Axillary versus femoral arterial cannulation in type A acute aortic dissection: evidence from a meta-analysis of comparative studies and adjusted risk estimates

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Abstract

OBJECTIVES: There is a growing perception that femoral arterial cannulation (FAC), by reversing the flow in the thoracoabdominal aorta, may increase the risk of retrograde brain embolization, dissection and organ malperfusion in type A aortic dissection. Axillary artery cannulation (AXC) has been reported to improve operative outcomes by allowing antegrade blood flow. However, FAC still remains largely utilized as a consensus for the routine use of AXC has not yet been reached.

METHODS: A meta-analysis on comparative studies reporting operative outcomes using AXC versus FAC was performed. Pooled weighted incidence rates for end points of interest (both adjusted and unadjusted) have been computed using an inverse variance model.

RESULTS: Overall, a total of 8 studies including 793 patients were analysed (AXC = 396, FAC = 397). AXC was associated with reduced risk for in-hospital mortality [risk ratio (RR): 0.41; 95% confidence interval (CI): 0.29–0.58; P < 0.001] and permanent neurological deficit (PND) (RR: 0.59; 95% CI: 0.37–0.93; P = 0.02) when compared with FAC. Pooled adjusted estimates confirmed that AXC was independently associated with a significantly reduced incidence of in-hospital mortality (adjusted OR: 0.54; 95% CI: 0.36–0.82; P = 0.004; I² = 57%) and PND (adjusted OR: 0.19; 95% CI: 0.07–0.54; P = 0.002; I² = 0%).

CONCLUSIONS: The present meta-analysis demonstrated that AXC is superior to FAC in reducing in-hospital mortality and the incidence of PND in patients operated on for type A acute aortic dissection.

Keywords: Cardiopulmonary bypass • Aortic dissection • Outcomes

INTRODUCTION

During surgery for type A acute aortic dissection, cerebrovascular injury is one of the major causes of morbidity and mortality [1]. Possible causes for this neurological complication are malperfusion, cerebral embolism and global ischaemia during deep hypothermic circulatory arrest (HCA) [2, 3]. The arterial cannulation approach may represent a main determinant of operative outcomes.

The femoral artery has been longer considered the usual site of cannulation for cardiopulmonary bypass in acute type A aortic dissection and a low complication rate has been reported [4, 5]. However, there is a growing perception that femoral arterial cannulation (FAC), by reversing the flow in the thoracoabdominal aorta, may increase the risk of retrograde brain embolization, dissection and organ malperfusion [6, 7].

To overcome this predicament, several groups have begun to cannulate the right subclavian/axillary artery. This technique allows a continuous antegrade body perfusion and additionally a selective cerebral antegrade perfusion during circulatory arrest, thus preventing organ malperfusion and neurological damage [8, 9]. However, the suggested superiority of axillary artery cannulation (AXC) over FAC is not based on randomized studies but rather on a few observational cohort studies of different quality reporting conflicting results and sometimes challenging each other [2].

As a consequence, a general agreement concerning the superiority of the use of AXC over FAC in type A aortic dissection has not yet been provided and FAC remains to be frequently used in type A aortic dissection [10, 11].

We aimed to get insights into the role of AXC over FAC in type A aortic dissection surgery by conducting a meta-analysis of
available observational cohort studies comparing the two cannulation strategies.

MATERIALS AND METHODS

Eligibility criteria

Observational studies included in the present meta-analysis met the following criteria: (i) patients underwent urgent/emergency proximal aortic and/or aortic arch surgery for type A aortic dissection; (ii) comparison of outcomes after AXC versus FAC was made. Non-English language, review articles and editorials were excluded. Care was taken to ensure that studies selected did not result in duplication of data. Studies that did not separate results for AXC and FAC or reported on one strategy only were excluded. Studies with <10 subjects per arm were excluded.

Search strategy

A literature search was done using MEDLINE, EMBASE and Web of Science to identify relevant articles on 8 April 2014. Search terms used the controlled vocabularies of MEDLINE and EMBASE alone or in combination with text words including ‘cannulation’, ‘cardiopulmonary bypass’, ‘central cannulation’, ‘peripheral cannulation’, ‘femoral artery’, ‘axillary artery’, ‘subclavian artery’, ‘proximal aorta’, ‘aortic arch’, ‘aortic dissection’ and ‘type A acute aortic dissection’. References from the selected studies were also manually searched to avoid missing any potentially suitable articles.

