Adverse cardiac events in children with Williams syndrome undergoing cardiovascular surgery: An analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database

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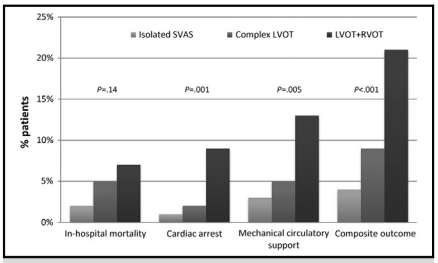
ABSTRACT

Objective: Patients with Williams syndrome (WS) undergoing cardiac surgery are at risk for major adverse cardiac events (MACE). Prevalence and risk factors for such events have not been well described. We sought to define frequency and risk of MACE in patients with WS using a multicenter clinical registry.

Methods: We identified cardiac operations performed in patients with WS using the Society of Thoracic Surgeons Congenital Heart Surgery Database (2000-2012). Operations were divided into 4 groups: isolated supravalvular aortic stenosis, complex left ventricular outflow tract (LVOT), isolated right ventricular outflow tract (RVOT), and combined LVOT/RVOT procedures. The proportion of patients with MACE (in-hospital mortality, cardiac arrest, or postoperative mechanical circulatory support) was described and the association with preoperative factors was examined.

Results: Of 447 index operations (87 centers), median (interquartile range) age and weight at surgery were 2.4 years (0.6-7.4 years) and 10.6 kg (6.5-21.5 kg), respectively. Mortality occurred in 20 patients (5%). MACE occurred in 41 patients (9%), most commonly after combined LVOT/RVOT (18 out of 87; 21%) and complex LVOT (12 out of 131; 9%) procedures, but not after isolated RVOT procedures. Odds of MACE decreased with age (odds ratio [OR], 0.99; 95% confidence interval [CI], 0.98-0.99), weight (OR, 0.97; 95% CI, 0.93-0.99), but increased in the presence of any preoperative risk factor (OR, 2.08; 95% CI, 1.06-4.00), and in procedures involving coronary artery repair (OR, 5.37; 95% CI, 2.05-14.06).

Conclusions: In this multicenter analysis, MACE occurred in 9% of patients with WS undergoing cardiac surgery. Demographic and operative characteristics were associated with risk. Further study is needed to elucidate mechanisms of MACE in this high-risk population. (J Thorac Cardiovasc Surg 2015;■:1-7)



Major adverse cardiac events, sorted by cardiac surgical procedure group.

Central Message

Major adverse cardiac events are common in patients with Williams syndrome following cardiac surgery. Demographic and operative characteristics are associated with risk of those events in patients with Williams syndrome, a high-risk population.

Author Perspective

Patients with Williams syndrome undergoing cardiac surgery are at risk for major adverse cardiac events. Further, patients' demographic and operative characteristics are associated with risk for those events. Findings from this study, the largest to date examining outcomes in patients with Williams syndrome, will help predict the risk associated with specific cardiac operations to better counsel patients and families.

CHD

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Abbreviations and Acronyms

CV = cardiovascular
LVOT = left ventricular outflow tract
MACE = major adverse cardiovascular events
RVOT = right ventricular outflow tract
QTc = corrected QT interval
STS-CHS = Society of Thoracic Surgeons Congenital Heart Surgery Database
SVAS = supravalvular aortic stenosis
WS = Williams syndrome

Supplemental material is available online.

Williams syndrome (WS) is a congenital, multisystem disorder caused by a chromosome 7 microdeletion.[1] Cardiovascular (CV) abnormalities occur in 80% of patients with WS and are the leading cause of morbidity and mortality.[2] The most common CV abnormalities are stenoses of medium and large arteries, including the left ventricular outflow tract (LVOT) and right ventricular outflow tract (RVOT).[2,3] These lesions often require intervention.[3]

Patients with WS are at increased risk for major adverse cardiac events (MACE), including sudden cardiac death.[4,5] The etiology of sudden cardiac death and other forms of MACE in WS has not been clearly elucidated; however, associations with supravalvular aortic stenosis (SVAS), coronary arteriopathy, and corrected QT interval (QTc) prolongation on electrocardiogram have been suggested.[6-8] Prior analyses of perioperative outcomes in patient with WS have largely focused on operative mortality and have not assessed the broader subset of MACE. Moreover, these analyses have been limited by relatively small procedural cohorts and/or outcomes data spanning decades of care.[9] Contemporary data on the prevalence and risk factors for MACE after surgery in patients with WS are lacking.

