Early and medium term outcomes of Alfieri mitral valve repair in the management of systolic anterior motion at septal myectomy

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Abstract

Background

This report studies the early and medium term clinical and echocardiographic outcomes of the Alfieri edge-to-edge mitral valve repair, as adjunctive therapy, to prevent and treat systolic anterior motion at time of septal myectomy for left ventricular outflow tract obstruction in hypertrophic cardiomyopathy.

Methods

From 2009-2015, 11 initial and consecutive patients had a trans-atrial Alfieri repair, to prevent (n=7) or treat (n=4) systolic anterior motion at the time of septal myectomy.

Results

No patients were lost to follow-up. There were no perioperative or late deaths. Pre-bypass, the mean left ventricular outflow tract gradient, measured directly by simultaneous needle insertion, was 40.7+/-19.9mmHg at rest and 115.8+/-30.4mmHg on provocation with Isoproterenol, which reduced after septal myectomy and Alfieri repair and discontinuation of bypass, to a mean gradient of 8.3+/-9.8mmHg at rest and 25.8+/-9.2mmHg on provocation. One patient who required mitral valve replacement on day 4, was hospitalised at 2.7 years with heart failure requiring diuresis and remains well at 6 years. One patient developed perioperative atrial fibrillation. There were no other early or late complications.

At a median follow-up of 6.6 years (IQR 1.2-7.4), clinical and echocardiographic data demonstrated maintained improvement in mean NYHA class from 2.6+/-0.9 preoperatively to 1.7+/-0.4 and reduction in mean grade of mitral regurgitation from 2.7+/-0.8 preoperatively to 0.7+/-0.6.

Conclusions

The Alfieri repair, as adjunctive therapy, for the prevention or treatment of systolic anterior motion at time of septal myectomy demonstrates satisfactory early and medium term clinical and echocardiographic outcomes supporting the ongoing utility of this approach.

Introduction

Septal myectomy (SM) is indicated in selected patients for the management of drug refractory symptomatic left ventricular outflow tract obstruction (LVOTO) in hypertrophic cardiomyopathy (HCM).[1] The mechanism of LVOTO involves both the left ventricular outflow tract (LVOT) and the mitral valve apparatus at various levels, especially when the anterior mitral valve leaflet is elongated.[2-4] Septal myectomy alone is adequate in the surgical management of LVOTO in the vast majority of patients with HCM.[5,6] Concomitant mitral valve repair at the time of SM can be used to prevent or treat post SM systolic anterior motion (SAM) related mitral regurgitation (MR) or residual unacceptably high LVOT gradients.[7-10] This approach to SAM which is required in a small minority of such patients can avoid mitral valve replacement (MVR) and its associated increased mortality and morbidity.[5,6,11,12] Previous studies using the “edge to edge” mitral repair technique described by Alfieri et al, have shown good outcomes in the correction of MR from diverse aetiologies such as degenerative, ischemic and functional.[13-17] This study investigates early and medium-term outcomes in a group of 11 consecutive patients undergoing an Alfieri mitral valve repair (AR) at the time of SM for the prevention and treatment of SAM.

Materials and Methods

A retrospective analysis was carried out in a cohort of patients with HCM who had a SM and AR for management of LVOTO by a single surgeon (CMcG). A diagnosis of HCM was defined as per international guidelines.[1] No patient had undergone previous management of LVOTO with surgery, alcohol septal ablation or dual chamber pacing. Preoperative clinical assessment was undertaken by a team of specialist HCM cardiologists in a national referral centre.

