Treatment strategies and outcomes following acute type A aortic dissection repair in patients with bicuspid and tricuspid aortic valves: A meta-analysis

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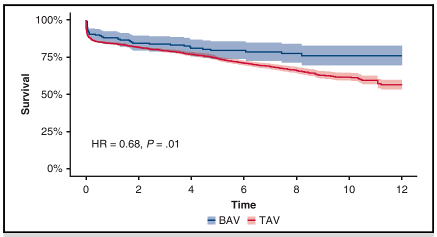
ABSTRACT

Background: There is no consensus regarding the strategies for repairing acute type A aortic dissection (ATAAD) in patients with bicuspid aortic valve (BAV). This meta-analysis aimed to compare the treatment strategies and outcomes of ATAAD repair between patients with BAV and those with tricuspid aortic valve (TAV).

Methods: A systematic review of databases were performed from inception through March 2023. The primary outcome of interest was all-cause mortality, with a minimum follow-up of 1 year. The secondary outcomes of interest included ratios of performed procedures and rate of distal aortic reoperation. Data were extracted, and pooled analysis was performed using a random-effects model.

Results: Eight observational studies including a total of 3701 patients (BAV, n = 349; TAV, n = 3352) were selected for a meta-analysis. Concerning proximal aortic procedures, BAV patients exhibited a higher incidence of necessary root replacement (odds ratio [OR], 6.53; 95% confidence interval [CI], 3.84 to 11.09; $P < .01$). Regarding distal aortic procedures, extended arch replacement was performed less frequently in BAV patients (OR, 0.69; 95% CI, 0.49 to 0.99; $P = .04$), whereas hemiarch procedure rates were comparable in the 2 groups. All-cause mortality was lower in the BAV group (hazard ratio, 0.68; 95% CI, 0.50 to 0.92; $P = .01$). Distal aortic reoperation rates were comparable in the 2 groups.

Conclusions: This study highlights distinct procedural patterns in ATAAD patients with BAV and TAV. Despite differing baseline characteristics, BAV patients exhibited superior survival compared to TAV patients, with comparable distal aortic reoperation rates. These findings may be useful for decision making regarding limited versus extended aortic arch repair. (JTCVS Open 2024;19:9-30)



BAV patients with ATAAD were associated with better survival compared to TAV patients.

CENTRAL MESSAGE

This study highlights distinct procedural patterns in acute type A aortic dissection patients with bicuspid aortic valve and patients with tricuspid aortic valve.

PERSPECTIVE

No specific guideline recommendations currently exist for acute type A aortic dissection in patients with bicuspid aortic valve (BAV). Our comparative analysis reveals significant distinctions in surgical approaches to the proximal and distal aorta between BAV and tricuspid aortic valve patients. Importantly, our findings highlight better survival rates in BAV patients, with comparable rates of distal aortic reoperations in the 2 groups.

Bicuspid aortic valve (BAV) is the most common congenital heart defect, with a prevalence of up to 2% in the general population.[1] BAV is often considered a valvulo-aortopathy, predisposing patients to aortopathies in addition to aortic valvular disease.[2,3] Among the BAV-associated aortopathies, acute type A aortic dissection (ATAAD) is the most serious complication, with an in-hospital mortality rate of up to 22%.[4] BAV increases the risk of ATAAD especially in a

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Abbreviations and Acronyms

- ATAAD = acute type A aortic dissection
- BAV = bicuspid aortic valve
- CI = confidence interval
- CPB = cardiopulmonary bypass
- HCA = hypothermic circulatory arrest
- HR = hazard ratio
- TAV = tricuspid aortic valve
- WMD = weighted mean difference
- XCL = aortic cross-clamp

Supplemental material is available online.

younger population, and the prevalence of BAV is as high as 9% in young patients with ATAAD, 10-fold higher than the prevalence of TAV.[5]

Both hemodynamic abnormalities and genetic intrinsic wall abnormalities of the ascending aorta have been suggested as the primary causes of ATAAD in BAV patients.[6,7] Abnormal valve morphology of bicuspid valves promotes eccentric, turbulent blood flow and alters wall shear stress, predisposing BAV patients to dilation of the ascending aorta and dissection.[6,8] Other studies have linked intrinsic abnormalities of the proximal aortic wall in BAV patients to ATAAD formation, including cystic medial degeneration, loss of elastic fibers, and decreased contractility of smooth muscle.[9-11] Despite efforts to elucidate the pathogenesis of ATAAD in BAV patients, clinical data on proper treatment strategies and outcomes remain limited for BAV patients experiencing ATAAD. Furthermore, there are no specific guidelines for managing ATAAD in BAV patients. Here we present the results of a systematic review and meta-analysis comparing treatment strategies and outcomes of ATAAD between patients with BAV and those with TAV.

METHODS

Ethics Statement

Given the nature of our study, Institutional Research Board or Informed Written Consent for Publication were not required. The review was conducted according to the Preferred Reporting items for Systematic Reviews and Meta-Analyses (PRISMA) statement standards.[12]

Protocol and Registration

The study protocol was registered on PROSPERO (CRD42023422688).

Eligibility Criteria

Included studies met the following criteria: the study design was an observational study, the study population was patients with ATAAD and either BAV or TAV, the study was a comparative study reporting outcomes of both BAV patients with ATAAD (BAV-ATAAD) and TAV patients with ATAAD (TAV-ATAAD), and the study included at least 1 of the following preoperative/intraoperative characteristics or perioperative/postoperative outcomes, including; intraoperatively performed procedures, durations of operative sequences, perioperative events, and postoperative events during follow-up period.

Information Sources and Search

All studies that investigated the treatment strategies for BAV and TAV patients with ATAAD were identified using a 2-level strategy. First, a search of the MEDLINE, Embase, and Cochrane Central databases was conducted to identify all the studies published from database inception to April 20, 2023, that investigated the comparison between BAV-ATAAD patients and TAV-ATAAD patients. The detailed retrieval strategy is shown in Tables E1-E3.

Study Selection and Data Collection Process

Relevant studies were identified through a manual search of secondary sources, including references of initially identified articles, reviews, and commentaries. All references were downloaded for consolidation, elimination of duplicates, and further analyses. Two independent and blinded authors (T.S. and Y.Y.) conducted a literature search and reviewed the search results separately to select the studies based on the inclusion and exclusion criteria after a full-text review. Disagreements were resolved by consensus between the 2 reviewers, with occasional arbitration by a third reviewer (T.K.).

Risk of Bias in Individual Studies

Study quality was assessed by 2 independent and blinded authors (T.S. and Y.Y.) using the Newcastle-Ottawa Scale for observational studies.[13] Disagreements were resolved by consensus.

Summary Measures

The primary outcome of interest was all-cause mortality following surgical repair with a $\geq$1-year follow-up. The secondary outcomes were intraoperatively performed procedures on the aortic root and aortic arch; duration of cardiopulmonary bypass (CPB), aortic cross-clamp (XCL), and hypothermic circulatory arrest (HCA); perioperative rates of stroke, myocardial infarction, and mortality, and postoperative rates of total reoperation and proximal and distal aortic reoperations.

Continuous variables, including aortic diameters and duration of CPB, XCL, and HCA, mean values with standard deviation were extracted. The ratios of performed surgical procedures were also extracted for both groups.

For comparisons of intraoperatively performed procedures, the number of events and the number of patients were extracted from each study for calculation of odds ratio (OR). For perioperative outcomes, the adjusted risk ratio (RR) was extracted if available from the studies. If the RR was not described in a study, it was calculated from the number of events and number of patients. For postoperative outcomes, the hazard ratio (HR) was extracted when available from studies. If the HR was not described in a study, it was calculated from a Kaplan-Meier (KM) curve if provided using the "HR calculations spreadsheet" provided by Tierney and colleagues[14] based on standard statistical methods reported by Parmar and colleagues[15] and Williamson and colleagues.[16] If a KM curve was not provided in a study, the RR was calculated from the number of events and number of patients and was converted to the HR by estimation.[17]

For all-cause mortality during follow-up, we analyzed the data from the approach described by Liu and colleagues for reconstructing time-to-event data at the individual level from KM curves.[18] Raw data coordinates, including time and event probabilities, were extracted from KM curves. Survival data at the individual level in each study were reconstructed from data coordinates and the numbers at risk at a given time point using the R package "IPDfromKM." To assess the accuracy of the calculated data compared to the originally extracted data, we evaluated root mean square error, mean absolute error, and maximum absolute error as measures of the precision of estimation based on Liu's algorithm.[18] The reconstructed KM curves in our study met the recommended thresholds of a root mean square error ≤.05, a mean absolute error ≤.02, and a maximum absolute error ≤.05.

In addition, we merged the reconstructed individual time-to-event data of all eligible studies and derived the pooled KM estimates.[18] To compare the incidence of each outcome between the BAV and TAV groups, we performed Cox proportional hazard model analyses stratified by study.

Synthesis of Results

Categorical values, including the ratios of the surgical procedures performed, are expressed as percentages. OpenMetaAnalyst version 12.11.14 (available from http://www.cebm.brown.edu/openmeta) was used to analyze ratios of the surgical procedures performed for single group meta-analysis. RevMan 5.4 (Nordic Cochrane Centre, the Cochrane Collaboration) was used to calculate the ORs of performed surgical procedures using the DerSimonian and Laird method in the random-effects model. RevMan 5.4 also was used to perform analyses for continuous variables. Two-group meta-analysis of continuous variables were performed using the DerSimonian and Laird method in the random-effects model. RevMan version 5.4 was also used to separately pool HRs and 95% confidence intervals (CIs) in the random-effects model using the inverse variance method, with the weights of each trial determined to be the inverse of the effect estimate. The analysis of all-cause mortality was conducted with R version 4.2.2 (R Foundation for Statistical Computing).

The random-effects model was used for each outcome regardless of heterogeneity among studies, which allowed for a more conservative assessment of the pooled effect size. A P value <.05 was considered statistically significant.

Risk of Bias Across Studies and Additional Analyses

ProMeta 3 software (https://idostatistics.com/prometa3) was used to perform sensitivity analyses and examine funnel plot asymmetry. Funnel plot asymmetry suggesting publication bias was assessed mathematically using Egger's linear regression test.[19] Significant heterogeneity was considered present when the I^2 index was >50% or the P value for heterogeneity was <.05. A sensitivity analysis was performed with ProMeta 3 by removing one study at a time (ie, the leave-one-out method) to confirm that our findings were not derived from a single study. A meta-regression analysis based on the difference in age between the BAV and TAV groups was performed with ProMeta 3.

RESULTS

Study Selection

Our study included 8 observational studies[20-27] that enrolled a total of 3701 patients with ATAAD, consisting of 349 patients with BAV and 3352 patients with TAV (Figure 1).

