EuroValve

November 8-9, 2013

Bicuspid Aortic Valve

Classification and natural history

Agnès Pasquet, MD, PhD
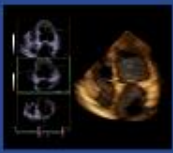
Pôle de Recherche Cardiovasculaire

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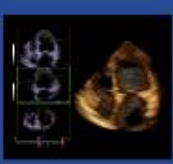IREC Institut de Recherche Expérimentale et Clinique
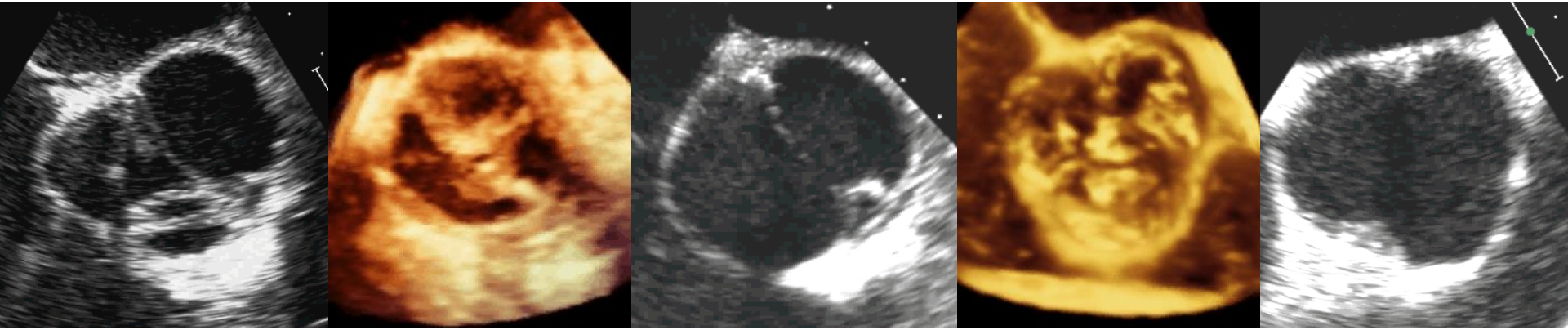
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I currently don't have, or have had over the last two years, an affiliation or financial interests or interests of any order with a company or I don't receive compensation or fees or research grants with a commercial company :
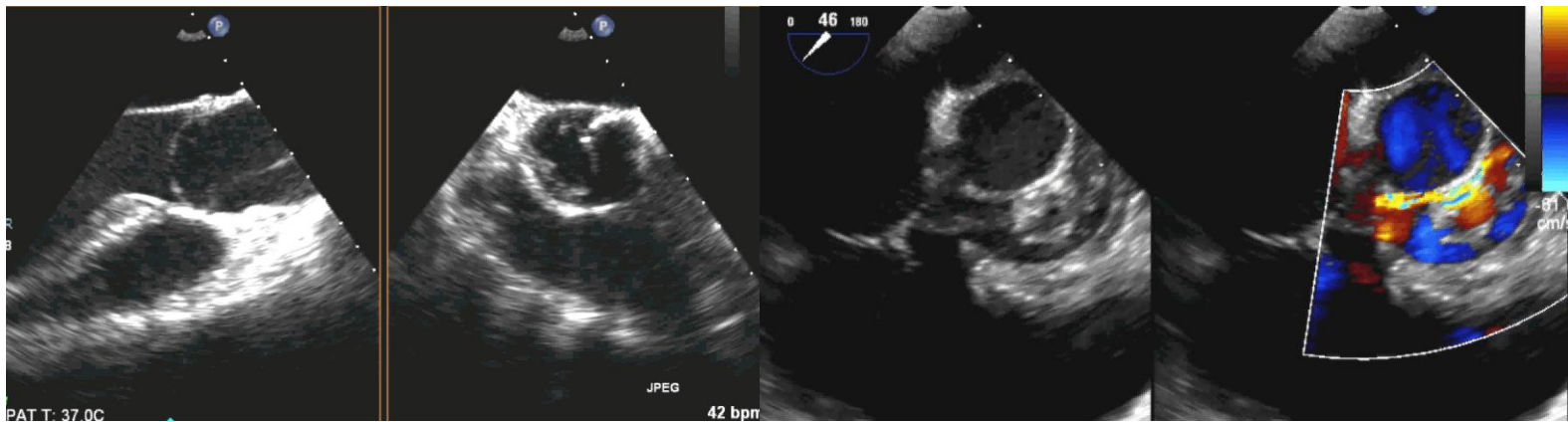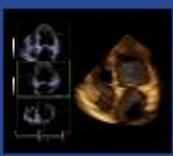
No relationship to disclose
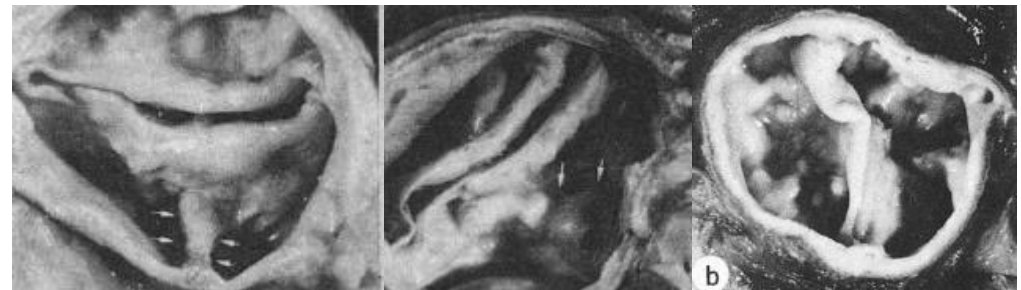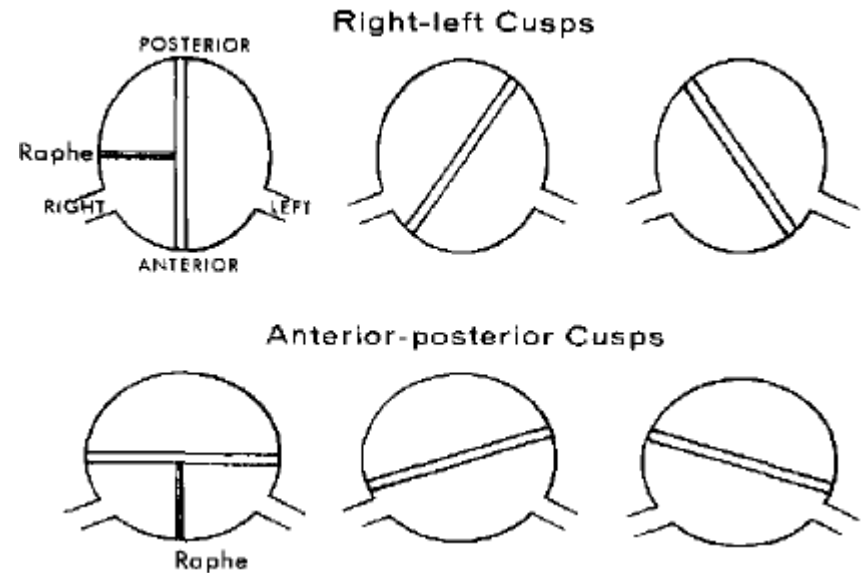
Bicuspid valve recover a wide range of morphology !

