

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form ([see an example](#)) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Mini-sternotomy for Aortic Valve Replacement Reduces the Length of Stay in the Cardiac Intensive Care: Meta-analysis of randomised controlled trials
<b>AUTHORS</b>	Khoshbin E, Prayaga S, Kinsella J, Sutherland FWH

### VERSION 1 - REVIEW

<b>REVIEWER</b>	J.Pepper, Professor of Cardiac Surgery, Royal Brompton Hospital, Sydney Street, London, SW3 6NP, UK. No competing interests
<b>REVIEW RETURNED</b>	29/07/2011

The reviewer filled in the checklist and made no further comments.

<b>REVIEWER</b>	Stephen McKellar Mayo Clinic Division of Cardiovascular Surgery No competing interests.
<b>REVIEW RETURNED</b>	30/07/2011

<b>THE STUDY</b>	The question has already been answered, this study provides no new data.  A consort diagram is needed to clarify their inclusion/exclusion criteria.
<b>RESULTS &amp; CONCLUSIONS</b>	The question has already been answered by previous studies.  I think the small advantage is overstated in the manuscript.
<b>REPORTING &amp; ETHICS</b>	Need a CONSORT diagram.

<b>REVIEWER</b>	Antonio Miceli, MD  Department of cardiac surgery Fondazione G. Monasterio CNR regione Toscana Massa Italy  Research fellow Bristol Heart Institute University of Bristol, Bristol, UK  Conflict of interest: none
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<b>REVIEW RETURNED</b>	17/08/2011
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<b>THE STUDY</b>	<p>1. This meta-analysis is based on old studies. Three out of 4 studies have been published between 1999 and 2003. Anesthetic and surgical techniques have changed in the last years. That could affect your outcomes. This is another limitation of your study and has to be mentioned in the limitation section.</p> <p>2. The first studies on minimally invasive AVR were conducted in 1996. Therefore authors should explain why their electronic search started from 1996. Moreover, authors should report:</p> <ul style="list-style-type: none"> <li>- Minimally invasive cardiac valve surgery improves patient satisfaction while reducing costs of cardiac valve replacement and repair. Cohn et al Ann Surg 1997;226:421-428.</li> <li>- Minimally invasive approach for aortic valve operations. Cosgrove et al. Ann Thorac surg 1996;62:596-7</li> </ul>
<b>RESULTS &amp; CONCLUSIONS</b>	<p>1. Although authors failed to prove a clear superiority in favor of ministernotomy in terms of blood loss (<math>p=0.08</math>) and length of stay (<math>p=0.06</math>), there is a trend of significance in both cases and that has to be highlighted in the discussion.</p> <p>2. Although Macheler's study was excluded due to the lack of data regarding ITU and length of hospital stay (as well as mean and SD of ventilation time and bleeding), authors should mention in their discussion the positive results reported by Macheler regarding the duration of ventilation and drainage bleed per 24 h.</p>
<b>GENERAL COMMENTS</b>	<p>In the manuscript "Ministernotomy for aortic valve replacement reduces the length of stay in the cardiac intensive unit care: a mini meta-analysis", Khoshbin et al identified 5 prospective randomized studies on ministernotomy vs full sternotomy. One study was excluded due to the lack of data. They concluded that ministernotomy for isolated AVR significantly reduced the length of ITU stay.</p> <p>A recent meta-analysis by Brown et al ( J Thorac Cardiovasc Surg 2009;137:670-9) reviewed 26 studies comparing ministernotomy and full sternotomy. Among these, there were 4 randomized studies which were studied separately in subgroup outcome analysis (according to your study --- ref 2:Dogan et al, ref 3:Bonacchi et al, ref 4:Aris et al, ref 7:Macheler et al). Specifically, they found a non statistical significant advantage in term of ventilation time, bleeding and ITU stay. Because 3 out of 4 studies are reported in your review, authors should deeply discuss and highlight the difference with the previous meta-analysis.</p> <p>Please report the authors' name in all the figures of the study instead of the numbers (01,02,03, 04)</p>

<b>REVIEWER</b>	<p>Orlando Santana, M.D.  Director, Echocardiography Laboratory  Columbia University Division of Cardiology at the Mount Sinai Heart Institute  Miami Beach, Florida. 33140  U.S.A.</p>
<b>REVIEW RETURNED</b>	12/09/2011

<b>GENERAL COMMENTS</b>	1st page, sentence 47 the word "Mini-sternotomy" is misspelled.
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## VERSION 1 – AUTHOR RESPONSE

### A) Questions for Discussion:

Question 1: This is a small study and larger studies on the topic have already been published. In both of the larger analyses, the RCTs were discussed separately and their findings were similar to what is described here. They reported marginal advantages, few objective advantages, and little difference for mini-sternotomy AVR.