Study Characteristics

Propensity score matching was used in 2 studies.[24,27] The study profile and patient characteristics are summarized in Table 1. For studies reporting mid-term outcomes, follow-up periods ranged from 3.1 years to 4.3 years.[21,22,24,25] Two studies did not report follow-up periods,[23,26] and 2

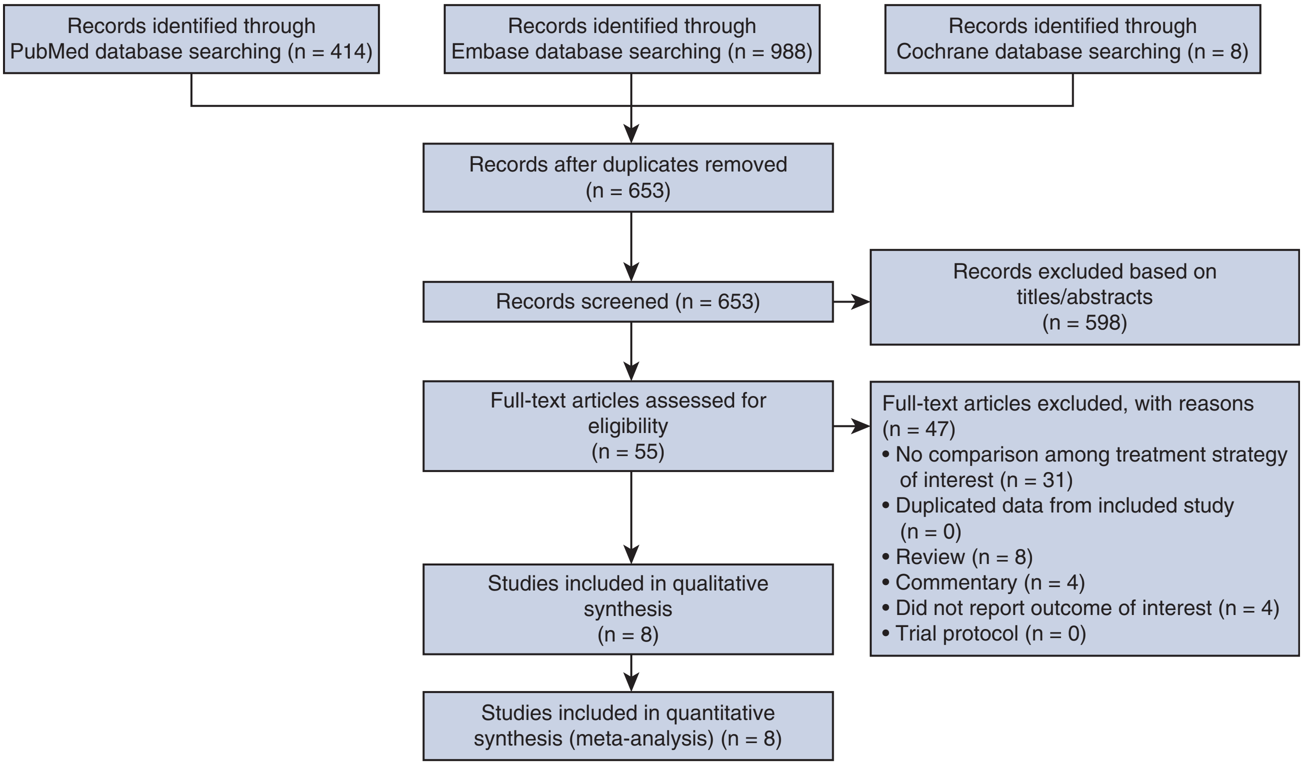

FIGURE 1. Workflow for selecting eligible articles according to PRISMA criteria in the search for original studies for this meta-analysis.

TABLE 1. Study profiles

First author	Year	Study period	Follow-up, y	Adjustment	CTD	Patients, n BAV	Patients, n TAV	Age, y BAV	Age, y TAV	Males, % BAV	Males, % TAV	HTN, % BAV	HTN, % TAV	DM, % BAV	DM, % TAV	Hyperlipidemia, % BAV	Hyperlipidemia, % TAV
Della Corte[26]	2023	N/A	N/A	None	N/A	15	142	59	67	80	62	87	91	N/A	N/A	N/A	N/A
Haunschild[27]	2022	2000-2018	N/A	PSM	None	34	34	49	51	74	68	67	65	3	3	N/A	N/A
Titsworth[25]	2022	1996-2021	4.3	None	None	60	655	54	61	82	67	67	78	1.7	8.5	N/A	N/A
Mennander[24]	2020	2005-2014	3.1	PSM	Included	65	260	55	55	83	83	49	49	N/A	N/A	14	8
Kreibich[23]	2020	2002-2017	N/A	None	None	72	1068	54	63	72	65	71	89	7	12	28	38
Etz[22]	2015	1995-2011	3.9	None	None	32	347	46.7	61.6	71.9	63.7	46.9	72	0	9.2	28.1	30.8
Rylski[21]	2014	1993-2013	4.1	None	Included	41	588	55	61	63.4	64.1	56.1	81.1	9.8	9.2	N/A	N/A
Wang[20]	2013	2007-2012	N/A	None	None	30	258	46	51	80	76	50	70.9	3.3	3.9	N/A	N/A

First author	CAD, % BAV	CAD, % TAV	FH of CTD, % BAV	FH of CTD, % TAV	CKD, % BAV	CKD, % TAV	Prior stroke, % BAV	Prior stroke, % TAV	Tamponade, % BAV	Tamponade, % TAV	AR, % BAV	AR, % TAV	DeBakey type I, % BAV	DeBakey type I, % TAV	History of cardiac surgery, % BAV	History of cardiac surgery, % TAV
Della Corte[26]	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Haunschild[27]	3	3	0	0	26	21	3	3	N/A	N/A	94	85	71	71	N/A	N/A
Titsworth[25]	22	17	0	0	1.7	5.3	1.7	4.1	5	12	47	39	N/A	N/A	10	6.6
Mennander[24]	N/A	N/A	7	7	0	3	N/A	N/A	46	40	N/A	N/A	67	78	3	1
Kreibich[23]	N/A	N/A	0	0	8	16	10	9	22	21	33	28	N/A	N/A	N/A	N/A
Etz[22]	6.3	12.7	0	0	0	2	6.3	16.5	N/A	N/A	N/A	N/A	75.0	79.3	6.0	7.8
Rylski[21]	17.1	18.5	4.9	4.6	7.3	8	9.8	7.1	34.1	23.8	51.2	34	65.9	69.6	12.2	8.7
Wang[20]	3.3	3.9	0	0	6.7	1.9	6.7	1.6	N/A	N/A	33.3	39.9	66.7	70.9	N/A	N/A

CTD, Connective tissue disorder; *HTN*, hypertension; *DM*, diabetes mellitus; *BAV*, bicuspid aortic valve; *TAV*, tricuspid aortic valve; *N/A*, not available; *PSM*, propensity score matching; *FH*, family history; *CKD*, chronic kidney disease; *AR*, moderate to severe aortic regurgitation; *CAD*, coronary artery disease.

studies reported only periprocedural outcomes.[20,27] BAV patients were generally younger than TAV patients. The percentage of males was higher in the BAV group. The rate of comorbidities, including hypertension and diabetes mellitus, was higher in the patients with TAV. Moderate to severe aortic regurgitation was more frequent in the BAV group, and DeBakey type I aortic dissection was more common in the TAV group. Patients with prior aortic interventions were excluded.

The weighted mean difference (WMD) for baseline age was lower in the BAV group (−7.22 years; 95% CI, −11.46 to −2.97 years; $P < .01$) (Figure E1, *A*). Five studies reported ascending aorta diameters, and 2 studies reported aortic arch diameters. Diameters of the aortic root and descending aorta were reported in 1 study each. BAV patients had larger ascending aorta diameters compared with TAV patients (WMD, 6.94 mm; 95% CI, 3.64- 10.25 mm; $P < .01$) (Figure E1, *B*). Meanwhile, aortic arch diameters were similar in BAV and TAV patients (WMD, −1.65 mm; 95% CI, −3.63 to 0.32 mm; $P = .10$) (Figure E1, *C*).

Risk of Bias Within Studies

The quality of observational studies is summarized in Table E4. The quality ranged from 6 to 9. Two studies were associated with an intermediate risk of bias and other studies were associated with a low risk of bias.

Results of Individual Studies and Synthesis of Results

Intraoperative procedures. The combined ratios of intraoperative procedures on the aortic root and aortic arch are summarized in Table 2. Aortic root replacement was performed in 73.6% of BAV patients and in 33.3% of TAV patients—a significantly higher rate in BAV group (OR, 6.53; 95% CI, 3.84-11.09; $P < .01$) (Figure E2, *A*). Meanwhile, aortic valve resuspension was performed in 21.8% of BAV patients and 58.5% of TAV patients—a significantly lower rate in the BAV group (OR, 0.19; 95% CI, 0.06-0.52; $P < .01$) (Figure E2, *B*). The 2 groups had similar rates of aortic valve replacement and no proximal aortic root

TABLE 2. Intraoperative procedures performed on the aortic root and aortic arch in acute type A aortic dissection

Procedure	BAV group, % (95% CI)	TAV group, % (95% CI)
Aortic root procedure		
None	4.3 (0-12.5)	16.1 (0-47.6)
Aortic valve replacement	5.7 (2.7-8.7)	4.0 (2.2-5.8)
Valve resuspension	21.8 (16.0-27.5)	58.5 (36.3-80.7)
Root replacement	73.6 (58.0-89.3)	33.3 (18.0-48.6)
Aortic arch procedure		
None	33.2 (7.3-59.2)	26.2 (9.9-42.5)
Hemiarch	46.8 (22.0-71.6)	46.4 (25.1-67.8)
Extended arch	18 (7.8-28.3)	26.3 (13.2-39.4)

BAV, Bicuspid aortic valve; *CI*, confidence interval; *TAV*, tricuspid aortic valve.

