VASCULAR DYSFUNCTION IN HYPOSPADIAS

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INTRODUCTION

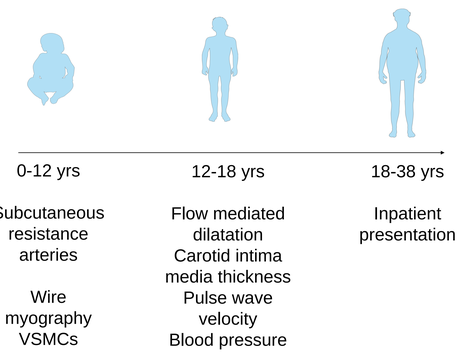
Hypogonadism has been associated with cardiovascular disease. However, little is known about the cardiovascular impact of hypogonadism during development. Using hypospadias as a surrogate of hypogonadism, we investigated whether hypospadias is associated with vascular dysfunction during childhood and whether it is a risk factor for adult cardiovascular disease.

AIM

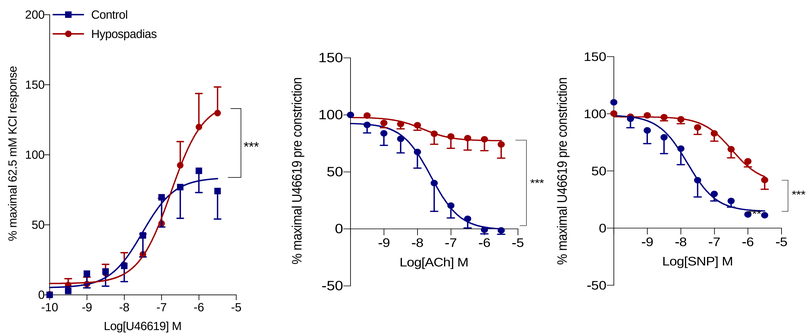
To investigate the association between hypospadias, as a surrogate for early onset hypogonadism and cardiovascular dysfunction across the lifespan.

HYPOTHESIS:
Boys with hypospadias exhibit vascular dysfunction and evidence of impaired cardiovascular outcomes in adolescence and adulthood.

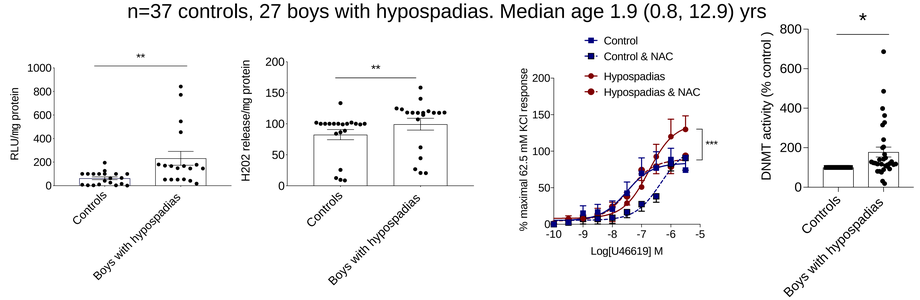
METHODS



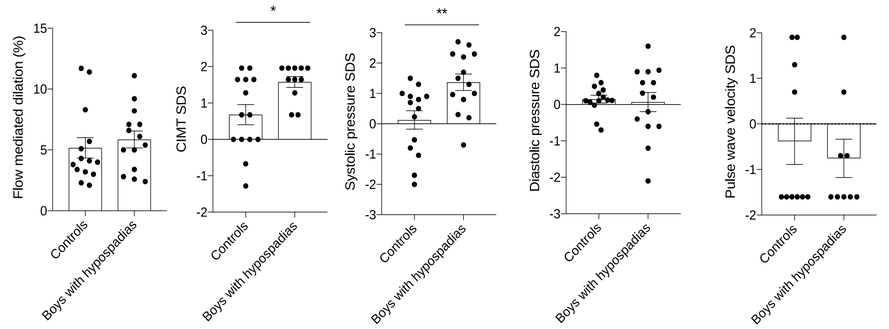
RESULTS



Resistance arteries from boys with hypospadias demonstrate increased U46619-induced contraction and reduced endothelial-dependent and endothelial-independent vasodilatation.
n=37 controls, 27 boys with hypospadias. Median age 1.9 (0.8, 12.9) yrs



The vascular dysfunction was mediated by increased reactive oxygen species (ROS) generation and associated with epigenetic alterations.
n=37 controls, 27 boys with hypospadias. Median age 1.9 (0.8, 12.9) yrs



Boys with hypospadias have subclinical evidence of vascular dysfunction in adolescence, namely increased carotid intima media thickness (CIMT) and increased blood pressure.
n=14 controls, 14 boys with hypospadias. Median age 13 (12, 18) yrs

Admission diagnosis	Univariate OR	95% CI	p	Multivariate OR	95% CI	p
Arrhythmia	2.5	1.4-4.6	0.003	2.8	1.4-5.6	0.003
Angina	4.7	0.3-74.7	0.30	5.9	0.07-524.5	0.43
Cardiomyopathy	0.0	0-0	0.99	0.0	0-0	0.99
Diabetes	1.5	0.9-2.5	0.09	1.5	0.8-2.6	0.15
Hypertension	2.3	0.9-5.8	0.05	4.2	1.5-11.9	0.04
Heart failure	11.7	2.2-60.4	0.03	1.7	0.7-114.3	0.02
Ischaemic heart disease	1.6	0.3-7.7	0.60	2.2	0.3-14.1	0.40
Myocardial infarction	0	0-0	0.90	0.0	0-0	0.90
Peripheral arterial disease	0.9	0.1-8.0	0.90	1.5	0.1-15.1	0.73
Renal failure	1.3	0.7-2.5	0.50	1.8	0.9-3.8	0.12
Stroke	0.0	0-0	0.99	0.0	0-0	0.99

Hospital admission data demonstrated that men born with hypospadias had increased risk of admission to hospital for arrhythmia, hypertension and HF, when adjusted for birthweight, gestation, deprivation index and maternal smoking.
n = 8,073 controls, 6,797 men with hypospadias. Median age 26 (18, 38) yrs.

CONCLUSIONS

- **First study to date examining vasoreactivity by wire myography in paediatric blood vessels.**
- **Boys with hypospadias demonstrate increased vasoconstriction and impaired vasorelaxation.**
- **Adolescents with hypospadias have increased CIMT SDS and systolic blood pressure SDS.**
- **Young men born with hypospadias are at increased risk of arrhythmia, hypertension and heart failure.**
- **Need for longitudinal studies to assess the clinical implications of these findings.**

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CONTACT INFORMATION

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