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Ascending aorta replacement *vs.* total aortic arch replacement in the treatment of acute type A dissection: a meta-analysis

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Abstract. – OBJECTIVE: Acute type A aortic dissection (ATAAD) is a severe, rapidly progressing disease which typically requires patients to undergo emergency surgical intervention. Despite advancements in surgical procedures, still, ATAAD remains a surgical emergency associated with high mortality. The aim of this systematic review and meta-analysis was to compare whether either ascending aorta replacement (AR) or total aortic arch replacement (TR) leads to improved short- and long-term clinical outcomes.

MATERIALS AND METHODS: A search of PubMed, Embase, Science Direct, Web of Science, SciELO, BIOSIS, and China National Knowledge Infrastructure (CNKI) databases were supplemented by searching through bibliographies of key articles. Thereafter, data on early and late prognostic factors were extracted. A systematic review and meta-analysis of 15 studies were performed to compare whether either AR or TR leads to a reduction in the risk of in-hospital and short-term mortality, postoperative complications, re-operation rate, and long-term mortality.

RESULTS: A total of 15 cohort studies (n = 2822 patients with ATAAD; AR with HA, partial arch = 1911, TR = 911) were deemed eligible and included in the meta-analysis. Compared with TR, AR led to a significantly lower risk of in-hospital mortality (RR = 0.77; 95% CI: 0.61-0.96), shorter cardiopulmonary bypass time (CPB, mean difference = -53.09; 95% CI: -56.68–-49.50), circulatory arrest time (CA, mean difference = -8.09; 95% CI: -9.04-7.15), and antegrade cerebral perfusion (ACP, mean difference = -28.62; 95% CI: -30.23–-27.00). Differences in the incidence rates of neurological dysfunctions and renal dialysis were not significant. The pooled rate of aortic re-operation was lower in TR group (AR 7.6% *vs.* TR 5.3%), albeit not significantly (risk ratio = 1.39; 95% CI: 0.94-2.07; *p* = 0.10).

CONCLUSIONS: These findings demonstrate that AR is associated with a lower early mortality rate and shorter operative times overall. Nevertheless, the incidence of postoperative complications in patients undergoing AR is comparable to that of patients undergoing TR. Further prospective follow-up data needs to be collected and analyzed to discern whether there are statistically significant differences in the risks of re-operation and long-term mortality between AR and TR procedures.

Key Words:
Acute type A aortic dissection, Ascending aorta replacement, Total aortic arch replacement, Systematic review, Meta-analysis.

Introduction

Acute type A Aortic Dissection (ATAAD), which involves the ascending aorta, the aortic arch, and the descending aorta, remains a

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challenging pathological entity for surgeons. ATAAD is characterized by a sudden onset of searing central chest pain that also involves the neck, back or abdomen[1]. The overall prevalence ranges from 5 to 10 cases per one million people worldwide with an estimated incidence of ~3-4 cases per 100,000 people each year[2]. Although diagnosis, surgical techniques, and postoperative care for ATAAD have improved significantly in recent years, perioperative outcomes showed high morbidity and an early/in-hospital and long-term mortality. The current in-hospital mortality has been estimated between 15% and 35%, with a five-year survival rate of 65%-75%[3].

ATAAD typically requires patients to undergo an emergency surgical intervention to prevent aortic rupture, minimize aortic valve insufficiency, and restore flow in the compromised branched vessels[4]. Conventional treatments such as Ascending aorta replacement (AR) with resection of the entry site, often in combination with hemiarch (HA) or an open distal anastomosis are considered the gold standard technique for treating ATAAD[5]. Although several medical studies[6-8] have supported the clinical value of AR as being the most optimal treatment for patients with ATAAD, the risk of progressive dilation with the possible need for reintervention over the long-term still remains. Due to this risk, a more extensive surgical intervention, a total aortic arch replacement (TR) procedure with the possible elephant trunk implantation in the proximal descending aorta has been adopted[9-10]. This to improve long-term prognosis by contrasting late aneurysm formation at the distal aorta that may require hazardous aortic reoperations or cause death by rupture and thus reduce the incidence of late aortic complication[11]. However, such a surgical procedure still represents a challenge to surgeons, particularly when treating patients incurring a high risk of complications. Indeed, the TR surgical procedure requires a high level of expertise and the perioperative outcomes of patients undergoing TR have been reported to be significantly lower than those regarding patients who underwent AR or HA[12].

Although clinical guidelines for treatment and patient management regarding ATAAD have been established, in many cardiac centers worldwide, long-term aortic events are still largely treated by extensive aortic replacement, rather than by AR with or without the HA, as its effectiveness remains controversial. Besides, there is no clinical consensus upon the most optimal treatment strategy for patients with ATAAD. Previous meta-analyses[13] assessed the efficacy and safety by comparing studies of hemiarch *vs.* total aortic arch replacement among patients with acute type A dissection. However, such studies considered all types of treatment techniques, including with and without frozen elephant trunk and, the entry sites, including the tubular part, the root, the arch or even the distal aorta.

In this systematic review and meta-analyses, we sought to compare the surgical outcomes of TR with and without elephant trunk or frozen elephant trunk and those of AR or/and with HA, partial arch replacement in patients with ATAAD with respect to primary outcomes such as the following:

- Early/in-hospital mortality;
- Intermediate mortality;
- Postoperative complications like neuro dysfunction, renal failure;
- Secondary outcomes, such as cardiopulmonary bypass (CPB), aortic cross-clamp (ACC), circulatory arrest (CA), antegrade cerebral perfusion (ACP), and coronary artery bypass grafting (CABG), respectively.

Materials and Methods

Sources of Data and Guidelines for the Systematic Review

A systematic review and meta-analysis were thoroughly conducted to compare early and late prognostic outcomes between patients undergoing either AR or TR. A systematic literature search of English databases, including MEDLINE (using the PubMed interface), Scopus Science direct, EMBASE, Web of Knowledge and The Cochrane Library and Chinese database, including China National Knowledge Infrastructure (CNKI), was performed for retrieving relevant observational studies published prior to December 31, 2017. The following search terms were adopted to aid the systematic literature survey: ‘total arch’, or ‘aortic replacement’, or ‘extensive replacement’, or ‘arch replacement’, or ‘arch repair’, or ‘ascending’ or ‘conservative management’ or ‘hemiarch’ or ‘proximal repair’ or limited ascending replacement’ or ‘open distal anastomosis’ or ‘stent’ or ‘frozen elephant trunk’ and 'acute type A dissection', 'acute type A aortic dissection' or 'DeBakey type 1 aortic dissection' as either keywords or MeSH terms. References of key studies were also assessed for eligibility. The systematic review was focused on retrieving full papers published in English. The PRISMA evidence-based guidelines (Table I) were strictly followed throughout this systematic review and meta-analysis[14].

Selection Criteria

Two independent investigators assessed all papers for eligibility for inclusion in the systematic review being performed; any discrepancies were resolved by a consensus process. Articles were included in the systematic review and meta-analysis if:

1. The authors reported data from an original, peer-reviewed study (review articles and conference/meeting abstracts, expert opinions, editorial comments, case reports, studies without full texts were excluded. Additional studies were scrutinized from the references lists of the studies);
2. The study was an observational study consisting of adult subjects (18 years of age or older), diagnosed with acute type A aortic dissection;
3. The study directly compared the prognostic results between patients undergoing either AR or TR, as well as a technique that combines open arch surgery and aortic endovascular treatment (i.e., frozen elephant trunk method) or hybrid technique; Hemiarch a substitute for the proximal arch repair is considered advanced compared to the level of innominate artery irrespective of the arch vessels; however, a substitution of supra-aortic vessels as an island or individual branched grafts are considered as a complete substitution of arch replacement. Replacement is defined as the proximal arch repair beyond the level of the innominate artery without involving the arch vessels, and total arch replacement is the replacement of supra-aortic vessels as an island or individual branched grafts.
4. The study achieved high rating (i.e., six stars or above) as per the Newcastle-Ottawa Quality Assessment Scale (NOS)[15].

Studies involving patients with chronic or subacute aortic dissection or acute type B aortic dissection were excluded due to the diverse clinical features exhibited. An initial screening of identified titles and abstracts was performed, followed by a thorough, systematic review of the full papers.

Data Extraction and Quality Assurance Assessment

The same two independent reviewers extracted the following information from the selected full-text articles:

1. Specific details of the studies, including first author, year of publication, country, duration of the study, number of patients involved in each of the AR or/and hemiarch and TR cohorts, mean follow-up time, etc.;
2. Characteristics of the patient population, including gender, age, comorbidity (hypertension, Marfan syndrome, stroke, and cardiogenic shock/tamponade);
3. Perioperative parameters (Table II), such as cardiopulmonary bypass (CPB), aortic cross-clamp (ACC), circulatory arrest (CA), antegrade cerebral perfusion (ACP), and coronary artery bypass grafting (CABG) times;
4. Prognostic outcome measures of clinical value (Table III), including in-hospital mortality, short term mortality, morbidity, the postoperative incidence of permanent/temporary neurological dysfunction, and renal failures, as well as long-term mortality.

The two independent reviewers in question also performed a quality assurance assessment of each study, carefully considering criteria deployed for recruiting patients, ascertainment of exposure, comparability of populations, and assessment of outcomes as per the Newcastle-Ottawa Scale[15] for meta-analysis of non-randomized studies. This scale deploys a qualitative star-based scoring system (0-9 stars can be attributed to any given study), while a score of ≥ 7 indicates the absence of substantial bias. Discrepancies in data extraction and quality assessment were resolved by consensus.

Study Endpoints

Primary outcomes of this study are listed as follows: in-hospital and short-term mortality, the postoperative occurrence of permanent/temporary neurological dysfunction, and renal failure. Short-term mortality is defined as any death occurring within 30 days of operation or before hospital discharge, while in-hospital mortality is defined as the death occurred at any time interval

Table I. Characteristics of the 15 Acute Type A AD (Disease) studies included in the meta-analysis.

