PBLD #3: Infant with Williams Syndrome for Cardiac Catheterization and Cardiac Surgery

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Objectives

Although trans-thoracic echocardiography can reveal a wealth of information for many congenital cardiac defects, some lesions require cardiac catheterization to fully delineate the anatomy prior to surgical repair.
In this problem based learning discussion, an infant with severe cardiac manifestations of Williams syndrome requires multiple anesthetics for diagnostic cardiac catheterization, surgical correction, and interventional cardiac catheterization. The learning objectives for this discussion are as follows:
1) To understand the features of Williams syndrome
2) To review the possible mechanisms for sudden death in patients with Williams syndrome
3) To formulate plans for preoperative, intraoperative, and postoperative management of severe biventricular obstruction with biventricular failure

Stem Case

Anesthetic # 1
A two-month-old girl with dysmorphic facies consistent with Williams syndrome presents for diagnostic cardiac catheterization. She was born at 41 weeks EGA and hospitalized in the NICU for 4 days for respiratory distress, but did not require mechanical ventilation. She was again hospitalized at 1month of age for pneumonia and found to have a murmur at that time. Parents report she is a fussy eater.

Key Questions
1) What is Williams Syndrome?
2) What are the cardiovascular defects associated with Williams syndrome?
3) How does one assess congestive heart failure in an infant?

Pre-admission data is as follows:
- VS   – HR 130s, RR 40s, BP 110/70, SpO_2 100%, Wt 4.5 kg
- EKG – NSR 130 bpm, rightward axis deviation, prominent LV forces, no Q's or ST Δ
- CXR – Enlarged cardiac silhouette, lungs appear wet
- TTE – Severe supravalvular Aortic stenosis with calculated gradient of 100 mmHg, severe supravalvular pulmonic stenosis with small branch PA's and calculated gradient of 78 mmHg

Key Questions
4) What are the anesthetic concerns for a patient with aortic stenosis?
5) What are the anesthetic concerns for a patient with severe supravalvular aortic stenosis extending across the entire arch and diffuse supravalvular pulmonary artery stenosis?
6) What are the risks of sedation or general anesthesia under these circumstances?
7) What monitors, equipment, personnel, and other resources would you like available before proceeding with this case?
8) Will you proceed with sedation or general anesthesia? What agents are safe? If you decide on general anesthesia, how will you induce this patient? Will you intubate?

Anesthetic # 2
The patient described above undergoes successful diagnostic cardiac catheterization. She returns one week later for definitive surgical correction.

Key Questions
9) How will you induce general anesthesia in this patient? What agents will you use for maintenance?
10) What invasive monitors are necessary for this case? Which monitors will you place prior to induction? Prior to incision?
11) After this type of aortic arch and pulmonary artery reconstruction, what difficulties do you anticipate upon separation from CPB?

Separation from CPB is unsuccessful and the decision to initiate ECMO is made. The post-operative course is as follows:
- ECMO d/c'd on POD #5
- Required CPR on POD #10
- Extubated on POD #12
- Weaned off infusions of vasopressin, epinephrine, and norepinephrine by POD #14
- Discharged from the hospital on Lasix, Methadone, and Ativan on POD #21

Anesthetic # 3
The patient is readmitted to the PICU one month later for respiratory distress and poor feeding. A dobutamine drip 5mcg/kg/min is initiated. The following data is gathered:
- VS   – HR 160s, RR 50-60, BP 100/40, SpO_2 100% on NC O_2, Wt 5.2 kg
- EKG – Sinus tachycardia 160 bpm, left superior axis deviation, RAE, ST abnormalities and T-wave inversions in lateral leads
- CXR – Large globular cardiac silhouette, very large PA, negative infiltrates or effusions
- TTE – Poor biventricular function, huge proximal PA aneurysm formation, severe bilateral branch PA stenoses

The cardiology team wants to attempt branch PA stenting in the Cath Lab under general anesthesia.

