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The Expanding Role of Mitral Valve Repair in Triple Valve Operations: Contemporary North American Outcomes in 8,021 Patients

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Abstract

Background—Although the operative risk of multivalve operations has historically been high, current outcomes are poorly understood. We sought to evaluate factors influencing contemporary results of triple-valve operations using The Society of Thoracic Surgeons Adult Cardiac Surgery Database.

Methods—Among patients undergoing combined mitral, aortic, and tricuspid valve (triple-valve) operations between 1993 and 2011, aortic valve repair patients were excluded and those having aortic valve replacement were analyzed according to whether they underwent repair vs replacement of the mitral valve (MV) and tricuspid valve (TV). Temporal trends in operative death and clinical outcomes were examined using unadjusted and adjusted analyses.

Results—A total of 8,021 triple-valve patients were studied. The median (25th percentile, 75th percentile) age was 67 years (59, 77 years), 4,809 (60%) were women, 4,488 (56%) had New York Heart Association class III to IV symptoms, and the mean (25th percentile, 75th percentile) ejection fraction was 50% (40%, 60%). MV repair was performed in 2,728 (34%) patients overall and increased over time from 13% (1993 to 1997) to 41% (2008 to 2011). TV repair was performed in 7,512 (94%) patients overall and increased over time from 86% (1993 to 1997) to

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96% (2008 to 2011). Unadjusted operative mortality decreased from 17% in 1993 to 9% in 2011. Adjusted odds ratios (95% confidence intervals) of operative mortality were lower in those having MV repair (0.72 [0.61 to 0.85]), TV repair (0.64 [0.50 to 0.83]), and MV D TV repair (0.46 [0.34 to 0.63]) compared with those having replacements. Unadjusted and adjusted odds of stroke were similar between groups and not significant for all.

Conclusions—This large series demonstrates that surgical results of triple-valve operations have continued to improve during the past 18 years. MV and TV repair were associated with improvements in early survival. Although further study is required to understand late outcomes, these data suggest that broader efforts to perform MV repair instead of replacement in this high-risk patient population appear warranted.

Surgical treatment of valvular heart disease involving the aortic (AV), mitral (MV), and tricuspid (TV) valves has traditionally been associated with a very high periprocedural mortality risk, ranging between 10% and 50%, along with a stroke hazard of 10% [1, 2]. These operations thus represent one of the highest-risk cardiac surgical procedures in the modern era. Compared with less developed countries, Western surgical practices have seen declining rates of rheumatic disease during the past 2 decades, resulting in growing numbers of elderly patients presenting with degenerative heart valve pathology. The majority of the available literature detailing the outcomes of triple-valve operations has been limited to single-center series.

In general, recent efforts to increase the frequency of both MV and TV repair vs replacement in isolated valve operations have been based on evidence derived from observational studies demonstrating both short-term and long-term survival benefits associated with native valve reconstruction [3–8]. This has particularly been true in the case of degenerative MV disease [8–11]. The veracity of using existing published outcomes to extrapolate the benefits of single-valve repair to patients with triple-valve disease, however, is uncertain. We therefore sought to evaluate temporal trends in outcomes of triple-valve operations in North America and, specifically, to examine the effect of MV and TV repair compared with replacement in this setting.

Patients and Methods

The Duke University Medical Center Institutional Review Board authorized the study and granted a waiver of the requirement for informed consent.

Study Population

The Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database (ACSD) is a clinical data registry promoting quality improvement in cardiac surgical outcomes since 1989. Baseline and intraoperative patient characteristics and operative outcomes are collected using standard definitions, with routine data auditing that has shown greater than 95% accuracy vs chart abstraction [12].

In this study, 10,440 triple-valve (AV + MV + TV) operations were identified among 864 participant surgical groups from 1993 to 2011. After excluding patients with an aortic dissection or aneurysm repair (n = 644), concurrent pulmonic valve operation (n = 136),

cardiac trauma or transplantation (n = 8), an emergency or salvage operations (n = 188), concurrent Batista and other major cardiac procedures (n = 1,099), concurrent operation for peripheral or carotid arterial disease (n = 78) or noncardiac thoracic procedures (n = 34), AV repair (n = 223), or those missing information for age or sex (n = 9), we identified 8,021 operations from 827 participating institutions for analysis (Fig 1). There were increases in the number of participating centers (range, 261 to 1,017) and in the proportion of operations (range, 0.09% to 0.29%) that were triple-valve operations over the duration of the study.

