



# Bicuspid Valvulopathy & Aortopathy

**Jae-Kwan Song, MD, PhD, FACC**

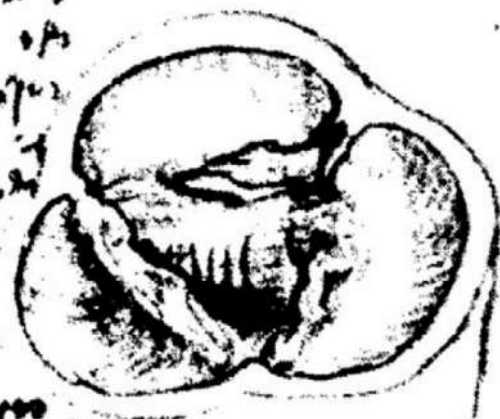
Asan Medical Center Heart Institute

Research Institute for Valvular Heart Disease

University of Ulsan College of Medicine

Seoul, South Korea

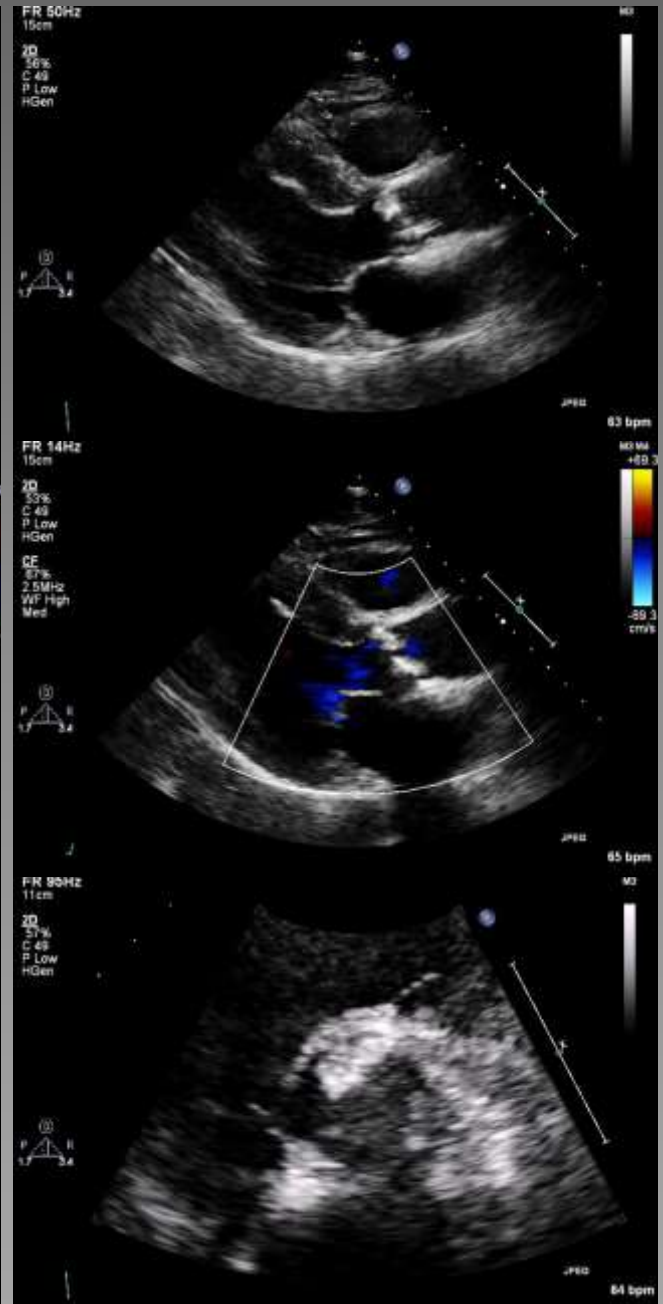
Handwritten text in Leonardo da Vinci's mirror script, likely describing anatomical observations or theories related to the heart and blood flow.



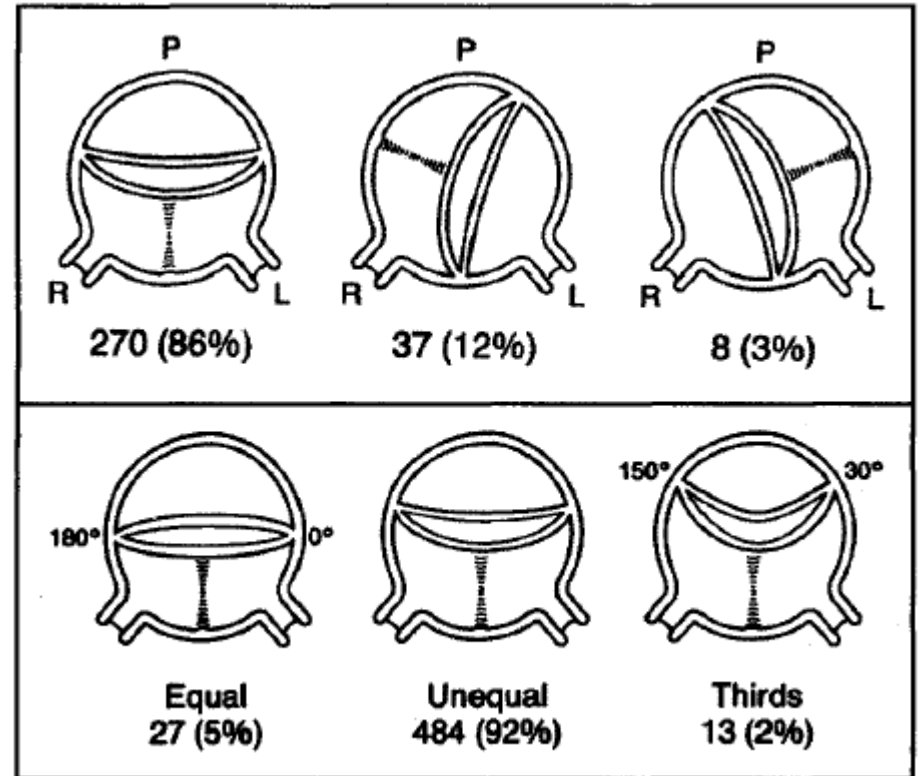
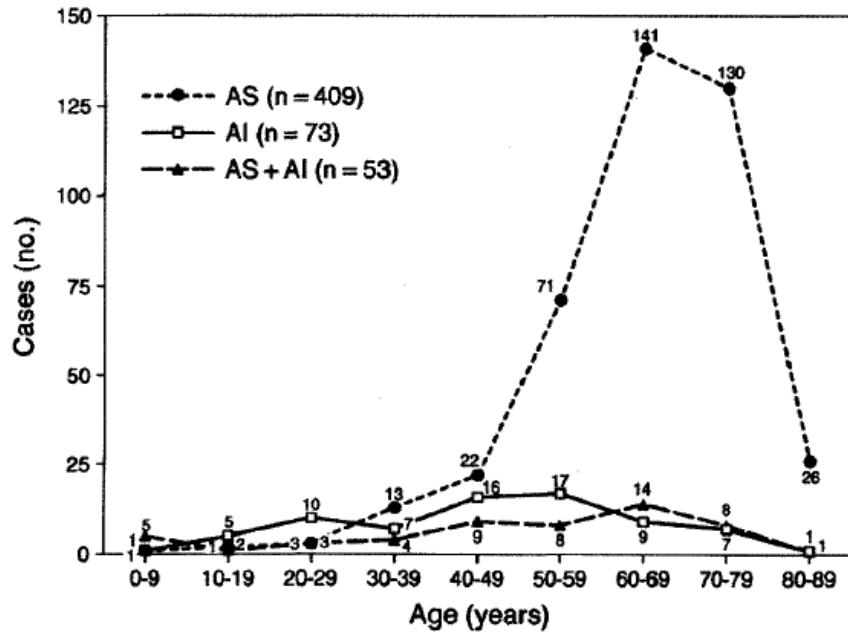
# Da Vinci's sketch

Over 400 Years ago

# Variable Clinical Presentation of BAV

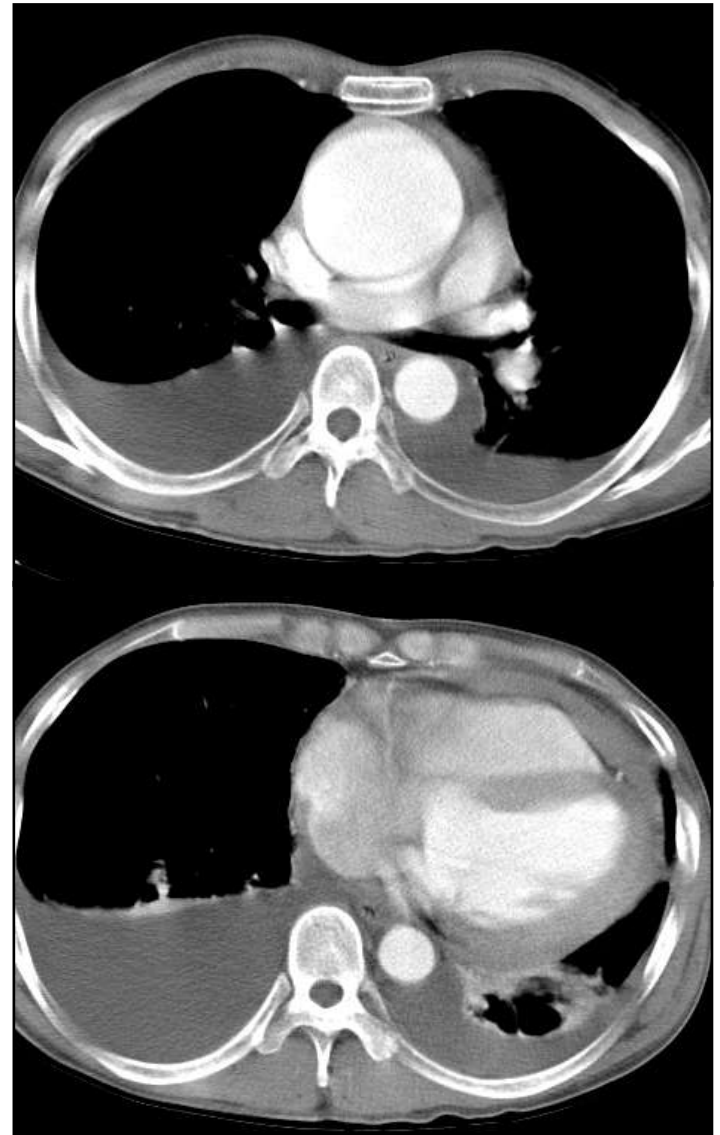
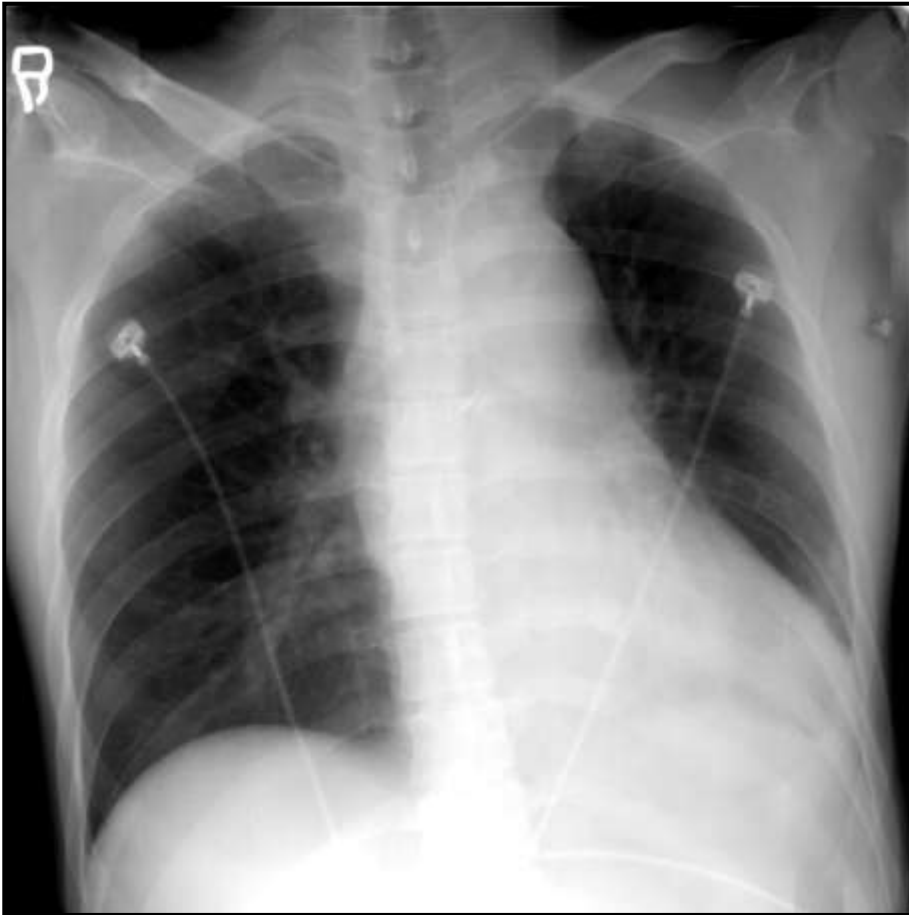


# Variable Clinical Presentation of BAV: 542 patients with BAV in Mayo Clinic - Surgery



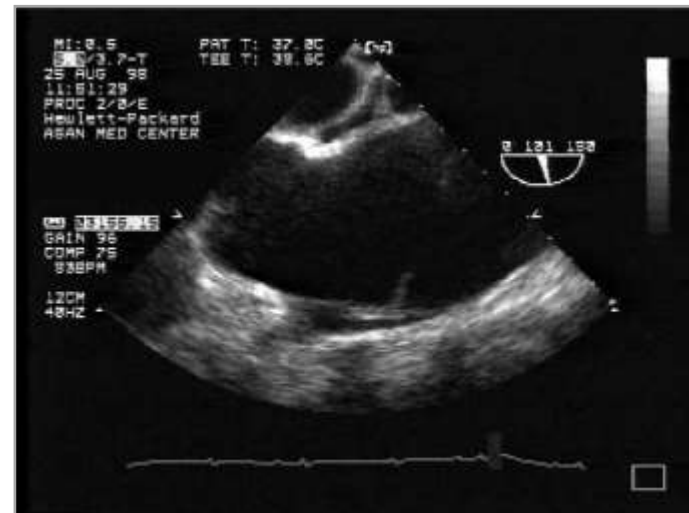
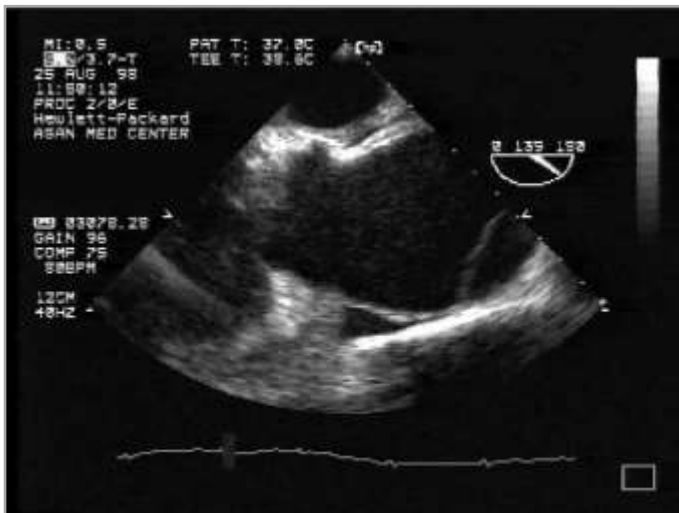
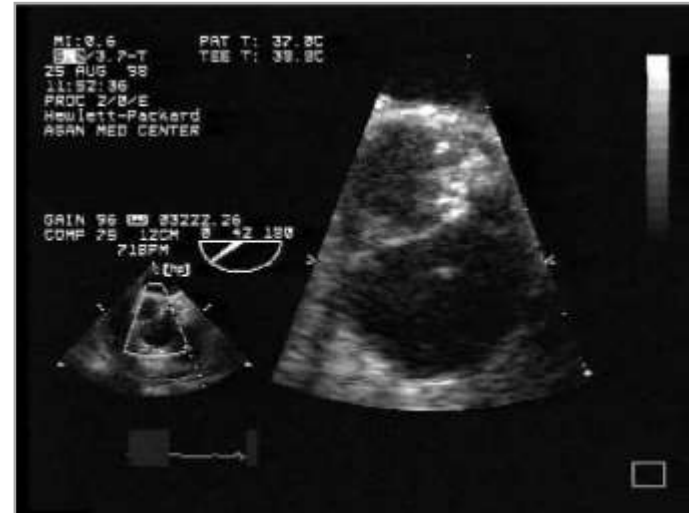
# Bicuspid Aortopathy