Key Questions

12) What are your anesthetic concerns at this time? Is there any way of optimizing this patient prior to catheterization?
13) IV access is lost prior to arrival in the Cath Lab, is an inhalational induction a reasonable option? Which agents would you choose?
14) The patient arrests upon placement of an ETT. What is the cause of this cardiovascular collapse?

The patient is successfully resuscitated with CPR and epinephrine in the Cath Lab. Despite initial stabilization, however, she arrests again the PICU, and the decision is made to place her on ECMO for the second time. She is brought back to the Cath Lab while on ECMO and undergoes bilateral branch PA stenting. Her post-interventional catheterization course is as follows:

- ECMO required x 4 days
- Mechanically ventilated x 21 days
- Vasopressors required x 31 days
- Discharged after 56 days of hospitalization

Anesthetic # 4
Over the next 6 weeks, this patient continues to exhibit irritability, poor growth, and dependency on continuous NGT feeds. Her medications include digoxin, aldactone, prilosec, and iron. The cardiology team feels that further stenting of the PAs is her only hope for survival and asks for your assistance in the Cath Lab. Pre-operative data includes:

- VS   – HR 150s-170s, RR 40s, BP 130s/70s, SpO_2 100%, Wt 6.5 kg
- EKG – Sinus tachycardia 150, left superior axis deviation, RAE, ST abnormalities and T-wave inversions in lateral leads, non-specific intraventricular block
- CXR – Cardiomegaly, markedly enlarged MPA, negative infiltrates or effusions
- TTE – Bilateral ventricular hypertrophy, bilateral diminished ventricular function, mild MR

Key Questions

15) The surgeons tell you that ECMO is not an option for this patient, because there are no available cannulation sites. How will this influence your pre-operative discussion with the patient's family?
16) Given her extremely complicated medical history, and the fact that she arrested during a previous inhalational induction, how will you induce general anesthesia in this patient? What will you do if peripheral IV access is not possible?
17) The patient has been taking prilosec for GERD symptoms related to the continuous NGT feeds. What elements of her history would affect your decision to perform a rapid sequence induction? What agents would you choose? Can you perform a rapid sequence induction safely in this patient?

Problem Based Learning Discussion

Anesthetic Concerns with Aortic Stenosis

- **Major alterations in O2 supply and demand occur**
  Demand is **increased** by:
  ↑ LV mass (increased systolic wall tension)
  ↑ Pressure work.
  Supply is **decreased** by:
  ↓ diastolic perfusion time
  ↓ coronary perfusion pressure secondary to ↓ systemic BP
  ↓ subendothelial perfusion due to increased LVEDP
  ↓ density of capillaries in the hypertrophied LV

- **Higher LV filling pressures are needed for optimal cardiac performance**
  Pressure overload of the LV leads to ventricular hypertrophy and low ventricular
  compliance. Left ventricular end-diastolic volume (LVEDV) must remain high to
  overcome this decrease in compliance to maintain adequate cardiac output. These
  higher filling volumes translate into higher left ventricular end-diastolic pressures
  (LVEDP), which are reflected backwards into the pulmonary circulation and result in
  pulmonary congestion and pulmonary hypertension. Adult patients with aortic
  stenosis almost always have radial arterial and pulmonary arterial catheters placed
  preoperatively to assist with volume status measurement and optimization;
  unfortunately, these lines are rarely in place prior to inducing an infant with this
  lesion.

- **Dysrhythmias are poorly tolerated**
  Dysrhythmias may interfere with diastolic perfusion time, which may affect coronary
  perfusion, and therefore increase the risk of ischemia. In adults, the "atrial kick"
  associated with normal sinus rhythm may account for 40% of atrial filling; hence,
  atrial fibrillation in the setting of AS can be ominous given the need for higher
  LVEDVs/LVEDPs. Finally, CPR is extremely difficult to accomplish in the setting
  of a fixed LV outflow tract obstruction.

