Early Off Pump Coronary Artery Bypass Grafting After Carotid Artery Stenting is Safer than On Pump Coronary Artery Bypass Grafting in Male Patients

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Abstract

Objectives: Our aim was to evaluate and compare the safety and reliability of the early coronary bypass operation either with off-pump or on-pump technique after carotid artery stenting (CAS) in ischemic patients.

Patients and methods: The data of 312 patients with combined coronary and carotid artery disease treated with CAS between 2010 and 2017 prior to CABG in two different centers: Saudi German Hospital in Saudi Arabia and central clinic Bad Berka in Germany were retrospectively reviewed. 189 patients were operated off-pump; they were referred to as group A. The remaining 123 patients were operated on-pump (group B). All patients were submitted for CAS hours before the CABG. In both groups the double antiplatelet therapy was given before and after the carotid stenting and continued after the CABG. Patients in both groups were investigated pre-and postoperative by CT brain and CT angiography of carotid artery. Patients were followed up for stroke, bleeding, MI and mortality for 2 years.

Results: Patients of group A had less mortality, less post-operative bleeding, less myocardial infraction and less stroke after CABG than those in group B. The early timing for the CAS prior to CABG was more safe and reliable in group A.

Conclusion: Early Off-pump CABG after CAS is safer for patients; with fewer complications and less mortality than in On-pump CABG.

Keywords: Off pump; CABG; Carotid stenting

Abbreviations: AF: Atrial fibrillation; CABG: Coronary Artery Bypass Grafting; CAS: Carotid Artery Stenting; CCU: Coronary Care Unit; CEA: Carotid End Artrectomy; CPB: Cardio Pulmonary Bypass; EF: Ejection Fraction; IUC: International Unit; MI: Myocardial Infarction; SD: Standard Deviation; TIA: Transient Ischemic Attack.

Introduction

The first technique using suture in the anastomosis was by Kolesov in 1964. This was the date of the real start of coronary revascularization that we know nowadays. Kolesov did not only launch the era of true CABG, but also, he is the godfather of the off-pump technique performing 82% of his cases for coronary revascularization without the CPB as he stated early the global inflammatory response of the CPB. 6 years later in 1970 he proved the reliability of the off-pump CABG by angiography follow up of his cases. Kolesov was not only the father of the surgical procedure but also the one who first introduced the magnifying goggles during surgery as well as the first surgeon ever to use clinically the coronary stapling technique in the anastomosis. Ever since the era of the heart lung machine flourished and all forgot the off-pump CABG [1].

The cardiac surgeries per se carry a risk of strokes. Statistically in the united states, the reported incidence of stroke in all cardiac surgeries is 2% in all cases operated, 6% in CABG patients and these figures increased to 12% in associated severe carotid artery lesions with cardiac surgeries [2,3]. In most of the cases this event is an intra and post-operative rather than preoperative insult. The proposed reasons were the atherosclerotic aorta, emboli from the machine (complement reaction), atrial fibrillation, mural or left atrial thrombi, cardiac tumours (myxoma), myocardial infarction and carotid lesions. The incidence of strokes with open heart increases with older ages> 70 years, females, hypertension, diabetes, renal failure, COPD, low EF<40%, aortic calcifications, carotid lesions, on-pump surgeries and long bypass time [4,5].

Most reports concluded that the incidence of strokes in off-pump CABG is decreased significantly compared to on-pump CABG. The
incidence was decreased between 50-58% in Off-pump than On-pump, with decreased in-hospital mortality due to stroke too [6-8].

An interesting study in 2004 reported a lower incidence of strokes with the off-pump (1%) and 2.5% in on-pump. 90% of strokes in off-pump had no neurologic deficits and they were delayed strokes (average 4 days after surgery) while they were early after the on-pump (average after 2 days). Notably the mortality rate was higher with early strokes [9].

The above-mentioned causes of strokes are mostly applied for the on-pump surgeries while the reasons of strokes with the off-pump are mostly attributed to the arrhythmias, carotid diseases and the atherosclerotic intracranial vessels. The protocols of most studies of the off-pump recommended not discontinuing the antplatelets before surgery especially in high risk patients [10-12].

With the belief of some authors that the Off-pump surgery is more reliable regarding the incidence of stroke, there is still a controversy and contradicting strategies to treat the associated carotid artery disease. The technique of solving the problem and the timing with the CABG or cardiac surgeries are still debatable. CABG after carotid procedures carry the risk of MI and the necessity to take double antplatelet therapy which may lead to postoperative bleeding or coagulopathies. CABG before solving the problem of the carotids carries the risk of post CABG strokes. Simultaneous CABG and carotid endarterectomy (CEA) or CAS may lead to devastating results and even the strategy within this plan is variable as some authors may start the carotid procedure under general anesthesia after harvesting the grafts for CABG and some others preferred to do the carotid procedures under local anesthesia then start the CABG just after the carotid was accomplished. Whether doing before, after or simultaneous; there was still the risk of the cardiopulmonary bypass (CPB) [13-15].

