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Predictors of low perioperative cardiac output in patients with heart valve surgery

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ARTICLE INFORMATION

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Acronyms
LCOS: low cardiac output syndrome
LVEF: left ventricular ejection fraction
NYHA: *New York Heart Association*
TAPSE: tricuspid annular plane systolic excursion

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ABSTRACT

Introduction: The perioperative low cardiac output syndrome (LCOS) is a frequent complication in the postoperative period of cardiac surgery which decreases short-term survival.
Objectives: To determine the variables that independently predict the incidence of LCOS in the perioperative period of heart valve surgery at the Instituto de Cardiología y Cirugía Cardiovascular, during the 2012-2014 triennium.
Method: A cohort study was conducted where two groups were formed: one with LCOS (46 patients) and the other without it (110 patients). A Kaplan-Meier curve was performed to determine survival 30 days after surgery. The groups were compared with the log-rank test. A multivariate analysis was carried out to determine the variables that independently influenced the appearance of LCOS. The level of statistical significance used was $p<0.05$.
Results: The sample was homogeneous according to clinical and demographic characteristics. The incidence and mortality of the LCOS were 29.5% and 28.3%, respectively. Preoperative renal dysfunction (OR=5.13, p=0.005), prolonged extracorporeal circulation time (OR=4.89, p=0.001) and elevated pulmonary vascular resistance (OR=7.52, $p<0.001$) were the variables independently associated with the appearance of low cardiac output.
Conclusions: The LCOS significantly reduces perioperative survival. Preoperative renal dysfunction, prolonged extracorporeal circulation and elevated pulmonary vascular resistance were variables of worse prognosis in these patients, associated with a higher probability of suffering this complication.
Keywords: Low cardiac output, Heart valve surgery, Perioperative survival, Survival analysis

Predictores de bajo gasto cardíaco perioperatorio en pacientes operados de cirugía cardíaca valvular

RESUMEN

Introducción: El síndrome de bajo gasto cardíaco (BGC) perioperatorio es una complicación frecuente en el postoperatorio de cirugía cardíaca la cual disminuye la supervivencia a corto plazo.
Objetivo: Determinar las variables que pronostican de manera independiente la

incidencia del BGC en el perioperatorio de cirugía cardíaca valvular en el Instituto de Cardiología y Cirugía Cardiovascular, durante el trienio 2012-2014.
Método: Se realizó un estudio de cohorte donde se conformaron dos grupos: uno con BGC (46 pacientes) y otro sin él (110 pacientes). Se realizó una curva de Kaplan-Meier para determinar la supervivencia a los 30 días de la cirugía, se compararon los grupos con la prueba de rangos logarítmicos (log-rank). Se efectuó un análisis multivariable para determinar las variables que influyeron de manera independiente en la aparición del BGC. El nivel de significación estadístico empleado fue de p<0,05.
Resultados: La muestra fue homogénea según características clínicas y demográficas. La incidencia y la mortalidad del BGC fueron del 29,5% y 28,3%, respectivamente. La disfunción renal preoperatoria (OR=5,13; p=0,005), el tiempo prolongado de circulación extracorpórea (OR=4,89; p=0,001) y la resistencia vascular pulmonar elevada (OR=7,52; p<0,001) fueron las variables que se asociaron de manera independiente a la aparición de bajo gasto.
Conclusiones: El BGC reduce significativamente la supervivencia perioperatoria. La disfunción renal preoperatoria, el tiempo prolongado de circulación extracorpórea y la resistencia vascular pulmonar elevada constituyeron variables de peor pronóstico en estos pacientes, asociadas a una mayor probabilidad de sufrir esta complicación.
Palabras clave: Bajo gasto cardíaco, Cirugía valvular cardíaca, Supervivencia perioperatoria, Análisis de supervivencia

INTRODUCTION

Low cardiac output syndrome (LCOS) continues to be a potential complication among patients in the postoperative period of cardiac surgery which prolongs hospital stay, increases healthcare costs and subsequently, increases perioperative morbidity and mortality[1,2]. Although cardiac surgery is indicated chiefly for coronary heart disease, valvular disease is frequent in our country and often diagnosed in advanced stages. This poses a challenge for surgical intervention as the risks of postoperative complications are higher; within which LCOS has a high incidence[1-3].

