ORIGINAL RESEARCH

Determinants of prolonged length of hospital stay after cardiac surgery: impact of rheumatic heart disease

Mariângela F Pato[I], Cláudio L Gelape[I], Tammy JM Cassiano[I], Adriano Carvalho[III], Priscila R Cintra[II], Luiz G Passaglia[II], Henrique S Costa[I], Timothy C Tan[IV], Paulo Cerqueira dos Santos Junior[V], Renato Bráulio[II], Maria CP Nunes[I,II]

[I] Universidade Federal de Minas Gerais, Faculdade de Medicina, Programa de Pós-Graduação em Moléstias Infecciosas e Medicina Tropical, Belo Horizonte, MG, Brazil
[II] Universidade Federal de Minas Gerais, Departamento de Cardiologia e Cirurgia Cardiovascular, Hospital das Clínicas, Belo Horizonte, MG, Brazil
[III] Universidade Federal de Minas Gerais, Hospital das Clínicas, Unidade de Terapia Intensiva, Belo Horizonte, MG, Brazil
[IV] Harvard Medical School, Massachusetts General Hospital, Cardiac Ultrasound Lab, Boston, MA, USA
[V] Universidade Federal de Minas Gerais, Departamento de Estatística, Belo Horizonte, MG, Brazil

BACKGROUND: Rheumatic heart disease remains a major health problem in developing countries. Several factors contribute to valve-related morbidity after cardiac surgery, but the role of rheumatic etiology of valve disease is not well defined. This study was designed to determine the additional value of rheumatic valve disease in predicting morbidity after cardiac surgery in the current era of heart valve disease treatment.
METHOD: This study prospectively included 164 patients for cardiac surgery from June 2010 to June 2011. The outcome was prolonged length of stay, defined as a length of stay greater than or equal to the 75th percentile for length of stay for each operation, including the day of discharge.
RESULTS: Rheumatic heart disease was present in 32 patients (20%) and all rheumatic patients underwent valve replacement. Rheumatic heart disease patients were younger with less comorbidities compared to non-rheumatic patients, with most (63%) having had previous surgery. Forty-one patients were classified as having a prolonged hospital length of stay; 11 (34%) patients with rheumatic and 30 (23%) non-rheumatic fever. Rheumatic heart disease was not associated with prolonged hospital stay in the univariate analysis; however, after adjustment for other factors including infectious endocarditis, surgery duration, mechanical ventilation time, EuroSCORE, and postoperative pneumonia, it was found to be a predictor of prolonged hospitalization.
CONCLUSION: This study demonstrates that rheumatic heart disease was an important factor associated with prolonged hospital, after adjustment for well-known risk factors of morbidity after cardiac surgery. Rheumatic fever is still prevalent among the patients who underwent to cardiac surgery in the current age, contributing to increase the postoperative morbidity.

KEYWORDS: Rheumatic valve disease, Cardiac surgery, Length of hospital stay, Postoperative morbidity, Valve replacement.

■ INTRODUCTION

Rheumatic heart disease (RHD), the long-term consequence of acute rheumatic fever, remains a public health concern around the world.[1,2] Despite its decreasing incidence, there is still a significant disease burden, especially in developing countries.[3,4] In Brazil, RHD is the main cause of valve disease, responsible for 70% of the cases.[5] The disease results in high cost for health services due to repeated hospitalizations, mostly for valve repair or replacement.[6,7]

Clinical management of heart valve disease depends on the clinical presentation and surgical treatment is frequently the only intervention that changes the natural progression of valve disease.[8] In the last decades, heart valve surgery has evolved with increased numbers of valve repairs, new prostheses, and novel repair methods.[9] Additionally, an enhanced understanding of patient- and

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disease-related factors affecting outcomes allows better selection of patients for appropriate intervention. However, the role of the rheumatic etiology of valve disease as a factor that may affect independently morbidity and mortality after cardiac surgery is not well defined.