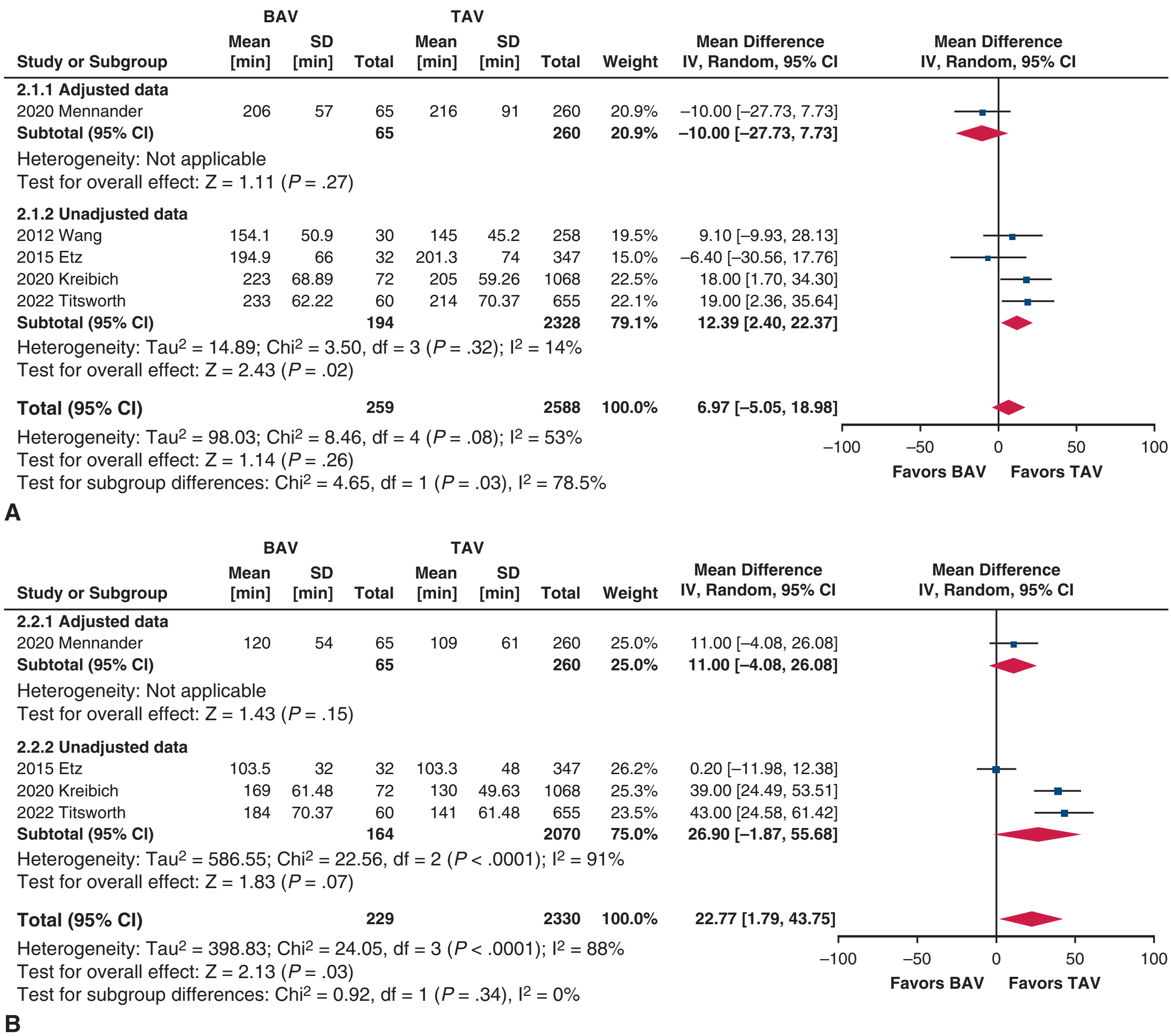

FIGURE 2. Forest plots of the duration of cardiopulmonary bypass (A), aortic cross-clamp (B), and hypothermic circulatory arrest (C) in patients with bicuspid aortic valve (*BAV*) and tricuspid aortic valve (*TAV*) undergoing surgical repair of acute type A aortic dissection, using a random-effects model. The *left portions of the figure* show the studies analyzed with their corresponding weighted mean difference and 95% confidence interval (*CI*). *IV*, Inverse variance; *SE*, standard error.

procedures (Figure E2, *C* and *D*). Definitions of aortic root replacement and aortic valve resuspension are provided in Table E5.

Regarding aortic arch procedures, the ratio of patients undergoing isolated ascending aortic repair was relatively higher in the BAV group, but the difference was not statistically significant (OR, 1.45; 95% CI, 0.99-2.14; $P = .06$) (Figure E3, *A*). Similarly, the ratio of patients needing hemiarch repair was similar, at 46.8% for the BAV group and 46.4% for the TAV group (OR, 1.08; 95% CI, 0.81-1.45; $P = .60$) (Figure E3, *B*). On the other hand, extended arch repair was performed in 18.0% of BAV patients and 26.3% of TAV patients, with a significantly higher rate in the BAV group (OR, 0.69; 95% CI, 0.49- 0.99; $P = .04$) (Figure E3, *C*).

Intraoperative data. The durations of CPB, XCL, and HCA were compared between BAV and TAV patients. Our analysis revealed a similar duration of CPB in the 2 groups (WMD, 6.97 minutes; 95% CI, −5.05 to 18.98 minutes; $P = .26$) (Figure 2, *A*). However, XCL time was significantly longer with BAV-ATAAD repair (WMD, 22.77 minutes; 95% CI, 1.79-43.75 minutes;

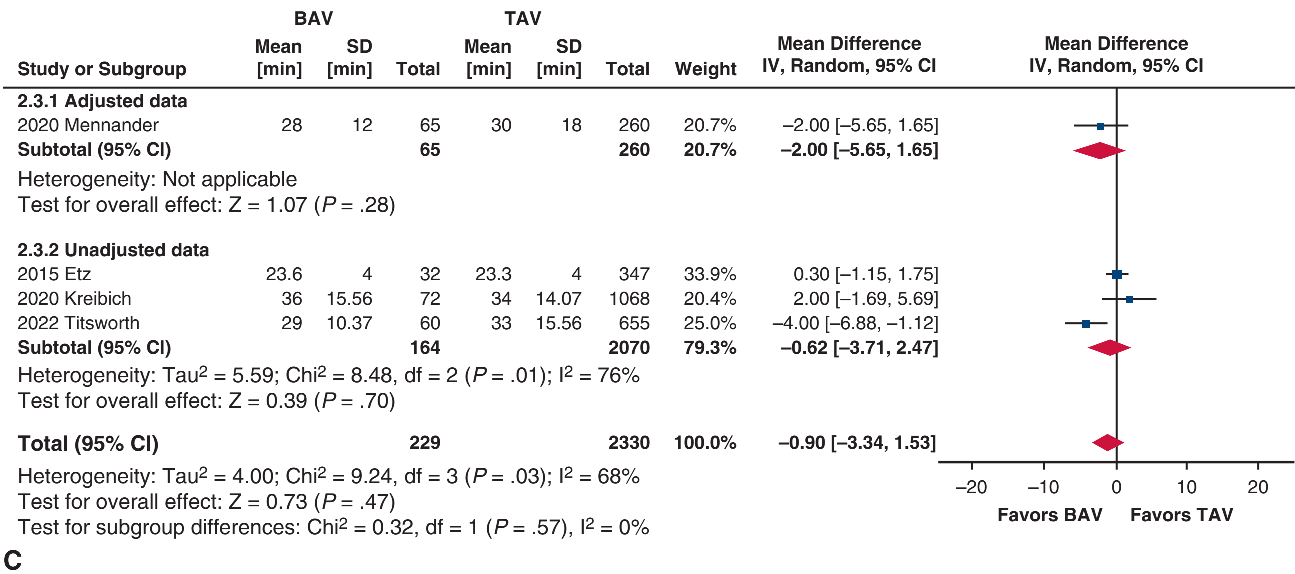

FIGURE 2. (*continued*).

P = .03) (Figure 2, *B*). The duration of HCA was similar in the 2 groups (Figure 2, *C*).

Perioperative outcomes. Perioperative mortality following repair was similar in the 2 groups (RR, 1.20; 95% CI, 0.74-1.94; P = .46) (Figure E4, *A*). Our analysis also demonstrated similar rates of myocardial infarction and stroke following repair in the 2 groups (Figure E4, *B* and *C*).

Postoperative outcomes. All-cause mortality following surgical repair with $\geq$1 year follow-up was better in the BAV group compared to the TAV group (HR, 0.68; 95% CI, 0.50-0.92; P = .01) (Figure 3). The total reoperation rate was similar in the 2 groups (HR, 0.91; 95% CI, 0.52-1.58; P = .74) (Figure 4, *A*), as were the distal aortic reoperation rate (HR, 1.59; 95% CI, 0.91-2.76; P = .10) (Figure 4, *B*) and the proximal aortic reoperation rate (Figure E4, *D*).

Additional Analyses

The results of leave-one-out analyses are summarized as forest plots (Figure E5). We confirmed the reproducibility of all the outcomes. Meta-regression analyses pertaining to the age differences between BAV and TAV patients, summarized in Figure E6, demonstrated no significant differences. Publication bias was assessed using funnel plots (Figure E7), which showed no evidence of publication bias.

DISCUSSION

Our study including 3701 patients is the first reported meta-analysis to compare the characteristics and outcomes

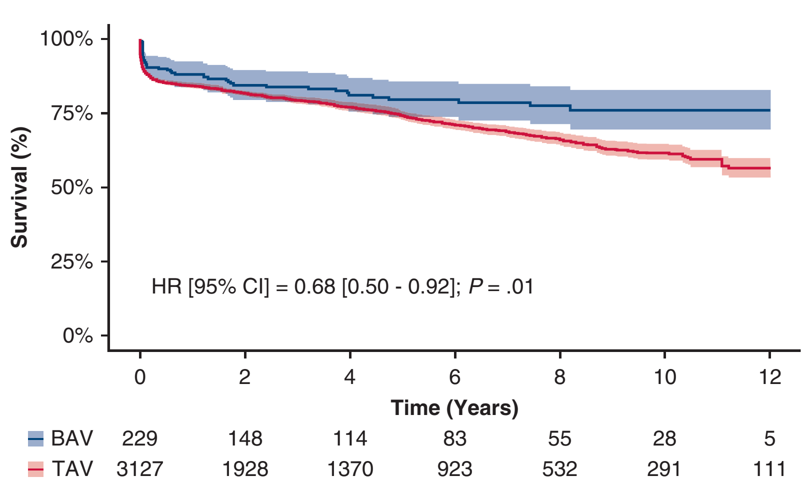

FIGURE 3. Kaplan-Meier analysis of all-cause mortality in bicuspid aortic valve (*BAV*) and tricuspid aortic valve (*TAV*) patients. *Solid lines* represent the estimates, and the *surrounding bands* represent 95% confidence intervals (*CIs*). *HR*, Hazard ratio.

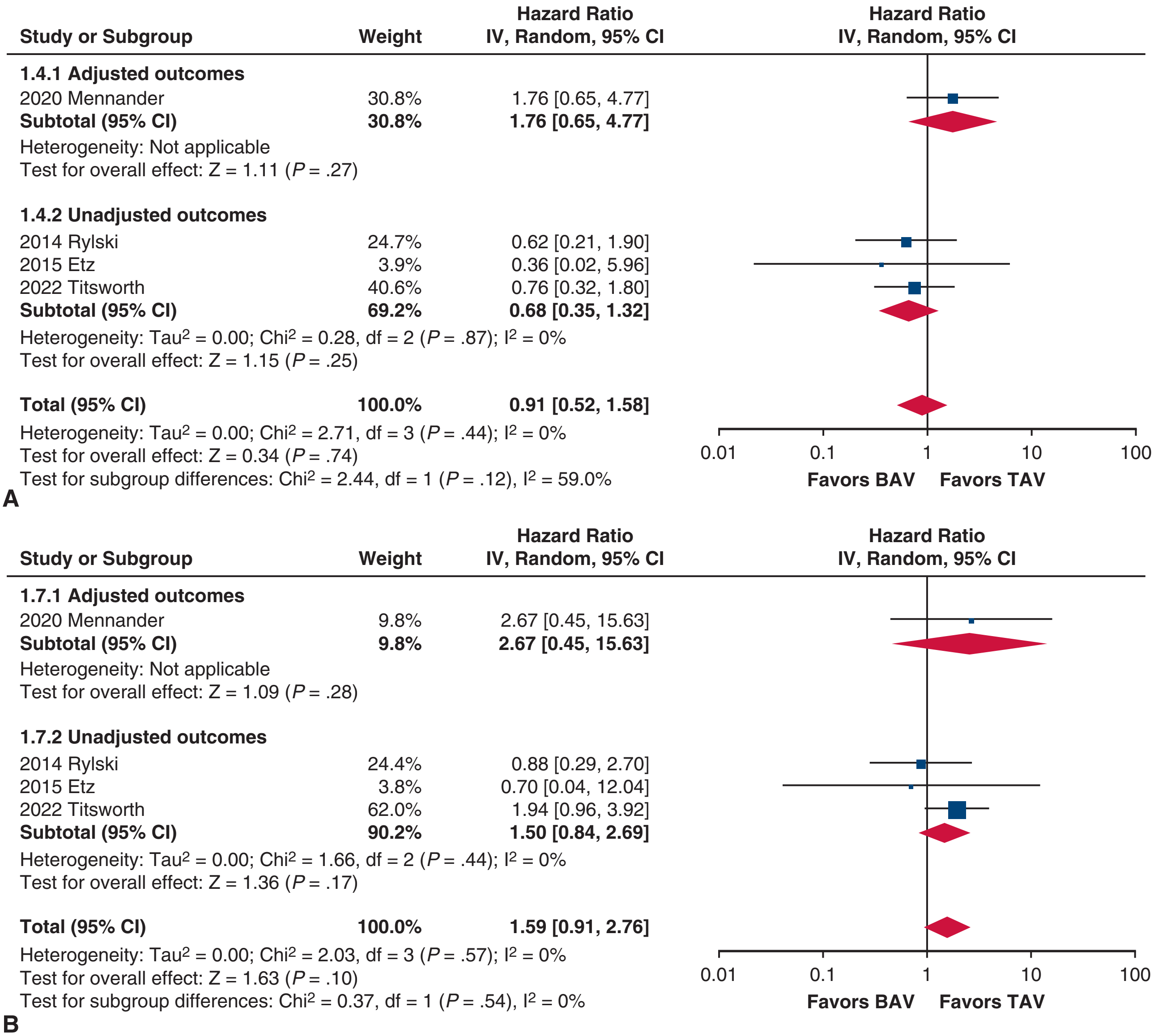

FIGURE 4. Forest plots of all-cause mortality and reoperation rates. Comparisons of reoperations (A) and distal reoperations (B) in bicuspid aortic valve (*BAV*) and tricuspid aortic valve (*TAV*) patients with acute type A aortic dissection using a random-effects model. The *left portions of the figures* show the studies analyzed with their corresponding hazard ratio (HR) and 95% confidence interval (*CI*). The *right portions* show a forest plot of the data. The *horizontal lines* represent the values within the 95% CI of the underlying effects. The *vertical line* indicates an HR of 1. *IV*, Inverse variance.

