Pressure Restrictive VSD: When to Intervene?

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Children's Hospital of Philadelphia

No disclosures

Scope of this talk

- Patient type
  - Asymptomatic
  - Beyond infancy
  - ≤ 18 years
- VSD type
  - Conoventricular/perimembranous
  - Conal septal hypoplasia/subpulmonic
- PA Pressure: predicted normal, mPAP ≤ 20

Indications to Intervene

- Anatomic complications
  - Aortic cusp prolapse/progressive aortic insufficiency (AI)
  - Double chamber right ventricle
  - Subaortic membrane
- Endocarditis: may be considered
- Persistent shunt of excessive magnitude
  - What is the threshold?
  - How long do you wait for spontaneous restriction?

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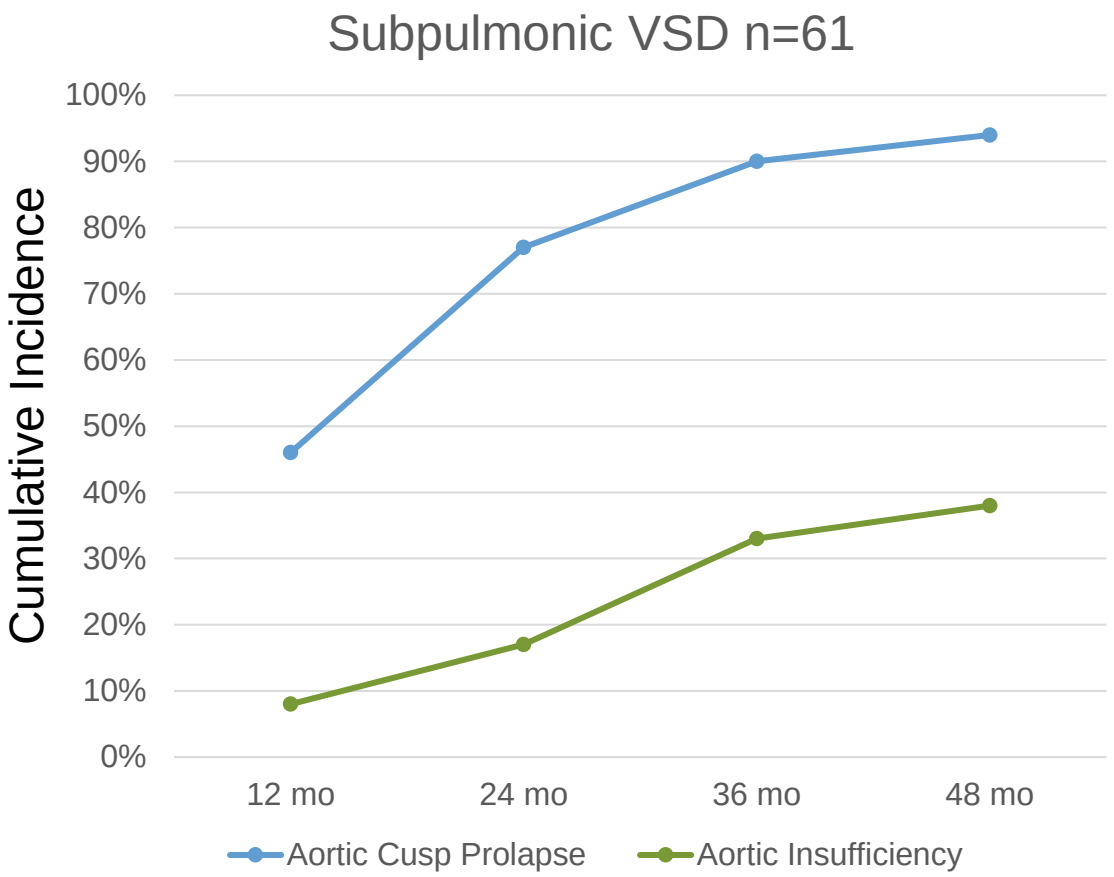
Case #1

