Title: Outcomes Following the Surgical Management of Left Ventricular Outflow Tract Obstruction; A Systematic Review and Meta-Analysis

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Abstract

Background

Left ventricular outflow tract obstruction (LVOTO) causes exertional symptoms in two thirds of patients with hypertrophic cardiomyopathy (HCM). Consensus guidelines recommend surgical intervention in patients with drug refractory symptoms. The primary aim of this study was to perform a systematic review and meta-analysis to determine morbidity and mortality after surgery.

Methods

Study Selection: Studies reporting outcomes following surgical intervention for symptomatic LVOTO in HCM.

Data Extraction: Articles from searching two scientific databases (PubMed and Web of Science) were reviewed and data were extracted by two investigators. Meta-analysis of data was performed with heterogeneity assessed using I^2 statistic.

Results

85 studies were included in the systematic review and 35 studies in the meta-analysis. Contemporary early (<30 days) and late (>30 days) mortality following septal myectomy were 1.4% (CI 0.8, 2.4) I^2 9.0%, p=0.36 and 0.7% (CI 0.3, 1.2) I^2 70.7%, p<0.05 respectively. Sixty-eight studies (80%) reported perioperative complications. The contemporary rate of a perioperative ventricular septal defect was 1.4% (0.8, 2.3) I^2 0%, p<0.05. Late morbidities including atrial fibrillation, stroke, heart failure and transplant were reported in fewer than 22% of studies and few studies compared mortality and clinical outcomes using different surgical approaches to LVOTO. The incidence rate (IR) of reintervention with a further surgical procedure was 0.3% (CI 0.2, 0.4) I^2 52.5%, p<0.05.

Conclusions

Contemporary surgical management of LVOTO is associated with low operative mortality rates but further studies are needed to investigate the impact of surgical therapy on non-fatal early and late complications.

Key Words: Septal Myectomy; Mitral Valve; Left Ventricular Outflow Tract Obstruction; Hypertrophic Cardiomyopathy

Introduction

Left ventricular outflow tract obstruction (LVOTO) caused by contact between the mitral valve (MV) leaflets and the interventricular septum during ventricular ejection occurs in up to two thirds of patients with hypertrophic cardiomyopathy (HCM).[1-4] In many patients, LVOTO results in disabling symptoms and predisposes to atrial and ventricular arrhythmia.[5,6] Pharmacological therapy with beta-blockers, non-dihydropyridine calcium channel antagonists and disopyramide are first-line treatment for symptomatic LVOTO but a proportion of patients are refractory to drug therapy.[7] In such cases, clinical practice guidelines recommend invasive interventions that either reduce the thickness of the interventricular septum or involve repair or replacement of the MV.[8] This advice is based largely on the experience of single centres and meta-analyses that analysed fewer than 16 papers each.[9-11] In this study we performed a systematic review and meta-analysis of the entire literature on surgical therapy of LVOTO. The aims were to determine early and late trends in surgical morbidity and mortality.

Methods

A systematic review of the literature and meta-analysis was carried out in accordance with the PRISMA statement.[12]

Systematic Review

A systematic literature search was performed using the search terms “myectomy”, “myotomy”, “myomectomy”, “hypertrophic cardiomyopathy”, “idiopathic hypertrophic subaortic stenosis”, “mitral valve replacement”, “mitral valve repair” “outcome”, “prognosis”, “mortality” using two databases (PubMed and Web of Science). Search terms were applied to titles and abstracts and the search was restricted to observational studies, clinical trials, comparative studies, controlled clinical trials, meta-analyses, randomised controlled trials, systematic reviews, journal articles, full texts, humans, and English language.

Original articles were reviewed and selected by two independent reviewers (RC, OW) to determine eligibility for the study. The search criteria were not limited to the date of publication. Case reports, editorials, systematic reviews and previous meta-analyses were removed. Articles unrelated to the topic along with those without a documented mortality rate were removed and database searches were corrected for duplicates. The reference lists of selected papers were scrutinised for additional eligible papers. The last search was carried out on 11/11/2015.

Variables extracted from each study included age, sex, date of study, date of publication, study location, New York Heart Association (NYHA) class, left ventricular outflow tract (LVOT) gradient, perioperative mortality, late mortality, cardiovascular mortality, rates of ventricular septal defect (VSD), stroke, permanent pacemaker (PPM) insertion and surgical re-intervention including myectomy, MV repair and replacement. Where reported, echocardiographic parameters including left ventricular (LV) ejection fraction, LV end diastolic diameter, maximum LV wall thickness, left atrial diameter and LVOT gradients were collected.

Early complications were defined as those occurring within the first 30 days post-operatively or during a post-operative stay. Long-term outcomes were defined as those occurring after this period. Sudden cardiac death and cardiovascular deaths were defined as per individual studies.

