ORIGINAL ARTICLE

Impact of Extended Septal Myectomy on Echocardiographic Changes in Hypertophic Obstructive Cardiomyopathy

Impacto de la miectomía septal ampliada sobre los cambios ecocardiográficos en la miocardiopatía hipertrófica obstructiva

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ABSTRACT

Background: Extended septal myectomy (ESM) has proven to be a useful strategy to improve symptoms in patients with hypertrophic obstructive cardiomyopathy (HOCM).

Objective: The aim of this study was to analyze the impact of ESM on short and mid-term structural and functional echocardiographic parameters in patients with HCM and left ventricular (LV) outflow tract dynamic obstruction.

Methods: Preoperative, immediate postoperative (1 month after surgery) and late postoperative (2 to 3 years) echocardiograms of patients undergoing ESM were analyzed.

Results: A total of 94 patients with mean age of 57.6 ± 13.8 years underwent surgery. A significant reduction was observed in maximum septal thickness in the immediate postoperative period, which was sustained in the late postoperative period, and in atrial size in the immediate postoperative period, which deepened in the late postoperative period (p <0.001). Intraventricular gradient at rest dropped from 49.2 to 6.4 mmHg (p <0.001) and then to 4.6 mmHg (p=0.224) in the immediate and late periods and with Valsalva maneuver from 93.9 to 8.7 mmHg (p <0.001), and then to 7.2 mmHg (p=0.226), respectively. Preoperative diastolic function was assessed as grade II in 58.5% of patients, decreasing to 51.7% in the immediate postoperative period and to 29% in the late postoperative period. In agreement with these results, a change was evidenced in the E/e´ ratio and pulmonary artery systolic pressure, degree of mitral regurgitation and left atrial dimensions.

Conclusion: In this cohort of patients with HOCM, ESM was associated with a significant improvement in LV diastolic function, reduction in filling and pulmonary pressures and degree of mitral regurgitation, and left atrial reverse remodeling. It is possible that this combination of effects explains the clinical benefits of the intervention.

Key words: Hypertrophic cardiomyopathy, septal myectomy, Echocardiography

RESUMEN

Introducción: La miectomía septal ampliada (MSA) ha demostrado ser una estrategia útil para mejorar los síntomas de los pacientes con miocardiopatía hipertrófica obstructiva (MCHO).

Objetivos: El objetivo de este trabajo fue analizar el impacto de la MSA en parámetros estructurales y funcionales ecocardiográficos a corto y mediano plazo, en pacientes con MCH y obstrucción dinámica del tracto de salida del ventrículo izquierdo (VI).

Material y métodos: Se analizaron los ecocardiogramas en los períodos preoperatorio, postoperatorio inmediato (1 mes post cirugía) y posoperatorio alejado (2 a 3 años) de pacientes sometidos a MSA.

Resultados: Se intervinieron 94 pacientes con una edad media de 57,6 ± 13,8 años. Se observó una reducción significativa del máximo espesor septal en el postoperatorio inmediato, que se mantuvo en el posoperatorio alejado, y en el tamaño auricular izquierdo en el postoperatorio inmediato que se profundizó en el alejado (p<0,001). El gradiente intraventricular en reposo pasó de 49,2 mmHg basal a 6,4 mmHg (p<0,001) y de allí a 4,6 mmHg (p=0,224) en los períodos inmediato y alejado, y con la maniobra de Valsalva de 93,9 mmHg a 8,7 mmHg (p<0,001) y de allí a 7,2 mmHg (p=0,226) respectivamente. La función diastólica fue valorada como grado II en el 58,5 % de los pacientes en el preoperatorio, 51,7 % en el postoperatorio inmediato y 29 % en el postoperatorio alejado. En la misma línea se evidenció un cambio en la relación E/e´ y la presión sistólica pulmonar, grado de insuficiencia mitral y dimensiones de la aurícula izquierda.

