I disclose the following financial relationships:

Consultant for Abbott, Boehringer Ingelheim, Valtech

Paid speaker for Edwards Lifesciences
Euro Heart Survey on Valvular Diseases

3547 Patients with Native Valve Disease

(Iung et al. Eur Heart J 2003;24:1244-53)
Single Native Valve Disease
Etiology

- AS
- AR
- MR
- MS

Categories:
- Other
- Ischemic
- Congenital
- Inflammatory
- Endocarditis
- Rheumatic
- Degenerative
Prevalence of BAV

• Systematic echocardiographic screening in children:
  – 0.6-0.8% in males
  – 0.2% in females

  (Tutar et al. Am Heart J 2005;150:513-5)

• Estimations in the USA
  – Prevalence 1.4%
  – Incidence of new cases estimated at 54 800 per year in the USA

  (AHA Heart Disease and Stroke Statistics--2012 Update
  Circulation 2012; 125:e2-e220)
Prevalence According to Anatomy

<table>
<thead>
<tr>
<th>main category: number of raphes</th>
<th>0 raphe - Type 0</th>
<th>1 raphe - Type 1</th>
<th>2 raphes - Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>21 (7)</td>
<td>269 (88)</td>
<td>14 (5)</td>
</tr>
<tr>
<td>1. subcategory: spatial position of cusps in Type 0 and raphes in Types 1 and 2</td>
<td>lat 13 (4)</td>
<td>ap 7 (2)</td>
<td>L – R 216 (71)</td>
</tr>
</tbody>
</table>

(Sievers et al. J Thorac Cardiovasc Surg 2007;133:1226-33)
Aortic Stenosis and BAV in Childhood

- 1135 children with bicuspid aortic valve
  Median age 3 years [1-18]
- 569 (50%) had isolated BAV
- BAV morphology and valve dysfunction

<table>
<thead>
<tr>
<th></th>
<th>R-L</th>
<th>R-N</th>
<th>L-N</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>59%</td>
<td>39%</td>
<td>2% Prevalence</td>
</tr>
<tr>
<td></td>
<td>10%</td>
<td>26%</td>
<td>0% V.max 3.5 m/sec.</td>
</tr>
</tbody>
</table>

- Age- and sex-adjusted link between AS and valve morphology: OR 2.3 [1.6-3.6] p<0.001
Progression of Aortic Stenosis

- 310 patients with BAV
  - 202 (65%) with R-L fusion
  - 108 (35%) with R-N fusion
Mean follow-up 14±7 yrs
Median age at end of follow-up: 16 years

(Fernandes et al. J Am Coll Cardiol 2007;22:2211-4)
Aortic Stenosis on BAV in the Adult

- In most cases, aortic stenosis is the consequence of a superimposed « degenerative » process

- Development of AS is also linked to cardiovascular risk factors in patients with BAV
  - Hypercholesterolemia OR 1.8 [1.1-2.8]
  - Hypertension OR 2.6 [1.1-6.6]

(Chan et al. Am J Cardiol 2001;88:690-3)
Etiologies of Aortic Stenosis

(Iung et al. Curr Prob Cardiol 2007;32: 609-61)
AS and Valve Morphology


• 49% had bicuspid aortic valves
• Age at intervention
  - bicuspid 67 ± 11 (27-91)
  - tricuspid 74 ± 8 (45-91)

(Roberts et al. Circulation 2005;111:920-5)
BAV and Valve Dysfunction

- Aortic valve surgery in 39 patients
  - 27 for severe AS
  - 6 for severe AR
  - 2 for severe mixed valve disease
  - 3 for moderate valve dysfunction and aortic dilatation
  - 1 for acute endocarditis
- Surgery for aortic coarctation in 8 patients
- Surgery for ascending aortic dilatation in 8 patients

(Michelena et al. Circulation 2008;117:2776-84)
AVR in Bicuspid/Tricuspid Valves

• Incidence of AVR (± CABG) in Olmsted County (1990-1999)
  – 19 / 100 000 pts/yrs for all patients
  – 1370 / 100 000 pts/yrs in patients with bicuspid aortic valves

• Age at AVR
  – 67 ± 16 yrs in patients with tricuspid aortic valves
  – 49 ± 20 yrs in patients with bicuspid aortic valves
    \( p<0.0001 \)

(Michelena et al. Circulation 2008;117:2776-84)
The Impact of Degenerative Disease

With age, valve degeneration (thickening, calcification, or mobility) was a strong independent predictor of all events

