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Stroke and ON-Pump Coronary Artery Bypass Grafting. Should We Change to OFF-Pump? Our Experience from the North of Jordan.

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Abstract

PRINCIPLES: Stroke is a well known complication after coronary artery bypass grafting (CABG) using cardiopulmonary bypass (CPB). We were interested in reviewing our experience with on-pump coronary artery bypass grafting, to evaluate its neurologic dysfunction and its impact on patient management. And to ask a question that recently applied. Should we change to OFF-Pump?MATERIAL AND METHODS: A retrospective review of 1.050 patients undergoing elective coronary artery bypass grafting (CABG) was performed from May 5, 2003, to December 31, 2007, in our institution. Stroke was defined as any new permanent global or focal neurological deficit, immediately after extubation (early) or within 5-6 day in the hospital (late). Medline literature was searched for all the studies published in the English language between 1999 and 2006 reporting neurological complications on patients undergoing CABG with emphasis on comparisons between off-pump coronary artery bypass surgery (OPCAB) and CPB techniques. The following terms were used: Stroke and on-pump coronary artery bypass grafting; on-pump versus off-pump; brain injury after coronary artery bypass grafting.RESULTS: Stroke occurred in 19 patients (1.81%). From this group thirteen were female (68.42%). Fifteen patients were diabetic (78.95%). History of previous transient ischemic attacks was found in 14 patients (73.68%). CONCLUSIONS: Female sex, diabetic patients and patients with previous transient ischemic attacks are associated with increased the risk of stroke and in-hospital mortality. Prospectively randomised trial is needed to give us a proper answer on our question.

INTRODUCTION

Coronary artery bypass grafting in the late 1960s was first performed without the use of cardiopulmonary bypass (CPB) [1]. But after the use of CPB and cardioplegic arrest this technique was largely abandoned [2]. With the use of cardiopulmonary bypass neurologic dysfunction is well documented as an associated complication of cardiac surgery [3]. Cerebral injury occurs in two distinct forms, and become an important cause of morbidity and mortality after open heart surgery [4]. Stroke, as devastating complication occurs in 3% of patients undergoing CABG [5]. Soon after open heart surgery using cardiopulmonary bypass (CPB), cognitive dysfunction, occurs in as many as 80% of patients and persists in one fourth of these patients six months after surgery and only by detailed neuropsychologic testing can be detected [4,6,7]. Many factors participate in the pathogenesis of cerebral injury and cognitive dysfunction after cardiac surgery, but there is increasing evidence that multiple microemboli arising from the ascending aorta, the heart chambers, or the bypass circuit are the primary pathophysiologic mechanisms producing diffuse ischemic cerebral injury [8]. Cardiopulmonary bypass requires cannulation and cross-clamping of the ascending aorta, which per se may dislodge atheromatous macroemboli, leading to stroke [9]. Cardiopulmonary bypass is a well known source that generates microemboli and increases the permeability of the blood-brain barrier which may adversely affect cognitive function [10,11].

