The added value of contrast-enhanced cardiac magnetic resonance to predict positive genetic testing in clinically suspected Lamin A/C cardiomyopathy

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Funding Acknowledgement: Type of funding source: None

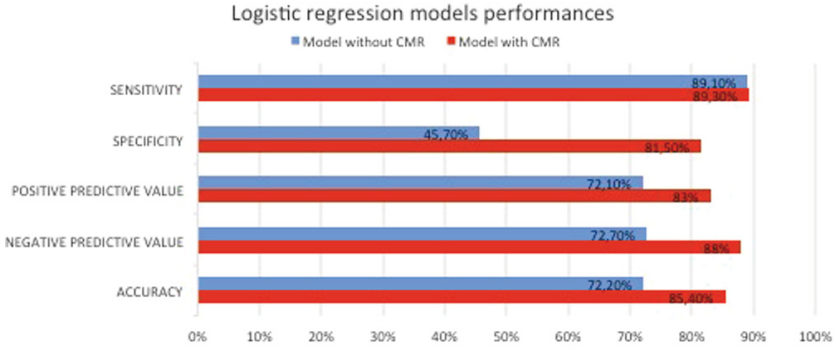
Background: Lamin A/C cardiomyopathy (CM) is an inherited disease due to LMNA gene mutation with particular phenotype that associates conduction disorders, frequent atrial fibrillation and life-threatening ventricular arrhythmias, with normal or altered ventricular systolic function. Cardiac magnetic resonance (CMR) studies suggest frequent late gadolinium enhancement (LGE) involving septal mid-myocardium.

Aims: To assess the added value of CMR to conventional clinical features of Lamin A/C CM for the prediction of a positive LMNA gene testing.

Methods: We performed a retrospective monocentric study in all index patients referred for genetic testing for a clinical suspicion of Lamin A/C CM. Clinical, ECG and imaging data including CMR at time of genetic testing in patients with a positive test (LMNA+) and patients without (LMNA-) were compared. The diagnostic performances of relevant parameters for the prediction of a positive LMNA gene testing were analyzed in several logistic regression models.

Results: 90 patients were included (55 LMNA+, 35 LMNA-).49% had significant left ventricular (LV) dilatation on echocardiography,57% had a LV ejection fraction (LVEF)<50%, 46% had a significant left atrial dilatation, and 17% had right ventricular dysfunction. None of these parameters were different comparing LMNA+ and LMNA- patients. LMNA+ patients had significantly more frequent familial history of sudden cardiac death (SCD) or CM. There were no significant differences between LMNA+ and LMNA- patients in terms of conduction disorders, ventricular and supra-ventricular arrhythmias. The only significant difference on ECG was a more frequent abnormal R-wave progression in V1-V3 in LMNA+ patients (87.8% vs 39.4%, p<0.001). 55 patients had a CMR (28/55 LMNA+, 27/35 LMNA-). The main reason for not performing CMR was the presence of cardiac implantable electronic device. LMNA+ patients had significantly more LGE than LMNA- (20/28 (71%) vs 9/27 (33%), p=0.011). The main differences in LGE features between the 2 groups were septal involvement (70% in LMNA+ vs 11% in LMNA-, p=0.005) and mid-myocardium localization (95% vs 44%, p=0.005). In a first logistic regression model without CMR data in all 90 patients, V1-V3 R-wave abnormalities, familial history of SCD and sinus node dysfunction were independent predictors of a positive LMNA gene testing (Sensitivity 89%, specificity 46%, accuracy 72%). A second model in the 55 patients who had a CMR showed better accuracy (85%), mainly driven by increased specificity (81%) with preserved sensitivity (89%). V1-V3 R-wave abnormalities, premature ventricular contractions, non-depressed LVEF and septal LGE predicted positive LMNA gene testing in this model (Septal LGE OR=31, 95% CI 4–715; p=0.005).

Conclusion: CMR, particularly septal mid-myocardium LGE, carries good diagnostic accuracy to predict a positive LMNA gene testing in clinically suspected Lamin A/C CM with increased specificity when added to conventional red flags.



	ACCURACY	NEGATIVE PREDICTIVE VALUE	POSITIVE PREDICTIVE VALUE	SPECIFICITY	SENSITIVITY
Model without CMR	72,20%	72,70%	72,10%	45,70%	89,10%
Model with CMR	85,40%	88%	83%	81,50%	89,30%