# Stroke After Coronary Artery Surgery: Incidence and Risk Factors Analysis

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## Abstract

Background. Stroke is a devastating complication of coronary surgery. In this report, the incidence, and correlates of stroke following coronary surgery were evaluated at King Abdullah University Hospital, in north of Jordan. Materials and Methods. Data were collected retrospectively. Between 2006 and 2009, 855 patients underwent coronary surgery. Stroke was defined as any new neurological deficit lasting more than 24 hours. Univariate and multivariate analysis were utilized as appropriate.Results. The incidence of stroke was 1.4% (n = 12). Age, previous stroke and emergency surgery were correlates by univariate analysis. Multivariate analysis revealed age, previous stroke and chronic renal impairment as predictors of stroke. Ten (83.3%) of the 12 patients were diagnosed to have stroke in the first 24 hours. Length of hospital stay was  $20.9 \pm 20.34$  days for stroke patients and  $9.2 \pm 5.17$  days for nonstroke patients (p  $\leq$  0.001). There were 4 (33.3%) deaths in the stroke group and 27 (3.2%) for nonstroke patients (p  $\leq$  0.001). Conclusion. Three independent risk factors for stroke were identified: age, prior stroke and chronic renal impairment. Vigilance in evaluating preoperative history of stroke is important. Patients with high risk for stroke should lead the surgeon to individualize his surgical technique.

# INTRODUCTION

Stroke remains a dreadful complication of coronary surgery. It can turn a nicely done procedure into a distressing situation for the patients, their family and the surgical team with exhaustion of staff and resources. In the 1960s, stroke was a complication of more than 9% of coronary artery bypass grafting (CABG) [1]. In the recent literature some investigators reported a lower rate of stroke between 3.8% and 1.4% [2-4]. Filsoufi et al. [2] reported in a recently published paper an incidence of 1.9% for on-pump CABG and 1.4% for beating heart CABG. In a large prospectively gathered database, including coronary and valve surgery, Bucerius et al. [3] reported an overall incidence of stroke of 4.6%, ranging from 9.7% for double or triple valve surgery to 1.9% for beating heart CABG and 3.8% for on-pump CABG. The low incidence of this postoperative key event limits the power of most published papers. Some accepted correlates that increase the risk of stroke include history of cerebrovascular disease (CVA), hypertension, increasing age, and diabetes mellitus [2-11]. Possible mechanisms of stroke include arteriosclerotic emboli from the aorta, air embolism, and carotid artery disease, hypotension during surgery and prolonged cardiopulmonary bypass time, as well as cerebral microvascular disease.<sup>4-6</sup> Stroke is known to

increase morbidity, mortality, hospital stay and cost [2-5,7].

Outcomes data on 855 isolated CABG procedures performed at King Abdulla University Hospital (KAUH), in north of Jordan between 2006 and 2009, provided for the first time, an opportunity to identify patient and disease factors associated with stroke. In addition, the impact of postoperative stroke on length of stay and hospital mortality was evaluated.

# MATERIALS AND METHODS

The present analysis includes all isolated CABG surgeries performed at KAUH from January 2006 to April 2009. Preoperative and perioperative data were retrospectively collected. Two groups were identified. Cases were defined as those who had suffered a postoperative stroke, and controls comprised all the remaining patients in the cohort. The population studied consisted of 855 consecutive patients undergoing on-pump coronary surgery. Of these, 12 patients had postoperative stroke.

