Individualised surgical strategies for left ventricular outflow tract obstruction in hypertrophic cardiomyopathy

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Word Count: 4910

Abstract

Objectives

Surgical strategies to treat drug refractory left ventricular outflow tract obstruction (LVOTO) in hypertrophic cardiomyopathy (HCM) include septal myectomy (SM), and less frequently mitral valve (MV) repair or replacement. The primary aim of this study is to report surgical technique and management outcomes in a consecutive group of patients with variable phenotypes of HCM in a broad national specialist practice.

Methods and Results

203 consecutive patients, 132 males (mean age 48.6 +/- 14.6 years) underwent surgery for the management of LVOTO. Surgical approaches included SM (n=159), SM with MV repair (n=25), SM with MV replacement (n=9) and MV replacement alone (n=10). Specific surgical approaches were performed based on the underlying mechanism of obstruction. Eleven patients (5.4%) had previous alcohol septal ablation for management of LVOTO. Concomitant non-mitral cardiac procedures were carried out in 22 patients (10.8%).

Operative survival rate was 99.0% with 2 deaths within 30 days. The mean bypass time was 92.9+/-47.8 minutes with a mean length of hospital stay of 10.5+/-7.8 days. Surgical complications included 3 ventricular septal defect's requiring repair (1.5%), 1 Gerbode defect surgically repaired, 2 aortic valve repairs (1.0%), 2 transient ischaemic attack's (1.0%) and 4 strokes (2.0%). Thirty-nine patients (19.2%) had perioperative new onset atrial fibrillation and 8 patients (3.9%) had unexpected atrioventricular block requiring a permanent pacemaker. Mean resting left ventricular outflow tract gradients improved from 70.6+/-40.3mmHg preoperatively to 11.0+/-10.5mmHg at 1 year (p<0.001). Mean NYHA Class improved from 2.6+/-0.5 preoperatively to 1.6+/-0.6 at 1 year.

Conclusions

In variable phenotypes of LVOTO in HCM, an individualised surgical approach achieved effective reductions in LVOT gradients and good symptomatic relief with acceptable mortality and morbidity.

Introduction

Hypertrophic cardiomyopathy (HCM) is the commonest genetically inherited cardiac condition affecting 1 in 500 of the population. Complications include left ventricular outflow tract obstruction (LVOTO), atrial fibrillation (AF), ventricular arrhythmias, sudden cardiac death and heart failure.[1-4] Severe drug refractory symptoms can persist in up to one third of cases. Expert consensus indicates surgical intervention to be the gold standard in the management of these patients.[2] Septal myectomy (SM) alone, is the surgical technique of choice in the vast majority of patients with HCM with excellent outcomes.[6-12] The mechanism of LVOTO can be complex with a varying non-classical phenotype also seen in HCM. This includes limited septal hypertrophy, angulation of the aorta, elongation of mitral leaflets and abnormalities of the sub-mitral apparatus. Abnormal mitral attachments include thickened or anteriorly displaced papillary muscles, direct insertion of the papillary muscle into the anterior mitral valve leaflet or fibrotic chordal attachments.[5] These non-classical phenotypes may, in individual circumstances, dictate a different surgical approach. With an improved understanding of the mechanism of obstruction, an increasing number of mitral valve (MV) repairs and replacements are performed both concomitantly with SM, or alone. The primary aim of this study is to evaluate early outcomes following individualised surgical strategies for the management of LVOTO in a wide spectrum of HCM patients.

Methods

Study

Between 2003 and 2015, 203 consecutive patients underwent surgical intervention for the management of LVOTO in HCM in a national specialised cardiomyopathy unit at the Heart Hospital, University College London Hospital. No patients were excluded. All patients were operated on by one of two surgeons (CMcG, VT).

