Long Term Outcomes For Different Surgical Strategies To Treat Left Ventricular Outflow Tract Obstruction

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Abstract

Aims:

Surgical intervention can treat dynamic left ventricular outflow tract obstruction (LVOTO) in hypertrophic cardiomyopathy (HCM). This study assesses the impact of different surgical strategies on long-term mortality and morbidity.

Methods and Results:

347 patients underwent surgical intervention for LVOTO (1988-2015). Group A (n=272) underwent septal myectomy; Group B (n=33), septal myectomy and mitral valve (MV) repair; Group C (n=22), myectomy and MV replacement and Group D (n=20), MV replacement alone. Median follow-up was 5.2 years (IQR 1.9 – 7.9 years).

The mean resting LVOT gradient improved postoperatively from 71.9+/-39.6mmHg to 13.4+/18.5mmHg ($p<0.05$). Overall, 75% of patients improved by >1 NYHA class. 61% of patients undergoing a MV replacement alone did not improve NYHA class. Complications included (>30 days'); atrial fibrillation (29.6%), TIA/stroke (2.4%), heart failure hospitalisation (3.2%) with 16 repeat surgical interventions (3.0 years (IQR 0.3 – 5.0 years).

There were 5 perioperative deaths and 20 late deaths (>30 days'). Survival rates at 1, 5 and 10 years respectively were 98.4%, 96.9%, 91.9% in group A; 97.0%, 92.4%, 61.6% in group B; 100.0%, 100.0%, 55.6% in group C; and 94.7%, 85.3%, 85.3% in group D ($p<0.05$).

Conclusion:

Septal myectomy is a safe procedure resulting in symptomatic improvement in the majority of patients. Ongoing clinical surveillance and medical therapy is required following surgery. MV replacement in patients with LVOTO is less successful in improving symptoms, with patients having a different phenotype to the majority undergoing surgical treatment for LVOTO.

Keywords: Hypertrophic Cardiomyopathy, Septal Myectomy, Left Ventricular Outflow Tract Obstruction

Abbreviations & Acronyms: hypertrophic cardiomyopathy (HCM), left ventricular outflow tract obstruction (LVOTO), mitral valve (MV), atrial fibrillation (AF), ventricular septal defect (VSD), permanent pacemaker (PPM), coronary artery bypass graft (CABG), aortic valve replacement (AVR), MAZE

Introduction

Hypertrophic cardiomyopathy (HCM) is a common myocardial disorder, usually inherited as an autosomal dominant trait, that causes premature death from heart failure (HF), stroke and ventricular arrhythmia.[1-6] Many patients experience debilitating symptoms due to obstruction of the left ventricular outflow tract caused by contact between the mitral valve (MV) leaflet(s) and the interventricular septum during ventricular systole. Factors predisposing to this abnormal movement of the valve include altered septal geometry, elongation of the mitral leaflets and malpositioning of the papillary muscles and mitral chordae.[7-12] Left ventricular outflow tract obstruction (LVOTO) typically increases with reductions in preload, afterload and ventricular contractility and so negatively inotropic drugs such as ß-blockers, calcium antagonists and disopyramide are used as first line therapy in symptomatic patients.[4] However, some patients continue to experience symptoms despite medical therapy and may be candidates for surgical interventions that reduce the thickness of the interventricular septum or alter the MV or submitral apparatus.

Many studies have shown that septal myectomy (SM) in which the thickness of the basal septum is reduced by removal of muscle via an aortic approach results in relief of obstruction and good long-term outcomes.[13-19] In patients with marked mitral leaflet elongation, SM has been combined with one of several adjunctive procedures including MV replacement and MV repair.[20-24] However, there are few data on their safety and long-term benefit compared to SM alone.

The aim in this retrospective analysis, is to compare and contrast the short and long-term outcomes in patients undergoing a range of different surgical approaches for the relief of LVOTO.

Methods

Study Design

This is an observational cohort study comprising all patients with HCM undergoing surgical treatment for LVOTO and followed up at a specialist cardiomyopathy clinic located sequentially at St George's Hospital (1988-2003), The Heart Hospital, University College London (2003-2015) and St Bartholomew's Hospital (2015-present). The majority of patients were operated on by three surgeons (CMcG, VT, VC). HCM was defined as a wall thickness ≥15mm in any left ventricular myocardial segment in the absence of other abnormal loading conditions.[2] Patients operated on for aortic valve (AV) replacement surgery and limited myectomy were removed if the underlying pathology was severe aortic stenosis. Patients were included if at least one year follow up data were available.