Conclusión: En esta cohorte de pacientes con MCHO, la realización de una MSA se asoció a una mejoría significativa de la función diastólica del VI, reducción de las presiones de llenado y pulmonares y grado de insuficiencia mitral, y remodelado reverso de la aurícula izquierda. Es posible que esta combinación de efectos explique los beneficios clínicos de la intervención.

Palabras claves: Miocardiopatía Hipertrófica - Miectomía septal - Ecocardiograma

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INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is a hereditary cardiac disease with complex genetic and phenotypic expression and an estimated prevalence of 1:500 in the general population. (1,2)

Approximately 70% of patients with HCM present some form of dynamic obstruction (HOCM) that contributes to the development of symptoms such as dyspnea and angina. In turn, sufficient evidence shows the impact of dynamic obstruction in the development of functional and structural changes at the cardiac level, as the increase in ventricular filling pressures, pulmonary pressure and left and right atrial dilation. (3,4)

Extended septal myectomy (ESM) has shown to be a useful strategy to improve symptoms and quality of life in patients with HOCM refractory to medical treatment. (3-5)

The purpose of this study was to evaluate the impact of this surgery on the structural changes associated with dynamic obstruction.

The objective was to analyze the short and midterm impact of ESM in structural and functional echocardiographic parameters in patients with HCM and left ventricular (LV) outflow tract dynamic obstruction.

METHODS

Study design

An observational study was carried out on a prospective cohort of patients undergoing ESM from November 2011 to December 2022. It included patients with possibility of follow-up and a control echocardiogram in the immediate and late postoperative periods.

HCM diagnosis

The HCM diagnosis was performed according to international guideline recommendations, with the presence of increased LV wall thickness in one or more myocardial segments, determined by any imaging technique, in the absence of any other cardiac or systemic cardiac disease that justified it. In adults, a LV wall thickness ≥15 mm, or a septal/posterior wall thickness ratio >1.3 was considered to determine a diagnosis, and for first-degree relatives of a patient with HCM, a LV wall thickness ≥13 mm was contemplated for the diagnosis. (2,3)

The HOCM diagnosis was performed according to international guideline recommendations by Doppler echocardiography, when the peak gradient obtained spontaneously and/or using maneuvers (Valsalva, exercise) was ≥30 mmHg. (2,3)

Echocardiographic assessment

A two-dimensional ultrasound was used to measure myocardial maximum septal thickness, left atrial (LA) anteroposterior diameter in the long parasternal axis, and atrial area and volume in apical 4-chamber view. Left atrial volume was calculated using the area-length biplane method and the LA volume index using body surface area.

Left ventricular systolic function was quantified by Simpson's rule, in apical 2-chamber and 4-chamber views. (6)

The apical 4-chamber view with pulsed Doppler mitral flow at the mitral valve leaflet tips was used to determine peak early (E) and late (A) diastolic wave velocities, the E/A ratio and E wave deceleration time, and to classify diastolic dysfunction according to echocardiographic quantification guidelines into normal and grade I, II and III. Early lateral and medial mitral annulus peak diastolic velocities were analyzed with tissue Doppler to assess ventricular filling pressures, considering the ratio between mitral peak E wave velocity and average peak e' wave velocity (E/e'). (7)

According to international recommendations, diastolic function assessment in HCM patients was considered through an integral approach, taking into account all the echocardiographic parameters that include and consider as abnormal values an E/e' ratio >14, indexed LA volume >34 ml/m², difference in the pulmonary vein retrograde A wave duration - transmitral flow antegrade A wave duration >30 msec, and peak tricuspid regurgitant jet velocity >2.8 m/s. Normal LA pressure and grade I diastolic dysfunction was considered if <50 % of these variables reached cut-off values, and elevated LA pressure and grade II diastolic dysfunction when > 50% of these variables did. In case of 50% discordance, the findings were not conclusive to estimate LA pressure. Grade III diastolic dysfunction was considered in the presence of a restrictive filling pattern and reduced Doppler tissue mitral annulus velocity (septal <7 cm/s, and lateral <10 cm/s). (7)