- M/44, sudden back pain



# Bicuspid Aortopathy: AD with normally functioning BAV

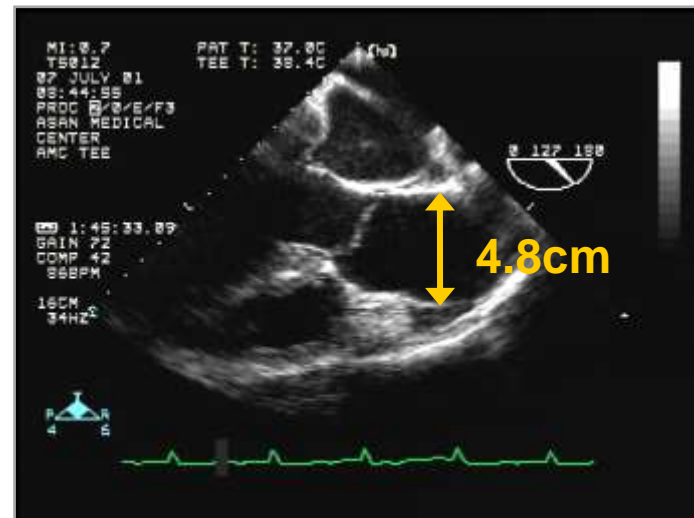
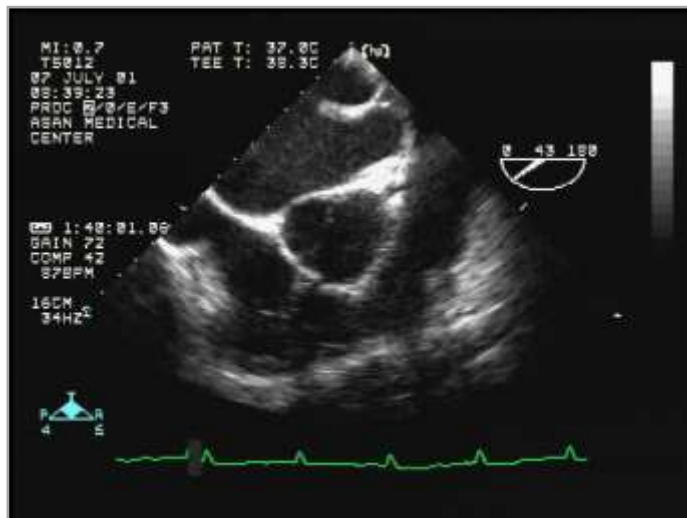
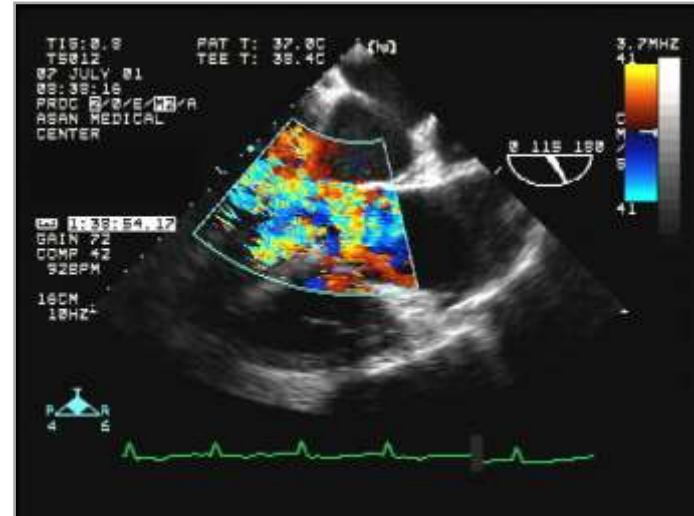
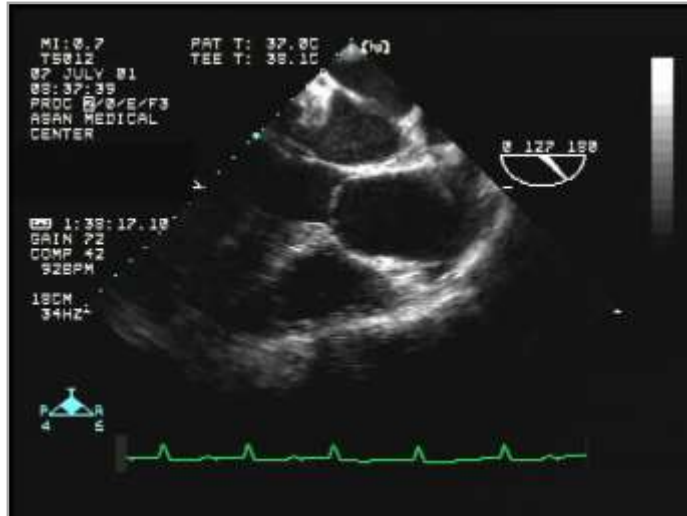
- M/44, sudden back pain





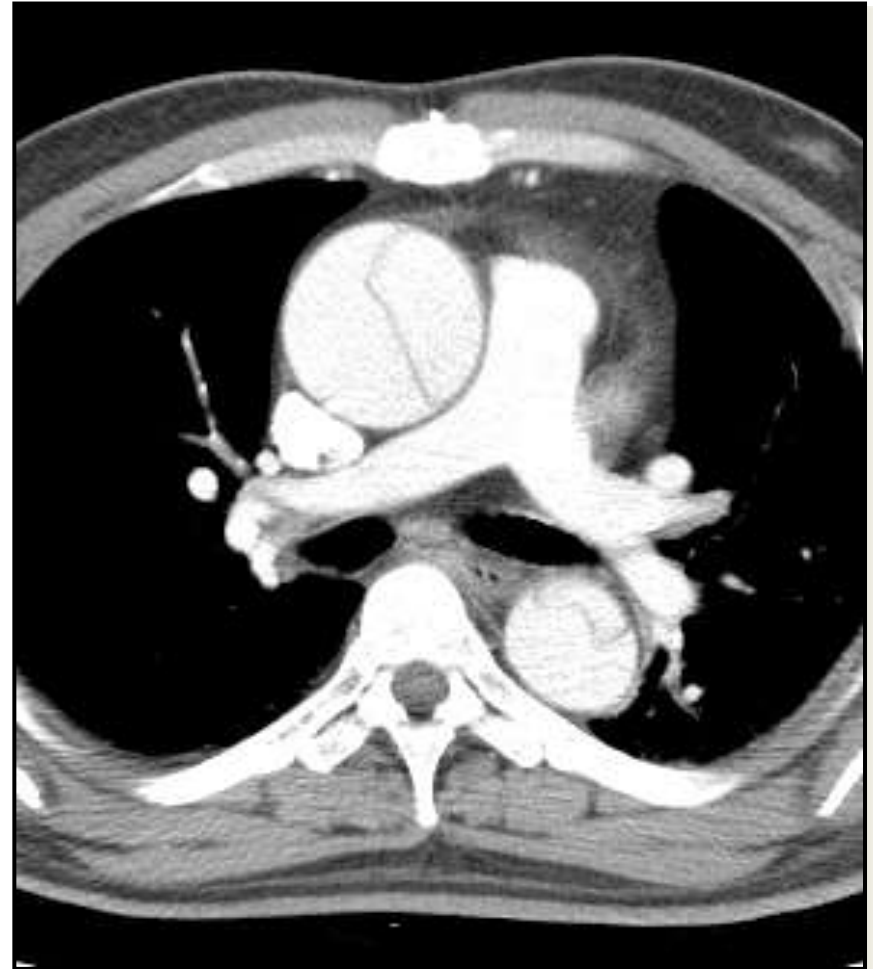
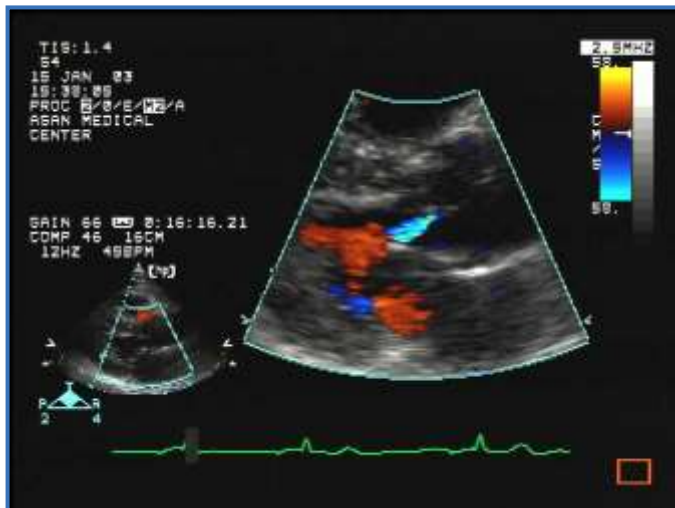
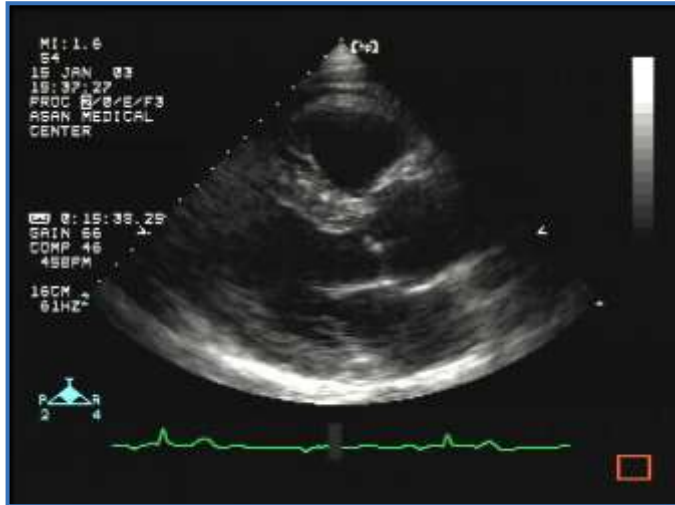
# Bicuspid Aortopathy: AD after aortic valve surgery

- M/56, aortic valve repair due to severe AR with BAV



# Bicuspid Aortopathy: AD after aortic valve surgery

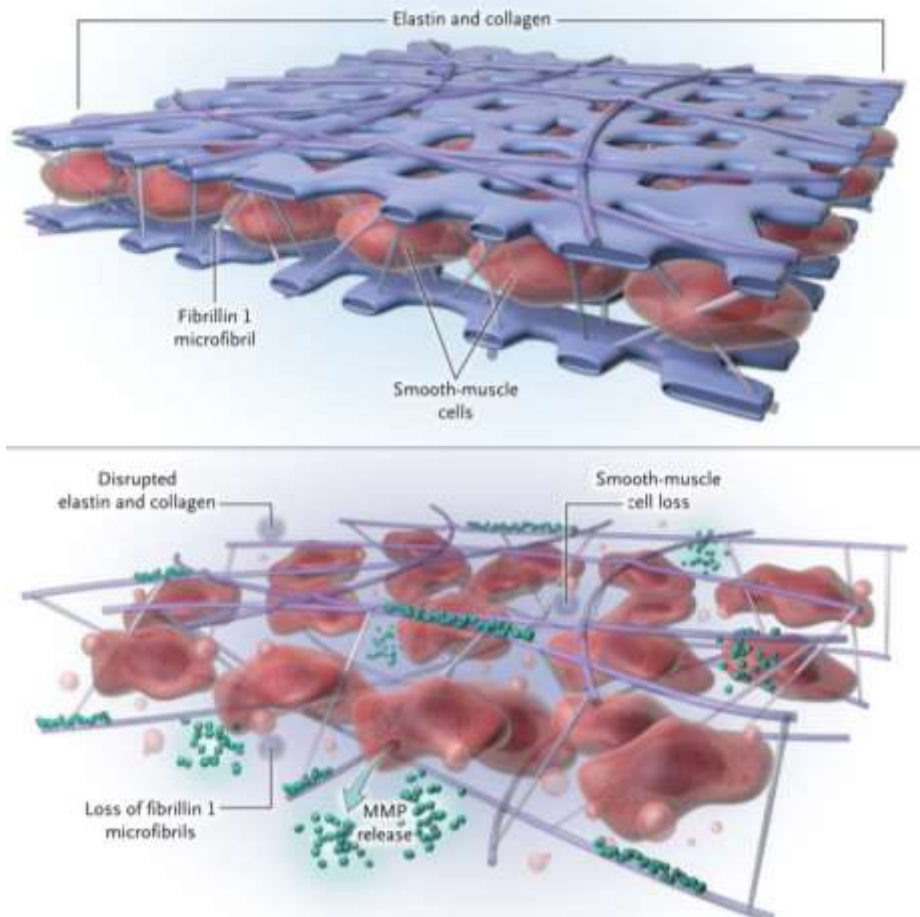
- Type 1 AD with markedly dilated aorta (48 → 57 mm)



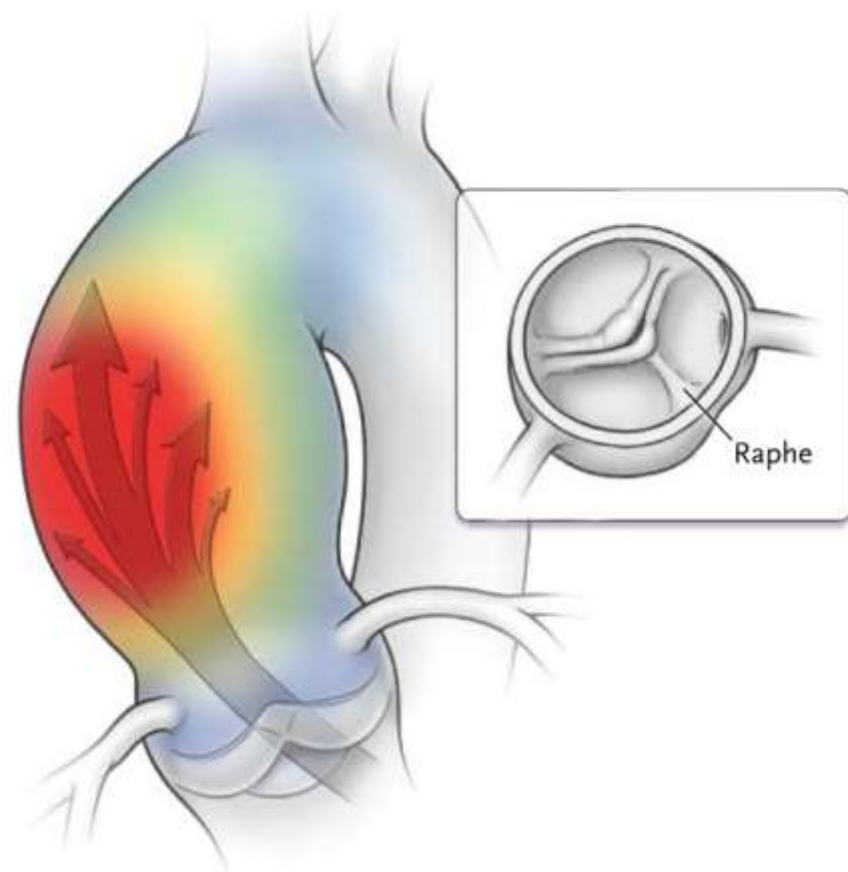


# Bicuspid Aortopathy: Two main contributors

## Matrix fragility



## Flow dynamics



# Bicuspid Aortopathy

ORIGINAL CONTRIBUTION

## Outcomes in Adults With Bicuspid Aortic Valves

Nikolaos Tzemos, MD

Judith Therrien, MD

James Yip, MD

George Thanassoulis, MD

Sonia Tremblay, MD

Michal T. Jamorski, BSc

Gary D. Webb, MD

Samuel C. Siu, MD, SM

**B**ICUSPID AORTIC VALVE IS THE most common congenital cardiac anomaly in the adult population.<sup>1-3</sup> Prior studies have reported significant mortality and morbidity in patients with bicuspid aortic valve related to the development of aortic valve dysfunction, endocarditis, and dissection.<sup>1,4,5</sup> It is uncertain whether these prior findings, based on necropsy and surgical series from earlier eras, can be applied to a contemporary patient population.<sup>1,6,7</sup> The purpose of this cohort study was to examine the cardiac outcomes and disease progression in a large contemporary group of adults with bicuspid aortic valve followed up over a prolonged period of observation.

### METHODS

This cohort study examined a referral population of consecutive adults with bicuspid aortic valve assessed at the University Health Network (Toronto General and Toronto Western Hospitals, Toronto, Ontario, Canada) ambulatory cardiac clinics from 1994 through 2001. Patients were identified using the hospital's echocardiography and congenital cardiac databases. The University Health Network is the main congenital cardiac center for the city of Toronto. The

**Context** Bicuspid aortic valve is the most common congenital cardiac anomaly in the adult population. Cardiac outcomes in a contemporary population of adults with bicuspid aortic valve have not been systematically determined.

**Objective** To determine the frequency and predictors of cardiac outcomes in a large consecutive series of adults with bicuspid aortic valve.

**Design, Setting, and Participants** Cohort study examining cardiac outcomes in 642 consecutive ambulatory adults (mean [SD] age, 35 [16] years; 68% male) with bicuspid aortic valve presenting to a Canadian congenital cardiac center from 1994 through 2001 and followed up for a mean (SD) period of 9 (5) years. Frequency and predictors of major cardiac events were determined by multivariate analysis. Mortality rate in the study group was compared with age- and sex-matched population estimates.

**Main Outcome Measures** Mortality and cause of death were determined. Primary cardiac events were defined as the occurrence of any of the following complications: cardiac death, intervention on the aortic valve or ascending aorta, aortic dissection or aneurysm, or congestive heart failure requiring hospital admission during the follow-up period.

**Results** During the follow-up period, there were 28 deaths (mean [SD], 4% [1%]). One or more primary cardiac events occurred in 161 patients (mean [SD], 25% [2%]), which included cardiac death in 17 patients (mean [SD], 3% [1%]), intervention on aortic valve or ascending aorta in 142 patients (mean [SD], 22% [2%]), aortic dissection or aneurysm in 11 patients (mean [SD], 2% [1%]), or congestive heart failure requiring hospital admission in 16 patients (mean [SD], 2% [1%]). Independent predictors of primary cardiac events were age older than 30 years (hazard ratio [HR], 3.01; 95% confidence interval [CI], 2.15-4.19;  $P < .001$ ), moderate or severe aortic stenosis (HR, 5.67; 95% CI, 4.16-7.80;  $P < .001$ ), and moderate or severe aortic regurgitation (HR, 2.68; 95% CI, 1.93-3.76;  $P < .001$ ). The 10-year survival rate of the study group (mean [SD], 96% [1%]) was not significantly different from population estimates (mean [SD], 97% [1%];  $P = .71$ ). At last follow-up, 280 patients (mean [SD], 45% [2%]) had dilated aortic sinus and/or ascending aorta.

**Conclusions** In this study population of young adults with bicuspid aortic valve, age, severity of aortic stenosis, and severity of aortic regurgitation were independently associated with primary cardiac events. Over the mean follow-up duration of 9 years, survival rates were not lower than for the general population.

JAMA. 2008;300(11):1317-1325

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inclusion criteria were bicuspid aortic valve documented on transthoracic echocardiography and the absence of com-

plex congenital cardiac defects. We excluded 260 patients who were referred for cardiac surgery, catheter-based treat-

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Heart Center, Children's Hospital of Philadelphia, Department of Medicine, University of Pennsylvania, Philadelphia (Dr Webb); and Division of Cardiology, University of Western Ontario, London, Ontario, Canada (Dr Siu).

