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Predictors of infection in post-coronary artery bypass graft surgery

Preditores de infecção no pós-operatório de cirurgia de revascularização miocárdica

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Abstract

Background: **Although coronary artery bypass grafting (CABG) is a good alternative therapy in severe arterial disease, it may evolve with complications, especially infections.**

Objectives: **To determine the incidence of infection in post-CABG and its clinical predictors in a cardiology reference center in Brazil.**

Methods: **Concurrent cohort study. Data were collected from all patients undergoing CABG between January/2004 and February/2006, excluding emergency surgery, absent record of blood glucose levels preoperatively and infection prior to surgery. Statistical analysis: Student's t test, chi square, logistic regression.**

Results: **We evaluated 717 Patients, 11 ± 61.9 years old, were men 67.1%, 29.6% with diabetes, of whom 137 (19.1%) developed infection (62% respiratory, 25% superficial wound, urinary 9.5%, 3.6% deep wound). Diabetes was more prevalent in those who developed infection, as well as prolonged time of indwelling central venous catheter (79.3 ± 40.5 vs. 61.0 ± 19.3 hours, *P* <0.001). After multivariate analysis (model adjusted for dyslipidemia, hypertension, smoking and leukocytes), both diabetes (OR 4.18 [2.60-6.74]), prolonged central venous line (1019 OR [1:00 to 1:02] and cardiac catheterism (OR 03.02 [1.14-3.60] remained predictors of infection. While diabetes is associated with a higher percentage of infections (*P* <0.001), preoperative serum glucose was not associated with increased risk of infection.**

Conclusions: **Diabetes and permanence of central venous catheters were associated with development of infection in post-CABG. The preoperative blood glucose was not a predictor of risk of infection. It is probably necessary to study with great detail glycemic control trans- and post-operatively.**

Descriptors: **Diabetes mellitus. Myocardial revascularization. Infection. Risk.**

Resumo

Introdução: **Embora a cirurgia de revascularização miocárdica (CRM) seja uma boa alternativa terapêutica na**

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doença arterial grave, pode evoluir com complicações, especialmente infecções.

Objetivos: **Determinar a incidência de infecção no pós-operatório de CRM e seus preditores clínicos em um centro de referência cardiológico brasileiro.**

Métodos: **Estudo de coorte. Foram coletados dados de todos os pacientes submetidos à CRM entre janeiro/2004 e fevereiro/2006, excluindo-se cirurgias de urgência, sem glicemia pré-operatória e com infecção prévia à cirurgia. Análise estatística: teste t-Student, qui quadrado e regressão logística.**

Resultados: **Foram avaliados 717 pacientes, 61,9 ± 11 anos, 67,1% homens, 29,6% com diabetes, dos quais 137 (19,1%) desenvolveram infecção (62% respiratória, 25% superficial de ferida operatória, 9,5% urinária, 3,6% profunda de ferida operatória). Diabetes foi mais prevalente naqueles que desenvolveram infecção, assim como maior tempo de permanência do cateter venoso central (79,3 ± 40,5 vs. 61,0 ± 19,3 h, *P*<0,001). Após análise multivariada (modelo ajustado para dislipidemia, hipertensão, tabagismo e leucócitos), tanto diabetes (OR 4,18 [2,60-6,74]), quanto tempo de permanência do cateter venoso central (OR 1,019 [1,00-1,02]) e cateterismo cardíaco durante a internação (OR 2,03 [1,14-3,60] mantiveram-se preditores do desfecho infecção (*P*<0,001). Apesar do diabetes estar associado a maior percentual de infecções (*P*<0,001), glicemia do pré-operatório não se associou a maior risco de infecção.**

Conclusões: **Diabetes e tempo de permanência do cateter venoso central se associaram ao desenvolvimento de infecção no pós-operatório de CRM. A glicemia pré-operatória não foi preditora de risco de infecção, provavelmente havendo necessidade de caracterização mais detalhada do controle glicêmico trans e pós-operatório imediato.**

