The impact of arterial cannulation strategy on operative outcomes in aortic surgery: Evidence from a comprehensive meta-analysis of comparative studies on 4476 patients

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Objectives: There is a growing perception that peripheral cannulation through the femoral artery, by reversing the flow in the thoracoabdominal aorta, may increase the risk of retrograde brain embolization in aortic surgery. Central cannulation sites, including the right axillary artery, have been reported to improve operative outcomes by allowing antegrade blood flow. However, peripheral cannulation still remains largely used because a consensus for the routine use of central cannulation approaches has not been reached.

Methods: A meta-analysis of comparative studies reporting operative outcomes using central cannulation versus peripheral cannulation was performed. Pooled weighted incidence rates for end points of interest were obtained using an inverse variance model.

Results: A total of 4476 patients were included in the final analysis. Central cannulation was used in 2797 patients, and peripheral cannulation was used in 1679 patients. Central cannulation showed a protective effect on in-hospital mortality (risk ratio, 0.59; 95% confidence interval, 0.48-0.7; $P < .001$) and permanent neurologic deficit (risk ratio, 0.71; 95% confidence interval, 0.55-0.90; $P = .005$) when compared with peripheral cannulation. A trend toward an increased benefit in terms of reduced in-hospital mortality was observed when only the right axillary artery was used as the central cannulation approach (risk ratio, 0.35; 95% confidence interval, 0.22-0.55; $P < .001$; $I^2 = 0\%$).

Conclusions: Central cannulation was superior to peripheral cannulation in reducing in-hospital mortality and the incidence of permanent neurologic deficit. This superiority was particularly evident when the axillary artery was used for central cannulation. (J Thorac Cardiovasc Surg 2014;148:2936-43)

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Injury to the central nervous system remains one of the major causes of morbidity and mortality after proximal aortic and arch operations, affecting not only quality of life postoperatively but also resulting in prolonged hospitalization and increased cost of treatment.[1]

Growing data have indicated that the cannulation of arteries preserving an antegrade flow (so-called central cannulation [CC] sites) in the thoracic aorta is associated with superior survival and better neurologic outcomes compared with the cannulation of the femoral artery (so-called peripheral cannulation [PC]).[2] In particular it has been advocated that the cannulation of the femoral artery, by reversing the flow in the thoracoabdominal aorta, may increase the risk of retrograde brain embolization and dissection in patients with severe atherosclerosis and of brain or organ malperfusion in those undergoing operation for type A acute aortic dissection (TAAAD).[3,4] However, the suggested superiority of CC sites over the femoral artery during proximal aortic and arch operations is not based on randomized studies but rather on a few observational cohort studies of different quality reporting and conflicting results.[3,4]

As a consequence, a general agreement concerning the use of CC sites during proximal aortic and arch operations has not been reached,[4] and PC is still preferred by many surgeons during aortic surgery.[5,6] We investigated the role of CC sites during proximal aortic and aortic arch surgery by conducting a meta-analysis of available

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Abbreviations and Acronyms

ASCP = antegrade selective cerebral perfusion
CC = central cannulation
CI = confidence interval
HCA = hypothermic circulatory arrest
PC = peripheral cannulation
PND = permanent neurologic deficit
RR = risk ratio
TAAAD = type A acute aortic dissection

observational cohort studies comparing the 2 cannulation strategies.

METHODS

Eligibility Criteria

Observational studies included in the present meta-analysis met the following criteria: (1) patients underwent elective or urgent/emergency proximal aortic and aortic arch surgery, and (2) a comparison of outcomes after CC versus PC was made. Patients undergoing cannulation of the ascending aorta, right axillary/subclavian artery, or innominate artery constituted the CC group. Patients undergoing femoral artery cannulation constituted the PC group.

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 CC and PC or reported on only 1 strategy were excluded. Studies with less than 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 April 8, 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," "innominate artery," "direct aortic," "ascending aorta," "proximal aorta," "aortic arch," "aortic aneurysm," and "aortic dissection." References from the selected studies also were manually searched to avoid missing any potentially suitable articles.

In-hospital mortality and permanent neurologic deficit (PND) were the primary end points of our meta-analysis. Two reviewers (U.B., S.G.R.) independently screened all studies for inclusion. The search strategy adopted is in accordance with the Meta-analysis of Observational Studies in Epidemiology guidelines.[7] Disagreements were resolved by consensus. Agreement between reviewers regarding study inclusion was assessed using the Cohen k statistic.[8] Quality of included studies was assessed with the Newcastle–Ottawa scale for observational studies.[9] 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) and metafor R package (Wolfgang Viechtbauer 2010. Conducting meta-analyses in R with the metafor package. *J Stat Softw.* 2010;36:1-48. Available at: http://www.jstatsoft.org/v36/i03/.) Pooled weighted incidence rates for end points of interest were obtained using an inverse variance model.[10] Operative mortality and PND were 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.[11] Studies without events in both cases and control groups did not contribute to the statistical result.[12] 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% to 49%, 50% to 74%, and 75% or greater, indicative of low, moderate, and high heterogeneity, respectively.[13] When the pooled estimate demonstrated moderate heterogeneity, a random-effect model was implemented to report the result. Leave-one-out and subgroup analyses were performed to investigate heterogeneity. Publication bias was visually assessed using the Funnel plot method and Egger's test. The 95% CIs have been reported where appropriate.

RESULTS

Selected Studies

From 2404 abstracts, we selected 20 full-text articles fitting our selection criteria. After evaluating the full-text articles, 14 were finally selected for the systematic review and meta-analysis.[14-27] An overview of the studies and study quality assessment are summarized in Tables 1 and 2, respectively. An outline of the systematic review process is depicted in Figure 1. A Cohen k statistic of 90% was obtained for the final selection process.

A total of 4476 patients were included in the final analysis. CC was used in 2797 patients, and PC was used in 1679 patients. The CC group included right axillary artery cannulation in 7 studies,[20-26] direct aortic cannulation in 2 studies,[18,19] both right axillary artery or direct aortic cannulation in 3 studies,[15-17] and right axillary artery or innominate artery or direct aortic cannulation in 2 studies.[14-27] A total of 8 of 14 studies reported on type A aortic dissection cases only,[16-18,20-23,25] whereas the others included mixed aortic pathologies.[14,15,19,24,26,27] Cerebral protection strategies included hypothermic circulatory arrest (HCA), antegrade selective cerebral perfusion (ASCP), and retrograde cerebral perfusion. A total of 6 studies used a unique cerebral protective strategy for all patients in both groups.[14,15,19,21-23] The study period ranged from 1990 to 2011. All studies included reported on in-hospital mortality, and all but 1 study[21] reported on the incidence of PND. All but 4 studies[20,23-25] showed a high-level quality.

