

Influence of Carotid Injury in Post-Myocardial Revascularization Surgery and Its Late Evolution

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Abstract

Background: Approximately 30% of perioperative CVA of myocardial revascularization surgery (MRS) are a result of carotid injuries, without reduction of risk confirmed by perioperative intervention.

Objectives: Evaluate the impact of carotid disease and perioperative intervention in patients subjected to MRS.

Methods: Observational, retrospective study, evaluating 1169 patients aged ≥ 69 years undergoing MRS from January, 2006 and December, 2010, monitored, on average, for 49 months. All patients were subjected to ultrasonography of carotids before MRS. It was defined as carotid disease when lesion $\geq 50\%$. The primary outcome was composed of CVA incidence, transitory ischemic accident (TIA) and death due CVA.

Results: Prevalence of carotid disease was of 19.9% of patients. The incidence of primary outcome between unhealthy and healthy patients was of 6.5% and 3.7%, respectively ($p = 0.0018$). In the first 30 days, there were 18.2% of events. Were related to carotid disease: renal dysfunction (OR 2.03, IC95% 1.34-3.07; $p < 0.01$), peripheral arterial disease (OR 1.80, IC95% 1.22-2.65; $p < 0.01$) and previous myocardial infarction (OR 0.47, IC95% 0.35-0.65; $p < 0.01$). Regarding the primary outcome, were associated the previous TIA (OR 5.66, IC95% 1.67-6.35; $p < 0.01$) and renal dysfunction (OR 3.28, IC95% 1.67-6.45; $p < 0.01$). In patients with lesion $\geq 70\%$, perioperative carotid intervention demonstrated an incidence of 16% in primary outcome compared to 4.3% in conservatory treatment ($p = 0.056$) with no difference between percutaneous and surgical approaches ($p = 0.516$).

Conclusion: Carotid disease increases the risk of CVA, TIA or death due to CVA in MRS. However, the carotid intervention was not related to reduction of primary outcome. (Arq Bras Cardiol. 2013;101(4):297-303)

Keywords: Carotid Stenosis / complications; Myocardial Revascularization; Peri operative Care.

Introduction

Cerebrovascular accident (CVA) is one of the risks related to myocardial revascularization surgery (MRS), which leads to a death rate of 19% and it has a significant social and functional impact¹.

About 30% of perioperative CVA result from lesions in carotids, and the more significant the vessel obstruction level and when both carotids are injured, the greater is the risk of this event².

Current recommendations regarding the treatment of carotid disease (CD) in MRS context are contradictory. Brazilian guidelines on surgical treatment for myocardial revascularization, valvulopathies and aorta recommend that patients with transitory ischemic accident (TIA), amaurosis, peripheral obstructive disease and age above 60 years carry out Doppler ultrasonography and arteriography. In case of carotid injury, symptomatic patient with injury above 60% and

unstable angina, stem and multiarterial injury, simultaneous surgery is recommended; in case of stable angina, simultaneous or staged surgery. If the patient is asymptomatic and has lesion below 60%, MRS is recommended³. However, according to the American College of Cardiology, in patients with indication for MRS and previous CVA or TIA, with significant carotid stenosis, it is reasonable to consider a carotid revascularization with MRS. But in patients with no history of CVA or TIA, intervention is considered if there are no significant bilateral carotid injuries or severe unilateral stenoses with contralateral occlusion⁴.

This study was designed to evaluate the prevalence of significant carotid injury, its association with more relevant cerebrovascular events (CVA, TIA, death) and clinical, demographic and angiographic characteristics of patients, considering population above the age of 65 years, subjected to MRS.

Methods

Study population

An observational, retrospective study was carried out, evaluating data obtained from medical charts of patients aged 65 or older, consecutively subjected to MRS, between January 2006 and December 2010, and prospectively followed-up for

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a period of 49 months. A retrospective analysis of outcomes and demographic and clinical data was then performed.

The study was approved by the local ethics committee, which was carried out with resources from the sector itself.