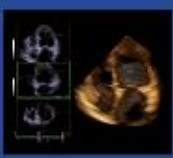# Classification: From autopsy studies..

85 autopsy cases

- *Group 1*: Aortic stenosis
- *Group 2*: Aortic regurgitation
- *Group 3*: Nl Valves

2 different type

- Right to left Cusp
- Anterio posterior cusp
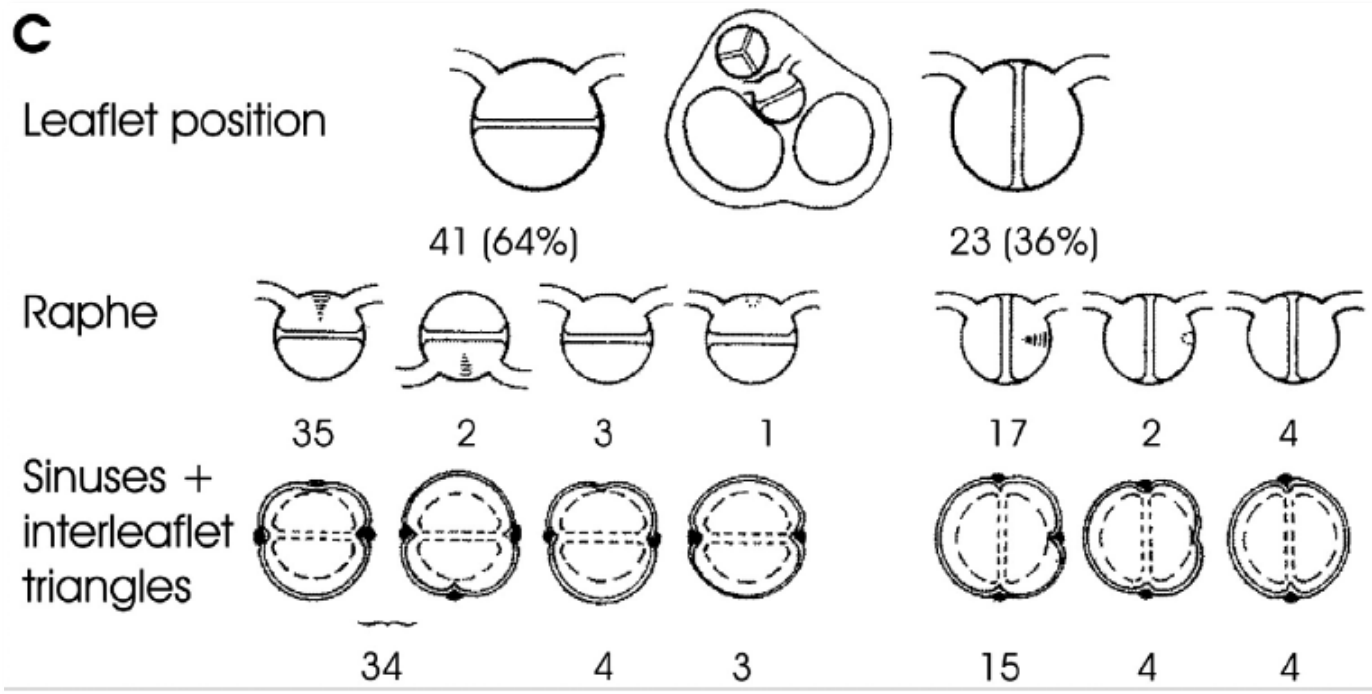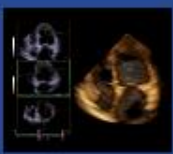

Roberts, Am J Cardiol 1970;26:72-83

EuroValve

Classification of BAV:

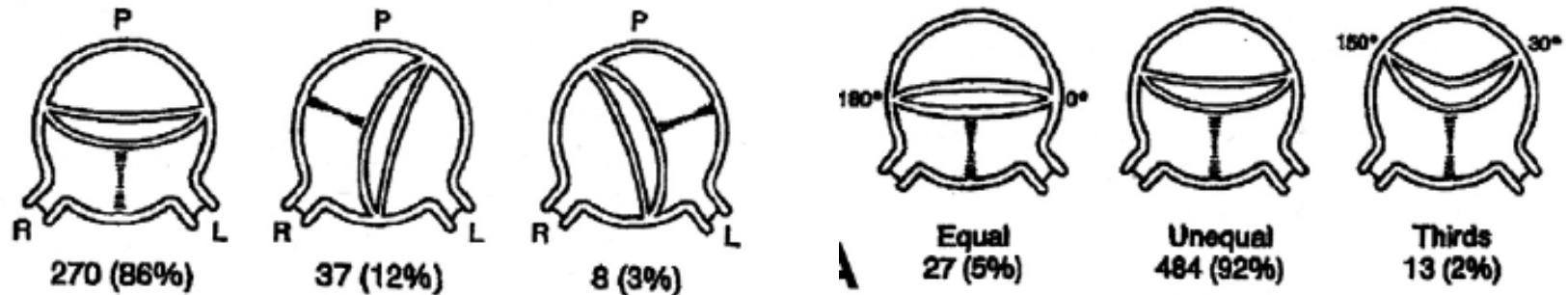- Angelini proposed a classification based on leaflet position, raphe and sinus plus interleaflet triangle (autopsy)


Angelini et al JTCS 1989;98:362-367

Classification of BAV: relation with pathology ?

270 (86%)   37 (12%)   8 (3%)   Equal 27 (5%)   Unequal 484 (92%)   Thirds 13 (2%)

Cusp maybe equal or unequal, with ou without raphe

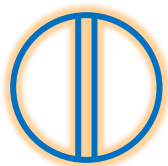| Functional state	Cusp size			Fused commissures			Calcification‡		Annular dilatation	
	Equal	Unequal	Thirds	One	Both	None	Present	Absent	Present	Absent
Pure AS	21	369	9	45	12	342	395	4	43	356
Pure AI	5	58	3	8	1	57	27	39	32	34
AS and AI	1	50	1	13	3	36	44	8	21	31
Normal	0	7	0	1	0	6	2	5	2	5
Total	27	484	13	67	16	441	468	56	98	426
Percent	5	92	2	13	3	84	89	11	19	81

Sabet et al Mayo Clin Pocess 1999;74:14-26
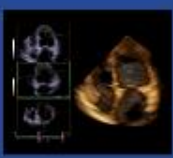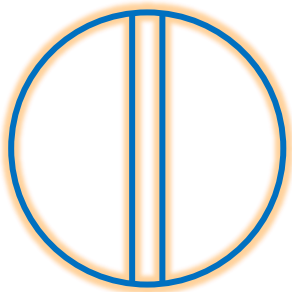
Classification: the surgical time !