We used a large, multicenter clinical registry to describe cardiac operations and outcomes in patients with WS. We defined MACE as postoperative death, cardiac arrest, or need for mechanical circulatory support, and evaluated the prevalence of MACE overall and across procedural cohorts, including those requiring coronary artery interventions or relief of left-sided obstructive lesions.

METHODS

Data Source

The Society of Thoracic Surgeons Congenital Heart Surgery (STS-CHS) database was used for this study. As of January 2014, the database contains de-identified data on more than 292,000 surgeries conducted since 2000 at 120 centers in North America. It is estimated that the database currently represents approximately 93% of all US centers that perform congenital heart surgery and >96% of all operations.[10] Preoperative, operative, and outcomes data are collected on all patients undergoing pediatric and congenital heart surgery at participating centers. Coding for this database is accomplished by clinicians and ancillary support staff using the International Pediatric and Congenital Cardiac Code[11] and is entered into the contemporary version of the STS-CHS data collection form.[12] The Duke Clinical Research Institute serves as the data warehouse and analytic center for all of the STS national databases. Evaluation of data quality includes the intrinsic verification of data, along with a formal process of in-person site visits and data audits conducted by a panel of independent data quality personnel and pediatric cardiac surgeons at approximately 10% of participating institutions each year.[10,13,14] This study was approved by the STS-CHS Database Access and Publications Committee and the Duke University Institutional Review Board, and was not considered human subjects research by the Duke University Institutional Review Board in accordance with the Common Rule (45 CFR 46.102(f)).

Patient Population

All index operations (first operation of a hospital admission) in the STS-CHS database (2000-2012) among patients with a diagnosis of WS or a 7q11 chromosomal abnormality were potentially eligible for inclusion (n = 493 operations from 89 centers). The index operation is defined by the STS-CHS database as the first CV operation (with or without cardiopulmonary bypass) of the hospitalization. Index operations for single ventricle heart defects (n = 6) and those missing information on postoperative complications (n = 40) were excluded (Figure 1).

Data Collection and Outcomes

Data collection included demographic information, preoperative risk factors as defined in the STS-CHS database, diagnostic and operative variables, and outcomes data.[15] Procedural cohorts were based on the primary and secondary components of the index operation and were defined as isolated SVAS intervention excluding all other interventions with the exception of patent ductus arteriosus closure, other LVOT procedures (including extended arch intervention), RVOT procedures, and combined LVOT/RVOT procedures.

The primary outcome of interest was the incidence of postoperative MACE, defined as postoperative death, cardiac arrest, or need for mechanical circulatory support.[16] Other outcomes evaluated included arrhythmia, neurologic deficit persistent at discharge, unplanned reoperation, presence of an open sternum after surgery, need for prolonged mechanical ventilation, and the presence of any postoperative complications. The outcomes were chosen a priori given their clinical significance and their potential association with MACE.

Analysis

Population characteristics were described collectively and stratified by procedural group using standard summary statistics, including counts and percentages and median and interquartile ranges. Standard statistical tests, including χ^2 tests of association and Wilcoxon rank sum tests were used to compare the distribution of categorical and continuous variables across the different procedural groups. The association between preoperative factors and MACE was also explored using univariate logistic regression. Preoperative factors evaluated were chosen a priori based on their association with morbidity and mortality after congenital heart surgery in general (age, weight, previous cardiac surgery, and any preoperative risk factor), or their previously described potential implication in MACE in patients with WS (eg, arrhythmia or coronary procedures). Given the descriptive nature of this study and unavailability in the database of other important variables likely to affect WS outcomes, multivariable analysis

