A Clinical Trial of Minothoracotomy versus Conventional Sternotomy for Mitral Valve Repair."

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KEY POINTS

Question: Is minimally invasive mitral valve repair (Mini) better at improving physical function at 12 weeks compared to conventional sternotomy (Sternotomy) mitral valve repair (MVr) for degenerative mitral regurgitation (DMR)?

Findings: In this randomized controlled trial of 330 patients, Mini is not superior to Sternotomy in recovery of physical function at 12 weeks. Mini achieves high quality and durable valve repair at 1 year with similar post operative complications to Sternotomy.

Meaning: Mini does not improve physical function at 12 weeks, but outcomes at 1 year shows Mini MVr is as safe and clinically effective a treatment as Sternotomy for DMR. These findings can inform shared decision-making discussions with patients being evaluated for MVr.

ABSTRACT

Importance:
The benefits, clinical effectiveness, and safety of mitral valve repair (MVr) via thoracoscopically-guided minithoracotomy (Mini) compared to median sternotomy (Sternotomy) in patients with degenerative mitral valve regurgitation (DMR) is uncertain.

Objective:
To determine the benefits, safety and clinical effectiveness of Mini versus Sternotomy MVr.

Design, Setting and Participants
A pragmatic multicenter, expertise-based, superiority, randomised controlled trial in 10 tertiary care institutions in the United Kingdom. Adults with degenerative mitral regurgitation undergoing mitral valve repair surgery

Interventions
Participants were randomized 1:1 with concealed allocation to receive either Mini or Sternotomy MVr performed by an expert surgeon.

Main Outcomes:
The primary outcome was physical functioning and associated return to usual activities measured by change from baseline in SF-36v2 physical functioning scale at 12 weeks following index surgery assessed by an independent researcher blinded to intervention. The primary analysis was modified intention-to-treat. Secondary outcomes included recurrent MR grade, physical activity, and quality of life. Safety outcomes (complications) were monitored for one year.

Results:
Between November 2016 and January 2021, 330 participants were randomized; 164 allocated to Sternotomy and 166 to Mini, of whom 309 underwent surgery and 294 reported the primary outcome. 30% of participants were female. At 12 weeks, mean difference between groups in the change in SF-36v2 physical function T scores was 0.68; 95% CI, -1.89 to 3.26. Valve repair rates (96%) were similar in both groups. Echocardiography demonstrated mitral regurgitation severity as none or mild for 92% of participants at 1 year with no difference between groups. Death, repeat mitral valve surgery, or heart failure hospitalisation occurred in 5.4% (9/166) of the Mini and 6.1% (10/163) of the Sternotomy participants at 1 year.

Conclusions and relevance:

Mini is not superior to Sternotomy in recovery of physical function at 12 weeks. Mini achieves high rates and quality of valve repair and has similar safety outcomes at 1 year to Sternotomy. The results provide randomized evidence about the relative clinical effectiveness and safety of Mini MVr and can inform shared decision-making discussions with patients who are being evaluated for MVr surgery.

Trial registration number: ISRCTN13930454.

Introduction (3411/3000)

Mitral valve repair (MVr) surgery is the optimal treatment for patients with degenerative mitral regurgitation (DMR) (1, X). When compared to mitral valve replacement (MVR), it results in lower mortality and better preservation of left ventricular function (2).

Conventional MVr surgery (Sternotomy) is routinely performed via full sternotomy, enabling easy access to the heart, flexibility in myocardial protection strategies, multiple ways of accessing the mitral valve, and eases de-airing to prevent air emboli which cause cerebrovascular accidents. The sternotomy is immobilised using wires, bands or plates, to allow sternal union around 12 weeks after surgery (3). The invasiveness of this approach limits physical activity, delays a rapid return to pre-surgery physical function levels, and increases the risk of post-operative complications (4).

A video assisted thoracoscopically guided minimally invasive approach to mitral repair (Mini), performed via a 4-7 cm lateral thoracotomy, completely avoiding sternotomy, is increasingly demanded by patients who believe it accelerates recovery and improves cosmesis (5). Surgeons who favor this approach argue it reduces the time taken to recover physical function after surgery, post-operative complications, and costs by reducing hospital stay (6,7).

Uptake of Mini is variable worldwide with low rates in the United States and the United Kingdom but high rates in Germany (8,9, Y). The main reason for the variation is the lack of clear and definitive evidence from robustly designed and adequately powered trials confirming equivalent or superior benefits of this approach relative to sternotomy (10,11). There are concerns that the relative complexity of Mini may increase the risk of peri-operative complications, particularly vascular injuries and stroke (12,13), and uncertainty around the ability to repair complex valve lesions through the Mini incision (14).

