

EARLY STROKE IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION: INCIDENCE, RISK FACTORS AND CLINICAL OUTCOMES

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Abstract

Background: Limited data is available about stroke developing after acute myocardial infarction (AMI). We investigated the incidence, risk factors and in-hospital outcome of stroke after AMI in clinical practice with and without use of thrombolysis.

Methods and results: We analyzed data from a prospective registry of consecutive patients admitted to the coronary care unit (CCU) at Mubarak Al Kabeer Hospital in Kuwait. Of 2481 patients admitted with AMI between 1999 and 2003, 29 (1.2%) developed stroke during their hospital stay. Age older than 60 years (OR 5.5; 95% CI 2.4 to 12.5; $P < 0.001$) and systolic blood pressure higher than 160 mmHg (OR 3.2; 95% CI 1.1 to 9.5; $P < 0.04$), were identified as independent predictors for stroke among patients with AMI. Patients who received thrombolytic therapy were not at an increased risk for developing stroke (OR 0.7; 95% CI 0.2 to 2.0). Patients developing stroke were 12 times more likely to die during hospitalization compared with patients who did not develop stroke (OR 12.6; 95% CI 5.4 to 26.7; $P < 0.001$).

Conclusions: Stroke is an infrequent but serious complication of AMI. Older age and high systolic blood pressure at admission are independent predictors of stroke. *Heart Views* 2007;8(4):142-146. © Gulf Heart Association 2007.

Key Words: ? stroke ? acute myocardial infarction ? risk factors ? prognosis

Introduction

Stroke is an uncommon but serious complication of acute myocardial infarction (AMI). The incidence and type of stroke has changed with the routine use of thrombolytic therapy for AMI. In the pre-thrombolytic era stroke occurred in 1.7-3.2% after AMI, and almost all strokes were thromboembolic¹. In the Thrombolytic era the incidence of stroke has decreased to about 1.2%, and intracerebral hemorrhage became a frequent type of stroke². Furthermore, some of the usual risk factors for stroke, such as anterior location of AMI, have recently been disputed^{3,4}. In this study we aim to determine the incidence, risk factors and in-hospital outcome of stroke after AMI in our clinical practice.

Methods

We analyzed data from a prospective registry of unselected patients consecutively admitted to the coronary care unit (CCU) of Mubarak-Al-Kabeer Hospital in Kuwait between 1999 and 2003. All patients admitted to the CCU during this period

were registered and followed up during their hospital stay. Using a structured data collection form. This form included information on patients' demographics, past medical history, risk factors, physical examination, ECG at presentation, cardiac enzymes, lipid profile, blood sugar, admission and discharge diagnosis, thrombolytic therapy administration, and in-hospital course and outcome.

The diagnosis of AMI was based on the following criteria: Ischemic type of chest pain, diagnostic serial ECG changes, and elevation of creatine kinase (twice or more the normal value with at least 3% MB fraction) or Troponin-I.

Stroke was defined as the presence of a new neurological deficit that persisted for longer than 24 hours. The diagnosis was confirmed and the stroke type identified by a CT scan in all but one of the patients with the clinical diagnosis of stroke.

Statistical analysis

Categorical variables were compared using chi-square test. When the assumptions related to use of chi-square test was violated Fisher's

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Table 1: Demographic and clinical characteristics at admission, co-morbid variables and early therapy of patients with and without stroke after AMI.

Variables	With Stroke (n=29)	Without Stroke (n= 2452)	P - value* (Univariate)
Age in years (mean \pm SD)	66 \pm 11	55 \pm 12	< 0.001
Male	75.9%	85.6%	NS
Previous Medical History			
MI	17.2%	23.0%	NS
CABG	0.0%	3.5%	NS
PTCA	0.0%	4.9%	NS
Known Risk Factors			
Diabetes**	41.4%	41.5%	NS
Hypertension	55.2%	35.9%	< 0.05
Smoking	17.2%	47.1%	< 0.001
Co-Morbid conditions			
Heart Rate > 100	27.6%	16.1%	NS
SBP > 160	37.9%	14.7%	< 0.01
SBP > 190	13.8%	3.6%	< 0.05
LVF	18.5%	11.9%	NS
Anterior MI	42.9%	34.3%	NS
Therapy			
Thrombolytic Therapy	81.8%	86.9%	NS
SK	27.8%	22.4%	NS
t-PA	33.3%	39.4%	NS
Other drugs	38.9%	38.2%	NS

