

# Evaluation of variables responsible for hospital mortality in patients with rheumatic heart disease undergoing double valve replacement

*Avaliação de variáveis responsáveis pela mortalidade hospitalar em pacientes portadores de doença reumática submetidos à dupla troca valvar*

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## Abstract

**Objective:** To describe the hospital mortality and associated clinical and echocardiographic variables in patients with rheumatic disease who underwent double valve replacement surgery.

**Methods:** This is a cross sectional descriptive study of mortality, performed in a referral hospital in Salvador, Bahia. Records from patients with rheumatic disease who underwent double valve replacement surgery during the years 2007-2011 were analyzed.

**Results:** The studied sample comprises 104 patients and 60 (57.7%) were male. The mean age was 38.04±14.45. Sixty five bioprostheses and 38 mechanical prostheses were used in these patients at the time of surgery. There were statistically significant differences between the two groups, when we analyzed the following variables: the mean age (36.30±13.03 vs. 45.35±17.8 years-old,  $P=0.011$ ), mean hemoglobin (11.10±2.19 vs. 9.22±2.26 g/dL,  $P=0.002$ ), mean hematocrit (34.22±5.86 vs. 28.44±6.62%,  $P<0.001$ ). New York Heart Association functional class III and IV (NYHA) ( $P=0.022$ ) was statistically associated with mortality.

**Conclusion:** We concluded that the mean hemoglobin/hematocrit level and the NYHA functional class was the major variables

associated to the mortality among these patients. Based on these data one may concern about the patient best moment for surgery and the patient hemoglobin level.

**Descriptors:** Rheumatic Fever. Heart Valve Diseases. Hospital Mortality. Preoperative Period.

## Resumo

**Objetivo:** Descrever a mortalidade hospitalar em pacientes reumáticos submetidos à cirurgia de dupla troca valvar e sua relação com variáveis clínicas e ecocardiográficas.

**Métodos:** Trata-se de um estudo de corte transversal. Foram estudados pacientes maiores que 18 anos, com valvopatia reumática que foram submetidos à cirurgia de DTV do período de janeiro de 2007 a dezembro de 2011 no Hospital Ana Nery - Salvador - Bahia. A coleta de dados se deu por meio de consulta aos prontuários dos pacientes.

**Resultados:** Foram estudados 104 pacientes, 60 (57,7%) eram do sexo masculino. A média de idade da população estudada foi de 38,04±14,45 anos. Foram utilizadas 65 próteses biológicas e 38 próteses metálicas. Houve diferença estatisticamente significativa entre os grupos comparados, pacientes que obtiveram alta versus pacientes que foram a óbito, em relação às seguintes

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Abbreviations, acronyms & symbols	
AR	Aortic regurgitation
CPB	Cardiopulmonary bypass
MR	Mitral regurgitation
NYHA	New York Heart Association
RF	Rheumatic fever

variáveis: média de idade dos pacientes que receberam alta para casa e foram a óbito, respectivamente (36,30±13,03 vs. 45,35±17,8,  $P=0,011$ ); média de hemoglobina, (11,10±2,19 vs.

9,22±2,26 g/dL,  $P=0,002$ ); média do hematócrito, (34,22±5,86 vs. 28,44±6,62%,  $P<0,001$ ). As classes funcionais III e IV (New York Heart Association) estiveram associadas estatisticamente com a mortalidade ( $P=0,022$ ).

**Conclusão:** Os dados encontrados no estudo apresentam uma população pouco estudada na qual os principais achados foram a média do nível de hemoglobina/hematócrito e classe funcional NYHA. Deve se levar em conta esses dados para a escolha do melhor momento de cirurgia para essa população.