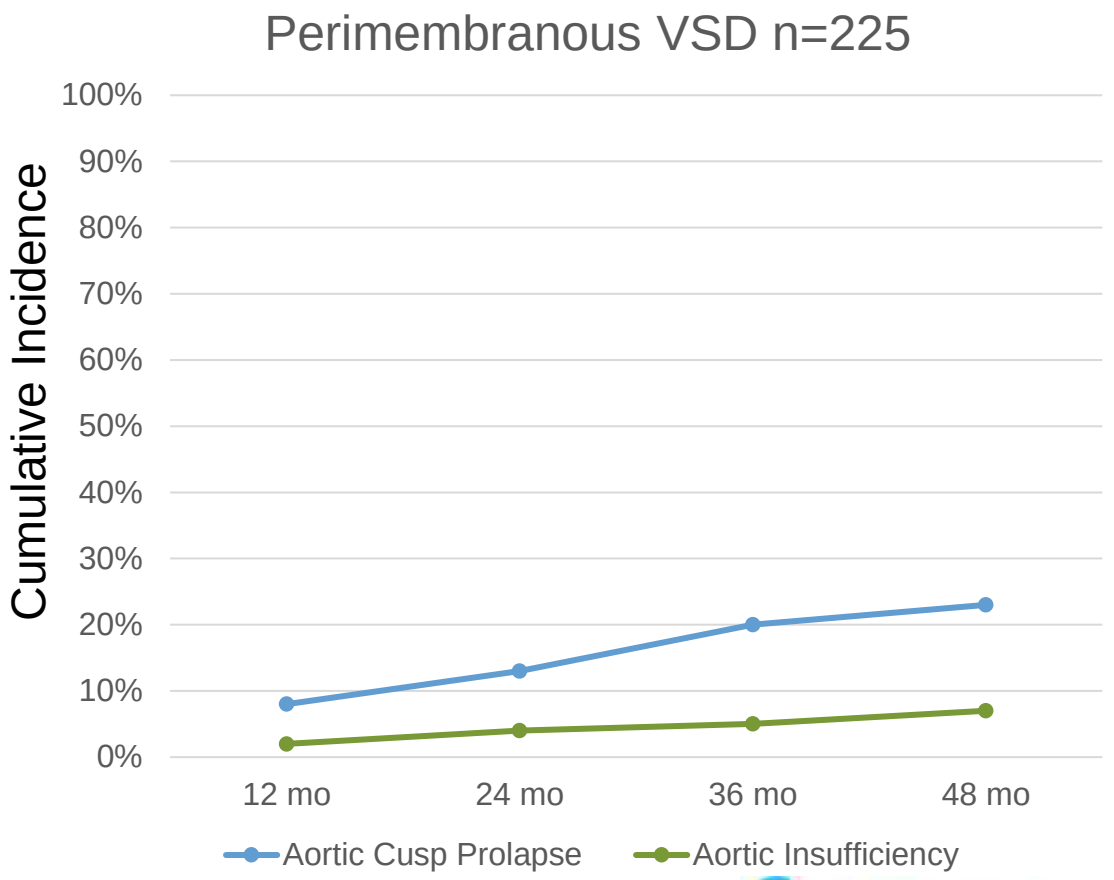
- 3 year old, asymptomatic boy
- Conal septal hypoplasia VSD
  - Peak gradient by echo 112 mmHg
  - LVEDD z-score 0.6
  - “Mild” right coronary cusp prolapse but no AI
  - No change in echo over serial follow up

Natural aortic valve complications of ventricular septal defect: a prospective cohort study

Thanarat Layangool [1], Tawatchai Kirawittaya, Chaisit Sangtawesin, Vichow Kojaranjit, Perapat Makarapong, Amornrat Pechdamrongsakul, Yanisa Intasorn, Putra Noisang

Children < 1 yo with isolated VSD
- N=321
- Subpulmonic 19%
- Perimembranous 70%





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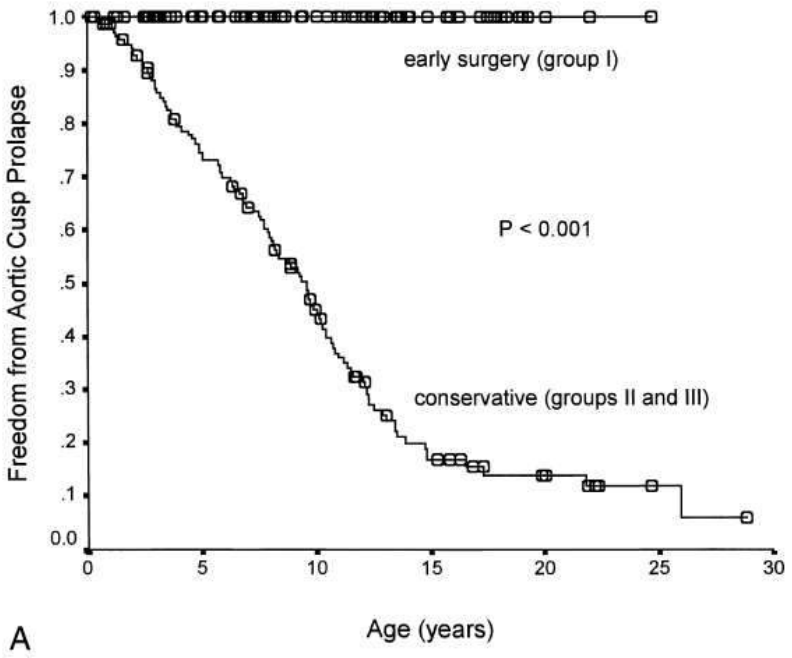
Subpulmonic VSD, Aortic Cusp Prolapse & Insufficiency

