

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

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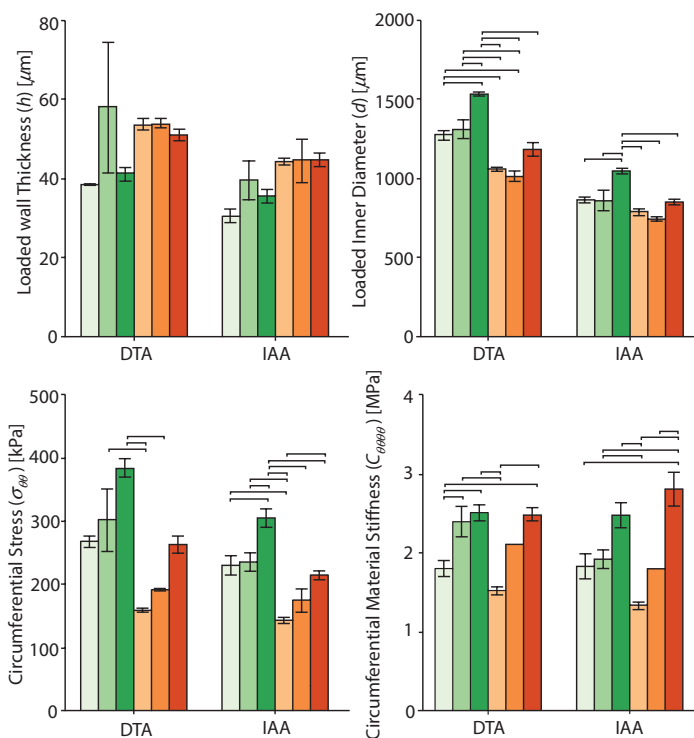
ABSTRACT

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.

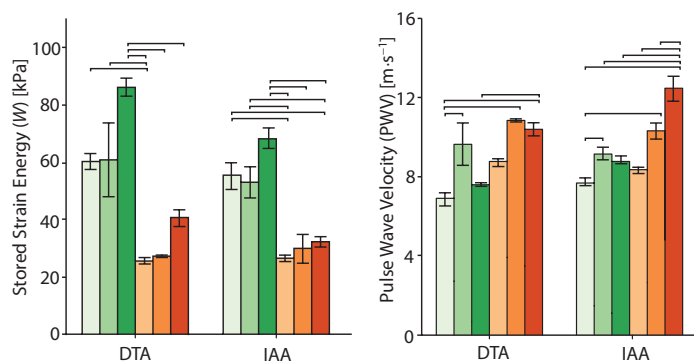
Methods: Adult male and female *Fbln5*^{+/+} and *Fbln5*^{-/-} mice were studied under three conditions: untreated, after 14-day 490 ng/kg/min angiotensin-II infusion (AngII), and after 13 weeks on 8%-NaCl chow + 3 g/L L-NAME drinking water (L-NAME-NaCl). After tail-cuff blood pressure (BP) measurement 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.



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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 \pm standard error, overbars indicate $p < 0.05$; ANOVA followed by Tukey's test.

<i>Fbln5</i> ^{+/+} groups	SBP/DBP	<i>Fbln5</i> ^{-/-} 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].

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