**Descritores:** Febre Reumática. Doenças das Valvas Cardíacas. Mortalidade Hospitalar. Período Pré-Operatório.

## INTRODUCTION

Rheumatic fever (RF) is a major public health problem, especially in developing countries<sup>[1]</sup>. Valvular heart disease accounts for a significant portion of cardiovascular hospital admissions in Brazil. Unlike most developed countries, its main cause is RF, responsible for 70% of the cases<sup>[2]</sup>. During the acute phase of the disease, mitral regurgitation (MR) is the most frequent impairment, followed by aortic regurgitation (AR). Obstructive valve lesions usually do not occur in the early stages of the RF. Recurrence of the acute phase of rheumatic heart disease increases the long term risk of permanent heart injuries and may cause multiple valves lesions<sup>[3]</sup>. Therefore, patients with rheumatic valve disease tend to have multiple valve lesions: either due to rheumatic valve involvement (stenosis and/or regurgitation) or secondary to ventricle dilation, leading to mitral or tricuspid insufficiency.

Surgical treatment is usually focused at the most severe valve lesion. However, double valve replacement surgery is being performed more frequently nowadays as an attempt to achieve better quality of life and to improve cardiovascular hemodynamics, reducing mortality among these patients<sup>[2,4]</sup>.

Present literature lacks data on clinical or echocardiographic variables associated to in-hospital mortality in rheumatic patients undergoing double valve replacement surgery. Thus, this study aims to assess which of these determinants has impact in this population.

## METHODS

This is a cross-sectional retrospective study including all rheumatic patients admitted to the Ana Neri Hospital, Salvador, BA, Brazil, older than 18 years old, that underwent double valve replacement surgery from January 2007 to December 2011. Medical records were reviewed and evaluated for data collection.

The surgical procedure was performed with the patient in the dorsal decubitus position, with a central arterial line to monitor the mean arterial pressure and a central venous line. Median sternotomy and systemic heparinization (0.4 mg/Kg) were

performed, followed by cannulation of the ascending aorta for cardioplegia, using hypothermia (32°C) as a protective strategy, followed by cardiopulmonary bypass (CPB). In the presence of AR, the Aorta was opened and then injected the cardioplegic solution into the coronary ostium. For those patients without AR, the cardioplegic solution was injected directly into the aortic root. Afterwards, the left atrium was opened to perform the mitral and aortic valve replacement, in this respective order, with mechanical or biological prostheses as indicated.

Statistical analysis was performed with SPSS (Version 17.0). Variables were tested for normality using the One Sample Test Kolmogorov-Smirnov and the appropriate statistical test was applied according to its distribution. Continuous variables were described as mean ± standard deviation. Continuous variables with normal distribution were compared using Student's t-test. Asymmetrical distribution variables were analyzed by the Mann-Whitney test, and their depiction was done by their median, maximum and minimum values. Categorical variables were described by their frequencies and analyzed with the Chi-square test. The level of statistical significance in this study was 5% ( $P<0.05$ ).

This study was approved by the institutional review board of the Ana Nery Hospital (protocol 59/10).

## RESULTS

This study sample was composed by 104 patients who underwent double valve replacement surgery between January 2007 and December 2011. The mean age±standard deviation was 38.04±14.45 years. Clinical and epidemiological characteristics of the study population are shown in Table 1.

In the study population, 100% of the patients underwent mitral and aortic valve replacement. This surgery was associated with another surgical procedure in only 30.8% of cases. The postoperative hospitalization period ranged from one day to a maximum of 56 days (median 13 days).

The aortic and mitral valves were the most affected in this study population, but the tricuspid and pulmonary valves were also impaired, as follows. Three patients presented mild tricus-

Table 1. Clinical and epidemiological characteristics of the study population. Salvador, 2007-2011.

