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Does diabetes mellitus increase immediate surgical risk in octogenarian patients submitted to coronary artery bypass graft surgery?

Diabetes mellitus aumenta risco cirúrgico imediato em pacientes octogenários submetidos à cirurgia de revascularização miocárdica?

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Abstract

Introduction: **Diabetes is a well known risk factor for early and late adverse outcomes in patients undergoing coronary artery bypass graft surgery (CABG); however, few studies have investigated the impact of this risk factor in the group of older patients, especially octogenarians.**

Objectives: **To compare in-hospital mortality and morbidity of diabetic and nondiabetic patients aged ≥ 80 years submitted to CABG.**

Methods: **A total of 140 consecutive cases were studied, of whom 37 (26.4%) were diabetics, in a retrospective cross-sectional study, that included all patients aged ≥ 80 years submitted to isolated/associated CABG. The patients' mean age was 82.5 ± 2.2 years and 55.7% were males.**

Results: **The hospital mortality rate did not significantly differ in multivariate analysis: 16.2% diabetic x 13.6% nondiabetic (*P* = 0.554), as well as morbidity: 43.2% x 37.9%, respectively (*P* = 0.533). Regarding to operative morbidity, the occurrence of stroke was significantly higher in diabetic patients in the univariate analysis (10.8% x 1.9%, *P* = 0.042). In multivariate analysis, however, the incidence of stroke was not associated with the presence of diabetes (*P* = 0.085), but it was associated with atrial fibrillation (*P* = 0.044). There was no significant difference related to other complications.**

Conclusion: **In this small consecutive retrospectively analyzed series, there was no significant increase in hospital mortality and morbidity related to diabetes for CABG in octogenarian patients. The impact of the results of this study is limited by the sample size and might be confirmed by future randomized clinical trials.**

Descriptors: **Myocardial revascularization. Aged. Aged, 80 and over. Diabetes mellitus.**

Resumo

Introdução: **O diabetes é um fator de risco conhecido para eventos adversos precoces e tardios em pacientes submetidos à cirurgia de revascularização miocárdica (CRM); entretanto, poucos estudos investigaram sua influência no grupo de pacientes mais idosos, especialmente nos octogenários.**

Objetivos: **Comparar a mortalidade e a morbidade hospitalar de pacientes com idade ≥ 80 anos diabéticos e não-diabéticos submetidos à CRM.**

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Abbreviations, acronyms & symbols	
ADA	American Diabetes Association
CPB	Cardiopulmonary bypass
CABG	Coronary artery bypass grafting
HbA1c	Glycosilated hemoglobin
IC/FUC	Instituto de Cardiologia do Rio Grande do Sul
IABP	Intra-aortic balloon pump
LVEF	Left ventricle ejection fraction
NYHA	New York Heart Association
ROC	Receiver operating characteristic

Métodos: **Foram estudados 140 casos consecutivos, sendo 37 (26,4%) diabéticos, em um estudo transversal retrospectivo incluindo todos os pacientes com idade ≥ 80 anos submetidos à CRM isolada/associada. A idade média dos pacientes foi de 82,5 ± 2,2 anos e 55,7% eram do sexo masculino.**

Resultados: **A taxa de mortalidade hospitalar não diferiu de maneira significativa na análise multivariada entre os grupos, 16,2% diabéticos x 13,6% não-diabéticos (*P*=0,554), assim como a morbidade pós-operatória, 43,2 x 37,9%, respectivamente (*P*=0,533). Em relação à morbidade, a ocorrência de acidente vascular cerebral foi significativamente maior em pacientes diabéticos na análise univariada (10,8% x 1,9%; *P* = 0,042). Na análise multivariada, no entanto, a incidência dessa complicação não foi associada com a presença de diabetes (*P*=0,085), mas com a presença de fibrilação atrial (*P*=0,044). Não se observou nenhuma diferença significativa em relação às outras complicações.**

Conclusão: **Nessa pequena série de casos retrospectiva, não houve um aumento significativo da morbimortalidade hospitalar no grupo de pacientes octogenários diabéticos. O impacto dos resultados desta série é limitado pelo tamanho amostral e poderá ser confirmado por futuros ensaios clínicos randomizados.**

Descriptors: **Revascularização miocárdica. Idoso. Idoso de 80 anos ou mais. Diabetes mellitus.**

INTRODUCTION

Diabetes is a well-known risk factor for ischemic heart disease. Coronary artery disease is not only more prevalent in diabetic patients (55%) compared with the rest of the population (2% to 4%) but tends to be more extensive, involving multiple vessels and being rapidly progressive. Moreover, diabetes is also a significant risk factor for early and late adverse outcomes after myocardial revascularization with coronary artery bypass grafting (CABG) [1].

