Does off-pump coronary artery surgery reduce the incidence of postoperative atrial fibrillation?

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Summary

A best evidence topic in cardiac surgery was written according to a structured protocol. The question addressed was whether off-pump coronary artery surgery reduces the incidence of postoperative atrial fibrillation. Altogether 107 papers were found using the reported search, of which 18 presented the best evidence to answer the clinical question. The author, journal, date and country of publication, patient group studied, study type, relevant outcomes, results, and study weaknesses of these papers are tabulated. We conclude that off-pump coronary artery surgery significantly reduces the incidence of postoperative atrial fibrillation with a number needed to treat of 20 to prevent one case of AF.

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expTachycardia, Supraventricular/ OR AF.mp] OR [meta-analysis.af AND exp Thoracic surgery/].

5. Search outcome

One hundred and seven papers were found of which 7 were deemed to be relevant. In addition cross-checking of the reference lists, suggestions from Journal Club members and hand checking Cardiothoracic Journals published this year revealed a further nine papers. These papers are presented in Table 1.

6. Results

Reston et al. [2] performed a comprehensive and well-balanced meta-analysis in 2003 of the short term and mid-term outcomes of ‘off-pump coronary bypass surgery’ (OPCAB) versus conventional coronary arterial bypass surgery (CABG). Using comprehensive search strategies and strict entry criteria, they selected 28 studies from 180 reviewed papers that reported the incidence of AF in these patients. They found that there was a highly significant reduction in AF in the OPCAB group (Odds ratio 0.69 in favour of OPCAB). There was, however, significant heterogeneity (or disagreement that cannot be explained by chance) between these studies that they could not account for. However, if only the randomised controlled trials were included, the difference was increased rather than decreased. They did caution that most studies excluded patients such as non-elective surgery, re-operation, renal failure and impaired ejection fraction.

While Reston et al. also found significant benefits in terms of stroke, MI and mortality, a meta-analysis by Van der Heijden et al. in 2004 [3] that assessed only RCTs disagreed with their meta-analysis, finding that there was no significant difference in the combined end-point of MI, death or stroke. Although this study did not look at AF it is interesting to note that this meta-analysis also included, the Octopus study [4], the SMART study [5] and an RCT from Hawaii [6]. This calls into question the measurement of AF in their study, which they did not describe in the protocol.

In addition, yet another meta-analysis by Parolari et al. in 2003 [7], also found no difference in this composite outcome measure of stroke, MI, or death. Again this meta-analysis did not extract data on AF but calls into question the findings by Reston et al. due to the marked difference in their findings.

Ascione and Angelini performed a pooled meta-analysis of BHACAS 1 and 2 [8]. They showed that the incidence of AF reduced from 37% to 13%, which was a highly significant finding. This was despite showing no difference in mortality or cardiac events.

A meta-analysis by Athanasiou et al. in 2004 [9] specifically asked the question of whether OPCAB reduced the incidence of AF in elderly patients undergoing coronary arterial surgery. They found that in the eight studies that they identified, the incidence in the OPCAB group was 22% but in the CABG group it was 28%, which was significant. However, this study had many flaws. It only included cohort studies from 1999 to 2003 identified from Medline although the reasons for this narrow timeframe were not explained. More importantly no attempt was made to contact the authors of the many RCTs in this area to ask for their data on AF in the over 70s age group. Thus, this is a small meta-analysis of non-randomised patients only.

Of the recent randomised trials not included in the Reston et al. meta-analysis. The SMART Trial [5] of 200 patients randomised to either OPCAB or CABG found no significant difference in AF but with an incidence of 16% in the OPCAB group and 22% in the CABG group there was a trend towards reduced incidence in OPCAB surgery.

In contrast, the PRAGUE-4 trial [10] that randomised 400 patients to OPCAB or CABG found no difference at all in the incidence of AF. The OPCAB group had an incidence of 20% compared to an incidence of 24% in the CABG group.


The OCTOPUS trial [13] found no difference in AF between the two groups with a 20% incidence in the OPCAB group and a 21% incidence in the CABG group.

Munero et al. performed a PRCT in 176 patients comparing total arterial OPCAB with total arterial CABG [14]. They found that the incidence of AF was 22% in the OPCAB group and 35% in the CABG group, which showed a strong trend towards a lower incidence in the OPCAB group but had a P value of 0.06.

Gerola et al. [19] performed an RCT in 2004 in Brazil in 160 patients and found a low incidence of AF in both groups. The finding of 9% in the OPCAB group and 5% in the CABG group was far lower than other studies, and calls into question the measurement of AF in their study, which was not described in the protocol.

Lee et al. in 2003 [6] performed a small RCT in 60 patients, and found an incidence of AF of 23% in OPCAB group and 39% in the CABG, but this was not statistically significant.

