Risk Factors of Unfavorable Outcome in Children with Mitral Valve Repair

Factores de riesgo de evolución desfavorable en niños con plástica de la válvula mitral

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ABSTRACT

Objectives: The aim of this study was to analyze risk factors of unfavorable outcome (UO) in children with mitral regurgitation (MR) undergoing mitral valve repair (MVR).
Methods: Patients with MR who had undergone MVR from 2004 to 2014 were retrospectively analyzed. Unfavorable outcome was defined as reoperation or significant MR [moderate to severe (3+) or severe MR (4+)] during follow-up. Variables were expressed as median. Univariate and multivariate logistic regression analyses were performed to identify predictive factors of UO.
Results: Sixty five patients with MR3+ and MR4+ underwent MVR. Etiology was dysplasia in 44.6% of cases, infective endocarditis in 13.8%, rheumatic fever in 18.4%, abnormal coronary origin in 7.7% and other disorders in 13.8%. Median follow–up time was 26.5 months (52 patients are still being followed-up). Ventricular dysfunction was documented in 44.6% of cases and 46.1% had pulmonary hypertension. Fifteen patients presented UO and 9 were reoperated (7 valve replacements and 2 re-repairs). Univariate analysis demonstrated a significant association between UO and the following conditions: rheumatic fever (p=0.005), preoperative mitral annulus ≥+5 SD (p=0.002), left ventricular end-systolic diameter ≥+4 SD (p=0.022), pulmonary hypertension (p=0.024) and immediate postoperative residual MR ≥ moderate (p=0.021). Multivariate analysis demonstrated mitral annulus diameter (p=0.012), rheumatic fever (p=0.026) and early residual MR (p=0.042) as independent variables of UO. No deaths occurred in this series.
Conclusions: Mitral valve repair in children with severe MR demonstrated mid-term favourable results. Rheumatic fever, mitral annulus diameter ≥+5 SD and immediate postoperative residual MR ≥2+ were predictive factors of UO. Neither age at surgery nor ventricular dysfunction showed statistically significant differences during follow-up.

Key words: Mitral regurgitation - Mitral valve repair - Unfavorable outcome.

RESUMEN

Objetivo: Analizar los factores de riesgo de evolución desfavorable (ED) en niños con insuficiencia mitral (IM) sometidos a plástica mitral (MVR).
Métodos: Se analizaron pacientes con IM sometidos a MVR entre los años 2004 y 2014. Se definió ED como la reoperación o la IM significativa (3+, moderada a grave, o 4+, grave) durante el seguimiento. Las variables se expresaron como mediana. Se realizó el análisis univariado y el de regresión logística multivariado de los factores predictores de ED.
Resultados: Se sometieron a MVR 65 pacientes con IM 3+ e IM 4+. La etiología incluyó displasia (44,6%), endocarditis infecciosa (13,8%), fiebre reumática (18,4%), anomalía coronaria (7,7%) y otras (13,8%). La mediana del tiempo de seguimiento fue 26,5 meses (52 pacientes se encuentran aún en seguimiento). El 44,6% presentó disfunción ventricular y el 46,1% hipertensión pulmonar. La cantidad de pacientes con ED fue de 15: 9 fueron reoperados (7 reemplazos valvulares y 2 replástica). El análisis univariado demostró asociación significativa entre ED y las siguientes condiciones: fiebre reumática (p=0,005), anillo mitral preoperatorio ≥+5 DS (p=0,002), diámetro sistólico del ventrículo izquierdo (DSVI) ≥+4 DS (p=0,022), hipertensión pulmonar (p=0,024) e IM residual posoperatoria inmediata ≥ moderada (p=0,021). El análisis multivariado demostró como variables independientes de ED el diámetro del anillo mitral (p=0,012), la fiebre reumática (p=0,026) y la IM residual temprana (p=0,042). No se produjo mortalidad.
Conclusiones: La plástica mitral en niños con IM grave demostró resultados favorables a mediano plazo. La fiebre reumática, el diámetro del anillo mitral ≥+5 DS y la IM residual ≥2+ fueron factores predictores de ED. No se hallaron diferencias estadísticamente significativas durante el seguimiento en relación con la edad ni con la presencia de disfunción ventricular.

Palabras clave: Insuficiencia mitral - Plástica mitral - Evolución desfavorable

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INTRODUCTION

Mitral regurgitation (MR) in children is of heterogeneous etiology. Isolated congenital dysplasia is relatively rare. More frequently, MR is associated with other cardiac malformations or is acquired as a complication of other diseases that affect the heart. Due to this variety of lesions, the surgical management of MR in children remains a challenge. There are several series that describe good mid- and long-term results of mitral valve repair (MVR) in the pediatric population, which is why it is preferred as the first surgical option. The advantages with respect to valve replacement is that it allows the growth of the mitral annulus, preserves the subvalvular apparatus, as well as the geometry and ventricular function, and also avoids the need for anticoagulation and its complications.

