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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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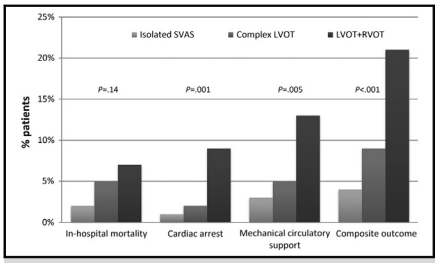
ABSTRACT

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;149:1516-22)



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.

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.

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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