Descritores: **Diabetes mellitus. Revascularização miocárdica. Infecção. Risco.**

INTRODUCTION

Coronary artery disease is a condition with widespread impact on the population, and accounts for significant morbidity and mortality nowadays. Treatment for coronary artery bypass graft (CABG) has been shown to improve survival in patients with severe coronary artery disease [1]. However, several studies have shown, after heart surgery, still significant rate of postoperative complications, especially superficial and shallow infections [2-8]. A multicenter study conducted in Australia showed that of 4,474 patients undergoing CABG, the risk of wound infection was 4.5 to 10.7 per 100 procedures. Multivariate analysis showed age, obesity and diabetes mellitus (DM) as independent risk factors for this outcome [7]. In relation to DM, Guven et al. [9] demonstrated that hyperglycemia at pre-CABG was the main risk factor for developing post-operative infections; risk can be reduced with improved glycemic control in the perioperative period [10]. Similar results were observed by some authors [11], but not by others [12]. In Brazil, a recent study also shows a high incidence of postoperative mediastinitis in cardiac surgery [8].

Based on information from the registry of infections in post-CABG developed in Australia, it has been developed a risk score for infections that could be applied aiming to identify the patients most prone to this complication, acting preventively more intensively in the latter [13], which was also been suggested in a Brazilian study [14]. The identification of clinical and laboratory factors evaluated in the preoperative of patients who are treated at institutions that perform CABG and its relationship with outcomes after surgery, especially the risk of infection, are essential for the implementation of measures aimed at preventing these outcomes improving prognosis and reducing costs. Hence, the knowledge about local factors is essential for a better planning of assistance, the study aimed to evaluate the relationship between clinical and laboratory factors assessed preoperatively, especially the presence of DM, and rate of postoperative infections in patients undergoing CABG in a reference center in southern Brazil, searching for associations between preoperative variables and risk of postoperative infection.

METHODS

This study was approved by the Institutional Ethics Committee, under registration number 3413/03. The authors signed a commitment pledging to use the information solely for scientific purposes, while fully preserving the anonymity of patients.

We conducted a cohort study in which data were collected on all patients who underwent CABG from January 2004 to February 2006, in a reference center in Rio Grande do Sul, Brazil. Exclusion criteria were: emergency surgery, no record of fasting blood glucose on admission,

no evidence of infection until 36 hours after surgery and evidence of any infection in the preoperative period (presence of positive culture tests or antibiotics).

The study included 717 patients, of whom 212 (29.6%) had DM (defined by previous personal history of DM, use of oral hypoglycemic agents or fasting glucose greater than or equal to 126 mg / dl at the time of admission). Cardiopulmonary bypass was performed during all procedures, according to the routine of the institution.

Data were collected retrospectively, filling out a form that contained variables such as demographic and identification (name, sex, race, age), clinical (weight, height, blood pressure, heart rate, axillary temperature, current medications, blood glucose levels in capillary during the first 48 hours after surgery), laboratory (fasting plasma glucose, hematocrit, hemoglobin, leukocytes, platelets, creatinine, sodium, potassium), intraoperative (surgical time, cardiopulmonary bypass, aortic clamping, mechanical ventilation, central venous catheter, urinary catheter) and comorbidities (hypertension, diabetes mellitus, smoking, obesity, dyslipidemia, myocardial infarction, heart failure, chronic renal failure, chronic obstructive pulmonary disease, prior stroke, prior cancer) . The glomerular filtration rate was calculated using the Cockcroft-Gault equation [15].

