

## Risk Factors for Stroke after Coronary Artery Bypass Grafting

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### Summary

**Background:** Stroke is a feared complication after coronary artery bypass grafting surgery (CABG), with an incidence between 1.3 and 4.3%.

**Objective:** To identify predictive factors for stroke after CABG in the modern era of cardiac surgery.

**Methods:** This is a case-control study of 65 pairs of patients, paired by sex, age ( $\pm 3$  years) and date of CABG ( $\pm 3$  months). The cases were patients submitted to elective CABG with extracorporeal circulation (ECC) that presented stroke (defined as clinical neurological deficit up to 24 hours post-operatively and confirmed by imaging assessment) and the controls were those individuals submitted to elective CABG with ECC, but without stroke.

**Results:** The univariate analysis demonstrated that the number of revascularized vessels was associated with the occurrence of stroke after the CABG ( $3 \pm 0.8$  vs.  $2.76 \pm 0.8$ ,  $p = 0.01$ ). The multivariate analysis by conditional logistic regression showed that systemic arterial hypertension (SAH) [OR: 6.1 (1.5 – 24),  $p = 0.009$ ] and diabetes mellitus (DM) [OR: 3.1 (1.09 – 11),  $p = 0.03$ ] were the determinants of the highest chance of stroke after CABG, whereas acute myocardial infarction (AMI)  $> 1$  month, was the determinant of the lowest chance of stroke [OR: 0.1 (0.03 – 0.36),  $p = 0.003$ ].

**Conclusion:** Hypertension and diabetes mellitus were identified as independent predictors of stroke within the first 24 postoperative hours after CABG. In patients with such risk factors, it is possible that the knowledge of the causal mechanisms of brain injury represents a strategy capable of decreasing the incidence of stroke after CABG. (Arq Bras Cardiol 2008;91(4):213-216)

**Key words:** Cerebrovascular accident; myocardial revascularization / adverse effects; risk factors.

### Introduction

The coronary artery bypass grafting surgery (CABG) is an effective treatment to prolong and improve the life of patients with coronary artery disease (CAD)<sup>1</sup>.

Stroke is a feared complication of this surgery. Its incidence in the 60s reached up to 9%<sup>2</sup> and despite the improvement in surgical techniques in the last years, the incidence of this complication currently varies from 1.3 to 4.3%<sup>3-6</sup>.

Previous clinical studies identified stroke predictors after CABG; however, the low incidence of this event, the lack of standardization in the assessment of variables related to the brain injury and the sizes of the samples are all limiting factors of these studies<sup>7-9</sup>.

We believe that the analysis of the current risk factors is necessary to determine what the actual predictors of stroke are in this modern era of cardiac surgery.

A case-control study was carried out in order to identify predictive factors for stroke after CABG.

### Methods

This is a case-control study of 65 pairs of patients paired by sex, age ( $\pm 3$  years) and date of the CABG ( $\pm 3$  months). The cases were patients (pts) submitted to the first elective CABG with extracorporeal circulation (ECC) that presented stroke (defined as clinical neurological deficit up to 24 hours post-operatively and confirmed by imaging assessment) and the controls were those individuals also submitted to the first elective CABG with ECC, but without stroke.

The clinical and surgical characteristics that were evaluated were: systemic arterial hypertension (SAH), diabetes mellitus (DM), dyslipidemia (DLP), smoking, previous stroke, previous carotid lesion ( $\geq 60\%$ ), previous atrial fibrillation, ventricular function (defined by the left ventricular ejection fraction (LVEF) at the echocardiogram as: normal when the LVEF  $> 60\%$ , slight when it is between 50 and 60%, moderate when it is between 40 and 50% and severe when it is  $< 40\%$ ), number of revascularized vessels, time of ECC, chronic renal failure (creatinine  $\geq 1.5$  mg/dl), acute myocardial infarction (AMI)

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≤1 month and >1 month, previous percutaneous coronary intervention (PCI).

The continuous variables were described as means and standard deviations, whereas the categorical variables were described as percentages.

At the univariate analysis the marginal homogeneity test was used to evaluate the categorical variables and the Student's t test for the numerical ones. To calculate the Odds Ratio (OR), a multivariate analysis by conditional logistic regression was performed, with p being considered significant when ≤ 0.05.

The variables assessed by the multivariate model of conditional logistic regression (used to evaluate the probability of the variables to determine the cases) were those that presented p values ≤ 0.1 in the univariate models or the ones that were considered clinically relevant.

This study was approved by the Ethics Committee in Research of our institution.

## Results

From January 2000 to April 2006, a total of 3,420 patients were submitted to the first elective CABG with ECC and 65 (1.9%) presented stroke AVE, according to the study definition.

Sixty-five pairs of patients were included, according to the study design, of whom 41 were males and 24 were females. Mean age was  $70.6 \pm 8.1$  years.

The distribution frequency of the analyzed variables and their associations with the occurrence of stroke according to the univariate analysis, are shown in Tables 1 and 2. The variables that had a significant association with stroke in the postoperative period of CABG were the higher number of revascularized vessels and previous PCI.

The final model of multivariate analysis by conditional logistic regression included the following variables: SAH, DM, DLP, smoking, previous stroke, previous carotid lesion, previous atrial fibrillation, ventricular function, number of revascularized vessels, time of ECC, AMI ≤1 and > 1 month and previous PCI.

