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Contemporary prevalence and outcomes of rheumatic mitral valve surgery

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Abstract

Objective: Rheumatic mitral valve disease is often viewed as a historic disease in North America with limited contemporary data. We hypothesized that rheumatic pathology remains common and has worse short-term outcomes and higher resource utilization compared to other mitral valve pathologies.

Method: All patients undergoing mitral valve repair or replacement (2011–2019) were extracted from a regional Society of Thoracic Surgeons database. Resource utilization metrics included inflation-adjusted hospital costs. Patients were stratified by mitral valve pathology for univariate analysis.

Result: Out of the 6625 mitral valve procedures, 835 (12.6%) were from rheumatic disease, a proportion that incrementally increased over time (+0.39% per year, $p = .032$). Among 19 hospitals, there was high variability in number of rheumatic mitral operations (median: 22, interquartile range [IQR]: 5–80) and rate of rheumatic repairs (median: 3%, IQR: 0%–6%). Rheumatic patients were younger (62 vs. 65, $p < .0001$), more often female (75% vs. 43%, $p < .001$) and with greater burden of heart failure, multi-valve disease, and lung disease, but less coronary disease. There were no differences in operative mortality (5.2% vs. 5.0%, $p = .85$) or major morbidity (22.2% vs. 21.8%, $p = .83$). However, resource utilization was higher for rheumatic patients, including more frequent transfusions (43% vs. 39%, $p = .012$), longer ICU (73 vs. 64 h, $p < .0001$) and postoperative length of stay (8 vs. 7 days, $p < .0001$).

Conclusions: Rheumatic mitral disease accounts for a meaningful (12%) and rising percentage of mitral valve operations in the region, with high variability among hospitals. Rheumatic mitral surgery yielded similar short-term outcomes compared to nonrheumatic pathology, but required greater resource utilization.

KEYWORDS

mitral valve, outcomes research, resource utilization, rheumatic disease

Abbreviations: CONSORT, Consolidated Standards of Reporting Trials; ICU, intensive care unit; LOS, length of stay; O:E, observed to expected ratio; PROM, predicted risk of mortality; STS, Society of Thoracic Surgeons; VCSQI, Virginia Cardiac Services Quality Initiative.

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1 | INTRODUCTION

Rheumatic mitral valve disease, a complication of acute rheumatic fever, has declined significantly in prevalence in developed nations following the widespread adoption of penicillin for the treatment of streptococcal pharyngitis.[1,2] While developing nations continue to experience a high burden of the disease, the sentiment amongst many physicians and health policymakers in developed nations is that rheumatic valve disease contributes minimally to mitral valvular disease, relative to other etiologies (i.e., degenerative valve disease).[3–5]

The assumption that rheumatic mitral valve disease's burden on the United States' healthcare system is minimal is misguided. Current reports make use of literature review from which rates of rheumatic heart disease are extrapolated, and do not describe the specific prevalence of rheumatic mitral valve disease nor the prevalence of those patients requiring mitral valve surgery.[5,6] Prior reports from developed nations including surgical data are not contemporaneous and do not reflect current practice.[7] Recent patterns in immigration may have increased the prevalence of patients in the United States who have been exposed to acute rheumatic fever.

We hypothesized that rheumatic heart disease remains a significant contributor to the burden of mitral valve disease in the United States, and is a predictor of increased resource utilization and worse short-term outcomes among patients undergoing mitral valve surgery. To test these hypotheses, we undertook a multicenter, retrospective analysis of patients undergoing mitral valve surgery from 2011 to 2019.

2 | METHODS

2.1 | Patient data and variable definitions

The initial patient cohort consisted of all mitral valve operations performed within the Virginia Cardiac Services Quality Initiative between January 2011 and December 2019. Patients were then excluded for missing mitral valve pathology information. A subgroup analysis excluded patients with missing Society of Thoracic Surgeons (STS) predicted risk of mortality (PROM) scores. Cohort selection and patient exclusion details are provided in the Consolidated Standards of Reporting Trials (CONSORT) diagram as Figure 1.