of ATAAD in patients with BAV and patients with TAV (Figure 5). Our analysis demonstrated better survival in BAV patients following surgical repair of ATAAD but similar aortic reoperation rates in the 2 groups. Furthermore, our analysis confirmed that BAV patients experienced ATAAD at a younger age and with larger preoperative ascending aorta diameters. Analysis of intraoperatively performed procedures showed that BAV patients were more likely to require aortic root replacement, whereas TAV patients were more likely to undergo aortic valve resuspension. Concerning aortic arch procedures, BAV patients were less likely to undergo an extended arch replacement, whereas ratios of hemiarch and isolated ascending aortic repair were similar in the 2 groups.

ATAAD occurred roughly 7 years earlier in BAV patients compared to TAV patients, consistent with previous reports.[20,21] The preoperative ascending aorta diameter was approximately 7 mm larger in BAV patients compared to TAV patients, as reported previously.[7] Underlying proximal aortopathy may predispose BAV patients to ATAAD formation at a younger age, even in the absence of cardiovascular risk factors.[7,28]

Our study revealed different proximal aortic procedures in the BAV and TAV patient groups. BAV patients more

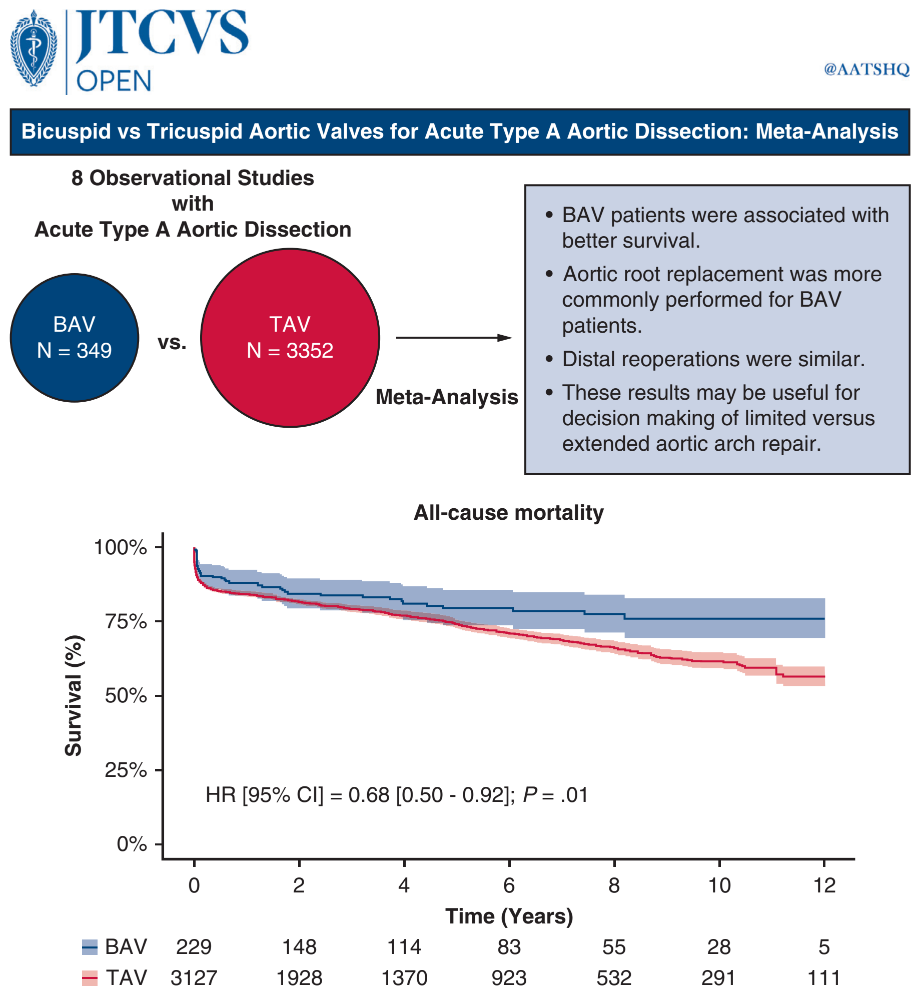

FIGURE 5. The meta-analysis of 8 observational studies comparing bicuspid aortic valve (*BAV*) and tricuspid aortic valve (*TAV*) patients with acute type A aortic dissection, showing better survival in the BAV group. *HR*, Hazard ratio; *CI*, confidence interval.

frequently underwent aortic root replacement, whereas TAV patients were more likely to undergo aortic valve resuspension. This phenomenon could be driven by the larger aortic root and ascending aorta diameters in BAV patients.[26] Whereas the choice between the root replacement and aortic valve resuspension technique is dependent on multiple factors, including age, location of entry tear, anatomy, concurrent aortic valve disease, and sickness (ie, presence of malperfusion syndrome, medical comorbidities), of the individual patient, the 2 procedures were associated with similar mortality in a multicenter analysis of BAV-ATAAD patients.[29] However, the association between aortic root status and proximal procedures was beyond the scope of this study, owing to limited data. The longer XCL observed with the BAV group could be attributed to the higher frequency of aortic root replacement procedures in this group. Despite their complexity and longer operative times, procedures including the modified Bentall operation and aortic valve replacement directly replace the abnormal BAV morphology, which has been reported to reduce the aberrant aortic hemodynamics.[30] The observed similarity in perioperative mortality and myocardial infarction rates indicate that aortic root replacement procedures can be safely performed in BAV-ATAAD patients. However, it must be noted that outcomes following ATAAD repair are strongly influenced by the presence of cardiac tamponade, cardiogenic shock, end-organ malperfusion, and the procedural volumes and experiences of the surgeons.[31,32] The articles included in our meta-analysis were published from tertiary centers, and careful interpretation of the data is necessary for low-volume centers.

The analysis of aortic arch procedures revealed comparable ratios of hemiarch repair in the BAV and TAV groups but a higher rate of extended arch replacement in the TAV group. This difference in the prevalence of aggressive arch replacement procedures in TAV patients may be related to the higher ratio of DeBakey type I aortic dissection. This phenomenon could be attributed to the limited distal extent of aortopathy in BAV patients owing to the embryonic origins of smooth muscle cell lineage.[9] Although extended arch replacement was less common in the BAV group, the reoperation rate for the distal aorta were comparable in the 2 groups. Recent research indicates that postoperative distal aortic diameter growth in BAV-ATAAD patients is similar to or progresses more gradually compared to that in the TAV-ATAAD group.[25] These findings imply that the aortic arch can be managed similarly in BAV-ATAAD patients and TAV-ATAAD patients, without the need for extensive aortic arch repair. In contrast, patients with Marfan syndrome need different management strategies for ATAAD, with more extensive arch repair associated with better outcomes.[33] The disparity in management of ATAAD in patients with BAV and Marfan syndrome is an intriguing area for further investigation, given the similar underlying cystic medial degeneration of the aortic wall in the 2 disorders.[34]

The all-cause mortality rates after surgical repair of ATAAD were more favorable in patients with BAV compared to those with TAV. Despite the higher rates of aortic root replacement, the survival in patients with BAV was not endangered in comparison to TAV patients.[24] Apart from the younger age of BAV patients, the differential survival rates could be attributed to distinct pathogenic mechanisms underlying ATAAD in both BAV and TAV patients. The causative factors for ATAAD in BAV patients—namely aberrant blood flow through the valve and reduced tensile strength of the proximal aorta[35]—can be effectively resolved following surgical repair. Conversely, driving factors of TAV-ATAAD, such as hypertension and atherosclerosis, persist after surgical repair.[25] Nonetheless, our results must be interpreted with caution, as the BAV patients were younger and had fewer comorbidities. Regarding the differences in performed surgical procedures, Haunschild and colleagues[27] reported similar mortality rates following aortic root replacement in BAV-ATAAD and TAV-ATAAD patients, although their data were limited to 30-day mortality. Additionally, the influence of dissection location on mortality and other outcomes remains underexplored. Therefore, the precise determinants of observed outcomes in current studies are unclear, and further research is imperative.

It must be noted that aortic/cardiovascular mortality was not measured in this study, owing to the lack of reported outcomes. Given the similar reintervention rates during follow-up in the 2 groups, the observed favorable mortality in the BAV group must be interpreted with caution. Future studies regarding all-cause and aortic mortality rates with longer follow-up and adherence to guideline-recommended follow-up imaging strategies are mandated. Moreover, only 2 studies reported propensity score–matched results, and other studies reported data without considering potential risk factors for adverse outcomes.[24,27]

Limitations

This study has several significant limitations. Despite the high prevalence of BAV, the number of BAV patients needing surgical repair of an ATAAD is relatively small, and thus only retrospective studies were available for the present investigation. However, it would be difficult to perform a randomized control study in this patient group from both a clinical and an ethical standpoint. Second, there is heterogeneity in the indications for operations/reoperations and variations in surgical techniques among studies. Third, the baseline characteristics of the BAV and TAV groups differed, and only 2 studies reported outcomes from propensity score–matched analysis.[24,27] However, the baseline characteristics of the 2 groups differed drastically in the clinical setting as well, and the reported data can be translated into clinical practice despite the baseline differences. To address this limitation, future large-scale studies using adjustment techniques such as propensity score matching are mandated. ATAAD is associated with a high mortality rate, and death is a competing event for outcomes during follow-up.[24] The limited number of reports in the literature led to the inclusion of only a few studies for each outcome analysis, potentially resulting in the significant heterogeneity observed in this study. Therefore, given the limited number of studies in this meta-analysis, the results should be interpreted with caution. Potential overestimation or underestimation of effect sizes may exist. In addition, although we found differences in operative techniques between our 2 study groups, we were unable to account for factors including the entry point of the dissection. There are limited existing data on aortic root morphology and dissection entry points. It must be noted that the choice of operative technique is influenced by a multitude of factors, including patient anatomy and surgeon preference.

Finally, in the analysis of mid-term data, including reintervention rate, the combined HRs were based on data with varying follow-up periods. This heterogeneity in follow-up duration introduced the potential for bias in the estimated risk of reintervention. Furthermore, reconstruction of time-to-event data at the individual level from KM curves might have introduced bias. To mitigate this, high-resolution KM curves were used for the analysis with a relatively reliable methodology.[18] However, despite these precautions, the potential for bias underscores the inherent limitations of this approach. Therefore, careful interpretation of results is mandated. Future large-scale investigations are warranted to validate the outcomes of this analysis.