Approximately 20% of patients who undergo CABG have diabetes mellitus. Diabetes has been associated with higher perioperative morbidity as well as decreased survival after this procedure. Diabetic patients who undergo surgical revascularization of coronary arteries represent a large and complex subgroup of bypass patients [2].

The elderly are expected to have a higher rate of morbid outcomes after surgery than younger patients, despite recent advancements in technology, pharmacotherapy, and perioperative management that are improving postoperative outcomes. Coronary artery disease is increasingly prevalent in the elderly population. With advances in surgical technique, the incidence of CABG surgery performed in elderly patients has been increasing over recent years [3].

Octogenarians are an expanding group of patients referred for cardiac surgery. Patients in this age group tend to have higher rates of comorbidities and risk factors, which may result in more frequent and severe complications, and higher mortality rates [4].

Few studies [5] have investigated the impact of diabetes in the group of older patients, especially octogenarians. This study aimed to compare mortality and morbidity in diabetic and nondiabetic octogenarian patients undergoing CABG.

METHODS

This retrospective cross-sectional study included consecutive patients aged 80 years or older who were submitted to CABG at Instituto de Cardiologia do Rio Grande do Sul (IC/FUC). The variables analyzed were age, gender, hypertension, severe 3-vessel or left main artery disease, New York Heart Association (NYHA) heart failure functional class, previous myocardial infarction, urgency/emergency surgery, left ventricle ejection fraction (LVEF), atrial fibrillation, renal dysfunction, previous CABG, associated surgery performed, cross-clamp and cardiopulmonary bypass (CPB) times.

Diabetes mellitus diagnosis was performed in order to American Diabetes Association (ADA) guidelines [6]: glycosilated hemoglobin (HbA1c) ≥ 6.5%, or fasting serum glycemia ≥ 126 mg/dL, or serum glycemia ≥ 200 mg/dL after ingestion of 75 g of glucose, or random serum glycemia ≥ 200 mg/dL accompanied by symptoms atributed to hyperglycemia. In the absence of unequivocal hyperglycemia, the first three criteria mentioned before, should be repeated to seal diagnosis.

Renal dysfunction, both pre- and postoperative, was defined as serum creatinine level ≥ 2 mg/dL. Coronary artery disease was considered severe if reduction of luminal area exceeded 70% in a coronary artery or 50% in the left main coronary artery. The involvement of the three main coronary arteries and their branches was analyzed to categorize the number of vessels involved. Low cardiac output was considered all hemodynamic instability requiring vasoactive drugs or intra-aortic balloon pump support (IABP). Focal neurological deficits or changes in level of consciousness for a period exceeding 24 hours were defined as stroke.

Hospital mortality was defined as the occurrence of death during hospitalization, regardless of its duration. Operative morbidity was defined as the occurrence of any of the following complications: trans-operative myocardial infarction, low cardiac output, need for IABP support, sepsis, operative wound or lower limb infection, renal dysfunction, stroke, bleeding requiring reoperation or prolonged mechanical ventilatory support (over 48 hours).

Cardiopulmonary bypass was performed in all cases, and it was established by cannulation of the ascending aorta and right atrium and maintained under mild hypothermia of 34ºC. Distal anastomosis were carried out under aortic clamping and myocardial protection using cardioplegic crystalloid solution model St. Thomas II, injected anterogradaly through puncture of the ascending aorta. Topycal hypothermia was performed during the ischemic phase with frozen saline solution and/or amorphous ice made of saline solution, that was put into pericardial cavity. The proximal aorta anastomosis were carried out under partial ascending aortic clamping with Lambert-Kay type clamp, performed during rewarming.

Data were collected directly from patients' records, and analyzed with the SPSS 15.0 software. The descriptive analysis for qualitative variables was performed from the distribution of absolute and relative frequency, and the quantitative as mean and standard deviation. The comparison of groups was performed by Student's t test for quantitative variables and by chi-square for categorical variables. In situations of low frequency, we used the Fisher exact test. Multivariate analysis was performed by logistic regression: there were included in the regression, all variables that showed $P < 0.30$ in univariate analysis, The level of significance in all tests was 5%.

