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Mini-sternotomy for Aortic Valve Replacement Reduces the Length of Stay in the Cardiac Intensive Care: A Mini Meta-analysis

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Mini-sternotomy for Aortic Valve Replacement Reduces the Length of Stay in the Cardiac Intensive Care: A Mini Meta-analysis.

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Abstract

Introduction: Mini-sternotomy for isolated aortic valve replacement aims to reduce operative trauma hastening recovery and improving the cosmetic outcome of cardiac surgery. The short-term clinical benefits from the mini-sternotomy are presumed to arise because the incision is less extensive and the lower half of the chest cage remains intact. The basic conduct of virtually all other aspects of the aortic valve replacement procedure remains the same. Therefore, similar long term outcomes are to be expected. Methods: We conducted a meta-analysis of the only available prospective randomised controlled trials in the published English literature since 1996. Four studies met our criteria: Prospective randomised controlled trials comparing minimally invasive [Inverted 'C' or 'L' (J) shaped] hemi-sternotomy versus conventional sternotomy for adults undergoing isolated aortic valve replacement using standard cardiopulmonary bypass technique. Our outcome measures were the length of positive pressure ventilation, blood loss, intensive care and hospital stay. Results: The length of ITU stay was significantly shorter by 0.57 days in favour of the mini-sternotomy group (CI: -0.95, -0.2; p = 0.003). There was no advantage in terms of duration of ventilation (CI:-3.48, 0.36; p = 0.11). However there was some evidence to suggest a reduction in blood loss and the length of stay in hospital in the mini-sternotomy group. This however did not prove to be statistically significant [154.17mls reduction (CI: -324.51, 16.17; p = 0.08) and 2.03 days less (CI:-4.12, 0.05; p = 0.06) respectively]. Conclusion: Mini-sternotomy for isolated aortic valve replacement significantly reduces the length of stay in cardiac intensive care. Other short term benefits may include a reduction in blood loss or the length of hospital stay.

Article summary

Article focus: This article tests the null hypothesis that, mini-sternotomy has no outcome benefit for aortic surgery. Key message: Min-sternotomy for aortic valve replacement reduces the length of stay in intensive care unit. Strengths: Use of highest quality evidence based medicine. Limitations: Lack of input from patients.

Introduction

A mini-sternotomy through an inverted C, L (or J) shaped hemi-sternotomy is a technique that aims to reduce the operative trauma thereby hastening recovery and improving the cosmetic outcome of cardiac surgery. Some may be of the opinion that the latter has the

potential to confer the greatest benefit. There have been a number of studies, some claim benefits of mini-sternotomy and others have been equivocal about postoperative outcomes such as ventilation requirement, bleeding, and intensive care and hospital stay for isolated aortic valve replacement. However there are only but a few prospective randomised controlled trials (PRCT) in this subject [1-4]. We conducted a meta-analysis of the available PRCTs.

Methods

Electronic search for relevant publications in the English language were conducted in MEDLINE, EMBASE and CENTRAL databases starting from 1996, including the keywords 'aortic valve surgery', 'controlled clinical trials' and 'minimally invasive surgery'. Reference lists of relevant articles were also searched. We only included prospective randomised controlled trials in our mini-meta-analysis.
Of the 21 studies found in our search, 4 studies met our criteria. We selected the studies according to the following inclusion criteria: 1. The type of studies: Prospective randomised controlled trials comparing minimally invasive versus conventional sternotomy, 2. Participants: Adult patients undergoing isolated aortic valve replacement using standard cardiopulmonary bypass technique. The exclusion criterions were, 1. Any other type of mini-sternotomy than hemi-sternotomy through inverted 'C' or 'L' (J) shaped approach. 2. The language of the article was limited to English.
Our outcome measures included the length of positive pressure ventilation, blood loss, intensive care and hospital stay.
Statistical analysis was performed using Review Manager (RevMan) version 5.0. As the data obtained was continuous, combined mean differences were measured using the Random effects model on the presumption that individual studies had varied outcomes. Tests for heterogeneity were perfumed using the chi square test, I^2 test and degrees of freedom.

Results

There were two meta-analyses in this subject [1, 2], four of five PRCTs were subjected to our meta-analysis [3-6]. One PRCT was excluded due to lack of data [7]. An attempt was made to contact the corresponding author for additional information with a view to include that study. This was unsuccessful. Other excluded studies [8-24], were either prospective non-randomized (n = 5), case control studies (n = 3), retrospective studies (n = 1), different type of incisions (n = 2) or studies with outcome measures irrelevant to our study (n = 4). The total number of patients included in this meta-analysis was the sum of the patients recruited in to the four PRCTs. That equals to 220 patients. Table 1 illustrates each of these studies characteristics. The following results are presented as mean differences in outcomes between mini-sternotomy and conventional sternotomy groups in the Random effects method.

Duration of mechanical ventilation in hours: There was a statistically insignificant reduction in the duration of ventilation (Figure 1). This was 1.56 hours less in the mini-sternotomy group (CI:-3.48, 0.36; $p = 0.11$).

Postoperative blood loss in the first 24 hours: There was a statistically insignificant reduction in blood loss of 154.17mls in the mini-sternotomy group compared to the full sternotomy (CI: -324.51, 16.17; $p = 0.08$). Illustrated by figure 2.

Lengths of Intensive Care Unit (ICU) stay in days: Combined mean difference of all the studies showed that the length of ITU stay was significantly shorter by 0.57 days in favour of mini-sternotomy group (CI: -0.95, -0.2; $p = 0.003$). Figure 3 illustrates this primary outcome measure.

Lengths of Hospital stay in days: As illustrated in figure 4, the duration of hospital stay was shorter by 2.03 days in favour of the mini-sternotomy group however the difference again failed to reach statistically significant levels (CI:-4.12, 0.05; $p = 0.06$).

Discussion

We performed a mini meta-analysis to compare the short term post-operative outcomes in four published studies, accounted for differences in their findings, and drew a consensus view on the potential benefits of a mini-sternotomy over a full median sternotomy for a standard aortic valve replacement. The following outcome measures were assessed: Duration of ventilation, postoperative blood loss, length of stay in the intensive care unit and the hospital stay.

Using only the best available level of evidence in this meta-analysis we have clearly illustrated the advantage of the mini-sternotomy approach in reducing the number of days spent in the intensive care unit ($p = 0.003$) and a lack of advantage in terms of number of hours ventilated ($p = 0.11$). We have however failed to prove a clear superiority in favour of mini-sternotomy in terms of reduction in blood loss ($p = 0.08$) or the length of hospital stay ($p = 0.06$). The difference may be of clinical importance. The reduction in ITU stay by 0.57 days is a more than 50% reduction in the length of stay in ITU for a typical isolated aortic valve replacement with potential financial advantages.

This study is limited as it only includes four PRCTs, with relatively small number of subjects and outcome variables. Lack of long term data is not exclusive to this meta-analysis. These limitations can only be addressed by conducting a well designed and adequately powered PRCT.

The total number of patients included in this study was 220. This is a small number considering isolated aortic valve replacement constitutes a large proportion of our cardiac surgical work. There were two extensive well conducted meta-analysis comparing mini-sternotomy versus conventional sternotomy for aortic valve replacement [1, 2]. They improved the power of the study by including several comparative non randomised studies, hence increasing the number of patients to 4,586 and 4,667 respectively. These studies looked at a wide variety of non-sternotomy incisions. They excluded studies if more than 50% of reported cases were not a mini-sternotomy, or operations other than isolated aortic valve replacement. Their combined conclusion was that mini-sternotomy can be performed safely for aortic valve replacement without increased risk of death or major complications [1] but with no clinical benefits [2]. In contrast the rational for our study was to focus on

mini-sternotomy incisions and the commonest variations thereof which included the inverted C and L or (J) mini-sternotomies.
An additional consideration is that minimally invasive surgery benefits patients because of the incision. Cosmesis does not appear to be a priority for patients in the western world [8]. A more cosmetic scar may be more of an issue in Asia due to younger patient population [3] (table 1). This was a limitation in this study for which there was insufficient data for comparisons to be made in this meta-analysis.

Conclusion

There is a significant reduction in the length of stay in cardiac intensive care unit and an overall benefit in short term outcomes from mini-sternotomy for isolated aortic valve replacement. This meta-analysis would no doubt prove useful when designing a much needed, larger and adequately powered prospective randomised controlled trial in this subject.

Acknowledgement

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Funding

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Competing Interest

None

Authors' contributions

All authors contributed equally in design, review of the literature analysis and intellectual discussion of this manuscript. The primary author Dr Espeed Khoshbin presented this work at the International Society of Minimally Invasive Cardiothoracic Surgery in Washington DC, June 2011.