From all patients subjected to MRS within the period, approximately 44% were at the age of 65 or older and, of these patients, 92.7% (1,169) were subjected to pre-operative investigation for carotid disease. Among the reasons for which patients did not undergo Doppler ultrasonography of carotids, were unstable coronary disease and emergency MRS.

Evaluation of carotid disease

The definition of carotid disease was based on peak systolic velocity in the internal carotid artery evaluated by Doppler ultrasonography and classified according to injury level: absent or mild stenosis (< 50%), moderate stenosis (50-69%), severe stenosis (70-99%) and occlusion (100%)⁵. In this study, significant and severe carotid disease were those classified with stenosis of level $\geq 50\%$ and $\geq 70\%$, respectively, considered in the presence of unilateral or bilateral disease.

Surgical procedures, indication and technique applied

MRS indication followed the guidelines for myocardial revascularization surgery³. Surgical procedure was carried out using median sternotomy, using electrical scalpel and opening of pericardium with inverted 'T' incision. The internal thoracic artery was used in almost all cases associated with the greater saphenous vein when necessary.

The surgical procedure was carried out with the aid of extracorporeal circulation in 97.4% of cases. Extracorporeal circulation was performed with membrane oxygenator; it was filled with saline.

Myocardial protection was achieved with intermittent clamping of aorta (anoxic clamping), clamping with no longer than 15 minutes and a two-minute interval between the clamping.

The decision for carotid procedure associated with MRS was made by the medical team. In cases where *percutaneous* implantation of endoprostheses was chosen, it was associated with acetylsalicylic acid the use of clopidogrel, 75mg, daily for 30 days.

Combined surgery

Combined surgery was indicated in the presence of symptomatic carotid disease associated with unstable or critical coronary disease. However, therapeutic options

were individualized, case by case, and decided by a multidisciplinary team.

Before the myocardial revascularization procedure, a neck incision was performed. The carotid artery had its plate removed. A patch could be used to close the artery. After revascularization and use of protamine, skin and subcutaneous tissue were sutured. All patients underwent surgical procedures on aspirin.

Statistical analysis

For comparisons of categorical variables, Fisher's exact test was applied and, for continuous variables, Student t-test. Values of $p < 0.05$ were considered statistically significant. A univariate analysis evaluating the relation between risk factors and level of carotid disease was performed. Variables that showed values of $p \leq 0.1$ in univariate models were analyzed by multivariate regression.

Objectives

Defined as primary outcome associated with carotid disease was the incidence of compound event CVA, TIA and death due to CVA, being CVA defined as clinical and *persistent neurological deficit* after 24 hours of its installation, confirmed or not by imaging test, and TIA as reverted deficit within 24 hours after installation. Secondary outcome was defined as all-cause mortality.

Results

We evaluated 1,169 patients, in which we found prevalence of significant carotid disease (injury on vessel $\geq 50\%$) was of 19.9%. It was observed severe lesions (injury on vessel $\geq 70\%$) in 8.6% of patients, and 2% of these showed total occlusion in at least one vessel (Table 1).

Mean age of study patients was of 71.6 years (SD ± 4.9), ranging from 65-95 years old. Among those with significant carotid injury, mean age was of 72.1 years old (SD ± 5.2) and, among those without significant disease, 71.4 years old (SD ± 4.8) ($p = 0.127$). For severe CD, mean age was of 73.1 years old (SD ± 5.4), while for patients without severe CD was of 71.4 years old (SD ± 4.8) ($p = 0.002$).

We found as predictors of significant carotid disease, in univariate analysis, systemic arterial hypertension (SAH), previous TIA, renal dysfunction and peripheral arterial disease (Table 2). Multivariate analysis showed the following predictors: renal dysfunction and peripheral vasculopathy (Table 3). In both, AMI was observed as protective factor.