## **PREOPERATIVE DATA**

Patient data were collected by review of medical records. Documentation of a prior stroke was verified from each patient's medical records, review of results of brain computerized tomography (CT) scan or magnetic resonance imaging (MRI), when available, or presence of unresolved neurological deficit. Recent myocardial infarction (MI) as a risk factor was defined, if patients had elevation of cardiac enzymes or as evidenced by electrocardiogram (ECG) within 4 weeks from time of surgery. Heart failure was considered if patients were symptomatic or on anti heart failure treatment. Most of the diabetic patients were type two controlled with oral hypoglycemic agents, Hypertensive patients were controlled with anti hypertensive treatment. Chronic renal impairment was defined if creatinin  $\geq 2.5$ mg/dl or on chronic dialysis. All patients with positive history for intermittent claudication or had a documented clinical evidence of ischemia, were considered to have peripheral vascular disease. Left ventricular function was assessed either angiographically or by echocardiography. Number of diseased coronary arteries was based on the coronary angiogram report. Carotid artery duplex scanning was performed routinely in all elective patients. Carotid artery luminal narrowing  $\geq 70\%$  was considered as a positive study. These patients were sent for surgical or percutaneous intervention before the bypass procedure. Emergency surgery was defined, if the patient was sent to the operating room within 24 hours from time of cardiac catheterization.

# INTRAOPERATIVE DATA

Although assessment of the ascending aorta was performed by digital palpation, no information concerning the eventual presence of aortic atherosclerotic plaques was reported in the operative note. So this variable was not assessed in this study. Patients were excluded if an additional surgical procedure on the ascending aorta was performed. Standard techniques were used for cardiopulmonary bypass (CPB). Perfusion was maintained at 2.0 to 2.4 L/min/m2, and systemic perfusion pressure was kept at 60-80 mmHg. Myocardial viability was preserved with cold antegrade potassium cardioplegia and topical hypothermia. Body temperature was maintained between 28 and 32°C.

# **NEUROLOGICAL COMPLICATIONS**

Stroke was defined as any new focal neurological dysfunction of presumed vascular origin lasting more than 24 hours. Nothing was mentioned, in the reviewed medical records, about any neurological event lasting less than 24 hours. Most likely, this is because evidence of these events is hindered postoperatively owing to residual anesthetics and sedative drugs. Stroke was initially diagnosed by the surgical team and confirmed by the neurologist on the basis of the clinical findings and brain imaging by CT scan or MRI.

# STATISTICAL ANALYSIS

All statistical analysis was conducted using the Statistical Package for Social Sciences (SPSS, version 16.0) software (SPSS Inc, Chicago, IL). Continuous variables were described as mean ± standard deviation (SD) and categorical variables were described using percentage. The differences in the incidence of stroke according to demographic and clinical characteristics were compared using X<sup>2</sup> test or Fisher exact test wherever appropriate. Multivariate analysis, using binary logistic regression analysis, was performed to determine factors associated with the risk of stroke. Crude odds ratios (OR) of the association between each factor and stroke were reported. Crude OR measures the strength of the association between the factor and stroke without taking into account the effect of the other variables. The adjusted OR with their 95% confidence interval for each factor was reported after adjusting for other variables in the model. Adjusted OR measures the association between the factor and stroke after adjusting for the effect of other variables. A  $p \le 0.05$  was considered statistically significant.

# RESULTS

Demographics and other univariate analysis of patient characteristics for the stroke and non stroke groups are listed in table 1. Of the 855 patients reviewed in this study who underwent on-pump CABG, 12 (1.4%) patients showed clinical evidence of stroke within their hospitalization; 10 (83.3%) were diagnosed in the first 24 hours, the other 2 patients were diagnosed on the third postoperative day. The mean age of stroke patients was  $67.4 \pm 6.93$  years, while for the nonstroke patients it was  $58.2 \pm 10.09$  years,  $p \le 0.001$ . Patients who suffered stroke were more likely to be diabetic  $(66.6\% \text{ vs. } 51.2\%, p \le 0.441)$ , hypertensive (83.3% vs.)54.6%,  $p \le 0.148$ ), in heart failure (33.3% vs. 22.2%, p  $\leq 0.272$ ) and in chronic renal failure (16.7% vs. 4.2%, p  $\leq$ 0.092) than patients who did not have stroke. In addition, they were more likely to have peripheral vascular disease (26% vs. 18%,  $p \le 0.629$ ) and perioperative blood transfusion (75% vs. 60%,  $p \le 0.224$ ) than patients who did not have stroke. There was no significant difference between both groups regarding; preoperative left ventricular ejection fraction (LVEF), number of coronary arteries diseased, pump run time and cross clamp time. However, patients who underwent an emergency operation (33.3% vs. 11.3%,  $p \le$ 0.04) had a significantly higher rate of stroke. Also patients with a history of previous stroke (41.7% vs. 8.4%,  $p \le$ 0.002) and recent MI (41.7% vs. 15.1%,  $p \le 0.025$ ), had a