CONCLUSIONS

This meta-analysis reveals that patients with BAV experience ATAAD at a younger age compared to TAV patients. Notably, survival following ATAAD was better in BAV patients, although the rate of reoperation was comparable in the 2 groups. Moreover, the BAV patients frequently underwent aortic root replacement for proximal aortic repair, while management of the distal aorta shows that BAV patients less frequently required extended arch repairs. These findings suggest that the presence of BAV alone does not inherently warrant extensive aortic arch repair in the context of ATAAD. Further studies are imperative to confirm these findings.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author on reasonable request.

Conflict of Interest Statement

Dr Fukuhara serves as a consultant for Terumo Aortic, Artivion, Medtronic, and Edwards Lifesciences. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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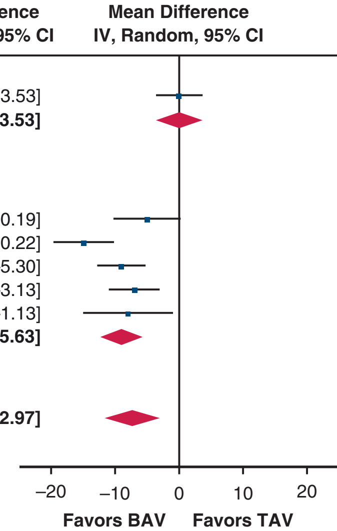
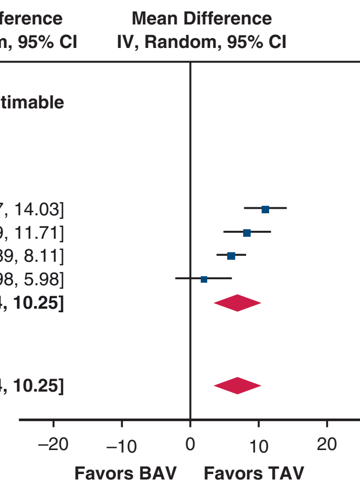
Key Words: acute type A aortic dissection, bicuspid aortic valve, tricuspid aortic valve

Study or Subgroup	BAV Mean [years]	BAV SD [years]	BAV Total	TAV Mean [years]	TAV SD [years]	TAV Total	Weight	Mean Difference IV, Random, 95% CI
2.4.1 Adjusted data								
2020 Mennander	55	13	65	55	13	260	18.2%	0.00 [−3.53, 3.53]
Subtotal (95% CI)			**65**			**260**	**18.2%**	**0.00 [−3.53, 3.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.00 (*P* = 1.00)								
2.4.2 Unadjusted data								
2012 Wang	46	14	30	51	11	258	15.9%	−5.00 [−10.19, 0.19]
2015 Etz	46.7	13	32	61.6	12	347	16.6%	−14.90 [−19.58, −10.22]
2020 Kreibich	54	15.56	72	63	14.81	1068	18.0%	−9.00 [−12.70, −5.30]
2022 Titsworth	54	14.81	60	61	12.59	655	17.8%	−7.00 [−10.87, −3.13]
2023 Della Corte	59	13	15	67	12	142	13.5%	−8.00 [−14.87, −1.13]
Subtotal (95% CI)			**209**			**2470**	**81.8%**	**−8.85 [−12.07, −5.63]**
Heterogeneity: $Tau^2 = 7.61$; $Chi^2 = 9.49$, df = 4 ($P = .05$); $I^2 = 58\%$								
Test for overall effect: Z = 5.39 ($P < .00001$)								
Total (95% CI)			**274**			**2730**	**100.0%**	**−7.22 [−11.46, −2.97]**
Heterogeneity: $Tau^2 = 22.54$; $Chi^2 = 27.67$, df = 5 ($P < .0001$); $I^2 = 82\%$								
Test for overall effect: Z = 3.33 ($P = .0009$)								
Test for subgroup differences: $Chi^2 = 13.17$, df = 1 ($P = .0003$), $I^2 = 92.4\%$								



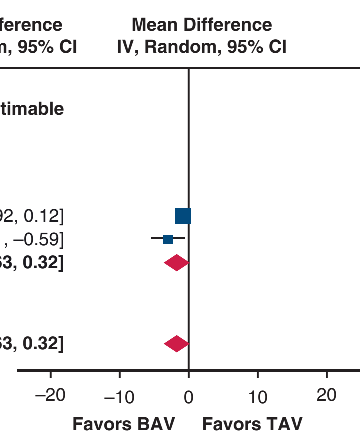
A

Study or Subgroup	BAV Mean [mm]	BAV SD [mm]	BAV Total	TAV Mean [mm]	TAV SD [mm]	TAV Total	Weight	Mean Difference IV, Random, 95% CI
2.5.1 Adjusted data								
Subtotal (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
2.5.2 Unadjusted data								
2012 Wang	59	8.15	30	48	6.67	258	25.4%	11.00 [7.97, 14.03]
2015 Etz	61.5	9	32	53.2	13	347	24.1%	8.30 [4.89, 11.71]
2020 Kreibich	56	8.89	72	50	8.15	1068	28.5%	6.00 [3.89, 8.11]
2023 Della Corte	53	7	15	51	11	142	22.0%	2.00 [−1.98, 5.98]
Subtotal (95% CI)			**149**			**1815**	**100.0%**	**6.94 [3.64, 10.25]**
Heterogeneity: $Tau^2 = 8.82$; $Chi^2 = 14.20$, df = 3 ($P = .003$); $I^2 = 79\%$								
Test for overall effect: Z = 4.11 ($P < .0001$)								
Total (95% CI)			**149**			**1815**	**100.0%**	**6.94 [3.64, 10.25]**
Heterogeneity: $Tau^2 = 8.82$; $Chi^2 =14.20$, df = 3 ($P = .003$); $I^2 = 79\%$								
Test for overall effect: Z = 4.11 ($P < .0001$)								
Test for subgroup differences: Not applicable								



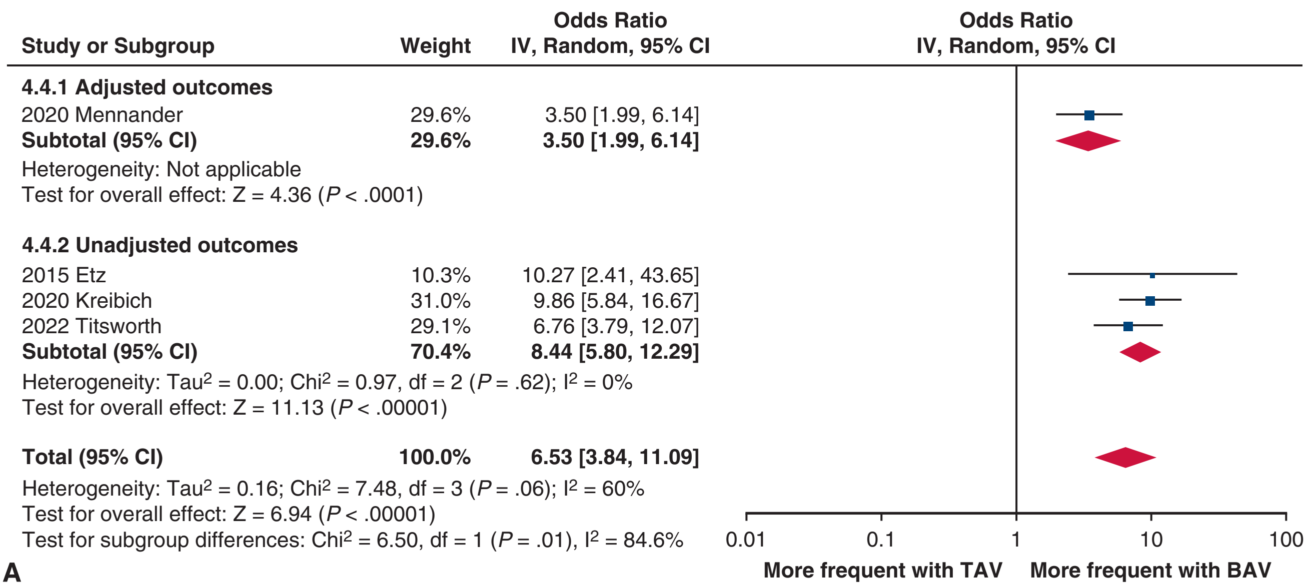
B

Study or Subgroup	BAV Mean [mm]	BAV SD [mm]	BAV Total	TAV Mean [mm]	TAV SD [mm]	TAV Total	Weight	Mean Difference IV, Random, 95% CI
2.6.1 Adjusted data								
Subtotal (95% CI)			**0**			**0**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
2.6.2 Unadjusted data								
2022 Titsworth	34.1	3.7	60	35	5.19	655	64.2%	−0.90 [−1.92, 0.12]
2023 Della Corte	41	4	15	44	8	142	35.8%	−3.00 [−5.41, −0.59]
Subtotal (95% CI)			**75**			**797**	**100.0%**	**−1.65 [−3.63, 0.32]**
Heterogeneity: $Tau^2 = 1.31$; $Chi^2 = 2.47$, df = 1 ($P = .12$); $I^2 = 59\%$								
Test for overall effect: Z = 1.64 ($P = .10$)								
Total (95% CI)			**75**			**797**	**100.0%**	**−1.65 [−3.63, 0.32]**
Heterogeneity: $Tau^2 = 1.31$; $Chi^2 = 2.47$, df = 1 ($P = .12$); $I^2 = 59\%$								
Test for overall effect: Z = 1.64 ($P = .10$)								
Test for subgroup differences: Not applicable								



C

FIGURE E1. Forest plot assessment of baseline characteristics. Comparisons of baseline age (A) and preoperative diameters of the ascending aorta (B) and aortic arch (C) for bicuspid aortic valve (*BAV*) and tricuspid aortic valve (*TAV*) patients with acute type A aortic dissection undergoing surgical repair, using a random-effects model. The *left portions of the figures* show the studies analyzed with their corresponding weighted mean difference and 95% confidence interval (*CI*). *IV*, Inverse variance.