It was considered as postoperative infection the patient that presented any of the following conditions: 1) respiratory infection (defined as positive or infiltrate sputum on recent chest radiography, clinically characterized as resulting from heart failure), 2) urinary tract infection (defined by positive or white cell urine culture), 3) superficial operative wound infection (clinical diagnosis recorded in medical records, in which the involvement was only skin and subcutaneous tissue), 4) deep operative wound infection (clinical diagnosis recorded in medical records, which involved the mediastinum, bone or cartilaginous tissue, with or without the presence of necrotic tissue). Antibiotic prophylaxis with cefazolin was performed preoperatively, according to the routine of the institution. In subjects who had more than one infection, we considered only the first one in order to calculate the incidence. Any deaths were also recorded.

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS version 17.0). We described the characteristics of the sample by mean, standard deviation, median, interquartile ranges and proportions. Possible associations between the characteristics studied were evaluated by chi-square or Fisher's exact test, when appropriate and Student's t test. Multivariate analysis was performed by stepwise backward regression that found infection as dichotomous outcome and included clinically significant variables of univariate analysis and variables considered clinically important according to the hierarchical conceptual model (technique described by Barros & Victora [16]). In cases of duplicate variables (systolic blood pressure and systemic hypertension, for example), we chose to use the variable in its continuous form. We did not include in the same model variables with strong linear relationship, such as cardiopulmonary bypass time and total time of surgery, for example. It was considered a critical alpha of 0.05 as level of statistical significance.

RESULTS

The patients studied had a mean age of 61.9 ± 11 years, 67.1% men and 29.6% had a previous diagnosis of DM. Age was similar between groups, however, it was observed among patients with diabetes lower proportion of males (60.8% vs. 70.1%), higher incidence of history of dyslipidemia (46.2% vs. 14.1%) and higher incidence of previous diagnosis of hypertension (89.2% vs. 56.6%). These patients also had fasting blood glucose levels preoperatively higher, as expected (114.2 ± 36.3 mg / dL vs. 102.8 ± 27.1 mg / dL, P <0.001).

One hundred and thirty-seven (19.1%) patients had some type of infection, of which 85 (62%) were respiratory, 13 (9.5%), urinary tract, 35 (25%) superficial operative wound infection and five (3.6%), deep operative wound infection. The occurrence of any type of infection was higher in patients with DM (n = 85, 62%) when compared with those without DM (n = 82, 38%), P <0.001. The incidence of respiratory infection was similar between patients with and without DM (P = 0.067). Deep operative wound infection occurred in 3.6% of patients with DM and in none without DM.

Univariate analysis with the characteristics of the patients, classified according to the outcome of infection, present or absent, is presented in Table 1. Smoking (P <0.001), duration of central venous catheter (P <0.001), cardiac catheterization during hospitalization (P = 0.024) and WBC (P = 0.041) were more prevalent or higher in subjects who developed infection than those who did not have this outcome. There was no difference between the number of deaths among patients who developed infections (7, 5.1%) or not (23, 4.1%), P = 0.716.

Table 2 presents the data in the multivariate analysis in model adjusted for dyslipidemia, hypertension, smoking, and leukocytes. DM (OR = 4.18, 95% CI [2.60 to 6.74]), duration of central venous catheter (OR 1.019 [1.00 to 1.02]) and cardiac catheterization during hospitalization (OR 2.03 [1.14 to 3.60] were the predictors of the outcome of infection (P <0.001), even after adjustment. There was no interaction between time spent with central venous catheters and the presence of DM (P = 0.215).

Figure 1 shows the length of stay in hospital according to the presence of diabetes mellitus and infection. The

Table 1. Clinical and demographic characteristics of 717 patients undergoing coronary artery bypass grafting according to the infection outcome (presence or absence).