Consequently, the best surgical approach for MVr is widely debated. A consensus document from the International Society of Minimally Invasive Cardiac Surgery (ISMICS) and recent guidelines have recommended a multi-centre randomised controlled trial (RCT) to assess the effectiveness and safety of Mini versus Sternotomy MVr (15,16). To inform decision-making for patients and clinicians, the United Kingdom (UK) Mini Mitral Trial reported here compared the benefits and risks of the two procedures and specifically aimed to determine if physical functioning and associated return to usual activities was superior after the Mini approach.

Methods

Study Design

UK Mini Mitral is a multi-center, expertise based superiority RCT of Mini (intervention) versus Sternotomy (control) in patients undergoing MVr. The trial design and protocol were previously published (17).
Conducted across 10 UK National Health Service (NHS) centres, day-to-day management was by a trial management group. Independent oversight committees were appointed by the funder. Ethical approval was given by NHS Wales REC 6 (16/WA/0156).

Participants

Participants were adults (age ≥18 years) with DMR requiring MVr. All participants were discussed by a mitral valve heart team where the diagnosis of DMR was made and suitability for valve repair was confirmed. Concomitant surgery for AF or tricuspid valve (TR) repair was allowed. Exclusions included

concomitant coronary or aortic valve surgery and redo surgery. An exhaustive list is included in the supplement. All participants provided written informed consent.

Expertise based Randomisation and Blinding

The key design challenge for the trial was to account for the learning curve of the procedures. This has been the major limitation and criticism of previous studies comparing the 2 procedures and is a challenge for all trials comparing surgical techniques.
Prior to designing the trial, we consulted widely on the need to account for expertise and reduce bias. Mini surgeons were concerned that Sternotomy surgeons may not necessarily be able to perform the mini procedure without training. Sternotomy surgeons were concerned that Mini surgeons may lack key expertise which may impact outcomes, e.g. techniques to limit the size of the sternal incisions, the use of specialised sternal retractors which reduces wide sternal opening, and special methods of closing the sternotomy e.g. the sternal bands or plates. To reduce such bias and allow the best comparison of the 2 procedures, surgeons agreed that only performing the one type of surgery in the trial for which they had expertise, would be the most robust method to limit significant bias which would have been introduced otherwise.

Consequently, individual expert surgeons performed only one type of operation. Before performing surgery within the trial, each surgeon completed a minimum of 50 procedures; the Trial Steering Committee reviewed records for each surgeon and agreed to their participation. Depending on allocation, participants were required to move to another surgeon following randomization if the original surgeon to which they were referred was not the designated expert for the randomized procedure. No participant refused to switch surgeons after randomization.

Eligible participants were randomized in a 1:1 ratio to MVr via Mini or Sternotomy by the center research teams using a 24-hour, central, secure, web-based randomization system with concealed allocation. A minimisation scheme accounted for baseline SF-36v2 physical functioning score, presence or absence of Atrial Fibrillation (AF), and presence and severity of TR.

Blinding of patients and clinical teams was not possible due to the nature of the surgical interventions. Instead, a central independent researcher, blind to allocation, collected all SF-36v2 data beyond baseline for all participants. Additionally, a central independent core laboratory, blind to allocation, reported all anonymised echocardiograms.

Trial Surgical Interventions

Trial interventions are described in detail in the supplementary material. For Mini, a 4-7cm right lateral minithoracotomy, and thoracoscopic guidance were used.

For Sternotomy, the sternum was divided completely.

Both procedures required cardiopulmonary bypass (CPB). For sternotomy CPB was established by siting cannulas centrally in the right atrium, venae cavae and ascending aorta, for Mini peripheral femoral vessels were used.

Mitral valve repair techniques were not specified in the trial protocol and were at the discretion of the operating surgeon. In both arms, valve and cardiac function were assessed with intraoperative

echocardiography. Repeat cross clamping to improve quality of valve repair after echo examination was encouraged.

Patients were followed, with trial visits at 6, 12, 18, 24, 36 and 1 year following surgery.

Outcomes

The primary outcome was physical functioning and associated return to usual activities measured by change in SF-36v2 physical functioning scale (18) at 12 weeks following index surgery assessed by an independent researcher blinded to intervention.

Secondary outcomes included SF-36v2 physical functioning scores at 6, 12, 18, 24, 36 and 1 year; physical activity and sleep captured by wrist-worn accelerometers at baseline, 6 and 12 weeks; residual MR assessed via transthoracic echocardiography at 12 and 1 year, reported by a core laboratory blinded to intervention and overall quality of life (QoL) assessed using EQ-5D-5L up to 1 year (19,20).