Characteristics	N°	%
Sex (n=104)		
Man	60	57.7
Woman	44	42.3
Origin (n=104)		
Capital	34	32.7
Interior	70	67.3
Body Mass Index (n=97)		
Underweight	8	8.2
Normal	67	69.1
Overweight	18	18.6
Obesity Grade 1	4	4.1
Diabetes Mellitus (n=104)		
Present	3	2.9
Absent	101	97.1
Systemic Arterial Hypertension (n=104)		
Present	50	48.1
Absent	54	51.9
Chagas Disease (n=104)		
Present	0	0
Absent	104	100
Atrial Fibrillation before DVRS (n=100)		
Yes	28	28
No	72	72
Class of Heart Failure NYHA (n=94)		
Class I	2	2.1
Class II	36	38.3
Class III	33	35.1
Class IV	23	24.5
Previous cardiac surgery (n=100)		
Yes	38	38
No	62	62
Type of prosthesis (n=103)		
Biological	65	63.1
Metallic	38	36.9
Hospital outcome (n=104)		
Death	20	19.2
Discharged home	84	80.8

DVRS- Double valve replacement surgery; NYHA- New York Heart Association.

pid stenosis and one patient had moderate tricuspid stenosis. Two patients presented with mild pulmonary regurgitation and one patient presented with severe insufficiency. No patients presented pulmonary stenosis (Figure 1).

The left atrium was analyzed through echocardiography in 96 patients, ranging from a minimum of 33 mm until 129 mm (median 53 mm). The left atrium size was not associated with hospital mortality ( $P=0.785$ ). The left ventricle diameters and left ventricular systolic function were also not associated with mortality (Table 2), as well as the degree of valve lesion.

When considering two distinct groups, those who were discharged after surgery and those who died during hospital stay, some statistically significant differences can be noticed: their mean age, respectively ( $36.30\pm 13.03$  vs.  $45.35\pm 17.8$  years old,  $P=0.011$ ), mean hemoglobin ( $11.10\pm 2.19$  vs.  $9.22\pm 2.26$  g/dL,  $P=0.002$ ); and mean hematocrit ( $34.22\pm 5.86$  vs.  $28.44\pm 6.62$  %,  $P<0.001$ ).

Comparisons of gender, city of origin, body mass index, diabetes mellitus, hypertension, atrial fibrillation, class of heart failure, urea, creatinine, previous cardiac surgery and kind of prosthesis between the groups and outcomes are presented in Table 3.

The anoxia time was  $129\pm 30$  minutes, CPB time was  $163\pm 40$  minutes, and the total time of surgery was  $305\pm 66$  minutes. The comparison between the mean anoxia time, CPB time, and total surgical time in both hospital outcomes (death x discharge) were, respectively,  $149.17\pm 40.99$  and  $123.99\pm 24.125$  ( $P=0.001$ ),  $185.53\pm 54.597$  and  $157.34\pm 34.623$  ( $P=0.006$ ),  $350.29$  and  $295.23\pm 56.692\pm 63.983$  ( $P=0.002$ ).

## DISCUSSION

Five clinical variables were associated with mortality during the hospitalization of rheumatic patients who underwent double valve replacement surgery: age, hemoglobin, hematocrit, diabetes mellitus and NYHA functional class (New York Heart Association (NYHA) functional classification of heart failure).

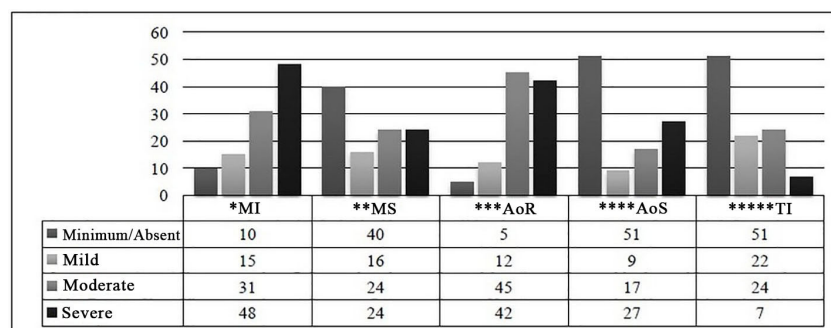


Fig. 1 - Distribution of studied patients by valvular's injury degree of. Salvador 2007-2011. \*MI=Mitral Regurgitation; \*\*MS=Mitral Stenosis; \*\*\*AoR=Aortic Regurgitation; \*\*\*\*AoS=Aortic Stenosis; \*\*\*\*\*TI=Tricuspid Regurgitation

Table 2. Average of echocardiography's measurements of normal distribution in the study population and average's comparison on hospital outcome. Salvador, 2007-2011.

