Association between MYH7 gene variants and cardiac conduction disease

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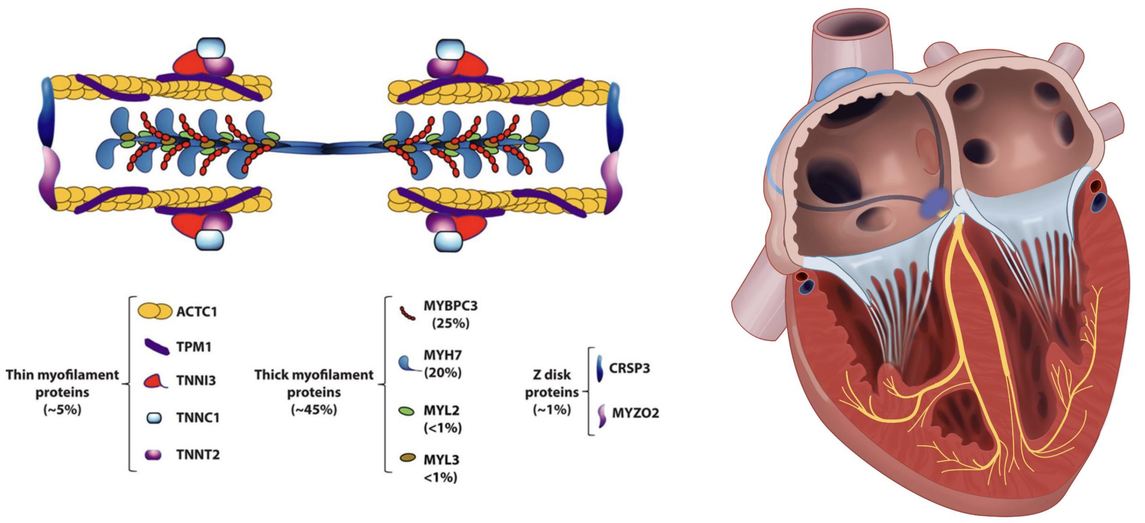
Background

Hypertrophic cardiomyopathy (HCM) is a genetic disease of cardiomyocytes. It is commonly caused by sarcomere mutations, including in the gene encoding beta-myosin heavy chain (MYH7). Current guidelines do not discriminate between genotypes for prediction of overall patient outcomes. Despite some evidence existing that MYH7 is associated with cardiac conduction disease, the underlying mechanism for this is poorly understood at present. The primary aim of this research was to determine if the presence of MYH7 gene mutation is associated with higher rates of conduction system disease or arrhythmia.



Methods

We conducted a retrospective cohort study of 86 patients from an inherited cardiac conditions centre in an Irish hospital. MYH7 variant positive patients (both with and without manifestation of left ventricular hypertrophy (LVH)) (MYH7+) were compared with sarcomere mutation negative HCM patients (HCM-). Medical records and investigations including electrocardiograms (ECGs) and cardiac MRIs (cMRI) were reviewed to determine if there were differences in the prevalence of atrioventricular (AV) conduction disease and arrhythmias.

	MYH7 (n=43)	Gene negative (n=43)	Mean difference (ms)	P value
Mean (IQR) PR interval (ms)	175.6 (147.8, 195.2)	170.8 (155, 183.2)	4.8	0.3098
PR >180 ms	50% (n=21)	30.95% (n=13)		<0.001
Conduction disease	25.58% (n=11)	11.63% (n=5)		
First degree heart block	16.28% (n=7)	9.3% (n=4)		
AVNRT ablation	4.66% (n=2)	0		
WPW ablation	2.32% (n=1)	0		
Short PR interval	2.32% (n=1)	0		
LBBB	0	2.32% (n=1)		
Atrial fibrillation	16.28% (n=7)	13.95% (n=6)		0.999
Documented VT	20.93% (n=9)	30.23% (n=13)		0.458

Means compared using Mann-Whitney U test, categorical variables compared using chi-square test. *p<0.05 is significant

Table 1: Results of arrhythmia identified between both MYH7 + and HCM- groups

Results

Our results revealed a trend towards higher rates of conduction disease in those with MYH7 mutation compared to the HCM-group. There was a significant trend of patients with a mean PR intervals >180 ms in MYH7+ compared to the gene elusive cohort, despite lower rates of beta blocker use. MYH7+ patients had a lower prevalence of late gadolinium enhancement on cMRI, likely owing to many not (yet) having LVH. There was a higher rate of atrial arrhythmias observed in the MYH7+ group.