To assess the relative safety of the two procedures, we measured pre specified post-operative complications up to 12 weeks after surgery, and Death, reintervention on the mitral valve, hospitalizations for heart failure and adverse events up to 1 year after surgery.

were reported.

Statistical Analysis

A full description of the sample size calculation is in the published protocol (17). The sample size was calculated using the SF-36v2 physical functioning at 12 weeks and a minimal clinically important change of 10 points with SD of 30 (18,21,22). Given these assumptions, 382 participants (191 in each arm) would be required to achieve 90% power at a two-sided significance level of 5% in the absence of correlation between baseline and 12 weeks. Due to challenges with recruitment, and to assess our assumptions, we performed a blinded sample size re-estimation using baseline SF-36v2 physical functioning scale data from 177 trial patients. Using the re-estimated SD of 26.3 with 90% power, 288 participants are required to detect a 10 point difference in SF-36v2 physical functioning at 12 weeks. The final sample size was therefore reduced to 330, which included attrition.

The primary analysis was performed according to the intention-to-treat principle and included the full analysis population, which included all the patients who underwent randomization, received surgery and had data on the primary outcome at week 12. Secondary analyses were based on ITT as well, where we have analysed all available data for the participants. There was no correction of the type I error rate for multiple testing across secondary end points because they were not powered and were considered exploratory. Thus, reported 95% confidence intervals have not been adjusted for multiplicity and do not imply definitive treatment effects.

The primary outcome of SF-36v2 PF T-score was analysed using a linear mixed-effects model that adjusted for the minimisation factors except for baseline SF-36v2 physical functioning score, which was included as part of the outcome to calculate change from baseline. Conversion to T scores is recommended and described in the user manual (18) and fully described in the Statistical Analysis Plan and enables comparability with a UK population. Initially, the model accounted for both intra-site and intra-patient correlation by using a nested covariance matrix to obtain robust standard errors. However, upon further analysis, it was observed that variation between the multiple sites was negligible, and thus, only intra-patient correlation was embedded in the final model.

Sensitivity analyses were performed according to participants who adhered to the eligibility criteria, received surgery based on randomization allocation and completed at least 12 weeks follow-up (per-protocol analysis), and actual surgical procedure the participants received (as-treated analysis). Subgroup analyses were performed under the same model as the primary analysis; results were visualized as a forest plot with sex, age, valve pathology, and baseline SF-36v2 as prespecified characteristics.

There were no item-level missing data in SF-36v2 physical functioning scale at 12 weeks and 294 participants have primary outcome data, which is more than the 288 participants required. Nonetheless, we also imputed the patient-level missing primary outcome data using an imputation model that was stratified according to randomization assignment and included minimisation variables for sensitivity analysis.

Remaining secondary outcomes, including echocardiogram data, were analysed using linear mixed-effects models for continuous variables.

The statistical analysis plan is included in the supplementary material.

Results

From Nov 2016 through Jan 2021, 1167 patients were screened, of which 330 were enrolled and randomized to either Sternotomy (n=164) or Mini (n=166). 11 participants withdrew prior to surgery, 1 Sternotomy participant was removed from the database at their request, 1 died pre-surgery, 3 remained asymptomatic, and 5 did not receive surgery for reasons unknown. 309 (94%) participants underwent surgery in the trial; 147 of 163 (90%) participants randomized to Sternotomy and 162 of 166 (98%) randomized to Mini **(Figure 1).**

The two groups had similar demographic, clinical and echocardiographic characteristics at baseline. Mean age was 67 years and 100 (30%) were women **(Table 1).**

All surgeons met the minimum expertise criteria. Mini and Sternotomy surgeons had performed a median of 86 and 162 procedures respectively prior to enrolling participants **(eTable 1 in Supplement 3).**

MVr was performed in 296 of 309 participants; repair rates were similar in both groups (95.6% in Mini and 97.3% in Sternotomy).

Average cardiopulmonary bypass times and aortic cross clamp times were longer in Mini than Sternotomy (32.9 minutes 95% CI, 19.46 to 46.34 and 11.42 minutes 95% CI, 5.21 to 17.63 respectively).

Primary Outcome

At 12 weeks following surgery SF-36v2 PF T scores had improved in both Mini (7.62; 95% CI, 5.49 to 9.78) and Sternotomy groups (7.20; 95% CI, 5.04 to 9.35). Although the change was higher in the Mini group, the primary outcome of mean difference between groups was not statistically different (mean difference 0.68, 95% CI, -1.89 to 3.26) (Figure 2). No statistically significant differences were detected in any subgroup analyses (eFigure 1 **in Supplement 3**).
Results were consistent across the per-protocol and as-treated analyses (eFigure 2 **in Supplement 3**). Results of the sensitivity analyses for the imputation of missing data were similar to the primary

analysis. The primary outcome was re-analysed on the percentage scale and the results are in agreement with the standardized T-score (see eTable 2 **in Supplement 3**).