In our hospital, MVR is the first surgical strategy in patients with MR. The technique of choice depends on the anatomical characteristics of the valve and the mechanism of MR. The aim of this study was to analyze the risk factors of unfavorable outcome (UO) in children with diagnosis of MR undergoing MVR.

METHODS

Between January 2004 and December 2014, 65 children (28 male and 37 female) with moderate to severe (MR 3+) or severe (MR 4+) MR underwent MVR at Hospital de Pediatría "Prof. Dr. Juan P. Garrahan". The medical histories and echocardiographic records were retrospectively analyzed. Patients with mitral stenosis, atrioventricular canal defect and univentricular pathology were excluded from the study.

The etiologies documented were dysplasia (n=29), rheumatic fever (n=12), infective endocarditis (n=9), abnormal coronary origin (n=6), collagen disorders (n=3) and others (n=6). Median age and weight at the time of repair were 8.2 years (IQR$_{25-75}$: 3.1–13.3) and 26.5 kg (IQR$_{25-75}$: 13.5–40.5), respectively. Eight patients were under one year of age and 12 weighed less than 10 kg.

All patients were evaluated preoperatively with clinical examination, chest X-ray, electrocardiogram and transthoracic echocardiogram. The severity of MR was assessed qualitatively and semiquantitatively, in accordance with the European Association of Echocardiography recommendations for the assessment of MR. We evaluated the anatomy of the valve (annulus, leaflets, subvalvular apparatus) and the hemodynamic consequences of MR (size of the left chambers, ventricular function, and pulmonary pressure). Based on these parameters, we defined 5 degrees of MR: mild (1+), mild to moderate (2+), moderate (3+), moderate to severe (4+) and severe (5+). The dimensions of the mitral annulus and the ventricular and left atrial diameters were evaluated calculating the Z score normalized by body surface area, according to the tables obtained from the regression equations to calculate the Z score for cardiac structures (JASE 2008). The systolic pressure of the pulmonary artery was estimated from the gradient of tricuspid valve regurgitation, whenever present.

The median Z score of the preoperative mitral annulus was +6.35 (IQR$_{25-75}$: +4.3– + 8.29), the left ventricular diastolic diameter was +3 (IQR$_{25-75}$: + 2– + 4) and the left ventricular systolic diameter was +2 (IQR$_{25-75}$: + 1– + 3). Some degree of ventricular dysfunction was present in 44.6% of the patients and 46.1% had pulmonary hypertension.

Intraoperative transesophageal echocardiography was performed in 78% of patients to evaluate the functionality of the mitral valve before and after repair.

The need for reoperation or the presence of significant MR (MR 3+ or MR 4+) at follow-up were defined as UO.

Statistical analysis

Continuous variables are expressed as median and interquartile range (IQR$_{25-75}$) and categorical variables as number (n) and percentage. The association between variables was evaluated with the Chi^2 test or Fisher's exact test. A univariate analysis was performed to assess the relationship between independent variables and the event of interest (UO, unfavorable outcome). Subsequently, a multivariate logistic regression analysis was done selecting the variables that presented p ≤0.2 associated with the Wald test, identifying those with statistically significant association (Wald test <0.05). The presence of confounders in an iterative process was evaluated until all biologically and statistically irrelevant variables were excluded. The robustness of the model was evaluated with the Hosmer-Lemeshow test.

Follow-up

All patients were clinically evaluated with chest x-ray, echocardiogram, Holter monitoring, ergometry and transthoracic echocardiogram before discharge and during outpatient follow-up. In 80% of cases patients (52 children) are being followed up (median follow-up 26.5 months (IQR$_{25-75}$: 12–41.5). The presence of symptoms, valve function, degree of MR, mean transvalvular gradient, Z score of the mitral annulus and ventricular dimensions, left ventricular function, presence of pulmonary hypertension and need for reoperation (mitral valve re-repair or valve replacement) were evaluated.

Ethical considerations

The study was carried out following research recommendations. A review of the medical records was performed and no data that might lead to patients´ identification were reported, according to current legal regulations (Personal Data Protection Law).