Valve presented as viewed from the surgeon's position :
left coronary sinus on the left side !

0 raphe Type 0   1 raphe Type 1   2 raphes Type 2

Lat   Ap   L-R   R-N   N-L   L-R/R-N

Sivers et al JTCS 2007;133:1226-33
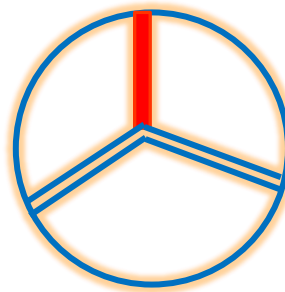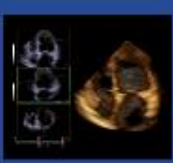
Classification: the surgical time !

0 raphe Type 0

Type 0 (no raphe)

1 raphe Type 1

Type 1 (one raphe)

2 raphes Type 2

Type 2 (two raphes)

Sivers et al JTCS 2007;133:1226-33
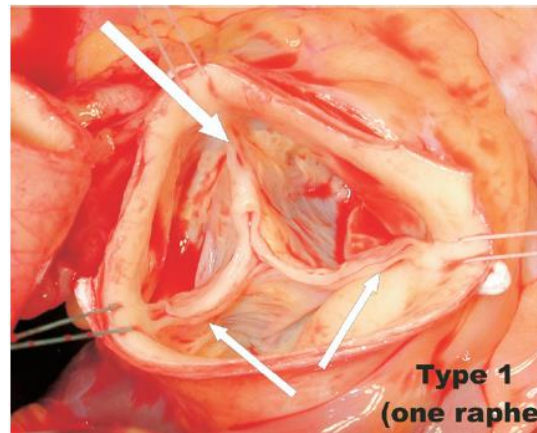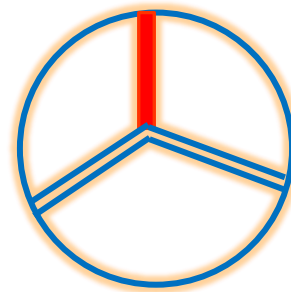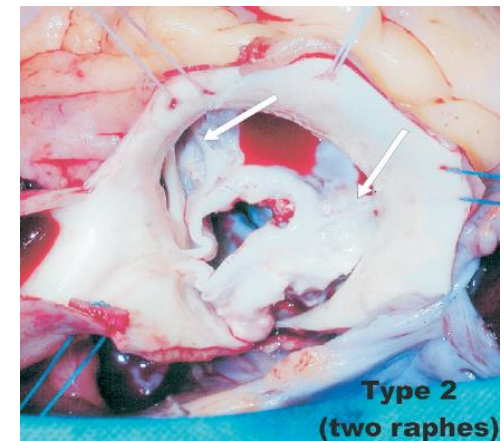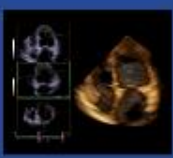
Classification: the echographic time !

Valve from ps short axis,   Root : ps long axis
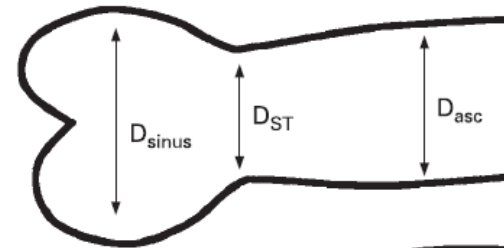
Schaffers et al Heart 2008;94:1634–1638

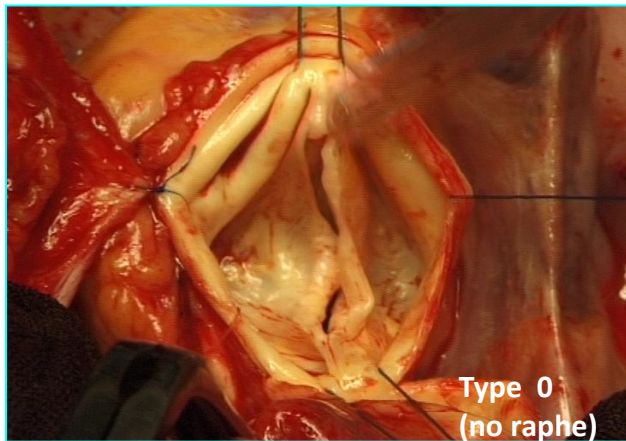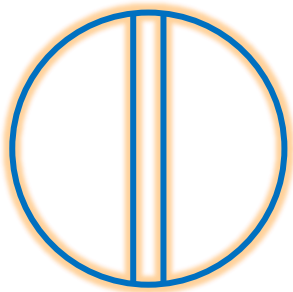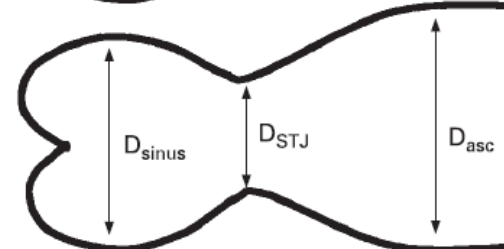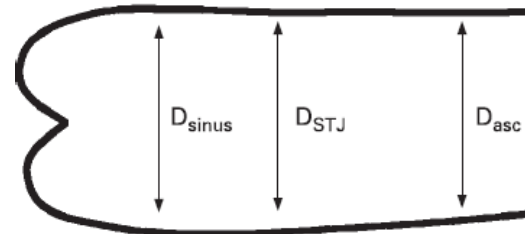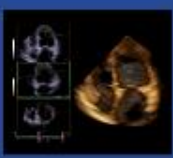# Classification: the echographic time !

Valve morphology	Aorta shape		
	N (%)	A (%)	E (%)
BAV type 1 (n = 144)*	86 (60)	50 (35)	8 (5)
BAV type 2 (n = 37)*	12 (32)	20 (54)	5 (14)

Schaffers et al Heart 2008;94:1634–1638

Classification: the MDCT time !