In particular, in the setting of RHD, structural prosthesis deterioration, valve thrombosis, embolism, bleeding events, operated valve endocarditis, and reintervention contribute to valve-related morbidity. The length of stay after thoracic surgery is also an important marker of morbidity, which is a direct consequence of the interaction between the patient and the surgery. Several variables can affect the length of stay, including preoperative, intraoperative, and postoperative factors.

We hypothesized that after adjustment for preoperative patient risk factors, RHD is an important predictor of prolonged length of stay after thoracic surgery. Therefore, the present study was designed to determine the additional value of RHD in predicting morbidity after cardiac valve surgery in the current era of heart valve disease treatment.

■ METHOD

This study prospectively included consecutive adult patients (> 18 years) who were admitted to the Hospital das Clínicas at Universidade Federal de Minas Gerais for elective or urgent cardiac surgery by thoracotomy from June 2010 to June 2011. Patients who underwent heart transplantation or device implantation, including pacemakers, were excluded. The postoperative evolution of the patients was followed by the researcher from the surgical act until discharge from the hospital or death. The protocol was approved by the Ethics Committee of Federal University of Minas Gerais, Brazil (protocol number ETIC 0616.0.203.000-10).

Demographic data including comorbidities and medications were collected prior to surgery. Preoperative patient clinical features included the presence of the following medical diagnoses: rheumatic fever, previous infective endocarditis or thoracic surgery, hypertension, diabetes, asthma, bronchitis, chronic obstructive pulmonary disease and chronic renal disease. All drugs that the patients were taking one day before the surgery were considered.

Definition of the outcome

For this study, the outcome of interest was prolonged length of stay, defined as a length of stay greater than or equal to the 75th percentile for the length of stay for each operation, including the day of discharge or death.[10] The surgery was considered urgent when the intervention was for acute onset or clinical deterioration of potentially life-threatening conditions, and performed within hours of decision to operate; it was considered elective when the procedure was planned or booked in advance to a routine admission to hospital.[11]

Intraoperative and Postoperative Variables

The length of the operation was defined as the time from the first incision to wound closure.[11] A neurologic event was defined as a change in neurologic function, including persistent disorientation, after the first days in the intensive care unit, and included strokes and reversible events.[12] Lung infection, surgical site infection and urinary tract infection were defined according to the definitions of the USA Center for Disease Control for nosocomial infections.[13] Mediastinitis was regarded as a deep wound infection with clinical evidence and or microbiological commitment of the retrosternal space.[14] Reoperation was defined as all surgical procedures that required the patient to be taken back to the operating room for intervention within the length of stay.[10]

Statistical analysis

Categorical data were presented as numbers and percentages, and continuous data were expressed as mean ± SD. The variables were compared using chi-squared test, unpaired Student's t-test or Mann-Whitney test, as appropriate.

Logistic regression was used to identify independent risk factors for prolonged hospitalization. To explore potential predictors of the length of stay after thoracic surgery, univariate analysis of clinical characteristics was performed. Odds ratios were calculated with 95% confidence intervals as an estimate of the risk associated with each variable. The multivariate logistic regression model incorporated pre and post operative variables that were associated with prolonged length of hospital stay in the univariate analysis and a significance level of $p < 0.05$. Additionally, variables that had clinical relevance in the context of cardiac surgery, specifically previous cardiac surgery and RHD were also entered in a multivariate analysis.

Potential predictive variables of duration of hospitalization included in the model were age, EuroSCORE, rheumatic fever, diabetes, infective endocarditis, coexistent lung diseases, previous thoracic surgery, surgery time, mechanical ventilation time, pulmonary infection, and urinary tract infection. A value of $p < 0.05$ was considered significant. SPSS version 18 (SPSS Inc., Chicago, IL) was used for all analyses.