Secondary outcomes

Early post-operative echocardiographic assessment demonstrated MR grade of none or mild for 147 of 155 (95%) in Mini and 134 of 139 (96%) in Sternotomy at 12 weeks. At 1 year 123 of 133 (92%) of Mini and 126 of 137 (92%) had MR grade of none or mild. At 12 weeks no participants had severe MR. At 52 weeks this had increased to 3 Sternotomy participants and 1 Mini participant. (Figure 3). Further details of echocardiographic assessments at 1 year are shown in eTable 3 **in Supplement 3**

The summary of PF T-scores up to 1 year are shown in eFigure 3 **in Supplement 3**. PF T-scores increased significantly at 6 weeks compared to baseline in the Mini group (2.30; 95% CI, 0.24 to 4.40, p= 0.03) but not in the sternotomy group (1.64; 95% CI, -0.44 to 3.72, p= 0.12).

Time spent in Moderate-to-Vigorous Physical Activity (MVPA) decreased from baseline to 6 and 12 weeks post-surgery in both surgical arms, although this change was smaller in the Mini group. There was a difference in the mean change in time spent in MVPA in favor of Mini surgery by 9.97 minutes (95% CI, 2.46 to 17.49) compared with Sternotomy at 6 weeks post-surgery (Figure 5). Sleep efficiency increased by 5% more (95% CI, 0 to 0.09) at 12 weeks in Mini versus Sternotomy compared to baseline (eFigure 4 **in Supplement 3**).

Median post operative length of hospital stay was significantly reduced after Mini by one day, (median days 5 (IQR=3) versus 6 days (IQR=3) for Sternotomy(1 day, 95%CI: (0.00003, 1.00002),p=0.0038).. The proportion of patients discharged early (defined as 4 days or less after surgery) was greater following Mini (33.1% for Mini versus 15.3% for Sternotomy; odds of being discharged early was 2.81 higher in Mini group (95% CI, 1.6 to 4.94).

QOL measured derived from responses to EQ-5D-5L questionnaire at each time point are shown in eTable 4 **in Supplement 3**. There was no clear difference in scores between groups at any timepoint.

Post operative complications
At 12 weeks, 1 (0.6%) Mini and 4 (2.5%) Sternotomy participants had died. Stroke with permanent neurological deficit had occurred in 1 (0.6%) Mini and 5 (3.5%) Sternotomy participants. Reoperation for bleeding during the index operative stay occurred in 1 (0.6%) of the Mini group and 4 (2.5%) of the Sternotomy group (Table 2). Changes in New York Heart Associations scores at 6 and 12 weeks were similar and are shown in eFigure 5 **in Supplement 3**.

At 1 year, 9 (5.4%) participants in Mini and 10 (6.1%) in Sternotomy had died (4 vs 4), had repeat mitral valve surgery (0 vs 1), or had been hospitalized for heart failure (3 vs 5).

At 1 year 136 (82%) Mini and 124 (76%) Sternotomy participants suffered an adverse event and 14 (8.4%) Mini and 9 (5.5%) Sternotomy participants suffered a serious adverse event (eFigure 6 **in Supplement 3**).

Discussion

This multicenter, expertise based, RCT of Mini- versus Sternotomy MVR demonstrated no difference in the primary outcome of mean change in SF-36v2 PF T-score from baseline to 12 weeks between the groups. This finding was consistent for all planned subgroups analysed and for the per protocol and as treated analysis.

Analysis of secondary outcomes demonstrated an increase in MVPA in the sternotomy group at 6 weeks but not at other time points. This suggests that physical activity among participants receiving Mini was less impacted in the early postoperative period, but the clinical significance of this change is uncertain. PF increased at 6 weeks compared to baseline in the Mini group but not in the sternotomy group. Changes in PF scores were in line with changes observed in the other QoL scores.

We converted the PF percentage score to the T score for comparability with the UK population. However, the observed change in the primary outcome on the PF percentage score from either operation was approximately 14 points and consistent with the minimum clinically important difference of 10 assumed at the outset of the trial. Re-analysis of the primary outcome using the percentage scale showed no difference to the reported outcomes.

The repair techniques used were not protocolised and surgeons were able to decide which approach to use. Leaflet resection was more commonly used in Sternotomy and chordal replaced more commonly used in Mini these but differences these did not affect repair rates or rates of recurrent mitral regurgitation as 12 weeks or 1 year. Cardiopulmonary bypass times were significantly longer with mini but did not lead to an increase in peri operative MI, renal failure or prolonged ventilation which are impacted by prolonged CPB.

