DIFFERENTIAL GENETIC EXPRESSION AND REDUCED LONGITUDINAL FUNCTION IN PATIENTS WITH DIABETES AND SEVERE AORTIC STENOSIS WITH A NORMAL EJECTION FRACTION

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Introduction Aortic stenosis and type 2 diabetes mellitus are common conditions and patients with cardiovascular disease and type 2 diabetes tend to have a worse outlook than those with cardiovascular disease alone. We compared patients with severe aortic stenosis and diabetes to patients with severe aortic stenosis but no diabetes. We compared left ventricular (LV) function and expression of key genes in the left ventricle.

Methods Two groups of patients with severe aortic stenosis (AVA of 1.0 cm² or less and LV ejection fraction >55%) and with (n=6) or without (n=8) type 2 diabetes were referred for aortic valve replacement. Patients had a full echocardiogram with speckle tracking prior to their operation and had a single apical LV needle biopsy taken just prior to the initiation of cardio-pulmonary bypass. The biopsies were flash frozen for mRNA expression. Expression of 48 mRNAs (responsible for ion channels and involved in energy metabolism and contractile performance in the heart) was measured by qPCR. Expression was normalised to 18S and differences were assessed using Student's t-test (*P<0.05).

Results Mean patient characteristics (with standard deviations) in both groups are shown below:

Mean echocardiogram parameters (with standard deviations) for the two groups are shown below:

Of the 48 genetic targets tested on the tissue samples we found an increase in patients with diabetes:

NFKB-a proinflammatory transcription factor

KIR 2.1 and KIR 3.1- potassium channels

NCX 1-sodium-calcium exchanger

ANKRD1- a transcription factor

We found a decrease in patients with diabetes in:

HERG- a potassium channel

MTATP 6- a mitochondrial energy production gene

NAV 1.5- a sodium channel

Discussion We have shown a significant reduction in longitudinal left ventricular function (as evidenced by reduced MAPSE and longitudinal strain) in patients with diabetes mellitus and severe aortic stenosis compared to non diabetic controls. There was no difference in weight, BMI, waist circumference, normal ejection fraction, LV septal thickness and LV end diastolic volume. The left ventricular changes are accompanied by differential expression in

several cardiac genes in patients with diabetes and may represent a subclinical cardiomyopathy that could be targeted for primary prevention of symptomatic cardiac disease.

Table 1

Group	Age (years)	Waist (cm)	Weight (kg)	BMI (Kg/m ²)	HbA1c (%)
Control	78.8 (8.3)	35.8 (2.7)	79.4 (11.47)	27.8 (2.3)	
Diabetes	74.9 (12.8)	39.7 (8.8)	84.8 (21.4)	31.3 (6.9)	6.9

Table 2

Group	LV Septal width (cm)	LV End-Diastolic Volume (ml)	LV Ejection Fraction (%)	LV Longitudinal strain (%)	MAPSE (cm)
Control	1.6 (0.23)	76.2 (26.5)	63.9 (6.5)	18.3 (3.7)	1.6 (0.23)
Diabetes	1.7 (0.48)	89.6 (15.6)	58.2 (2.6)	12.7 (2.5)*	1.1 (0.20)*