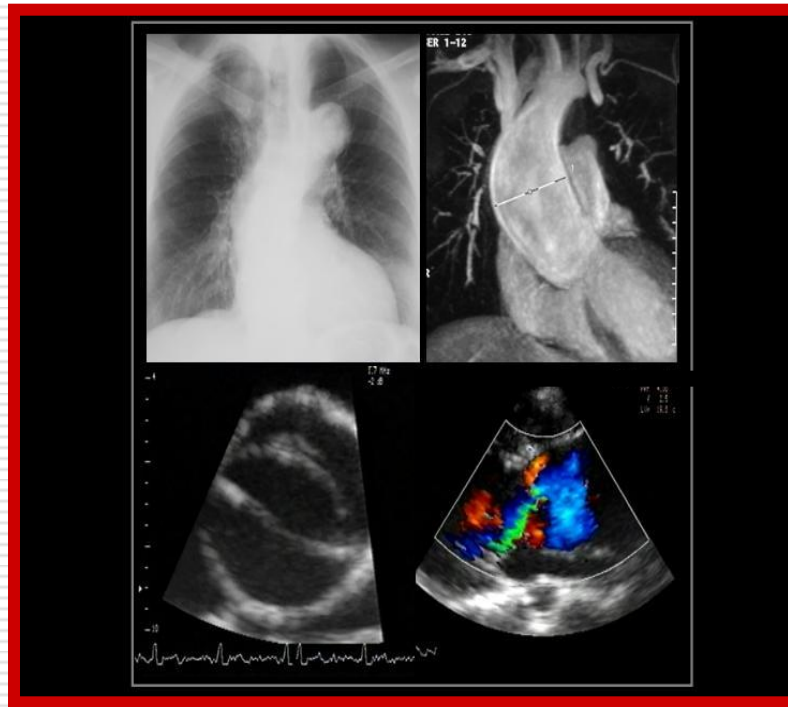


Bicuspid Aortic Valve Recognition:

Is this information useful in patients with aortic dilatation?



Bicuspid Aortic Valve

BAV the most common congenital heart defect (1%).

Familial occurrence noted in 9% of first-degree relatives.
Autosomal dominant pattern with incomplete penetrance.

BAV may coexist with other congenital CV defects:

Co Ao	50%
Turner S	30%
Supravalvular AS	30%
Valvula sinus aneurysm	20%
Ductus	
VSD	30%
Sones complex	60%



Aortic Dimensions in Patients With Bicuspid Aortic Valve Without Significant Valve Dysfunction

Moreno Cecconi, MD, Marcello Manfrin, MD, Alessandra Moraca, MD, Raffaele Zanolli, PhD, Pier Luigi Colonna, MD, Maria Grazia Bettuzzi, MD, Stefano Moretti, MD, Domenico Gabrielli, MD, and Gian Piero Perna, MD

(Am J Cardiol 2005;95:292-294)

TABLE 2 Aortic Dimensions at Different Levels in Patients With BAVs and Controls

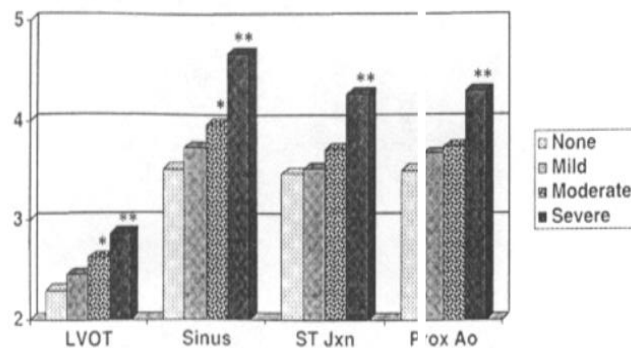
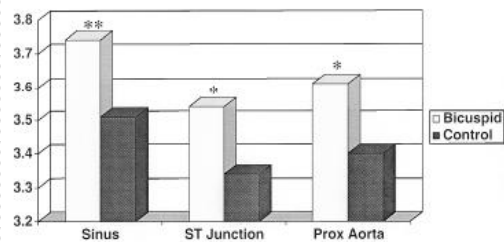
Variable	Patients With BAVs (n = 162)	Controls (n = 162)
Annulus (mm/m ²)	15.4 ± 4.7	14.4 ± 4
Sinuses of Valsalva (mm/m ²)	22 ± 6.5*	19.5 ± 5.1
Sinotubular junction (mm/m ²)	19.5 ± 6.3†	16.7 ± 4.1
Ascending aorta (mm/m ²)	23.7 ± 7.3†	18.6 ± 4.7
Aortic arch (mm/m ²)	15.1 ± 4.7	14.4 ± 3.8
Descending aorta (mm/m ²)	12.4 ± 3.2	12.3 ± 2.9
Abdominal aorta (mm/m ²)	10.2 ± 3	10.5 ± 2.5

Values are expressed as mean ± SD.

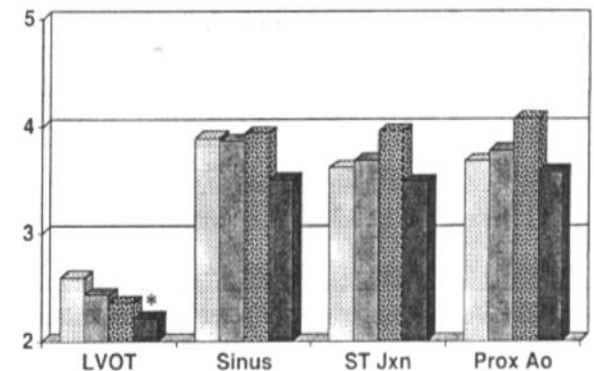
*p < 0.01; †p < 0.001.