The trial addresses a major area of uncertainty in cardiac surgery and a topic that has been identified as a research priority by participants.(23) The importance of identifying the best surgical approach is especially pressing as new percutaneous treatments for DMR emerge.

The trial has several strengths which enable robust comparison of the two surgical approaches. First, it is the largest ever RCT conducted to compare the two techniques and the first trial to account for the impact of the learning curve on outcomes.(24) Expertise based randomization meant challenges, with participants having to accept moving between expert surgeons after randomization, but it ensured a comparison of two techniques undertaken by skilled operators. It also reproduced the likely implementation of the intervention had one group been shown to be superior. We believe this approach to be the most robust and limited significant bias which would have been introduced otherwise No consenting participants refused to move surgeons.

Second, the choice of recovery of physical function as the primary measure of effectiveness was made after extensive patient engagement. Patients were clear that once they were assured of surgical expertise, the key question influencing their choice of procedure was speed of recovery of physical function after surgery. Use of such patient driven outcomes provides valuable evidence to inform shared decision-making, clinical guidelines, and health policy.(25)

Third, SF-36v2 has been used extensively in international trials to measure health status among patients, including in studies of mitral valve disease.(21,22,26) SF-36v2 has a 4-week recall period, takes only a few minutes to complete, has high precision, and in this trial was captured by an independent assessor blinded to allocation.

Fourth, the MCID was determined following extensive clinical and patient engagement to reach consensus, and reference to the literature.(21,22) The MCID, and conversion to T scores in our analysis is endorsed in the SF-36v2 user manual (18) and enables comparability with a UK population.

Only one RCT comparing Mini versus Sternotomy MVR has been reported previously.(27) This single centre RCT trial recruited 140 participants with Barlow's disease, and reported broadly similar results, specifically no difference in mortality, morbidity, or recurrent MR between the groups. Propensity matched comparisons previously suggested that the risk of short-term adverse events are either similar or better with Mini and that there are no differences in long term outcomes. (28) These have been limited by lack of echocardiographic or clinical data beyond the immediate post operative period. Meta-analyses of mainly observational data consistently reported longer operating times with Mini and better short-term outcomes but with higher rates of mitral valve reoperation.(14, 29)

The trial has important limitations. First, this was not a blinded trial, with participants and surgeons aware of allocation. To minimise bias, SF-36v2 and all echocardiographic measures were independently assessed, by personnel blinded to allocation. Detection bias attributable to participant unblinding would also have likely favored the less invasive therapy, suggesting that this was not an important source of bias.
Second, to avoid the impact of a learning curve and need to account for surgical expertise, set criteria for the minimum number of operations performed for all surgeons were achieved prior to performing surgery in the trial. As such, the results may not be applicable for non-expert surgeons or centres but have allowed comparison of the interventions rather than surgeons.

Conclusions

The UK Mini Mitral trial confirms for the first time in a multicentre RCT that Mini MVr achieves high quality and durable valve repair up to 1 year with similar safety and adverse event outcomes to Sternotomy. Change in physical function from baseline to 12 weeks was not significantly different.

Contributors

The study design was conceived by EA, JZ, RM, AK, GM, LV, and HH, who together were awarded funding. EA was the Chief Investigator. Trial management and oversight was done by EA, AM, NH, ZW,

RM, AK, EO, HH and LV. Statistical analysis was undertaken by EK, AK, JW, and EO vouched for the results. Health economic analysis were performed by LV and CF. NH, ZW and AM had access to and verified the data. All authors participated in writing the final manuscript, had full access to all the data in the study, reviewed and approved the final manuscript. EA had final responsibility for the decision to submit for publication.

Declaration of interests

EA, RM, AK, EK, EO, GM, CF-G, LV and HH report grants from the National Institute for Health and Care Research, Heart Research UK, British Heart Foundation, and The Sir Bobby Robson Foundation during the conduct of this trial.
JZ declares speaker and consultancy fees from Medtronic, Edwards Lifesciences and Cambridge Medical robotics.
AK's main contribution was during his employment by Durham University. He currently works for GSK, UK.
None are directly relevant to UK Mini Mitral.
All others declare no competing interests.

Data sharing

All data requests should be submitted to the corresponding author (EA) for consideration. After publication, access to anonymised data might be granted for non-commercial research at the discretion of the corresponding author and Sponsor following review by the CTU.

Acknowledgments

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A special thanks goes to Stephen Owen who was our patient representative on the trial steering committee (TSC), and to all members of the TSC and IDMEC (full details are in the supplementary material). We would also like to acknowledge the support of the NIHR Clinical Research Network.