Presence of mitral regurgitation was evaluated with color Doppler ultrasound, and qualitatively graded as mild, moderate and severe, and whether its mechanism was secondary to anterior systolic mitral valve motion, or as a consequence of a valve abnormality, such as prolapse, chordal rupture, mitral valve ring calcification or incorrect positioning of a papillary muscle, or mitral subvalvular apparatus abnormalities. (7)

To assess pulmonary artery systolic pressure (PASP), peak tricuspid regurgitant jet velocity continuous Doppler was used, added to right atrial diastolic pressure, according to the inferior vena cava diameter and its percentage of inspiratory collapse. (7)

The obstructive gradient was identified with color Doppler and quantified with continuous Doppler according to the Bernoulli formula, at rest and with Valsalva maneuver/exercise. (7)

The clinical preoperative, postoperative and follow-up evaluation of patients was performed by cardiologists of the Cardiomyopathy center, and functional class for dyspnea, according to the New York Heart Association (NYHA) classification, presence or absence of angina, syncope, family history of sudden death, cardiovascular risk factors and optimal medical treatment were established (Figure 1).

Follow-up

Transthoracic echocardiograms were performed in the following periods:
- Preoperative period: up to 3 months before surgery
- Immediate postoperative period: 1 month after surgery
- Late postoperative period: between 2 and 3 years after surgery.

Statistical analysis

Quantitative variables are expressed as mean or median with their corresponding standard deviation (SD) or interquartile range (IQR) as appropriate. Categorical variables are presented as frequency and percentage. The Kolmogorov-Smirnov test (n ≥30) and the Shapiro-Wilk test (n <30) were used to evaluate the normality of variables and the application assumptions of each of the tests used.

Chi-square, McNemar, sign, Wilcoxon or ANOVA tests were used as appropriate (2 samples or more, independent or paired)

A two-tailed p value <0.05 was considered significant.

SPSS 19 (Statistical Package for the Social Sciences) was used to perform the analyses.

Ethical considerations

The study was carried out according to national ethical regulations (CABA law 3301), the national law of clinical research in human beings and the declaration of Helsinki, and was approved by the Institutional Teaching and Ethics Committee.

Patients signed an informed consent for the anonymous use of their personal data.

RESULTS

A total of 94 patients, with mean age 57.6±13.8 years, 53% female, underwent surgery during the study period, with a median follow-up of 3.3 years (IQR 1.1-5.1) Table 1.

All patients underwent ESM and 43 of them (45.7%) were also subjected to concomitant treatment of the mitral valve or the subvalvular mitral apparatus (9 underwent mitral valve repair, 26 mitral valve plication, 14 second order chord resection, 8 accessory muscle resection, and 3 mitral valve replacement). In addition, aortic valve replacement was performed in 3 patients (3.1%), coronary bypass surgery in 19 (20.2%) and Maze surgery in 17 (18%).

All patients presented complete left bundle branch block after the intervention, and 7.4% required definite pacemaker for complete atrioventricular block, in 5.3% of cases in patients with isolated septal myectomy. Two patients presented atrial fibrillation (AF) in the immediate preoperative and postoperative periods and 5 in the late postoperative period.

Fig. 1. Echocardiographic evaluation of a patient with hypertrophic obstructive cardiomyopathy.

Table 1. Baseline population characteristics.

Variables	n= 94
Age (years), mean ±SD	57.3 ± 13.2
Female gender, n (%)	50 (53.1)
HTN, n (%)	59 (62.7)
Dyslipidemia, n (%)	54 (57.4)
Diabetes, n (%)	11 (11.7)
Smoking, n (%)	21 (22.3)
Syncope, n (%)	13 (13.8)
Angina, n (%)	17 (18)
Coronary artery disase, n (%)	19 (20.2)
Pharmacological treatment, n (%)	
Betablockers	65 (69.1)
Verapamil	2 (2.1)
Amiodarone	23 (24.4)
Diuretics	35 (36.1)
ARBs	17 (18)
Family history of sudden death, n (%)	11 (11.7)
Prior alcohol septal ablation, n (%)	6 (6.3)
Prior ICD, n (%)	11 (11.7)

ARBs: Angiotensin receptor blockers; HTN: Hypertension; ICD: Implantable cardioverter defibrillator; SD: Standard deviation

There were 3 (3.1%) interventricular septal defects related with the surgical procedure, and 30-day perioperative mortality was 1 patient (1.06%). Nine patients (9.5%) died during follow-up, 3 related to their underlying disease (3.2%)

Regarding functional class, 89% of patients were asymptomatic during the long-term follow-up.

