Perioperative mortality in diabetic patients undergoing coronary artery bypass graft surgery

Mortalidade perioperatória em diabéticos submetidos à cirurgia de revascularização miocárdica

Michel Pompeu Barros de Oliveira Sá[1]; Evelyn Figueira Soares[2]; Cecília Andrade Santos[2]; Omar Jacobina Figueiredo[2]; Renato Oliveira Albuquerque Lima[2]; Rodrigo Renda Escobar[3]; Fábio Gonçalves de Rueda[3]; Ricardo de Carvalho Lima[4]

A B S T R A C T

Objective: Investigate risk factors for in-hospital death in diabetic patients undergoing isolated CABG. **Methods:** Retrospective study of 305 consecutive diabetic patients undergoing CABG in the Division of Cardiovascular Surgery of our institution from April 2004 to April 2010. Univariate analysis for categorical variables was performed with the chi-square test or Fisher's exact as appropriate. Potential risk factors with P <0.05 in univariate analysis were included in multivariate analysis, which was performed by backward logistic regression. P values <0.05 were considered statistically significant. **Results:** The study population had a mean age of 61.44 years (± 9.81) and 65.6% (n=200) were male. The in-hospital mortality rate was 11.8% (n=36). The following independent risk factors for death were identified: on-pump CABG (OR 6.15, 95% CI 1 0.57 to 24, 03, P=0.009) and low cardiac output in the postoperative period (OR 34.17, 95% CI 10.46 to 111.62, P <0.001). The use of internnal thoracic artery (ITA) was an independent protective factor for death (OR 0.27, 95% CI 0.08 to 0.093, P=0.038). **Conclusion:** This study identified the following independent risk factors for death after CABG: on-pump CABG and low cardiac output syndrome. The use of ITA was an independent protective factor.

Key words: Risk factors. Diabetes *mellitus*. Surgery. Coronary artery bypass. Myocardial revascularization.

INTRODUCTION

The prevalence of diabetes mellitus (DM) throughout the western world has been increasing at an alarming rate in recent years[1]. Coronary artery disease (CAD) is often an associated condition[2]. Diabetic patients have a worse prognosis when compared to non-diabetics in relation to coronary heart disease and display different evolutions when treated by percutaneous intervention with catheter or by surgery[3]. Studies show that the presence of DM is an independent risk factor for postoperative mortality of coronary artery bypass grafting (CABG), with an odds ratio of 1.73 for death from cardiovascular causes[4] and 2.94 for overall mortality[5].

Medical evidence leads to a greater tendency of indicating CABG in diabetics with multivessel disease[2]. In such patients CABG should always be considered in view of the benefits in the medium and long term when compared to medical and interventional treatments. However, when indicating surgery in the presence of DM, one should consider the potential increased surgical risk and special care in pre-operative and postoperative handling[2].

The search for factors that increase surgical risk, especially modifiable, is essential in order to decrease operative mortality.

The aim of this study was to investigate risk factors for in-hospital deaths of diabetic patients undergoing CABG at our local institution.

METHODS

Study Population

After approval by the ethics committee, we reviewed the records of 305 consecutive diabetic patients undergoing CABG at our institution from April 2004 to April 2010.

Definition of Diabetes and Variables

The presence of diabetes was defined as reported by patient and/or use of oral hypoglycemic medication and/or insulin.

Work performed at the Division of Cardiovascular Surgery, Emergency Hospital of Pernambuco - PROCAPE. Faculty of Medical Sciences / University of Pernambuco - FCM / UPE.

1. Resident, General Surgery, Barao de Lucena Hospital – HBL; 2. Medical School Graduate, Faculty of Medical Sciences, University of Pernambuco - FCM / UPE-PE-BR; 3. Cardiovascular Surgeon, Emergency Hospital of Pernambuco - PROCAPE-PE-BR; 4. Head, Division of Cardiovascular Surgery, Emergency Hospital of Pernambuco - PROCAPE-PE-BR.