Study Outcomes

The primary outcomes for this analysis were operative death and stroke. Secondary outcomes included renal failure and multisystem organ failure. All outcomes were defined as occurring during the index hospitalization or within 30 days of the index procedure.

Statistical Analysis

Baseline patient and procedural characteristics are summarized as counts and percentages for categorical variables and as median with 25th and 75th percentiles for continuous variables. Characteristics were compared for categorical variables using Pearson χ^2 tests and for continuous variables using Kruskal-Wallis test. Statistical significance was defined as a *p* value of 0.05 or less. All analyses were performed by the Duke Clinical Research Institute using SAS 9.2 software (SAS Institute, Cary, NC).

Valve treatment strategies were compared, including MV repair vs replacement, TV repair vs replacement, and double valve (MV+TV) repair vs replacement in this cohort of patients who all underwent AV replacements (AVRs). The unadjusted odds ratio (OR) and 95% confidence interval (CI) for each comparison were estimated for operative death and stroke using logistic regression models, with generalized estimating equations to generate robust standard error estimates that accounted for clustering of like patients at individual centers.

Adjusted ORs were calculated after conditioning on the following set of clinical variables: age, body surface area, gender, race (black and others), diabetes (diet control, oral control, insulin control, diabetes without treatment, no diabetes), hypertension, renal function (renal failure with dialysis, renal failure without dialysis [serum creatinine >2 mg/dL], no renal failure), endocarditis, cerebrovascular accident, immunosuppressive treatment, prior myocardial infarction (< 1 week, 1 to 3 weeks, >3 weeks, none), unstable angina with no recent MI (< 7 days), cardiogenic shock, arrhythmia, status (urgent or elective), preoperative intraaortic balloon pump, first reoperation, second reoperation or more, concomitant coronary artery bypass procedure, and time periods (1993 to 1997, 1998 to 2002, 2003 to 2007, and 2008 to 2011), mitral stenosis, tricuspid stenosis, and prior valve operation.

Results

Population Characteristics

Between 1993 and 2011, 8,021 triple-valve operations were performed at 827 participating centers (Fig 1), including 448 operations (6%) with triple-valve replacement, 61 (1%) with tricuspid replacement and mitral repair, 4,845 (60%) with tricuspid repair and mitral

replacement, and 2,667 (33%) with tricuspid and mitral repair (Table 1). The median (25th, 75th percentile) age of the overall cohort was 70 years (59, 77 years), and 60% were women. Chronic renal failure was prevalent in 10% (including dialysis in 5%), prior stroke in 11%, severe lung disease in 5%, and coronary artery disease in 38%. A previous valve operation was noted in 21%, and 11% had undergone a coronary artery bypass grafting operation. Clinical heart failure was present in 67%, including 56% with New York Heart Association class III or IV symptoms (Table 1).

Total volume of triple-valve operations captured by the STS ACSD rose from 96 in 1998 to 812 annually in 2010 (Fig 2). During the study interval, the likelihood of MV repair increased from 13% (1993 to 1997) to 41% (2008 to 2011). Patients receiving a MV repair (vs replacement) had a lower prevalence of previous valve operation (10% vs 26%) and MV stenosis (6% vs 44%); however, severe left ventricular dysfunction (ejection fraction <0.35) was more common in the MV repair cohort (23% vs 9%).

TV replacement was relatively uncommon (509 [6%]) and decreased in frequency from 14% to 4% of triple-valve procedures during the study interval. Among tricuspid replacement procedures, 18% had active or treated endocarditis, and 14% had tricuspid stenosis. When valve replacement was performed, biologic devices (compared with mechanical) were implanted in 62.6% of AVRs, 52% of MVRs, and in 57.4% of those undergoing TV replacement.

We next sought to determine whether the performance of valve preservation/reconstruction during MV/TV repair (plus AVR) affected operative times compared with those who underwent triple-valve replacement. Median cardiopulmonary bypass time overall was 200 minutes and was significantly less in those undergoing double (MV + TV) repair vs triple-valve replacement (189 vs 220 minutes, $p < 0.0001$). Similarly, median ischemic (cross-clamp) time was 153 minutes overall and significantly less in those undergoing double-valve repair vs triple-valve replacement (143 vs 156 minutes, $p < 0.0001$).

The administration of warfarin at the time of dismissal from the hospital was documented in 3,330 patients (41.5%) overall and was more likely to be administered in those undergoing AVR plus double-valve repair (1,192 [44.7%]) vs triple-valve replacement (120 [26.8%], $p < 0.0001$).