RESULTS

Median cardiopulmonary bypass and aortic cross-clamping times were 86 (IQR$_{25-75}$: 64-104) and 62 (IQR$_{25-75}$: 41–77) minutes, respectively. The surgical techniques performed were pericardial annuloplasty (n=59), cleft closure (n=19), commissuroplasty (n=14), perforation closure (n=9), resection of valvar tissue (n=10), chordal shortening or replacement (n=4), pericardial leaflet expansion (n=2) and Alfieri procedure (n=2) (Figure 1). Fifteen associated procedures were performed (ventricular and atrial septal defect closure, patent ductus arteriosus closure). Median hospital stay was 5 days (IQR$_{25-75}$: 4–7) (Table 1). Only 10 patients presented serious complications (morbidity: 15.6%), such as low cardiac output syndrome (n=9), arrhythmias (n=9), respiratory complications (n=5) and severe infections (n=3). Two patients (3.08%) required early valve replacement, one for severe MR and the other for infective endocarditis, at 8 and 14 days postoperatively, respectively. No early or remote mortality was reported in this series.

Fig. 1. Surgical techniques
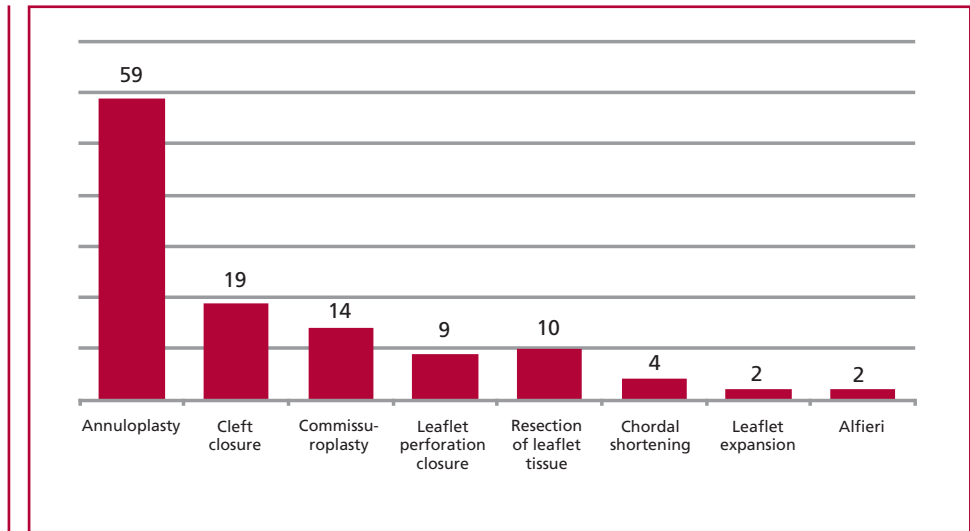
Among the 52 patients under follow-up, 15 presented UO. During follow-up, 9 of these patients progressed to severe MR, requiring reoperation within 2 to 55 months after surgery. Bidisc mechanical prostheses were placed in 7 patients and 2 children underwent mitral valve re-repair, with good results. From the 6 patients with UO (MR3+/MR 4+) that did not require reoperation, one was lost to follow-up and the other 5 remain in functional class I, with adequate weight progress, without ventricular dysfunction, mitral stenosis or pulmonary hypertension.

In 73% of cases patients on mid-term follow-up are free from reoperation or significant MR (favorable outcome), all of them asymptomatic. During their evolution, nearly all of these patients showed a decrease in the Z score of end-systolic and end-diastolic ventricular diameters, and in the Z score of left atrial diameter, as well as improvement of echocardiographic systolic function parameters and decrease of pulmonary artery pressure. Two patients were the exception, maintaining a Z score of LV diastolic diameter > +2 SD, one for non-compact cardiomyopathy and the other for associated moderate aortic regurgitation. The average and median mean mitral transvalvular gradient after repair was 4.1 and 5 mmHg (IQR$_{25-75}$: 3–7), respectively.

Risk analysis

Among the variables studied, univariate analysis showed a significant association between UO and rheumatic fever (p=0.005), preoperative mitral annulus diameter ≥+5 DS (p=0.002), left ventricular diastolic diameter ≥+4 DS (p=0.039), left ventricular systolic diameter ≥+4 SD (p=0.022), preoperative pulmonary hypertension (p=0.024) and immediate post-surgical residual MR ≥ 2+ (p=0.021) (Table 2).

In the multivariate logistic regression model, only preoperative mitral annulus diameter > +5 DS (p=0.012), rheumatic fever (p=0.026) and the degree of early residual MR (p=0.031) were predictive variables (Table 3). No statistically significant differences were observed in the evolution with respect to weight, age or preoperative ventricular function.

