## **ORIGINAL ARTICLE**

# Epidemiological Characteristics and Mortality Predictors in Patients Over 70 Years Submitted to Coronary Artery Bypass Grafting

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### Abstract

**Background:** Coronary artery disease is the leading cause of death worldwide, with age being an independent risk factor for mortality in patients submitted to surgical revascularization.

**Objective:** To evaluate the mortality risk predictors in patients older than 70 years submitted to myocardial revascularization.

**Methods:** This is a retrospective cohort study of a cardiac surgery database. Logistic regression was used to assess independent death predictors.

**Results:** A total of 372 patients submitted to surgical revascularization from 2004 to 2012 were assessed. The main cardiovascular risk factor was hypertension, followed by diabetes mellitus. Mortality at 30 days was 19.35%. The presence of peripheral vascular disease (OR: 2,47), emergency surgery (OR: 4,86) and combined valve procedure (OR: 3,86) were independent predictors of death.

**Conclusion:** The surgical procedure in elderly patients showed a higher mortality than in the general population. Peripheral vascular disease, emergency surgery and combined valve procedures increased the risk of death in these patients. (International Journal of Cardiovascular Sciences. 2018;31(3)258-263)

Keywords: Coronary Artery Disease / surgery; Myocardial Revascularization; Hypertension; Diabetes Mellitus; Aged.

## Introduction

Cardiovascular disease is currently one of the main causes of hospitalization in Brazil in the general population, being the main cause of hospitalization in elderly patients.<sup>1</sup>

With the advent of new technologies for the treatment of cardiovascular disease, the survival of the patient with heart disease increases and, with aging, other comorbidities, such as hypertension, diabetes, kidney failure and cognitive dysfunction appear.<sup>2,3</sup>

With the aging process, the cardiovascular system itself shows physiological changes, such as progressive increase in systolic blood pressure, reduction of aerobic capacity and of reflex responses of the autonomic nervous system.<sup>4</sup>

The aging process alone increases the patient's cardiovascular risk, either by the Framingham and SCORE risk score evaluation, which are used in asymptomatic patients, or by assessing the prevalence of coronary heart disease using the Diamond score.<sup>5,6</sup>

In patients with coronary disease, age is an important predisposing risk factor for future events, both in acute coronary disease scores, such as GRACE, as well as in preoperative risk assessment, such as the EuroSCORE.<sup>7,8</sup>

There are still doubts related to the predictive factors of surgical death, defined as death occurring within 30 days

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of the surgical procedure, in the Brazilian population of patients aged 70 years or older.

The aim of our study was to evaluate the epidemiological characteristics of patients undergoing coronary artery bypass grafting at a specialized hospital of the Brazilian Unified Health System (*Sistema Único de Saúde* - SUS), and to analyze the risk predictors of surgical death and complications inherent to the procedure.

## Methods

Retrospective cohort of the cardiac surgery database of Instituto Nacional de Cardiologia, in Rio de Janeiro (RJ), of patients operated from December 2004 to March 2012.

This database included demographic, clinical, laboratory, echocardiographic and angiographic variables of the preoperative, intraoperative and immediate postoperative periods at the Intensive Care Unit (ICU) and the late postoperative period at the infirmary, totaling 327 variables, in addition to vital status at 30 days. In the present study, we assessed the demographic, clinical, laboratory, echocardiographic and angiographic data of the patient's preoperative period and the need for combined valve surgery, considering the type of evolution (discharge vs. death within 30 days of the procedure). Angina pectoris was classified according to the Canadian Class Society (CCS) criteria.<sup>9</sup>

The institutional Research Ethics Committee authorized the performance of this study, approval number 0117/110906.

#### Statistical analysis

Statistical analysis was performed by recording the frequencies, the means and their respective standard deviations, or the median and quartiles, when appropriate. Student's *t* test was used to compare the outcome groups, when the variables showed a normal distribution, or Mann-Whitney U test, when normality was not observed. For dichotomous variables, chi-squared or Fisher's exact test were applied, as appropriate. To study the association between the independent variables and the outcome, two-phase multivariate logistic regression was used and the variables that had p < 0.20 in the first stage were included in the final stage. The StataCorp 14 program (by StataCorp LP) was used. It was considered an alpha value of 0.05. All tests were two-tailed.

## Results

The epidemiological characteristics are shown in table 1. There were 372 patients, most of them males, with a median age of 74.26 years and a mean body mass index of 26.2 kg/m<sup>2</sup>. Regarding the risk factors, the patients had systemic arterial hypertension (93.2%), diabetes (29.0%) and were current smokers (4.3%). Even with a mean creatinine level within the normal range, patients had decreased creatinine clearance. The mortality rate of the study population was 19.35% (72 patients) at 30 days.