Structural parameters showed a significant reduction in maximum septal thickness, from 21.3 mm in the preoperative period to 14 mm in the immediate postoperative period, ($p<0.001$) which was maintained in the late postoperative period.

A significant reduction was observed in the left atrial size; its anteroposterior diameter decreased from 49.7 mm to 48.2 mm in the immediate postoperative period ($p<0.001$) to 46.2 mm in the late postoperative period ($p< 0.001$). Left atrial volume indexed by body surface area decreased from 57.6 ml/m² to 51.2 ml/m² ($p<0.001$) in the immediate postoperative period, and to 46.1 ml/m2 ($p<0.001$) in the late postoperative period. Moreover, left atrial area decreased from 30.1 cm2 to 28.2 cm² ($p<0.001$) in the immediate postoperative period, and to 26.3 cm2 ($p<0.001$) in the late postoperative period (Table 2 and Figure 2).

Regarding functional parameters, the intraventricular gradient at rest decreased from 49.2 mmHg to 6.4 mmHg ($p<0.001$), and then to 4.6 mmHg ($p=0.224$) in the immediate and late postoperative periods, and

with the Valsalva maneuver from 93.9 mmHg to 8.7 mmHg ($p<0.001$), and 7.2 mmHg ($p=0.226$), respectively. Diastolic function was assessed as grade II in 59.3% of patients in the preoperative period, in 51.6% in the immediate postoperative period, and in 29% in the late postoperative period (Figure 3). Similarly, a change in the E/e´ ratio and pulmonary artery systolic pressure was evidenced. Moderate to severe mitral regurgitation decreased from 53.1% in the preoperative period to 8.7% in the late postoperative period and pulmonary pressure from 32 mmHg to 27 mmHg, respectively. Left ventricular ejection fraction (LVEF) decreased from 65% to 60% ($p<0.001$) in the immediate postoperative period and remained at 60% ($p=0.953$) in the late postoperative period .

DISCUSSION

The importance of the results obtained in this work is the significant impact of ESM on the different hemodynamic parameters studied by echocardiography and the clinical improvement of patients. We would like to highlight 4 findings.

First, from a structural point of view, a reduction was evidenced in the LA size measured in all its forms, which appears to be intensified with the passage of time. The probable mechanisms that we understand are involved in this phenomenon are the reduction of mitral regurgitation and of LV filling pressure. In

Table 2. Modification of echocardiographic parameters with the ESM

| Variable	Preoperative	Immediate POP	Late POP	p
Maximum thickness (mm), mean ±SD	21.3 ± 3.9	14 ± 3	14 ± 3	<0.001
Gradient at rest (mmHg), mean ±SD	49.2 ± 31.4	6.4 ± 9.3	4.6 ± 9.4	<0.001
Valsalva gradient (mmHg), mean ±SD	93.9 ± 39.7	8.7 ± 13	7.2 ± 14	<0.001
LA volume (ml/m2), mean ±SD	57.6 ± 18.4	51.2 ± 17.2	46.1 ± 16.5	<0.001
LA area (cm2), mean ±SD	30.1 ± 5.9	28.2 ± 5.4	26.3 ± 5.6	<0.001
LA anteroposterior diameter (mm), (mean ±SD)	49.7 ± 6	48.2 ± 5.8	46.2 ± 5.4	<0.001
Diastolic function, n (%)				
Normal	0	0	1 (1.2)	
AF	2 (2.1)	2 (2.1)	5 (5.3)	
Grade I	36 (38.3)	40 (43)	57 (61.3)	<0.001
Grade II	55 (58.5)	48 (51.7)	27 (29)	
Grade III	1 (1.1)	0	0	
Mitral valve prosthesis	0	3 (3.2)	3 (3.2)	
E/e´ ratio, mean ±SD	15.7 ± 4.8	13 ± 3.3	11.1 ± 3.2	<0.001
LVEF (%), mean ±SD	65 ± 6.2	59.9 ± 6.1	60 ± 6.8	<0.001
PASP (mmHg), mean ±SD	32.9 ± 9.5	30.1 ± 7.9	27.5 ± 8.4	<0.001
Mitral regurgitation, n (%)				
None	0	3 (3.2)	3 (3.2)	
Mild	44 (46.7)	80 (87.9)	80 (87.9)	<0.001
Moderate	38 (40.4)	8 (8.7)	8 (8.7)	
Severe	12 (12.7)	0	0	