Several parameters, both bloody and bloodless, have been established to diagnose LCOS, but from the clinical point of view it can be identified by oliguria (diuretic rhythm less than 0.5 ml/kg/h) and the need to use intravenous inotropics, counterpulse balloon or both to achieve adequate hemodynamics[1].

Several prospective and observational studies have described different factors that can predict LCOS. Among them are: previous systolic dysfunction of the left ventricle, poor functional class and prolonged extracorporeal circulation times (cardiopulmonary bypass), to name but a few[2,4,5]. This complication has been poorly assessed in our field and the studies are based more on coronary surgery than on heart valve surgery.

Therefore, we found interesting and useful to carry out a study in patients who underwent heart valve surgery, in order to determine the variables that can independently predict the appearance of such a complex cardiac postoperative syndrome; as well as the perioperative survival of those who may develop it.

METHOD

A cohort study was carried out to assess all patients diagnosed with mitral or aortic valve disease, or both, who underwent heart valve repair or replacement surgery at the Instituto de Cardiología y Cirugía Cardiovascular de La Habana, Cuba, from January 1st, 2012 to December 31, 2014.

Data from variables of interest were collected from admission to 30 days, after reviewing medical records. The study was conducted in accordance with the guidelines proposed in the Declaration of Helsinki and approved by the Ethics Committee of the aforementioned institution. We excluded all patients with coronary disease in the preoperative studies.

Definition of the variables

Low perioperative cardiac output (dependent varia-

ble): was considered when, due to hemodynamic conditions, inotropic support was necessary for more than 12 hours or the use of intraaortic balloon counterpulsation, or both, associated with a diuretic rhythm less than 0.5 ml/kg/h.

Independent variables

General: age, sex, body surface (DuBois), personal pathological history, smoking habit, rheumatic/non rheumatic-valve disease etiology, functional class III-IV of the New York Heart Association (NYHA).

Perioperative: type of surgery, surgical and extracorporeal circulation time, hospital stay and condition at discharge, living or deceased.

Laboratory: Complete blood count, hematocrit, glycemia, creatinine, uric acid and glomerular filtration calculated by CKD-EPI.

Echocardiogram: left ventricular ejection fraction (LVEF), tricuspid annular plane systolic excursion (TAPSE), mean pulmonary artery pressure using Mahan's regression equation: (79- [0.45×time of pulmonary acceleration]), pulmonary artery systolic pressure calculated by the gradient of tricuspid regurgitation plus pressure in the right atrium, estimation of mean right atrial pressure from diameter and inspiratory collapse of the inferior vena cava, left atrium area in 4-chamber view, Pulmonary vascular resistance calculated by equation: maximum velocity of tricuspid regurgitation (m/s)/right ventricular outflow tract velocity time integral×10+0.16.

Statistical analysis

The SPSS program for Windows, version 15.0, was used for data analysis. The patients were divided into two groups: LCOS patients (46 patients) and non-LCOS patients (110 patients). Qualitative variables were expressed in absolute and relative frequencies and Chi-square test was applied for homogeneity, as well as the Fisher test for expected frequencies below five. Kolmogorov-Smirnov normality test was applied to the quantitative variables, t-Student test was used in those with normal distribution, as well as Mann-Whitney U test in those who did not; these variables were expressed as mean ± standard deviation.

Perioperative survival was determined using the Kaplan–Meier curve and logarithmic rank test for comparing survival between the groups. A multivariate logistic regression was performed, where the presence of LCOS was used as a dependent variable and the variables showing differences between the groups ($p<0.05$) were included in the model (gradually analyzed). Quantitative variables were grouped by ranges for processing. We evaluated the model by means of the goodness-of-fit test. The level of significance used in all cases was $p<0.05$.

Table 1. General characterization of patients according to low cardiac output.

Variables	Low cardiac output		Total (N=156)	p value
	Yes (n=46)	No (n=110)		
Age (years)	58.59±10.24	53.46±12.14	54.97±11.85	0.013
Female sex	23 (50.0)	50 (45.5)	73 (46.8)	0.61
Body surface area (m^2)	1.75±0.21	1.76±0.20	1.75±0.20	0.76
Rheumatic etiology	13 (28.3)	33 (30.3)	46 (29.5)	0.82
FC III-IV (NYHA)	41 (89.1)	81 (73.6)	122 (78.2)	0.03
High blood pressure	24 (52.2)	47 (42.7)	71 (45.5)	0.28
Diabetes mellitus	4 (8.7)	15 (13.6)	19 (12.2)	0.39
COPD	1 (2.2)	10 (9.1)	11 (7.1)	0.12
Permanent AF	13 (28.3)	15 (13.6)	28 (17.9)	0.03
Smoking habit	14 (30.4)	28 (25.5)	42 (26.9)	0.52

Values express mean ± standard deviation and n (%).
AF, atrial fibrillation; COPD, chronic obstructive pulmonary disease; FC, functional class; NYHA, New York Heart Association
Source: Medical records.