BAV A-P

BAV R-L

Kang et al J Am Coll Cardiol Img 2013;6:150–61
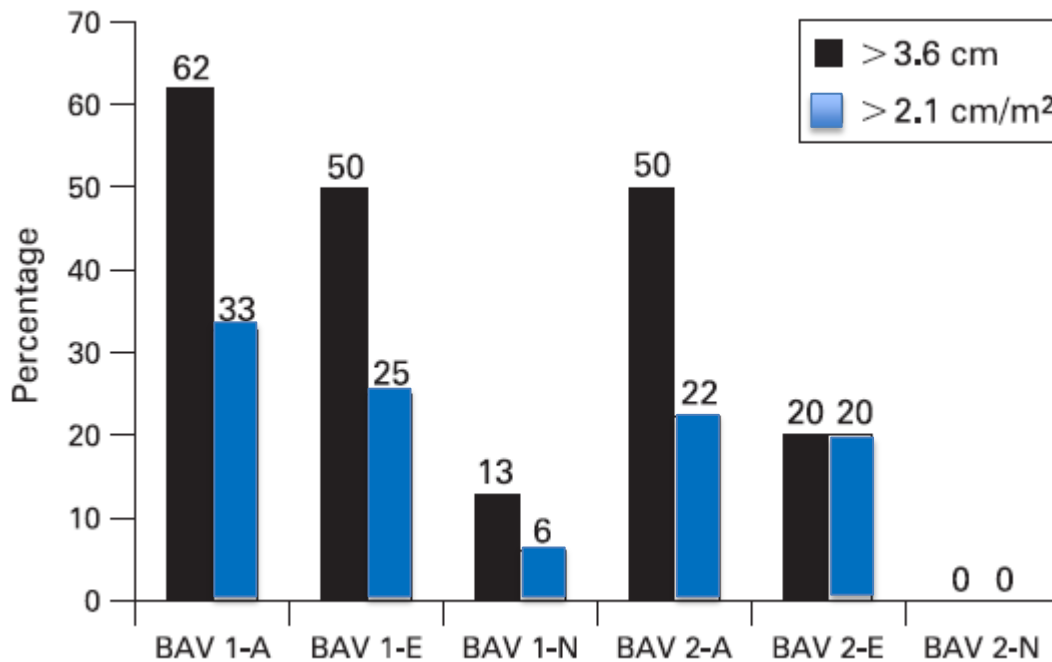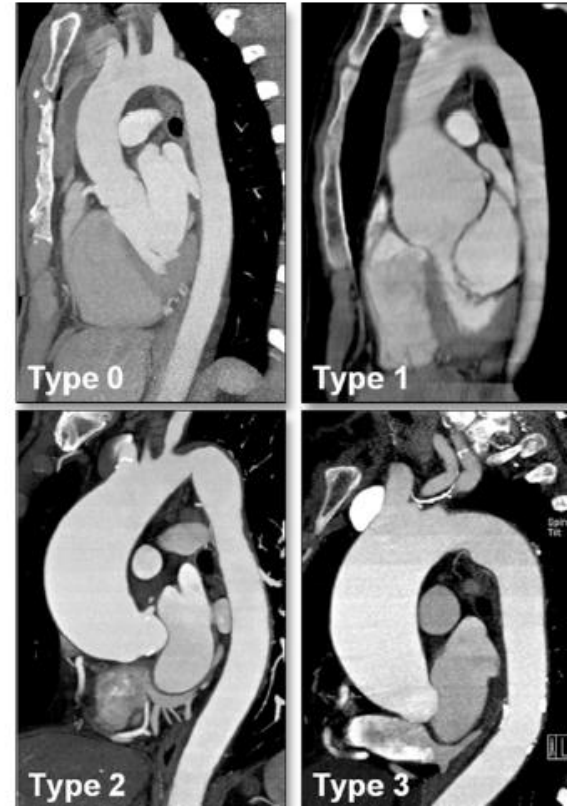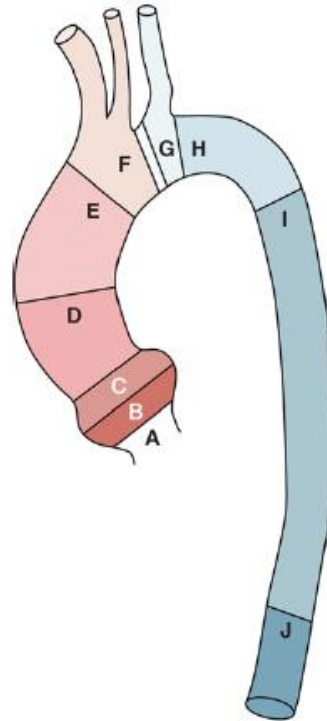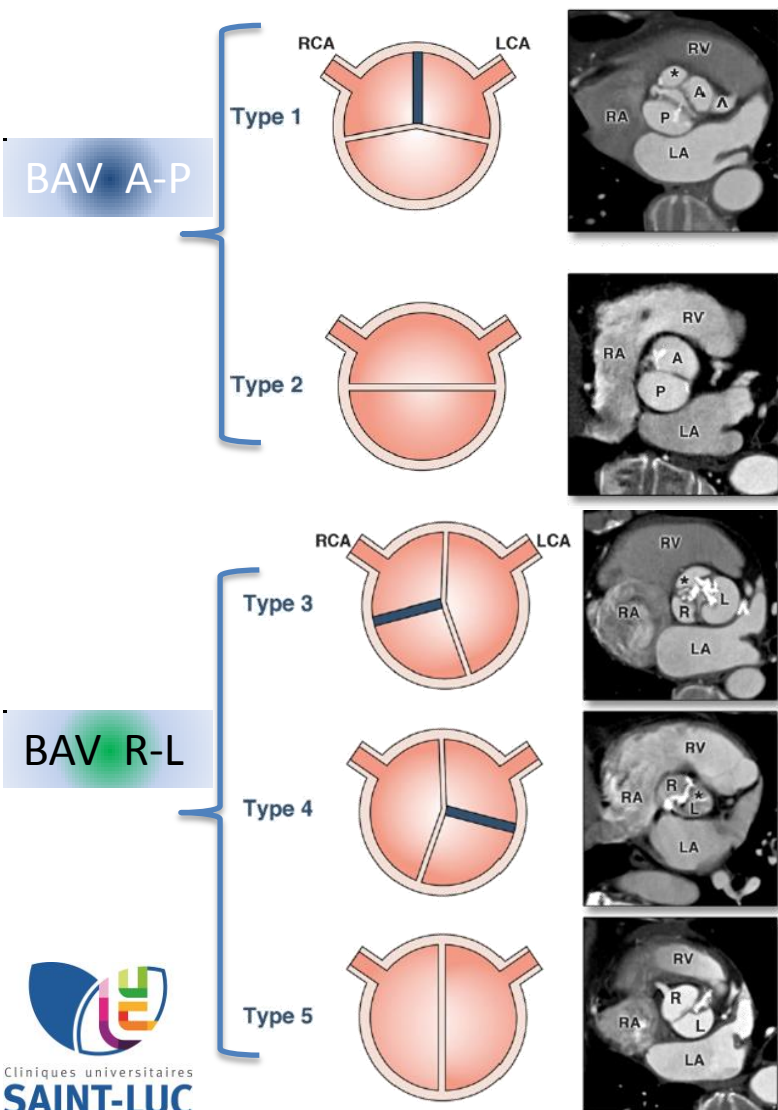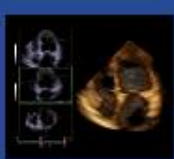
Classification: the MDCT time !