Characteristics	Presence of infection n=137	Absence of infection n = 580	*P*-value
Age (years)	62.9 ± 10.8	61.7 ± 10.8	0.248
Elderly (> 65 years)	60 (43.8)	244 (42.1)	0.120
Male	91 (66.4)	392 (67.6)	0.873
Race			0.703
White	112 (91.8)	473 (93.3)	
Non-white	10 (8.2)	34 (6.7)	
Diabetes mellitus	85 (62)	127.0 (21.9)	<0.001
Neoplasia	0	3 (0.5)	0.529
Cardiac catheterization during hospitalization	112 (81.8)	416 (71.8)	0.024
Percutaneous coronary intervention during hospitalization	9 (6.6)	33 (5.7)	0.848
AMI	31 (22.6)	95 (16.4)	0.109
Sequelae of stroke	12 (8.8)	58 (10)	0.779
COPD	20 (14.6)	62 (10.7)	0.253
Dislipidemia	47 (34.3)	122 (21.0)	0.001
BMI (kg/m²)			0.938
<25	61 (45.2)	257 (45.1)	
25-30	49 (36.3)	214 (37.5)	
>30	25 (18.5)	99 (17.4)	
Hypertension	113 (82.5)	362 (62.4)	<0.001
Smokers	37 (27.0)	54 (9.3)	<0.001
Medications in use			
ACEI	81 (59.1)	252 (44.4)	0.003
Statins	88 (64.2)	288 (50.1)	0.004
Oral antidiabetic	48 (35.0)	138 (23.8)	0.010
Blood pressure (mmHg)			
Systolic	133.4 ± 17.1	129.6 ± 15.7	0.013
Diastolic	78.9 ± 11.1	76.4 ± 9.9	0.008
Heart rate	80.7 ± 10.0	78.8 ± 9.5	0.039
Cardiopulmonary bypass time (min)	80.4 ± 24.5	78.7 ± 25.5	0.504
Aortic clamping time (min)	52.3 ± 19.9	51.6 ± 19.6	0.722
Duration of surgery (hours)	4.4 ± 0.7	4.3 ± 0.7	0.162
Time of central venous catheter (hours)	79.3 ± 40.5	61.0 ± 19.3	<0.001
Mechanical ventilation time (hours)	12 (9.2-17.9)	12 (10-14.3)	0.159
Fasting plasma glucose (mg/dL)	110.0 ± 36.1	105.8 ± 29.4	0.220
GFR (ml/min)	81.2 ± 39.9	85.9 ± 39.3	0.213
Leukocytes	7196.8 ± 2118	6807.5 ± 1322.8	0.041

Data expressed as mean ± SD (Student t-test), n and percentage in parentheses (Chi-square test) or median (p25-p75). AMI: acute myocardial infarction, COPD: chronic obstructive pulmonary disease, BMI: body mass index, ACEI: angiotensin-converting enzyme inhibitors, GFR: glomerular filtration rate calculated by Cockcroft-Gault equation

Table 2. Multivariate analysis evaluating the association between infection and diabetes.

Variables	OR	CI 95%	*P*	Adjusted OR*	CI 95%	*P*
Diabetes mellitus	5.567	3.54-8.73	<0.001	4.141	2.53-6.75	<0.001
Time of central venous catheter (hours)	1.029	1.01-1.03	<0.001	1.019	1.00-1.02	<0.001
Cardiac catheterization	1.755	1.09-2.80	<0.001	2.013	1.14-3.60	<0.001

** Adjusted OR: Odds ratio adjusted for dyslipidemia, hypertension, smoking, and leukocytes*

length of stay in hospital was higher in patients with DM who developed infection (9.7 ± 4.6 days) compared to all other groups of patients (8.1 ± 3.3 days for patients with DM who did not develop infection, 6.5 ± 1.6 days for patients without diabetes who developed infections and 6.4 ± 1.4 days for patients without diabetes who did not develop infection), *P* <0.001. Patients with DM who did not develop infection also remained longer in hospital compared with patients without DM (*P* <0.05).

