Subaortic Membrane : Revisited

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Plan of Talk

- Prevalence
- Anatomy
- Natural history
- Pathophysiology
- Surgical management and FU
Epidemiology

- Second most common form of AS
- In children; 10 – 14% are subvalvular
- 67 – 75% are males
- Associated; PDA, VSD, CoA, PS and others
- Seldom seen in newborns, rare in infants
- Most consider it an acquired lesion
- In some, only detected after repair of VSD or CoA
- Familial occurrence has been described

Anatomy

- Subvalvular aortic stenoses are a variety of lesions:
  - A thin membrane (the commonest)
  - Thick fibromuscular ridge
  - Diffuse tunnel-like obstruction
  - Abnormal mitral valve attachments
  - Accessory endocardial cushion tissue
Anatomy

- Membrane attached to the IVS or encircles LVOT
- Immediately below the valve or further down in LV
- AV is usually trileaflet
- Muscular IVS hypertrophy in up to 75% of cases
- Diffuse “tunnel-like” narrowing of LVOT is rare

Discrete Fibrous Ring

Histology

- The typical fibrous ring has distinct five layers.
  - Endothelial layer
  - Mucopolysaccharide-rich subendothelial layer
  - Fibroelastic layer
  - Smooth muscle layer
  - Central fibrous layer

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Morphology of Subvalvar Aortic Stenosis

1. **Aortic valve**
   Usually normal
   Trivial or mild AR in 2/3 due to leaflet thickening or effect of eddy current

2. **Left ventricle**
   Usually concentrically hypertrophied
   Subendocardial ischemia and fibrosis

3. **Coexisting cardiac anomalies**
   Isolated in 1/2-2/3
   VSD, COA, TOF, AP window

4. **Other types of discrete Subvalvar Stenosis**
   Mitral valve anomalies: accessory tissue or leaflet malposition
   Localized muscular obstruction: related to malalignment
Natural progression

- Chronic turbulence
- Vessel wall stress
- Anomalous endothelial proliferation
- Obstruction
  - Ventricular hypertrophy
  - Ischaemia
  - Arrhythmia
  - Aortic insufficiency
  - Endocarditis

Natural history

- Rarely important obstruction in infancy
- Evident and progressive with age; probably more rapidly than valvular stenosis
- Aortic incompetence is a progressive lesion secondary to leaflet thickening and injury
  - normal pop.
  - several studies
- Graph shows that DSS, like AS, is not a benign lesion and may be worse

Julien and Hofman, 2009
Relation between age at diagnosis and odds ratio of at least moderate AR

McMahon, et al, 2004

Relation between highest peak Doppler gradient and frequency of at least moderate AR

McMahon, et al, 2004
Congenital or Acquired?

Pathophysiologic Theories
Discrete Subaortic Stenosis
A possible four stage etiology

Geometric Theory

- Most patients who developed a DSS had a malaligned VSD with anterior deviation of infundibular septum
  Zielinsky, et al, 1987
- 2X increase in mitral-aortic separation
  Rosenquist, et al, 1979
- Aortoseptal angle < 130° is a prominent feature
  → turbulence → abnormal proliferative response
**Turbulence Theory**

- Abnormal flow patterns are present in patients with DSS
- Chronic flow disturbances stimulate the endothelium to undergo transformation; the cause of the stenosis and its recurrence
- Reasons for the flow disturbance may be:
  - Muscular ventricular bands
  - Septal ridges
  - Malalignment of the IVS
  - A long LVOT associated with increased M-A separation

*Gewillig, et al. 1992*

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**Shear Stress And Cardiovascular Development**

What is the role of shear stress in the morphogenesis and differentiation of the cardiovascular system?
Haemodynamics regulate Cardiogenesis

- Biomechanical forces, exerted by blood flow are important factor that modulates embryonic patterning, morphogenesis, and function
- Flow forces control genetic expression and cellular differentiation

Shear stress distribution in the developing heart

- Different areas in developing heart have different geometry and shear stress profile
- Morphogenesis and differentiation of the cardiovascular system is controlled by shear stress
- There is a delicate balance between genetic determination and hemodynamic modulation
Haemodynamics regulate valvulogenesis

- Valves arise from endocardial cushions
- The cardiac cushions begin as
  - Endocardial bulges caused by regional swellings of the cardiac jelly, then
  - “Seeded” by migrating cardiac endothelial cells that metamorphose cardiac mesenchymal cells and
  - Begin proliferating
- Shear stress on the endocardial cells ➞ alter genetic program or the signals

Laminar flow vs turbulent in LVOT

- Laminar flow is essential for normal development of LVOT
- LVOT geometry set the scene for turbulent flow in the LVOT
- Turbulent flow & shear stress ➞ progression of subaortic stenosis
Genetic Predisposition

- Has been documented in Newfoundland dogs

- Familial occurrence of DSS has been reported in humans
  (Gale, et al, 1974; Abdalla, et al, 1994)
Surgical resection must include myectomy as well; membranectomy alone is not sufficient.
A) Aortoseptal angle, preoperatively

B) Aortoseptal angle, postoperatively

Freedom from re-operation
Resection vs concomitant myectomy
Age of resection

Kaplan Meier survival curve for the study cohort; overall probability of freedom from reoperation

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Kaplan Meier survival curves separating patients by independent predictors of reoperation

A) Patients in whom the distance in systole between the DSS and the AV was <6mm were significantly more likely to require reoperation

B) Patients with peak pre-op PG across the LVOT of >60mmHg were significantly more likely to require reoperation


Freedom from reoperation; simple vs complex subaortic stenosis

Take Home Message

- Discrete subortic stenosis is not as benign as its name implies
  - Progressive in nature,
  - Severe left ventricular hypertrophy (LVH)
  - Significant aortic insufficiency (AI).
  - Recurrence rates are high

Looking at the aetiology; it feels as if nature is trying to make a new valve where it should not be??

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Thank you

Dr. Ahmed Mahrous, MD