Supravalvular Aortic Stenosis

**Definition**

=> obstruction of the ascending aorta at / above the sinutubular junction

Morphologic spectrum:

- *discrete stenosis*: distinct hourglass shaped obstruction at the sinutubular junction
- *diffuse stenosis*: partial or complete hyoplasia of the ascending aorta +/- both the descending thoracic and abdominal aorta
- isolated / part of complex LVOTO, mostly involving the aortic valve
Supravalvular Aortic Stenosis

**Pathophysiology**

- microdeletion / mutation of the elastin precursor gene on chromosome 7 may lead to **elastin deficiency in the wall of the great arteries**

### 'Elastin Arteriopathy'

<table>
<thead>
<tr>
<th>WT</th>
<th>Eln⁺⁻⁻</th>
<th>hBAC-mNull</th>
</tr>
</thead>
<tbody>
<tr>
<td>100% elastin</td>
<td>50-60%</td>
<td>30-40%</td>
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*mouse model; Am J Physiol Heart Circ Physiol 315: H189–H205, 2018*
Supravalvular Aortic Stenosis
Pathophysiology

\textbf{Elastin Arteriopathy}

structurally altered aortic wall: aortic \textit{media is thickened} and dysplastic with \textit{increased numbers of smooth muscle cells} and collagenous fibers while \textit{elastic fibers are decreased} and elastin is abnormal

\Rightarrow \text{may cause discrete obstruction or diffuse hypoplasia}
\Rightarrow \text{results in increased aortic stiff-ness and impaired Windkessel effect}

\textit{Am J Physiol Heart Circ Physiol} 315: H189–H205, 2018
## Supravalvular Aortic Stenosis

### Associated lesions

<table>
<thead>
<tr>
<th>Elastin arteriopathy</th>
<th>Aortic valve disease</th>
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</thead>
<tbody>
<tr>
<td>• diffuse hypoplasia of thoracic or abdominal aorta</td>
<td>• up to 50% of symptomatic patients</td>
</tr>
<tr>
<td>• aortic coarctation</td>
<td>• may cause diminished coronary artery perfusion due to obstruction by redundant, dysplastic aortic valve leaflets</td>
</tr>
<tr>
<td>• coronary artery stenosis due to focal or diffuse coronary narrowing (5-15% of surgical patients)</td>
<td>• may be present at diagnosis of develop during f/u</td>
</tr>
<tr>
<td>• ostial stenoses of carotid, subclavian, renal, mesenteric, iliac, and other peripheral arteries (~ 20%)</td>
<td></td>
</tr>
<tr>
<td>• supravalvular/peripheral pulmonary artery stenosis (in &gt; 50% of patients with symptomatic SVAS)</td>
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Supravalvular Aortic Stenosis

Epidemiology

- incidence ~ 1:20,000 live births
- ~ 0.05 - 0.25 % of patients with congenital heart disease

Underlying disease

- Williams-Beuren-syndrome (autosomal dominant)
- Familial Supravalvular Aortic Stenosis (autosomal dominant)
- Supravalvular Aortic Stenosis (sporadic)
- Familial Hypercholesterinaemia (rare)

Williams-Beuren-Syndrome

- incidence 1:7,500 bis 1:10,000 live births
- de novo deletion on chromosome 7 (7q11.23)
  - healthy parents
  - offspring with 50 % genetic deficiency
Supravalvular Aortic Stenosis

Epidemiology

- multi-system disorder with associated syndromal findings e.g. failure to thrive, elfin face, intellectual impairment, arterial hypertension, and others
- estimated prevalence of SVAS 69%
- cardio-vascular anomalies in ~ 80% of patients, in symptomatic infants > 90%
- arterial hypertension ~ 50% (with or without stenosis of the renal arteries or hypoplasia of the abdominal aorta)

Williams-Beuren-Syndrome

- short up-turned nose
- long philtrum
- full lips
- widely spread teeth
- periorbital fullness
<table>
<thead>
<tr>
<th><strong>pressure load of the left ventricle</strong></th>
</tr>
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<tbody>
<tr>
<td>its extent depending on the severity of aortic stenosis and additional involvement of aorta of peripheral arteries</td>
</tr>
<tr>
<td><strong>myocardial hypertrophy</strong></td>
</tr>
<tr>
<td>subsequent aortic valve and/or mitral valve regurgitation</td>
</tr>
<tr>
<td>underperfusion of the poststenotic vascular bed in peripheral artery disease</td>
</tr>
<tr>
<td>systemic arterial hypertension</td>
</tr>
<tr>
<td>prestenotic dilation of the aortic root or coronary arteries may develop</td>
</tr>
<tr>
<td>diastolic coronary perfusion may be impaired.</td>
</tr>
<tr>
<td>the risk of subendocardial ischemia is increased even in the absence of additional coronary obstructions</td>
</tr>
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</table>
Supravalvular Aortic Stenosis

Pathophysiology

Systole (A) before repair and (B) after repair. Diastole (C) before repair and (D) after repair.

