Stroke after Coronary Artery Surgery: A Single Center Report

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Abstract

Stroke or cerebrovascular accident (CVA) is a devastating complication of coronary surgery. In this report, the incidence, and correlates of CVA following isolated coronary artery bypass grafting (CABG) surgery were evaluated. Data were collected retrospectively. Between 2006 and 2009, 855 patients underwent isolated CABG surgery. CVA was defined as any new neurological deficit lasting more than 24 hours. Univariate and multivariate analyses were utilized as appropriate. The incidence of CVA was 1.4% ($n = 12$). Age, previous CVA, and emergency surgery were correlated by univariate analysis. Multivariate analysis revealed age, previous CVA, and chronic renal impairment as predictors of CVA. Ten (83.3%) of the 12 patients were diagnosed to have CVA in the first 24 hours. Length of hospital stay was 20.9 ± 20.34 days for CVA patients and 9.2 ± 5.17 days for non-CVA patients ($p \leq 0.001$). There were 4 (33.3%) deaths in CVA group and 27 (3.2%) for non-CVA patients ($p = 0.001$). Postoperative CVA is a major contributor to mortality, prolonged hospitalization, and other adverse postoperative complications. Further studies are needed to develop better strategies to minimize the occurrence of CVA among patients undergoing CABG.

Keywords

- coronary bypass
- complications
- stroke
- CVA
- CABG surgery

Cerebrovascular accident (CVA) remains a dreadful complication of coronary surgery. In the 1960s, more than 9% of coronary artery bypass grafting (CABG) surgeries were complicated by CVA.¹ In recent literature, rates between 3.8 and 1.4% were reported.^{2–4} Filsoufi et al² in a recently published paper reported an incidence of 1.9% for on-pump CABG and 1.4% for off-pump CABG. The low incidence of this postoperative key event limits the power of most published articles. Some accepted correlates that increase the risk of CVA include history of cerebrovascular disease, hypertension, increasing age, and diabetes mellitus.^{2–11} Possible mechanisms of CVA include arteriosclerotic emboli from the aorta, air embolism, carotid artery disease, hypotension during surgery, and prolonged cardiopulmonary bypass (CPB) time, as well as cerebral microvascular disease.^{4–6} CVA is known to increase morbidity, mortality, hospital stay, and cost.^{2–5,7}

Outcomes data on 855 isolated on-pump CABG surgeries performed at King Abdulla University Hospital (KAUH), in

the north of Jordan between 2006 and 2009, provided an opportunity to identify patient and disease factors associated with CVA. In addition, the impact of postoperative CVA on length of hospital stay and in-hospital mortality was evaluated.

Patients and Methods

The present analysis includes all isolated CABG surgeries performed between January 2006 and April 2009. Preoperative and perioperative data were retrospectively collected. After isolation of data, patients with atrial fibrillation (preoperative and postoperative), due to small number and none of them had CVA, were excluded from the study. The studied population consisted of 855 consecutive patients undergoing isolated on-pump CABG surgery. Two groups were identified: group 1, 12 patients who had postoperative CVA; and group 2, remaining patients in the cohort. This work was approved by

the ethical committee in the hospital and patients' signature was waived.

Preoperative Data

Patients medical records were reviewed for: prior CVA; results of brain computerized tomography (CT) scan or magnetic resonance imaging (MRI), when available, or presence of unresolved neurological deficit, recent myocardial infarction (MI); elevation of cardiac enzymes or as evidenced by electrocardiogram 4 weeks before surgery, heart failure; symptomatic patients or on antiheart failure treatment, diabetes mellitus; most patients were type 2 on oral hypoglycemic agents, hypertension; previously diagnosed and on antihypertensive treatment, chronic renal impairment; creatinine ≥ 1.5 mg/dL or on chronic dialysis, peripheral vascular disease; positive history of intermittent claudication, or a documented clinical evidence of peripheral ischemia, left ventricular ejection fraction (LVEF); by either angiography or echocardiography, number of diseased coronary arteries; based on coronary angiogram and operative reports, emergency surgery; within 24 hours from time of cardiac catheterization.

Carotid artery duplex scanning was performed routinely in all elective patients (80% of the studied cohort); 10% had severe stenosis (luminal narrowing $\geq 70\%$); and 24.5% had moderate disease. Patients with severe stenosis were sent for surgical or percutaneous intervention before bypass surgery.