Table 1 - Distribution of patients according to the carotid stenosis level according to Doppler ultrasonography of the carotid

Level of carotid stenosis	Absolute number of patients	Percentage of patients in relation to the general population
Without injury	148	12.7
<50%	789	67.5
50-69%	132	11.3
70-99%	77	6.6
Total occlusion	23	2.0
Total	1.169	100

Table 2 - Clinical characteristics of patients with significant carotid disease ($\geq 50\%$)

Variables	CD < 50% (n = 937)	CD $\geq 50\%$ (n = 232)	Odds ratio	p
Female	34.7%	40.5%	0.78 (0.58-1.05)	0.10
SAH	88.4%	93.5%	1.89 (1.08-3.31)	0.02
DM2	46.4%	43.1%	0.88 (0.66-1.17)	0.37
FH CD	10.7%	10.8%	1.01 (0.63-1.60)	1.00
Smoking	10.4%	10.8%	-	0.77
Previous CVA	4.4%	5.6%	1.29 (0.68-2.45)	0.48
Previous TIA	1.6%	3.9%	2.47 (1.07-5.72)	0.03
Renal dysfunction	10.9%	18.1%	1.80 (1.22-2.67)	<0.01
Peripheral vasculopathy	12.2%	20.3%	1.83 (1.26-2.67)	<0.01
Dyslipidemia	9.9%	9.5%	0.96 (0.60-1.56)	1.00
Previous AMI	50.9%	34.1%	0.50 (0.37-0.67)	< 0.01

TIA: transitory ischemic accident; CVA: cerebrovascular accident; CD: carotid disease; DM2: diabetes mellitus type 2; SAH: systemic arterial hypertension; FH CD: family history of coronary disease; AMI: acute myocardial infarction.

Table 3 - Multivariate analysis of clinical characteristic of patients with significant carotid disease ($\geq 50\%$) which p < 0.10

Clinical characteristic	Odds ratio	p
Sex	0.75 (0.55-1.02)	0.06
SAH	1.71 (0.97-3.04)	0.06
TIA	2.03 (0.85-4.82)	0.11
Peripheral vasculopathy	1.80 (1.22-2.65)	<0.01
Renal dysfunction	2.03 (1.34-3.07)	<0.01
Previous TIA	0.47 (0.35-0.65)	<0.01

TIA: transitory ischemic accident; SAH: systemic arterial hypertension.

The incidence of primary outcome was of 3.7%, with 18.2% having occurred in the first 30 days after surgery. From the total events, 3% were observed in the group without carotid injury and 6.5% in the group with significant carotid injury ($p = 0.0018$). Only previous TIA (OR 5.66, IC95% 1.67-6.35; $p < 0.01$) and renal dysfunction (OR 3.28, IC95% 1.67-6.45; $p < 0.01$) were defined as predictors for the primary outcome in univariate analysis (Table 4). All-cause mortality at the end of the follow-up was of 11.1%, and in 6.8% the basic cause was CVA.

Among patients with severe CD (lesion $\geq 70\%$ and < 100%) and underwent an intervention for its treatment in the perioperative period, the incidence of primary outcome was of 12.5%. But among those who, as decided by the medical team, were not subjected to any procedure, the incidence of primary outcome was of 3.4% ($p = 0.24$).

As for the type of approach (percutaneous versus surgical), when compared with each other, there was no statistical difference in the primary outcome incidence ($p = 0.516$) (Table 5).

In the first 30 days after MRS, the incidence of neurological events was of 12% among patients who underwent procedures against 4.5% among those who were not subjected to procedures, with $p = 0.28$. After 30 days of MRS and until the end of the follow-up, the incidence of neurological event was of 0% in the group without procedure and 7% in the group with procedure, with $p = 0.24$.

Survival in 60 months for patients without carotid injury was of 90.7% and, in the group with carotid disease above 50%, was of 83.5%, (HR = 1.9, IC95% 1.3-2.8), $p = 0.001$ (Figure 1).

Discussion

The incidence of primary outcome in this population was 3.7% and correlated with data from the literature, which values range from 2-6%^{6,7}. It is estimated that such data may be underestimated, once studies show that neurological disorders such as delirium, agitation, memory loss and cognition loss, in post-MRS, show incidences of up to 13.8%, with many related to cerebral infarction⁶.