ECO	Global average	Outcome	Average	P Value
LVDD (n=92)	63.73±15.77	Discharged home	63.52±13.5	0.792
		Death	64.65±23.89	
LVSD (n=91)	42.81±12.56	Discharged home	43.53±12.50	0.261
		Death	39.71±12.76	
EF (n=94)	60.74±12.27	Discharged home	60.78±11.51	0.948
		Death	60.56±15.92	
PASP (n=63)	58.63±22.19	Discharged home	57.38±22.14	0.335
		Death	64.55±22.49	

LVDD=Left Ventricular Diastolic Diameter; LVSD=Left Ventricular Systolic Diameter; EF=Ejection Fraction; ECO=Echocardiographic Measurements; PASP=Pulmonary Artery Systolic Pressure

Table 3. Clinical and epidemiological characteristics and comparison between groups of hospital outcome.

Variable	Discharged Home		Death		P value
	Nº	%	Nº	%	
Sex (n=104)					0.816
Man	48	46.2	12	11.5	
Woman	36	34.6	8	7.7	0.192
Origin (n=104)					
Capital	25	24	9	8.7	
Interior	59	56.7	11	10.6	0.698
Body Mass Index (n=97)					
Normal	56	57.7	11	11.3	
Not normal	26	26.8	4	4.1	0.034
Diabetes Mellitus (n=104)					
Present	1	1	2	1.9	
Absent	83	79.8	18	17.3	0.092
Arterial Hypertension (n=104)					
Present	37	35.6	13	12.5	
Absent	47	45.2	7	6.7	0.181
Atrial Fibrillation (n=100)					
Present	20	20	8	8	
Absent	60	60	12	12	0.022
Class of HF NYHA (n=94)					
I or II	35	37.2	3	3.2	
III or IV	41	43.6	15	16	0.056
Urea (n=97)					
Normal	55	56.7	9	9.3	
Not normal	23	23.7	10	10.3	0.088
Creatinine (n=99)					
Normal	65	65.7	12	12.1	
Not normal	15	15.2	7	7.1	0.471
Previous cardiac surgery (n=100)					
Yes	29	29	9	9	
No	51	51	11	11	0.219
Type of prosthesis (n=103)					
Biological	50	48.5	15	14.6	
Metallic	33	32	5	4.9	

HF NYHA=Class of Heart Failure New York Heart Association

The double valve replacement surgery is a risk factor for death independent of preoperative data<sup>[5]</sup>, mainly due to longer duration of surgery, CPB and aortic clamping<sup>[2,6,7]</sup>.

The mortality rate in the study population was 19.2%.

Despite elevated when compared to other referral centers in developed countries, different socioeconomic profiles and different access to health between developed and developing countries lead to a comparison limitation<sup>[8,9]</sup>.

In this study population, 59.6% of patients had functional New York Heart Association (NYHA) class III or IV, and 24.5% were in NYHA functional class IV. No other study has a number of patients in a so severe functional class. Studies with low mortality rates show a maximum of 8% of the population with NYHA functional class IV<sup>[8,10]</sup>. The lowest mortality rate was 0.7% presented by a study which had only 0.5% of patients in NYHA functional class IV<sup>[11]</sup> and NYHA functional class IV has been presented as an independent risk factor for operative mortality in double valve replacement surgery. Possibly, this is due to an increased release of proinflammatory vasodepressive cytokines in NYHA functional class IV<sup>[12]</sup>. Patient with advanced heart failure presents a state of chronic inflammation, especially in episodes of decompensation, generating greater degree of difficulty and complications during the surgical technique performing<sup>[12]</sup>.

