Featured Article

Aortic root replacement in bicuspid versus tricuspid aortic valve patients

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Background: Concomitant replacement of the aortic root and aortic valve is a widely used treatment strategy in elective patients with aortic valve stenosis and root aneurysm. It is also a strategy frequently employed in patients with acute aortic dissection type A (AADA), involving the aortic root. Although more patients have undergone valve sparing procedures over the past decades, the classic 'modified Bentall technique' remains a valid option, particularly for patients with a bicuspid aortic valve (BAV). We aimed to compare the results of elective and emergency modified Bentall procedures in patients with bicuspid and tricuspid aortic valves (TAVs).

Methods: We retrospectively reviewed our database for patients undergoing either elective or emergency modified Bentall procedures between 2000 and 2018 and identified 827 elective cases (44% BAV) and 258 emergency cases (15% BAV). Analysis of intra- and postoperative outcomes and early mortality was performed. Due to inequality of the groups, a matching analysis was performed.

Results: We found BAV patients to be significantly younger (elective: 58±18 *vs.* 65±14, P<0.001; emergency: 49±17 *vs.* 62±19, P<0.001) and healthier at time of surgery. In the AADA cohort, malperfusion rate was not different between bicuspid and tricuspid patients, however bicuspid AADA patients presented more often with an entry in the aortic root. After matching, procedure times and early outcomes did not differ between the groups, except for significantly higher rates of respiratory failure in elective TAV patients (10% *vs.* 5%, P=0.033). The 30-day mortality was 2% in elective cases and 22% in emergency AADA surgery. A subgroup analysis of elective patients with aortic diameter <55 mm also showed excellent outcomes.

Conclusions: After adjustment for preoperative inequalities, no differences in early mortality and outcomes were found between bicuspid and tricuspid patients receiving elective or emergency modified Bentall surgery.

Keywords: Aortic root aneurysm; acute aortic dissection; aortic valve replacement; bicuspid aortic valve (BAV)

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Introduction

Replacement of the aortic root is necessary in patients with aortic root aneurysms or acute aortic dissection type A (AADA) involving the aortic root, and can be either performed in combination with aortic valve replacement [as described by Bentall and De Bono (1)] or by a valve-sparing approach [using aortic valve reimplantation or remodeling technique (2,3)]. Approximately 1 out of 9 AADA patients is a carrier of a bicuspid aortic valve (BAV), the most common cardiac anomaly affecting up to 2% of the general population (4). In an elective setting the current guidelines treat BAV as an important risk factor for AADA and thoracic aortic aneurysm development, by setting the cut-off diameter for elective replacement 5 mm lower than in patients with a tricuspid aortic valve (TAV) (5). However, several studies have raised doubts about the utilization of the absolute aortic diameter as an ideal risk marker for patients with either BAV or TAV (6).

Elective aortic root replacement is associated with excellent short- and long-term results (7,8) and, as recently published, does not increase the perioperative risk in emergency AADA surgery (9). Little data exists on comparison between BAV and TAV patients undergoing modified Bentall surgery. Our aim was to therefore compare patients with a BAV and TAV receiving either elective (group A) or emergency (group B) concomitant replacement of the aortic valve and root as a modified Bentall procedure. Our data may serve as contemporary benchmark for high-volume expert centers.

Methods

Patient selection

The study was approved by the ethics committee of the medical faculty of the University of Leipzig (#177/15). We retrospectively reviewed our institutional database and included all patients ≥18 years who underwent (I) elective modified Bentall surgery or (II) a modified Bentall procedure in case of AADA at our institution between 2000 and 2018. Exclusion criteria were previous cardiac or aortic surgery, known hereditary connective tissue disorder (e.g., Marfan syndrome, Ehlers-Danlos syndrome), surgery for acute endocarditis, prior cardiac or aortic surgery, and patients without sufficient data about the aortic valve morphology.

All patient charts, echocardiographic data and computed tomography (CT) scans were reviewed by two examiners. Aortic diameter was determined by contrast enhanced CT for aortic root and ascending aorta at the level of the pulmonary artery bifurcation.

Operative technique

All operations were performed via either full median sternotomy or upper J- or T-shaped hemi-sternotomy at the level of the 3rd or 4th intercostal space. In elective cases, cardiopulmonary bypass (CPB) was usually established via distal ascending aorta and right atrium cannulation. In the AADA group, arterial cannulation was performed via axillary cannulation or, infrequently, via femoral cannulation, and venous access was gained via direct cannulation of the atrial appendage. A left ventricular vent was used in all operations, usually via the right superior pulmonary vein. Antegrade application of crystalloid or blood cardioplegia was conducted in most cases, with retrograde cardioplegia used in select patients. In patients with moderate or severe aortic insufficiency, cardioplegia was usually administered directly into the coronary ostia using mushroom- or olive-tipped catheters. According to patient's age and risk profile, standard biological prostheses sewn into a tubular dacron prostheses, xeno- or homograft root prostheses, or commercially available mechanically-valved conduits were used for root replacement. The modified Bentall procedure, routinely utilized at our institution, was just recently described by Khachatryan *et al.* (10).