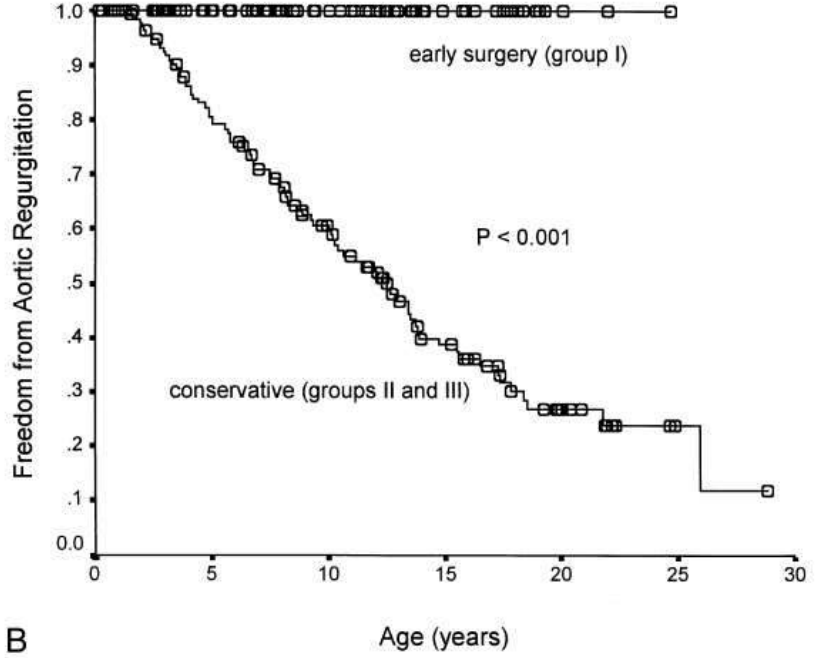
214 consecutive patients with subpulmonic VSD

- Group I: n=75 (35%), early surgery for heart failure
- Group II: n=102 (48%), asymptomatic, eventually developed cusp prolapse ± AI
  48/102 (47%) underwent surgery (mean age 9.8 y)
- Group III: n=37 (17%), managed medically, no valvar complications
  followed for 6.9 ± 5.8 years (range 0.3 to 24.3)

Freedom from Aortic Cusp Prolapse



Freedom from Aortic Insufficiency



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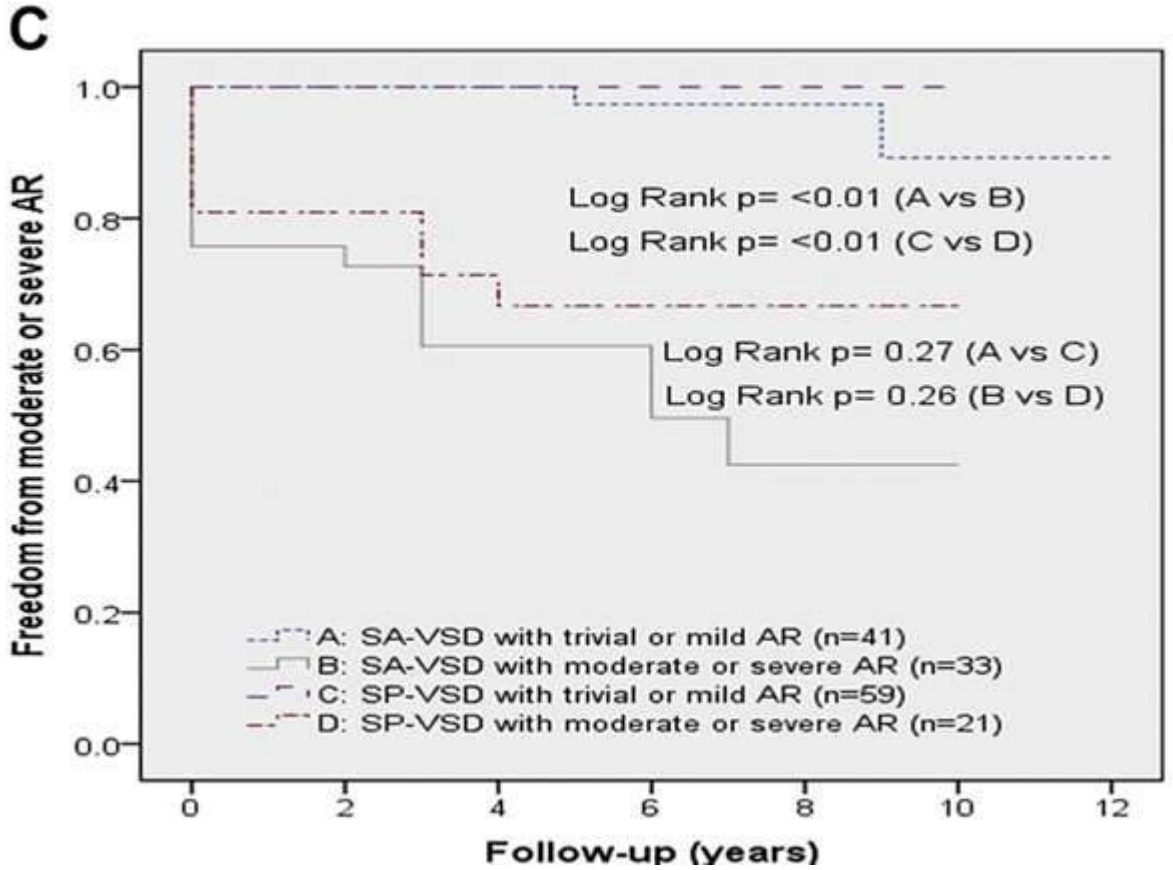
Lun K et al **Am J Cardiol 2001;87:1266–1270**