AF: Atrial fibrillation; ESM: extended septal myectomy; LA: Left atrial; LVEF: Left ventricular ejection fraction;
PASP: Pulmonary artery systolic pressure; POP: Postoperative; SD: Standard deviation

relation to the first, patients undergoing surgery for isolated mitral regurgitation usually show this phenomenon, correlated in the case of mitral valve repair surgery with the degree of residual mitral regurgitation. Regarding filling pressures, the reduction of the dynamic gradient has a verified impact at the level of end-diastole pressure and contributes to this phenomenon. From a prognostic viewpoint, LA size is an independent risk factor for adverse outcomes in patients with HCM, and increased LA volume is associated with an increased risk of atrial fibrillation, thromboembolic stroke, heart failure and cardiovascular mortality, which appears to represent much more than a simple structural change. (8-18) Our findings have been previously reported by Tower-Rader et al., who in a review of 25 patients observed a significant decrease in atrial volume 2 years after myectomy. (19) Similarly, Finocchiaro et al. demonstrated a marked reduction of LA volume in a cohort of 40 patients undergoing septal reduction therapy (myectomy or alco-

hol septal ablation). (20) In a cohort of 44 operated-on patients, Kyung Eun Ha et al. observed a reduction in atrial volume and increased strain of this chamber, consistent not only with the reduction in size but with an improvement in fiber function. (21)

Second, echocardiographic "hemodynamic" assessment showed a reduction in the E/e′ ratio and changes in the transmitral filling pattern. These modifications seem to be related with the reduction in LV end diastolic pressure, secondary to the significant reduction that the procedure achieved in the dynamic left ventricular outflow tract gradients both at rest and with Valsalva maneuver. Evidence of this is that the changes are noticeable in the immediate postoperative period. Moreover, both variables tend to improve even more in the late postoperative period, a fact that could be explained by the gradual recovery in diastolic function produced by the relief of the obstruction. This has been also reported by others, such as Nguyen et al, who found in a cohort of 656 patients

Fig. 2. Extended septal myectomy and changes in left atrial volume and E/e′ ratio.
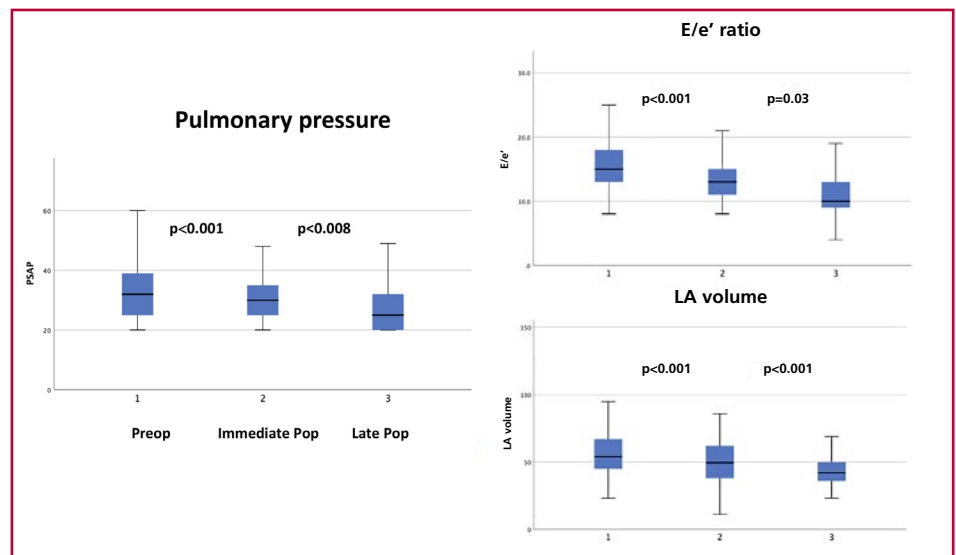
IQR: Interquartile range.LA: Left atrial.