* Categorical variables in the two populations were compared using chi-square test; when the assumptions related to use of chi-square test was violated Fisher's exact test replaced the chi-square test. Normal continuous variables between stroke and non-stroke groups were compared using t-test.

** includes all NIDDM and IDDM

exact test replaced the chi-square test. Normal continuous variables between stroke and non-stroke groups were compared using t-test.

Results

During the study period, 2481 consecutive patients with AMI were identified. Of these, 29 patients (1.2%) developed stroke during their hospital stay. More than half of these strokes (62%) were hemorrhagic. There was no significant difference in stroke rates between patients who received thrombolytic therapy and patients who did not (1.2% vs 1.8% respectively). Table 1 shows the characteristics of patients with AMI according to the development of stroke. Patients who developed a stroke following AMI were significantly older and more likely to be smokers. These patients were also more likely to have a history of hypertension and to have a systolic blood pressure higher than 160 mmHg at presentation.

In a logistic regression model including 11

variables, risk factors for stroke were analyzed (Table 2). Age > 60 years was the strongest predictor of stroke after AMI among the variables we studied (OR 5.8; 95%CI 2.6 to 13.1; $P < 0.001$). Other predictors of stroke were systolic blood pressure at presentation higher than 160 mmHg (OR 4.2; 95% CI 1.4 to 12.4; $P < 0.01$) and a past medical history of hypertension (OR 2.2; 95% CI 1.1 to 4.6; $P < 0.05$). Female gender and diabetes mellitus were not associated with a higher risk of stroke. Anterior location of AMI was also not associated with a higher risk of stroke (OR 1.4; 95% CI 0.7 to 3.0). Patients who received thrombolytic therapy were not at an increased risk for developing stroke (OR 0.7; 95% CI 0.2 to 2.0).

Using multivariate adjusted logistic regression two factors were identified as independent predictors for stroke among patients with AMI: age > 60 (OR 5.5; 95% CI 2.4 to 12.5; $P < 0.001$) and systolic blood pressure higher than 160 mmHg at presentation (OR 3.2; 95% CI 1.1 to 9.5; $P < 0.04$) (Table 3).

Table 2: Determinants of stroke after AMI as quantified by logistic regression model

Determinants	Odds Ratio (95% CI)	p-value
Age >60	5.8 (2.6-13.1)	< 0.001
Female gender	1.9 (0.8-4.5)	NS
Past Medical History		
LVF	1.7 (0.6-4.5)	NS
CABG	0.0 (0.0 - -)	NS
PTCA	0.0 (0.0- -)	NS
DM	0.9 (0.5-2.1)	NS
Hypertension	2.2 (1.1 -4.6)	< 0.05
Vital signs at Presentation		
SBP >190	4.2 (1.4-12.4)	< 0.01
Heart rate >100/min	1.9 (0.9-4.5)	NS
Thrombolytic therapy	0.7 (0.2-2.0)	NS
Anterior MI	1.4 (0.7- 3.0)	NS

As would be expected, outcomes in patients who developed stroke after AMI were worse than in those who did not develop stroke (Table 4). Patients developing stroke were 12 times more likely to die during hospitalization compared with patients who did not develop stroke (OR 12.6; 95% CI 5.4 to 26.7; $P < 0.001$). Patients who developed stroke after receiving thrombolytic therapy had a higher mortality than patients developing stroke without receiving this treatment (47% vs 0%). Among patients who survived after stroke, the length of hospital stay was significantly longer than it was for patients who did not develop stroke (HR 4.9; 95% CI 2.1 to 8.6; $P < 0.001$).

