



## Artery Research

ISSN (Online): 1876-4401

ISSN (Print): 1872-9312

Journal Home Page: <https://www.atlantis-press.com/journals/artres>

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### **P4.03: ORAL LYCOPENE SUPPLEMENTATION IMPROVES ENDOTHELIAL FUNCTION IN PATIENTS WITH CARDIOVASCULAR DISEASE: A RANDOMISED CONTROLLED TRIAL**

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**To cite this article:** P.R. Gajendragadkar, A. Hubsch, K. Mäki-Petäjä, M. Serg, I.B. Wilkinson, J. Cheriyan (2012) P4.03: ORAL LYCOPENE SUPPLEMENTATION IMPROVES ENDOTHELIAL FUNCTION IN PATIENTS WITH CARDIOVASCULAR DISEASE: A RANDOMISED CONTROLLED TRIAL, Artery Research6:4, 183–184, DOI: <https://doi.org/10.1016/j.artres.2012.09.151>

**To link to this article:** <https://doi.org/10.1016/j.artres.2012.09.151>

Published online: 21 December 2019

Modulation of venous capacitance may be an important effect of baroreceptor activation in hypertension and heart failure.

\* Wright CI *et al.*, *Can J Cardiol* 2004; 20:1127.

### P3.22

#### EFFECT OF TISSUE TRANSGLUTAMINASE (TG2) ON CARDIAC AND VASCULAR FUNCTION IN YOUNG TG2 KNOCKOUT MICE

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**Background:** Structural changes of the arterial wall are associated with increased arterial stiffness and hypertension. Tissue transglutaminase (TG2), an enzyme ubiquitously expressed in the vasculature, forms stable crosslinks between extracellular matrix proteins, including collagen. Due to its role in small artery remodelling, calcification and atherosclerosis, TG2 has been implicated in cardiovascular disease. The aim of this study was to compare parameters of cardiac and vascular function between TG2 knockout mice and wild-type littermates.

**Methods:** Male TG2<sup>-/-</sup> (n=4) and TG2<sup>+/+</sup> (n=4) mice, aged 16 weeks, were anaesthetized with isoflurane. Aortic pressure was recorded with a 1.2F high fidelity sensor via the left carotid artery. Mean and pulse pressure and augmentation index were determined from the pressure signal; baroreflex sensitivity computed from directional changes of systolic pressure and interbeat interval (ECG), and aortic pulse transit time from the R wave to foot of the aortic pulse. Ventricular weight was expressed as percentage of total body weight.

**Results:** TG2<sup>-/-</sup> mice showed significant differences only in relative ventricular weight compared to wild-type controls (Table).

| Table                            | Cardiovascular parameters in TG2 <sup>-/-</sup> and wild-type mice (Mean ± SEM) |                    |
|----------------------------------|---------------------------------------------------------------------------------|--------------------|
| Parameter                        | Wild-type                                                                       | TG2 <sup>-/-</sup> |
| Heart rate (bpm)                 | 619 ± 31                                                                        | 639 ± 26           |
| Ventricle/body weight (%)        | 0.39 ± 0.016                                                                    | 0.44 ± 0.011*      |
| Mean arterial pressure (mmHg)    | 76.5 ± 1.1                                                                      | 72.1 ± 4.2         |
| Pulse pressure (mmHg)            | 30.4 ± 0.40                                                                     | 28.1 ± 1.1         |
| Augmentation index (%)           | 20.0 ± 1.9                                                                      | 18.0 ± 1.8         |
| Baroreflex sensitivity (ms/mmHg) | 2.04 ± 0.72                                                                     | 2.17 ± 0.55        |
| ECG - aortic pulse delay (ms)    | 15.43 ± 0.71                                                                    | 14.80 ± 1.9        |

\*p<0.05

**Conclusion:** Although findings suggest a tendency for increased ventricular mass, TG2 does not influence other baseline cardiovascular parameters in young healthy mice. This is consistent with TG2 activity, which is modulated by Ca<sup>2+</sup> and endothelial nitric oxide, being generally increased in inflammation and ageing. However, this study lays the ground work for future experiments in which inflammation or endothelial dysfunction will be induced, whereby TG2<sup>-/-</sup> mice would be expected to be protected from associated increase in vascular dysfunction and stiffness.