significantly higher rate of postoperative stroke. In the multivariate analysis (table 2), the factors associated with the risk of developing stroke were increased for age, history of previous stroke, and preoperative chronic renal impairment. The odds of stroke increased by 12%, for each one year increase in age ( $p \le 0.005$ ). Having a history of CNS disease (OR = 10.8, 95% CI: 2.8 to 41.7) and having renal impairment (OR=6.7, 95% CI: 1.5to 30.8) were significantly associated with increased odds of stroke. The length of inhospital stay for the stroke group was  $20.9 \pm 20.34$  days, while for the nonstroke group was  $9.2 \pm 5.6$  days,  $p \le 0.001$ . There were 4 (33.3%) inhospital mortalities in the stroke group and 27(3.2%) inhospital mortalities in the nonstroke group, with  $p \le 0.001$ .

#### Figure 1

Table 1. Clinical characteristics of patients with stroke and no stroke

Variable	Stroke	No stroke	P Value	
	(n = 12)	(n = 843)		
Age (year)	67.4±6.93	58.2 ± 10.09	0.001	
≥65	8 (66.7%) 283 (24%)		0.0206	
Female	4(33.3%)	202(24%)	0.326	
Systemic hypertension	10(83.3%)	545(64.6%)	0.148	
Diabetes mellitus	8(66.6%)	432(51.2%)	0.441	
Smoking	5(41.7%)	452(53.6%)	0.597	
COPD	3(25%)	124(14.7%)	0.258	
Hyperlipidemia	6 (50%)	449(53.2%)	0.947	
Heart failure	4(33.3%)	187(22.2%)	0.272	
Chronic renal failure	2(16.7%)	35(4.2%)	0.092	
Previous stroke	5(41.7%)	71(8.4%)	0.002	
Peripheral vascular disease	2(26%)	152(18%)	0.629	
Prior recent myocardial infarction	5(41.7%)	127(15.1%)	0.025	
Ejection fraction	-		-	
≥ 50%	7(58.4%)	478(56.7%)	0.857	
40-49%	4(33.3%)	237(28.1%)	0.451	
30-39%	1(8.3%)	124(14.7%)	0.456	
Coronary stenosis				
Left main	2(16.7%)	187(22.2%)	0.484	
Two vessels	1(8.3%)	168(19.9%)	0.27	
Three vessels	11(91.7%)	662(78.5%)	0.238	
Emergency	4(33.3%)	95(11.3%)	0.04	
Pump run time(min) Mean	75.9±23.5	89.22±28.31		
≥ 90	7(58.3%)	374(44.4%)	0.333	
230	7(58.5%)	374(44.476)	0.555	
Cross clamp time(min)		62 20 11 8 27		
Mean	50.3±13.75	52.29±18.27		
≥60	4(33.3%)	249	0.49	
Perioperative blood transfusion	9(75%)	506(60%)	0.224	
Length of hospital stay (days)	$20.9 \pm 20.34$	9.2 ± 5.6	0.001	
Mortality	4(33.3%)	27(3.2%)	0.001	

## Figure 2

Table 2. Crude and Adjusted Odds Ratio (OR) and their 95% Confidence Intervals (CI) for the Factors Associated with Stroke