**Table 1 – Patients' clinical characteristics and complementary examinations**

Variables	Case (n = 65 pts)	Control (n = 65pts)	p value
SAH (%)	68	75	0.2
Diabetes mellitus (%)	49	35	0.1
Dyslipidemia (%)	52	58	0.4
Smoking (%)	28	24	0.6
Stroke (%)	3	0	0.2
CRF (%)	8	6	0.7
CS ≥ 60% (%)	15	15	0.9

SAH - systemic arterial hypertension; CRF - chronic renal failure; CS - carotid stenosis; pts - patients.

**Table 2 – Patients' clinical profile**

Variables	Patients (n =65)	Controls (n = 65)	p value
AMI ≤ 1 month (%)	15	18	0,6
AMI > 1 month (%)	18	14	0,4
Atrial fibrillation (%)	3	1,5	0,5
PCI (%)	1,5	15	0,007
MRS (%)	12	12	0,9
LVEF 40% to 50% (%)	17	23	0,4
LVEF < 40% (%)	7	9	0,3

AMI - acute myocardial infarction; PCI - percutaneous coronary intervention; MRS - myocardial revascularization surgery; LVEF - left ventricular ejection fraction

After the control for these factors, we identified SAH [OR: 6.1 (1.5 –24), p = 0.009] and DM [OR: 3.1 (1.09 – 11), p = 0.03] as the determinant factors of the highest chance of stroke in the postoperative period of CABG, whereas AMI >1 month [OR: 0.1 (0.03 – 0.36), p = 0.003] was the factor associated with the lowest chance of this event.

## Discussion

The present study, carried out in the contemporary era of CABG, identified two factors in the clinical profile of the patients, SAH and DM, which were determinants of a higher chance of stroke in the postoperative period of CABG.

The two mechanisms responsible for stroke are ischemia and hemorrhage<sup>10</sup>. Ischemia can be caused by embolic phenomena (cardiac, of the aorta or of proximal arteries), thromboembolism of intra or extracranial vessels and systemic hypoperfusion. Hemorrhage occurs in association with systemic arterial hypertension or to reperfusion of the infarcted areas<sup>10</sup>. In the hemorrhagic stroke, the blood accumulates outside the blood vessel and can contribute to the elevation in the intracranial pressure and the neural cell death<sup>10</sup>.

In the ischemic injury caused by cardiac embolism, the emboli generally originate from the atrium, as in the atrial fibrillation, or from the left ventricle, as in the recent AMI. Usually, multiple infarctions occur, predominantly at the site of the middle cerebral artery. When there is lacunar thromboembolism, the cause is hypertension-induced atherosclerosis or stenoses of the arteries that penetrate the brain. The thrombotic thromboembolism is related to the atherosclerosis of the intracranial vessels or hematologic abnormalities, such as increase in red blood cells or platelets<sup>10</sup>.

The brain damage caused by hypoperfusion is the result of the combination of extracranial stenosis and systemic hypotension, being more frequently unilateral, when related to embolism, and bilateral, when related to important and persistent systemic hypotension<sup>10</sup>.

When the brain injury has two or more causative mechanisms, it is classified as being of multiple causes and those

without known mechanisms are classified as “others”<sup>10</sup>.

Neurological events that occur after CABG are classified as type 1, when they are focal stroke, transient ischemic attack or fatal brain damage and type 2, when they reflect diffuse brain injury with disorientation or intellectual deterioration, which are normally reversible<sup>8</sup>.

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, as demonstrated by Glance et al<sup>11</sup> in a study that evaluated 51,750 patients submitted to CABG and, after adjustment for preoperative risk factors, the stroke determined a four-fold higher chance of death<sup>12</sup>.

The identification of predictive factors for stroke and, whenever possible, the actions that can be taken against these factors in order to decrease the incidence of this event, have been sought for more than 4 decades<sup>2</sup>. In this sense, one analysis of 16,528 individuals submitted to CABG in the 90s disclosed the following independent predictors: chronic renal failure, AMI < 24 hours, previous stroke, carotid disease, SAH, DM, age > 75 years, LVEF ≤ 34%, decreased cardiac output and atrial fibrillation in the postoperative period<sup>11</sup>.

Other studies also identified SAH and DM as independent predictors of stroke in the postoperative period of CABG. Although the rapid progression of aortic atherosclerosis, as well as carotid atherosclerosis and thrombotic alterations are associated with brain injury, the exact mechanism of the stroke in hypertensive and diabetic patients is not fully clarified and needs further investigation<sup>13-17</sup>.

The surgical techniques and the pre, intra and postoperative care have changed in the recent years, contributing to an improvement in CABG outcome<sup>18</sup>. However, due to the same changes, it is not possible to infer that all results of clinical studies performed at another moment of cardiac surgery can be transported to the current moment.

The identification of patients with characteristics of higher

risk for the occurrence of brain damage will allow us to adopt prophylactic measures based on the previous knowledge (as previously described) of the causative mechanisms of stroke.

Thus, we believe that in hypertensive and diabetic patients, measures such as adequate control of blood pressure (preventing periods of hypertension and hypotension), the tracking of possible cardiac emboligenic sources or other vascular sites and the careful assessment and handling of the aortic artery can contribute to reduce the incidence of stroke after CABG.

## Conclusions

The SAH and the DM were determinant factors of higher chance of stroke within the first 24 hours of the PO period after CABG. In patients with these risk factors, it is possible that incisive actions against the mechanisms that cause stroke contribute to reduce its incidence.

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## Potential Conflict of Interest

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

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## Study Association

This study is not associated with any graduation program.

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