Meta-analysis

Studies reporting prevalence data for different types of mortality were included in the meta-analysis. Not all studies provided standard error (SE) of the prevalence and so SE was calculated using the prevalence data and sample size in each study and the same formula commonly used for binomial proportion.[13] Assuming that the estimated values for prevalence follow a normal distribution for large number of studies, we calculated 95% confidence intervals (CI) for population prevalence. The incidence rate for each study was calculated using the number of new cases and median follow-up time provided by the study. SE of incidence rate was calculated assuming Poisson distribution of number of new cases. A random effect meta-regression model was then used to combine both the prevalence and incidence data and to obtain the pooled (overall) prevalence and incidence for different types of mortality separately. The overall prevalence (or incidence) rate was the weighted average of the prevalence (or incidence) across different studies, where weights were calculated using measures of precision (inverse of the variance of the prevalence). Intra- and inter-study variances were used in the calculation of precision. The intra-study variance was the variance of the prevalence (incidence) obtained as above (square of SE) for each study. The inter-study variance, a parameter of the random effects meta-regression model, was estimated using method of moments. The inter-study variance was used to adjust for the heterogeneity in prevalence (or incidence) between studies. Heterogeneity between studies was further assessed using the I^2 statistic.[13] A random effect meta-analysis was conducted to obtain an overall prevalence (or incidence) rates of different types of mortality. The analysis was further extended for different subgroups based on surgical technique and study year to see if the results vary across the subgroups. To reduce centre bias, studies from the same centre were isolated according to study period and the largest cohort was used in the meta-analysis. Paediatric studies were excluded from the meta-analysis. Selected studies with a non-classical baseline population were also excluded from the meta-analysis.[61,75] All these computations were conducted using Stata V.11 and Comprehensive Meta-Analysis V.3.

Results

The results of the search strategy are shown in *figure 1*. Eighty-five papers were included in the systematic review *(table 1).* Following exclusion of multiple studies from the same centres, 35 papers were included in the final meta-analysis. The systematic review included 9738 patients from 1958 -2012. All studies were observational and used retrospective data collection. The median number of patients per study was 56 (IQR 25 -127). The mean age at surgery was 45.2 years and 55.1% were men; the mean follow-up was 5.5 years.

Systematic Review

Geographical Location

Fifty-seven (67.1%) studies came from North American centres (7557 patients) and 23 (27.1%) from European centres (2020 patients). The remainder comprised of 2 studies from China, 1 from Australia and 1 from Brazil. Of the 57 articles from North America, 21 (36.8%) were published from the Mayo Clinic in Rochester, Minnesota. This introduced bias in the meta-analysis due to overlapping cohorts from the same centre. We sought to eliminate this bias in the meta-analysis as described above. The origin of individual studies is shown in *table 1*.

Surgical Procedures

The 85 studies included patients undergoing septal myectomy (SM) alone, SM with concomitant MV intervention and MV replacement alone. 11 studies (12.9%) focused on MV intervention in the surgical management of LVOTO which were analysed separately in the

meta-analysis. Selected cohorts reported outcomes in patients undergoing redo surgical procedures and one reported outcomes in patients undergoing apical myectomy which were not included in the meta-analysis.[61,75]

Clinical Assessment

Sixty-eight studies (80.0%) referenced NYHA class and 47 studies (55.3%) reported a mean improvement of 1.4. Mean ejection fraction reduced from 65.4% (CI 65.0, 65.6) preoperatively to 59.4% (CI 59.0, 59.8) postoperatively. Left ventricular end diastolic diameter increased from 42.5mm (CI 42.3, 42.8) to 45.0 mm (CI 44.6, 45.5) postoperatively. Mean maximum wall thickness reduced from 22.1mm (CI 22.0, 22.2) to 17.1mm (CI 16.7, 17.4) postoperatively. The mean left atrial diameter reduced 45.9mm (CI 45.6, 46.2) to 45.3mm (CI 45.2, 45.4) postoperatively. Mean resting peak left ventricular outflow tract gradient reduced from 74.0 mmHg (CI 73.0, 75.0) to 9.2mmHg (CI 8.9, 9.4) postoperatively.

Early Complications

Sixty-eight studies (80.0%) documented rates of at least one non-fatal perioperative complications. PPM insertion was the most frequently documented complication with 60 studies (70.6%) reporting rates of perioperative PPM insertion. Fewer studies documented other perioperative complications with 31 studies (36.5%) documenting rates of VSD and 24 studies (28.2%) documenting rates of perioperative CVA *(table S1, supplementary material).* Twenty-one studies (24.7%) documented postoperative AF with 5 studies (5.9%) documenting specific new onset of AF postoperatively.