	Crude OR (95% Confidence Interval)	P-value	Adjusted OR (95% Confidence Interval)	P-value
Age (year)	1.10 (1.02 - 1.18)	0.010	1.12 (1.04 - 1.22)	0.005
History of CNS disease	7.8 (2.4 - 25.5)	0.001	10.8 (2.8 - 41.7)	0.001
Renal impairment	9.7 (2.4 - 39.3)	0.002	6.7 (1.5 - 30.8)	0.015

# DISCUSSION

There is a decreasing incidence of stroke following coronary artery procedures, when in the 1960s; stroke complicated more than 9% of CABG [1]. In the recent literature there is a variation in the reported incidence, ranging from 3.8% to as low as 1.4% [2-9]. The incidence of stroke in this study was 1.4%. This low incidence is multifactorial; first- most of the strokes (75%) occurred in patients who were more than 70 years old, while more than 60% of our patients needed coronary operation at an age less than 60 years, second- the use of carotid ultrasound in all elective patients and sending those with significant carotid disease to intervention before coming to coronary surgery, third- although, nothing was mentioned in the operative note about the status of the ascending aorta, this may be related to the observed negligible incidence of atherosclerotic changes of the ascending aorta, which is the major source of emboli to the brain. Fourth- lack of proper workup or documentation for some patients who were in coma on a ventilator for a long time and died without proper diagnosis.

Several studies have evaluated risk factors for stroke during coronary surgery [5,8-19]. McKhann et al. [8] reported multiple comorbidities associated with increased risk of stroke, including; presence of carotid bruit, previous stroke, history of hypertension, increasing age and history of diabetes mellitus in addition to cardiopulmonary bypass time. Among the other preoperative variables, D'Ancona et al. [10] found that redosurgery and chronic renal failure were independent determinants for stroke. In a recent case-control study by de Oliveira et al. [11] they found that systemic arterial hypertension and diabetes mellitus were the determinants of the highest chance of stroke after CABG. This finding has been reported earlier by Craver et al.[12]. In one of the largest analysis of stroke determinants, Stamou et al. [14] found depressed LVEF% (<30%) was one of the strongest preoperative determinant for CVA. This letter finding was also supported by D'Ancona et al. [10] and Calafiore et al. [15]. Intraoperative physiologic variables and their impact on postoperative neurologic outcome, were studied by Van Wermeskerken et al. [13], who found no correlation between CPB time and the incidence of stroke by both univariate and multivariate analysis. Hogue et al. [16] found CPB time a strong correlate of early stroke, but not of delayed stroke. Some reports demonstrated that the number of revascularized vessels ( $\geq$ 3) was associated with a higher incidence of stroke after the CABG operations [18]. However, Toumpolis et al. [19] found no correlation between the number of diseased coronaries and the risk of

stroke.

In our study diabetes mellitus, smoking, symptoms of heart failure and peripheral vascular disease were found not to be correlates of stroke by both univariate and multivariate analysis. Although systemic hypertension was present in 83.3% of the stroke group, as compared to 64.6% of the nonstroke group, however, it was not statistically significantly associated with stroke by both univariate and multivariate analysis. We think this is because, most of our patients are young with a short history of chronic illnesses, like diabetes mellitus and hypertension, with less complications related to these illnesses, this may explain why they were not relevant associates of stroke in our study, while they were so in some of the above mentioned studies [8,11]. On the other hand, Filsoufi et al. [2] found that diabetes mellitus is not a correlate of stroke by both univariate and multivariate analysis.

In this study preoperative LVEF, number of diseased coronaries, CPB time, aortic cross clamp time and perioperative blood transfusion, did not have any statistically significant impact on the incidence of stroke. We think this was may be related to the short and safe period of both, CPB time and aortic cross clamp time, as our cohort of patients, all were primary cases.

Univariate analysis revealed that age, previous stroke, MI within a month from date of surgery, and emergency surgery were all associated with a higher risk of stroke. Multivariate logistic regression analysis was used to identify independent risk factors and odds ratios for variables associated with stroke. The three variables shown to be statistically significant independent predictors of stroke included age, previous stroke, and chronic renal impairment.

