

Imaging and Clinical Predictors of Unfavorable Outcome in Medically Treated Symptomatic Intracranial Atherosclerotic Disease

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Background: Patients with symptomatic intracranial atherosclerotic disease (sICAD) have an increased risk of stroke and vascular death. The aim of the study was to evaluate the natural history and outcome of patients with sICAD treated medically. *Methods:* The study population was first-ever transient ischemic attack (TIA) or stroke patients presenting to our institute who on vascular imaging had isolated intracranial atherosclerosis as cause of their symptoms and have a follow-up of 90 days. Unfavorable outcome was defined as occurrence of TIA, stroke, acute coronary event, and/or vascular death. *Results:* Fifty-three (11.8%) of the 449 ischemic stroke patients had sICAD. The risk of stroke in sICAD was 8.9%, 11.1%, 13.3%, and 15.6% in first 7 days, 30 days, 90 days, and 1 year, respectively. Five (11.1%) had cardiovascular events and accounted for 50% of mortality. The predictors of unfavorable outcome were presented as limb weakness (85.7% versus 58.8%, hazard ratio 1.5; 95% confidence interval [CI], .05-.9; $P = .04$), National Institutes of Health Stroke Scale (NIHSS) score 8 at admission (50% versus 5.9%, hazard ratio 8.5; 95% CI, .007-.5; $P = .02$), magnetic resonance imaging (MRI) with multiple diffusion-weighted imaging (DWI) lesions (65.4% versus 26.7%; 95% CI, .04-.7; $P = .01$), and angiography suggestive of diffuse atherosclerosis (50% versus 11.8%; 95% CI, odds ratio .02-.7; $P = .009$). On stepwise multiple regression, variables for unfavorable outcome were NIHSS score of 8 or more at admission ($P = .001$), multiple DWI lesion on MRI ($P = .04$), and diffuse atherosclerosis on angiography ($P = .006$). *Conclusion:* The patients with sICAD have a high risk of stroke and cardiac events even on aggressive medical treatment. Clinical and imaging features can identify this high-risk group. **Key Words:** Intracranial atherosclerotic disease—predictors—stroke—intracranial stenosis—treatment—TIA.

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There is no conflict of interest, and the study has received ethics approval.

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Introduction

Intracranial atherosclerotic disease (ICAD) is a leading cause of ischemic stroke, accounting for 8%-50% of patients,¹ with higher incidence and prevalence in the Asian as compared with the Caucasian population.^{1,2} Following the stenting versus aggressive medical therapy for intracranial arterial stenosis (SAMMPRIS) study, the present consensus opinion recommends medical management with dual antiplatelet agents for 90 days followed by aspirin and aggressive control of risk factors including hypertension, diabetes, smoking, and dyslipidemia.³ The annual recurrent stroke or

vascular death in the first year in patients with ICAD on medical management was 10%-17%.^{4,5} The risk persists and increases on long-term follow-up. In addition, silent myocardial ischemia was found in more than 50% of patients with ICAD, which is an important factor deciding the outcome.⁶ There is a need of risk stratification and risk prediction in this group of patients to determine effective management plans. The main aim of our study was to define predictors of unfavorable prognosis in symptomatic intracranial atherosclerotic disease (sICAD) patients on medical management.

Methods

Study Patients

We reviewed charts of all patients with a diagnosis of acute stroke or transient ischemic attack (TIA) attending the emergency department, general neurology clinic, or the stroke clinic of this tertiary care center. The study period was from January 2008 to March 2011. The inclusion criteria for the study were patients presenting with first-ever ischemic stroke or TIA, age more than or equal to 18 years, on contrast angiography either with computed tomography (CT) or magnetic resonance imaging (MRI) or catheter angiography showing isolated ICAD in the symptomatic vessel, a minimum follow-up of 3 months, and other potential causes like extracranial ipsilateral carotid stenosis or vertebral artery stenosis of more than 50%, and cardioembolic source have been ruled out.

Imaging Analysis

All the imaging was reviewed independently by 2 experienced neuroradiologist (C.K. and B.T.) both having experience in neuroradiology of more than 10 years. The images reviewed included the CT head, MRI brain, and vessel imaging. When patients had multiple angiography images, catheter angiogram was considered gold standard followed by CT angiography and then contrast-enhanced MR angiography, and time-of-flight MR angiography was excluded from the study. Symptomatic ICAD was defined as the degree of stenosis, measured at its point of maximal narrowing, and compared with normal section of the vessel distal to the stenosis ($[\text{normal distal lumen diameter} - \text{residual lumen}] / \text{normal distal lumen diameter}$) or proximal to the stenosis if ectasia or bifurcation was identified downstream of stenosis.⁷ Diffuse intracranial disease was modified from the previous definition given by Kumar et al.⁸ as stenosis in multiple intracranial arteries and multiple segments of stenosis in 1 artery. Diffusion-weighted imaging (DWI) and apparent diffusion coefficient MRI lesion pattern were classified as described by Bang et al.⁹ The MRI brain and vessel imaging of a patient with ICAD is shown in [Figure 1](#).

Treatment and Follow-up

All patients received standard of care, antiplatelet therapy either dual or single for the study duration depend-

ing on the discretion of the clinician, statins irrespective of the cholesterol status, and optimal management of the risk factors including hypertension, diabetes, and smoking. All patients with stroke and/or TIA were followed up 3 months after the index event and every 6 months thereafter in the stroke prevention clinic. Patients who were lost to follow-up were contacted by phone first, if no response then a letter was sent to them, and if still no response then a social worker visited the patient. Patients who were not traceable were considered lost to follow-up and were excluded from the study results.

Outcome Measures

The primary outcome measure was unfavorable outcome at the end of 90 days defined as the occurrence of TIA, stroke, acute coronary event, or vascular death and modified Rankin Scale score of 3 or more. The secondary outcome measure was recurrent stroke at the end of 90 days and 1 year.

Statistical Analysis

We used SPSS version 17.0 for Windows (SPSS, Inc., Chicago, IL) for statistical analysis. Descriptive statistics was used to measure the frequencies, mean, and median. We used univariate analysis with *P* less than .05 to identify variables predicting unfavorable outcome. Hazard ratio was calculated for each significant variable. We further applied multiple logistic regressions with 2-tailed tests to those variables to identify independent predictors of unfavorable outcome with *P* less than .05.

Results

Natural History

Of the total 449 patients with first-ever stroke, 11.8% (*n* = 53) had isolated ICAD. Forty-five (men = 30, 66.6%) patients with mean age of 58.16 ± 9.7 years and median National Institutes of Health Stroke Scale (NIHSS) score 4 (range 0-21) at admission had a complete 3 months follow-up and formed the study population. Because of the late arrival (median [interquartile range] 5 days [1-11]) to emergency or stroke prevention clinic, none of our study patients received thrombolysis. The neurovascular imaging including CT angiography or MR angiography or catheter angiography was performed at median (interquartile range) of 6 days (2-14). Twenty-eight (62.2%) patients had unfavorable outcome after mean follow-up of 15 ± 10.4 months (range 3-40 months). Recurrent stroke occurred in 16.9% (*n* = 9) or recurrent TIA in 13.2% (*n* = 7), acute cardiac event in 9.4% (*n* = 5, 1 had sudden cardiac death, 2 had acute coronary event, 1 had congestive cardiac failure, and the last one had unstable angina), early neurologic deterioration in 5.7% (*n* = 3), and 7.5% died during the follow-up

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