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Risk factors for low cardiac output syndrome after coronary artery bypass grafting surgery

Fatores de risco para síndrome de baixo débito cardíaco após cirurgia de revascularização miocárdica

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Abstract

Objectives: **Low cardiac output syndrome (LCOS) is a serious complication after cardiac surgery and is associated with significant morbidity and mortality. The aim of this study is to identify risk factors for LCOS in patients undergoing coronary artery bypass grafting (CABG) in the Division of Cardiovascular Surgery of Pronto Socorro Cardiológico de Pernambuco - PROCAPE (Recife, PE, Brazil).**

Methods: **A historical prospective study comprising 605 consecutive patients operated between May 2007 and December 2010. We evaluated 12 preoperative and 7 intraoperative variables. We applied univariate and multivariate logistic regression analysis.**

Results: **The incidence of LCOS was 14.7% (n = 89), with a lethality rate of 52.8% (n = 47). In multivariate analysis by logistic regression, four variables remained as independent risk factors: age ≥ 60 years (OR 2.00, 95% CI 1.20 to 6.14, *P* = 0.009), on-pump CABG (OR 2.16, 95% CI 1.40 to 7.08, *P* = 0.006), emergency surgery (OR 4.71, 95% CI 1.34 to 26.55, *P* = 0.028), incomplete revascularization (OR 2.62, 95% CI 1.32 to 5.86, *P* = 0.003), and ejection fraction <50%.**

Conclusions: **This study identified the following independent risk factors for LCOS after CABG: age ≥ 60 years of off-pump CABG, emergency surgery, incomplete CABG and ejection fraction <50%.**

Descriptors: **Risk factors. Cardiac output, low. Myocardial revascularization.**

Resumo

Objetivos: **A síndrome de baixo débito cardíaco (SBDC) é uma complicação grave após cirurgias cardíacas, estando associada à significativa morbidade e mortalidade. O objetivo deste estudo é identificar fatores de risco para SBDC em pacientes submetidos à cirurgia de revascularização miocárdica (CRM), na Divisão de Cirurgia Cardiovascular do Pronto Socorro Cardiológico de Pernambuco - PROCAPE (Recife, PE, Brasil).**

Métodos: **Estudo prospectivo histórico compreendendo 605 pacientes consecutivos operados entre maio de 2007 e dezembro de 2010. Avaliaram-se 12 variáveis pré-operatórias e sete variáveis intraoperatórias. Aplicaram-se análises univariada e multivariada por regressão logística.**

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Abbreviations, acronyms & symbols	
AMI	Acute myocardial infarction
BMI	Body mass index
CABG	Coronary artery bypass grafting
CI	Confidence interval
CK	Creatine kinase
CK-MB	Creatine kinase-MB fraction
COPD	Chronic obstructive pulmonary disease
CPB	Cardiopulmonary bypass
CRM	Cirurgia de revascularização miocárdica
EF	Ejection fraction
ICU	Intensive care unit
ITA	Internal thoracic artery
LCOS	Low cardiac output syndrome
NYHA	New York Heart Association
OR	Odds ratio
SBDC	Síndrome de baixo débito cardíaco
SPSS	Statistical Package for Social Sciences

Resultados: **A incidência de SBDC foi de 14,7% (n = 89), com taxa de letalidade de 52,8% (n = 47). Na análise multivariada por regressão logística, quatro variáveis permaneceram como fatores de risco independentes: idade ≥ 60 anos (OR 2.00, IC 95% 1,20 a 6,14, *P* = 0,009), CRM com circulação extracorpórea (OR 2,16, IC 95% 1,40 a 7,08, *P* = 0,006), cirurgia de emergência (OR 4,71, IC 95% 1,34 a 26,55, *P* = 0,028), CRM incompleta (OR 2,62, IC 95% 1,32 a 5,86, *P* = 0,003) e fração de ejeção < 50% (OR 1,87, IC 95% 1,17 a 3,98, *P* = 0,007).**

Conclusões: **Este estudo identificou os seguintes fatores de risco independentes para SBDC após CRM: idade ≥ 60 anos, CRM com CEC, cirurgia de emergência, CRM incompleta e fração de ejeção < 50%.**

Descritores: **Fatores de risco. Baixo débito cardíaco. Revascularização miocárdica.**

INTRODUCTION

Low cardiac output syndrome (LCOS) is one of the most important complications after cardiac surgery [1] and regardless of the specific characteristics of studied groups, LCOS is associated with high mortality, reaching up to 38% [2], being considered the largest cause of mortality in coronary artery bypass grafting (CABG) surgeries performed in an emergency [1].

