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Coronary Artery Bypass and Stroke: Incidence, Etiology, Pathogenesis, and Surgical Strategies to Prevent Neurological Complications

Marco Gennari, Gianluca Polvani,
Tommaso Generali, Sabrina Manganiello,
Gabriella Ricciardi and Marco Agrifoglio

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Abstract

Current data suggest that cardiac bypass surgery is the single largest cause of iatrogenic stroke. Among the strategies to decrease or eliminate aortic manipulation, there is the use of off-pump coronary artery bypass grafting (CABG) through an aortic “no touch” technique, which reduces significantly the stroke rate. However, this off-pump aortic “no touch” technique is not always applicable, and, when saphenous vein and/or free arterial aortocoronary grafts are used, there is still risk of neurological injury due to tangential aortic clamp applied during the proximal anastomosis sewing. We aim to analyze the current incidence, etiology, and physiopathology of the neurological complications after coronary artery bypass surgery. We describe the methods and techniques that provide reduction in the occurrence of neurological complications. CABG with multiple clamp technique failed to find a better outcome in terms of neuropsychological deficit in the OPCABG group. By the way, patients undergoing CABG with single clamping seems to have better outcomes, suggesting that the cross-clamping technique used and minimal aortic manipulation could have had a role in reducing neurocognitive impairment. Moreover, surprisingly, CPB seemed to be a neuroprotective factor, and this aspect could be linked to the mild hypothermia used during on-pump surgery.

Keywords: coronary artery bypass, stroke, cardiac surgery, aortic cross clamp, neurologic impairment

1. Introduction

In 1978 the World Health Organization defined a stroke as a focal or global neurologic deficit due to cerebrovascular cause that persists beyond 24 hours or is interrupted by death within 24 hours [1].

Strokes are classified by etiology into **ischemic strokes** (85%) and **hemorrhagic strokes** (15%). Ischemic strokes result from a critical reduction in blood flow and are categorized as embolic, thrombotic, hemodynamic, or hypotensive [2].

Cerebrovascular accidents (CVAs) remain one of the most common complications after surgical myocardial revascularization despite the increased quality of treatment. Cerebral injuries are associated with substantial increases in mortality, morbidity, length of hospitalization, and an impaired quality of life [3].

Ischemic stroke occurs in 1.5–5.2% of patients. Percentage varies across studies and depends on study design, patient risk profile, operative techniques, and the length of study follow-up. Although advances in surgical and medical management have occurred across the last 10 years, the risk of stroke after coronary artery bypass grafting (CABG) has not significantly declined likely because of the progressive aging of the CABG population [4].

The etiology of postoperative stroke is multifactorial. Previous studies showed that the risk factors for postoperative stroke following CABG include age, low left ventricular ejection fraction, unstable angina, atherosclerosis of the ascending aorta, chronic renal failure, chronic obstructive pulmonary disease, calcified aorta, a history of previous stroke, carotid stenosis, duration of cardiopulmonary bypass, peripheral vascular disease, smoke, and diabetes mellitus. The age seems the most important risk factor for postoperative stroke, followed by palpable calcification in the ascending aorta and arch [5, 6].

1.1. Epidemiology

The prevalence of stroke after surgery varies according to the different types of surgery and patient comorbidities. A postoperative stroke is reported to occur in 0.08–0.7% of patients after general surgery, in 0.8–3% after peripheral vascular surgery, in 4.8% after head and neck surgery, in 2–3% after carotid endarterectomy, in 8.7% after aortic repair, and in 5.7% after cardiac surgery. Furthermore, patients with advanced age, previous stroke or transient ischemic attack (TIA), or postoperative atrial fibrillation are at increased risk for postoperative strokes [7, 8].

Most postoperative strokes do not occur immediately after surgery; there is usually a symptom-free interval before ischemia becomes apparent. In a recent retrospective study, only 8% of strokes appeared in the postanesthesia care unit. Approximately 45% of occurrences are identified within the first day after surgery [9].

The incidence of early stroke within 30 days of the myocardial surgery revascularization is reported to be 2–4%. Other studies indicated that the rate of postoperative stroke in octogenarians ranged from 2 to 9% [10].