Statistical analysis

Statistical analysis was performed using R version 4.1.2. (The R Foundation for Statistical Computing), and RStudio 4.1.2. (RStudio: Integrated Development Environment for R, PBC, Boston, USA). Continuous variables were expressed as median and interquartile range (IQR), categorical data presented as counts and percentages throughout the manuscript. Distribution of continuous variables was controlled by means of Shapiro-Wilk test and QQ-plots. Unmatched groups were compared using the Wilcoxon sum rank test, two-sided Fisher's exact test, or Chi-square test, as appropriate.

In the elective cohort, propensity score matching was performed using 1:1 nearest neighbour method with 0.2 calliper. The following covariates were used for the matching in the elective cases: age, gender, body mass index, arterial hypertension, hyperlipidemia, diabetes mellitus, history of smoking, chronic obstructive pulmonary disease (COPD), peripheral arterial disease, coronary artery disease, prior myocardial infarction, prior stroke, preoperative glomerular filtration rate (GFR), preoperative left ventricular ejection fraction (LVEF), New York Heart Association (NYHA) class III–IV heart failure prior to the surgery, American Society of Anesthesiologists (ASA) class, type of the conduit used for the Bentall procedure (mechanical, biological or xeno-/homograft conduit), minimally invasive approach, extension of the aortic replacement [isolated ascending aortic replacement (AAR), hemiarch procedure or extended aortic arch surgery], aortic root enlargement, Morrow procedure, coronary

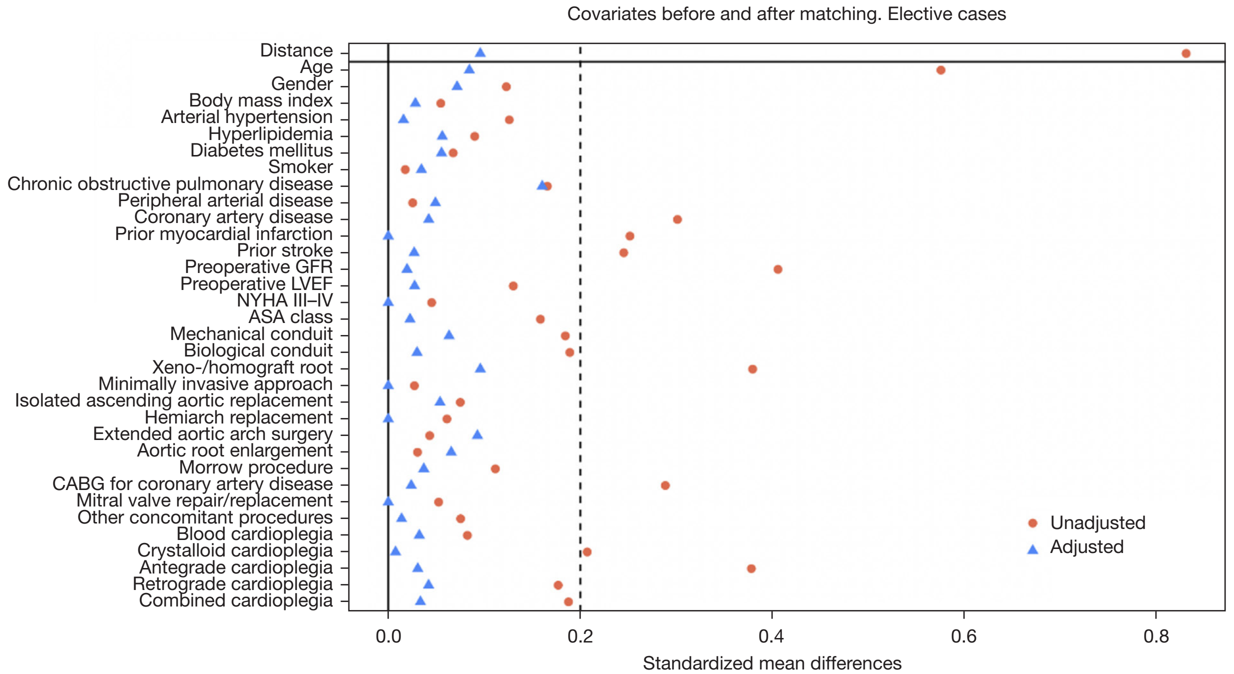

Figure 1 Covariates before and after propensity score matching (elective cases). GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association classification of heart failure; ASA, American Society of Anesthesiologists physical status classification; CABG, coronary artery bypass grafting.

artery bypass grafting (CABG) for coronary artery disease, mitral valve (MV) replacement or repair, other concomitant procedures, type of cardioplegia (blood, crystalloid, antegrade, retrograde or combined), displayed in Figure S1.

In the AADA cases, genetic matching (a form of nearest neighbour matching using generalized Mahalanobis distance) was performed in 1:1 fashion. The following covariates were used for the matching analysis in the AADA cases: age, gender, arterial hypertension, diabetes mellitus, history of smoking, COPD, peripheral arterial disease, coronary artery disease, prior stroke, chronic kidney disease, moderate or severe aortic stenosis (AS), NYHA III–IV class heart failure prior to surgery, preoperative LVEF, type of the conduit used for the Bentall procedure, preoperative malperfusion (coronary, cerebral, visceral or extremity malperfusion), CABG for coronary artery disease, and extended aortic arch surgery.

The covariates included in the propensity score model and genetic matching are presented in *Figures 1,2*.

Missing values (not exceeding 8% of analyzed covariate) were replaced by means of multiple imputations based on Rubin's rules. For comparison of the matched groups, we used the Wilcoxon-signed rank test for continuous, and McNemar's test for categorical data. Statistical significance was set at a P value of ≤0.05 for two-tailed testing.

