Meta-analysis of open surgical repair versus hybrid arch repair for aortic arch aneurysm

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Abstract

OBJECTIVE: To conduct a meta-analysis of available comparative studies evaluating hybrid arch repair versus open surgical repair of aortic arch aneurysm.

METHODS: A literature search was performed using PubMed, Embase and Web of Science to identify any studies comparing the results of hybrid arch repair with open surgical repair of aortic arch aneurysm. Study quality was assessed with the Newcastle-Ottawa Scale. Statistical heterogeneity was estimated using the chi-square test. A random-effects model was used to illustrate heterogeneity. Publication bias was evaluated by funnel plots.

RESULTS: Seven retrospective cohort studies from 2009 to 2016 comprising 727 patients were included. Among these patients, 269 were treated with hybrid arch repair and 458 with open surgical repair. There was no significant difference in operative mortality (OR 0.75; 95% CI 0.41–1.39; P = 0.37), permanent neurological deficit (OR 1.24; 95% CI 0.73–2.13; P = 0.42), late mortality (2 years) (OR 3.41; 95% CI 0.83–14.03; P = 0.09) or renal failure (OR 0.80; 95% CI 0.40–1.61; P = 0.53). Interestingly, the meta-analysis indicated that the hybrid group needed more reinterventions (OR 3.43; 95% CI 1.72–6.84; P = 0.0005).

CONCLUSIONS: We found no strong evidence indicating that hybrid arch repair is superior to open surgical repair. Furthermore, the hybrid arch repair resulted in more reinterventions despite the fact that it was a less invasive procedure; it also required fewer days in the hospital. Further studies with large numbers of participants and long-term follow-ups are necessary to confirm the effectiveness of hybrid arch repair.

Keywords: Aortic arch aneurysm • Open surgical repair • Hybrid arch repair
proximal extension of aneurysmal disease into the ascending aorta (diameter >40 mm). This surgical method can create an appropriate proximal landing zone by replacing the ascending aorta; endovascular aortic repair is finished later with supra-aortic debbranching (Fig. 1C). Type III hybrid arch repair entails a total arch replacement with an elephant trunk procedure and a delayed endovascular repair of the descending aorta, which is appropriate for extensive aortic disease (Fig. 1D). It is noteworthy that type III is an elephant trunk procedure with or without total arch replacement, depending on the shape of the proximal aortic arch. After a long elephant trunk graft is inserted into the aneurysm, the concomitant endovascular therapy can cause massive haemorrhage and lead to spinal cord ischaemia, so the elephant trunk procedure is considered. Usually, type II and III hybrid arch repairs require CPB for proximal aortic reconstruction; therefore, the risk of using CPB must be carefully considered on a case-by-case basis.

Hybrid arch repair is intended to reduce operative, bypass and circulatory arrest times in order to overcome the serious complications associated with open surgical repair [6]. However, thus far, no randomized controlled trials have been conducted to study this innovative technique, and whether hybrid arch repair is superior to open surgical repair is still controversial. The purpose of the present study was to integrate data from all of the relevant published articles on outcomes after open surgical repair and hybrid arch repair. We conducted a meta-analysis focusing on operative mortality, late mortality (2 years), related major complications and the need for reintervention to evaluate if hybrid arch repair has an advantage over open surgical repair.

MATERIALS AND METHODS

Search strategy

We applied the guidelines for Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [7]. Two authors (Ling Miao and Lei Song) performed a systematic search using the following databases: PubMed, Embase and Web of Science. The final search was done on 8 April 2016. The keywords included ‘aortic arch aneurysm’, ‘open surgical repair’ and ‘hybrid arch repair’. Our goal was to identify articles that reported the results of hybrid arch repair of aortic arch aneurysm compared with those of open surgical repair. In addition, a manual electronic search of the reference lists of relevant articles was used to broaden the search. No language limitations were applied. We identified 171 articles after duplicate checking.

Inclusion criteria

Two independent reviewers (Ling Miao and Lei Song) screened the titles and abstracts of the papers to identify potentially relevant articles. A third reviewer (Zhen-Guo Wang) helped to reach a consensus when necessary. To be included, articles had to satisfy the following requirements: (i) compare outcomes of hybrid arch repair of aortic arch aneurysm versus open surgical repair; (ii) report at least one outcome of interest; and (iii) be published in full text form. Articles were excluded if they met the following criteria: (i) were review articles, editorials or case reports; (ii) had no open surgical repair cohort comparison; (iii) discussed thoracic aortic aneurysms rather than aortic arch aneurysms; (iv) contained ambiguous, incorrect or no original data, or data from administrative databases because the credibility of administrative data was lower. Several articles that reported on thoracic aortic pathologies other than aortic arch aneurysm were excluded if the results of the aortic arch aneurysm were presented separately. In the end, we identified seven studies [2, 8–10, 12–14] that were appropriate for our meta-analysis (Supplementary Figure 1).