Meta-Analysis

Weighted pooled estimates for outcomes of interest are shown in Figure 2. CC showed a protective effect on hospital mortality when compared with PC (RR, 0.59; 95% CI, 0.48-0.7; $P < .001$). There was no significant heterogeneity among studies with regard to this outcome ($I^2 = 18\%$). In the leave-1-out analysis, CC was confirmed to be associated with reduced in-hospital mortality (RR ranged from 0.54 to 0.62). Pooled analysis showed that CC was associated with a reduced risk for PND (RR, 0.71; 95% CI, 0.55-0.90; $P = .005$). There was no significant heterogeneity among studies ($I^2 = 20\%$). In a leave-1-out analysis, CC was

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TABLE 1. Overview of studies

Study, reference	Institution	Study period	No. of CC sites	No. of PC	Indication for surgery	TAAAD (%)	Brain protection strategy
Di Eusanio and colleagues 2013[14]	University of Bologna, Bologna, Italy	1996-2011	DA (n = 46) RAA (n = 128) IA (n = 26)	237	Aortic arch repair for acute or chronic post-dissection or chronic nondissected aneurysm	37	HCA and ASCP in all cases
Etz and colleagues 2008[15]	Mount Sinai School of Medicine, New York, NY	1990-2005	DA (n = 157) RAA (n = 451)	261	Ascending aorta and arch aneurysm, aortic dissection	7.4	HCA only in all cases
Etz and colleagues 2014[16]	University of Leipzig, Leipzig, Germany	1995-2011	DA (n = 15) RAA (n = 297)	89	TAAAD	100	CC: 61% ASCP, 3% retrograde, 36% HCA PC: 21% ASCP 11% retrograde, 67% HCA
Haldenwang and colleagues 2012[17]	Ruhr-University, Bochum, Germany	2003-2010	DA (n = 15) RAA (n = 92)	15	TAAAD	100	Early period: HCA only Late period HCA and ASCP
Kamiya and colleagues 2009[18]	University Hospital Heidelberg, Germany	1988-2007	DA (n = 82)	153	TAAAD	100	CC: 13% ASCP, 87% HCA only PC: 9% ASCP; 91% HCA only
Lakew and colleagues 2005[19]	Cardiovascular Center, Bad Neustadt, Germany	1996-2000	DA (n = 166)	161	Chronic nondissected ascending aorta aneurysm	0	HCA only in all cases
Lee and colleagues 2012[20]	Seoul National University College, Seoul, South Korea	2001-2009	RAA (n = 58)	53	TAAAD	100	CC: 59% ASCP, 2% retrograde, 39% HCA PC: 45% ASCP 19% retrograde, 36% HCA
Moizumi and colleagues 2005[21]	Sendai City Medical Center, Sendai City, Japan	1992-2004	RAA (n = 69)	37	TAAAD	100	HCA and ASCP in all cases
Nouraei and colleagues 2007[22]	Newcastle, UK	1999-2004	RAA (n = 20)	29	TAAAD	100	HCA and RCP in all cases
Pasic and colleagues 2003[23]	Herzzentrum, Berlin, Germany	2000-2002	RAA (n = 20)	50	TAAAD	100	HCA and RCP in all cases
Polat and colleagues 2012[24]	Bağcılar Training and Research Hospital, İstanbul, Turkey	2000-2009	RAA (n = 84)	88	Ascending aorta and arch aneurysm, aortic dissection	60	CC: HCA and ASCP in 65% cases PC: HCA and RCP in 61% cases
Reuthebuch and colleagues 2004[25]	University Hospital Zurich, Zurich, Switzerland	1997-2003	RAA (n = 62)	60	TAAAD	100	CC: HCA and ASCP in all cases PC: HCA and RCP in all cases
Strauch and colleagues 2005[26]	Heart Center Lahr, Lahr/Schwarzwald, Germany	1999-2004	RAA (n = 49)	71	Arch aneurysms, type A dissections	30	CC: HCA and ASCP PC: HCA only
Svensson and colleagues 2004[27]	The Cleveland Clinic Foundation, Cleveland, Ohio	1993-2003	DA (n = 471) RAA (n = 466) IA (n = 24)	375	Atherosclerosis, aortic arch aneurysms, acute dissections	32	HCA using ASCP or RCP at surgeon's discretion

ASCP, Antegrade selective cerebral perfusion; *CC*, central cannulation; *DA*, direct aortic; *HCA*, hypothermic circulatory arrest; *IA*, innominate artery; *PC*, peripheral cannulation; *RAA*, right axillary artery; *RCP*, retrograde cerebral perfusion; *TAAAD*, type A aortic acute dissection.

TABLE 2. Newcastle–Ottawa Quality Assessment Scale

	Selection				Comparability	Outcomes			
Study, reference	Representativeness of the CC groups	Selection of the PC group	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Indication for surgery = ★ Age and cerebral protection strategy = ★	Assessment of outcome	Follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Total ★
Di Eusanio and colleagues 2013[14]	★	★	★		★	★	★	★	7
Etz and colleagues 2008[15]	★	★	★		★	★	★	★	7
Etz and colleagues 2014[16]	★	★	★		★	★	★	★	7
Haldenwang and colleagues 2012[17]	★	★	★			★	★	★	6
Kamiya and colleagues 2009[18]	★	★	★		★★	★	★	★	8
Lakew and colleagues 2005[19]	★	★			★★		★	★	6
Lee and colleagues 2012[20]	★	★			★		★	★	5
Moizumi and colleagues 2005[21]	★	★			★★		★	★	6
Nouraei and colleagues 2007[22]	★	★	★		★	★	★	★	7
Pasic and colleagues 2003[23]	★	★			★		★	★	5
Polat and colleagues 2012[24]	★	★					★	★	4
Reuthebuch and colleagues 2004[25]	★	★			★		★	★	5
Strauch and colleagues 2005[26]	★	★	★			★	★	★	6
Svensson and colleagues 2004[27]	★	★	★			★	★	★	6

CC, Central cannulation; *PC*, peripheral cannulation.

confirmed to be associated with a reduced risk for PND (RR ranged from 0.65 to 0.77). Pooled estimates among high-quality studies[14-19,21,22,26,27] (≥6 stars according to the Newcastle Ottawa scale, Figure E1) showed CC to be associated with a reduced rate of in-hospital mortality (RR, 0.61; 95% CI, 0.50-0.75; $P < .0001$, $I^2 = 33\%$) and PND (RR, 0.69; 95% CI, 0.54-0.89; $P = .004$; $I^2 = 7\%$).