Preoperative anemia is associated with increased morbidity and mortality among patients undergoing cardiac surgery<sup>[13]</sup>. Patients with lower hemoglobin levels and preoperative hematocrit are more likely to be transfused, and the use of blood derivatives bags is an independent risk factor for mortality and clinical complications such kidney failure, infections, and cardiac complications, pulmonary and neurological in the first thirty postoperative days<sup>[14,15]</sup>. Studies evaluating mortality in patients undergoing double valve replacement not present data on hemoglobin and hematocrit preoperatively patients<sup>[9-11]</sup>. This prevents a proper comparison of the results of this study which showed hemoglobin and hematocrit significantly lower in patients who had hospital death. The magnitude of the effect of anemia in the preoperative surgical double valve replacement as well as the optimal management of these patients lack of data in literature.

The mean age of patients who died was 45.35±17.8 years. Age as a mortality predictor in cardiac surgery is described in the literature as one of the main risk factors in most scores<sup>[15-22]</sup>. However, it should be noted that each score has its own cut-off point from which the surgical risk is established. The EuroSCORE indicates that there is an increased risk of death above 60 years old and one point is given for every 5 additional years<sup>[16,17]</sup>.

A previous study states that patients who were at least 50 years old had higher in-hospital mortality, regardless of the valve surgery performed: aortic or mitral valve replacement, double valve replacement, with or without coronary bypass revascularization<sup>[23]</sup>. This study shows a higher surgical risk among those with a lower mean age when compared to previously published data, since it is a more complex surgery in critically ill patients. Therefore, existing scores in the literature may not be suitable for predicting the actual risk for this specified population. It is possible that the relative risk with age is established at a lower age range for this group of patients.

Some clinical variables assessed in this study showed no influence on in-hospital mortality. Some are part of major

risk scores for mortality risk in heart surgery, such as: female gender, previous cardiac surgery and serum creatinine<sup>[16,19]</sup>. However, most studies evaluated these variables in all types of cardiac surgeries, not specifically double valve replacement. Otherwise, one study that presented independent risk factors for double valve replacement surgery, also found no influence of the variables mentioned above. It is noteworthy that most of these studies were conducted in major medical centers of the United States and Europe. This demonstrates the need to develop scores of preoperative risk in populations with different socioeconomic characteristics.

Echocardiography's measurements of the left ventricle compared between the two groups of patients (who were discharged home and who died) were not statistically significant, in agreement with previously published data<sup>[7]</sup>. Because they are variables characteristic of chronic disease, it seems possible that a certain degree of adaptation to the hemodynamic status may occur, with no impact on in-hospital mortality. However, it is necessary to investigate the influence of these variables on morbidity and mortality in a long term way.

The study has quite few limitations. It was a single center study, which may cause bias due to the restricted population size, limiting extrapolation of data to other populations.

## CONCLUSION

This study is remarkable for highlighting the value of age, hemoglobin, hematocrit, diabetes mellitus and NYHA functional class as possible variables associated to in-hospital mortality of rheumatic patients undergoing double valve replacement surgery.

A precise cut off point in the hemoglobin value to determine and predict mortality risk should be studied in order to improve the therapeutic management of patients who will undergo double valve replacement. Furthermore, early indication of heart valve surgeries may avoid a delayed procedure at an advanced stage of the disease.

Therefore, new prospective studies in national territory are needed to compare mortality rates between different Brazilian centers, enabling an advance in the management of this disease that still represents a serious public health problem.

### Authors' roles & responsibilities

AMSF	Planning and writing of the manuscript
GMA	Collection and analysis of data and writing of the manuscript; statistical analysis; conception and design of the study; completion of the operations and/or experiments
RMO	Collection and analysis of data
GTB	Collection and analysis of data
FFBR	Interpretation and review of the manuscript
CRM	Interpretation and review of the manuscript
ARD	Review of the manuscript and approval of final version
RAJ	Review of the manuscript and approval of final version

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