Prognosis of AI after VSD closure

154 patients with VSD/AI underwent surgery from 2006-2012

- Anatomic type:
  - 80 subpulmonic
  - 74 subaortic
- Preop AI:
  - 100 trivial-mild
  - 54 moderate-severe
- Mean age at surgery 10.5 ± 9 y
- Mean postop follow up: 6.3 ± 2.3 y

Freedom from moderate or severe AI



Giridhara et al, Ann Thorac Surg 2022;114:873-80

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Summary: VSD with Cusp Prolapse/AI

- Most commonly a concern for conal septal hypoplasia VSD
  - Typically during childhood/early adolescence
- Reasonable to follow, refer for surgery if progressive while AI is still trivial-mild
- Prepare families that they are not “out of the woods” after the first 1-2 years of life

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Population-based incidence of IE in VSD

- Population-based cohort study in Denmark using nationwide medical registries
- 8006 patients dx VSD before 2018
- 79,568 randomly selected controls from general Danish population, matched by birth year and sex.
- Median follow up ~23 years

Time period assessed	Incidence (per 10,000 person-years)		HR (95% CI)	Incidence (per 10,000 person-years)		HR (95% CI)
	VSD unrepaired (n=7324)	Controls (n=72765)		VSD surgically closed (n=682)	Controls (n=6803)	
Birth-end of follow up	4.8	0.2	28.0 (19.2-40.9)	29.1	0.4	82.7 (37.3-183.2)
From 1 year post dx or surgery	3.8	0.2	19.3 (11.9-31.1)	0.9	0.4	2.4 (0.3-20.6)

Eckerstrom F, *J Am Heart Assoc.* 2023;12:e027477

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Case #2:

- Conoventricular VSD
  - No CHF
  - Pressure restrictive by 6 weeks of age
- Cardiac Cath at 4 years of age
  - LVIDd Z-score +6
  - Qp:Qs 2:1
  - Mean pulmonary artery pressure 20-21 mmHg. PVR 1.1 WU.

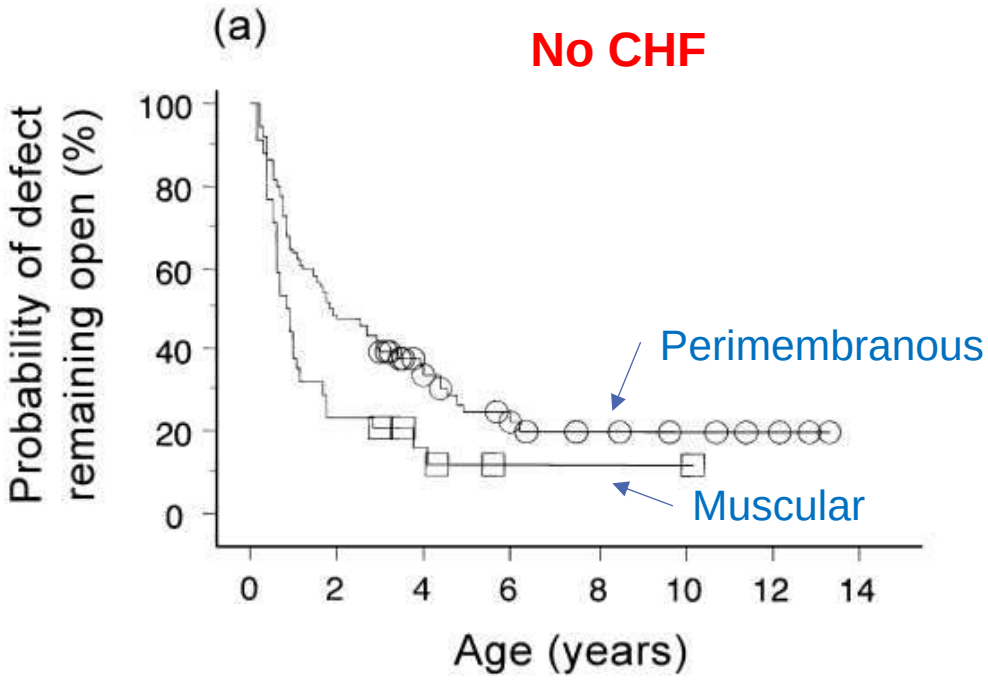
Case #2:

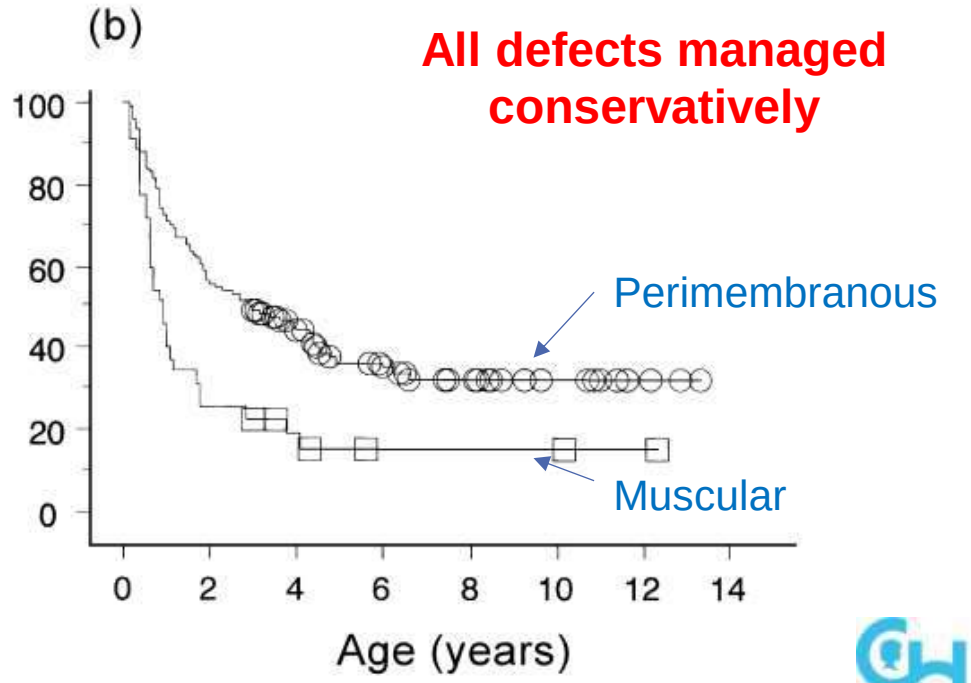
- Followed conservatively
  - Asymptomatic
  - Persistent LV dilation with LVIDd Z-score ~4-6
  - No other anatomic complications
- Age 14 years:
  - LVIDd Z-score +4.7

Spontaneous Closure of VSD

- 225 infants diagnosed with isolated VSD < 3 months of age
- Surgical closure performed in 59 (26%)
- Spontaneous closure rate in remainder:

VSD type	n	% Spontaneous Closure
Perimembranous	159	47%
- No CHF		74%
- With CHF		23%
Subpulmonary	31	10%