TABLES AND FIGURES

Figure 1 (awaiting updated version form Sonya) Patient selection allocation and flow in the UK Mini Mitral Trial.

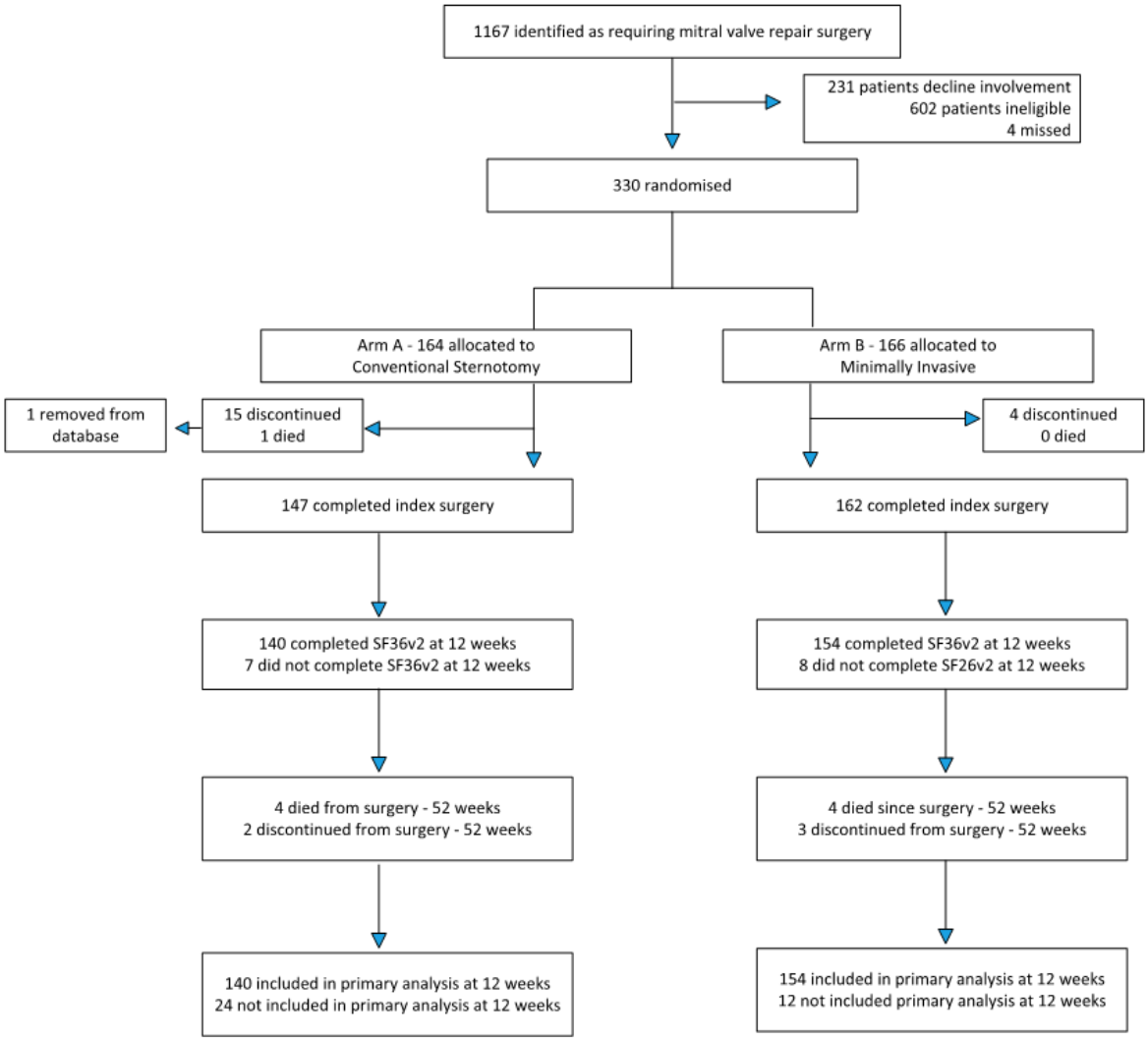

Table 1 Demographics, Baseline Clinical Data and Operative Data

Characteristic*, **	Conventional Sternotomy (N=163)	Minithoracotomy (N=166)
Demographic		
Age at randomization— yr	66.99±11.51	67.29±10.13
Male Sex — no. (%)	111 (68.1)	118 (71.1)
Race — no. (%)†		
White	158 (96.9)	166 (100)
Non white	5 (3.1)	0 (0)
BMI—mean±SD; no. ‡	26.2±4.21; 160	26.5±4.20; 165
Clinical — no./total no. (%)		
History of Atrial Fibrillation	69/160 (43.1)	69/165 (41.8)
History of Heart Failure	45/160 (28.1)	42/165 (25.5)
History of Renal Failure	5/160 (3.1)	6/165 (3.6)
History of Diabetes	15/160 (9.4)	7/165 (4.2)
History of Stroke	13/160 (8.1)	7/165 (4.2)
History of previous MI	5/160 (3.1)	6/165 (3.6)
History of Chronic Obstructive Pulmonary Disease	11/160 (6.9)	14/165 (8.5)
Asthma	13/160 (8.1)	17/165 (10.3)
History of Peripheral Vascular Disease	1/160 (0.6)	4/165 (2.4)
History of Pulmonary Hypertension	24/150 (16)	30/162 (18.5)
Mild (vs No)	0 (0)	0 (0)
Moderate (vs No)	16/150 (10.7)	17/162 (10.5)
Severe (vs No)	8/150 (5.3)	13/162 (8)
NYHA functional class III/IV (vs I/II)	77/150 (51.3)	87/162 (53.7)
Urgency¥		
Elective patient	132/150 (88)	148/162 (91.4)
In-house urgent patient	18/150 (12)	14/162 (8.6)
Euroscore II — mean±SD; no.	1.7±1.43; 150	1.72±1.67; 162
Baseline physical function (SF-36 PF score) §		
Low	36 (22.1)	36 (21.7)
Medium (vs Low)	58 (35.6)	60 (36.1)
High (vs Low)	69 (42.3)	70 (42.2)
Echocardiographic Assessments		
Baseline mitral regurgitation — no./total no. (%)		
Mild	0/155 (0)	0/158 (0)
Moderate	33/155 (21.3)	25/158 (15.8)
Severe (vs Moderate)	122/155 (78.7)	133/158 (84.2)
Left ventricular end systolic vol — ml., mean±SD; no.	49.71±21.37; 155	47.02±17.99; 157
Left ventricular end diastolic vol — ml., mean±SD; no.	148.67±46.58; 155	147.25±45.56; 157