The dependent variable was the in-hospital outcome (survival or death). The independent variables were divided into three categories:

1. CHARACTERISTICS OF PATIENTS

a. Age >70 years

b. Gender (male or female)

c. Obesity (body mass index e" 30Kg/m^2)

d. Hypertension (reported by patient and/or use of anti-hypertensive medication)

e. Smoking (reported by patient; active or inactive for less than 10 years)

f. Chronic obstructive pulmonary disease - COPD (dyspnea or chronic cough AND prolonged use of bronchodilators or corticosteroids AND/OR compatible radiological changes - hypertransparency by hyperinflation and/or rectification of ribs and/or diaphragmatic rectification)

g. Renal disease (creatinine e" 2.3 mg/dL or pre-operative dialysis)

h. Previous cardiac surgery

i. New York Heart Association (NYHA) functional class

j. Ejection fraction < 50%

k. Insulin-dependence

2. CHARACTERISTICS OF THE PROCEDURE

a. Emergency surgery (during acute myocardial infarction, ischemia not responding to therapy with intravenous nitrates, cardiogenic shock)

b. Use of internal thoracic artery (ITA)

c. Number of bypasses

d. Use of cardiopulmonary bypass – CPB (on-pump or off-pump)

3. COMPLICATIONS IN THE POSTOPERATIVE PERIOD

a. Hyperglicemia (first blood glucose after closure of skin >200mg/dL)

b. Low cardiac output syndrome (signs of poor peripheral and/or central perfusion – decreased level of consciousness, cold extremities and/or oliguria/anuria – and need for inotropic support with dopamine 4ìg/kg/min for a minimum of at least 12 hours or intraaortic balloon)

c. Reoperation (new sternotomy for bleeding, tamponade, or other reasons during the intra-hospital period)

d. Respiratory complications (pulmonary infection, acute respiratory distress syndrome, atelectasis, need for intubation for more than 48 hours)

e. Renal complications (creatinine e" 2,3 mg/dL or postoperative dialysis)

f. Multiple transfusions (more than 3 units of any blood products in the postoperative period before diagnostic definition of mediastinitis)

g. Sternal wound infection

Statistical Analysis

The data were stored in SPSS program (Statistical Package for Social Sciences) version 15, from which calculations were performed with statistical analysis and interpretation. The data storage was done in double-entry to validation and conduction of data consistency analysis, in order to ensure minimal error in recording information in the software.

Univariate analysis for categorical variables was performed with the chi-square test or Fishers exact test, as appropriate. Potential risk factors with P<0.05 in univariate analysis were included in multivariate analysis, which was performed by backward logistic regression. P values <0.05 were considered statistically significant.

RESULTS

Description of Population and Mortality

The study population had a mean age of 61.44 years (± 9.81), 65.6% (n = 200) were male and 34.4% (n = 105) were female. The mortality rate was 11.8% (n = 36). The study population was identified among 849 coronary artery bypass surgeries, showing a prevalence of 35.9% (n = 305) of diabetes among patients undergoing this type of surgical procedure in our local institution.

Univariate Analysis

Variables that were associated with increased risk of in-hospital deaths were:

1. CHARACTERISTICS OF PATIENTS (Table 1): age> 70 years (OR 2.67, 95% CI 1.30 to 5.46, p = 0.007), NYHA functional class IV (OR 3.24, 95% CI 1.15 to 9.12, p = 0.026), ejection fraction <50% (OR 2.08, 95% CI 1.01 to 4.30, p = 0.048);

2. CHARACTERISTICS OF THE PROCEDURE (Table 2): CPB (OR 2.62, 95% CI 1.21 to 5.64, p = 0.014);

3. POSTOPERATIVE COMPLICATIONS (Table 3): low cardiac output syndrome (OR 34.21, 95% CI 14.3 to 81.3, p <0.001), renal complications (OR 12.5, 95% CI 4.05 to 38.6, p <0.001), respiratory complications (OR 4.54, 95% CI 1.93 to 10.6, p = 0.001) and multiple transfusions (OR 2.93, 95% CI 1.39 to 6.13, p = 0.004).

The use of ITA was a protective factor for in-hospital death (OR 0.26, 95% CI 0.12 to 0.54, p <0.001), see table 2.

Multivariate Logistic Regression Analysis

We identified the following independent risk factors for in-hospital deaths: CPB (OR 6.15, 95% CI 1.57 to 24.03, p = 0.009) and low cardiac output in the postoperative period (OR 34.17, 95% CI 10.46 to 111.62, p <0.001). The use of ITA was an independent protective factor for in-hospital death (OR 0.27, 95% CI 0.08 to 0.093, p = 0.038).

