) had other CSE. In the latter group, 8 patients (25%) had non-valvular atrial fibrillation. In the entire group with CSE, 30 were candidates for anticoagulation; among them, 14 (46.6%) were anticoagulated, but only 6 (20%) were within therapeutic range at the time of stroke.

CONCLUSIONS: Rheumatic valvular disease seems to be the most common CSE in Iran. Many patients with rheumatic or non-rheumatic CSE are not adequately managed for secondary prevention of cardioembolic stroke.

Key Words: Cardioembolic, stroke, rheumatic.

ARYA Journal 2006; 2(1): 7-9 Archive of SID

Introduction

While a quarter of strokes are cardioembolic, Cardiac Source of Embolism (CSE) is considered a modifiable risk factor of stroke.

The distribution of cardiac pathology as the cause of embolic stroke varies between countries.

While non-valvular atrial fibrillation is the most prevalent CSE in developed countries, rheumatic valvular disease continues to prevail as the most common cause of CSE in the developing world.¹

Data on the incidence and prevalence of rheumatic heart disease in developing countries is lacking.²

Adequate anticoagulation offers stroke prevention in patients with rheumatic valvular disease or other potential CSE.

Prevention of rheumatic valvular disease and its complications is inadequate in developing countries.²

The incidence of stroke complicating rheumatic valvular disease is in the range of 1.5% to 4.7%.³

Unfortunately, epidemiologic studies on rheumatic valvular disease and its complications are in short supply. However, many tertiary care centers are involved with managing the complications of this preventable childhood disease. Below, we present our experience on CSE in a tertiary care center in Iran.

Materials and methods

Valie-Asr Hospital is a tertiary care university hospital in Khorasan, Iran, serving a population of 400,000.

All consecutive patients admitted to this hospital with a diagnosis of non-hemorrhagic stroke were included in this prospective observational study between June 2005 and June 2006. Stroke was defined as an ischemic focal neurological deficit persisting for at least 24 hours.⁴ Etiologic classification of stroke was made by a stroke neurologist according to the PIC criteria.⁵ Patients underwent a standard battery of diagnostic investigations.

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Date of submission: July 14, 2006

Date of acceptance: July 30, 2006

This included brain CT, ECG, blood electrolytes, blood count and differential, coagulation profile, carotid Doppler, trans-thoracic echocardiogram, and measurement of fasting blood glucose (FBS) and lipid profile. Trans-esophageal echocardiogram was obtained in patients with non-diagnostic trans-thoracic echocardiogram despite high suspicion of CSE. 24-hour Holter monitoring was performed for patients with history of syncope and/or palpitation, or high suspicion of CSE with non-diagnostic echocardiography and ECG. Three serial blood cultures were requested for any stroke patient with fever and heart murmur or valvular vegetation detected by echocardiography.

Data on patient demographics, clinical presentation, and diagnostic workup was kept in a database.

Results were expressed as mean \pm standard deviation for quantitative variables and number with percentage for qualitative variables.

Univariate analysis was performed using independent sample t-test, Mann-Whitney-U test, and Pearson chi-square test, when appropriate. P values less than 0.05 were considered as statistically significant.

Results

Non-hemorrhagic stroke was diagnosed in 302 patients (159 females, 143 males) in 2005. CSE was diagnosed in 60 (19.8%) of these patients, 37 (61.6%) of whom were female. Mean age of the group with CSE was 65.61 ± 17.48 years. Mean ages of female and male patients were 64.59 ± 2.80 years and 67.26 ± 3.83 years, respectively. Among patients with CSE, rheumatic valvular disease was detected in 28 (46.6%), 19 (67.8%) of whom had atrial fibrillation. The remaining 32 patients (32/60; 53.3%) had other types

of CSE; 8 patients in the latter group (8/32; 25%) had non-valvular atrial fibrillation.

Table 1 represents the frequency of various types of CSE in our 302 stroke patients.

In the rheumatic valvular disease group, there were significantly more female patients (OR=2.34, CI*=0.97-6.24, P=0.036).

Gender was not a significant factor in the non-rheumatic CSE group (OR=1.02, CI=0.46-2.26, P=0.89). The average age of female patients in the rheumatic valvular disease group was 59.30 ± 16.6 years, and that for male patients was 61.12 ± 17.54 years, with no significant difference between the two genders (P=0.899). The average age of female patients in the non-rheumatic CSE group was 70.82 ± 15.82 years, and that for male patients was 70.53 ± 18.59 years, with no significant difference between the two genders (P=0.894).

No significant difference was observed between the number of patients referred from urban or rural areas in the rheumatic CSE group (OR=1.0, CI=0.45-2.31, P=0.96).

Twenty-four patients were candidates for anticoagulation in the rheumatic valvular disease group, however, only 11 (11/24; 45.8%) were anticoagulated and INR was found to be within therapeutic range only in 5 (5/24; 20.8%). Among the non-rheumatic patients, 6 were candidates for anticoagulation, but only 3 (3/6; 50%) were anticoagulated, and only 1 (1/6; 16.6%) was within therapeutic range.

A total of 30 patients in the entire group with CSE were candidates for anticoagulation and among them, 14 (14/30; 46.6%) were anticoagulated but only 6 (6/30; 20%) were within therapeutic range.

*Confidence Interval

TABLE 1. CSE in 302 stroke patients

<i>Cardiac disorders</i>	<i>Female</i>	<i>Male</i>	<i>Total</i>
Valvular atrial fibrillation (VAF)	12	7	19
Non-valvular atrial fibrillation (NVAf)	4	4	8
Mechanical mitral valve (1 with VAF)	1	-	1
Mitral annular calcification (MAC)	2	-	2
Rheumatic mitral stenosis (18 with VAF)	7	1	8
Mitral valve prolapse (MVP)	7	2	9
Non-bacterial endocarditis	1	1	2
Left ventricular thrombus	-	1	1
Acute myocardial infarction (1 with NVAf)	-	1	1
Left ventricular aneurysm	-	1	1
Left ventricular akinetic segment	-	1	1
Congestive heart failure (CHF) (1 with NVAf)	2	4	6
Patent foramen ovale (PFO)	1	-	1
All CSE	37	23	60

Discussion

Rheumatic heart disease is an important cause of mitral and aortic valve disease in developing countries.⁶⁻⁸ Almost half of the cardioembolic strokes in developed countries are secondary to non-valvular atrial fibrillation and 7.6% of the cases of CSE are due to rheumatic heart disease.⁹ Rheumatic valvular disease accounted for 46% of the cases of CSE in our patients and was present in 70.3% of atrial fibrillation cases. The incidence of rheumatic valvular disease was significantly higher in females. This is in agreement with previous reports.^{8,10} The cause of this gender discrepancy is unknown.⁸

Epidemiologic studies on rheumatic heart disease in Iran are lacking. Therefore data is not available on early diagnosis and management of streptococcal throat infection and its complications. This hampers the institution of effective primary and secondary prevention measures. Further improvement in quality of manufacturing and storage of antibiotics is recommended in developing countries.²

There are clear indications for anticoagulant therapy in patients with CSE,^{11,12} whereas adequate anticoagulation was achieved in 20% of our patients who were candidates for this treatment. The reasons for inadequate management of CSE are largely unknown, nonetheless, inadequacies in logistics and infrastructure may be contributing factors.^{13,14}

Through our study, we opened only a small window to rheumatic valvular disease as a public health concern. Much work is needed on the epidemiology and prevention of rheumatic valvular disease and its complications in Iran, as well as other developing countries.

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