How Does Current Knowledge on BAV Aortopathy Impact Valve Repair?

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Disclosure of Interest

Speaker name: Alessandro Della Corte

- I do not have any potential conflict of interest
The current understanding of BAV aortopathy: searching for knowledge to translate into clinical management…

**Thursday September 13**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>08.30</td>
<td>The complex genetic architecture of bicuspid aortic valve related aortopathy, Bart Loeys</td>
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<tr>
<td>08.38</td>
<td>Protein-altering and regulatory genetic variants near GATA4 implicated in BAV, Simon Body</td>
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<tr>
<td>08.46</td>
<td>New insights in the genetics of aortopathy and BAV in Turner syndrome, Aline Verstraeten</td>
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<tr>
<td>08.54</td>
<td>Circulating microRNAs in bicuspid aortopathy, Evaldas Girdauskas</td>
</tr>
<tr>
<td>09.02</td>
<td>TGF-b/ENG ratio in bicuspid aortopathy, Alessandro Della Corte</td>
</tr>
<tr>
<td>09.10</td>
<td>Discussion</td>
</tr>
<tr>
<td>09.35</td>
<td>Fluid dynamics simulations to understand BAV aortopathy mechanisms and risks, Luca Koechlin</td>
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<tr>
<td>09.43</td>
<td>Searching for early biomechanically-driven indexes of aortic remodeling: where are we at? Emiliano Votta</td>
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<tr>
<td>09.51</td>
<td>Advanced imaging biomarkers in bicuspid aortic valve disease surveillance, Malenka Bissell</td>
</tr>
<tr>
<td>09.59</td>
<td>Gender-related differences in bicuspid aortopathy history and outcomes, Hector Michelena</td>
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Towards Personalized Surgical Indications for BAV aortopathy?

Phenotypic heterogeneity of bicuspid aortopathy: a potential key to decode the prognosis?

Alessandro Della Corte

**Knowledge–Practice Interconnection**

The clinical and basic research on bicuspid aortic valve (BAV) and associated conditions is an exponentially expanding field. As of 23 October 2013, according to a PubMed article search for the ‘bicuspid aortic valve’ (BAV) keyword, there is no recent replacement of the ascending aorta from the American Heart Association (AHA)/American College of Cardiology (ACC) do include BAV among those syndromic aortopathies, when recommending prophylactic surgery at a diameter between 40 and 50 mm. A recent survey among cardiac surgeons demonstrated that considerable genetic risk markers for BAV aortopathy, these predictors could be distinguished into phenotypic predictors or functional predictors (these latter including functional imaging parameters such as aortic wall distensibility or shear stress).

Also in our above-mentioned recent study, baseline diameter did not predict the progression of the aortopathy; however, the pattern of aortic dimensions (the so-called ‘aortic phenotype’) did: the only independent determinant of a fast growth (>0.9 mm/year) of the tubular ascending aorta in BAV patients was the root phenotype, that is, a dilated aorta with diameter at Valsalva sinuses exceeding the diameter of the tubular tract. The root

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**Pathogenetic mechanisms**

**Phenotype**

**Prognosis**

**Management Criteria**
Classification of BAV-associated aortopathy

Predictors of ascending aortic dilatation with bicuspid aortic valve: a wide spectrum of disease expression

Alessandro Della Corte *,1, Ciro Bancone, Cesare Quarto, Giovanni Dialetto, Franco E. Covino, Michelangelo Scardone, Giuseppe Caianiello, Maurizio Cotrufo

Non-dilated Aorta  Ascending phenotype (dilated, asc>root)  Root phenotype (dilated, root>asc)

80% dilatations  20% dilatations

Della Corte A, et al. EJCTS 2007;31:397-405
Combinations of different causative mechanisms

Ascending phenotype
- Aortic stenosis
- Older age
- Hypertension
- (RN type)

Root phenotype
- No AV stenosis
- Younger age
- Male sex
- RL type
- Taller stature
**Ascending phenotype**: regional aortopathy, probably predictable by flow imaging

**J Cardiovasc Med 2009**

The association of bicuspid aortic valve disease with asymmetric dilatation of the tubular ascending aorta: identification of a definite syndrome
Maurizio Cotrufo and Alessandro Della Corte

**EJCTS 2014**

Correlation between systolic transvalvular flow and proximal aortic wall changes in bicuspid aortic valve stenosis
Evaldas Girdauskas, Mina Rouman, Kushtrim Disha, Thorsten Scholle, Beatrix Fey, Bernhard Theis, Iver Petersen, Michael A. Borger and Thomas Kuntze

**JACC 2015**

Valve-Related Hemodynamics Mediate Human Bicuspid Aortopathy
Insights From Wall Shear Stress Mapping

Guzzardi et al. JACC 2015
Root phenotype: diffuse asc aortopathy, probably more genetically homogeneous