Anesthetic Goals for Aortic Stenosis

One must optimize the patient's tenuous myocardial O_2 supply/demand status
throughout the induction of anesthesia, and subsequent periods of anesthetic maintenance
and emergence. Major anesthetic goals can be summarized as follows:
- Maintain normal heart rate and rhythm
- Maintain a high preload
- Maintain diastolic blood pressure and coronary perfusion pressure
- Avoid agents that cause myocardial depression

Williams Syndrome

In 1961, Williams et al. first described a disorder in four unrelated children with mental deficiency, an unusual facies, and supravalvular aortic stenosis. These findings have been further characterized as follows:

General Findings

- "Elfin" Facies – medial eyebrow flare, short palpebral fissures, epicanthal folds, depressed nasal bridge, periorbital fullness of subcutaneous tissues, anteverted nares, long philtrum, prominent lips with open mouth, mandibular hypoplasia, blue eyes with stellate pattern of the iris,
- Growth Retardation – mild prenatal growth deficiency, post-natal growth 75% of normal, failure to thrive, GERD, constipation, colic, mild microcephaly. Idiopathic infantile hypercalcemia can sometimes cause the symptoms of irritability, constipation, vomiting, and muscle cramps.
- Performance – average I.Q. of 56 (range 41-80), verbal/memory performance >> perceptual/motor function; Children: loquacious, outgoing, strong interest in others, especially adults; Adults: ↑ hyperactivity, ↑ intensity, ↑ distractibility, ↓ adaptability, ↓ arousal threshold
- Neurological Exam – hoarse voice (bilateral vocal cord paralysis secondary to elastin abnormality), hypersensitivity to sound, mild spasticity, tight heel cords, ↑DTR's, poor coordination
- Etiology – majority of cases are sporadic, deletion of one elastin allele located within chromosome subunit 7q11.23 identified, both sporadic and inherited cases demonstrate chromosome deletion, deletion is diagnosed via FISH (fluorescent-in-situ-hybridization. This elastin deletion may explain some of the characteristics such as facial features, cardiovascular disease, vocal cord dysfunction, bowel/bladder diverticulae, and orthopedic problems.
- Renal – renal artery abnormalities, solitary kidney, pelvic kidney, bladder diverticula, frequent UTIs, cystic dysplasia, hypertension (secondary to arterial malformations or persistent hypercalcemia). Severe infantile hypercalcemia (15% incidence) usually resolves during childhood, but lifelong abnormalities of calcium and vitamin D metabolism may persist. Nephrocalcinosis is associated with persistent hypercalcemia.
- Occasional Abnormalities – pectus excavatum, strabismus, hyperopia, enamel hypoplasia/hypodontia, chronic OM, inguinal hernias, bowel diverticula, rectal prolapse

Cardiovascular Findings

- Supravalvular Aortic Stenosis – localized and diffuse
- Peripheral Pulmonary Artery Stenosis
- Pulmonic Valvular Stenosis
- VSD/ASD
- Renal Artery Stenosis with Hypertension

Supravalvular Aortic Stenosis (SVAS)

SVAS is the most common cardiac lesion associated with Williams syndrome. This stenosis may be localized or diffuse in nature. In the localized form, a coarctation exists at the supravalvular area of the aorta just above or at most the superior level of the attachments of the valve commisures. There is a variable amount of intimal thickening in the form of an internal shelf, which increases the stenosis significantly and may obstruct or even close the ostium of the Left main coronary artery (CA). In the diffuse form, there may be hypoplasia of the artery extending across the entire arch, the carotid and subclavian arteries, and into the descending aorta. Diffuse hypoplasia of the main pulmonary artery (MPA) may be associated with this diffuse form of SVAS, and both arteries may show marked wall thickening, fibromuscular dysplasia, and replacement of the elastic tissue of the media. Sudden death in infancy is common in this group.

In general, repair is recommended for LV→Ao gradients of 50 mmHg or more. Without repair, rapid progressive stenosis can occur. Primary repair of isolated, localized stenosis has a low mortality rate (0%), but the early risks are greater with diffuse SVAS (40%).

