Differences in left ventricular mass and morphology and right ventricular function differentiate phenotype-negative sarcomere gene mutation carriers from healthy volunteers

Van Der Velde N.[1]; Huurman R.[2]; Hassing H.[1]; Budde R.[1]; Van Slegtenhorst M.[3]; Verhagen J.[3]; Schinkel A.[2]; Michels M.[2]; Hirsch A.[1]

[1]Erasmus University Medical Centre, Cardiology and Radiology, Rotterdam, Netherlands (The)
[2]Erasmus University Medical Centre, Cardiology, Rotterdam, Netherlands (The)
[3]Erasmus University Medical Centre, Clinical Genetics, Rotterdam, Netherlands (The)

Funding Acknowledgements: Type of funding sources: None.

Carriers of pathogenic DNA variants (G+) causing hypertrophic cardiomyopathy (HCM) can be identified by genetic testing, before manifestation of left ventricular hypertrophy (LVH). These G+/LVH- subjects are routinely monitored for phenotypic expression, which, alongside LVH, can include other HCM-related abnormalities, including crypts and myocardial fibrosis. Cardiovascular magnetic resonance (CMR) imaging has emerged as a valuable technique in diagnosing and follow-up of HCM. In this study, we identified clinical features of subclinical HCM in a G+/LVH- population compared to healthy subjects.

We studied 33 G+ subjects with CMR and a maximal wall thickness (MWT) <13mm, and compared them to an age- and gender-matched group of 35 healthy controls (44 ± 14 vs 48 ± 10 y, p = 0.17; 11 (33%) vs 12 (34%) men, p = 0.93). The CMR imaging protocol consisted of 1) steady state free procession cine imaging, 2) 2-dimensional late gadolinium enhancement (LGE) images in the G+ patients and 3) pre-contrast T1 mapping using a modified look-locker inverse recovery sequence. We assessed CMR examinations for features of HCM. Forward logistic regression analysis was performed to determine which of the CMR characteristics were predictive of G+ status.

G+ subjects had a higher MWT (10.9 ± 1.6 vs 10.2 ± 1.3 mm, p = 0.04), a similar interventricular septal wall (IVS) thickness (8.8 ± 1.6 vs 8.7 ± 1.6 mm, p = 0.85), a smaller posterior wall (PW) and a higher IVS/PW ratio (6.6 ± 1.2 vs 7.7 ± 1.3mm, p < 0.001; 1.4 ± 0.3 vs 1.1 ± 0.2, p = 0.001). Indexed left ventricular (LV) mass was significantly lower in the G+ group (Table). LV function was similar (63 ± 6 vs. 61 ± 5%, p = 0.12), but right ventricular (RV) function was higher in the G+ group. They often had a characteristic hook-shaped thickening of the basal anterior wall (7 (21%) vs 0, p < 0.004; Figure) and more frequently exhibited myocardial crypts. Midwall LGE was present in 3 (9%) G+ subjects. Native septal T1 values were elevated in G+ patients compared to controls, although mostly within the normal range (986 ± 31 vs 963 ± 28 ms, p < 0.01). Crypts, indexed LV mass and RV ejection fraction were significant predictors of G+ status in logistic regression analysis (Table).

CMR demonstrates significant morphological differences between the G+/LVH- population and healthy controls. Further studies are needed to assess the prognostic significance of these morphological features.

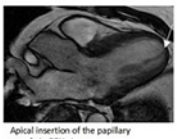
Predictors of genotype-positive status

Variables	G+ subjects (n = 33)	Controls (n = 35)	P value	OR for G+ status	P value
Left ventricular mass/BSA (g/m²)	45 ± 7.4	53 ± 7.9	<0.001	0.86 [0.78-0.95]	0.003
Right ventricular ejection fraction (%)	58 ± 6	53 ± 4	<0.001	1.15 [1.00-1.32]	0.047
Crypts	17 (55%)	4 (11%)	<0.001	9.62 [1.93-48.00]	0.006

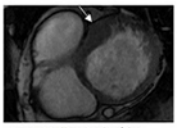
G+: genotype-positive, OR: odds ratio

Abstract Figure. CMR findings

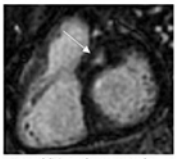
Crypt (*) and hook shaped thickening (↓) of the basal anterior wall in 2CH view



Apical insertion of the papillary muscle in 3CH view



Asymmetrical hypertrophy of the basal anterior wall in SA view



Late gadolinium enhancement at the site of the hypertrophy in SA view