Clinical assessment

All patients were assessed in a clinic specialising in cardiomyopathy. Baseline demographic data including age, sex, past medical and family history were documented, as was pre and postoperative New York Heart Association (NYHA) functional class. Variables from transthoracic echocardiography (TTE) including interventricular septal wall thickness (IVS), posterior wall thickness (PWT), left ventricular end diastolic diameter (LVEDD), left atrial diameter (LAD), left ventricular ejection fraction (EF), resting and provoked left ventricular outflow tract gradients (LVOT) and severity of mitral and aortic regurgitation were collected. Drug refractory symptomatic LVOTO with a LVOT gradient >50mmHg was the principal indication for surgery as per international guidelines.[2] All patients were discussed at a joint medical and surgical cardiac conference and the most suitable surgical approach discussed. Particular attention was paid to the MV on multimodality imaging preoperatively to decide if MV intervention might be required at the time of surgery.

Surgical technique

After median sternotomy and before cardiopulmonary bypass, direct simultaneous pressure measurements were performed with needles in the aorta and left ventricle. Provocation was measured following a bolus of Isoproterenol (5mcg) intravenously and repeated if an increase in heart rate and/or reduction in blood pressure was not achieved. Over the time of the study the surgical technique of SM evolved from the classical Morrow myectomy to the Danielson modification of the classic Morrow myectomy.[13,14] After the initial planned surgery and cessation of cardiopulmonary bypass, transoesophageal echocardiography (TOE) was done to assess the LVOT and MV. Direct simultaneous pressure measurements were repeated with and without provocation as done pre-bypass. Indications to resume bypass and perform further surgery at this point were principally a significant residual gradient, and/or persistent SAM related MR. Mitral valve repairs included trans-atrial Alfieri edge to edge repair, transaortic mitral plication, cleft repair, division of papillary muscles or artificial

chordal repair. Mitral annuloplasty was avoided in all patients. Mitral valve replacement was done at the time of SM using standard techniques and MV replacement was done alone without SM again using standard techniques. Perioperative complications were defined as those occurring within the first 30 days following surgery.

Follow up

All patients were followed up clinically at regular annual visits or more frequent intervals based on clinical status. At 1 year, postoperative echocardiographic data was available in 83.7% of patients. The remainder of patients were followed up by their local cardiologist.

Statistical analysis

Variables were collected and assessed using SPSS software, version 24 (IBM, Chicago). Tests of normality were carried out based on histogram distribution and the Shapiro-Wilks test. For data with a normal distribution, continuous variables were expressed as a mean ± standard deviation. For data with a non-normal distribution, continuous variables were expressed as a median with interquartile range. For normally distributed data, comparison of means was performed using a paired student t test. For non-normally distributed data comparisons were performed using a Mann Whitney U test. All echocardiographic variables were normally distributed and comparison of means was performed using a paired student t test. A p-value of <0.05 was considered significant.

Results

Of the 203 patients in the study, baseline demographics are documented in *Table 1*. The mean age at surgery overall was 48.6+/-14.6 and in those undergoing a SM alone was 47.5 +/- 14.2 years, SM

with MV Repair was 48.7+/- 15.0 years, SM with MV replacement was 55.4 +/- 15.0 years and MV replacement alone was 57.7 +/- 14.3 years. Eleven patients (5.4%) previously underwent alcohol septal ablation for the management of LVOTO with recurrence of symptoms.