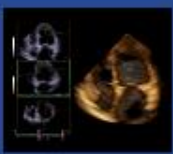|	BAV-AP (n = 93)	BAV-RL (n = 74)	p Value
Age, yrs	54.6 ± 14.9	54.8 ± 13.7	0.910
Men	69 (74.2)	46 (62.2)	0.150
Hypertension	31 (35.2)	16 (22.2)	0.072
Calcification			0.390
None	32 (34.4)	21 (28.4)	
Mild	12 (12.9)	12 (16.2)	
Moderate	10 (10.8)	14 (18.9)	
Severe	39 (41.9)	27 (36.5)	
Valvular dysfunction			<0.0001
Normal, mild AS, or mild AR	10 (10.8)	11 (14.9)	
Moderate-to-severe AS	43 (46.2)	49 (66.2)	
Moderate-to-severe AR	31 (32.3)	5 (6.8)	
Moderate-to-severe ASR	10 (10.8)	9 (12.2)	
Vmax, m/s	4.2 ± 1.5	4.9 ± 1.2	0.005
Ascending aorta dimension, mm			
Annulus	23.1 ± 3.7	22.1 ± 3.6	0.074
Sinus of Valsalva	38.1 ± 6.6	38.7 ± 6.3	0.522
Sinotubular junction	30.2 ± 5.3	31.8 ± 6.4	0.070
Tubular portion	41.0 ± 8.1	42.3 ± 8.0	0.284
BAV aortopathy			<0.0001
Type 0	31 (33.3)	14 (18.9)	
Type 1	23 (24.7)	11 (14.9)	
Type 2	30 (32.3)	19 (25.7)	
Type 3	9 (9.7)	30 (40.5)	

Kang et al J Am Coll Cardiol Img 2013;6:150–61
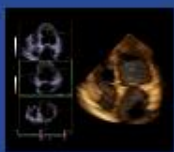
Could phenotype predict the pathology ?

First Author (Ref. #)	Mean Patient Age (yrs)	Number of Patients (AP/RL Type)	Major Findings
Fernandes et al. (5)	3	1,135 (70%/30%)	More significant valvular dysfunction in BAV-RL.
Cecconi et al. (13)	23.6	162 (55%/45%)	Only patients without significant valvular dysfunction were included. No correlation between BAV type and aortic enlargement.
Fernandes et al. (14)	16.1	310 (65%/35%)	More rapid progression of AR and AS with shorter time of intervention in BAV-RL.
Thanassoulis et al. (15)	33.1	156 (61%/38%)	Increased risk of rapid aortic dilation in BAV-AP.
Schaefer et al. (16)	Mid 40s	192 (80%/20%)	No association with valvular dysfunction; BAV-RL was associated with ascending aorta dilation.
Buchner et al. (18)	54	105 (72%/13%)	No correlation with aortopathy phenotype or valvular dysfunction.
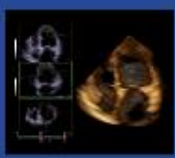
Natural history

- In 1844, Paget called attention to the peculiar liability of congenitally bicuspid aortic valves to disease, but their importance as something other than a pathologic curiosity was not appreciated .

- In 1858, Peacock pointed out that bicuspid aortic valves tended to become "thick . . . ossified . . . inducing first obstruction . . . and then incompetency"

- Osler in 1886 first described the abnormal liability of the bicuspid aortic valve to develop infective endocarditis .
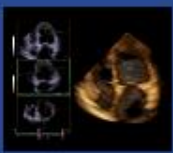
Survival of asymptomatic patient with BAV