Sensitivity Analysis on Subgroups

Pooled estimates according to the aortic causes (Figure E2) did not significantly differ among subgroups for both in-hospital mortality and PND (test for subgroup differences $P = .78$ and $P = .84$, respectively). When studies reporting only on patients with type A aortic dissection[16-18,20-23,25] were pooled, CC remained associated with a significantly lower risk for in-hospital mortality (RR, 0.48; 95% CI, 0.30-0.77; $P = .002$; $I^2 = 52\%$) and a trend toward a lower risk for PND (RR, 0.60; 95% CI, 0.31-1.15; $P = .1$; $I^2 = 56\%$) when compared with PC.

Pooled estimates according to the CC sites (Figure E3) showed a trend toward an extra benefit for in-hospital mortality (test for subgroup differences $P = .1$) but not for PND ($P = .75$) when only the right axillary/subclavian artery was used as the CC approach. By pooling data from studies including only the right axillary/subclavian artery as the CC site,[20-26] CC showed a significant association with a lower risk for in-hospital mortality (RR, 0.35; 95% CI, 0.22-0.55; $P < .001$; $I^2 = 0\%$) and a trend toward a lower incidence of PND (RR, 0.61; 95% CI, 0.32-1.14; $P = .1$, $I^2 = 45\%$) when compared with PC. When studies including only direct aortic cannulation as the CC strategy were included,[18,19] CC showed a nonsignificant association with a lower incidence of in-hospital mortality (RR, 0.93; 95% CI, 0.47-1.84; $P = .8$; $I^2 = 0\%$) and PND (RR, 0.92; 95% CI, 0.38-2.22; $P = .8$; $I^2 = 0\%$). However, 2 studies included only direct aortic cannulation as the CC strategy, and the paucity of evidence limits the consistency of the present findings on the impact of direct

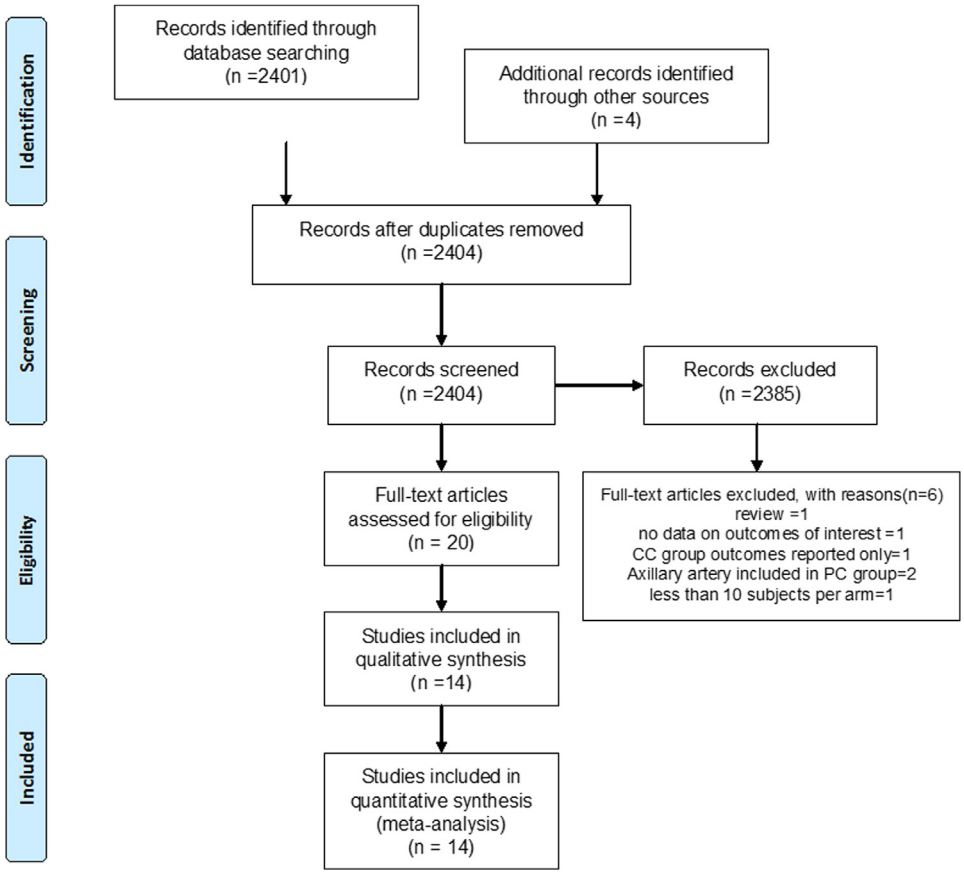

FIGURE 1. Flow chart depicting study selection for meta-analysis. *CC*, Central cannulation; *PC*, peripheral cannulation.

aortic cannulation. No study reported a comparison of innominate artery cannulation only and femoral artery cannulation.

Because cerebral protection strategies may play a main role in determining PND, thus affecting in-hospital mortality during aortic surgery, we pooled data from studies including patients undergoing operation using a single cerebral protection strategy for both CC and PC groups to support an independent effect of arterial cannulation approach on operative outcomes. Among 5 studies meeting this criteria,[14,15,19,21-23] cerebral protection strategy consisted of only HCA in both groups in 2 studies,[15,16] HCA combined with retrograde cerebral perfusion in 2 studies, and HCA combined with ASCP in 1 study. Pooled estimates from this subgroup (Figure E4) confirmed CC to be associated with a significantly lower risk for in-hospital mortality (RR, 0.41; 95% CI, 0.28-0.60; $P = <.0001$; $I^2 = 0\%$) and PND (RR, 0.55; 95% CI, 0.35-0.89; $P = .01$; $I^2 = 0\%$).

Assessment of Publication Bias

Visual assessment of funnel plot did not show outliers (Figure E5), and Egger's test excluded publication bias for both in-hospital mortality and PND ($P = .2$ and $P = .1$, respectively).