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## Valvular Heart Disease

### Natural History of Asymptomatic Patients With Normally Functioning or Minimally Dysfunctional Bicuspid Aortic Valve in the Community

Hector I. Michelena, MD; Valerie A. Desjardins, MD; Jean-François Avierinos, MD; Antonio Russo, MD; Vuyisile T. Nkomo, MD; Thoralf M. Sundt, MD; Patricia A. Pellikka, MD; A. Jamil Tajik, MD; Maurice Enriquez-Sarano, MD

**Background**—Bicuspid aortic valve is frequent and is reported to cause numerous complications, but the clinical outcome of patients diagnosed with normal or mildly dysfunctional valve is undefined.

**Methods and Results**—In 212 asymptomatic community residents from Olmsted County, Minn (age, 32±20 years; 65% male), bicuspid aortic valve was diagnosed between 1980 and 1999 with ejection fraction ≥50% and aortic regurgitation or stenosis, absent or mild. Aortic valve degeneration at diagnosis was scored echocardiographically for calcification, thickening, and mobility reduction (0 to 3 each), with scores ranging from 0 to 9. At diagnosis, ejection fraction was 63±5% and left ventricular diameter was 48±9 mm. Survival 20 years after diagnosis was 90±3%, identical to the general population ( $P=0.72$ ). Twenty years after diagnosis, heart failure, new cardiac symptoms, and cardiovascular medical events occurred in 7±2%, 26±4%, and 33±5%, respectively. Twenty years after diagnosis, aortic valve surgery, ascending aortic surgery, or any cardiovascular surgery was required in 24±4%, 5±2%, and 27±4% at a younger age than the general population ( $P<0.0001$ ). No aortic dissection occurred. Thus, cardiovascular medical or surgical events occurred in 42±5% 20 years after diagnosis. Independent predictors of cardiovascular events were age ≥50 years (risk ratio, 3.0; 95% confidence interval, 1.5 to 5.7;  $P<0.01$ ) and valve degeneration at diagnosis (risk ratio, 2.4; 95% confidence interval, 1.2 to 4.5;  $P=0.016$ ; >70% events at 20 years). Baseline ascending aorta ≥40 mm independently predicted surgery for aorta dilatation (risk ratio, 10.8; 95% confidence interval, 1.8 to 77.3;  $P<0.01$ ).

**Conclusions**—In the community, asymptomatic patients with bicuspid aortic valve and no or minimal hemodynamic abnormality enjoy excellent long-term survival but incur frequent cardiovascular events, particularly with progressive valve dysfunction. Echocardiographic valve degeneration at diagnosis separates higher-risk patients who require regular assessment from lower-risk patients who require only episodic follow-up. (Circulation. 2008;117:2776-2784.)

**Key Words:** aorta ■ echocardiography ■ surgery ■ survival ■ valves

**B**icuspid aortic valve (BAV) is a common congenital heart abnormality affecting 0.5% to 2% of the population.<sup>1-3</sup> It is often considered a serious condition with notable valvular risk, particularly of aortic valve endocarditis<sup>4,5</sup>; frequent progression to aortic valve stenosis,<sup>6,7</sup> especially in men<sup>8</sup>; and frequent aortic regurgitation requiring aortic valve replacement (AVR).<sup>8,9</sup> Furthermore, BAV is not just a peculiar valve morphology; it is a disease of the ascending aorta characterized at an early stage by asymptomatic dilatation of the ascending aorta<sup>10</sup> and later by frequent susceptibility to aneurysm formation of the aorta<sup>11-13</sup> and to the most dreaded complication, aortic dissection.<sup>2,8,14</sup> However, these implied serious prognostic consequences of BAV were derived mostly from autopsy or studies at referral centers with a high

concentration of patients who already have these complications. Few longitudinal data are available on asymptomatic, initially uncomplicated patients detected in the community who are not referred and may never be accounted for until autopsy.<sup>1</sup> Thus, the real complication burden of BAV in the community has not been measured. Although it is well established that patients with clinically significant aortic valve stenosis or regurgitation incur serious outcome consequences whether they have bicuspid and tricuspid valves,<sup>15,16</sup> limited data are available on patients with initially normally functioning or minimally dysfunctional BAV,<sup>17,18</sup> in whom mortality and cardiac and vascular event rates are undefined. To resolve these uncertainties, assessment of all cases diagnosed in a geographically defined community with high use

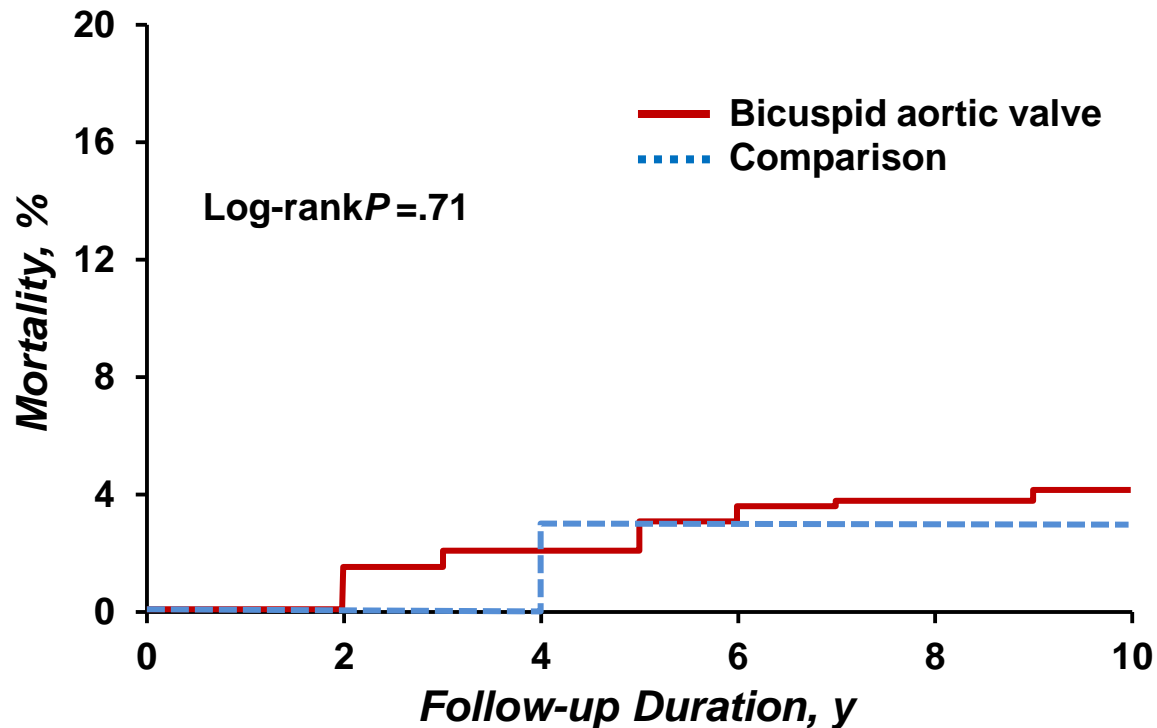
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Correspondence to Maurice Enriquez-Sarano, MD, Mayo Clinic, 200 First St. SW, Rochester, MN 55905. E-mail: sarano.maurice@mayo.edu  
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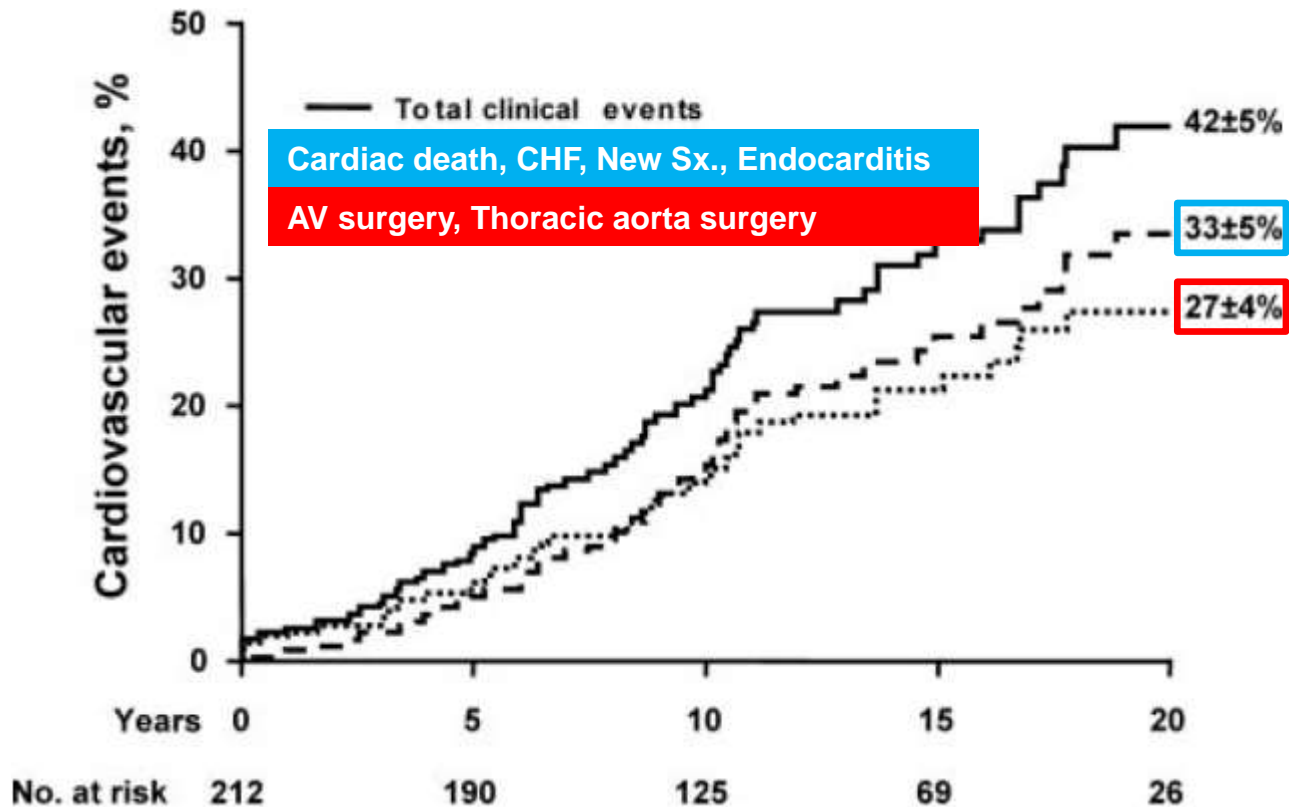
DOI: 10.1161/CIRCULATIONAHA.107.740878

# Overall Mortality Rate was Similar With Population Estimates

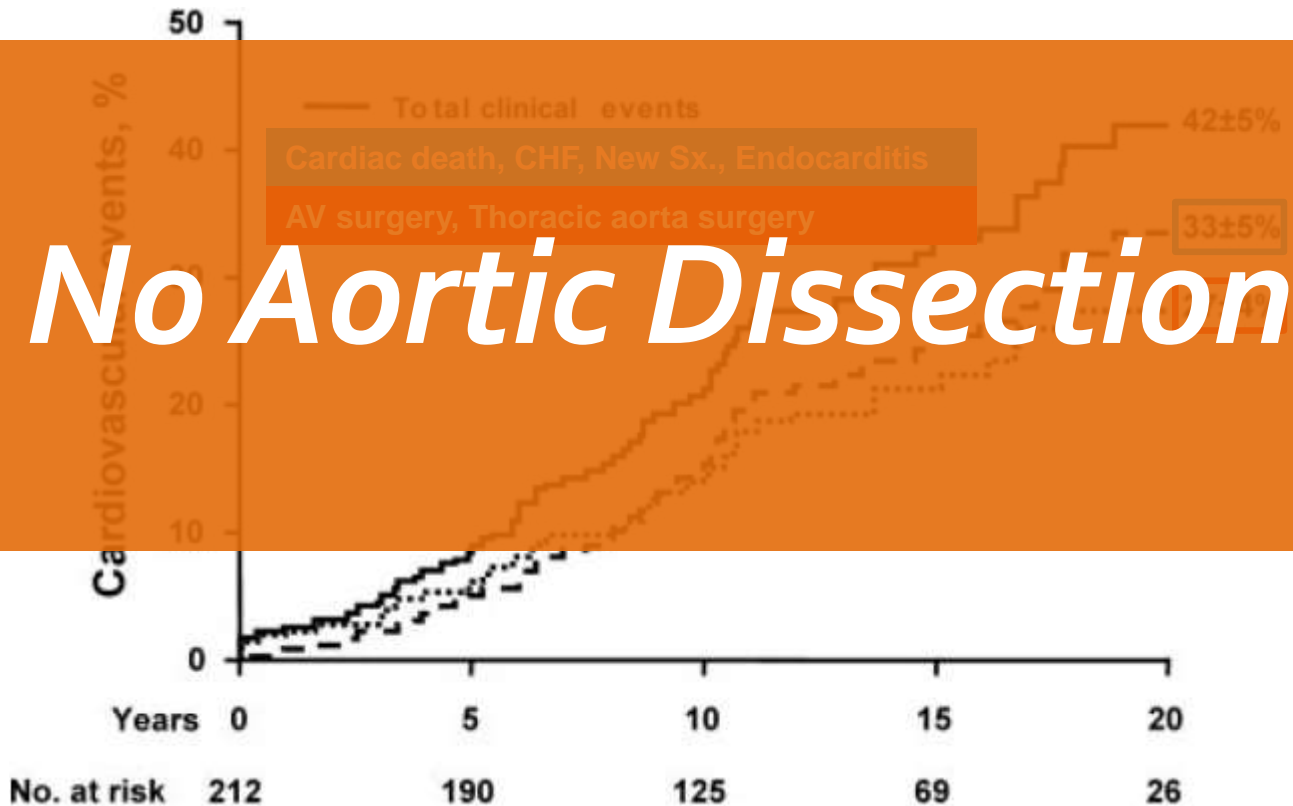


No. at risk	0	2	4	6	8	10
Bicuspid aortic valve	642	641	576	476	373	258
Comparison	642	642	642	622	622	622

# Cardiovascular Events



# Cardiovascular Events





# Bicuspid Aortopathy: Fact vs. Factoid

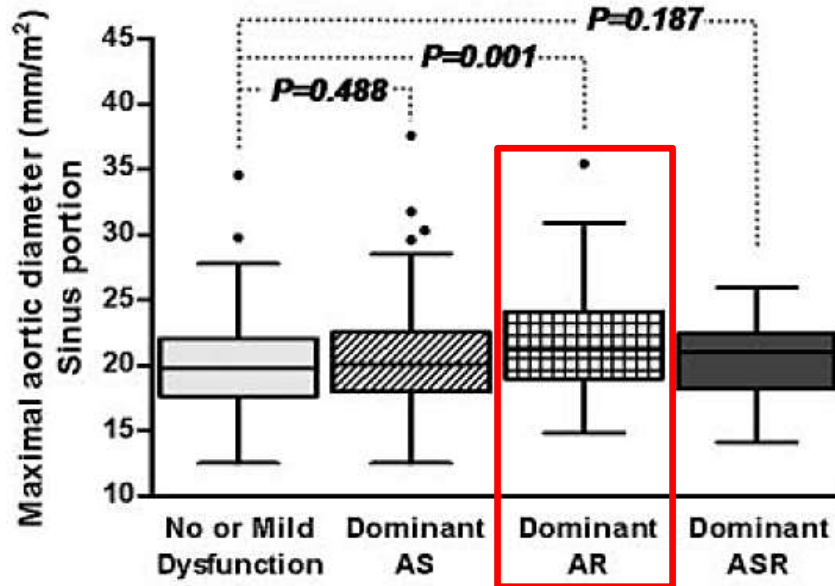
- Excellent overall survival in recent outcome studies

**Table 1** Late Outcomes in Adults With BAV Disease

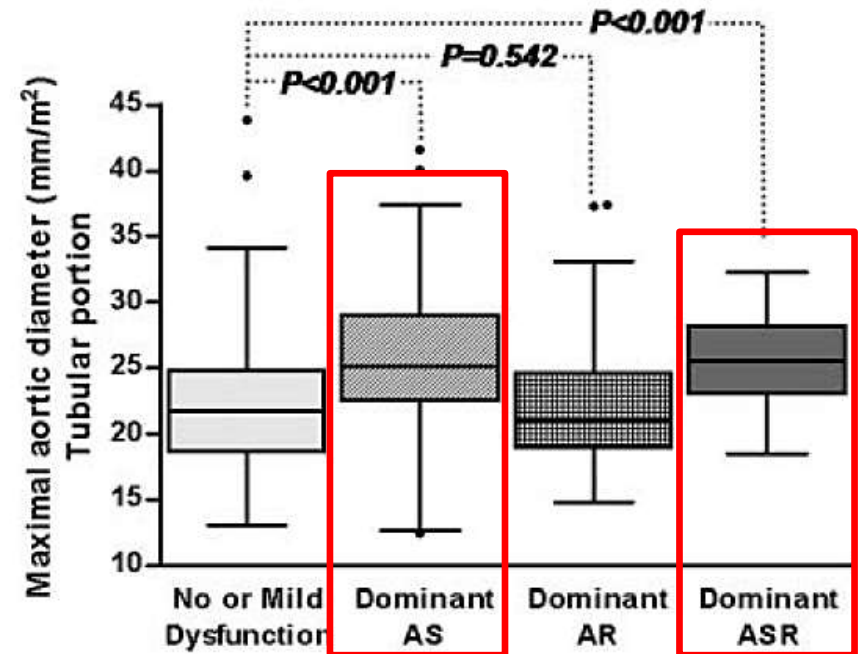
	Patients With BAV and No Significant Aortic Valve Dysfunction (n = 212)*	Patients With BAV With a Spectrum of Valve Function (n = 642)†
Mean follow-up, yrs (range)	15 ± 6 (0.4-25)	9 ± 5 (2-26)
Mean age at baseline, yrs	32 ± 20	35 ± 16
<b>Outcomes</b>		
Overall survival	90 ± 3% at 20 yrs	96 ± 1% at 10 yrs
Cardiac deaths		3 ± 1%
Aortic valve or ascending aorta surgery	27 ± 4%‡	22 ± 2%
Cardiovascular medical events	33 ± 5%	NA
Aortic dissection	0	2 ± 1%
Hospital admission for heart failure	7 ± 2%	2 ± 1%
Endocarditis	2%	2%
<b>Predictors of outcomes</b>		
Predictors of cardiac events (medical and surgical)	Age ≥50 yrs Valve degeneration	Age >30 yrs Moderate or severe aortic stenosis Moderate or severe aortic regurgitation

