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VALVULAR HEART DISEASE

TARGETED MYBPC3 KNOCK-OUT MICE WITH NON-OBSTRUCTIVE HYPERTROPHIC CARDIOMYOPATHY EXHIBIT STRUCTURAL MITRAL VALVE ABNORMALITIES

ACC Poster Contributions
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Background: Mutations in MYBPC3 encoding cardiac myosin-binding protein C typically cause hypertrophic cardiomyopathy (HCM). Moreover, anterior mitral valve leaflet elongation is frequently seen in HCM and is thought to be due to turbulence from outflow obstruction. Our aim was to measure mitral leaflets in mice with HCM without outflow obstruction compared to wild-type (+/+) controls.

Methods: High frequency, high resolution echocardiography (VeVo 2100, Visualsonics) was used to measure LV end-diastolic volume (EDV), mass (LVM), ejection fraction, anterior (AML) & posterior (PML) mitral leaflet length (L) & thickness (T). We compared Mybpc3 -/- (n=29), +/- (n=33), and +/+ (n=22) ages 3-6 months.

Results: Mybpc3 -/- mice have concentric LVH, globular LV dilation, and systolic dysfunction compared to +/- and +/+ mice (see Table) without LV outflow obstruction. Unadjusted AML-L was greatest in -/- mice compared to +/- and +/+ (P<0.0001). PML-L was similar. The +/- and +/+ mice were indistinguishable. After adjusting for LV size (EDV or LVM), the difference in -/- AML-L persists (P<0.002 and <0.0002 respectively). To assess total MV volume, AML-T was added to PML-T. Cumulative MV-T was increased in -/- mice (P<0.001).

Conclusions: Homozygous Mybpc3 -/- mice with marked LV dilation and hypertrophy but without LV outflow obstruction exhibit increased length of the AML. This suggests that mitral valve elongation may be due to paracrine effects and may be a target for mechanistic and therapeutic studies.

Results Table				
Unadjusted:	+/+ (avg+SD)	+/- (avg+SD)	-/- (avg+SD)	P
AML-L (mm)	1.73 +0.08	1.73 +0.07	1.92 +0.08	<0.0001
PML-L (mm)	1.36 +0.07	1.33 +0.07	1.35 +0.07	NS
A+PML-T (mm)	0.15 +0.02	0.18 +0.04	0.23 +0.04	<0.001
LVM (mg)	80 +16	88 +7	129 +26	<0.0001
EF (%)	63 +5	62 +7	35 +7	<0.0001
EDV (ul)	67 +11	63 +11	118 +40	<0.0001