Patients

The study consisted of 11 initial and consecutive patients, 7 males, 4 females, having an AR as part of SM surgery for LVOTO with HCM from April 2009 to August 2015 out of a total of 123 SM patients operated on in that period. The mean age of the AR patients was 47.5+/-13.9 years. All patients preoperatively had drug refractory symptomatic LVOTO at rest (n=8) or on provocation with the Valsalva manoeuvre (n=3). Surgical strategy was individualised preoperatively, including a multidisciplinary team review of all imaging. In particular, the potential use of adjunctive AR was considered and discussed in patients with reduced septal thickness or those with intrinsic mitral valve abnormalities. The aim of the AR was to reduce anterior leaflet SAM by attachment to a normal or tethered posterior leaflet. Specific attention was made to posterior mitral leaflet length to avoid bileaflet anterior motion post AR. The indications for an AR in this series included; elongated anterior mitral valve leaflets (n=5), leaflet prolapse (n=2), significant residual SAM related MR or residual unacceptable LVOT gradients on provocation after SM on the discontinuation of cardiopulmonary bypass (n=4). Eight patients had concomitant surgery to suture close the orifice of the left atrial appendage and 1 had a MAZE procedure for atrial fibrillation (AF).

Assessment and Follow-up

Echocardiograms were assessed preoperatively, and postoperatively, at regular follow-up intervals, including annually. Provocation using Valsalva or exercise echocardiography was performed if clinically indicated. No patients were lost to follow-up. Perioperative complications were defined as those occurring during hospitalisation or within 30 days of surgery. Late complications were defined as those occurring after this period.

Surgical Assessment and Technique

Perioperative transoesophageal echocardiography (TOE) was performed. 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. The technique of SM is based on the Danielson modification of the classic Morrow Myectomy.[18] Following this if planned preoperatively, the AR was done trans left atrially in a standard fashion by approximating the central free edges of the A2 and P2 scallops of the mitral valve using a pledgeted 4-0 Goretex suture.[15,16] After cardiopulmonary bypass TOE was done to assess the LVOT and mitral valve function. In addition, direct simultaneous pressure measurements were repeated with and without provocation as done pre-bypass. Indications to resume bypass and perform an AR at this point were a significant residual gradient, and/or persistent SAM related MR. Mitral annuloplasty was avoided in all patients.

Statistical Analysis

Data was analysed using SPSS Version 24 (IBM, Chicago). Variables collected included baseline demographics, New York Heat Association (NYHA) clinical classification, echocardiographic parameters (MR grade, SAM, ejection fraction, LVOT gradients) and postoperative outcomes. Variables were expressed as a mean with standard deviation or median with interquartile range as appropriate. Comparisons were made using paired t-tests. A p-value of <0.05 was considered significant.

Results

There were no perioperative or late deaths. The median follow-up duration was 6.6 years (IQR 1.2-7.4). No patient was lost to follow-up. Septal tissue excised at myectomy weighed a mean of 4.3+/-3.6 grams. Intraoperatively, pre-bypass, the mean resting LVOT gradient was 40.7+/- 19.9mmHg and on provocation with Isoproterenol was 115.8+/-30.4mmHg. Following surgical resection and AR, the mean resting LVOT gradient reduced to 8.3+/-9.8mmHg and on provocation was 25.8+/-9.2mmHg. The mean hospital stay was 10+/-3 days. One patient required a MVR on day 4 postoperatively due to severe MR. This was a 46-year-old man who preoperatively had a right atrial pressure of 21mmHg, pulmonary pressures >60mmHg, severe concentric left ventricular hypertrophy, complete SAM and severe MR with a dilated left atrium. He firstly underwent an extended SM (10 grams of tissue removed), with a MAZE procedure and planned AR. Intraoperatively there was resolution of obstruction with no significant gradient on provocation. Postoperatively, over the following days, he required increasing inotropic support to maintain adequate circulation. Echocardiography revealed severe MR. A MVR, inserting a 33mm St Jude mechanical prosthesis, was performed on day 4. The papillary muscles were found to be thickened and fibrosed. The patient was discharged home well on day 12. He had 1 hospitalisation at 2.7 years for management of heart failure with diuresis, and continues to be symptomatically well on latest follow-up at 6 years. Another patient had a brief episode of AF perioperatively, successfully chemically cardioverted. One patient, a 73-year-old man, with preoperative first degree atrioventricular block and left bundle branch block had a planned prophylactic dual chamber pacemaker inserted postoperatively.