Perioperative Antithrombotic Treatment

Most of patients were taking aspirin (100 mg once daily), it was not discontinued preoperatively. Heparin (3.0 mg/kg) was administered intravenously before completion of internal thoracic artery harvesting to maintain an activated clotting time (ACT) of more than 400 seconds and it was neutralized at the end of the procedure by protamine sulfate (3.0 mg/kg). Further protamine was given if ACT was greater than 140 seconds before chest closure. Neither aprotinin nor tranexemic acid was used in any of the patients. Packed red blood cells, fresh frozen plasma, and platelets were transfused according to the amount of bleeding, international normalized ratio (INR) levels, and platelet counts. Clopidogrel was used postoperatively in patients with allergy to aspirin, recent percutaneous coronary intervention, and in some with small diffusely diseased coronaries, as well as patients who developed CVA. Enoxaparin (40 mg once daily) was started in all patients on the next morning of the day of surgery. Warfarin was not used in any of the studied population.

Intraoperative Data

Assessment of the ascending aorta was performed by digital palpation. None of CVA patients had a documented atherosclerotic disease of the ascending aorta, 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 CPB. Perfusion was maintained at 2.0 to 2.4 L/min/m², and systemic perfu-

sion pressure was kept at 60 to 80 mm Hg. Myocardial viability was preserved with cold antegrade potassium cardioplegia and topical hypothermia. Body temperature was maintained between 28 and 32°C.

Neurological Complications

CVA was defined as any new focal neurological dysfunction of presumed vascular origin lasting more than 24 hours. A neurological assessment is routinely done by the surgical team if patients were extubated within 24 hours. Patients with positive neurological examination, suspected neurological deficit, and/or prolonged time on ventilator are usually assessed by the neurologists. CVA diagnosis was based on clinical findings and brain imaging by CT scan or MRI.

Statistical Analysis

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 $\pm$ standard deviation (SD) and categorical variables were described using percentage. The differences in the incidence of CVA according to demographic and clinical characteristics were compared using chi-squared 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 ratio (OR) of the association between each factor and CVA were reported. Crude OR measures the strength of the association between the factor and CVA without taking into account the effect of the other variables. The adjusted OR with its 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 CVA after adjusting for the effect of other variables. A $p \leq 0.05$ was considered statistically significant.

Results

Demographics and other univariate analyses of patient characteristics in groups 1 and 2 are listed in ►Table 1. Of the 855 patients reviewed in this study who underwent isolated on-pump CABG, 12 (1.4%) patients showed clinical evidence of CVA within their hospitalization, all were ischemic in nature; 10 (83.3%) were diagnosed in the first 24 hours, the other 2 were diagnosed on the third postoperative day. Mean age of group 1 was 67.4 ± 6.93 years, and group 2 was 58.2 ± 10.09 years, $p = 0.001$. Patients who suffered CVA were more likely to be diabetic, hypertensive, in heart failure and in chronic renal failure. In addition, they were more likely to have peripheral vascular disease and perioperative blood transfusion. There was no significant difference between both groups regarding; preoperative LVEF, number of diseased coronary arteries, CPB time, and aorta cross-clamp time. Postoperative CVA was significantly higher in patients who had emergency surgery, history of CVA, and recent MI. In multivariate analysis (►Table 2), the factors associated with increased risk of developing CVA were increased age, history of CVA, and

Table 1 Univariate analysis of clinical characteristics of patients in groups 1 and 2