## P4 – Clinical Science

### P4.01

#### PROXIMAL AND DISTAL AORTIC STIFFNESS AND CARDIAC FUNCTION IN YOUNG WOMEN

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**Introduction:** Diabetes and Hypertension affect cardiovascular structure and function. We investigated the relationship between large artery

structure (ascending aortic intima-medial thickness -aIMT), stiffness (ascending aortic distensibility-AAD & aortic pulse wave velocity-aPWV) and other cardiac structure and functional parameters by transthoracic echocardiogram (TTE) in a group of young pre-menopausal women without any cardiac disorder.

**Patients and Methods:** 83 women (age 35.8 years, 95% CI 34.7-36.8) underwent anthropometric, biochemical assessments, TTE and aPWV measurements. The aIMT was measured by 2-D mode by parasternal long axis view. AAD was computed using measurements of aortic root diameter in systole and diastole and aPWV by Doppler USS technique over descending aorta and thoraco-abdominal aorta between the origin of left subclavian artery and the bifurcation of the aorta.

**Results:** There was correlation between LV-Isovolumic relaxation time and AAD (r=0.336; p=0.03) but not with aPWV. There was no relation between LV posterior wall thickness and aIMT. After adjustment for age, body mass index, smoking history, day in menstrual cycle, systolic velocity time integral and total cholesterol only diastolic blood pressure was independently related to AAD (β: -0.18; 95% CI: -0.029 to -0.007; p=0.001) and to aPWV (β: 0.082; 0.027 to 0.138; p=0.004). Fasting plasma glucose influenced AAD (β: -0.212; -0.407 to -0.018; p=0.033) but not aPWV.

**Conclusion:** In young women, without overt diabetes, hypertension or pre-existing cardiac disease, proximal but not distal aortic stiffness was related to LV stiffness, in part influenced by BP, while glycaemia influenced only the proximal aortic stiffness independent of LV systolic function.

### P4.02

#### ASSESSING VENTRICULAR-VASCULAR INTERACTIONS NON-INVASIVELY IN HEALTHY ADOLESCENTS

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Withdrawn by the author.

### P4.03

#### ORAL LYCOPENE SUPPLEMENTATION IMPROVES ENDOTHELIAL FUNCTION IN PATIENTS WITH CARDIOVASCULAR DISEASE: A RANDOMISED CONTROLLED TRIAL

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**Introduction:** Lycopene is a potent antioxidant and carotenoid in the 'Mediterranean diet'. Plasma and adipose lycopene concentrations have previously been inversely correlated with cardiovascular disease (CVD) risk. We hypothesised that a standardised preparation of lycopene would improve endothelial function.

**Methods:** 36 healthy volunteers (HV) and 36 stable CVD patients on statins were randomised unequally (2:1) to either 7mg lycopene or placebo daily for 2 months (NCT01100385). Forearm blood flow responses to intra-arterial infusions of acetylcholine (endothelium-dependent vasodilatation,EDV); sodium nitroprusside (endothelium-independent vasodilatation,EIDV); and N<sup>G</sup>-monomethyl-L-arginine (measuring basal nitric oxide,NO) were measured using venous plethysmography.

**Results:** At baseline, both groups were similar in age, BP and hs-CRP but the CVD group had a lower LDL (2.4 ±0.6 vs. 3.6 ±0.9mmol/L, P<0.001). The CVD group had impaired EDV to ACh compared with HV (30% lower; 95%CI: -45, -10, P=0.008). Lycopene improved EDV in CVD patients by 53% (95%CI: +9, +93, P=0.03 vs. placebo) independent of changes in EIDV or basal NO. Lycopene did not change EIDV, EDV or basal NO in HV. Home blood pressure, LDL, HDL and hs-CRP levels were unchanged in both groups. A post-hoc analysis demonstrated that lycopene treatment improved EDV in CVD patients towards HV levels at baseline (3% lower; 95% CI: -30, +30, P=0.85), suggesting normalization of vascular function.

**Conclusion:** Lycopene supplementation improves endothelial function in CVD patients but not HV, and may require further investigation in larger outcome studies.