Results

Patient cohort

Elective Bentall

A total of 827 patients met the inclusion/exclusion criteria, of which 44% had a BAV and 56% a TAV anatomy. Bicuspid patients were approximately 7 years younger (P<0.001) and significantly healthier (less coronary artery disease, less prior stroke and chronic kidney disease) at the time of surgery. A total of 584 patients were successfully matched by 1:1 propensity score matching resulting in two matched groups with no differences in preoperative variables. Characteristics of the matched and unmatched cohort are displayed in *Table 1*. Covariates before and after propensity score matching are displayed in *Figure 1*.

Emergency Bentall

A total of 258 patients admitted for AADA underwent a concomitant replacement of the aortic valve and aortic

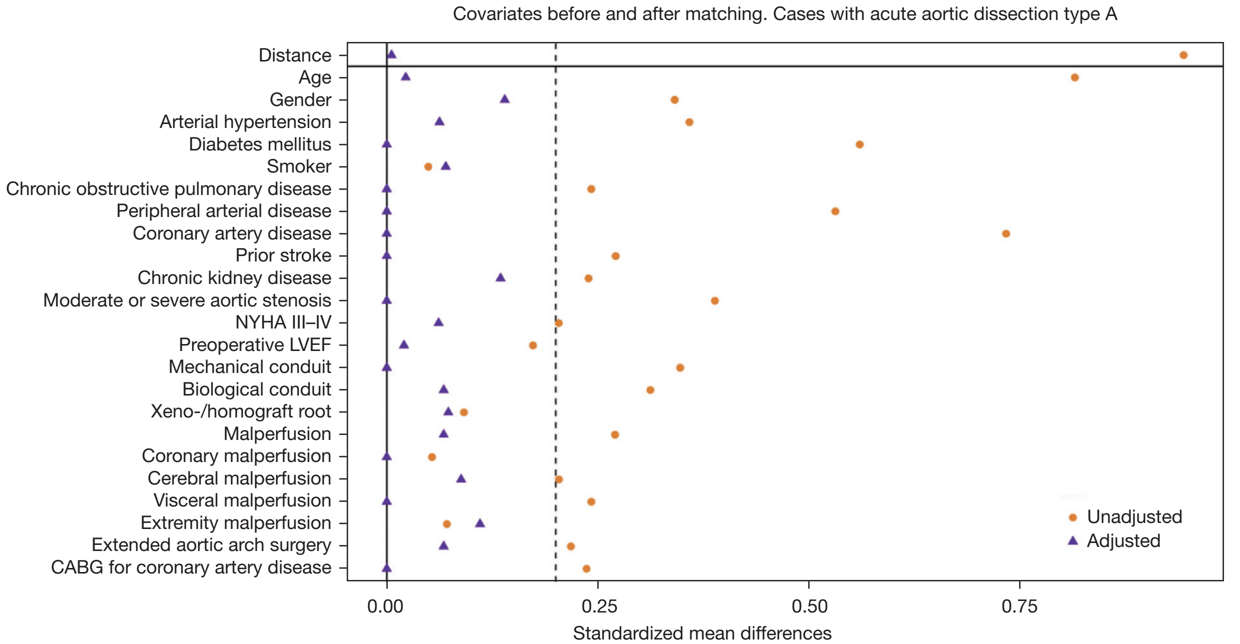

Figure 2 Covariates before and after genetic matching (cases with AADA). NYHA, New York Heart Association classification of heart failure; LVEF, left ventricular ejection fraction; CABG, coronary artery bypass grafting; AADA, acute aortic dissection type A.

root, of which 15% had a BAV and 85% a TAV. Baseline characteristics displayed significant differences in age, with BAV patients being 13 years younger at time of dissection (49±17 *vs.* 62±19 years, P<0.001), previously known arterial hypertension (P=0.01), and preoperative aortic valve stenosis (P=0.005). Preoperative malperfusion rate was not different between bicuspid and tricuspid patients. After adjusting and matching 68 patients, 34 in each group, no differences remained (see *Table 2*). Covariates before and after propensity score matching are displayed in *Figure 2*.

Operative details

Elective Bentall

Prior to matching, significantly more patients with a BAV received a mechanical valve conduit with a bigger prosthesis size (27±2 *vs.* 25±2, P=0.01) than TAV patients. Due to pre-existing co-morbidities, more concomitant CABG was performed in patients with TAV (P<0.001). Crystalloid cardioplegia was used significantly more often in BAV patients, although operative, CPB and aortic cross-clamp times were significantly longer in the TAV group before matching. After matching, no relevant differences remained between the two groups. All intraoperative details of the elective patients before and after matching are displayed in *Table 3*.

Emergency Bentall

As in the elective surgery cohort, significantly more BAV patients received a mechanical valved conduit compared to tricuspid patients prior to matching (54% *vs.* 37%, P=0.04). In the TAV group, more frozen elephant trunk procedures were performed (10% *vs.* 0%, P=0.05), resulting in a significantly longer circulatory arrest (CA) time (P=0.04) (see *Table 4*).

