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Relationship between preoperative variables and early postoperative outcome in patients with mitral valve replacement surgery

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ABSTRACT

Introduction: Preoperative variables in mitral valve replacement surgery allow an objective preoperative assessment of each patient.

Objective: To determine the influence of preoperative risk factors on mortality and major complications occurring in mitral valve replacement surgery.

Method: Analytical, longitudinal, prospective follow-up study of 158 patients who underwent surgery for mitral valve disease at the Cardiocentro Ernesto Che Guevara of Villa Clara, from 2007 to 2010. A bivariate study was conducted for each independent variable. Mortality and major complications were the dependent variables.

Results: The mean age was 65.2 years, female patients predominated. Smoking, ventilatory disorders, pulmonary hypertension and atrial fibrillation were the most important risk factors. Most patients underwent surgery electively, in functional class II, with left ventricular ejection fraction greater than 50% and predominance of mitral stenosis. The variables that were associated with the risk of major complications were: heart failure, age over 50 years, emergency surgery, the use of hemoderivatives, atrial fibrillation, ventilatory disorders in spirometry and pulmonary acceleration time. Those related to death were: reduced left ventricular ejection fraction, pulmonary acceleration time, heart failure, the use of hemoderivatives, creatinine > 1.5 mg/dl, cardiomegaly and atrial fibrillation.

Conclusions: The relationship between preoperative variables and postoperative morbidity and mortality behaved indistinctly in each surgical center.

Key words: Surgery, Mitral valve stenosis, Mitral valve insufficiency

Relación de variables preoperatorias y evolución posquirúrgica precoz en pacientes con cirugía de sustitución valvular mitral

RESUMEN

Introducción: Las variables preoperatorias en la cirugía de reemplazo valvular mitral permiten realizar una evaluación preoperatoria objetiva de cada paciente.

Objetivo: Determinar la influencia de los factores de riesgo preoperatorios en la mortalidad y las complicaciones mayores que ocurren en la cirugía de sustitución valvular mitral.

Método: Estudio analítico, longitudinal, de seguimiento prospectivo en 158 pacientes intervenidos quirúrgicamente por enfermedad valvular mitral en el Cardiocentro "Ernesto Che Guevara", de Villa Clara, durante los años 2007-2010. Se realizó un estudio bivariado por cada variable independiente, las variables dependientes fueron la mortalidad y las complicaciones mayores.

Resultados: La edad media fue de 65,2 años, predominó el sexo femenino, y el hábito de fumar, los trastornos ventilatorios, la hipertensión pulmonar y la fibrilación auricular fueron los factores de riesgo que se destacaron. La mayoría de los pacientes se operaron de forma electiva, con clase funcional II, fracción de eyección del ventrículo izquierdo mayor del 50 % y predominio de la estenosis mitral. Las variables que se asociaron con el riesgo de sufrir complicaciones mayores, fueron: la insuficiencia cardíaca, la edad mayor de 50 años, la cirugía de urgencia, el uso de hemoderivados, la fibrilación auricular, los trastornos ventilatorios en la espirometría y el tiempo de aceleración pulmonar. Las que se relacionaron con el hecho de morir, fueron: la fracción de eyección del ventrículo izquierdo disminuida, el tiempo de aceleración pulmonar, la insuficiencia cardíaca, el uso de hemoderivados, creatinina > 1,5 mg/dl, la cardiomegalia y la fibrilación auricular.

Conclusiones: La relación entre las variables preoperatorias y la morbilidad y mortalidad postoperatoria se comportó indistintamente para cada centro quirúrgico.

Palabras clave: Cirugía, Estenosis valvular mitral, Insuficiencia valvular mitral

INTRODUCTION

Mortality and morbidity are indicators that measure the results of medical interventions; however, they lack operationality if they are not followed by studies to determine the causes which are influencing them, and their origin.

The patient's preoperative variables have been and are used to determine the surgical risk by most prediction models in cardiovascular surgery. If we consider that the preoperative status of the patient is the only one that can be theoretically modified or attenuated, then, knowledge and assessment of these variables in this period is essential.

In recent years, in cardiac surgery, several studies have identified many preoperative risk factors in relation to morbidity and mortality. In descending order, these are the most significant ones[1,2]:

- Urgent or emergency surgery.
- Reoperation.
- Age over 75 years.
- Impaired left ventricular function.