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PRISMA 2009 Checklist

Section/topic	#	**Mini-sternotomy for Aortic Valve Replacement Reduces the Length of Stay in the Cardiac Intensive Care: A Mini Meta-analysis.** Khoshbin E, Prayaga S, Kinsella J, Sutherland FWH.	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	1
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	1&2
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	2
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	2
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	2
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	2
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	2
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	2
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	2
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	2
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	2

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Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	2
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	2
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	2-3
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	2&Table1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Figures1-4
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figures1-4
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Figures1-4
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Figures1-4
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Figures1-4
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	3
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	3-4
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	4
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	4

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

Figure 1: Duration of ventilation in hours.

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
01	2	3	30	6.43	1.14	30	27.8%	-4.43 [-5.58, -3.28]
02	13	1.3	20	13.2	1.5	20	29.1%	-0.20 [-1.07, 0.67]
03	4.4	0.9	40	5.3	1.8	40	29.9%	-0.90 [-1.52, -0.28]
04	9.9	8	20	9.9	4.5	20	13.1%	0.00 [-4.02, 4.02]
Total (95% CI)			**110**			**110**	**100.0%**	**-1.56 [-3.48, 0.36]**

Heterogeneity: Tau² = 3.11; Chi² = 36.63, df = 3 (P < 0.00001); I² = 92%
Test for overall effect: Z = 1.59 (P = 0.11)

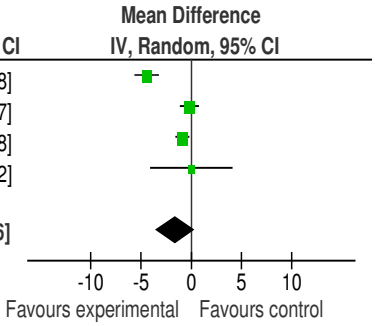

Figure 2: Post operative bleeding in the first 24 hours measured in milliliters.

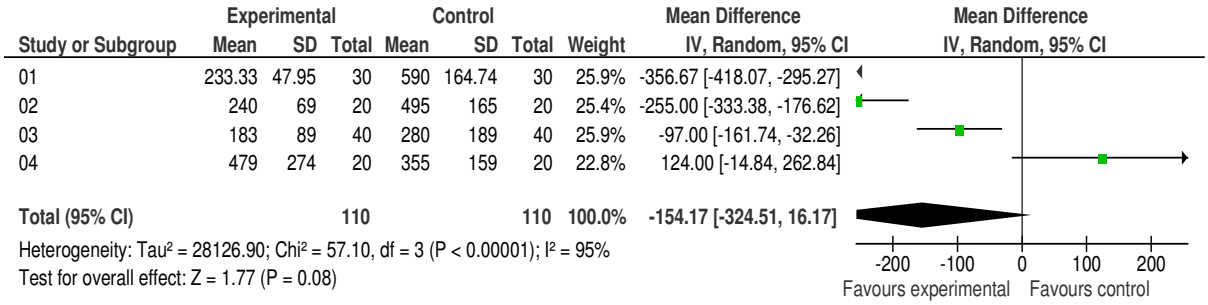

Figure 3: Length of ITU stay in days.

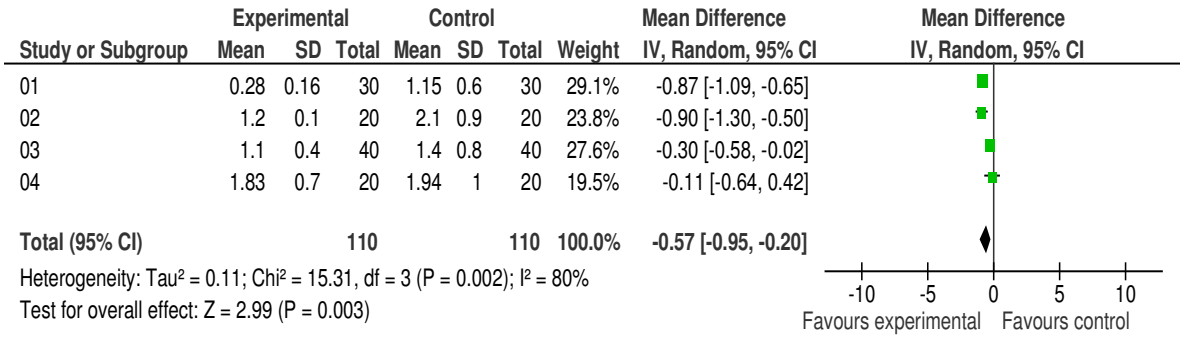

Figure 3: Length of ITU stay in days.

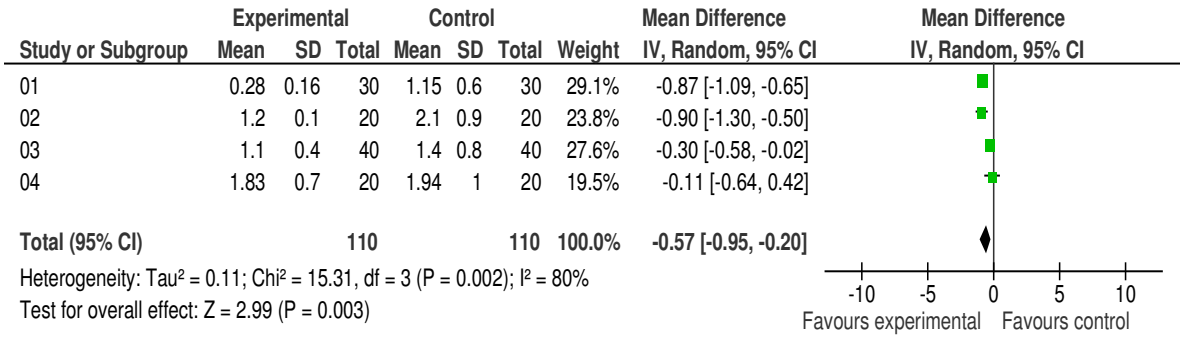

Figure 4: Length of hospital stay in days.

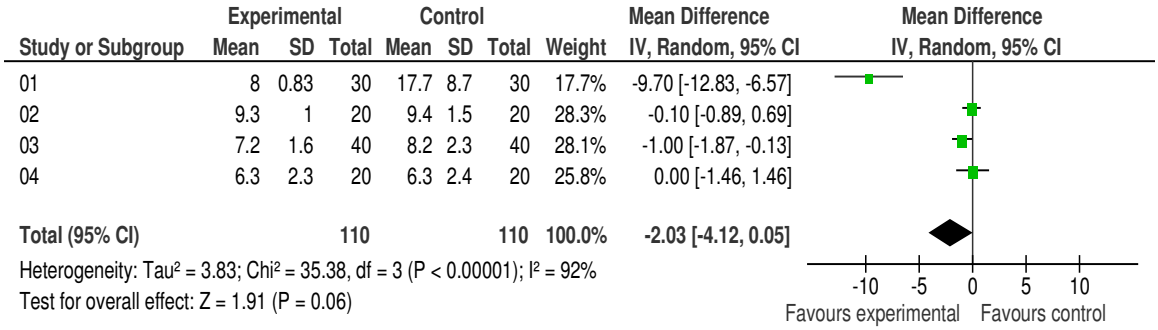

Table 1 : Study characteristics

Study	Moustafa et.al. 2007	Dogan et.al. 2003	Bonacchi et. al. 2002	Aris et. al. 1999
Methods	PRCT	PRCT	PRCT	PRCT
Number of Participants	30 + 30 = 60	20 + 20 = 40	40 + 40 = 80	20 + 20 = 40
Mean age in years (Full/Mini)	23.8 / 22.9	64.3 / 65.7	62.6 / 64.0	62.2 / 66.5
Sex M:F (Full/Mini)	15:15 / 16:14	11:9 / 9:11	-	-
Operation	Isolated AVR	Isolated AVR	Isolated AVR	Isolated AVR
Interventions	Full sternotomy VS. L shaped Mini-sternotomy Pain management with tenoxicam	Complete sternotomy VS. L shaped Mini-sternotomy	Standard sternotomy VS. C or L shaped Mini-sternotomy	Median sternotomy VS. C or L shaped Mini-sternotomy Pain management with metamizol
Outcomes	Duration of ventilation Post op blood loss Length of ITU stay Pulmonary function Analgesic requirement Length of hospital stay Cross clamp time Bypass time Operation time Survival to discharge	Duration of ventilation Post op blood loss Length of ITU stay Pulmonary function - Length of hospital stay Cross clamp time Bypass time Operation time Survival to discharge	Duration of ventilation Post op blood loss Length of ITU stay Pulmonary function Analgesic requirement Length of hospital stay Cross clamp time Bypass time Operation time Survival to discharge	Duration of ventilation Post op blood loss Length of ITU stay Pulmonary function - Length of Hospital stay Cross clamp time Bypass time Operation time Survival to discharge