Data extraction

Data were extracted independently by three coauthors (Ling Miao, Lei Song and Sheng-Kai Sun). A standard form was used to record the data from these papers, which included first
author, year of publication, country, study period, sample size, patients at follow-up, operative mortality rate, permanent neurological deficit (PND) (stroke, paraplegia), renal failure, late mortality (2 years) and need for reintervention. Operative mortality was defined as death during hospitalization or within 30 days after surgery. PND was defined as the presence of either new permanent focal or global neurological dysfunction persisting at discharge. No attempt was made to obtain missing data from the authors. Any disagreement was resolved by discussion until all the reviewers reached a consensus. All the necessary data from the available reports are listed in Table 1.

### Study quality

Two reviewers (Ling Miao and Lei Song) independently assessed the methodological quality of the included studies. Because all of the articles that we finally cited were retrospective cohort studies, we used a quality assessment tool based on the Cochrane Collaboration’s tool—the Newcastle-Ottawa Scale (NOS)—to assess the risk of bias. The NOS is a nine-star rating system designed for non-randomized studies, especially case-control and cohort studies. For cohort studies, the corresponding criteria cover the following domains: selection of participants, comparability of study groups and outcomes of interest. Each criterion gets a single star if appropriate methods have been reported (http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm). The risk of bias within the studies is reported in Table 2. Any disagreement was resolved by discussion among all the coauthors.

### Statistical analysis

Statistical analyses were performed by two coauthors (Ling Miao and Lei Song) using Review Manager Software (RevMan 5.3; The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). For dichotomous outcomes, a meta-analysis was performed by calculating the pooled odds ratio (OR) with 95% CI (confidence interval). The OR represents the odds of an adverse event occurring in the hybrid arch repair group divided by the odds of it occurring in the open surgical repair group. An OR of <1 favours the hybrid arch repair, and the point estimate of the OR is considered statistically significant at the \( P < 0.05 \) level if the 95% CI does not include the value 1.0. The weighted mean differences and the 95% CI were calculated for continuous outcomes. Statistical heterogeneity was assessed using the chi-square test; \( P < 0.10 \) or \( I^2 > 50\% \) was considered indicative of heterogeneity [15]. A random-effects model was used to account for important heterogeneity that existed among the studies included, whereas the fixed-effects model was used to

### Table 1: Characteristics of included studies

<table>
<thead>
<tr>
<th>Author, year, country</th>
<th>Study period</th>
<th>Sample size</th>
<th>Patients at follow-up</th>
<th>Operative mortality</th>
<th>PND</th>
<th>Renal failure</th>
<th>Late mortality</th>
<th>Need for reintervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iba, 2014, Japan</td>
<td>2008–2013</td>
<td>193</td>
<td>50 143</td>
<td>1 4</td>
<td>3</td>
<td>3</td>
<td>0 2</td>
<td>28 63 5 1</td>
</tr>
<tr>
<td>Kang, 2015, Korea</td>
<td>2006–2014</td>
<td>55</td>
<td>35 20</td>
<td>4 6</td>
<td>3</td>
<td>3</td>
<td>2 2</td>
<td>13 8 9 0</td>
</tr>
<tr>
<td>Lee, 2011, USA</td>
<td>2005–2009</td>
<td>58</td>
<td>37 21</td>
<td>6 4</td>
<td>4</td>
<td>2</td>
<td>- -</td>
<td>- - 7 4</td>
</tr>
<tr>
<td>Milewski, 2010, USA</td>
<td>2000–2009</td>
<td>72</td>
<td>27 45</td>
<td>3 7</td>
<td>3</td>
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<td>5 5</td>
<td>22 23 - -</td>
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<tr>
<td>Murphy, 2009, USA</td>
<td>2005–2006</td>
<td>30</td>
<td>18 12</td>
<td>1 2</td>
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<tr>
<td>Sood, 2014, USA</td>
<td>1993–2013</td>
<td>137</td>
<td>44 93</td>
<td>3 6</td>
<td>2</td>
<td>7</td>
<td>1 4</td>
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<tr>
<td>Tokuda, 2016, Japan</td>
<td>2002–2014</td>
<td>182</td>
<td>58 124</td>
<td>2 0</td>
<td>11</td>
<td>16</td>
<td>4 4</td>
<td>48 23 2 0</td>
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</tbody>
</table>

H: hybrid arch repair; O: open surgical repair; PND: permanent neurological deficit.