The deidentified data was provided by VCSQI, which is a regional consortium that consisted of 19 member hospitals in the Mid-Atlantic region at the time of data extraction. Business associate and data use agreements are in place between all member institutions, VCSQI, and the database vendor ARMUS Corporation. The clinical data submitted by member institutions is derived from the STS adult cardiac surgery database data forms. In addition, Uniformed Billing-04 charge files are submitted and matched at the patient level. Total hospital cost is estimated using cost-to-charge ratios provided by the Centers for Medicare and Medicaid Services. Cost data is adjusted for inflation using the Medicare inpatient prospective payment system yearly adjustments and presented in 2019 dollars. As a secondary analysis

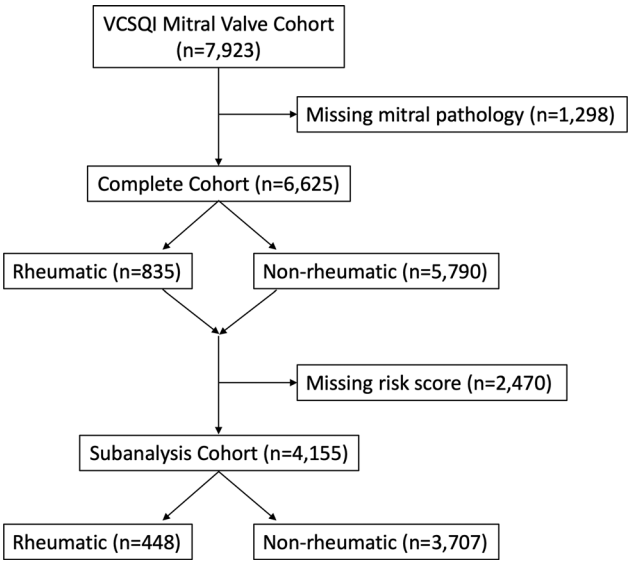

FIGURE 1 Consolidated Standards of Reporting Trials (CONSORT) diagram demonstrating inclusion and exclusion criteria for both complete and PROM cohorts

of the VCSQI quality database lacking Health Insurance Portability and Accountability Act patient identifiers, this study met the criteria for exemption from the Institutional Review Board review.

All variable definitions follow standard STS definitions.[8] Operative mortality includes in-hospital and 30-day deaths. Major morbidity includes renal failure, reoperation, permanent stroke, prolonged ventilation, and deep sternal wound infection.

2.2 | Statistical analysis

Categorical variables are presented as count (%) while continuous variables as median [Q1, Q3], except for cost data and risk scores that are presented as mean ± standard deviation to better represent total cost/risk. Patients were stratified by rheumatic mitral pathology (rheumatic vs. nonrheumatic) for univariate analysis. Categorical variables were analyzed by X^2 test and continuous variables by Mann–Whitney *U*-test. Risk-adjusted analyses were performed using hierarchical generalized linear modeling including STS predicted risk scores to account for operative risk and including hospital as a random effect to account for clustering. Statistical significance was defined by $p < .05$ and all statistical tests were performed using SAS Version 9.4 (SAS Institute).

3 | RESULTS

3.1 | Time varying and hospital characteristics

After exclusions, 6625 mitral patients were included in the primary cohort (Figure 1) with 835 (12.6%) classified as rheumatic. The rate of

patients classified as rheumatic varied over time from a low of 10.1% to a high of 14.6%. As seen in Figure 2, over time there was a significant trend of an increasing proportion of mitral patients with rheumatic pathology (+0.4% per year, $R^2 = 0.504$, $p = .032$). Figure S1 shows the overall rheumatic mitral volume did not statistically change over time (+2.6 cases, $R^2 = 0.002$, $p = .906$), with variation from 57 to 111 cases/year.

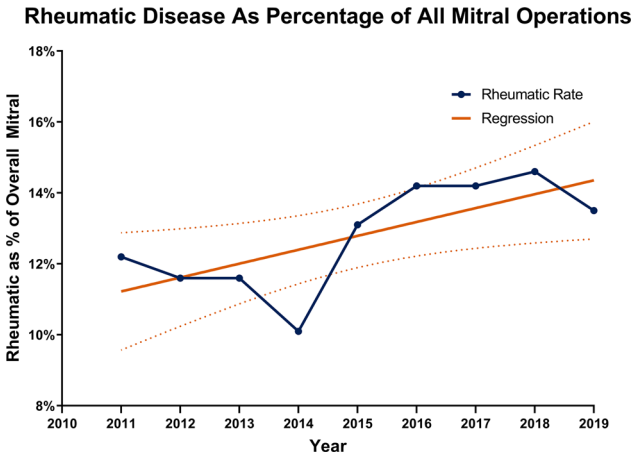

FIGURE 2 Rate of rheumatic etiology as percentage of all mitral valve operations over time for entire mitral cohort

The 19 hospitals demonstrated very high variation in number and rate of rheumatic cases. The median number of rheumatic mitral cases was 22 [5–80] and the median rate of rheumatic mitral pathology was 10.6% [7.1%–21.4%] with a coefficient of variation of 125%. The total number of rheumatic cases per hospital is shown in Figure 3 along with the mitral repair rate. The median rate of rheumatic repairs was 3% [0%–6%] with coefficient of variation of 137%. The distributions for individual hospital data on rate of rheumatic mitral disease, rheumatic repair rate, repair volume, and overall rheumatic volume are shown in Figure S2.