Long-Term Follow Up

Forty-five articles (52.9%) documented long-term complications following surgery. Re-operation for LVOTO or heart transplantation was most frequent (43 articles (50.6%); *table S2, supplementary material*). Late PPM was reported in 10 studies (11.8%) with rates ranging from 0%-6.4%. On late follow-up only 7 studies (8.2%) reported on stroke (range: 1.1% - 8.6%). Seven studies (8.2%) reported heart failure related hospitalisations after surgery (range: 0% - 13.6%). One study reported 6 HF hospitalisations during follow-up in a cohort of 44 patients undergoing apical myectomy.[75]

Meta-analysis

Thirty-five studies were included in the meta-analysis as illustrated in *figure 1*.

Early Mortality

The overall incidence of early perioperative mortality in SM studies, without MV intervention, was 2.7% (CI 0.7, 9.6) I^2 58.7%, p<0.05 *(figure 2).* There was a decline in perioperative mortality over time with an incidence of 5.2% (CI 3.4, 7.8) I^2 42.9%, p=0.06 in studies prior to 2000 and 1.4% (CI 0.8, 2.4) I^2 9.0%, p=0.36 in contemporary studies since 2000 (between groups p<0.05).

The incidence of early perioperative mortality in patients undergoing MV intervention, as seen in *figure 3*, was 1.4% (CI 0.5, 3.7) I^2 0%, p=0.70 in studies reporting outcomes in SM with MV repair, 7.3% (CI 2.4, 20.3) I^2 0%, p=0.73 in studies reporting outcomes in SM and MV replacement and 7.9% (CI4.3, 14.1) I^2 0%, p=0.93 in studies reporting outcomes in MV replacement alone (between groups p<0.05). Studies including MV replacement however, were older compared to those focusing on MV repair *(figure 3).*

Late Mortality

The overall annual IR late mortality (>30days) following SM surgery was 1.3% (CI 0.1, 2.5), I^2 75.6%, p<0.05 (*figure F1, supplementary material)*. There was a similar temporal decline in late mortality: IR prior to 2000 was 2.0% (CI 1.2, 2.8) I^2 2.5% p=0.38 and after 2000 was 0.7% (CI 0.3, 1.2) I^2 70.7%, p<0.05 (between groups p<0.05).

As seen in *figure F2, supplementary material*, the overall annual IR of late mortality (>30days) in those undergoing MV intervention, was 1.1% (CI 0.5, 1.7) I^2 51.3%, p<0.05. The annual IR of late mortality in studies reporting outcomes in SM with MV repair was 1.1% (CI 0.3, 1.8) I^2 59.2%, p<0.05, in studies reporting outcomes in SM and MV replacement was 0.8% (CI -0.8, 2.3) I^2 0%, p=1.00 and in studies reporting outcomes in MV replacement alone was 1.5% (CI 0.3, 2.8) I^2 40.7%, p=0.19 (between groups p=0.73).

Morbidity

Early Complications

The overall incidence of a VSD was 2.2% (CI 0.9, 5.7) I^2 48.6%, p<0.05. Contemporary studies since 2000, showed a decline in the incidence of VSD to 1.4% (0.8, 2.3) I^2 0%, p<0.05. The overall incidence of perioperative CVA was 2.1% (CI 1.5, 3.1) I^2 1.0%, p=0.44. The overall prevalence of perioperative PPM insertion was 5.0% (CI 4.0, 6.2) I^2 25.69%, p=0.09 which did not differ significantly overtime in comparing contemporary to earlier studies (p=0.22).

Late Morbidity

The overall incidence of reintervention was 2.8% (CI 1.8, 4.3) I^2 60.6% $p<0.05$ with an annual IR of reintervention of 0.3% (CI 0.2, 0.4) I^2 52.5%, $p<0.05$."

Discussion

Randomised trials comparing surgical intervention with medical therapy in patients with obstructive HCM are unlikely and so systematic reviews and meta-analyses will remain the major source of evidence for the study of surgical treatments for LVOTO. For the first time, we examine pooled data on mortality and morbidity among various surgical techniques in the management of LVOTO in HCM. The findings show that in the modern era (and in specialist centres) operative mortality in SM is low with similar low operative mortality rates in studies reporting outcomes in SM with MV repair. Contemporary data on the use of MV replacement in LVOTO are less robust and therefore difficult to draw conclusions from however higher operative mortality rates were seen in earlier studies. We also identify gaps in evidence with respect to reporting of perioperative complications and long-term disease related morbidity following surgical treatment.

Geographical location

Most data on surgical intervention come from large specialised centres in North America (25% from a single institution, the Mayo Clinic). This concentration of data from a small number of centres means that the good surgical outcomes reported in the literature may not be representative of results from less experienced low volume surgical units. Evidence suggesting that this is the case come from a recently published audit of North American centres carrying out septal myectomy procedures that reports an incidence of early mortality of 3.8% in high volume centres and 15.6% in low volume centres.[100] Furthermore, alcohol

septal ablation has been introduced in recent years as an alternative to surgical septal reduction therapy which may have resulted in a reduction in the number of surgical myectomies performed in Europe.