Operative Outcomes

During the entire interval studied, the operative mortality for triple-valve operations was 13%, which decreased over time from 17% in 1993 to 9% in 2011 (Fig 2). Renal failure occurred in 15% of patients, stroke in 2.8%, and multisystem organ failure in 5.2% overall (Table 2).

Operative mortality was highest among patients in whom both the TV and MV required replacement (19%, $p < 0.001$). After risk adjustment, MV repair (vs replacement) was associated with a lower odds of operative death (adjusted OR, 0.72; 95% CI, 0.61 to 0.85). Similarly, TV repair (vs replacement) was associated with a lower adjusted odds of operative death (adjusted OR, 0.64; 95% CI, 0.50 to 0.83). Finally, MV + TV repair plus

AVR (vs triple-valve replacement) was also associated with a lower adjusted odds of death (adjusted OR, 0.46; 95% CI, 0.34 to 0.63).

The observed incidence of stroke was similar across the four treatment groups ($p = 0.6$, Table 2). After risk adjustment, the risk was again similar across categories ($p = 0.4$). Finally, MV + TV repair (vs triple-valve replacement) was again not associated with a difference in the risk of stroke ($p = 0.5$; Table 3).

Comment

This multicenter registry experience of 8,021 patients from the STS ACSD undergoing triple-valve operations is the largest reported series to date to our knowledge. The number of recorded patients undergoing multivalve operations has continued to expand over time in North America. Trends noted in the current study include the increasing performance of both MV and TV repair along with declining mortality rates, with an unadjusted operative mortality of 12.6% in the most recent era (2008 to 2011). TV repair (vs replacement) is now nearly universally applied in this setting, whereas MV repair is performed in less than half of such cases. MV and TV repair were both associated with improved early survival in unadjusted and adjusted analyses. The risk-adjusted hazard of death was diminished by approximately one-quarter in those undergoing MV repair, one-third in patients having TV repair, and by more than half in those undergoing MV and TV repair. The postoperative incidence of stroke was also low in this cohort, totalling only 2.8% in the most recent era. The association between temporal increases in atrioventricular valve repair and improved early survival in patients undergoing triple-valve operations during the past 18 years presents a potential opportunity for further quality improvement in this technically challenging and high-risk surgical population.

Recent single-center series studying early outcomes after triple-valve operations have demonstrated similar outcome trends to those we report presently. Hermans and colleagues [2] described the early results of 166 patients undergoing triple-valve operations between 1972 and 2006, with a 30-day mortality of 10%. Operative risk was highest in patients receiving 3 biologic valves; however, none of the patients in their series underwent MV repair, and it is interesting that TV repair did not appear to influence results.

Gravel and colleagues [13] detailed the outcomes of 170 patients undergoing triple-valve operations between 1977 and 2008, concluding that operative mortality had improved (12% in 1999 to 2008) but was negatively impacted by tricuspid regurgitation severity and the presence of an intraventricular pacing lead. Tricuspid repair vs replacement was again not influential upon early death in the Gravel and colleagues' report ($p = 0.248$).

Finally, a recent study from Hannover [14] detailing outcomes of 90 patients undergoing triple-valve operations between 1996 and 2010 revealed an early mortality risk of 16%, which was predicted by the need for emergency surgery and the presence of preoperative intra-aortic balloon counterpulsation.

Recent changes in population demographics have been associated with the migration of multivalve disease etiology away from rheumatic valvulopathy and toward degenerative

pathology in patients requiring triple-valve operations. Some authors believe that despite an aging surgical population with degenerative multivalve disease, improvements in (1) the technical aspects of these operations and (2) perioperative care have been the predominant drivers of better outcomes [14]. The frequency of both MV and TV repair have also increased over time; which has been shown to be influenced by a variety of additional factors, including valve pathoanatomy, along with surgeon and institutional experience and volume [6, 15]. It is therefore unclear to what extent the increased frequency of valve repair performed at higher volume “referent” valve centers is linked to institutional differences in early safety and quality outcomes versus shifts in pathobiology using the current data set [15].

We sought to include mitral stenosis (likely rheumatic) and other subsets less likely to be repaired to understand the breadth of the triple-valve population, not to predict repair rates. Undoubtedly, the ability to perform both MV and TV repair is influenced by the absence of significant leaflet calcification, retraction, or tissue destruction; however, we were unable to distinguish these in the current data set. Nonetheless, even after adjusting for mitral stenosis, endocarditis, urgent presentation, and other potentially influential variables, atrioventricular valve preservation increased over time and was associated with a prognostic benefit.

