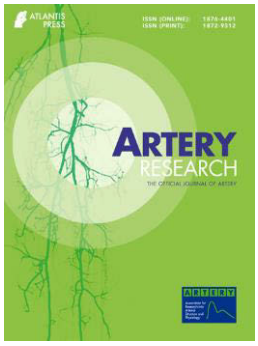

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# 2.7: THE GUT-DERIVED METABOLITE TRIMETHYLAMINE N-OXIDE INDUCES LARGE ELASTIC ARTERY STIFFENING AND ENDOTHELIAL DYSFUNCTION IN YOUNG MICE

Vienna Brunt, Rachel Gioscia-Ryan, Zachary Sapinsley, Melanie Zigler, James Richey, Douglas Seals

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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: $392 \pm 20$ vs. TMAO: $483 \pm 32$ cm/sec, $p = 0.04$) and impaired EDD (peak dilation, Control: $93.7 \pm 3.2$ vs. TMAO: $79.9 \pm 3.4\%$, $p = 0.01$).
Suppression of oxidative stress with TEMPOL restored EDD in TMAO-treated animals (peak dilation: $92.1 \pm 4.7\%$, $p = 0.46$ 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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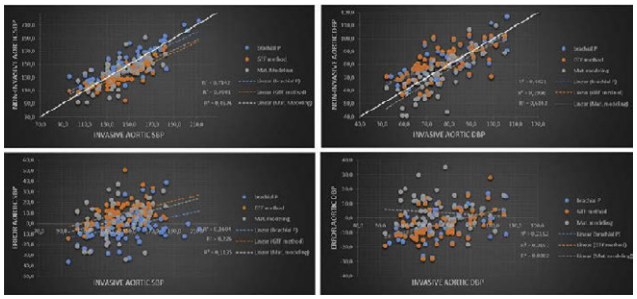
**Purpose:** Aortic blood pressure has a superior prognostic value with respect to the brachial pressure [1]. Nonetheless, the low efficacy of the most used non-invasive methods (i.e., approaches based on the generalized transfer function (GTF)) may hamper the detection of this superiority in population 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 ($2.4 \pm 12.6$ mmHg, $R^2 = 0.71$) and diastolic ($3.7 \pm 9.8$ mmHg, $R^2 = 0.48$) aortic pressure. GTF method underestimated systolic ($9.4 \pm 11$ mmHg, $R^2 = 0.71$) and overestimated diastolic ($4.5 \pm 10.2$ mmHg, $R^2 = 0.4$) aortic pressure. Mathematical model underestimated both systolic ($4 \pm 16.5$ mmHg, $R^2 = 0.47$) and diastolic ($3.9 \pm 10.4$ 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