Left ventricular volume end systolic dimension — cm mean±SD; no.	3.52±0.68; 157	3.40±0.61; 156

Left ventricular volume end diastolic dimension — cm., mean±SD; no.	5.51±0.67; 157	5.47±0.68; 156
Left atrial volume — ml., mean±SD; no.	118.54±55. 5; 155	117.97±48.98; 158
Mitral regurgitation vena contracta — mm, mean±SD; no.	0.74±0.17; 131	0.75±0.14; 127
Mitral regurgitation effective regurgitant orifice area (EROA) — cm2., mean±SD; no.	0.59±0.24; 137	0.59±0.28; 139
Regurgitant volume (calculated by PISA method) — ml., mean±SD; no.	80.72±30.92; 137	79.2±30.62; 138
LV Function (LVEF) — no./total no. (%)		
Good > 50%	134/150 (89.3)	120/162 (74.1)
Moderate 31-50%	15/150 (10)	40/162 (24.7)
Poor 21-30%	1/150 (0.7)	1/162 (0.6)
Very poor <20%	0/150 (0)	1/162 (0.6)
Valve pathology — no./total no. (%)		
Posterior leaflet prolapse	99/147 (67.3)	114/159(71.7)
Anterior leaflet prolapse	11/147 (7.5)	14/159 (8.8)
Bileaflet prolapse	29/147 (19.7)	27/159 (17)
Normal leaflets	8/147 (5.4)	4/159 (2.5)
Operative data — no./total no. (%)		
Mitral valve repair	142/146 (97.3)	153/160 (95.6)
AF surgery	20/147 (13.6)	21/160 (13.1)
TV surgery	10/111 (9)	2/120 (1.7)
Repair technique		
Resection	28/146 (19.2)	10/157 (6.4)
Chords	39/146 (26.7)	22/157 (14)
Premeasured loops	48/146 (32.9)	89/157 (56.6)
Edge to Edge	4/146 (2.7)	8/157 (5.1)
Mitral valve ring size— mm., mean±SD; no.	32.73±2.56; 142	31.5±2.9; 153
CPB time — m., mean±SD; no.	102.01±74.59; 146	134.77±41.04; 159
Aortic cross clamp time — m., mean±SD; no.	74.53±24.52; 146	85.6±30.82; 158
Duration of procedure — m., mean±SD; no.	184.34±42.65; 145	228.73±56.38; 159
Repeat bypass run for valve re repair or replacement	7/146 (4.8)	5/160 (3.1)

Table 1: Demographics, Baseline Clinical Data and Operative Data

* Plus–minus values are means ±SD. NYHA denotes New York Heart Association, TV tricuspid valve, LV Left ventricular and AF Atrial fibrillation.