PRCT = Prospective randomized controlled trial, AVR = Aortic valve replacement, VS. = Versus, ITU = Intensive care unit

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Abstract

Introduction: Mini-sternotomy for isolated aortic valve replacement aims to reduce operative trauma hastening recovery and improving the cosmetic outcome of cardiac surgery. The short-term clinical benefits from the mini-sternotomy are presumed to arise because the incision is less extensive and the lower half of the chest cage remains intact. The basic conduct of virtually all other aspects of the aortic valve replacement procedure remains the same. Therefore, similar long term outcomes are to be expected. Methods: We conducted a meta-analysis of the only available prospective randomised controlled trials in the published English literature since 1996. Four studies met our criteria: Prospective randomised controlled trials comparing minimally invasive [Inverted 'C' or 'L' (J) shaped] hemi-sternotomy versus conventional sternotomy for adults undergoing isolated aortic valve replacement using standard cardiopulmonary bypass technique. Our outcome measures were the length of positive pressure ventilation, blood loss, intensive care and hospital stay. Results: The length of ITU stay was significantly shorter by 0.57 days in favour of the mini-sternotomy group (CI: -0.95, -0.2; p = 0.003). There was no advantage in terms of duration of ventilation (CI:-3.48, 0.36; p = 0.11). However there was some evidence to suggest a reduction in blood loss and the length of stay in hospital in the mini-sternotomy group. This however did not prove to be statistically significant [154.17mls reduction (CI: -324.51, 16.17; p = 0.08) and 2.03 days less (CI:-4.12, 0.05; p = 0.06) respectively]. Conclusion: Mini-sternotomy for isolated aortic valve replacement significantly reduces the length of stay in cardiac intensive care. Other short term benefits may include a reduction in blood loss or the length of hospital stay.

Article summary

Article focus: This article tests the null hypothesis that, mini-sternotomy has no outcome benefit for aortic surgery. Key message: Mini-sternotomy for aortic valve replacement reduces the length of stay in intensive care unit. Sample search strategy: Medline Embase and Central databases. Strengths: Use of highest quality evidence based medicine. Limitations: This study is not a "Gold Standard" systematic review in the sense of searching grey literature but a confirmatory study.

Introduction

A mini-sternotomy through an inverted C, L (or J) shaped hemi-sternotomy is a technique that aims to reduce the operative trauma thereby hastening recovery and improving the cosmetic outcome of cardiac surgery. Some may be of the opinion that the latter has the potential to confer the greatest benefit. There have been numerous studies in this subject, some claim benefits in terms of postoperative outcomes, such as ventilation requirement, bleeding, and intensive care and hospital stay for isolated aortic valve replacement performed in this way, others have been equivocal. The two larger meta-analyses in the published literature[1-2], included data from a spectrum of sources ranging from prospective randomised controlled trials (PRCT) to non randomised studies. They addressed important broad questions of safety and efficacy[1] and mortality and morbidity[2] associated with this method. However failed to show any specific advantages in terms of length of positive pressure ventilation, blood loss, intensive care and hospital stay. We believe these outcomes are best assessed by way of PRCTs, and hence conducted a mini meta-analysis to address these specific questions using only the available PRCTs[3-6] published in this subject.

Methods

Electronic search for relevant publications in the English language were conducted in MEDLINE, EMBASE and CENTRAL databases starting from 1996, when the first study of minimal invasive AVR was conducted. We searched for the keywords 'aortic valve surgery', 'controlled clinical trials' and 'minimally invasive surgery'. Reference lists of relevant articles were also searched. We only included prospective randomised controlled trials in our mini-meta-analysis.

Of the 21 studies found in our search, 4 studies met our criteria. We selected the studies according to the following inclusion criteria: 1. The type of studies: Prospective randomised controlled trials comparing minimally invasive versus conventional sternotomy, 2. Participants: Adult patients undergoing isolated aortic valve replacement using standard cardiopulmonary bypass technique. The exclusion criterions were, 1. Any other type of mini-sternotomy than hemi-sternotomy through inverted 'C' or 'L' (J) shaped approach. 2. The language of the article was limited to English (Table 1).

Our outcome measures included the length of positive pressure ventilation, blood loss, intensive care and hospital stay.

Statistical analysis was performed using Review Manager (RevMan) version 5.0. As the data obtained was continuous, combined mean differences were measured using the Random effects model on the presumption that individual studies had varied outcomes. Tests for heterogeneity were perfumed using the chi square test, I^2 test and degrees of freedom.

Results

There were two meta-analyses in this subject [1, 2], four of five PRCTs were subjected to our meta-analysis [3-6]. One PRCT was excluded due to lack of data [7]. An attempt was made to contact the corresponding author for additional information with a view to include that

study. This was unsuccessful. Other excluded studies [8-24], were either prospective non-randomized (n = 5), case control studies (n = 3), retrospective studies (n = 1), different type of incisions (n = 2) or studies with outcome measures irrelevant to our study (n = 4). The total number of patients included in this meta-analysis was the sum of the patients recruited in to the four PRCTs. That equals to 220 patients. Table 2 illustrates each of these studies characteristics. The following results are presented as mean differences in outcomes between mini-sternotomy and conventional sternotomy groups in the Random effects method.

Duration of mechanical ventilation in hours: There was a statistically insignificant reduction in the duration of ventilation (Figure 1). This was 1.56 hours less in the mini-sternotomy group (CI:-3.48, 0.36; $p = 0.11$).

Postoperative blood loss in the first 24 hours: There was a statistically insignificant reduction in blood loss of 154.17mls in the mini-sternotomy group compared to the full sternotomy (CI: -324.51, 16.17; $p = 0.08$). Illustrated by figure 2.

Lengths of Intensive Care Unit (ICU) stay in days: Combined mean difference of all the studies showed that the length of ITU stay was significantly shorter by 0.57 days in favour of mini-sternotomy group (CI: -0.95, -0.2; $p = 0.003$). Figure 3 illustrates this primary outcome measure.

Lengths of Hospital stay in days: As illustrated in figure 4, the duration of hospital stay was shorter by 2.03 days in favour of the mini-sternotomy group however the difference again failed to reach statistically significant levels (CI:-4.12, 0.05; $p = 0.06$).

Discussion

We performed a mini meta-analysis to compare the short term post-operative outcomes in four published studies, accounted for differences in their findings, and drew a consensus view on the potential benefits of a mini-sternotomy over a full median sternotomy for a standard aortic valve replacement. The following outcome measures were assessed: Duration of ventilation, postoperative blood loss, length of stay in the intensive care unit and the hospital stay.

Using only the best available level of evidence in this meta-analysis we have clearly illustrated the advantage of the mini-sternotomy approach in reducing the number of days spent in the intensive care unit ($p = 0.003$) and a lack of advantage in terms of number of hours ventilated ($p = 0.11$). We have however failed to prove a clear superiority in favour of mini-sternotomy in terms of reduction in blood loss ($p = 0.08$) or the length of hospital stay ($p = 0.06$). However this shows a trend of significance. None of the previous meta-analyses showed such trend. Our meta-analysis therefore highlights a much needed, larger and adequately powered prospective randomised controlled trial for these specific outcomes. The reduction in ITU stay by 0.57 days is a more than 50% reduction in the length of stay in ITU for a typical isolated aortic valve replacement with potential financial advantages.

This study is limited as it is not a "Gold Standard" systematic review in the sense of searching grey literature but a confirmatory study. It only includes four PRCTs, with a relatively small number of subjects and outcome variables. A fifth PRCT by Macheler et, al. was excluded due to the lack of data regarding ITU and length of hospital stay, however it should be noted that this trial supported our findings regarding the duration of ventilation and blood drainage per 24 hours. It should also be mentioned that in the meta-analysis by Morgan et, al.[1] three out of four of the above studies were analyzed separately as a sub group[4-6]. They found a non statistical advantage in terms of ventilation time, bleeding and ITU stay. In contrast this mini meta-analysis excludes the PRCT by Macheler et, al. but includes the most recent PRCT by Moustafa et, al.[3]. Lack of long term data is not exclusive to this meta-analysis.