Clinical Assessment

All patients were assessed in a specialist clinic with baseline and follow-up clinical data and their data were stored on a relational database. Background history was documented including previous arrhythmia or cardiovascular complications. Atrial Fibrillation (AF) and Ventricular Tachycardia (VT) as documented on ECG or prolonged ECG monitoring were recorded as well as family history of HCM or sudden cardiac death (SCD). These definitions were consistent with previous studies.[5,6] Clinical assessment included documentation of New York Heart Association (NYHA) class, a 12-lead electrocardiogram and a transthoracic echocardiogram. Maximum left ventricular wall thickness (MWT), left ventricular ejection fraction (LVEF) by visual assessment, left atrial dimensions and LVOT pressure gradients at rest and with Valsalva provocation were documented. Exercise stress echocardiography using a bicycle ergometer was performed on clinical grounds to evaluate a provoked gradient when no resting LVOT gradient was documented. Cardiopulmonary Exercise Testing (CPET) was carried out using a bicycle ergometer in accordance with published methods.[6] Peak oxygen consumption, percentage target heart rate achieved, systolic and diastolic blood pressure response to exercise were documented. Prior to surgery, patients were presented at a joint

cardiothoracic conference to a team of cardiac surgeons and cardiologists specialising in inherited cardiovascular disease to determine the most suitable management plan.

Follow-Up

Following surgical intervention, patients were assessed post operatively by surgical and medical teams at six weeks and then at regular intervals based on their clinical condition. For the purposes of this analysis, clinical data were reviewed from follow-up clinics at 1, 5 and 10 years post operatively. Perioperative complications and death were defined as events occurring during a perioperative stay or within the first 30 days postoperatively. Long term outcomes (occurring at least 30 days after surgical intervention) used in the analysis were: stroke or transient ischaemic attacks, new onset AF, permanent pacemaker (PPM) implantation and HF hospitalisations, defined as an acute admission to hospital with shortness of breath and/or fluid overload requiring treatment with intravenous diuretics.

Study End-Points

The primary survival endpoint was all cause mortality. Secondary end-points were cardiovascular death, SCD, aborted SCD and heart transplantation. Cardiovascular death was defined as death secondary to SCD, stroke or HF. SCD was defined as witnessed sudden death within 1 hour of the onset of new symptoms or nocturnal deaths with no recent history of worsening symptoms. Aborted SCD was defined as successful defibrillation with spontaneous restoration of circulation. This included ICD shocks due to ventricular arrhythmias. HF death was defined as death preceded by signs and symptoms of HF of >1 hour duration or cardiogenic shock. These definitions were consistent with previous studies.[5,6]

Statistical Analysis

Continuous variables are expressed as mean ± standard deviation or as median with interquartile range based on distribution of data. Tests of normality were carried out using the Shapiro-Wilk test. Comparisons were made with the use of the Student *t* test, Mann–Whitney test, ANOVA and Kruskal–Wallis test based on normality of the data. Statistical analysis was performed using SPSS version 24 (SPSS Inc, Chicago, IL). A *P* value of <0.05 was considered significant. Primary and secondary end-points were assessed as above and cumulative probability of an end-point were analysed using the Kaplan-Meier method.

Results

Patient characteristics

347 patients (217 males) undergoing surgery between 1988 and 2015 were included in the study. The median age at diagnosis of HCM was 39.7 ± 17.6 years and age at time of surgery was 47.0 ± 16.7 years. Prior to surgery, 23 patients had undergone dual chamber pacemaker insertion to treat LVOTO and 15 had undergone alcohol septal ablation with no improvement in symptoms.

Patients were divided into groups based on their surgical intervention: Group A (n=272) SM alone; group B (n=33) SM with MV repair; group C (n=22) SM with MV replacement; and group D (n=20) MV replacement alone. MV repair procedures included intervention on papillary or chordal attachments, valve leaflet plication, Alfieri and cleft repair of the MV leaflets.