# Hemodynamic Burden and Bicuspid Aortopathy

## Sinus diameter



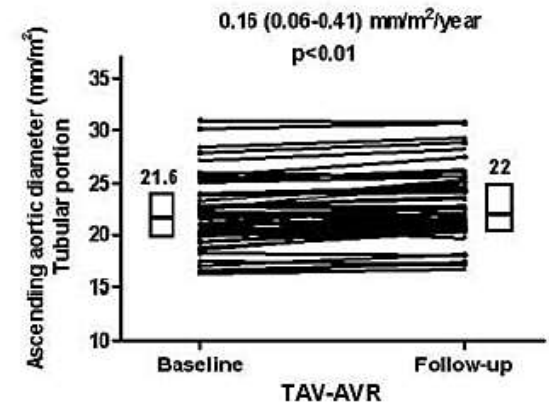
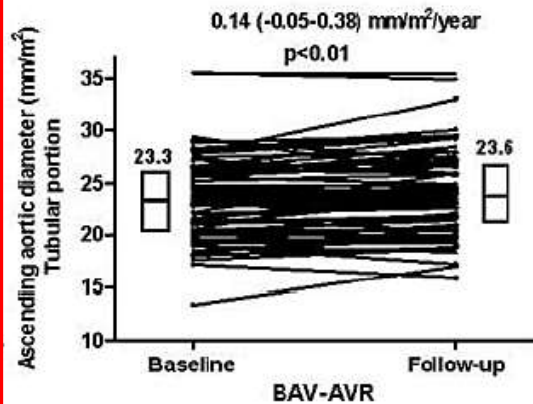
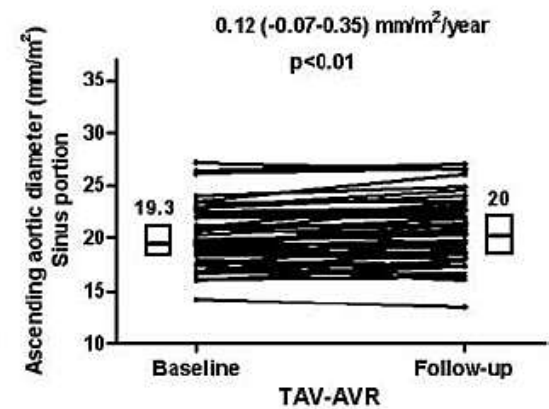
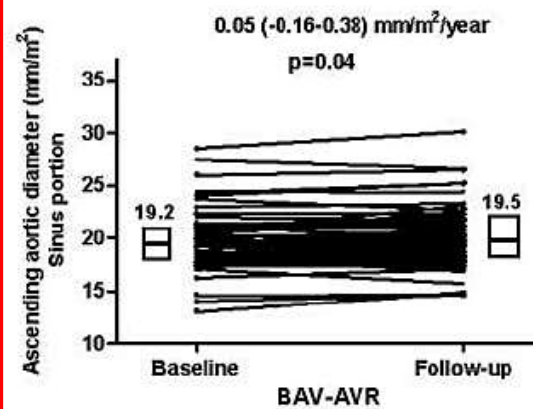
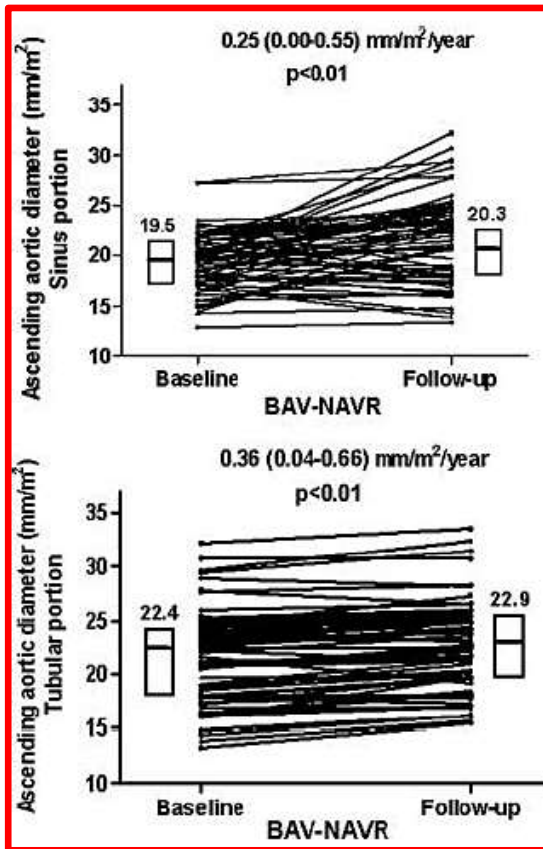
## Tubular diameter



*Sinus diameter is larger in AR,*

*whereas Tubular diameter is larger in AS*

# Valve Surgery Protected Aorta From Progressive Dilatation



# Etiology of AS



**Bicuspid**

- congenital
- 1-2% of general population



**Rheumatic**

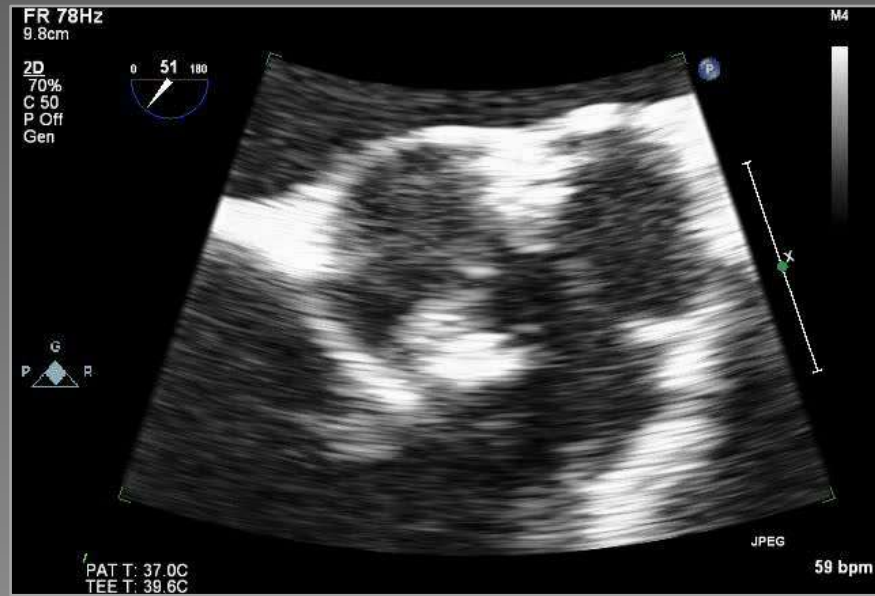
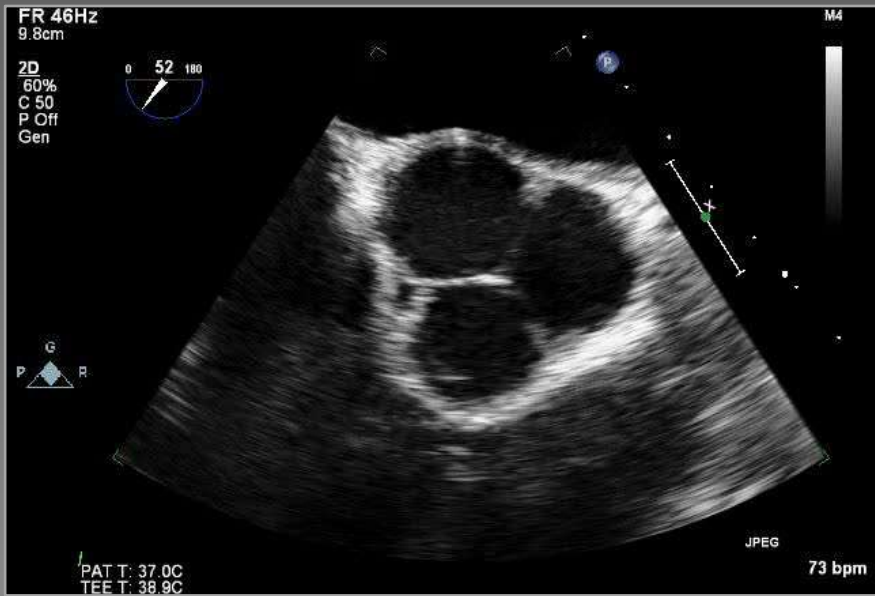
- multivalvular involvement
- commissural fusion (+)



**Degenerative**

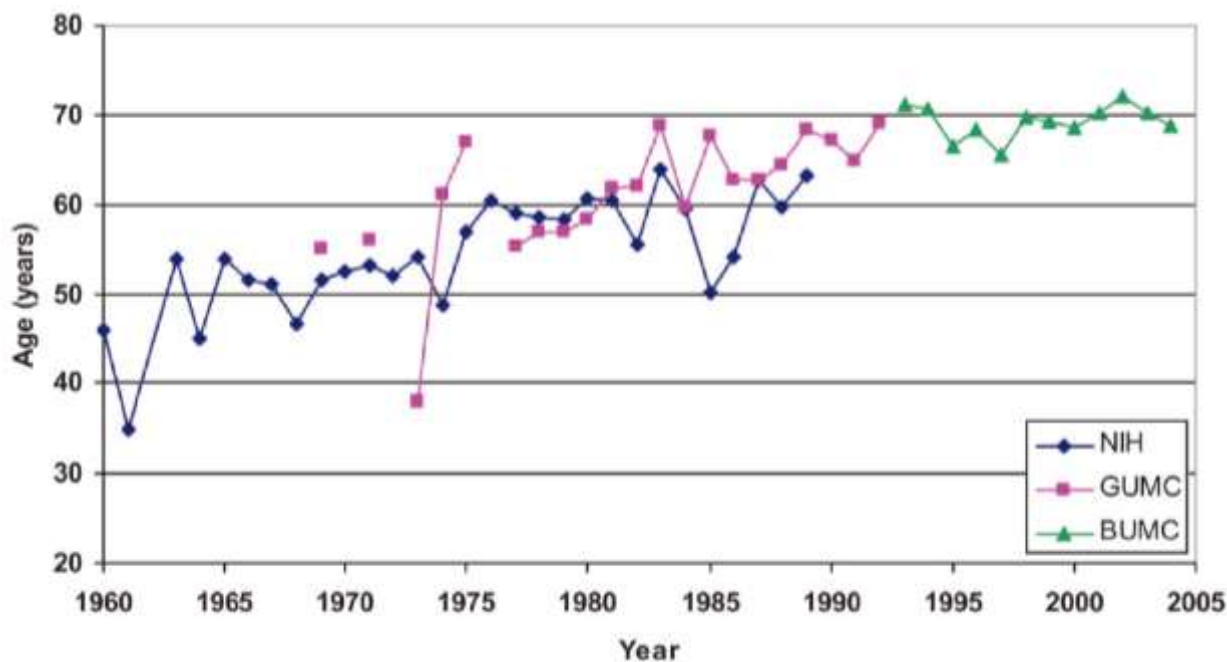
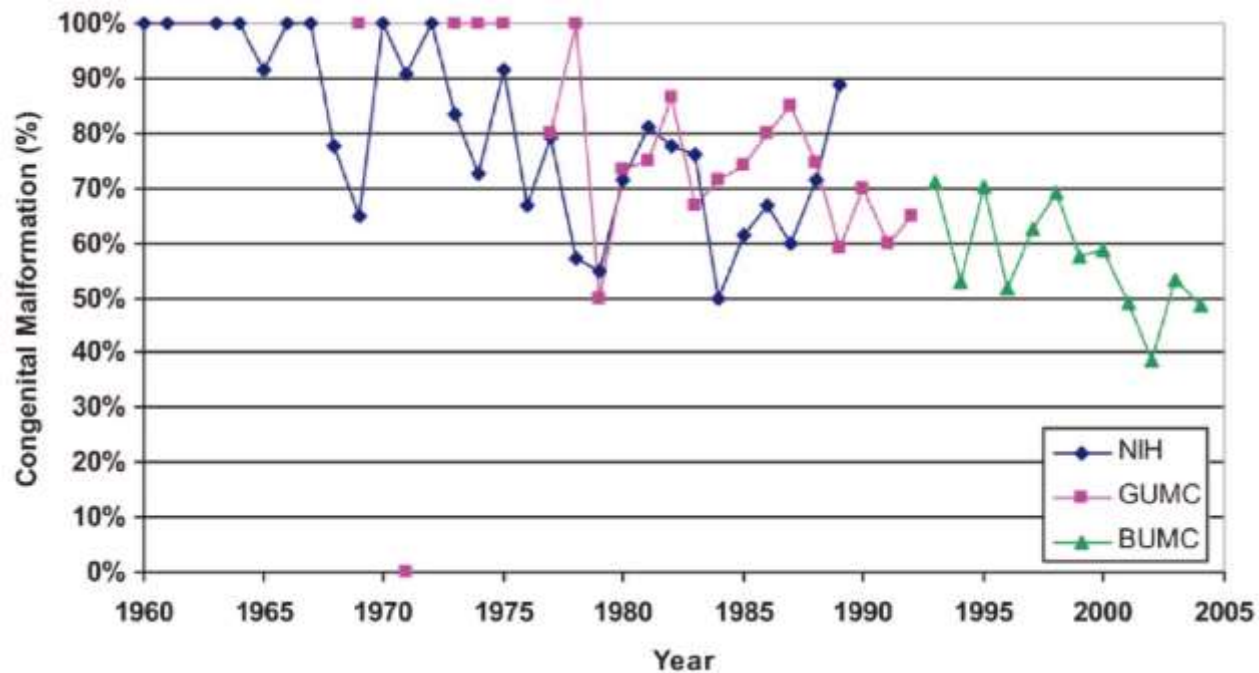
- disease of the aged population

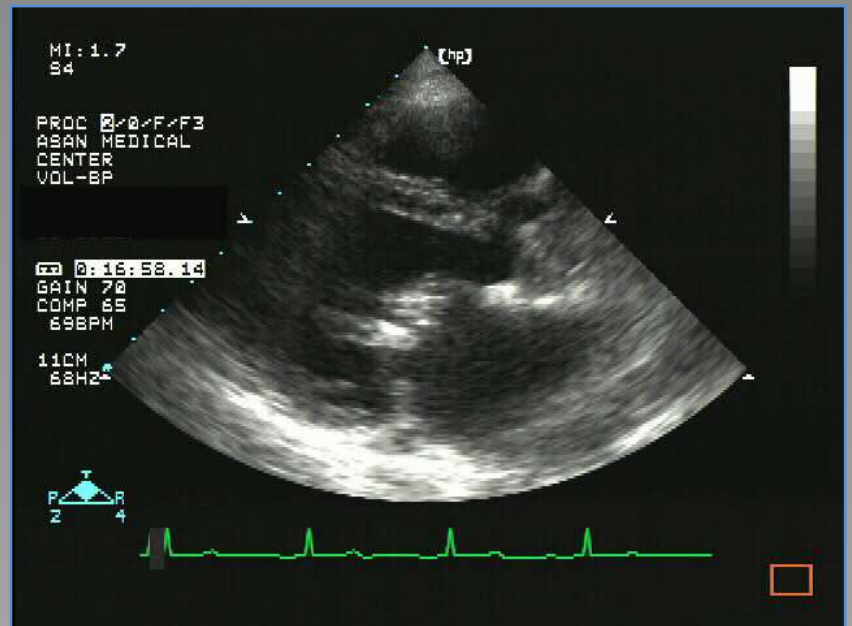
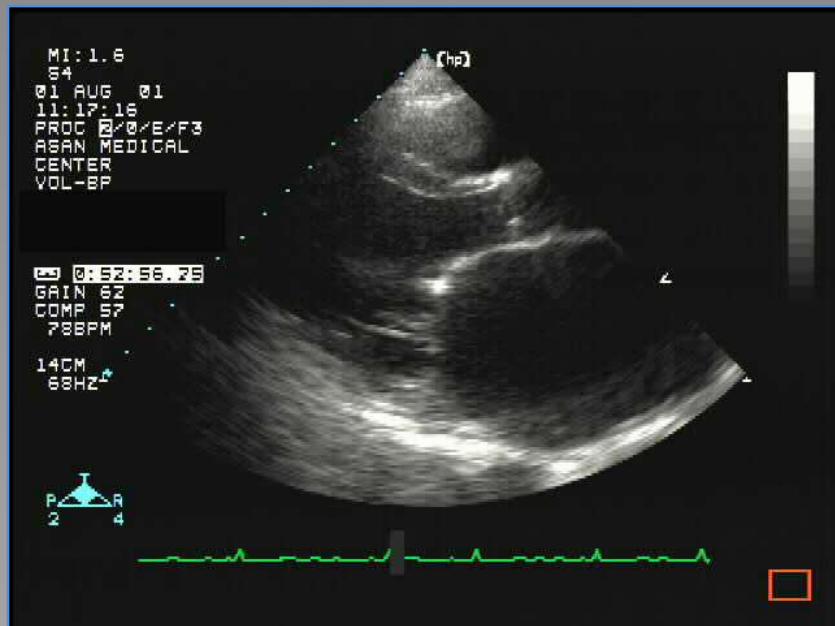
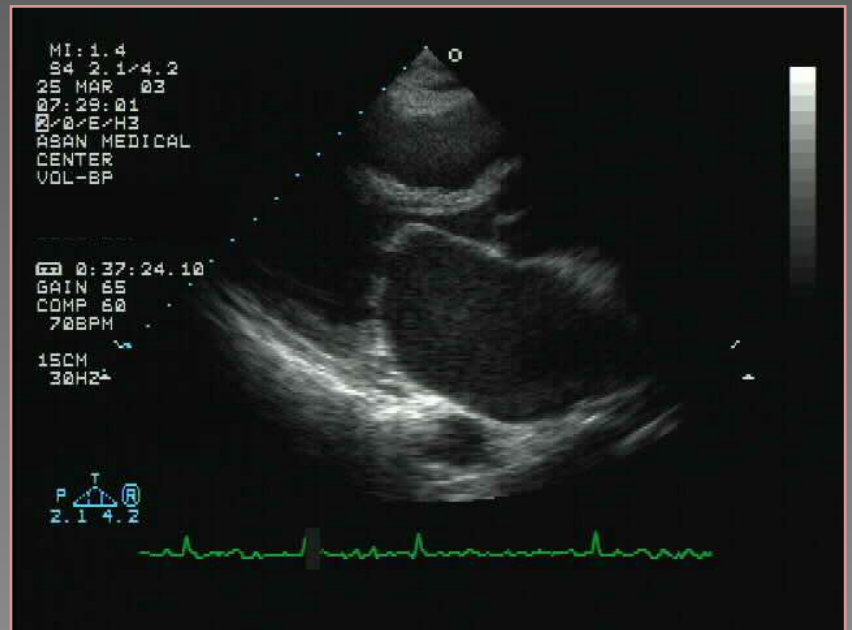
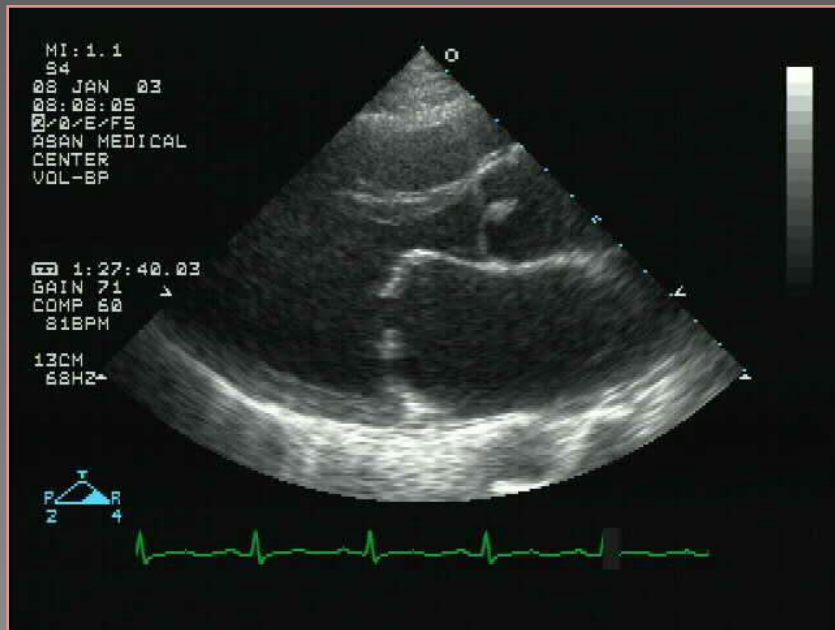