Recent studies using sensitive brain magnetic resonance imaging (MRI) with diffusion-weighted imaging report that 45% of patients who have undergone cardiac surgery have new ischemic brain lesions that are often clinically undetected. For this reason, the prevalence of stroke can be higher than documented [11, 12].

2. Incidence and etiology of neurological events after cardiac surgery

2.1. Cerebral embolism

It is possible to divide emboli into two categories: microemboli and macroemboli according to size (200 μm or greater). This distinction reflects different clinical manifestations: a single macroembolus can result in hemiplegia; instead, a microembolus is unlikely to have a noticeable effect except when these emboli are numerous. Macroemboli are unlikely to arise from the extracorporeal circuit but rather from surgical manipulation of the heart and the aorta. There are other categories: gaseous, biologic, inorganic, etc [13].

Gaseous emboli are usually derived from air or anesthetic gas (such as nitrous oxide). These emboli are introduced into the left side of the heart (during aorta or mitral valve replacement) or into the aorta (from the bypass circuit). The superiority of membrane oxygenators compared with bubble oxygenators in reducing cardiopulmonary bypass (CPB)-generated embolism has been demonstrated by ultrasound and retinal angiography [14].

Inorganic embolism which can arise from embolization of fragments of polyvinyl chloride tubing exposed to roller pump has been described.

Biologic aggregates include thrombus, platelets, and fat. Thrombus can arise from the left appendage, the left ventricular aneurysm, or from the CPB circuit. Heparin may contribute to create fat embolism by stimulating endothelial lipoprotein lipase. It seems that the principal sources of cholesterol embolism are large vessels of atherosclerotic plaques.

2.2. Cerebral hypoperfusion

Although a postoperative stroke is most often embolic in origin, an association between intraoperative hypotension and the occurrence of a postoperative stroke is often assumed.

Some authors identified the watershed infarcts; these are areas of the brain that are between non-anastomosing arterial vessels and arteries. They are termed watershed or border-zone areas. They are critically dependent on adequate perfusion pressure in the border-zone vessels. A reduction in perfusion below a critical value will result in ischemia because of inadequate collateral circulation. Infarction of watershed areas has been regarded as the hallmark of hemodynamic strokes. There are two major watershed regions. The cortical watershed areas are between the cortical branches of the anterior, middle, and posterior cerebral arteries. The internal or subcortical watershed is located in the white matter along and slightly above the lateral ventricles between the deep (lenticulostriate) and the cortical branches of the middle cerebral artery and the anterior cerebral arteries. There is much controversy about the relative contribution of low-flow pathophysiology. For example, it is hard to determine whether a local low-flow state due to hypoperfusion results in platelet microemboli or whether platelet microemboli result in local hypoperfusion. Irrespective of the sequence, there is a synergistic interaction [15, 16].

Intraoperative hypotension is a common event during surgery. Bijker et al. reviewed four major anesthesia journals for their definitions of hypotension. Almost 50 different definitions

were found utilizing systolic pressure and/or mean pressure either as an absolute or as a percentage of the baseline value. Diastolic pressure was never used. The most frequent definitions were as follows [17, 18]:

1. A 20% decrease in systolic pressure from the baseline value.
2. A combination of systolic pressures below 100 mmHg or greater than 30% decrease from the baseline value.
3. A systolic pressure below 80 mmHg. A definition of “baseline” was provided in only 50% of the manuscripts but was most frequently the blood pressure immediately before induction of anesthesia.

The majority of the articles stated how frequently blood pressure was measured, but only 10% of the articles specified a minimum duration for which reduced blood pressure would constitute hypotension.

Furthermore, it is possible to find a congenital variation of the circle of Willis. A persistent complete fetal-type posterior circulation results in the complete separation of the posterior and anterior circulations and occurs in 1–4% of the population. Development of collaterals usually occurs slowly, although hypoplastic vessels may have the capacity to be more acutely dilated. The contribution of the abnormalities to perioperative stroke is unknown, although, as shown in a recent case report, they may be an important factor for some patients [19, 20].