### Table 2: Newcastle-Ottawa quality assessment of included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Selection Representativeness</th>
<th>Selection Ascertainment of exposure</th>
<th>Outcome not present at start of study</th>
<th>Comparability Comorbidity based on the design or analysis</th>
<th>Outcome Assessment of outcome</th>
<th>Follow-up long enough</th>
<th>Adequacy of follow-up</th>
<th>Scores</th>
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<tr>
<td>Iba et al.</td>
<td>★ ★ ★ ★ ★ ★ ★ ★ ★ ★</td>
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<td>Kang et al.</td>
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analyse outcomes with non-significant heterogeneity. The pooled data were displayed as Forest plots. Publication bias was assessed by funnel plots. Using the data related to reintervention, sensitivity analysis was performed to evaluate the effect of the results.

RESULTS

Literature search

Supplementary Figure 1 shows the results of the literature search. The initial screening of the electronic databases yielded 174 citations. After removing duplicates, reviewing selected titles and abstracts and browsing full texts, seven potentially relevant retrospective cohort studies met the inclusion criteria [2, 8–10, 12–14]. All were non-randomized; no prospective randomized trials were found. The characteristics of the eligible articles are listed in Table 1. Among the seven studies, comprising a total of 727 patients, 269 patients were treated with hybrid arch repair and 458 patients with open surgical repair. All papers reported data on operative mortality rates and PND; four papers [2, 8, 9, 13, 14] reported data on late mortality (2 years) rates; five papers [2, 10, 12–14] contained data on the need for reintervention and all but one [2, 8, 9, 12–14] paper reported data on renal failure. As mentioned before, we used the NOS to assess the methodological quality (Table 2). Of all the citations, three papers [8, 10, 12] did not provide late mortality at 2 years; according to our standards, we defined their follow-up as not long enough for outcomes to occur.

Results of meta-analysis

The incidence of operative mortality was provided by 7 series, totalling 727 patients (269 hybrid repairs; 458 open repairs). There were 20 deaths in the hybrid group and 29 deaths in the open-repair group. The pooled results showed no significant difference between the hybrid or open-repair groups in operative mortality (OR 0.75; 95% CI 0.41–1.39; P = 0.37) with no heterogeneity (P = 0.50, I² = 0%) (Fig. 2).

Information regarding PND was available from all 7 articles, totalling 727 patients (269 hybrid repairs; 458 open repairs). PND occurred in 28 hybrid patients and 36 open-repair patients. The pooled results showed no significant difference between the hybrid and open-repair groups in PND (OR 1.24; 95% CI 0.73–2.13; P = 0.42) with no heterogeneity (P = 0.78, I² = 0%) (Fig. 3).

Late mortality (2 years) was reported by 4 series, totalling 502 patients (170 hybrid repairs; 332 open repairs). There were 111 deaths in the hybrid group and 117 deaths in the open-repair group. The pooled results showed no significant difference between the hybrid or open-repair groups in late mortality (2 years) (OR 3.41; 95% CI 0.83–14.03; P = 0.09) with high heterogeneity (P < 0.00001, I² = 90%) (Fig. 4).
Six series provided data regarding renal failure, totalling 669 patients (232 hybrid repairs; 437 open repairs). The number of renal failures was 12 in the hybrid group and 22 in the open-repair group. The pooled results showed no significant difference between the hybrid or open-repair groups in renal failure (OR 0.80; 95% CI 0.40–1.61; P = 0.53) with moderate heterogeneity (P = 0.17, I² = 35%) (Fig. 5).

Five series covered relevant data regarding the need for reintervention, totalling 610 patients (214 hybrid repairs; 396 open repairs). Reintervention was required in 31 hybrid patients and 13 open-repair patients. The pooled results showed that the hybrid group needed more reintervention compared with the open-repair group (OR 3.43; 95% CI 1.72–6.84; P = 0.0005) with moderate heterogeneity (P = 0.16, I² = 39%) (Fig. 6).

We tested the sensitivity by removing each of the studies one at a time and evaluating the effect on the results; however, this procedure made no difference to the overall study results.

When we looked at the funnel plot for operative mortality, we found that the study results displayed appropriate dispersion and that there was little publication bias (Supplementary Figure 2).