Moreover, the choice between the two strategies for carotid stenosis treatment has been long debated. For 20 years, the value of the CEA outweighed the aspirin. Since the FDA approval for the carotid stents in August 31, 2004 [15] there is a continuous debate for the indications of both the CAS and the CEA. The American College of Cardiology (ACC) and multisociety updated the guidelines in 2016 for the indications of either of them (Table 1) [16,17].

Patients and Methods

Our retrospective observational study took place between 01/2010 and 01/2017 where 312 patients were operated for combined CABG and carotid stent. The patients were operated in two different centres; Saudi German Hospital in Saudi Arabia and central clinic of Bad Berka in Germany using the same strategy in timings for both the CABG and the carotid stenting (first the CAS then the CABG hours after the stent). 189 patients were operated off-pump and they were referred as group A. Group B patients were operated on-pump (123 patients).

All patients of both groups were submitted to the CAS under local anesthesia. The same pre- and post-operative investigations were performed for both groups with follow up period of 2 years for all patients regarding the incidence of strokes, TIA, MI and mortality.

Inclusion criteria

All male patients whom were operated for combined early CABG after carotid stent between 01/2010 and 01/2017.

Exclusion criteria

1. Recent or old strokes
2. Left ventricular ejection fraction less than 40%.
3. Associated intracranial artery diseases
4. Patients on hemodialysis.
5. Associated atrial fibrillation, ventricular aneurysm, mural thrombus, recent MI (3 weeks or less) and redo cardiac operations.
6. If the Intra-Aortic Balloon (IAB) was inserted.

Pre-operative investigations

All patients were submitted for CBC, Liver and kidney functions, Coagulation profile, Thyroid profile, CT brain and CT angiogram for the great vessels showing the intracranial parts. Transthoracic echocardiography, thorough neurological assessment clinically, femoral duplex, Off-pump CABG technique.

The used procedure in all cases of group A was off-pump without CPB. The procedure was performed early after the carotid procedure from 1 hour to 22 hours maximum. All patients received double antplatelet therapy. The approach median full sternotomy. The hemodynamics of all patients were stable, the systolic blood pressure was almost always kept above 110 mmHg. All patients had full revascularization. Protamine was given as required according to the surgeon’s decision. It was not needed in 37 patients only.

Carotid artery stent (CAS) technique was performed for all patients in group A and B. The patients were in the supine position under local anesthesia in the Cath Lab Room. Heparin 80 IU/Kg was given IV. Seldinger technique was used to insert a hydrophilic guide-wire; the puncture was dilated reaching to 6F sheath. The guide-wire was advanced under fluoroscopy. The catheter was advanced and directed to the selected CCA (right or left). The guide wire was advanced to the ECA guiding an H1 catheter in the ECA. An angiography of the carotids was done. Balloon angioplasty was done prior to the deployment of the stent. A final look angiogram was performed before withdrawal of the wires.

Follow up investigations

1. Thorough neurological examination.
2. Blood picture, Liver and kidney functions, and Coagulation profile.
3. Carotid duplex performed just few hours after the CABG.
4. Transthoracic echocardiography.
5. CT brain and CT angiography for the carotids, CT angiogram for the carotids was performed before patient’s discharge from hospital, 6 months and 2 years after the operations.

Statistical analysis

Standard definitions were used for patient variables and outcomes. Categorical variables are expressed as percentages and continuous variables are expressed as mean ± SD with range throughout the manuscript. All statistical analyses were performed with the IBM SPSS 19.0 software (IBM Corp, New York, USA). All p values of < 0.05 were considered statistically significant.
Results

We reviewed the data of 312 patients grouped as A (Off-pump) and B (on-pump). All patients of both groups were males. The mean age in group A was 52.16 years ± 11.7 years and 51.3 years ± 12.4 years in B with no statistical significant difference. There was also no statistical significant difference regarding other risk factors as smoking, hypertension, diabetes and lipid profile (Table 2).

