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Machine-learning based exploration of echocardiographic patterns and clinical parameters to understand their relation to death or transplant in pediatric dilated cardiomyopathy

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Background: Pediatric dilated cardiomyopathy (DCM) affects left ventricular (LV) function and carries a high risk of death or heart transplantation. However, the relation of LV regional function and inefficiency to clinical outcomes is underexplored.

Purpose: The aim of this study was to understand the relationship of regional LV mechanics, global LV function and clinical characteristics to the outcomes of death or heart transplant in children with DCM; through the integration of a vast amount of information enabled by unsupervised machine learning techniques.

Methods: DCM was defined by a LV end-diastolic dimension z-score>2 and LV ejection fraction (EF) <55%. Longitudinal strain curves were sampled at 6 LV lateral wall and septal locations from the 4ch apical view. In addition, we analyzed other echo parameters including the aortic outflow pattern as a measure of LV pump function, QRS duration, LV EF, indexed end-diastolic LV dimension, global longitudinal strain and patient characteristics including age, weight, body surface area and medications (diuretics, ACE inhibitor, beta-blockers, mineralocorticoid receptor antagonist, digoxin, inotropes, antiarrhythmics). We used an unsupervised machine learning algorithm (multiple kernel learning) to reduce the dimensionality of these data, and position patients based on similarities. We subsequently used k-means clustering to recover homogeneous groups of patients. We then interpreted the data patterns associated to each of the groups for the occurrence of death or transplant through non-linear regression analysis (multi-scale kernel regression).

Results: 50 children with DCM (age 0 to 18 years) were analyzed. Clustering on the two first dimensions of the low-dimensional space resulted in three clusters (Figure A), with significantly different proportions of the composite outcome of death or heart transplant (Cl1 = 79%, Cl2 = 50%, Cl3 = 20%; p = 0.01). The group with the highest proportion of death or transplant (cluster 1) comprised the oldest and most frequently medicated subjects, with impaired LVEF and GLS, and with the widest QRS duration (p<0.01) (Figure B). The group with the second highest proportion of death or transplant (cluster 2) comprised patients with the lowest LVEF (p<0.01) and GLS (p<0.001), reduced and delayed peak aortic outflow velocity and severely impaired basal and apical LV strain (Figure C). In contrast, the group with highest transplant-free survival (cluster 3) had the highest LVEF and GLS values, the most synchronous LV contraction as assessed by strain and QRS duration and the highest amplitude and earliest peaking aortic flow.

Conclusion: Our results serve as a proof-of-concept that machine-learning based approaches can be useful to explore and understand which regional and global echo parameters in combination with clinical parameters are associated with a higher risk of death or transplant in pediatric DCM.
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