POST-CORONARY ARTERY BYPASS GRAFT STROKE AND ITS RELATED RISK FACTORS

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Abstract

INTRODUCTION: Cerebrovascular accident (CVA) or stroke remains a devastating complication of cardiac surgical procedures, especially coronary artery bypass graft (CABG) despite advances in perioperative monitoring and management. An individual's risk of stroke is based in part on preoperative characteristics, but also on intra- and postoperative factors. The purpose of this study was to determine the prevalence and predictors of stroke in a large group of patients undergoing cardiac surgery.

METHODS: Data were collected on 1467 patients who underwent CABG at Chamran Heart Center from 1995 to 2003. Stroke was defined as "a new focal neurological deficit which appears and is still at least partially evident more than 24 hours after its onset". Logistic regression identified significant predictors of stroke.

RESULTS: Among the preoperative and postoperative factors, significant correlates of stroke included chronic renal insufficiency (P=0.0001), hypertension (P=0.0001), diabetes (P=0.0001), and atrial fibrillation (P=0.0001). However, stroke had no significant correlation with sex (P=0.054), age (P=0.28), severe LV failure (P=0.062), history of CVA (P=0.723) or shock state (P=0.802).

DISCUSSION: Neurologic complications after cardiac surgical procedures remain a relatively common problem despite improvements in anesthetic and surgical techniques, as well as in perioperative monitoring and management. Increased stroke risk can be predicted by preoperative and postoperative clinical factors.

Keywords • Stroke • Cerebrovascular accident • Coronary artery bypass graft (CABG)

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Introduction

Stroke is a devastating complication of coronary artery bypass graft (CABG) surgery. Its incidence ranges in the medical literature from 1.3% to 4.3%,[1-3] and sometimes nearly 8%, depending on how the deficit is defined.[4-6]

Neurological derangement after CABG has been attributed to hypoxia, emboli, hemorrhage, and metabolic abnormalities.[7-8] Stroke is associated with increased morbidity, cost, length of stay, and mortality.[9]

Moreover, the case-fatality rate among patients with stroke after CABG is 20%, whereas mortality for all CABG patients is 2-4%.[10] In addition to the suffering of patients, the economic impact of stroke is substantial; stays in the intensive care unit (ICU) and in the hospital are significantly longer, and hospital costs are doubled.[11]

The etiology of stroke is complex; many preoperative risk factors have been identified, such as age, vascular disease, renal failure, and diabetes.[12-15]

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A contemporary risk factor analysis is therefore necessary to determine the predictors of stroke in the era of modern cardiac surgery. The aim of the present study therefore was to investigate the incidence and predictors of pre- and perioperative stroke in patients undergoing CABG in a large retrospectively compiled database from a single institution.

Materials and methods

Study population: A total of 1467 consecutive patients who underwent pure CABG between May 1996 and September 2002 at Chamran Heart Center constituted the population of the present study. Baseline demographics, procedural data, and perioperative outcomes were prospectively collected using standardized data-entry forms. Clinical events were source-documented.

Preoperative variables: Chronic renal insufficiency was defined as serum creatinine ≥2.0 mg/dL. Carotid artery disease was considered as a history of carotid artery disease verified by angiography or duplex ultrasonography. Recent myocardial infarction was defined as a myocardial infarction occurring at least 24 hours before CABG. Moderate left ventricular dysfunction was defined as an ejection fraction of 35-50% and severe left ventricular dysfunction was defined as an ejection fraction below 35%. Diabetes mellitus was defined as serum fasting blood sugar ≥120 mg/dL. Systemic hypertension was defined as blood pressure higher than 140/90 mmHg, or being on antihypertensive medications.

Operative variables: Clamp time was defined as the duration of time between clamping of the aorta and opening of the clamp.

Postoperative variables: Postoperative stroke was defined as any new major neurological deficit presenting in the hospital and persisting more than 24 hours.[16]

Transient ischemic attacks were not included in this analysis. Strokes were confirmed by an independent neurologist and/or appropriate brain imaging.

Atrial fibrillation was detected based on ECG obtained after CABG in ICU.

Patient characteristics are displayed in Table 1. Patients older than 65 years accounted for 20.6% and those less than 65 years for 79.4% of the study population. The majority of patients were male (75.1%) and 0.4% had a history of cerebrovascular disease.

