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Off Pump CABG and Stroke: Incidence and Mechanisms: A Single Center Experience

Sudhir Adalti*, Vivek Wadhawa, Vijay Gupta***, Sanjay Patel******

Authors Affiliation
*Assistant Professor **Associate Professor, Department of Cardiovascular and Thoracic Surgery ***Assistant Professor, Department of Nuclear Medicine ****Research Assistant, Department of Research, U. N. Mehta Institute of Cardiology and Research Center (Affiliated to BJ Medical College, Ahmedabad). Civil Hospital Campus, Asarwa, Ahmedabad, Gujarat 380016, India.

Reprints Requests
Vivek Wadhawa,
Associate Professor, Department of Cardiovascular and Thoracic Surgery, U.N. Mehta Institute of Cardiology and Research Center, Civil Hospital Campus, Asarwa, Ahmedabad, Gujarat 380016, India.
E-mail: getwadhawa@gmail.com

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Abstract

Background: Perioperative stroke is a distressing complication and it can lead to severe debilitation and excess mortality [1-4]. Perioperative strokes are mostly ischemic and the occurrence of perioperative stroke was different in the existing studies and ranges from 0.5 to 4.5% [5-7]. OPCAB has been conveyed to propose an inferior risk of stroke [8-9]. However, there is unavailability of adequate information on the timing and mechanisms of perioperative stroke in the setting of OPCAB. The aim of the study was to assess the incidence and mechanisms of perioperative stroke after OPCAB. *Methods and Materials:* We designed a retrospective, observational study and enrolled 2375 patients operated for isolated OPCAB between January 2014 and December 2016. Perioperative stroke is distinct as a neurologic deficit of abrupt onset affected by a disturbance in cerebral blood supply (ischemic or hemorrhagic) that did not resolve within 24 hours after CABG and continued for more than 72 hours [10]. Perioperative stroke does not include the neurologic deficits of confusion, delirium, and (or) encephalopathic (anoxic or metabolic) events. *Result:* The incidence of stroke in our study was 1.01% (24 patients out of total 2375 patients suffered stroke). There were fifteen men and nine women with the median age of 64 years (range, 60 to 68 years).Fourteen patients had a history of stroke prior to surgery. All the patients had impaired left ventricular ejection fraction. Three fourths of our patients were diabetic and two thirds hypertensive. Almost half of our patients were in atrial fibrillation and had previous myocardial infarction and coexistent peripheral vascular disease. *Conclusion:* Stroke rate in present study is on lower side of the reported range of stroke incidence as reported in various studies. Risk factors that we identified in the present study are similar to other studies as well but owing to its observational nature, results cannot be generalized.

Keywords: OPCAB; Stroke; CABG.

Introduction

Coronary artery bypass grafting (CABG) is one of the most common cardiac surgery performed in adult cardiothoracic patients. Associated with it are complications among which Perioperative stroke is a distressing complication and it can lead to severe debilitation and excess mortality [1-4]. Roach and colleagues addressed this issue in 1996 in a sample of 2108 patients undergoing elective CABG in the United States [1]. They reported an overall incidence of 6.1% on adverse cerebral outcomes. In their study, type 1 (major focal deficits, stupor and coma) deficits occurred in 3.1% patients while 3% had type 2 deficits (deterioration in intellectual function and memory). Perioperative strokes are mostly ischemic and the occurrence of perioperative stroke was

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different in the existing studies and ranges from 0.5 to 4.5% [5-7]. Several randomized and observational trials have reported no difference or a tendency toward reduced stroke in patients undergoing OPCAB compared with on pump coronary bypass. OPCAB has been conveyed to propose an inferior risk of stroke [8-9]. However, there is unavailability of adequate information on the timing and mechanisms of perioperative stroke in the setting of OPCAB. The aim of the study was to assess the incidence and mechanisms of perioperative stroke after OPCAB.

Methods and Material

Study Setting, Patient Sample and Data Collection

We designed a retrospective, observational study that required to characterize off-pump as a preventative stroke-risk factor during isolated OPCAB surgery. Consecutive adult (≥18 years of age) patients undergoing OPCAB surgery as a single procedure were retrospectively collected. We enrolled 2375 patients operated for isolated OPCAB between January 2014 and December 2016. All patients were managed intraoperatively and postoperatively according to our institutional protocols. The study was approved by the institutional ethics committee(UNMICRC/CVTS/2013/04), and consent was waived off for all patients. In order to meet the inclusion criteria, only OPCAB as a single surgical procedure was considered. All the patients who underwent OPCAB with concomitant surgical procedures were thus excluded. Patients who started off with off pump and converted to on pump were also excluded. The data were then entered in a computer database.