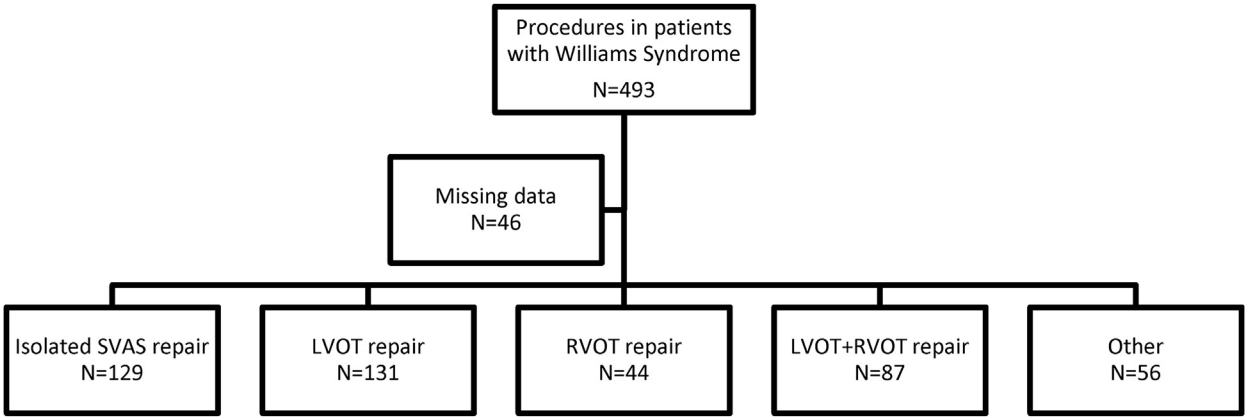

FIGURE 1. Flowchart of most common surgical procedure distributions in patients with Williams syndrome in the Society of Thoracic Surgeons Congenital Heart Surgery database. *SVAS*, Supravalvular aortic stenosis; *LVOT*, left ventricular outflow tract; *RVOT*, right ventricular outflow tract.

was not conducted. All analyses were done using SAS (version 9.3, SAS Institute, Inc, Cary, NC).

RESULTS

Study Population Characteristics

The cohort included 447 index CV operations at 87 surgical centers (Figure 1). The most common procedures and diagnoses are shown in Table E1. Overall, 77% of procedures involved the LVOT (isolated SVAS, LVOT, or LVOT/RVOT), whereas 30% involved the RVOT (RVOT or LVOT/RVOT). Combined LVOT/RVOT procedures were performed in 19% of the operations. Concomitant coronary artery procedures were rare (20 out of 447 [5%]), occurring most frequently in the cohort undergoing combined LVOT/RVOT procedures (10 out of 87 [11%]). SVAS was the primary diagnosis in more than half of all procedures (247 out of 447 [55%]). The majority of patients did not have a history of prior sternotomy (343 out of 447 [77%]).

Operative Characteristics

The median age and weight at surgery were 2.4 years (interquartile range, 0.6-7.4 years) and 10.5 kg (interquartile range, 6.5-21.5 years), respectively. Patients who underwent combined LVOT/RVOT procedures were younger at the time of surgery compared with those who underwent isolated SVAS repair or complex LVOT interventions ($P < .0001$) (Table 1). STS-CHS-defined preoperative risk factors were present in 112 out of 447 total procedures

