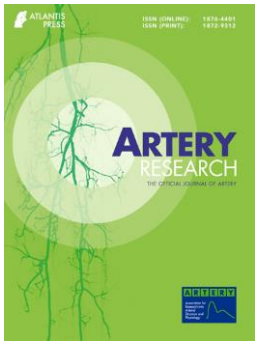

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3.1: INTEGRATED CENTRAL PRESSURE-STIFFNESS RISK SCORE: A NEW OPPORTUNITY FOR CARDIOVASCULAR RISK STRATIFICATION. FIRST RESULTS ON CHRONIC KIDNEY DISEASE PATIENTS

János Nemcsik, Orsolya Cseprekál, Ádám Tabák, Dóra Batta, József Egresits, István Kiss, András Tislér

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significantly and independently associated with MAP ($\beta = 0.008$, 95% CI 0.003, 0.013, $p = 0.003$). There was a significant difference in the strength of association between the ab-ratio and MAP between patients with disease and healthy individuals ($z > 2.2$, $p < 0.05$ for all).
Conclusion: Although ab-ratio is purported to be a risk marker that is independent of BP, this was observed only among patient populations, and not in healthy individuals. Therefore, the ab-ratio is influenced by disease status and may have restricted value as a BP-independent risk marker.

2.7
THE GUT-DERIVED METABOLITE TRIMETHYLAMINE N-OXIDE INDUCES LARGE ELASTIC ARTERY STIFFENING AND ENDOTHELIAL DYSFUNCTION IN YOUNG MICE

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The gut microbiome, an emerging mediator of host physiological function, is adversely altered by aging and many diseases, termed "gut dysbiosis." One consequence of gut dysbiosis is elevated circulating levels of the gut-derived metabolite trimethylamine N-oxide (TMAO), which has been directly linked to cardiovascular (CV) risk, including the development of atherosclerosis. However, it is unknown whether TMAO mediates arterial dysfunction that precedes the onset of clinical disease, and if so, the underlying mechanisms.
Purpose: To determine whether TMAO independently induces large elastic artery stiffening and endothelial dysfunction via increased superoxide-related oxidative stress.
Method: Twenty young (6 mo) male C57BL/6 mice were fed a chemically-defined choline (0.08–0.09%) diet supplemented without (Control; $N = 9$) or with ($N = 11$) 0.12% TMAO for 6 months. Arterial stiffness was assessed as aortic pulse wave velocity (aPWV). Endothelial function was evaluated *ex vivo* as carotid artery endothelium-dependent dilation (EDD) to increasing doses of acetylcholine (10^{-9} to 10^{-4}M) in the absence or presence of the superoxide dismutase mimetic TEMPOL.
Results: TMAO increased aPWV (Control: 392 ± 20 vs. TMAO: 483 ± 32 cm/sec, $p = 0.04$) and impaired EDD (peak dilation, Control: 93.7 ± 3.2 vs. TMAO: 79.9 ± 3.4%, $p = 0.01$).
Suppression of oxidative stress with TEMPOL restored EDD in TMAO-treated animals (peak dilation: 92.1 ± 4.7%, $p = 0.46$ vs. Control).
Conclusions: TMAO independently induces large elastic artery stiffening and endothelial dysfunction in mice. Dysfunction appears to occur through increases in oxidative stress. These data may explain, at least in part, why TMAO increases CV risk and provide a potential target for prevention/treatment of arterial dysfunction.
Supported by R01 HL134887 & T32 HL007822.