2.3. Atherosclerosis of the aorta

Aortic atherosclerosis is characterized by the formation of intimal plaques with the usual morphologic features of atherosclerosis, including cellular proliferation, lipid accumulation, inflammation, necrosis, fibrosis, and calcifications. Ulceration of these plaques can result in embolization of plaque elements or thrombus formation, which can lead to neurologic deficit, stroke, and death. Cardiac surgery usually involves manipulation of the ascending aorta by arterial cannulation and cross clamping. All of which can increase the risk of embolization of atherosclerotic material to the brain. The prevalence of atherosclerotic disease in the ascending aorta varies across studies, depending on the patient population, the criteria used to define the disease, and the diagnostic tool implemented to detect the disease. This type of disease has significantly increased in recent years, likely due to better diagnostic methods and an increasing population of elderly. Peripheral vascular disease, age, hypertension, and diabetes have been reported to be independent predictors of atherosclerotic disease of the ascending aorta [21].

The magnitude of this problem was well illustrated in a large prospective study by Roach et al. involving 24 centers. They reported a 3.1% incidence of type 1 neurologic injury (focal injury or stupor or coma at discharge) after CABG. Affected patients had a higher in-hospital mortality rate than patients without neurologic complications (21% vs. 2%), as well as a longer hospital stay (25 days vs. 10 days). Predictors of type I outcomes were palpable proximal aortic atherosclerosis, a history of neurologic disease, and older age. A high correlation between atherosclerosis of the ascending aorta and atheroembolism during CABG surgery has been established by several studies. Observational studies have shown, for example, that

atherosclerosis of the ascending aorta detected at the time of surgery is an independent risk factor for stroke. A previous study documented that the presence of atherosclerosis alone in this region in patient undergoing cardiac surgery increased the risk of early postoperative stroke from 1.8 to 8.7%. It is widely postulated that the proximate cause of atheroembolism is disruption of the atheroma during surgical manipulations such as for aortic cannulation, aortic cross clamping, or proximal coronary artery anastomosis. These interventions are associated with increases in Doppler-detected cerebral embolic signals, but the composition of these emboli cannot be determined. Disruption of atherosclerotic lesions was verified in a study of 472 patients who underwent epiaortic ultrasound before and after CPB, with new mobile lesions of the ascending aorta identified in 10 (3.4%) of patients after surgery at sites of aortic clamping or cannulation and stroke occurring in 3 of these 10 patients. A smaller study by Ribakove et al. revealed a similar rate of stroke (3 out of 10) in patients with identified mobile lesions (31). Swaminathan et al. demonstrated the potential of atheroma disruption due to the “sandblasting” effect of CPB at the site of the aortic cannula [22, 23].

Injury involving atherosclerotic lesions not only can result in emboli during surgery but may also expose lipid-laden, prothrombotic material that could promote thrombus formation postoperatively after heparin neutralization. Finally, atherosclerosis of the ascending aorta identifies patients likely to have severe atherosclerosis of cerebral arteries who are prone to cerebral injury from hypoperfusion. For this reason, avoidance of significant hypotension during and after surgery may be prudent to avoid neurologic injury [24, 25].

2.4. Atrial fibrillation

Atrial fibrillation (AF) is the most common sustained arrhythmia encountered in clinical practice. Its prevalence increases with age, affecting approximately 1% of the total population and 8% of individuals over 80 years old. The incidence of postoperative AF following coronary artery bypass grafting (CABG) surgery is high and ranges between 20 and 40% of patients. It increases the length of hospital stay and hospital costs and is associated with increased morbidity and mortality including postoperative stroke, as well as in-hospital and 6-month mortality. Postoperative AF typically develops within the first week post surgery, at a median time of 2 days after the operation. It generally resolves within 24–48 hours, and most patients are discharged in sinus rhythm. Several factors have been found to predict the risk of postoperative AF following CABG, including enlarged left atrial size and prolonged hospitalization post surgery [26].