This study is a subanalysis of a previous study [7] that was submitted to and approved by the local Research Ethics Committee, approved in January of 2008.

RESULTS

The sample included 140 patients aged 80 years or greater of whom 37 (26.4%) were diabetics. In the diabetic group, nine (24.3%) patients were in use of insulin therapy. The demographic characteristics are described in Table 1: no significant difference in variables between the two groups was observed.

Table 1. Demographic baseline characteristics of diabetic and nondiabetic patients.

Variable	Diabetic (n=37)	Nondiabetic (n=103)	Total	*P* value
Mean age (±SD)	82.7 ± 2.5	82.4 ± 2.1	82.5 ± 2.2	0.388
Male (%)	21 (56.8)	57 (55.3)	78 (55.7)	1.000
Hypertension (%)	31 (83.8)	71 (68.9)	102 (72.9)	0.127
Severe 3-vessel disease (%)	25 (67.6)	67 (65.0)	92 (65.7)	0.940
NYHA functional class III/IV (%)	13 (35.1)	32 (31.1)	45 (32.1)	0.803
Severe left main artery disease (%)	8 (21.6)	32 (31.1)	40 (28.6)	0.379
Previous MI (%)	11 (29.7)	26 (25.2)	37 (26.4)	0.754
Non-elective surgery (%)	6 (16.2)	16 (15.5)	22 (15.7)	1.000
LVEF < 50% (%)	5 (13.5)	9 (8.7)	14 (10.0)	0.523
Atrial fibrillation (%)	4 (10.8)	4 (3.9)	8 (5.7)	0.208
Renal dysfunction (%)	1 (2.7)	6 (5.8)	7 (5.0)	0.675
Previous CABG (%)	1 (2.7)	2 (1.9)	3 (2.1)	1.000
Associated CABG (%)	13 (35.1)	37 (35.9)	50 (35.7)	1.000
Cross-clamp time ≥ 90 min (%)	5 (13.5)	8 (7.8)	13 (9.3)	0.328
CPB bypass time ≥ 120 min (%)	4 (10.8)	10 (9.7)	14 (10.0)	1.000

SD, standard deviation; NYHA, New York Heart Association; MI, myocardial infarction; LVEF, left ventricle ejection fraction; CABG, coronary artery bypass graft; CPB, cardiopulmonary bypass

From the 140 CABG surgeries performed, 90 were isolated and 50 associated with other procedures. The implantation of an aortic bioprosthesis was the major associated procedure. The list of procedures performed is described in Table 2.

Table 2. Surgical procedures performed.

Surgery	n (%)
Isolated CABG	90 (64.3)
Associated CABG	50 (35.7)
Aortic bioprosthesis	28 (20)
Carotid endarterectomy	5 (3.6)
Aortic valvuloplasty	5 (3.6)
Mitral valve repair	3 (2.1)
Mitral bioprosthesis	3 (2.1)
Aortic bioprosthesis + Aortoplasty	2 (1.4)
Aortic bioprosthesis + Mitral valve repair	2 (1.4)
Endoaneurysmorrhaphy	1 (0.7)
Patent ductus arteriosus correction	1 (0.7)

CABG - coronary artery bypass graft

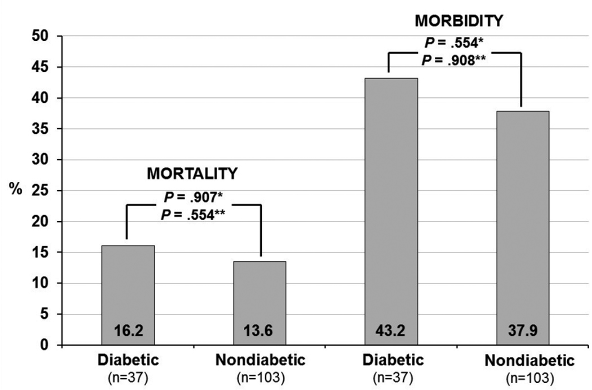

*Fig. 1 - Comparison of diabetic and nondiabetic patients regarding to the occurrence of mortality and morbidity outcomes. *Univariate analysis; **Multivariate analysis: adjusted for hypertension and atrial fibrillation*

The hospital mortality rate was slightly higher in diabetic patients, as well as morbidity; however, this difference was not significant in univariate and multivariate analysis. The results of these analyses are described in Figure 1.