For the discrete form of SVAS, the patient is placed on CPB and moderately cooled. After aortic cross-clamping and cardioplegia, the proximal Ao is opened through the area of stenosis, with an incision carried into both the Right and Non-coronary sinuses of Valsalva. A Y-shaped patch is then used to enlarge the ascending Ao. Alternatively, excision of the narrowed area followed by end-to-end anastomosis can be performed, but there is a risk of valve leaflet and coronary artery injury when the narrowing is proximal and diffuse.

For the diffuse form of SVAS, deep hypothermic circulatory arrest (DHCA) is required for aortic arch reconstruction. Sometimes arterial cannulation may need to be achieved via the femoral route. Once DHCA is achieved, a longitudinal incision is made through the area of stenosis and patched with homograft. The head vessels must be clamped, and sometimes the incision is carried into the proximal portion of these vessels if stenosis exists at this level. Post-operative complications include bleeding from the extensive suture lines and strokes from air trapped in the ascending Ao that embolizes into the cerebral circulation.

Coronary Artery Pathology

Surgical correction of the SVAS does not necessarily guarantee a good post-operative result. Indeed, severe ventricular dysfunction can occur despite elimination of the stenosis. Furthermore, some patients who underwent necropsy after experiencing sudden death have been shown to have no discernable left ventricular outflow tract obstruction (LVOTO). Coronary artery (CA) dysfunction appears to be the most likely cause. The proposed mechanisms are as follows:

- The free edges of the aortic valve leaflet near the aortic wall may become adherent to the obstructing ridge of tissue immediately above the ostium, thereby obstructing CA flow. This is more common in the Left sinus, but can occur on the Right.
- Under extreme circumstances, the proliferative process of the intimal ridge may extend into and narrow (or even obstruct) the ostium of the Left coronary sinus.
- In the absence of obstruction to inflow into the sinus of Valsalva (or of ostial stenosis) the CAs are exposed to high pressures transmitted proximal to the SVAS, which leads to severe CA dysplasia, narrowing, tortuosity, medial hypertrophy, and early onset of atherosclerosis.

These CA findings help explain the difficulties often seen during separation from CPB. For example, if a patient with severe SVAS has a systolic pressure of 100 mmHg and a calculated gradient of 100 mmHg across the stenosis, then pre-operative CA perfusion occurs at a pressure head of 200 mmHg. After repair, these same CAs simply cannot perfuse in the setting of "normal" blood pressures, which leads to ischemia, infarction, ventricular dysfunction, and death. Various maneuvers including aggressive vasoactive therapy, angioplasty, LVAD, and temporary placement on ECMO have been attempted with variable results.

Sudden Death in Williams Syndrome

Sudden death is a recognized complication of Williams syndrome. **Kececioglu et al.** documented a 3% incidence of sudden death in a group of 104 patients with Williams syndrome over the span of 30 years. The true incidence, however, may be higher. **Bird et al.** reported 10 new cases of sudden death and reviewed 9 previous cases in the literature. Of the19 cases of studied, 11 occurred in the setting of anesthetic agents and cardiac catheterization. The anesthetics included ketamine, valium, chloral hydrate, morphine, midazolam, meperidine, phenergan, thorazine, and halothane. Some patients arrested during catheter manipulation, while others arrested before the procedure began or even hours after apparently successful catheterization. Two of these patients had previously experienced cardiac arrest during hernia repair under general anesthesia.

Impaired coronary perfusion (with subsequent myocardial ischemia and infarction) and arrhythmia are the most likely mechanisms for sudden death. **Bird et al.** documented abnormal EKG findings in 7/19 patients who suffered sudden death. Of the 15 necropsy results studied, ischemia (11/15) and coronary stenosis (12/15) were the most prevalent pathological findings. The degree of SVAS did not correlate with the severity of coronary stenosis (4/15 patients with coronary stenosis had either mild or no discernible LVOTO). Surprisingly, 2 patients with severe bilateral outflow tract obstruction and biventricular hypertrophy did not show any evidence of coronary stenosis or chronic ischemia. Under these circumstances, hemodynamic stress may have lead to decreased cardiac output, which lead to myocardial ischemia and sudden biventricular collapse. One can imagine then that patients with severe biventricular outflow obstruction and evidence of ischemia/ST changes on EKG probably comprise the most fragile subset of patients with Williams syndrome.