Postoperative outcomes

Elective Bentall

Prior to matching, more TAV patients had a postoperative cerebrovascular accidents and pulmonary complications, but both outcomes were not significantly different after matching. Thirty-day mortality was significantly higher in the tricuspid patients before matching (4% *vs.* 1%, P=0.05). Rate of in-hospital mortality was not different; this contrasts with the causes of death, which differed qualitatively (not formally tested due to low numbers). In the whole cohort, 4 out of 4 in-hospital deaths of BAV patients were due to

Table 1 Preoperative patient characteristics in elective cases

Variables	Unmatched				Matched				SMD
	Total (n=827)	BAV (n=365, 44%)	TAV (n=462, 56%)	P value	Total (n=584)	BAV (n=292, 50%)	TAV (n=292, 50%)	P value	
Age (years)	62±16	58±18	65±14	<0.001	62±15	61±16	62±18	0.28	0.084
Male gender	658 [80]	300 [82]	358 [77]	0.10	468 [80]	238 [82]	230 [79]	0.38	0.072
BMI (kg/m^2)	27±5	27±5	27±5	0.43	27±5	27±5	27±5	0.62	0.028
Arterial hypertension	646 [78]	274 [75]	372 [81]	0.06	462 [79]	230 [79]	232 [79]	0.84	0.016
Hyperlipidemia	342 [41]	142 [39]	200 [43]	0.20	246 [42]	119 [41]	127 [43]	0.50	0.056
Diabetes mellitus	98 [12]	39 [11]	59 [13]	0.36	77 [13]	36 [12]	41 [14]	0.52	0.055
History of smoking	363 [44]	162 [44]	201 [43]	0.80	245 [42]	125 [43]	120 [41]	0.68	0.035
COPD	38 [5]	11[3]	27 [6]	0.05	30 [5]	11 [4]	19 [7]	0.12	0.160
Peripheral arterial disease	495 [60]	221 [61]	274 [59]	0.72	345 [59]	176 [60]	169 [58]	0.53	0.049
Coronary artery disease	145 [18]	44 [12]	101 [22]	<0.001	76 [13]	40 [14]	36 [12]	0.61	0.042
Prior myocardial infarction	51 [6]	13 [4]	38 [8]	0.005	24 [4]	12 [4]	12 [4]	1.00	0.000
Prior stroke	28 [3]	6 [2]	22 [5]	0.01	11 [2]	6 [2]	5 [2]	0.74	0.027
Preoperative GFR (mL/min/1.73 m^2)	95±42	102±44	90±42	<0.001	98±42	97±43	98±40	0.87	0.020
Chronic kidney disease	88 [11]	27 [7]	61 [13]	0.007	54 [9]	27 [9]	27 [9]	1.00	–
Prior dialysis	1 [<1]	0 [0]	1 [<1]	0.37	0 [0]	0 [0]	0 [0]	1.00	–
Preoperative LVEF (%)	60±14	60±11	60±15	0.13	60±13	60±12	60±13	0.60	0.027
NYHA class III–IV	126 [5]	59 [16]	67 [15]	0.51	90 [15]	45 [15]	45 [15]	1.00	0.000
ASA class	2±1	2±1	3±1	0.01	2±1	2±1	2±1	0.75	0.023

Data expressed as n [%] or median ± IQR. BMI, body mass index; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association classification of heart failure; ASA, American Society of Anesthesiologists physical status classification; BAV, bicuspid aortic valve; TAV, tricuspid aortic valve; SMD, standardized mean difference (presented for the matching covariates); IQR, interquartile range.

low cardiac output, whereas of the 17 TAV patients that died in hospital, 57% were due to low cardiac output, 14% major cerebral injury, 14% sepsis, and 7% died of multiorgan failure. Intraoperative death, in-hospital mortality and 30-day mortality rates were not different between the groups. Length of hospital stay was similar after matching with 16 to 17 days in median (see *Table 5*).

Emergency Bentall

In emergency cases, postoperative respiratory failure was present in nearly half of the patients with TAV, compared to 21% in BAV patients (P=0.003). Although in-hospital mortality was not different with 15% and 17% respectively (P=1.0), the causes varied qualitatively between the groups (not formally tested due to low numbers). In the tricuspid group low cardiac output was the cause of death most frequently, whereas bicuspid patients more frequently died from multiorgan failure (1/6 *vs.* 4/38) or major cerebral injury (3/6 *vs.* 13/38). Due to the small patient numbers in the BAV group, these differences cannot be statistically