DISCUSSION

Surgical management of MR in pediatric patients is considered a challenge due to its broad etiology and concomitant cardiac injuries. Surgical options include valve repair and mechanical replacement. Valve replacement in pediatrics entails significant problems, including the limited availability of prostheses with infant size, the potential growth of children, which implies patient-prosthesis mismatch needing prosthesis replacement, and the need for anticoagulation

Table 1. Associated procedures

Associated procedures	%
Closure of ventricular septal defect	2
Aortic valve repair	2
Closure of atrial septal defect	1
Coronary reimplantation	2
Aortic valve replacement	1
Ross surgery	1
Myectomy	4
Tricuspid valve repair	2

Table 2. Univariate analysis

Variables	Favorable outcome	Unfavorable outcome	p
Mitral annulus Z ≥5	56.7%	93.3%	0.002
Reumathic fever	8.1%	40%	0.005
LVSD Z ≥ +4	13.5%	20%	0.022
PHT	37.8%	80%	0.024
Immediate postoprative MR	13.5%	33.3%	0.021

LVSD: Left Ventricular systolic diameter, PHT: Pulmonary hypertension. MR: Mitral regurgitation.

RISK FACTORS IN PEDIATRIC MITRAL VALVE REPAIR / Sandra E. Sepúlveda et al.

337

Table 3. Univariate analysis

Variables	Odds ratio	95% CI	p
Mitral annulus Z≥5	12.3	1.39 – 4.69	0.024
Residual MR	6.3	1.18 – 3.4	0.031
Reumathic fever	5.8	1.23 – 3.3	0.026

MR: Mitral regurgitation.

and its associated complications, increasing early and late mortality that results in a 10-year survival rate of 33–74%. (1, 2) Due to the advantages of valve repair, which preserves the subvalvular apparatus and ventricular geometry, with less deleterious effects on function (3-8), this is the first surgical option in patients with MR in our institution

Preoperative echocardiographic evaluation, based on the analysis of valvular and subvalvular anatomy and the regurgitation mechanism, is essential, since it determines the surgical strategy. Similarly, intraoperative transesophageal echocardiography allows evaluating the immediate results of MVR. The optimal outcome of MVR is the restoration of valve function, with minimal stenosis and residual regurgitation. (3) Mitral valve repair improves the degree of MR. In patients with favorable outcome and presence of nonsignificant residual MR (<MR 3+), no progression of MR was observed during follow-up. Improvement was observed in relation to chamber diameters and ventricular function, and decrease in the estimated pulmonary pressures.

Several publications have evaluated the mid- and long-term results of MVR in children. (5-7, 9-13) Good results have been reported, with 67% of cases free from reoperation at 8 years and 86% free from valve replacement at 10 years. (7, 9) Our results are similar to those mentioned, since 73% of patients are free from reoperation, maintaining a degree of nonsignificant MR and with 100% survival rate.

Few series have reported predictive factors of reoperation or adverse effects after valve repair in the child population. Kalfa et al. identified left outflow tract obstruction (possibly as a marker of ventricular dysfunction) and young age at the time of surgery as the main independent factors for reoperation. (7)

On the other hand, Lee and Oppido described in their series that postoperative residual MR is the main risk factor for reoperation. (9, 11) Based on a multivariate analysis, Baghaei defined age < one year, weight < 6 kg and associated heart defects (pulmonary stenosis) as strong risk factors for mortality and poor outcome. (6)

In our series, univariate analysis showed that the strongest association between significant residual MR and need for reoperation was preoperative mitral annulus dilation with Z ≥+5 SD (p=0.002), immediate post-surgical residual MR ≥ 2+ (p=0.021), history of rheumatic fever (p=0.005), left ventricular systolic diameter ≥+4 DS (p=0.022) and preoperative pulmo-

nary hypertension (p=0.024).

Unlike previous studies, no association between UO and age and weight at the time of surgery (<3 years; p=0.904) was found in the multivariate analysis of risk. On the other hand, mitral annulus dilation ≥+5 SD (p=0.012), immediate postoperative residual MR (p=0.031) and rheumatic fever (p=0.026) were independent predictive variables of UO. The study is limited by its retrospective design.

CONCLUSIONS

Mitral valve repair performed in children with MR is a surgical technique that has good short- and midterm outcome, with low morbidity, and prevents valve replacement and its complications. Patients with MR secondary to rheumatic fever, those with worse presurgical condition of the left chambers and with greater hemodynamic repercussions (greater mitral annulus and ventricular diameter dilation and pulmonary hypertension) and those with postoperative residual MR, showed worse outcome. Patients who presented valvular competence or mild MR (1+, 2+) in the immediate post-repair echocardiographic control maintained the degree of residual regurgitation in the long-term evolution.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material).

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