DISCUSSION

For many years, the femoral artery has been routinely used as favorite arterial cannulation site for extracorporeal circulation. With the routine use of the ascending aorta as an arterial cannulation site,[28] the femoral artery was used only in complicated cases when aortic cannulation was deemed not to be feasible, such as in the case of aortic dissection or chronic proximal aortic and aortic arch aneurysm. However, the perceived increased risk of retrograde cerebral embolization, organ malperfusion, perfusion of the false lumen, and retrograde dissection[2] due to flow reversal in the thoracoabdominal aorta when using femoral artery cannulation, and increasing evidence for the benefits of antegrade cerebral perfusion during aortic arch surgery[3,4] resulted in the search for alternative CC sites during aortic surgery. The axillary artery was described as a safe and easy cannulation site for extracorporeal circulation, especially in patients with a diseased ascending aorta.[29] In addition, direct cannulation of the true lumen is an emerging method for a quick and easy establishment of cardiopulmonary

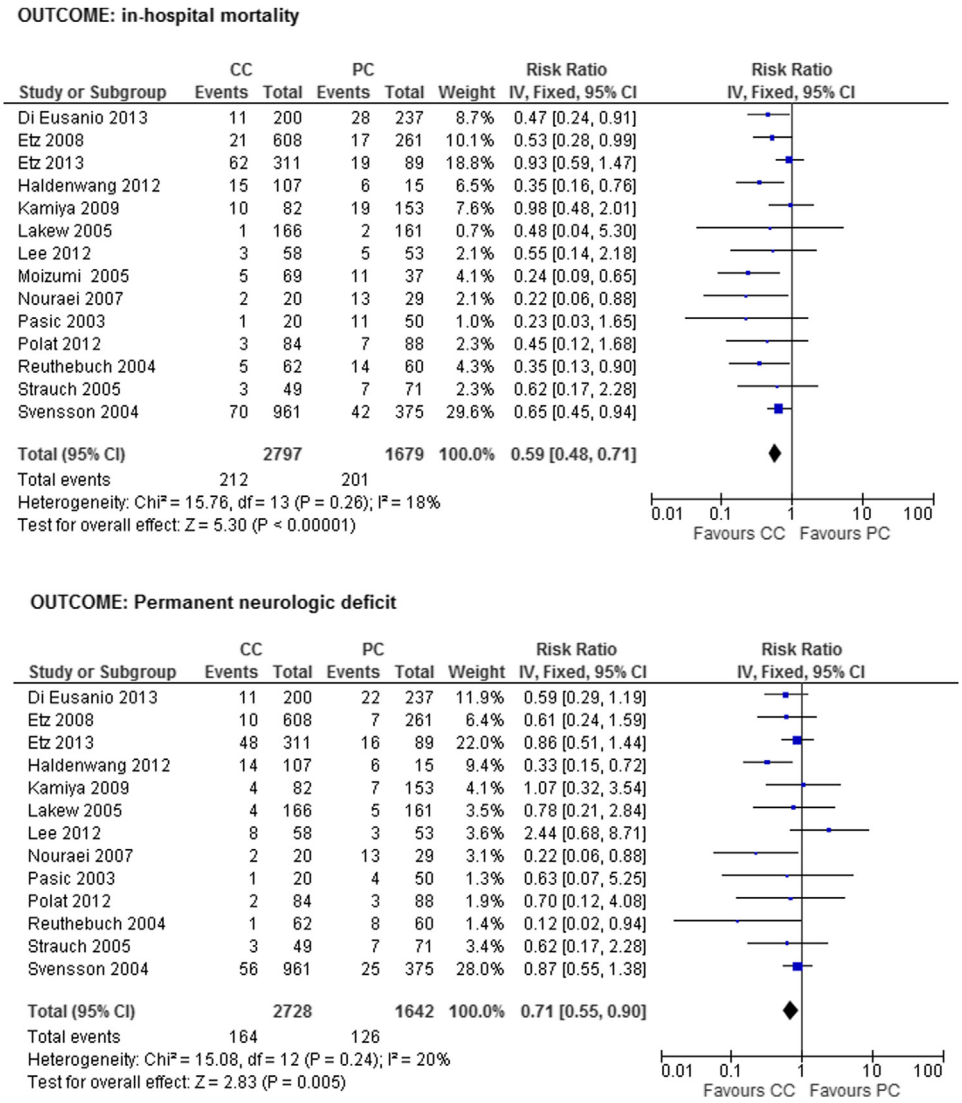

FIGURE 2. Forest plot for in-hospital mortality (*top*) and PND (*bottom*). *CC*, Central cannulation; *PC*, peripheral cannulation; *CI*, confidence interval.

bypass.[30] Despite concerns regarding the fragility of vessels and distal embolization during ascending aortic cannulation of a dissected aorta, it has been reported to be associated with promising results.[18] Innominate artery cannulation recently was proposed as an alternative cannulation site for ASCP with larger arterial access and avoidance of additional incisions.[31]

However, whether CC sites should be routinely used in proximal aortic and aortic arch surgery is still a matter of controversy. The lack of prospective randomized trials has not allowed a general recommendation for routine use of central arterial cannulation. Thus, summary of evidence from observational cohort studies is a logical approach to guide decision making in the treatment of such a high-risk setting. On the other hand, because patients with chronic proximal aortic or aortic arch aneurysms normally do not present on an emergency basis, every effort must be made to standardize the best surgical approach to reduce the perioperative risk for stroke or other complications.

The present meta-analysis pooling data from available evidence strongly supports the superiority of CC over PC in proximal aortic and aortic arch surgery. We found CC to be associated with a 41% and 29% absolute risk reduction of in-hospital mortality and PND, respectively, when compared with PC. The advantage from CC over PC was more pronounced in patients undergoing operation for TAAAD with an absolute risk reduction of 52% and 40% for in-hospital mortality and PND, respectively. Our results support the potential superiority of axillary artery cannulation over other CC sites. In studies in which only axillary artery cannulation was used as the CC strategy,[20-26] there was a 65% and 39% absolute risk reduction for in-hospital mortality and PND, respectively, whereas there was a 7% and 8% absolute risk reduction for the same

outcomes when only direct aortic cannulation was used. However, there is still a paucity of comparisons between direct aortic versus femoral cannulation in the treatment of aortic aneurysm to draw definitive conclusions. In addition, because of the absence of studies reporting comparative outcomes of innominate artery cannulation, at present it is difficult to determine the effectiveness of innominate artery cannulation compared with femoral cannulation.