Aortic Dilatation in Bicuspid Valve Coexistent Valvular Lesions

- Aortic dimensions larger in BAV than in comparable TAV.
- Intrinsic pathology responsible for aortic dilatation beyond that predicted by haemodynamic factors in BAV



AR



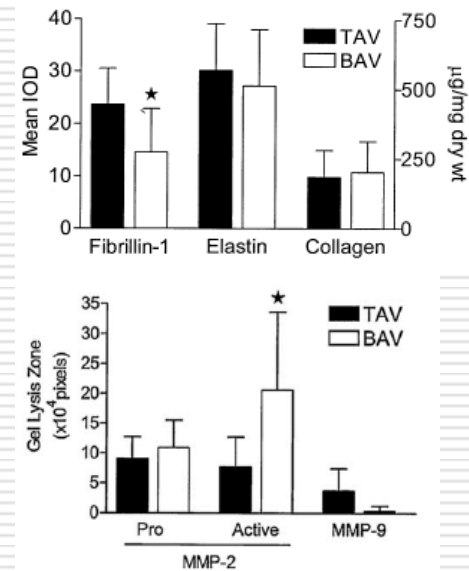
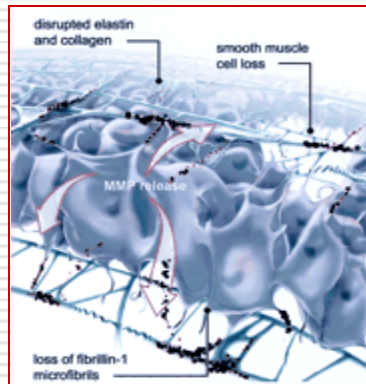
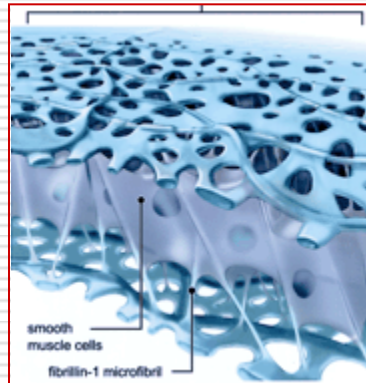
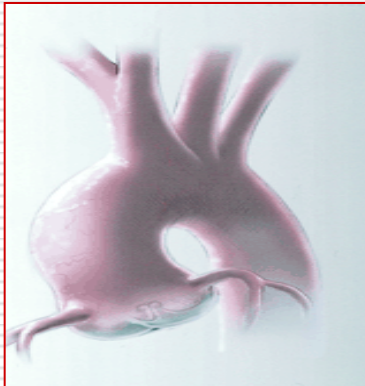
AS

Pathophysiology of Aortic Dilatation in Marfan and BAV

- **Mechanisms of aortic dilatation**
 - Congenital aortic fragility from genetic predisposition
 - Mechanical stress
 - **Aortic media affected by damage and repair events**
 - Excessive injury: Valve dysfunction, Hypertension, Age
 - Impaired repair: Connective tissue disorders
-

Vascular matrix remodeling in patients with bicuspid aortic valve malformations: Implications for aortic dilatation

Fedak, J Thorac Cardiovasc Surg 2003;126



- Deficient microfibrillar elements :
 - Smooth muscle cell detachment
 - MMP release
 - Matrix disruption
 - Cell death
 - Loss structural support and elasticity

Spatial Patterns of Matrix Protein Expression in Dilated Ascending Aorta with Aortic Regurgitation: Congenital Bicuspid Valve versus Marfan's Syndrome

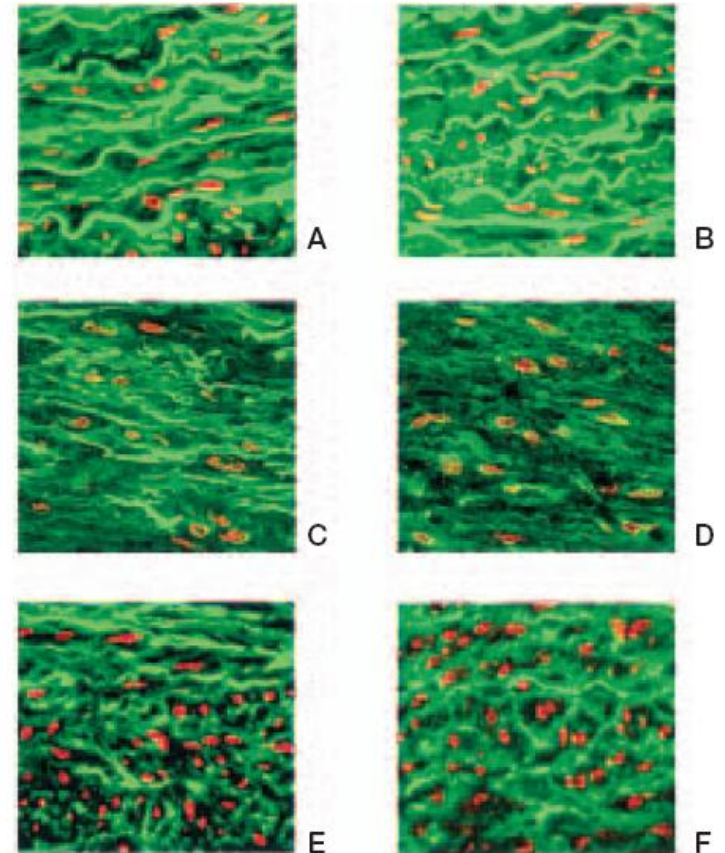
Alessandro Della Corte¹, Luca S. De Santo¹, Stefania Montagnani², Cesare Quarto¹, Gianpaolo Romano¹, Cristiano Amarelli¹, Michelangelo Scardone¹, Marisa De Feo¹, Maurizio Cotrufo¹, Giuseppe Caianiello¹