Girdauskas E, et al. EJCTS 2017
Pattern of Ascending Aortic Dimensions Predicts the Growth Rate of the Aorta in Patients With Bicuspid Aortic Valve

Alessandro Della Corte, MD, PhD,* Ciro Bancone, MD, PhD,* Marianna Buonocore, MD,* Giovanni Di Ietto, MD,* Franco E. Covino, MD,* Sabrina Manduca, MD,* Giancarlo Scognamiglio, MD,*† Veronica D’Oria, MD,* Marisa De Feo, MD, PhD*

Aortic events after isolated aortic valve replacement for bicuspid aortic valve root phenotype: echocardiographic follow-up study†

Evaldas Girdauskas,* Kishtrum Disha,* Mina Rouman,* Andres Espinoza,* Michael A. Borger* and Thomas Kuntze*

† Department of Cardiac Surgery, Heart Center, Central Hospital Bad Berka, Bad Berka, Germany
‡ Cardiovascular Institute, Columbia University Medical Center, New York, USA

Impact of Aortic Insufficiency on Ascending Aortic Dilatation and Adverse Aortic Events After Isolated Aortic Valve Replacement in Patients With a Bicuspid Aortic Valve

Yongshi Wang, MD,* Boting Wu, MD,* Jun Li, MD, Lili Dong, MD, Chunsheng Wang, MD, and Xianhong Shu, MD, PhD

Della Corte A, et al. JACC Img 2013

Girdauskas E, et al. EJCTS 2015

How does Knowledge of Phenotypic Heterogeneity Impact on Aorta Repair?

Review

Bicuspid aortic valve aortopathy in adults: Incidence, etiology, and clinical significance

Hector I. Michlena a, a, Alessandro Della Corte b, Siddharth K. Prakash c, Dianna M. Milewicz c, Artur Evangelista d, Maurice Enriquez-Sarano a

*If first-time patient, may reimage at 6 months and if no progression then yearly
The American Association for Thoracic Surgery consensus guidelines on bicuspid aortic valve–related aortopathy: Full online-only version

Michael A. Borger, MD, PhD, a Paul W. M. Fedak, MD, PhD, b Elizabeth H. Stephens, MD, PhD, c Thomas G. Gleason, MD, d Evaldas Girdauskas, MD, PhD, e John S. Ikonomidis, MD, PhD, f Ali Khoynezhad, MD, PhD, g Samuel C. Siu, MD, h Subodh Verma, MD, PhD, i Michael D. Hope, MD, j Duke E. Cameron, MD, k Donald F. Hammer, MD, l Joseph S. Coselli, MD, m Marc R. Moon, MD, n Thoralf M. Sundt, MD, o Alex J. Barker, PhD, p Michael Markl, PhD, q Alessandro Della Corte, MD, PhD, r Hector I. Michanela, MD, s and John A. Elefteriades, MD t

<table>
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<th>Recommendation</th>
<th>Class/LOE</th>
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<td>Repair of the ascending aorta/root is recommended when the aortic diameter is ≥55 mm in patients without risk factors</td>
<td>I/B  26,27,33,155,226</td>
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<tr>
<td>Repair of the ascending aorta/root should be performed when the aortic diameter is ≥50 mm in patients with risk factors (ie, root phenotype or predominant AI, uncontrolled hypertension, family history of aortic dissection/sudden death, coarctation, aortic growth &gt;3 mm/y)</td>
<td>IIa/B  26,27,33,155,226</td>
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How does Knowledge of Phenotypic Heterogeneity Impact on Valve Repair?

This is the phenotypic context in which BAV repair is considered, indicated and practiced.

- No AV stenosis
- Younger age
- Male sex
- RL type
- Taller stature
- Faster aortic growth
- Post-AVR events
- Familial forms
- (AML prolapse)
- Higher dissection risk?
- Connective tissue disease?
- Earlier indications for surgery?
Timing of Operation

The current knowledge of the ‘malignant behaviour’ of dilatation in patients with root phenotype justifies a more aggressive timing (diameter >50 mm if BAV is not severely regurgitant, otherwise >45mm)

• Young patients (prosthesis-related complications)
• Increased chances to repair the valve

Surgical treatment of bicuspid aortic valve disease: Knowledge gaps and research perspectives

Alessandro Della Corte, MD, PhD, Simon C. Body, MBChB, MPH, Anna M. Booher, MD, Hans-Joachim Schaefers, MD, Rita K. Milewski, MD, PhD, Hector I. Michieleana, MD, Arturo Evangelista, MD, PhD, Philippe Pibarot, DVM, PhD, Patrick Mathieu, MD, Giuseppe Limongelli, MD, PhD, Prem S. Shekar, MD, Sary F. Aranki, MD, Andrea Ballotta, MD, Giuseppe Di Benedetto, MD, Natzi Sakalihasan, MD, PhD, Gianantonio Nappi, MD, Kim A. Eagle, MD, Joseph E. Bavaria, MD, Alessandro Frigola, MD, and Thoralf M. Sundt, MD, on behalf of the International Bicuspid Aortic Valve Consortium (BAVCon) Investigators
Valve sparing-root replacement with the reimplantation technique to increase the durability of bicuspid aortic valve repair