#### Table 1 - Demographic and clinical characteristics of the study population

Characteristic	
Age, years (median and interquartile range)	74.26 (71.77-77.08)
Men	67.2
Body mass index	$26.2\pm4.1$
Systemic arterial hypertension	93.2
Diabetes Mellitus	29.0
Smoking	4.3
Previous acute myocardial infarction	19.4
Previous stroke	5.3
Creatinine clearance	51.77 (42.38-61.86)
Creatinine	1.1 (1.0-1.38)
Previous coronary artery bypass grafting	2.1
Previous percutaneous coronary angioplasty	9.1
Angina	80.9
Unstable angina	27.6
Stable angina	72.4
Left main coronary artery lesion	41.9
Proximal anterior descending artery lesion	62.0
Trivascular	75.0
Ejection fraction	62.0 (49.0-69.0)
NYHA functional class III or IV	9.2
Death at 30 days	19.3

Results expressed in median (interquartile range), percentage or mean ± median. NYHA: New York Heart Association.

In the univariate analysis (Tables 2 and 3), the following were markers of surgical death: emergency surgery, combined valvular surgery, previous surgery, peripheral vascular disease, NYHA functional class III/IV, increased left atrial diameter, lower preoperative statin use, increased need for preoperative nitrate use, moderate/ severe aortic regurgitation, moderate/severe aortic stenosis, and moderate/severe tricuspid regurgitation.

The multivariate analysis was performed in two stages and, in the final stage, the presence of peripheral vascular disease, the need for emergency surgery and the combined procedure with valve replacement were found to be independent predictors of death (Tables 4 and 5).

### Discussion

The objective of coronary artery bypass grafting is to correct myocardial ischemia resulting from coronary artery obstruction, aiming at relieving symptoms, improving quality of life and allowing the patient to return to work, as well as increasing life expectancy.<sup>9</sup>

It is a revascularization method with higher percentage of complete revascularization and reduction of anginal episodes. In contrast, there is a longer hospital length of stay and a higher incidence of complications during surgical hospitalization, which makes this surgery a second alternative for patients requiring revascularization.<sup>9</sup>

The epidemiological characteristics of patients submitted to coronary artery bypass grafting show that most patients are males, with a mean age of 60 years, arterial hypertension as the most prevalent risk factor and preserved left ventricular function.<sup>10,11</sup>

However, elderly patients have a greater number of comorbidities, when compared to younger patients. In addition to these comorbidities, the elderly's Table 2 - Univariate analysis of surgical mortalityby the presence of categorical variables potentiallypredictive of surgical death

Variable	Death (%)	Survivor (%)	p-value
Combined surgery	40.00	15.82	< 0.001
NYHA Functional class III or IV	38.24	17.26	0.003
Emergency surgery	40.91	18.00	0.004
Use of statins in the preoperative period	16.84	30.43	0.017
Peripheral vascular disease	30.16	17.12	0.018
Previous surgery	31.37	17.35	0.019
Moderate/severe tricuspid regurgitation	60.00	18.44	0.019
Moderate/severe aortic regurgitation	38.89	18.07	0.029
Moderate/severe mitral regurgitation	34.78	17.93	0.040
Moderate/severe aortic stenosis	32.81	16.03	0.002
Nitrates in the preoperative period	33.33	17.99	0.051
Beta-blocker in the preoperative period	32.81	28.57	0.056
Male gender	17.60	22.95	0.220
Diabetes	15.74	20.91	0.253
Left main coronary artery lesion	18.59	19.52	0.822

NYHA: New York Heart Association.

Table 3 - Univariate analysis of surgical mortality by the presence of continuous variables potentially predictive of surgical death

Variable	Survivor	Death	p-value
Left atrial dimension, cm	3.91 (3.84-3.98)	4.13 (3.94-4.32)	0.0129
Body mass index, kg/m <sup>2</sup>	26.11 (25.72-26.50)	26.80 (25.36-28.24)	0.3162
Age, years	74.15 (71.73-7.08)	74.81 (72.16-77.23)	0.3505
Left ventricular ejection fraction, $\%$	58.77 (57.12-60.43)	55.76 (51.62-59.90)	0.7250
Pulmonary artery systolic pressure, mmHg	35.50 (32.11-38.89)	39.83 (33.97-45.68)	0.9114