3.2 | Demographic, baseline and operative characteristics

The rheumatic patients were younger (median age 62 vs. 65, $p < .0001$) and more commonly female (75% vs. 43%, $p < .0001$) as compared with the nonrheumatic mitral patients. These patients also had a higher burden of comorbid conditions, heart failure, and multivalve disease (Table 1). Exceptions included, lower rates of coronary artery disease (29% vs. 39%, $p < .0001$) and dialysis-dependent renal failure (3.0% vs. 4.6%, $p = .032$).

Rheumatic patients were more commonly elective status cases (74% vs. 68.4%, $p < .0001$). Although rheumatic patients had higher rates of prior valve surgery, they had a lower rate of prior coronary bypass surgery (Table 2). Rates of concomitant aortic and tricuspid

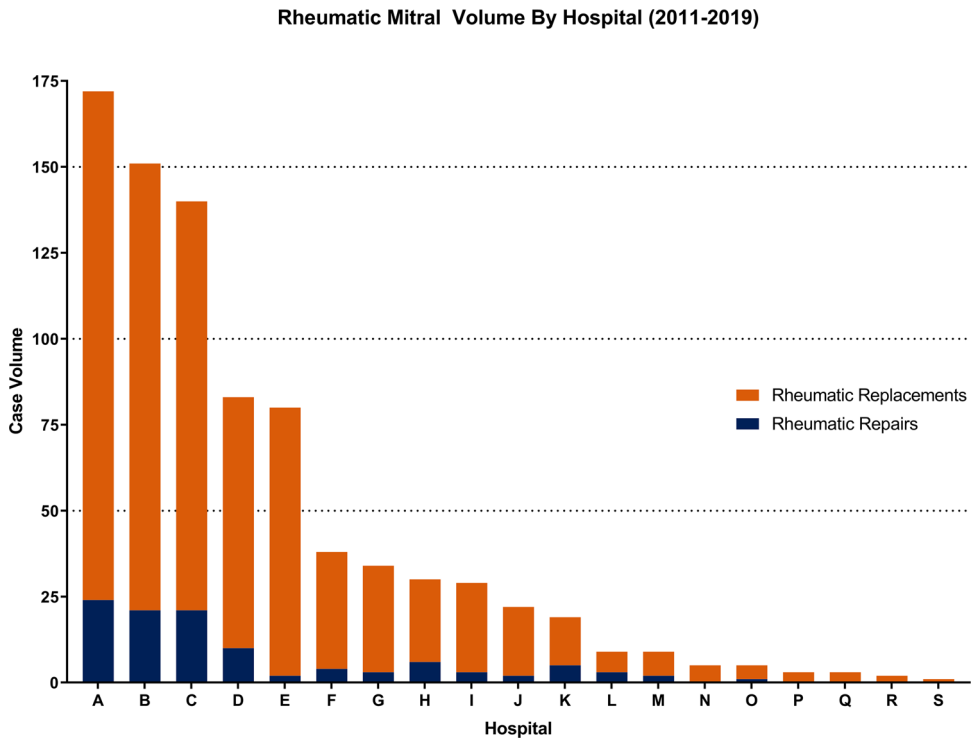

FIGURE 3 Rheumatic mitral valve operations by hospital for the duration of study period (2011–2019) stratified by repairs and replacements