Author, year	Country	Study period	Study design	Total sample size	Follow-up (months)	AR, *n*	TR, *n*	Dissection	Quality¥
Dai et al[16]	Fujian, China	2008-2010	Observational Cohort	93	64 ± 5.3 months	41	52	TAR: triple branched stent graft reconstruction of the aortic arch; AR with hemiarch and AAR replacement	7
Di Eusanio et al[17]	Bologna, Italy	1997-2012	Observational Cohort	240	4.8 ± 3.9 years (0.1-15.5 years)	187	53	TAR: Elephant trunk technique (Classic/frozen); AR: partial arch replacement + ascending aorta + hemiarch	8
Easo et al[18]	Oldenburg, Germany	2006-2010	Observational Cohort	658	–	518	140	TAR: Elephant trunk technique (Classic/frozen); AR: ascending aorta + hemiarch/open anastomosis	7
Kim et al[26]	Seoul, South Korea	1999-2009	Observational Cohort	188	47.5 months (0-130.4 months) (4.0 years)	144	44	TAR: AR: ascending aorta + hemiarch	9
Lio et al[27]	Rome, Italy	2006-2013	Observational Cohort	92	19.5 months (interquartile range [IQR], and 30.5 ± 29.8 months (IQR range, 0-100 mo.).	59	33	TAR: AR: ascending aorta + hemiarch	8
Ohtsubo et al[28]	Saga, Japan	1989-2001	Observational Cohort	47	42.0 ± 36 months (0-147 months) 3.5 years	23	24	TAR: AR: ascending aorta + hemiarch	7
Omura et al[19]	Kobe, Japan	1999-2014	Observational Cohort	197	60 ± 48 months	88	197	TAR: Elephant trunk technique (Classic/frozen); AR: partial arch replacement + ascending aorta + hemiarch	9
Rice et al[20]	Texas, USA	NS	Observational Cohort	489	49 months	440	49	TAR: AR: ascending aorta + hemiarch	9
Rylski et al[21]	Freiburg, Germany	2001-2013	Observational Cohort	51	4.9 years 45% > 5 years	37	14	TAR: AR: ascending aorta + hemiarch	9
Shi et al[29]	Shenyang, China	2006-2011	Observational	155	42.7 ± 17.8 months 8 (3.6 years)	71	84	TAR: Elephant trunk technique; AR: Aorta+stented elephant trunk+ ascending aorta + hemiarch	
Shiono et al[7]	Tokyo, Japan	1995-2005	Observational Cohort	134	FU Up to 10 years	105	29	TAR: AR: ascending aorta + hemiarch	8
Shen et al[31]	China	Jan to Nov 2010		38	12 ± 3 months (range, 8-18 months)	16	22	TAR: With Elephant Trunk Techniques VS AR: ascending aorta	8
Tan et al[22]	Nieuwegein, The Netherland	1986-2001	Observational Cohort	70	2.6 years (0-14.5 years)	53	17	TAR: AR: ascending aorta + hemiarch	8
Uchida et al[23]	Hiroshima, Japan	1997-2008	Observational Cohort	120	67 months (3-124 months) (5.6 years)	55	65	TAR: AR: ascending aorta + hemiarch	7
Zhang et al[24]	Shanghai, China	2002-2010	Observational Cohort	162	55.7 ± 33.1 months (4.6 years)	74	88	PR (AS+HA) VS ER (TA+descending)	7

*Number of patients *Study Sample size; ¥Study quality was evaluated using the Newcastle-Ottawa scale.

Table II. Characteristics of the patients 15 Acute Type A AD (Disease) studies included in the meta-analysis.

Author, year	Mean age (years)		Male gender n (%)		Hypertension n (%)		Marfan syndrome n (%)		Stroke n (%)		Cardiogenic shock-tamponade n (%)	
	TR	AR	TR	AR	TR	AR	TR	AR	TR	AR	TR	AR
Dai et al[16]	49.8 ± 9.6	49.1 ± 10.4	29 (65.0)	25 (61.3)	49 (94.2)	40 (97.6)	3 (5.8)	2 (4.9)				
Di Eusanio et al[17]	59.2 ± 12.3	64.4 ± 11.2	41 (77.4)	125 (66.8)	40 (75.5)	138 (80.2)	3 (5.7)	5 (2.7)	3 (5.7)	7 (3.7)	2 (3.8)	25 (13.4)
Easo et al[18]	–	–	–	–	–	–	–	–	–	–	–	–
Kim et al[26]	55.0 ± 12.1	57.6 ± 11.5	26 (59.1)	69 (47.9)	24 (54.5)	92 (63.9)	1 (2.3)	7 (4.9)	–	–	4 (9.1)	13 (9.0)
Lio et al[27]	61 ± 12	66 ± 10	< 28 (85)	43 (73)	30 (91)	51 (86)	–	–	–	–	–	–
Ohtsubo et al[28]	68	68	13 (54.2)	7 (30.4)	–	–	–	–	–	–	–	–
Omura et al[19]	61 ± 13	70 ± 11	62 (70.5)	50 (45.9)	–	–	–	–	–	–	–	–
Rice et al[20]	62.4 ± 13.4	57.9 ± 14.8	38 (77.5)	313 (71.1)	44 (89.8)	370 (84.1)	1 (2.0)	9 (2.1)	6 (12.2))	30 (6.8)	9 (18.4)	69 (15.7)
Rylski et al[21]	55	66	8 (57)	21 (57)	13 (93)	31 (84)	0	2 (5)	1 (7)	2 (5)	1 (7)	3 (8)
Shi et al[29]	53.9 ± 12.2	55.9 ± 10.1	57 (67.9)	53 (74.6)	67 (79.8)	55 (77.5)	22 (26.2)	10 (14.1)	1 (1.2)	0	12 (14.3)	13 (18.3)
Shiono et al[7]	61.9 ± 12.6	82.0 ± 2.4	52 (47.3)	10 (41.7)	96 (87.2)	23 (95.8)	8 (7.3)	0	10 (9.1)	2 (8.3)	46 (41.8)	11 (45.8)
Shen et al[31]	45.4 ± 10.4	42.4 ± 11.5	16 (72.7)	12 (75.0)	13 (59.1)	8(50.0)	3 (13.6)	2 (12.5)	–	–	2 (9.1)	1 (6.25)
Tan et al[22]	–	–	–	–	–	–	–	–	–	–	–	–
Uchida et al[23]	64.4	72.3	28 (43.1)	25 (45.4)	–	–	–	–	6 (9)	12 (22)	–	–
Zhang et al[24]	45.5 ± 13.5	49.1 ± 12.6	74 (84.1)	55 (74.3)	64 (72.7)	47 (63.5)	21 (23.9)	13 (17.6)	1 (1.1)	2 (2.7)	17 (23.0)	25 (28.4)

*Number of patients.

Table III. Early postoperative complications.

Author, year	Pulmonary complications (%)		Temporary neurological dysfunction		Paraplegia		Postoperative hoarseness		Acute renal failure (%)	
	TR	AR	TR	AR	TR	AR	TR	AR	TR	AR
Dai et al[16]	4 (7.69)	4 (9.76)	3 (5.77)	2 (4.88)	1 (1.92)	1 (2.44)	0 (0)	1 (2.44)	3 (5.77)	2 (4.88)
Di Eusanio et al[17]	–	–	–	–	–	–	–	–	13 (24.5)	35 (18.7)
Easo et al[18]	–	–	–	–	–	–	–	–	–	–
Kim et al[26]	–	–	1 (2.3)	4 (2.8)	1 (2.3)	1 (0.7)	–	–	–	–
Lio et al[27]	4 (12.0)	20 (34.0)	1 (3.0)	6 (10.2)	–	–	–	–	5 (15.0)	15 (25.0)
Ohtsubo et al[28]	–	–	1 (4.2)	1 (2.4)	–	–	–	–	–	–
Omura et al[19]	–	–	3 (3.4)	4 (3.7)	–	–	–	–	–	–
Rice et al20	–	–	–	–	–	–	–	–	–	–
Rylski et al[21]	–	–	4 (28.6)	11 (10.8)	–	–	–	–	–	–
Shi et al[29]	–	–	–	–	0	0	–	–	–	–
Shiono et al[7]	–	–	–	–	–	–	–	–	–	–
Uchida et al[23]	–	–	–	–	–	–	–	–	0	1 (1.8)
Zhang et al[24]	–	–	11 (12.5)	8 (10.8)	–	–	–	–	1 (1.4)	2 (2.3)

further to a surgical procedure if the patient had not been discharged from the hospital. Secondary outcomes will be the following operative characteristics: (CPB), (ACC), (CA), (ACP), and (CABG).

Statistical Analysis

The Risk Ratios (RRs) were estimated for dichotomous variables based on the relative frequencies from the selected studies. Forest plots were generated to qualitatively assess the RRs and quantify the corresponding 95% confidential interval (95% CI) across studies. For continuous data, the mean differences were employed as an effective measure. Heterogeneity was evaluated *via* the Cochrane Q statistic ($p<0.10$ was considered indicative of statistically significant heterogeneity) and the I^2 statistic (values of <50% and ≥ 50% were considered to represent low and high heterogeneity, respectively). The RRs were pooled using the DerSimonian and Laird random-effects model. The weights were equal to the inverse variance of each study's effect estimation. The possibilities of publication bias were assessed *via* the Begg & Mazumdar rank correlation, Egger's regression test, and a qualitative assessment of a funnel plot. All statistical analyses were performed using "Review Manager (REVMAN) 5.3 Copenhagen" (The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). For all analyses, a two-sided p-value <0.05 was considered statistically significant.

Results

Literature Search

2,104 unique citations were identified through the conducted literature search. After screening articles based on titles and abstracts, 290 of them were shortlisted. After careful assessment, 275 articles were excluded from the review and meta-analysis. Finally, 15 articles met the eligibility criteria and were included in this study[6,7,16-30]. An overview of the article selection process is illustrated in Figure 1. The initial percentage of agreement upon the eligibility of the studies considered among reviewers was 96%, demonstrating a considerably high agreement between the two reviewers.

Study Characteristics

The basic characteristics of the 15 included studies from eight (8) countries (China, Germany, Italy, Japan, the Netherlands, South Korea, UK, and the USA) are summarized in Table IV. All studies were retrospective observational cohort studies. The pooled sample consisted of 1911 patients who underwent AR with hemiarch, partial arch, and stented elephant technique, while 911 patients had TR. The mean follow-up time ranged from 12 months to 10 years. Amongst the fifteen included studies, six obtained a NOS score equal to 7; five obtained 8 stars and the remaining six obtained 9 stars. A total of fifteen-study analysis was performed with AR, HA, partial arch, and stented elephant trunk (Classic/frozen) technique were compared with total arch replacement with and without elephant trunk techniques. Four studies with AR compared to TR. Four studies with HA compared to TR. Two studies with TR compared to AR compared to HA and one each of HA and PA compared to TR with the elephant technique; AR and HA compared to TR and HA with elephant technique compared to TR with elephant technique, respectively. Aortic dilatation at distal was included besides dissection.

Patients Characteristics

Baseline characteristics of patients included in the selected studies are summarized in Table V. The proportion of male patients was higher in the AR with HA cohort as compared to the TR cohort. The distributions of age and incidences of hypertension, Marfan syndrome, and stroke were similar between the two cohorts of patients considered.

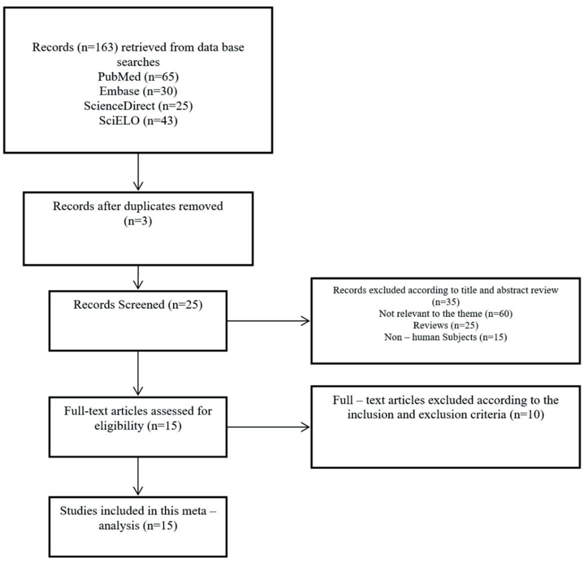


Figure 1. A flowchart illustrating the selection process of studies included in this review and meta-analysis.