All variables to be analyzed were entered in a retrospective fashion by two physicians involved in the project, resulting in a complete data set for each patient.

Statistical analysis: Continuous variables are expressed as mean ± SD throughout the manuscript, and categorical data as proportions. Categorical variables were compared with the chi square test. Univariate analyses of risk factors were performed calculating odds ratios (OR) with 95% confidence intervals (CI). Variables with a P value less than 0.05 were considered significant. All statistical analyses were performed using the SPSS statistical package 11.00 (SPSS, Birmingham, AL).

Results

Data were collected from 1503 patients who underwent CABG at Chamran Heart Center from 1995 to 2003. Thirty-six patients were excluded owing to incomplete data. Baseline clinical characteristics of patients are presented in Table 1.

A total of 1467 consecutive patients undergoing CABG were included in the present study. Postoperative stroke occurred in 30 patients (2.0%).

The baseline clinical characteristics of patients with and without stroke are summarized in Table 2.

Patients with postoperative stroke were significantly more likely to have diabetes, hypertension, and chronic renal insufficiency than patients without stroke.

Postoperative new-onset atrial fibrillation occurred in 30% of the patients who developed postoperative stroke and in 6.8% of the patients without stroke (P<0.0001).

TABLE 1. Baseline Clinical Characteristics

Age >65 y	20.6%
Female sex	24.9%
Diabetes	22.6%
Hypertension	32.3%
Moderate systolic left ventricular failure	37.8%
Severe systolic left ventricular failure	10.3%
Postoperative atrial fibrillation	7.2%
Previous cerebrovascular accident	0.4%
Chronic renal failure	1.5%
Emergency CABG in cardiogenic shock state	0.2%

TABLE 2. The baseline clinical characteristics of patients with and without stroke

		Postoperative stroke N	%	P value	Odds Ratio	Confidence Interval 95%
Sex	Male	18	60	0.054	-	-
	Female	12	40			
Age	<65	19	63.3	0.028	2.28	1.073-4.844
	>65	11	36.7			
Diabetes mellitus	No	14	46.7	0.0001	4.054	1.96-8.4
	Yes	16	53.3			
Chronic renal failure	No	27	90	0.0001	8.29	2.32-29.7
	Yes	3	10			
Hypertension	No	7	23.3	0.0001	7.2	3.1-16.9
	Yes	23	76.7			
Sever left ventricular failure	No	23	76.7	0.062	-	-
	Yes	7	23.3			
Cerebrovascular accidents	No	30	100	0.723	-	-
	Yes	0	0			
Shock state	No	30	100	0.802	-	-
	Yes	0	0			
Postoperative atrial fibrillation	No	21	70	0.0001	5.92	2.64-13.28
	Yes	9	30			

Cross-clamp time evaluation by Mann-Whitney U was conducted. Cross-clamp time was not significantly higher in those who developed postoperative stroke (66 minutes mean clamp time for stroke patients versus 60.5 minutes for non-stroke patients, P=0.067).

Discussion

Neurologic complications after cardiac surgical procedures remain a relatively common problem despite improvements in anesthetic and surgical techniques, as well as in perioperative monitoring and management. Several previous studies have demonstrated that permanent neurologic deficits occur in as many as 6% of patients undergoing cardiac surgery.[16-18]

In his prospective large-scale series, Bucerius J found the incidence of stroke to be 4.6% with significant variation among different surgical procedures.[19] He noted that they had overestimated the incidence of stroke because they had included temporary neurologic deficits (e.g. TIA) in their definition of stroke, in contrast to previous studies that have generally focused on permanent deficits.

In the current study, the incidence of stroke (permanent deficits) was about 2%.

Cerebral micro-emboli generated during CABG with cardiopulmonary bypass might be implicated in postoperative neurological impairment.[20,21]

Pathological examination by Moody et al. of the brain after conventional CABG revealed the presence of multiple emboli lodged in small cerebral arterioles and capillaries.[22] BhaskerRao et al. documented in a prospective study that cerebral dysfunction was significantly lower after CABG without cardiopulmonary bypass compared to on-pump CABG.[20]

We did not find any significant statistical relation between sex and post-CABG stroke (P=0.054). But Sotiris C found the female sex to be an independent risk factor for post-CABG stroke.[23]

In the current study, age higher than 65 years had no significant statistical relationship with post-CABG stroke (P=0.028).