The total number of patients included in this study was 220. This is a small number considering isolated aortic valve replacement constitutes a large proportion of our cardiac surgical work. There were two extensive well conducted meta-analysis comparing mini-sternotomy versus conventional sternotomy for aortic valve replacement [1, 2]. They improved the power of the study by including several comparative non randomised studies, hence increasing the number of patients to 4,586 and 4,667 respectively. These studies looked at a wide variety of non-sternotomy incisions. They excluded studies if more than 50% of reported cases were not a mini-sternotomy, or operations other than isolated aortic valve replacement. Their combined conclusion was that mini-sternotomy can be performed safely for aortic valve replacement without increased risk of death or major complications [1] but with no clinical benefits [2]. In contrast the rational for our study was to focus on mini-sternotomy incisions and the commonest variations thereof which included the inverted C and L or (J) mini-sternotomies.

There also exists a degree of geographical variation which should be taken in to consideration. For example: the benefits due to the incision. Cosmesis does not appear to be a priority for patients in the western world [8]. A more cosmetic scar may be more of an issue in Asia due to younger patient population [3] (table 2). This was a limitation in this study for which there was insufficient data for comparisons to be made. However minimally invasive valve surgery is already known to improve patient satisfaction while reducing costs of cardiac valve replacement[25-26].

Conclusion

There is a significant reduction in the length of stay in cardiac intensive care unit and an overall benefit in short term outcomes from mini-sternotomy for isolated aortic valve replacement. This meta-analysis would no doubt prove useful when designing a much needed, larger and adequately powered prospective randomised controlled trial in this subject.

Acknowledgement

We would like to thank the department of biostatistics at Robertson Centre, University of Glasgow for their help with the statistical methods, the library staff at Glasgow Royal Infirmary and the audit office staff at the Golden Jubilee National Hospital for their help with the literature search.

Funding

We would also like to thank Mark Woolley from Cardiosolutions for providing funding to present this work at the International Society of Minimally Invasive Cardiothoracic Surgery in Washington DC, June 2011.

Competing Interest

None

Authors' contributions

All authors contributed equally in design, review of the literature analysis and intellectual discussion of this manuscript. The primary author Dr Espeed Khoshbin presented this work at the International Society of Minimally Invasive Cardiothoracic Surgery in Washington DC, June 2011.

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Table 1: Consort diagram

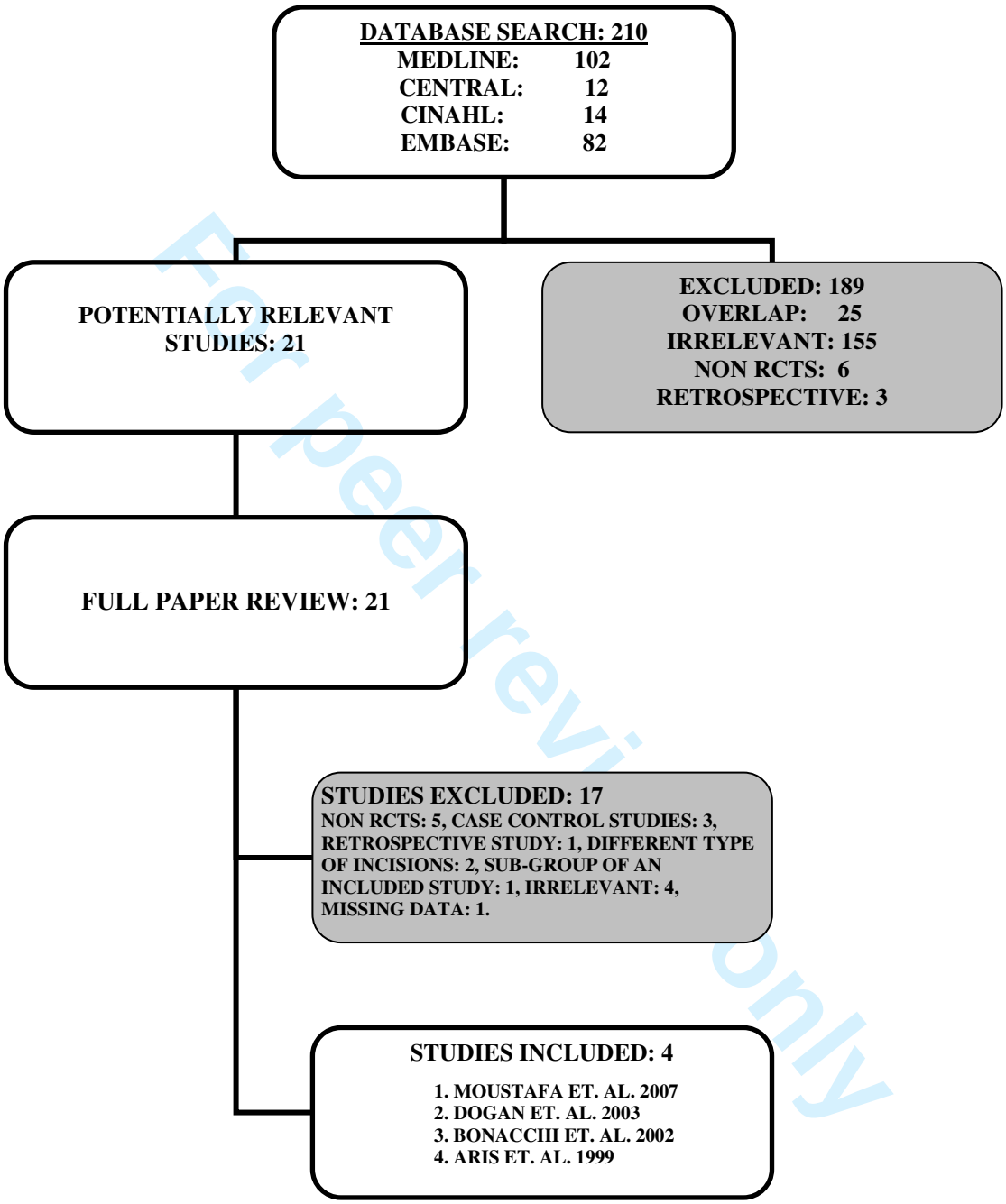


Table 2 : Study characteristics

Study	Moustafa et.al. 2007	Dogan et.al. 2003	Bonacchi et. al. 2002	Aris et. al. 1999
Methods	PRCT	PRCT	PRCT	PRCT
Number of Participants	30 + 30 = 60	20 + 20 = 40	40 + 40 = 80	20 + 20 = 40
Mean age in years (Full/Mini)	23.8 / 22.9	64.3 / 65.7	62.6 / 64.0	62.2 / 66.5
Sex M:F (Full/Mini)	15:15 / 16:14	11:9 / 9:11	-	-
Operation	Isolated AVR	Isolated AVR	Isolated AVR	Isolated AVR
Interventions	Full sternotomy VS. L shaped Mini-sternotomy Pain management with tenoxicam	Complete sternotomy VS. L shaped Mini-sternotomy	Standard sternotomy VS. C or L shaped Mini-sternotomy	Median sternotomy VS. C or L shaped Mini-sternotomy Pain management with metamizol
Outcomes	Duration of ventilation Post op blood loss Length of ITU stay Pulmonary function Analgesic requirement Length of hospital stay Cross clamp time Bypass time Operation time Survival to discharge	Duration of ventilation Post op blood loss Length of ITU stay Pulmonary function - Length of hospital stay Cross clamp time Bypass time Operation time Survival to discharge	Duration of ventilation Post op blood loss Length of ITU stay Pulmonary function Analgesic requirement Length of hospital stay Cross clamp time Bypass time Operation time Survival to discharge	Duration of ventilation Post op blood loss Length of ITU stay Pulmonary function - Length of Hospital stay Cross clamp time Bypass time Operation time Survival to discharge

PRCT = Prospective randomized controlled trial, AVR = Aortic valve replacement, VS. = Versus, ITU = Intensive care unit

PRISMA 2009 Checklist

Section/topic	#	**Mini-sternotomy for Aortic Valve Replacement Reduces the Length of Stay in the Cardiac Intensive Care: A Mini Meta-analysis.** Khoshbin E, Prayaga S, Kinsella J, Sutherland FWH.	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	1
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	1&2
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	2
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	2
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	2
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	2
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	2
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	2
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	2
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	2
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	2

PRISMA 2009 Checklist

Section/topic	#	**Mini-sternotomy for Aortic Valve Replacement Reduces the Length of Stay in the Cardiac Intensive Care: A Mini Meta-analysis.** Khoshbin E, Prayaga S, Kinsella J, Sutherland FWH.	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	2
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	2
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	2-3
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	2&Table1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Figures1-4
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figures1-4
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Figures1-4
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Figures1-4
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Figures1-4
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	3
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	3-4
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	4
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	4

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Figure 1: Duration of ventilation in hours.

