Searching for early biomechanically-driven indexes of aortic remodeling: where are we at?

Emiliano Votta
Politecnico di Milano
Department of Electronics, Information and Bioengineering
Biomechanics Research Group

www.biomech.polimi.it
Speaker name: Emiliano Votta

- I do not have any potential conflict of interest
BAV: Aortopathy & Biomechanics

Fluid-dynamics

Magnitude Image

Phase Difference, Flow

Structural response

cine-sequence
High prevalence (20-84%) of aortic dilation in BAV-affected population.

[Evangelista et al., Heart, 2018]

Colocalization of high \textbf{wall shear stress (WSS)} and increased concentration of transforming growth factor TGF-β1 and activation of aortic wall matrix metalloproteinase (MMP)

[Guzzardi et al., JACC, 2015]

\textit{In vitro} stimulation (48 hours) of healthy porcine aortic tissue with BAV-related WSS histories caused an increase in the expression of MMPs involved in the degradation of the aortic wall tunica media

[Atkins et al., Biomech in Mech, 2014]
BAV: Aortopathy & Fluid dynamics

The American Association for Thoracic Surgery consensus guidelines on bicuspid aortic valve–related aortopathy: Executive summary

Michael A. Borger, MD, PhD, Paul W. M. Fedak, MD, PhD, Elizabeth H. Stephens, MD, PhD, Thomas G. Gleason, MD, Evaldas Girdauskas, MD, PhD, John S. Ikonomidis, MD, PhD, Ali Khoynehzad, MD, PhD, Samuel C. Siu, MD, Subodh Verma, MD, PhD, Michael D. Hope, MD, Duke E. Cameron, MD, Donald F. Hammer, MD, Joseph S. Coselli, MD, Marc R. Moon, MD, Thoralf M. Sundt, MD, Alex J. Barker, PhD, Michael Markl, PhD, Alessandro Della Corte, MD, PhD, Hector I. Michanela, MD, and John A. Elefteriades, MD

ABSTRACT

Bicuspid aortic valve disease is a common congenital cardiac disorder, being present in 1% to 2% of the general population. Associated aortopathy is a common finding in patients with bicuspid aortic valve disease, with thoracic aortic dilation noted in approximately 40% of patients in referral centers. Several previous consensus statements and guidelines have addressed the management of bicuspid aortic valve–associated aortopathy, but none focused entirely on this disease process. The current document is an executive summary of “The American Association for Thoracic Surgery Guidelines on Bicuspid Aortic Valve–Related Aortopathy.” All major aspects of bicuspid aortic valve aortopathy, including natural history, phenotypic expression, histology and molecular pathomechanisms, imaging, indications for surgery, surveillance, and follow-up, and recommendations for future research are contained within these guidelines. The current executive summary serves as a condensed version of the guidelines to provide clinicians with a current and comprehensive review of bicuspid aortic valve aortopathy and to guide the daily management of these complex patients. (J Thorac Cardiovasc Surg 2018;156:473-80)
4D flow MRI

Volumetric coverage + 3D velocity field + Time = 4D Flow

Anatomy

Blood velocity data

- $V_1$: Head-Foot
- $V_2$: Posterior-Anterior
- $V_3$: Right-Left

[Diyerfeldt et al., 2015, JCMR]
Assessing in vivo fluidynamic stimuli

Repeatable analysis protocol

3D anatomy

3D Velocity field
**Fluidynamic indexes**

Wall shear stress ($\overline{WSS}$) and related indexes (the most commonly assessed ones)

\[
\tau_{ij} = \frac{1}{2} \left( \frac{\partial v_i}{\partial x_j} + \frac{\partial v_j}{\partial x_i} \right)
\]

\[
T = \tau \cdot n
\]

\[
\overline{WSS} = n \times (T \times n)
\]

- Numerically (hence, non exactly) computed
- Sensitive to noise

**At best, errors by a factor of two affect results**

[Piatti et al., J Biomech, 2017]

Uncertainty on wall position and inward normal

\( \Delta x = \text{average voxel dimension} \)
WSS-related indexes

How strong is the drag force on the endothelium?

• Maximum wall shear stress ($\left| \overrightarrow{WSS} \right|_{\text{max}}$)
WSS-related indexes

How strong is the drag force on the endothelium?

• Maximum wall shear stress ($|\vec{WSS}|_{\text{max}}$)

How is this drag force aligned in space?

• Components along mutually orthogonal directions (axial and circumferential)
• Transverse WSS, i.e., WSS component orthogonal to the main flow direction
WSS-related indexes

How strong is the drag force on the endothelium?

• Maximum wall shear stress \(\left|\overrightarrow{WSS}\right|_{\text{max}}\)

How is this drag force aligned in space?

• Components along mutually orthogonal directions (axial and circumferential)
  • Transverse WSS, i.e., WSS component orthogonal to the main flow direction

How much do magnitude and direction of the drag force change in time?