TABLE 1. Patient and operative characteristics

Characteristic	Overall (N = 447)	Isolated SVAS (n = 129)	Complex LVOT (n = 131)	Isolated RVOT (n = 44)	LVOT/RVOT (n = 87)	Other (n = 56)	*P* value
Demographic factors							
Age at surgery (y)	2.4 (0.6-7.4)	3.8 (2.4-7.6)	2.1 (0.6-9.1)	0.9 (0.4-2.3)	0.7 (0.4-1.2)	6.9 (0.9-15.3)	< **.001**
Weight at surgery (kg)	10.6 (6.5-21.5)	13.6 (10.2-24.1)	11.3 (6.4-25.8)	7.6 (5.2-10.4)	6.9 (5.4-9.3)	19.2 (7.9-42.3)	< **.001**
Male gender	257 (57.5)	81 (62.8)	74 (56.5)	24 (54.5)	58 (66.7)	20 (35.7)	**.004**
Preoperative factors							
Any preoperative risk factors	112 (25.1)	22 (17.1)	35 (26.7)	20 (45.5)	19 (21.8)	16 (28.6)	**.005**
Mechanical circulatory support	6 (1.3)	1 (0.8)	2 (1.6)	0 (0)	2 (2.3)	1 (1.9)	.802
Mechanical ventilator support	26 (5.9)	3 (2.4)	8 (6.3)	3 (6.8)	6 (7.0)	6 (11.1)	.219
Neurologic deficit	14 (3.2)	2 (1.6)	5 (3.9)	3 (6.8)	3 (3.5)	1 (1.9)	.478
Prior sternotomy							< **.001**
0	343 (76.7)	121 (93.8)	80 (61.1)	33 (75.0)	75 (86.2)	34 (60.7)	
1	53 (11.9)	3 (2.3)	24 (18.3)	5 (11.4)	9 (10.3)	12 (21.4)	
≥2	38 (8.5)	1 (0.8)	22 (16.8)	5 (11.4)	3 (3.4)	7 (12.5)	
Operative factors							
Cardiopulmonary bypass time (min)	117 (82-163)	92 (69-130)	129 (86-175)	100 (66-132)	162 (111-205)	130 (101-144)	< **.001**
Crossclamp time (min)	63 (42-95)	56 (44-79)	64 (41-91)	38 (0-68)	96 (55-121)	75 (39-109)	< **.001**
Concomitant coronary artery repair	20 (4.5)	0 (0)	6 (4.6)	1 (2.3)	10 (11.5)	3 (5.4)	.002
Subsequent coronary artery repair	2 (0.4)	1 (0.8)	0 (0)	0 (0)	1 (1.1)	0 (0)	.680

Data are presented as n (%) or median (interquartile range). Boldface type indicates statistical significance. *SVAS*, Supravalvular aortic stenosis; *LVOT*, left ventricular outflow tract; *RVOT*, right ventricular outflow tract.

TABLE 2. Postoperative outcomes

Outcome	Overall (N = 447)	Isolated SVAS (n = 129)	Complex LVOT (n = 131)	Isolated RVOT (n = 44)	LVOT/RVOT (n = 87)	Other (n = 56)	*P* value
Major adverse coronary event	41 (9.2)	5 (3.9)	12 (9.2)	0 (0)	18 (20.7)	6 (10.7)	< **.001**
In-hospital mortality	20 (4.5)	2 (1.6)	7 (5.3)	0 (0)	6 (6.9)	5 (8.9)	.071
Cardiac arrest	14 (3.1)	1 (0.8)	2 (1.5)	0 (0)	8 (9.2)	3 (5.4)	**.003**
Mechanical circulatory support	25 (5.6)	4 (3.1)	7 (5.3)	0 (0)	11 (12.6)	3 (5.4)	**.015**
Postoperative length of stay (d)	6.0 (4.0-10.0)	4.0 (4.0-6.0)	6.0 (4.0-10.0)	6.0 (4.0-10.0)	8.0 (5.0-18.0)	7.0 (4.0-11.0)	< **.001**
Any postoperative complication	188 (42.1)	33 (25.6)	59 (45.0)	16 (36.4)	51 (58.6)	29 (51.8)	< **.001**
Arrhythmia	32 (7.2)	6 (4.7)	13 (9.9)	5 (11.4)	6 (6.9)	2 (3.6)	.289
Neurologic deficit (persisting at discharge)	6 (1.3)	2 (1.6)	1 (0.8)	0 (0)	3 (3.4)	0 (0)	.327
Unplanned reoperation	22 (4.9)	3 (2.3)	9 (6.9)	1 (2.3)	7 (8.0)	2 (3.6)	.231
Sternum left open	47 (10.5)	6 (4.7)	10 (7.6)	7 (15.9)	20 (23.0)	4 (7.1)	< **.001**
Prolonged mechanical ventilator support	15 (3.4)	4 (3.1)	2 (1.5)	3 (6.8)	4 (4.6)	2 (3.6)	.491

Data are presented as n (%) or median (interquartile range). Boldface type indicates statistical significance. *SVAS*, Supravalvular aortic stenosis; *LVOT*, left ventricular outflow tract; *RVOT*, right ventricular outflow tract.