Surgery

The mean cardiopulmonary bypass-time was 92.9+/-47.8 minutes with a mean length of hospital stay of 10.5+/-7.8 days. The mean weight of septal tissue removed, available in 87 patients (42.3%), weighed 6.6+/-4.3 grams. Surgical procedures are illustrated in *Table 2*. One hundred and fifty-nine patients (78.3%) had a SM alone. Twenty-five patients (12.3%) had a SM with MV repair which included edge-to-edge (Alfieri) repair, valve plication, cleft repair, chordal repair and division of papillary muscle. Nine patients (4.4%) underwent a SM with MV replacement, two of which were bioprosthetic MV replacements. In 6 of these 9 patients concomitant MV replacements were unplanned following unsuccessful repair, the remainder were planned replacements. Four of these 6 patients had degenerative MV disease with residual moderate to severe MR following initial bypass and SM. The other 2 patients had a MV repair after SM with residual moderate to severe MR. None of these 6 patients had residual SAM following the initial SM. Ten patients (4.9%) had a MV replacement alone without a SM, one of which was a bioprosthetic MV replacement. Other concomitant procedures included coronary artery bypass grafting (n=4), aortic valve replacement (n=3), surgical MAZE with or without pulmonary vein radiofrequency ablation (n=9), resection of subaortic membrane (n=7), closure of a patent foramen ovale (n=3) or atrial septal defect (n=1). Forty-six patients (22.7%) underwent closure of the left atrial appendage at the time of surgery. Thirteen patients (6.4%) of the 203 patients required reinstitution of cardiopulmonary bypass following initial SM. This was required for a mitral valve repair due to residual SAM/MR (n=7), a MV replacement for residual MR following initial repair (n=2) and a MV replacement directly without an intermediate repair attempt (n=4). Anatomical and echocardiographic indications for individual surgical approaches to the MV are shown in *Table 3*.

Early Mortality

Operative survival was 99.0% with 2 perioperative deaths within 30 days of surgery. One patient, a 67-year-old female sustained a ventricular septal defect (VSD) identified on an intraoperative transoesophageal echocardiogram (TOE) following a SM with staple excision of the left atrial appendage. This was repaired immediately through a right ventriculotomy using bovine pericardial patches and continuous prolene sutures to close the defect and the right ventricle. This patient developed progressive low cardiac output and died on day 3. A second patient, a 30-year-old male, undergoing an extended SM for severe concentric left ventricular hypertrophy and pulmonary vein isolation for the management of AF developed an aortic valve tear to the left coronary cusp which was repaired using two 8-0 prolene sutures. This patient died on day 3 from heart failure in the setting of aortic regurgitation, severe diastolic dysfunction and external pacemaker dysfunction. Survival at 1 year was 98.5% with 1 further death at 4 months due to heart failure postoperatively. There were no other deaths within the first year of surgery.

Complications

Fifty-six patients (27.6%) had documented postoperative AF, thirty-nine of which were new onset of postoperative AF. There were 2 perioperative TIA's (1.0%) with 4 perioperative strokes (2.0%). One stroke was assumed cardioembolic in nature in the setting of new onset AF. The remaining cases had no documented AF. Thirteen patients (6.4%) had a permanent pacemaker (PPM) device inserted for atrioventricular block. Five of these 13 patients had a planned prophylactic insertion of a permanent pacemaker for pre-existing high grade atrioventricular block during the primary surgical admission. These patients were deemed at high risk for complete heart block with the additional inevitable left bundle branch block from SM. Eight further patients (3.9%) developed unexpected atrioventricular block requiring permanent pacemaker insertion. Ten patients (4.9%) had an implantable cardioverter device (ICD) in the perioperative period, 3 of which were implanted to treat complete atrioventricular

block in the setting of associated risk factors for sudden cardiac death. The remaining 7 patients had an ICD implanted based on risk factors associated with SCD. As described above, 3 patients (1.5%) suffered a VSD requiring repair intraoperatively. One additional patient developed an acquired Gerbode defect postoperatively which was successfully surgically repaired.[15] Two patients (1.0%) had an unplanned aortic valve repair due to a new valve tear intraoperatively. Two patients (1.0%) required further operative intervention during the initial surgical stay. These patients who initially underwent SM with MV repair required reintervention with MV replacement on day 4 and 14 respectively due to severe MR.

Clinical and Echocardiogrpahic Outcomes

The mean NYHA Class improved from 2.6+/-0.5 preoperatively to 1.6+/-0.6 postoperatively at 1 year (p<0.001). The vast majority of patients improved symptomatically with 78.7% of patients improving by at least one NYHA class postoperatively, with 19.5% of patients remaining in the same NYHA functional class and a minority of patients (1.7%) in a higher NYHA function class at 1 year. Echocardiographic variables are shown in *Table 4*. The mean IVS wall thickness reduced from 19.1+/-4.1mm preoperatively to 13.9+/-4.0mm postoperatively (p<0.001). Resting LVOT gradients reduced from 70.6+/-40.3 preoperatively to 11+/-10.5mmHg after surgery at 1 year (p<0.001). One hundred and eighty-three patients (90.1%) had no evidence of resting or provoked LVOTO on the postoperative echocardiogram at 1 year. Individual NYHA class and MR grade are compared pre and postoperatively in *Table 5*.