2.8
INVASIVE STUDY FOR TESTING NON-INVASIVE METHODS OF AORTIC PRESSURE ESTIMATION

Andrea Guala [1], F. Tosello [2], D. Leone [2], L. Sabia [2], F. D'Ascenzo [3], T. Crea [2], C. Moretti [3], F. Gaita [3], F. Veglio [2], L. Ridolfi [4], A. Milan [2]
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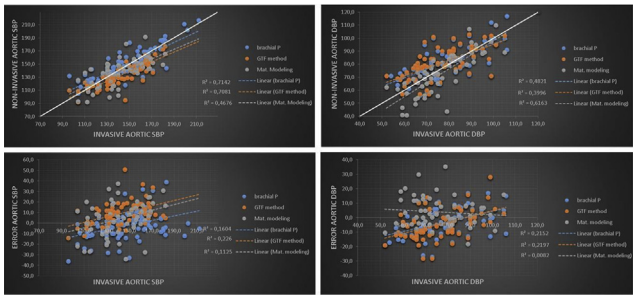
Purpose: Aortic blood pressure has a superior prognostic value with respect to the brachial pressure [1]. Nonetheless, the low efficacy of the most used non-invasive methods (i.e., approaches based on the generalized transfer function (GTF)) may hamper the detection of this superiority in population studies [2]. In this sense, low-order, patient-specific whole-body mathematical models might help to bridge brachial to aortic pressure waveforms. We aimed to compare (i) GTF, (ii) a patient-specific 1D-0D mathematical model, and (iii) brachial blood pressure in the estimation of invasive aortic pressure measured through catheter.
Method: One-hundred patients referred to diagnostic coronary angiography were included in this study. Brachial pressure was measured with a validated automatic oscillometric device simultaneously to invasive aortic pressure, which was measured with a calibrated fluid-filled catheter. End-systolic and end-diastolic left ventricular volumes, carotid-femoral pulse wave velocity and tonometric radial waveform were measured immediately prior to the invasive procedure and were used to set GTF and the mathematical model.
Results: Oscillometric brachial pressure overestimated both systolic (2.4 ± 12.6 mmHg, $R^2 = 0.71$) and diastolic (3.7 ± 9.8 mmHg, $R^2 = 0.48$) aortic pressure. GTF method underestimated systolic (9.4 ± 11 mmHg, $R^2 = 0.71$) and overestimated diastolic (4.5 ± 10.2 mmHg, $R^2 = 0.4$) aortic pressure. Mathematical model underestimated both systolic (4 ± 16.5 mmHg, $R^2 = 0.47$) and diastolic (3.9 ± 10.4 mmHg, $R^2 = 0.62$) aortic pressure. Brachial pressure and GTF methods presented trends toward systolic and diastolic pressure overestimation for higher aortic pressure, while mathematical modeling not.



Conclusions: Systolic and diastolic oscillometric brachial pressures give a better predictor of aortic pressure extremes with respect to both GTF- and mathematical model-based methods.
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Oral session III – Models and Technology
3.1
INTEGRATED CENTRAL PRESSURE-STIFFNESS RISK SCORE: A NEW OPPORTUNITY FOR CARDIOVASCULAR RISK STRATIFICATION. FIRST RESULTS ON CHRONIC KIDNEY DISEASE PATIENTS

János Nemcsik [1], Orsolya Cseprekál [2], Ádám Tabák [3], Dóra Batta [1], József Egresits [4], István Kiss [5], András Tislér [3]
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Background: The evaluation of arterial stiffness and central haemodynamics represent a new tool of cardiovascular (CV) risk stratification. Our aim was to create an integrated central pressure-stiffness risk score (ICPS score) which incorporate the predictive potential of identical parameters.
Methods: 100 chronic kidney disease patients on conservative therapy (CKD 1–5) were involved in our study. Pulse wave velocity (PWV), augmentation index (Aix), central systolic blood pressure (csys) and central pulse pressure (cPP) were measured.
Patients were followed for 59.7 months and CV morbidity and mortality were registered. Patients were classified into tertiles based on their PWV, Aix, csys and cPP values. After the analysis of the predictive values of the tertiles of the identical parameters, patients were scored. One score was given, when a patient had a third tertile value of PWV, csys or cPP or a second or third tertile value of Aix. Then the CV outcome was analyzed with Cox regression analysis of the groups of patients with different scores.
Results: During follow-up 37 CV events occurred. Compared with the zero-point group ($n = 21$), the one-point group ($n = 25$) did not have significantly

increased odds ratio (OR) for CV events (OR: 1.10; 95% confidence interval (CI): 0.27—4.44), but the risk has been significantly elevated in the two-point group (n = 29, OR: 4.59, CI: 1.39—15.22) and it increased further in the three-point group (n = 16, OR: 9.03, CI: 2.22—36.65), as well as in the four-point group (n = 9, OR: 11.84, CI: 2.52—55.64).
Conclusion: The ICPS score can help in the identification of chronic kidney disease patients with high CV risk.