90 ± 3%

Expected survival

Observed survival

p: 0.72

Survival, %

Years   0   5   10   15   20

No. at risk   212   206   155   95   42
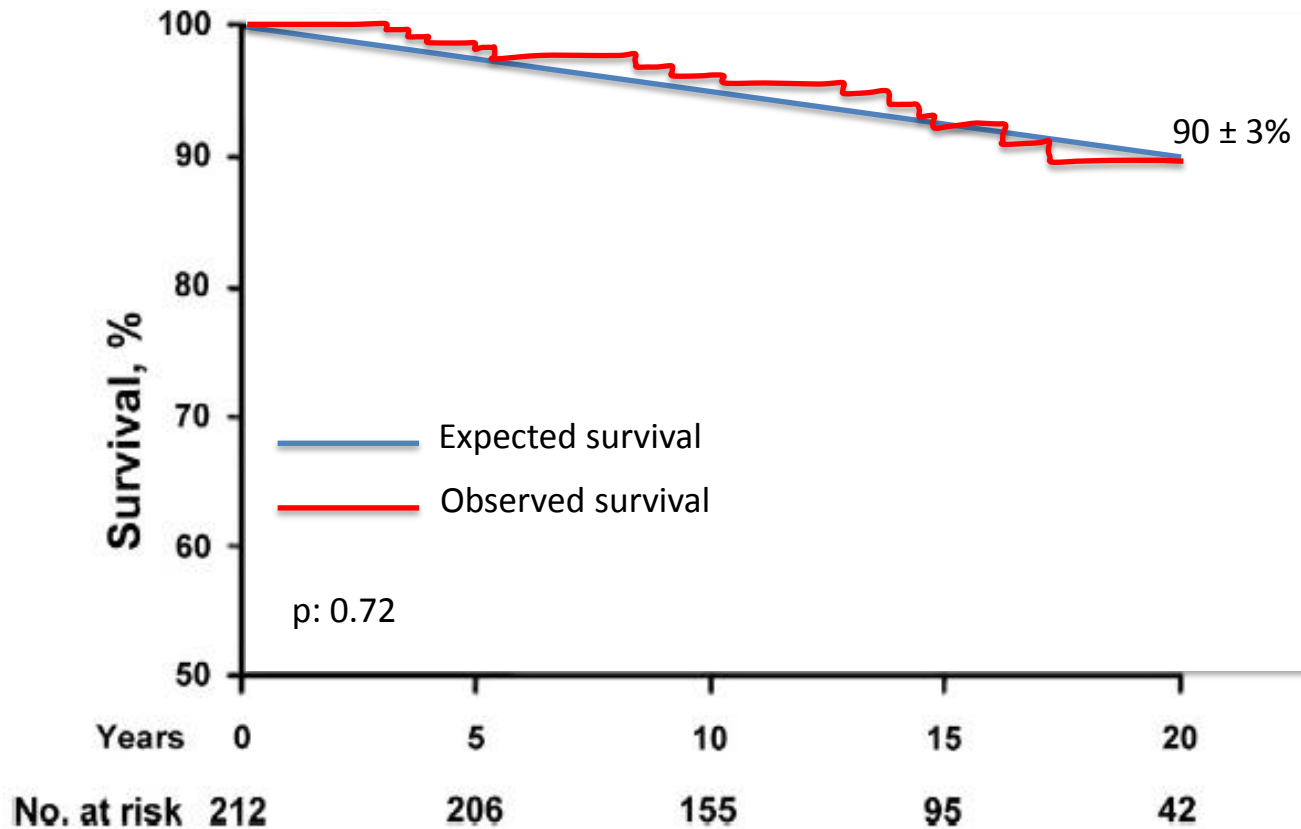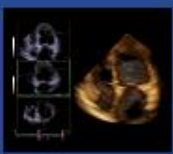
Natural history: medical event BAV
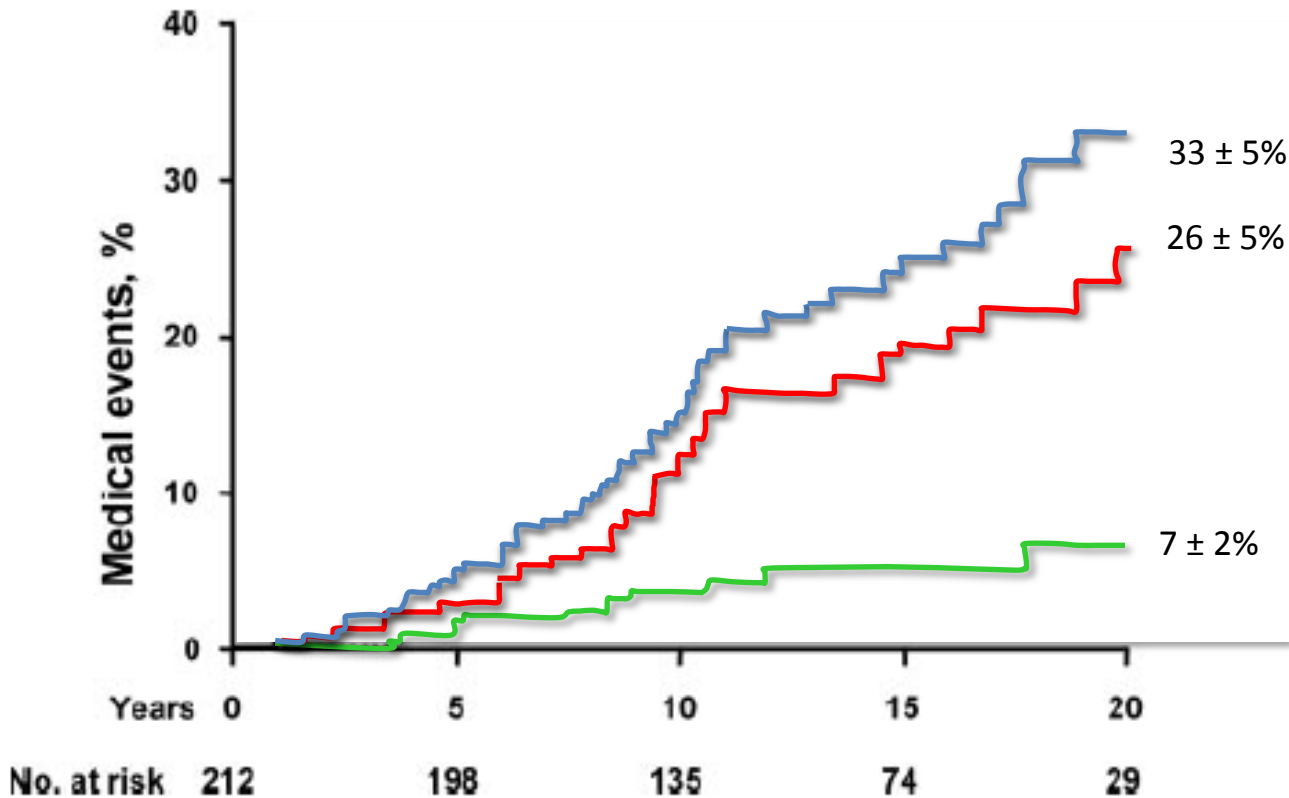
Med events: cardiac death, CHF, new cardiac symptoms, stroke, and endocarditis;

New cardiac symptoms: dyspnea, cardiac chest pain, and syncope

CHF

33 ± 5%

26 ± 5%

7 ± 2%

Michelina et al Circulation. 2008;117:2776-2784.)
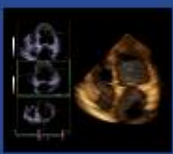
Natural history: surgical event BAV

Total surgical events aortic valve, ascending aorta, aortic coarctation

Ao Valve surgery: AVR or surgical valvotomy

Asc Aorta surgery

Aortic Coarct surgery

27 ± 4%
24 ± 4%
5 ± 2%
4 ± 1 %

Michelina et al Circulation. 2008;117:2776-2784.)

BAV Risk factor for events:

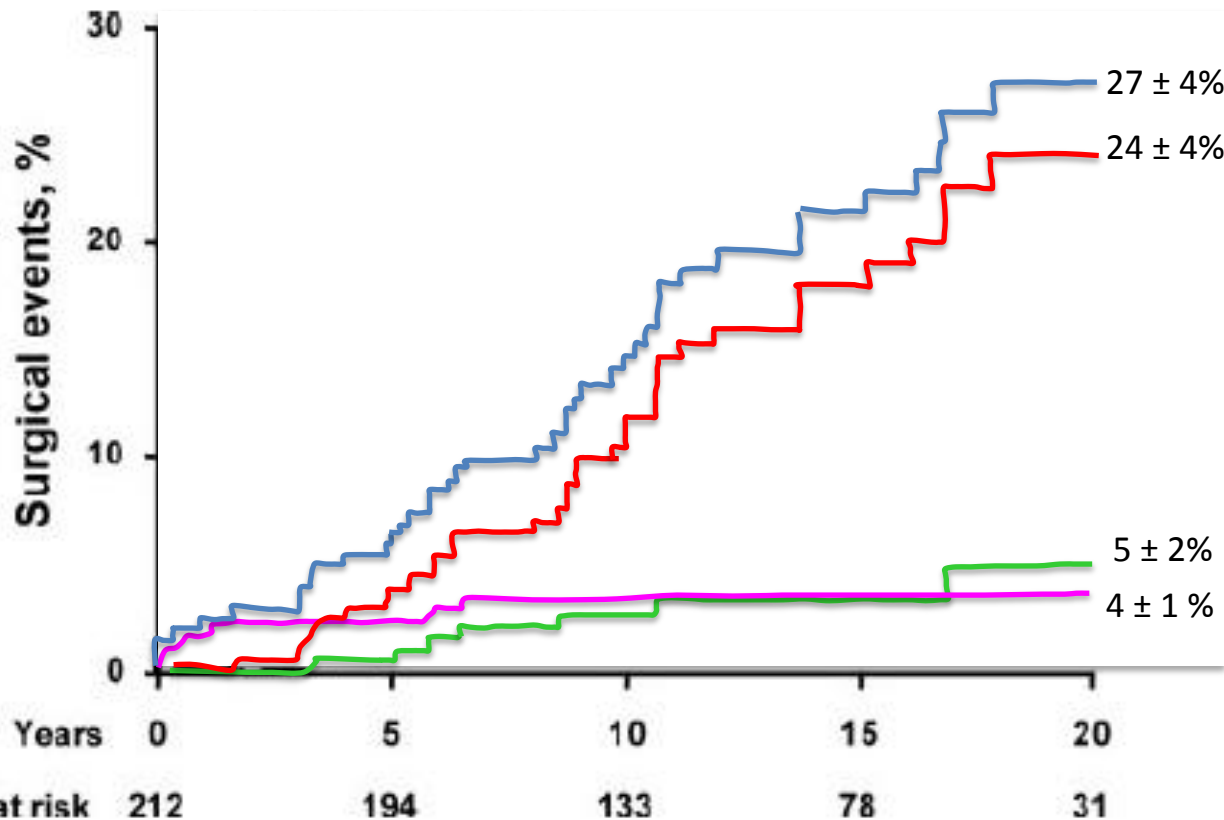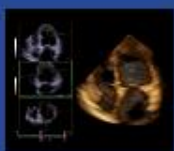| Candidate Variables	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	P Value	HR (95% CI)	P Value
Baseline age >30 y	2.11 (1.56-2.87)	<.001	3.01 (2.15-4.19)	<.001
Male sex	1.82 (1.27-2.62)	.002		
Hypertension	1.65 (1.24-2.20)	.002		
Hyperlipidemia	2.66 (1.70-4.18)	<.001		
Diabetes mellitus	1.00 (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		

Abbreviations: CI, confidence interval; HR, hazard ratio.
[a] Calculated as weight in kilograms divided by height in meters squared.

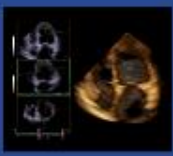*Tzemos et al JAMA. 2008;300(11):1317-1325*
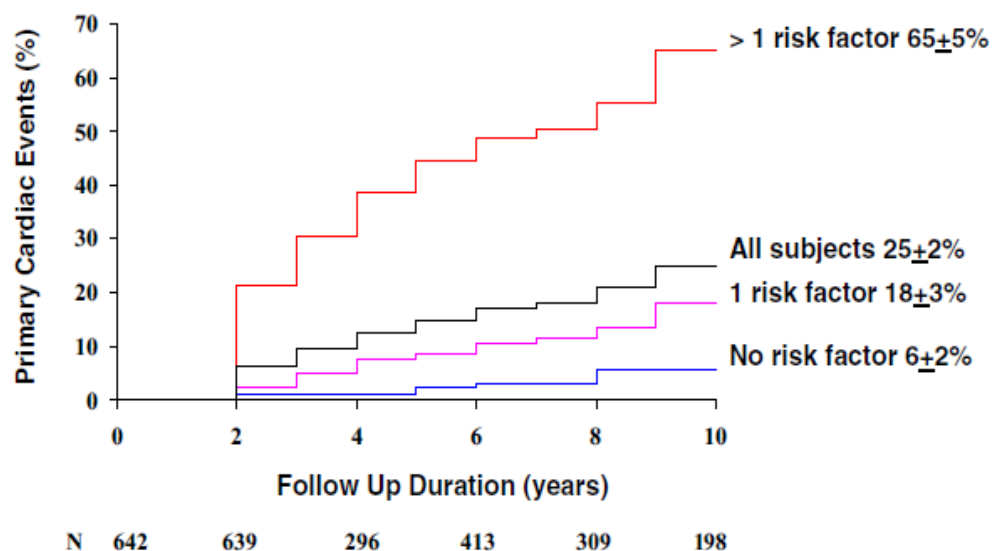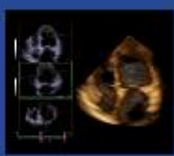
Natural history :

	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
Outcomes		
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%
Predictors of outcomes		
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

*Adapted from Michelena et al. (6). Cardiovascular medical events = cardiac death, congestive heart failure, new cardiovascular symptoms (dyspnea, syncope, anginal pain), stroke, and endocarditis. Surgical events = aortic valve surgery (aortic valve replacement, repair, or valvulotomy) and surgery of the thoracic aorta (for aneurysms, dissection, or coarctation). †Adapted from Tzemos et al. (7). Primary cardiac events = surgery on the aortic valve or ascending aorta, percutaneous aortic valvotomy, aortic complications (dissection or aneurysm development), congestive heart failure requiring hospital admission, or cardiac death. ‡Includes surgery for coarctation of the aorta.
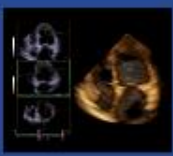
BAV = bicuspid aortic valve.