In addition to increased mortality related to LCOS, previous studies reported high rates of morbidity associated with this complication, such as increased incidence of pulmonary complications, myocardial infarction, stroke, renal failure and need for reoperation [2-6].

In addition to increased morbidity and mortality, patients who develop LCOS stay longer in ventilatory support, have a longer stay in intensive care unit and longer hospitalization [2,3], factors that are also reported as risk factors associated with higher mortality [1], with consequent increase of the economic impact of this entity [6].

The available data in the literature mainly refers to general cardiac surgery and recently there is a tendency to define risk factors for LCOS in specific subtypes of cardiac surgery such as aortic and mitral valve surgery with the definition of specific risk factors for each situation [2,3].

The identification of risk factors associated with the development of LCOS in coronary artery bypass surgery is essential to optimize pre-operative risk factors involved in strategies to improve myocardial protection and early intra-operative hemodynamic support [3], and set high-risk groups hemodynamically stable that may benefit from prophylactic use of intra-aortic balloon [6,7].

Therefore, the aim of this study is to identify risk factors for low cardiac output syndrome after CABG surgery.

METHODS

Source population

After approval by the ethics committee, in accordance with Resolution 196/96 (National Board of Health - Ministry of Health - Brazil) [8,9], we reviwed the records of consecutive patients undergoing CABG at our institution from May 2007 to December 2010. At first, we identified 647 patients eligible for the study. Forty-two were excluded due to lack of information from medical records, leaving 605 patients for data analysis, which complied with the minimum sample size calculated for the type of study required. Data collection was performed by trained staff (four people), and they did not know the purpose of the study (blind data collection).

Sample size

The sample was calculated from the work of Maganti et al. [3], which had as main objective the identification of predictors of LCOS after surgery for mitral valve surgery alone. It was selected the variable "emergency surgery", which in this study had a frequency of 5.09% of LCOS among those non-exposed to this factor, with an odds ratio (OR) of 2.90. Considering á error as 5%, â error of 20%, and the study power as 80%, we obtained a minimum sample of 422 individuals for a cohort study.

Study design

It was a historical prospective study. The dependent variable was LCOS after the surgical procedure. This variable was categorized into yes or no. LCOS were considered with those who met the following criteria before discharge from first hospitalization in the intensive care unit immediately after surgery (built from studies about

LCOS after mitral valve surgery [3], after aortic valve surgery [2] and patients with descompensated severe heart failure [10]):

1. Need for inotropic support with vasoactive drugs (dopamine 4 ì g/kg/min at least for a minimum of 12 hours and / or dobutamine) to maintain systolic blood pressure greater than 90 mmHg

OR

2. Need for mechanical circulatory support with intraaortic balloon to maintain systolic blood pressure greater than 90 mmHg

AND

3. Signs of impairment of body perfusion - cold extremities, hypotension, oliguria / anuria, lowered level of consciousness or a combination of these signs.

The independent variables were divided into two categories:

1. Pre-operative factors:

a. Age $\geq$ 60 years;

b. Gender (male or female);

c. Obesity (body mass index > 30 kg/m^2 - BMI);

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

e. Diabetes (reported by a patient and/or use of oral hypoglicemic medication and/or insulin);

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

g. 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 rectification diaphragmatic);

h. Renal disease (creatinine > 2.3 mg/dL or pre-operative dialysis);

i. Previous cardiac surgery;

j. Ejection fraction (EF) < 50%;

k. New York Heart Association (NYHA) functional class (I, II, III, IV);

l. Recent acute myocardial infarction (AMI < 90 days).

2. Intra-operative factors:

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

b. Concomitant cardiac surgery;

c. Use of internal thoracic artery (ITA);

d. Number of bypass (1, 2, 3 or more);

e. Use of cardiopulmonary bypass - CPB (on-pump or off-pump; according to the surgeon's preference);

f. Use of intraaortic baloon pump;

g. Completeness of revascularization (comparing significantly stenotic vessels at cardiac catheterization with surgically grafted coronary vessels; grafting of all the significantly stenotic coronary vessels was considered complete revascularization).