At 1 year follow-up, the mean NYHA class had improved from 2.6+/-0.9 preoperatively to 1.6+/-0.7 and on most recent follow-up (median 6.6 years) was 1.7+/-0.4. Nine of the 11 patients showed an improvement in NYHA functional class to NYHA Class I/II, while 2 patients remained in the same functional class (NYHA III). One of the 2 patients who remained in the same functional class, was diagnosed with lung and liver metastases of

unknown primary. He subsequently underwent chemotherapy with an ongoing good response. The other patient was a 64-year-old woman with multiple comorbidities limiting her functional capacity, including ongoing smoking, chronic obstructive pulmonary disease and severe osteoarthritis, subsequently having a knee replacement and who remains limited (NYHA III) at 7 years. There were no other late complications in the series.

Echocardiographically (Table 1), the mean interventricular septal wall thickness (IVS) reduced from 17.5+/-3.0mm preoperatively to 15.5+/-3.8mm at 1 year and 16.1+/-3.5mm at most recent follow-up (median 6.6 years). Changes in left atrial diameter (LAD) and left ventricular end diastolic dimensions (LVEDD) were not significant at 1 year or on most recent follow-up compared to preoperatively. The mean grade of MR improved from 2.7+/-0.8 preoperatively to 1.0+/-0.9 at 1 year, and 0.7+/-0.6 at most recent follow-up. The mean resting left ventricular outflow tract gradient reduced from 59.8+/-28.2mmHg preoperatively to 20.7+/-16.6mmHg at 1 year and 16.2+/-15.7 at most recent follow-up. All 11 patients had documented SAM on the preoperative echocardiogram. No patient had SAM on the postoperative echocardiogram at 1 year.

Discussion

Isolated septal myectomy is the only surgical procedure required in the vast majority of patients with LVOTO in HCM.[4,5] The incidence of SM with concomitant mitral valve repair in this study (11 of 123 overall SM cases) is consistent with the 7% reported recently in the largest study to date of over 2000 patients from the Mayo Clinic, also discussed subsequently in an editorial.[5,6] The type of mitral repair was not described in the Mayo study. A number of surgical techniques have been utilised on the mitral valve to eliminate SAM in the context of SM.[7-10] The optimal surgical strategy remains uncertain.[5] Systolic anterior

motion of the anterior mitral valve leaflet after SM can result in residual unacceptable levels of LVOTO and/or MR post procedure. As in the Mayo study, if further septal resection was judged inappropriate due to limited septal thickness, mitral valve repair was our preferred approach to reduce this residual LVOTO and/or MR whenever possible, and avoid the limitations of valve replacement.[5,11,12] Alfieri and colleagues introduced a technique in 1995 describing an edge to edge repair to approximate the central mitral valve edges creating a double orifice to alleviate MR.[15] This technique has been studied in larger cohorts undergoing surgery for primary MR with good long term outcomes.[13-17] Previous studies with long term follow up from AR showed rates of freedom from reoperation of 90% at 5 years and survival rates of 94% at 5 years.[16]

There are few papers describing AR in the context of LVOTO in HCM. These report short term results only with limited echocardiographic follow-up. In a subgroup of 14 patients who underwent AR without annuloplasty after SM at the Cleveland Clinic, two patients required subsequent MVR.[17] This study, using the trans aortic AR technique, reported an encouraging early experience of AR in HCM, but had limited follow up data compared to the longer clinical and echocardiographic follow-up in this current study. A further study by Shah et al, focused on perioperative complications following trans aortic AR in 24 patients with LVOTO in HCM with short, limited follow-up data with 1 early mortality from a ventricular septal defect (VSD).[19] Recently Obadia et al, report outcomes in 22 patients with trans aortic AR after SM with shorter follow-up and early echocardiographic data only.[20] The remainder of the literature consists of case reports.