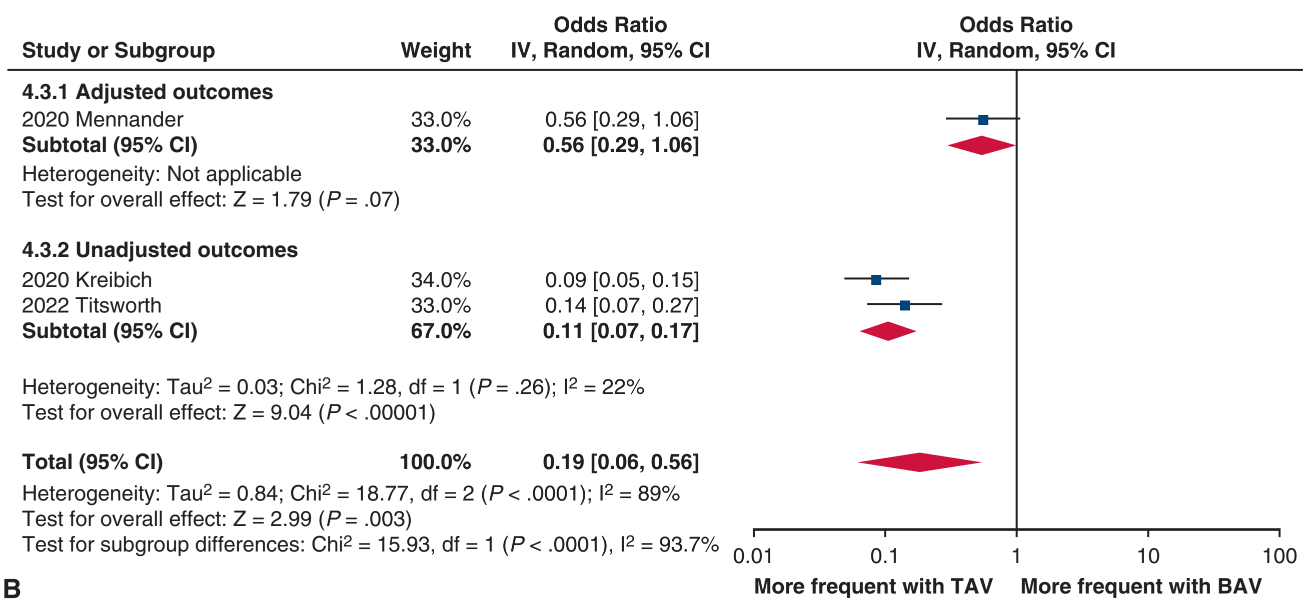
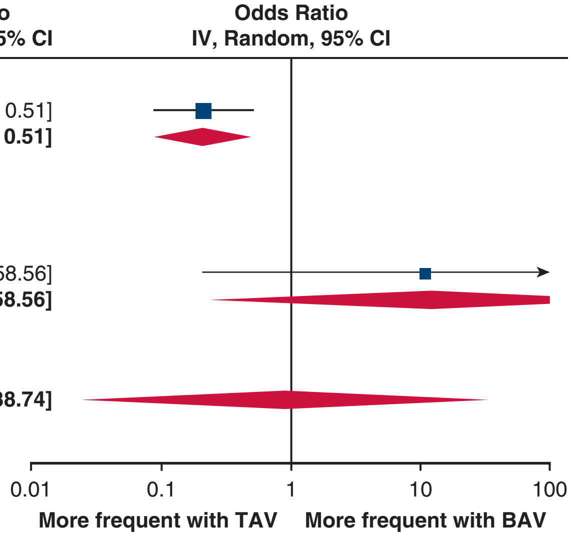


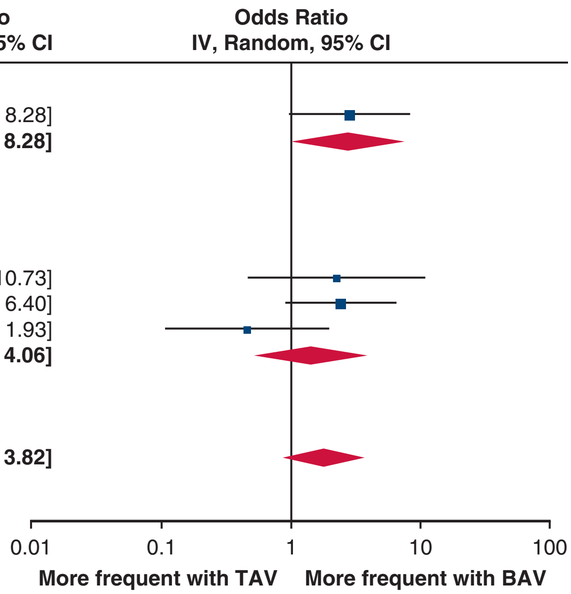
FIGURE E2. Forest plot assessment of intraoperatively performed procedures. Comparisons of the ratios of aortic root replacement (A), aortic repair (B), (C) no proximal repair, and (D) aortic valve replacement for bicuspid aortic valve (*BAV*) and tricuspid aortic valve (*TAV*) patients with acute type A aortic dissection undergoing surgical repair, using a random-effects model. The *left portions of the figure* show the studies analyzed with their corresponding odds ratio (OR) and 95% confidence interval (*CI*). *IV*, Inverse variance.

Study or Subgroup	log [Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
4.1.1 Adjusted outcomes				
2020 Mennander	−1.5461	0.4486	62.5%	0.21 [0.09, 0.51]
Subtotal (95% CI)			**62.5%**	**0.21 [0.09, 0.51]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 3.45 (P = .0006)				
4.1.2 Unadjusted outcomes				
2022 Titsworth	2.3823	2.0118	37.5%	10.83 [0.21, 558.56]
Subtotal (95% CI)			**37.5%**	**10.83 [0.21, 558.56]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 1.18 (P = .24)				
Total (95% CI)			**100.0%**	**0.93 [0.02, 38.74]**
Heterogeneity: Tau^2 = 5.59; Chi^2 = 3.63, df = 1 (P = .06); I^2 = 72%				
Test for overall effect: Z = 0.04 (P = .97)				
Test for subgroup differences: Chi^2 = 3.63, df = 1 (P = .06), I^2 = 72.5%				



C

Study or Subgroup	log [Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
4.2.1 Adjusted outcomes				
2020 Mennander	1.0425	0.5465	29.5%	2.84 [0.97, 8.28]
Subtotal (95% CI)			**29.5%**	**2.84 [0.97, 8.28]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 1.91 (P = .06)				
4.2.2 Unadjusted outcomes				
2015 Etz	0.8094	0.7977	17.7%	2.25 [0.47, 10.73]
2020 Kreibich	0.8821	0.4971	32.9%	2.42 [0.91, 6.40]
2022 Titsworth	−0.7841	0.7353	19.9%	0.46 [0.11, 1.93]
Subtotal (95% CI)			**70.5%**	**1.44 [0.51, 4.06]**
Heterogeneity: Tau^2 = 0.40; Chi^2 = 3.78, df = 2 (P = .15); I^2 = 47%				
Test for overall effect: Z = 0.70 (P = .49)				
Total (95% CI)			**100.0%**	**1.79 [0.84, 3.82]**
Heterogeneity: Tau^2 = 0.20; Chi^2 = 4.58, df = 3 (P = .21); I^2 = 34%				
Test for overall effect: Z = 1.52 (P = .13)				
Test for subgroup differences: Chi^2 = 0.79, df = 1 (P = .37), I^2 = 0%				



D

FIGURE E2. (*continued*).

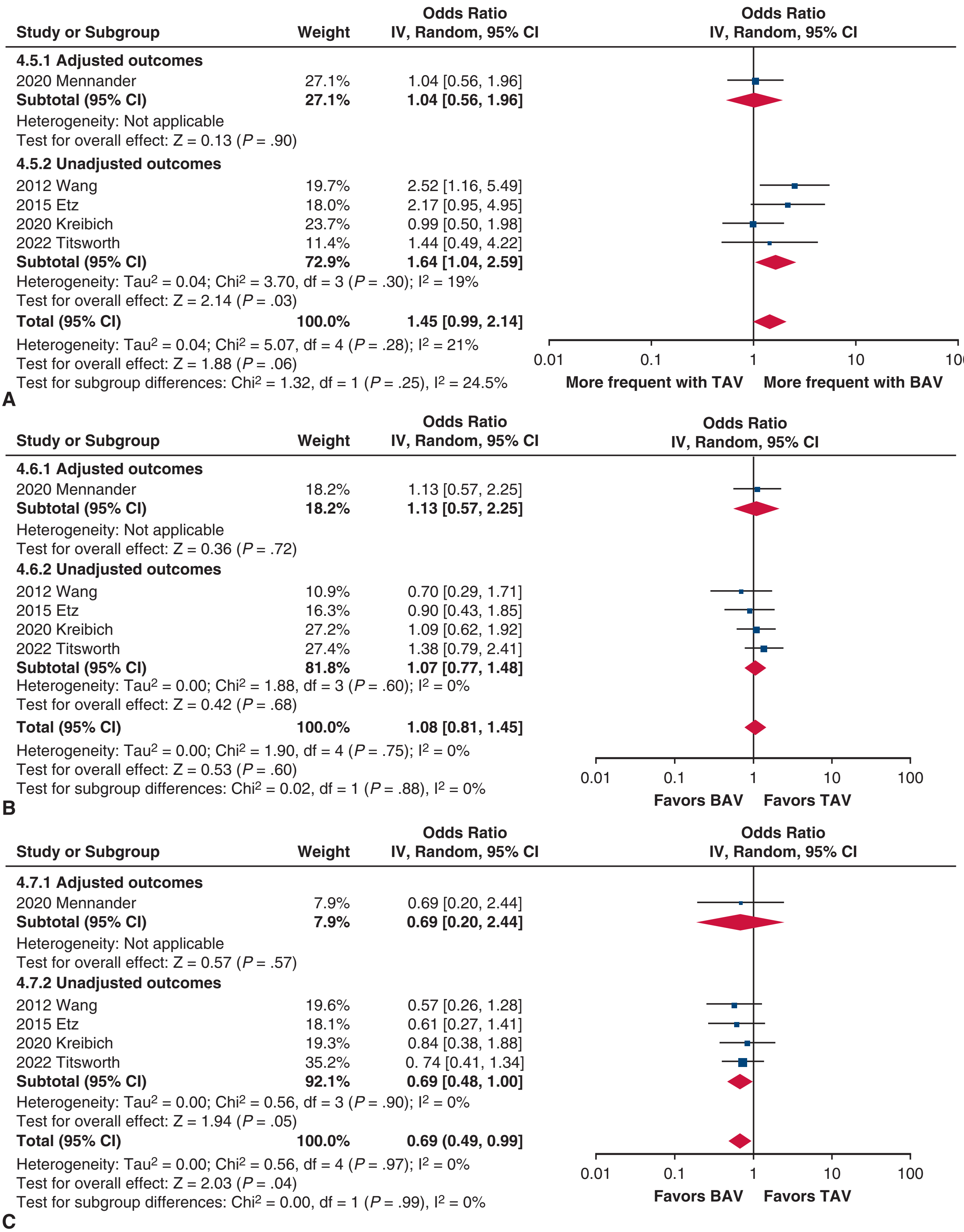


FIGURE E3. Forest plot assessment of intraoperatively performed procedures. Comparisons of the ratios of isolated ascending aortic repair (A), hemiarch repair (B), and extended arch repair (C) for bicuspid aortic valve (*BAV*) and tricuspid aortic valve (*TAV*) patients with acute type A aortic dissection undergoing surgical repair, using a random-effects model. The *left portion of the figure* shows the studies analyzed with their corresponding odds ratio (OR) and 95% confidence interval (*CI*). *IV*, Inverse variance.

