Risk Factors for Acute Cardioembolic Brain Stroke in Acute Myocardial Infarction

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ABSTRACT

Background and Objectives : An ischemic brain stroke following acute myocardial infarction (AMI) has a poor clinical prognosis, which primarily results from a thromboembolism. We determined the risk factors of acute cardioembolic brain stroke events that developed concurrently with, or soon after, the onset of AMI. **Subjects and Methods :** We evaluated 38 AMI patients, who developed subsequent acute cardioembolic brain stroke during their index admission, by comparing their clinical and angiographic characteristics with those of 1,443 consecutive patients that had not experienced a brain stroke. Strokes that occurred between the onset of the AMI and patient discharge were analyzed. The incidences of cardiovascular risk factors, and the clinical and angiographic characteristics, of patients admitted to Ewha Womans University Mokdong Hospital, with a diagnosis of AMI over a 10-year period, were compared. **Results :** In the univariate analysis, the frequencies of atrial fibrillation (21% vs. 4%, p=0.011) and hypertension (71% vs. 48%, p=0.030), and a left ventricular ejection fraction <40% (52% vs. 33%, p=0.039) were significantly higher in patients that had had an acute cardioembolic brain stroke. In a logistical regression analysis, atrial fibrillation was found to be a significant contributor to the subsequent development of an acute cardioembolic brain stroke in the AMI patients (p=0.023, β =2.025, odds ratio=7.6). Mean follow-up period, which was mainly determined as the time to death after the AMI, was shorter in the acute cardioembolic brain stroke patients (8.5 month vs. 24.3 month, p=0.002). The death rate during the mean follow-up period was much higher in these patients (50% vs. 29%). **Conclusion :** We found that the presence of atrial fibrillation at the time of admission for an AMI was associated with an increased risk of a subsequent acute cardioembolic brain stroke. **(Korean Circulation J 2005;35:353−356)**

KEY WORDS : Myocardial infarction ; Stroke, acute ; Atrial fibrillation ; Thromboembolism.

Introduction

Epidemiological studies have shown that an acute stroke (AS) and acute myocardial infarction (AMI) have common risk factors, like age, gender and hypertension.[1-5] Moreover, stroke after an AMI occurs due to pathological conditions of the heart. The total incidence of strokes after an AMI, including patients without a thrombolysis, ranges from 1.0 to 1.3%, and about 0.8% are ischemic strokes due to cardioembolism or an unknown etiology.[6-10] No data concerning a cardioembolic brain stroke after the onset of AMI are available for the Korean population. Therefore, we evaluated the AMI patients that subsequently experienced a cardioembolic brain stroke to identify the risk factors contributing to a cardioembolic brain stroke.

Subjects and Methods

Subjects

We evaluated 38 AMI patients, who developed a subsequent cardioembolic stroke during their index admission, by comparing their clinical and angiographic characteristics with those of 1,443 consecutive patients that had not experienced a brain stroke. Patients that had suffered strokes between the onset of the AMI and their discharge were analyzed. The cardiovascular risk factors, and clinical or angiographic characteristics, of the patients admitted to Ewha Womans University Hospital, with a diagnosis of acute myocardial infarction over a 10-year period, were assessed and compared between these two patient groups.

The AMI was diagnosed using the WHO definition;

i.e., when patients had at least two of the following three criteria: a chest pain typical of myocardial ischemia, initial and serial conventional electrocardiographic changes in the standard or precordial leads, and enzymatic evidence of myocardial necrosis.[11] An acute stroke was defined using the WHO definition as, "rapidly developing clinical signs of focal (or global) disturbance of cerebral function lasting more than 24h (unless interrupted by surgery or death), with no apparent cause other than one of vascular origin". Patients with intracerebral hemorrhage were excluded. The definition used for a cardioembolic stroke was similar to that of the National Institute of Neurological Disorders and Stroke Classification.[12] Patients with a recorded history of hypertension, or with three or more successive blood pressure measurement exceeding 140/90 mmHg during hospitalization, were considered hypertensive. Diabetes mellitus was determined to be present if documented in medical records or if a patient required dietary sugar restriction, insulin, or oral hypoglycemic drugs during hospitalization, in addition to having positive criteria for diabetes.[13]

Statistical analysis

Data were expressed as means ± SD for continuous variables, and as frequencies for variables on a nominal scale. For group comparisons Student's t-, ANOVA or chi-squared tests were used. Logistical regression analysis was used to determine the risk factors for cardioembolic stroke after an AMI. P<0.05 were considered significant.