The characteristics of each surgical group are summarised in *table 1*. Patients in group D were older at diagnosis and at the time of surgery had a higher prevalence of hypertension and AF. The mean left ventricular wall thickness prior to surgery was smallest in group D, with 11 of 20 patients having a MLVWT less than 17.0 mm. Mitral regurgitation was more severe in those undergoing a MV procedure, particularly in those requiring a MV replacement (table 2, *supplemental data*). All patients in group D had a planned MV replacement. In group C, 13 of the MV replacements were unplanned and were carried out at the time of intervention due to persistence of MR despite SM and/or MV repair.

Perioperative course for each surgical subgroup

There were five perioperative deaths (3 in Group A, 1 in Group B, 0 in Group C and 1 in Group D). The mean by-pass time was 93.3+/-47.2mins overall and 81.9+/-41.1mins, 121.8+/-35.0mins, 157.1+/-21.6mins, 124.3+/-37.5mins respectively in Groups A to D. 121 concomitant procedures were carried out including 18 coronary artery bypass grafts, 10 AV replacements, 11 maze procedures (9 radiofrequency pulmonary vein isolation), 55 left atrial appendage removal and 21 other minor procedures. The mean length of hospital stay was 11.3 days (9.5, 11.7, 17.2, 18.8 days respectively for groups A to D).

Perioperative complications are documented in *table 2*. There were 4 ventricular septal defects (VSD) requiring repair, all of which were in Group A with LVMWT of 15mm, 16mm, 18mm, 21mm respectively. There was 1 LV rupture of the lateral wall which was repaired successfully at the time of SM. There were two unplanned AV repairs due to aortic valve injury during surgery. All remaining AV procedures were carried out for pre-existing aortic regurgitation.

There were 8 perioperative strokes and 5 transient ischaemic attacks (TIAs). Of these 13 cases, 4 had previously documented AF and 4 had new onset AF. Five patients had no documented AF. One patient had an air embolus and one patient had a deep vein thrombosis with an associated patent foramen ovale and paradoxical embolism. Pre-operatively the mean left atrial diameter in patients who suffered a perioperative CVA was 50.5+/-13.7mm with a mean left atrial area of 41.5+/-19.1cm^2.

Twenty-four patients required a perioperative PPM insertion for high grade atrio-ventricular heart block. Nine patients had an implantable cardioverter defibrillator (ICD) inserted for primary prevention in the perioperative period and 1 patient for secondary prevention of aborted SCD following an in hospital cardiac arrest with successful defibrillation.

Symptoms following surgery

In the cohort as a whole, 95.1% of patients described symptoms of dyspnoea preoperatively. NYHA functional class improved from a mean of 2.5+/- 0.6 to 1.6+/-0.6 at one year. Overall, 75% of patients in the entire cohort described an improvement in symptoms with an improvement in NYHA class of at least one class. The change in NYHA class varied between the surgical subgroups (*figure 1*) with the greatest change in group B (mean 1.2+/-0.7) followed by Group A (0.9+/-0.7), Group C (0.8+/-0.7) and Group D (0.4+/-0.7), p=0.08). In Group D, NYHA class remained unimproved at 1 year in 62.0% of patients compared to 27.5% in Group A. Clinical response, $\geq$1 NYHA class was compared to those who did not improve postoperatively as illustrated in *figure 1*.

Symptoms other than dyspnoea are described in *table 1, supplemental data*. Preoperatively 162 patients (46.2%) described symptoms of exertional chest pain; 114 patients (32.8%) and 46 patients (13.3%) described symptoms of presyncope and syncope, respectively; and with 122 patients (35.2%) complained of palpitations. On follow up at one year, 50 patients (14.4%) described exertional chest pain; 27 patients (7.8%) had symptoms of presyncope and 8 (2.3%) patients had further episodes of syncope; 51 patients (14.7%) described symptoms of palpitations.

Changes in echocardiographic parameters at 1 Year

The mean resting gradient improved from 71.9+/-39.6mmHg preoperatively to 13.4+/-18.5mmHg postoperatively ($p<0.05$). This gradient improved significantly in all groups. There was a similar reduction in LVMWT in all groups except Group D with a significant difference on analysis between groups ($p<0.05$). This was similar for septal wall thickness. LVEDd increased in group A and B but was seen to reduce in in those undergoing MV replacement in group C and D. EF reduced in those undergoing myectomy and increased in group D. Changes in echocardiographic variables are documented in *table 2, supplemental data.*

Changes in functional status using cardiopulmonary exercise testing

There was no change in per cent predicted or absolute peak VO_2 following surgery. There was an improvement in percent predicted target heart 0.70 to 0.74 ($p<0.05$) and in systolic blood pressure response to exercise (32.4mmHg to 38.7mmHg ($p<0.05$)). Although full CPEX data was not available in those undergoing a MV replacement there appeared to be a poorer response in both groups C and D which show a reduction in predicted VO2, target heart rate and systolic blood pressure response postoperatively (*table 3, supplemental data)*.

