Diagnostic and Prognostic Efficiency of Genotype Versus Phenotype in Genetic Cardiomyopathies

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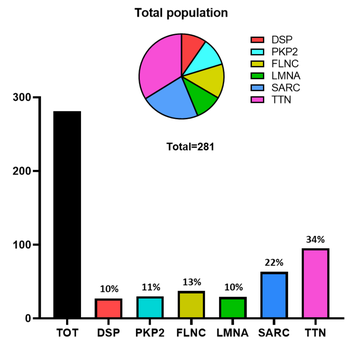
Background

- In cardiomyopathies (CMP), genetic background may show phenotypic heterogeneity.
- We aimed to define the efficiency of the phenotype- versus the genotype-based classification in the diagnostic and prognostic definition of a large cohort of patients with positive genetic testing and different CMPs:
  - Dilated Cardiomyopathy (DCM)
  - Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)
  - Left Ventricular Arrhythmogenic Cardiomyopathy (ALVC)
  - Biventricular ARVC (BiV).

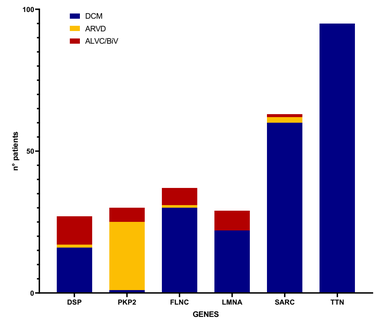
Methods

- 281 patients (80% DCM) carrying pathogenic or likely pathogenic variants (P/LP) were included in this study.
- Phenotypes were classified as DCM, ARVC, ALVC, and BiV according to current consensus criteria.
- Primary and secondary outcomes included: 1) all-cause mortality/heart transplant (D/HT); 2) heart failure-related death/heart transplant/left ventricular device implantation (DHF/HT/VAD); and 3) sudden cardiac death/life-threatening ventricular arrythmias (SCD/MVA).
- Statistical tests performed included the analysis of variance (ANOVA) test with the Brown-Forsythe statistic, nonparametric Mann-Whitney test, chi-square test and the Fisher's exact test.

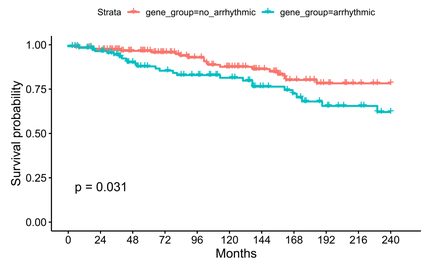
Results



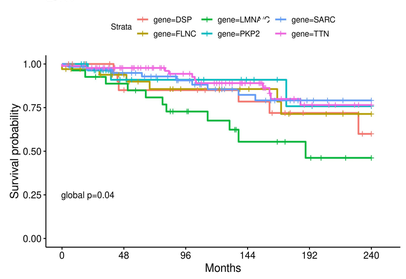
A. Gene Variants Distribution



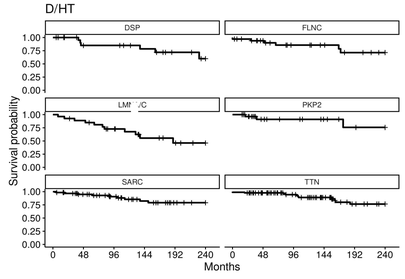
B. Phenotypic Distribution for Each Gene



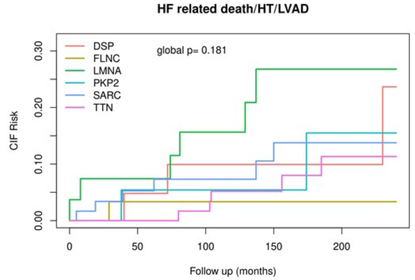
C. Kaplan Meier Plot for Non-Arrhythmic vs Arrhythmic Genes



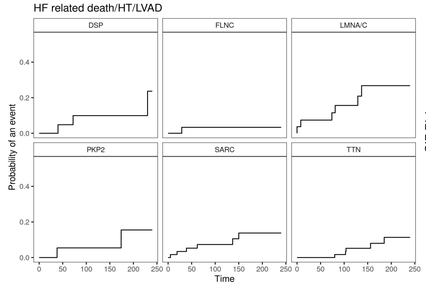
D. Kaplan Meier Plot for Primary Outcome



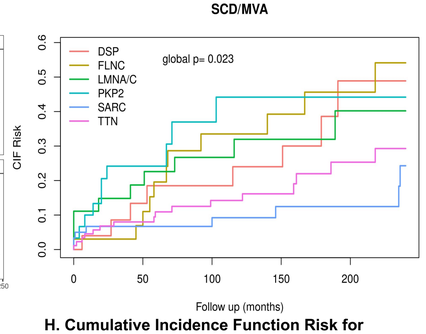
E. Kaplan Meier plot for Primary Outcome by Genotype



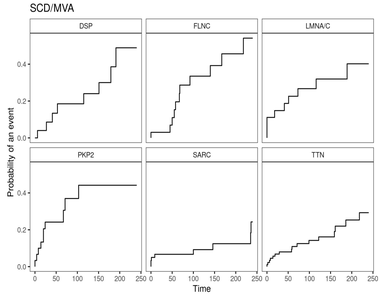
F. Cumulative Incidence Function Risk for Heart Failure Secondary Outcome



G. Kaplan Meier Plot for Heart Failure Secondary Outcome



H. Cumulative Incidence Function Risk for Arrhythmic Secondary Outcome



I. Kaplan Meier Plot for Arrhythmic Secondary Outcome

Conclusions

- In genetic cardiomyopathies, the genotype is associated with significant phenotypic heterogeneity.
- Nevertheless, the genotype showed higher accuracy in differentiating patients with CMPs and predicting their outcome compared to the phenotype-based classification.

Implications

- Our findings provide strong evidence of the necessity to include genotype predictors, in addition to phenotypic expression, in the evaluation and clinical management of cardiomyopathies.

Disclosures

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