Williams Syndrome and the Anesthetic Literature

Although repair of SVAS has been documented extensively in the surgical literature, relatively few papers describe in detail the anesthetic agents used for patients with Williams syndrome.

In 1998, **Kawahito et al.** described the successful anesthetic management of a patient with WS undergoing aortoplasty for SVAS. The patient was a 15 y/o, 40 kg girl with SVAS gradient 80mmHg, LVH by EKG and CXR criteria, but no CHF or ischemia. After pre-medication with IM atropine and midazolam, she underwent induction with fentanyl (200mcg), thiamylal (100mg), and vecuronium. Maintenance was then achieved with sevoflurane, oxygen, nitrous oxide, and fentanyl infusion. Initial separation from CPB was complicated by hypotension and ST depression thought secondary to mechanical distortion of a coronary artery, but she was successfully weaned off CPB on dopamine, prostaglandin, and nitroglycerin after artery repair.

In 2000**, Audrzejowski et al.** described a successful general anesthetic for MRI angiography in a patient with WS. The patient was a 21 y/o, 39 kg man with murmurs over the chest, carotids, and abdomen, limited exercise tolerance, occasional peripheral cyanosis, and LVH by EKG criteria. A preoperative echo was not possible due to poor patient cooperation. After pre-medication with temazepam, he was induced with remifentanil (1 mcg/kg), etomidate (0.3 mg/kg), and atracurium (0.6mg/kg). Maintenance was achieved with sevoflurane, oxygen, nitrous oxide, and intermittent boluses of remifentanil (0.5mcg/kg). He was extubated while awake. The MRI revealed an abnormal pulmonary tree and absent Left renal artery/kidney, but there was no evidence of SVAS.

In 2002, **Horowitz et al.** documented two deaths.

- Case #1: A 6 y/o WS girl with history of syncope and known main and right pulmonary artery stenoses, multiple branch pulmonary stenosis, and SVAS with a gradient of 100 mmHg by echo, underwent catheterization and IM sedation with meperidine, promethazine, and chlorpromazine. Twenty minutes after catheter removal, she developed bradycardia, apnea, complete heart block, and subsequent vfib arrest. Resuscitation was unsuccessful.

- Case #2: A 3 y/o WS girl (who previously underwent catheterization and IM sedation with meperidine, promethazine, and chlorpromazine at 22months) presented for surgical repair of SVAS. Preoperative echo revealed severe LVH, hyperdynamic LV function, and a peak aortic gradient of 150 mmHg; EKG revealed LVH and abnormal ST changes. She was premedicated with PO midazolam (0.5mg/kg) and subsequently induced with IV ketamine (4mg/kg) and pancuronium (0.2mg/kg). Tracheal intubation was uneventful. After placing the patient in Trendelenberg position and administering isoflurane 0.2% and oxygen, the HR slowed from 150 to 70 BPM, pulse oximetry was lost, and atropine, phenylephrine, and epinephrine were required to stabilize the blood pressure. Isoflurane 0.2% was again administered prior to incision with resultant systolic blood pressure drop from 130 to 50 mmHg, and the development of irregular heartbeats at 60-70 bpm. She was immediately placed on CPB. Separation from CPB was unsuccessful despite surgical repair of SVAS, Right CA angioplasty, and LIMA to LAD bypass. After three days of LVAD therapy, life support was discontinued.