Table 4 - Multivariate analysis of clinical characteristic of patients with primary outcome

Variables	No event	Event	Odds ratio	p
SAH	89.3%	93.0%	1.59 (0.49-5.23)	0.61
DM2	46.2%	32.6%	0.56 (0.29-1.07)	0.09
FH CD	10.9%	7.0%	0.61 (0.19-2.02)	0.61
Smoking	16.3%	10.2%	-	-
Previous CVA	4.5%	9.3%	2.20 (0.76-6.40)	0.13
Previous TIA	1.8%	9.3%	5.66 (1.85-17.34)	0.01
Renal dysfunction	11.7%	30.2%	3.28 (1.67-6.45)	<0.01
Peripheral vasculopathy	13.5%	20.9%	1.69 (0.79-3.59)	0.17
Dyslipidemia	9.7%	11.6%	1.22 (0.47-3.17)	0.60
Previous AMI	47.7%	41.9%	0.79 (0.42-1.46)	0.53
Prior AMI	11.8%	14.0%	1.22 (0.50-2.94)	0.63
Previous PCA	1.9%	4.7%	2.56 (0.58-11.28)	0.21
Postoperative AF				
Arrhythmia	18.0%	20.5%	1.17 (0.53-2.59)	0.67
Transoperative AMI	21.6%	27.9%	1.40(0.71-2.78)	0.35
Previous heart surgery				
LMCA injury	3.7%	4.7%	1.28 (0.30-5.49)	0.67
ECC				
Age				
Time of anoxia (min)				
Time of ECC (min)	3.2%	2.3%	0.72 (0.10-5.37)	1.00
	33.1%	33.3%	1.01 (0.48-2.11)	1.00
	97.4%	97.7%	1.11 (0.15-8.37)	1.00
	71.6	71.4	-	0.85
	54.4	59.4	-	0.18
	81.2	89.9	-	0.16

TIA: transitory ischemic accident; PCA: percutaneous coronary angioplasty; CVA: cerebrovascular accident; ECC: extracorporeal circulation; DM2: diabetes mellitus type 2; AF: atrial fibrillation; SAH: systemic arterial hypertension; FH CD: family history of coronary disease; AMI: acute myocardial infarction; LMCA: left main coronary artery.

Table 5 - Incidence of primary outcome in relation to carotid disease approach

Procedure	Primary outcome (n = 1.169)	Primary outcome related to CD approach (n=9)	p
None	79.1%	-	-
Previous endarterectomy	2.3%	6.7%	
Endarterectomy during MR or until 30 days later	7%	17.2%	p = 0.516
Stent pre-MRS	11.6%	20%	
Stent post-MRS	0	0	

CD: carotid disease; MRS: myocardial revascularization surgery.