TABLE 1 Baseline characteristics and demographics

	Rheumatic (*n* = 835)	Nonrheumatic (*n* = 5790)	*p*
Age	62 [53–71]	65 [56–74]	<.0001
Sex (female)	629 (75.3%)	2464 (42.6%)	<.0001
Body mass index	27.8 [23.6–32.6]	26.6 [23.5–30.6]	<.0001
Tobacco use	349 (41.9%)	1865 (32.3%)	<.0001
Heart failure	625 (74.9%)	3696 (63.9%)	<.0001
Hypertension	583 (69.8%)	4045 (69.9%)	.964
Coronary artery disease	237 (29.2%)	2135 (39.1%)	<.001
Prior myocardial infarction	90 (10.9%)	1059 (18.4%)	<.0001
Prior stroke	114 (13.7%)	673 (11.7%)	.096
Peripheral arterial disease	79 (9.5%)	512 (8.9%)	.569
Dialysis dependent renal failure	25 (3.0%)	268 (4.6%)	.032
Diabetes mellitus	221 (26.5%)	1313 (22.7%)	.015
Chronic lung disease	389 (46.6%)	1809 (31.2%)	<.0001
Aortic insufficiency (>mild)	136 (16.3%)	622 (10.7%)	<.0001
Aortic stenosis	153 (18.4%)	494 (8.5%)	<.0001
Mitral regurgitation (>mild)	669 (80.1%)	5359 (92.7%)	<.0001
Mitral regurgitation grade			<.0001
None	17 (2.1%)	68 (1.1%)	
Trace/mild	143 (17.3%)	340 (5.9%)	
Moderate	222 (26.8%)	840 (14.6%)	
Severe	447 (53.9%)	4519 (78.4%)	
Mitral stenosis	560 (67.2%)	515 (8.9%)	<.0001
Mitral stenosis grade			<.0001
None	273 (32.7%)	5257 (90.8%)	
Mild	63 (7.5%)	132 (2.3%)	
Moderate	176 (21.1%)	143 (2.5%)	
Severe	323 (38.7%)	258 (4.5%)	
Tricuspid regurgitation (>mild)	298 (35.8%)	1443 (24.9%)	<.0001

valve procedures were higher in rheumatic patients, which concomitant coronary bypass was lower. For rheumatic patients, the rate of mitral valve replacement was dramatically higher than nonrheumatic patients (87.2% vs. 37.5%, $p < .0001$). Cross-clamp and bypass times were not different between groups.

TABLE 2 Operative characteristics

	Rheumatic (*n* = 835)	Nonrheumatic (*n* = 5790)	*p*
Nonelective status	200 (24.0%)	1830 (31.6%)	<.0001
Prior sternotomy	130 (15.6%)	883 (15.3%)	.852
Prior valve procedure	162 (19.4%)	678 (11.7%)	<.0001
Prior coronary surgery	22 (2.6%)	339 (5.9%)	.0001
Mitral replacement	727 (87.2%)	2172 (37.5%)	<.0001
Coronary artery bypass grafting	129 (15.5%)	1343 (23.2%)	<.0001
Aortic valve procedure	180 (21.6%)	789 (13.6%)	<.0001
Tricuspid valve procedure	165 (19.8%)	684 (11.8%)	<.0001
Other cardiac surgery	450 (53.9%)	2396 (41.4%)	<.0001
Other noncardiac surgery	7 (0.8%)	60 (1.0%)	.593
Cardiopulmonary bypass time	152 [117–192]	154 [120–195]	.301
Cross-clamp time	107 [80–138]	110 [83–141]	.118

3.3 | Short-term outcomes

The unadjusted rates of operative mortality (5.2% vs. 5.0%) and major morbidity (22.2% vs. 21.8%) were not statistically different between groups (Table 3). Individual complications were also not significantly different (all $p > .05$). However, resource utilization was generally higher for rheumatic patients. The rate of red blood cell transfusion was higher (39.6% vs. 34.8%, $p = .007$). The length of stay (LOS) was longer, both for the intensive care unit (ICU) with a median of 73 versus 64 h ($p < .0001$), and median postoperative days of 8 versus 7 ($p < .0001$). There was no significant difference in total hospital cost.

3.4 | Subgroup analysis with STS risk scores

A total of 4155 mitral patients had STS risk scores available (Figure 1) with 448 (10.8%) classified as rheumatic. Complete baseline, demographic and operative characteristics are available in Tables S1 and S2. Differences between groups mirrored those found in the entire cohort. Short-term outcomes similarly mirrored the entire cohort with no significant differences in operative mortality (2.9% vs. 3.7%, $p = .395$) or major morbidity (17.6% vs. 18.0%, $p = .852$). The observed to expected ratio (O:E) for mortality was 0.63 ($p = .087$) for rheumatic and 0.84 ($p = .037$) for nonrheumatic patients. Rheumatic patients had higher transfusion rates, longer ICU and postoperative LOSs (Table S3).