The better outcomes from CC approaches over femoral cannulation have been suggested to be mainly caused by maintaining antegrade cerebral blood flow through the whole procedure and by avoiding complete circulatory arrest.[3] To reduce the effect of cerebral protection strategies on the overall impact of the arterial cannulation strategy, we performed a subgroup analysis on studies in which a single cerebral protection strategy was adopted in both the CC and PC groups. CC was still associated with a strongly significant absolute risk reduction of 59% and 45% over PC for in-hospital mortality and PND, respectively. These results support the hypothesis that PC increases per se the risk of operative mortality and PND by reversing the flow in the thoracoabdominal aorta.[3]

Study Limitations

There are several caveats to the interpretation of the results of this review, primarily arising out of the observational design and retrospective data collection in the included studies. Because the decision to treat patients using either modality was at the discretion of treating physicians, selection bias was inevitable. This may have resulted in systematic differences in variables, which could have influenced outcomes with either treatment modality. It must be emphasized that the data included in this review originate from centers with expertise in aortic surgery. Therefore, the conclusions cannot be extrapolated to smaller, less-experienced centers. An additional bias may occur because more experienced surgeons were more likely to use the axillary artery, whereas surgeons with less experience might have preferred the femoral artery even in these centers with expertise. 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. Lastly, we are unable to unambiguously attribute the increased risk for in-hospital mortality and PND to PC because of the paucity of data regarding the incidence of complications directly related with the cannulation strategy, such as malperfusion, embolic stroke, and retrograde dissection.

CONCLUSIONS

Current surgical results in patients presenting with TAAAD are still unsatisfactory with an operative hospital mortality ranging from 20% to 30% worldwide.[32] On the other hand, chronic proximal aortic and arch aneurysm repair is performed frequently in elective asymptomatic patients.[1] Therefore, every effort must be made to standardize the best surgical approach to reduce the perioperative risk for stroke and other complications.

Cannulation strategy represents a critical choice that may play a crucial role in determining operative outcomes in aortic surgery. The results of this meta-analysis question the current extended and often exceedingly liberal use of PC through the femoral artery. Our findings strongly support a standardized approach by using CC through the right axillary artery regardless of the cerebral protection strategy adopted during proximal aortic and arch surgery to improve operative outcomes.

References

1. Misfeld M, Leontyev S, Borger MA, Gindensperger O, Lehmann S, Legare JF, et al. What is the best strategy for brain protection in patients undergoing aortic arch surgery? A single center experience of 636 patients. *Ann Thorac Surg*. 2012; 93:1502-8.
2. Di Eusanio M, Schepens MA, Morshuis WJ, Dossche KM, Di Bartolomeo R, Pacini D, et al. Brain protection using antegrade selective cerebral perfusion: a multicenter study. *Ann Thorac Surg*. 2003;76:1181-8.
3. Gulbins H, Pritisanac A, Ennker J. Axillary versus femoral cannulation for aortic surgery: enough evidence for a general recommendation? *Ann Thorac Surg*. 2007;83:1219-24.
4. Tiwari KK, Murzi M, Bevilacqua S, Glauber M. Which cannulation (ascending aortic cannulation or peripheral arterial cannulation) is better for acute type A aortic dissection surgery? *Interact Cardiovasc Thorac Surg*. 2010;10:797-802.
5. Fusco DS, Shaw RK, Tranquilli M, Kopf GS, Elefteriades JA. Femoral cannulation is safe for type A dissection repair. *Ann Thorac Surg*. 2004;78:1285-9.
6. Ayyash B, Tranquilli M, Elefteriades JA. Femoral artery cannulation for thoracic aortic surgery: safe under transesophageal echocardiographic control. *J Thorac Cardiovasc Surg*. 2011;142:1478-81.
7. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. *JAMA*. 2000;283:2008-12.
8. Carletta J. Assessing agreement on classification tasks: the kappa statistic. *Comput Linguist*. 1996;22:249-54.
9. Wells G, Shea B, O'Connell J, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analysis. 3rd Symposium on Systematic Reviews: Beyond the Basics. July 3-5, 2000, Oxford.
10. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. *J Natl Cancer Inst*. 1959;22:719-48.
11. Friedrich JO, Adhikari NK, Beyene J. Inclusion of zero total event trials in meta-analyses maintains analytic consistency and incorporates all available data. *BMC Med Res Methodol*. 2007;7:5.
12. Higgins JPT, Green S, eds. Cochrane Handbook for Systematic Reviews of Interventions 4.2.6 [updated September 2006]. In: The Cochrane Library, Issue 4, 2006. Chichester, UK: John Wiley & Sons, Ltd.
13. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327:557-66.
14. Di Eusanio M, Pantaleo A, Petridis FD, Folesani G, Cefarelli M, Berretta P, et al. Impact of different cannulation strategies on in-hospital outcomes of aortic arch surgery: a propensity-score analysis. *Ann Thorac Surg*. 2013;96:1656-63.
15. Etz CD, Plestis KA, Kari FA, Silovitz D, Bodian CA, Spielvogel D, et al. Axillary cannulation significantly improves survival and neurologic outcome after atherosclerotic aneurysm repair of the aortic root and ascending aorta. *Ann Thorac Surg*. 2008;86:441-6.
16. Etz CD, von Aspern K, da Rocha E Silva J, Girrbach FF, Leontyev S, Luehr M, et al. Impact of perfusion strategy on outcome after repair for acute type a aortic dissection. *Ann Thorac Surg*. 2014;97:78-85.
17. Haldenwang PL, Wahlers T, Himmels A, Wippermann J, Zeriouh M, Kröner A, et al. Evaluation of risk factors for transient neurological dysfunction and adverse outcome after repair of acute type A aortic dissection in 122 consecutive patients. *Eur J Cardiothorac Surg*. 2012;42:e115-20.