■ RESULTS

Baseline features of the study population

A total of 164 patients with mean age of 55.6 ± 13.9 years, 70 women (43%) were included. RHD was present in 32 patients (20%) and of these patients, 20 (63%) had previous mitral valve replacement (70% of the cases). All patients with RHD underwent valve replacement (29 mitral valve, 2 aortic valve, 1 aortic and mitral valve); none had

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valve repair. The most frequently found comorbidities were hypertension and diabetes. The baseline characteristics of the patients stratified by the presence of rheumatic fever are shown in Table 1. The rheumatic patients were younger, had less comorbidities and used fewer medications than non-rheumatic patients, while 16% of them had infective endocarditis and most of them (63%) had already had surgery.

There was no difference in the frequency of oral anticoagulation therapy in patients who had prolonged length of hospital stay compared to those with standard hospitalization time.

During this period of the study, five types of thoracic surgeries were performed at the hospital: coronary artery bypass grafting (CABG) in 86 of the cases (52.4%); valve replacement in 59 (36.0%); atrial septal defect correction in 10 (6.1%); combined surgery (CABG with valve replacement) in 7 (4.3%); and mitral valve repair in 2 cases (1.2%).

Blood transfusion was administrated to 128 patients, while 112 were on vasoactive amines, and 60 on antibiotic therapy. Fifty-one patients (31%) had heart arrhythmias, the most common being atrial fibrillation. Intraoperative and postoperative variables stratified by the presence of rheumatic fever are shown in Table 2.

Regarding postoperative infections, 32 patients showed lung infections, 11 presented urinary tract infection, and 4 patients had mediastinitis. Thirteen patients required reoperation, 22 had cardiopulmonary arrest, and 19 died. Some post-surgical complications occurred only in non-rheumatic patients such as surgical site infection (13), neurological events (6) and mediastinitis (4).

Length of stay after surgery

Of the 164 patients 41 were computed as prolonged length of stay in hospital after thoracic surgery. Patients with RHD had prolonged hospitalization with median of 15 hospitalized days compared to 10 days for the non-rheumatic patients (p = 0.002; Figure 1). The determinants factors of prolonged hospitalization are shown in Tables 3 and 4.

In the univariate analysis, RHD was not associated with prolonged stay after surgery.

Among the variables associated with prolonged stay after thoracic surgery, infective endocarditis was an important determinant factor in the patients with RHD, while diabetes was in non-rheumatic patients. Previous thoracic surgery was also a predictor of prolonged stay, which occurs in the majority in rheumatic patients (63%).

The intra and postoperative variables that have influence on the length of stay were duration of surgery, duration of mechanical ventilation and lung infection. The patients who had been operated previously had more complications that those who underwent first surgical intervention. Likewise, the mechanical ventilation time was strongly correlated with prolonged stay (Figure 2). In addition, we found that blood transfusion, use of amines, the presence of arrhythmias and urinary tract infection were

Table 1 - Preoperative clinical features of the rheumatic compared with non-rheumatic patients

Variables*	Cardiac surgery by rheumatic valve disease (n = 32)	Cardiac surgery by other causes (n = 132)	P value
Age (years)	45.9 ± 14.0	58.0 ± 12.9	< 0.001
Male	10 (31)	84 (64)	0.001
Infective endocarditis[†]	5 (16)	6 (5)	0.021
Hypertension	19 (63)	109 (83)	0.015
Diabetes mellitus	4 (13)	44 (34)	0.029
Lung diseases	2 (7)	11 (8)	0.789
Renal insufficiency	3 (10)	10 (8)	0.629
Previous cardiac surgery	20 (63)	11 (8)	< 0.001
Valve prostheses	14 (70)	2 (18)	0.006
EuroSCORE	5.5 [2.1/7.9]	2.4 [1.5/4.5]	< 0.001
Medication			
Beta-blockers	10 (31)	43 (33)	0.219
Aspirin	6 (21)	76 (65)	< 0.001
Diuretics	25 (86)	28 (24)	< 0.001
ACE inhibitor	19 (59)	74 (56)	0.429
Statin	3 (10)	66 (57)	< 0.001

* Values are expressed as the mean value ± SD, median (interquartile range), or absolute numbers (percentage); [†] Cardiac surgery was performed for complications of IE earlier in the course of the infection or after treatment; ACE: Angiotensin Converting Enzyme Inhibitors. The patients who had prolonged length of stay had higher EuroSCORE, more prevalence of valve prostheses and infective endocarditis compared to patients with standard length of hospitalization.