RESULTS

Our study population consisted of 156 patients who underwent left heart valve surgery; 46 patients (29.5%) developed postoperative LCOS. The sample was homogeneous according to the general characteristics; there was only a significant difference in terms of age, which was higher in the LCOS group, as well as poor preoperative functional class and chronic atrial fibrillation which were also more frequent in this group (**Table 1**).

Regarding perioperative variables, extracorporeal and surgical circulation times were significantly longer in the LCOS group, as well as longer stay (p<0.0001). Thirteen patients died in this period, all from the LCOS group, which represents a mortality of 28.3%. Overall mortality was 8.3% (**Table 2**).

Among the laboratory variables studied, only those related to preoperative renal function were significantly different, being worse in the group with LCOS, expressed by creatinine (p<0.0001) and glomerular filtration (p<0.0001); as well as uric acid, also higher in patients with LCOS (p<0.0001) (**Table 3**).

Echocardiographic variables showed that LCOS patients had lower TAPSE (**Table 4**), as well as higher mean pulmonary artery and right atrial pressure, and higher pulmonary artery systolic pressure, all with significant differences (p<0.05). Pulmonary vascular resistance was greater than 3 U/Wood in 37% of patients in the LCOS group, compared to the 10% in the non-LCOS group, so the difference was also significant (p<0.0001).

General perioperative survival was lower in the LCOS group (p<0.0001), greater reduction between both groups occurred in the first 10 days of the

Table 2. Caracterización perioperatoria de los pacientes estudiados según bajo gasto cardíaco.

Variables	Low cardiac output		Total (N=156)	p value
	Yes (n=46)	No (n=110)		
Isolated mitral surgery	18 (39.1)	50 (45.5)	68 (43.6)	0.46
Isolated aortic surgery	20 (43.5)	51 (46.4)	71 (45.5)	0.74
Double valve replacement	8 (17.4)	9 (8.2)	17 (10.9)	0.09
Surgical time (min)	404.11±160.53	288.14±61.04	322.33±113.65	<0.0001
CPB time (min)	199.78±18.70	122.68±36.50	145.42±70.77	<0.0001
Stay (days)	19.43±15.33	11.62±6.51	13.92±10.53	<0.0001
Deceased	13 (28.3)	0 (0)	13 (8.3)	<0.0001

Values express mean ± standard deviation and n (%). CPB, cardiopulmonary bypass.
Source: Medical records.

Table 3. Laboratory variables of the patients according to low cardiac output.

Preoperative laboratory variables	Low cardiac output		Total (N=156)	p value
	Yes (n=46)	No (n=110)		
Hemoglobin (g/l)	13.33±1.67	13.22±1.43	13.26±1.51	0.66
Hematocrit	0.40±0.05	0.40±0.04	0.40±0.42	0.92
Glycemia (mmol/l)	5.06±0.76	5.38±1.27	5.29±1.15	0.05
Creatinine (µmol/l)	88.17±23.24	72.96±17.34	77.44±20.41	<0.0001
Uric acid (mmol/l)	405.89±141.56	320.72±118.57	345.84±128.09	<0.0001
eGFe (ml/min/1.73m^2)	78.03±30.07	97.68±30.01	91.88±31.25	<0.0001

Values express mean ± standard deviation and n (%). eGF, estimated glomerular filtration.
Source: Medical records.

Table 4. Echocardiographic variables of patients according to low cardiac output.