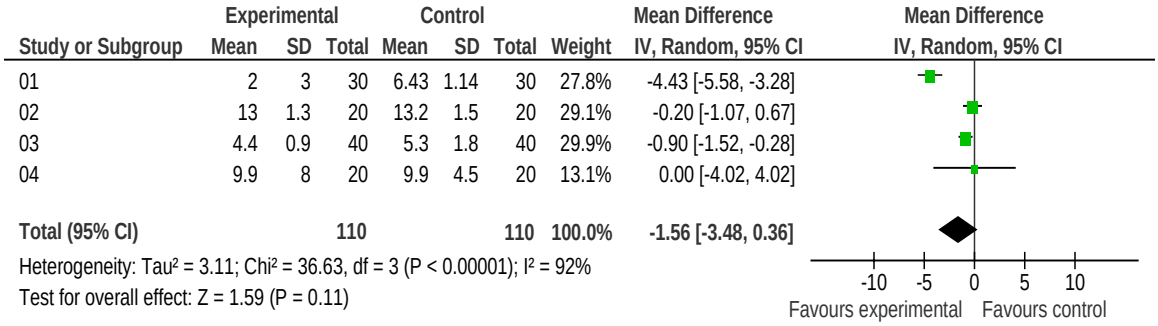


Figure 2: Post operative bleeding in the first 24 hours measured in milliliters.

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
01	233.33	47.95	30	590	164.74	30	25.9%	-356.67 [-418.07, -295.27]
02	240	69	20	495	165	20	25.4%	-255.00 [-333.38, -176.62]
03	183	89	40	280	189	40	25.9%	-97.00 [-161.74, -32.26]
04	479	274	20	355	159	20	22.8%	124.00 [-14.84, 262.84]
Total (95% CI)			**110**			**110**	**100.0%**	**-154.17 [-324.51, 16.17]**

Heterogeneity: Tau² = 28126.90; Chi² = 57.10, df = 3 (P < 0.00001); I² = 95%

Test for overall effect: Z = 1.77 (P = 0.08)

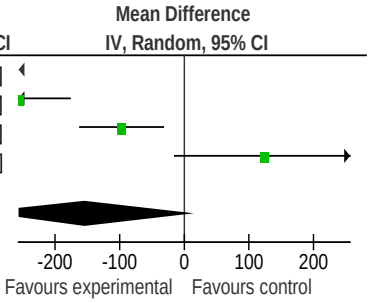


Figure 3: Length of ITU stay in days.

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
01	0.28	0.16	30	1.15	0.6	30	29.1%	-0.87 [-1.09, -0.65]
02	1.2	0.1	20	2.1	0.9	20	23.8%	-0.90 [-1.30, -0.50]
03	1.1	0.4	40	1.4	0.8	40	27.6%	-0.30 [-0.58, -0.02]
04	1.83	0.7	20	1.94	1	20	19.5%	-0.11 [-0.64, 0.42]
Total (95% CI)			**110**			**110**	**100.0%**	**-0.57 [-0.95, -0.20]**

Heterogeneity: Tau² = 0.11; Chi² = 15.31, df = 3 (P = 0.002); I² = 80%

Test for overall effect: Z = 2.99 (P = 0.003)

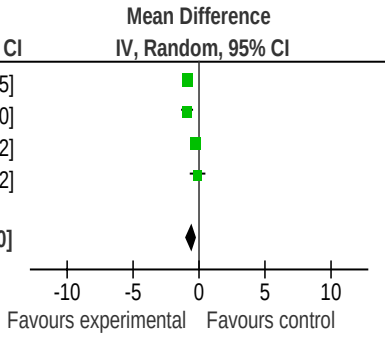
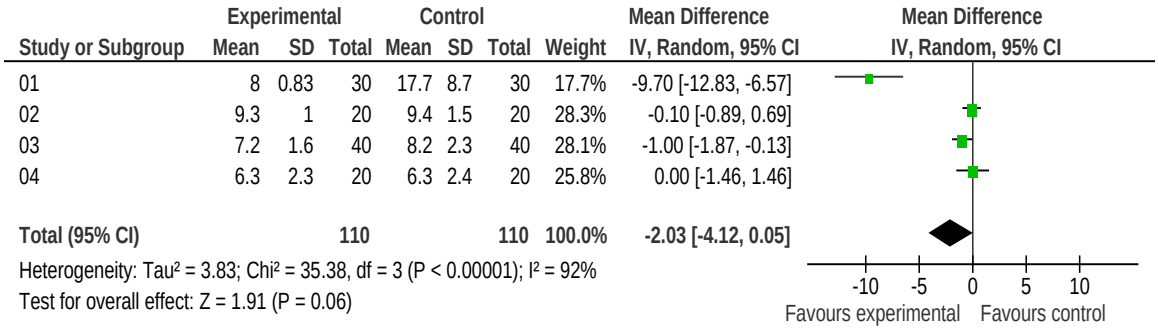


Figure 4: Length of hospital stay in days.



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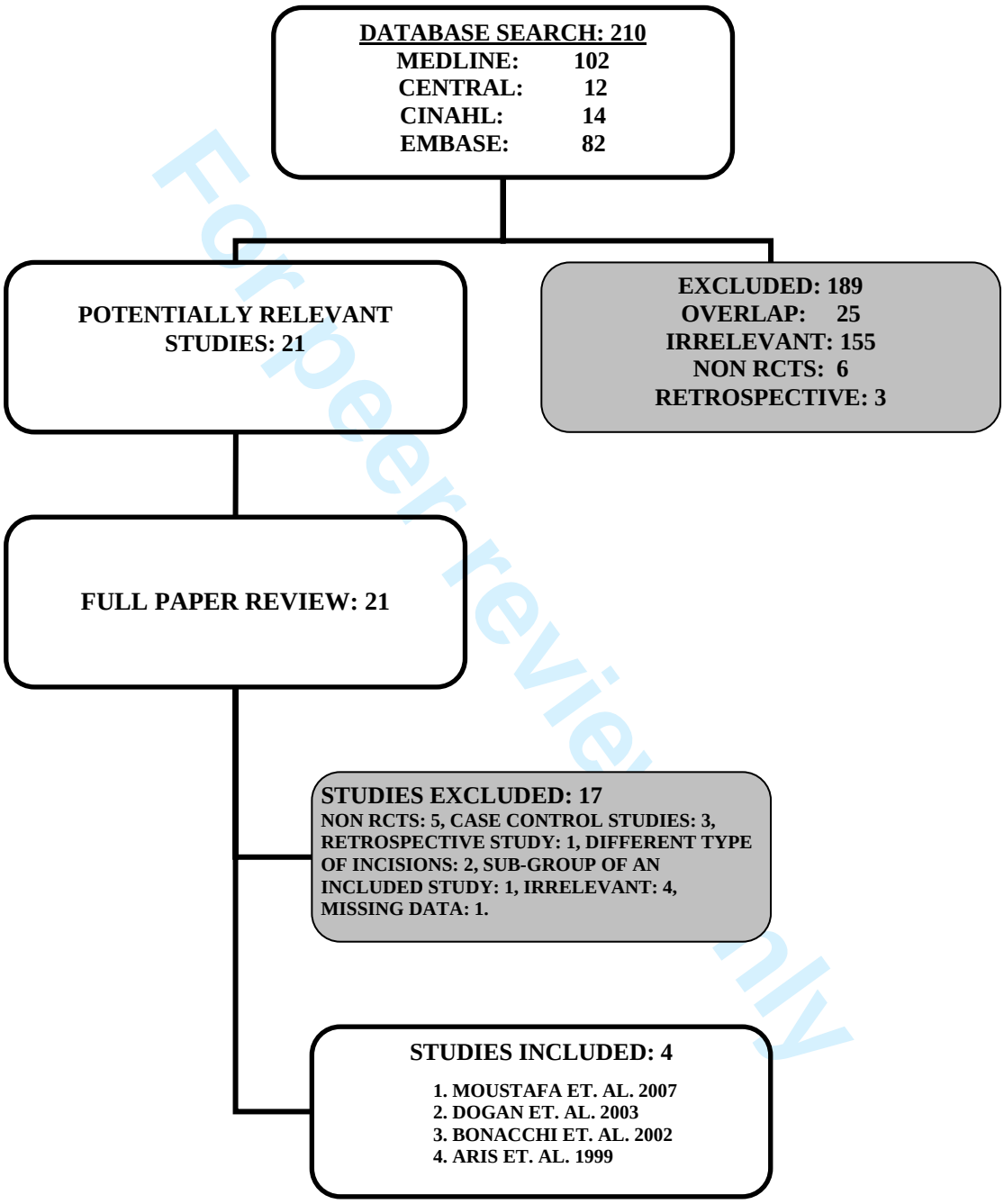

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PRCT = Prospective randomized controlled trial, AVR = Aortic valve replacement, VS. = Versus, ITU = Intensive care unit

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Mini-sternotomy for Aortic Valve Replacement Reduces the Length of Stay in the Cardiac Intensive Care: Meta-analysis of randomised controlled trials.