Although not an RCT, Salamon et al. performed a retrospective cohort study in 2003 [15] that specifically looked at whether OPCAB reduced the incidence of AF. The 252 patients having OPCAB had an incidence of 8.8%, whereas the incidence of AF in 1470 CABG pts receiving prophylactic B-Blockers was 11.6%. When a matched group for number of grafts was found the CABG AF frequency of AF reduced to 9.4%. It should be remembered that there are many weaknesses inherent to the retrospective cohort design of this study including intergroup demographic
Table 1
Best evidence papers

<table>
<thead>
<tr>
<th>Author, date and country</th>
<th>Patient group</th>
<th>Study type (level of evidence)</th>
<th>Outcomes</th>
<th>Key results</th>
<th>Comments/Weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van der Heijden et al. (2004), Eur J Cardiothorac Surg, Holland [3]</td>
<td>Meta-analysis of RCTs comparing OPCAB with CABG</td>
<td>Meta-analysis (level 1a)</td>
<td>Combined endpoint of mortality stroke and MI, at 1 year (5 studies)</td>
<td>OPCAB group 23/412 (5.6%) CABG group 34/410 (8.2%) ( P=0.15 )</td>
<td>Inadequate search strategies, Embase, grey literature, experts and search for unpublished studies were not examined</td>
</tr>
<tr>
<td>Athanasiou et al. (2004), Ann Thorac Surg, UK [9]</td>
<td>Meta-analysis of all observational studies comparing OPCAB and CABG in patients over 70 years of age</td>
<td>Meta-analysis (level 2a)</td>
<td>Incidence of AF</td>
<td>OPCAB group 168/764 (22%) CABG group 641/2253 (28%) Odds 0.70 (0.56–0.86)</td>
<td>Unclear why studies were not sought prior to 1999 or why authors of RCTs were not contacted in order to obtain their data in their over 70s groups, which would have lead to much greater numbers from studies with superior methodology</td>
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<tr>
<td>Straka et al. for the PRAGUE-4 study (2004), Ann Thorac Surg, Czech Republic [10]</td>
<td>RCT comparing OPCAB (N=204) with CABG (N=184) in a single centre</td>
<td>Single blind RCT (level 1b)</td>
<td>Incidence of AF</td>
<td>OPCAB group 40/204 (20%) CABG group 44/184 (24%) ( P=0.30 )</td>
<td>Cross-over in 5.4% of patients in each group, preoperatively and 9.8% intraoperatively in OPCAB group</td>
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<tr>
<td>Gerola et al. (2004), Ann Thorac Surg, Brazil [19]</td>
<td>160 low risk patients randomized to OPCAB (N=80) and CABG (N=80)</td>
<td>PRCT (level 1b)</td>
<td>Incidence of AF</td>
<td>OPCAB group 4/80 (5%) CABG group 7/80 (8.7%) ( P=0.53 )</td>
<td>Methods for measurement of AF not given</td>
</tr>
<tr>
<td>Reston et al. (2003), Ann Thorac Surg, USA [2]</td>
<td>Meta-analysis of RCTs and cohort studies comparing OPCAB with standard CABG</td>
<td>Meta-analysis (level 1a)</td>
<td>Odds of AF in OPCAB group compared to CABG group</td>
<td>Odds of AF was 0.69 (95%CI 0.58–0.81) in favour of OPCAB ( P=0.00001 ) When only RCTs considered the effect was even bigger in favour of OPCAB</td>
<td>A significant heterogeneity was found between studies for AF indicating significant disagreement between studies but the reasons for this were not clear</td>
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<td></td>
<td>Searched 21 databases up to Jan 2003, 180 studies reviewed, 10 RCTs, five prospective and 38 retrospective cohort studies found</td>
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<td>PRAGUE-4 trial, Brompton Trial and Smart trial not included</td>
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<td>28 studies were included in their analysis of atrial fibrillation</td>
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<td>Stroke (38 studies)</td>
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<td>Mid term Mortality (7 studies)</td>
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<tbody>
<tr>
<td>Parolari et al. (2003), Ann Thorac Surg, Italy [7]</td>
<td>Meta-analysis of RCTs comparing OPCAB with CABG</td>
<td>Meta-analysis (level 1a)</td>
<td>Combined end-point of mortality stroke and MI</td>
<td>OPCAB group 7/532 (1.3%), CABG group 17/558 (3%), ( P = 0.08 )</td>
<td>Several RCTs not found that were included in the meta-analyses above</td>
</tr>
<tr>
<td>Puskas et al. for the SMART study (2003), J Thorac Cardiovasc Surg, USA [5] and J Am Med Assoc (2003) [16]</td>
<td>RCT comparing OPCAB (N=98) with CABG (N=99)</td>
<td>Single blind PRCT (level 1b)</td>
<td>Incidence of AF</td>
<td>OPCAB group 16/98 (16%), CABG group 22/99 (22%), ( P = 0.367 )</td>
<td>Four patients crossed over in this study</td>
</tr>
<tr>
<td>Lee et al. (2003), Ann Thorac Surg, Hawaii [6]</td>
<td>60 patients randomized to OPCAB (N=30) or CABG (N=30)</td>
<td>PRCT (level 2b)</td>
<td>Incidence of AF</td>
<td>OPCAB group 7/30 (23%), CABG group 11/30 (37%), ( P = \text{NS} )</td>
<td>Small study. Methods for AF measurement not described</td>
</tr>
<tr>
<td>Salamon et al. (2003), Ann Thorac Surg, USA [15]</td>
<td>2569 patients undergoing OPCAB and CABG</td>
<td>Retrospective Cohort study (level 2b)</td>
<td>Incidence of AF</td>
<td>Gp I, OPCAB group 8.8%, Gp II, CABG group 11.6%, Gp III: Graft matched CABG 9.4%, Gp IV: no B-Blocker CABG 28%</td>
<td>Retrospective cohort study, therefore the definitions of AF may have varied and there were significant differences in demographics between all groups</td>
</tr>
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<td>Muneretto et al. (2003), Ann Thorac Surg, Italy [14]</td>
<td>176 patients randomized to total arterial OPCAB (N=88) or CABG (N=88)</td>
<td>PRCT (level 1b)</td>
<td>Incidence of AF</td>
<td>OPCAB group 19/88 (21.6%), CABG group 31/88 (35.2%), ( P = 0.06 )</td>
<td>Methods for measurement of AF not given</td>
</tr>
<tr>
<td>Ascione et al. (2002), Lancet UK [8] and Circulation (2000) [18]</td>
<td>Pooled meta-analysis of BHACAS 1 and 2 studies</td>
<td>Pooled meta-analysis (level 1a)</td>
<td>Incidence of AF</td>
<td>OPCAB group 25/200 (13%), CABG group 74/201 (37%), ( P &lt; 0.0001 )</td>
<td>Selection bias. Continuous Holter ECG monitoring not done after first 72 h</td>
</tr>
<tr>
<td>Van Dijk for the OCTOPUS Trial (2001), Circulation, and N Eng J Med (2003), Holland [13,17]</td>
<td>Multicentre PRCT comparing OPCAB (N=142) with CABG (N=139)</td>
<td>Single blind PRCT (level 1b)</td>
<td>Incidence of AF</td>
<td>OPCAB group 28/142 (20%), CABG group 29/139 (21%), ( P = 0.79 )</td>
<td>Event free survival</td>
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<td>Exclusion for reoperation, poor EF, MI &lt;6weeks</td>
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<td>OPCAB group 132/142 (93%), CABG group 131/139 (94%)</td>
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**OPCAB**: Off-pump coronary artery bypass; **CABG**: Coronary artery bypass grafting; **EF**: Ejection fraction; **MI**: Myocardial infarction; **IABP**: Intra-aortic balloon pump; **AF**: Atrial fibrillation; **PRCT**: Prospective randomized controlled trial; **GH**: Gender; **BHACAS**: British Heart Valve and Aortic Stenosis; **CCTR**: Cochrane Central Register of Controlled Trials; **Cochrane register of unpublished trials**: Cochrane register of unpublished randomized controlled trials.
differences and possible variation in AF definition. Therefore, although we found further cohort studies we excluded these from this topic.