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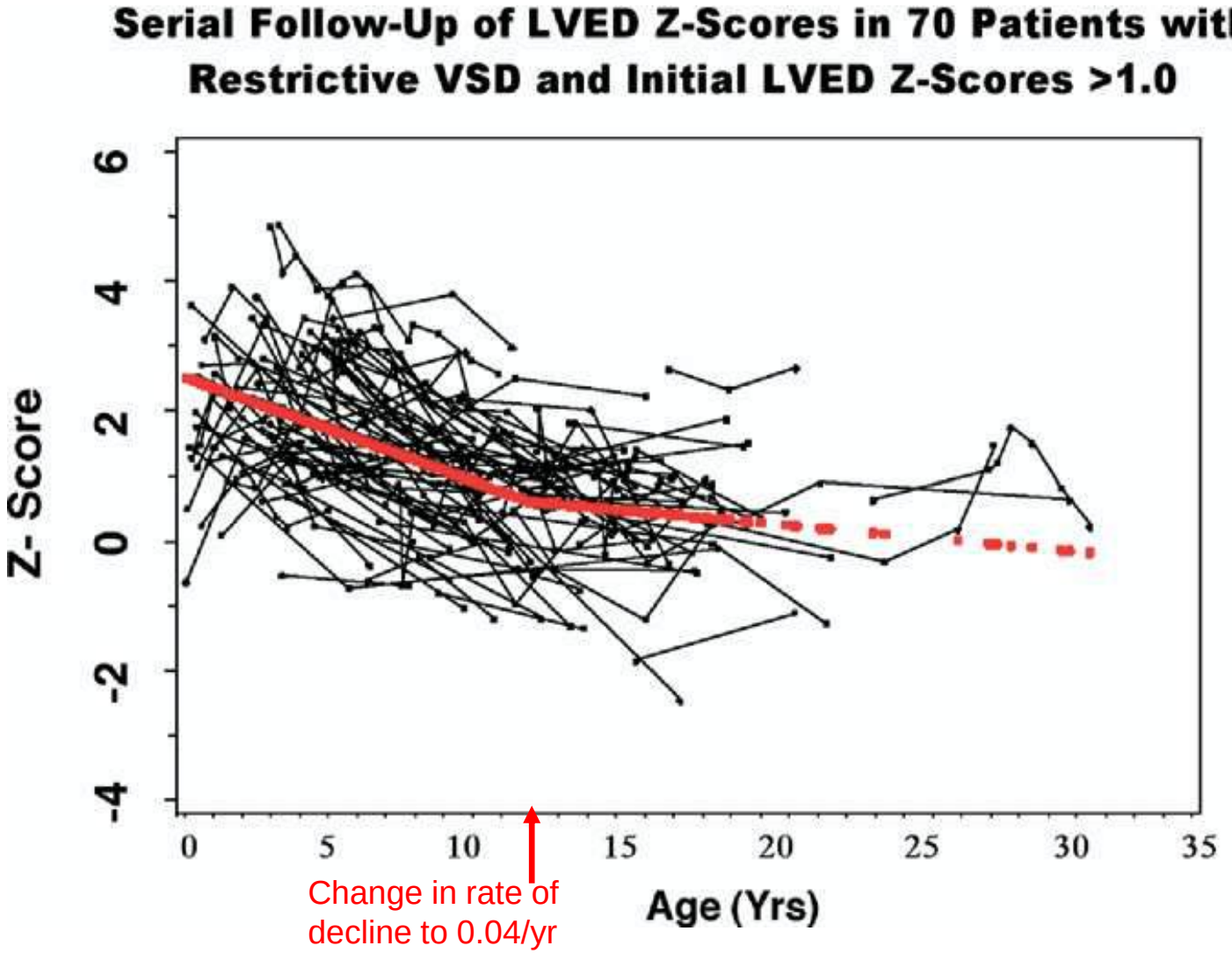
Miyake T, Pediatrics International (2004) 46, 135–140

Spontaneous Regression of LV Dilation



- None had CHF, PAH, or FTT

Kleiman C, et. al. Spontaneous Regression of Left Ventricular Dilation in Children with Restrictive Ventricular Septal Defects. J Pediatr. 2007 Jun;150(6):583-6

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Long-term Outcomes "Simple" VSD—mostly unoperated

- Population based registry: Denmark
  - Born 1948-1973, still alive at age 15 without significant comorbidity
  - VSD n=598, 8.7% operated on <15y
- 10 controls/pt matched birth year and gender
- Follow up complete through 2012 except 2.3% who emigrated
  - Median age at f/u for VSD 45.9y

Mortality

	Number of deaths (pct)	Mortality per 1,000 patient-years	adjusted Hazard ratio (95 % CI)
All CHD	86 (100)	2.16	1.87 (1.49 – 2.36)
Atrial septal defect	16 (18.6)	2.17	1.71 (1.01 – 2.90)
Patent ductus arteriosus	19 (22.1)	2.06	1.83 (1.12 – 2.99)
Pulmonary stenosis	10 (11.6)	2.09	1.51 (0.77 – 2.94)
Ventricular septal defect	41 (47.7)	2.23	2.08 (1.48 – 2.92)

Cardiac Morbidity*

	Number of patients with critical cardiac morbidity (%)	Critical cardiac morbidity Incidence rate per 1,000 patient-years	Adjusted hazard ratio (95% CI)
All CHD	142 (100)	3.91	5.66 (4.62-6.93)
Atrial septal defect	31 (21.8)	4.95	6.82 (4.29-10.86)
Patent ductus arteriosus	22 (15.5)	2.56	3.74 (2.28-6.13)
Pulmonary stenosis	22 (15.5)	5.04	6.32 (3.67-10.88)
Ventricular septal defect	67 (47.2)	3.92	6.37 (4.67-8.70)