18. Kamiya H, Kallenbach K, Halmer D, Ozsöz M, Ilg K, Lichtenberg A, et al. Comparison of ascending aorta versus femoral artery cannulation for acute aortic dissection type A. *Circulation*. 2009;120(11 Suppl):S282-6.
19. Lakew F, Pasek P, Zacher M, Diegeler A, Urbanski PP. Femoral versus aortic cannulation for surgery of chronic ascending aortic aneurysm. *Ann Thorac Surg*. 2005;80:84-8.
20. Lee HK, Kim GJ, Cho JY, Lee JT, Park I, Lee YO. Comparison of the outcomes between axillary and femoral artery cannulation for acute type A aortic dissection. *Korean J Thorac Cardiovasc Surg*. 2012;45:85-90.
21. Moizumi Y, Motoyoshi N, Sakuma K, Yoshida S. Axillary artery cannulation improves operative results for acute type A aortic dissection. *Ann Thorac Surg*. 2005;80:77-83.
22. Nouraei SM, Nouraei SA, Sadashiva AK, Pillay T. Subclavian cannulation improves outcome of surgery for type a aortic dissection. *Asian Cardiovasc Thorac Ann*. 2007;15:118-22.
23. Pasic M, Schubel J, Bauer M, Yankah C, Kuppe H, Weng YG, et al. Cannulation of the right axillary artery for surgery of acute type A aortic dissection. *Eur J Cardiothorac Surg*. 2003;24:231-5.
24. Polat A, Tuncer A, Tuncer EY, Mataracı I, Keleş C, Aulasaleh S, et al. Is axillary arterial cannulation better than femoral arterial cannulation? *Turk Gogus Kalp Dama*. 2012;20:186-93.
25. Reuthebuch O, Schurr U, Hellermann J, Prêtre R, Künzli A, Lachat M, et al. Advantages of subclavian artery perfusion for repair of acute type A dissection. *Eur J Cardiothorac Surg*. 2004;26:592-8.
26. Strauch JT, Böhme Y, Franke UF, Wittwer T, Madershahian N, Wahlers T. Selective cerebral perfusion via right axillary artery direct cannulation for aortic arch surgery. *Thorac Cardiovasc Surg*. 2005;53:334-40.
27. Svensson LG, Blackstone EH, Rajeswaran J, Sabik JF III, Lytle BW, Gonzalez-Stawinski G, et al. Does the arterial cannulation site for circulatory arrest influence stroke risk? *Ann Thorac Surg*. 2004;78:1274-84.
28. Berger RL, Saini VK, Dargan EL. Clinical applications of femoral vein-to-artery cannulation for mechanical cardiopulmonary support and bypass. *Ann Thorac Surg*. 1973;15:163-9.
29. Neri E, Massetti M, Capannini G, Carone E, Tucci E, Diciolla F. Axillary artery cannulation in type A aortic dissection operations. *J Thorac Cardiovasc Surg*. 1999;118:324-9.
30. Conzelmann LO, Weigang E, Mehlhorn U, Vahl CF. How to do it: direct true lumen cannulation technique of the ascending aorta in acute aortic dissection type A. *Interact Cardiovasc Thorac Surg*. 2012;14:869-70.
31. Preventza O, Bakaeen FG, Stephens EH, Trocciola SM, de la Cruz KI, Coselli JS. Innominate artery cannulation: an alternative to femoral or axillary cannulation for arterial inflow in proximal aortic surgery. *J Thorac Cardiovasc Surg*. 2013; 145:S191-6.
32. Trimarchi S, Eagle KA, Nienaber CA, Rampoldi V, Jonker FH, De Vincentiis C, et al. International Registry of Acute Aortic Dissection Investigators. Role of age in acute type A aortic dissection outcome: report from the International Registry of Acute Aortic Dissection (IRAD). *J Thorac Cardiovasc Surg*. 2010; 140:784-9.