Coronary artery involvement

Type I
- Ostial Narrowing

Type II
- Cusp-Ridge Fusion

Type III
- Fusiform Narrowing


J Thorac Cardiovasc Surg 2000;120:1040-6)
Clinical presentation

- Isolated supravalvular aortic stenosis usually remains asymptomatic for a long time
- Systolic murmur conducted to the carotid arteries without typical ejection click
- With increasing pressure gradients there is a thrill in the jugular notch
- Systemic hypertension; asymmetric upper extremity blood pressures are often noted
- Peripheral bruits (thoracic / abdominal) with additional aortic, peripheral, or pulmonary artery stenoses
Supravalvular Aortic Stenosis

Diagnostic work-up

Aim

⇒ Confirmation of the diagnosis
⇒ Displaying the entire thoracic and abdominal aorta including originating arteries to define the amount and severity of additional lesions

Echocardiography

• primary diagnostic tool. The following details should be described:
  - localization, form and severity of supravalvular aortic stenosis
  - Doppler calculations of mean and maximum gradients
  - left ventricular outflow tract, aortic valve, and ascending aorta
  - aortic arch (coarctation?) including head and neck vessels and descending aorta
• left ventricular function and extend of myocardial hypertrophy
• right ventricular outflow tract obstruction / branch pulmonary artery stenosis
• prenatal diagnosis by fetal echocardiography usually detects severe stenoses with potential clinical manifestation in infancy
Supravalvular Aortic Stenosis

Echocardiography
Supravalvular Aortic Stenosis

Echocardiography
Supravalvular Aortic Stenosis

Diagnostic work-up

**Chest X-ray**
- no specific diagnostic value
- should be performed prior to invasive procedures / anaesthesia

**Magnetic Resonance Imaging** / **Computer Tomography**
Supravalvular Aortic Stenosis

Diagnostic work-up

**Magnetic resonance imaging / computer tomography:**

- MR and CT angiography are equally suited for investigation of aorta and its major branches as well as pulmonary arteries.

**Drawbacks:**
- MRI: requires (long) sedation / general anaesthesia in infants / young children increasing the risk of procedural complications
- CT: radiation exposure
Supravalvular Aortic Stenosis

Computertomography

newborn with diffuse SVAS

adult with discrete SVAS
Supravalvular Aortic Stenosis

Computed Tomography

Elastin arteriopathy in a male adolescent with WBS
## Supravalvular Aortic Stenosis

### Diagnostic work-up

<table>
<thead>
<tr>
<th>Abdominal ultrasonography</th>
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<tbody>
<tr>
<td>• may detect stenoses of the abdominal aorta or large visceral arteries</td>
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<table>
<thead>
<tr>
<th>Diagnostic cardiac catheterization and angiocardiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>• may be indicated in selected cases, e.g. suspected coronary artery obstruction, peripheral pulmonary artery stenosis or distal systemic artery obstruction</td>
</tr>
<tr>
<td>• patients with more severe supravalvular stenosis, coronary stenosis or bilateral outflow tract obstruction have in addition to procedure related sedation or general anaesthesia a significantly higher risk for hemodynamic instability caused by catheter manipulation</td>
</tr>
<tr>
<td>• therefore, cardiac catheterization in this high risk group of patients should only be performed in experienced centers which are able to treat cardiac decompensation</td>
</tr>
</tbody>
</table>
Supravalvular Aortic Stenosis

Angiography

- Severe discrete stenosis
- LCA stenoses and hypoplasia of the descending aorta
- Diffuse stenosis and marked dilation of the coronary arteries
Supravalvular Aortic Stenosis

Diagnostic work-up

**ECG**
- the extend of left ventricular myocardial hypertrophy correlates with the severity of supravalvular aortic stenosis
- repolarization abnormalities may occur with progressive disease or coronary involvement
- right ventricular or biventricular hypertrophy may be found in additional supravalvular / peripheral pulmonary artery stenosis
- QT-interval prolongation may occur in WBS patients (QTc > 460 msec in 14%)
- right atrial hypertrophy in up to 25% of WBS patients

**Genetic tests and counseling**
- recommended in the presence of phenotypic abnormalities or familial forms
- prenatal genetic diagnostics may be applicable in familial forms
Supravalvular Aortic Stenosis