Age higher than 70 years, one of the most commonly reported independent predictors of stroke,[14,24,25,26] was present in approximately one-fifth of our patient population.

However, our analysis did not reveal age as an independent predictor of stroke. Advanced age is not thought to be a cause of stroke per se, but rather a marker of increased atherosclerotic burden.[25]

Bucerius J did not find any significant statistical relation between advanced age and stroke after CABG.[19] The explanation of why advanced age did not arise as an independent predictor of stroke in our study may have been: first, more than 79% of the study group was under 65 years of age and

atherosclerosis in this group is less severe than in older age groups; and second, our surgeon used long cross-clamp method with minimum manipulation of the aorta.

Diabetes was one of the independent predictors of stroke in our analysis (OR: 4.054). This risk factor placed the patients at increased risk of atherosclerotic embolization as well as impaired autoregulation of cerebral blood flow.[27]

The same results have been reported by other investigators.[19,23,27]

History of Chronic renal failure (Cr>2) was the most powerful predictor of stroke (OR: 8.29) in our study, possibly due to preoperative renal insufficiency secondary to renal artery arteriosclerosis.

Arteriosclerosis has been well documented to be a systemic disease affecting multiple parts of the systemic circulation. Anderson and associates found renal failure to be a predisposing factor for adverse outcomes including neurologic deficits in patients undergoing coronary bypass surgery.[12]

We found that patients with hypertension were at increased risk for stroke (OR: 7), similar to other studies.[19,26,28,29]

Cautious management of blood pressure in severely hypertensive patients is important because of the risk of precipitating ischemic stroke during aggressive blood pressure reduction.[30]

In the current study, we did not find left ventricular (LV) dysfunction and shock state to be significantly related to post-CABG stroke as independent risk factors (P=0.062), however, Sotiris C and Roach GW reported severe LV dysfunction and shock state to be significantly related to post-CABG stroke.[23,31]

The smaller number of cases of severe LV dysfunction who underwent CABG (10.3%) might have been the cause of fewer strokes after CABG.

Statistical analyses in the current study did not show any significant relationship between the history of cerebrovascular disease and post-CABG stroke (P=0.723).

History of cerebrovascular disease denotes the existence of pathologic conditions within the cerebrovascular system or an underlying stenosis of one or both carotid arteries.[19]

Other investigators have demonstrated a 7% to 13% incidence of postoperative stroke in patients with history of previous neurologic events.[32,33]

The lower incidence of postoperative stroke in patients with history of previous neurologic events in our study is probably due to the fewer cases of carotid artery stenosis.

In the current study, postoperative atrial fibrillation was an independent risk factor for postoperative stroke (P=0.0001) (OR=6).

As demonstrated by a previous study by Hogue et al. atrial fibrillation is most probably related to the development of postoperative, but not intraoperative stroke. In their study, postoperative atrial fibrillation combined with low cardiac output correlated only with late (postoperative) stroke because early (intraoperative) strokes precede the onset of postoperative atrial fibrillation.[18]

Among the postoperative variables, new-onset atrial fibrillation was associated with a higher risk of postoperative stroke.[23]

Patients with stroke had a prolonged intensive care stay compared with patients without stroke, probably due to the increased incidence of respiratory insufficiency and reintubation, as well as to delayed mobilization. Furthermore, stroke patients had a markedly higher mortality rate.[19]

According to current data, patients with history of diabetes mellitus, systemic hypertension and chronic renal failure are at very high risk for post-CABG stroke. This complication also occurs in the setting of postoperative atrial fibrillation.

At the end some questions are raised:

1. What is the mechanism whereby diabetes mellitus, systemic hypertension and chronic renal failure put patients at greater risk?
2. Strokes occurring around the time of cardiopulmonary bypass are presumed to be embolic; what is it about chronic renal failure, for example, that might increase the risk of embolism?
3. Is there any role for hyperhomocysteinemia or other coagulopathies in patients with chronic renal failure?
4. Can statins reduce the risk of stroke in high-risk patients undergoing CABG?

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