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Table 2 - Intraoperative and Postoperative Variables compared between rheumatic and non-rheumatic patients

Variables*	Cardiac surgery by rheumatic valve disease (n = 32)	Cardiac surgery by other causes (n = 132)	P value
Mitral prosthesis	29 (91)	7 (21)	< 0.001
Blood transfusions[†]	28 (90)	100 (78)	0.124
Extracorporeal circulation time (min)	94.6 ± 67.2	81.6 ± 44.6	0.195
Mechanical ventilation time (days)	6.9 ± 15.0	9.1 ± 47.1	0.793
Use of amines	22 (71)	90 (70)	0.896
Arrhythmias	13 (43)	38 (30)	0.142
Pulmonary infection	7 (26)	25 (20)	0.493
Urinary tract infection	3 (10)	8 (6)	0.450
Use of antibiotics	13 (45)	47 (37)	0.453
Reoperation	3 (10)	10 (8)	0.695
In-hospital death	3 (10)	16 (12)	0.663
ICU time (days)	14.9 ± 32.9	9.0 ± 14.3	0.138
Anticoagulant therapy	15 (60)	10 (9)	< 0.001
Length of stay (days)	15 [12/28]	10 [7/19]	0.002

* Values are expressed as the mean value ± SD, median (interquartile range), or absolute numbers (percentage); [†] yes or no; ICU: Intensive care unit.
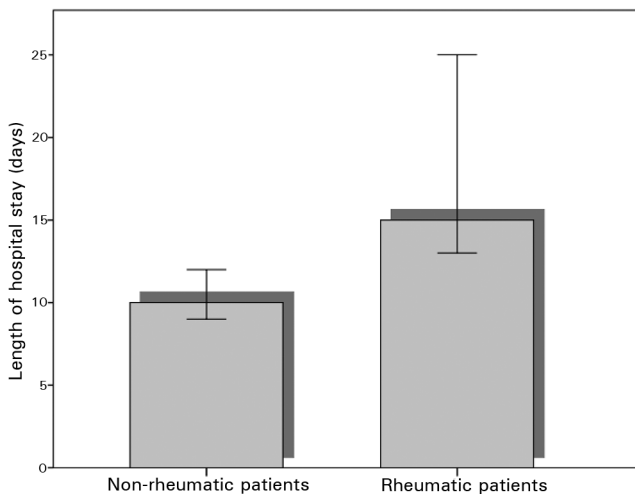

Figure 1 - Length of stay in rheumatic compared with non-rheumatic patients.

associated with hospitalization time. In the multivariate analysis, RHD remained an important predictor of prolonged hospitalization, independent of infective endocarditis, operative duration, mechanical ventilation time, and nosocomial pneumonia. Therefore, although RHD was not an isolated factor determining prolonged hospitalization, it appeared to add itself to other factors that contribute to prolonged hospitalization, as this variable remained in the multivariate analysis.

■ DISCUSSION

RHD constitutes a serious health problem, responsible for 20% of the thoracic surgeries performed at a referral center in the current age. The patients with RHD were younger with less associated comorbidities than those who underwent to coronary artery bypass grafting or other types of thoracic surgery. The mortality rate was similar but the length of stay was longer in the patients with RHD compared to those with non-rheumatic heart disease independent of other well-known risk factors of morbidity after cardiac surgery, including pulmonary infection, technical issues that increase the duration of the surgery, and infective endocarditis.