Discussion

Surgical management of LVOTO by SM is considered by expert consensus to be the gold standard in the management of drug refractory symptomatic cases in HCM, with excellent outcomes in the vast majority of cases.[2] Multiple large surgical series have reported the outcomes of SM alone, which reflect in part, referral patterns to large US centers.[7,9,10] The earliest surgical approaches included the

standard SM introduced by Morrow et al. (1961) and MV replacement by Cooley et al. (1971); both of which have been shown to be successful in improving symptoms and alleviating LVOT gradients.[14,16] In the vast majority of patients, SM is the only procedure required to treat LVOTO in HCM. Mitral abnormalities however, do play an important role in the mechanism of LVOTO in individual patients such as those with limited hypertrophy, and we believe an individualised surgical approach is necessary for optimal surgical management.[5] The current series reflects experience of surgery for LVOTO in HCM in a national centre with referral of a wide phenotypic variation performing >70% of such UK practice over the period of the study.

Preoperative and intraoperative imaging, including TTE and TOE are essential in the characterisation of phenotypic abnormalities to allow for strategic surgical planning to address causes of MR and SAM. Intrinsic MV abnormalities can pre-exist including annular, leaflet or chordal calcification or fibrosis which may need to be addressed at the time of operation. Specific abnormalities of the MV apparatus, commonly seen in HCM patients can contribute to the mechanism of LVOTO including both elongation of MV leaflets and abnormal mitral attachments.[17] Abnormal MV attachments, commonly seen with LVOTO include anterior papillary muscle displacement, thickened bifid papillary muscles, direct insertion of papillary muscle into the AMVL or fibrotic chordal attachments. Complex cases with involvement of both the mitral and submitral apparatus can be managed with a combination of SM and repair or replacement of the MV. The use of an extended SM can address this issue somewhat by extending the resection in a fan like fashion moving distally in the septum. Ferrazi et al. report good outcomes in patients undergoing a limited SM with trans aortic selective division of fibrosed secondary chordae attached to the AMVL body believed to be contributing to SAM.[18] Elongation of the MV leaflets, in particular the anterior leaflet result in SAM related MR. In cases of limited septal hypertrophy, MV replacement has been performed as primary surgery in the past, however, a range of newer surgical techniques for MV repair have evolved to address such cases in which adequate resection is technically challenging.[19-21] Controversy remains over individual techniques of MV repair in patients with LVOTO. The rate of concomitant MV intervention with SM

has varied from 8% in a recent large study of over 2000 patients from the Mayo Clinic operated on with SM for LVOTO to 25% in a paper from the Cleveland Clinic.[7,11]

Multiple surgical approaches have been advocated in the presence of elongated leaflets with post SM SAM and/or MR with good outcomes, including the edge to edge Alfieri repair, MV plication and AMVL extension using a pericardial patch.[19-21] The edge to edge Alfieri mitral valve repair was our preferred surgical approach to address elongated anterior mitral leaflets with SAM related MR with good resolution of LVOT gradients and improved symptoms. This was done using a trans-atrial rather than trans-aortic approach which allowed us to inspect the submitral apparatus in more detail. The Alfieri technique has been used successfully in MR of various aetiologies.[21] There have been no early or late mortalities in this group of 11 patients in the current study, who documented good medium term outcomes.[22] If an Alfieri repair is contemplated, assessment of the posterior MV leaflet length is important, as excess length can lead to bileaflet prolapse with SAM making this type of repair less likely to be effective.