Table 4 - Multivariate analysis of surgica	al death predictors in the initial stag
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Factor	Odds ratio	Standard error	95%CI	p-value
Emergency surgery	4.4952	2.5857	1.4559-13.879	0.009
Peripheral vascular disease	2.5038	0.9111	1.2271-5.1091	0.012
Left atrial dimension	1.4488	0.3623	0.8874-2.3655	0.138
Combined surgery	2.1760	1.2039	0.7357-6.4358	0.160
Previous surgery	1.6740	0.6984	0.7390-3.7925	0.217
Moderate/severe tricuspid regurgitation	3.1501	3.1348	0.4479-22.152	0.249
Beta-blocker in the preoperative period	0.6536	0.2706	0.2903-1.4715	0.304
Moderate/severe aortic stenosis	1.4779	0.7335	0.5587-3.9096	0.431
Statins in the preoperative period	0.8023	0.3059	0.3800-1.6941	0.564
NYHA III-IV	1.3249	0.6894	0.4777-3.6742	0.589
Nitrates in the preoperative period	1.2760	0.8513	0.3451-4.7179	0.715
Moderate/severe aortic regurgitation	0.9405	0.5882	0.2761-3.2041	0.922
95% CI: 95% confidence interval; NYHA: New York Heart Association.				

Table 5 - Multivariate analysis of the factors predicting surgical death in the final stage				
Factor	Odds ratio	Standard error	95%CI	p-value
Combined surgery	3.8651	1.2871	2.0123-7.4236	< 0.001
Emergency surgery	4.8608	2.3881	1.8558-12.732	0.001
Peripheral vascular disease	2.4773	0.8218	1.2931-4.7463	0.006
95% CI: 95% confidence interval.				

circulatory system has alterations caused by the aging process, such as increased arterial stiffness, diastolic function worsening and greater extent of coronary artery disease.<sup>12-14</sup>

Compared to younger patients, elderly ones have higher mortality in relation to revascularization – be it surgical or percutaneous. However, in comparison with percutaneous revascularization, the long-term benefits of undergoing surgery are better for the elderly, especially in relation to greater symptomatic relief and the less need for new revascularizations.<sup>15</sup>

Several studies have shown that age leads to an increased risk of death. Santos et al. observed that patients over 65 years of age have a 2.3-fold higher risk of death than younger patients; Rocha et al. compared

patients older and younger than 70 years, and found a mortality rate of 8.9% in the older patients and 3.6% in the younger patients – this cohort did not involve patients submitted to the combined surgery, which is an important predictor of mortality.<sup>16,17</sup>

Contrarily, Aikawa did not identify an impact on the mortality in older patients (>65 years) (5.8% vs. 2.0%), but identified a higher rate of postoperative complications in the elderly, when compared to the younger patients (30% vs. 14%).<sup>14</sup>

We already have reports of surgical series involving octogenarians submitted to isolated myocardial revascularization procedures, showing that these patients have a higher risk of developing in-hospital death; however, when compared with patients who undergo elective surgery or those with fewer comorbidities, the risk is similar to that of younger patients.<sup>18,19</sup>

The mortality among older patients was much higher than that assessed in the general population, according to a previous study performed by our group. The assessment of all patients showed an index of 10.3%, compared to 22.3% in the current cohort. However, when we compare it with some cohorts of patients over 70 years of age, one observes very similar mortality rates.<sup>10,20</sup>

Regarding the predictors of mortality, it is known that emergency surgery in the elderly has a negative impact on prognosis in the postoperative evolution of patients, with a risk of death up to 55-fold higher in some series.<sup>21</sup>

The presence of peripheral atherosclerotic disease is closely related to age and the highest number of risk factors for coronary disease. Associated with this, there have been reports that graft quality is worse in these patients. The PREVENT IV study demonstrated that patients with peripheral vascular disease have a 3.3-fold increased risk of death, infarction or new revascularization in 5 years, but without an impact in the first 30 days after surgery. This fact is supported by two other studies that demonstrated that the impact of peripheral vascular disease lies in the long term. However, none of these studies have studied only the elderly population, a fact that may explain why the combination of advanced age with peripheral vascular disease shows a worse prognosis than isolated peripheral vascular disease in the postoperative period of coronary artery bypass grafting.<sup>22-24</sup>

When making comparisons with other populations, one needs to keep in mind some peculiarities of the assessed patients. Our patients were from the Brazilian Unified Heath System (SUS), which, for the most part, have a more unfavorable socioeconomic condition than those from the private health care network and from other countries, in addition to having less access to specialized care.<sup>25</sup>

#### Conclusion

The predictors of surgical death in the septuagenarians of this assessed sample were the need for emergency surgery, combined valvular procedure and the presence of peripheral vascular disease.