Impact of rheumatic fever on morbidity after thoracic surgery

Several factors contribute to an increase in the length of stay after thoracic surgery in RHD. In general, patients with RHD have been shown to have a higher incidence of need for reoperation.[15] The need for further surgery occurs in 8-10% of the cases. Beside symptoms, the most important predictors of postoperative outcome are age, preoperative left ventricular function, pulmonary hypertension, and reparability of the valve.[8] Even though surgical expertise in valve repair is improving overall, the repair of rheumatic lesions can still be challenging, even in experienced hands.[16] Therefore, in the absence of evidence from randomized clinical trials, the decision to interfere in a patient with RHD relies on an individual risk-benefit analysis suggesting that improvement of prognosis, as compared with natural history, outweighs the risk of intervention and its potential late consequences, particularly prosthesis-related complications.[17]

In our study, 63% of the patients with RHD had had previous surgical intervention, and 70% of these had been subjected to valve replacement." Length of stay appears also

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Table 3 - Variables associated with prolonged stay after cardiac surgery (Univariate analysis)

Variables	Odds ratio	(95% CI)	P value
Preoperative			
Age (years)	1.024	0.997 - 1.052	0.082
Rheumatic disease	1.781	0.772 - 4.106	0.176
Infective endocarditis	10.00	2.508 - 39.869	0.001
Type of surgery	4.015	1.264 - 12.747	0.018
Diabetes mellitus	2.146	1.016 - 4.534	0.045
Previous cardiac surgery	1.888	0.815 - 4.377	0.138
EuroSCORE	1.254	1.120 - 1.405	< 0.001
Intraoperative/Postoperative			
Time of surgery (hours)	1.632	1.135 - 2.348	0.008
Mechanical Ventilation time (days)	1.327	1.171 - 1.504	< 0.001
Blood transfusion	6.122	1.391 - 26.954	0.017
Use of Amines	7.703	2.246 - 26.417	0.001
Arrhythmias	2.612	1.238 - 5.514	0.012
Surgical site infection	13.218	3.417 - 51.140	< 0.001
Mediastinitis	9.750	0.984 - 96.647	0.052
Pulmonary infection	32.143	11.491 - 89.913	< 0.001
Urinary tract infection	6.125	1.686 - 22.246	0.006
Reoperation	8.625	2.485 - 29.937	0.001
Cardiopulmonary arrest	3.190	1.254 - 8.112	0.015

Table 4 - Multivariate predictors of prolonged hospitalization after cardiac surgery

Variables	Odds ratio	(95% CI)	P value
Rheumatic fever	11.668	1.043 - 113.503	0.042
Mechanical ventilation time (days)	1.290	1.092 - 1.525	0.003
Pulmonary Infection	11.952	2.588 - 55.202	0.001
Infective endocarditis	12.487	1.649 - 94.579	0.001
Length of the surgery (hours)	2.498	1.268 - 4.921	0.008

to be prolonged in RHD because of a need for long-term anticoagulation. There are some variables that influence the level of anticoagulation, which can lead to inadequate protection or excessive anticoagulation with the risk of bleeding. Therefore, in the patients with RHD in whom valve replacement was frequent, careful control at regular intervals is necessary before discharge from the hospital. In our study, 60% of rheumatic patients were on oral anticoagulants, requiring strict postoperative control until discharge, and thus leading to prolonged hospitalization.[18-20]

Determinants of prolonged length of stay in hospital after thoracic surgery

Infective endocarditis remains a dangerous condition with high morbidity and mortality. Surgery is potentially lifesaving and is required in 25% to 50% of cases during acute infection and 20% to 40% during convalescence. Operative procedures are often technically difficult, requiring radical debridement and reconstruction, which is associated with a high risk of complications. Surgical treatment of heart valve disease is an increasingly common heart intervention and as a result, the number of patients at risk of developing prosthetic valve endocarditis is growing. Although prosthetic valve endocarditis was diagnosed promptly and usually treated with surgical intervention, the morbidity and in-hospital mortality rates were very high. Rates of recurrent prosthetic valve endocarditis are high at 6% to 15%, and further surgery for this indication or dysfunction of the newly implanted prosthesis is required in up to 25% of patients.[21,22]