The advantage of MV repair is that it obviates the need for MV replacement and its associated complications.[23] Late survival following SM with MV repair was superior to SM with MV replacement in the large Mayo clinical experience.[11] Contemporary data on MV replacement alone for relief of LVOTO in HCM in the literature is less robust than that for SM. Initial studies reported by Cooley et al. showed good symptomatic relief and resolution of gradients. Further long-term studies by the same group showed good outcomes at ten years.[24] Other early studies showed similar symptomatic and gradient reduction with MV replacement, however, higher mortality rates and complication rates were seen in these cohorts.[25,26] More recent studies of MV replacement in patients with LVOTO have reported on SM with MV replacement rather than MV replacement alone.[11,27,28,29] Mitral valve replacement alone can be a successful approach in cases unsuitable for repair or when used alone in those patients with thinner septae unsuitable for SM.

In the early part of the series, there were few concomitant MV procedures performed. With an improved understanding of the mechanism of obstruction, over time, more complex HCM phenotypes were operated on particularly in older patients with concomitant cardiac disease with an increasing number of MV repairs and replacements. The decision to proceed with a MV replacement directly, rather than a further bypass run to explore a potentially intermediate MV repair was carefully considered. In this study it was noted that patients who required MV replacement were older and had more comorbidities than those who did not require a MV replacement. The preoperative phenotype as well as cardiac and non-cardiac comorbidities were factored into the surgical decision making process i.e. in consideration of the tolerance of a more extensive, longer operation. In selected older patients with atypical phenotypes and multiple comorbidities in whom SM alone was felt unlikely to be adequate and who were felt to be unsuitable for multiple bypass runs, an upfront decision to perform MV replacement alone was made in this series.

Figure 1, illustrates a flowchart for consideration in the strategic planning of surgery in the management of non-classical LVOTO in HCM. These phenotypes include aortic angulation, limited hypertrophy or abnormally distributed hypertrophy along with abnormalities of the MV commonly including elongated leaflets, abnormal MV attachments or other intrinsic abnormalities of the MV. A stepwise approach is taken in the planning of individual cases which is re-evaluated intraoperatively following the initial procedure and initial bypass run to evaluate if further intervention is needed to the MV. The recent Mayo study of 174 patients surgically managed with SM and MV intervention revealed no difference in ICU length of stay, hospital length of stay or late mortality in those undergoing single or multiple cardiopulmonary bypass runs indicating the safety of this approach in appropriate patients.[11]

Hospital volume plays an important role in mortality outcomes of surgery for HCM. A recent national database study analysing 6386 SM's reported that surgery in lower volume centres was an independent predictor of mortality in the USA.[30] In high volume centres early surgical outcomes following SM have shown very low mortality rates with good resolution of symptoms.[6,7,10,30] Mortality within this current study is low and comparable to current reported outcomes in high volume centres for SM.[9] Additionally, 21.7% of patients included in the current study had MV surgery and 10.8% had concomitant non-mitral surgery. This study reports good echocardiographic follow up with 83.7% of all patients at 1 year, a rate which is not available in many other studies of this size. Almost 80% of patients in this study showed an improvement in NYHA class postoperatively comparable to previous large studies.[10,12] Over 90% of patients demonstrated a resolution of obstruction with a LVOT gradient of <30mmHg on postoperative echocardiography at 1 year. This individualised approach to the management of LVOTO in variable phenotypes of HCM adopted by our institution has not compromised, at least, 1 year surgical, clinical and echocardiographic outcomes.

Limitations

This study represents a single centre, retrospective consecutive experience representing limitations inherent to this study design. We acknowledge that as a national referral centre with a large population of HCM patients attending for regular clinical review that this may introduce referral bias, however, we believe that, a more variable set of phenotypes may be seen within such an environment, requiring a more individualised surgical approach. There was incomplete data on the exact distribution of hypertrophy from echocardiography in individual patients.

Conclusion

This study from a single centre experience reports individualised surgical approaches to the management of LVOTO in HCM with low mortality rates and good clinical outcomes. Surgical

strategy should be individualised depending on the underlying mechanism of obstruction with appropriate evaluation of the MV.

