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WILLIAMS SYNDROME

Surgical Specialty:	Cardiac
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Background:

- General Considerations[1, 2]
  - Williams syndrome, also known as Williams-Beuren syndrome, has an incidence of 1 in 7,500 to 20,000 people.
  - Occurs due to a deletion in the long arm of chromosome 7 (7q11.23) which codes for the elastin gene.
  - Williams syndrome affects multiple organ systems, but most commonly the cardiovascular system.
  - Prevalence is similar for both biological sexes; however, males are more likely to have severe cardiac disease.
  - Characteristic features include elfin facies and a "musical" and hyper-social personality.
- Patient Considerations
  - Disease-specific Considerations[1,2]
    - Over 80% of patients have cardiovascular manifestations, including elastin arteriopathy of the medium and large-sized arteries such as valvular and supravalvular aortic stenosis (SVAS) and aortic coarctation.
    - Arterial stenotic lesions, specifically SVAS, occur in 45-70% of cases and are the leading cause of morbidity and mortality.
    - Stenoses may also involve the pulmonary arteries, origins of the coronary arteries, and renal arteries.
  - Associated Comorbidities[3]
    - **Developmental and Neurological**: developmental delay, hypotonia
    - **Eyes and Ear**: strabismus, recurrent otitis media, tear duct hypoplasia, hearing loss, sound sensitivity (hyperacusis).
    - **Endocrine and Growth**: early puberty, slow physical growth, hypercalcemia, diabetes, obesity, hypothyroidism.
    - **Gastrointestinal**: feeding difficulties, diverticulitis, constipation, gastroesophageal reflux disease.
    - **Genitourinary**: enuresis, urinary frequency.
    - **Behavioral and Psychiatric**: attention deficit hyperactivity disorder, anxiety, depression, hyper-social personality.
    - **Craniofacial and Dental**: characteristic facial appearance, malocclusion, microdontia.

- **Cardiovascular**: hypertension, vascular stenoses, cardiovascular collapse (with or without anesthesia), QTc prolongation, right and left ventricular outflow tract obstruction, ventricular septal defect, mitral valve prolapse, and aortic insufficiency. Common heart defects include supravalvar aortic stenosis, pulmonary stenosis (both valvular and peripheral), aortic coarctation and mitral valve prolapse
- **Musculoskeletal**: decreased bone mineral density, scoliosis, joint laxity, and contractures.

Anesthetic Planning:

- Pre-Anesthetic Evaluation
  - Additional labs/tests indicated during work-up
    - A thorough cardiovascular assessment, including an echocardiogram, should be done within 1 month of the anesthetic and surgery.
    - Electrocardiogram (ECG) within 2 hours of the start of the procedure[4].
  - The patient should be scheduled for the first case of the day, and intravenous (IV) fluids should be administered if the NPO time is expected to be greater than 2 hours.
  - If preoperative IV access cannot be obtained, clear fluids should be continued up until 2 hours before the surgery to maintain intravascular volume status.
  - If the patient has neurodevelopmental delays, attention-deficit disorder, or autistic behavior, premedication may be warranted.
  - Depending on the planned procedure, consider obtaining albumin, ionized calcium, serum calcium, basic metabolic panel (to evaluate BUN and creatinine), and thyroid function tests (thyroid-stimulating hormone and triiodothyronine levels)
  - Risk stratification[4]
    - Risk factors for sudden death—young age (less than 3 years), sedation or general anesthesia, biventricular outflow tract obstruction, and coronary artery stenosis.
    - Risk stratification is discussed in more detail in this article.
  - Discussions to have with surgeon/family
    - Code status
    - Extracorporeal Membrane Oxygenation (ECMO) candidate. In the event of a cardiac arrest, ECMO would need to be activated if return of spontaneous circulation is not achieved quickly after initiation of Pediatric Advanced Life Support.
- Specific or Unique Room Set-Up Requirements
  - Airway—not known to be difficult to mask ventilate or intubate.
  - Drugs/Infusions—standard induction drugs and vasoactive emergency drugs. (including vasopressors as they should be the first line drugs for SVAS to preserve myocardial oxygen supply/demand balance)
  - Monitors—standard American Society of Anesthesiologists monitors, including a 5-lead ECG and possibly an arterial line.

Intraoperative Considerations:

- General
  - Cath lab procedures take place in 1/3rd of patients, with 75% of those undergoing their first intervention by age 5.
  - If the patient requires multiple procedures, all attempts should be made to combine them under one anesthetic.

- Induction
    - There is no optimal induction technique for patients with William's syndrome.
    - Meticulous attention should be paid to avoiding hypotension and maintaining coronary perfusion pressure.
    - Balanced and careful titration of induction agents.
    - Noise-free operating room as many William's syndrome patients have hyperacusis.
- Maintenance
    - Maintain age-appropriate heart rate, sinus rhythm, adequate preload, contractility, and systemic vascular resistance ~~(SVR).~~
    - Avoid increases in pulmonary vascular resistance ~~(PVR).~~
    - For prolonged procedures, a calcium level should be monitored.
- Hemodynamic/Physiologic goals
    - There is no specific anesthetic technique that is recommended over another; the primary goal is to maintain hemodynamic stability.
    - Maintain coronary perfusion pressure.
    - Avoid increases in myocardial oxygen demand and decreases in myocardial oxygen supply.
    - Maintain euvolemia.
    - Monitor the patient's volume status, including blood loss and urine output.
- Surgical Considerations
    - Because these children often display muscular weakness, neuromuscular blocking drugs should be used with caution.
- Emergence/Disposition
    - Standard monitoring until the patient has fully recovered from anesthesia.
    - Early parental presence to allay anxiety in the postoperative period.

Case Specific Complications/Pitfalls

- Williams syndrome is one of the leading causes of cardiac arrest listed in the Pediatric Cardiac Arrest ~~(POCA)~~ registry.
- The risk of sudden cardiac death is reported to be 25 to 100 times more likely than in the general population and is more likely to occur under anesthesia.
- Sudden death has also been reported in patients without evidence of coronary or outflow tract obstruction.
- If the patient does go into cardiac arrest, attempts to resuscitate the child are frequently unsuccessful and often refractory to all efforts to regain a normal heart rhythm
- At some institutions, these patients are cared for by pediatric cardiac anesthesiologists. Alternatively, some insist on having two attendings present for induction and emergence due to the increased chance of cardiac decompensation.

References

1. Miller-Hance WC and Gertler R. "Essentials of Cardiology." In: Cote CJ, Lerman J, and Anderson BJ. *A Practice of Anesthesia For Infants and Children*. 6th ed. Philadelphia, PA. (2019):366-7.
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3. Kozel BA, Barak B, Kim CA, et al. Williams syndrome. *Nat Rev Dis Primers. 2021;* 7:42. PubMed Link
4. Collins RT, Collins MG, Schmitz ML, Hamrick JT. Peri-procedural risk stratification and management of patients with Williams syndrome. *Congenit Heart Dis*. 2017; 12:133-42. PubMed Link

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