Risk-adjusted hierarchical regression results are shown in Table 4 where estimates represent the odds of risk for each mitral pathology

TABLE 3 Outcomes

	Rheumatic (*n* = 835)	Nonrheumatic (*n* = 5790)	*p*
Operative mortality	43 (5.2%)	289 (5.0%)	.845
Major morbidity	185 (22.2%)	1264 (21.8%)	.832
Stroke	11 (1.3%)	88 (1.5%)	.652
Atrial fibrillation	213 (25.5%)	1396 (24.1%)	.381
Renal failure	44 (5.3%)	275 (4.8%)	.515
Prolonged ventilation (>24 h)	145 (17.4%)	991 (17.1%)	.860
Deep sternal wound infection	0	6 (0.2%)	.364
Reoperation for bleeding	38 (4.6%)	243 (4.2%)	.635
Any transfusion	359 (43.1%)	2229 (38.5%)	.012
Red blood cell transfusion	330 (39.6%)	2012 (34.8%)	.007
Intensive care unit (h)	73 [41–139]	64 [28–120]	<.0001
Postoperative length of stay (days)	8 [6–12]	7 [5–11]	<.0001
Total cost (2019 dollars)	$71,877 ± 80,108	$72,808 ± 88,027	.279
Discharge to home	646 (77.4%)	4402 (76.0%)	.396

TABLE 4 Risk-adjusted outcomes with rheumatic disease as reference

	Degenerative	*p*	Ischemic	*p*	Endocarditis	*p*	Other	*p*
Mortality	1.08 (0.66–1.78)	.761	1.32 (0.67–2.58)	.427	1.78 (0.97–3.17)	.062	1.12 (0.64–1.96)	.695
Major morbidity	1.10 (0.85–1.41)	.476	1.12 (0.77–1.63)	.565	1.39 (1.01–1.91)	.044	1.31 (0.99–1.74)	.061
ICU LOS (h)	9.3 (−12.0 to 30.6)	.392	10.1 (−20.7 to 40.9)	.521	16.6 (−10.8 to 44.0)	.235	−1.4 (−25.9 to 23.2)	.913
Postop LOS (days)	0 (−1.0 to 1.04)	.988	−0.2 (−1.7 to 1.3)	.769	1.8 (0.5–3.1)	.008	−0.3 (−1.5 to 0.9)	.636
Total cost ($)	4784 (−5229 to 14,796)	.349	10,592 (−2248 to 23,432)	.106	17,863 (6224–29,503)	.003	−1899 (−12,688 to 8889)	.730

Abbreviations: ICU, intensive care unit; LOS, length of stay.

as compared with rheumatic patients. There were no significant risk-adjusted outcomes as compared with degenerative, ischemic, and other classified pathologies. However, endocarditis patients had significantly higher odds of major morbidity (odds ratio: 1.4, $p = .044$), longer postoperative stays (1.8 days, $p = .008$), and higher cost ($17,863, $p = .003$) compared with rheumatic patients.

4 | COMMENT

In this multicenter retrospective cohort study, rheumatic mitral valve disease was identified to be a significant, and increasing, contributor to mitral valve surgery in the mid-Atlantic region of the United States. Patients undergoing mitral valve surgery for rheumatic valve disease have comparatively high resource utilization relative to those with nonrheumatic mitral valve disease. Importantly, however, morbidity and major mortality were not significantly increased among patients undergoing mitral valve surgery for rheumatic valve disease.

Rhematic fever and its cardiac sequelae are perceived by some physicians in the United States to be a largely historic disease. At the turn of the 20th century, rheumatic fever was the leading cause of death among Americans aged 5–20 years and the second most likely cause among those aged 20–30. Prevalence and incidence of this deadly disease were observed to steadily decline over time in the United States, with the cause of this decline largely attributed to improving living conditions and sanitation as well as the advent of penicillin antibiotics.[1–7,9] Rheumatic fever is no longer designated as a nationally notifiable disease by the Centers for Disease Control and Prevention and as such prevalence data are not collected nor publicly available.[10] By extension, data regarding the prevalence of rheumatic heart disease in the United States are also unavailable. However, rheumatic fever and heart disease remain endemic in the developing world where it is a leading cause of premature death among young adults.[11] Prevalence of rheumatic heart disease is highest among indigenous populations (such as those in Australia) and in sub-Saharan Africa, where prevalence is as high as 30 per 1000 and 37 per 1000, respectively.[11–13] Despite these statistics, there is

comparatively little emphasis on preventing and treating rheumatic fever compared with other global public health priorities.[14] While prevention measures are cost-effective, cardiac surgical programs are expensive and require intensive longitudinal investment. However, where cardiac surgical centers are established, an emphasis should be placed on rheumatic valvular disease management which can account for a majority of cardiac cases.[15] This requires a collaboration between cardiac surgery, anesthesiology, cardiology, government, and industry to ensure access to valve replacement (bioprosthetic and mechanical) and balloon valvuloplasty at affordable prices. Although lessons can be learned from the continued rheumatic disease treatment in the United States, successful pioneering work in Nepal and other locations may offer more salient insights into program development in other low and middle income countries.[16]