Repair of both MVs [11] and TVs [16] has been increasingly recognized as important in optimizing patient outcomes. Isolated MV repair is safe and effective and is associated with a very low periprocedural risk (<0.3%) in recent reports [6, 17, 18]. Moreover, MV repair is durable and conveys a significant midterm to late-term survival advantage over MV replacement in patients with similar risk profiles [19]. Whereas prior studies have not specifically studied the assertion that a survival advantage is conveyed by MV repair (over replacement) in patients with triple-valve disease [13, 14, 20], our results clearly demonstrate that MV repair is associated with protection from early death in unadjusted and adjusted analyses. Potential explanations include the maintenance of ventricular-valvar continuity, diminished risk of atrioventricular disruption, and shorter operative times, as demonstrated in the current report. A growing body of evidence also supports the performance of concomitant surgical correction of functional TV regurgitation at the time of left-sided surgery, particularly in the setting of multivalve disease and myocardial dysfunction [21–23]. Finally, recent single-center [16] and registry experiences have advocated for the utility of tricuspid repair over replacement, when technically feasible, in improving early outcomes [24].

The current report is the first large registry study to analyze the effect of atrioventricular valve repair on early outcomes in patients undergoing triple-valve operations and specifically demonstrates an independent protective effect of repair techniques that spare the MV and TV. The large sample size and multiinstitutional nature increase the likelihood that the results are generalizable to many institutions performing heart valve operations in North America as well as those abroad. The robust analysis performed accounts for center clustering and consistently demonstrates a survival benefit associated with the performance of MV and TV repair. Taken together, this experience provides important evidence supporting the use of valve repair over replacement in contemporary triple-valve operation populations.

The limitations of this report are consistent with its retrospective and multicenter registry-based nature. As with any observational study, unmeasured confounders may lead to bias. We recognize that the data collection forms for the years included in this study provided limited information about the specific causes of the valve disease. These variables undoubtedly influence outcomes and will be available in forthcoming data harvests using newer versions of the STS ACSD data collection form for future analyses.

Although the current report only included patients undergoing AVR (representing most triple-valve surgical patients), we acknowledge that the data are only generalizable to this patient population. Finally, we present early postsurgical outcomes only because midterm to long-term data are not available in the STS ACSD database for linkage analysis in the current study. Patients with mitral stenosis and endocarditis were included to describe the full spectrum of patients undergoing triple-valve operations, but the severity of stenosis/restriction and tissue destruction cannot be assessed from the currently available data set. Despite this, the early prognostic benefit of valve repair in this high-risk population was reconfirmed after adjustment for these potentially confounding factors.

In conclusion, although the early mortality risk after triple-valve operations remains substantial at 9% in the most recent year of data available, surgical outcomes continue to improve. The performance of both MV and TV repair is independently associated with enhancements in early survival. Although almost all patients currently undergo TV repair, MV repair is still performed in less than half of patients in this setting. Together these data provide strong evidence supporting atrioventricular valve repair over replacement advocating for continued efforts to increase the performance of MV repair when technically feasible. Further studies examining long-term survival, freedom from morbidity, and durability of valve repair vs replacement among patients undergoing triple-valve operations in Western surgical practices are necessary to better understand whether the early advantages identified in this report are durable.

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Fig 1.
Flow diagram details the study population included in the analysis.

Fig 2.

Temporal trends are shown for operative mortality (red line), stroke (green line), and annual volume (blue line) of triple-valve operations amongst North American cardiac surgical centers participating in The Society of Thoracic Surgeons Adult Cardiac Surgery Database.