Table 2 Preoperative patient characteristics in cases with AADA

Variables	Unmatched				Matched				SMD
	Total (n=258)	BAV (n=39, 15%)	TAV (n=219, 85%)	P value	Total (n=68)	BAV (n=34, 50%)	TAV (n=34, 50%)	P value	
Age (years)	60±20	49±17	62±19	<0.001	50±17	49±18	51±15	0.90	0.014
Male	167 [65]	30 [77]	137 [63]	0.084	48 [71]	25 [74]	23 [68]	0.53	0.129
DeBakey type I dissection	179 [69]	25 [64]	154 [70]	0.44	48 [71]	24 [71]	24 [71]	1.00	–
Arterial hypertension	209 [81]	26 [67]	183 [84]	0.01	45 [66]	23 [67]	22 [65]	0.74	0.062
History of smoking	55 [21]	9 [23]	46 [21]	0.83	13 [13]	7 [21]	6 [18]	0.76	0.075
Coronary artery disease	32 [12]	1 [3]	31 [14]	0.060	2 [3]	1 [3]	1 [3]	1.00	0.000
Prior myocardial infarction	16 [6]	1 [3]	15 [7]	0.48	1 [1]	1 [3]	0 [0]	1.00	–
COPD	15 [6]	1 [3]	14 [6]	0.48	2 [3]	1 [3]	1 [3]	1.00	0.000
Prior stroke	16 [6]	1 [3]	15 [7]	0.48	2 [3]	1 [3]	1 [3]	1.00	0.000
Diabetes mellitus	26 [10]	1 [3]	25 [11]	0.14	2 [3]	1 [3]	1 [3]	1.00	0.000
Peripheral arterial disease	25 [10]	1 [3]	24 [11]	0.14	1 [2]	1 [3]	0 [0]	1.00	0.000
Chronic kidney disease	89 [34]	10 [26]	79 [36]	0.21	16 [24]	9 [26]	7 [21]	0.41	0.139
Preoperative AR ≥ moderate	230 [89]	35 [90]	195 [89]	1.00	61 [90]	32 [94]	29 [85]	0.26	–
Preoperative AS ≥ moderate	29 [11]	10 [26]	19 [9]	0.005	12 [18]	6 [18]	6 [18]	1.00	0.000
NYHA III/IV	114 [56]	14 [36]	100 [46]	0.26	25 [37]	13 [38]	12 [35]	0.78	0.061
Preoperative LVEF (%)	55±10	60±9	55±10	0.09	55±7	59±7	55±8	0.52	0.024
Cardiopulmonary resuscitation	20 [8]	3 [8]	17 [8]	1.00	3 [4]	3 [9]	0 [0]	0.25	–
Inotropic support	55 [21]	11 [28]	44 [20]	0.25	15 [22]	10 [29]	5 [15]	0.10	–
Ventilation	47 [18]	9 [23]	38 [17]	0.38	15 [22]	9 [27]	6 [18]	0.35	–
Pericardial effusion	103 [40]	16 [41]	87 [40]	0.88	26 [38]	14 [42]	12 [35]	0.62	–
Malperfusion syndrome	92 [36]	10 [26]	82 [37]	0.16	17 [25]	9 [26]	8 [24]	0.78	0.068
Cerebral malperfusion	48 [19]	5 [13]	43 [20]	0.38	9 [13]	5 [15]	4 [12]	0.74	0.087
Coronary malperfusion	37 [14]	5 [13]	32 [15]	0.86	8 [12]	4 [12]	4 [12]	1.00	0.000
Visceral malperfusion	15 [6]	1 [3]	14 [6]	0.48	2 [3]	1 [3]	1 [3]	1.00	0.000
Extremity malperfusion	24 [9]	3 [8]	21 [10]	1.00	5 [7]	3 [9]	2 [6]	0.56	0.113

Data expressed as n [%] or median ± IQR. Cases with connective tissue disorders; and unknown type of aortic valve were not included. Categorical unmatched variables compared using Chi-square or Fisher test; continuous unmatched variables—by means of Wilcoxon sum rank test. In the matched cohort; McNemar's test and Wilcoxon-signed rank test were used. AADA, acute aortic dissection type A; COPD, chronic obstructive pulmonary disease; AR, aortic regurgitation; AS, aortic stenosis; NYHA, New York Heart Association classification of heart failure; ASA, American Society of Anesthesiologists physical status classification; BAV, bicuspid aortic valve; TAV, tricuspid aortic valve; SMD, standardized mean difference (presented for the matching covariates); IQR, interquartile range.

Table 3 Intraoperative patient data, elective cases

Variables	Unmatched				Matched				SMD
	Total (n=827)	BAV (n=365, 44%)	TAV (n=462, 56%)	P value	Total (n=584)	BAV (n=292, 50%)	TAV (n=292, 50%)	P value	
Types of conduits									
Mechanical valve conduit	278 [34]	141 [38]	137 [30]	0.007	191 [33]	100 [34]	91 [31]	0.41	0.060
Biological valve conduit	207 [25]	109 [30]	98 [21]	0.004	168 [29]	86 [29]	82 [28]	0.70	0.030
Xeno-/homograft root	342 [41]	115 [32]	227 [49]	<0.001	225 [39]	106 [36]	119 [41]	0.20	0.096
Prosthesis size (mm)	27±2	27±2	25±2	0.01	27±2	27±2	27±2	0.02	–
Concomitant procedures									
CABG for iatrogenic injury	13 [2]	2 [1]	11 [2]	0.04	5 [1]	2 [1]	3 [1]	0.65	0.037
CABG for coronary artery disease	113 [14]	33 [9]	80 [17]	0.001	56 [10]	29 [10]	27 [9]	0.78	0.024
Morrow procedure	39 [5]	13 [4]	26 [6]	0.16	28 [5]	13 [4]	15 [5]	0.71	0.037
Aortic root enlargement	3 [<1]	1 [<1]	2 [<1]	1.00	3 [1]	1 [<1]	2 [1]	0.56	0.066
MV repair or replacement	1 [<1]	0 [0]	1 [<1]	0.44	0 [0]	0 [0]	0 [0]	1.00	0.000
Hemiarch	12 [1]	4 [1]	8 [2]	0.56	8 [1]	4 [1]	4 [1]	1.00	0.000
Operative data									
Minimally invasive approach	83 [10]	35 [10]	48 [10]	0.70	58 [10]	29 [10]	29 [10]	1.00	0.000
CPB time (min)	115±46	111±46	118±46	<0.001	114±44	112±49	114±40	0.12	–
Cross-clamp time (min)	88±34	87±31	89±35	0.03	88±33	88±32	88±32	0.07	–
Operative time (min)	195±73	195±70	200±75	0.02	192±67	195±77	190±65	0.32	–
Cardioplegia type									
Blood cardioplegia	211 [26]	86 [24]	125 [27]	0.25	136 [23]	66 [23]	70 [24]	0.68	0.032
Crystalloid cardioplegia	541 [65]	258 [71]	283 [61]	0.005	411 [70]	206 [71]	205 [70]	0.92	0.008
Antegrade cardioplegia	662 [80]	318 [87]	344 [74]	<0.001	501 [86]	249 [85]	252 [86]	0.70	0.031
Retrograde cardioplegia	36 [4]	10 [3]	26 [6]	0.043	18 [3]	8 [3]	10 [3]	0.59	0.042
Combined cardioplegia	54 [7]	16 [4]	38 [8]	0.026	28 [5]	15 [5]	13 [4]	0.69	0.034
Nonselective root cardioplegia	9 [1]	4 [1]	5 [1]	1.00	6 [1]	4 [1]	2 [<1]	0.41	–
Cardioplegia unknown	66 [8]	17 [5]	49 [11]	0.002	31 [5]	16 [5]	15 [5]	0.84	–