Early complications

This systematic review and meta-analysis demonstrates improved surgical outcomes following surgical management of LVOTO since its first introduction in the 1950s. Similar falls in reported late mortality were seen. The incidence of complications arising directly from removal of septal muscle such as VSD and need for PPM insertion perioperatively was low, particularly in contemporary studies but there was limited reporting of other perioperative complications such as atrial fibrillation and stroke.

Late complications

While this review and meta-analysis confirms the success of surgery in treating symptoms attributable to LVOTO, the underling myocardial disease retains the potential for progression in spite of surgical intervention. While most series included data on long-term survival, less than 22% reported the incidence of non-fatal complications such as AF, stroke and HF. Documentation of long-term morbidity was less robust than the reporting of early complications. This may be accounted by the fact that many studies are reported by large tertiary referral centres that discharge patients to local physicians following surgery. This represents a major gap in current knowledge as most series suggest that patients with and without LVOTO are at risk of adverse outcomes and the impact of surgery on the incidence of non-fatal disease related morbidity is unknown. Further studies are required to assess long-term non-fatal outcomes

Comparison of different surgical approaches

MV replacement for the management of LVOTO was introduced in the 1970s, but higher complication rates mean that it is reserved mostly for individuals considered unsuitable for myectomy.[101] With improved imaging techniques and surgical advances, MV repair in combination with SM in the management of LVOTO is increasingly advocated. This can involve plication of the MV leaflet, anterior MV leaflet extension with patch repair, edge to edge (Alfieri) repair or reorientation of papillary muscles. In this review, studies investigating outcomes following MV replacement alone, although older, reported higher perioperative mortality rates.[26, 27] Contemporary studies have focused on SM with MV repair using various techniques. [40, 44, 54, 56, 63, 64, 71, 72, 74, 99] but studies comparing outcomes of different MV interventions including MV replacement with SM alone are lacking.

Conclusions

Contemporary surgical management of LVOTO in specialist centres is associated with low operative mortality rates. Reporting of long-term morbidity is less robust than that of early complications. Further studies are needed to investigate the long-term outcomes for different surgical approaches to the management of LVOTO and to determine the impact of relief of LVOTO on non-fatal disease related complications.

Contributions

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

All authors have given final approval of the version published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Competing interests: None declared.

