

Conference Abstract

YI 2.2 Spontaneous Cardiovascular Ageing of C57BL6 Mice Results in the Development of Aortic Stiffness Prior to Peripheral Blood Pressure Alterations

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Keywords

Arterial stiffness
 ageing
 aorta

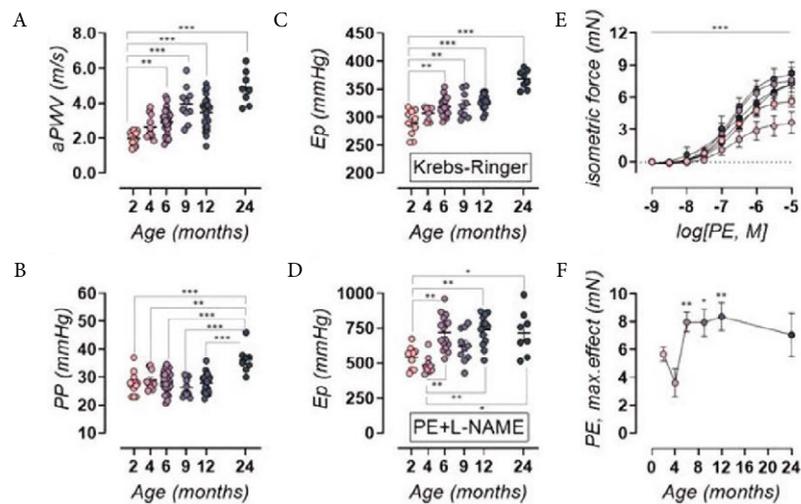
ABSTRACT

Background: Although generally assumed to be an adaptive response to increased blood pressure (BP), arterial stiffness is now recognized as an independent predictor of cardiovascular (CV) events [1]. Moreover it precedes hypertension in at least two mouse models [2,3]. Therefore, the present study aims to investigate the temporal development of aortic stiffening and peripheral blood pressure (BP) alterations in spontaneously ageing mice.

Methods: A longitudinal cardiovascular characterization of spontaneously ageing C57Bl6 mice (2, 4, 6, 9, 12 and 24-month old) (male, $n > 8$) was performed. This includes *in vivo* analysis of peripheral BP (Coda) and aortic pulse wave velocity (aPWV, Vevo2100), combined with *ex vivo* aortic studies of isometric reactivity (organ baths) and aortic stiffness measurements (Peterson modulus, E_p) in the Rodent Oscillatory Tension set-up for Arterial Compliance (ROTSAC).

Results: *In vivo* and *ex vivo* characterisation confirms that aortic stiffness precedes peripheral BP alterations in spontaneously ageing C57Bl6 mice, with significantly increased aPWV from 6 months of age (Figure A), whereas peripheral BP measurement only shows elevated pulse pressure in 24-month-old mice (30% increase vs. all other ages, Figure B). *Ex vivo* investigation of the thoracic aorta further reveals that the aortic stiffening is both contraction-independent (Figure C) and dependent (Figure D), since older mice display increased contractions to phenylephrine (PE) (Figure E and F).

Conclusion: Spontaneously ageing C57Bl6 mice present with significant aortic stiffness by 6-months of age, which is both contraction-dependent and independent in origin. Aortic stiffness thereby precedes the development of peripheral BP alterations by 18 months.



Significantly increased aPWV after 6-months (A) and increased peripheral pulse pressure after 18-months (B)
 Isobaric *ex vivo* aortic stiffness in uncontracted (Krebs-Ringer, C) and maximally contracted (PE+L-NAME, D) aortic rings
 Heightened contractions using a PE dose-response curve of *ex vivo* aortic rings (E) and its maximal effect (F).

Figure

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REFERENCES

- [1] Mattace-Raso FUS, van der Cammen TJ, Hofman A, van Popele NM, Bos ML, Schalekamp MA, et al. Arterial stiffness and risk of coronary heart disease and stroke: the Rotterdam Study. *Circulation* 2006;113:657–63.
- [2] Le VP, Knutsen RH, Mecham RP, Wagenseil JE. Decreased aortic diameter and compliance precedes blood pressure increases in postnatal development of elastin-insufficient mice. *Am J Physiol Heart Circ Physiol* 2011;301:H221–H9.
- [3] Weisbrod RM, Shiang T, Al Sayah L, Fry JL, Bajpai S, Reinhart-King CA, et al. Arterial stiffening precedes systolic hypertension in diet-induced obesity. *Hypertension* 2013;62:1105–10.

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