Table IV. Perioperative parameters.

Author, year	Perioperative parameters									
	Cardiopulmonary bypass time (min)		Cardiac arrest (min)		Aortic cross-clamp time (min)		Antegrade cerebral perfusion (ACP) (min)		Coronary artery-bypass grafting time	
	TR	AR	TR	AR	TR	AR	TR	AR	TR	AR
Dai et al[16]	153 ± 23.1	150 ± 19.4	25.9 ± 6.6	23.8 ± 7.2	88.3 ± 11.2	88.3 ± 11.2	–	–	6	6
Di Eusanio et al[17]	249.9 ± 75.4	202.8 ± 62	–	–	–	–	86.9 ± 33.3	45.1 ± 13.7	4	8
Easo et al[18]	–	–	44.8 ± 29.7	24.3 ± 14.4	–	–			15	49
Kim et al[26]	314.6 ± 100.5	233.4 ± 90.7	50.2 ± 44.3	24.6 ± 13.9	–	–	61.4 ± 0	29.2 ± 0	3	14
Lio et al[27]	249 ± 87	175 ± 63	66 ± 39	32 ± 23	–	–	–	–	0	5
Ohtsubo et al[28]	292 ± 20.0	170 ± 7.8	48 ± 4.2	28 ± 1.2	–	–	106 ± 6.0	0	–	–
Omura et al[19]	244 ± 88	187 ± 71	–	–	–	–	124.0 ± 42.5	48.1 ± 26.6	4	3
Rice et al[20]	172.6 ± 50.1	160.3 ± 51.4	43.1 ± 14.3	27.2 ± 9.3	106 ± 29.1	100.6 ± 33.8	–	–	2	38
Rylski et al[21]	274 ± 0	189 ± 0	–	–	134 ± 0	97 ± 0	71 ± 0	25 ± 0	–	–
Shi et al[29]	164.7 ± 19.6	103.6 ± 20.9	29.3 ± 4.3	30.6 ± 4.9	108.9 ± 18.4	75.7 ± 15.7	55.2 ± 6.2	30.6 ± 4.9	6	7
Shiono et al[7]	–	–	–	–	–	–	–	–	1	8
Uchida et al23	163 ± 43	108 ± 16	–	–	–	–	70 ± 18	21 ± 12	–	–
Zhang et al[24]	182.4 ± 34.3	179.7 ± 39.5	35.4 ± 11.6	28.1 ± 10.1	113.4 ± 25.8	102.4 ± 30.3	–	–	8	8

Table V. Mortality and morbidity.

Author, year	Operative outcome and follow-up							
	30-day mortality		In hospital death		Late death (≥ 1 year)		Subsequent operation	
	TR	AR	TR	AR	TR	AR	TR	AR
Dai et al[16]	2 (3.85)	1 (2.44)	2 (3.85)	2 (4.88)	–	–	–	–
Di Eusanio et al[17]	–	–	12 (22.6)	45 (24.1)	–	–	–	–
Easo et al[18]	–	–	36 (25.7)	97 (18.7)	–	–	–	–
Kim et al[26]	6 (13.6)	14 (9.7)	–	–	10 (22.7)	14 (9.7)	–	–
Lio et al[27]	–	–	11 (33.3)	9 (15.2)	–	–	–	–
Ohtsubo et al[28]	6 (25)	2 (4.8)	8 (33.3)	3 (7.3)	–	–	–	–
Omura et al[19]	6 (6.8)	12 (11.0)	9 (10.2)	16 (14.7)	15 (13.8)	9 (10.2)	–	–
Rice et al[20]	10 (20.4)	57 (12.9)	–	–	–	–	–	–
Rylski et al[21]	–	–	4 (28.6)	10 (9.8)	–	–	–	–
Shi et al[29]	5 (5.9)	3 (4.2)	–	–	–	–	–	–
Shiono et al[7]	6 (5.5)	3 (12.5)	2 (6.9)	7 (6.7)	10 (9.1)	9 (37.5)	–	–
Tan et al[22]	–	–	4 (23.5)	45 (21.7)	–	–	–	–
Uchida et al[23]	–	–	3 (4.6)	2 (3.6)	3 (4.6)	9 (16.4)	–	–
Zhang et al[24]	5 (5.7)	4 (5.4)	–	–	–	–	–	–

The aortic cross-clamp time of -12.60 (95% CI, -15.64- -9.56) min (Appendix, Figure 2) was found with higher efficiency compared with cardiopulmonary bypass time of -53.09 (95% CI, -56.68- -49.50) min (Appendix, Figure 3) later with selective antegrade cerebral perfusion time of -28.62 (95% CI, -30.23-27.00) min (Appendix, Figure 4), hypothermic circulatory arrest time of -8.09 (95% CI, -9.04- -7.15) min (Appendix, Figure 5), higher in AR patients with -12.46 (95% CI: -29.89-4.96) min (Appendix, Figure 6), long term mortality of 0.86% (95% CI, 0.74-1.00%; Appendix B, Figure 7).

Surgical Technique

Indirect incision by eliminating the major section of the minute curvature of the arch along with open distal anastomosis is necessary for the efficient hemiarch replacement. Re-implantation of supra-aortic vessels is established in patients who are advised with total arch replacement procedure through *en bloc*, which is like an island or vessels that are connecting independently through a cleft or any instrument having three forks to insert. A few diagnostic centers prefer the practice of intraluminal stent graft merged along with true lumen of the distal arch through the application of open aortic technique. The tissue was found to be cross-clamped, and antegrade perfusion was extended from a side branch. The purpose of Hemiarch replacement is achieved when an innermost membrane is cut, confined to the rising aorta or the lesser curvature involved in the transverse arch. However, total arch replacement is implemented in patients showing an internal membrane cut which is restricted laterally with a larger curvature that is in proximity to the supra-aortic vessels. The arrangement of stent graft was quite novel with the implication of the total arch replacement with frozen elephant trunk. In short, it was decided that the stent graft was carried out in a normal forward angle into the true lumen of the descending thoracic aorta. As soon as the stent graft is successfully implanted, the distal aorta which is effectively integrating the stent graft is tagged to the distal trunk of the cleft consisting of the prosthetic graft by the open aortic technique. The insertion of a ball-shaped object into the true lumen of the sliding down aorta under transoesophageal ultrasound guidance has been described[23,24].

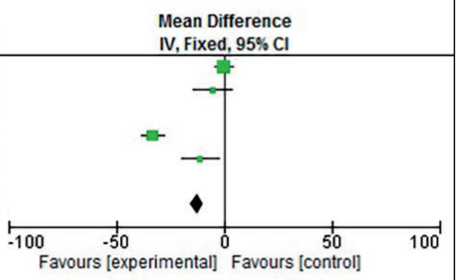
Primary Outcome

Mortality

Ten (n=10) studies[7,16-19,21-23,27,28] reported in-hospital mortality. As illustrated in Figure 8, there was no significant evidence of heterogeneity amongst trials as assessed by the Cochran's Q (p=0.18), and the I^2 value (29%). Using a fixed-effects model, it was found that the AR, including HA and partial arch surgical procedure may lead to a significantly lower risk of in-hospital mor-

Study or Subgroup	ARR Mean	ARR SD	ARR Total	TAAR Mean	TAAR SD	TAAR Total	Weight	Mean Difference IV, Fixed, 95% CI
Dai et al 2015	88.3	11.2	41	88.3	11.2	52	43.9%	0.00 [-4.58, 4.58]
Rice et al 2015	100.6	33.8	440	106	29.1	49	12.1%	-5.40 [-14.14, 3.34]
Rylski et al 2014	97	0	102	134	0	14		Not estimable
Shi et al 2014	75.7	15.7	71	108.9	18.4	84	32.0%	-33.20 [-38.57, -27.83]
Zhang et al 2013	102.4	30.3	74	113.4	25.8	88	12.0%	-11.00 [-19.76, -2.24]
Total (95% CI)			**728**			**287**	**100.0%**	**-12.60 [-15.64, -9.56]**

Heterogeneity: Chi² = 88.32, df = 3 (P < 0.00001); I² = 97%
Test for overall effect: Z = 8.13 (P < 0.00001)



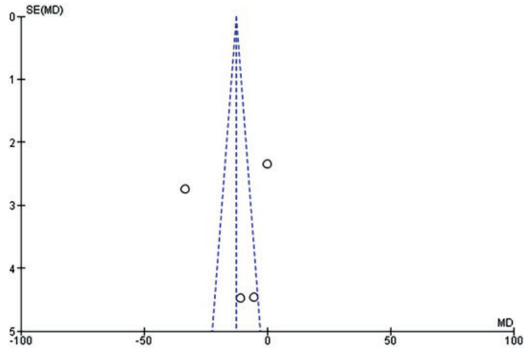
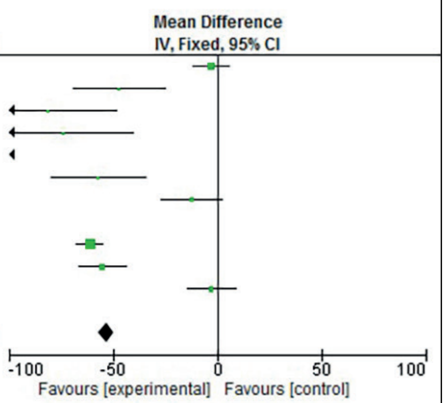


Figure 2. Comparison of in-hospital mortality between patients undergoing either ascending aortic replacement (AR) or total arch replacement (TR). RR=0.70; 95% CI: 0.59-0.84; *p*=0.0001. Seventeen (N=17) studies were considered. AR: ascending aortic replacement; TR: total arch replacement; CI, confidence interval.