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Figures

Figure 1

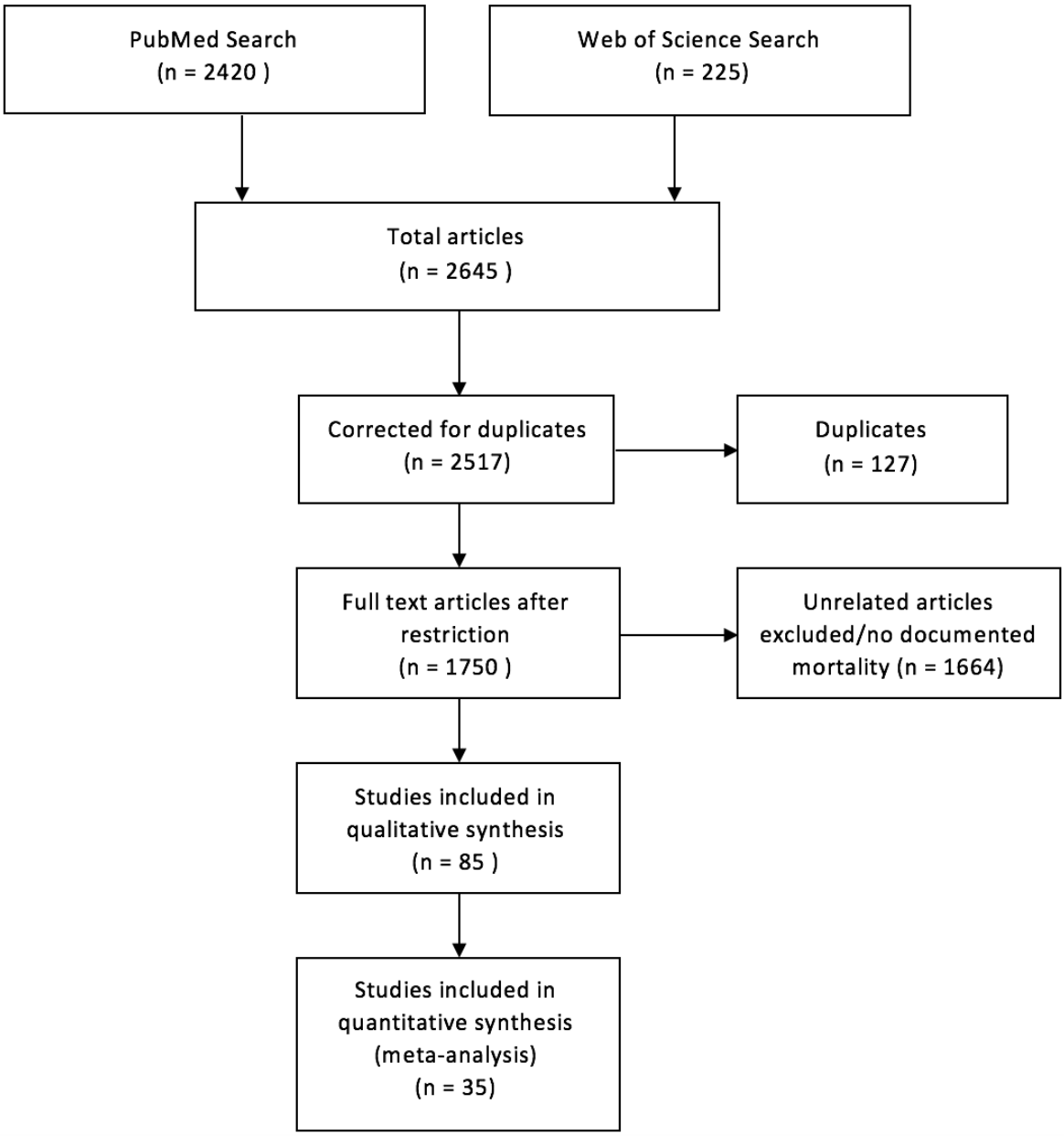

Figure 2

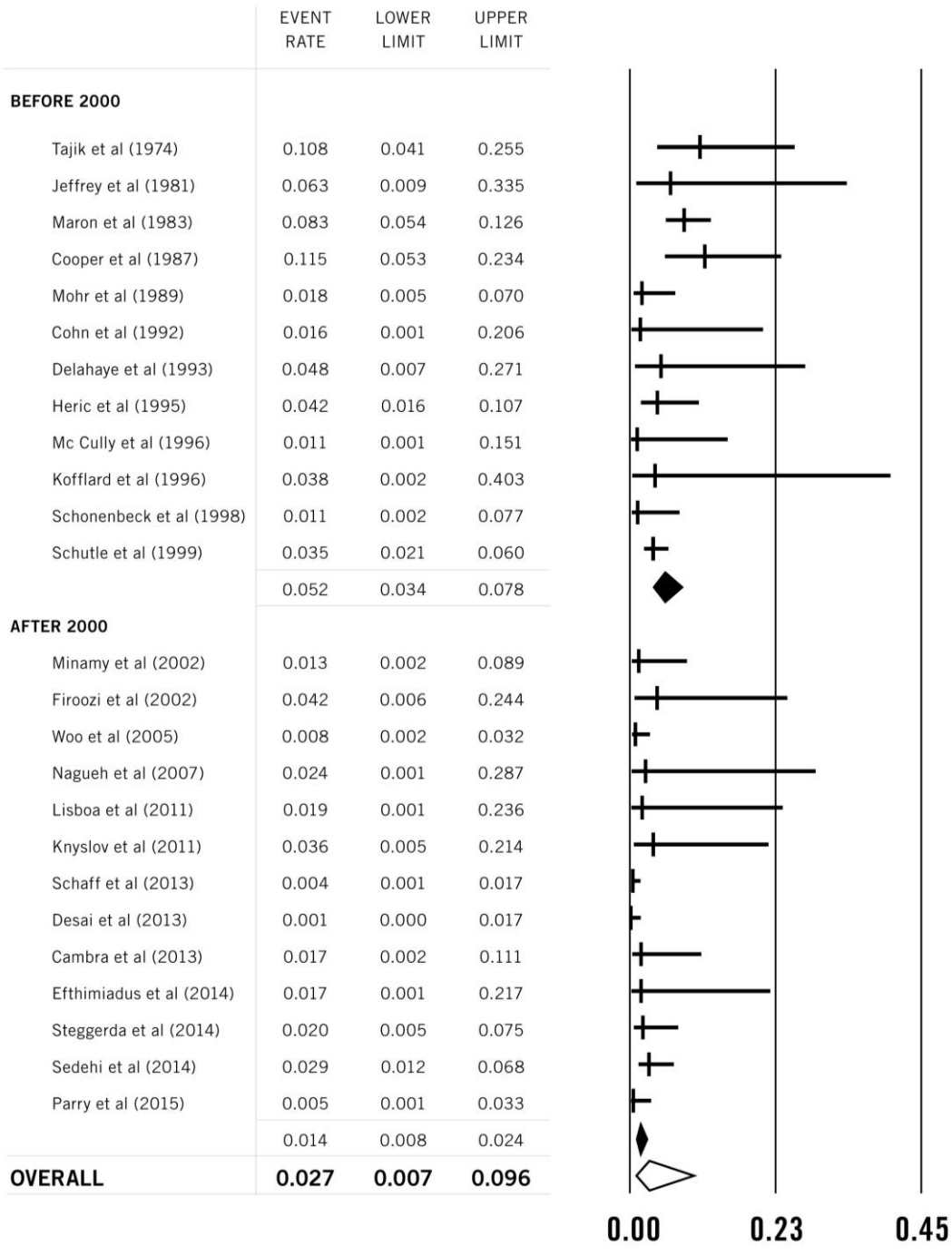
EVENT RATE
LOWER LIMIT
UPPER LIMIT
BEFORE 2000
Tajik et al (1974) 0.108 0.041 0.255
Jeffrey et al (1981) 0.063 0.009 0.335
Maron et al (1983) 0.083 0.054 0.126
Cooper et al (1987) 0.115 0.053 0.234
Mohr et al (1989) 0.018 0.005 0.070
Cohn et al (1992) 0.016 0.001 0.206
Delahaye et al (1993) 0.048 0.007 0.271
Heric et al (1995) 0.042 0.016 0.107
Mc Cully et al (1996) 0.011 0.001 0.151
Kofflard et al (1996) 0.038 0.002 0.403
Schonenbeck et al (1998) 0.011 0.002 0.077
Schutle et al (1999) 0.035 0.021 0.060
0.052 0.034 0.078
AFTER 2000
Minamy et al (2002) 0.013 0.002 0.089
Firoozi et al (2002) 0.042 0.006 0.244
Woo et al (2005) 0.008 0.002 0.032
Nagueh et al (2007) 0.024 0.001 0.287
Lisboa et al (2011) 0.019 0.001 0.236
Knyslov et al (2011) 0.036 0.005 0.214
Schaff et al (2013) 0.004 0.001 0.017
Desai et al (2013) 0.001 0.000 0.017
Cambra et al (2013) 0.017 0.002 0.111
Efthimiadus et al (2014) 0.017 0.001 0.217
Steggerda et al (2014) 0.020 0.005 0.075
Sedehi et al (2014) 0.029 0.012 0.068
Parry et al (2015) 0.005 0.001 0.033
0.014 0.008 0.024
OVERALL 0.027 0.007 0.096
0.00
0.23
0.45