Table 4 shows the data from multiple logistic regression analysis.

Table 1 – Outcomes according to clinical characteristics (univariate analysis).

	OUTCOME						OR	CI 95%	p value
	Survival		Death		Total				
	N	%	N	%	N	%			
Age > 70 years									
No	207	77.0	20	55.6	227	74.4	1.00		
Yes	62	23.0	16	44.4	78	25.6	2.67	1.30 - 5.46	0.007
Gender									
Female	89	33.1	16	44.4	105	34.4	1.00		
Male	180	66.9	20	55.6	200	65.6	0.62	0.30 - 1.25	0.181
Obesity									
No	234	87.0	34	94.4	268	87.9	1.00		
Yes	35	13.0	2	5.6	37	12.1	0.39	0.09 - 1.70	0.213
Hipertension									
No	35	13.0	4	11.1	39	12.8	1.00		
Yes	234	87.0	32	88.9	266	87.2	1.20	0.39 - 3.58	0.749
Smoke									
No	165	61.3	20	55.6	185	60.7	1.00		
Yes	104	38.7	16	44.4	120	39.3	1.27	0.62 - 2.56	0.505
COPD									
No	239	90.5	33	91.7	277	90.7	1.00		
Yes	25	9.5	3	8.3	28	9.3	0.87	0.24 - 3.03	0.826
Renal disease									
No	259	96.3	34	94.4	293	96.1	1.00		
Yes	10	3.7	2	5.6	12	3.9	1.52	0.32 - 7.24	0.597
NYHA class									
I	193	71.7	21	58.3	214	70.2	1.00		
II	35	13.0	5	13.9	40	13.1	1.31	0.46 – 3.71	0.608
III	24	8.9	4	11.1	28	9.2	1.53	0.48 – 4.84	0.468
IV	17	6.3	6	16.7	23	7.5	3.24	1.15 – 9.12	0.026
PCC									
No	249	92.6	33	91.7	282	92.5	1.00		
Yes	20	7.4	3	8.3	23	7.5	1.13	0.31 - 4.01	0.848
EF < 50%									
No	206	76.6	22	61.1	228	74.8	1.00		
Yes	63	23.4	14	38.9	77	25.2	2.08	1.01 - 4.30	0.048
Use of insulin									
No	212	78.8	28	77.7	240	78.7	1.00		
Yes	57	21.2	8	22.3	65	21.3	1.06	0.42 - 2.61	0.887

OR: odds ratio*; CI: confidence interval; COPD: chronic obstructive pulmonary disease; NYHA: New York Heart Association; PCC: previous cardiac surgery; EF: ejection fraction*

DISCUSSION

This study showed 35.9% prevalence of DM in patients undergoing CABG at our institution during the reference period. This rate was 33.4% higher than the one reported in the study of Lauruschkat *et al.*[6] involving 7310 patients who consecutively underwent CABG, which observed a prevalence of 29.6% of DM diagnosed preoperatively.

The observed in-hospital post-CABG mortality rate of 11.8% is considered high. We should take into account that this study deals with a population under additional surgical risk, with a greater tendency to complications that can lead to death in the postoperative period, since all the individuals are diabetics[2]. Another aspect is the fact that we are studying a population operated at a public institution. Moraes *et al.*[7] conducted a study involving 752 patients undergoing CABG in a private institution, showing a 1.7% mortality. Moreover, Oliver *et al.*[8] recently published a work involving public hospitals and showed in-hospital mortality ranging from 7.0% to 14.3%. Another recent work[9] involving 600 patients undergoing CABG in public

Table 2 – Outcomes according to procedure characteristics (univariate analysis).