Long Term Outcomes

Median follow up was 5.2 years (IQR 1.9 – 7.9 years). 191 patients continue to be followed up at St. Bartholomew's Hospital and 122 patients are followed by local physicians. 9 patients were lost to follow up.

Mortality

Excluding perioperative deaths, there were 20 deaths during follow up (15 in Group A, 2 in Group B, 2 in Group C, and 1 in Group D). There were 5 cardiovascular deaths, 1 from SCD, 3 from HF and 1 from a stroke. There were 7 non-cardiac deaths and 8 who died of unknown causes.

Estimated survival rates for all-cause mortality post-operatively at 1, 5 and 10 years respectively were 98.4%, 96.9%, 91.9% in group A; 97.0%, 92.4%, 61.6% in group B; 100.0%, 100.0%, 55.6% in group C; and 94.7%, 85.3%, 85.3% in group D ($p<0.05$). Estimated survival rates including appropriate ICD shock therapy at 1, 5 and 10 years were 98.4%, 96.9%, 91.1% in group A; 97.0%, 92.4%, 61.6% in group B; 100.0%, 100.0%, 55.6% in group C; and 94.7%, 85.3%, 85.3% in the group D ($p<0.05$).

Morbidity

At follow up, 72 patients (20.7%) had documented paroxysmal AF and 31 patients (8.9%) persistent AF. There were 4 TIAs and 4 strokes, three of which were presumed cardioembolic as seen in *table 3*. The mean left atrial diameter was 51.5+/-8.0mm postoperatively in this subgroup.

Nine patients (2.6%) received a PPM and 45 patients (13.0%) an ICD. All ICDs were inserted for primary prophylaxis purposes on late follow up. Nine of these 45 patients undergoing ICD insertion had CRT-D devices. There were 10 CRT-P devices inserted on follow-up. In total 99 patients had an ICD in situ postoperatively which was either inserted before or after the operation; there were 3 appropriate ICD shocks for VT/VF and 5 inappropriate shocks during the follow up period.

The median time to first HF hospitalisation was 5.2 years (IQR 0.9 -6.4 years). Sixteen patients underwent a second surgical procedure with a median time to reintervention of 3.0 years (IQR 0.3 – 5 years): 7 re-do myectomies, 8 MV replacements, 1 MV repair and 3 AV replacements.

Discussion

Most studies of SM in HCM have focused on long-term mortality rather than morbidity.[14,18,25] `The novel finding in this study is that in spite of low procedural and long term death rates, the incidence of non-fatal disease related complications after surgical treatment of LVOTO is relatively high during follow-up, illustrating the need for ongoing clinical surveillance and medical therapy. We also identify an older cohort of patients that have LVOTO associated with milder hypertrophy but severe mitral regurgitation who respond less well to intervention.

Single centre studies and meta-analyses show that SM is an effective procedure with a low mortality rate in high volume specialist centres, but relatively few studies have reported on the outcomes of MV surgery in patients with HCM.[26, 27] The findings in the present study are broadly in line with the published literature in that a reduction in resting LVOTO to less than 30 mmHg was achieved in more than 90% of patients undergoing SM alone with an operative mortality and an annual all-cause approximately 1%. The change in symptoms, as measured by NYHA class was also similar to published data in that 75% of patients reported an improvement.[27] Patients undergoing SM and MV

repair had similar outcomes to those treated with SM alone, but those receiving MV replacements had poorer outcomes with less symptomatic benefit in spite of a similar reduction in LVOT gradients. These findings suggest that patients with LVOTO and other indications for mitral surgery need to be carefully selected for intervention and that further study is required to optimize surgical strategies in this group.