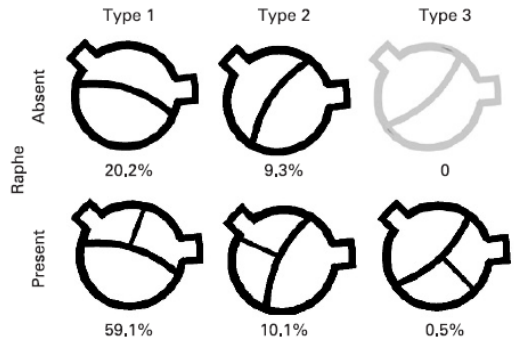
¹Department of Cardiothoracic and Respiratory Sciences, Second University of Naples, V. Monaldi Hospital, Naples,

²Department of Biomorphological and Functional Sciences, Federico II University, Secondo Policlinico, Naples, Italy

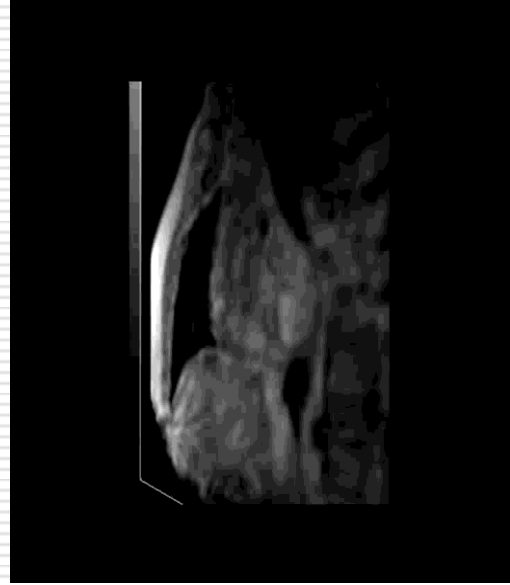
Expression of extracellular matrix proteins in BAV and Marfan aortic aneurysms is similar, but differences are remarkable in terms of type, grade and spatial distribution

- asymmetrical in BAV
- symmetrical in Marfan

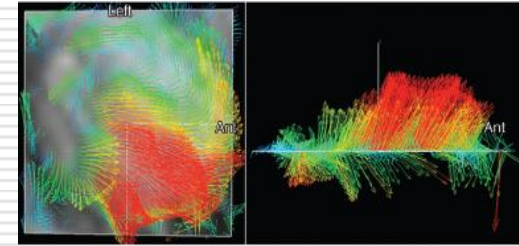
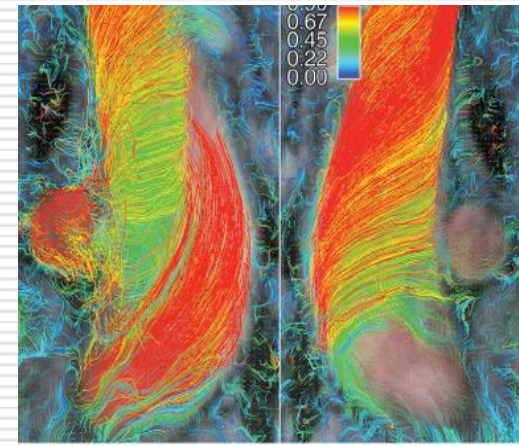




Bicuspid phenotypes and flows

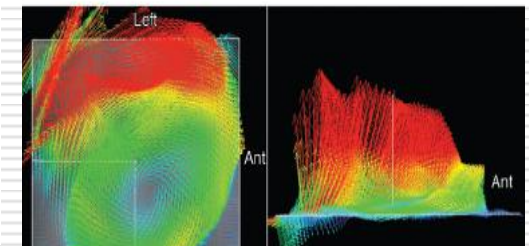
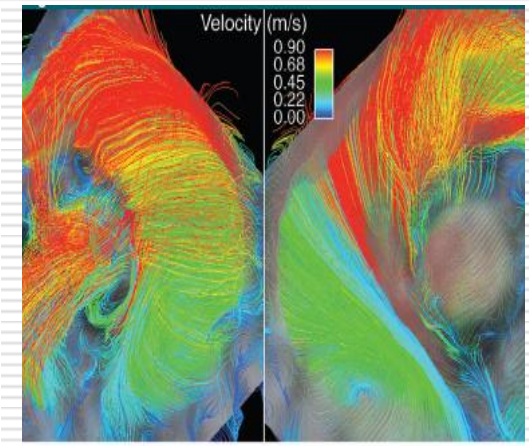


4-D flow MRI



R-L leaflet fusion (I)