| Multidisciplinary carotid artery stenting guidelines | Guidelines |
|-----------------------------------------------|------------|
| Indications | | |
| Symptomatic high surgical risk | | |
| >70% stenosis | American Heart Association (AHA) |
| Difficulty to access surgically | American Stroke Association (ASA) |
| Associated medical conditions which increase surgical risk | | |
| Radiation induced stenosis | | |
| Restenosis after CEA | | |
| Unfavorable neck anatomy | Multisociety guidelines |
| Symptomatic with average surgical risk | | |
| Non-invasive imaging shows reduced internal carotid artery diameter to >70%. With risk <6%. | Multisociety guidelines |
| Invasive (angiography) imaging showing reduced diameter >50% with anticipated perioperative stroke or mortality of <6%. | | |
| Symptomatic with low or average risk | | |
| Non-invasive imaging: >70%. | American Heart Association (AHA) |
| Invasive imaging: >50%. | American Stroke Association (ASA) |
| Asymptomatic high surgical risk | | |
| Comorbid conditions | Multisociety guidelines |
| Life expectancy | | |
| Other individual factors | | |
| Asymptomatic with unfavorable neck anatomy for arterial surgery. | Multisociety guidelines |
| Asymptomatic average surgical risk | | |
| Prophylactic CAS. To be evaluated as it is used in 60% stenotic lesions (by angiog) or 70% by validated Doppler ultrasound. | Multisociety guidelines |

Table 1: The American Heart Association Multidisciplinary guidelines (2016) for carotid stenting [16].

The number of symptomatic patients for TIA were almost the same in both groups. The critical left main lesion of coronaries were 23 patients in A (12.1%) and 14 patients in B (11.3%) with p-value of 0.5. The cardiac function in both groups was almost equal with a mean EF % of 52% ± 11.7% in A and 53% ± 12% in B. The average time between the CAS procedure and the start of CABG was: 4.2 hours ±2.3 hours in A and 4 hours ± 1.9 hours in B. The dose of the heparin used during CABG was markedly low in group A than B. Protamine was not needed in only 37 patients in group A (19.6%) while it was given to all patients of B. Group A patients had better results than those of B; regarding the post-operative blood loss, duration of mechanical ventilation, AF, re-exploration for bleeding and CCU stay.

The incidence of strokes was higher in group B than in A. The perioperative mortality in group A was 0%, while in group B there were 2 mortalities; one related to the stroke and the other was due to multi-organ failure after extensive postoperative MI (Table 3). The CAS was patent in all patients of group A post CABG, but it was occluded totally in one patient in B. Postoperatively there were 3 patients that had neurologic deficit while it was just one case who suffered of transient lower limb paresis which recovered after 4 days. The one year follow up as well as the 2 years follow up of both groups revealed no differences in each group regarding the cardiac status, the CAS or the neurological status.
Table 2: Baseline characteristic difference between the two groups.

| Variables          | Group A (off-pump) No.189 patients | Group B (on-pump) No.123 patients | P-value |
|--------------------|------------------------------------|-----------------------------------|---------|
| Age. Mean IQR      | 52.16 (42-63 years)                | 51.3 (39-64 years)                | 0.14    |
| Hypertensive       | 82 pt. 43.33%                      | 51 pt. 41.46%                     | 0.63    |
| Diabetic           | 91 pt. 48.14%                      | 61 pt. 49.59%                     | 0.87    |
| Smoker             | 60 pt. 31.74%                      | 41 pt. 33.33%                     | 0.73    |
| Dyslipidemic       | 81 pt. 42.85%                      | 53 pt. 43.08%                     | 0.65    |
| Status post TIA    | 33 pt. 17.46%                      | 20 pt. 16.25%                     | 0.51    |
| Asymptomatic       | 156 pt. 82.54%                     | 103 pt. 83.74%                    | 0.6     |
| Pre-operative EF%  | 52% ± 11.7%                        | 53% ± 12%                         | 0.81    |

IQR: Interquartile Range; TIA: Transient Ischemic Attack; EF: Ejection Fraction.

Table 3: Operative and end points difference between the two groups.

| Variables                  | Group A (off-pump) No.189 patients | Group B (on-pump) No.123 patients | P-value |
|----------------------------|------------------------------------|-----------------------------------|---------|
| Heparin                    | 150 IU/kg                          | 450 IU/kg                         | 0.001   |
| Heparin antidote           | 152 (80.42%)                       | 123 (100%)                        | 0.0012  |
| Postoperative mech. Vent. time in hours mean ± SD | 5.3 ± 2                  | 8.1 ± 3.6                         | 0.02    |
| Postoperative blood drain in ml mean ± SD  | 450 ± 220                      | 600 ± 350                         | <0.001  |
| Postoperative strokes      | 0%                                  | 2.43%                             | 0.04    |
| Postoperative CAS occlusion| 0%                                  | 1 (0.813%)                        | 0.21    |
| Postoperative MI           | 1(0.529%)                          | 2 (1.626%)                        | 0.09    |
| Postoperative AF           | 12 (6.34%)                         | 27 (21.9%)                        | <0.001  |
| Re-exploration             | 1 (0.529%)                         | 3 (2.43%)                         | 0.00271 |
| Postoperative bleeding, more than 1000 cc | 2 (1.05%)                    | 9 (7.31%)                         | <0.001  |
| Postoperative CCU stay time in days mean ± SD  | 2.7 ± 1.1                     | 3.6 ± 2                           | 0.06    |
| Hospital stay in days mean ± SD     | 8.8 ± 1.5                         | 12.3 ± 4.6                        | 0.02    |
| Postoperative mortality     | 0%                                  | 2 (0.813%)                        | <0.03   |
| Post-operative neurologic deficits | 1 (0.529%)                   | 3 (2.43%)                         | 0.05    |
| Mortality related to stroke | 0%                                  | 1 (0.813%)                        | 0.2     |