3.2
ASCENDING AND DESCENDING AORTA PULSE WAVE VELOCITY AND DISTENSIBILITY IN BICUSPID AORTIC VALVE PATIENTS

Andrea Guala [1], Jose Rodriguez-Palomares [2], Lydia Dux-Santoy [2], Gisela Teixido-Tura [2], Giuliana Maldonado [2], Nicolas Villalva [2], Filipa Valente [2], Laura Galian [2], Marina Huguet [1], Laura Gutierrez [1], Teresa Gonzalez [1], Ruben Fernandez [1], Augusto Sao-Aviles [1], David Garcia-Dorado [1], Artur Evangelista [2]
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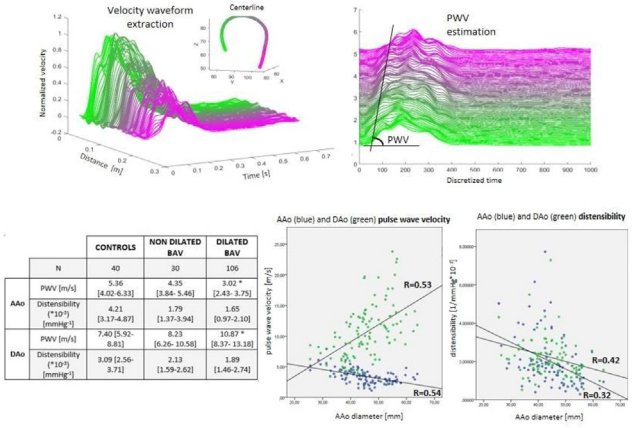
Purpose: Bicuspid aortic valve (BAV) is a cardiac congenital disease associated with ascending aorta (AAo) dilation. The study of the impact of aortic biomechanics in this population has been limited by technical difficulties. Contrasting results have been reported for distensibility while studies including regional pulse wave velocity (PWV) are still lacking. Using 4D-flow MRI, we assessed AAo and descending aortic (DAo) biomechanical properties and determined their association in BAV aortopathy.
Methods: One-hundred thirty-six BAV patients with no severe valvular disease and 40 healthy volunteers were recruited. The protocol included a 4D-flow acquisition and a set of 2D CINE PC-MRI at 1.5 T. Aortic 3D geometry was reconstructed from 4D-flow-derived angiography and at least 100 analysis planes were identified in the thoracic aorta. Transit time was calculated on the velocity upslope through wavelet analysis [1]. CINE PC-MRI were used to compute distensibility. Statistical significance is reported corrected for confounding factors.
Results: Non-dilated BAV and controls have similar AAo and DAo PWV and distensibility. Dilated patients presented lower AAo PWV and higher DAo PWV compared to non-dilated ($p < 0.001$ and $p = 0.017$, respectively). Distensibility did not differentiate dilated from non-dilated patients and presented lower association with dilation severity (see Figure).



		CONTROLS	NON DILATED BAV	DILATED BAV
	N	40	30	106
AAo	PWV [m/s]	5.36 [4.02-6.33]	4.35 [3.84- 5.46]	3.02 * [2.43- 3.75]
AAo	Distensibility (*10⁻³) [mmHg⁻¹]	4.21 [3.17-4.87]	1.79 [1.37-3.94]	1.65 [0.97-2.10]
DAo	PWV [m/s]	7.40 [5.92- 8.81]	8.23 [6.26- 10.58]	10.87 * [8.37- 13.18]
DAo	Distensibility (*10⁻³) [mmHg⁻¹]	3.09 [2.56- 3.71]	2.13 [1.59-2.62]	1.89 [1.46-2.74]