Data expressed as n [%] or median ± IQR. CABG, coronary artery bypass grafting; MV, mitral valve, CPB, cardiopulmonary bypass; BAV, bicuspid aortic valve; TAV, tricuspid aortic valve; SMD, standardized mean difference (presented for the matching covariates).

analyzed. However, after matching, all postoperative outcome variables were not significantly different (see *Table 5*). Prior to matching, BAV patients had a 2-day shorter length of stay in the hospital, but after matching, both patient groups were similar with a median of 16 days.

Subgroup analysis of elective patients with aortic diameter <55 mm

Preoperative characteristics before and after matching were similar to the whole group—co-variates before and

Table 4 Intraoperative data, patients with AADA

Variables	Unmatched				Matched				SMD
	Total (n=258)	BAV (n=39, 15%)	TAV (n=219, 85%)	P value	Total (n=68)	BAV (n=34, 50%)	TAV (n=34, 50%)	P value	
Indication for Bentall procedure									
Dissected root and/or coronary arteries	170 [66]	25 [64]	145 [66]	0.80	45 [66]	23 [68]	22 [65]	0.81	–
Calcified aortic valve	14 [5]	1 [3]	13 [6]	0.70	4 [6]	0 [0]	4 [12]	0.13	–
Severely dilated aortic root	49 [19]	9 [23]	40 [18]	0.51	9 [13]	7 [21]	2 [6]	0.10	–
Failure of supracoronary AAR or aortic valve sparing procedure	9 [3]	2 [5]	7 [3]	0.63	5 [7]	2 [6]	3 [9]	0.65	–
Unknown	16 [6]	2 [5]	14 [6]	1.00	5 [7]	2 [6]	3 [9]	0.56	–
Types of conduits									
Mechanical valve conduit	101 [39]	21 [54]	80 [37]	0.04	36 [53]	18 [53]	18 [53]	1.00	0.000
Biological valve conduit	96 [37]	10 [26]	86 [39]	0.10	17 [25]	9 [26]	8 [24]	0.71	0.068
Xeno-/homograft root	61 [24]	8 [21]	53 [24]	0.69	15 [22]	7 [21]	8 [24]	0.56	0.071
Prosthesis size (mm)	25±2	25±2	25±2	0.06	25±2	25±2	24±2	0.47	–
Concomitant procedures									
CABG (total)	54 [21]	2 [5]	52 [24]	0.008	7 [10]	1 [3]	6 [18]	0.13	–
CABG for coronary artery disease	10 [4]	0 [0]	10 [5]	0.37	0 [0]	0 [0]	0 [0]	1.00	0.000
MV repair	1 [<1]	1 [3]	0 [0]	0.15	1 [1]	1 [3]	0 [0]	1.00	–
Extent of distal aortic resection									
Isolated AAR	21 [8]	3 [8]	18 [8]	1.00	5 [7]	2 [6]	3 [9]	0.65	–
Hemiarch	150 [58]	26 [67]	124 [57]	0.24	42 [62]	22 [65]	20 [59]	0.53	–
Total arch	24 [9]	5 [13]	19 [9]	0.38	6 [9]	5 [15]	1 [3]	0.10	–
Total arch and DTA	3 [1]	1 [3]	2 [1]	0.39	1 [1]	1 [3]	0 [0]	1.00	–
Elephant trunk	41 [16]	5 [13]	36 [16]	0.81	12 [18]	5 [15]	7 [21]	0.48	–
Frozen elephant trunk	22 [9]	0 [0]	22 [10]	0.05	3 [4]	0 [0]	3 [9]	0.25	–
Extended aortic arch surgery	87 [34]	10 [26]	77 [35]	0.25	21 [31]	10 [29]	11 [32]	0.65	0.064
Operative data									
CPB time (min)	201±84	194±55	202±89	0.51	197±98	195±51	203±125	0.17	–
Aortic cross-clamp time (min)	120±47	120±33	121±55	0.31	120±41	120±32	125±57	0.17	–
CA time (min)	25±22	21±14	26±6	0.04	24±17	24±15	23±22	0.23	–
Operative time (min)	325±140	310±80	325±154	0.53	315±102	308±84	327±157	0.21	–
CA body temperature (℃)	26±6	26±4	26±6	0.63	26±6	27±4	25±7	0.11	–