Risk factors are often interrelated, so that, in univariate analyzes, the impact of similar factors on morbidity and mortality may be overestimated. Likewise, some risk factors, identified in the univariate analyzes, are actually reflecting other variables which are more independent[3].

Significant changes have occurred in the assessment and treatment of patients with mitral valve disease in recent years; for this reason, there have been changes in preoperative variables, as well as in the incidence of early morbidity and mortality[4-6].

Surgical intervention on the mitral valve has evolved from closed mitral commissurotomy, valve replacements and repairs, to minimally invasive access. Hence, it is today one of the most regulated and safe surgical procedures in cardiovascular surgery. In spite of this, patients are not exempt from postoperative and surgical complications[7].

The analysis of outcomes in cardiac surgery, specifically in mitral valve replacement surgery, has

become very important due to the volume of cases of this type of intervention in thoracic surgery.

The figures of death and major complications in mitral valve replacement surgery are not negligible, both in domestic and foreign hospitals. It is estimated that deaths from this type of surgery should range from 2.5 % to 10 % of operated patients, and major complications may reach up to 30% of them[8-10].

Knowledge of predictors of mortality and major complications plays a key role because it allows an objective, individualized preoperative assessment of patients. The aim of this study was to determine the relationship between preoperative variables and morbidity and mortality in patients who underwent mitral valve replacement surgery at the Cardiocentro Ernesto Che Guevara in Santa Clara, Villa Clara, Cuba.

METHOD

The study was conducted at the department of cardiovascular surgery of the above-mentioned hospital. It was a non-experimental study, with a prospective follow-up in patients who underwent mitral valve replacement surgery. It included 158 patients, 7 died and 29 had major complications. The data from each of these patients was introduced into a database with SPSS statistical system, version 15.0, for statistical processing.

The postoperative variables that were analyzed in the study were: the fact of dying or not dying and the existence or not of major complications.

Mortality: Deaths that occur during hospitalization as a result of surgery, regardless of the length of stay, or within 30 days of surgical intervention[11].

Major complications: major complications include low cardiac output requiring intraaortic balloon counterpulsation or mechanical ventilation; severe arrhythmias (ventricular fibrillation and complete atrioventricular block); respiratory complications requiring mechanical ventilation for more than 48 hours; focal neurological injuries which are confirmed by clinical method, computerized tomography, or both; diffuse encephalopathy for more than 24 hours requiring mechanical ventilation, or showing a very impaired mental status; renal failure requiring dialysis or ultrafiltration; reoperation; mediastinitis and generalized sepsis[11].

Techniques and procedures for implementation of the surgical technique

All patients underwent surgery through a longitudinal median sternotomy, a detour avoiding the venae cavae, arterial cannulation in the ascending aorta and in the right atrium for both venae cavae, partial and full bypass with roller pump at 32 degrees Celsius, administration of cold crystalloid cardioplegia at 4 degrees Celsius, valve replacement through Guiraudon technique, implantation of St Jude Medical or CarboMedics bileaflet mechanical prosthesis, placement of drains into anterior and posterior mediastinum and sternal closure with stainless steel sutures[7].

Statistical analysis

Descriptive statistics of all variables included in the study: quantitative variables were expressed as mean $\pm$ standard deviation. Qualitative variables were expressed as absolute values and percentages.

To determine the predictor variables, four bivariate studies were conducted, where the dependent variables were mortality and the existence of major complications, first with quantitative variables, and then with qualitative variables.

For quantitative variables, the comparison of means was performed using the Mann-Whitney test after determining the normality of variables with Kolmogorov-Smirnov test. The association between qualitative variables was performed by χ^2 statistics. Based on these bivariate studies, the predictor variables of mortality and major complications were identified.

In all cases, when the significance associated with the statistical test used was less than 0.05, it was considered statistically significant, values less than 0.01 were considered highly significant.

RESULTS

General characteristics

The mean age of the patients was 65.2 ± 9.5 years; 39.2 % of them were in the age group between 40 and 49 years old and 71.5% were female. Preoperative

variables included hypertension in 32 patients (20.2 %), smoking in 60 (37.9 %), a history of diabetes mellitus in 7 (4.4 %), 5 patients (3.2 %) had a personal history of infectious endocarditis or infectious endocarditis at the time of surgery, 41 patients (26 %) had pulmonary hypertension and 49 (31%) showed ventilatory disorders in the pulmonary function test.