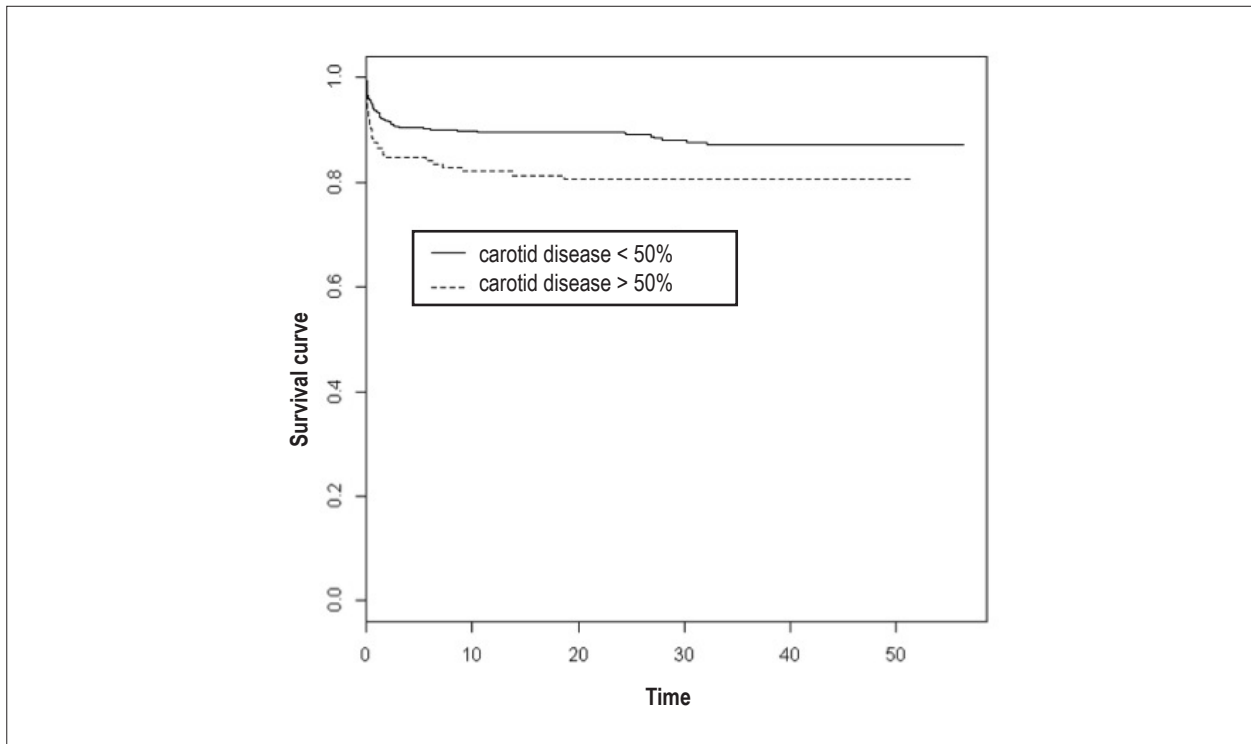


Figure 1 - Kaplan-Meier curves for survival free from events in 60 months of follow-up.

In the primary outcome, 18.2% of events occurred in the first 30 days after surgery. Even though 34.5% of total CVA of study population had occurred in the group without significant carotid disease, the presence of carotid disease $\geq 50\%$ aggregates an OR = 2.2 ($p = 0.0018$) for compound outcome of CVA, TIA and death due to cardiovascular. In the literature, the relation between carotid disease and post-CVA is controversial. Even though it is related that the risk for CVA is higher than 2% among those with non-significant CD against 5% in the group with significant CD, reaching 11% in case of occlusion, most perioperative CVA are not related to carotid disease². In previous studies with patients subjected to MRS, only 23.7% had significant carotid disease, suggesting that alternative causes were related to the development of the event⁸.

It is recognized that 50-79% of CVA cannot be attributed to CD alone, with contribution of embolic events secondary to extracorporeal circulation, postoperative arrhythmias, hypotension, state of hypofibrinolysis and aortic calcification such as etiological factors^{6,9-11}. In the literature are also identified as predictors of perioperative CVA: age, female gender, diabetes mellitus, SAH, peripheral vasculopathy, polytransfusion and emergency surgery^{12,13}. In our study, only previous TIA and renal dysfunction were defined as predictors for the primary outcome.

In the current cohort, the prevalence of significant carotid disease of 19.9% was similar to that from the literature, which values range between 4-18.7%^{14,15}. The prevalence of unilateral occlusion (2%) was higher than that

from the literature (0.06%), however there were no cases of bilateral occlusion, which prevalence is estimated at 0.04%.

For preoperative carotid evaluation in MRS, we currently recommend screening with Doppler ultrasonography of patients aged 65 or older, in addition to those with stenosis of the left main coronary artery and previous CVA or TIA, SAH, DM^{2,4}. In this study, CD $\geq 50\%$ predictors, after multivariate analysis, were the factors: renal dysfunction, peripheral arterial disease and previous myocardial infarction, this as protective factor. It has been hypothesized that the presence of previous AMI as protective factor can be explained by the current conduct of initiating the treatment with inhibitors of angiotensin-converting enzymes (ACE), angiotensin II receptor blockers (ARB) and statins, medications that have impact on the evolution of atherosclerotic disease¹⁶.