• Oscillatory shear index (OSI) - measures the tendency of the WSS to change direction throughout the cardiac cycle
  • Relative residence time, similar to OSI
WSS-related indexes

Preliminary study on real subjects [Piatti et al., Frontiers in Physiol, 2017]

• Population:
  • 10 Healthy volunteers (age= 23±7)
  • 5 BAV patients (age=25±10; fusion RL:RN:LN=4:1:0; Aortic diameter = 24.2±2.7 mm Cardiac Output = 5.2 ± 1.0)
WSS-related indexes

Preliminary study on real subjects

• Population:
  • 10 Healthy volunteers (age= 23±7)
  • 5 BAV patients (age=25±10; fusion RL:RN:LN=4:1:0; Aortic diameter = 24.2±2.7 mm
    Cardiac Output = 5.2 ± 1.0)

• Tested hypotheses:
  • some of the WSS-related indexes reveal derangements in absence of aortic
dilation (tested based on 4D flow data analysis)
  • derangements, if any, may cause adverse aortic remodeling (tested by 3-year
    follow-up diameter measurements)
WSS-related indexes

Preliminary study on real subjects

Aortic wall reference system for 2D mapping

2D template definition

A: \( r(\hat{s}) = 0 \)

P: \( r(\hat{s}) = 0.5 \)

BrA

PA

LVOT

s = 0

s = 0.5

s = 1

L

R

s = 0

s = 1

5

6

7

8

1

2

3

4

A

R

P

L

A
WSS-related indexes

Preliminary study on real subjects: space distribution of indexes

Statistical heat maps for the Healthy Volunteers (HVs) group

10th percentile

50th percentile

90th percentile

BAV-specific heat maps
WSS-related indexes

Preliminary study on real subjects: patient specific areas of derangements

BAV01

BAV04

BAV05

Higher than HV 90th percentile
Lower than HV 10th percentile
Between HV 90th and 50th percentiles
Between HV 50th and 10th percentiles
WSS-related indexes

Preliminary study on real subjects: time course of indexes at hot spots

BAV05

SSS

ISO

HV distribution

BAV

Higher than HV 90th percentile
Lower than HV 10th percentile
Between HV 90th and 50th percentiles
Between HV 50th and 10th percentiles
WSS-related indexes

Preliminary study on real subjects: key findings

• Some indexes highlight greater (and notable!) derangements in BAV vs. HVs
  • Transverse WSS
  • Circumferential component of the WSS
  • OSI computed for the circumferential component of the WSS
  • Time course of WSS magnitude and orientation together is relevant

• These major derangements are observed prior to anatomical remodeling

  Possible causative relationship with remodeling

• No anatomical remodeling at 3-year follow up in these patients

High risk for of complications: 20 years after diagnosis, valve or cardiovascular surgery is required in 25% of patients. [Michelena et al., Circulation, 2008; Tzemos et al., JAMA, 2008]
WSS-related indexes

Our findings on WSS-related indexes were recently confirmed

• **4Dflow-based study on a large cohort of patients** (101 BAV patients, aortic diameter ≤ 45 mm, no severe valvular disease vs. 20 healthy subjects)

  • WSS magnitude lacks significance since its value is similar in controls and BAV
  • helical flow in BAV increases circumferential WSS
  • variation in WSS components may also influence the aortic morphotype

  [Rodríguez-Palomares et al., J Magn Res Imag, 2018]

• CFD study with 4Dflow-based boundary conditions

  • stronger impact of the BAV anatomy on circumferential WSS than on axial WSS
  • OSI reveals differences between BAV and healthy conditions only if computed for the single components and not for the WSS as a vector
  • a new potential marker is proposed: the Shear Magnitude and Directionality Index (SMDI)

  [Liu et al., Frontiers in Physiol, 2018]
WSS-related indexes

Final Remarks

• **Large cohorts of patients** undergoing 4Dflow acquisitions are needed and longitudinal follow-up studies are required
  
  • multi-center studies would be beneficial

• **The devil is in the detail**: small differences in the algorithms that compute WSS can lead to huge differences in WSS quantification
  
  • for different studies to be really comparable and for thresholds to be identified for risk assessment/stratification, these algorithms should be standardized

• **Need for consensus guidelines also for engineers and radiologists?**
My Partners in Crime

Francesco Sturla
Filippo Platti
Alberto Redaelli
Selene Pirola
Giovanni Rossini
Malenka Bissell
Alessandro Della Corte
BAV: Aortopathy & Fluid dynamics

- Inherent fibrillin 1 deficiency
- ECM matrix disruption
- Smooth muscle cells detachment
- Elevated aortic WSS generated by aberrant flow
- More severe ECM dysregulation
Fluidynamic indexes

Wall shear stress computation: a general and benchmarked method

• Volumetric WSS: properly computes trends over space, but not local values

[Piatti et al., J Biomech, 2017]
Fluidynamic indexes

Wall shear stress computation: a general and benchmarked method

• Volumetric WSS: properly computes trends over space, but not local values
• Local 2D WSS computation: improves local assessment

[Piatti et al., J Biomech, 2017]