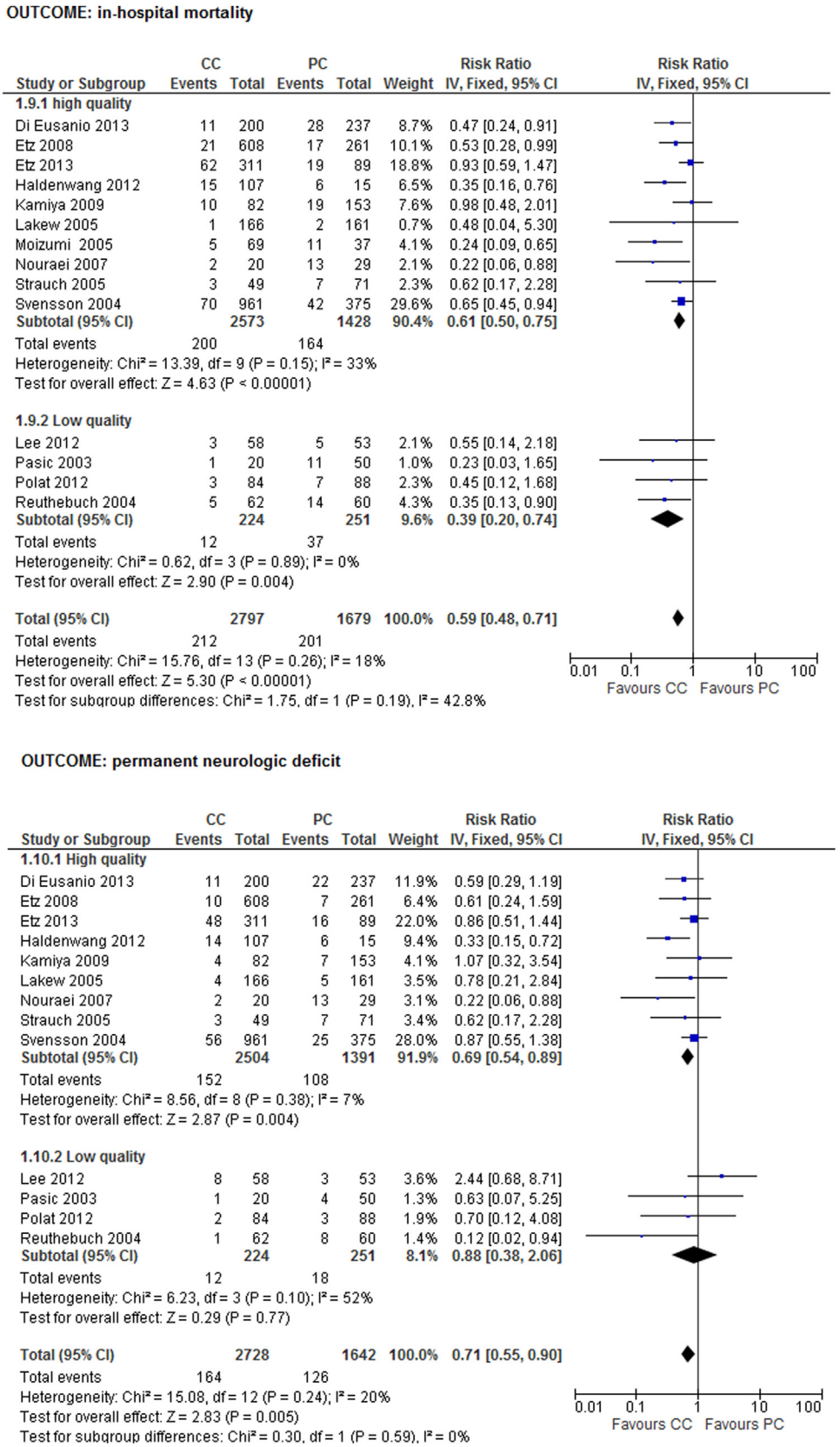

FIGURE E1. Forest plot according to study quality for in-hospital mortality (*top*) and PND (*bottom*). *CC*, Central cannulation; *PC*, peripheral cannulation; *CI*, confidence interval.

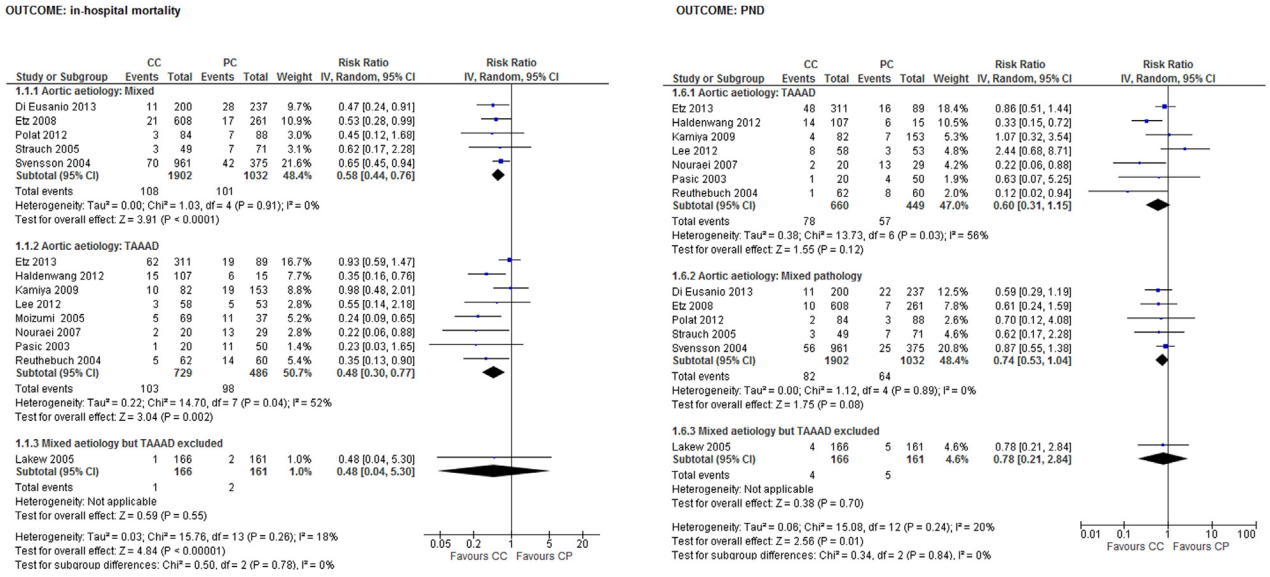

FIGURE E2. Forest plot according to aortic cause for in-hospital mortality (*left*) and PND (*right*). *CC*, Central cannulation; *PC*, peripheral cannulation; *CI*, confidence interval; *TAAAD*, type A aortic acute dissection; *CP*, peripheral cannulation.

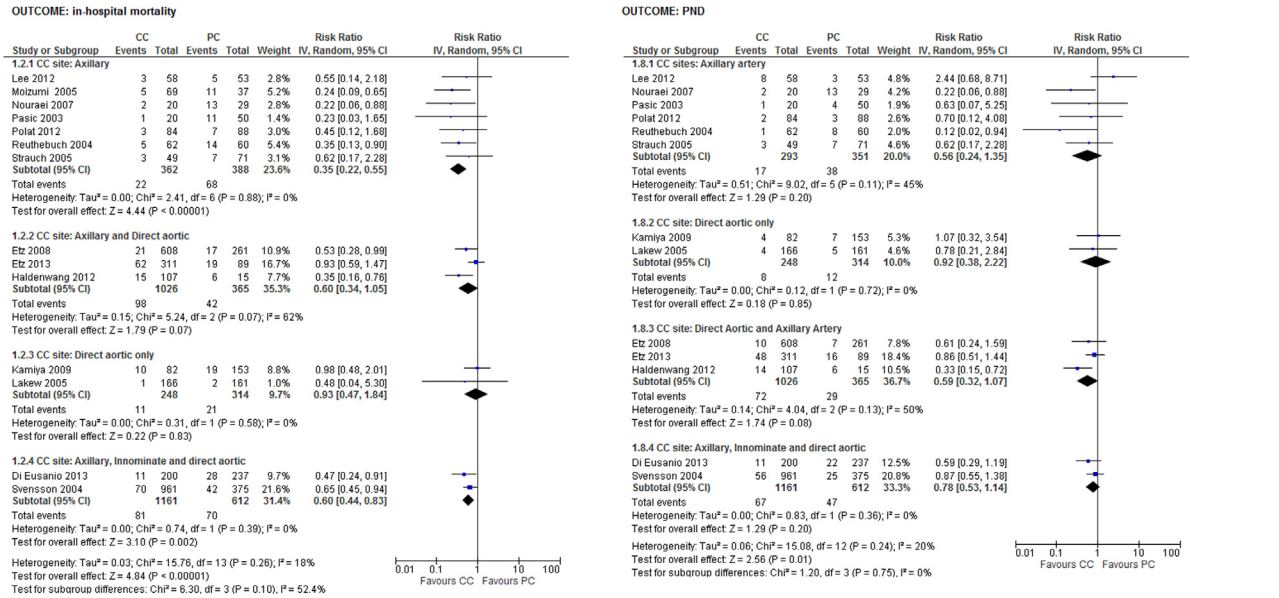

FIGURE E3. Forest plot according to central cannulation site for in-hospital mortality (*left*) and PND (*right*). *CC*, Central cannulation; *PC*, peripheral cannulation; *CI*, confidence interval.