In medical patients with chronic or recurrent AF, the cause and effect relationship between the arrhythmia and the cerebrovascular event has been unquestionably proven [27].

Lahtinen and colleagues from Finland analyzed data of 52 stroke patients after CABG operation and found that in 19 patients (36%) the first AF episode preceded the development of stroke by a mean of 21.3 hours (average, 2.5 AF episodes before stroke). The stroke was attributed to calcification in the ascending aorta in 13 patients (25%), and 16 patients (31%) had greater than 70% internal carotid artery stenosis [28].

The pathophysiology of postoperative AF is not completely understood. Apart from obvious comorbid conditions such as valvular heart disease, atrial enlargement, congestive heart failure, and history of preoperative atrial arrhythmias, several other risk factors predispose

cardiac surgical patients for postoperative AF. Advanced age is the strongest, followed by systemic hypertension, left ventricular hypertrophy, peripheral vascular disease, and chronic lung disease. Longer cardiopulmonary bypass time and aortic cross-clamping time have been shown to be associated with increased incidence of postoperative AF. Postoperative pericardial fluid collection and pericarditis have also been associated with atrial arrhythmias [29].

2.5. Genetic predisposition

It has been suggested that genetic predisposition might explain the marked variability in individual susceptibility for cerebral injury from cardiac surgery despite similar risk. Tardiff was the first to show a relationship between the risk of postoperative neurocognitive dysfunction and the presence of the apolipoprotein E ϵ 4 allele. The apolipoprotein E (APOE) ϵ 4 genotype is a plausible candidate gene since it has been shown to increase risk for Alzheimer's disease and cognitive decline after cerebral injury. Other investigators have examined for a relationship between polymorphisms of genes involved in pathways regulating coagulation, cell adhesion, and inflammation with perioperative cerebral injury [30].

The C-reactive protein minor allele 1059G/C SNP and the P-selectin allele SELP 1087G/A allele were further found to be associated with decline in cognition 6 weeks after CABG surgery.

Grocott et al. documented that the presence of at least one minor allele at each of the two loci (CRP, 3'_UTR 1846C/T; IL-6, 74G/C) is a risk factor for stroke, increasing risk more than three-fold (60). The observation that the interaction of these two inflammatory SNPs contributes to perioperative stroke suggests that inflammatory pathways may be important mechanistic factors in either initiating or otherwise modulating stroke after cardiac surgery. This interpretation is consistent with the current knowledge regarding CPB initiating and IL-6 mediating a robust inflammatory response. This finding is also consistent with the view that inflammation plays an important role in the etiology of stroke in the general population [31].

2.6. Carotid stenosis

Carotid artery atherosclerosis often accompanies significant coronary atherosclerotic lesions. Hypoperfusion arising from a severely stenotic carotid artery or embolization from an ulcerated plaque, calcific debris from a diseased valve, and introduction of air during the procedure are important mechanisms. The risk of stroke in patients with carotid artery disease after CABG has been estimated 1.8% in patients with stenosis <50%, 3.2% in patients with stenosis between 50 and 99%, and 10% in patients with contralateral occlusion. It is thought that carotid intra-plaque hemorrhage can result in plaque destabilization and intimal ulceration, creating a nidus for thromboembolism. Intra-plaque hemorrhage detected by magnetic resonance imaging is associated with increase of ipsilateral stroke in symptomatic and asymptomatic nonsurgical patients. Impaired cerebral hemodynamic functional distal to carotid artery stenosis is another determinant of postoperative stroke. Maximally dilated vessels distal to carotid artery stenosis can no longer vasodilate in response to hemodynamic compromise. Therefore, perioperative reduction in blood pressure or cardiac output in this group of patients is hypothesized to lead to cerebral ischemia [32, 33].

3. Pathogenesis of neurological complications in conventional coronary artery bypass grafting (CABG)

3.1. Risk factors of stroke after myocardial revascularization

The risk factors of postoperative stroke can be divided into preoperative, intraoperative, and postoperative factors [34].