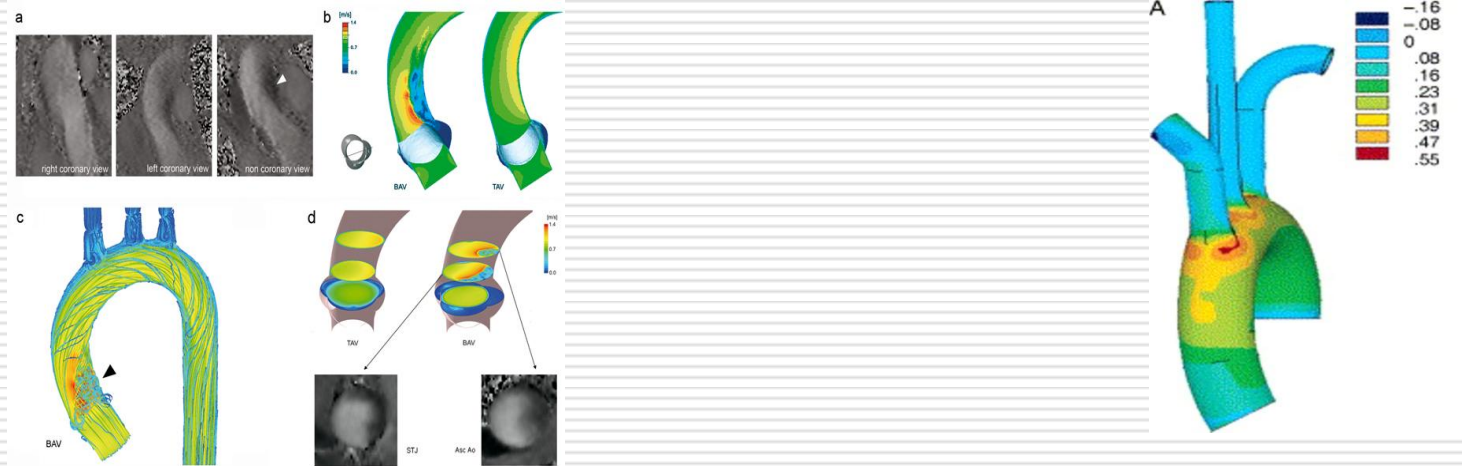
Right-handed helical flow
Right anterior eccentric jet



R-NC leaflet fusion (II)

Left-handed helical flow
Left posterior eccentric jet

Flow and Stress Patterns in Bicuspid Valve.



- In fully opened BAV, the orifice is not only asymmetrical, but also stenotic and turbulent flow is present in normofunctioning BAV
- BAV induces extensive recirculation vortices not trapped in the Valsalva sinuses but extended into the AA.
- Longitudinal stress 2 cm above STJ is 32% > in AR than in controls

Valvular Heart Disease

Reduced Aortic Elasticity and Dilatation Are Associated With Aortic Regurgitation and Left Ventricular Hypertrophy in Nonstenotic Bicuspid Aortic Valve Patients

Heynric B. Grotenhuis, MD,*†§|| Jaap Ottenkamp, MD,†§|| Jos J. M. Westenberg, PhD,*
Jeroen J. Bax, MD,‡ Lucia J. M. Kroft, MD,* Albert de Roos, MD*

Leiden and Amsterdam, the Netherlands

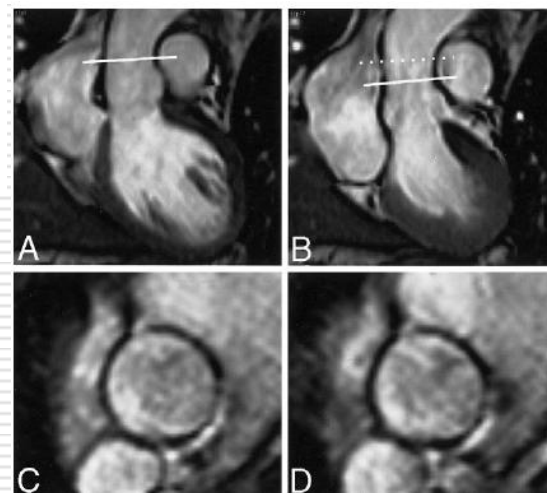
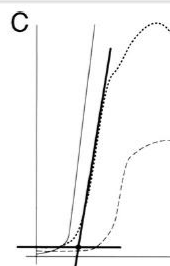
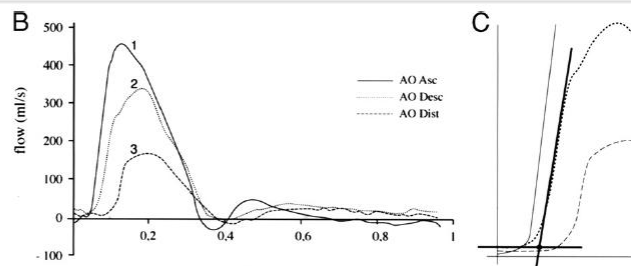
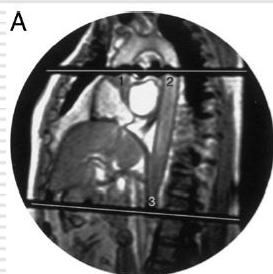
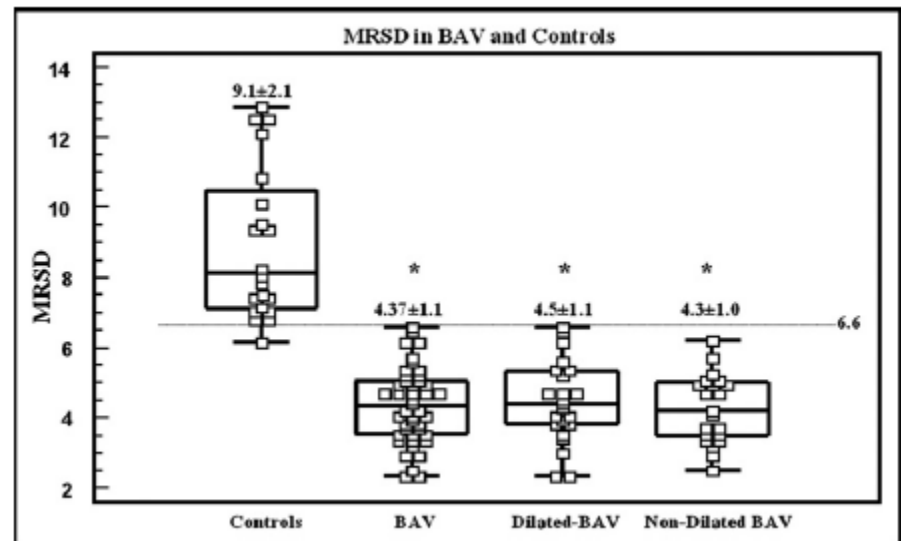
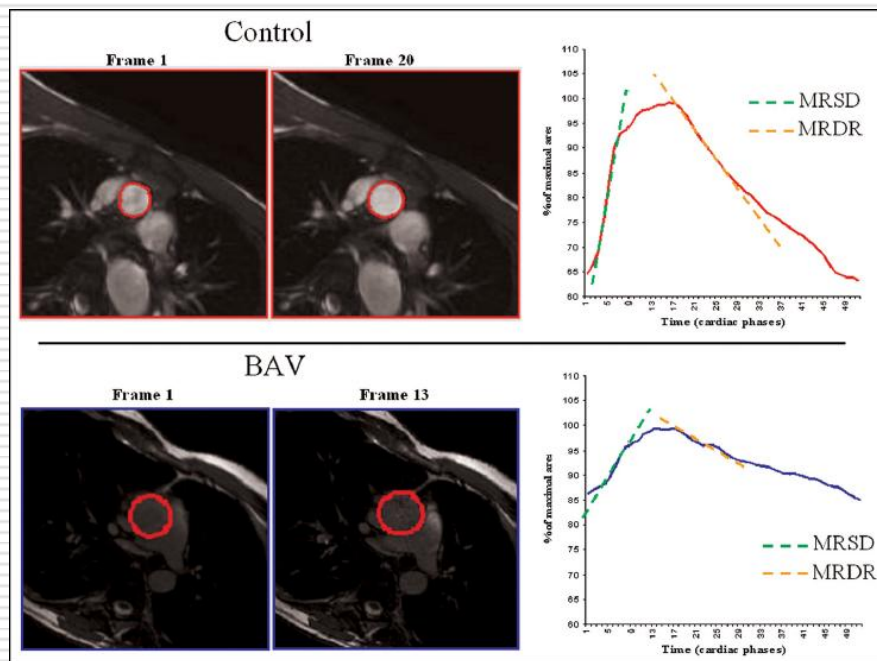