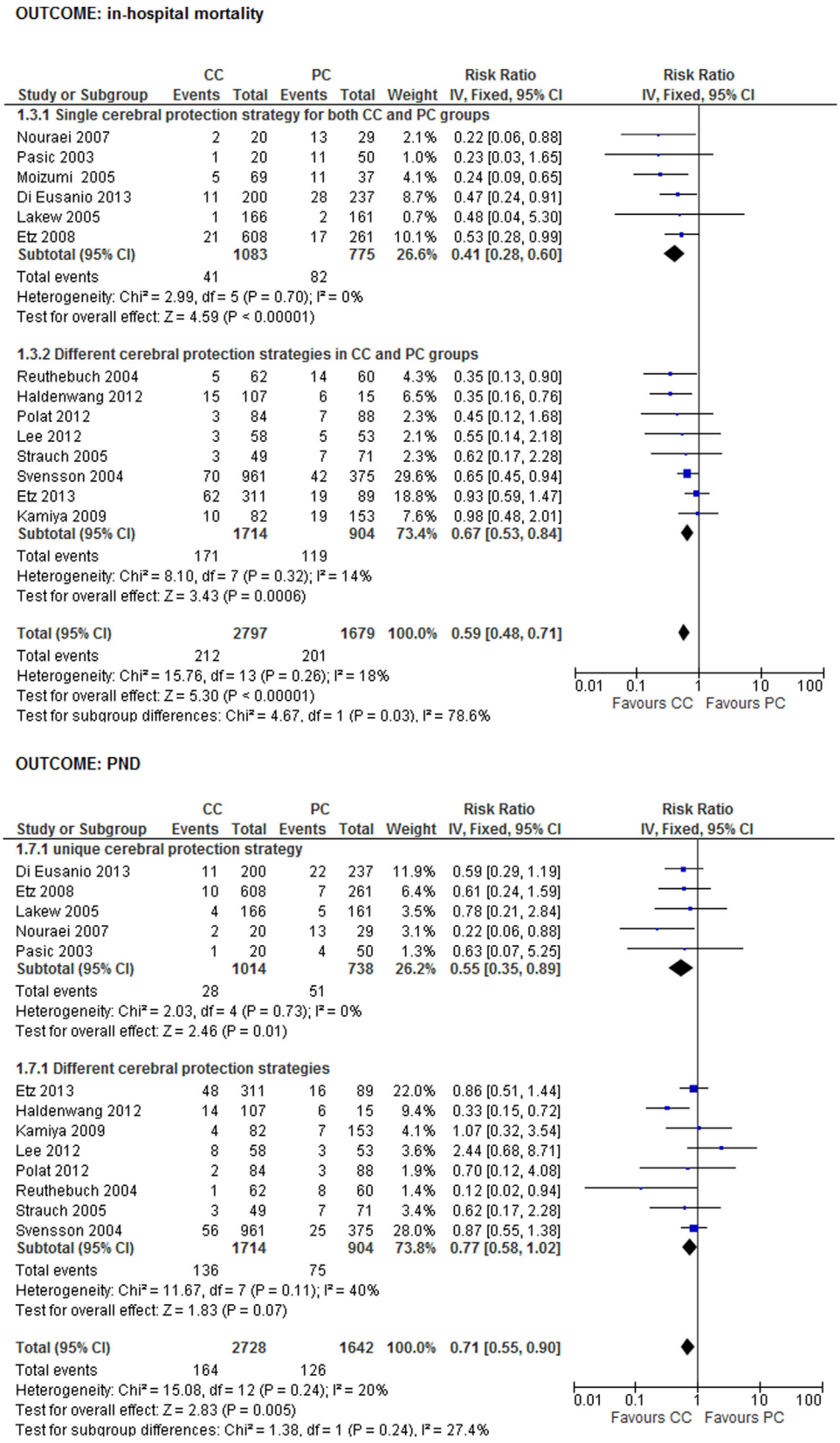

FIGURE E4. Forest plot according to cerebral protection strategy for in-hospital mortality (*left*) and PND (*right*). *CC*, Central cannulation; *PC*, peripheral cannulation; *CI*, confidence interval; *PND*, permanent neurologic deficit.

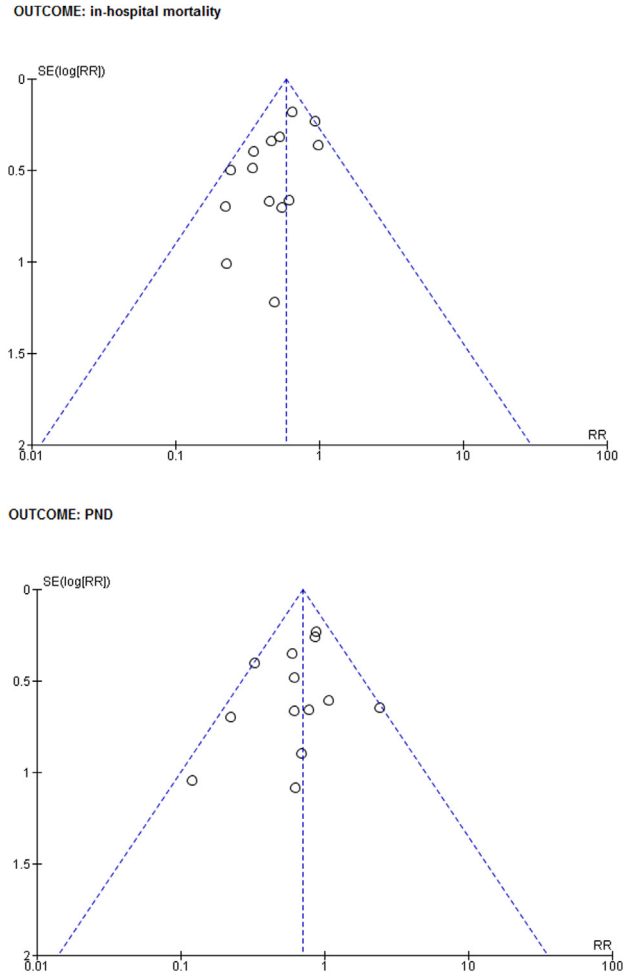

FIGURE E5. Funnel plot for publication bias assessment for in-hospital mortality (*top*) and PND (*bottom*). *PND*, Permanent neurologic deficit; *RR*, risk ratio; *SE*, standard error.