(Michelena et al. Circulation 2008;117:2776-84)
Aortic Regurgitation and BAV

• Less frequent occurrence than aortic stenosis on bicuspid valves

• Mechanisms
  – Valve prolapse
  – Dilatation of sinotubular junction
  – Endocarditis
AR and BAV

  - 122 related to valve disease
  - 146 related to disease of ascending aorta

- 77 (29%) bicuspid aortic valves
  - 74/122 (61%) among valve-related AR
    - 59 without endocarditis
    - 15 with signs of healed or active endocarditis
  - 3/146 (2%) among aorta-related AR (all aortic dissection)

(Roberts et al. Circulation 2006;114:422-9)
AR and BAV in Childhood

- 164 children with BAV and serial echocardiographic examinations

<table>
<thead>
<tr>
<th>AR ≥ moderate (%)</th>
<th>R-L (n=103)</th>
<th>R-N (n=61)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>At first echo</td>
<td>11</td>
<td>33</td>
<td>0.004</td>
</tr>
<tr>
<td>At last echo</td>
<td>26</td>
<td>64</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

- Progression of ≥ 1 grade of AR in 44% of patients with R-N fusion vs. 27% with R-L fusion
  
BAV and Ascending Aorta

More frequent dilatation of ascending aorta with bicuspid vs. tricuspid aortic valves independently of valve function

(Nistri et al. Heart 1999;82:19-22)
(Keane et al. Circulation 2000;102suppl.:III-35-9)

<table>
<thead>
<tr>
<th>R-L Fusion (n=144)</th>
<th>R-N fusion (n=37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60%</td>
<td>32%</td>
</tr>
<tr>
<td>35%</td>
<td>54%</td>
</tr>
<tr>
<td>5%</td>
<td>14%</td>
</tr>
</tbody>
</table>

(Schaefer et al. Heart 2008;94:1634-8)
BAV and Ascending Aorta

- Histological abnormalities of the aortic wall

- Maximal aortic dilatation rate does not differ between BAV and Marfan syndrome (0.42±0.6 vs 0.49±0.5 mm/yr.)

(Detaint et al. Heart, in press)

(Fedak et al. Circulation 2002;106:900-4)
Aortic Dilatation and Valve Function

The rate of progression of ascending aorta diameters

• Does not depend on aortic valve function

(Ferencik et al. Am J Cardiol 2003;92:43-6)

• Does not differ in patients with or without AVR

<table>
<thead>
<tr>
<th>Progression</th>
<th>No AVR</th>
<th>AVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valsalva sinuses</td>
<td>0.02±0.13</td>
<td>0.03±0.06</td>
</tr>
<tr>
<td>Ascending aorta</td>
<td>0.08±0.06</td>
<td>0.10±0.06</td>
</tr>
</tbody>
</table>

Aortic Dissection and BAV

• Necropsy
  186 patients with aortic dissection
  14 (7.5%) had a bicuspid aortic valve
  
  (Roberts et al. J Am Coll Cardiol 1991;17:712-6)

• IRAD registry
  951 patients from 18 centres (1996-2001)
  Aortic valve morphology was available in 516
  18 (3.5%) had a bicuspid aortic valve
  – 9% before 40 years
  – 1% after 40 years

  (Januzzi et al. J Am Coll Cardiol 2004;43:665-9)
Genetic Component in BAV

• High heritability of BAV (75-89%)
  - 50 probands with BAV
  - 259 first-degree relatives: 24% with BAV
  (Cripe et al. J Am Coll Cardiol 2004;44:138-43)

• Prevalence of aortic root dilatation of 32% in first-degree relatives of subjects with BAV
  (Biner et al. J Am Coll Cardiol 2009;53:2288–95)
Genetic Component in BAV

• Association between mutations of NOTCH-1 gene and BAV in a family comprising 11 case of congenital heart disease (6 with BAV)

(Garg et al. Nature 2005;437:270-4)

NOTCH-1 signalling pathway is involved in the septation of the common arterial trunk
Conclusion (I)

- Bicuspid aortic valve is frequent in the population.

- It seldom causes aortic valve dysfunction during childhood and adolescence.

- Aortic valve dysfunction occurs progressively in the adult and is most often aortic stenosis, due to superimposed degenerative valve remodelling.

- Aortic stenosis occurs more frequently and at a younger age on bicuspid than on tricuspid valve.
Conclusion (II)

• Aortic dilatation
  – is due to structural abnormalities of the aortic wall
  – follows different patterns which are linked to aortic valve morphology
  – does not depend on valve function

• Growing evidence suggests a genetic component in bicuspid aortic valve.