Videbaek J, ***Circulation*. 2016;133:474-483.**

*ACHD surgery, HF, VF/VT, resuscitated arrest, IE, new dx PAH, aortic dissection

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Long-term Outcomes of VSD: operated and unoperated

- Population-based cohort study in Denmark using nationwide medical registries
- 8006 patients dx VSD before 2018 (8.5% closed surgically)
- 79,568 randomly selected controls from general Danish population, matched by birth year and sex.
- Median follow up ~23 years
- Incidence of morbid events from 1 year post dx or surgery

Morbidity	Incidence (per 10,000 person-years)		HR (95% CI)	Incidence (per 10,000 person-years)		HR (95% CI)
	VSD unrepaired (n=7324)	Controls (n=72765)		VSD surgically closed (n=682)	Controls (n=6803)	
Arrhythmia	12.6	5.9	2.2 (1.8-2.6)	27.6	7.7	3.6 (2.3-5.4)
Pulmonary Hypertension	1.9	0.3	5.7 (3.5-9.4)	4.4	0.3	13.7 (3.7-51)
Heart Failure	8.6	3.0	2.9 (2.3-3.6)	20.8	3.0	7.0 (4.1-12.1)

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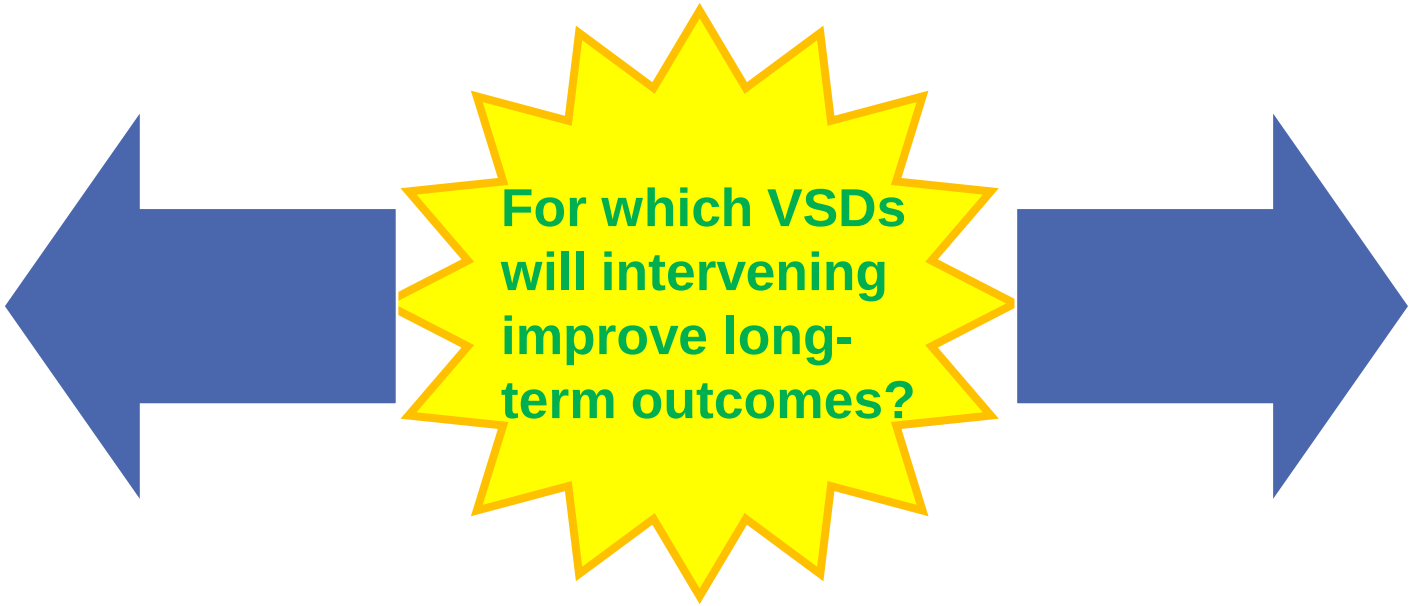
The Challenge



Questions with no good data:

Mechanisms of the adverse outcomes?

If one mechanism is volume load, **by when** should it be relieved to improve outcome?

Is there an **era effect** in operated VSDs? (later age at repair, surgical technique such as right ventriculotomy)?

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How have our ACHD colleagues answered this question?

LV volume load, Qp:Qs >1.5:1 → closure

I	B-NR	1. Adults with a VSD and evidence of left ventricular volume overload and hemodynamically significant shunts (Qp:Qs >1.5:1) should undergo VSD closure, if PA systolic pressure is less than 50% systemic and pulmonary vascular resistance is less than one third systemic.[S4.1.3-1]

Stout KK et al. *Circulation.* 2019;139:e637–e697.