Figure 3

	EVENT RATE	LOWER LIMIT	UPPER LIMIT
SEPTAL MYECTOMY WITH MITRAL VALVE REPAIR			
McIntosh et al (1992)	0.029	0.004	0.177
Schoendube et al (1995)	0.009	0.001	0.125
Minakata et al (2004)	0.009	0.001	0.125
Wan et al (2009)	0.036	0.005	0.214
Balaram et al (2012)	0.004	0.000	0.057
Vriesendorp et al (2015)	0.005	0.000	0.076
	0.014	0.005	0.037
SEPTAL MYECTOMY WITH MITRAL VALVE REPLACEMENT			
Delahaye et al (1993)	0.083	0.021	0.279
Stassano et al (2004)	0.056	0.008	0.307
	0.073	0.024	0.203
MITRAL VALVE REPLACEMENT ALONE			
Krajcer et al (1989)	0.069	0.026	0.170
McIntosh et al (1989)	0.086	0.036	0.191
Walker et al (1989)	0.091	0.013	0.439
	0.079	0.043	0.141
OVERALL	**0.044**	**0.014**	**0.135**

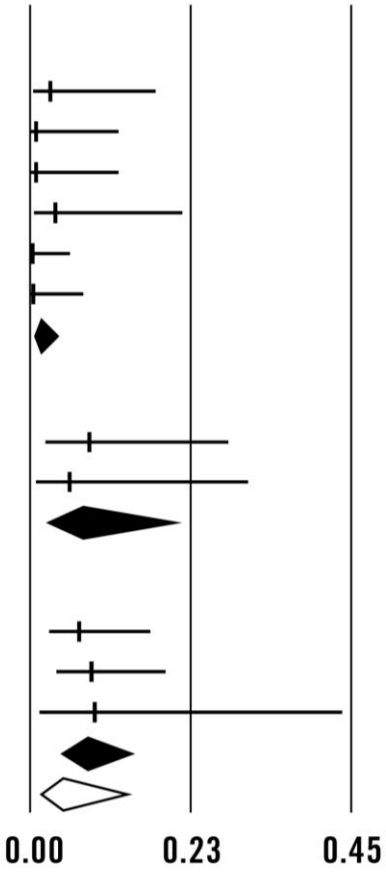

Figure Legends

Figure 1: Flow chart indicating search methods

Figure 2: Meta-analysis of incidence of early perioperative mortality over time in septal myectomy studies

Figure 3: Meta-analysis of incidence of early perioperative mortality in MV intervention studies