Within the narrow population of patients with WS, it is clear that congenital defects can vary greatly in scope and severity. The anesthetic risks for a given patient will most likely depend on the degree of ventricular failure, ischemia, and dysrhythmia seen in the preoperative period. Patients with normal coronary artery anatomy and myocardial tissue perfusion will most likely tolerate a number of different agents, including those that affect SVR and myocardial contractility. On the contrary, patients who suffer from abnormal CA perfusion and ischemia may arrest with the slightest change in hemodynamics. Similarly, patients with normal RV function will most probably tolerate agents that affect PVR, whereas patients with severe RVOTO may experience RV failure and hemodynamic collapse in the setting of airway manipulation or coughing/valsalva. Furthermore, it is important to recognize that sedation is not necessarily safer than general anesthesia for these patients. Chloral hydrate, benzodiazepines, morphine, and various combinations of IM sedatives have been associated with deaths during cardiac catheterization. Whether these deaths occurred as a direct result from pharmacologic changes, mechanical dysfunction from the catheterization process itself, or a combination of factors is unknown.

A Cautious Approach to Anesthesia for Patients with Williams Syndrome

<u>**PRE-OPERATIVE PERIOD**</u>

As described above, the degree of cardiovascular pathology can vary greatly amongst patients with Williams syndrome, and no one piece of information can accurately predict the risks associated with an anesthetic or invasive procedure. Thus, it is critically important to assess the patient's baseline hemodynamic status by history, physical examination, and non-invasive data measurement.

History

In its most severe cardiovascular form, patients with Williams syndrome can present with diffuse SVAS, Pulmonic Valvular stenosis, diffuse peripheral Pulmonary Artery stenosis, carotid artery stenosis, renal artery stenosis, and hypertension. This frightening combination of defects will lead to biventricular hypertrophy, dysfunction, and failure. Thus, the signs and symptoms of congestive heart failure must be explored during the preoperative interview. Infants suffering from severe CHF will often demonstrate episodes of tachypnea, tachycardia, diaphoresis, pallor, poor peripheral perfusion, and fatigue during feeds (the infant equivalent of a stress test). Older children and adults may be asymptomatic at rest, but then develop fatigue, dyspnea, angina, or syncope during play or other forms of exercise. On physical exam, "wheezing" due to engorgement of the bronchial venous system may be incorrectly diagnosed as reactive airway disease in infants, whereas older children and adults are more likely to reveal classic "rales" during lung auscultation. CXR may show biventricular enlargement, pulmonary edema, and alveolar infiltrates.

Any episodes of syncope or "life threatening events" must be documented, as these may indicate the presence of severe coronary artery pathology, ischemia, carotid artery insufficiency, and/or malignant arrhythmia. Hemodynamic instability associated with a previous general anesthetic or sedation is an ominous sign of cardiovascular fragility.

Signs and symptoms of renal dysfunction should also be explored given the WS association of renal artery abnormalities, calcium homeostasis abnormalities, and persistent hypertension. Four-limb BPs may help identify a coarctation, while abdominal bruits are consistent with renal artery abnormalities. Infants with colic, irritability, constipation, vomiting, and muscle cramps should be screened for idiopathic infantile hypercalcemia. An abnormal chemistry-7 may reveal an elevated creatinine level, or a low bicarbonate value consistent with chronic acidosis secondary to poor perfusion.

There have been reported cases of masseter spasm and elevated enzymes (CK, GOT, LDH) in WS patients who have received halothane and succinylcholine, but it is not clear if these cases were true episodes of malignant hyperthermia (one patient tested negative on muscle biopsy). Recent work has shown that the α_2/δ subunits (CACNL2A) of the ryanodine receptor are localized to chromosome 7q11.23-q21.1, and this places the locus outside the WS deleted region. No specific MH precautions are indicated at this time, but it is always prudent to ask for any family history of MH or adverse anesthetic events as you would any prospective patient.

EKG

As noted in the work by **Bird et al.,** EKG abnormalities were common in patients who later suffered sudden death, as were histologic abnormalities consistent with acute and chronic ischemia at the time of autopsy. Ischemia from CA pathology is probably the most important reason for death. It is imperative to obtain an EKG looking for signs ventriculomegaly, LV strain, ischemia, and infarct.

ECHO

WS patients with > 50 mmHg SVAS gradients are usually candidates for surgical correction. Echo helps define the location of SVAS, arch integrity, extent of pulmonary tree involvement, overall ventricular function, and areas of focal wall motion abnormality. It is important to remember that gradients do not always correlate with the severity of CA pathology; some patients with relatively mild SVAS were later found to have severe CA abnormalities on autopsy.