PATIENTS AND METHODS

1050 consecutive patients who were undergoing coronary artery bypass grafting (CABG) from May 5, 2003, to December 31, 2007, were enrolled in this retrospective study. Our cardiac center is a new one in the north since May 5, 2002. All patients had undergone conventional CABG using a left internal mammary artery (LIMA) graft with different surgeons. Stroke was defined as any new permanent global or focal neurological deficit. Stroke was first detected by cardiac surgeon immediately after extubation (early) or within 5-6 day in the hospital (late), then neurologist will be consulted, and in the majority of patients they were confirmed by CT head scan. Patients having cardiac valve surgery, ASD (atrial septal defect) repair, LVEF (left ventricular ejection fraction) <0.40, and undergoing repeat CABG surgery were excluded. Mortalities not related to neurological complications were excluded. Twenty seven patients with severe carotid artery disease were excluded from the study as they were transferred to other cardiac center for combined surgery with carotid endarterectomy by vascular surgeons as a complex case. Patients with incomplete intraoperative or postoperative data from medical files were excluded from study. TABLE 1- 754 men (71.81%) and 296 women (28.19%) (mean age, 59.5 years; range, 35-75 years) were enrolled. Patients were examined before surgery, after extubation in cardiac intensive care unit (ICU), in the ward during daily follow up round, after discharge at one week in the clinic, and at 3 to 4 weeks after surgery, according to our cardiac surgery follow up protocol. Carotid artery duplex scanning was done in 481 of patients (45.80%) ≥60 years old (not routinely), but it's done when clinically carotid bruit was documented, including transient ischemic attacks (TIA).[12] Intraoperative epiaortic ultrasound to assess for ascending aorta atherosclerosis is not available in our department yet. Carotid artery stenosis was graded as follows: insignificant or no disease (luminal narrowing 50%); moderate disease (narrowing >50% but <80%); severe disease (narrowing 80 but 99%); and complete occlusion.[13] A P value <0.05 was regarded as statistically significant. Surgical Techniques: The skin was incised with a sterile lancet, midline sternotomy, and pericardial and presternal tissues were cut by electrocauterization. Bone wax was used. Cardiopulmonary bypass was instituted with a single right atrial two stage cannula and an ascending aorta perfusion cannula. Standard bypass management included membrane oxygenators, arterial line filters, systemic hypothermia down to 32°C, and non-pulsatile flow of 2.4 l/min/m^2, with a mean arterial pressure greater than 50 mm Hg. The myocardium was protected by using intermittent antegrade cold blood cardioplegia (4:1 blood to crystalloid ratio). Anticoagulation was achieved using 300 U/kg of heparin. If required, heparin was supplemented to maintain the activated clotting time above 480 seconds and was reversed by protamine at the end of the procedure. All patients underwent standard placement of mediastinal and left pleural chest drains. Steel wires were used for closing the sternum, and 2 layers of Vicryl 2.0 dyed suture were used to close subcutaneous tissues avoiding dead spaces between the subcutaneous tissues. Subcuticular closure was performed with (polyglactin 910) absorbable Vicryl undyed for intracutaneous closure group. intravenous (IV) zinaceff 30 minutes before the operation followed by 750mg IV zinaceff every 8 hours. Patients who were allergic to penicillin received 1-g IV vancomycin every 12 hours, until their drains were removed. Postoperatively, patients were observed in the cardiovascular intensive care unit until they were hemodynamically stable and extubated. The drains were retained until drainage was less than 100 cc in 12 hours. Hemodynamic stable Patients were transferred to cardiac ward at 2nd day post operation.

RESULTS

Stroke occurred in 19 patients (1.81%). Fifteen of these cases (78.95%) discovered at first day post operation in the ICU. Four of them developed stroke in the ward after they were discharged from the ICU (21.05%) 2nd-3rd day post operation. All of these patients were ≥ 65 years old. Brain CT-scan was done in nine patients. Eleven of the 19 patients with stroke had moderate carotid artery disease and history of TIA (transient ischemic attacks) (57.89%). The patients with severe carotid artery disease transferred to other cardiac center for combined surgery with carotid endarterectomy by vascular surgeons as complex cases and were excluded from the study. Thirteen of the 19 patients who developed stroke were female (68.42%). Ten of these female patients were diabetic. Four of these female patients died in the hospital. Six of the 19 patients who developed stroke were male (31.58%). Five of them were diabetic. Two of these patients died in the hospital. The overall mortality related to stroke from the total number of patients in this study was (0.57%). The mortality in the stroke group (n=19) was (31.57%). Total diabetic patients who developed stroke were 15 patients (8.24%) from the total diabetic number of patients (n= 182). TABLE 2- Most strokes after coronary artery bypass grafting occur after initial uneventful neurological recovery from surgery. Female sex was independently associated with stroke. Diabetes and history of previous TIA or presence of significant carotid artery stenosis were other independent predictors of stroke.

Figure 1

DEMOGRAFIC CHARACTIRISTICS AND RISK FACTORS

	Study group patients (n= 1.050)
Age	mean age, 59.5 years; range, 35-75 years
Female	296
Male	754
Angina pectoris	298
Left main coronary lesion	248
History of cardiac surgery	-
History of MI	225
History of TIA	24
Carotid artery stenosis	336
Moderate right stenosis	55
Severe right stenosis	8 Excluded from the study
Moderate left stenosis	43
Severe left stenosis	19 Excluded from the study
Nonsignificant carotid stenosis	211
Diabetes mellitus	182
Male	94
Female	88
Chronic renal failure	5
Peripheral vascular disease	13
Ascending aorta atherosclerosis	-
COPD	54
History of cerebral embolism	9
Smoking	279
Steroid use	3
Reopening for bleeding	11
LVEF	0.40-0,54
Emergency surgery	6
Dyspnea	246
Hypertension	267
Body mass index	<30