Despite divergent, international guidelines recommend intervention on symptomatic carotid stenoses above 70% and asymptomatic above $\geq 80\%$ ⁴. In our study, there was no difference in compound outcome between patients with CD $\geq 70\%$ evaluated by Doppler ultrasonography who underwent or not an intervention in carotid disease ($p = 0.24$). Moreover, when compared with each other, there was no statistical difference in the primary outcome incidence between the different approaches (percutaneous versus surgical – $p = 0.516$). Some studies indicate that performing the correction of carotid injury associated with MRS can also increase the risk of postoperative CVA and death^{17,18}.

The type of intervention related to the lower number of neurological events and the best moment for approaching CD remain controversial. In our results, the difference between these factors was not statistically significant.

In the literature, studies are divergent. In one study analyzing patients with carotid disease which underwent MRS, it was observed that the incidence of postoperative CVA was of 15.1% among patients subjected to MRS combined with endarterectomy and of 20% in patients who underwent angioplasty with stent prior to surgery. There was no postoperative CVA in patients with CD $\geq 70\%$ who did not undergo a carotid revascularization procedure⁸. Levi et al¹⁹ monitored 80 patients who underwent endarterectomy combined with MRS and found a neurological events rate of 7.6% in 10 years.

In this study, the incidence of CVA in the group subjected to endarterectomy prior to MRS was of 6.7%. Van der Heyden et al²⁰ evaluated endarterectomy followed by MRS in 356 patients neurologically asymptomatic, in a 30-day follow-up; rate of death and CVA was of 4.8%.

Ziada et al²¹ compared endarterectomy and carotid angioplasty with stent, followed by heart surgery. There was a smaller proportion of CVA in a 30-day follow-up in the group which was subjected to carotid angioplasty with stent. On the other hand, a meta-analysis of 11 studies comparing carotid endarterectomy and carotid angioplasty with stent prior to MRS found similar rates of CVA and AMI²². Currently, the European directive of myocardial revascularization, published in 2011, recommends the carotid intervention on symptomatic patients when stenosis 70-99%; the procedure can be considered for asymptomatic male patients with bilateral stenosis of 70-99% or stenosis of 70-99% associated with contralateral occlusion. The same directive claims the approach of CD in MRS is controversial and hypothesizes the decision to intervene and the type of procedure to be performed (surgery or angioplasty) must be individualized after discussion by a multidisciplinary team, including a neurologist²³.

Currently, conflicting results could be justified by the fact that in the literature, studies on this topic are based on retrospective studies. Limitations on this study are due to the presence of possible variables not balanced in the sampling. Randomized studies are necessary for

a better assessment on the impact of CD approach in perioperative MRS.

Study limitations

This is a retrospective study, based on the analysis of medical charts. The choice of clinic therapeutic strategy, surgery strategy or stenting was decided by the medical team responsible for the patient, which did not allow the comparative analysis of results.

Conclusion

Carotid disease is an important marker of neurological events related to MRS. The presence of significant carotid injury is a risk factor for CVA, TIA or death due to CVA in patients subjected to MRS. However, the surgical approach for carotid disease was not significantly related to the primary outcome.

Author contributions

Conception and design of the research: Batista CC, Petisco AC, Oliveira DP, Farsky PS, Arantes FBB, Asséf JE, Barbosa JEM, Friolani SC, Revelo MSC; Acquisition of data: Batista CC, Petisco AC, Oliveira DP, Arantes FBB, Barbosa JEM, Revelo MSC; Analysis and interpretation of the data: Batista CC, Petisco AC, Oliveira DP, Farsky PS, Arantes FBB, França JID, Barbosa JEM, Friolani SC, Revelo MSC; Statistical analysis: França JID, Revelo MSC; Writing of the manuscript: Batista CC, Oliveira DP, Farsky PS, Arantes FBB, Friolani SC, Revelo MSC; Critical revision of the manuscript for intellectual content: Batista CC, Petisco AC, Oliveira DP, Farsky PS, Arantes FBB, Asséf JE, Friolani SC, Revelo MSC.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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