**DISCUSSION**

From an anatomical standpoint, operative treatment of the aortic arch is a huge challenge. With the continuous improvement of technology and innovation, hybrid arch repair, a combination of aortic branch vessel revascularization and thoracic endovascular...
aortic repair, has evolved as an effective and feasible means for treatment of aortic arch aneurysm. Several studies have shown that the therapeutic effect is acceptable. However, the current studies are small and lack credible evidence of the superiority of hybrid arch repair compared with open surgical repair. By searching the database, we found one previous meta-analysis [16] that pooled data from four available reports [8–11] on hybrid arch repair versus open surgical repair. They only compared the results of operative mortality and PND; simultaneously, the relevant data were completely lacking. Therefore, on the basis of the four studies described earlier, we did another search and added another four papers [2, 12–14] to conduct a more comprehensive meta-analysis of the outcomes of the two therapies. After careful comparison, we found that two references were from the same institution and that study periods overlapped, so we deleted the older study [11, 13]. Although the sample size increased slightly, there were no differences in terms of operative mortality rates and PND (Figs 2 and 3). When we pooled the data from four references regarding late mortality at 2 years, we found no advantage with hybrid arch repair (Fig. 4). Six of seven papers provided data on renal failure; unfortunately, the results did not demonstrate any difference (Fig. 5). To our surprise, hybrid arch repair was strongly associated with more frequent need for reintervention (Fig. 6). Most of the reinterventions were performed because of the relatively high incidence of type I endoleak, which gave rise to continued dilation of the aneurysm with a high risk of rupture. In general, the reasons for type I endoleak are (i) insufficient proximal or distal seal; (ii) spread of pathological lesions; and (iii) the technical limitations of endovascular devices. Among the hybrid arch repair cases, patients with the repair in zone 0 tended to have lower incidence rates of endoleak and reintervention. Hence, implantation of an additional stent graft, which was performed at a longer and more proximal site and extended to zone 0, may reduce type I endoleak. Nevertheless, perioperative aortic dissection in type I hybrid arch repair was also noteworthy, especially when the stent graft was positioned proximally in zone 0 or 1. Although there were no relevant data regarding why the perioperative aortic dissection was performed, researchers found that all of the patients had one thing in common: The diameters of their ascending aortas were >40 mm. Therefore, Bavaria et al. [6] suggested that type II hybrid arch repair is more suitable than type I and that the ascending aorta should be replaced when the diameter is >40 mm. As mentioned earlier, however, the repair of type II and III hybrid arch requires CPB, which is a significant disadvantage. Aside from the higher rate of reintervention with hybrid arch repair, the evidence indicated that the hybrid strategy yielded a shorter length of stay in the intensive care unit and fewer days in the hospital. In addition, hybrid arch repair played a leading role in high-risk cases, especially elderly patients older than 75 years with significant comorbidities that should be taken into account when considering whether to use the hybrid method [2, 8, 9]. Nevertheless, the higher costs of and the lower insurance indemnity for hybrid arch repair should also be considered [8]. Therefore, the choice of surgical procedure requires careful consideration of a number of factors. The hybrid method is still associated with many uncertainties.

Our meta-analysis has some limitations. First, all of the reports were retrospective cohort studies, with no randomized controlled trials, so the level of evidence tended to be weak. Second, the study population was relatively small, and there were only 7 eligible studies totalling 727 patients (269 hybrid repairs, 458 open repairs). Generally speaking, a larger sample size would provide more reliable results. Third, the cited references reported limited follow-up periods. In one paper, the potential follow-up time could have been 5 years [2]; nevertheless, the author failed to provide data with sufficient long-term follow-up. Two of three additional papers did not provide details on follow-up [8, 12], and one provided follow-up information for only 1 year [10]. This issue is serious, especially for high-risk patients, because it may result in an overestimation of the survival rate. For those patients who may have a long lifetime, longevity is likely to have a positive effect on the development of aortic arch aneurysm. Fourth, potential bias may exist, although the result of the funnel plot for operative mortality showed no apparent publication bias. Future studies should focus on this issue. Fifth, the discussions of risk factors in the seven studies contained discrepancies and were inadequate. As was mentioned before, hybrid arch repair might be an appropriate alternative for patients >75 years, so age could be viewed as a risk factor. Other risk factors included female gender, duration of follow-up and postoperative complications. Investigators should consider all of these issues for future research.

In conclusion, our meta-analysis substantiated the fact that there is no strong evidence verifying the advantages of hybrid arch repair over open surgical repair. In addition, hybrid arch repair resulted in more reinterventions even though it is less invasive and requires fewer days in the hospital. However, hybrid arch repair should be still considered as an appropriate alternative for elderly and high-risk patients. Thus, the selection of the appropriate surgical procedure for aortic arch aneurysm should take into consideration the characteristics of the patient and the cost of the operation. Further higher-quality comparative studies with large numbers of participants and long-term follow-up periods are necessary to confirm the effectiveness of hybrid arch repair for aortic arch aneurysm.

SUPPLEMENTARY MATERIAL

Supplementary material is available at ICVTS online.

Conflict of interest: none declared.

REFERENCES