Study or Subgroup	ARR Mean	ARR SD	ARR Total	TAAR Mean	TAAR SD	TAAR Total	Weight	Mean Difference IV, Fixed, 95% CI
Dai et al 2015	150	19.4	41	153	23.1	52	17.2%	-3.00 [-11.64, 5.64]
Di Eusanio 2015	202.8	62	187	249.9	75.4	53	2.6%	-47.10 [-69.26, -24.94]
Kim et al 2011	233.4	90.7	144	314.6	100.5	44	1.2%	-81.20 [-114.39, -48.01]
Lio et al 2016	175	63	59	249	87	33	1.1%	-74.00 [-107.76, -40.24]
Ohtsubo 2002	170	7.8	41	292	20	24	18.5%	-122.00 [-130.35, -113.65]
Omura et al 2015	187	71	109	244	88	88	2.5%	-57.00 [-79.71, -34.29]
Rice et al 2015	160.3	51.4	440	172.6	50.1	49	5.9%	-12.30 [-27.13, 2.53]
Rylski et al 2014	189	0	102	274	0	14		Not estimable
Shi et al 2014	103.6	20.9	71	164.7	19.6	84	31.2%	-61.10 [-67.52, -54.68]
Uchida et al 2009	108	16	55	163	43	65	10.1%	-55.00 [-66.28, -43.72]
Zhang et al 2013	179.7	39.5	74	182.4	34.3	88	9.7%	-2.70 [-14.20, 8.80]
Total (95% CI)			**1323**			**594**	**100.0%**	**-53.09 [-56.68, -49.50]**

Heterogeneity: Chi² = 504.17, df = 9 (P < 0.00001); I² = 98%
Test for overall effect: Z = 29.01 (P < 0.00001)



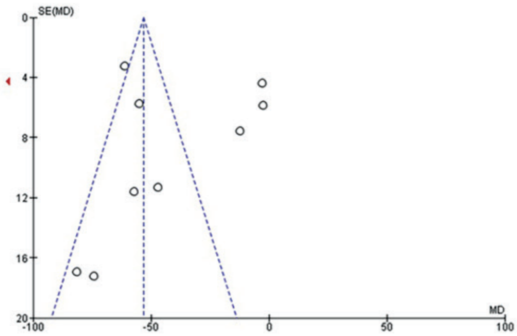


Figure 3. Comparison of cardiopulmonary by-pass time (CPB) between patients undergoing either ascending aortic replacement (AR) or total arch replacement (TR). Mean=-53.58 (95% CI: -81.02 - -26.14), *p*=0.0001. Seventeen (N=17) studies were considered. AR: ascending aortic replacement; TR: total arch replacement; CI, confidence interval.

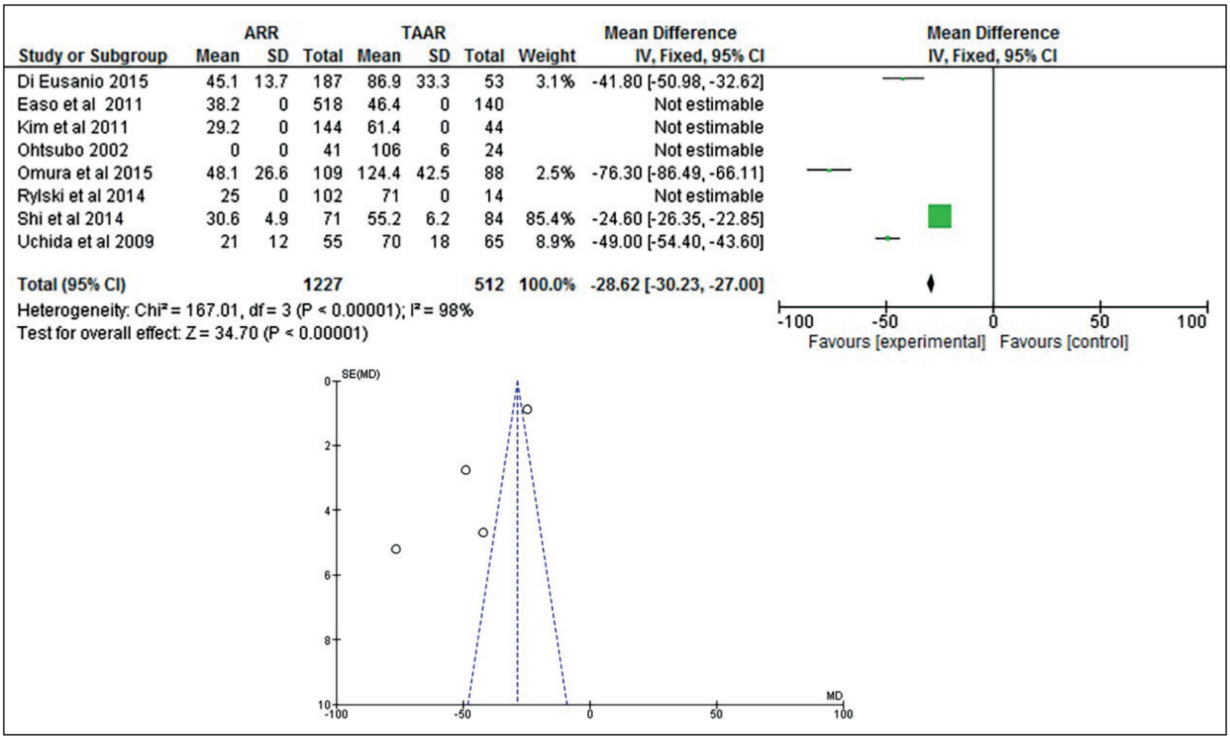


Figure 4. Comparison of circulatory arrest time (CA) between patients undergoing either ascending aortic replacement (AR) or total arch replacement (TR). Mean=-12.84 (95% CI: -20.61 - -5.06), p=0.001. AR: ascending aortic replacement; TR: total arch replacement; CI, confidence interval.

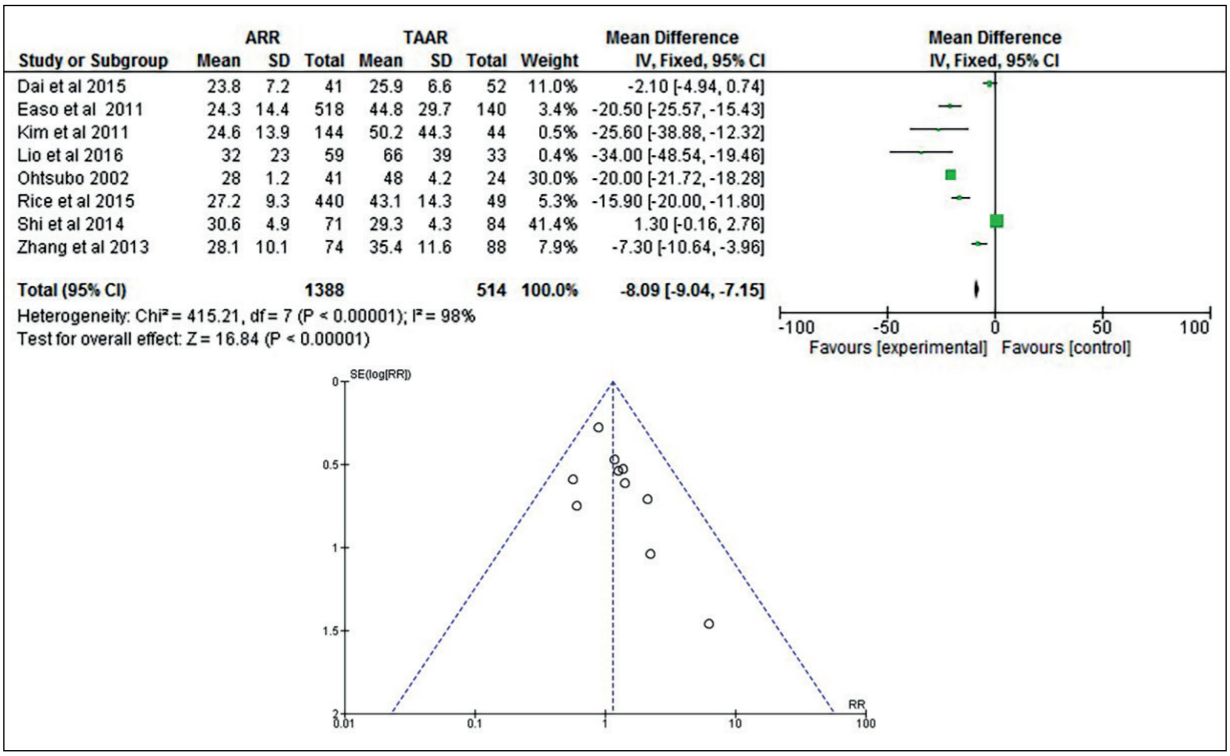


Figure 5. Comparison of antegrade cerebral perfusion (ACP) between patients undergoing either ascending aortic replacement (AR) or total arch replacement (TR). Mean=-39.12 (95% CI: -57.74 - -20.49), p<0.0001. AR: ascending aortic replacement; TR: total arch replacement; CI, confidence interval.

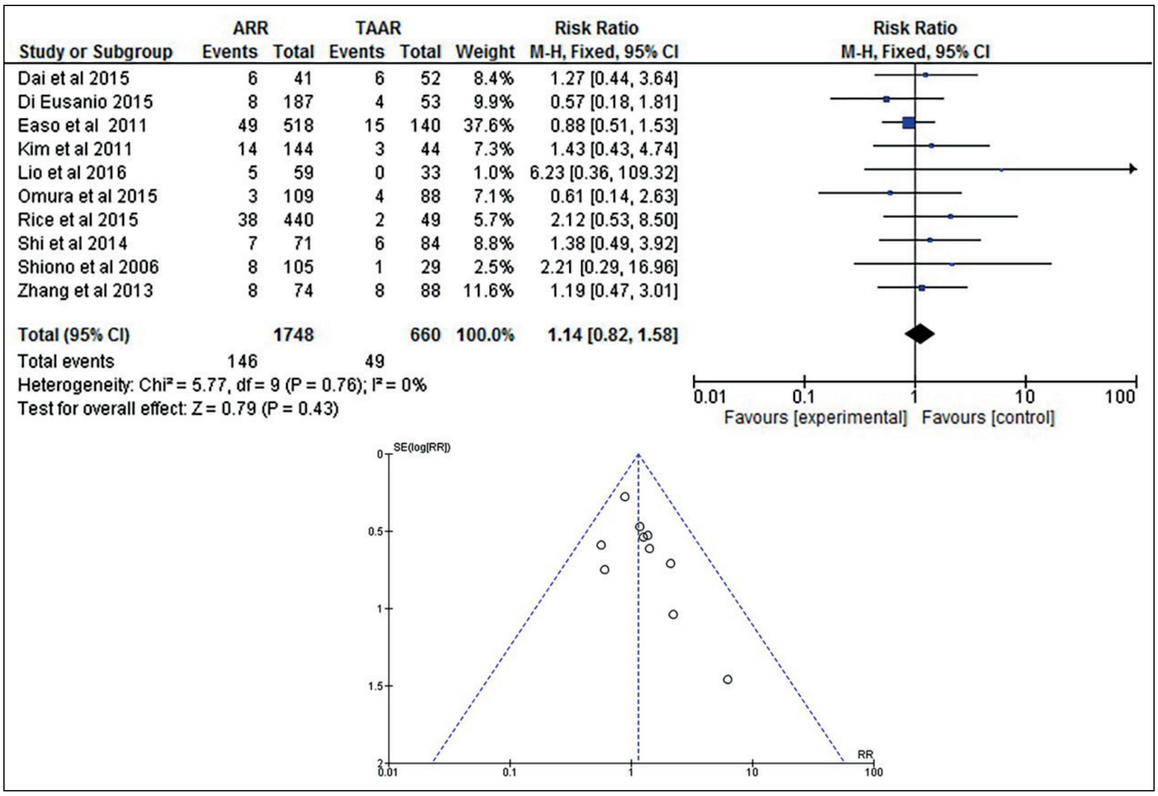


Figure 6. Comparison of aortic cross-clamp (ACC) time between patients undergoing either ascending aortic replacement (AR) or total arch replacement (TR). Mean=-12.46 (95% CI: -29.89-4.96), p=0.16. AR: ascending aortic replacement; TR: total arch replacement; CI, confidence interval.

