ASSOCIATION OF GENETIC VARIANTS WITH MYOCARDIAL MECHANICS AND MORPHOMETRY IN PATIENTS WITH NONISCHEMIC DILATED CARDIOMYOPATHY

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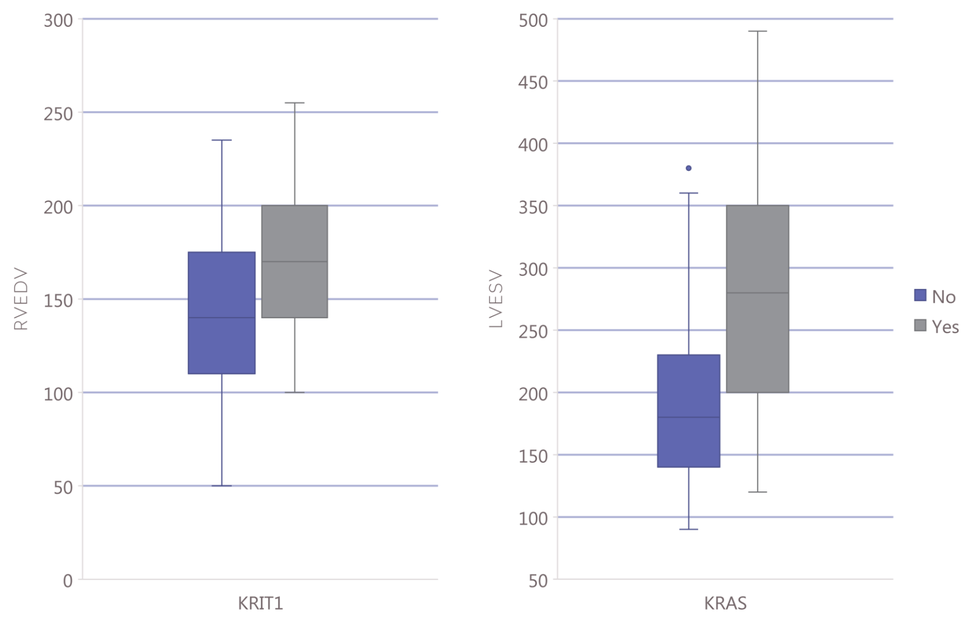
Dilated Cardiomyopathy (DCM) is characterized by ventricular dysfunction and dilatation, independent of loading conditions or coronary artery disease. DCM's prevalence ranges from 1:250 to 1:2500, making it a major cause of global heart failure in the young and heart transplantation. Disease progression in DCM is influenced by factors like toxic damage, delayed treatment, and genetic predisposition. Genetic evaluation aids in prognosis prediction for DCM. Despite standard imaging methods, the study underscores the importance of whole-heart mechanics evaluation due to DCM's diverse phenotypic presentation.

GOALS

- Explore how cardiac-related gene variants relate to changes in heart mechanics or morphometrics in nonischemic dilated cardiomyopathy (NIDCM) patients.
- Investigate the impact of novel gene variants (GATAD1, LOX, RASA1, KRAS, KRIT1) on clinical and cardiac parameters, advancing our understanding of their role in dilated cardiomyopathy for improved patient care.

METHODS

- **Study population:** 95 patients with nonischemic DCM (NIDCM).
- **Inclusion:** outpatients and hospitalized patients with first time diagnosed NIDCM.
- **Exclusion:** patients with ischemic disease, valve issues, inflammatory conditions, kidney disease, tachycardia-induced HF, peripartum cardiomyopathy, toxic damage, age <18, and poor imaging quality.
- **Data includes:** clinical parameters, 2D echocardiography, magnetic resonance imaging (MRI) parameters
- **Genetic analysis:** Utilized Illumina NextSeq 550 and a 233-gene commercial panel covering validated cardiomyopathy and cardiovascular-related genes.



- **Statistical analysis:** utilizing a variety of tests, including Shapiro-Wilk, ANOVA, Kruskal-Wallis, and chi-square, the analysis whether there are significant differences in clinical, 2D echocardiographic, and MRI parameters between patients with the genes variants and those without was performed. Significance is inferred at a 0.05 threshold.

RESULTS

Genes with the most cases of statistically significant differences in clinical, 2D echocardiographic, and MRI parameters between patients with and without gene variants were selected. The largest differences in total cardiac myocardial mechanics and morphometry between those patients were observed in the genes KRAS, KRIT1, GATAD1, LOX and RASA1. KRAS and KRIT1 gene variants in patients with NIDCM were related to enlargement of both ventricles and atria and worse RV function.

	KRAS			KRIT1		
	No gene variants	Gene variants	p-value	No gene variants	Gene variants	p-value
2D echocardiographic parameters				2D echocardiographic parameters		
LVEDD, mm	62.0	64.5	0.041	RVEDV, ml	131.1	174.0	0.002
LVESV, ml	138.0	161.5	0.043	RVEDVi, ml/2	61.9	77.0	0.004
MRI parameters				MRI parameters			
RVEF, %	43.5	40.0	0.003	RVEF, %	43.5	38.0	0.037
LVEDD, mm	69.0	75.0	0.003	RVESV, ml	96.0	117.0	0.022
LVEDV, ml	272.0	356.0	0.000	RVESVi, ml/m^2	36.9	45.8	0.001
LVEDVi, ml/m^2	135.0	174.0	0.000	LVEDV, ml	290.0	377.0	0.038
LVESV, ml	186.0	274.0	0.001	RDVEDV,ml	192.5	228.0	0.004
LVESVi, ml/m^2	90.0	126.4	0.001	RAA, cm^2	26.7	31.0	0.006
RVEDV, ml	188.0	219.0	0.033				
LAA, cm^2	30.5	36.5	0.009				

CONCLUSION

Our study suggests that novel gene variants linked to cardiomyopathy can significantly impact clinical, morphometric, and myocardial mechanics parameters. To validate these findings and explore greater variation, further research with larger cohorts and broader sequencing panels, such as whole exomes or genomes, is essential. Emphasizing our focus on protein-coding regions sheds light on significant differences in variant dispersion.

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