(25%). Preoperative mechanical ventilatory support was the most common (26 out of 447 [6%]). Preoperative mechanical circulatory support was reported in 1.3% (6 out of 447). Preoperative risk factors were more frequent in patients undergoing isolated RVOT procedures ($P = .005$), with the most common risk factors in that group being labeled as other risk factor (9 out of 44 [21%]), mechanical ventilator support (3 out of 44 [7%]), and neurologic deficit (3 out of 44 [7%]). Unplanned reoperations were performed in 22 out of 447 patients (4.9%).

Outcomes and Risk Factors

Overall in-hospital mortality in the cohort was 20 out of 447 (5%) (Table 2). Mortality was higher in patients undergoing combined LVOT/RVOT procedures (6 out of 87 [7%]), whereas there were no mortalities in the group of patients undergoing isolated RVOT procedures (Figure 2). There was no significant difference in in-hospital mortality between combined LVOT/RVOT procedures and complex LVOT or isolated SVAS repairs ($P = .07$ and $P = .54$, respectively). Postoperative complications were common, occurring in 188 out of 447 cases (42%). The most common postoperative complications included sternum left open and arrhythmias (47 out of 447 [11%] and 32 out of 447 [7%], respectively).

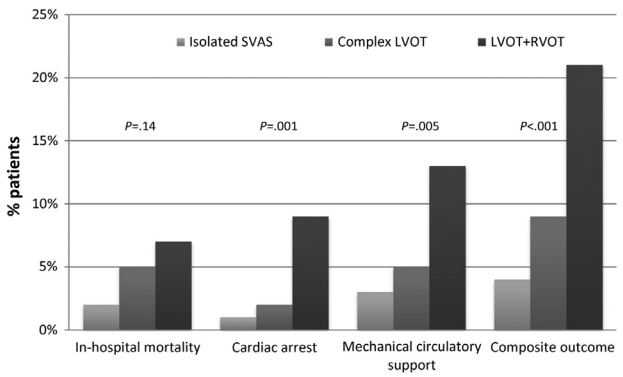

FIGURE 2. Major adverse cardiac events by cardiac surgical procedure group. *SVAS*, Supravalvular aortic stenosis; *LVOT*, left ventricular outflow tract; *RVOT*, right ventricular outflow tract.

Overall, MACE occurred after 41 out of 447 procedures (9%), including 20 deaths, 25 episodes of postoperative mechanical circulatory support (11 out of 25 [44%] with mortality), and 14 postoperative cardiac arrests (4 out of 14 [29%] with mortality). MACE were significantly more common after combined LVOT/RVOT (18 out of 87 [21%]) procedures than after complex LVOT or isolated SVAS procedures ($P < .001$ and $P = .01$, respectively). There were no MACE reported after isolated RVOT procedures. MACE occurred most frequently following procedures involving coronary artery repair either as primary or concomitant procedure (7 out of 22 [32%]), and in patients with preoperative arrhythmias (3 out of 15 [20%]). Median aortic crossclamp times were longer in patients with MACE compared with those without (86.5 minutes [interquartile range, 59-139 minutes] vs 61 minutes [interquartile range, 41-92 minutes]; $P = .004$). This difference was driven by the longer crossclamp time in patients who experienced MACE after isolated SVAS repair (median, 101 minutes [interquartile range, 61-151 minutes] vs 55 minutes [interquartile range, 43-77 minutes]; $P = .03$). Aortic crossclamp times did not differ between patients with and without MACE undergoing any other procedure.