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Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Surgery
Keywords:	Mini-sternotomy , Aortic Valve Replacement , Meta analysis

Mini-sternotomy for Aortic Valve Replacement Reduces the Length of Stay in the Cardiac Intensive Care: Meta-analysis of randomised controlled trials.

Khoshbin E, Prayaga S, Kinsella J, Sutherland FWH.
Department of Cardiothoracic Surgeon, Golden Jubilee National Hospital, and Academic Unit of Anaesthesia, Pain and Critical Care, University of Glasgow, Scotland, UK.

Abstract

Background: Mini-sternotomy for isolated aortic valve replacement aims to reduce operative trauma hastening recovery and improving the cosmetic outcome of cardiac surgery. The short-term clinical benefits from the mini-sternotomy are presumed to arise because the incision is less extensive and the lower half of the chest cage remains intact. The basic conduct of virtually all other aspects of the aortic valve replacement procedure remains the same. Therefore, similar long term outcomes are to be expected. Objectives: To conduct a meta-analysis of the only available randomised controlled trials in the published English literature. Data sources: Electronic search for relevant publications in MEDLINE, EMBASE and CENTRAL databases were performed. Four studies met our criteria. Study eligibility criteria: Randomised controlled trials comparing minimally invasive [Inverted 'C' or 'L' (J) shaped] hemi-sternotomy versus conventional sternotomy for adults undergoing isolated aortic valve replacement using standard cardiopulmonary bypass technique. Methods: Our outcome measures were the length of positive pressure ventilation, blood loss, intensive care and hospital stay. Results: The length of ITU stay was significantly shorter by 0.57 days in favour of the mini-sternotomy group (CI: -0.95, -0.2; $p = 0.003$). There was no advantage in terms of duration of ventilation (CI:-3.48, 0.36; $p = 0.11$). However there was some evidence to suggest a reduction in blood loss and the length of stay in hospital in the mini-sternotomy group. This however did not prove to be statistically significant [154.17mls reduction (CI: -324.51, 16.17; $p = 0.08$) and 2.03 days less (CI:-4.12, 0.05; $p = 0.06$) respectively]. Limitations: This study includes a relatively small number of subjects (n = 220) and outcome variables. The risk of bias was not assessed during this meta-analysis. Conclusion: Mini-sternotomy for isolated aortic valve replacement significantly reduces the length of stay in cardiac intensive care. Other short term benefits may include a reduction in blood loss or the length of hospital stay.

Article summary

Article focus: This article tests the null hypothesis that, mini-sternotomy has no outcome benefit for aortic surgery. Key message: Mini-sternotomy for aortic valve replacement reduces the length of stay in intensive care unit. Sample search strategy: Medline Embase and Central databases. Strengths: Use of highest quality evidence based medicine. Limitations: This study is not a "Gold Standard" systematic review in the sense of searching grey literature but a confirmatory study.

Introduction

A mini-sternotomy through an inverted C, L (or J) shaped hemi-sternotomy is a technique that aims to reduce the operative trauma thereby hastening recovery and improving the cosmetic outcome of cardiac surgery. Some may be of the opinion that the latter has the potential to confer the greatest benefit. There have been numerous studies in this subject, some claim benefits in terms of postoperative outcomes, such as ventilation requirement, bleeding, and intensive care and hospital stay for isolated aortic valve replacement performed in this way, others have been equivocal. The two larger meta-analyses in the published literature[1-2], included data from a spectrum of sources ranging from randomised controlled trials (RCT) to non randomised studies. They addressed important broad questions of safety and efficacy[1] and mortality and morbidity[2] associated with this method. However failed to show any specific advantages in terms of length of positive pressure ventilation, blood loss, intensive care and hospital stay. We believe these outcomes are best assessed by way of RCTs, and hence conducted a meta-analysis to address these specific questions using only the available RCTs[3-6] published in this subject.

Methods

Electronic search for relevant publications in the English language were conducted in MEDLINE, EMBASE and CENTRAL databases starting from 1996, when the first study of minimal invasive AVR was conducted. The eligibility of each study was assessed by more than one author during the search of databases and references. We searched for the keywords 'aortic valve surgery', 'controlled clinical trials' and 'minimally invasive surgery'. Reference lists of relevant articles were also searched. We only included randomised controlled trials in our meta-analysis.

Of the 21 studies found in our search, 4 studies met our criteria. We selected the studies according to the following inclusion criteria: 1. The type of studies: Randomised controlled trials comparing minimally invasive versus conventional sternotomy, 2. Participants: Adult patients undergoing isolated aortic valve replacement using standard cardiopulmonary bypass technique. The exclusion criterions were, 1. Any other type of mini-sternotomy than hemi-sternotomy through inverted 'C' or 'L' (J) shaped approach. 2. The language of the article was limited to English (Table 1).

Our outcome measures included the length of positive pressure ventilation, blood loss, intensive care and hospital stay.

Statistical analysis was performed using Review Manager (RevMan) version 5.0. As the data obtained was continuous, combined mean differences were measured using the Random effects model on the presumption that individual studies had varied outcomes. Tests for heterogeneity were performed using the chi square test, I^2 test and degrees of freedom. In this meta-analysis the risk of bias wasn't assessed.

Results

There were two meta-analyses in this subject [1, 2], four of five RCTs were subjected to our meta-analysis [3-6]. One RCT was excluded due to lack of data [7]. An attempt was made to contact the corresponding author for additional information with a view to include that

study. This was unsuccessful. Other excluded studies [8-24], were either prospective non-randomized (n = 5), case control studies (n = 3), retrospective studies (n = 1), different type of incisions (n = 2) or studies with outcome measures irrelevant to our study (n = 4). The total number of patients included in this meta-analysis was the sum of the patients recruited in to the four RCTs. That equals to 220 patients. Table 2 illustrates each of these studies characteristics. The following results are presented as mean differences in outcomes between mini-sternotomy and conventional sternotomy groups in the random effects method.

Duration of mechanical ventilation in hours: There was a statistically insignificant reduction in the duration of ventilation (Figure 1). This was 1.56 hours less in the mini-sternotomy group (CI:-3.48, 0.36; $p = 0.11$).

Postoperative blood loss in the first 24 hours: There was a statistically insignificant reduction in blood loss of 154.17mls in the mini-sternotomy group compared to the full sternotomy (CI: -324.51, 16.17; $p = 0.08$). Illustrated by figure 2.

Lengths of Intensive Care Unit (ICU) stay in days: Combined mean difference of all the studies showed that the length of ITU stay was significantly shorter by 0.57 days in favour of mini-sternotomy group (CI: -0.95, -0.2; $p = 0.003$). Figure 3 illustrates this primary outcome measure.

Lengths of Hospital stay in days: As illustrated in figure 4, the duration of hospital stay was shorter by 2.03 days in favour of the mini-sternotomy group however the difference again failed to reach statistically significant levels (CI:-4.12, 0.05; $p = 0.06$).

Discussion

We performed a meta-analysis to compare the short term post-operative outcomes in four published studies, accounted for differences in their findings, and drew a consensus view on the potential benefits of a mini-sternotomy over a full median sternotomy for a standard aortic valve replacement. The following outcome measures were assessed: Duration of ventilation, postoperative blood loss, length of stay in the intensive care unit and the hospital stay.

Using only the best available level of evidence in this meta-analysis we have clearly illustrated the advantage of the mini-sternotomy approach in reducing the number of days spent in the intensive care unit ($p = 0.003$) and a lack of advantage in terms of number of hours ventilated ($p = 0.11$). We failed to prove a clear superiority in favour of mini-sternotomy in terms of reduction in blood loss ($p = 0.08$) or the length of hospital stay ($p = 0.06$). However this shows a trend of significance. None of the previous meta-analyses showed such a trend. Our meta-analysis therefore highlights a much needed, larger and adequately powered randomised controlled trial for these specific outcomes. The reduction in ITU stay by 0.57 days is a more than 50% reduction in the length of stay in ITU for a typical isolated aortic valve replacement with potential financial advantages.

