Artery Research
Vol. **25(S1)**; 2019, *pp.* S8–S9
DOI: https://doi.org/10.2991/artres.k.191224.007; ISSN 1872-9312; eISSN 1876-4401
https://www.atlantis-press.com/journals/artres

2.2 Modest Region-Specific, Sex-Independent Aortic Remodelling when Hypertension is Superimposed on Aging

Bart Spronck[1,2,*], Jacopo Ferruzzi[1], Alexander W. Caulk[1], Sae-Il Murtada[1], Jay D. Humphrey[1,3]

[1]*Yale University, New Haven, CT, USA*
[2]*Maastricht University, Maastricht, The Netherlands*
[3]*Yale School of Medicine, New Haven, CT, USA*

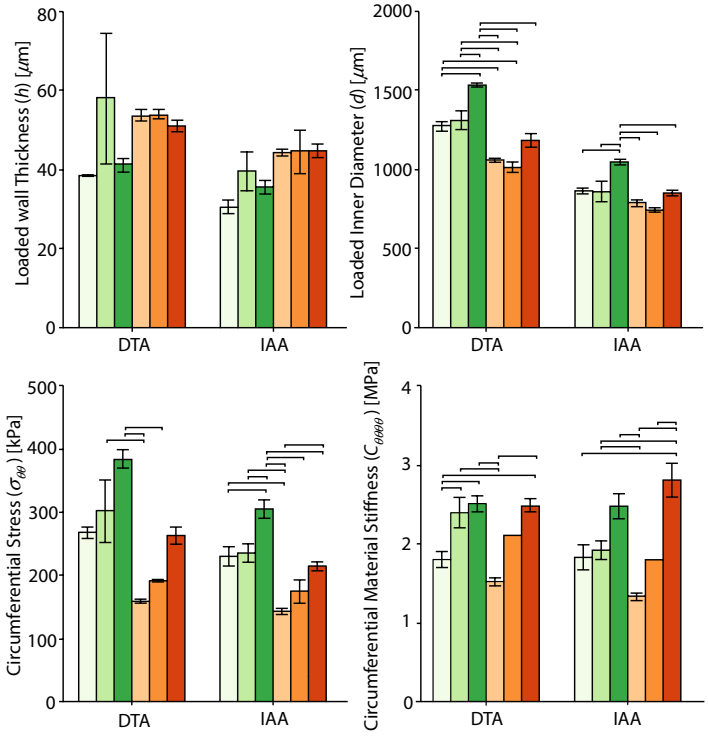
ABSTRACT

Background: Aging and hypertension often co-occur, which complicates distinguishing their biomechanical effects on arteries clinically. While aortic elastin (half-life ~70 years) is reduced in human aging, in mouse aging (lifespan ~2 years) it remains mostly intact. Knock-out of elastin-associated glycoprotein fibulin-5 (*Fbln5*$^{-/-}$) in mice however yields a biomechanical phenotype that resembles human aging.

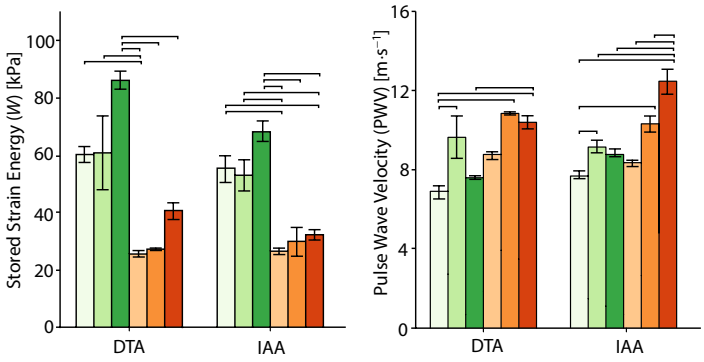
Methods: Adult male and female *Fbln5*$^{+/+}$ and *Fbln5*$^{-/-}$ mice were studied under three conditions: untreated, after 14-day 490 ng/kg/min angiotensin-II infusion (AngII), and after 13 weeks on 8%-NaCl chow + 3 g/L L-NAME drinking water (L-NAME-NaCl). After tail-cuff blood pressure (BP) measurement and euthanasia, descending thoracic (DTA) and infrarenal abdominal (IAA) aortas were dissected and tested using a computer-controlled biaxial testing device.

Results: Salt+L-NAME led to adaptive remodelling (circumferential stress homeostasis) and maladaptive remodelling (lack thereof) in the IAA and DTA, respectively (figure, males), while AngII caused luminal dilatation but little remodelling of the wall. Effects of aging (*Fbln5*$^{-/-}$) were more dramatic than those due to induced hypertension. Consequently, superimposing hypertension on aging led to modest additional changes in luminal radius and wall thickness, though increased stress and stiffness metrics due to increased pressure loading of the wall [3] Trends in females were similar to those in males.

Conclusions: Effects of hypertension on aortic remodelling are modest when superimposed on aging in mice. These findings are consistent with general observations in humans [4,5], though separated here for the first time in a rodent model characterized by a severe loss of elastic fiber integrity similar to that found in the aged human aorta.



*Corresponding author. Email: bart.spronck@yale.edu



Male data. h, d, $\sigma_{\theta\theta}$, W, and $C_{\theta\theta\theta\theta}$ calculated for SBP; PWV calculated using Bramwell-Hill equation for SBP/DBP. Bars and whiskers indicate mean ± standard error, overbars indicate $p<0.05$; ANOVA followed by Tukey's test.

***Fbln5*$^{+/+}$ groups**	SBP/DBP	***Fbln5*$^{-/-}$ groups**	SBP/DBP
Untreated (*n*=5)	120/84	**Untreated (*n*=5)**	121/85
L-NAME-NaCl (*n*=9)	160/118	**L-NAME-NaCl (*n*=2)**	152/110
AngII (*n*=5)	153/110	**AngII (*n*=5)**	168/120

SBP/DBP: systolic and diastolic blood pressures [mmHg].

REFERENCES

[1] Ferruzzi J, Bersi MR, Uman S, Yanagisawa H, Humphrey JD. Decreased elastic energy storage, not increased material stiffness, characterizes central artery dysfunction in fibulin-5 deficiency independent of sex. J Biomech Eng 2015;137:031007.

[2] Ferruzzi J, Bersi MR, Humphrey JD. Biomechanical phenotyping of central arteries in health and disease: advantages of and methods for murine models. Ann Biomed Eng 2013;41:1311–30.

[3] Spronck B, Heusinkveld MH, Vanmolkot FH, Roodt JO, Hermeling E, Delhaas T, et al. Pressure-dependence of arterial stiffness: potential clinical implications. J Hypertens 2015;33:330–8.

[4] Benetos A, Laurent S, Hoeks AP, Boutouyrie PH, Safar ME. Arterial alterations with aging and high blood pressure. A noninvasive study of carotid and femoral arteries. Arterioscler Thromb 1993;13:90–7.

[5] Bussy C, Boutouyrie P, Lacolley P, Challande P, Laurent S. Intrinsic stiffness of the carotid arterial wall material in essential hypertensives. Hypertension 2000;35:1049–54.