COPD: Chronic obstructive pulmonary disease; LVEF: Left ventricular ejection fraction; MI: Myocardial infarction. TIA: Transient ischemic attacks

Moderate and severe carotid artery stenosis refer to stenosis of ≥50% but <80% and ≥80% to ≤99%, respectively.[13]

Figure 2

DISTRIBUTION OF (19) PATIENTS WITH STROKE

	n=	P value
Female	13	0.026
Male	6	
Diabetic	15	0.000
TIA with significant carotid stenosis	14	0.004

TIA: Transient ischemic attacks

DISCUSSION

Stroke is a well known and unwanted complication after coronary artery bypass grafting (CABG) using cardiopulmonary bypass (CPB) [13]. With the use of cardiopulmonary bypass, we are facing evidence suggesting increase in morbidity associated with coronary artery bypass grafting (CABG) surgery [14]. Stroke after coronary bypass grafting is usually embolic and related to CPB, manipulation of the aorta during cannulation, or surgical [15]. Bowles, et al [16] have demonstrated a significant reduction in the number of microemboli detected by transcranial Doppler ultrasonography (TCD), as they comparing off-pump coronary artery bypass grafting (OPCAB) with on-pump CABG (coronary artery bypass grafting using CPB), they noticed a reduction in the stroke rate in patients undergoing off-pump coronary artery bypass. But they believed that true clinical significance of this dramatic reduction in cerebral microemboli, however, remains to be determined.

From the randomized controlled trials (RCTs) [5] available evidence with respect to occurrence of stroke and postoperative neurocognitive dysfunction does not unequivocally show that OPCAB is better than conventional CABG (on-pump CABG) [14,17-31]. Postoperative stroke after OPCAB may be related to aortic manipulation during construction of the proximal anastomoses that requires the use of a side-biting clamp [32]. Recently in off-pump surgery the non-touch technique of the ascending aorta, which avoids intraoperative dislodgment of the atheromatous macroemboli from the atherosclerotic aorta into the cerebral circulation, may improve neurologic outcomes after OPCAB [33]. Sedrakyan, et al [34] in their meta-analysis of systematically reviewed trials, concluded that off-pump CABG is associated with reduced risk of stroke, AF and infections as compared with CABG with CPB, but they believed that evidence should be generalized taking in consideration randomized controlled trial (RCT) enrollment limitations, drawbacks related to training requirements, propensity to perform fewer grafts and likely reinterventions after off-pump surgery. Lev-Ran, et al [35] included a total of 700 consecutive patients undergoing multiple-vessel off-pump coronary artery bypass grafting between 2000 and 2003. They compared 429 patients undergoing aortic no-touch technique with 271 patients in whom partial aortic clamps were applied. The aorta was evaluated with manual palpation, and screened by epiaortic ultrasonography which was used selectively. They concluded that avoiding partial aortic clamping during off-pump coronary artery bypass grafting provides superior neurologic outcome. The results are reproducible and irrespective of the severity of aortic disease or the method of aortic screening. They recommended this technique whenever technically feasible. Kapetanakis, et al [36] from January 1998 to June 2002, enrolled 7,272 patients underwent isolated CABG surgery through three levels of aortic manipulation: full plus tangential (side-biting) aortic clamp application (on-pump surgery; n = 4,269), only tangential aortic clamp application (OPCAB surgery; n = 2,527) or an “aortic no-touch” technique (OPCAB surgery; n = 476). Their result showed a significant association for postoperative stroke correspondingly increasing with the extent of aortic manipulation was demonstrated by the univariable analysis (cerebrovascular accidents (CVA) incidence respectively increasing from 0.8% to 1.6% to a maximum of 2.2%, p < 0.01). In the logistic regression model, patients who had a full and a tangential aortic clamp applied were 1.8 times more likely to have a stroke versus those without any aortic manipulation (95% confidence interval: 1.15 to 2.74, p < 0.01) and 1.7 times more likely to develop a postoperative stroke than those with only a tangential aortic clamp applied (95% confidence interval: 1.11 to 2.48, p < 0.01). They concluded that aortic manipulation during CABG is a contributing mechanism for postoperative stroke. The incidence of postoperative stroke increases with increased levels of aortic manipulation. Bergman, et al [37] studied 28 consecutive patients with extensive atherosclerosis in the ascending aorta undergoing coronary surgery. Extensive atherosclerosis, detected by epiaortic ultrasound, was defined as involvement of 6 or more out of 12 segments. Since 1998 they have converted 15 patients with extensive atherosclerosis in the ascending aorta from on-pump to off-pump. Thirteen patients with similar disease who underwent on-pump before the introduction of off-pump were used as controls. The incidence of stroke in the off-pump group was 0% as compared with 31% in the coronary artery bypass grafting group (P = 0:03). Y-grafts were used more often in the off-pump (47%) than in the on-pump group (0%, P < 0:01). The non-touch technique of the ascending aorta was also more frequently used in the off-pump group (73 versus 0%, P< 0:001). Off-pump reduces the incidence of stroke in patients with aortic atherosclerosis when the disease occupies 50% or more of the ascending aorta. Completeness of revascularization remains a limiting factor in OPCAB. Apart from the internal thoracic arteries, saphenous veins and radial arteries, which are the most commonly used grafts, necessitate a proximal anastomosis unless Y-grafts are used. The preferred area to place these anastomoses is the ascending aorta. Bergman, et al [37] in their study, OPCAB patients received about the same number of distal anastomoses as patients undergoing conventional CABG, but with fewer proximal anastomoses. This was due to the use of sequential grafting and Y-grafts. Recently, Kim, et al [38] reported the complete avoidance of proximal anastomoses by performing OPCAB complete arterial revascularization with internal mammary and radial Y-grafts. This technique [37] may be ideal for patients with atherosclerosis in the ascending aorta. In fact, with Bergman, et al [37] study the ascending aorta was not touched in 11 of the 15 patients (73%) that were converted to OPCAB, and almost half of the patients received Y-grafts.