SD: Standard Deviation; IU: International Unit; CAS: Coronary Artery Stenting; AF: Atrial Fibrillation; MI: Myocardial Infarction; CCU: Coronary Care Unit; TIA: Transient Ischemic Attack; CABG: Coronary Artery Bypass Grafting.

The overall incidence of stroke with CPB was reported to be between 1- 6% with more incidence being ischemic [23-26]. In our study we excluded patients with possible source of thrombus rather than the carotid artery lesions being a stratified risk factor alone [4]. Other patients that had high risk for perioperative strokes whether they were cardiac or neurological factors were also excluded so as to avoid biased results. Strokes occurred only in the group where the CPB was used with an incidence of 2.43% and were all ischemic strokes. In patients performed off-pump there was no reported neurological insults. Despite our optimistic results; some other authors reported the...
same outcomes in both on and off-pump surgeries [7] and others had results near to ours with an incidence of 1% stroke in their series and 50% reduced rate than the on-pump [8,9]. The lower incidence of post CABG strokes we reported (2.43%) with the on-pump compared to other reports that had almost double this (4.6%-6%) and our 0% incidence with the off-pump CABG was compared to other authors reported 1% might be due to our strict exclusion criteria which might add in return to the limitation of our study [23]. Meanwhile other studies reported higher incidence of strokes (10%) with the staged procedures using off-pump CABG and CAS and the combined procedures (both hybrid and staged) [24-26].

The timing of the CAS procedures in all cases in A and B was few hours before the CABG and they all received double antiplatelet therapy pre-CABG and post as well. In group B there was significant bleeding post CABG that necessitated re-exploration in 3 patients (2.43%) and all had no surgical sources. Despite many authors reported almost equal results of off-pump and on-pump as regards the complications and even they condemned the off-pump for the long-term outcomes, yet they reported lower incidences of strokes and they contradicts for the bleeding and re-exploration postoperatively [27,28]. The timing for CAS in our patients was few hours on average just before CABG, we do not see differences with other authors in the timing except if they used the hybrid strategy as this would never assess the neurologic complications that might happen during the CAS unless they had performed it under local anaesthesia [24]. Barrera and his colleagues reported 2 hours between the CAS and the CABG as the ideal timing and they recorded neither stroke nor mortality or MI or late complications. The limited number in their study may lead to these results. Other authors used different strategy, but they reported almost same results where CABG was performed 5-6 weeks after the CAS and the clopidogrel was discontinued one week prior to CABG.

The hypothesis of selecting male patients was that, most of the study cohort group was collected from Saudi hospitals rather than the German hospital. The demographic distribution of the population in Saudi Arabia is tilting more towards male gender because the data were collected from a private hospital where most of the admitted patients are males who are employed in Saudi Arabia. It’s worth noting that most of the foreigners employed in Saudi Arabia are living as singles leaving their families in home land. Consequently, we selected only males in our study.

Conclusion

It is safe and reliable to perform synchronous CAS/CABG starting by CAS under local anesthesia then no matter after how many hours we can perform the CABG which was preferred to be off-pump than using the CPB as it gave better outcomes regarding the early mortality, bleeding and strokes.

Notes

Ashraf Fawzy, Mahmoud Salah Eldin and Farouk Hassan Elalfy: conceived of the presented idea. A.B. developed the theory and performed the computations. Tamer Owais, Ashraf Fawzy, Martin Breuer, Thomas Kuntze: cardiac surgeon carried out bypass operations. Mahmoud Salah Eldin and Farouk Hassan Elalfy: carried out carotid stenting. Mohammad El Garhy: cardiologist followed up the patients after the operations and verified the analytical methods. Tamer Owais: took the lead in writing the manuscript and is the corresponding author. Mohammad El Garhy: contributed to the final version of the manuscript. Thomas Kuntze: supervised the findings of this work.

All authors discussed the results and provided critical feedback and helped shape the research, analysis and manuscript.

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