Study limitations

The case report form used in our registry did not include information on known risk factors for stroke such as chronic atrial fibrillation, previous history of stroke or transient ischemic attacks. Accordingly, these variables could not be considered in the analysis.

Table 4: Short term morbidity and mortality of patients with stroke after AMI

	With Stroke (n=27)	Without Stroke (n=2424)	Adjusted Odds Ratio (95% CI)	P -value
In-Hospital Mortality	48.1% (n=21)	5.4% (n=2381)	12.6 (5.4 -26.7)* Hazard Ratio (95% CI)	<0.001
Length of Hospital Stay in days (Median ± IQR)	8 (16)	5 (2)	4.3 (2.1 -8.6)*	<0.001

*Adjusted odds ratio obtained using multiple logistic regression; adjusted for age, hypertension, smoking, SBP > 160 or SBP > 190 and Diabetes.

Table 3: Independent predictors for the development of stroke among AMI patients as identified by multivariate adjusted logistic regression

Predictors	Odds Ratio	95% CI	P value
Age > 60	5.5	2.4-12.5	<0.001
SBP > 160	3.2	1.1-9.5	0.04

Discussion

The incidence of stroke after AMI in our study was 1.2% which is comparable to that reported from National Registry of Myocardial Infarction-2 (NRMI-2) and from Maximal Individual Therapy in Acute Myocardial Infarction Trial (MIR/MITRA)^{5,6}. Our results support a decline in the incidence and event rate of ischemic stroke after AMI. In the 1970s and 1980s the risk of stroke after AMI was high at a rate of 2.3 to 3.8% in studies examining the effect of warfarin in AMI and at a rate of 0.9 to 1.9% in observational studies from coronary care units^{7,8,9}. In the 1990s, the stroke event rate was lower at a rate of 0.8 to 1.1% in the placebo groups of large thrombolysis trials^{10,11,12}. In a recently conducted registry of acute coronary syndromes in Kuwait, the incidence of stroke was 0.3% among Patients with AMI³.

The decrease in the incidence of post AMI ischemic stroke in recent decades is possibly explained by early mobilization of patients with AMI and the routine use of thrombolytics and aspirin. The use of aspirin has resulted in impressive reduction (42%) of post AMI stroke in a large randomized study¹¹. Our finding that thrombolytic therapy is not associated with an increased risk of developing stroke is in agreement with results from the 3 largest placebo – controlled trials of thrombolytic treatment after AMI^{11,12,14}.

Our results show that older age and hypertension are associated with a higher event rate of stroke, This is in agreement with findings

from Behar S et al¹⁵. Advanced age is consistently shown to be a strong predictor of stroke following AMI in clinical trials and registries. Patients aged 65-75 and patients aged over 75 were respectively 2.1 and 2.42 times more likely to have a stroke after AMI than those under 65 years¹². Severe AMI complicated by reduced cardiac output and poor cerebral perfusion predisposes to the development of stroke especially in elderly patients usually having subcritical cerebrovascular stenosis¹⁶.