Tables

Table 1

Author	*Location*	*Year*	*FU (Yrs)*	*Cohort*	*SM*	*SM &MV Repair*	*SM & MVR*	*SM & MVR/MV rep*	*MVR alone*
Tajik et al	Mayo Clinic, USA	1974	7.0	43	38	1	1	-	0
Morrow et al	NHLBI, Maryland, USA	1975	5.7	83	83	-	-	-	-
Koch et al	NHLBI, Maryland, USA	1980	4	20	20	-	-	-	-
Jeffrey et al	St Luke's Hospital, Wisconsin, USA	1981	5.8	20	17	0	3	-	1
Beahrs et al	Mayo Clinic, USA	1982	13.4	40	40	0	0	0	0
Binet et al	Centre Chirurgical Marie Lanuelongue, France	1983	8.2	76	73	0	3	-	0
Maron et al	NHLBI, Maryland, USA	1983	5.8	240	240	-	-	-	-
Rothlin at al	University Hospital, Zurich, Switzerland	1983	7.6	63	58	0	5	-	0
Schaffer et al	Sick Kids, Toronto, Canada	1983	6.1	3	3	0	0	-	0
Fighali et al	Texas Heart Institute, USA	1984	4.0	36	12	0	11	-	13
Cooper et al	NHLBI, Maryland, USA	1987	4.5	52	52	0	0	-	0
Leachman et al	Texas Heart Institute, USA	1987	10.0	54	0	0	0	0	54
Williams et al	Sick Kids, Toronto, Canada	1987	3.0	61	60	1	0	-	0
Krajcer et al	Texas Heart Institute, USA	1988	9.8	185	127	0	0	-	58
Cecchi et al	NHLBI, Maryland, USA	1989	7.0	18	17	-	-	-	1
Lewis et al	NHLBI, Maryland, USA	1989	3.4	18	12	0	0	-	6
McIntosh et al	NHLBI, Maryland, USA	1989	2.0	58	0	0	0	-	58
Mohr et al	Mayo Clinic, USA	1989	5.1	115	109	0	2	-	4
Siegman et al	NHLBI, Maryland, USA	1989	4.8	28	24	0	0	-	4
Walker et al	Western General Infirmary, Edinburgh, UK	1989	8.2	21	11	0	0	-	10
Seiler et al	University Hospital, Zurich, Switzerland	1991	9.4	79	79	-	-	-	-
Cohn et al	Brigham & Women's Hospital, Boston, USA	1992	6.5	31	31	0	0	-	0
McIntosh et al	NHLBI, Maryland, USA	1992	2.2	36	0	35	1	0	0
Delahaye et al	Hopital Cardiovasculaire et Pulmonologique, Lyon, Fr.	1993	5.7	47	21	0	24	-	2

Schulte et al	Heinrich Heine University Hospital, Dusseldorf, Germany	1993	8.2	364	338	7	19	-	0
Stone et al	NHLBI, Maryland, USA	1993	10.1	17	14	0	1	-	2
Ten Berg et al	St Antonius Hospital, Nieuwegein, Netherlands	1994	6.8	38	30	0	8	-	0
Heric et al	Cleveland Clinic, USA	1995	3.7	178	136	4	17	-	3
Schoendube et al	Klinikum RWTH Aachen, Germany	1995	7.0	58	0	58	0	-	0
Kofflard et al	University Hospital Dijkzigt, Rotterdam, Netherlands	1996	-	20	12	8	0	-	0
Mc Cully et al	Mayo Clinic, USA	1996	2.4	65	60	3	2	-	0
Robbins et al	Stanford University, USA	1996	6.1	158	133	0	5	-	0
Theodoro et al	Mayo Clinic, USA	1996	6.4	25	23	2	0	-	0
Gol et al	Cardiology Clinic, Ankara, Turkey	1997	3.7	69	62	4	3	-	0
Schonenbeck et al	University Hospital, Zurich, Switzerland	1998	11.7	110	98	10	2	-	0
Schutle et al	Heinrich Heine University Hospital, Dusseldorf, Germany	1999	8.5	368	368	0	0	-	0
Havndrup et al	Copenhagen, Denmark	2000	3.6	11	9	0	2	-	0
Merrill et al	Vanderbilt University, USA	2000	6.6	22	21	0	1	-	0
Qin et al	Cleveland Clinic, USA	2001	0.4	26	26	-	-	-	-
Firoozi et al	St George's Hospital, London, UK	2002	3.8	24	24	-	-	-	-
Minami et al	Heart Center NRW, Bad Oeynhausen, Germany	2002	5.5	125	110	0	15	-	0
Van der Lee et al	Erasmus Medical Centre, Rotterdam, Netherlands	2003	3.4	29	0	29	0	-	0
Jiang et al	Anzhen Hospital, Beijing, China	2004	2.0	11	11	-	-	-	-
Minakata et al	Mayo Clinic, USA	2004	2.8	56	54	2	0	-	0
Stassano et al	Texas Heart Institute, USA	2004	21.9	18	0	0	18	-	0
Balaram et al	St Luke's-Roosevelt Centre, NYC, USA	2005	2.4	19	0	19	0	-	0
Minakata et al	Mayo Clinic, USA	2005	5.8	13	13	0	0	-	0
Minakata et al	Mayo Clinic, USA	2005	8.6	56	49	7	0	-	0
Ommen et al	Mayo Clinic, USA	2005	5.8	289	289	-	-	-	-
Ralph-Edwards et al	Toronto General Hospital, Canada	2005	2.3	48	48	0	0	-	0