Results

The mean time from admission due to the AMI to the taking of brain CT or MRI for the detection of brain stroke was 4.2 ± 2.1 days. The frequencies of atrial fibrillation (21% vs. 4%, p=0.011) and hypertension (71% vs. 48%, p=0.030), and a left ventricular ejection fraction <40% (52% vs. 33%, p=0.039) were significantly higher in patients that had experienced a cardioembolic brain stroke (Table 1). Age, gender, frequency of anterior myocardial infarction, ST segment myocardial infarction, previous myocardial infarction, a previous ischemic stroke, diabetes mellitus or hypercholesterolemia were no different between the two groups. The drug histories, including aspirin, ticlopidine or clopidogrel, were similar in the two groups. The peak CK-MB level, frequency of thrombolytic treatment, left anterior descending artery (as an infarct-related artery), TIMI 3 flow of an infarct-related artery and extension of coronary disease, including normal or 1-vessel disease, were comparable between the two groups. In the logistical regression

Table 1. Characteristics of the patients with an acute myocardial infarction, according to the development of a cardioembolic brain stroke

	With cardioembolic brain stroke (n=38)	Without cardioembolic brain stroke (n=1,443)	p
Age (yrs)	70 ± 11	69 ± 12	0.568
Male	53%	50%	0.806
Anterior myocardial infarction	44%	64%	0.108
STEMI	50%	60%	0.367
Atrial fibrillation on admission	21%	4%	0.011
Previous myocardial infarction	8%	12%	0.571
Previous ischemic stroke	11%	8%	0.643
DM	45%	25%	0.051
Hypertension	71%	48%	0.030
Hypercholesterolemia	174 ± 51	178 ± 41	0.740
Smoking	45%	69%	0.020
LVEF<40%	52%	33%	0.039
Peak CK-MB (IU/L)	100.1 ± 143.3	250.7 ± 488.1	0.069
Use of aspirin before admission	18%	14%	0.524
Use of ticlopiding/clopidogrel before admission	8%	14%	0.409
Thrombolysis	16%	17%	0.849
Coronary angiography	29%	69%	0.000
Coronary angioplasty	24%	58%	0.012
Normal or 1-vessel coronary artery	30%	31%	0.777
IRA in LAD	61%	62%	0.949
TIMI 3 flow in IRA	30%	27%	0.733
Mean follow-up time (months)	8.5 ± 10.7	24.3 ± 17.4	0.002
Follow-up patient	50%	46%	0.170

Mean ± SD. STEMI: ST segment elevation myocardial infarction, DM: diabetes mellitus, LVEF: left ventricular ejection fraction, LAD: left anterior descending artery, IRA: infarct related artery

Table 2. Logistical regression analysis for the occurrence of an acute cardioembolic stroke accompanied by an acute myocardial infarction

	Atrial fibrillation	Hypertension	Smoking	Left ventricular ejection fraction
Odds ratio	7.6	0.4	2.2	0.8
β	2.025	-1.014	0.778	-0.171
p	0.023	0.050	0.113	0.730

analysis, atrial fibrillation was identified as a significant contributory risk factor for the subsequent development of a cardioembolic stroke in patients with an AMI (p= 0.023, β=2.025, odds ratio=7.6) (Table 2). Follow-up was achieved in nearly half the patients, and the mean follow-up period, mainly determined by the time to death after the AMI, was shorter in the cardioembolic stroke group (8.5 month vs. 24.3 month, p=0.002) (Table 1). The death rate during the mean follow-up period was much higher in these patients (50% vs. 29%).

Discussion

This study demonstrated the presence of atrial fibrillation at the time of admission for an AMI was associated with an increased risk of a subsequent acute cardioembolic brain stroke.