In regard to operative morbidity, the occurrence of stroke was significantly higher in diabetic patients in the univariate analysis: no significant difference in relation to other complications was observed. In multivariate analysis, the incidence of stroke was not associated with the presence of diabetes, but it was associated with the presence of atrial fibrillation (P = 0.044). The occurrence of complications that were summarized in the surgical morbidity endpoint is described in Table 3.

DISCUSSION

In this relatively small series of patients, it was not observed higher rate of fatal or nonfatal outcomes in diabetics, as compared to nondiabetic octogenarian patients, similarly to other previous studies that are cited in this section. However, the majority of these studies did not analyze specifically octogenarian patients, beyond it did not specifically evaluate the impact of diabetes as a preoperative risk factor.

The reported incidence of postoperative complications after coronary artery bypass procedures in diabetic patients has varied. Fietsam et al. [8] found an increase in morbidity among diabetic patients; however, they did not find any increase in the occurrence of reoperation, stroke, or perioperative myocardial infarction, iin agreement with our findings in this series. In contrast, Kuan et al. [9] reported that diabetics had an increased risk of stroke, hemorrhage, and perioperative myocardial infarction [2].

Brazilian studies observed association of diabetes with general infections in the post-operative period [10],

Table 3. Comparison of diabetic and nondiabetic patients for the occurrence of postoperative morbidity.

Complication	Diabetic (n=37)	Nondiabetic (n=103)	Total	*P* value*	*P* value**
Low cardiac output (%)	13 (35.1)	26 (25.2)	39 (27.9)	0.348	
Renal dysfunction (%)	4 (10.8)	10 (9.7)	14 (10.0)	1.000	
Mechanical ventilation > 48h (%)	6 (16.2)	7 (6.8)	13 (9.3)	0.105	
IABP support (%)	2 (5.4)	8 (7.8)	10 (7.1)	1.000	
Bleeding requiring reoperation (%)	2 (5.4)	6 (5.8)	8 (5.7)	1.000	
Peri-operative MI (%)	1 (2.7)	6 (5.8)	7 (5.0)	0.675	
Sepsis (%)	1 (2.7)	6 (5.8)	7 (5.0)	0.675	
Stroke (%)	4 (10.8)	2 (1.9)	6 (4.3)	0.042	0.085
Operative wound infection (%)	2 (5.4)	3 (2.9)	5 (3.6)	0.608	
Lower limb infection (%)	1 (2.7)	2 (1.9)	3 (2.1)	1.000	

IABP, intra-aortic balloon pump; MI, myocardial infarction.
** Univariate analysis.*
*** Multivariate analysis: adjusted for hypertension and atrial fibrillation*

sternal wound infection [11] and mediastinitis [12,13]. In this series, there was not higher incidency of sepsis, sternal wound infection or lower limb wound infection, probably due to lack of statistical power, due to its relatively small sample to show such relation.

Thourani et al. [2] found that diabetic patients had worse in-hospital and long-term outcome after CABG. Diabetic patients had a higher incidence of postoperative death (3.9% versus 1.6%) and stroke (2.9% versus 1.4%) (both, $P < 0.05$). Diabetics had lower survival (5 years, 78% versus 88%; 10 years, 50% versus 71%; both, $P < 0.05$) and lower freedom from percutaneous transluminal coronary angioplasty (5 years, 95% versus 96%; 10 years, 83% versus 86%; latter, $P < 0.05$). In our report, although there was numerically higher mortality in diabetic patients, it was not observed statistically significant difference in regard to mortality. In relation to the higher incidence of stroke in the diabetic patients observed initially, it was shown further, in multivariate analysis, that it was in fact related to atrial fibrillation.

Herlitz et al. [14] reported that diabetic patients undergoing CABG more frequently required reoperation and had a higher incidence of peri- and postoperative neurological complications. In addition, they observed that diabetic patients during the 2 years after CABG had 2-fold increase in mortality rate compared to nondiabetic patients, both early and late after surgery: 30-day mortality was 6.7% in diabetic patients and 3.0% in nondiabetics ($P < 0.01$) and between 30 days and 2 years 7.8% and 3.6%, respectively ($P < 0.01$).

Postoperative glycemic control in this series (150-200 mg/dL) was not aggressive. In relation to this issue, two recent randomized clinical trials observed no benefit of aggressive glycemic control (90-120 mg/dL) compared with moderate glycemic control (120-180 mg/dL) [15,16].