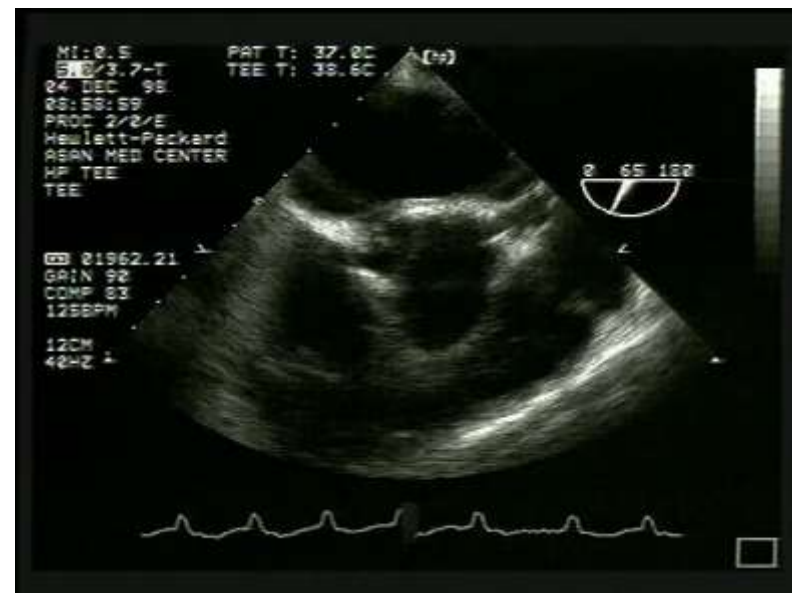
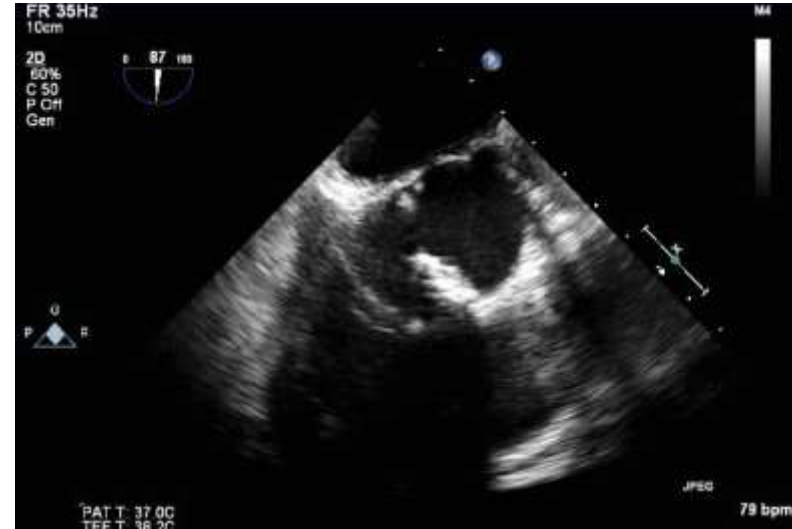
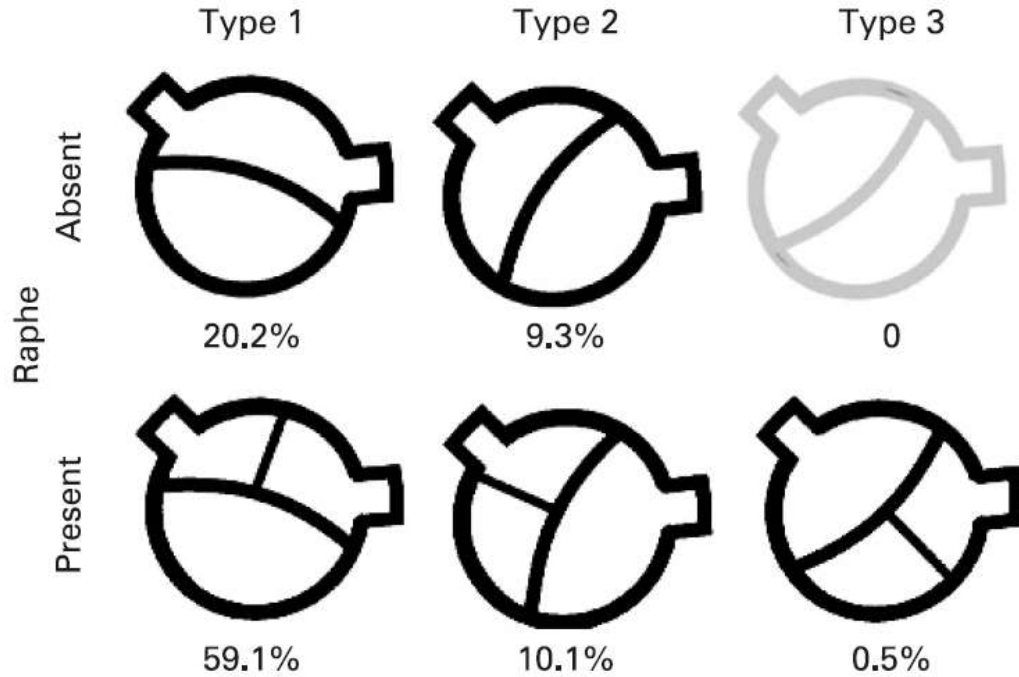
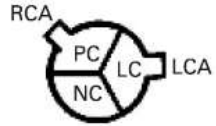


**Temporal Trend  
of AVR for AS:  
1,849 pts >40 yrs**





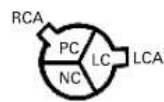
# Bicuspid Aortic Valve



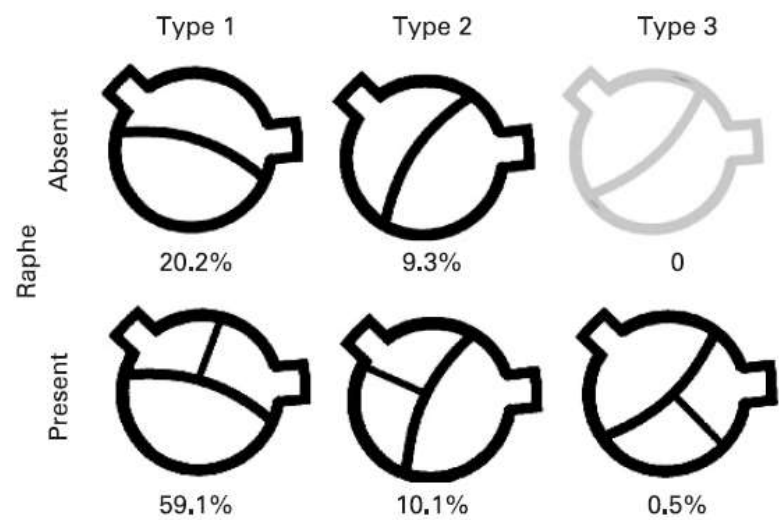
# Bicuspid Phenotype Classification

From 304 surgical specimens

Non-invasive imaging data



main category: number of raphes	0 raphe - Type 0		1 raphe - Type 1			2 raphes - Type 2
	21 (7)	269 (88)				14 (5)
1. subcategory: spatial position of cusps in Type 0 and raphes in Types 1 and 2	lat 13 (4)	ap 7 (2)	L - R 216 (71)	R - N 45 (15)	N - L 8 (3)	L - R / R - N 14 (5)
2. subcategory:						
V F I	6 (2)	1 (0.3)	79 (26)	22 (7)	3 (1)	6 (2)
A U S	7 (2)	5 (2)	119 (39)	15 (5)	3 (1)	6 (2)
L N B (I + S)		1 (0.3)	15 (5)	7 (2)	2 (1)	2 (1)
V C			3 (1)	1 (0.3)		
U L						
A I						
D O						
R N No						

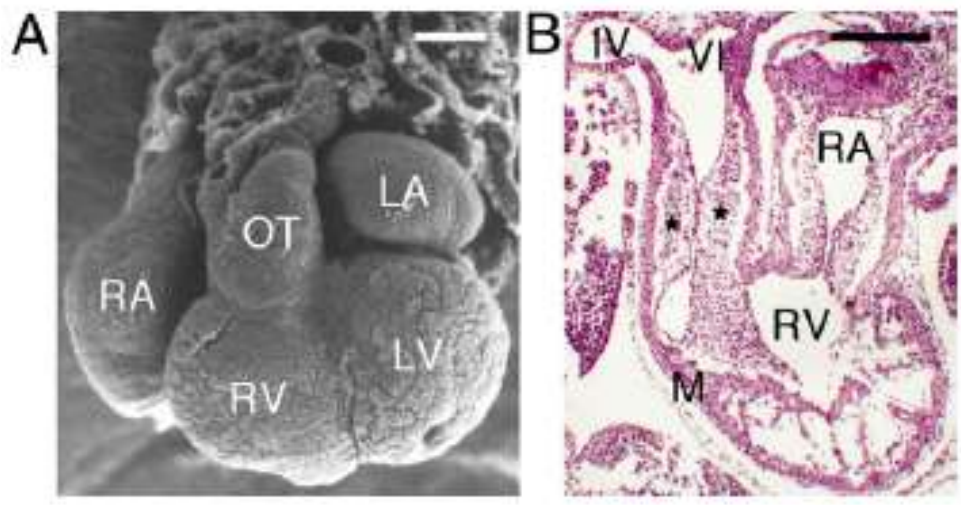
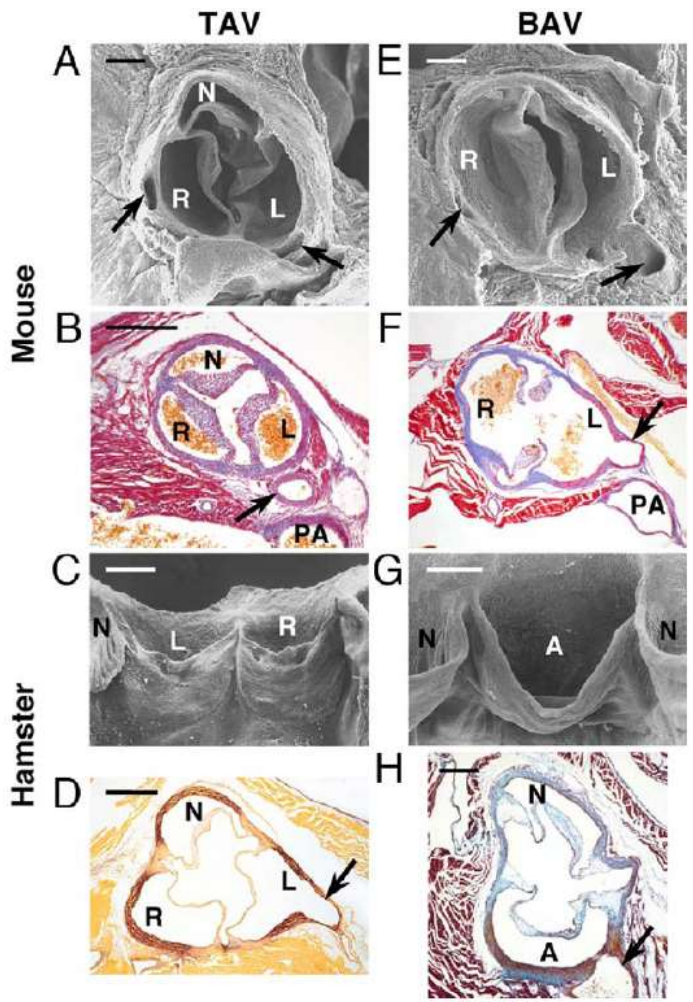


*J Thorac Cardiovasc Surg 2007;133:1226-33*

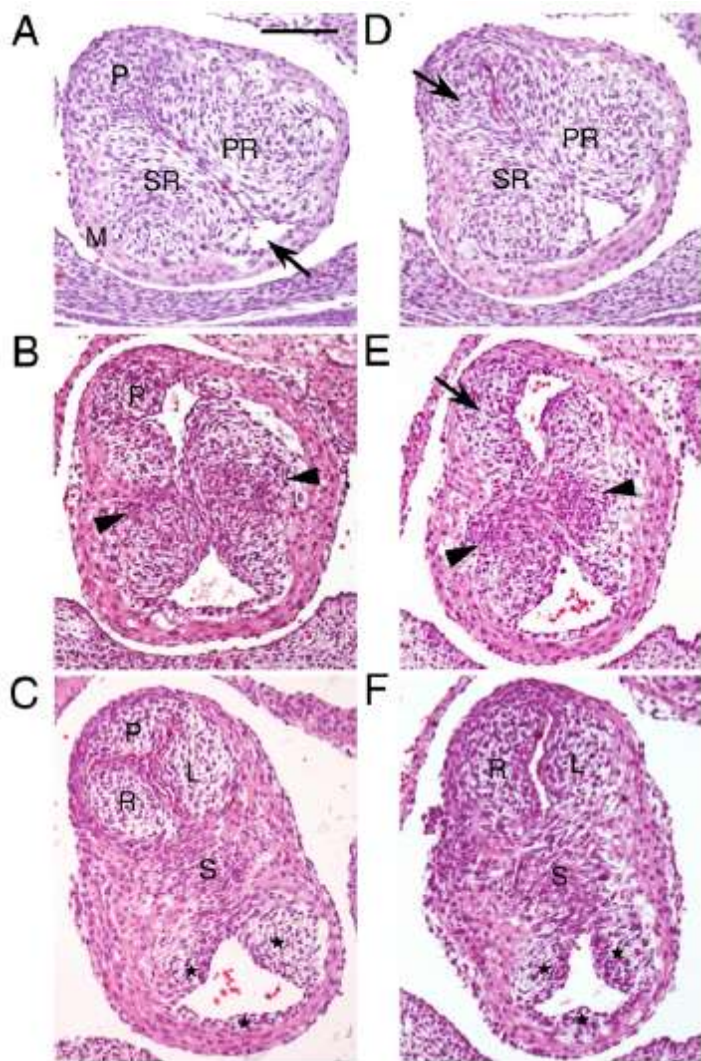
*Heart 2008;94:1634-38*



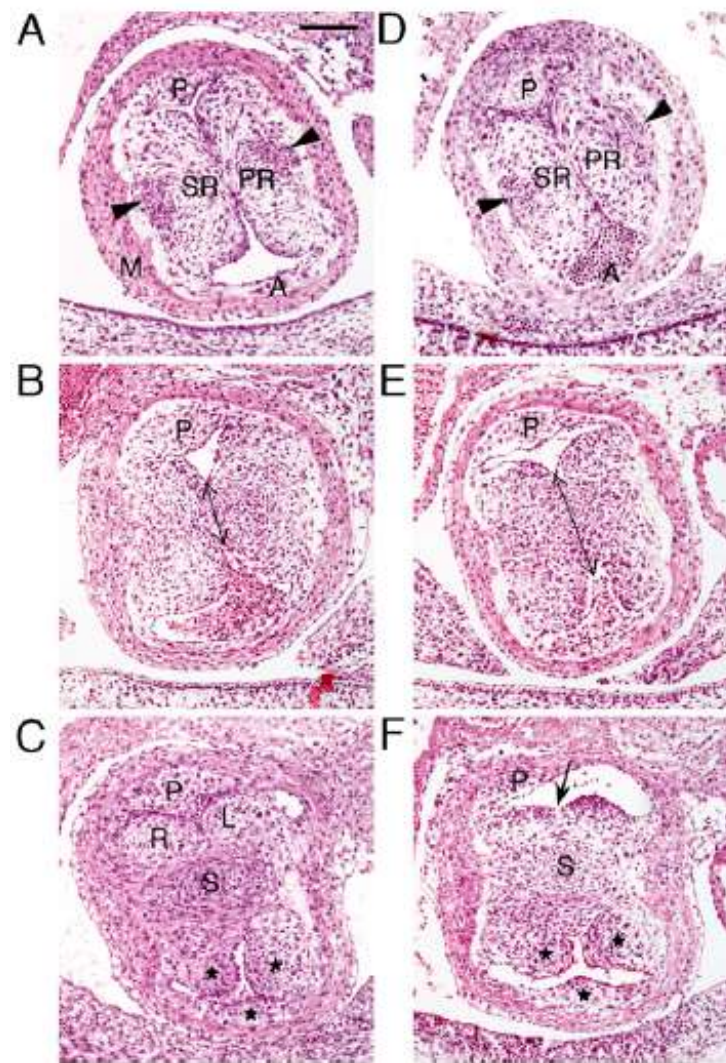
# Bicuspid Aortic Valves With Different Spatial Orientations of the Leaflets Are Distinct Etiological Entities