Perioperative stroke is distinct as a neurologic deficit of abrupt onset affected by a disturbance in cerebral blood supply (ischemic or hemorrhagic) that did not resolve within 24 hours after CABG and continued for more than 72 hours [10]. Perioperative stroke does not include the neurologic deficits of confusion, delirium, and (or) encephalopathic (anoxic or metabolic) events.

All the stroke outcomes included in this study were diagnosed by a neurologist and in most cases brain CT-scan or MRI were used for lesion assessment. The study excluded patients with diffuse postoperative brain encephalopathy presenting as delirium, confusion, prolonged alteration of mental status and anxiety in the immediate postoperative period, as this could imitate longer revelation to anaestheia.

The risk variables of strokes included the 13 variables in the study, major nine factors such as: age, gender, diabetes mellitus, arterial hypertension, peripheral arteriopathy (including all extracardiac vascular disease manifestations as intermittent claudication, amputation, absent pedal pulse and/or lower extremity ulcers; previous surgery and/or percutaneous intervention on the abdominal, thoracic aorta, lower extremity and supraaortic vessels), previous stroke events (ictus with/without residual neurological defect or transient ischaemic attack), chronic renal failure (known glomerular filtration impairment <60 ml/min/1.73 m^2, patients requiring dialysis and/or preoperative creatininemia ≥2 mg/dl), preoperative cardiac failure (left ventricular ejection fraction <40% by echocardiography or ventriculography and/or preoperative New York Heart Association functional class III–IV), non-elective priority of surgery (urgency: operation required within 24 h to reduce the chance of further clinical weakening; or emergency: in which case there should be no delay in providing operative intervention).

Presence of preoperative atrial fibrillation (defined by ECG and/or Holter recording showing paroxysmal or persistent arrhythmia during the qualifying admission/consultation or in the preceding 12 months) was also considered. The mechanism of stroke was classified by clinical presentation and imaging findings [4,5,11]. There are two types of strokes: ischemic and hemorrhagic. There are three major mechanisms of ischemic stroke: thrombotic, embolic, and hypoperfusion. Hemorrhagic and thrombotic strokes are extremely rare after isolated CABG [4,5,11].

Statistical Analysis

The statistical calculations were performed using SPSS software v 20.0 (Chicago, IL, USA). Continuous data were expressed as mean±SD. Univariate analysis of the continuous data was performed using student's t-test, whereas chi-square test was used for the categorical data. The cut off value of $p<0.05$ was considered for the statistical significance.

Result

The incidence of stroke in our study was 1.01% (24 patients out of total 2375 patients suffered stroke). Preoperative and operative characteristics are presented in Tables 1 & 2. Table 3 presents all the complications after OPCAB which includes stroke.

The mechanisms as shown in Table 4 were classified as embolic in eight patients (30%) and hypoperfusion in fifteen patients (62.5%). Imaging studies showed multiple cerebral infarcts in all embolic episodes, lacunar infarcts (hypo- perfusion) in twelve episodes, and single acute cerebral infarct (hypoperfusion) in three episodes. One patient had large posterior cerebellar bleed on second day after his surgery.

There were fifteen men and nine women with the median age of 64 years (range, 60 to 68 years). Fourteen patients had a history of stroke prior to surgery. All the patients had multivessel coronary artery disease, and six patients had significant left main disease. All the patients had impaired left ventricular ejection fraction. Three fourths of our patients were diabetic and two thirds hypertensive. Almost half of our patients were in atrial fibrillation and had previous myocardial infarction and coexistent peripheral vascular disease.

Patients experiencing a stroke after CABG also experienced substantially more hospital morbidity, mortality, and resource utilization than those not experiencing a stroke.