** Where the full randomized data set was not available, the number of cases analysed has been given.

†Race and ethnicity were reported as two separate variables by the patient.

‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.

¥ Patients who were classed as in house urgent were those who were admitted to hospital in heart failure and required urgent surgery during that admission.

§ The baseline physical function (SF-36 PF scores) on the 36-Item Survey (SF-36) are reported in 0 -100 scale with higher scores indicating better health status.

¶ Isolated posterior leaflet pathology- patients with only posterior leaflet prolapse (with P1 or P2 or P3 or PMC and none of A1, A2, A3, and AMC). Isolated anterior leaflet pathology - patients with only anterior leaflet prolapse (A1 or A2 or A3 or AMC and none of P1, P2, P3, and PMC). Bileaflet pathology -patients with any one of P1 or P2 or P3 or PMC or any one of A1 or A2 or A3 or ALC). Normal leaflets- patients with no P1, P2, P3, PMC and no A1, A2, A3, and ALC)

Figure 2 Primary outcome (ideally a parallel line plot)

Figure 3 Echo data as a Sankey diagram

Table 2 Post operative complications at 12 weeks and 1 year

	Conventional Sternotomy (N=163)	Minithoracotomy (N=166)	Diff/OR (95% CI); p-value
Early post operative complication measured up to 12 weeks after surgery	Patients no.(%)	Patients no.(%)	
Death	4* (2.5)	1 (0.6)	0.24 (0.03,2.2); 0.2
Neurological event			
Temporary stroke/TIA	3 (1.8)	7 (4.2)	2.52 (0.61,10.47); 0.2
Stroke with permanent deficit	5 (3.1)	1 (0.6)	0.19 (0.02,1.67); 0.13
MI**	1 (0.6)	0 (0)	-
Tracheostomy	0 (0)	3 (1.8)	-
Renal impairment- AKIN criteria (150% increase over baseline /- replacement therapy)	4 (2.5)	3 (1.8)	0.63 (0.14,2.92); 0.55
Prolonged ventilation (>48 Hrs)	3 (1.8)	4 (2.41)	1.19 (0.26,5.47); 0.82
ICU LOS (hours).-median (IQR)	21.7 (9.2)	23.03 (21.6)	p=0.07[$]
Proportion of prolonged CICU stay (>48 hours)	19 (11.7)	21 (12.7)	1.25 (0.62,2.52); 0.54
MV Replacement	5 (3.1)	8 (4.8)	1.36 (0.43,4.35); 0.6
Reoperation for bleeding during index hospital stay	4 (2.5)	1 (0.6)	0.25 (0.03,2.26); 0.21
Number of patients receiving RBC or blood product transfusion	45 (27.6)	44 (26.5)	0.86 (0.52,1.41); 0.54
Wound pain scores – mean±SD			
Day 3	2.96 ±2.26	2.62±2.41	-0.35 (-0.89,0.19); 0.21
6wks	1.86±1.85	1.50±1.85	-0.32 (-0.75,0.11); 0.15

12wks	0.986±1.58	0.788±1.32	-0.16 (-0.5,0.18); 0.34
New Post op AF (in SR pre-op and in AF post op)	22 (13.5)	20 (12.1)	0.86 (0.43,1.73); 0.67
Thoracotomy wound infection			
Sternal wound infection			
Groin wound infection			
Hospital LOS – median (IQR)	6 (3)	5 (3)	p=0.003[$]
Early discharge (<=4 days post-surgery)	25 (15.3)	55 (33.1)	2.81 (1.6,4.94); <0.001
Post operative complications measured up to 1 year after surgery			
Death	4* (2.5)	4 (2.4)	0.98 (0.24,4.05); 0.98
Any Hospitalization at 1 year	50 (30.7)	65 (39.2)	1.48 (0.93,2.35); 0.09
Heart failure hospitalisation at 1 year	5 (3.1)	5 (3)	0.98 (0.27,3.51); 0.97
Repeat mitral valve surgery at 1 year	1 (0.6)	0 (0)	-
Number of deaths, repeat surgery on the MV at 1 year	5 (3.1)	4 (2.4)	0.78 (0.2,2.99); 0.72
Number of deaths, repeat surgery on the MV, HHF at 1 year	10 (6.1)	9 (5.4)	0.88 (0.34,2.25); 0.78

*One additional patient died prior to surgery in the Sternotomy group

** One patient with a myocardial infarction died.

[$]p-value obtained by non-parametric Wilcoxon test.

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