Our results confirm that the morbidity of thoracic surgery was increased when infective endocarditis occurred

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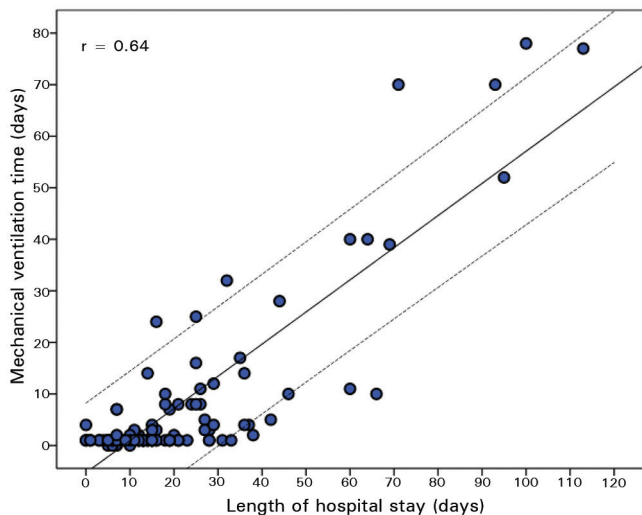Pato MF et al.

Figure 2 - Correlation between mechanical ventilation time and prolonged length of stay after cardiac surgery.

in patients with rheumatic valve abnormalities or prosthetic valves. Although surgical treatment results in improved survival at both immediate and long-term follow-up, the hospital stay is prolonged.

After cardiac surgery, patients are often extubated as soon as the anesthetic effect ceases. However, approximately 3-6% of patients may require prolonged mechanical ventilation due to the complexity of their heart disease, or to pulmonary or other systemic problems. In such cases, the usual criteria for extubation, as analysis of blood gases, vital capacity and minute volume often fail to predict successful extubation.[23]

The factors responsible for prolonging the mechanical ventilation, specifically after thoracic surgeries, are the preoperative conditions, the surgical incision and the need for extracorporeal circulation. Therefore, patients who have risk factors associated with preoperative surgical aggression may show impairments in lung function in the immediate postoperative period, requiring ventilatory support.[24] A previous study showed that there was no correlations of preoperative and postoperative pulmonary function with length of hospital stay.[25] Similarly, there was no association between pain in patients submitted to heart surgery via sternotomy and the length of hospital stay.[26] In another study, preoperative respiratory muscle dysfunction does not seem to lead to pulmonary complications after cardiac surgery.[27]

Ventilator-associated pneumonia is defined as any case of lung infection occurring in a patient within 48 hours or more after intubation and which was not present before. It is also the most common and fatal infection of intensive care units, which increases length of stay in intensive care units by 28%. Approximately 86% of hospital associated pneumonia is linked with mechanical ventilation.[28] The present study also highlights

the role of ventilator-associated pneumonia in predicting prolonged hospitalization after thoracic surgery, which was independent of mechanical ventilation time and chronic lung disease. Diagnosis of ventilator-associated pneumonia remains challenging because many conditions have similar clinical signs and there is no clearly accepted gold standard for diagnosis of this type of pneumonia.

After adjusting for pulmonary infection, mechanical ventilation duration, previous endocarditis and RHD, we found that operative time predicted prolonged length of stay. The length of the surgery may be a marker for patient characteristics, the severity of the primary disease at the time of operation, the skill of the primary surgeon, or the experience of the surgical team. Similarly, Collins et al.[10] demonstrated that operative time was associated with a risk for prolonged length of stay after vascular surgery. Previous studies have highlighted that variations in length of stay are affected by many factors, including patient, physician, and hospital characteristics.[10,29]

Red blood cell transfusion is an independent risk factor for increased hospital length of stay in patients undergoing cardiac surgery.[30] Observational studies demonstrated an association between transfusion and adverse outcomes in cardiac surgery.[31,32] In our study, blood transfusion appeared to be a surrogate marker of operative complications or higher morbidity, but it was not an independent predictor of hospital length of stay.