Table 1: Preoperative Characteristics of Patients Undergoing Coronary Artery Bypass

Variables	No of Patients (N=2375)
Age (Years;mean±SD)	59.04 ± 9.92
Sex (Female/Male)	(642/1733) (27.03%/72.96%)
Prior Stroke(n;%)	98 (4.12%)
Diabetes(n;%)	582 (24.5%)
Unstable Angina(n;%)	506 (21.3%)
Atrial Fibrillation(n;%)	236 (9.9%)
Hypertension(n;%)	754 (31.4%)
COPD (n;%)	423 (17.81%)
Myocardial Infarction(n;%)	1123 (47.3%)
Peripheral Vascular Disease(n;%)	156 (6.6%)
Chronic Renal Failure(n;%)	189 (7.95%)
NYHA Class (N;%)	
Class – I	95 (4%)
Class – II	902 (37.9%)
Class – III	1187 (49.9%)
Class – IV	191 (8.1%)
Extent of coronary artery disease	
1-vessel disease(n;%)	423 (17.81%)
2-vessel disease(n;%)	855 (26.00%)
3-vessel disease(n;%)	1097 (46.18%)
Left ventricular ejection fraction (mmHg;mean±SD)	41.1 ±14.55

COPD: Chronic Obstructive Pulmonary Disease, NYHA: New York Heart Association

Table 2: Operative Data

Variables	No. of Patients (N=2375)
≤2 Grafts(n;%)	177 (07.45%)
3 Graft(n;%)	1575 (66.3%)
≥ 4 Graft(n;%)	623 (26.23%)
Mean no. of grafts(mean±SD)	3.28 ± 1.22
Homologous blood transfused (ml) (range)	350 ± 105

Table 3: Post-operative data and complication

Variables	No. of Patients
Reintubation (n;%)	112 (4.71%)
Low cardiac output syndrome (n;%)	89 (3.74%)
Postoperative dialysis (n;%)	145 (6.1%)
New-onset atrial fibrillation(n;%)	227 (9.55%)
Ventricular fibrillation (n;%)	44 (1.85%)
Stroke	24(1.01%)
Hypoperfusion (n;%)	15 (0.63%)
Embolic (n;%)	8 (0.33%)
Hemorrhage (n;%)	1 (0.04%)
Time on ventilator (hrs;mean±SD)	4.5 ± 5.49
Intensive care unit stay (days;mean±SD)	2.1 ± 2.6
Total hospital stay (days;mean±SD)	6.23 ± 5.9

Table 4: Comparison of Stroke after cardiac surgery

Variables	Patient with stroke after surgery (n = 24)	Patient without stroke after surgery (n = 2351)	P value
Age (Years;mean±SD)	64 ± 4.2	57.6± 5.1	**<0.0001**
Sex (Female/Male)	9/15	633/1718	0.3528
Prior Stroke(n;%)	14 (58.3%)	10(0.4%)	**<0.0001**
Diabetes(n;%)	19 (79.1%)	563 (23.9%)	**<0.0001**
Unstable Angina(n;%)	9(37.5%)	497 (21.1%)	0.0897
Atrial Fibrillation(n;%)	11(45.8%)	225 (9.5%)	**<0.0001**
Hypertension(n;%)	16(66.6%)	738 (31.3%)	**0.0005**
COPD(n;%)	6(25%)	417 (17.7%)	0.5111
Myocardial Infarction(n;%)	13(54.1%)	1110 (47.2%)	0.6360
Peripheral Vascular Disease(n;%)	14 (58.3%)	142(6.03%)	**<0.0001**
Chronic Renal Failure(n;%)	9(37.5%)	180 (7.5%)	**<0.0001**
LVEF (mmHg;mean±SD)	27± 5.4	46.2± 8.7	**<0.0001**
Mean no. of grafts(mean±SD)	2.92 ± 1.18	3.29 ± 1.24	0.1458

COPD: Chronic Obstructive Pulmonary Disease, LVEF: Left Ventricular Ejection Fraction

Discussion

In the present study, incidence of perioperative stroke was 1.01% which is in the lower side of the observed incidence as reported by other studies [1-7]. The theoretical benefits of OPCAB were avoidance of cardiopulmonary bypass. However, the effect of OPCAB on perioperative stroke remains a topic of controversy, with recent reports offering opposite conclusions, some showing a reduction in stroke but others showing no effect [12,13,14]. In an updated meta-analysis of 59 randomized trials encompassing 8961 patients, the incidence of stroke after OPCAB was 1.4%, and there was a 30% reduction in the occurrence of perioperative stroke with OPCAB [9]. The post-OPCAB stroke incidence varies between studies and it depends on the center's or surgeon's experience. The stroke incidence after OPCAB was low (<1%) in experienced centers [15], intermediate (1.4%) in randomized studies, 9and high (3%) in the real-world registry data [16].