Data expressed as n [%] or median ± IQR. Categorical unmatched variables compared using Chi-square or Fisher test, continuous unmatched variables—by means of Wilcoxon sum rank test. In the matched cohort, McNemar's test and Wilcoxon-signed rank test were used. AADA, acute aortic dissection type A; AAR, ascending aortic replacement; CABG, coronary artery bypass grafting; MV, mitral valve; DTA, descending thoracic aorta; CPB, cardiopulmonary bypass; CA, circulatory arrest; BAV, bicuspid aortic valve; TAV, tricuspid aortic valve; SMD, standardized mean difference (presented for the matching covariates); IQR, interquartile range.

Table 5 Outcomes of matched patients undergoing elective and emergency surgery

Variables	Matched elective cohort				Matched type A dissection patients			
	Total (n=584)	BAV (n=292, 50%)	TAV (n=292, 50%)	P value	Total (n=68)	BAV (n=34, 50%)	TAV (n=34, 50%)	P value
Complications								
Low cardiac output syndrome	11 [2]	8 [3]	3 [1]	0.13	7 [10]	3 [9]	4 [12]	0.71
Perioperative myocardial infarction	1 [<1]	0 [0]	1 [<1]	1.00	2 [3]	0 [0]	2 [6]	0.48
Stroke	16 [3]	7 [2]	9 [3]	0.62	2 [3]	0 [0]	2 [6]	0.48
Re-exploration for bleeding	44 [8]	21 [7]	23 [8]	0.75	4 [6]	0 [0]	4 [12]	0.13
Sepsis	8 [1]	4 [1]	4 [1]	1.00	18 [26]	11 [32]	7 [21]	0.25
Gastrointestinal complications	25 [4]	11 [4]	14 [5]	0.55	2 [3]	1 [3]	1 [3]	1.00
Respiratory failure	45 [8]	16 [5]	29 [10]	0.03*	9 [13]	4 [12]	5 [15]	0.74
Renal failure requiring dialysis	16 [3]	10 [3]	6 [2]	0.32	21 [31]	7 [21]	14 [41]	0.09
Pacemaker implantation	21 [4]	14 [5]	7 [2]	0.13	10 [15]	5 [15]	5 [15]	1.00
Hospital stay (days)	10±6	10±6	11±6	0.75	16±11	16±11	16±10	0.86
Mortality								
Intraoperative death	0 [0]	0 [0]	0 [0]	1.00	3 [4]	1 [3]	2 [6]	0.62
In-hospital mortality	6 [1]	4 [1]	2 [1]	0.41	13 [19]	6 [18]	7 [21]	0.71
30-day mortality	10 [2]	5 [2]	5 [2]	1.00	15 [22]	8 [24]	7 [21]	0.71

Data expressed as n [%] or median ± IQR. *, odds ratio 0.480 (95% confidence interval 0.220–0.991). BAV, bicuspid aortic valve; TAV, tricuspid aortic valve; IQR, interquartile range.

after matching are displayed in Figure S2. All significant intraoperative differences from the original cohort (see Table S1) were equalized after matching the patients. Outcome variables also showed no difference with very low in-house (1%) and 30-day mortality (2%). Before matching, rates of re-exploration for bleeding and respiratory failure were significantly higher in TAV subgroup; after matching, no differences could be detected. For all details see Table S2.

Discussion

In the current study, we compared perioperative outcomes in BAV and TAV patients undergoing elective and emergency modified Bentall surgery. After adjusting for preoperative characteristics, statistically significant differences in early outcomes were observed only with regards to respiratory failure rates in elective Bentall procedures. Prior to propensity matching, the group of BAV patients was younger and healthier at time of surgery. After matching, however, the two groups of patients were comparable with regards to all preoperative variables.

Over the past few decades, awareness for aortic root aneurysmal disease has increased resulting in timely preventive surgical intervention in root aneurysm patients and, in most AADA cases, immediate referral to emergency surgery (11). Outcomes of elective and emergency aortic root replacement have improved over time, resulting in decrease of mortality rates to about 3% in elective cases (12,13) and approximately 10–30% in emergencies, with higher mortality rates in AADA patients presenting with preoperative organ malperfusion (14,15). In our cohort of elective patients, 30-day mortality was 2% in both groups after matching, slightly lower than that reported in a large meta-analysis including 46 studies and 7,629 patients (16). This very low mortality rate in our high-volume center is reflective of the known association between center volume and outcomes in aortic surgery (17).

The analyzed group of AADA patients displayed a mortality rate of 28% in the current series, with no significant differences between the groups before and after matching. We have previously reported similar findings in these high-risk patients (18), as have several other large German centers with aortic expertise (19). As no difference in organ malperfusion [one of the major determinants of outcomes in AADA (15)] was present preoperatively between our two patient groups, no significant outcome differences could be detected. It has been shown in a study by Yang *et al.* that operative mortality is higher in AADA patients receiving modified Bentall surgery compared to David procedure, probably due to patient selection (20). Patients receiving modified Bentall tend to be in worse condition preoperatively, leading to higher in-hospital mortality.