This study is limited as it is not a "Gold Standard" systematic review in the sense of searching grey literature but a confirmatory study. It only includes four RCTs, with a relatively small number of subjects and outcome variables. The risk of bias wasn't assessed during this meta-analysis. A fifth RCT by Macheler et, al. was excluded due to the lack of data regarding ITU and length of hospital stay, however it should be noted that this trial supported our findings regarding the duration of ventilation and blood drainage per 24 hours. It should also be mentioned that in the meta-analysis by Morgan et, al.[1] three out of four of the above studies were analyzed separately as a sub group[4-6]. They found a non statistical advantage in terms of ventilation time, bleeding and ITU stay. In contrast this meta-analysis excludes the RCT by Macheler et, al. but includes the most recent RCT by Moustafa et, al.[3]. Lack of long term data is not exclusive to this meta-analysis.

The total number of patients included in this study was 220. This is a small number considering isolated aortic valve replacement constitutes a large proportion of our cardiac surgical work. There were two extensive well conducted meta-analysis comparing mini-sternotomy versus conventional sternotomy for aortic valve replacement [1, 2]. They improved the power of the study by including several comparative non randomised studies, hence increasing the number of patients to 4,586 and 4,667 respectively. These studies looked at a wide variety of non-sternotomy incisions. They excluded studies if more than 50% of reported cases were not a mini-sternotomy, or operations other than isolated aortic valve replacement. Their combined conclusion was that mini-sternotomy can be performed safely for aortic valve replacement without increased risk of death or major complications [1] but with no clinical benefits [2]. In contrast the rational for our study was to focus on mini-sternotomy incisions and the commonest variations thereof which included the inverted C and L or (J) mini-sternotomies. In this meta-analysis there are no non mini-sternotomy cases and all cases underwent isolated aortic valve replacement.

There exists a degree of geographical variation which should be taken in to consideration. For example: the benefits due to the incision. Cosmesis does not appear to be a priority for patients in the western world [8]. A more cosmetic scar may be more of an issue in Asia due to younger patient population [3] (table 2). This was a limitation in this study for which there was insufficient data for comparisons to be made. However minimally invasive valve surgery is already known to improve patient satisfaction while reducing costs of cardiac valve replacement[25-26].

Conclusion

There is a significant reduction in the length of stay in cardiac intensive care unit and an overall benefit in short term outcomes from mini-sternotomy for isolated aortic valve replacement. This meta-analysis would no doubt prove useful when designing a much needed, larger and adequately powered randomised controlled trial in this subject.

Acknowledgement

We would like to thank the department of biostatistics at Robertson Centre, University of Glasgow for their help with the statistical methods, the library staff at Glasgow Royal Infirmary and the audit office staff at the Golden Jubilee National Hospital for their help with the literature search.

Funding

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Competing Interest

None

Authors' contributions

All authors contributed equally in design, review of the literature analysis and intellectual discussion of this manuscript. All authors critically revised the manuscript and approved the final version. The primary author Dr Espeed Khoshbin presented this work at the International Society of Minimally Invasive Cardiothoracic Surgery in Washington DC, June 2011.

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Table 1: PRISMA flow diagram

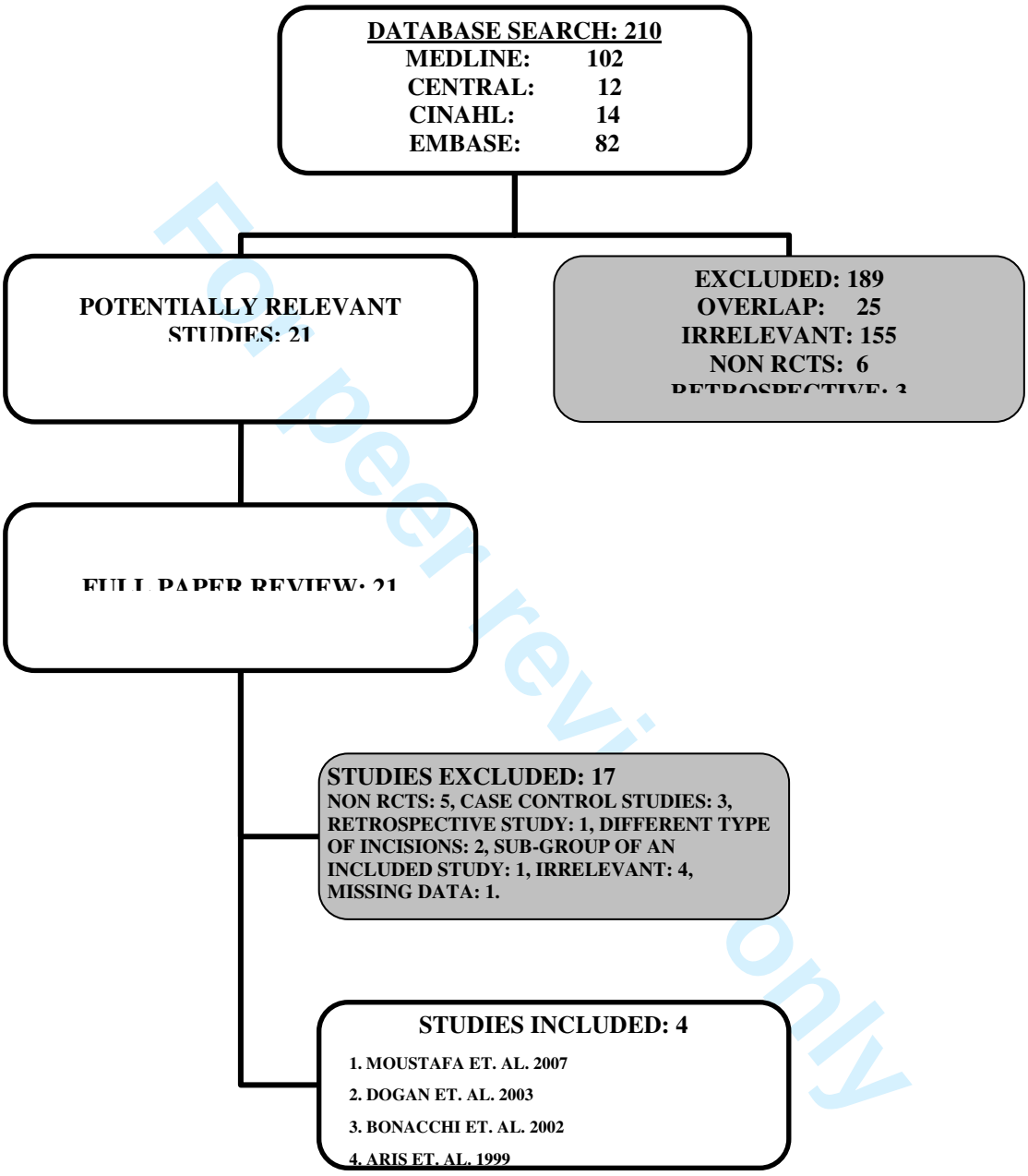

Table 2 : Study characteristics

Study	Moustafa et.al. 2007	Dogan et.al. 2003	Bonacchi et. al. 2002	Aris et. al. 1999
Methods	PRCT	PRCT	PRCT	PRCT
Number of Participants	30 + 30 = 60	20 + 20 = 40	40 + 40 = 80	20 + 20 = 40
Mean age in years (Full/Mini)	23.8 / 22.9	64.3 / 65.7	62.6 / 64.0	62.2 / 66.5
Sex M:F (Full/Mini)	15:15 / 16:14	11:9 / 9:11	-	-
Operation	Isolated AVR	Isolated AVR	Isolated AVR	Isolated AVR
Interventions	Full sternotomy VS. L shaped Mini-sternotomy Pain management with tenoxicam	Complete sternotomy VS. L shaped Mini-sternotomy	Standard sternotomy VS. C or L shaped Mini-sternotomy	Median sternotomy VS. C or L shaped Mini-sternotomy Pain management with metamizol
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PRCT = Prospective randomized controlled trial, AVR = Aortic valve replacement, VS. = Versus, ITU = Intensive care unit

PRISMA 2009 Checklist

Section/topic	#	**Mini-sternotomy for Aortic Valve Replacement Reduces the Length of Stay in the Cardiac Intensive Care: Meta-analysis of randomised controlled trials.** Khoshbin E, Prayaga S, Kinsella J, Sutherland FWH.	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	1
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	1&2
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	-
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	2
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	2
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	2
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	2
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	2
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	-
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	2