Preoperative echocardiographic variables	Low cardiac output		Total (n= 156)	p value
	Yes (n=46)	No (n=110)		
LVEF (%)	58.33±16.25	62.97±11.70	61.60±13.32	0.08
TAPSE (mm)	19.24±4.89	21.87±4.92	21.10±5.04	0.003
PA mean pressure (mmHg)	36.91±12.98	30.02±12.01	32.05±12.65	0.002
RA pressure (mmHg)	9.02±6.14	6.00±4.91	6.89±5.49	0.004
PA systolic pressure (mmHg)	54.01±26.24	40.10±21.87	44.19±24.02	0.001
LA area in 4-chamber view (cm^2)	30.02±10.85	29.25±12.47	29.48±11.99	0.71
PVR ≥ 3 (U/Wood)	17 (37.0)	11 (10.0)	28 (17.9)	<0.0001

Values express mean ± standard deviation and n (%).
LA, left atrium; LVEF, left ventricular ejection fraction; PA, pulmonary artery; PVR, pulmonary vascular resistance; RA, right atrium; TAPSE, tricuspid annular plane systolic excursion
Source: Echocardiographic report.

postoperative period (**Figure**).

The multivariate analysis (**Table 5**) found that the main predictors for LCOS were pulmonary vascular resistance more than 3 U/Wood (OR 7.52, p<0.001), prolonged extracorporeal circulation time (OR 4.89, p=0.001) and preoperative renal dysfunction (OR 5.13, p=0.005), after results were adjusted for age over 65 years, sex and LVEF≤40%.

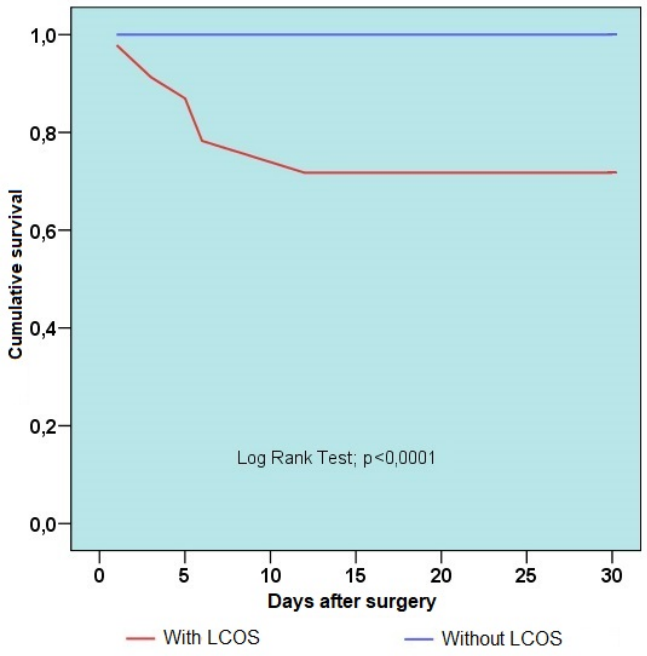

Figure. Kaplan-Meier curve of perioperative general survival according to low cardiac output (LCOS).

DISCUSSION

Our results showed that LCOS is a really serious complication that affects patients in both overall cardiac surgery and valve surgery, as is the case in our study. Its incidence in our series is consistent with what is reported in the literature[1,2,6]. The increase in age, female sex, an extreme body surface area, a poor functional class and decreased LVEF are some of the variables established in the prediction of risk in cardiac surgery[2,3,7,8].

It has been demonstrated that women are more likely to request health services in advanced stages of the disease, which increases surgical risks[2,8]. Extreme body surface area, both obesity and malnutrition, have been observed to predispose to a worse postoperative outcome[3,4].

Comorbidities such as diabetes mellitus, high blood pressure and chronic obstructive pulmonary disease are also associated with complications[9]. Patients with double valvular replacement present a greater risk due to prolonged extracorporeal circulation times, among other factors[2]. In our series, except for age, functional class and chronic atrial fibrillation, these variables were homogeneously distributed so they did not influence the incidence of LCOS.

Advanced age is one of the predictors of perioperative complications, including LCOS, which justi-

Table 5. Independent predictor variables of low cardiac output. Multivariable analysis.