Age showed a strong correlation with stroke by univariate and multivariate analysis. For each one year increase in age the odds of stroke increased by 12%. This is consistent with several other previous reports [8,16-19]. Some investigators reported female gender as a risk factor for post operative stroke [16], while others found males to be at higher risk [3]. In this study although the prevalence of stroke was higher among females, gender was not a correlate of stroke by both univariate and multivariate analysis. We think this may be related to the small number of patients who had stroke in this study. A history of stroke, in our study, was a correlate of postoperative stroke by both univariate and multivariate logistic regression analysis. Bucerius et al. [3] in their analysis of 16,184 consecutive patients undergoing cardiac surgery found that history of cerebrovascular disease was the strongest preoperative predictor of stroke. Several centers have shown that prior stroke correlates with a greater risk of postoperative neurologic complications by univariate or multivariate analysis [5,6,20-24]

MI within a month from the time of surgery was found to be a correlate of stroke by univariate analysis. This is in concordance with some peer reviews. Toumpolis et al. [19] found a significantly increased incidence of early and delayed stroke in patients with recent MI. Some others like Antunes et al. [25] found no correlation between recent MI and the incidence of post-operative stroke.

Emergency surgery performed for critical left main coronary artery disease ( $\geq$  70% luminal narrowing with or without angina) or unstable cardiac conditions, was found in our study to be a significant predictor of stroke by univariate analysis but not in multivariate regression analysis. This group of patients is more likely to have extracardiac atherosclerotic disease in addition to the increased risk of perioperative hemodynamic instability. This result was consistent with peer reviews [3,18]. However, Filsoufi et al. [2] found no correlation between the occurrence of stroke and urgency of surgery by both univariate and multivariate analysis.

Also we found patients with creatinin  $\geq 2.5\%$  or on chronic dialysis were at higher risk for stroke by multivariate regression analysis. Charlesworth et al. [18] reported a creatinin serum level of more than 2% or renal failure was a strong predictor of risk of stroke. John et al. [4] reported a serum creatinin  $\geq 2.5\%$  as a statically significant correlate of stoke by univariate analysis, as well as renal failure by multivariate analysis. Several other peer reviews came to the same conclusion [10,14,19].

Patients who had a stroke in this study had an inhospital mortality of 33.3% and a mean hospitalization of  $20.9 \pm 20.34$  days, compared to 3.2% mortality and a mean hospitalization of  $9.1 \pm 5.6$  days for the nonstroke patients. This high mortality has been similarly reported by others and has not changed during the past decade [2,4,14]. The exact reason for this high mortality rate associated with stroke remains unclear. However, we think most of the patients who develop stroke are old with multiple comorbidities and they spend a long time on the ventilator and in the intensive care unit (50% in our study), which make them prone for major complications, particularly respiratory failure and sepsis.

# LIMITATIONS OF THE STUDY

This is a retrospective analysis with low number of stroke and conclusions are possibly limited in their application. Neurological events and risk factors may be underreported in the patients' files. Also we had no follow-up data on readmission for stroke, which may further contributed to the low incidence of stroke in this study. Despite the observed low incidence of atherosclerotic disease of the ascending aorta in this region, however, lack of use of epiaortic ultrasound and missing information about the ascending aorta is another limiting factor. The contribution of postoperative atrial fibrillation to stroke risk was not studied, due to the lack of proper documentation of its occurrence and the timing in relation to stroke.

# CONCLUSION

Stroke is a major contributor to mortality and prolonged hospitalization after CABG. Three significant independent risk factors for stroke were identified in this study: age, prior stroke and chronic renal impairment. Vigilance in evaluating preoperative history of stroke, particularly in elderly patients is important. Patients with high risk for stroke should lead the surgeon to individualize his surgical technique. The use of epiaortic ultrasound, when available, utilization of offpump CABG, and decreasing manipulation of the ascending aorta by using single cross clamp in addition to maintaining high perfusion pressure may decrease the incidence of this complication.

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