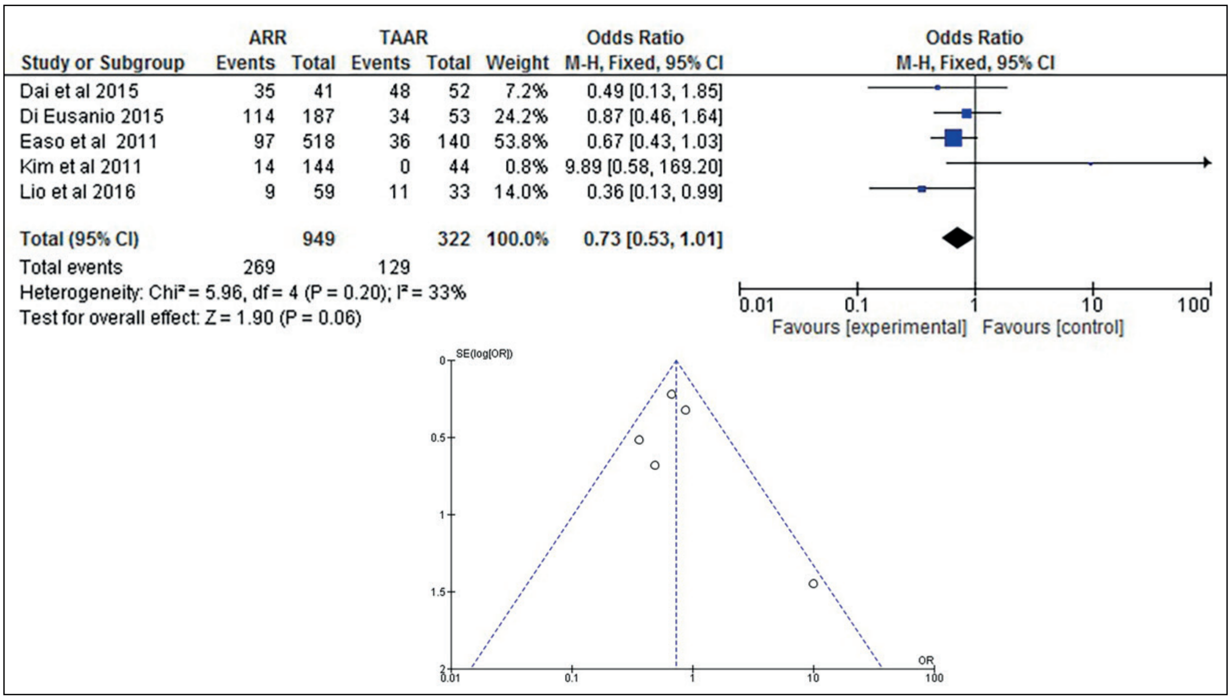


Figure 7. Comparison of coronary artery by-pass grafting (CABG) between patients undergoing either ascending aortic replacement (AR) or total arch replacement (TR). Risk ratio (RR)=1.06 (95% CI: 0.76-1.48), p=0.73. AR: ascending aortic replacement; TR: total arch replacement; CI, confidence interval.

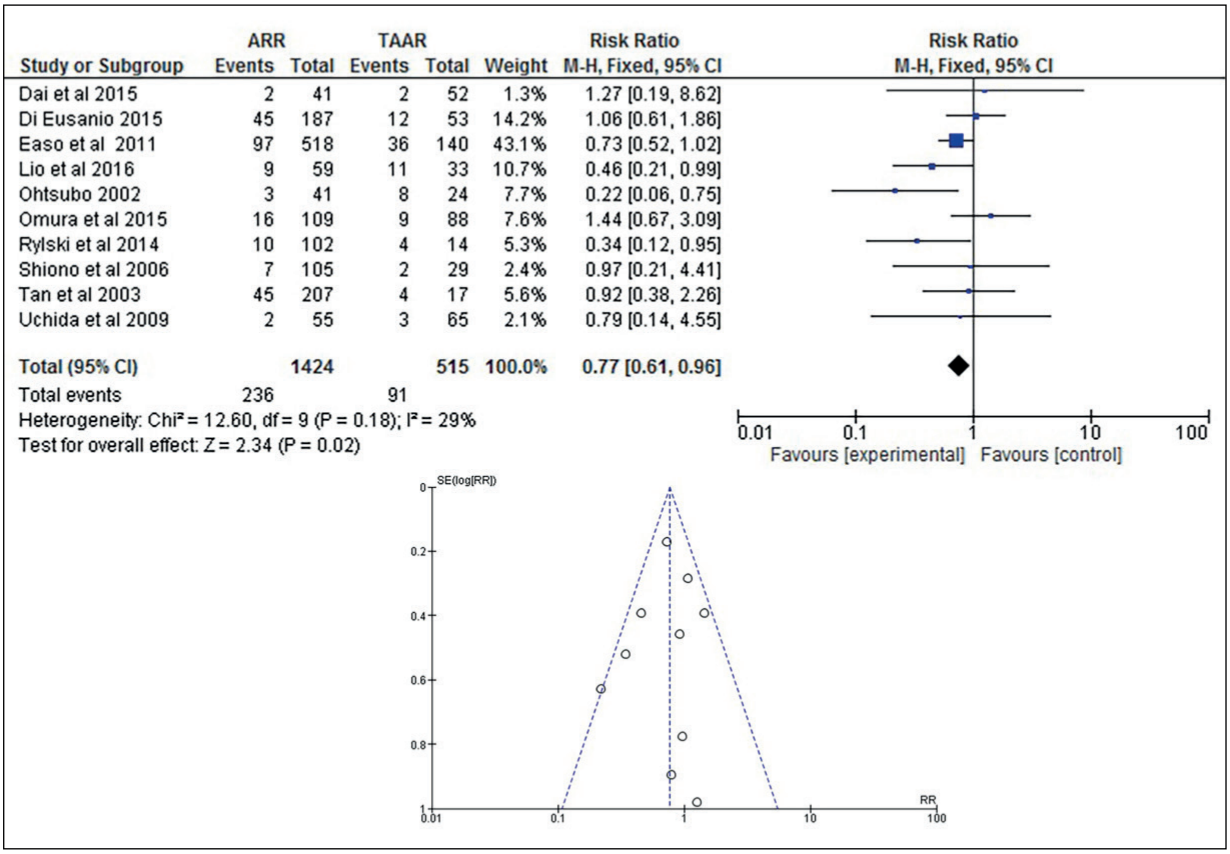


Figure 8. Comparison of permanent neurological dysfunction between patients undergoing either ascending aortic replacement (AR) or total arch replacement (TR). Risk ratio=1.15 (95% CI: 0.78, 1.69), p=0.50. AR: ascending aortic replacement; TR: total arch replacement; CI, confidence interval. Funnel plot of in-hospital mortality. SE: standard error; RR: risk ratio.

tality as compared to the TR (RR=0.77; 95% CI: 0.61-0.96; p=0.02) (Figure 8). The mortality rate ranged from 20.3-46.9 for hemiarch, 11.7-59.1 for AAD, and 2.7-27.2 for the total arch, 31.7-68.3 for the total arch with elephant trunk.

In subgroup analysis, using fixed-effect model, it was found that in three studies[21,22,28] (n=3) showed no significant differences in terms of in-hospital mortality between hemiarch (HA) and Total arch replacement TR; [TR (RR=0.55; 95% CI: 0.29-1.05, I^2=0%, p=0.07)] (**Supplementary Figure S1**), while AR surgical procedure alone significantly lowered the risk of in-hospital mortality as compared to the TR (RR=0.47; 95% CI: 0.26-0.83, I^2=50%, p=0.009) (**Supplementary Figure S8**)[21,22,28]. When Shen et al[31] was included[21,22,28,31] statistically significance remained as such (RR=0.48; 95% CI: 0.28-0.84, I^2=27%, p=0.010; **Supplementary Figure S13**). No statistically significant difference in in-hospital mortality was observed when HA, partial arch with AR were applied as surgical procedure[17,19] (n=2; RR=1.19; 95% CI: 0.76-1.87, I^2=0%, p=0.45; **Supplementary Figure S14**). Similarly, no significance difference was also observed when AR + HA was compared with the TR[18,23] (n=2) using elephant trunk technique (RR=0.73; 95% CI: 0.53-1.02, I^2=0%, p=0.06; **Supplementary Figure S24**) or without elephant technique[7,16,27] (RR=0.62; 95% CI: 0.33-1.17, I^2=0%, p=0.14; **Supplementary Figure S35**).

As illustrated in Table VI, solely the German Registry for Acute Aortic Dissection Type A (GERAADA) study did not report the 5-year-survival rate, whilst the other studies reported it. Such data were summarized in Table VI. Data on short-term mortality was extracted for a total of 1271 patient from five studies (n=5)[16-18,26,27] and it was found slightly higher in TAAR patients as opposed to HA although mostly not significantly (risk ratio=0.35; 95% CI: 0.08- 1.55; p=0.17; Figure S7) (Figures S23, S34, S45) and in a few cases significantly (risk ratio=0.2; 95% CI: 0.04-0.89; p=0.03, Figure S12). The 5-year survival

Table VI. Prisma.

Section/ topic	#	Checklist item	Reported on page #
Title			
Title	1	Ascending aorta replacement versus total aortic arch replacement in the treatment of acute Type A dissection: a meta-analysis	1
Abstract			
Structured summary	2	Provide a structured summary including, as applicable: objectives; methods, results; conclusion and keywords	2
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	The aim of this systematic review and meta-analysis was to compare early and late prognostic factors in patients with ATAAD undergoing ascending aorta replacement (AR) versus total aortic arch replacement (TR) surgical procedures	2
Methods			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., Prospective or retrospective cohort study) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	9
Summary measures	13	State the principal summary measures (e.g., Risk ratio).	9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., HR, I2 and Chi2) for each meta-analysis.	9
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity and subgroup analyses), if done, indicating which were pre-specified.	44
Results			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	6
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, design, participants, outcome) and provide the citations.	27
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	33
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	34
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	35
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	15
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity and subgroup analyses [see Item 16]).	44
Discussion			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	19
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	20
Funding			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	–

rate in the patient cohort undergoing AR was higher than for the patient cohort undergoing TR; however these results were found to be statistically insignificant (OR=0.73, 95% CI: 0.53-1.01; *p*=0.06) (Figures S19 and S29). Evidence of low heterogeneity was observed amongst the included studies (I^2=33%; Figure 7).

In subgroup analysis, using fixed-effect model, it was found that in two studies[26,27] (n=2) HA surgical procedure was not associated with 5 year survival rate as compared to the TR (RR=0.90; 95% CI: 0.45-1.79, I^2=82%, *p*=0.76). Similar results were observed even AR was combined with HA[16,26,27] as compared to the TR without elephant trunk technique (RR=0.92; 95% CI: 0.74-1.13, I^2=65%, *p*=0.42; **Supplementary Figure S40**).