The predominant functional class, according to the New York Heart Association (NYHA), was functional class II with 84 patients (53.2 %) and 9 patients (5.7 %) had signs of heart failure; 151 patients (95.6 %) had an ejection fraction greater than 50%; 132 patients (83.5 %) showed normal levels of creatinine and 26 (16.4%) had cardiomegaly.

Atrial fibrillation was found in 39 patients (24.7 %). The average size of the left atrium was 50.6 ± 7.3 mm, and 13 patients (8.2%) had thrombi in this chamber.

Preoperatively, 58.9 % of patients had been treated with diuretics, 41.8 % with angiotensin-converting enzyme inhibitors and 39.9% with digitalis.

With regard to the variables related to surgery, 8 patients (5.1 %) underwent emergency surgery, only 9 patients (5.7%) had a history of cardiac surgery, and there was a predominance of stenotic mitral valve disease in 61 patients (38.6%), followed by double valve lesion (36.7 %); 130 patients (82.3 %) had no calcification of the ring or valve leaflets; 50 % of patients had a preoperative hospital stay of more than 7 days. Seven patients died, out of 158 included in the study, for a mortality rate of 4.4%, and 29 (18.3 %) had severe complications.

Study of major complications

In the first bivariate analysis, the quantitative variables showing statistical significance between patients who had major complications and those without them (**Table 1**) included age (p = 0.007) and pulmonary acceleration time (p = 0.015).

When analyzing age, the mean was higher in those who had major complications compared to those who did not, with a high statistical significance. The mean pulmonary acceleration time in those who had complications was farthest away from the normal range. The mean was 100.6 ms in those who did not have complications and was very close to the lower limit of normalcy, which is 100 ms.

In the bivariate analysis, the qualitative variables that were significantly associated with the development of major complications (**Table 2**) included heart failure (p = 0.000), ventilatory disorders in pulmonary

Table 1. Bivariate analysis of qualitative variables taking into account the differences between living patients and patients with major complications. Mitral valve surgery. Cardiocentro Ernesto Che Guevara, Villa Clara. 2007-2010.

Variables	Major complications						p
	Yes			No			
	n	Mean	SD	n	Mean	SD	
Age	29	50,1	13,7	129	44,1	9,3	0.007
PAcT	29	92,6	19,5	129	100,6	15,2	0.015

Source: Department of Statistics. Cardiocentro Ernesto Che Guevara. Santa Clara, Villa Clara, Cuba.
Legend. PAcT: Pulmonary acceleration time.

Table 2. Qualitative variables that were significant in the bivariate analysis taking into account the differences between living patients and patients with major complications.

Variables	95 % Confidence interval		OR	p
	Lower	Higher		
Heart failure	3,9	103,7	20,2	0.000
Emergency surgery	1,4	31,9	6,7	0.007
Preoperative use of hemoderivatives	1,2	21,3	5	0.018
Ventilatory disorders	1,8	9,5	4,1	0.001
Atrial fibrillation	1,3	7,1	3,1	0.007

Table 3. Quantitative variables which were significant in the bivariate analysis with regard to mortality.

Variables	Death						p
	Yes			No			
	n	Mean	SD	n	Mean	SD	
PAcT	7	83,9	15,4	151	100	16,1	0.01
LVEF	7	50,6	7,4	151	63,8	7,3	0.03

Legend. PAcT: Pulmonary acceleration time, LVEF: Left ventricular ejection fraction.

Table 4. Qualitative variables which were significant in the bivariate analysis with regard to mortality.

Variables	95 % Confidence interval		OR	p
	Lower	Higher		
Heart failure	6,8	222,3	38,9	0.000
Cardiomegaly	1,57	35,4	7,4	0.004
Creatinine > 1,5 mg/dl	6,8	222,3	14,6	0.01
Preoperative use of hemoderivatives	1,5	60,4	9,7	0.004
Atrial fibrillation	1,6	35,4	7,4	0.04

function test (p = 0.001), preoperative use of hemoderivatives (p = 0.018), emergency surgery (p = 0.007) and atrial fibrillation (p = 0.007).

Study of the deceased

The quantitative variables that were statistically significant in patients who died (**Table 3**) included pulmonary acceleration time (p = 0.01) and ejection fraction (p = 0.03).