In an interesting study performed by Halkos et al. [17], an elevated hemoglobin A1c level was strongly associated with adverse events after CABG, suggesting that a preoperative hemoglobin A1c testing may allow for more accurate risk stratification in patients undergoing this procedure. An elevated hemoglobin A1c level predicted in-hospital mortality after CABG: odds ratio 1.40 per unit increase ($P = 0.019$). Receiver operating characteristic (ROC) curve analysis revealed that hemoglobin A1c greater than 8.6% was associated with a 4-fold increase in mortality. For each unit increase in hemoglobin A1c, there was a significantly increased risk of myocardial infarction and deep sternal wound infection.

On the other hand, regarding specifically to octogenarian patients undergoing CABG, Bardakci et al. [3] did not observe the presence of diabetes as an independent risk factor for hospital mortality, similar to data observed in this study. Previous studies involving octogenarian patients undergoing cardiac procedures had already described the lack of association of diabetes with this outcome [18-24]. Studying even older patients, Speziale et al. [25] described the non-elective surgery and the existence of previous myocardial infarction as predictors of mortality in nonagenarian patients undergoing cardiac procedures, not observing the presence of diabetes as a risk factor for this outcome.

In a Brazilian study performed by Alves Júnior et al. [26], including patients 70 years or greater submitted to CABG or heart valve surgeries, diabetes was not associated with increased risk for in-hospital mortality. In the other hand, Iglézias et al. [27], while analyizing patients also with 70 years or greater, that had been submitted to CABG, found that diabetes was associated with surgical mortality. In a study that included patients aged 80 years or more, similarly to this, Guimarães et al. [28] also did not observed diabetes as a predictor of mortality; although, this study was not designed with this objective.

In this study, there was no association of diabetes with increase in the incidence of postoperative complications. López-Rodríguez et al. [29], when analyzed patients older than 75 years, did not observe this association as well. Ji et al. [5] reported that diabetic patients aged over 70 years had a higher rate of deep sternal wound infection, while sharing similar rates for other morbidities compared with nondiabetic patients aged over 70 years. Nagpal et al. [4], when analyzed octogenarian patients undergoing CABG with or without cardiopulmonary bypass, described that diabetes was not as a risk factor for the occurrence of the combined endpoint of death and major complications.

Patients aged 80 years and over have a significantly higher risk for any complication with cardiac surgery, including neurologic events, pneumonia, dysrhythmias, and wound infection. Independent predictors of cerebrovascular accident, coma, or stupor are proximal aortic atherosclerosis, history of neurologic disease, age greater than 70 years, and history of pulmonary disease. The strongest predictor of focal cerebrovascular accident (4-fold increase in risk) is proximal aortic atherosclerosis as judged by surgeons' intraoperative palpation. Older age also seems to be a predictor of more subtle neurologic injury, such as memory deficit and cognitive decline [30]. Regarding to pre-operative atrial fibrillation as a risk factor for stroke, Tarakji et al. [31] in a recent study reported an odds ratio of 2.4 (95% confidence interval 1.38-4.2) for intra-operative stroke and 3.0 (95% confidence interval 1.64 -5.4) for stroke in the postoperative period. Risk factors common to both intraoperative and postoperative stroke were older age, smaller body surface area, previous stroke, preoperative atrial fibrillation, and on-pump CABG with hypothermic circulatory arrest.

In relation to long-term survival, the literature is inconsistent in defining diabetes as an unfavorable prognostic factor in octogenarian patients undergoing cardiac procedures. Kohl et al. [20] noted that octogenarian patients undergoing cardiac procedures did not have lower survival compared to nondiabetics. On the other hand, Peterson et al. [21], in a large study involving 24,461 patients undergoing CABG, reported that the presence of complicated diabetes was a risk factor for mortality in 3 years. Long term survival of patients included in this report is being analyzed, and it will be reported further.

CONCLUSIONS

In this small consecutive retrospectively analyzed study, there was no significant increase in in-hospital mortality for CABG in octogenarian diabetic patients and the rate of nonfatal complications was similar to nondiabetic octogenarians. The impact of the results found in this report is limited by its small sample size and might be confirmed by future clinical trials. Other limitations of this report are its retrospective method and to be done in a single center; however, results found in this study suggest, based on previous findings, that CABG may be performed in diabetic octogenarians without increase of risk related to diabetes.

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