	OUTCOME						OR	CI 95%	p value
	Survival		Death		Total				
	N	%	N	%	N	%			
ITA									
No	38	14.1	14	38.9	52	17.0	1.00		
Yes	231	85.9	22	61.1	253	83.0	0.26	0.12 - 0.54	0.000
N° of bypasses									
1	50	18.6	5	13.9	55	18.0	1.00		
2	118	43.9	15	41.7	133	43.6	1.27	0.43 - 3.68	0.659
3	88	32.7	14	38.9	102	33.4	1.59	0.54 - 4.67	0.399
4	13	4.8	1	2.8	14	4.6	0.77	0.08 - 7.16	0.818
5	0	0.0	1	2.8	1	0.3	-	-	-
CPB									
Off-pump	135	50.2	10	27.8	145	47.5	1.00		
On-pump	134	49.8	26	72.2	160	52.5	2.62	1.21 - 5.64	0.014
Emergency surgery									
No	266	98.9	35	97.2	301	98.7	1.00		
Yes	3	1.1	1	2.8	4	1.3	2.53	0.25 - 25.0	0.426

OR: odds ratio*; CI: confidence interval; ITA: internnal thoracic artery; CPB: cardiopulmonary bypass.*

Table 3 – Outcomes according to postoperative complications (univariate analysis).

	OUTCOME						OR	CI 95%	p value
	Survival		Death		Total				
	N	%	N	%	N	%			
Hiperglicemia									
No	121	45.0	10	27.8	131	43.0	1.00		
Yes	148	55.0	26	72.2	174	57.0	2.13	0.94 - 4.93	0.050
Low cardiac output									
No	250	92.9	10	27.8	260	85.2	1.00		
Yes	19	7.1	26	72.2	45	14.8	34.21	14.3 - 81.3	0.000
Renal complications									
No	263	97.8	28	77.8	291	95.4	1.00		
Yes	6	2.2	8	22.2	14	4.6	12.5	4.05 - 38.6	0.000
Respiratory complications									
No	248	92.2	26	72.2	274	89.8	1.00		
Yes	21	7.8	10	27.8	31	10.2	4.54	1.93 - 10.6	0.001
Sternal wound infection									
No	253	94.1	31	86.1	284	93.1	1.00		
Yes	16	5.9	5	13.9	21	6.9	2.55	0.87 - 7.44	0.087
Reoperation									
No	260	96.7	35	97.2	295	96.7	1.00		
Yes	9	3.3	1	2.8	10	3.3	0.83	0.10 - 6.71	0.858
Multiple transfusion									
No	221	82.2	22	61.1	243	79.7	1.00		
Yes	48	17.8	14	38.9	62	20.3	2.93	1.39 - 6.13	0.004

OR: odds ratio*; CI: confidence interval.*

hospitals showed a mortality rate during hospital stay of 12.2%. Sá *et al.*[10] showed a mortality rate during hospital stay of 13% involving 500 patients undergoing CABG in a public institution. Apparently there is some influence of the institutional factor (public versus private), with in-hospital mortality of public institutions being higher than in private

Table 4 - Independent risk factors for death (multivariate logistic regression analysis).

	OR	CI 95%	p value
ITA			
No	1.00		
Yes	0.27	0.08 - 0.93	0.038
CPB			
Off-pump	1.00		
On-pump	6.15	1.57 - 24.03	0.009
Postoperative low cardiac output syndrome			
No	1.00		
Yes	34.17	10.46 - 111.62	0.000

OR: odds ratio*; CI: confidence interval; ITA: internnal thoracic artery; CPB: cardiopulmonary bypass.*

ones. This may be related to the probable difference between the population assisted by private institutions (population that has better access to basic and complex health services) and the population assisted by public institutions (population that has restricted access to basic health services and even more restricted access to high-tech services).

Lima *et al.*[11] identified an important strategy to decrease surgical morbidity and mortality: off-pump CABG. In this study, which addressed specifically the diabetic population, it was observed that the use of CPB was an independent risk factor for in-hospital deaths. Taking into account that diabetes is a systemic disease with an important inflammatory component [2], it is assumed that there is a significant disarray after CPB. Off-pump CABG eliminates the non-pulsing flow and hypothermic myocardial ischemia, decreases release of inflammatory cytokines (tumor necrosis factor alpha, interleukins) and free radicals that are associated with cardiopulmonary bypass[12]. It has been noted that CPB is associated with higher levels of activated complement factors and markers of endothelial injury[12]. These effects are expressed in the clinical arena with a decrease of complications that increase mortality, such as renal failure, stroke, infections, atrial fibrillation, need for blood transfusions and low cardiac output[13].