Neurological Events

The incidences of permanent and temporary neurological dysfunction were reported in eight[7,17-21,24,28] (n=8) and seven articles[16,19,21,24,26-28] (n=7), respectively. A transient neurological impairment can be explained with following clinical symptoms like partial loss of orientation, unclear speech, and delay in reply to the command or with further significant nervous disorders, which were entirely cured during the clinical review. However, long-lasting neurological disorders persist after the post-surgery of the neurological problems, which could not cure the medical condition, and resulted in coma and stroke, which were further diagnosed by the neuro specialist or radiography.

As illustrated in Figures 9 and 10, there was no statistically significant difference either in the permanent (RR=1.15; 95% CI: 0.78-1.69; *p*=0.50; I^2=0%) and temporary (RR=0.89; 95% CI: 0.53-1.48; *p*=0.65; I^2=0%) neurological dysfunctions between two cohorts of patients considered.

In sub group analysis, using fixed-effect model, it was found that in two studies[21,28] (N=2) HA surgical procedure showed no difference in the temporary neurological dysfunction as compared to the TR (RR=1.52; 95% CI: 0.42-5.48, I^2=0%, *p*=0.52; **Supplementary Figure S2**). Similarly, in two studies[17,19] (N=2) HA combined with AS and partial arch surgical procedure no significant difference in the permanent dysfunction (RR=1.42; 95% CI: 0.59-3.39, I^2=0%, *p*=0.43; **Supplementary Figure S15**) and temporary (RR=1.05; 95% CI: 0.50-2.19, I^2=0%, *p*=0.90; **Supplementary Figure S16**) as compared to the TR.

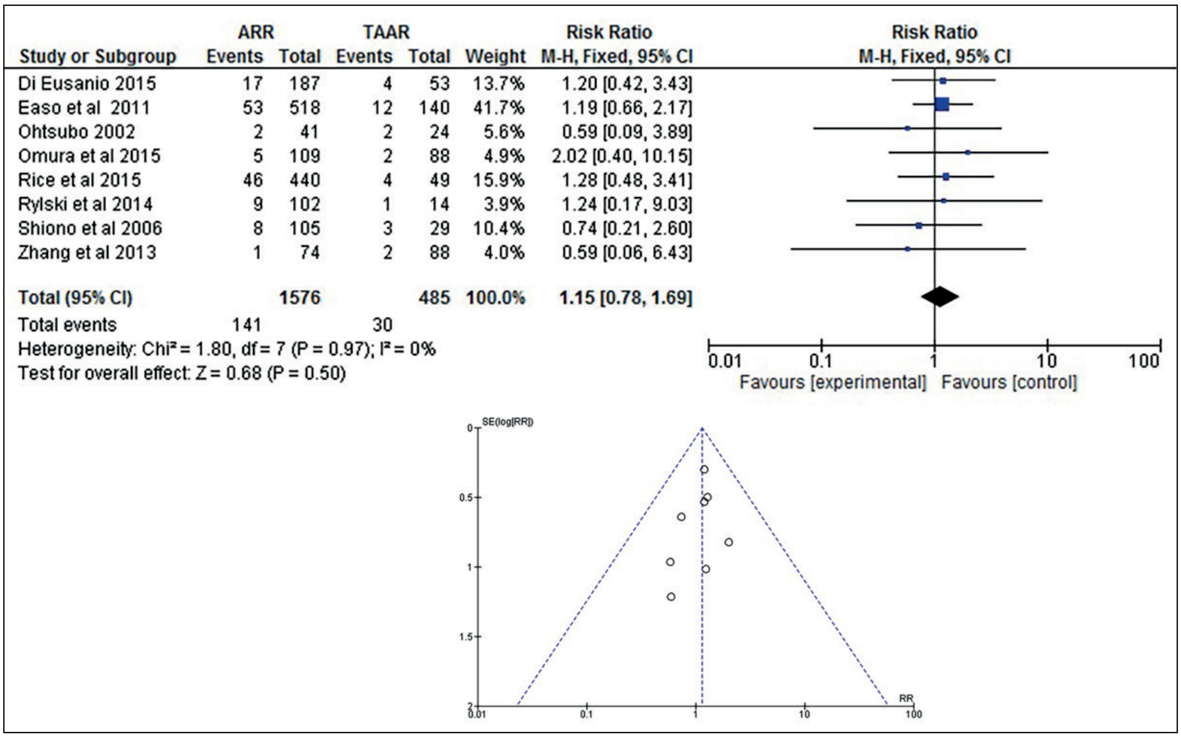


Figure 9. Comparison of temporary neurological dysfunction between patients undergoing either ascending aortic replacement (AR) or total arch replacement (TR). Risk ratio (RR)=0.79 (95% CI: 0.48-1.28), *p*=0.34. AR: ascending aortic replacement; TR: total arch replacement; CI, confidence interval.

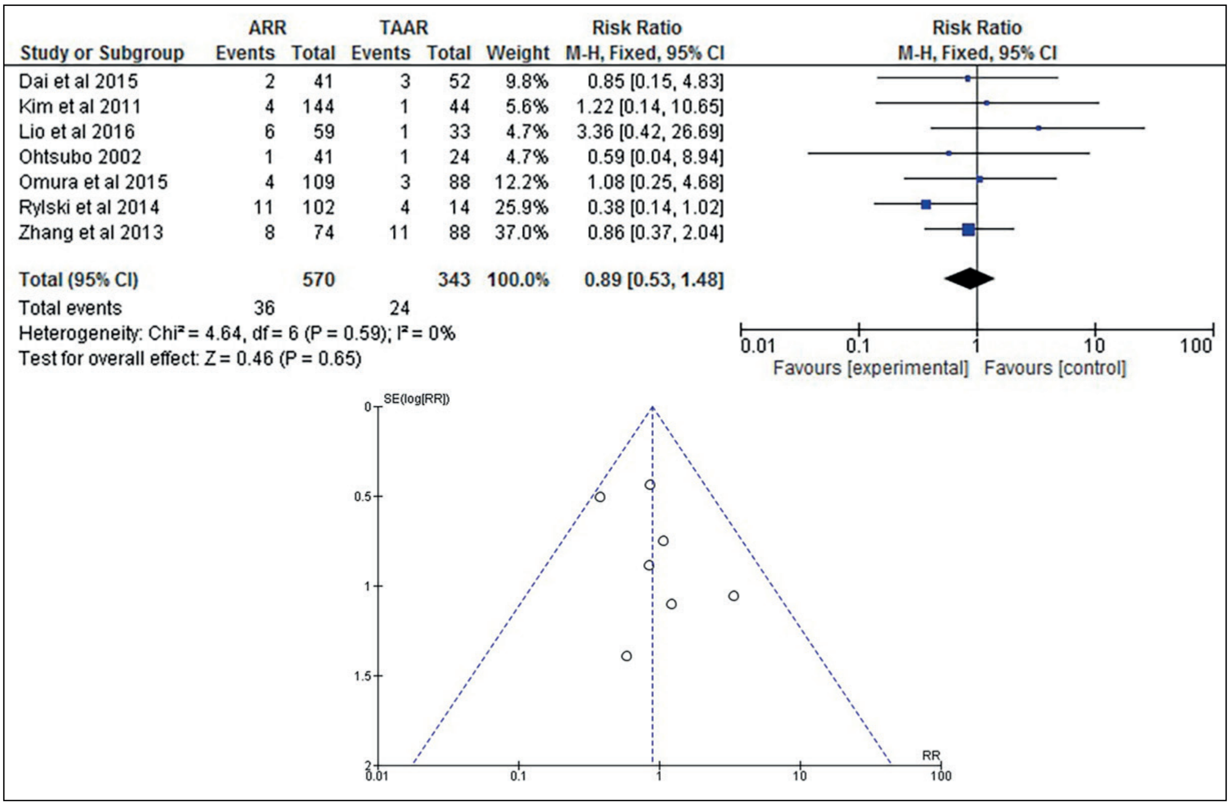


Figure 10. Results of ascending aortic replacement (AR) *vs.* total arch replacement (TR) on renal dialysis. Risk ratio=0.73 (95% CI: 0.56-0.95), p=0.02. AR: ascending aortic replacement; TR: total arch replacement; CI, confidence interval.

In three studies[18,20,24] (N=3) AR combined with HA surgical procedure insignificantly high risk of permanent dysfunction as compared to the TR using elephant trunk technique (RR=1.18; 95% CI: 0.72-1.94, I^2=0%, p=0.52; **Supplementary Figure S25**) (Figure S36). In three studies[16,26,27] (N=3), AR combined with HA surgical procedure insignificantly led to a high risk of temporary dysfunction as compared to the TR without elephant trunk technique (RR=1.54; 95% CI: 0.52-4.61, I^2=0%, p=0.44; **Supplementary Figure S37**) (Figure S26).

Renal Dialysis

With regards to the incidence of renal dialysis, the pooled RR, including 9 studies[7,17,19,20,23,24,26,27,29] (n=9) was 0.74 (95% CI: 0.56-0.96; p=0.03; I^2=0%). These results thus indicated that the incidence of renal dialysis was significantly higher in the cohort of patients undergoing AR (p=0.03) (Figure 11).

In subgroup analysis, using fixed-effect model, it was found that in two studies[17,19] (N=2), HA combined with AS and partial arch surgical procedure insignificantly lowered the risk of renal dialysis (RR=0.84; 95% CI: 0.52-1.36, I^2=0%, p=0.48; **Supplementary Figure S17**). In four studies[20,23,24,29] (N=4), AR combined with HA surgical procedure insignificantly lowered the risk of renal dialysis as compared to the TR using elephant trunk technique (RR=0.64; 95% CI: 0.40-1.01, I^2=0%, p=0.06; **Supplementary Figure S27**). In three studies[7,26,27] (N=3), AR combined with HA surgical procedure insignificantly lowered the risk of renal dialysis as compared to the TR without elephant trunk technique (RR=0.75; 95% CI: 0.47-1.20, I^2=0%, p=0.23; **Supplementary Figure S38**).