The determination of the risk factors and clinical features of a cardioembolic brain stroke are highly relevant issues, given the high mortality and risk associated with recurrent embolism, such that anticoagulation might be used as an effective prophylaxis. A cardiac source of an embolism has been reported in around one third of patients with cerebral infarction.[14-22] The various sources of a cardiogenic embolism represent distinct types of heart disease, each with unique demographic features and risks of primary or secondary emboli.[22] Recent data has shown that hypertrophic hypertensive cardiac disease, complicated by atrial fibrillation, is the most frequent cardiac source of emboli in cardioembolic stroke patients. Other important cardiac sources identified include; isolated atrial fibrillation, rheumatic mitral valve disease, and systolic left ventricular dysfunction of ischemic and non-ischemic causes. However, the incidences of traditional emboligenous-prone cardiac disorders, such as mitral valve prolapse and mitral annular calcification, have been reported to be low.[17]

The total incidence of strokes after an AMI has been reported to be 1.0%.[6-8] In the present study, 2.5% of the AMI cases experienced a cardioembolic brain stroke, which is somewhat higher than that reported previously. A recent report showed that for patients <75 years old with an AMI, almost 60% of those that developed a stroke presented with an anterior wall myocardial infarction, compared with only 38% of those not developing a stroke.[23] These data support the hypothesis that, "em-

boli from the left ventricle following an AMI are an important cause of a peri-AMI associated stroke". In the setting of an acute transmural infarction, patients with an anterior infarction and severe apical-wall-motion abnormality (akinesis or dyskinesis) are at high risk of developing a left ventricular thrombus; these thrombi were diagnosed an average of five days after the infarction.[24] Left ventricular thrombi, which project into the lumen, are more likely to embolize, and a trend of an association between greater mobility and embolization has been reported.[25] A cardioembolism tends to occur more in the acute phase rather than the chronic phase after an AMI.[26] Although, in the present study, we could not check for either the existence of a left ventricular thrombus or the exact extent of the left ventricular regional wall motion abnormality, due to the retrospective nature of our study. A left ventricular ejection fraction <40% was more prevalent in those that had experienced a cardioembolic brain stroke. Our study suggests that left ventricular wall motion abnormality might be associated with cardioembolization, although this was not found to be significant in the logistical regression analysis.

Atrial fibrillation is widely accepted as one of most significant risk factors for a cardioembolic brain stroke.[17] Recent data from cardioembolic brain stroke patients has shown that atrial fibrillation, without organic heart disease, was present in 22.1%, but with organic heart disease this figure was 57.7%.[17] However, in those with ischemic heart disease only, severe left ventricular systolic dysfunction was identified as a high risk cardiac source of embolism. The presence of intraventricular thrombosis, and the predominance of cases with a sinus rhythm, confirms the primary role of severe left ventricular systolic dysfunction, rather than atrial fibrillation, as a cardiologic substrate in patients with a cardioembolic stroke.[17] This observation differed somewhat from the findings of the present study, which indicate that atrial fibrillation is the most significant risk factor for a cardioembolic brain stroke, even in those with an acute myocardial infarction, one of most important ischemic heart diseases. The difference in the follow-up duration might be one of the possible reasons for these discrepancies. We followed the acute phase after AMI onset; whereas, the previous report followed the patient over several years. The OPTIMAAL trial aimed to determine the frequency of atrial fibrillation, its impact on the clinical outcomes of patients with AMI and the left ventricular dysfunction.[27] This trial included 5,477 patients with both an AMI and signs of left ventricular dysfunction. Patients with atrial fibrillation at the baseline were found to have a higher risk of mortality than those without. New-onset atrial fibrillation was associated with an increased subsequent mortality over the first 30 days.

A recent study showed a small subset of patients that

presented with a stroke, but without any signs or symptoms of AMI. 1.6% of the total AMI, 22% of the "stroke complicating MI" cases, presented with a stroke at the time of admission. The nature of these presentations highlights the importance of urgent EKG in all cases of an acute stroke.[28]

The provision of long-term anticoagulation is currently a class Ia recommendation in patients with a documented left ventricular thrombus, but a class IIa recommendation for patients with significant apical wall motion abnormalities.[29] In view of these recommendation, and the findings of the present study, anticoagulation can not be overemphasized, in patients with atrial fibrillation following a large anterior AMI, with regard to the prevention of a cardioembolism.

The present study had several limitations; firstly, due to the small numbers of echocardiographic studies available, we could not evaluate the coexistence of a left ventricular thrombus, or regional wall motion abnormalities, with a cardioembolic stroke. Secondly, the onset times of atrial fibrillation or brain stroke were not determined due to incomplete data. in the near future, we hope to conduct well-organized, prospective studies.

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