Woo et al	Toronto General Hospital, Canada	2005	7.7	338	325	0	0	13	0
Swistel et al	St Luke's-Roosevelt Centre, NYC, USA	2006	3.1	42	4	34	3	-	1
Elbardissi et al	Mayo Clinic, USA	2007	1.9	16	14	2	0	-	0
Monteiro et al	Mayo Clinic, USA	2007	3.0	150	150	-	-	-	-
Nagueh et al	DeBakey Heart Centre, Texas, USA	2007	1.5	20	20	-	-	-	-
Vural et al	Bursa Yuksek Ihtisas Hospital, Turkey	2007	1.1	24	9	15	0	-	0
Kaple et al	Cleveland Clinic, USA	2008	3.8	115	0	67	35	-	13
Smedira et al	Cleveland Clinic, USA	2008	3.6	323	323	0	0	-	0
Wan et al	Mayo Clinic, USA	2009	5.6	32	0	28	4	-	0
Brown et al	Mayo Clinic, USA	2010	3.6	416	345	62	9	-	0
Kwon et al	Cleveland Clinic, USA	2010	0.9	182	143	0	0	39	0
Schaff et al	Mayo Clinic, USA	2010	2.6	44	43	0	1	-	0
Ball et al	Toronto General Hospital, Canada	2011	7.2	287	287	-	-	-	-
Knyslov et al	National Institute of Cardiovascular Surgery, Ukraine	2011	3.8	28	28	-	-	-	-
Lisboa et al	Heart Institute, Sao Paolo, Brazil	2011	9.6	34	26	8	0	-	0
Balaram et al	St Luke's-Roosevelt Centre, NYC, USA	2012	5.6	132	32	86	14	-	0
Hickey et al	Sick Kids, Toronto, Canada	2012	8.2	32	32	-	-	-	-
Iacovani et al	Ospedali Riuniti, Bergamo, Italy	2012	1.7	124	115	7	2	-	0
Schaff et al	Mayo Clinic, USA	2012	-	749	639	95	15	-	0
Altarabseh et al	Mayo Clinic, USA	2013	8.3	127	97	29	1	-	0
Cambra et al	Hospital Universitari I Politecnic La Fe, Spain	2013	2.2	69	66	-	-	3	0
Desai et al	Cleveland Clinic, USA	2013	6.2	699	518	154	27	0	0
Kunkala et al	Mayo Clinic, USA	2013	1.6	56	56	-	-	-	-
Orme et al	Mayo Clinic, USA	2013	4.7	239	239	-	-	-	-
Wang et al	Fuwai Hospital, Beijing, China	2013	0.9	93	74	9	10	-	0
Cho et al	Mayo Clinic, USA	2014	-	52	48	4	0	-	0
Efthimiadus et al	AHEPA, Thessaloniki, Greece	2014	1.4	32	29	3	0	-	0
Geske et al	Mayo Clinic, USA	2014	3.1	306	306	-	-	-	
Helder et al	Mayo Clinic, USA	2014	2.6	16	15	1	0	-	0

Kunkala et al	Mayo Clinic, USA	2014	4.6	23	23	0	0	-	0
Panaich et al	NIS, USA	2014	-	665	665	-	-	-	-
Samardhi et al	Prince Charles Hospital, Brisbane, Australia	2014	3.8	23	20	1	2	-	0
Sedehi et al	Stanford University, USA	2014	13.7	171	171	0	0	-	0
Steggerda et al	St Antonius Hospital, Nieuwegein, Netherlands	2014	9.1	102	102	-	-	-	-
Parry et al	Toronto General Hospital, Canada	2015	4.4	211	209	2	0	-	0
Vriesendorp et al	Erasmus Medical Centre, Rotterdam, Netherlands	2015	8.3	139	24	98	14	-	0

Table 1: Systematic Review with study location and type of surgical procedure.

"-": Not reported in study

FU: Mean Follow-Up Duration

SM: Septal Myectomy without Mitral Valve Intervention

SM & MV Repair: Septal Myectomy and Mitral Valve Repair

SM & MVR: Septal Myectomy and Mitral Valve Replacement

SM & MVR/MVrep: Septal Myectomy and unspecified Mitral Valve Replacement or Repair

MVR: Mitral Valve Replacement