The mechanism of stroke was classified as ischemic and hemorrhagic by clinical presentation and imaging findings [4,5,11]. There are three major mechanisms of ischemic stroke: thrombotic, embolic, and hypoperfusion. Hemorrhagic and thrombotic strokes are extremely rare after isolated CABG [4,5,11]. We divided the possible mechanism of perioperative stroke into either embolic or hypoperfusion strokes.

Embolic stroke was characteristic of multiple infarcts in multiple territories and predominantly occurred in the distribution of the middle cerebral artery [5,17]. Hypoperfusion strokes may arise from a combination of extracranial or intracranial cerebral artery stenosis and systemic hypotension [5,11,17]. Typically, hypoperfusion stroke in patients with carotid or cerebral artery stenosis leads to watershed or large cerebral infarcts. Hypoperfusion stroke in patients with stenosis of the small penetrating arteries in the deep cerebral white matter leads to lacunar stroke.

In the current study, more than half of the strokes were hypoperfusion strokes (62.5%) which resulted from three major mechanisms: (1) atherosclerotic emboli from manipulations of the atherosclerotic aorta; (2) intraoperative hypoperfusion in the setting of preexisting stenosis of carotid artery or small penetrating cerebral artery; and (3) cardiogenic embolization. The remaining strokes were embolic strokes predominantly resulting from cardiogenic embolization, which was attributed to perioperative cardiac events and postoperative atrial fibrillation.

Consistent with other studies [4,18-21], we found previous stroke, diabetes, hypertension, peripheral vascular disease, and renal failure to be significant risk factors for stroke within 30 days after OPCAB. In addition, we found advanced age and low EF to be significant factors. Age may represent the increased arteriosclerotic burden leading to stroke and low EF leading to low cardiac output state. Patients who experienced a stroke had substantially worse hospital outcomes prolonged ventilation, renal failure. They also experienced substantially longer intensive care unit and postoperative lengths of stay.

Previous studies have identified arteriosclerotic emboli from intraoperative manipulation of the aorta as the main culprit [17,18]. We similarly identified factors associated with arteriosclerotic burden as major risk factors for stroke. Preoperative and intraoperative imaging (eg, computed tomography, intraoperative transesophageal echocardiography,

and epiaortic echocardiography) may be used to assess ascending aortic arteriosclerosis. If it is found, surgical techniques could be used that avoid or minimize aortic manipulation to eliminate risk of arteriosclerotic embolization. These include total arterial off pump CABG with no aortic manipulation.

In addition to atherosclerotic embolus, intraoperative hypoperfusion is a potential cause of stroke during CABG and highlights the importance of maintaining adequate blood pressure during manipulation of the heart during off-pumpCABG. Hypotension with resulting hypoperfusion may occur during retraction of the heart in off-pump CABG; The inflammatory process and hypercoagulability after surgery might provide some explanation for patients developing thrombotic or embolic stroke. Identifying the etiology of this postoperative risk factor for stroke may lead to better strategies to prevent it, whether through more aggressive use of antithrombotic and antiplatelet agents, prophylactic prevention of atrial fibrillation, or both. Atrial fibrillation continues to be a common postoperative problem with peak incidence on the second day, suggesting a possible mechanism. To treat new-onset atrial fibrillation, we initially try early medical conversion or electroconversion and, if atrial fibrillation recurs or is persistent, rate control and anticoagulation. This strategy appears to be associated with not only preventing an anticipated increased risk of postoperative stroke but perhaps with actually lowering the risk.

It should be noted that this study has several limitations. It is limited by its dependence on a retrospective observational study, and the conclusions derived are limited in application. We did not assess OPCAB performance under 'touch' or 'non-touch' aorta schemes. As 'touch' schemes have been reported to limit the benefit of OPCAB in terms of perioperative stroke incidence.

Finally, as diffuse brain encephalopathy was excluded, this may potentially have underestimated the real prevalence of small perioperative strokes, even though other studies have reported diffuse brain encephalopathy, mainly related to intraoperative factors such as cardiopulmonary bypass and general an aesthesia times.

Conclusion

Stroke rate in present study is on lower side of the reported range of stroke incidence as reported in various studies. Risk factors that we identified in the present study are similar to other studies as well but owing to its observational nature, results cannot be generalized.

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