The latter complication, low cardiac output, occurs in 9.1% of CABGs[14]. Our study found a 14.8% occurrence of this complication in the postoperative period (n = 45), which means an increase of 62.6% in the incidence of low cardiac output compared with that described in the literature. This probably occurred because we studied a population with diabetes, a condition associated with an increase of 1.6 times the risk of low cardiac output postoperatively[14]. Rao *et al,* in a study involving 4558 consecutive CABGs, observed that operative mortality was higher in patients who developed low cardiac output in comparison to those who did not (16.9% versus 0.9%, p <0.001)[14]. Oliveira *et al.*[8] and Pivatto *et al.*[15] also identified low cardiac output as a risk factor for increased operative mortality. Our study also found that low cardiac output was an independent risk factor for in-hospital deaths. The low cardiac output syndrome is a clinical outcome that may result from inadequate myocardial protection or perioperative ischemia. Patients at high risk for low cardiac output should be the focus of trials of new techniques of myocardial protection to resuscitate the ischemic myocardium.

Despite the later impairment caused by diabetes, surgical treatment of diabetic patients (especially those with multivessel disease) is associated with significant improvement in event-free survival when compared to those undergoing medical treatment and percutaneous angioplasty, as reported in the BARI study[16] and ratified by the BARI 2D study[17]. The better survival in the BARI study (mortality of 5.8% in the surgical group compared with 20.6% in the percutaneous group, with average follow up 5.4 years) was related to the implantation of at least one ITA, emphasizing the importance of such graft in improving late prognosis. It is known that implantation of ITA in the left anterior descending artery coronary constitutes an independent factor of improved survival in the long term. In some situations, surgeons are afraid to use the ITA in diabetics, especially if they are elderly and/or obese and/or present a poor quality sternum, because of the risk of a catastrophic infectious event secondary to postoperative sternal ischemia by the artery harvest of its original bed: the mediastinitis[18,19]. In other situations ITA is not used due to the discovery, during the operation, that its flow is inadequate. However, our study showed that the use of ITA in the making of a coronary bypass was an independent protective factor for death, showing that the benefit of using this type of graft in diabetics may already be initiated during hospitalization.

Being a retrospective analysis of medical records is this study's major limitation, leaving it at the mercy of all the biases associated with this type of study and also the quality of records' filling.

CONCLUSION

This study identified the following independent risk factors for in-hospital deaths after CABG in diabetics: CPB and low cardiac output syndrome. The use of ITA was an independent protective factor for death.

R E S U M O

Objetivo: *Investigar fatores de risco para óbito intra-hospitalar em diabéticos submetidos à cirurgia de revascularização miocárdica isolada.* ***Métodos****: Estudo retrospectivo de 305 pacientes. Foram avaliadas média de idade, taxa de mortalidade intra-hospitalar, uso de circulação extracorpórea, débito cardíaco no período pós-operatório e uso da artéria torácica interna. Análise univariada para variáveis categóricas foi executada com teste qui-quadrado de Pearson ou exato de Fisher, conforme apropriado. Potenciais fatores de risco com valor de P <0,05 na análise univariada foram incluídos na análise multivariada, que foi realizada por regressão logística backward. Valores de P <0,05 foram considerados estatisticamente significativos.* ***Resultados:*** *A população estudada apresentou média de idade de 61,44 anos (±9,81), sendo 65,6% (n=200) do sexo masculino. A taxa de mortalidade intra-hospitalar foi de 11,8% (n=36). Os fatores de risco independentes para óbito mostraram: uso de circulação extracorpórea OR 6,15; IC 95% 1,57-24,03; P=0,009 e baixo débito cardíaco no período pós-operatório com OR 34,17; IC 95% 10,46-111,62; P<0,001. O uso de artéria torácica interna foi fator protetor independente para óbito com OR 0,27; IC 95% 0,08-0,093; P=0,038.* ***Conclusão:*** *Este estudo identificou como fatores de risco independentes para óbito após a operação o uso de circulação extracorpórea e síndrome de baixo débito cardíaco. O uso da artéria torácica inerna foi fator protetor independente.*

Palavras-chave*: Fatores de Risco. Diabetes* mellitus. *Cirurgia. Ponte de artéria coronária. Revascularização miocárdica.*

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Mailing address:
Michel Pompeu Barros de Oliveira Sá
michel_pompeu@yahoo.com.br