Table 2 Results in 20 BAV Patients and 20 Age- and Gender-Matched Healthy Subjects

Parameters	Patients	Healthy Subjects	p Value
Annulus diameter (mm)	30.1 ± 6.9	26.2 ± 3.3	0.03
Annulus area (cm ²)	7.4 ± 3.5	5.5 ± 1.4	0.03
Sinus of Valsalva diameter (mm)	33.4 ± 5.7	29.2 ± 3.2	<0.01
Sinus of Valsalva area (cm ²)	9.0 ± 3.4	6.8 ± 1.5	<0.01
Sinotubular junction diameter (mm)	30.4 ± 6.2	26.8 ± 3.4	0.04
STJ area (cm ²)	7.5 ± 3.5	5.7 ± 1.5	0.04
Ascending aorta diameter (mm)	30.0 ± 6.3	25.7 ± 3.1	<0.01
Ascending aorta area (cm ²)	7.4 ± 3.4	5.2 ± 1.3	<0.01
Distensibility (in 10 ⁻³ mm Hg ⁻¹)*	3.1 ± 1.2	5.6 ± 3.2	<0.01
PWV aortic arch (m/s)	5.6	4.5	0.01
PWV descending aorta (m/s)	5.2	4.3	0.03
Aortic regurgitation fraction (%)	6 ± 8	1 ± 1	<0.01

Elastic Properties of Aortic Wall in Patients With Bicuspid Aortic Valve by Magnetic Resonance Imaging

Giovanni Donato Aquaro, MD^{a,*†}, Lamia Ait-Ali, MD, PhD^{b,†}, Maira Levorato Basso, MD^c, Massimo Lombardi, MD^a, Alessandro Pingitore, MD, PhD^b, and Pierluigi Festa, MD^a

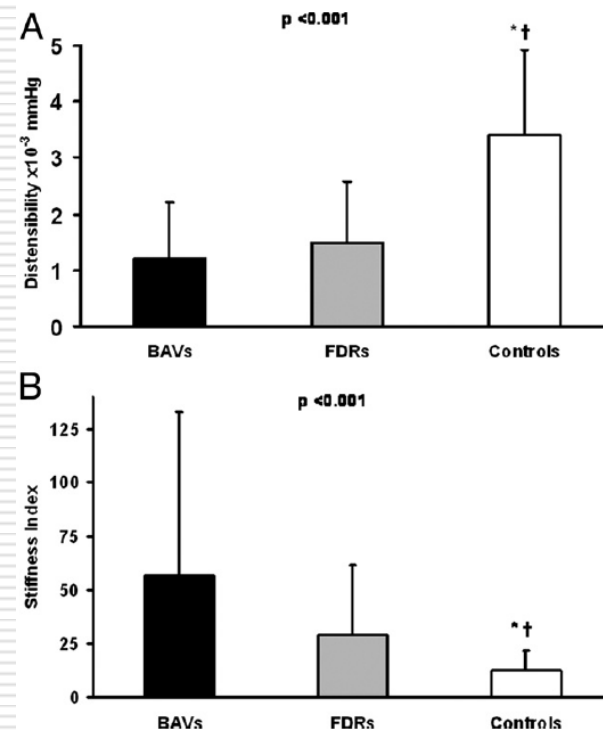
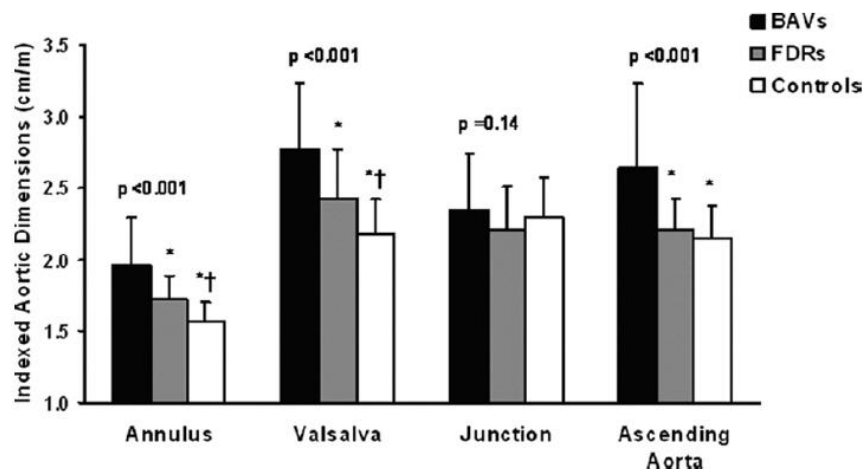