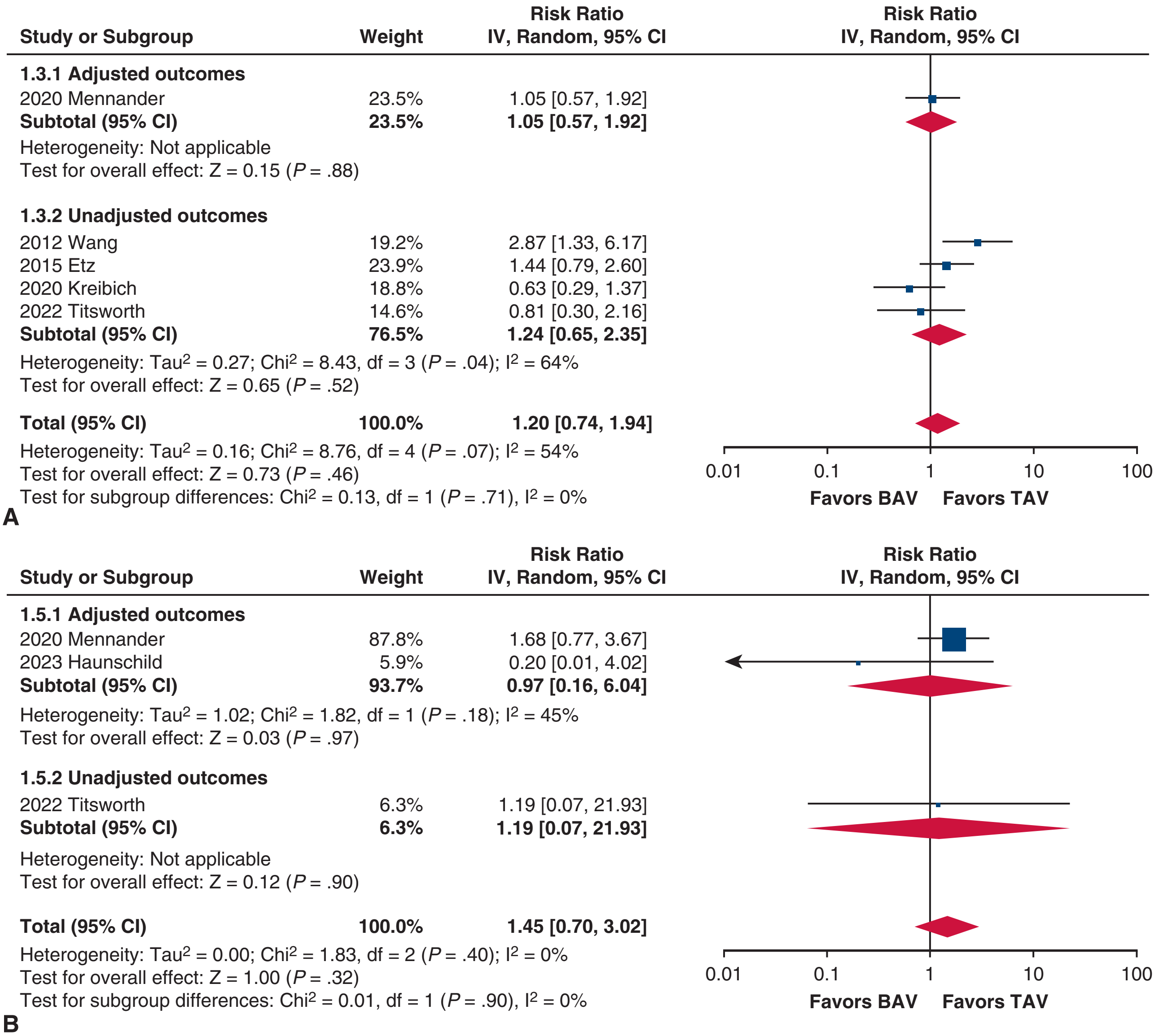
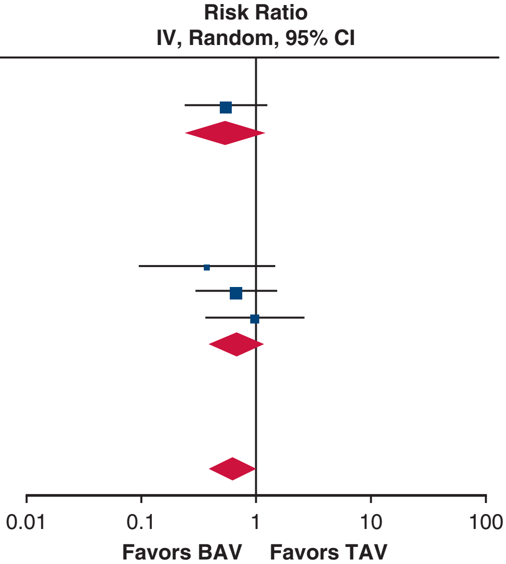


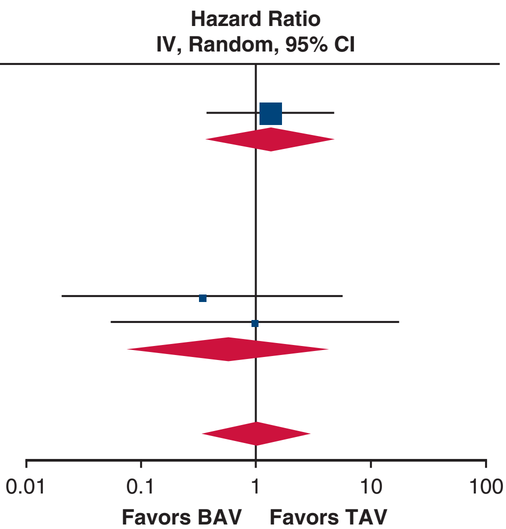
FIGURE E4. Forest plot for myocardial infarction and perioperative death rates. Comparisons of perioperative mortality (A), myocardial infarction (B), stroke (C), and proximal aortic reoperations (D) for bicuspid aortic valve (*BAV*) and tricuspid aortic valve (*TAV*) patients with acute type A aortic dissection undergoing surgical repair using a random-effects model. The *left portions of the figure* show the studies analyzed with their corresponding risk ratio (RR) and 95% confidence interval (*CI*). The *right portion of the figure* shows a forest plot of the data. The *horizontal lines* represent the values within the 95% CI of the underlying effects. The *vertical line* indicates an RR of 1. *IV*, Inverse variance.

Study or Subgroup	Weight	Risk Ratio IV, Random, 95% CI
1.2.1 Adjusted outcomes		
2020 Mennander	32.4%	0.55 [0.24, 1.22]
Subtotal (95% CI)	**32.4%**	**0.55 [0.24, 1.22]**
Heterogeneity: Not applicable		
Test for overall effect: Z = 1.47 (*P* = .14)		
1.2.2 Unadjusted outcomes		
2015 Etz	11.4%	0.37 [0.10, 1.46]
2020 Kreibich	34.6%	0.67 [0.31, 1.46]
2022 Titsworth	21.7%	0.97 [0.36, 2.61]
Subtotal (95% CI)	**67.6%**	**0.68 [0.39, 1.20]**
Heterogeneity: Tau^2 = 0.00; Chi^2 = 1.24, df = 2 (*P* = .54); I^2 = 0%		
Test for overall effect: Z = 1.33 (*P* = .18)		
Total (95% CI)	**100.0%**	**0.64 [0.40, 1.01]**
Heterogeneity: Tau^2 = 0.00; Chi^2 = 1.44, df = 3 (*P* = .70); I^2 = 0%		
Test for overall effect: Z = 1.93 (*P* = .05)		
Test for subgroup differences: Chi^2 = 0.20, df = 1 (*P* = .65), I^2 = 0%		



C

Study or Subgroup	Weight	Hazard Ratio IV, Random, 95% CI
1.10.1 Adjusted outcomes		
2020 Mennander	71.1%	1.33 [0.37, 4.79]
Subtotal (95% CI)	**71.1%**	**1.33 [0.37, 4.79]**
Heterogeneity: Not applicable		
Test for overall effect: Z = 0.44 (*P* = .66)		
1.10.2 Unadjusted outcomes		
2014 Rylski	14.9%	0.34 [0.02, 5.56]
2022 Titsworth	14.0%	0.98 [0.05, 17.47]
Subtotal (95% CI)	**28.9%**	**0.57 [0.08, 4.22]**
Heterogeneity: Tau^2 = 0.00; Chi^2 = 0.26, df = 1 (*P* = .61); I^2 = 0%		
Test for overall effect: Z = 0.55 (*P* = .58)		
Total (95% CI)	**100.0%**	**1.04 [0.35, 3.06]**
Heterogeneity: Tau^2 = 0.00; Chi^2 = 0.76, df = 2 (*P* = .68); I^2 = 0%		
Test for overall effect: Z = 0.07 (*P* = .94)		
Test for subgroup differences: Chi^2 = 0.49, df = 1 (*P* = .48), I^2 = 0%		



D

FIGURE E4. (*continued*).

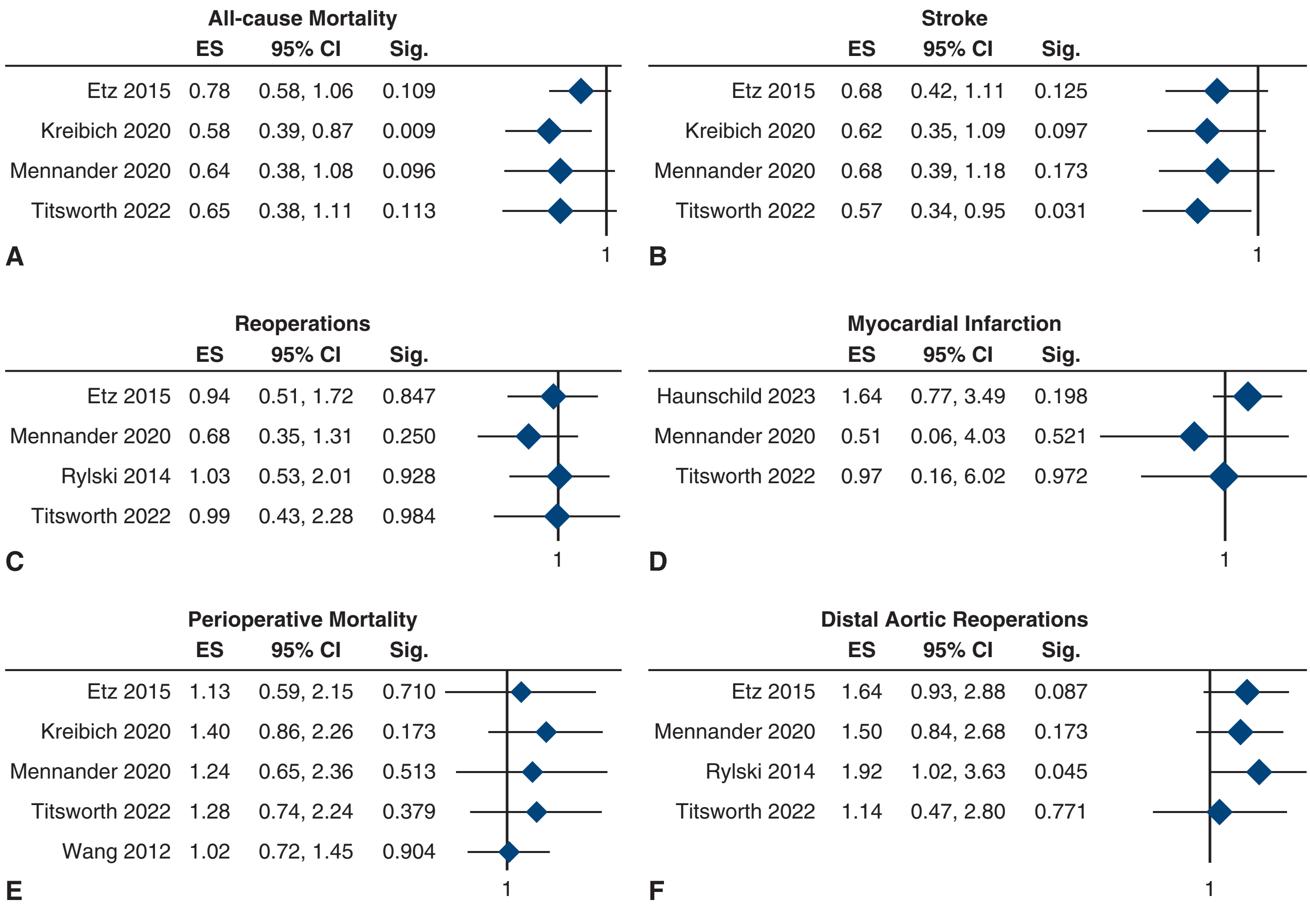


FIGURE E5. Sensitivity analyses by leave-one-out analysis. The *left portion of the figure* shows the studies analyzed. (A) All-cause mortality. (B) Stroke rate. (C) Reoperation rate. (D) Myocardial infarction rate. (E) Perioperative mortality. (F) Distal aortic reoperation rate. The *vertical line* indicates a hazard ratio (HR) of 1. The *forest plots* represent the meta-analytic data with removal of 1 study each. *ES*, Effect size; *Sig*, significant difference.