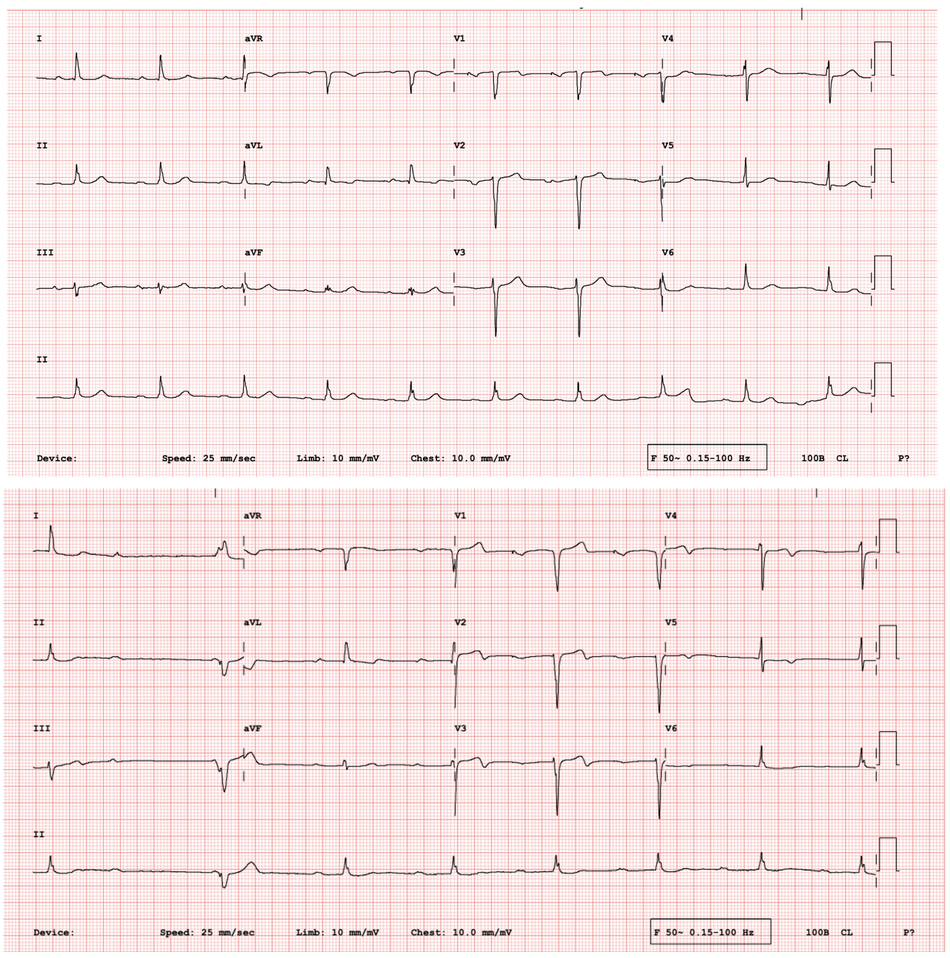


Figure 1: ECG of Patient X in 2018; MYH7+, PR Prolongation (PR 267 msec)
Figure 2: ECG of Patient X in 2023; MYH7+, ICD in situ, Ventricular pacing

Conclusion

These findings suggest that MYH7 genetic variations in HCM is associated with conduction disease and prolongation of the PR interval. Therefore, the presence of conduction disease in HCM patients should prompt consideration for genetic testing for MYH7 gene variation, in the appropriate clinical context, and heightened suspicion of variant positivity in relatives of MYH7+ patients with PR prolongation >180 msec. Additionally, there appears to be a suggestion of higher rates of atrial arrhythmias in this group, but overall numbers are low. Judicious usage and dosage of beta-blocker therapy should be considered in this cohort of patients. Further studies are necessary to elucidate the underlying pathophysiologic mechanism for this conduction disorder.

References

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