We also assessed the following characteristics: postoperative incidence of cerebrovascular accident and renal failure, length of stay in intensive care unit (days) and hospital stay (days); outcome (survival or death).

Data analysis

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

Univariate analysis for categorical variables was performed with the chi-square test or Fisher's exact test as appropriate. For continuous variables we used t-Student test. Verification of the hypothesis of equality of variances was performed using the Levene F test. Potential risk factors with P <0.05 in the univariate analysis were included in multivariate analysis in ascending order, which was performed by backward logistic regression. P values <0.05 were considered statistically significant.

RESULTS

Incidence

Study population had a mean age of 62.00 years (± 10.06) and 58.7% (n = 355) were male and 41.3% (n = 250) were female. It was found an incidence of 14.7% (n = 89) of cases of LCOS after CABG.

Univariate analysis

Variables that were associated with increased risk of LCOS after CABG with P <0.05: were age $\geq$ 60 years, emergency surgery, no use of ITA, EF < 50% and on-pump CABG. Data from the univariate analysis were shown in Tables 1 and 2.

Multivariate analysis by logistic regression

We identified the following independent risk factors for developing LCOS after CABG: age $\geq$ 60 years (OR 2.00, 95% CI 1.20 to 6.14, P = 0.009), on-pump CABG (OR 2.16, 95% CI 1.40 to 7.08, P = 0.006), emergency surgery (OR 4.71, 95% CI 1.34 to 26.55, P = 0.028), incomplete revascularization (OR 2.62, 95% CI 1.32 to 5.86, P = 0.003), and ejection fraction <50% (OR 1.87, 95% CI 1.17 to 3.98, P = 0.007). Through specific tests, it was found that the model is well accepted (P <0.001) and showed a degree of explanation of 82.1% (Table 3).

Table 1. Incidence of LCOS according to preoperative variables.

Variable	LCOS Yes		LCOS No		TOTAL		*P* Value	OR (95% CI)
	N	%	N	%	N	%		
Total Group	89	14.7	516	85.3	605	100		
Age (years)								
< 60	18	8.0	208	92.0	226	37.4	0.001(1)*	1.00
≥ 60	71	18.7	308	81.3	379	62.6		2.66 (1.50 - 4.78)
Gender								
Male	49	13.8	306	86.2	355	58.7	0.452(1)	1,00
Female	40	16.0	210	84.0	250	41.3		1.19 (0.76 - 1.87)
Obesity								
Yes	9	9.5	86	90.5	95	15.7	0.177(1)	0.56 (0.25 - 1.21)
No	80	15.7	430	84.3	510	84.3		1.00
Hypertension								
Yes	79	14.5	465	85.5	544	89.9	0.396(1)	0.87 (0.40 - 1.90)
No	10	16.4	51	83.6	61	10.1		1.00
Diabetes								
Yes	38	16.2	196	83.8	234	38.7	0.399(1)	1.22 (0.77 - 1.92)
No	51	13.7	320	86.3	371	61.3		1.00
COPD								
Yes	9	17.3	43	82.7	52	8.6	0.580(1)	1.24 (0.58 - 2.64)
No	80	14.5	473	85.5	553	91.4		1.00
Renal failure								
Yes	8	17.4	38	82.6	46	7.6	0.593(1)	1.24 (0.56 - 2.76)
No	81	14.5	478	85.5	559	92.4		1.00
AMI < 90 days								
Yes	39	13.9	242	86.1	281	46.4	0.591(1)	0,88 (0.55 - 1.42)
No	50	15.4	274	84.6	324	53.6		1.00
Smoke								
Yes	41	14.0	252	86.0	293	48.4	0.629(1)	0.89 (0.56 - 1.44)
No	48	15.4	264	84.6	312	51.6		1.00
NYHA Class								
I/II	68	13.7	429	82.3	497	82.1	0.125(1)	1.00
III/IV	21	19.4	87	80.6	108	17.9		0.66 (0.37 - 1.17)
EF < 50%								
Yes	38	22.4	132	77.6	170	28.1	0.001(1)*	1.91 (1.30 - 2.79)
No	51	11.7	384	88.3	435	71.9		1.00
Previous cardiac surgery								
Yes	12	21.1	45	78.9	57	9.4	0.156(1)	1.63 (0.83 - 3.22)
No	77	14.1	471	85.9	548	90.6		1.00