Conclusions: Confirming for the first time previous findings in abdominal aorta aneurysm and fluid-mechanics theory, AAo PWV is reduced in aneurysmatic BAV patients. BAV aortopathy is related to a stiffer DAo. Regional PWV outperforms distensibility as a marker of local aortic biomechanics. These data exclude congenital aortic wall pathology related to BAV
Reference
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3.3
ASSESSMENT OF AORTIC MORPHOLOGY IN A BICUSPID AORTIC VALVE POPULATION

Froso Sophocleous [1], Benedetta Biffi [2], Elena Giulia Milano [3,4], Cha Rajakaruna [3,4], Massimo Caputo [3,4], Costanza Emanueli [1,5], Chiara Bucciarelli-Ducci [3,4], Tom Gaunt [1], Silvia Schievano [2], Giovanni Biglino [1]
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Background: Bicuspid aortic valve (BAV) is a congenital heart disease associated with aortic wall abnormalities and co-existing with other congenital defects (e.g. aortic coarctation). This study aimed to explore aortic shape features in a BAV population, identifying sub-groups with different aortic morphologies.
Methods: Single-centre retrospective study. Patients with an MRI scan and native BAV diagnosis between 2011 and 16 were studied (n = 525); those with a 3D MRI dataset were included for shape analysis (n = 108, 64% males, 38 ± 16.5 years). MRI-derived 3D aortic reconstructions were analysed using a statistical shape modelling framework [1]. A mean aortic shape ('template') was computed and shape deformations were correlated with demographic, volumetric and functional data.
Results: Aortic coarctation (n = 71) was significantly associated with a more gothic arch ($p = 0.02$), more tubular ascending aorta and descending aorta dilation ($p < 0.001$). Also, smaller aortic size in patients with coarctation was associated with the younger age of this group (33 ± 13 vs. 47 ± 19, $p < 0.001$), given the overall relationship between aortic size and age ($p < 0.001$). Aortic stenosis

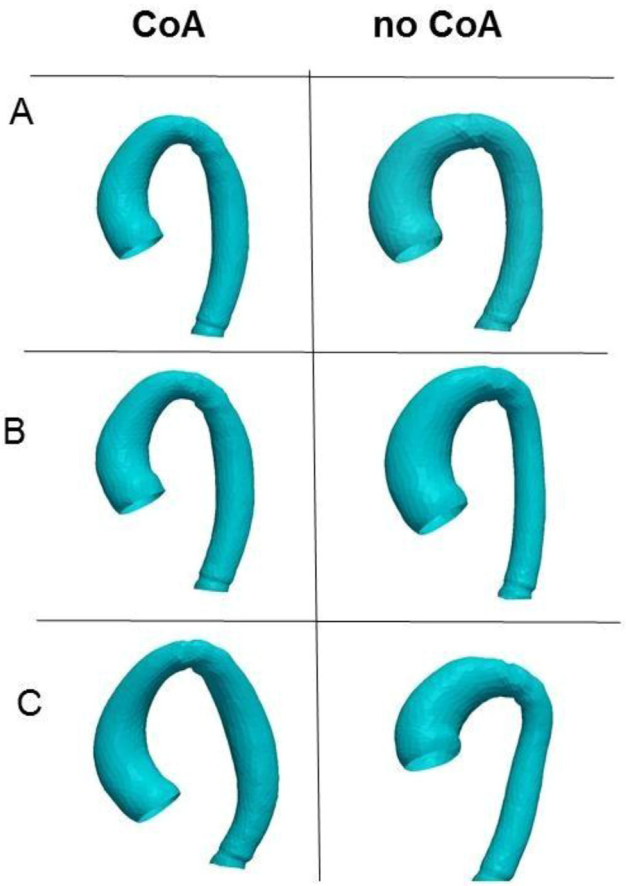

Figure 1 Shape features of coarctation (CoA) vs no CoA in BAV population. A) The 'template' (or average shape) for patients with CoA on the left, and patients without CoA on the right. B) Patients with CoA have tubular ascending aortas (left), while patients without CoA tend to have increased ascending aortic dilation (right). C) Patients with CoA have more a gothic arch (left), whereas patients without CoA have a rounder arch (right).