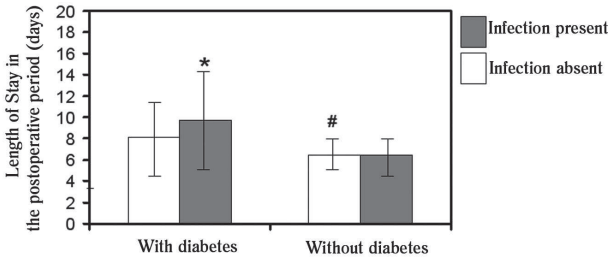

Fig. 1 - Length of stay in hospital according to the presence of diabetes mellitus and infection. * P *<0.001, #* P *<0.05.*

DISCUSSION

In this cohort study of incidence of infection in the postoperative period of myocardial revascularization, focusing on clinical and laboratory predictors of the occurrence of various types of infection, stand out as an original contribution in Brazil the following findings: 1. The high incidence of infections in post-CABG (19.1%), more common in patients with diabetes, especially deep operative wound infections (3.6%) 2. The duration of central venous catheter, presence of diabetes and cardiac catheterization during hospitalization as independent predictors of development of any infection in the postoperative period of CABG and 3. The increased length of hospital stay due to the presence of diabetes, especially the combination of diabetes associated with infection in the postoperative period of myocardial revascularization.

Prevalence of any infection in the postoperative period of CABG surgery was estimated between 16.9 and 24.3% [17.18] in other series, including all the patients operated and only patients with diabetes, respectively, data that are similar to that found in our study. Specifically, the number of patients who developed deep wound infection was similar to that observed in other studies [7,8,14,17-21], with some exceptions [22-24]. The expectation that new preventive and therapeutic approaches focusing on the prevention of surgical infection could reduce the incidence of infections over the past years did not occur in most of the studies cited, probably because more patients that underwent CABG during that period were elderly of high surgical risk and higher surgical complexity [25].

Considering the patients with diabetes, their disadvantage remains compared to the patients without diabetes regarding the risk of any infection in the post-CABG, especially deep operative wound infection, as other authors have shown [18]. A study in our group has not demonstrated this association [14], but it must be considered the possibility of measurement bias, since the data were collected retrospectively and the evaluation of the presence of DM was performed only by the patient's history, since the patient is unaware of carrying this disease in 46% of cases [26]. The fact that there was no difference between the capillary blood glucose in the immediate 48 hours after surgery and the presence of infection in our patients, unlike what was previously shown [18.27], may be due to the small number of patients with DM evaluated and the retrospective nature of this study, in addition to the average of postoperative glucose not having been as high as that described by Jones et al. [27].

The presence of diabetes as an independent predictor of development of any infection in post-CABG was demonstrated in this study, in agreement with previous reports [7,24,28]. We did not observe, however, the association between age, obesity [7,14,20], females [28,29] and presence of hypertension [29] with the development of infection, described in other series. Longer duration of central venous catheter and cardiac catheterization during hospitalization as independent predictors of development of any infection in the postoperative period of CABG were shown only in our study, regardless of the presence of DM they retained their association with the risk of infection.

The increased length of hospital stay due to the presence of diabetes, especially the combination of diabetes associated with infection in the post-CABG period was expected but it needs to be highlighted by the likely increase in costs that entails. Once identified the association between diabetes and diabetes/infection with increased length of hospital stay, it is up to the managers the implementation of measures that are able to reduce these outcomes [21,23,30,31], aiming at cost reduction as already demonstrated in other institutions [22].

Importantly, as in any observational study , it is not possible to rule out residual confounding factors, even after adjustment in multivariate analysis. In addition, the constant evolution of surgical techniques and changing patterns of infection lead to the need for constant review of the findings. Another limitation of this study is that we

do not have accurate data on how many patients were excluded.

We conclude that the incidence of infections in post-CABG remains higher than the ideal, with a distinct disadvantage in patients with diabetes, especially deep operative wound infections. These events contribute to the increased length of hospital stay due to the particular combination of diabetes associated with infection, and they could be minimized by the implementation of continuous insulin infusion protocol as a routine in the postoperative of coronary artery bypass grafting, thus, reducing morbidity, mortality and hospital costs.

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