Variable	Group 1 (n = 12)	Group 2 (n = 843)	p Value
Age (y), mean $\pm$ SD	67.4 $\pm$ 6.93	58.2 $\pm$ 10.09	0.001
≥ 65 , n (%)	8 (66.7)	283 (24)	0.0206
Female, n (%)	4 (33.3)	202 (24)	0.326
Systemic hypertension, n (%)	10 (83.3)	545 (64.6)	0.148
Diabetes mellitus, n (%)	8 (66.6)	432 (51.2)	0.441
Smoking, n (%)	5 (41.7)	452 (53.6)	0.597
COPD, n (%)	3 (25)	124 (14.7)	0.258
Hyperlipidemia, n (%)	6 (50)	449 (53.2)	0.947
Heart failure, n (%)	4 (33.3)	187 (22.2)	0.272
Chronic renal failure, n (%)	2 (16.7)	35 (4.2)	0.092
Previous CVA, n (%)	5 (41.7)	71 (8.4)	0.002
Peripheral vascular disease, n (%)	2 (26)	152 (18)	0.629
Prior recent myocardial infarction, n (%)	5 (41.7)	127 (15.1)	0.025
Ejection fraction (%)			
≥ 50 , n (%)	7 (58.4)	478 (56.7)	0.857
40–49, n (%)	4 (33.3)	237 (28.1)	0.451
30–39, n (%)	1 (8.3)	124 (14.7)	0.456
Coronary stenosis			
Left main, n (%)	2 (16.7)	187 (22.2)	0.484
Two vessels, n (%)	1 (8.3)	168 (19.9)	0.27
Three vessels, n (%)	11 (91.7)	662 (78.5)	0.238
Emergency, n (%)	4 (33.3)	95 (11.3)	0.04
Pump run time (min)			
Mean	75.9 $\pm$ 23.5	89.22 $\pm$ 28.31	
≥ 90 , n (%)	7 (58.3)	374 (44.4)	0.333
Cross-clamp time (min)			
Mean	50.3 $\pm$ 13.75	52.29 $\pm$ 18.27	
≥ 60 , n (%)	4 (33.3)	249 (29.5)	0.49
Perioperative blood transfusion, n (%)	9 (75)	506 (60)	0.224
Length of hospital stay (d)	20.9 $\pm$ 20.34	9.2 $\pm$ 5.6	0.001
Mortality, n (%)	4 (33.3)	27 (3.2)	0.001

Abbreviations: COPD, chronic obstructive pulmonary disease, CVA, cerebrovascular accident; SD, standard deviation.

preoperative chronic renal impairment. The odds of CVA increased by 12%, for each 1 year increase in age, $p = 0.005$. Having history of CVA and/or renal impairment was significantly associated with increased odds of CVA. The mean length of in-hospital stay in group 1 was 20.9 ± 20.34 days and group 2 was 9.2 ± 5.6 days, $p = 0.001$. There were 4 (33.3%) in-hospital CVA-related mortalities in group 1 and 27 (3.2%) in-hospital mortalities in group 2, $p = 0.001$.

Discussion

The etiopathogenesis of CVA is complex, multifactorial, and related to a large number of perioperative factors and patient comorbidities. In this study, we sought to report the incidence

and mortality rate as well as to evaluate the predictors of postoperative CVA in patients undergoing isolated CABG surgery.

The reported incidence of CVA ranges from 3.8% in on-pump CABG surgery to as low as 1.4% in off-pump cases.^{2–9} The incidence of CVA in this study was 1.4%. This low incidence may be related to the fact that; most of the studied population were relatively young, and CVA was more likely to occur in patients older than 70 years. The use of carotid artery Doppler ultrasound in all elective patients and sending those with significant carotid disease to intervention before coming to coronary surgery might have impacted the result. Nothing was mentioned in the operative note about the status of the ascending aorta; this may be related to the observed

Table 2 Crude and adjusted OR and their 95% CI for the factors associated with CVA

	Crude OR (95% CI)	p Value	Adjusted OR (95% CI)	p Value
Age (y)	1.10 (1.02–1.18)	0.010	1.12 (1.04–1.22)	0.005
History of CVA	7.8 (2.4–25.5)	0.001	10.8 (2.8–41.7)	0.001
History of renal impairment	9.7 (2.4–39.3)	0.002	6.7 (1.5–30.8)	0.015

Abbreviations: CI, confidence interval; CVA, cerebrovascular accident; OR, odds ratio.

negligible incidence of atherosclerotic changes of the ascending aorta, which is the major source of emboli to the brain.

Different chronic comorbidities were reported as predictors of CVA.^{5,8–19} In our study, diabetes mellitus, systemic hypertension, smoking, heart failure, and peripheral vascular disease were not predictors of CVA. This may be related to the short history of such chronic illnesses, as majority of studied patients were young.

MI was significantly associated with CVA by univariate analysis. This is in concordance with some peer reviews. Toupoulis et al¹⁹ found a significantly increased incidence of early and delayed CVA in patients with recent MI. However, others such as Antunes et al²⁰ found no correlation between recent MI and the incidence of postoperative CVA.