Aortopathy Is Prevalent in Relatives of Bicuspid Aortic Valve Patients

Simon Biner, MD,*† Asim M. Rafique, MD,* Indraneil Ray, MD,* Olivera Cuk, MD,* Robert J. Siegel, MD,* Kirsten Tolstrup, MD*

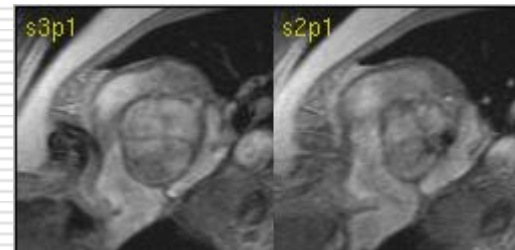
Los Angeles, California; and Tel Aviv, Israel

Aortic root was dilated and functionally abnormal of 32% of FDR.



Aortic complications of BAV and implications on management

- Dilation of the aorta is an independent risk factor for surgery.
- Real aortic complication is aortic dissection.
- Risk of dissection with smaller diameters?



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

212 patients (20 y follow-up)

40% ascending aorta > 40mm

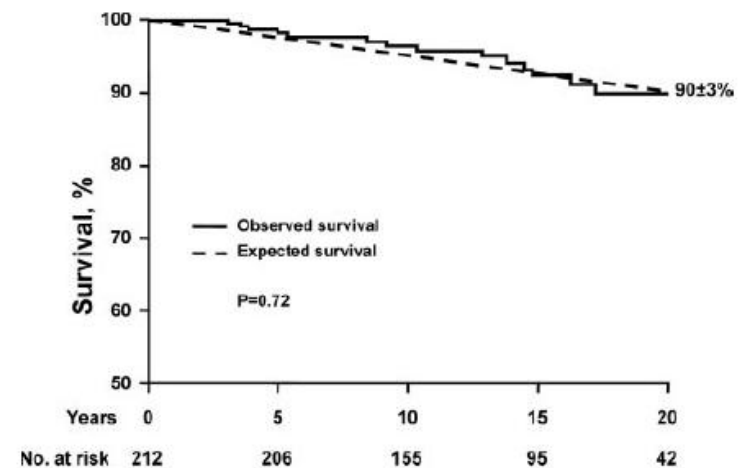
10% mortality identical to the general population

24% aortic valve surgery

5% aortic surgery

“no aortic dissection”

Independent predictors: age > 50 and valve degeneration at diagnosis

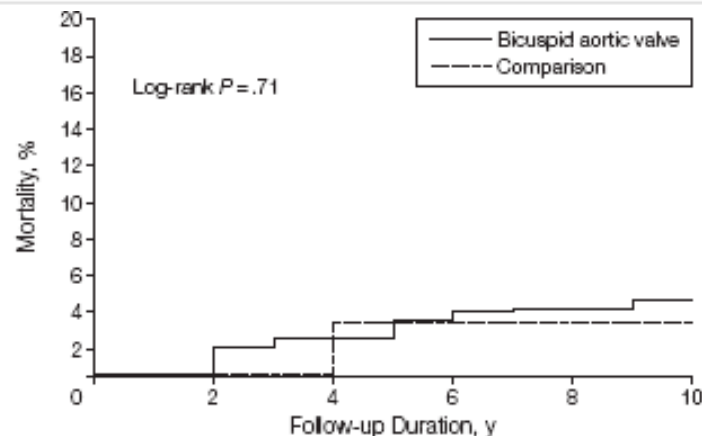


Outcomes in Adults With Bicuspid Aortic Valves

642 patients
 Follow-up : 9y

JAMA 2008; 300 (11) : 1317

Mortality 4% vs 3%
 Cardiac surgery 22%
 Aortic dissection 0.4%



Candidate Variables	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	P Value	HR (95% CI)	P Value
* Baseline age >90 y	2.11 (1.56-2.87)	<.001	3.01 (2.15-4.19)	<.001
Male sex	1.82 (1.27-2.62)	.002		
Hypertension	1.65 (1.24-2.20)	.002		
Hyperlipidemia	2.66 (1.70-4.18)	<.001		
Diabetes mellitus	1.00 (0.35-2.84)	.95		
Smoking	5.36 (1.89-15.24)	.004		
Family history of coronary artery disease	0.52 (0.21-1.29)	.20		
Body mass index ^a	1.00 (0.97-1.04)	.91		
Prior diagnosis of aortic coarctation	0.30 (0.19-0.48)	<.001		
Prior aortic valvuloplasty or valvotomy	1.92 (1.29-2.85)	.004		
Prior pregnancy	0.38 (0.13-1.08)	.10		
Right-left leaflet orientation	1.57 (1.11-2.21)	.02		
* Moderate or severe aortic stenosis	5.31 (3.98-7.09)	<.001	5.67 (4.16-7.80)	<.001
* Moderate or severe aortic regurgitation	2.61 (1.96-3.48)	<.001	2.68 (1.93-3.76)	<.001
Left ventricular ejection fraction <55%	3.22 (1.98-5.24)	<.001		
Aortic sinus >35 mm	1.93 (1.45-2.58)	<.001		