Table 4 shows qualitative variables that were significant in the bivariate analysis of deceased patients. There is a significant association between death and heart failure, with p = 0.000; the preoperative use of hemoderivatives and cardiomegaly, both with the same statistical significance, p = 0.004; a preoperative creatinine between 1.5 and 2.5 mg/dl, with p = 0.01, and preoperative atrial fibrillation, with p = 0.04.

DISCUSSION

Age cannot be analyzed as a risk factor in isolation, but associated with other comorbidities that are influenced by aging. It is a variable related to major complications, but not with death.

In a multivariate analysis conducted with large series of surgical patients between 1978 and 2001, it was found that an age over 50 years was an independent predictor of cardiac death, especially when it exceeded 70 years. They also observed a decline in PO_2 at rest, which decreases linearly with age after age 50. However, the risk of respiratory complications increases significantly only between 70 and 80 years, in patients who have no other pulmonary risk factors[12,13].

Mortasawi *et al.*[13] found age to be a predictor of major complications in the immediate postoperative period of cardiac surgery with extracorporeal circulation, which linearly increases complications with

increasing age. Furthermore, as in our study, the age variable was not statistically significant in its relationship with death, which is consistent with other studies, such as those conducted at the Sao Lucas Hospital of the Catholic University of Rio Grande do Sul, Brazil, and demonstrates that age is not a contraindication *per se* to mitral valve replacement surgery[13,14].

At the Institute of Cardiology and Cardiovascular Surgery in Havana, it was found that increased age was directly related to the increase in major complications; hence patients older than 50 years were considered the age group most prone to major complications, mainly infectious complications[10].

The multicenter study ESMUCICA did not find age as an independent risk factor associated with the development of major complications in the immediate postoperative period following mitral valve replacement, which does not match the findings in our research. This study was conducted in 41 cardiovascular centers in the Southern Cone, with around 1450 patients[11].

Pulmonary acceleration time was another quantitative variable with statistical significance. Although it is not the best indicator for assessing pulmonary pressures, it was the only preoperative parameter available to estimate it in our patients.

Although the usefulness of routine preoperative pulmonary function assessment is controversial, it has been observed that those patients exhibiting, in the first second, a forced expiratory volume less than 50 % of predicted would have an increased risk of complication with prolonged mechanical ventilation in the immediate postoperative period[15].

Karel Morlans *et al*[10] have identified preoperative pulmonary arterial hypertension as a predictor of complications in the immediate postoperative period of mitral valve replacement surgery, primarily because it has prolonged intubation time, low cardiac output and respiratory sepsis, which coincides with the findings of Roques and Joao Carlos Vieira[10,14,16].

Lung diseases imply a significant risk of perioperative cardiac complications. Hypoxemia is the main risk factor for myocardial ischemia; equally, the conditions that cause the increase in respiratory work also increase the demand for cardiac output, as much as 25 % of the oxygen provided by the heart is used for respiratory work. Thus pulmonary hypertension increases the risk of cardiac complications[17].

Perhaps heart failure and emergency surgery are the least controversial qualitative preoperative variables with high statistical significance in its relation to the occurrence of major complications. The former, due to the exhaustion of compensatory mechanisms, and the latter, due to the low probability of creating them, as a result of the acute clinical symptoms.

Hidalgo *et al*[18] reported, in a paper on blood conservation in patients undergoing cardiac surgery in our hospital, that the use of hemoderivatives increases the risk of nosocomial infections and a higher incidence of heart failure. They also consider that morbidity and mortality is increased up to 100 days after surgery, which is consistent with the data found in our study[18].

Heart failure and atrial fibrillation are signs or symptoms of advanced stages of mitral valve disease, this finding may be due to the fact that a large number of patients do no undergo surgery at the ideal time, as a result of the imbalance between demand and surgical possibilities.

The presence of preoperative atrial fibrillation is the result of a long-term volume overload, which first generates dilation and then electrophysiological changes[19].

Rodriguez *et al*[20], from the University Hospital of Valladolid, found, as predictors of major complications, a serum creatinine greater than 1.4 mg/dl, age over 74 years, ventricular dilatation, emergency surgery and NYHA functional class III-IV, which coincides with Joao Carlos Vieira[14].

The ESMUCICA study identified atrial fibrillation and nonoliguric renal failure without dialysis as predictors of major complications in both, stenosis and mitral regurgitation[11].