Conflicts of Interest

None declared

Figure Legend

Figure 1: Flowchart in decision making for surgical management

Tables

Table 1

Overall number of patients	203 (100%) ( ) = % of total
Age at Surgery (mean+/-SD)	48.6+/-14.6
Male	132 (65.0%)
Past History	
Atrial Fibrillation	28 (13.8%)
Previous PPM	14 (6.9%)
Previous PPM for LVOTO	9 (4.4%)
Previous ASA	11 (5.4%)
Stroke	3 (1.5%)
Peripheral Vascular Disease	1 (0.5%)
Diabetes Mellitus	9 (4.4%)
Hypertension	58 (28.6%)

Table 1: Baseline demographics

Table 2

Overall number of patients	203 (100%)
	( ) = % of total
Septal Myectomy	159 (78.3%)
Septal Myectomy with MV repair	25 (12.3%)
Plication	4
Edge-to-edge Alfieri repair	11
Cleft repair	3
Division of papillary muscles	1
Chordal repair	6
Septal Myectomy with MV replacement	9 (4.4%)
MV replacement alone	10 (4.9%)
Concomitant Procedures (in 22 patients)	27
CABG	4 (2.0%)
Planned aortic valve replacement	3 (1.5%)
MAZE	9 (4.4%)
Resection of subaortic membrane	7 (3.4%)
Closure of PFO	3 (1.5%)
Closure of ASD	1 (0.5%)

Table 2: Surgical procedures

Table 3:

Category of MV intervention (N = number in each category)	ASH <18mm	Angulation of aorta	Long AMVL	Abnormal MV attachments	Myxomatous MV	Prolapse	MR	SAM
Papillary division (N=1)	1	0	0	0	0	0	1	1
Cleft Repair (N=3)	0	0	1	0	0	0	3	3
Plication (N=4)	1	1	3	0	0	1	4	4
Chord Repair (N=6)	1	0	0	3	2	1	4	5
Alfieri (N=11)	4	3	5	2	1	2	9	10
SM and MV replacement (N=9)	2	1	3	2	3	1	9	9
MV replacement alone (N=10)	7	1	1	0	6	0	7	9

Table 3: Anatomical and echocardiographic features in individual surgical mitral interventions.

Numbers in each vertical column represent the number of patients with the listed specific feature.

ASH: Asymmetric Septal Hypertrophy

AMVL: Anterior MV Leaflet

MR: Grade 3 or 4 mitral regurgitation

Table 4

	Preoperative N=203	Postoperative N=170	P-Value
IVS (mm)	19.1+/-4.1	13.9+/-4.0	<0.001
PWT (mm)	10.8+/-2.8	10.1+/-2.3	0.022
LAD (mm)	47.2+/-7.7	45.8+/-7.1	0.002
LAA (cm^2)	30.6+/-8.0	27.1+/-7.0	0.003
LVEDd (mm)	46.0+/-5.9	48.9+/-6.3	<0.001
EF (%)	69.0+/-6.8	62.1+/-8.4	<0.001
Resting Grad (mmHg)	70.6+/-40.3	11.0+/-10.5	<0.001
Provoked Grad (mmHg)	91.1+/-39.8	24.5+/-32.0	<0.001
MR grade	2.4+/-0.9	1.4+/-0.7	

Table 4: Comparison of pre and post-operative echocardiographic variables using a paired t test.

Table 5

	Overall (n=203)		SM Alone (n=159)		MV Intervention (n=44)	
	Preop	*Postop*	*Preop*	*Postop*	*Preop*	*Postop*
NYHA Class						
1	2.0%	47.4%	2.6%	45.7%	0%	53.8%
2	36.7%	48.6%	37.3%	50.0%	34.1%	43.6%
3/4	61.3%	4.0%	60.1%	4.3%	65.9%	2.6%
MR Grade						
0/1	14.2%	52.9%	17.3%	51.2%	2.4%	59.5%
2	42.4%	43.0%	44.7%	44.4%	34.1%	37.8%
3	31.9%	4.1%	29.3%	4.4%	41.5%	2.7%
4	11.5%	0%	8.7%	0%	22.0%	0%

Table 5: Comparison of individual NYHA Class and MR grade pre and postoperatively overall and in those undergoing SM alone and those undergoing a MV intervention.