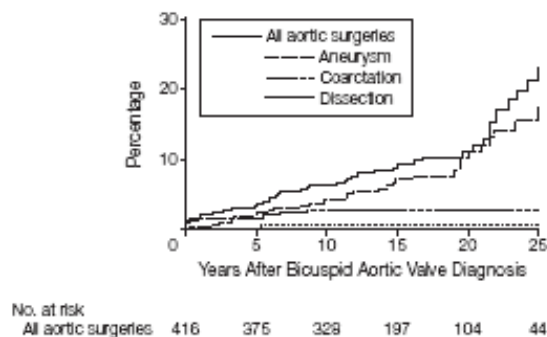
Incidence of Aortic Complications in Patients With Bicuspid Aortic Valves

Hector L. Michelena, MD

Context Bicuspid aortic valve (BAV), the most common congenital heart defect, has

N: 416, 25-y risk
2 AD,
26% AA
25% aortic surgery
53% AVR

Figure 5. Risk of Aortic Surgery After Definite Bicuspid Aortic Valve Diagnosis



Kaplan-Meier risk of aortic surgery 25 years after echocardiographic bicuspid aortic valve in 416 patients.

Table 3. Predictors of Aortic Aneurysm Formation

Variable	No. of Events	Denominator	Univariate Analysis, Hazard Ratio (95% CI)	P Value
Age, y ^a	N/A	416	1.0 (0.98-1.02)	.05
Sex				
Men	288	416	1.7 (0.9-3.5)	.10
Hypertension	93	416	1.2 (0.5-2.4)	.69
Smoking	132	416	1.3 (0.7-2.4)	.34
Diabetes	15	416	1.3 (0.2-13.9)	.81
Atherosclerotic disease ^b	21	416	0.7 (0.03-3.1)	.68
Total cholesterol, mg/dL ^a	N/A	255	1.0 (0.99-1.01)	.44
Typical bicuspid aortic valve	350	416	0.98 (0.5-2.3)	.98
Any aortic regurgitation	247	416	1.8 (0.99-3.4)	.05
Baseline aorta diameter ≥ 40 mm	90	416	3.4 (1.7-6.4)	.001
Baseline aortic stenosis	94	416	2.9 (1.6-5.2)	<.001
Multivariate, Hazard Ratio (95% CI)				
Age, y			1.0 (0.98-1.02)	.76
Sex				
Male			1.2 (0.6-2.5)	.68
Hypertension			0.95 (0.4-2.1)	.91
Any aortic regurgitation			1.5 (0.8-2.9)	.17
Baseline aorta diameter ≥ 40 mm			3.3 (1.5-7.2)	.004
Baseline aortic stenosis			3.4 (1.8-6.3)	<.001

Risk of Aortic Root or Ascending Aorta Complications in Patients with Bicuspid Aortic Valve With or Without Coarctation Of The Aorta

J Oliver, R Alonso, A González, P Gallego, A Sánchez-Recalde, E Cuesta, A Aroca, and JL Lopez-Sendon

Am J Cardiol 2009; 104:1001

BAV + A Co
(N=138)

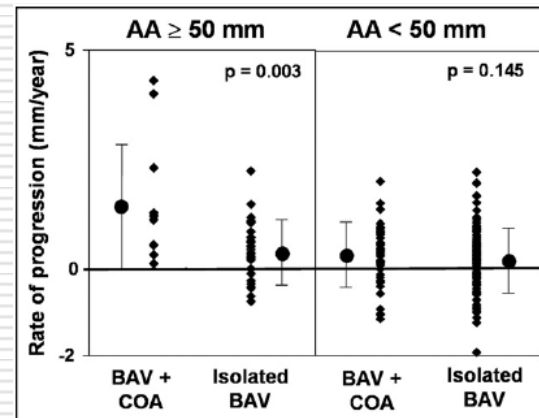
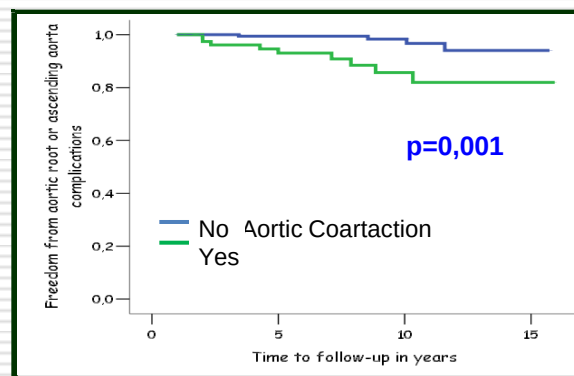
BAV without A Co
(N=484)

Total
(N=622)

1.1 (2.9%)

1.5 (2.9%)

p=0,037



Natural History of Ascending Aortic Aneurysms in the Setting of an Unreplaced Bicuspid Aortic Valve

Ryan R. Davies, MD, Ryan K. Kaple, BA, Divakar Mandapati, MD, Amy Gallo, MD, Donald M. Botta, Jr, MD, John A. Elefteriades, MD, and Michael A. Coady, MD, MPH

Section of Cardiothoracic Surgery, Yale University School of Medicine, New Haven, Connecticut; Department of Surgery, Columbia University College of Physicians and Surgeons, New York, New York; and Landmark Medical Center/Beth Israel Deaconess Medical Center, Woonsocket, Rhode Island

Ann Thorac Surg 2007; 83:1338-44

514 patients, AA>35 mm

70 BAV, 445 TAV

Aortic growth rate (1.9 vs 1.3 mm/y; $p<0.01$)