Laurent de Kerchove, MD, a Munir Boodhwani, MD, MMSC, d David Glineur, MD, a Michel Vandyck, MD, b Jean-Louis Vanoverschelde, MD, PhD, c Philippe Noirhomme, MD, a and Gebrine El Khoury, MD a

Group 1 (unmatched, n= 87) | Group 2 (unmatched, n= 74)
---|---
Definition: BAV repair without VAJ annuloplasty or with subcommissural annuloplasty (SCA) | Definition: BAV repair with circumferential VAJ annuloplasty
- No annuloplasty (cusp repair only) | 5 (6%)
- SCA | 48 (55%)
- Ascending aorta replacement | 4 (5%)
- Ascending aorta replacement + SCA | 13 (15%)
- Aortic root remodeling1 | 7 (8%)
- Aortic root remodeling1 + SCA | 10 (11%)
- Valve sparing reimplantation technique 2 | 74 (100%)

Freedom from recurrent aortic insufficiency greater than 2+
Concerns of post-BAV-repair calcification and stenosis?

- Awareness of the differences between the patient phenotypes (probably subtended by different genetic background)

- “Root phenotype”: association with AS very uncommon → Very low risk of evolution to calcific stenosis following BAV repair as long as performed in root phenotype patients?

Della Corte A et al., EJCTS 2007

Schneider U et al., JTCVS 2017
Need to re-configure commissural orientation?

Effect of Geometry on the Leaflet Stresses in Simulated Models of Congenital Bicuspid Aortic Valves

PAUL N. JERMIHOY,1 LU JIA,2 MICHAEL S. SACKS,3 ROBERT C. GORMAN,4 JOSEPH H. GORMAN III,5 and KRISHNAN B. CHANDRAN6

Valve Configuration Determines Long-Term Results After Repair of the Bicuspid Aortic Valve

Diana Aicher, MD; Takashi Kunihara, MD; Omar Abou Issa, MD; Brigitte Brittner, MD; Stefan Gräber, MD; Hans-Joachim Schäfers, MD

Circulation 2011
Morpho-functional features of the BAV

- Commissural orientation
- RL vs RN
- Presence and completeness of the raphe
- Indentation of the fused cusp free margin (“restrictive raphe”)
- Height of the false commissure
- Others?
## Morpho-functional features of the BAV

<table>
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<tr>
<th>Group 1: 120°-139° Asymmetric BAV</th>
<th>Group 2: 140°-159° Intermediate BAV</th>
<th>Group 3: 160°-180° Symmetric BAV</th>
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<tr>
<td>n=20</td>
<td>n=53</td>
<td>n=42</td>
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1. **Type of cusp fusion**  
   (R:right, N:non, L:left coronary cusp)  
   (Basal ring line)  
   - **Height of non-functional commiss.**  
   - **Length of fusion**  
   - **gH fused cusp**  
   - **gH non-fused cusp**  
   - **Ascending aorta**  
   - **Sino-tubular junction**  
   - **Sinus of Valsalva**  
   - **Muscular inclusion**  
   - **Aorto-ventricular junction**  

- **R/L 75%, R/N 20%, N/L 5%**  
- **18.4±5**  
- **8.3±3**  
- **18.6±2**  
- **129±5**  
- **21.2±3**  
- **37.5±10**  
- **34.3±6**  
- **39.8±5**  
- **26.6±4**  

- **R/L 87%, R/N 11%, N/L 2%**  
- **13.8±4**  
- **14.3±3**  
- **18.7±2**  
- **148±4**  
- **23.5±2**  
- **33.9±6**  
- **39.7±7**  
- **28±4**  

- **R/L 79%, R/N 21%, N/L 0%**  
- **8.2±6**  
- **21.1±2**  
- **18.3±4**  
- **168±8**  
- **24.2±3**  
- **35.3±7**  
- **39.9±6**  
- **28.3±4**

*De Kerchove L et al., EACTS 2017*
Conclusions

• As long as clinical and basic research elucidates more and more aspects of this disease (e.g. phenotypic heterogeneity), our surgical approach can improve (e.g. phenotypic stratification).

• In BAV repair, there is still space for improvement: optimization of indications (e.g. timing), patient selection (e.g. root phenotype patients), technical aspects (e.g. commissural reorientation)…

• In-depth understanding of the morpho-functional heterogeneity of the valve is expected to provide the basis for such an improvement.