Mitral valve replacement as a primary therapy for LVOTO was first advocated in the 1970s, but subsequent studies reported higher rates of perioperative and late mortality compared to SM alone.[28-30] Nevertheless, MV abnormalities that contribute to LVOTO are common in patients with HCM and as result, numerous valve sparing repair procedures have been explored. In the present study, MV replacement was considered the most appropriate management in a minority of patients. Although numbers are small in group D, patients undergoing MV replacement for LVOTO had higher perioperative mortality and stroke rates compared to patients undergoing SM alone and nearly two thirds had no improvement in NYHA class at one year. However, individuals undergoing MV replacement were significantly older and had more comorbidities including AF and hypertension. Their cardiac morphology also differed in that they had less hypertrophy, greater MR and larger left atria. Together these findings suggest that the patients undergoing MV replacement had a more severe cardiac phenotype than those undergoing SM alone and that this may account for their poorer surgical outcomes.

Very few studies have investigated changes in exercise performance after surgical treatment for LVOTO. In the sub-set of patients that underwent CPET before and after surgery there was an improvement in systolic blood pressure response but no change in peak oxygen consumption. The lack of improvement in pVO2 seems counterintuitive given the improvement in NYHA class reported by most patients, but it probably reflects the complex mechanism of exercise limitation in HCM. For example, it is possible that the relief of SAM related MR and exercise induced myocardial ischaemia could result in symptomatic improvement without an increase in LV stroke volume sufficient to increase peak oxygen consumption. Similarly, the increase in exercise blood pressure might reflect changes in centrally mediated vascular behaviour during exercise rather than an increase in cardiac

output. Whatever the explanation, these findings suggest that peak oxygen consumption may be an unreliable indicator of the success of surgical intervention for LVOTO.

Conclusions

Septal myectomy for LVOTO is a safe procedure in high volume centres and results in symptomatic improvement in the majority of patients. Ongoing clinical surveillance and medical therapy is still required following surgery as disease related complications such as AF are common following successful surgical treatment of LVOTO. Mitral valve replacement in patients with LVOTO is associated with higher mortality and morbidity and is less successful in improving symptoms, but the characteristics of patients requiring MV replacement suggest that this group is at higher pre-operative risk and has a different phenotype to the majority of patients undergoing surgical treatment for LVOTO.

Contributions

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

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This study conforms to the principles of the declaration of Helsinki.

There are no conflicts of interest.

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Figure Legends

Figure 1: Percentage of NYHA responders Vs non-responders.

Figure 2: Kaplan- Meier curves for survival analysis in the surgical groups at 10 year follow up.

(a): K-M Overall survival analysis

(b): K-M survival analysis by groups

(c):K-M analysis for appropriate ICD shock or death

Tables

	Total	***Group A***	***Group B***	***Group C***	***Group D***
N	347	272 (78.4%)	33 (9.5%)	22 (6.3%)	20 (5.8%)
Demographics					
Male	217 (62.5%)	171 (62.9%)	23 (69.7%)	13 (59.1%)	10 (50%)
Age at Diagnosis (years)	39.7+/-17.6	38.0+/-17.4	42.3+/-16.1	49.4+/-17.0	51.5+/-17.7
Age at Surgery (years)	47.0+/-16.7	44.9+/-16.0	48.6+/-16.8	55.8+/-15.1	62.4+/-16.1
BMI (units)	28.6+/-5.1	28.8+/-5.4	27.1+/-3.2	29.5+/-4.7	26.9+/-4.1
Past Medical History					
Prior history of AF	44 (12.7%)	27 (9.9%)	6 (18.2%)	4 (18.2%)	7 (35.0%)
History of any VT	16 (4.6%)	13 (4.8%)	2 (6.1%)	0 (0%)	1 (5.0%)
History of Ventricular Fibrillation	4 (1.2%)	3 (1.1%)	1 (3.0%)	0 (0%)	0 (0%)
Hypertension	83 (23.9%)	60 (22.1%)	7 (21.2%)	10 (45.5%)	6 (30.0%)
Diabetes Mellitus	12 (3.5%)	9 (3.3%)	1 (3.0%)	1 (4.5%)	1 (5.0%)
TIA/Stroke	7 (2.0%)	5 (1.8%)	1 (3.0%)	0 (0%)	1 (5.0%)
Coronary Artery Disease	12 (3.5%)	10 (3.7%)	1 (3.1%)	1 (4.5%)	0 (0%)