Procedural complication risk

- the incidence of sudden death in WBS patients comes to 1/1,000 pt. years
- the risk of sudden death in WBS patients is 25–100-fold higher compared to the age-matched normal population


- any procedure requiring deep sedation or general anesthesia in patients with haemodynamically relevant supravalvular aortic stenosis is at elevated risk for severe complications and sudden cardiac death due to impaired coronary perfusion
- patients at highest risk are infants with the Williams-Beuren syndrome, particularly those with biventricular outflow tract obstruction

- both syndromal (WBS) and non-syndromal patients are affected
- periprocedural death has also been reported in patients with moderate stenosis and those without coronary artery involvement
## Supravalvular Aortic Stenosis

### Procedural complication risk

### Table 2. Risk stratification and prehydration plan prior to anesthetic administration in patients with Williams syndrome

<table>
<thead>
<tr>
<th>Low risk (standard anesthetic care)</th>
<th>Moderate risk (morning IV placement and hydration ≥2 h prior to anesthetic)</th>
<th>High riska (admit preceding evening with IV fluid administration overnightb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;20 years</td>
<td>Hypertension</td>
<td>Age &lt;3 years</td>
</tr>
<tr>
<td>No cardiac involvement greater than mild supravalvar or branch PAS</td>
<td>Moderate supravalvar or branch PAS</td>
<td>History of adverse cardiovascular event</td>
</tr>
<tr>
<td>Normal ECG</td>
<td>Mild bilateral outflow tract obstruction</td>
<td>Preprocedural arrhythmia</td>
</tr>
<tr>
<td>No renal artery involvement</td>
<td>Renal artery stenosis</td>
<td>Bilateral outflow tract obstruction of ≥moderate severity</td>
</tr>
<tr>
<td></td>
<td>Renal dysfunction</td>
<td>SVAS gradient of ≥40 mmHg and the presence of left ventricular hypertrophy</td>
</tr>
<tr>
<td></td>
<td>QTC on ECG &gt;450 ms, but &lt;500 ms</td>
<td>Coronary artery involvement</td>
</tr>
<tr>
<td></td>
<td>Airway abnormalities, lung disease, or severe gastroesophageal reflux</td>
<td>Diffuse stenosis of the thoracic aorta</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Right ventricular pressure ≥75% systemic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥Moderate left or right ventricular hypertrophy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Symptoms or ECG signs of ischemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>QTC on ECG ≥500 ms</td>
</tr>
</tbody>
</table>

Collins RT  Cardiovascular disease in Williams syndrome  Curr Opin Pediatr 2018, 30:609–615
Supravalvular Aortic Stenosis
Management

Indications for treatment

Symptomatic patients
• chest pain,
• dyspnoe or
• syncope

Asymptomatic patients
• progressive left ventricular hypertrophy
• repolarization disorders in ECG
• peak / mean Doppler gradient > 70 / 50 (40) mmHg
• peak-to-peak gradient (catheter) > (30 to) 50 mmHg

Drug treatment:
• there is no medical treatment for relief of supravalvular aortic stenosis
• secondary left heart failure should be treated according to guidelines
• systemic arterial hypertension should be treated according to guidelines
Supravalvular Aortic Stenosis
Management

Catheter intervention

- there is no indication for interventional treatment of supravalvular aortic stenosis
- balloon or stent angioplasty may be considered in concomitant vascular lesions

Williams-Beuren syndrome:
- Stenoses might recede over time
  => 'wait and watch' strategy might be considered if LV pressure load is acceptable

Transcatheter interventions for arterial stenoses in Williams syndrome are rarely of any benefit and may be detrimental.

Collins RT Cardiovascular disease in Williams syndrome. Current opinion in pediatrics 2018
the treatment of choice combines the resection of the stenosis with an aortoplasty mostly using patches performed on cardiopulmonary bypass
Supravalvular Aortic Stenosis
Surgical Repair

Extended 3-patch supravalvular aortic stenosis repair. (A and B) The ascending aorta is transected at its narrowest point, and 3 incisions are extended into the sinuses of Valsalva. (C) The sinuses are enlarged with 3 pericardial patches, and the patch from the noncoronary sinus is extended into the ascending aorta to ensure symmetrical enlargement of the narrow segment.

Modified Brom technique

In this modification of the Brom repair, the ascending aorta is enlarged by extending each sinus patch into counter-incisions made in the ascending aorta. This is most useful for patients with diffuse disease that is confined to the ascending aorta.