Secondary Outcomes

Operative Time

The durations of CPB (mean difference=-53.09; 95% CI: -56.68- -49.50; p<0.0001; I^2=98%; Figure 3) (mean difference=-102.00; 95% CI: -110.93- -93.07; p<0.00001; Figure S4) (Figure S10), CA (mean difference MD=-8.09; 95% CI: -9.04–7.15; p<0.001; I^2=98%; Figure 5) (mean difference=-16.00; 95% CI: -17.99- -14.01; p<0.00001;

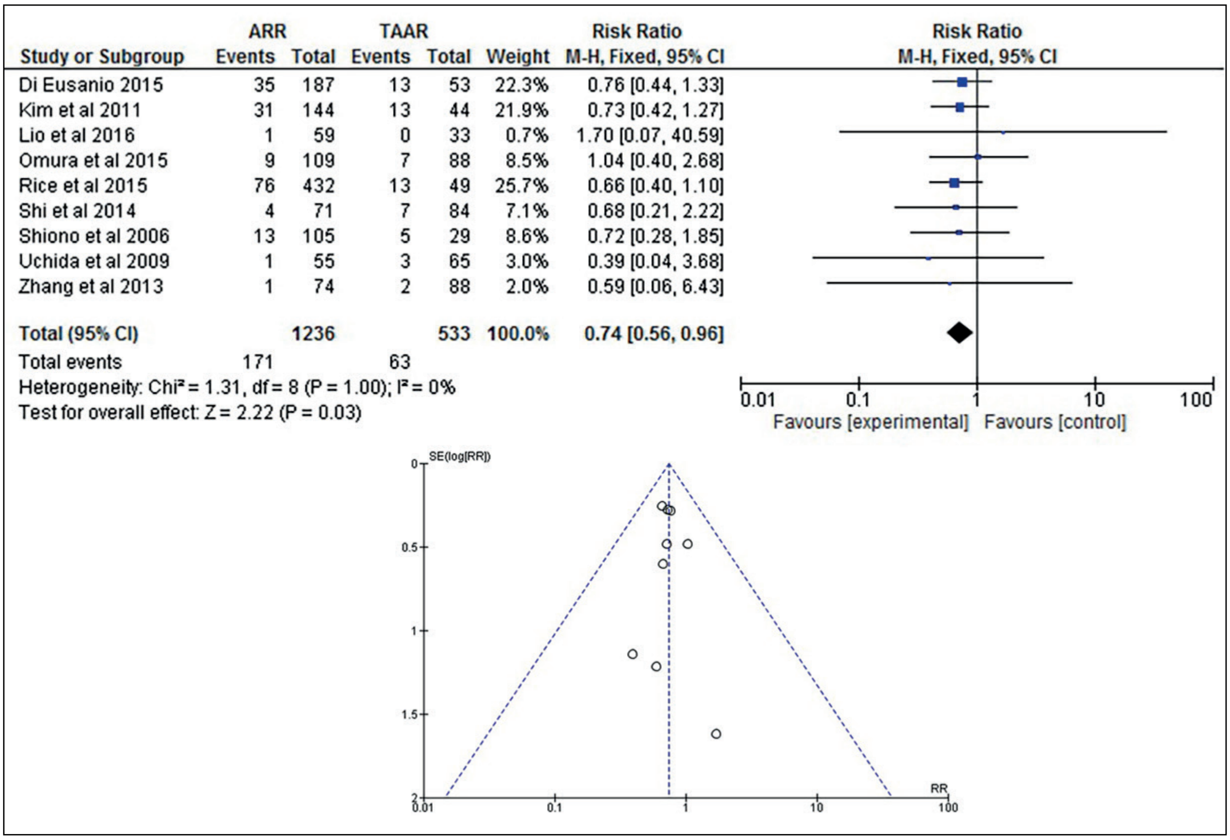


Figure 11. Results of AR *vs.* TR on re-operation rate. Risk ratio=1.39 (95% CI: 0.95, 2.04), p=0.09. AR: ascending aortic replacement; TR: total arch replacement; CI, confidence interval.

Figure S5) (Figures S11 and S42) and ACP (MD=-28.62; 95% CI: -30.23- -27.00; p<0.0001; I^2 = 98%; Figure 4) (mean difference=-77.00; 95% CI: -82.72- -71.28; p<0.00001; Figure S6) were significantly shorter in the cohort of patients undergoing AR as compared to the cohort of patients undergoing TR. As presented in Figure 2 and Figure 6, there was no statistically significant difference in the duration of ACC (mean difference= -12.60; 95% CI: -15.64–9.56; p<0.001; I^2=97%) (Figure S43) and CABG (RR=1.14; 95% CI: 0.82-1.58; p=0.76) between the two cohorts of patients.

In sub-group analysis, based on 2 studies (n=2) the duration of CPB (mean difference= -51.93; 95% CI: -67.79- -36.07; p<0.0001; I^2=0%; **Supplementary Figure S20**) and ACP (MD=-57.26; 95% CI: -64.26–50.44; p<0.0001; I^2=96%; **Supplementary Figure S21**) were significantly shorter in the cohort of patients undergoing HA combined with AR and partial arch as compared to the cohort of patients undergoing TR. As presented in **Supplementary Figure S22**, there was no statistically significant lower risk in CABG (RR=0.58; 95% CI: 0.23-1.45; I^2=0%, p=0.25) between the two cohorts of patients.

In four studies[20,23,24,29] (n=4), the durations of CPB (mean difference=-45.02; 95% CI: -49.78- -40.27; p<0.0001; I^2=97%; **Supplementary Figure S30**), CA (MD=-2.74; 95% CI: -3.97- -1.50; p<0.0001; I^2=98%; **Supplementary Figure S31**), while in three studies[18,23,29] (N=3) the ACP (MD=-26.91; 95% CI: -28.58- -25.25; p<0.0001; I^2=99%; **Supplementary Figure S32**), were significantly shorter in the cohort of patients undergoing AR combined with HA surgical procedure as compared to the TR using elephant trunk technique. In four studies[18,20,24,29] (N=4), as presented in **Supplementary Figure S33**, there was no statistically insignificantly high risk in CABG (RR=1.12; 95% CI: 0.74-1.68; I^2=0%, p=0.59) between the two cohorts of patients.

In three studies[16,26,27] (N=3), the durations of CPB (mean difference=-11.78; 95% CI: -19.90- -3.67; p<0.0001; I^2=94%; **Supplementary Figure S41**), CA (MD=-4.22; 95% CI: -6.95- -1.49;

p<0.0001; I^2=93%) were significantly shorter in the cohort of patients undergoing AR combined with HA surgical procedure as compared to the TR using no elephant trunk technique. In four studies[7,16,26,27] (N=4), as presented in **Supplementary Figure S44**, there was no statistically insignificantly high risk in CABG (RR=1.71; 95% CI: 0.84-3.48; I^2=0%, p=0.14) between the two cohorts of patients.

Aortic Re-operation (Proximal and Distal)

Eleven studies[7,16,17,19,21-24,26,27,29] (n=11) reported that the pooled rate of aortic re-operation was 7.6% in the cohort of patients undergoing AR and 5.3% in that undergoing TR, respectively (Figure 12). The difference in the re-operation rate between the two cohorts of patients was not statistically significant (RR=1.39; 95% CI: 0.94-2.07; p=0.109 I^2=0%).

The proximal and distal aorta was observed to be with 5.6% for the overall rate of aortic reoperation. 12 follow up studies has included 1,651 patients exhibited the frequency of proximal and distal aorta with 7.3% in hemiarch and 3.3% with an overall arch replacement without any statistical significance observed among these two groups (RR =1.45; 95% CI: 0.93–2.28; p=0.10, I^2=23%).

In the subgroup analysis, using fixed-effect model, it was found that in two studies[21,22] (N=2) HA surgical procedure insignificantly high risk of aortic re-operation as compared to the TR (RR=2.20; 95% CI: 0.40-12.05, I^2=12%, p=0.36; **Supplementary Figure S3**), AS surgical procedure insignificantly high risk of aortic re-operation as compared to the TR (RR=1.14; 95% CI: 0.22-5.81, I^2=0%, p=0.88; **Supplementary Figure S9**). Two studies (N=2)[17,19] HA combined with AS and partial arch surgical procedure insignificantly high risk of aortic re-operation as compared to the TR (RR=1.23; 95% CI: 0.61-2.48, I^2=50%, p=0.57; **Supplementary Figure S18**).

In three studies[23,24,29] (N=3) AR combined with HA surgical procedure significantly high risk of aortic re-operation as compared to the TR using

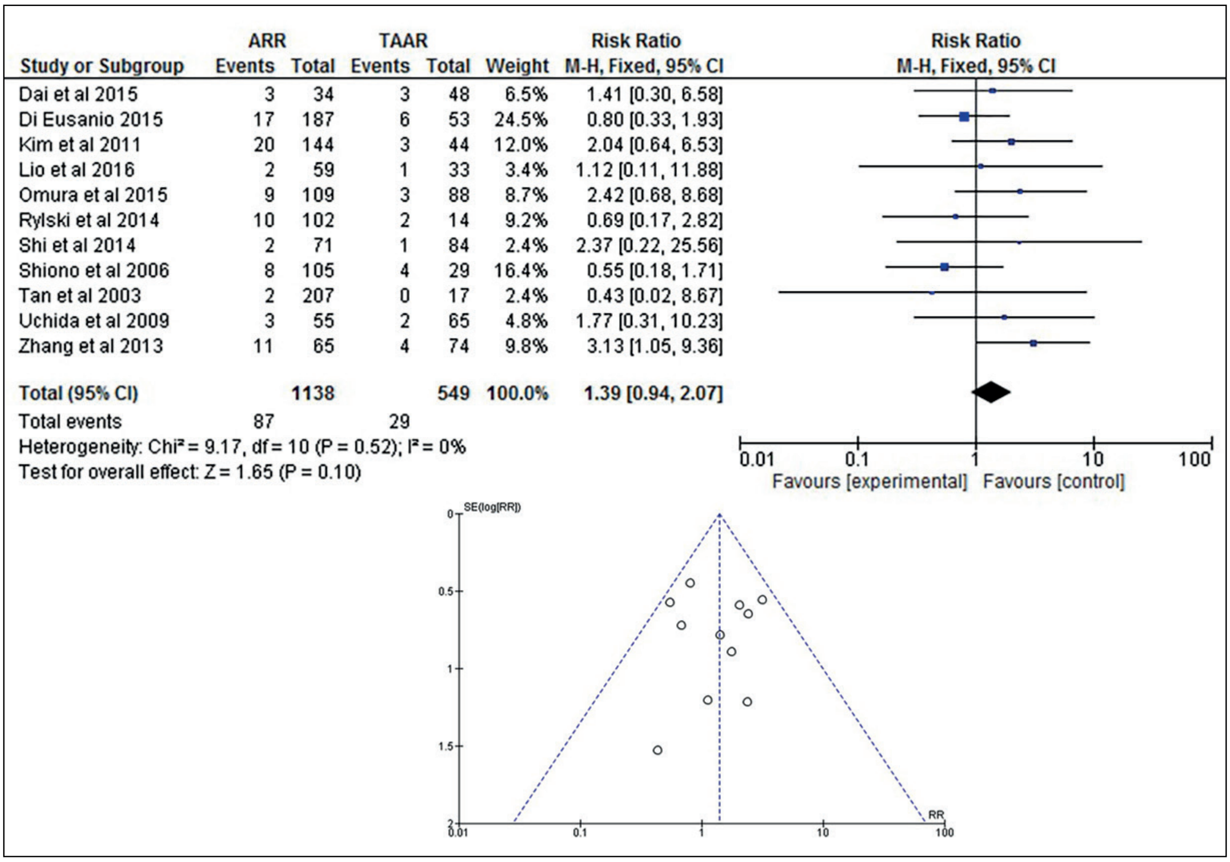


Figure 12. Results of AR *vs.* TR on long-term survival. Risk ratio=0.85 (95% CI: 0.73, 0.98), p=0.03. AR: ascending aortic replacement; TR: total arch replacement; CI, confidence interval.

elephant trunk technique (RR=2.64; 95% CI: 1.12-6.23, I^2=0%, p=0.03; **Supplementary Figure S28**). Four studies[7,16,26,27] (N=4) AR combined with HA surgical procedure insignificantly high risk of aortic re-operation as compared to the TR without elephant trunk technique (RR=1.21; 95% CI: 0.62-2.37, I^2=0%, p=0.57; **Supplementary Figure S39**).