Our data reports, for the first time, medium term clinical and echocardiographic outcomes of AR after SM in HCM with a median follow-up of 6.6 years. Interventricular septal wall thickness was reduced from 17.5+/-3.0 preoperatively to a mean of 15.5+/-3.8

postoperatively at 1 year. An AR was performed rather than further resection either because residual thickness was such that a further resection was regarded as high risk for VSD, or the patient had a known mitral leaflet abnormality. This partly reflects the varying clinical phenotype of patients in HCM, with less hypertrophy seen in the sub group of patients treated in this study compared to Obadia et al, who report a mean septal wall thickness preoperatively of 25mm.

As in the Cleveland series, a concomitant mitral annuloplasty, almost uniformly done at the time of general mitral repair including the AR, was avoided in this series of HCM patients, to avoid any propensity to worsening SAM.[17] The use or lack of use of mitral annuloplasty in the subset of patients with mitral valve repair after septal myectomy was not reported in the large Mayo series or by the studies from Shah et al and Obadia et al.[5, 19, 20] The avoidance of annuloplasty has not compromised the results of AR in the current series at medium term follow-up.

The relative merits of trans atrial AR, done in this study, versus trans aortic AR remain to be clarified by larger series with longer follow up. In the context of LVOTO and HCM there is limited experience with the trans aortic approach.[17,19, 20] Literature on the AR for other aetiologies of MR has principally used the trans atrial approach which was utilised in this cohort.

The favourable early and medium term clinical and echocardiographic outcomes in the current study demonstrate the benefit of trans atrial AR for the prevention or treatment of SAM at the time of SM in the management of LVOTO. In the current study, functional outcomes, assessed using NYHA classification, were comparable to a recent meta-analysis looking at long term follow-up in general septal reduction therapy.[21] There was no early or

late mortality, few early or late complications and good symptomatic and echocardiographic outcomes.

Limitations

This paper represents a small, single centre, single surgeon, retrospective experience. The sample size is small, so that conclusions must be guarded, but appears to be the largest study to date looking at more medium term as well as early, clinical and echocardiographic outcomes of the AR for the treatment of SAM post SM in HCM. The absence of measured, documented mitral valve morphometry is a weakness in this, as in most relevant studies.

Conclusions

This study of good early and medium term, clinical and echocardiographic outcomes in 11 consecutive patients using trans atrial AR without annuloplasty, as adjunctive therapy, for the prevention or treatment of SAM at the time of SM in the management of LVOTO in HCM supports further study of the ongoing utility of this approach to address a sometimes difficult surgical challenge.

Contributions

Contributors RC and CMG conceived and designed the research. RC, OW, MTE acquired the data. RC analysed, interpreted and performed statistical analysis of the data. RC drafted the manuscript. RC, OW, AP, MTE, PME and CMG made critical revision of the manuscript for important intellectual content.

Conflicts of interest

None declared.

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Table 1

	Preoperatively	1 Year (n=11)	P Value (Comparison at 1 year and preoperatively	Most recent follow-up (n=11)	P Value (Comparison on most recent follow-up and preoperatively)
Interventricular Septal Thickness (mm)	17.5+/-3.0	15.5+/-3.8	<0.05	16.1+/-3.5	0.07
Posterior Wall Thickness (mm)	9.6+/-2.1	9.7+/-0.9	0.77	11.1+/-2.3	0.22
Left Atrial Diameter (mm)	46.6+/-8.7	47.7+/-8.1	0.89	44.3+/-8.8	0.23
Left Ventricular End Diastolic Diameter (mm)	45.5+/-4.9	45.4+/-5.4	0.88	43.5+/-6.5	0.41
Ejection Fraction (%)	72.0+/-9.8	64.4+/-9.9	0.59	62.2+/-6.2	<0.05
Resting Left Ventricular Outflow Tract Gradient (mmHg)	59.8+/-28.2	20.7+/-16.6	<0.05	16.2+/-15.7	<0.05
Mitral Regurgitation	2.7+/-0.8	1.0+/-0.9		0.7+/-0.6	

Table 1: Mean echocardiographic variables with pre and post-operatively comparisons using paired t-tests (significance, $p<0.05$)