PRISMA 2009 Checklist

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency ($e.g., I^2$) for each meta-analysis.	2

Section/topic	#	**Mini-sternotomy for Aortic Valve Replacement Reduces the Length of Stay in the Cardiac Intensive Care: A Mini Meta-analysis.** Khoshbin E, Prayaga S, Kinsella J, Sutherland FWH.	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	-
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	2
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	2-3&Table1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	2&Table2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Figures1-4
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figures1-4
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Figures1-4
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	-
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Figures1-4
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	3
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	4
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	4
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	5

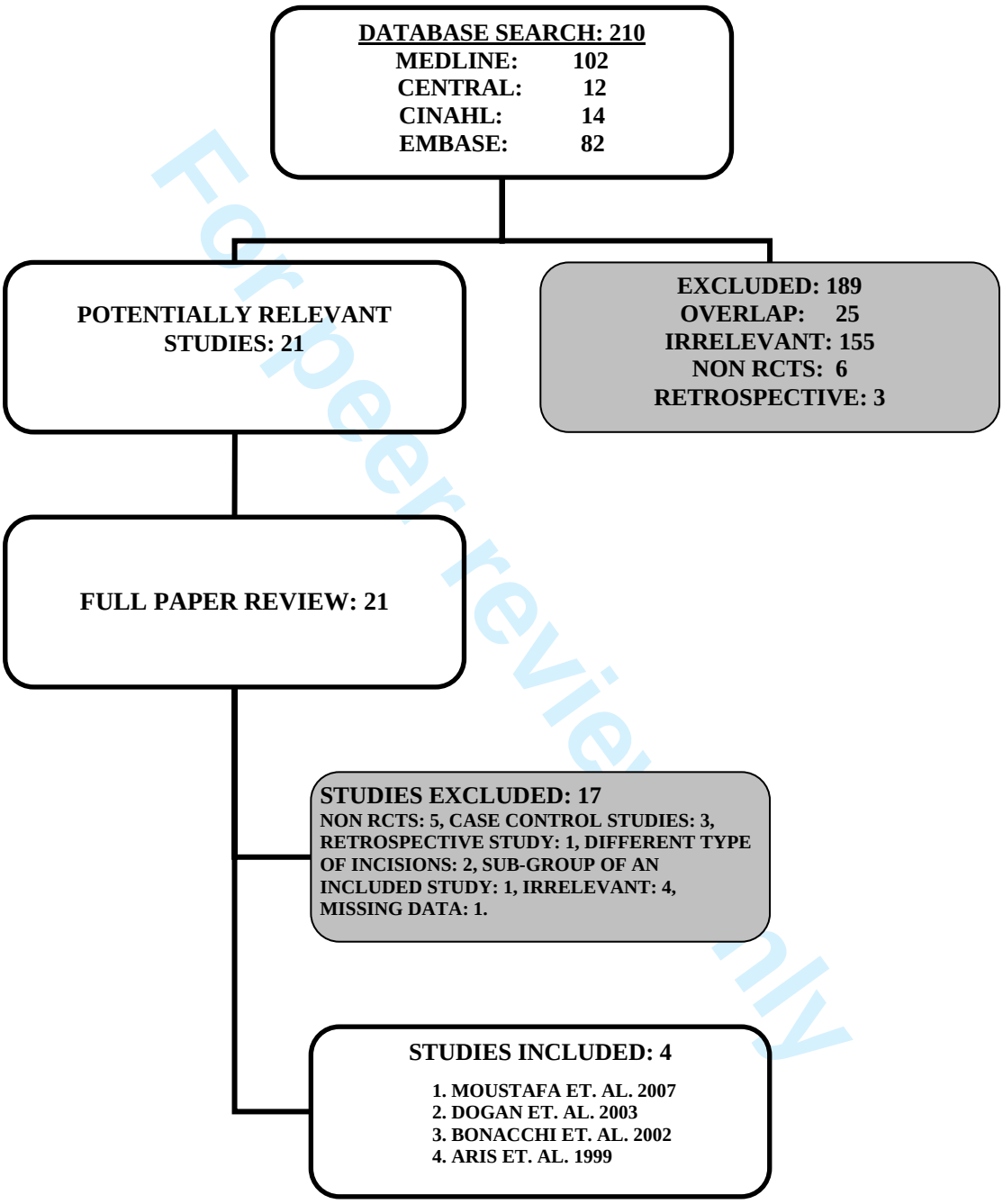
From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097.

PRISMA 2009 Checklist

doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Table 1: PRISMA flow diagram



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PRCT = Prospective randomized controlled trial, AVR = Aortic valve replacement, VS. = Versus, ITU = Intensive care unit

Figure 1: Duration of ventilation in hours.

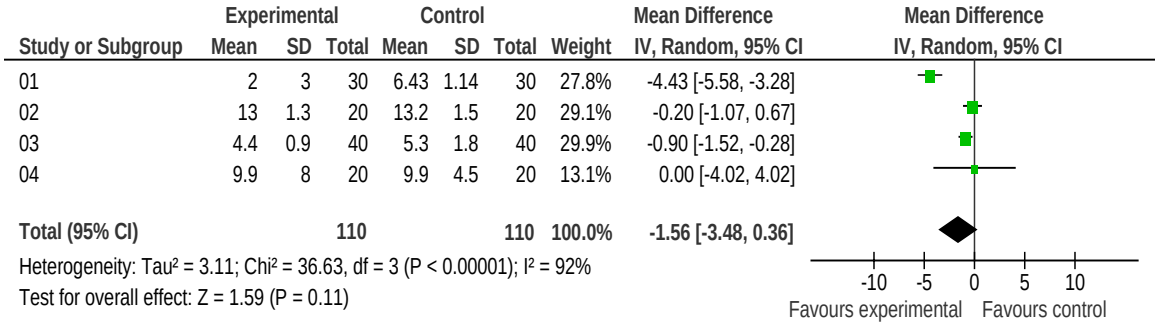

Figure 2: Post operative bleeding in the first 24 hours measured in milliliters.

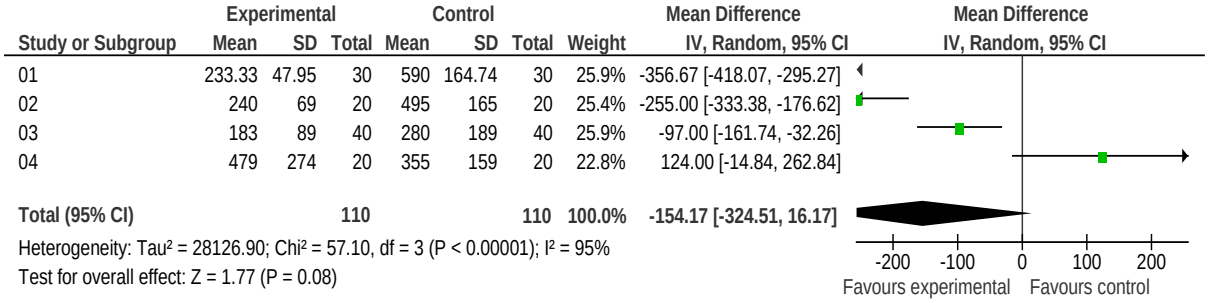

Figure 3: Length of ITU stay in days.

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
01	0.28	0.16	30	1.15	0.6	30	29.1%	-0.87 [-1.09, -0.65]
02	1.2	0.1	20	2.1	0.9	20	23.8%	-0.90 [-1.30, -0.50]
03	1.1	0.4	40	1.4	0.8	40	27.6%	-0.30 [-0.58, -0.02]
04	1.83	0.7	20	1.94	1	20	19.5%	-0.11 [-0.64, 0.42]
Total (95% CI)			**110**			**110**	**100.0%**	**-0.57 [-0.95, -0.20]**

Heterogeneity: Tau² = 0.11; Chi² = 15.31, df = 3 (P = 0.002); I² = 80%

Test for overall effect: Z = 2.99 (P = 0.003)

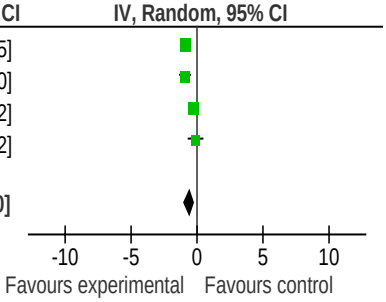

Figure 4: Length of hospital stay in days.