#### Author contributions

Conception and design of the research: Azevedo VMP, Xavier RMA, Chaves RBM. Acquisition of data: Azevedo VMP, Xavier RMA, Chaves RBM. Analysis and interpretation of the data: Kaufman R, Azevedo VMP, Sá RMG, Geller M, Xavier RMA, Chaves RBM, Castier MB. Statistical analysis: Kaufman R, Azevedo VMP, Geller M. Writing of the manuscript: Kaufman R, Azevedo VMP, Sá RMG, Xavier RMA, Chaves RBM, Castier MB. Critical revision of the manuscript for intellectual content: Kaufman R, Azevedo VMP, Castier MB.

#### **Potential Conflict of Interest**

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

#### Sources of Funding

There were no external funding sources for this study.

#### **Study Association**

This article is part of the thesis of Doctoral submitted by Renato Kaufman, from *Universidade do Estado do Rio de Janeiro*.

#### Ethics approval and consent to participate

This study was approved by the Ethics Committee of the *Instituto Nacional de Cardiologia* under the protocol number 0117/110906. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

#### References

- Brasil. Ministério da Saúde. Datasus. [Internet]. Banco de dados do Sistema Único de Saúde. [Acesso em 2015 jun 18]. Disponível em: http:// www.datasus.org.br
- Grundy EMD. The epidemiology of aging. In: Tallis RC, Fillit HW. (editors). Brocklehurst's textbook of geriatric medicine and gerontology. Philadelphia: Elsevier Science Ltd; 2003. p. 3-20.

Schramm JM, Oliveira AF, Leite IC, Valente JG, Gadelha AM, Portela MC, et al. Epidemiological transition and the study of burden of disease in Brazil. Ciênc Saúde Coletiva 2004;9(4):897-908. doi: http://dx.doi. org/10.1590/S1413-81232004000400011.

Fechine BR, Trompieri NO. Processo de envelhecimento: as principais alterações que acontecem com o idoso com o passar dos anos. Rev

Cient Int. 2012;20(1):106-132. doi: http://dx.doi.org/10.6020/1679-9844/2007.

- Xavier HT, Izar MC, Faria Neto JR, Assad MH, Rocha VZ, Sposito AC, et al; Sociedade Brasileira de Cardiologia. [V Brazilian Guidelines on Dyslipidemias and Prevention of Atherosclerosis]. Arq Bras Cardiol. 2013;101(4 Suppl 1):1-20. doi: http://dx.doi.org/105935/abc20135010.
- Cesar LA, Ferreira JF, Armaganijan D, Gowdak LH, Mansur AP, Bodanese LC et al; Sociedade Brasileira de Cardiologia. Guideline for stable coronary artery disease. Arq Bras Cardiol. 2014;103(2 Suppl 2):1-56. doi: http://dx.doi.org/10.5935/abc.2014S004.
- Roques F, Nashef SA, Michel P, Gauducheau E, deVincentiis C, Baudet E, et al. Risk factors and outcome in European cardiac surgery: analysis of the EuroSCORE multinational database of 19030 patients. Eur J Cardiothorac Surg. 1999;15(6):816-22. PMID: 10431864.
- Nicolau JC, Timerman A, Marin-Neto JA, Piegas LS, Barbosa CJ, Franci A, et al; Sociedade Brasileira de Cardiologia. [Guidelines of Sociedade Brasileira de Cardiologia for unstable angina and non-ST-segment elevation myocardial infarction (II edition, 2007) 2013-2014 update]. Arq Bras Cardiol. 2014;102(3 Suppl 1):1-61. doi: http://dx.doi.org/10.5935/ abc.2014S001
- Hueb W, Soares PR, Gersh BJ, César LA, Luz PL, Puig LB, et al. The medicine, angioplasty, or surgery study (MASS-II): a randomized, controlled clinical trial of three therapeutic strategies for multivessel coronary artery disease: one-year results. J Am Coll Cardiol. 2004;43(10):1743-51. doi: 10.1016/j.jacc.2003.08.065.
- Kaufman R, Kuschnir MC, Xavier RM, Santos MA, Chaves RB, Müller RE, et al. Perfil epidemiológico na cirurgia de revascularização miocárdica. Rev Bras Cardiol. 2011;24(6):369-76.
- Cruz LC, Kaufman R, Azevedo VM, Militão RC, Schneider F, Treml FT, et al. Análise das metas terapêuticas na prevenção secundária de DAC após CRM. Rev Bras Cardiol. 2012;25(4):309-12.
- 12. Scott BH, Seifert FC, Grimson R, Glass PS. Octogenarians undergoing coronary artery bypass graft surgery: resource utilization, postoperative mortality, and morbidity. J Cardiothorac Vasc Anesth. 2005;19(5):583-8. doi: 10.1053/j.jvca.2005.03.030.
- Graham MM, Ghali WA, Faris PD, Galbraith PD, Norris CM, Knudtson ML; Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH) Investigators. Survival after coronary revascularization in the elderly. Circulation. 2002;105(20):2378-84. doi: https://doi.org/10.1161/01.CIR.0000016640.99114.3D.
- Aikawa P, Cintra AR, Leite CA, Marques RH, da Silva CT, Afonso Mdos S, et al. Impact of coronary artery bypass grafting in elderly patients. Rev Bras Cir Cardiovasc. 2013;28(1):22-8. doi: http://dx.doi. org/10.5935/1678-9741.2013000.