(*): Significant difference at 5.0%; (1): Chi-square test; LCOS: low cardiac output syndrome; COPD: chronic obstructive pulmonary disease; AMI: acute myocardial infarction; NYHA: New York Heart Association; EF: ejection fraction; OR: Odds Ratio; CI: Confidence Interval

Table 2. Incidence of LCOS according to intraoperative variables.

Variable	LCOS Yes N	LCOS Yes %	LCOS No N	LCOS No %	TOTAL N	TOTAL %	*P* Value	OR (95% CI)
Total Group	89	14.7	516	85.3	605	100		
Use of ITA								
Yes	64	12.9	431	87.1	495	81.8	0.009(1)*	0.50 (0.29 - 0.88)
No	25	22.7	85	77.3	110	18.2		1.00
Number of bypasses								
1	15	12.3	107	87.7	122	20.2	0,670(1)	1.00
2	41	15.8	219	84.2	260	43.0		1.28 (0.74 - 2.23)
3 or more	33	14.8	190	85.2	223	36.8		1.20 (0.68 - 2.13)
Emergency surgery								
Yes	6	50.0	6	50.0	12	2.0	0.004(2)*	6.14 (1.94 - 19.51)
No	83	14.0	510	86.0	593	98.0		1.00
Additional procedure								
Yes	7	26.9	19	73.1	26	4.3	0.087(2)	2.23 (0.91 - 5.48)
No	82	14.2	497	85.8	579	95.7		1.00
Cardiopulmonary bypass								
On-pump	69	20.6	266	79.4	335	55.4	< 0.001(1)*	3.24 (1.86 - 5.69)
Off-pump	20	7.4	250	92.6	270	44.6		1.00
Intraaortic baloon pump								
Yes	8	34.7	64	65.3	72	11.9	0.870(1)	0.60 (0.28 - 1.31)
No	81	12.0	452	88.0	533	88.1		1.00
Completeness of revascularization								
Complete	60	11.8	448	88.2	508	84.0	< 0.001(1)*	1.00
Incomplete	29	29.9	68	70.1	97	16.0		3.22 (1.92 - 5.26)

(*): Significant difference at 5.0% (1): Chi-square test (2): Fisher's exact test; LCOS: low cardiac output syndrome; ITA: internal thoracic artery; OR: Odds Ratio; CI: Confidence Interval

Table 3. Multivariate analysis by logistic regression

Variable	Adjusted OR	*P* Value
Age ≥ 60 years	2.00 (1.20 - 6.14)	0.009*
On-pump CABG**	2.16 (1.40 - 7.08)	0.006*
Emergency surgery	4.71 (1.34 - 26.55)	0.028*
Incomplete revascularization***	2.62 (1.32 - 5.86)	0.003*
EF < 50%	1.87 (1.17 - 3.98)	0.007*

(*): Significant difference at 5.0%. Constant P < 0.001; (**): Compared to Off-pump CABG.; (***): Compared to Complete revascularization.; EF: ejection fraction; CABG: coronary artery bypass graft; OR: Odds Ratio; CI: Confidence Interval

Evolution and outcome

Patients who developed LCOS after CABG stayed more days in the intensive care unit (8.45 ± 3.26 days versus 2.38 ± 1.21 days; $P < 0.001$) and longer hospital stay (21.87 ± 7.24 versus 10.54 ± 5.23; $P < 0.001$) compared with those who did not develop LCOS after CABG. Patients who developed LCOS after CABG presented higher rates of stroke (41.6% versus 3.5%; P <0.001) and renal failure (23.6% versus 5.8%; P <0.001) in comparison to the group that did not have postoperative LCOS. Forty-seven (52.8%) cases resulted in death.