In 2006, the Department of Cardiothoracic Surgery of the University of Tel-Aviv found a mortality of 2.0 % in 51 mitral valve replacement surgeries. Other authors, as Heikkinen *et al*, reported a similar study in 2007, and found a mortality of 20.5 % after mitral valve replacement. The high mortality was attributed to a large number of emergency interventions and interventions in octogenarian patients[21,22].

Although Parsonnet and Euroscore do not to give a high score to an ejection fraction between 30 and 50 %, our study is consistent with several articles that identify a left ventricular ejection fraction of 60 % as a cutoff point in the outcome and prognosis of this surgical procedure[23,24].

Pizarro *et al*[25] identified a preoperative left ventricular ejection fraction of less than 60 % as a strong prognostic factor of postoperative ventricular dysfunction, heart failure and death.

Studies comparing mortality among patients with or without sinus rhythm, who underwent mitral valve replacement, found that those who had sinus rhythm showed a higher immediate survival, which had a high statistical significance after five years[26,27].

Numerous reports and cohort studies relate blood transfusions to increased immediate mortality. An explanation for this phenomenon is the fact that there is a greater use of allogeneic blood and its derivatives compared to other surgeries, the use of extracorporeal circulation, hypothermia, anticoagulants, and a direct deterioration of the hemostatic system, by consuming coagulation factors, platelet destruction and fibrinolysis activation[28-31].

We agree with Van Gameren *et al* in identifying a serum creatinine above 2.0 mg/dl as an independent predictor of mortality in mitral valve surgery [32].

The reasons why cardiovascular patients with renal impairment have an increased morbidity and mortality after undergoing surgery are manifold: First, by the association with impaired hemostasis, with an increased risk of reoperation due to bleeding; secondly, by the presence of arterial calcifications and the involvement of multiple segments of the aorta, which poses technical difficulties for the surgeon when performing valve excision, cannulation and placement of the anoxic arrest clamp; and also due to malnutrition, advanced arterial disease, hypertension and diabetes mellitus, which are associated with it[33-37].

Although Euroscore gives more importance to the increase in creatinine above 2.1 mg/dl, this result does not coincide with ours, which shows statistical significance for creatinine > 1.5 mg/dl. This is consistent with the results of Cooper *et al*[33], who analyzed retrospectively over 48 000 patients undergoing cardiac surgery with cardiopulmonary bypass, and identified a serum creatinine greater than 1.5 mg/dl and a glomerular filtration rate lower than 60 ml/min/1.73 m^2 as independent predictors of hospital mortality. In this study, it is noteworthy the exponential growth in mortality when the glomerular filtration rate falls below 60 ml/min/1.73 m^2.

By consulting some studies conducted with patients treated in the country and abroad, it was found that Morlans *et al*[10] identified severe cardiomegaly and emergency operation as the most important preoperative predictors of mortality in mitral valve replacement, with statistical significance of p = 0.01 and p = 0.06, respectively. Also significant were infectious endocarditis, renal disease, age over 50 years and pulmonary hypertension, all with p<0.05. This was in contrast with our findings, which did not find an association between mortality and the origin of mitral valve disease, a history of cerebrovascular disease, diabetes mellitus, increased diameter of the left atrium, the presence of thrombus within it, hypertension and sex[10].

Discrepancies with this study[10] include the statistical significance of the decreased left ventricular ejection fraction and congestive heart failure, with high statistical significance in our patients.

In the multicenter study ESMUCICA, conducted in Argentina on predictors of death in patients undergoing valve surgery, the bivariate analysis only showed statistical significance in the relationship between the fact of dying and mitral valve replacement, an age over 70 years and a history of previous cardiac surgery; variables that in our study did not show the same behavior[11].

Roques *et al*[16] identified an age over 70 years, a preoperative creatinine greater than 200 mmol/l, a history of cardiac surgery, left ventricular systolic dysfunction, heart failure and pulmonary hypertension as risk factors predictive of early mortality after mitral valve surgery.

Although the study was conducted in 2001 and did not discriminate between valve replacement and valve repair, it is thought that repairing or replacing the mitral valve does not change the pathological substrate caused by this background.

CONCLUSIONS

The relationship between preoperative variables and postoperative morbidity and mortality behaved indistinctly in each surgical center. The pulmonary acceleration time of less than 100 ms, heart failure, ventilatory disorders in pulmonary function test and atrial fibrillation are common preoperative variables for major complications and death.

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