In-hospital mortality and permanent neurological deficit (PND) were the primary end points of our meta-analysis. Two reviewers (U.B. and P.V.) independently screened all studies for inclusion. The search strategy adopted is in accordance with the Meta-analysis of Observational Studies in Epidemiology guidelines [12]. Disagreements were resolved by consensus. Agreement between reviewers regarding study inclusion was assessed using the Cohen’s k statistic [13]. The quality of included studies was assessed with the Newcastle-Ottawa scale for observational studies [14]. The total score was 9 stars, and the quality was graded as low level (<6 stars) or high level (≥6 stars).

Statistical analysis

Statistical analysis was conducted using Review Manager (RevMan, Computer program. Version 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012). Pooled weighted incidence rates for end points of interest have been obtained using an inverse variance model [15]. Operative mortality and PND are reported as a risk ratio (RR) with a 95% confidence interval (CI). Yates correction was implemented if a cell contained a zero in the 2 × 2 contingency table [16]. Pooled estimates were reported using a fixed-effect model. We used the I^2 statistic, which estimates the percentage of total variation across studies that is due to heterogeneity rather than chance. Suggested thresholds for heterogeneity were used, with I^2 values of 25–49%, 50–74% and ≥75%, indicative of low, moderate and high heterogeneity [17]. In the presence of high heterogeneity, estimates were also calculated using a random-effect model.

Since clinical and operative variables affecting outcomes investigated might have also influenced the choice of cannulation site, we performed sensitivity analysis including subgroup analysis and pooled adjusted risk estimates computation to support an independent effect of arterial cannulation strategy on operative outcomes. Subgroup analyses were conducted including only studies with comparable prevalence (Fisher’s exact test, P > 0.1) between AXC and FC groups of the following risk factors: preoperative mal-perfusion, cardiac tamponade, cerebral protection strategy and hemi/total arch replacement.

We finally computed pooled adjusted risk estimates from individual studies when reported by using log transformation and a generic inverse-variance weighting method. Publication bias was assessed by Egger’s test. A P-value < 0.05 was used as the level of significance and 95% (CIs) have been reported where appropriate.

RESULTS

Selected studies

From 2404 abstracts, we selected 18 full-text articles fitting our selection criteria. After evaluating the full-text articles, 8 were finally selected for the systematic review and meta-analysis [18–25]. An overview of studies and study quality assessment are summarized in Tables 1 and 2, respectively. An outline of the systematic review process is depicted in Fig. 1. Cohen’s k statistic of 90% was obtained for the final selection process.

Overall, a total of 793 patients were included in the final analysis. AXC was used in 396 cases and FAC in 397 cases. Cerebral protection strategies adopted in the included cohorts were HCA, antegrade selective cerebral perfusion (ASCP) and retrograde cerebral perfusion (RCP). A total of five studies used a unique cerebral protective strategy for all patients in both the AXC and FAC groups [18, 19, 22–24]. The study period ranged from 1990 to 2011. All studies included reported on in-hospital mortality and all but one reported on the incidence of PND. All but three studies [21, 24, 25] showed a high level of quality.

Overall meta-analysis

Weighted pooled estimates for outcomes of interest are shown in Fig. 2. AXC was associated with reduced in-hospital mortality when compared with FAC (RR: 0.41; 95% CI: 0.29–0.58; P < 0.0001). There was low heterogeneity among studies with regard to this outcome (I^2 = 38%). Pooled analysis showed AXC being associated with a significant trend towards a reduced risk for PND when compared with FAC (RR: 0.59; 95% CI: 0.37–0.93; P = 0.02) with a moderate heterogeneity among studies (I^2 = 56%). When high-quality studies only were included (≥6 stars according to the Newcastle-Ottawa scale) [18–20, 22, 23], AXC was still associated with a reduced risk for in-hospital mortality (RR: 0.43; 95% CI: 0.29–0.63; P < 0.001; I^2 = 62%) and a reduced risk of PND (RR: 0.51; 95% CI: 0.31–0.86; P = .01; I^2 = 52%).