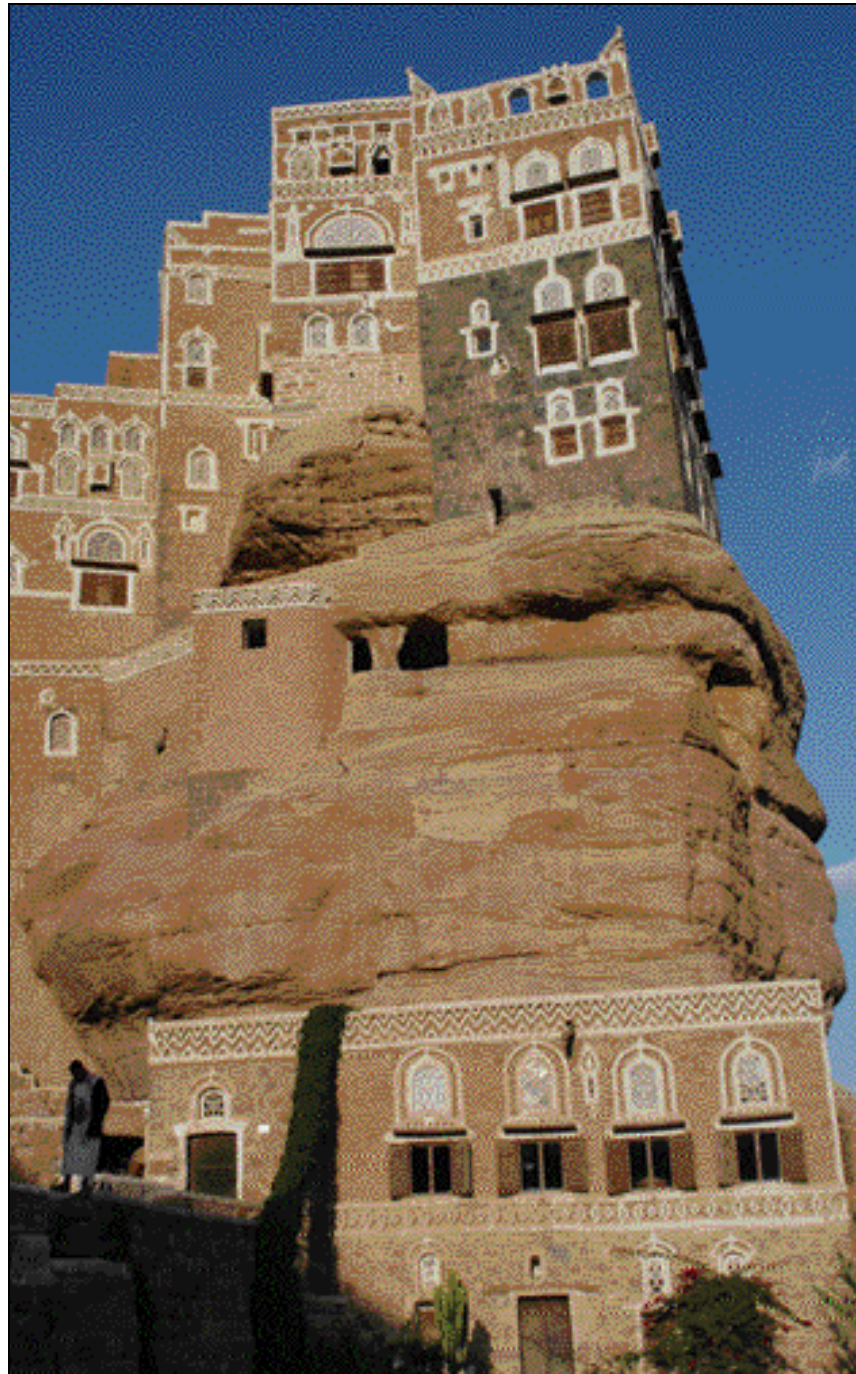
Hypertension is the most powerful, prevalent and treatable risk factor for stroke¹⁷. Both systolic and diastolic blood pressures are independently related to stroke incidence. Isolated systolic hypertension which is common in the elderly consistently increases the risk of stroke by 2 to 4 times. The importance of an anterior location of infarction and left ventricular thrombus as risk factors for stroke has recently been disputed³⁴. We did not find that anterior location of the infarction to be an important predictor of stroke, this is in accordance with previous studies^{12,15}. Embolization from a left ventricular thrombus can explain only a small fraction of AMI-related strokes. Haemodynamic changes, cerebral vessels atherosclerosis, the inflammatory response to infarction and hemostatic abnormalities¹⁸, may be other factors predisposing to ischemic stroke.

In conclusion, stroke is an infrequent but serious complication of AMI, older age and high systolic blood pressure at admission are independent predictors of stroke. Patients who received thrombolytic therapy are not at increased risk for developing stroke.?