Preoperative factors include advanced age, atherosclerosis in the ascending aorta, unstable angina, hypertension, history of stroke, and redo surgery. Emergency surgery is performed for critical left main coronary artery disease (more or equal to 70% luminal narrowing with or without angina), or unstable cardiac conditions are also significant predictors of stroke after CABG procedure.

Intraoperative factors include the endurance of extracorporeal circulation and aorta clamping or operation type. Some reports demonstrate that the number of revascularized vessels (more or equal to three) is associated with a higher incidence of stroke after CABG procedure.

Finally, **postoperative factors** include atrial fibrillation, microembolism detachment, and hypotension.

The single most important risk factor for post-myocardial revascularization stroke is atrial fibrillation, newly onset or chronic. This arrhythmia occurs in up to 20% of patients following a STEMI and is associated with a significant increase in risk for an in-hospital stroke.

It is also well known that a high correlation exists between atherosclerosis of the ascending aorta and atheroembolism during CABG surgery, as several studies show.

In a prospective multicenter study including more than 2000 patients, atherosclerosis of the ascending aorta was the strongest independent predictor of stroke associated with CABG. In the study by Bergman et al., extensive atherosclerotic disease of the ascending aorta was associated with a 31% risk of postoperative stroke. The risk depends on the presence, location, and extent of disease, whenever the aorta is surgically manipulated.

Age > 75, black race, peripheral vascular disease, diabetes, renal impairment, hypertension, any frailty, and no aspirin therapy on discharge are also strong independent predictors of ischemic stroke [8]. In particular, age shows a strong correlation with stroke: for each 1 year increase in age, the odds of stroke increases by 12% [35].

In addition, the incidence of postoperative stroke in patients with a history of stroke is significantly higher than in patient with no previous history of stroke. Maybe, these data are due to associated older age and more complicated comorbidities of these patients.

3.2. Pathogenesis of stroke after myocardial revascularization

The two mechanisms responsible for stroke after CABG procedure are ischemia and hemorrhage. Some studies suggest that pan-vascular inflammation may also play a role, especially in the setting of acute coronary syndromes.

Ischemia can be due to embolic events (from cardiac chambers, aorta, or other peripheral arteries), thromboembolism of intra- or extracranial vessels, or systemic hypoperfusion. Hypoperfusion stroke arises from hemodynamic compromise distal to the carotid/cranial artery stenosis and has been associated with the patients' capacity for cerebral autoregulation [36].

Hemorrhage is instead associated with hypertension or reperfusion of infarcted area. The interaction between embolism and hypoperfusion is generally considered to be a major cause of postoperative stroke. Hypoperfusion may contribute to embolism retention. Several studies have found multiple emboli in the cortical watershed of patients who died after cardiac surgery. A recent study from Cao and co-workers suggests that unstable angina, LVEF <50%, and hypotension are risk factors of postoperative recurrent stroke. All of these factors decrease brain perfusion, leading to stroke.

Embolic ischemic stroke is generally caused by an embolus from the left atrium, as in atrial fibrillation, or from the left ventricle, as in recent AMI. Embolization of atheromatous debris from the aorta, instead, is likely to occur at the time of cannulation of the vessel to establish cardiopulmonary bypass, when the aortic clamp is applied or released or when proximal graft anastomoses are performed using side-biting clamp. Cerebral emboli often coexist with intraoperative hypoperfusion, which impairs the clearance of microemboli and may be responsible of bilateral watershed infarcts after CABG. Cerebral hypoperfusion may be exacerbated by the coexistence of carotid artery stenosis, which is another important risk factor for intraoperative stroke [37].

Thrombotic thromboembolism is related to the atherosclerotic disease of the intracranial vessels or hematologic pathologies. Thromboembolic strokes are most frequently caused by thrombus formation at the site of the ulcerated atherosclerotic plaque on the carotid/cranial arteries, although the aortic arch can also be a site of thrombus formation.

Neurological events after CABG are classified as:

- **Type 1:** in case of focal stroke, transient ischemic attack, or fatal brain damage.
- **Type 2:** in case of diffuse brain injury with disorientation and intellectual deterioration, which are normally reversible.