Khoshbin answers: Thank you for your comment. This study is a mini meta-analysis and does not intend to be a “Gold Standard” systematic review in the sense of searching grey literature but more of a confirmatory study. 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 broader questions of safety and efficacy(1) and mortality and morbidity(2) associated with mini-sternotomy of all types. The disadvantage of recruiting in this way is that the analysis is less specific for a particular type of procedure. This study in contrast addressed more specific questions such as the quantity of blood lost, length of positive pressure ventilation, intensive care and hospital stay which we believe are best answered through PRCTs. For example in our meta-analysis we only recruited studies which performed inverted C or L (J) shape sternotomies. Previous meta-analyses have not made this distinction in selecting studies for inclusion. In summary our study is more focused and also more rigid in its inclusion criteria (and therefore smaller). Such subtle changes have an impact on the results of the analysis and therefore on the conclusions that can be drawn from our study in comparison with the conclusions drawn in previous meta-analyses.

Question 2: I would consider a difference in ICU stay of 0.5 days a marginal advantage. Considering each individual patient, is it more cost effective and advantageous to leave the ICU in the morning versus in the late afternoon or evening? Do the authors have more meaningful cost savings data on the relevance of this statistical difference?

Khoshbin answers: The marginal advantages you refer to in this meta-analysis are a statistically significant reduction in the length of stay in cardiac intensive care unit and a trend of significance in both quantity of blood loss ( $p = 0.08$ ) and the length of stay in hospital ( $p = 0.06$ ). 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 advantage of a half a day reduction in ICU stay clearly depends upon mean length of stay. 0.5 days in a care pathway that typically involves only 1 day in ICU is a 50% reduction. That is a significant reduction. In order to translate this benefit into cost savings, one should consider that if the critical care unit is staffed on a 12 hourly shift basis then 0.5 day is one nursing shift i.e. saving is the cost of a nursing shift OR half a day in an economic model. Cost of an ICU bed is £1500 per day in the UK. As regards morning, afternoon or evening discharge from ICU, this issue is immaterial to the cost saving as ICU is staffed on a 24 hourly basis. Furthermore, the importance of early discharge from ICU is not just about cost saving, it is a surrogate for the speed of patient recovery from a major operation and therefore patient well being. This is the main reason for offering minimally invasive surgery to patients.

Question 3: There is no mortality or intraoperative information included in this study.

Khoshbin answers: We did not set out to study cross clamp / bypass times. It is well known that these times are longer for minimally invasive procedures. The focus of our meta-analysis was not on intra-operative procedure differences (which have been well documented previously) but on meaningful postoperative clinical outcomes. It is reasonable to request mortality, however considering the relatively small number of patients in this meta-analysis; we only investigated the outcomes that were

common to all four PRCT.

Question 4: There is no CONSORT diagram reporting why certain studies were included or excluded. Also, were the studies independently reviewed by different authors? If so, how were differences resolved?

Khoshbin answers: We have now included the consort diagram reporting the study criterion. Trials identified according to the study criterion were independently reviewed by each author, and differences resolved by discussion.

Question 5: Were funnel plots used to look for publication bias?

Khoshbin answers: We did not use funnel plot as the total number of studies in this mini meta-analysis was quite small.

B) Suggestions for alteration in the manuscript:

Your suggestions are important to us and we have made adjustments in the body of text to cover them.

1. This meta-analysis is based on old studies. Three out of 4 studies have been published between 1999 and 2003. Anesthetic and surgical techniques have changed in the last years. That could affect your outcomes. This is another limitation of your study and has to be mentioned in the limitation section.

Reply: Thank you for this suggestion. However it is 1999 to 2007. The surgical and anaesthetic techniques have not significantly changed since then. However we have stressed the geographic variation as a limitation.

2. The first studies on minimally invasive AVR were conducted in 1996. Therefore authors should explain why their electronic search started from 1996. Moreover, authors should report: - Minimally invasive cardiac valve surgery improves patient satisfaction while reducing costs of cardiac valve replacement and repair. Cohn et al Ann Surg 1997;226:421-428.-Minimally invasive approach for aortic valve operations. Cosgrove et al. Ann Thorac surg 1996,62:596-7

Reply: This has been added to the body of the manuscript.

3. Although authors failed to prove a clear superiority in favor of ministernotomy in terms of blood loss ( $p=0.08$ ) and length of stay ( $p=0.06$ ), there is a trend of significance in both cases and that has to be highlighted in the discussion.

Reply: This has been added in the discussion section.

4. Although Macheler's study was excluded due to the lack of data regarding ITU and length of hospital stay (as well as mean and SD of ventilation time and bleeding), authors should mention in their discussion the positive results reported by Macheler regarding the duration of ventilation and drainage bleed per 24 h.

5. A recent meta-analysis by Brown et al ( J Thorac Cardiovasc Surg 2009:137:670-9) reviewed 26 studies comparing ministernotomy and full sternotomy. Among these, there were 4 randomized studies which were studied separately in subgroup outcome analysis (according to your study --- ref 2:Dogan et al, ref 3:Bonacchi et al, ref 4:Aris et al, ref 7:Macheler et al). Specifically, they found a non statistical significant advantage in term of ventilation time, bleeding and ITU stay. Because 3 out of 4 studies are reported in your review, authors should deeply discuss and highlight the difference with the previous meta-analysis.

Reply: this has been addressed in the discussion section.

6. Please report the authors' name in all the figures of the study instead of the numbers (01,02,03, 04)

Reply: Unfortunately I am unable to alter the diagrams at this late stage. However I have made sure they are clearly marked.