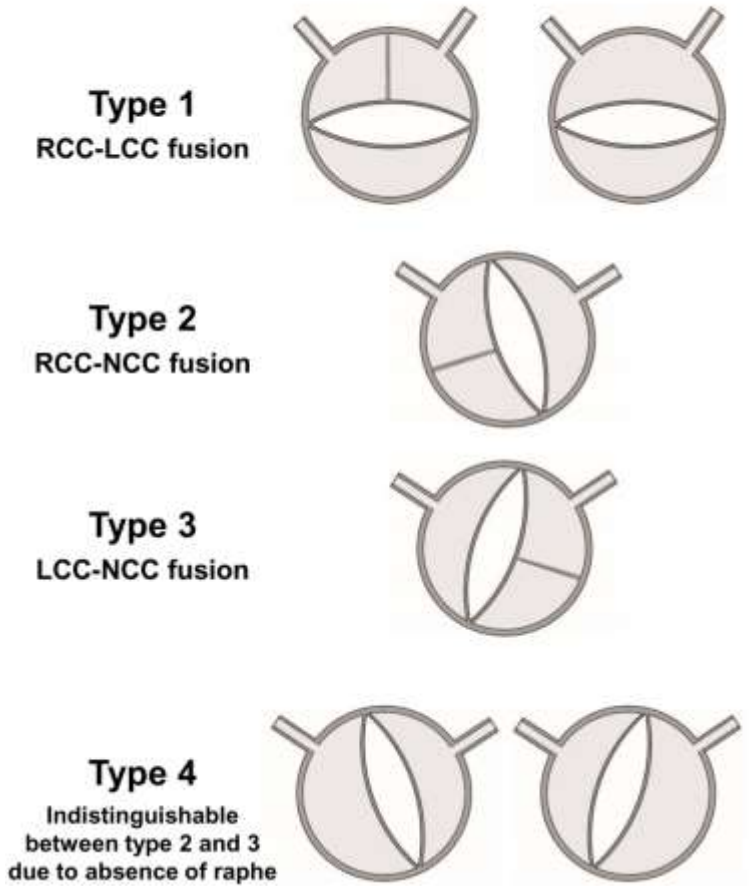
**R-N fusion; defective development of the OT endocardial cushion**



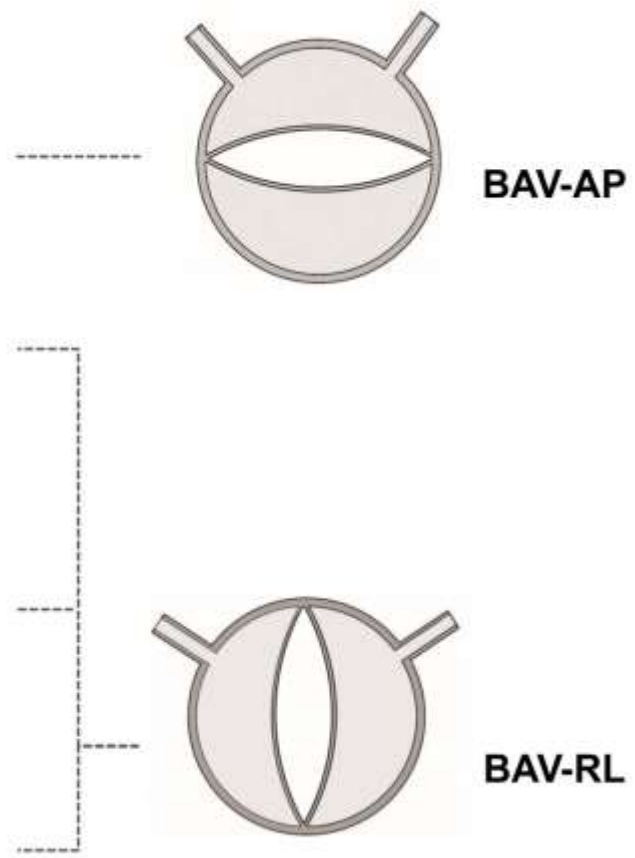
**R-L fusion; normal cardiac outflow tract (OT) septum**

# Bicuspid Phenotype Classification

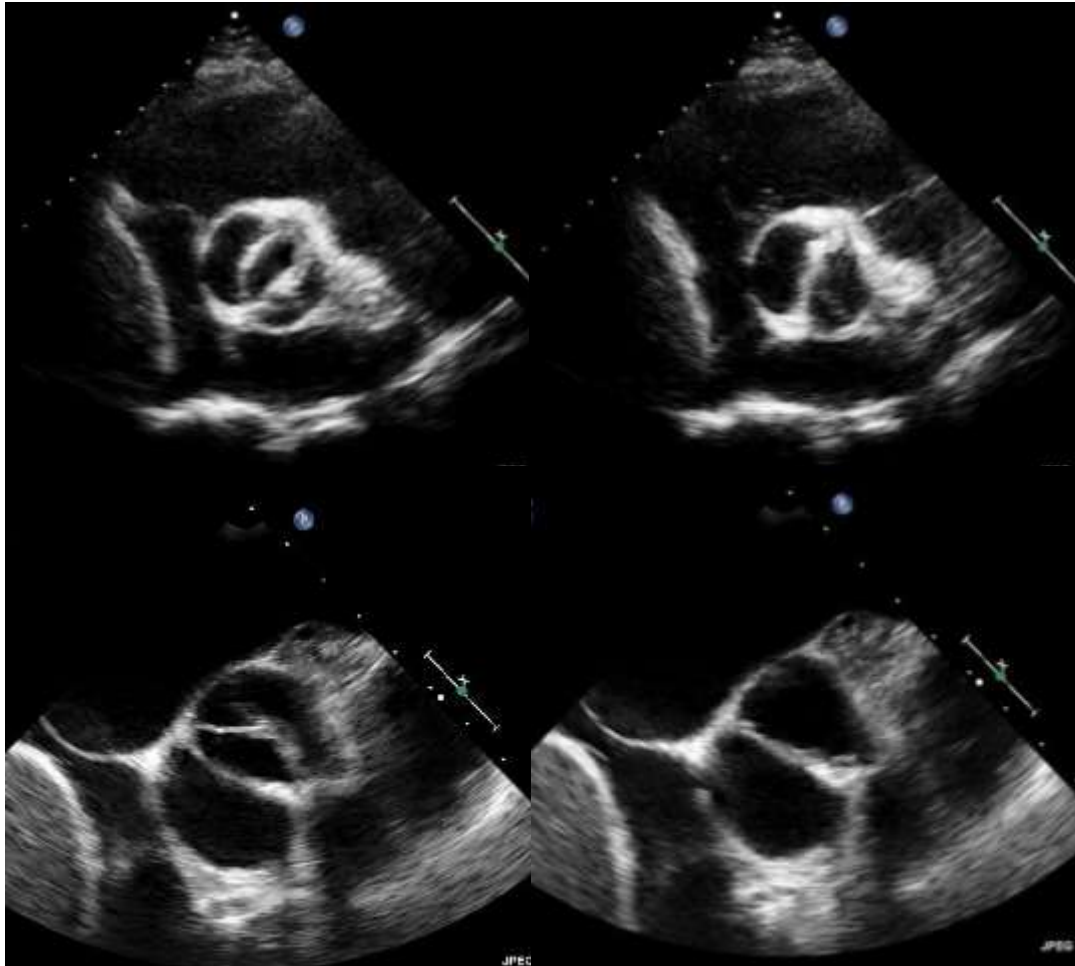
## Conventional classification



## Dichotomous classification

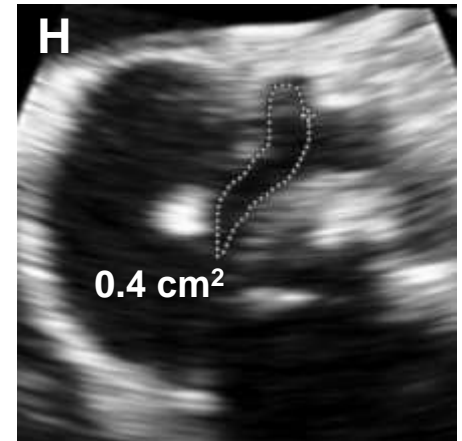
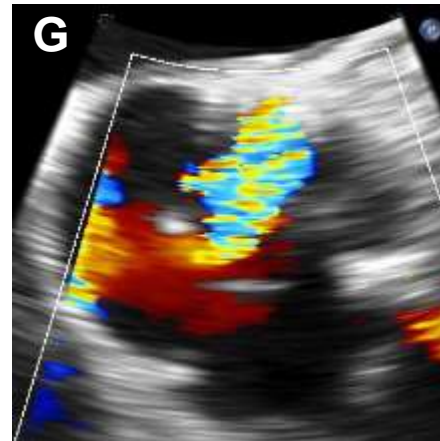
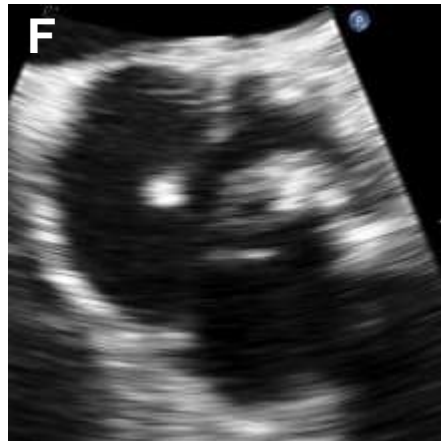
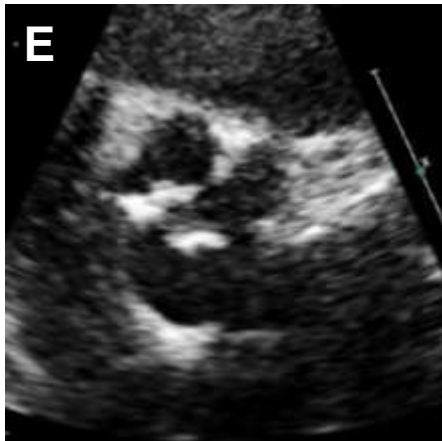
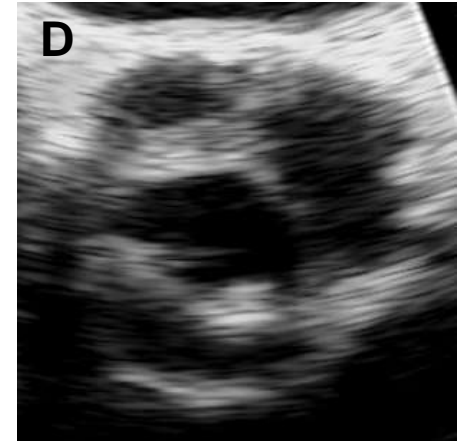
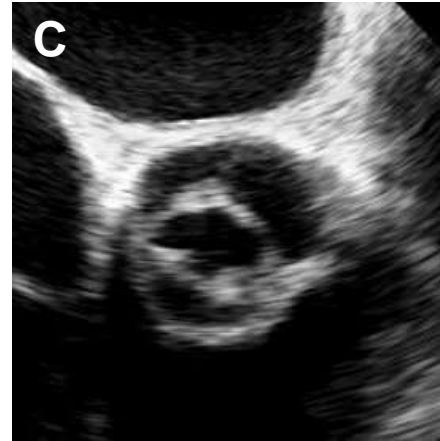
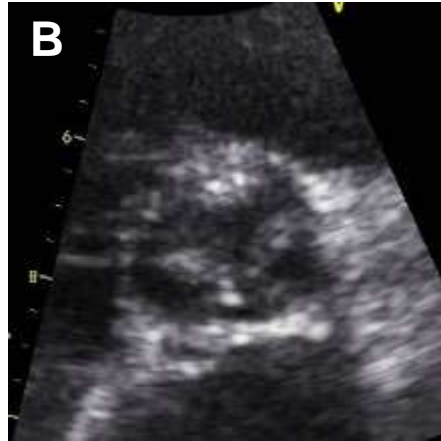
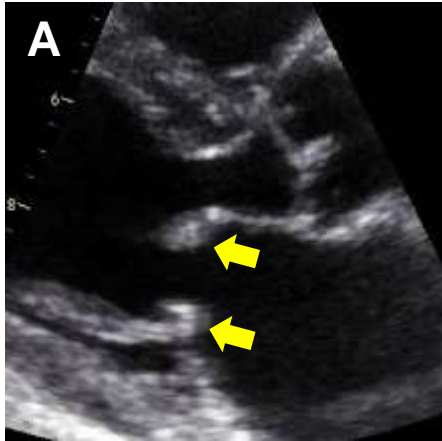


*Echocardiography is a main tool!*

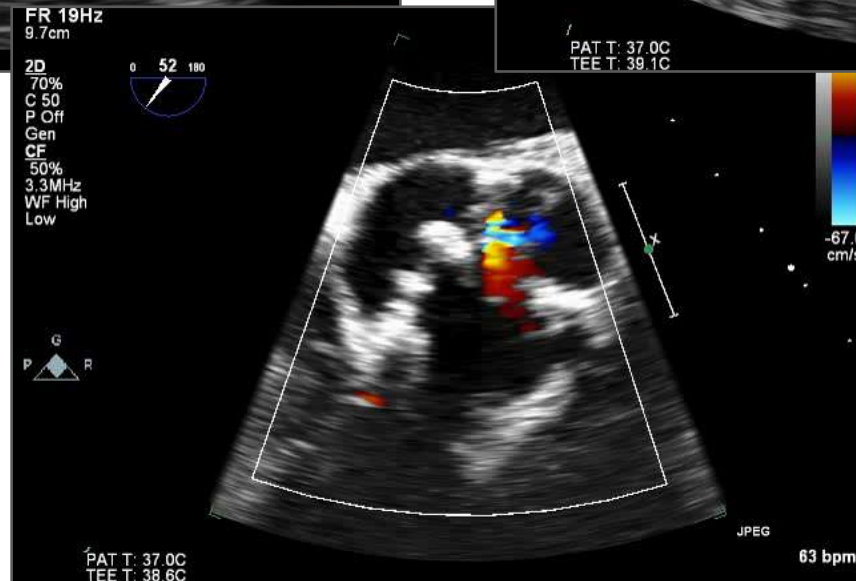
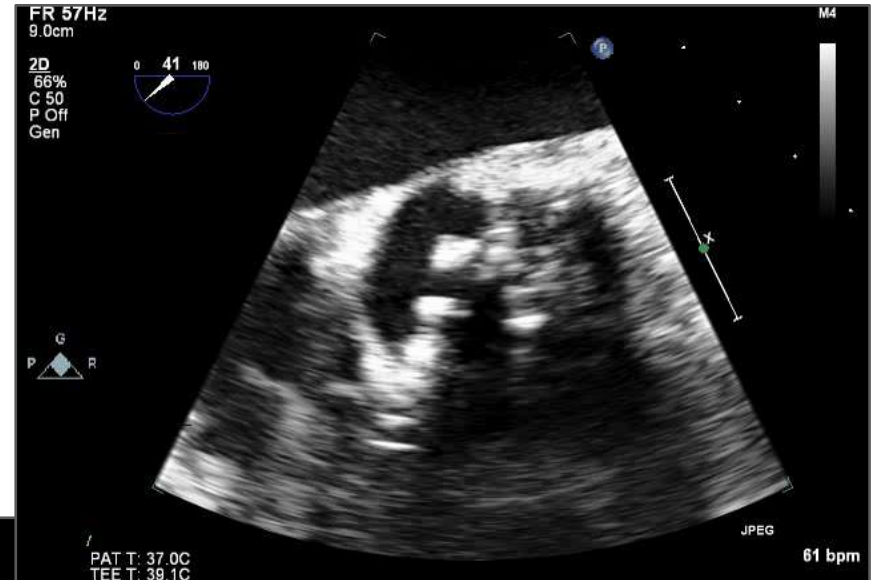




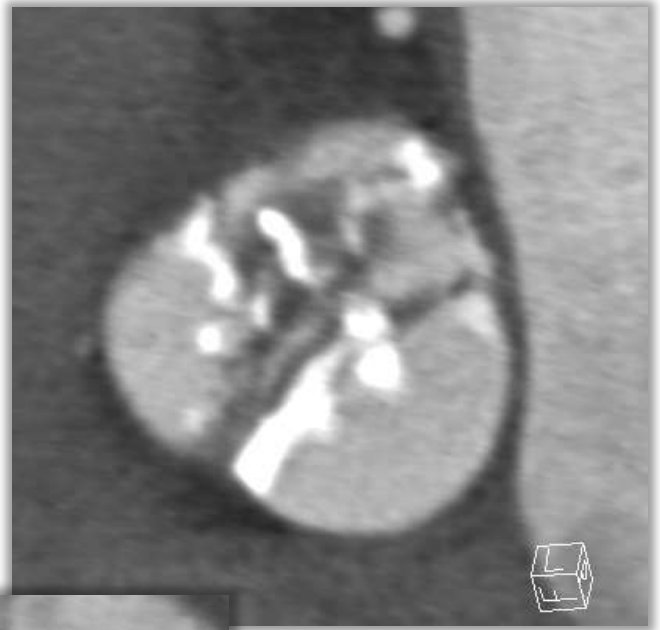
# Any Role of TEE?