References

1. Nishimura RA, Holmes DR. Hypertrophic obstructive cardiomyopathy. N Engl J Med 2004;350:1320-7

2. Elliott PM, Anastasakis A, Borger MA, Borggrefe M, Cecchi F, Charron P et al. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: the Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC). Eur Heart J 2014;35:2733-9

3. Maron BJ. Hypertrophic cardiomyopathy: a systematic review. JAMA. 2002 Mar 13;287(10):1308-20

4. Spirito P, Seidman CE, McKenna WJ, Maron BJ. The management of hypertrophic cardiomyopathy. N Engl J Med. 1997;336:775-85

5. Maron MS, Olivotto I, Harrigan C, Appelbaum E, Gibson CM, Lesser JR et al. Mitral valve abnormalities identified by cardiovascular magnetic resonance represent a primary phenotypic expression of hypertrophic cardiomyopathy. Circulation 2011;124:40-7

6. Iacovoni A, Spirito P, Simon C, Iascone M, Di Dedda G, De Filippo P et al. A contemporary European experience with surgical septal myectomy in hypertrophic cardiomyopathy. Eur Heart J. 2012;33:2080-7

7. Desai MY, Bhonsale A, Smedira NG, Naji P, Thamilarasan M, Lytle BW et al. Predictors of long-term outcomes in symptomatic hypertrophic obstructive cardiomyopathy patients undergoing surgical relief of left ventricular outflow tract obstruction. Circulation 2013;128:209-16

8. Liebregts M, Vriesendorp PA, Mahmoodi BK, Schinkel AF, Michels M, ten Berg JM. A Systematic Review and Meta-Analysis of Long-Term Outcomes After Septal Reduction Therapy in Patients With Hypertrophic Cardiomyopathy. JACC Heart Fail. 2015;3:896-905

9. Maron BJ, Dearani JA, Ommen SR, Maron MS, Schaff HV, Nishimura RA et al. Low Operative Mortality Achieved With Surgical Septal Myectomy: Role of Dedicated Hypertrophic Cardiomyopathy Centers in the Management of Dynamic Subaortic

Obstruction. J Am Coll Cardiol. 2015;66:1307-8

10. Ommen SR, Maron BJ, Olivotto I, Maron MS, Cecchi F, Betocchi S et al. Long-term effects of surgical septal myectomy on survival in patients with obstructive hypertrophic cardiomyopathy. J Am Coll Cardiol. 2005;46:470-6

11. Hong JH, Schaff HV, Nishimura RA Abel MD, Dearani JA, Li Z et al. Mitral Regurgitation in Patients With Hypertrophic Obstructive Cardiomyopathy: Implications for Concomitant Valve Procedures. J Am Coll Cardiol. 2016;68:1497-504

12. Woo A, Williams WG, Choi R, Wigle ED, Rozenblyum E, Fedwick K et al. Clinical and echocardiographic determinants of long-term survival after surgical myectomy in obstructive hypertrophic cardiomyopathy. Circulation. 2005;111:2033-41

13. Dearani JA, Ommen SR, Gersh BJ, Schaff HV, Danielson GK. Surgery Insight: septal myectomy for obstructive hypertrophic cardiomyopathy—the Mayo Clinic experience. Nat Clin Pract Cardiovasc Med. 2007;4:503-12

14. Morrow AG, Brockenbrough EC. Surgical Treatment of Idiopathic Hypertrophic Subaortic Stenosis: Technic and Hemodynamic Results of Subaortic Ventriculotomy. Ann Surg. 1961;154:181–9.