The unadjusted odds of MACE were lower with increasing age and weight at surgery (odds ratio [OR], 0.99 per year of age; 95% confidence interval [CI], 0.98-0.99; and OR, 0.97 per kg; 95% CI, 0.93-0.99). These effects were seen in isolated SVAS repairs but not in LVOT or combined LVOT/RVOT procedures (Table 3). The presence of any preoperative risk factor was associated with increased odds of MACE (OR, 2.08; 95% CI, 1.06-4.00).

TABLE 3. Unadjusted odds ratios (95% confidence interval) of major cardiac adverse event

Effect	Overall (N = 447)	Isolated SVAS (n = 129)	Complex LVOT (n = 131)	LVOT/RVOT (n = 87)	Other (n = 56)
Demographic characteristic					
Age at surgery (mo)	**0.99 (0.98-0.99)**	**0.97 (0.92-1.00)**	1.00 (0.99-1.01)	1.00 (1.0-1.01)	**0.96 (0.88-0.99)**
Weight at surgery (kg)	**0.97 (0.93-0.99)**	**0.82 (0.63-0.99)**	1.00 (0.96-1.03)	1.01 (0.96-1.05)	**0.81 (0.59-0.96)**
Female gender	1.07 (0.56-2.03)	2.45 (0.46-15.16)	0.66 (0.18-2.11)	1.03 (0.34-2.94)	2.27 (0.41-23.35)
Other preoperative factor					
Any preoperative risk factors	**2.08 (1.06-4.00)**	1.61 (0.16-9.26)	3.07 (0.94-10.06)	1.56 (0.46-4.78)	**5.54 (1.09-35.20)**
Previous cardiac surgery	0.69 (0.26-1.54)	2.44 (0.02-28.02)	0.97 (0.27-3.11)	0.86 (0.15-3.37)	0.12 (0.00-1.15)

Boldface type indicates statistically significant odds ratios. *SVAS*, Supravalvular aortic stenosis; *LVOT*, left ventricular outflow tract; *RVOT*, right ventricular outflow tract.

Gender, race, presence of preoperative arrhythmias, and a history of prior cardiac surgery were not associated with odds of MACE. Procedures involving coronary artery repair had higher unadjusted odds of MACE (OR, 5.37; 95% CI, 2.05-14.06), whereas the presence of a postoperative arrhythmia was not associated with higher odds of MACE.

DISCUSSION

The major finding of our study—which was the largest analysis to date of outcomes in patients with WS undergoing cardiac surgical procedures—was a 9% overall prevalence of MACE, which ranged from 0% after isolated RVOT procedures to 21% after combined LVOT/RVOT procedures.

Distribution of Surgical Procedures

Most surgical procedures in our cohort involved the LVOT. This finding is consistent with the previously reported experience from the Children's Hospital of Philadelphia, where 33 out of 48 surgical interventions (69%) were for SVAS,[8] and the multicenter 19-year experience of the Pediatric Cardiac Care Consortium, where 32 out of 48 (67%) of all surgical interventions were performed for SVAS or combined SVAS and pulmonary artery stenosis.[9] Isolated RVOT procedures were the least common procedures in our cohort, perhaps reflecting that only the most severe forms of RVOT obstruction are referred for surgical intervention and the availability of nonsurgical alternative forms of therapy.[17] The finding that the majority of patients undergoing isolated RVOT were younger than age 1 year is consistent with previous reports and likely reflects the higher severity of obstruction requiring earlier surgical intervention in these patients.[3]

Coronary artery procedures are of particular interest in patients with WS, because coronary ostial stenosis has been proposed as etiologic in the occurrence of sudden death, particularly around the time of anesthetic induction.[4] Similar to prior studies, coronary artery procedures were uncommon (5%) and occurred predominantly in patients with complex LVOT or combined LVOT/RVOT procedures (77%). It is possible that some of these patients may have undergone coronary artery procedures in response to an intraoperative complication, and not because of a primary coronary anomaly.