The stroke that occurs within the first 24 hours after the CABG is a potentially devastating complication. It is associated with the increased hospital mortality.

3.3. Risk stratification

Identification of vulnerable patients at increased risk of stroke before CABG is of paramount importance for the surgical decision-making approach and informed consent. As previously said, age, diabetes, hypertension, peripheral vascular disease, renal failure, left ventricular dysfunction, and nonelective surgery have consistently been reported as risk factors of perioperative stroke in patients undergoing CABG surgery. All these risk factors can be assessed before surgery. The combination of these variables has generated several risk stratification tools that can be implemented before surgery, to determine the individual probability of stroke in patients undergoing CABG [38].

In the Charlesworth score, generated from 33,000 consecutive patients undergoing isolated CABG, seven variables are integrated, including age, diabetes, left ventricular ejection fraction <40%, female gender, priority of surgery, renal dysfunction, and peripheral vascular disease. In the simpler model generated by McKhann et al., only three variables are considered: age, hypertension, and history of stroke. More recently, Hornero et al. generated and validated a new risk model (Pack2 score), including priority of surgery, peripheral vascular disease, preoperative cardiac failure/left ventricular ejection fraction <40%, and chronic kidney failure. Interestingly, in patients with Pack2 score ≥ 2 , off-pump CABG significantly reduced the risk of stroke compared with on-pump CABG, whereas no difference was apparent between the two strategies of revascularization in patients with Pack2 score < 2. Further studies should externally validate this score and assess whether it is useful in clinical practice to select the optimal strategy of revascularization between on-pump and off-pump CABG in high-risk patients.

However, these risk stratification tools share a major limitation in disregarding two important risk factors—atherosclerotic disease of the ascending aorta and pre-existing cerebrovascular disease. These factors should always be analyzed to make the optimal strategy of coronary revascularization within Heart Team environment.

Unfortunately, severe atherosclerosis of the ascending aorta is often an unexpected intraoperative finding during CABG, especially if preoperative risk stratification has not been accurate. It still represents a challenge for the surgeon, and sometimes the operative strategy must be changed at the time of surgery. The methods to diagnose severe atherosclerosis in the ascending aorta before surgery include computed tomography scanning, transesophageal echocardiography, or magnetic resonance imaging. Intraoperative ultrasonographic scanning of the aorta can also be used to find atherosclerotic changes in the entire ascending aorta. It is a rapid, safe, and sensitive method, and in some studies, it has been found to be more accurate than both transesophageal echocardiography and computed tomography in detecting atheromatous debris in the ascending aorta.

Assessment of the neurological risk profile of patients before CABG is another essential step to plan the surgery and predict the patients' risk for postoperative stroke. The neurological profile of the patient should be carefully characterized, seeking for a history of stroke, the presence of initial neurocognitive disorders, or the presence of pre-existing cerebrovascular disease. Recent studies have also suggested that detection of cerebral ischemia by magnetic resonance imaging before CABG is strongly associated with the risk of postoperative stroke. Searching for carotid artery disease with echo Doppler before CABG is also a safer and cheaper method of screening, especially in high-risk patients.

4. Off-pump coronary artery bypass (OPCAB) and “no touch technique” as strategies to reduce the neurological risk

CPB is still the most diffused technique used to perform CABG. Even if debate on the superiority of on-pump CABG over off-pump CABG (OPCABG) is still open, evidences of prospective studies like ROOBY trial showed better results in terms of cumulative 1-year events

for myocardial infarction and revascularization procedures and better rate of venous graft patency at 1 year, along with better Fitz-Gibbon grade for on-pump CABG [39].

While other studies such as the SMART trial highlighted no significant differences between the two techniques in terms of mortality, myocardial infarction, stroke, and recurrent angina or readmission for cardiac or noncardiac events, on-pump CABG is still the gold standard procedure, and CPB is the most widely applied technique.

However, the use of CPB has been advocated to be related with a certain risk of neurocognitive sequelae linked with inflammatory response and microembolism [40].

On the other hand, cannulation itself, cross clamping, and, more widely, aortic manipulation have showed to be linked with neurocognitive impairment.