Meyers repair: 3-sinus all-autologous slide aortoplasty

*Semin Thorac Cardiovasc Surg Pediatr Card Surg Ann 2011; 14:85-91*
Supravalvular Aortic Stenosis
Surgical Repair

Severe ‘diffuse disease’ requiring separate patch augmentation of the entire ascending aorta and aortic arch

Supravalvular Aortic Stenosis

Prognosis I

Natural history

- mean Echo gradients of less than 20 mm Hg in infancy generally remain unchanged during the first two decades of life; mean Doppler gradients exceeding 35 mm Hg usually increase during childhood
  

- if diagnosed beyond infancy, a large portion of children with congenital supravalvular aortic stenosis may avoid surgical intervention because the lesion gradually regresses over time
  

- ~50% of patients diagnosed with SVAS beyond infancy will need surgery within 10 y of those, ~80% are operated within 1 y after diagnosis

Supravalvular Aortic Stenosis
Nonsurgical Outcome

- many children—particularly those with Williams syndrome—show regression of stenosis without intervention.
- children who undergo operation have high LVOT gradients and smaller LVOT z scores that do not improve over time

• surgical results are generally favourable
• perioperative mortality is ~ 5% for the whole age group (operation between 1990 and 2015; mean age at operation 2 – 4 years)
• in recent years hospital mortality has decreased to 1.3 to 3.3% [ECHSA, NICOR, STS]
• there is an elevated risk of early mortality after operation in infancy, potentially representing more severe disease

• surgical intervention alters the natural history: LVOT obstruction is relieved and does not recur, and ascending aortic dimensions progressively enlarge towards normal values

Supravalvular Aortic Stenosis

Surgical Outcome

Risk of severe adverse events

- In-hospital mortality
- Cardiac arrest
- Mechanical circulatory support
- Composite outcome

STS Congenital Heart Surgery Database
J Thorac Cardiovasc Surg 2015;149:1516-22
Supravalvular Aortic Stenosis

Prognosis after surgery

- After surgical repair, residual obstruction, aortic regurgitation and coronary complications may occur.
- The risk of reoperation varies between 7 and 20% in the entire group being highest after surgical repair in infancy (up to 50% after 5 years).
- There is no difference between the surgical techniques concerning perioperative mortality or reoperation rate.
- However, more recent publications are in favour of 'multi-sinus reconstructions and extended aortoplasty.'
Supravalvular Aortic Stenosis
Follow-up in childhood

- **Infants** diagnosed with supravalvular aortic stenosis require close f/u (≤ 3 mo)
- a tertiary pediatric center should be involved early for complete imaging and timing of surgical intervention

- **asymptomatic patients** beyond infancy with low gradients should be followed at 12 months intervals; school-aged children at 1-2-year intervals.
- restriction of physical activity is not required, if the pressure gradient is less than 20 mmHg
- long term follow-up after surgical repair is mandatory for residual obstructions, aortic regurgitation and systemic arterial hypertension.
Supravalvular Aortic Stenosis
Adult Congenital Heart Disease

• 1/3 of surgical patients are late primary diagnoses of supravalvular aortic stenosis
• 2/3 of patients are reoperations after SVAS surgery in childhood, often involving the aortic valve
• besides Echocardiography and CPET, additional imaging +/- invasive pressure monitoring is warranted in many pts.
Supravalvular Aortic Stenosis
Adult Congenital Heart Disease

Indication for surgery in adult SVAS

SVAS with a mean Doppler gradient > 50 mmHg and clinical symptoms:
• chest pain,
• dyspnoe on exertion
• syncope

SVAS with a mean Doppler gradient < 50 mmHg and clinical symptoms and
• LV dysfunction or
• LV myocardial hypertrophy

• Lifelong f/u is advised, involving specialists in Adult CHD
Supravalvular Aortic Stenosis

Pregnancy

Maternal risk:
• SVAS mean Doppler gradient < 40 mmHg are expected to be well tolerated
• SVAS mean Doppler gradient > 40 mmHg:
  - may tolerate pregnancy
  - close monitoring in tertiary center
• SVAS mean Doppler gradient > 50 mmHg = severe stenosis or clinical symptoms => caesarean section
• Patients with severe stenosis or clinical symptoms or reduced LVEF should be counseled against pregnancy

Fetal risk:
• In patients with > moderate aortic stenosis, there is an 25 % risk of preterm delivery and growth retardation
Supravalvular Aortic Stenosis

Summary

- Supravalvular Aortic Stenosis is a manifestation of a generalized elastin arteriopathy

- Many children with mild to moderate stenosis may show regression of stenosis without intervention

- Children with SVAS have a markedly increased risk for severe complications and sudden death related to procedures requiring anaesthesia

- Surgical repair by resection of stenosis and aortoplasty is the treatment of choice

Vielen Dank!