Outcomes

MACE are common after cardiac surgery in patients with WS, but the risk varies by procedure. Although our overall in-hospital mortality of 5% is comparable to the mortality reported for surgery-related deaths in the Pediatric Cardiac Care Consortium study[8] and the report from the Children's Hospital of Philadelphia,[9] our study is the first to report incidence of MACE following surgical intervention in patients with WS. Given the reported mortality rate and the high morbidity associated with MACE, the risks associated with cardiac surgery in WS are significant. This finding is further emphasized when considering that patients with WS generally undergo surgery beyond the neonatal period, and that our cohort consists only of patients with biventricular circulation. Indeed, among the 35 most common procedures performed in children and recorded in the STS-CHS database during the period from 2008 to 2012, only revision or conversion of a Fontan had a higher mortality (9%), and mechanical aortic root replacement was the only procedure with similar mortality in patients with biventricular circulation (5%).[18] In comparison, mortality in children during the same time period was only 0.4% following the Ross procedure, only 0.3% following RVOT procedures, and only 0.2% following aortic stenosis repair. Overall, this information is critical when discussing risk of surgical interventions with patients with WS and their families.

MACE were most common after combined LVOT/RVOT procedures (21%). This finding is consistent with prior reports of higher mortality in patients with WS requiring biventricular outflow tract surgery.[9] It remains unclear whether risk in these patients is increased because of a more severe, underlying WS-related, vascular disease substrate, or simply because of the greater complexity of simultaneous surgical intervention on both outflow tracts. No MACE occurred after isolated RVOT surgery, possibly reflecting both the reduced surgical complexity and the decreased burden of WS-related CV pathology. It should be noted that patients undergoing isolated RVOT surgery still had a relatively high frequency of postoperative

complications (36% vs 41% for all other procedures combined). The absence of MACE in these patients despite a 36% postoperative complication rate may support the possibility that MACE in patients with WS is related to the underlying WS-related disease substrate and not just the increased surgical complexity associated with left-sided interventions.

Mechanisms of MACE

The exact mechanism of MACE in patients with WS is unknown. Surgical relief of either SVAS or more distal arch obstruction will substantially decrease coronary perfusion pressure. Because coronary ostial stenosis has previously been implicated as a potential explanation for cardiac arrest in patients with WS, we postulated that MACE would be more common after these left-sided cardiac surgeries.[4,6] However, MACE was significantly less frequent in our cohort after isolated SVAS repair when compared with other left-sided cardiac surgeries, suggesting that the mechanisms may be more complex. Similar to several smaller studies, we found that bilateral outflow tract obstruction and coronary ostial stenoses were both risk factors. However in our analysis and in others, MACE occurred in the absence of both findings.[8,9] Arrhythmias may play an important role, because prolongation of the QTc interval has been found in a subset of patients with WS.[5] This may be related to myocardial ischemia, as QTc interval prolongation has also been correlated with the occurrence of ventricular ectopy.[19] Although MACE occurred more frequently in patients with preoperative arrhythmias, the unadjusted odds of MACE were not significantly different in these patients. Known surgical risk factors such as lower age and weight at surgery, the presence of any preoperative complication, and longer aortic crossclamp time were associated with increased odds of MACE. As a whole, the increased risk of MACE in patients with WS may be mediated by several different factors, including the need for surgical intervention at younger age and lower weight in the most severely affected patients; coronary artery anomalies requiring intervention, seen more frequently in combined LVOT/RVOT procedures and complex LVOT procedures; and unforeseen intraoperative complications requiring longer aortic crossclamp times even in overall lower risk groups such as isolated SVAS repair.