Pathology related to BAV:

- Aortic stenosis

- Aortic incompetence
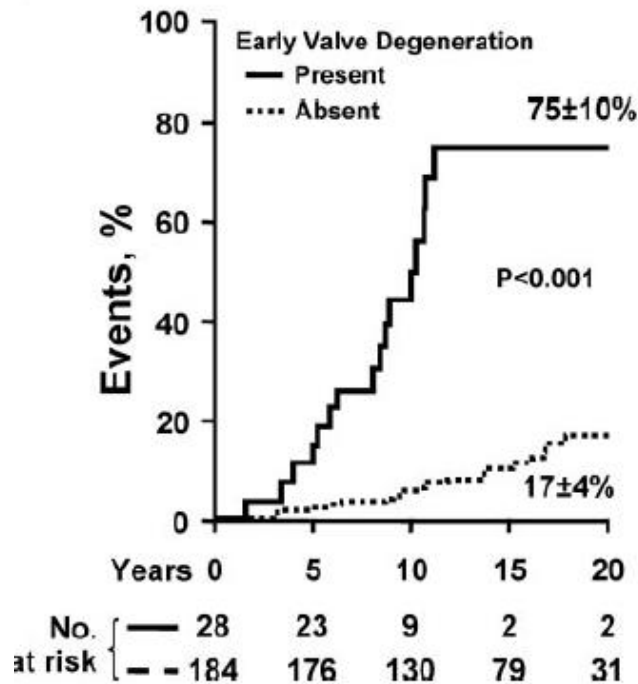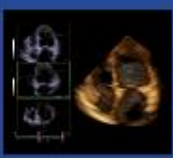
- Aortopathy and aortic dissection

- Endocarditis

BAV and aortic stenosis:

- Most commun complication of BAV

- Leaflet calcification, which occurs in a similar fashion to that seen in patients with trileaflet leaflet calcification.

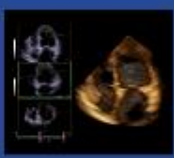- Calcification is often present by 40 years of age (age ⬆, risk ⬆.
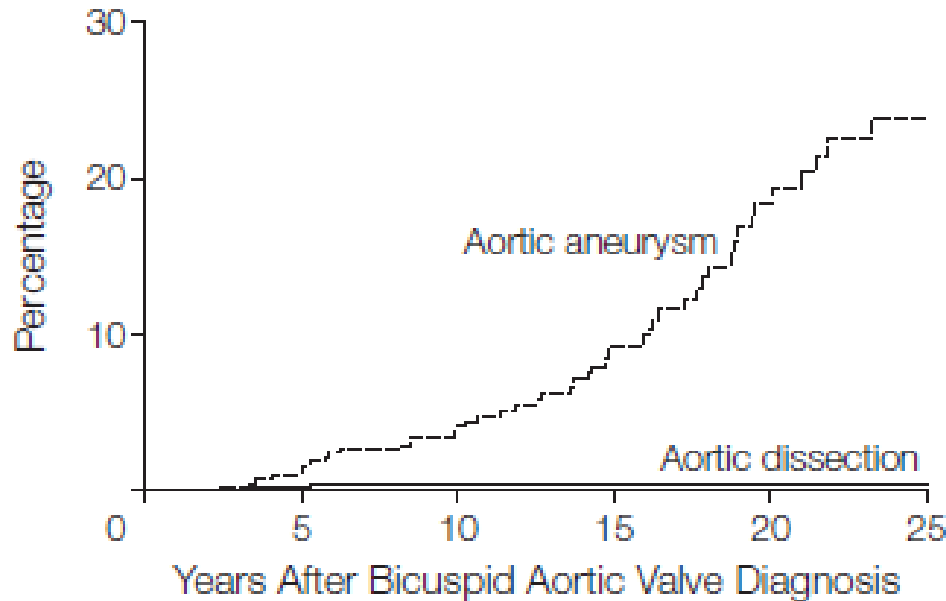
BAV and aortic incompetence:

- With age, aortic incompetence may also develop secondary to dilation of the ascending aorta.

- Frequence: rare to common ! (13% in a large serie)

- *In the Olmstead county*: 47% pt some degree of AR at baseline; however, interventions for severe AR were uncommon: only 3%

- *In the Toronto study*, 21% pt moderate or severe AR at baseline; however, only 6% interventions for symptomatic AR

- Despite variations in prevalence, moderate or severe aortic incompetence is clinically important and is an independent predictor for late adverse cardiac events.

Aortopathy and aortic dissection:

At 20y: 26% will develop aneuvrysm

84.9/10 000 pts year BAV

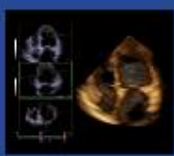1.04/10 000 pts year all population

RR:84 x !

Risk of aneurysm formation in pt without aneurysm at diagnosis

Michelena et al JAMA. 2011;306(10):1104-1113

Aortopathy and aortic dissection:

| 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

Abbreviation: N/A, nonapplicable (measurements).
SI conversion factor: to convert total cholesterol from mg/dL to mmol/L, multiply by 0.0259.
[a] Hazards ratios of continuous variables represent risk increase per unit of the regressor variable. For age, it is for each 1-year increase; total cholesterol, for each 1 mg/dL increase.
[b] History of stroke, transient ischemic attack, or myocardial infarction at baseline.

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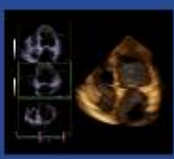
Aortopathy and aortic dissection:

⬆ Risk for ao dissection:
  aortic size
  aortic stiffness
  male sex
  Family history
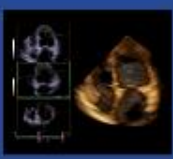 Marfan
  coarctation of the aorta
  Turner syndrome

Olmstead country

2 ao dissec/416 pts FU: 20 y

3.1/10 000 pts year BAV

0.31/10 000 pts year all population

RR:8.4 x !

Michelena et al JAMA. 2011;306(10):1104-1113

BAV and endocarditis:

- Endocarditis risk, based on earlier case series, was estimated to range between 10% and 30%.

- But more recent estimates of the incidence of endocarditis are much lower at **2% or 0.3%/**year

- Because the risk of endocarditis is felt to be low, the ESC, ACC/AHA practice guidelines **no longer suggest bacterial endocarditis prophylaxis** in patients with straightforward BAV disease, except in patients with a prior history of endocarditis
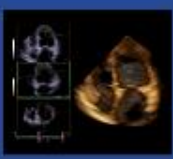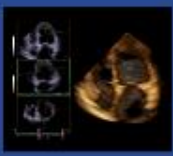
Conlusion:

- Several classification of BAV have been proposed but until know none has proved being predictive of natural history.

- The long term prognosis of BAV is favorable nevertheless a number of patient will experience medical event of need a cardiac surgery.

- Therefore, these patients must be carefully followed to detect complications (root dilatation, stenosis, regurgitation) and treat them on time !
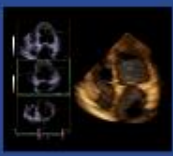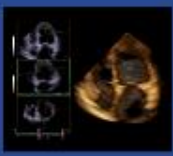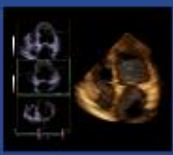
Thank you for your attention !

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Angelini et al JTCS 1989;98:362-367

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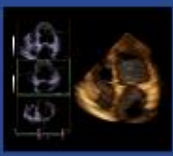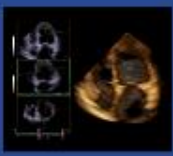
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Thank you for your attention !