Publication Bias

Funnel plot, Begg & Mazumdar rank correlation, and the Egger's regression test were performed to estimate the risk of publication bias among the selected studies. As illustrated in Figure 8, the shape of the Funnel plot seems to be symmetrical, suggesting that there is no significant publication bias. Begg's & Mazumdar rank correlation (Kendall's Tau=0.07; p=0.18) and Egger regression test (Intercept=1. 18, 2-tailed p=0.06) supported the results derived from the Funnel plot.

Discussion

There is always a confusion among surgeons about which efficient procedure to take up, whether hemiarch or ascending aorta replacement or total arch replacement for patients suffering from ATAAD. As per the records of the German Registry for Acute Aortic Dissection Type A (GERAADA) study, a huge database comprising the details of patients getting operated for ATAAD and segmentation restricted to the short proximal fragment was alone was documented in 20% of all the patients[25]. For most ATAAD patients, the dissection process affects the entire length of the aortic arch[26]. Thus, there is still no clinical consensus upon the optimal surgical treatment strategy for ATAAD patients. Other largest registry for acute aortic dissection is International Registry of Acute Dissection (IRAD) with 43 aortic centres enrolling patients[32]. Similar to GERAADA, IRAD data shows no statistical significance between early mortality rate of ascending aorta replacement 22.9% and total arch replacement 23.7% respectively[33]. Similarly, there was no statistical difference between AR, TR, and HA (20.9%)

Currently, a few aortic centers advocate for the TR with frozen elephant technique surgical procedure as the optimal treatment for subjects with ATAAD[34]. The replacement of the entire dissected aorta could decrease the incidence of false lumen patency and decrease the risk of aortic dilatation, as well as that of late aortic re-operation[27,28]. Besides, the factors such as an aneurysm or extensive arch destruction, syndromic disease, and age push surgeon to perform TR. Conversely, other surgeons have supported the use of the conventional strategy, i.e., AR, arguing that the major goal of an emergency surgical procedure is the immediate survival of the patients. The TR surgical procedure may lead to higher risks of bleeding complications and prolonged cerebral ischemia, which may thus outweigh the long-term benefit if performed by surgeons with inadequate experience in aortic dissection[29,30].

2734 subjects from the included 15 studies were analyzed in this systematic review and meta-analysis.

In-Hospital Mortality

From the primary analysis based on 10 studies we infer that AR, HA, and PA showed statistically lower risk of in hospital mortality when compared to TR *(p*=0.02). However, based on 3 studies analysis, there was no statistical significance mortality rate among HA and TR. Furthermore, an analysis of findings from 3 studies suggests that AR alone has significantly lower risk of in-hospital mortality rate when compared to TR procedure *(p*=0.009). Based on few studies, we infer that there was no statistical significance between HA, PA with AR and AR, including HA when compared to TR with and without elephant technique.

5-Year-Survival Rate

There was no heterogeneity or statistical significance between AR and TR procedure on analyzing the 5-year-survival rate. Similarly, from subgroup analysis we infer that there is survival rate relationship between HA or AR with HA and TR procedure.

In regard to mortality rate, Rice et al[20] found comparable 1-, 5-, and 10-year survivals between the two cohorts of patients in question (those undergoing either AR or TR), 72.8%, 69.9%, and 61.2% for the cohort of patients undergoing TR, and 80.2%, 75.6%, and 61.3% for patients undergoing AR, respectively, albeit such findings were found not to be statistically significant. These results support the conclusions drawn from other six studies, outlined as follows. Dai et al[16] suggest that survivals were higher in the cohort of patients undergoing TR than in patients undergoing AR, with 1-, 3- and 5-year survivals were 96.1%, 94.1%, and 94.1% in the cohort of patients undergoing TR, and 90.5%, 83.3% and 83.3% in patients undergoing AR, respectively. Both Ohtsubo et al[28] (AR 44.4%±14.3% *vs.* TR 91.3%±5.9%, p=0.02) and Uchida et al[23] (AR 69.0% *vs.* TR 95.3%, p=0.03) reported significantly higher 5-year survivals in the cohort of patients undergoing the TR surgical procedure. As some of the included studies did not report the hazard ratios or exact survivals within the follow-up interval, it was not possible to pool the results of long-term mortality data from them.

Neurological Dysfunction and Renal Dialysis

There is no statistical significance in occurrence of permanent or temporary neurological dysfunction among both AR and TR procedure. However, from subgroup analysis on 2 studies, we can infer that AR with HA procedure pose higher risk of developing permanent neuro-dysfunction when compared to TR with elephant technique (p=0.52). Similarly, from 2 studies we infer that AR with HA procedure significantly increases the risk of temporary neuro-dysfunction when compared to TR procedure (p=0.44).

From 9 studies included in this meta-analysis we conclude that AR procedure statistically increases the risk of renal dialysis when compared to TR (p=0.03). Under subgroup analysis, from different combination of studies we infer that AR in combination with HA and PA significantly lowers the risk of renal dialysis. Based on 2 studies subgroup analysis it is evident that HA with AR and PA has lower risk of renal dialysis than TR alone (p=0.48), AR with HA lowers renal dialysis more significantly in TR alone procedure when compared to TR with elephant technique (p=0.23 and p=0.06), respectively. From the above, we conclude that though AR procedure along with increase the risk of renal dialysis, in combination with HA and PA it lowers the risk of renal dialysis when compared to TR procedure. This could be attributed to prolonged cerebral perfusion involved in the TR surgical procedure, which may contribute to further increase in-hospital mortality in the cohort of patients undergoing TR.

Duration of CPB, CA, ACP, ACC, and CABP

Overall, the duration of CPB, CA, and ACP was less in patients who underwent AR procedure compared to TR. However, the duration of ACC and CABG remained the same for both the procedures. From the subgroup analysis we infer that AR along with HA and/ or PA also decreased the CPB, CA, and ACP duration when compared to TR with or without elephant trunk technique, at the same time the duration of CABG remained same.

Aortic Re-Operation

From 11 studies it is evident that AR procedure results in higher aortic re-operation (7.6%) when compared to TR (5.3%); however, it was not statistically significant. From subgroup analysis we infer that both HA or AR alone or in combination with PA statistically increases the risk of aortic re-operation when compared to TR (p=0.36; p=0.88 and p=0.57), respectively. Similarly, AR in combination with HA significantly increases the risk of re-operation in TR with or without elephant technique p=0.03 from 3 studies and p=0.57 from 4 studies, respectively. Kim et al[26] reported risk of aortic dilatation (>55 mm) at distal for both TA and HA groups and Omura et al[19] reported one distal aortic dilatation case following HA for ADIAD Omura et al[19] reported 2 cases of distal aortic dilatation. Notably, there was no relation either with aortic re-operation both proximally and distally among the type of arch replacement and complete thrombosis of false lumen. However, there was minimum death rate observed with re-operation for aortic dilation. False lumen is the most widespread risk factor for ATAAD leading to an aortic aneurysm and to the need for re-intervention on the aortic arch or descending aorta further to ATAAD surgical repair. As anastomotic leakage or a small tear in the proximal descending thoracic aorta may occur during the AR surgical procedure, the false lumen is susceptible to dilation due to the shear stress acting on the proximal descending aorta[23]. Zhang et al[24] observed that a residual false lumen in the descending thoracic aorta is found in 50-70% of patients with ATAAD after undergoing ascending aortic or hemiarch replacement. Conversely, the TR surgical procedure would completely repair the intimal tear in the ascending aorta and the entire aortic arch concurrently by replacing the dissecting aorta affected. A residual false lumen is found in approximately 30% of the patients with ATAAD also after undergoing the TR surgical intervention[24]. Thus, Zhang et al[24] found that the cohort of patients undergoing TR may be associated with a significantly lower rate of re-operation at 10-year follow-up (AR 16.9%

vs. TR 5.4%, $p<0.05$). In this meta-analysis, the pooled results suggest that the TR surgical procedure seems to be associated with a lower incidence of aortic re-operation, albeit these results were found not to be statistically significant.

The present analysis did not confer any statistical significance with respect to the death rate, incidence of transient and long-lasting neurological disorder, and renal dialysis between the two groups during the surgery. Circulatory arrest times, aortic cross-clamp, cardiopulmonary bypass times were considerably extensive in total arch replacement, signifying that AR is the best treatment option compared to TR.

In the GERAADA study, a logistic regression analysis of clinical presentation and surgery upon 30-day mortality showed that the length of CA was a significant risk factor for early postoperative mortality. Other studies suggested that longer CPB and CA times might be directly related to cardiac, cerebral, and organ injuries. The higher baseline incidence of cardiogenic shock and tamponade in the cohort of patients undergoing AR may increase the risk of early mortality; nevertheless, this conclusion contradicts the findings derived from the systematic review and meta-analysis conducted. Thus, a more conservative surgical treatment strategy is recommended for patients with cardiogenic shock and tamponade.

Hence, from the meta-analysis we can infer that AAR cannot be recommended as standard surgical procedure to be followed by all surgeons unanimously. The type of surgical procedure should be case-specific based on the patient's clinical data, anatomic condition, clinical experience of the surgeon, volume of similar operations performed at that institution and patient's preference.

This systematic review and meta-analysis was limited by several factors. First, all studies included were retrospective observational cohort studies with inherent limitations, including detection and publication bias exists. Second, without appropriate randomization, selection, and treatment biases may arise. The proportion of female patients was found to be higher in the cohort of patients undergoing AR, which is a surgical procedure typically performed in patients with cardiogenic shock or tamponade. Third, a significant level of heterogeneity still exists in the studies analyzed, which may reflect the varying degree of complexity in the surgical procedure for ATAAD patients and the relative variability in experience among operative centers. Especially, TR was performed more among younger patients than in those with Marfan syndrome. Finally, information upon the duration of some research studies was lacking, and this may also limit the generalization of the results derived from this systematic review and meta-analysis.

Conclusions

This systematic review and meta-analysis suggest no significant difference in mortality, incidence in temporary and permanent neurological dysfunctions, and renal dialysis between the two groups while AR surgical procedure is associated with a significantly shorter CPB, CA, and ACP times. This research enhanced the significance of performing the total aortic arch procedure despite its immediate risks in the organization to achieve the better- outcomes as compared to AR as most of the studies conducted mid-term survivorship instead of focusing on long term survival rate. Hence, a firm conclusion on modified and long-lasting effective data is necessary to strongly recommend a standard procedure. Hence, AAR cannot be recommended as a principal surgical procedure to be followed in all organizations of surgeons regardless of patient characteristics. However, relatively to the subject-specific surgical treatment strategy should be designed according to patient-specific data and clinical experience. This investigation would benefit physicians to practice such surgical procedures on a patient who is specific for that surgery, thereby enhancing the quality treatment outcome in patients for their better survival.

Conflict of Interest
The Authors declare that they have no conflict of interests.

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