Variables	B ± ET*	Wald	OR	CI 95%	p value
eGF < 60 (ml/min/1.73m^2)	1.635±0.57	7.97	5.13	1.64-15.96	0.005
Prolonged CPB	1.589±0.45	11.99	4.89	1.99-12.03	0.001
PVR ≥ 3 (U/Wood)	2.018±0.52	14.95	7.52	2.70-20.93	<0.001
Adjustment variables					
Age ≥ 65 years	0.059±0.59	1.42	0.55	0.20-1.46	0.23
LVEF ≤ 40%	0.214±0.75	0.08	0.8	0.18-3.56	0.80
Female sex	0.011±0.42	0.01	0.98	0.42-2.28	0.98

* Regression coefficient ± Standard error.
CI, confidence interval; CPB, cardiopulmonary bypass greater than 120 minutes; eGF, estimated glomerular filtration; LVEF, left ventricular ejection fraction; OR, *odds ratio*; PVR, pulmonary vascular resistance.
Goodness of fit: x^2=22,21, p=0,567.

fies it being significantly higher in this group[1,2,10]. A (NYHA) functional class III or IV indicates greater severity of the disease and, therefore, more operative risk, which makes it a known predictor of LCOS, as observed in our series[1]. Chronic atrial fibrillation per se is not a risk factor described for low cardiac outcome[1], but it is more frequently found in advanced stages of valvular diseases[3], which is why its greater presence is justified in the LCOS group.

It is known that LCOS significantly prolongs patient stay in cardiovascular therapy units,[4] as occurred in our study. Prolonged periods of extracorporeal and surgical circulation increase the probability of postoperative LCOS[1], multiple pathophysiological mechanisms which require an extracorporeal circulation machine may favor this state; among them we could mention immunological mechanisms that, through the activation of the complement, favor a state of systemic inflammatory response, vasoactive changes and hemostasis disturbances, among others[11]. Such activation was essential in our patients, all with valvular diseases, which visibly favored the LCOS with highly significant differences (p<0.0001) between the groups compared.

Some studies link hyperuricaemia with heart failure[12,13]. If we understand low cardiac output as a specific variety of heart failure[1], then our results may have a causal relationship, and should be subject to thorough further studies.

Preoperative renal dysfunction is an established risk factor for cardiac surgery[1,9,14], as it increases the risk of acute renal failure and mortality. Therefore, it is logical to find a worse renal function in the patients with LCOS before surgery, which is a predictor for its development[1,2,15].

Pulmonary hypertension is found in several predictive models of surgical risk as one of the most important factors[1,3,4], prior right ventricular dysfunction is associated with LCOS[1,16], which justifies the finding of severe levels of preoperative pulmonary hemodynamic variables in LCOS patients.

Pulmonary hypertension is one of the most important factors in many models of surgical risk prediction[1,3,4], prior right ventricular dysfunction is associated with LCOS[1,16], consistent with our finding of severe levels of preoperative pulmonary hemodynamic variables in patients with LCOS.

Overall mortality in our patients was 8.3%, similar to levels reported in literature. Different studies range from 2 to 7%[4-7,14]. Survival was significantly lower (p<0.0001) in the LCOS group, for a higher mortality 28.3%, which is similar to our review[1,3,14], and even lower than that reported in a study of more than a thousand cases where mortality due to LCOS was 40% 15. We obtained positive results, taking into account the substantial resources this type of surgery requires[17].

After processing all significantly different variables between both groups in a multivariate regression model, only preoperative renal dysfunction, extracorporeal circulation time greater than 120 minutes and pulmonary vascular resistance higher than 3 U/Wood remained independent. A study performed in patients with valvular diseases also found preoperative renal dysfunction as one of the strongest predictors of low cardiac output and mortality, as

well as machine times (extracorporeal circulation) greater than 120 minutes in patients with LCOS[15]. In addition, several studies consider that these two factors are fundamental in the prognosis of cardiac surgery[1,3,10,14].

Finally, it is striking that pulmonary vascular resistance greater than 3 U/Wood acts as a predictor of low cardiac output, but other variables that evaluate pulmonary hemodynamics such as mean and systolic pulmonary pressures are not included, although they are recognized factors[1,2, 16]. This, in our opinion, occurs because this variable distinguishes a greater remodeling in the pulmonary vasculature, which occurs in pulmonary hypertension,[16,18] and could better stratify patients with previous pulmonary hypertension, although they would be in a subgroup with a higher risk of suffer low expenditure and, therefore, higher mortality. However, as this is a small study, further investigations should be conducted.

CONCLUSIONS

Low cardiac output in the postoperative period of cardiovascular surgery is a fearsome complication that significantly reduces the perioperative survival of the patients studied when compared with those without this complication. The variables independently associated to LCOS were: preoperative renal dysfunction, prolonged extracorporeal circulation time and pulmonary vascular resistance greater than 3 U/Wood.

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