This point was also taken into consideration in ROOBY trial, where patient evaluation with neuropsychological testing was performed in every case in order to investigate memory, attention, and visuospatial skills. All the tests failed to find any clinically significant difference between the two groups, but a better scoring in the clock-drawing test was reported for the off-pump group.

This aspect was also investigated in other studies with no clear results. Remarkably, Hammon et al. prospectively analyzed 237 high-risk patients undergoing OPCABG vs. CABG with single clamp technique [41].

CABG with multiple clamp technique failed to find a better outcome in terms of neuropsychological deficit in the OPCABG group. By the way, patients undergoing CABG with single clamping had better outcome, suggesting that the cross clamping technique used and minimal aortic manipulation could have had a role in reducing neurocognitive impairment. Moreover, surprisingly, CPB seemed to be a neuroprotective factor, and this aspect could be linked to the mild hypothermia used during on-pump surgery [42].

In our study, the aim was to evaluate the acute rate of neurovascular outcome in two relatively homogeneous groups of patients, treated by the same senior surgeon in the same time frame. Neurological evaluation included clinical exam and CT scan. Five patients were found to have experienced ischemic stroke (2%) with no significant clinical sequelae, probably because of the limited interested cerebral area. However, no difference in the stroke rate between the SAC and DAC groups could be found. This is in contrast with other studies. Tsang et al. in 2003 randomized 268 patients either to single or multiple clamps with a higher rate of cerebrovascular accident in the multiple clamp group.

This fact should be taken into account if considering their results. In our study, patients were selected to be at low risk of cerebrovascular accident in order to have less confounding factors [43].

Gerriets et al. have also advocated the use of intra-aortic filter but failed to show a clinical significant benefit in their randomized trial.

Other parameters such as biochemical markers have been evaluated. Dar et al. showed that in a series of 50 patients randomized to single or multiple clamping CABG, S-100 protein levels

were significantly higher in the second group; the troponin T levels were also evaluated with no significance. However, no clinically significant differences were found between the two groups.

In our cohort, none of the techniques used showed to be superior in terms of stroke incidence over the other. As each technique has its own surgical advantages and disadvantages (for instance, more space to perform proximal anastomosis in SAC and direct evaluation of graft's length in DAC), the surgeon should choose the technique with which he is more confident in order to have the best surgical result, as good outcome with very low complications rate can be achieved with both techniques. However, in selected patients, according to the literature, it can be rational to reduce aortic manipulation in the presence of aortic atheromas and to use mild hypothermia in order to have better cerebral protection, and SAC strategy could be preferred over DAC. OPCABG and the use of double mammary graft or Y configuration could be advocated in the case of porcelain aorta in order to avoid aortic manipulation [44].

An interesting aspect, as reported by Hammon et al., is that neuropsychological deficits, even if absent and even not radiologically detectable early after operation, can appear over a period of 6 months, suggesting that a closer neurological follow-up should be taken into consideration especially in high-risk patients to better estimate the real neurological outcome [45].

Regarding the so-called no touch technique, i.e., performing CABG without touching the aorta by anastomosing the grafts to the in situ left and/or right mammary arteries, the main concern is the technical feasibility and the need for adequate mammary arteries caliber and coronary arteries run-off, in order to adequately distribute the blood flow to the coronary bed [46].

5. Conclusion

In conclusion, incidence of stroke seems to be independent from cross-clamping technique, and, more generally, we could infer that the global rate of stroke after CABG is probably more influenced by the presence of subjacent risk factors as aortic atheromas, carotid stenosis, and peripheral vascular disease.

Author details

Marco Gennari^{1*}, Gianluca Polvani^{1,2}, Tommaso Generali³, Sabrina Manganiello¹, Gabriella Ricciardi¹ and Marco Agrifoglio^{1,2}

*Address all correspondence to: marcogennari.md@gmail.com

1 Centro Cardiologico Monzino, IRCCS, Milan, Italy

2 Department of Cardiovascular Sciences and Community Health, University of Milan, Italy

3 San Donato Hospital, IRCCS, Italy

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