Emergency surgery performed for critical left main coronary artery disease ($\geq 70\%$ luminal narrowing with or without angina) or unstable cardiac conditions, was significantly associated with CVA by univariate analysis. These patients are more likely to have extracardiac atherosclerotic disease in addition to the increased risk of perioperative hemodynamic instability. This result was consistent with some peer reviews.^{3,18} On the contrary, Filsofi et al² found no correlation between the occurrence of CVA and urgency of surgery by both univariate and multivariate analysis.

Preoperative LVEF, number of diseased coronaries, CPB time, and aortic cross-clamp time did not have any significant impact on the incidence of CVA in this study. We think this was related to the short CPB and aortic cross-clamp times, as all studied patients were primary cases. This coincides with some peer reviews.^{13,19}

Patients who had blood and blood products transfusion in the postoperative period, were reported by Mikkola et al²¹ to have a significantly increased risk of CVA. In our study, CVA patients were more likely to have transfusion of blood and blood products but did not reach a statistical significance, most likely due to the small number of patients with CVA.

In our study, increasing age, history of CVA, and chronic renal failure were the independent predictors of CVA. We think these patients may have widespread cerebrovascular disease, impaired cerebral blood flow, and/or increased susceptibility to atheroembolism or thromboembolism. This is consistent with multiple peer reviews.^{3,5,6,8,10,14,16–19,22–26} In the study of Bucerius et al³, having a history of CVA was the strongest predictor of postoperative CVA. Charlesworth et al¹⁸ reported a creatinine serum level of more than 2 mg/dL or renal failure was a strong predictor of CVA.

Hospital length of stay was significantly longer in group 1 compared with group 2. Also in-hospital mortality was

significantly higher. 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 associated with CVA remains unclear. We think most of CVA patients are elderly with multiple comorbidities, spend long time on ventilator, which make them prone for major complications, particularly respiratory failure and sepsis.

Intraoperative CVA may result from embolism, thrombosis, or hypoperfusion. Previous studies have identified atherosclerotic emboli from intraoperative manipulation of the aorta as the main source.²⁷ In our study, CVA patients had a negligible incidence of atherosclerotic changes of the ascending aorta, all had ischemic CVA involving different areas of the brain, with no dominance to certain lobe or area. Still the role of various contributing factors is difficult to ascertain or investigate including the bypass circuit, clots at tip of the aortic cannula especially if left inside after protamine infusion, as well as blood and blood products transfusion.²¹

We think proper preoperative evaluation of extracardiac arteriopathy with complete neurological assessment; including carotid artery duplex scanning are important factors in decreasing the incidence of CVA. In our study, 10% of the screened patients, had a significant carotid artery stenosis and were sent for intervention before coming to cardiac surgery. None of them had postoperative CVA. Also brain CT scan and MRI of some CVA patients, with no history of prior neurological event, showed recurrent old infarction(s), which may be a clue of cerebrovascular disease that may favor a hypoperfusion etiology. Whether brain imaging for high risk patients would change the outcome is still to be investigated in larger prospectively planned studies.

Use of off-pump surgery and a no-touch aorta technique in the case of diseased ascending aorta,^{28,29} improving CPB techniques and materials,³⁰ reducing CPB and aorta clamping times,³¹ and avoidance of intraoperative hypoperfusion,³² are measures which may significantly reduce the risk of postoperative CVA.

In conclusion, despite advances in cardiac surgery that has led to an overall improvement in outcome after coronary revascularization, the incidence of CVA after CABG surgery has remained constant over the past decade. Postoperative CVA is a major contributor to mortality, prolonged hospitalization, and other adverse postoperative complications. Knowledge of the risk factors offers an opportunity to implement preoperative as well as intraoperative measures to reduce the incidence of CVA and should influence patient selection. Further studies are needed to develop better

strategies to minimize the incidence of CVA among patients undergoing CABG surgery.

Limitations of the Study

This is a retrospective analysis with low number of CVA patients and conclusions are possibly limited in their application. Neurological events and risk factors may be underreported in patients' files. Despite the observed low incidence of atherosclerotic disease of the ascending aorta in this region, lack of use of epiaortic ultrasound is another limiting factor. The contribution of postoperative atrial fibrillation to CVA was not studied, due to the small number of patients with atrial fibrillation, however, none of them developed CVA and so, it cannot be a predictor of this event. We were unable to determine whether each CVA was embolic, thrombotic, or hypoperfusive in etiology.

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