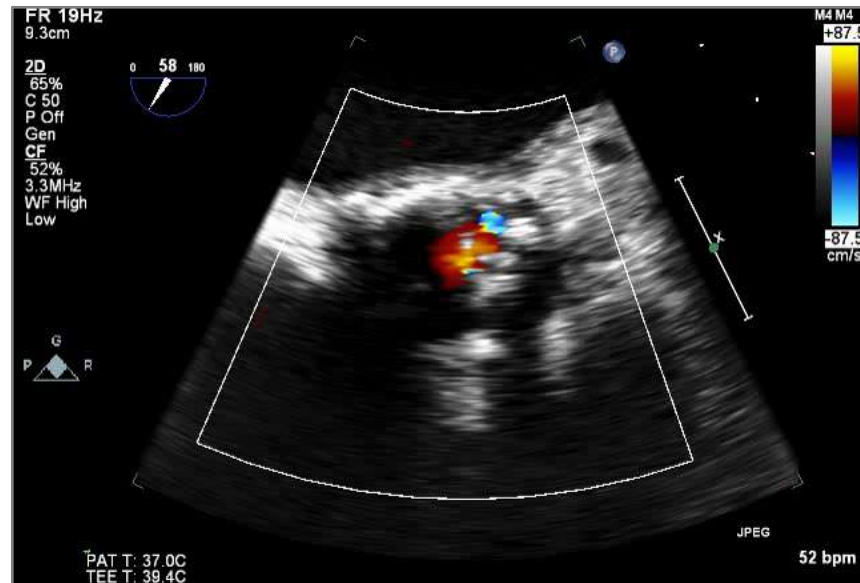
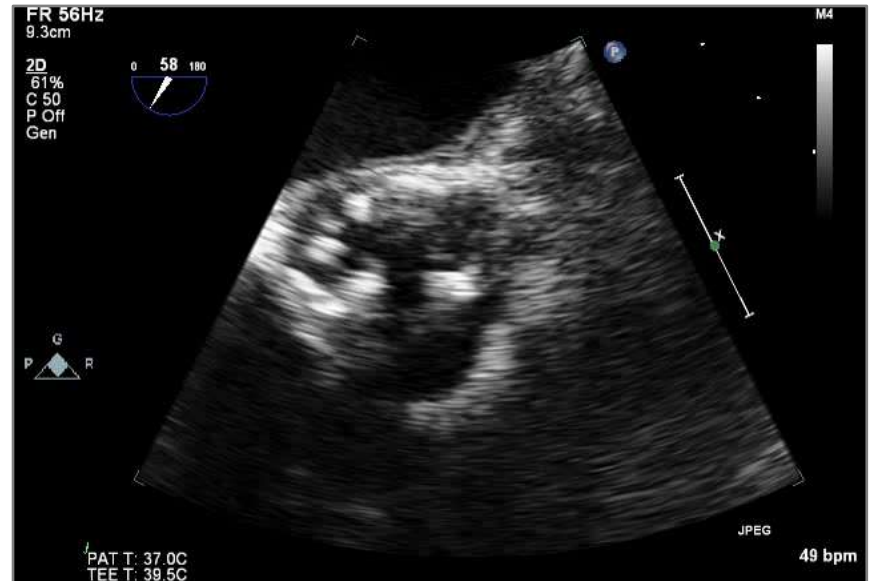


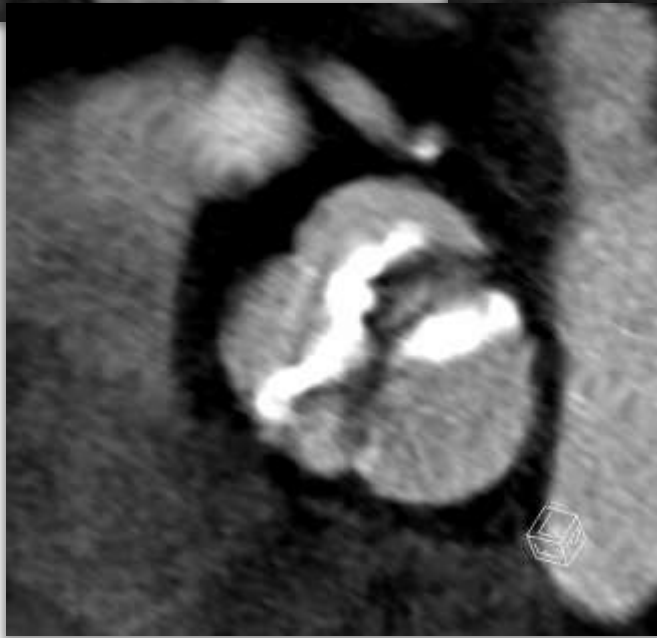
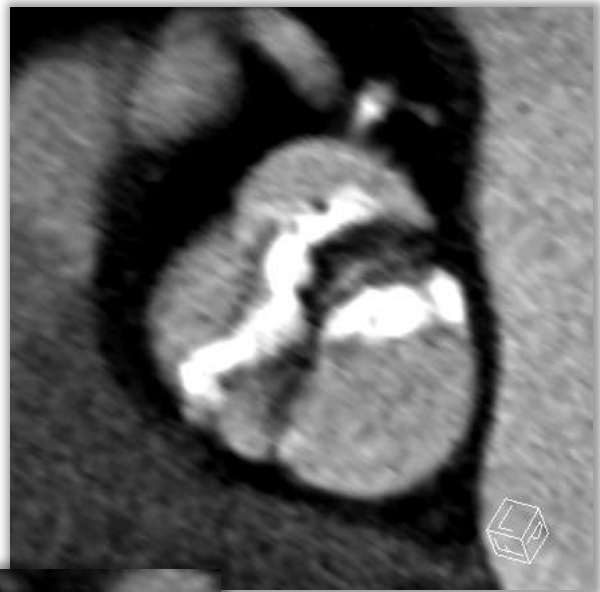
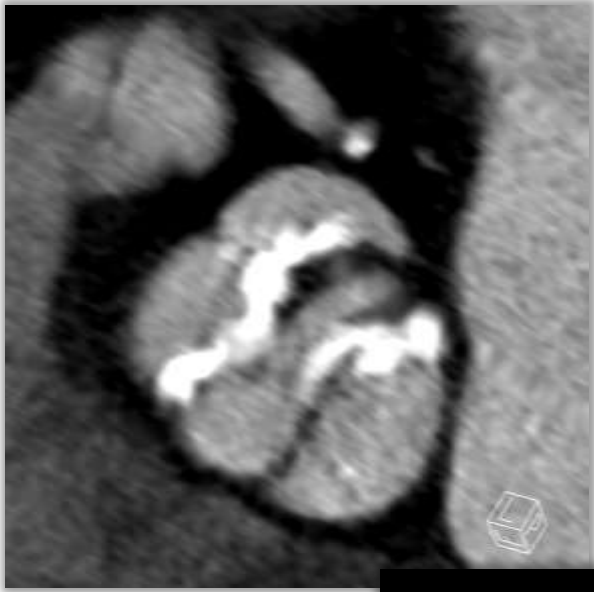
# Any Role of CT?

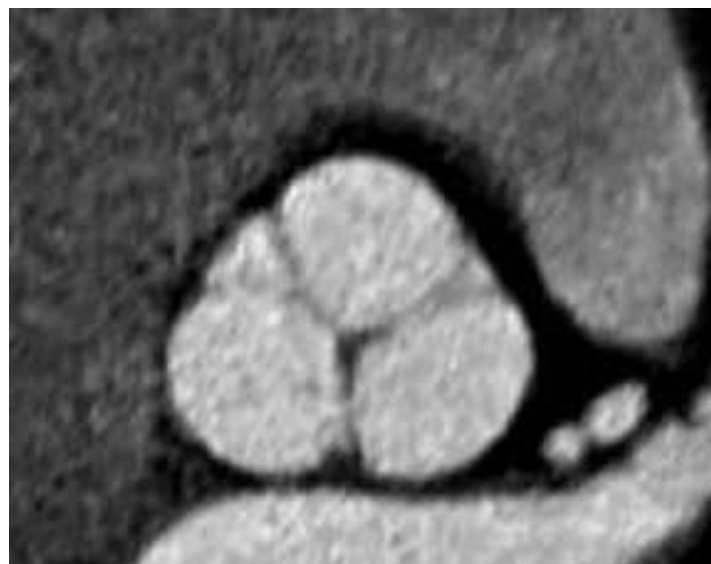
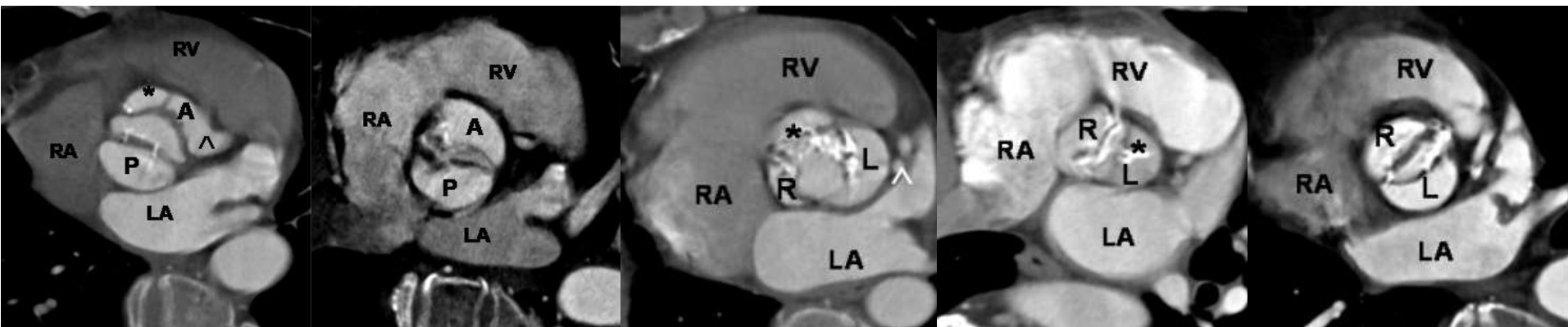






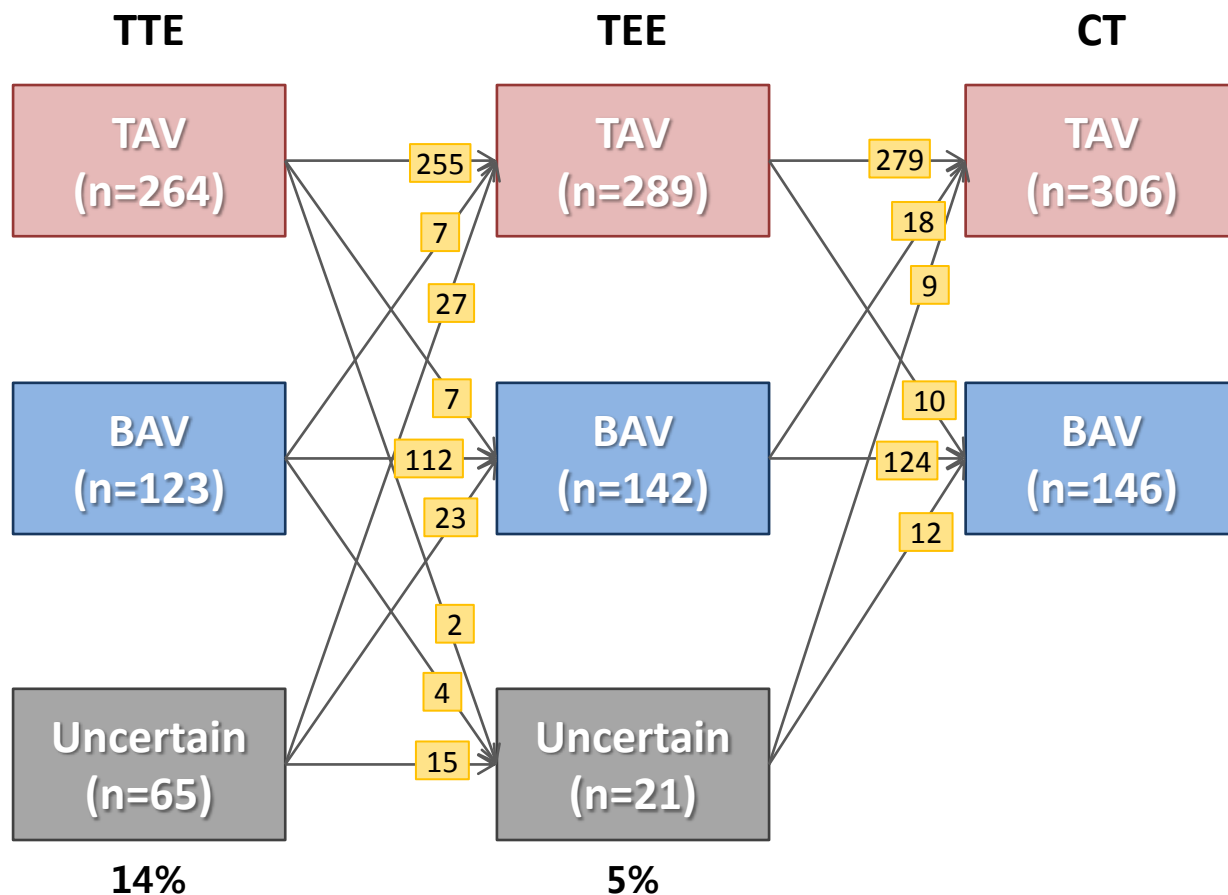








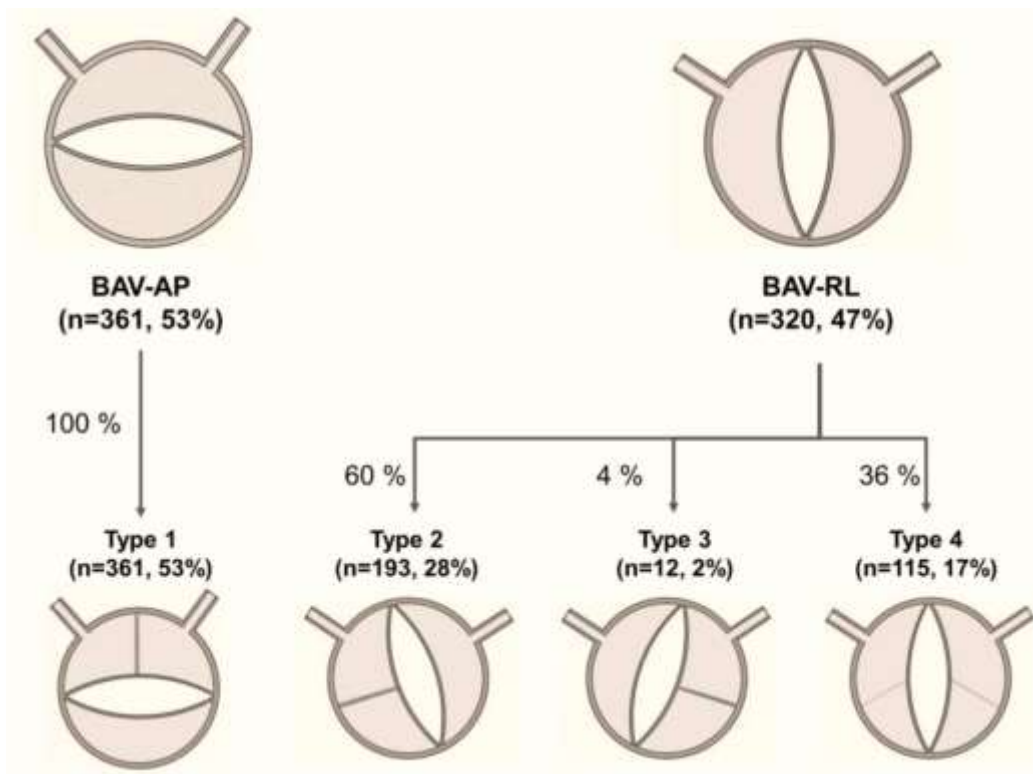
**AMC data: 452 AS patients underwent TTE, TEE and CT ('03 – '14)**  
**- age  $65 \pm 11$  years; Vmax  $4.6 \pm 1.1$  m/s**



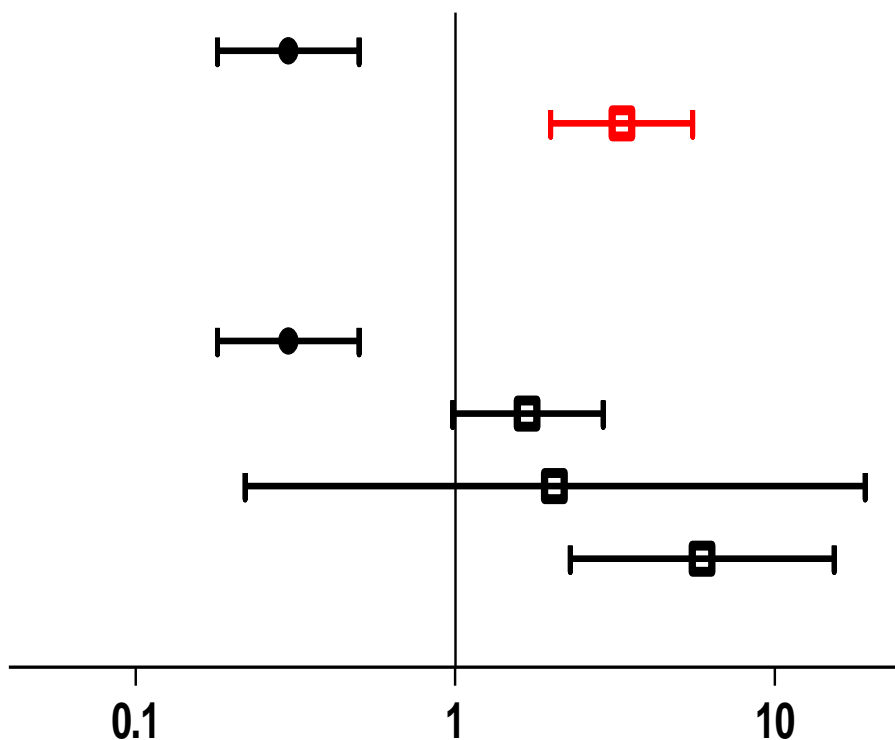
- TTE diagnosis of BAV: sensitivity 83%, specificity 74%
- TEE diagnosis of BAV: sensitivity 91%, specificity 85%