References:

1. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomized trials of more than 1000 patients. *Lancet*. 1994; 343: 311-322.
2. Maggioni AP, Franzosi MG, Santoro E, et al. The risk of stroke in patients with acute myocardial infarction after thrombolytic and antithrombotic treatment. *N Engl J Med*. 1992; 327: 1-6.
3. Longstreth WT Jr, Litwin PE, Weaver WD, for the MITI Project Group. Myocardial infarction, thrombolytic therapy, and stroke: a community-based study. *Stroke*. 1993; 24: 587-590.
4. Bodenheimer MM, Sauer D, Shareef B, Brown MW, Fleiss JL, Moss AJ. Relation between myocardial infarct location and stroke. *J Am Coll Cardiol*. 1994;24:61-66.
5. Mooe T, Eriksson P, Stegmayr B. Ischemic stroke after acute myocardial infarction: a population-based study. *Stroke*. 1997 Apr; 28(4): 762-767.
6. Wienbergen H, Schiele R, Gitt AK, et al ; for the MIR and MITRA Study Groups. Incidence, risk factors, and clinical outcome of stroke after acute myocardial infarction in clinical practice. *Am J Cardiol*. 2001 Mar 15;87(6):782-5, A8.
7. Puletti M, Morocutti C, Tronca M, Fattapposta F, Borgia C, Curione M, Cusmano E. Cerebrovascular accidents in acute myocardial infarction. *Ital J Neurol Sci*. 1987;8:245-248.
8. Thompson PL, Robinson JS. Stroke after acute myocardial infarction: relation to infarct size. *Br Med J*. 1978;2:457-459.
9. Komrad MS, Coffey CE, Coffey KS, McKinnis R, Massey EW, Califf RM. Myocardial infarction and stroke. *Neurology*. 1984;34:1403-1409.
10. Wilcox RG, von-der-Lippe G, Olsson CG, Jensen G, Skene AM, Hampton JR. Trial of tissue plasminogen activator for mortality reduction in acute myocardial infarction: Anglo-Scandinavian Study of Early Thrombolysis (ASSET). *Lancet*. 1988;2:525-530.
11. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17 187 cases of suspected acute myocardial infarction: ISIS-2. *Lancet*. 1988;2:349-360.
12. Maggioni AP, Franzosi MG, Farina ML, Santoro E, Celani MG, Ricci S, Tognoni G. Cerebrovascular events after myocardial infarction: analysis of the GISSI trial: Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI). *Br Med J*. 1991;302:1428-1431.
13. Mohammad Zubaid , Wafa A. Rashed, Hisham Saad, Ali Attiya, Bassam Abu Al-Banat, Mustafa Ridha, Muhammad H. Al-Kandari, Ghassan Baidas, Rashed Al-Hamdan, Shaheed Zubair, Lukman Thalib, Kuwait Acute Coronary Syndromes Registry: Baseline Characteristics, Management Practices and In-Hospital Outcomes of Patients Hospitalized with Acute Coronary Syndromes in Kuwait: *Med Princ Pract* 2007; 16:407-412.
14. Mahaffey KW, Granger CB, Sloan MA, et al. Risk factors for in-hospital nonhemorrhagic stroke in patients with acute myocardial infarction treated with thrombolysis: results from GUSTO-I. *Circulation*. 1998; 97: 757-764.
15. Behar S, Tanne D, Abinader E, Agmon J, Barzilai

- J, Friedman Y, Kaplinsky E, Kauli N, Kishon Y, Palant A, Peled B, Reisin L, Schlesinger Z, Zahavi I, Zion M, Goldbourt U, for the SPRINT Study Group. Cerebrovascular accident complicating acute myocardial infarction: incidence, clinical significance and short- and long-term mortality rates. *Am J Med.* 1991;91:45-50.
16. Chin PL, Kamiski J, Rout M. Myocardial infarction coincident with cerebrovascular accidents in the elderly. *Age Aging* 1977; 6:29-37.
17. Mac Mahon S, Rodgers A. Blood Pressure, antihypertension treatment and stroke risk. *J Hypertens suppl.* 1994; 12:S5-S14.
18. Gustafsson C, Blomb?ck M, Britton M, Hamsten A, Svensson J. Coagulation factors and the increased risk of stroke in nonvalvular atrial fibrillation. *Stroke.* 1990;21:47-51.



Typical Yemeni building and external architecture.