15. Collis R, Afoke J, McGregor CG. An acquired Gerbode defect from the left ventricle to the coronary sinus following mitral valve replacement. J Card Surg. 2017;32:361-3

16. Cooley DA, Leachman RD, Hallman GL, Gerami S, Hall RJ. Idiopathic hypertrophic subaortic stenosis. Surgical treatment including mitral valve replacement. Arch Surg. 1971;103:606-9

17. Patel P, Dhillon A, Popovic Z, Smedira NG, Rizzo J, Thamilarasan M et al. Left Ventricular Outflow Tract Obstruction in Hypertrophic Cardiomyopathy Patients Without Severe Septal Hypertrophy. Implications of Mitral Valve and Papillary Muscle Abnormalities Assessed Using Cardiac Magnetic Resonance and Echocardiography. Circ Cardiovasc Imaging. 2015;8(7)e003132

18. Ferrazzi P, Spirito P, Iacovoni A, Calabrese A, Migliorati K, Simon C et al. Transaortic Chordal Cutting: Mitral Valve Repair for Obstructive Hypertrophic Cardiomyopathy With

Mild Septal Hypertrophy. J Am Coll Cardiol. 2015;66:1687-96

19. Vriesendorp PA, Schinkel AF, Soliman OI, Kofflard MJ, de Jong PL, van Herwerden LA et al. Long-term benefit of myectomy and anterior mitral leaflet extension in obstructive hypertrophic cardiomyopathy. Am J Cardiol. 2015;115:670-5

20. Balaram SK, Ross RE, Sherrid MV, Schwartz GS, Hillel Z, Winson G et al. Role of mitral valve plication in the surgical management of hypertrophic cardiomyopathy. Ann Thorac Surg. 2012;94:1990-7

21. Bhudia SK, McCarthy PM, Smedira NG, Lam B, Rajeswaran J, Blackstone EH. Edge-to-edge (Alfieri) mitral repair: results in diverse clinical settings. Ann Thorac Surg. 2004;77:1598-606

22. Collis R, Watkinson O, Pantazis A, Tome-Esteban M, Elliott PM, McGregor CGA. Early and medium term outcomes of Alfieri mitral valve repair in the management of systolic anterior motion during septal myectomy. J Card Surg. 2017; Accepted for publication

23. Yun KL, Miller DC. Mitral valve repair versus replacement. Cardiol Clin. 1991;9:315-27

24. Krajcer Z, Leachman RD, Cooley DA, Coronado R. Septal myotomy-myomectomy versus mitral valve replacement in hypertrophic cardiomyopathy. Ten-year follow-up in 185 patients. Circulation. 1989;80:I57-64

25. McIntosh CL, Greenberg GJ, Maron BJ, Leon MB, Cannon RO 3rd, Clark RE. Clinical and hemodynamic results after mitral valve replacement in patients with obstructive hypertrophic cardiomyopathy. Ann Thorac Surg. 1989;47:236-46

26. Walker WS, Reid KG, Cameron EW, Walbaum PR, Kitchin AH. Comparison of ventricular septal surgery and mitral valve replacement for hypertrophic obstructive cardiomyopathy. Ann Thorac Surg. 1989;48:528-34

27. Kaple RK, Murphy RT, DiPaola LM, Houghtaling PL, Lever HM, Lytle BW et al. Mitral valve abnormalities in hypertrophic cardiomyopathy: echocardiographic features and surgical outcomes. Ann Thorac Surg. 2008;85:1527-35

28. Stassano P, Di Tommaso L, Triggiani D, Contaldo A, Gagliardi C, Spampinato N. Mitral valve replacement and limited myectomy for hypertrophic obstructive cardiomyopathy: a 25-year follow-up. Tex Heart Inst J 2004;31:137–42

29. Wan CK, Dearani JA, Sundt TM 3rd, Ommen SR, Schaff HV. What is the best surgical treatment for obstructive hypertrophic cardiomyopathy and degenerative mitral regurgitation? Ann Thorac Surg. 2009;88:727-31

30. Kim LK, Swaminathan RV, Looser P, Minutello RM, Wong SC, Bergman G et al. Hospital Volume Outcomes After Septal Myectomy and Alcohol Septal Ablation for Treatment of Obstructive Hypertrophic Cardiomyopathy: US Nationwide Inpatient Database, 2003-2011. JAMA 2016;1:324-32