- Mullany CJ, Mock MB, Brooks MM, Kelsey SF, Keller NM, Sutton-Tyrrell K, et al. Effect of age in the Bypass Angioplasty Revascularization Investigation (BARI) randomized trial. Ann Thorac Surg. 1999;67(2):396-403. doi: https://doi.org/10.1016/S0003-4975(98)01191-6.
- Santos CA, Oliveira MA, Brandi AC, Botelho PH, Brandi Jde C, Santos MA, et al. Risk factors for mortality of patients undergoing coronary artery bypass graft surgery. Rev Bras Cir Cardiovasc. 2014;29(4):513-20. doi: 10.5935/1678-9741.20140073.
- Rocha AS, Pittella FJ, Lorenzo AR, Barzan V, Colafranceschi AS, Brito JO, et al. Age influences outcomes in 70-year or older patients undergoing isolated coronary artery bypass graft surgery. Rev Bras Cir Cardiovasc. 2012;27(1):45-51. doi: http://dx.doi.org/10.5935/1678-9741.20120008.
- Alexander KP, Anstrom KJ, Muhlbaier LH, Grosswald RD, Smith PK, Jones RH, et al. Outcomes of cardiac surgery in patients > or = 80 years: results from the National Cardiovascular Network. J Am Coll Cardiol. 2000;35(3):731-8. doi: https://doi.org/10.1016/S0735-1097(99)00606-3.
- Wang W, Bagshaw SM, Norris CM, Zibdawi R, Zibdawi M, MacArthur R. Association between older age and outcome after cardiac surgery: a population-based cohort study. J Cardiothorac Surg. 2014 Nov 18;9:177. doi: 10.1186/s13019-014-0177-6.
- Almeida FF, Barreto SM, Couto B, Starling CE. Predictive factors of in-hospital mortality and of severe perioperative complications in myocardial revascularization surgery. Arq Bras Cardiol. 2003;80(1):41-50. doi: http://dx.doi.org/10.1590/S0066-782X2003000100005.
- Guimarães IN, Moraes F, Segundo JP, Silva I, Andrade TG, Moraes CR. Risk factors for mortality in octogenarians undergoing myocardial revascularization surgery. Arq Bras Cardiol. 2011;96(2):94-8. doi: http:// dx.doi.org/10.1590/S0066-782X2011005000008.
- Harskamp RE, Alexander JH, Schulte PJ, Jones WS, Williams JB, Mack MJ, et al. Impact of extracardiac vascular disease on vein graft failure and outcomes after coronary artery bypass surgery. Ann Thorac Surg. 2014;97(3):824-30. doi: 10.1016/j.athoracsur.2013.09.099.
- Chu D, Bakaeen FG, Wang XL, Dao TK, LeMaire SA, Coselli JS, et al. The impact of peripheral vascular disease on long-term survival after coronary artery bypass graft surgery. Ann Thorac Surg. 2008;86(4):1175-80. doi: 10.1016/j.athoracsur.2008.06.024.
- vanStraten AH, Firanescu C, Soliman H, Tan ME, TerWoorst JF, Martens EJ, et al. Peripheral vascular disease as a predictor of survival after coronary artery bypass grafting: comparison with a matched general population. Ann Thorac Surg. 2010;89(2):414-20. doi: 10.1016/j. athoracsur.2009.11.036.
- Gomes WJ, Mendonça JT, Braile DM. Cardiovascular surgery outcomes: oportunity to rediscuss medical and cardiological care in the Brazilian Public Health System. Rev Bras Cir Cardiovasc. 2007;22(4):3-4. doi: http://dx.doi.org/10.1590/S0102-76382007000400002.