# Bicuspid Phenotype Classification

- 681 BAV patients who underwent aortic valve surgery
- Predominant cause of surgery was AS (n=546, 80%)
- Concomitant aortic surgery in 31% (n=214)
- Phenotype classification using TTE, TEE and CT



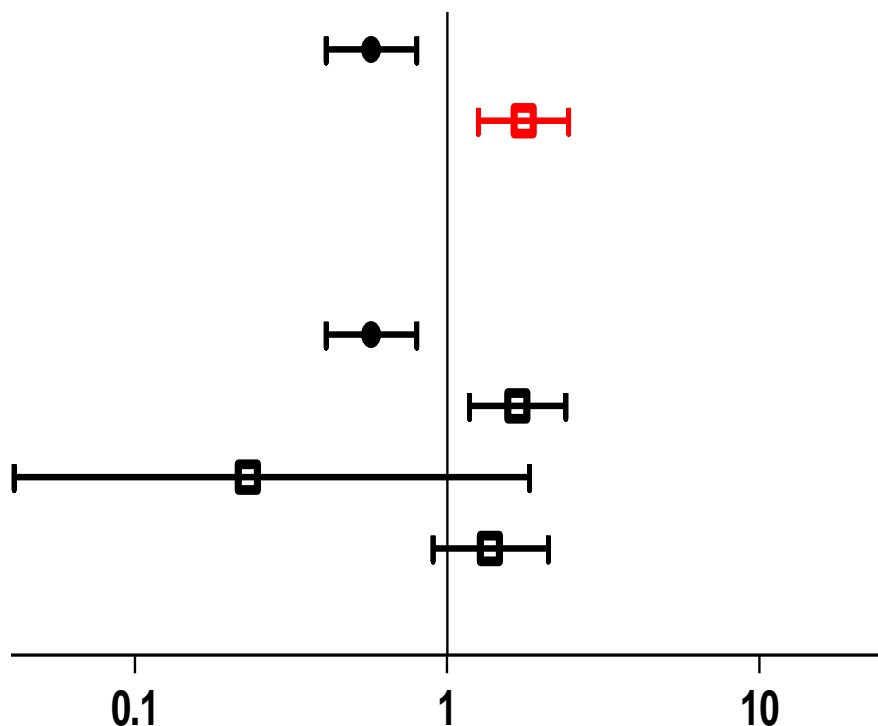
# Bicuspid Phenotype Classification



	Odds ratio	95% C.I.	P-value
<b>New dichotomous classification</b>			
BAV-AP	0.30	0.18 - 0.50	< 0.001
<b>BAV-RL</b>	<b>3.32</b>	<b>1.99 - 5.54</b>	
<b>Conventional classification</b>			
Type 1	0.30	0.18 - 0.50	< 0.001
Type 2	1.68	0.98 - 2.90	0.061
Type 3	2.04	0.22 - 19.17	0.535
Type 4	5.92	2.29 - 15.35	< 0.001

Odds ratio > 1 favors surgery for AS dominant valvulopathy

# Bicuspid Phenotype Classification



Odds ratio > 1 favors concomitant aortic surgery

	Odds ratio	95% C.I.	P-value
<b>New classification</b>			
BAV-AP	0.57	0.41 - 0.80	0.001
BAV-RL	1.76	1.26 - 2.45	
<b>Conventional classification</b>			
Type 1	0.57	0.41 - 0.80	0.001
Type 2	1.68	1.18 - 2.40	0.004
Type 3	0.23	0.03 - 1.84	0.167
Type 4	1.37	0.90 - 2.11	0.146

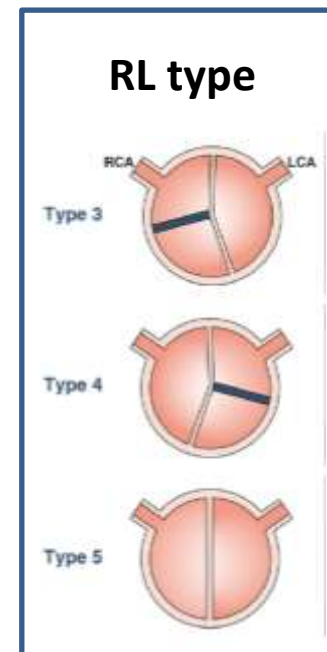
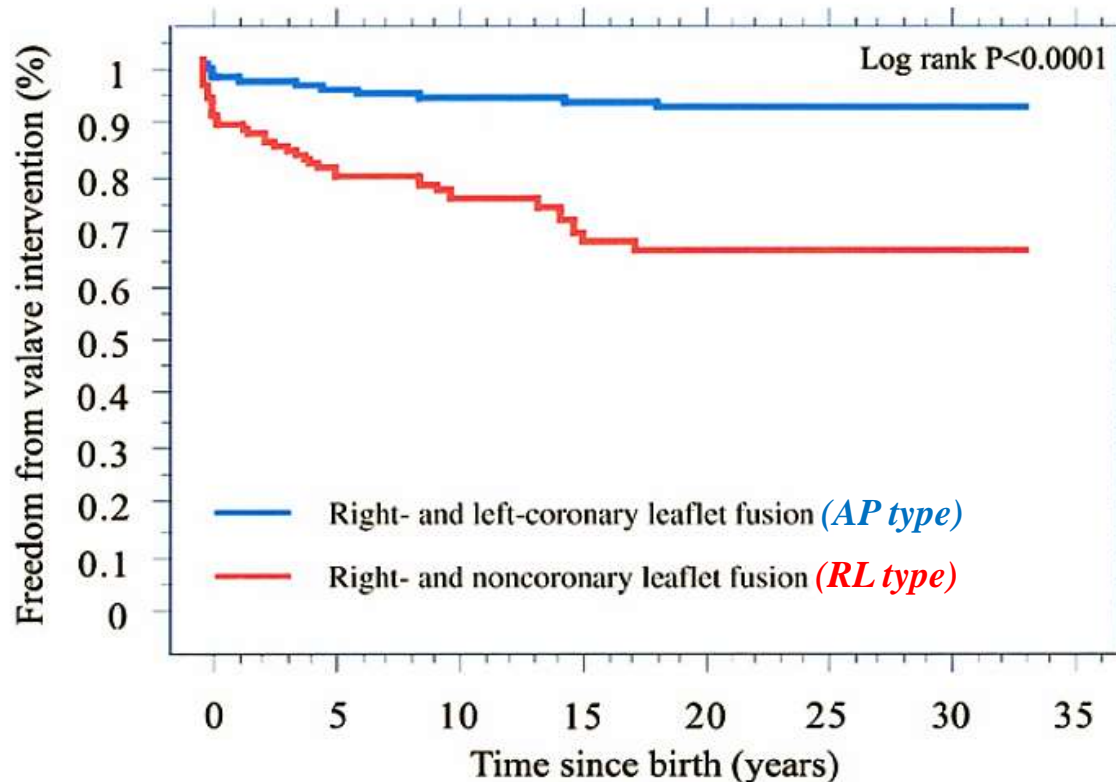
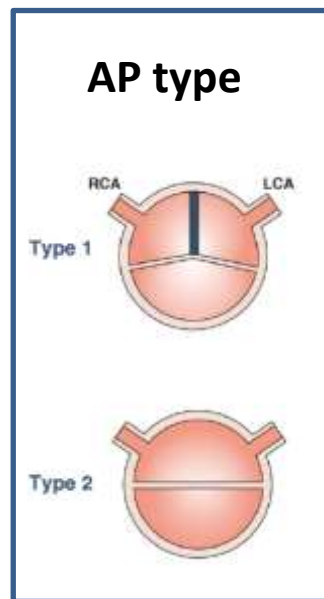


# Bicuspid Phenotype Classification: Performance using TTE data only

Cardiologist	Feasibility		Accuracy	
	Conventional	Dichotomous	Conventional	Dichotomous
A	90 %	97 %	73 % (66/90)	91 % (88/97)
B	97 %	99 %	70 % (68/97)	86 % (85/99)
C	95 %	97 %	67 % (65/95)	86 % (83/97)
D	94 %	95 %	67 % (63/94)	87 % (83/95)
<b>Overall</b>	<b>94 %</b>	<b>97 %</b>	<b>70 % (262/376)</b>	<b>87 % (339/388)</b>

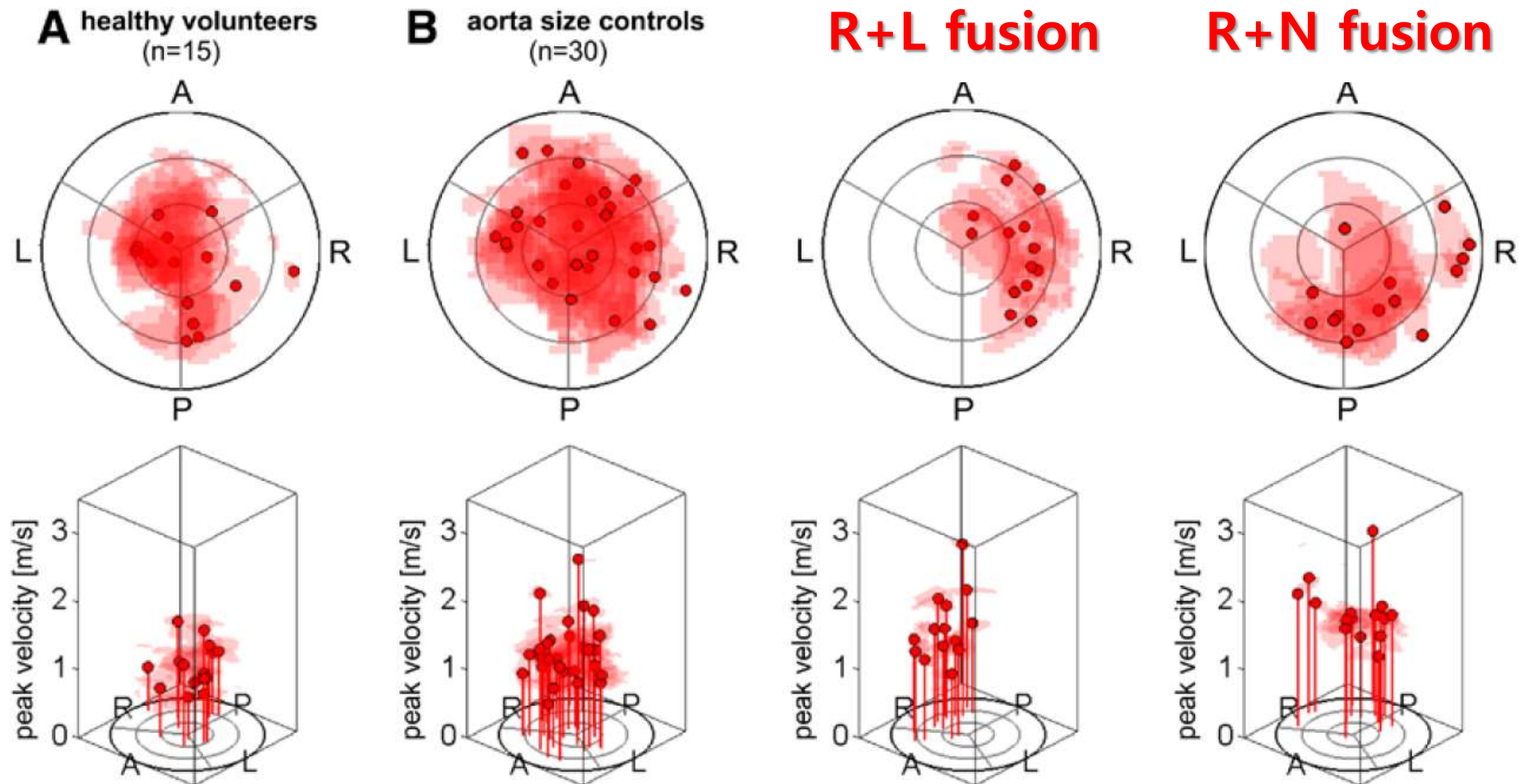
Cardiologist A and B had clinical experience in echo over 5 years, whereas Cardiologist C and D less than 2 years.

# BAV phenotype and valvular intervention in the young

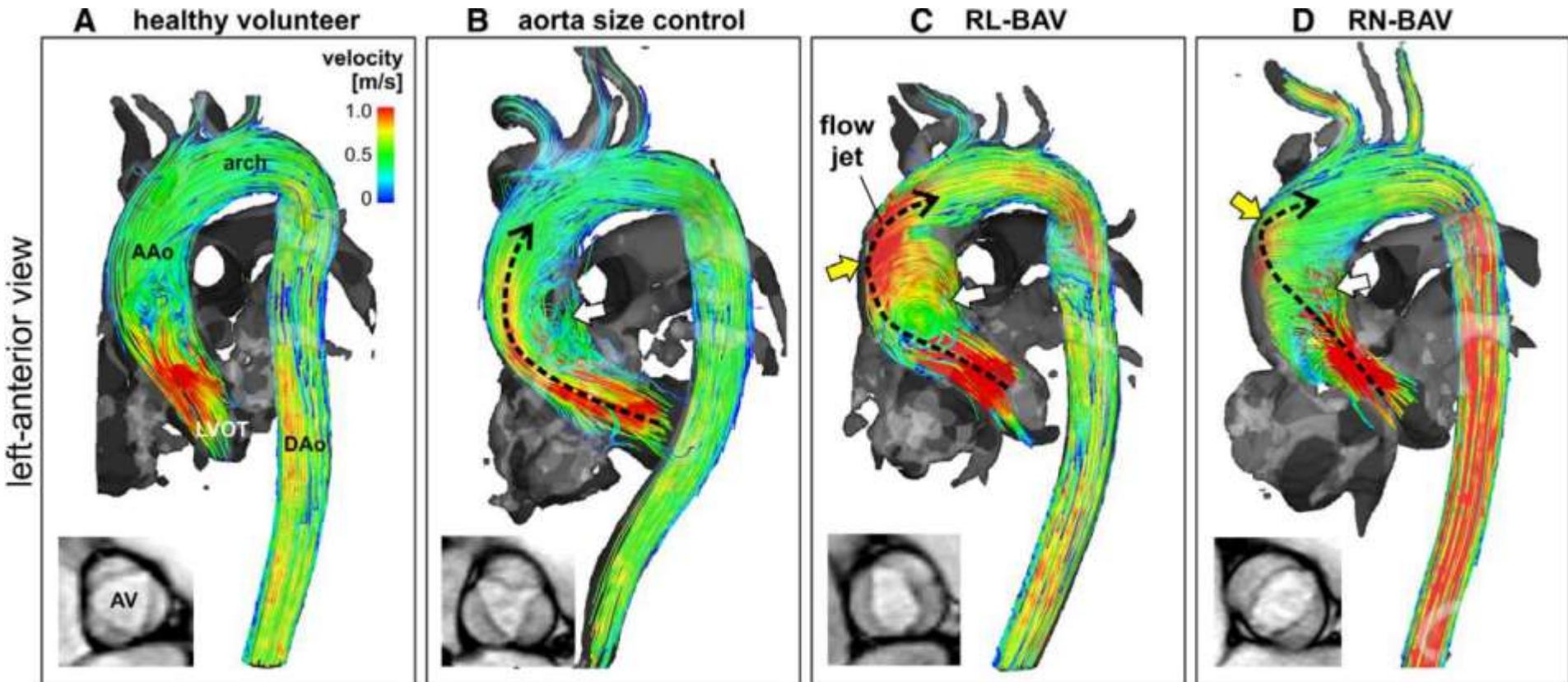


- Age 16.1 years (5.6 – 34.4): Children hospital, Boston

# Patterns of hemodynamic stress



# Phenotypes and flow dynamics



**R+L fusion**

**R+N fusion**



# Knowledge Gap & Bias

- 1. BAV phenotype prevalence**
- 2. BAV phenotype vs. patterns of valvular dysfunction**
- 3. BAV phenotype vs. patterns of aortopathy**
- 4. BAV phenotype vs. long-term outcome**
  - prediction or risk stratification?
- 5. Pathogenesis of aortopathy**
  - inherent fragility vs. hemodynamic burden

# **Bicuspid Aortic Valve**

## **Identifying Knowledge Gaps and Rising to the Challenge**

### **From the International Bicuspid Aortic Valve Consortium (BAVCon)**

Hector I. Michelena, MD; Siddharth K. Prakash, MD, PhD;  
Alessandro Della Corte, MD, PhD; Malenka M. Bissell, MD, BM, MRCPCH;  
Nandan Anavekar, MB, BCh; Patrick Mathieu, MD; Yohan Bossé, PhD;  
Giuseppe Limongelli, MD; Eduardo Bossone, MD; D.Woodrow Benson, MD, PhD;  
Patrizio Lancellotti, MD, PhD; Eric M. Isselbacher, MD; Maurice Enriquez-Sarano, MD;  
Thoralf M. Sundt III, MD; Philippe Pibarot, DVM, PhD; Artur Evangelista, MD, PhD;  
Dianna M. Milewicz, MD, PhD; Simon C. Body, MBChB, MPH; on behalf of the  
BAVCon Investigators\*

# **Korean BAV Registry (KoBAV)**

# Registry data

## Contemporary Reviews in Cardiovascular Medicine

### Bicuspid Aortic Valve

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BAVCon Investigators\*

#### International Bicuspid Aortic Valve Consortium (BAVCon)

**This study is currently recruiting participants.** (see [Contacts and Locations](#))

*Verified November 2013 by Brigham and Women's Hospital*

**Sponsor:**

Brigham and Women's Hospital

**Information provided by (Responsible Party):**

Simon Body, Brigham and Women's Hospital

**ClinicalTrials.gov Identifier:**

NCT01980797

First received: November 5, 2013

Last updated: November 8, 2013

Last verified: November 2013

[History of Changes](#)

[Full Text View](#)

[Tabular View](#)

[No Study Results Posted](#)

[Disclaimer](#)

[How to Read a Study Record](#)

#### Purpose

Bicuspid aortic valve (BAV) disease is the most frequent congenital cardiac malformation, occurring in 0.5-1.2% of the US population. In young adults, it is generally a benign abnormality; but in older adults it is associated with thoracic aortic aneurysm or dissection in 20-30% of those with