Although the pathologic effects of extracorporeal circulation have been well documented, in our study extracorporeal circulation time was not a determinant factor of morbidity. In agreement with our results, Torrati et al.[33] found that complications occurring after cardiac surgery were similar between the patients who had extracorporeal circulation duration of up to 85 minutes and those who had a time of over 85 minutes. Recent technical advances in pump oxygenators and closer attention to hemodynamic parameters intra-operatively have reduced long-term effects of extracorporeal circulation.

Study limitations

Several confounding factors may have contributed to the association between RHD and prolonged hospitalization, including the need of anticoagulation therapy, prosthesis implantation, critically ill patients or some another factors. Subsequent studies will be warranted to define the role of rheumatic etiology as a risk factor for length of stay regardless of these comorbidities.

■ CONCLUSIONS

This study highlights the importance of RHD as a contributing factor for prolonged hospital stay after thoracic surgery, after adjustment for the presence of infective

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endocarditis, operative time, and postoperative pneumonia. Rheumatic fever is still prevalent among the patients who underwent cardiac surgery, contributing to increase the postoperative morbidity.

■ DECLARATION OF INTEREST

The authors report no conflict of interest.

DETERMINANTES DE INTERNAÇÃO HOSPITALAR PROLONGADA APÓS CIRURGIA CARDÍACA: IM-PACTO DE CARDIOPATIA REUMÁTICA

OBJETIVO: A doença cardíaca reumática continua a ser um problema grave de saúde nos países em desenvolvimento. Vários fatores contribuem para a morbidade relacionada com a cirurgia valvar cardíaca, mas o papel da etiologia reumática das valvopatias não está bem definido. Este estudo foi desenhado para determinar participação adicional de valvopatias reumáticas na previsão de morbidade após cirurgia cardíaca na era atual de tratamento da doença.

MÉTODOS: Este estudo incluiu prospectivamente 164 pacientes submetidos a cirurgia cardíaca, entre junho de 2010 a junho de 2011. O resultado medido foi a duração da estadia prolongada, definido como tempo de permanência maior ou igual ao percentil 75 para a duração da estada para cada operação, incluindo a dia da alta.

RESULTADOS: A cardiopatia reumática esteve presente em 32 pacientes (20%) e em todos os pacientes submetidos à substituição da válvula. Pacientes com doenças cardíacas reumáticas eram mais jovens e com menos comorbidades comparados com pacientes não-reumáticos; a maioria deles (63%) tinha tido cirurgia prévia. Quarenta e um pacientes foram classificados como tendo um tempo de permanência hospitalar prolongado; 11 (34%) pacientes com doenças reumáticas e 30 (23%) com doenças não-reumáticas. A doença reumática não se apresentou associada com período de internação prolongado, na análise univariada; No entanto, após o ajuste para outros fatores, incluindo endocardite infecciosa, duração da cirurgia, tempo de ventilação mecânica, EuroSCORE, e pneumonia no pós-operatório, a doença reumática revelou-se um preditor de hospitalização prolongada.

CONCLUSÕES: Este estudo demonstra que a doença cardíaca reumática é um importante fator associado com internação prolongada, após o ajuste para fatores de risco bem conhecidos de morbidade após cirurgia cardíaca. A febre reumática ainda é prevalente entre os pacientes que se submeteram à cirurgia cardíaca na época atual, contribuindo para aumentar a morbidade pós-operatória.

UNITERMOS: doença reumática da válvula, cirurgia cardíaca, tempo de permanência hospitalar, morbidade pós-operatória, a substituição da válvula.

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