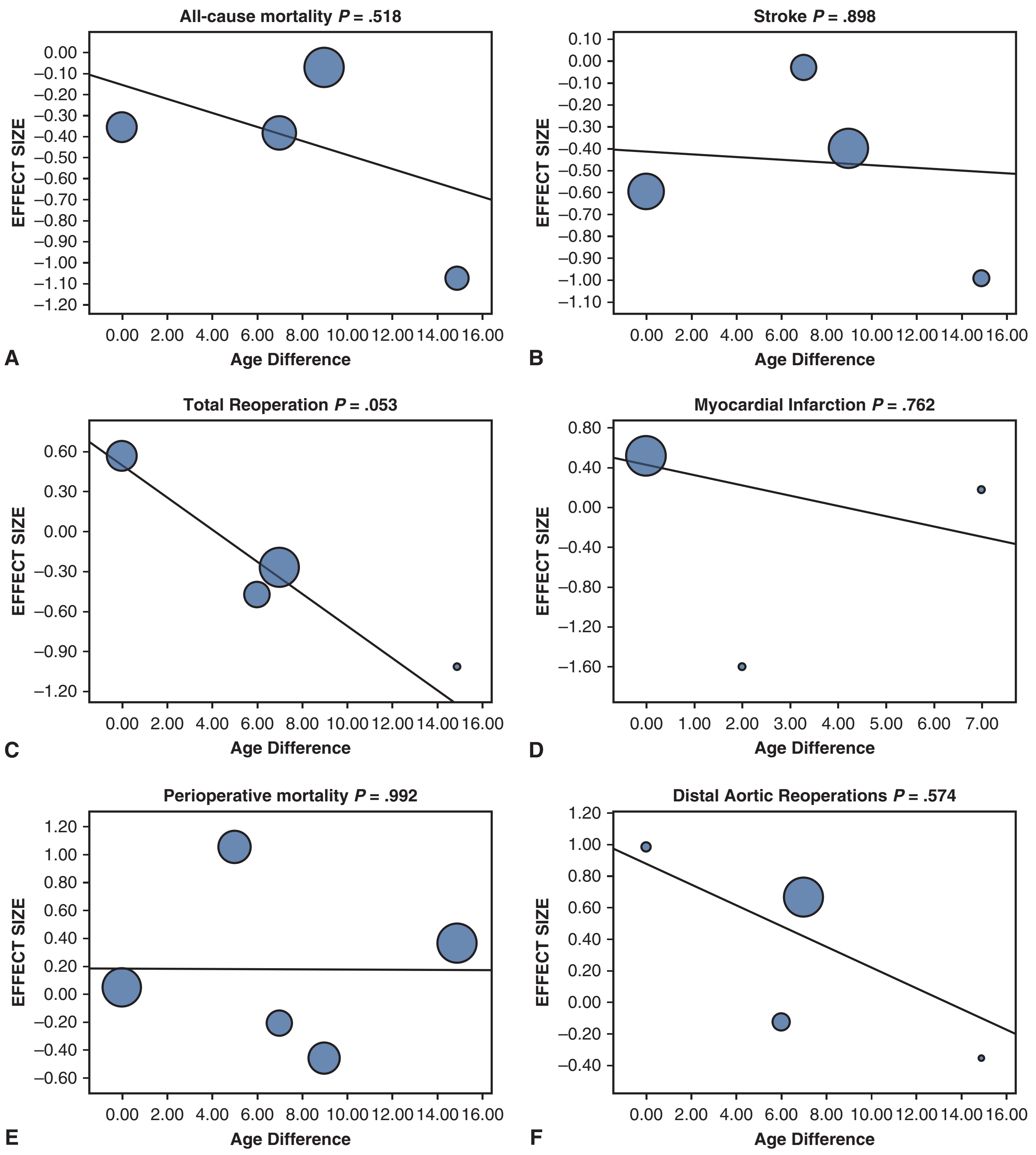


FIGURE E6. Meta-regression analysis results for all-cause mortality (A), stroke (B), total reoperations (C), myocardial infarction (D), perioperative mortality (E), and distal aortic reoperation rate (F).

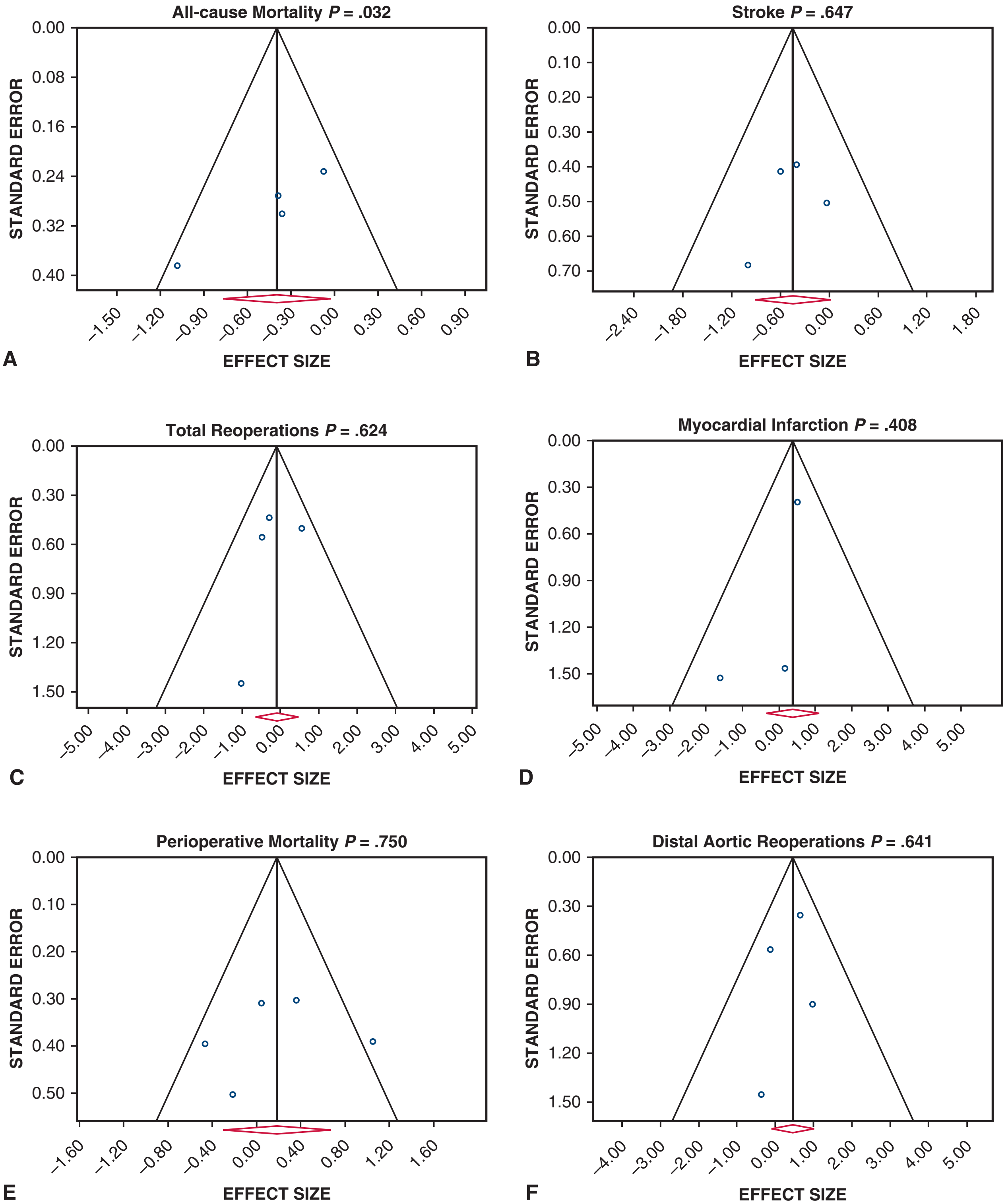


FIGURE E7. Funnel plots for assessing publication bias. Funnel plots for each outcome for all-cause mortality (A), stroke rate (B), reoperation rate (C), myocardial infarction rate (D), perioperative mortality (E), and distal aortic reoperation rate (F).

TABLE E1. Search strategy for MEDLINE

Number	Search	Results
1	"Aortic Dissection"[mh]	20,959
2	"aortic dissection"[tiab]	16,933
3	"type a aortic dissection"[tiab]	3805
4	"acute type a aortic dissection"[tiab]	2043
5	"dissecting aneurysms"[tiab]	1117
6	"Bicuspid Aortic Valve Disease"[mh]	2373
7	"bicuspid aortic valve"[tiab]	4114
8	"bav"[tiab]	2005
9	"bicuspid"[tiab]	5996
10	"patients"[tiab]	6,895,607
11	#1 OR #2 OR #3 OR #4 OR #5	27,498
12	#6 OR #7 OR #8 OR #9	7407
13	#10 AND #11 AND #12	414

TABLE E2. Search strategy for Embase

Number	Search	Results
1	aortic dissection	31,183
2	type a aortic dissection	4873
3	acute type a aortic dissection	2437
4	dissecting aortic aneurysms	2349
5	bicuspid aortic valve	9603
6	Bav	3778
7	bicuspid	11,816
8	patients	10,487,581
9	#1 OR #2 OR #3 OR #4	32,759
10	#5 OR #6 OR #7	12,963
11	#8 AND #9 AND #10	988

TABLE E3. Search strategy for Cochrane Central

Number	Search	Results
1	"Aortic Dissection"[mh]	142
2	"aortic dissection"[tiab]	695
5	"dissecting aneurysms"[tiab]	91
6	"Bicuspid Aortic Valve Disease"[mh]	17
7	"bicuspid aortic valve"[tiab]	72
8	"bav"[tiab]	59
11	#1 OR #2 OR #3	754
12	#4 OR #5 OR #6	105
13	#7 AND #8	8

TABLE E4. Quality assessment based on the Newcastle-Ottawa Scale

Study	Representa-tiveness of exposed cohort	Selection of nonexposed cohort	Ascertain-ment of exposure	Absence of outcome at start of study	Compar-ability of cohorts	Outcome assessment	Length of follow-up	Adequacy of follow-up	NOS score
Della Corte[26]	1	1	1	1	0	1			5
Haunschild[27]	1	1	1	1	2	1			7
Titsworth[25]	1	1	1	1	0	1	1	1	7
Mennander[24]	1	1	1	1	2	1	1	1	9
Kreibich[23]	1	1	1	1	0	1	1	1	7
Etz[22]	1	1	1	1	0	1	1	1	7
Rylski[21]	1	1	1	1	0	1	1	1	7
Wang[20]	1	1	1	1	0	1			5

NOS, Newcastle-Ottawa Scale (range, 1-9).

TABLE E5. Definitions of aortic valve resuspension and root replacement in each study

Author	Valve resuspension	Root replacement
Della Corte[26]	N/A	N/A
Haunschild[27]	N/A	N/A
Titsworth[25]	Root repair	Root replacement
Mennander[24]	Supracoronary graft and aortic valve resuspension	Mechanical Bentall, biological Bentall, David
Kreibich[23]	Valve resuspension	Valved conduit, valve-sparing aortic root replacement
Etz[22]	N/A	Yacoub, David, glue/suture, composite root replacement
Rylski[21]	Aortic valve resuspension	Composite valved graft, valve-sparing aortic root replacement
Wang[20]	N/A	N/A

N/A, Not available.