Subgroup analysis

Overall four studies [21, 22, 24, 25] reported on AXC and FAC groups with comparable (P > 0.1) prevalence of preoperative mal-perfusion. Subgroup pooled estimates confirmed AXC to be associated with a significantly lower in-hospital mortality (RR: 0.32; 95% CI: 0.18–0.57; P = 0.0001; I^2 = 0%) and a trend towards lower incidence of PND (RR: 0.65; 95% CI: 0.11–4.01; P = 0.6; I^2 = 67%).
<table>
<thead>
<tr>
<th>Study</th>
<th>Institution</th>
<th>Study period</th>
<th>AXC</th>
<th>FAC</th>
<th>AXC approach</th>
<th>Preoperative malperfusion</th>
<th>Cardiac tamponade</th>
<th>Brain protection strategy</th>
<th>Hemi/total arch replacement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Di Eusanio et al. [18]</td>
<td>University of Bologna, Bologna, Italy</td>
<td>1996–2011</td>
<td>44</td>
<td>122</td>
<td>Direct or interposition graft</td>
<td>Not reported</td>
<td>Not reported</td>
<td>HCA and ASCP in all cases</td>
<td>Not reported</td>
</tr>
<tr>
<td>Etz et al. [19]</td>
<td>Mount Sinai School of Medicine, New York, NY, USA</td>
<td>1990–2005</td>
<td>31</td>
<td>31</td>
<td>Directly</td>
<td>Not reported</td>
<td>Not reported</td>
<td>HCA only in all cases</td>
<td>Not reported</td>
</tr>
<tr>
<td>Haldenwag et al. [20]</td>
<td>Ruhr-University Bochum, Bochum, Germany</td>
<td>2003–2010</td>
<td>92</td>
<td>15</td>
<td>Direct or interposition graft</td>
<td>Total 45 Not reported separately</td>
<td>Total 57 Not reported separately</td>
<td>Early period: HCA only Late period: HCA and ASCP</td>
<td>Total 52 Not reported separately</td>
</tr>
<tr>
<td>Lee et al. [21]</td>
<td>Seoul National University College of Medicine, Seoul, Korea</td>
<td>2001–2009</td>
<td>58</td>
<td>53</td>
<td>Direct or interposition graft</td>
<td>AXC: 4 (6.9%) FAC: 4 (7.5%) (P = 1)</td>
<td>AXC: 5 (8.6%) FAC: 11 (20.8%) (P = 0.06)</td>
<td>CC: 59% ASCP, 2% retrograde, 39% HCA only PC: 45% ASCP, 19% retrograde, 36% HCA only</td>
<td>AXC: 29 (42%) FAC: 15 (40%) (P = 1.0)</td>
</tr>
<tr>
<td>Mizumi et al. [22]</td>
<td>Sendai City Medical Center, Sendai, Japan</td>
<td>1992–2004</td>
<td>69</td>
<td>37</td>
<td>Interposition graft</td>
<td>AXC: 26 (37%) FAC: 9 (24%) (P = 0.8)</td>
<td>AXC: 31 (45%) FAC: 20 (54%) (P = 0.4)</td>
<td>HCA and ASCP in all cases</td>
<td>AXC: 29 (42%) FAC: 15 (40%) (P = 1.0)</td>
</tr>
<tr>
<td>Nouraei et al. [23]</td>
<td>London, UK Deutsches Herzcentrum Berlin, Berlin, Germany</td>
<td>1999–2004</td>
<td>20</td>
<td>29</td>
<td>Interposition graft</td>
<td>Not reported</td>
<td>Not reported</td>
<td>HCA and RCP in all cases</td>
<td>Not reported</td>
</tr>
<tr>
<td>Pasic et al. [24]</td>
<td>Deutsches Herzcentrum Berlin, Berlin, Germany</td>
<td>2000–2002</td>
<td>20</td>
<td>50</td>
<td>Direct or interposition graft</td>
<td>AXC: 5 (25%) FAC: 7 (14%) (P = 0.3)</td>
<td>Not reported</td>
<td>HCA and RCP in all cases</td>
<td>Not reported</td>
</tr>
<tr>
<td>Reuthebuch et al. [25]</td>
<td>University Hospital Zurich, Zurich, Switzerland</td>
<td>1997–2003</td>
<td>62</td>
<td>60</td>
<td>Direct or interposition graft</td>
<td>AXC: 18 (29%) FAC: 21 (35%) (P = 0.5)</td>
<td>AXC: 17 (28%) FAC: 20 (32%) (P = 0.5)</td>
<td>CC: HCA and ASCP in all cases PC: HCA and RCP in all cases</td>
<td>AXC: 31 (50%) FAC: 22 (36%) (P = 0.13)</td>
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AXC: axillary cannulation; FAC: femoral cannulation; HCA: hypothermic circulatory arrest; ASCP: antegrade selective cerebral perfusion; RCP: retrograde cerebral perfusion; TAAAD: type A aortic acute dissection.
Two studies [22, 25] reported on AXC and FAC groups with comparable prevalence of preoperative cardiac tamponade. Subgroup pooled estimates confirmed AXC to be associated with a significantly lower in-hospital mortality (RR: 0.29; 95% CI: 0.15–0.58; \( P = 0.0004; I^2 = 0\%\)) and a trend towards lower incidence of PND (RR: 0.12; 95% CI: 0.02–0.94; \( P = 0.04\)). As cerebral protection strategies may play a main role in determining PND thus affecting in-hospital mortality, we pooled data from studies including patients operated on using a single cerebral protection strategy for both AXC and FAC groups to support an independent effect of the arterial cannulation approach on outcomes investigated. Among five studies meeting this criterion [18, 19, 22–24], the cerebral protection strategy consisted of HCA only in one study [19], HCA combined with RCP only in two studies [23, 24] and HCA combined with selective antegrade cerebral perfusion only in two studies [18, 22]. Pooled estimates from this subgroup confirmed AXC to be associated with a significantly lower risk for in-hospital mortality (RR: 0.42; 95% CI: 0.28–0.61; \( P < 0.0001; I^2 = 55\%\)) and PND (RR: 0.52; 95% CI: 0.31–0.86; \( P = 0.01; I^2 = 37\%\)). Finally, a total of 3 studies [21, 22, 25] reported on AXC and FAC groups with comparable (\( P > 0.1\)) prevalence of hemi/total arch replacement. Subgroup pooled estimates confirmed AXC to be associated with a significantly lower in-hospital mortality (RR: 0.33; 95% CI: 0.18–0.61; \( P = 0.0004; I^2 = 0\%\)) and a non-significant trend towards lower incidence of PND (RR: 0.61; 95% CI: 0.03–11.42; \( P = 0.7; I^2 = 83\%\)).