Resources

There have been documented WS deaths with sedation, general anesthesia, and a variety of invasive procedures. Some patients arrested and died even hours after successful completion of the procedure. ICU admission for close hemodynamic monitoring is clearly indicated for patients who have baseline evidence of cardiac dysfunction. ECMO has been required in some cases to rescue children from total CV collapse. Thus, elective cases should be scheduled during times of maximum staff support, and arrangements for surgical/perfusion stand-by should be coordinated well in advance.

Consent

There is always the small possibility of respiratory and/or cardiovascular compromise during sedation or general anesthesia, but death is a very real component of care for patients with severe cardiac manifestations of WS. The risk of sudden death cannot be simply made on the basis of an ECHO study or otherwise. Although some patients demonstrate very obvious features of severe cardiovascular dysfunction and carry great anesthetic/surgical risk, parents must understand in no uncertain terms that complete hemodynamic collapse and death can occur even in patients with "mild" disease.

NPO Status

Patients with severe biventricular outflow obstruction and biventricular failure are extremely fragile. They must maintain a consistent intravascular volume to preserve adequate LVEDV and subsequent LVEDP. It is important to encourage liberal fluid intake until shortly before the procedure per standard NPO guidelines. Early IV placement and correction of any outstanding fluid deficits is paramount.

INDUCTION

        In many ways, the goals for induction in a patient with severe WS are similar to those with severe AS:
- Maintain normal heart rate and rhythm
- Maintain a high preload/optimize intravascular volume status
- Avoid fluctuations in SVR and PVR
- Avoid agents that cause myocardial depression

As noted in the discussion above, some patients with normal CA anatomy and only mild SVAS or mild RVOTO can tolerate a variety of anesthetic agents without untoward effects. Indeed, **Kawahito et al.** induced with thiamylal and separated from CPB with nitroglycerin and prostaglandin. In complete contrast, **Horowitz et al.** documented complete cardiovascular collapse with the addition of 0.2% isoflurane. Given the unpredictable nature of WS lesions, it may be best to use a narcotic based induction to avoid any changes in SVR/PVR, especially for those patients who cannot be properly assessed in terms of exercise stress tolerance.

MAINTENANCE

        The choice of maintenance agents once again depends on the patient's underlying lesion and hemodynamic status. If there is any doubt about the patient's ability to tolerate fluctuations in SVR and PVR, care should be made to avoid agents that would change these parameters. One must also consider the deleterious effects of $PaCO_2$/PVR elevation when respirations are not controlled, as well as the potential devastating effects of coughing/valsalva upon extubation. Deep extubation with subsequent mask ventilation may be an appropriate alternative to bucking/coughing for patients with severe RVOTO and RV failure.

POST-OPERATIVE PERIOD

        As discussed above, close post-operative monitoring is essential. Be it in the PICU or the PACU, the team of nurses and physicians must anticipate and correct any early signs of hemodynamic dysfunction. Resuscitation can be extremely difficult, if not impossible, once the patient arrests with severe SVAS and CA pathology. Care must be given to minimize changes in SVR and PVR. Pain, for example, must be adequately treated to avoid the deleterious effects of increasing catecholamines. Hypothermia and shivering can also lead to increased catecholamines and markedly increased SVR. Excessive sedation with subsequent elevated $PaCO_2$ and PVR may cause RV collapse in a patient with severe RVOTO and RV failure. Even vomiting or coughing, by virtue of rapidly changing PVR and SVR states can lead to total hemodynamic collapse in certain patients. Thus, clear postoperative planning and early intervention are the hallmarks of life-saving care for patients with WS.

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Web Sites

Online Mendelian Inheritance in Man: National Center for Biotechnology Information
Extensive review of the Williams syndrome literature
http://www.ncbi.nlm.nih.gov/omim/

Williams syndrome Association
Helpful information for family members and doctors
http://www.williams-syndrome.org/fordoctors/index.html