Peripheral Vascular Disease	1 (0.3%)	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)
PPM	29 (8.4)	20 (7.4%)	2 (6.1%)	3 (13.6%)	4 (20.0%)
ICD	44 (12.7%)	38 (14.0%)	3 (9.1%)	2 (9.1%)	1 (5.0%)
Family History					
HCM	103 (29.7%)	86 (31.6%)	10 (30.3%)	4 (18.2%)	3 (15.0%)
SCD	63 (18.2%)	51 (18.8%)	7 (21.2%)	4 (18.2%)	1 (5.0%)
HCM with SCD	31 (8.9%)	26 (9.6%)	4 (18.2%)	2 (9.1%)	1 (5.0%)

Table 1: Demographic of surgical population

	Total	***Group A***	***Group B***	***Group C***	***Group D***
Death	5 (1.4%)	3 (1.1%)	1 (3.0%)	0 (0%)	1 (5.0%)
VSD	4 (1.2%)	4 (1.5%)	0 (0%)	0 (0%)	0 (0%)
LV Rupture	1 (0.3%)	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)
Unplanned AV Surgery	2 (0.6%)	2 (0.7%)	0 (0%)	0 (0%)	0 (0%)
Postop AF	84 (24.2%)	56 (20.6%)	9 (27.3%)	9 (40.9%)	10 (50.0%)
New Postop AF	56 (16.1%)	42 (15.4%)	5 (15.2%)	5 (22.7%)	4 (20.0%)
TIA	5 (1.4%)	4 (1.5%)	0 (0%)	1 (4.5%)	0 (0%)

Stroke	8 (2.3%)	6 (2.2%)	0 (0%)	0 (0%)	2 (10.0%)
PPM	24 (6.9%)	21 (7.7%)	2 (6.1%)	0 (0%)	1 (5.0%)
ICD	10 (2.9%)	8 (2.9%)	1 (3.0%)	1 (4.5%)	0 (0%)

Table 2: Perioperative complications

	Total	***Group A***	***Group B***	***Group C***	***Group D***
Paroxysmal AF	72 (20.7%)	51 (18.8%)	9 (27.3%)	4 (18.2%)	8 (40.0%)
Persistent AF	31 (8.9%)	22 (8.1%)	2 (6.1%)	3 (13.6%)	4 (20.0%)
Postop TIA	4 (1.2%)	1 (0.4%)	1 (3.0%)	2 (9.1%)	0 (0%)
Postop Stroke	4 (1.2%)	3 (1.1%)	0 (0%)	0 (0%)	1 (5.0%)
Late PPM	9 (2.6%)	6 (2.2%)	0 (0%)	2 (9.1%)	1 (5.0%)
Late ICD	45 (13.0%)	40 (14.7%)	3 (9.1%)	2 (9.1%)	0 (0%)
Late CRT	19 (5.5%)	18 (6.6%)	1 (3.0%)	0 (0%)	0 (0%)
HF Admission	11 (3.2%)	8 (2.9%)	1 (3.0%)	2 (9.1%)	0 (0%)
Reintervention	16 (4.6%)	14 (4.9%)	2 (6.3%)	1 (4.5%)	1 (5.0%)
Redo Myectomy	7 (2.0%)	6 (2.2%)	0 (0%)	0 (0%)	1 (5.0%)
Redo MVR	8 (2.3%)	5 (1.8%)	2 (6.1%)	1 (4.5%)	0 (0%)

Redo MV Repair	1 (0.3%)	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)
Redo AVR	3 (0.9%)	3 (1.1%)	0 (0%)	0 (0%)	0 (0%)
Transplant	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Death	20 (5.8%)	15 (5.5%)	2 (6.1%)	2 (9.1%)	1 (5.0%)

Table 3: Long-term outcomes following surgical intervention.