Table 3. Cumulative Incidence of Negative Events

Event	BAV	TAV	<i>p</i> Value	Odds Ratio (95% CI)
Aortic dissection	4 (5.7%)	38 (8.4%)	0.4382	0.6587 (0.2276 to 1.9060)
Aortic rupture	2 (2.9%)	15 (3.3%)	0.8373	0.8549 (0.1913 to 3.8214)
* Aortic rupture <i>or</i> dissection	6 (8.6%)	47 (10.4%)	0.6338	0.8059 (0.3310 to 1.9617)
Aortic rupture, dissection, <i>or</i> mortality	6 (8.6%)	116 (25.7%)	0.0016 ^a	0.2707 (0.1142 to 0.6418)
Death before operation	0 (0.0%)	78 (17.3%)	0.0002 ^a	N/A
Death	3 (4.3%)	137 (30.4%)	< 0.0001 ^a	0.1026 (0.0317 to 0.3320)
* Aortic size at rupture (mean, cm)	5.24	5.35	0.4394	

^a Statistically significant at the $p < 0.05$ level.

BAV = bicuspid aortic valve; CI = confidence interval; TAV = tricuspid aortic valve.

Should the ascending aorta be replaced more frequently in patients with bicuspid aortic valve disease?

Michael A. Borger, MD, PhD^{a,b}

Mark Preston, BSc^{a,b}

Joan Ivanov, RN, PhD^{a,b}

Paul W. M. Fedak, MD, PhD^{a,b}

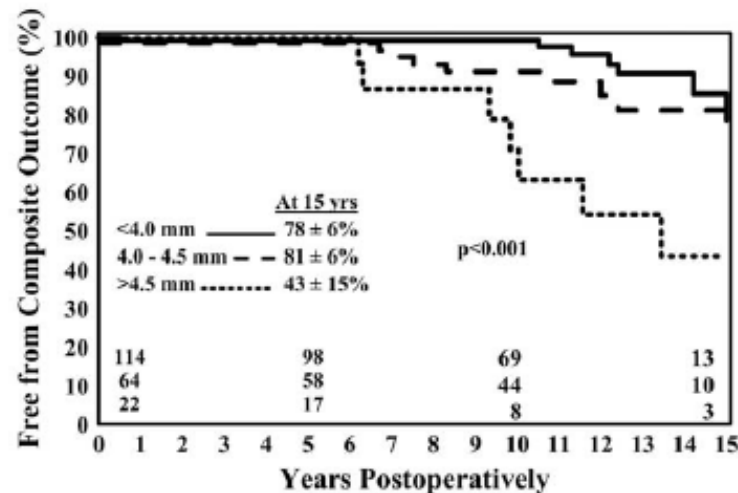
Piroze Davierwala, MD^{a,b}

Susan Armstrong, MSc^{ab}

Tirone E. David, MD^{a,b}

J Thorac Cardiovasc Surg 2004;128:677

- BAV with moderate dilatation (45-49mm) have a significant higher risk of long-term aortic complications.



Natural History of Ascending Aortic Aneurysms in the Setting of an Unreplaced Bicuspid Aortic Valve

Ryan R. Davies, MD, Ryan K. Kaple, BA, Divakar Mandapati, MD, Amy Gallo, MD, Donald M. Botta, Jr, MD, John A. Elefteriades, MD, and Michael A. Coady, MD, MPH

Section of Cardiothoracic Surgery, Yale University School of Medicine, New Haven, Connecticut; Department of Surgery, Columbia University College of Physicians and Surgeons, New York, New York; and Landmark Medical Center/Beth Israel Deaconess Medical Center, Woonsocket, Rhode Island

- Aortic stenosis higher risk of rupture/dissection OR:10, 95% CI: 1.1-95
- Despite faster rates of growth, BAV has a similar rate of aortic complications than TAV.

in patients with Marfan syndrome, we have previously demonstrated an increased propensity toward rupture, resulting in a lower threshold for operative intervention at 5.0 cm rather than 5.5 cm in the ascending aorta [11]. In the current study, we were not able to find a similarly increased risk of complications,

Indications for elective surgery in the Bicuspid Aortic Valve



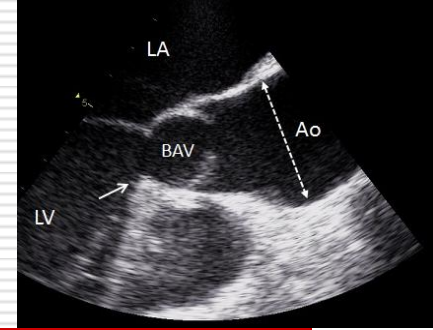
Aortic diameter ≥ 55 mm

Aortic diameter ≥ 50 mm if:

- Aortic coarctation, corrected or not
- First-degree family relative with Ao dissection/rupture
- Small body size:
 - Aortic area/height $> 10 \text{ cm}^2/\text{m}$
 - Aortic diameter / BSA $> 2.75 \text{ cm}/\text{m}^2$
- Severe AS or AR without surgical criteria (?)
- Expansion rate $\geq 2 \text{ mm}/\text{y}$ *

Aortic diameter > 45 mm with concomitant indication for elective AVR

Conclusions



- Ascending aortic dilatation occurs commonly in BAV, even in absence of AS or AR.
- Ascending aorta dilatation appears depend on:
 - a) Different haemodynamic factors such as increase wall stress secondary to jet excentricity and valve dysfunction.
 - b) Genetic factors that could lead to intrinsic aortic wall weakness.
- Although BAV patients present wall abnormalities that cause progressive aortic dilatation, the risk of dissection or aortic rupture is clearly lower than in Marfan Syndrome.
- In BAV, without severe dysfunction of the valve, timing of ascending aorta surgery (at 50 mm vs 55 mm) should be individualised considering the presence of aortic coarctation, body size, progressive dilatation, age and comorbidities.