Patients with a BAV are known to receive surgery approximately 10 years earlier compared to the tricuspid peers (21). In our retrospective analysis, BAV patients were 7 years younger in the group of elective modified Bentall surgery and 13 years younger in the emergency group (see *Tables 1,2*), leading to a different risk profile including less co-morbidities (e.g., chronic kidney disease, prior stroke, prior myocardial infarction). Respiratory failure after cardiac surgery is a well-known major adverse event, and its risk factors are critical preoperative state, poor left ventricular function, COPD, age and others (22). Especially in an acute setting, age itself is an important risk factor associated with higher mortality and morbidity (23,24). Hsu *et al.* analyzed nearly 4,000 AADA patients in Taiwan and found a respiratory failure rate of 29.1% in AADA patients at the age of 80 years and older *vs.* 17.2% in non-octogenarians (25). Similar results were observed in the present study. In the AADA group, respiratory failure was more prevalent in TAV patients (before matching: 46% *vs.* 21%, P=0.003 and after matching: 41% *vs.* 21%, P=0.09) despite similar operating times. This difference did not reach statistical significance in the matched cohort. Higher respiratory failure rates in TAV patients were, however, statistically significant in elective cases (12% *vs.* 5%, P<0.001 before matching, and 10% *vs.* 5%, P=0.03 after matching). This could be explained by the older and sicker TAV patients that even after matching, presented with a slightly higher rate of COPD, compared to BAV patients.

In elective cases the higher incidence of severe co-morbidities resulted in significantly worse 30-day mortality (4% *vs.* 1%) before matching; after matching no mortality differences were present. It is important to mention that even though matching analyses were performed to compare the results of Bentall procedure in BAV and TAV groups, in real-life scenario these two categories of patients do differ dramatically, particularly because of the significant age difference. Because the Bentall procedure is based on aortic valve replacement, and not reimplantation or reconstruction, superior outcomes in BAV patients are not surprising. At the same time, these age and comorbidity differences may be not as relevant in the decision-making process when a valve-sparing procedure (technically more complex in BAV) is to be performed. The increased complexity of repair and high rate of aortic valve stenosis in BAV patients are the main reasons that a consistently small number of David procedures are reported in this population.

BAV patients are being increasingly considered for transcatheter aortic valve replacement (TAVR) therapy, often with suboptimal results due to technical complexities (e.g., coronary anomalies, heavy calcification of the valve, elliptical annulus shape) associated with BAV (26). In contrast, the herein presented data demonstrates equally impressive results between BAV and TAV patients undergoing the modified Bentall procedure. A significant portion of the included patients (i.e., patients with aortic diameter <55 mm) may also fall into an area where TAVR could be considered as a possible therapeutic option. For these patients, as demonstrated in our subgroup analysis, Bentall results are excellent and not associated with higher complication rates when compared to TAV patients.

The pathological risk of the presence of a BAV has been more frequently investigated over the past decade, impacting guidelines for aortic replacement and shifting the absolute aortic diameter as indicator for aortic surgery between 45 and 50 mm for this specific patient group (5). Studies have demonstrated that every ninth AADA patient is a carrier of a BAV and that the dissection entry is more often located in the aortic root leading to a more extensive surgical repair (18). Apparently, no difference in incidence of rupture or dissection between BAV and TAV patients has been detected in the past (21). However, controversies exist on diameter at time of AADA in BAV patients. In 2013, Eleid *et al.* reported that the mean aortic diameter of BAV patients was 1 cm larger than their tricuspid peers (66±15 *vs.* 56±11 mm) (6), whereas a recent collaboration between Freiburg and the University of Pennsylvania showed that 76% of BAV patients had a diameter <5 cm (27). Furthermore, the presence of AS is associated with a higher risk for aortic rupture, dissection and death before operative repair with BAV patients (21). In our unmatched AADA patients, BAV carriers presented significantly more often with severe AS at the time of dissection. Furthermore, aortic disease in BAV patients is oftentimes limited to the proximal aorta, whereas in TAV patients the aorta is diseased as a whole—underlined by the higher rate of frozen elephant trunk procedures in the herein presented TAV patients (10% *vs.* 0%, P=0.05).

Our findings show that the early outcome of surgery is almost not different in patients with divergent aortic valve morphology, particularly when they are matched for preoperative characteristics. However, BAV patients present at a younger age with less comorbidities when receiving their aortic repair, and therefore tend to have better results in the unmatched cohort. For this reason, it is essential to establish a proper follow-up program monitoring for echocardiographic and CT controls over an extended time span in BAV patients. For TAV patients, CT imaging of the remaining aorta, especially after AADA, is key as in these patients, aortic disease is not limited to the proximal aortic segment, rather involving the aorta in its entirety. We have previously demonstrated that AADA patients undergoing retrograde perfusion (femoral-femoral cannulation) during AADA repair is associated with worse 10-year survival, compared to antegrade perfusion (71% *vs.* 51% survival at 10 years) (28) and general re-operation probability of AADA patients at 10 years has been previously published with 16% (29). These findings underscore the importance of long-term surveillance in TAV patients post-AADA repair.

Limitations

As this is a retrospective study data, could only be analyzed as documented. Patients with missing aortic valve morphology had to be excluded. The total number of patients with a documented BAV and AADA was relatively small. Finally, the current study focusses on early mortality and perioperative complications; follow-up data is not presented.

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Footnote

Conflicts of Interest: The authors declare no conflicts of interest.

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