DISCUSSION

Although some authors have reported that LCOS is a rare event after cardiac surgery using cardiopulmonary bypass with incidence rates reaching 0.1 to 2% [11,12], these numbers may be considerably higher in patients undergoing CABG surgery. Regarding the Brazilian data about LCOS after CABG, few studies have been published. A study evaluating 814 patients between 2002 and 2003 in Sao Paulo showed that LCOS was responsible for 54.2% of postoperative deaths and affected 16.1% of patients [13]. Similarly, a retrospective study of 546 patients undergoing CABG in Rio de Janeiro found LCOS as the most frequent postoperative complication [14]. The incidence of LCOS in our study was similar to other Brazilian series (14.7%).

Advanced age has been documented as a risk factor for LCOS after heart surgery such as mitral valve surgery [3] and aortic valve surgery [2]. In patients undergoing aortic valve replacement, for example, the development of LCOS continues to be an important complication and has, as one of its risk factors, advanced age [2]. The same type of phenomenon was observed in our study, which specifically addressed CABG surgery.

Misare et al. [15] demonstrated an age-dependent sensitivity to myocardial ischemia in an ovine model, introducing the term "senescent myocardium", concluding that elderly patients may be at increased risk for myocardial injury because of their senescent myocardium, and developing higher rates of LCOS after CABG.

Another risk factor for LCOS in our study was EF <50%. Low ventricular function is the most important predictor of postoperative morbidity and mortality [16]. Patients with poor ventricular function have a limited margin for myocardial protection, which makes patients experiment more intraoperative myocardial injury and develop LCOS after surgery [17]. However, the dysfunctional myocardium may not be irreversibly damaged and may be "stunned" or "hibernating", so the role of myocardial protection in these patients may be to limit the extent of myocardial injury.

We have demonstrated on-pump CABG as a risk factor for LCOS after surgery. This finding suggests a lower degree of myocardial injury in off-pump CABG. Some studies [18,19] show lower release of enzymes from myocardial injury in the postoperative period (CK, CK-MB, troponin T, parameters of myocardial injury) in patients undergoing off-pump CABG. The regional normothermic ischemia in off-pump CABG, the temporary interruption of coronary flow approached, seems to cause less myocardial injury compared to hypothermic global ischemia induced by cardioplegic arrest [20], which makes patients develop smaller rates of LCOS after CABG.

We also have demonstrated incomplete revascularization as a risk factor for LCOS after surgery. We note that our rate of incomplete revascularization is the same as reported in the CABG-arm of ARTS-II trial, that it was 16.0% [21]. Someone might say that this observation of increased risk is due to the dicotomy of "on-pump *vs.* off-pump CABG" (also related to the dicotomy "complete and incomplete revascularization", creating a confounding field), but we must observe that this risk factor is independently associated with this complication, being on-pump CABG also an independent risk factor for this complication. So we must deduce that, independently of use or not use CPB, incomplete revascularization, *per si*, is prejudicial for myocardium. Beyond this aspect, some series have shown the absence of any such disparity of completeness of revascularization between off-pump and on-pump CABG, giving more reinforcement to the rationale that incomplete revascularization is an independent risk factor for LCOS [22].

We also observed emergency surgery as a risk factor for LCOS after CABG. Kim et al. [1] observed that emergency CABG (defined in their study as surgery done within 24h after diagnostic angiography) presents higher rates of mortality compared to elective CABG, pointing that LCOS after surgery as the major cause of death.

Length of stay in intensive care unit (ICU) and hospital stay after cardiac surgery is associated with higher costs and may be correlated with an increased mortality, and some studies imply LCOS as a risk factor for this outcome. In a retrospective review of 3.523 patients undergoing CABG and/or valve surgery, multivariate logistic regression analysis showed that LCOS was an independent predictor of longer hospital stay and readmission to the ICU and a longer hospital stay [23]. We also observed that patients who developed LCOS in the postoperative period have average length of stay in ICU and hospital stay longer than patients without this complication.

It was observed that 52.8% of patients who developed LCOS after CABG in our institution died. Other studies have shown that LCOS after cardiac surgery is associated with increased mortality [3,13], and a Brazilian study identified mortality associated with this complication very similar to that observed in our institution (54.2%) [3].

CONCLUSION

We identified the following risk factors for LCOS after CABG: age ≥ 60 years, on-pump CABG, emergency surgery, incomplete revascularization and ejection fraction < 50%. Patients with LCOS after CABG present longer ICU and hospital length of stay, with high lethality rates.

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