Figures

Figure 1:

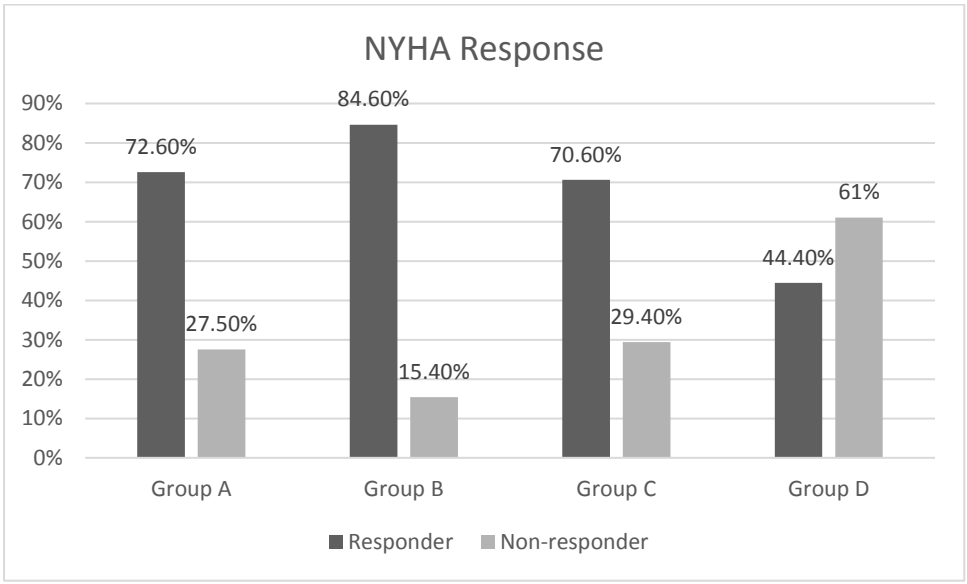
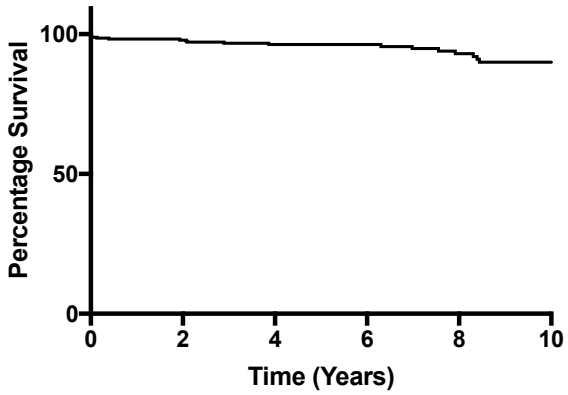
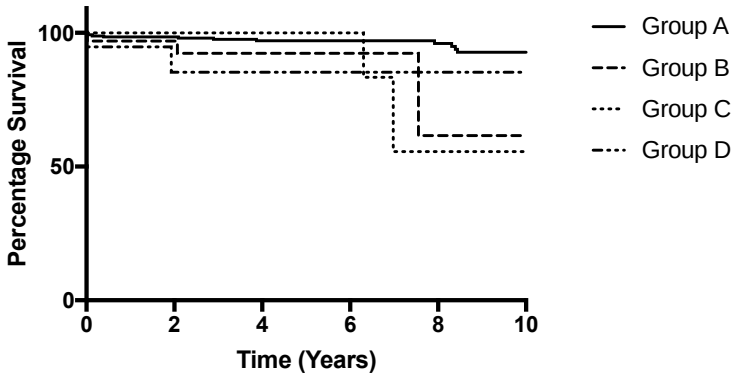


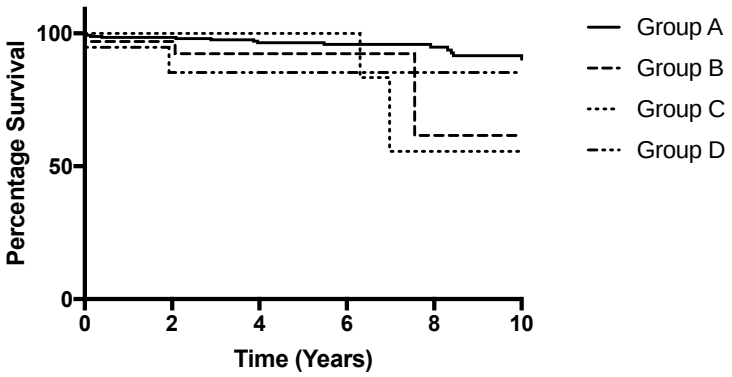
Figure 2:


Percentage Survival
100
50
0
0
2
4
6
8
10
Time (Years)

(a)


Percentage Survival
100
50
0
0
2
4
6
8
10
Time (Years)
Group A
Group B
Group C
Group D

(b)


Percentage Survival
100
50
0
0
2
4
6
8
10
Time (Years)
Group A
Group B
Group C
Group D

(c)