Proposed approach

- Pressure-restrictive VSD with persistent LV dilation but no anatomic complications
  - Conal septal hypoplasia type: recommend surgery given low likelihood of spontaneous closure, high likelihood of aortic valve complications
  - Conoventricular type:
    - Observe for decrease in dilation
    - LVIDd Z-score >2 at age 12 years→cMR for Qp:Qs, LV volume
    - Qp:Qs >1.5, evaluate for transcatheter closure
    - If not a candidate for transcatheter closure, consider surgical closure

Case #2

- Age 14 years: LVIDd Z-score +4.7
- Age 16 years: Cardiac Cath
  - Baseline Qp:Qs 1.9:1, mPAP 12, PVRI 0.7 WU/m2
  - ADO II placed in TV windsock, small residual shunt
  - Developed hemolysis, resolved by 5 months post-procedure
- Age 18 years
  - Small residual VSD
  - LVIDd Z 2.5
  - cMR:
    - Qp:Qs 1.1:1
    - Top normal LVEDV 95 mL/m2
    - LVEF 68%

Thank you

NHS I & II

Group	Severity Class	N (NHS-1)	PA Pressure	Qp:Qs	Rp:Rs
Ia	Trivial	390	Low*	<1.5	
	Trivial/mild	6	Low*	Missing	
Ib	Mild	234	Low*	≥1.5	
II	Moderate	328	High		<0.2 or Rp≤4
	Moderate-severe	27	High	>1.2 or age <2y	Missing
III	Severe	189	High		≥0.2, <0.7 or Rp>4
IV	Eisenmenger	98	High		>0.7

*Pressure low = PA/Ao <0.3 or MPA mean pressure <20 mmHg or MPA systolic pressure <35 mmHg

- Of the original 630 trivial-mild participants, only 318 (50.4%) were fully re-evaluated at NHS-II
- 24% of trivial-mild participants managed surgically
- For the mild group, survival free from operation at 25 years was 48.5%

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Kidd L, Circulation Vol 87(2S) Supplement, February 1993, pp I38-I51.

Ventricular Septal Defect and Aortic Valve Regurgitation: Pathophysiology and Indications for Surgery

James S. Tweddell,[*,‡] Andrew N. Pelech,[†,‡] and Peter C. Frommelt[†,‡]

Table 1 A Summary of Hemodynamic Characteristics of Ventricular Septal Defects With Aortic Valve Prolapse With or Without AI

Study	Year	n Total	VSD Position	No. With AVP With or Without AI	Qp/Qs	PA Pressure (mmHg)	
						Systolic PA Pressure	Mean or Median PA Pressure
Schmidt et al[19]	1988	48	SA	28	Mean, 1.5 ± 0.5	NA	
Rhodes et al[20]	1990	92*	PM	62	Median, 1.6		Median, = 15
			SA	21	Range, 1 – 4		Range, 4 – 36
Komai et al[13]	1997	27	SA	12	Mean, 1.44 ± 0.47		Mean, 22.0 ± 16.3
Sim et al[21]	1999	128	SA	36	Range, 1.1 – 2.6	NA	
Lun et al[17]	2001	214	SA	102	Mean, 1.6 ± 0.6	Mean, 28.2 ± 11	
Cheung et al[22]	2002	135	SA	56	Mean, 1.7 ± 0.6§	Mean, 30.5 ± 9.5§	
					Mean, 1.8 ± 0.7‖	Mean, 28.2 ± 5.7‖	
Chiu et al[18]	2005	677	SA	209	Mean, 1.62 ± 0.92		Mean, 15.7 ± 7.0
			PM	103	Mean, 1.71 ± 0.77		Mean, 17.1 ± 8.3
			MO	61	Mean, 1.45 ± 0.64		Mean, 13.4 ± 5.2

Abbreviations: SA, subarterial; PM, perimembranous; MO, muscular outlet; AVP, aortic valve prolapse; AI, aortic insufficiency.
*Position of VSD unknown in 9 patients.
§Patients with AVP and < moderate AI = 39.
‖Patients with AVP and ≥ moderate AI n = 17.

Other Long-term Functional Outcomes

- Relatively small studies have identified deficits in adults with both surgically repaired VSDs and small unoperated VSDs:
  - Pulmonary function:
    - At rest: surgically repaired VSDs
    - With exercise: surgically repaired and unoperated VSDs
  - Exercise capacity
  - Biventricular contractility: rest and exercise

Eckerstrom *Am J Cardiol* 2020;125:1710−1717
Eckerstrom International Journal of Cardiology 306 (2020) 168–174
Maagaard *J Am Heart Assoc.* 2020;9:e015956.
Maagaard *Am J Cardiol* 2020;133:139−147
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