Fig. 3. Modifications in the transmitral filling pattern.
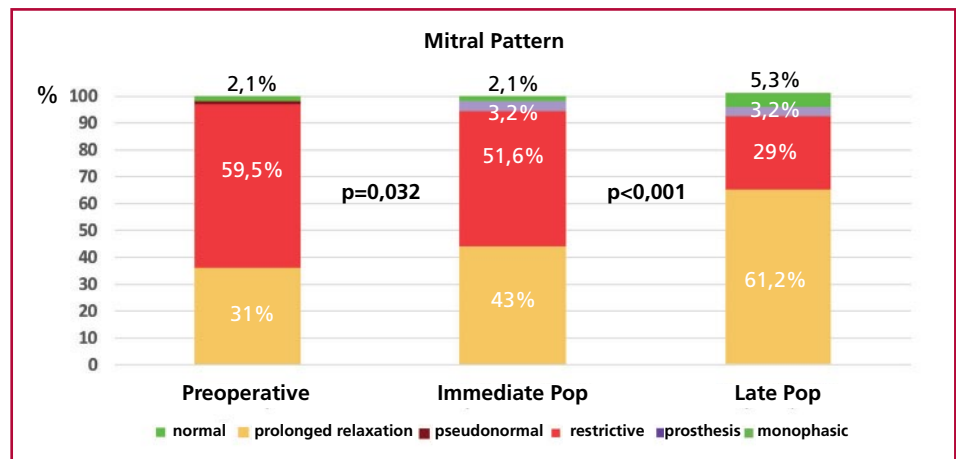
POP: postoperative

an improvement in the E/e' ratio, which occurred in the early postoperative phase and was maintained in the long-term follow-up. (22) There is evidence that correlates dynamic obstruction with the development of myocardial ischemia and interstitial fibrosis, so we hypothesize that this relief could be generating a retrograde phenomenon. (23,24)

Third, the LVEF drop in the immediate postoperative period could be associated with the impact of the pump used for cardiopulmonary bypass during surgery, but above all to the development of left bundle branch block due to the myectomy. This last phenomenon causes mechanical dyssynchrony and a drop in ejective volume, without ruling out that it has an impact on the reduction of the dynamic gradient. The analysis of the late postoperative period shows a numerical though not significant recovery, requiring greater follow-up for analysis. (23-26) Along the same line, Ha et al. observed a relationship between postmyectomy QRS duration and the drop in LVEF, accompanied by a reduction in non-septal LV longitudinal strain. (21)

Fourth, patients showed a reduction in echocardiographic assessed pulmonary artery systolic pressure that deepened over time. This fact shows that changes in left filling pressures and improvement in diastolic function have an impact on the pulmonary circuit and right chambers, which probably contributes to explaining the clinical improvement of patients. (25,26)

Limitations

The number of patients included may decrease the reliability of several of the data obtained. However, the consistency of the findings suggests a direct relationship between the intervention and the observed changes. We also understand the limitations of the methods to accurately estimate ventricular filling pressures in this scenario, though there is sufficient information to consider that changes in these variables are associated with improvement in diastolic function.

CONCLUSION

In this cohort of patients with HOCM, ESM was associated with a significant improvement in LV diastolic function, reduction in filling and pulmonary pressures and degrees of mitral regurgitation, and reverse remodeling of the left atrium.

It is possible that this combination of effects explains the clinical benefits of the intervention.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web).

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