Pooled adjusted risk estimates

Overall four studies [18, 20, 22, 23] reported on adjusted effect size from AXC over FAC for outcomes investigated. The effect of arterial cannulation site on in-hospital mortality was adjusted for several clinical and perfusion variables including: gender [18, 20, 22, 23], age [18, 20, 22, 23], critical acute dissection (including shock, tamponade, aortic rupture, cerebral ischaemia, visceral ischaemia, cardiopulmonary resuscitation) [18, 20, 22, 23], re-intervention [18, 22, 23], renal failure [18, 20, 22, 23], coronary artery disease [18, 22, 23], hemiarch/total arch replacement [18, 22, 23], ASCP time [18, 20, 22, 23], deep HCA time [18, 20, 22], and AXC time [18, 20, 22]. Pooled adjusted estimates of individual log odds ratios (ORs) confirmed that AXC was independently associated with a significantly reduced incidence of in-hospital mortality (adjusted OR: 0.54; 95% CI: 0.36–0.82; \( P = 0.004; I^2 = 57\%\)) and PND (adjusted OR: 0.19; 95% CI: 0.07–0.54; \( P = 0.002; I^2 = 0\%\)) (Fig. 3).

Assessment on publication bias

Egger’s test excluded publication bias for both in-hospital mortality and PND (\( P = 0.1 \) and \( P = 0.3 \), respectively).

COMMENT

Femoral artery cannulation has been used for cardiopulmonary bypass since the 1950s and the femoral artery has been the primary site for arterial cannulation in surgery for type A aortic dissection [4, 5]. However, FAC has been associated with a greater risk of stroke, particularly those with concurrent thoracoabdominal aortic or iliac aneurysmal disease. This was probably due to debris or thrombi in these segments that had been pumped from dissection sites retrogradely to the brain [6, 7]. In addition, retrograde perfusion through the femoral artery may further exacerbate dissected intimal flaps and cause organ malperfusion, progressive