This study found that rheumatic heart disease remains a significant contributor to the burden of surgical mitral valve disease in the United States, despite the low prevalence of acute rheumatic fever in the United States. We hypothesize that this may be in part due to migration from areas where acute rheumatic fever remains endemic. Condemi and colleagues reported the results of a screening program for migrants aged 13–26 years old in Rome, Italy. Out of 653 patients screened, 17 were found to have definite rheumatic heart disease and another 122 were classified as borderline rheumatic heart disease suggesting a prevalence ranging from 2.6% to 21%.[17] Economically distressed communities may also suffer from a relative lack of access to medical care, resulting in unrecognized acute rheumatic fever and resultant rheumatic heart disease.[18] This was observed in the wake of the fall of the Soviet Union, when central Asian republics experienced severe economic decline which was concomitant with a sharp increase in acute rheumatic fever.[19] As societal unrest, climate change, and other yet unrecognized disruptive trends promote continued migration from developing to industrialized nations such as the United States, it is reasonable to expect rheumatic heart disease to remain a significant contributor to mitral valve disease despite seemingly low rates of acute rheumatic fever.

In our cohort, patients undergoing mitral valve surgery for rheumatic disease have significantly longer ICU and total LOSs, relative to patients with nonrheumatic valve disease. Patients with rheumatic mitral disease were more likely to have comorbid conditions and concomitant valvular disease, which may explain this finding. Several prior studies have reported increased LOS among patients with rheumatic valve disease. Pato and colleagues performed an analysis on LOS and found that patients with rheumatic valve disease had significantly longer LOS (15 vs. 10 days; $p = .002$). Notably, all patients with rheumatic valvular disease underwent replacement in this study.[20] The vast majority of the rheumatic patients included in our manuscript underwent mitral valve replacement—this has been identified as an independent risk factor for increased LOS (vs. mitral valve repair).[21,22] It is notable that despite this increased LOS, there was no difference in hospital cost between groups. We have previously identified complications as drivers of hospital cost, and the additional non-ICU care for rheumatic patients should be accounted for in term of expected resources but may not have a meaningful impact of hospital cost.[23]

Notably, the presence of rheumatic disease was not significantly associated with significantly increased odds of morbidity or mortality in our cohort. Our overall rate of mortality (5.2%) for rheumatic valve disease is comparable to other published series.[7,22] This complication rate is also in line with the preoperative risk of the cohort, with a high rate of concomitant valvular and coronary disease, and with our rate of mortality for nonrheumatic valve disease at 5.0%. For the nonrheumatic cohort, this may also reflect the high proportion of ischemic and endocarditis mitral valve disease requiring concomitant operations which made up our nonrheumatic cohort. The mortality rates for both cohorts were lower in the PROM sub-group of patients (2.9% and 3.7%). Although the O:E ratio for rheumatic patients was lower than nonrheumatic patients (0.63 vs. 0.84) only the nonrheumatic group was statistically lower due to sample size.

We acknowledge several limitations to this study. This study is retrospective in nature and is vulnerable to the effects of unmeasured confounding. However, these results reflect robust risk adjustment utilizing STS PROM, which is an established variable for accounting for differences in preoperative risk. The cohort utilized is drawn from the mid-Atlantic region and as such may not be generalizable to other geographic areas. Nevertheless, the cohort of hospitals included is diverse in both size and structure (i.e. Academic vs. Private). Finally, we acknowledge that some patients with rheumatic mitral valve disease may have been misclassified as nonrheumatic and vice-versa. This error should be random and should not influence our findings to favor or reject the null hypothesis.

In this large, regional, observational study we found that rheumatic disease remains a significant and increasing driver of mitral valve surgery. Rheumatic disease was associated with increased resource utilization. Further work could focus on identifying patient populations at increased risk of requiring mitral valve surgery for rheumatic disease in the current era.

CONFLICT OF INTERESTS

Dr. Ailawadi is a consultant for Abbott, Edwards, Medtronic, Anteris, Atricure, and Gore. Dr. Joseph is a speaker for Angiodynamics.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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