The strengths of our study include its sample size and data source. The STS-CHS database captures the majority of congenital heart surgeries performed in the United States. The detailed data collection allowed us to separate patients by type of surgery performed, and uncovered differences between types of LVOT procedures, combined LVOT/RVOT procedures, and cases with concomitant coronary artery interventions. The knowledge of postoperative complications, including cardiac arrest and need for mechanical circulatory support, allowed us to identify the meaningful and much more common outcome of MACE, rather than focusing on postoperative mortality alone. Although the overall incidence of MACE was high, the population was heterogeneous with respect to surgical procedures and risk factors, and the number of events by subgroups was limited. Despite the wealth of data collected in the STS-CHS database, details of individual cases, including unusual intraoperative findings that may be common in this population, are not available. Further, at the time of our analysis, details of the anesthetic management, postulated to play a significant role in MACE in patients with WS, were not reliably captured in the database and therefore could not be included in this analysis. Finally, additional measures of postcardiotomy cardiovascular compromise such as intermittent episodes of ischemia or prolonged need for inotropic support were not available in the database and could therefore not be evaluated in the analysis. Taken together, these limitations would have diminished the interpretability of a multivariable analysis, and for these reasons we elected a primarily descriptive focus for this study.

CONCLUSIONS

We found a 9% incidence of MACE after surgical intervention in patients with WS, highlighting the significant risk associated with certain operations in these patients. Although the exact mechanism of MACE is difficult to elucidate in a retrospective, database-driven study, our findings suggest a multifactorial etiology of this outcome in the WS population.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: Williams syndrome, major adverse cardiac events, risk factors

TABLE E1. Surgical procedures

Primary procedure	Overall (N = 447)	Isolated SVAS (n = 129)	Complex LVOT (n = 131)	Isolated RVOT (n = 44)	LVOT/RVOT (n = 87)	Other (n = 56)
Aortic stenosis, supravalvular, repair	181 (40.5)	129 (100.0)	24 (18.3)	0 (0.0)	28 (32.2)	0 (0.0)
Aortic arch repair	53 (11.9)	0 (0.0)	39 (29.8)	0 (0.0)	14 (16.1)	0 (0.0)
Coarctation repair, patch aortoplasty	11 (2.5)	0 (0.0)	11 (8.4)	0 (0.0)	0 (0.0)	0 (0.0)
Valvuloplasty, aortic	12 (2.7)	0 (0.0)	9 (6.9)	0 (0.0)	3 (3.4)	0 (0.0)
Coarctation repair, end to end	6 (1.3)	0 (0.0)	6 (4.6)	0 (0.0)	0 (0.0)	0 (0.0)
Coarctation repair, end to end, extended	5 (1.1)	0 (0.0)	5 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)
Aortic aneurysm repair	5 (1.1)	0 (0.0)	5 (3.8)	0 (0.0)	0 (0.0)	0 (0.0)
Valvuloplasty, mitral	17 (3.8)	0 (0.0)	2 (1.5)	0 (0.0)	1 (1.1)	14 (25.0)
Pulmonary artery, reconstruction, branch, central (within the hilar bifurcation)	48 (10.7)	0 (0.0)	0 (0.0)	15 (34.1)	33 (37.9)	0 (0.0)
RVOT procedure	10 (2.2)	0 (0.0)	0 (0.0)	10 (22.7)	0 (0.0)	0 (0.0)
Pulmonary artery, reconstruction, main (trunk)	7 (1.6)	0 (0.0)	0 (0.0)	7 (15.9)	0 (0.0)	0 (0.0)
Pulmonary artery, reconstruction, branch (at or beyond the hilar bifurcation)	6 (1.3)	0 (0.0)	0 (0.0)	3 (6.8)	3 (3.4)	0 (0.0)
Ventricular septal defect repair, patch	5 (1.1)	0 (0.0)	0 (0.0)	1 (2.3)	0 (0.0)	4 (7.1)

Results presented are limited to those procedures reported in >1% of the entire cohort. Values are presented as n (%). *SVAS*, Supravalvular aortic stenosis; *LVOT*, left ventricular outflow tract; *RVOT*, right ventricular outflow tract.

000 Adverse cardiac events in children with Williams syndrome undergoing cardiovascular surgery: An analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database

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Major adverse cardiac events occur in 9% of all cardiac operations in patients with Williams syndrome. Risk varies with the type of operation and is highest for left-sided lesions. Preoperative risk factors and concomitant coronary artery procedures are associated with increased risk.