<table>
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<th>Table 2: Newcastle-Ottawa quality assessment scale</th>
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<tbody>
<tr>
<td>Selection</td>
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<tr>
<td>FAC group</td>
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<tr>
<td>AXC: axillary cannulation; FAC: femoral cannulation.</td>
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<tr>
<td>Di Eusanio et al. (2013)</td>
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<td>Etz et al. (2013)</td>
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<td>Haldenwang et al. (2012)</td>
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<td>Lee et al. (2012)</td>
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<td>Moizumi et al. (2005)</td>
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<td>Nose et al. (2007)</td>
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<td>Reuthebuch et al. (2004)</td>
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<tr>
<td>Pasic et al. (2003)</td>
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<td>U. Benedetto et al. / European Journal of Cardio-Thoracic Surgery</td>
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arch vessel compromise, and neurological injury [21]. Previous studies have reported an incidence of malperfusion syndrome with femoral cannulation of 2.5–13% [2, 10]. The right axillary or subclavian artery was introduced as an alternative site for an arterial cannulation in patients requiring proximal aortic and arch surgery and type A acute aortic dissection. Recently, the theoretical advantages of AXC have become apparent [8, 9]. These possible advantages include a decreased risk of stroke from embolic material, a lower likelihood of malperfusion and less disruption of the atheroma or calcified plaques [2]. Also, AXC facilitates continuous antegrade cerebral blood flow during the steps where a bloodless field is required for the operation [18, 22, 25]. For these reasons, an increasing number of surgeons prefer cannulating the axillary artery instead of the femoral artery in patients with type A aortic dissection. However, whether the axillary artery should be used routinely in type A aortic dissection surgery has been controversial [2] and FAC still remains the standard option in many centres due to the lack of a general consensus [10, 11]. The lack of randomization is an important issue which limits the value of available evidences. However, different individual situations in which patients with type A dissection present with at the time of surgery demand a personalized approach and these patients are very unlikely to be suitable for any prospective, randomized trials. In addition, the number of patients of each center is rather small. Therefore, summary of evidence from observational cohort studies is a candidate to guide decision-making in the treatment of such a high-risk setting.

The present meta-analysis, pooling data from available evidence, strongly supports the superiority of central cannulation over peripheral cannulation in proximal aortic and aortic arch surgery. We found AXC to be associated with a 59 and 41% absolute risk reduction of in-hospital mortality and PND when compared to FAC, respectively and this benefit was confirmed by pooled adjusted risk estimates. It can be argued that as right AXC is more time consuming than femoral cannulation, femoral artery was systematically preferred in patients with a severely compromised clinical and anatomical condition (malperfusion syndrome, cardiac tamponade, need for arch replacement) thus affecting outcomes in this group. To rule out a potential bias due to patient selection, we performed sensitivity analysis including subgroup analysis and adjusted risk estimates. These analyses supported an independent effect of arterial cannulation site on operative outcomes investigated. Moreover, none of the included studies reported a higher preoperative malperfusion syndrome prevalence among patients receiving FAC, thus challenging the common perception that FAC is preferentially used in more compromised patients.

Figure 1: Flowchart depicting study selection for meta-analysis. AXC: axillary cannulation; FAC: femoral cannulation.
Finally, cerebral protection strategies play a main role in determining PND, thus affecting in-hospital mortality during aortic surgery [21, 25]. The superior results of AXC compared with FAC have been suggested to be mainly caused by facilitating continuous antegrade cerebral flow and not by reversing the flow in the thoracoabdominal aorta *per se* [2]. However, our sensitivity
analysis supports an independent effect of the arterial cannulation strategy on operative mortality and PND regardless of the cerebral protection strategy adopted.

**Study limitations**

There are several caveats to the interpretation of the results of this review, primarily arising out of the observational design in the included studies. In observational studies, unadjusted risk estimates are prone to selection and performance bias and meaningful statistical inference can be problematic as many clinical and perfusion variables in acute type A aortic dissection repair may affect operative outcomes. We thus addressed known confounders in included observational studies by using subgroup analysis and the multivariable analysis method previously validated. Sensitivity analysis supported the benefit of AXC over FAC.

AXC can be established using direct cannulation or by means of an interposition graft. Both the strategies were used in most of the studies included in the present analysis. Unfortunately, data on outcomes investigated were not provided separately for direct and interposition graft approaches from individual studies and therefore no conclusion can be drawn on potential differences.

It must be emphasized that the data included in this review originate from centres with expertise in aortic surgery. Therefore, the conclusions cannot be extrapolated to smaller, less experienced centres. An additional bias may occur because both the approaches were used in a single centre: more experienced surgeons were more likely to use the axillary artery, whereas others might have preferred the femoral artery. In all the included studies, outcomes were objectively measured but definitions were not prespecified and may not have been consistently applied in an unbiased manner to both treatment groups.

**Conclusions and implications for clinical practice**

Current surgical results in patients presenting with type A acute aortic dissection are still unsatisfactory with an operative hospital mortality rate ranging from 20–30% worldwide [1]. Therefore every effort must be made to decrease surgical morbidity and mortality. The cannulation strategy represents a critical choice that may play a crucial role in determining operative outcomes.

The results of the present meta-analysis should give pause to the current extended liberal use of peripheral cannulation through the femoral artery. Our findings strongly support a standardized approach in type A aortic dissection by using AXC regardless of the cerebral protection strategy adopted.

**Conflict of interest:** none declared.

**REFERENCES**