As we observed from our study we found that female sex was independently associated with stroke, but this finding was observed before in other studies [39-46]. Prior neurological event, carotid artery stenosis, diabetes mellitus, and advanced age have been found in many studies to increase susceptibility to perioperative stroke, possibly by identifying individuals with widespread cerebrovascular disease, impaired cerebral blood flow, and/or increased susceptibility to atheroembolism or thromboembolism [39-49]. Atrial fibrillation was observed as transient due to electrolyte disturbances, the heart rate returned to sinus after electrolyte correction. Atrial fibrillation is a frequent complication of cardiac surgery that has been reported to increase the risk of perioperative stroke in some, but not all, studies [39-46]. Hogue, et al [46] found that an equally important explanation may be the strong interaction they observed between postoperative atrial fibrillation combined with low cardiac output syndrome and delayed stroke, an interaction that has not been reported previously and because both complications are associated with cardiac thrombus formation and cerebral hypoperfusion, aggressive therapy may be beneficial for patients with both conditions. Unfortunately epiaortic ultrasound of the ascending aorta was not performed to evaluate for atheromatous disease. The finding that ascending aorta atherosclerosis was an independent predictor of delayed strokes suggests that risk of stroke associated with this condition may result from mechanisms other than direct atheroembolism. In addition to being a potential cause of cerebral embolism, ascending aorta atherosclerosis may be a marker of widespread atherosclerosis of the aortic arch and cerebral vessels [46,50-58].

LIMITATIONS OF THE STUDY

This is a retrospective nonrandomized study in a new cardiac surgery center, as well as we are in the starting period in cardiac surgery in the north of Jordan, our cases are more selective. Inspite of the fact that the quality of patients in the recent years and the improvement of invasive cardiology techniques and the experience of cardiologists, leaving us without a wide range of selections. Carotid artery ultrasound was performed in 45.80% of patients ≥60 years old (not routinely) and the prevalence of carotid artery disease could have been underestimated. Epiaortic ultrasound was not available to evaluate the ascending aorta for atheromatous disease. Detailed preoperative neurological assessment was not performed in our patients. We could not find a clear cut answer for the question if we should change to off-pump, many of these studies going toward off-pump, we think a prospective randomized study with a large number of patients will give us a proper answer.

CONCLUSIONS

Female sex, diabetic patients and patients with previous transient ischemic attacks and significant carotid artery stenosis are associated with increased the risk of stroke and in-hospital mortality. The literature does not offer a clear answer about the common question that recently applied - Should We Change to OFF-Pump? The proper answer would come from one surgeon with a prospective randomize trial.

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