Thus in summary three meta-analyses were found that assessed AF in OPCAB versus CABG. They all found a significant reduction in AF with OPCABG. Six further RCTs were identified that were published after several of these meta-analyses. None of them identified a significant difference individually however if you summate their findings there was a 17.8% AF rate in the OPCAB group (114/642) but a 23% rate of AF in the CABG group (144/620). This corresponds to an odds of 0.76 (using a random effects model) with a probability of 1.6% that the results are non-significant (Fig. 1). This finding, therefore, agrees with the already performed meta-analyses that found significant differences. Our summary of the recent RCTs gives a number needed to treat of 20 to avoid one incidence of AF.

7. Clinical bottom line

OPCAB reduces the incidence of postoperative atrial fibrillation with a number needed to treat of 20 to prevent one case of AF.

References


Appendix A. ICVTS on-line discussion

Author: Dr. John Pepper, Royal Brompton Hospital, Department of Surgery, Sydney Street, London SW3 6NP, UK

Date: 23-Aug-2004

Message: This is a very interesting systematic review. As the authors point out, AF is very rarely the primary outcome measure in randomised controlled trials of on versus off-pump in coronary artery surgery. Furthermore, off-pump is a heterogeneous group, not only with respect to the conduct of the operation but to the use of prophylactic antiarrhythmic agents.

An important unanswered question is to what extent does a reduction in the incidence of AF in OPCAB lead to a reduction in stroke? It is probably in the over 70 age group that this difference will be detectable, but dissecting out AF from other causes of stroke will be very difficult.