Table 1

Patient Characteristics

Variable	Overall (N = 8,021)	MV + TV Replacement (n = 448)	MV Repair + TV Replacement (n = 61)	TV Repair + MV Replacement (n = 4,845)	MV + TV Repair (n = 2,667)	p Value
Age, y	70.0 (59.0, 77.0)	62.0 (51.0, 72.0)	63.0 (52.0, 73.0)	68.0 (58.0, 76.0)	74.0 (65.0, 79.0)	<0.001
Female	4,809 (60.0)	298 (66.5)	30 (49.2)	3,162 (65.3)	1,319 (49.5)	<0.001
Diabetes	1,968 (24.5)	102 (22.8)	7 (11.5)	1,170 (24.1)	689 (25.8)	0.0392
Hypertension	5,206 (64.9)	215 (48.0)	38 (62.3)	3,002 (62.0)	1,951 (73.2)	<0.001
Dialysis	422 (5.3)	32 (7.1)	3 (4.9)	237 (4.9)	150 (5.6)	0.1695
Renal failure						
No dialysis	349 (4.4)	19 (4.2)	2 (3.3)	186 (3.8)	142 (5.3)	0.0317
With dialysis	422 (5.3)	32 (7.1)	3 (4.9)	237 (4.9)	150 (5.6)	
Prior CVA	850 (10.6)	59 (13.2)	7 (11.5)	538 (11.1)	246 (9.2)	0.0145
Previous CABG	907 (11.3)	30 (6.7)	7 (11.5)	454 (9.4)	416 (15.6)	<0.001
CLD, moderate-severe	928 (11.6)	46 (10.3)	12 (19.7)	543 (11.2)	327 (12.3)	0.1403
NYHA CHF						
I, II	924 (11.5)	36 (8.0)	12 (19.7)	544 (11.2)	332 (12.4)	<0.001
III, IV	4,488 (56.0)	264 (58.9)	34 (55.7)	2,679 (55.3)	1,511 (56.7)	
Ejection fraction	0.500 (0.400, 0.600)	0.550 (0.450, 0.600)	0.490 (0.400, 0.600)	0.550 (0.450, 0.600)	0.470 (0.350, 0.560)	<0.001
Diseased coronary vessels, No.						
0	3,857 (48.1)	201 (44.9)	35 (57.4)	2,395 (49.4)	1,226 (46.0)	<0.001
1	1,174 (14.6)	48 (10.7)	10 (16.4)	689 (14.2)	427 (16.0)	
2	773 (9.6)	28 (6.3)	4 (6.6)	422 (8.7)	319 (12.0)	
3	1,129 (14.1)	32 (7.1)	4 (6.6)	551 (11.4)	542 (20.3)	
Missing	1,088 (13.6)	139 (31.0)	8 (13.1)	788 (16.3)	153 (5.7)	
Infectious endocarditis	678 (8.5)	75 (16.7)	16 (26.2)	374 (7.7)	213 (8.0)	<0.001
Previous valve operation	1,663 (20.7)	169 (37.7)	18 (29.5)	1,217 (25.1)	259 (9.7)	<0.001
Stenosis						
Aortic	4,791 (59.7)	221 (49.3)	29 (47.5)	2,928 (60.4)	1,613 (60.5)	0.0022
Mitral	2,480 (30.9)	185 (41.3)	7 (11.5)	2,128 (43.9)	160 (6.0)	<0.001
Tricuspid	312 (3.9)	65 (14.5)	6 (9.8)	194 (4.0)	47 (1.8)	<0.001

Categorical data are shown as counts (%) and continuous data as median (25th percentile, 75th percentile).
 CABG = coronary artery bypass grafting; CHF = congestive heart failure; CLD = chronic lung disease; CVA = cerebrovascular accident (stroke); MV = mitral valve; NYHA = New York Heart Association; TV = tricuspid valve.

Table 2**Unadjusted Operative Outcomes**

Outcome	Overall (N = 8,021)	MV + TV Replacement (n = 448)	MV Repair + TV Replacement (n = 61)	TV Repair + MV Replacement (n = 4,845)	MV + TV Repair (n = 2,667)	p Value
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	
Operative death	1,040 (13.0)	86 (19.2)	8 (13.1)	644 (13.3)	302 (11.3)	<0.0001
Permanent stroke	221 (2.8)	14 (3.1)	0 (0.0)	133 (2.7)	74 (2.8)	0.5640
Post-op renal failure	1,206 (15.0)	80 (17.9)	18 (29.5)	706 (14.6)	402 (15.1)	0.0035
Multisystem failure	417 (5.2)	37 (8.3)	1 (1.6)	240 (5.0)	139 (5.2)	0.0070

MV = mitral valve; TV = tricuspid valve.

Table 3

Adjusted Operative Outcomes

Variable	Operative Mortality		Stroke	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
MV repair vs replacement	0.82 (0.71–0.96)	0.72 (0.61–0.85)	0.98 (0.73–1.30)	0.86 (0.62–1.19)
TV repair vs replacement	0.66 (0.52–0.84)	0.64 (0.50–0.83)	1.01 (0.60–1.69)	0.94 (0.55–1.60)
MV + TV repair vs dual replacement	0.55 (0.42–0.72)	0.46 (0.34–0.63)	0.98 (0.55–1.76)	0.81 (0.44–1.48)
MV repair only vs TV repair only	1.24 (0.94–1.64)	1.12 (0.83–1.50)	0.97 (0.53–1.77)	0.91 (0.48–1.73)

CI = confidence interval; MV = mitral valve; OR = odds ratio; TV = tricuspid valve.