Development of Machine Learning Models for Prediction of Left Ventricular Systolic Dysfunction in Patients with Isolated Left Ventricular Dilation

Ahmed Saleh, MD[1], Miguel Sotelo, PhD[2], Paul Nona, MD[2], Loren Wagner, PhD[2], Chris Rogers[2], Julian Booker, MD[1], Efstathia Andrikopoulou MD[3]
[1]The University of Alabama at Birmingham, Birmingham, Alabama // [2]Tempus AI, Inc., Chicago, Illinois // [3]The University of Washington, Seattle, Washington

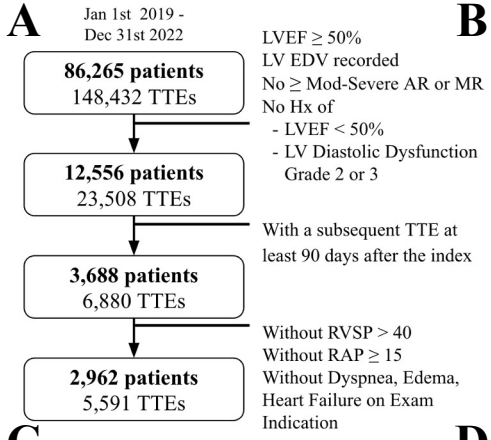
Introduction

- Isolated left ventricular dilation (ILVD) refers to an enlargement of the left ventricle (LV) without concurrent significant systolic dysfunction or other structural heart diseases such as valvular heart disease, coronary artery disease, or congenital heart defects, and is typically characterized by an increase in the left ventricular end-diastolic diameter (LVEDD) greater than 52 mm or above the 95th percentile for the population.[1]
- Echocardiographic changes may indicate preclinical stages of the progression to dilated cardiomyopathy with reduced left ventricular ejection fraction (LVEF).[2,3]
- There are currently no available predictive models for disease progression. Here, we developed such a model using real-world data from patients with ILVD.

Methods

- De-identified patient records in the Tempus Database were retrospectively analyzed, with the follow-up period ending in January 2023 (Figure A)
- Patients with ILVD were defined based on echocardiographic parameters as those with LVEF > 50% and LV end diastolic volume indexed (LVEDVi) > 75 and 62 mL/m^2 for males and females, respectively.
- The endpoint was LVEF < 40% on future (≥90 days) TTE ("progression")
- Five ML models and one soft voting ensemble model were trained with data parsed from TTE reports (Figure A). Model training and feature importance details are shown in Figure B

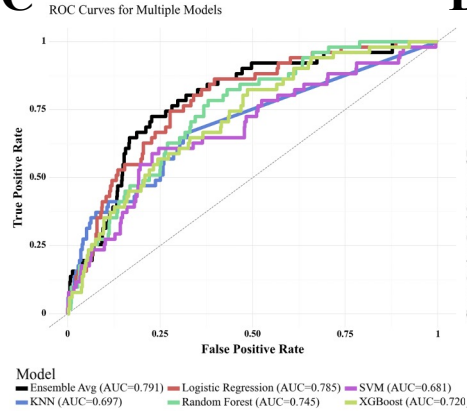
A



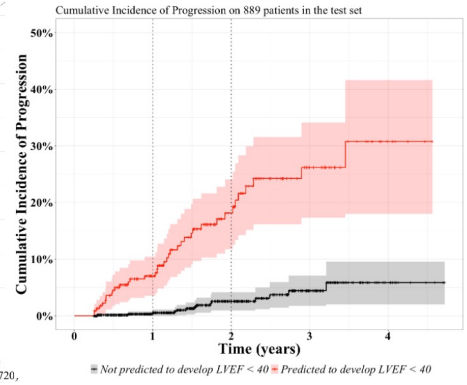
B

- **Data split:** 70:30
- **Feature selection:**
  - At least a 70% completeness rate
  - Median Imputed continuous variables with missingness
- **Model:**
  - L1-regularized regression
  - XGBoost with hyperparam tuning
  - RF with hyperparam tuning
  - SVM with hyperparam tuning (linear vs radial)
  - KNN with hyperparam tuning
  - Ensemble: average prediction probabilities
- **Operating point:** maximum of Youden's J statistic
- **SHAP Interpretability** on all models

C



D



Results

- 2,962 patients met the inclusion criteria (median time from index to last TTE was 578 (IQR = 500) days).
- 6% of patients met the endpoint (177 patients, median 478 days to endpoint, IQR = 535 days).
- **The ensemble model had the highest ROC area under the curve (0.791, Figure C), precision (0.163), F1-score (0.266), and specificity (0.773).**
- **Patients predicted to develop LVEF < 40% had an 8.2x higher risk of developing LVEF < 40% within five years of index (p < 0.001, Figure D).**
- Male gender, higher heart rate, lower LVEF at index TTE, higher LVEDVi, and lower tricuspid annular plane systolic excursion had the highest mean absolute impact on the model's output probability.

Conclusion

- Using only data parsed from the index TTE, ensembling a model for the prediction of developing LVEF < 40% in patients with ILVD and without a history of LV diastolic or systolic dysfunction performed the best.
- Additional analyses including clinical variables such as comorbidities, symptoms, and medications may improve the model's performance.

References:
1. Yeboah J, Bluemke DA, Hundley WG, Rodriguez CJ, Lima JA, Herrington DM. Left ventricular dilation and incident congestive heart failure in asymptomatic adults without cardiovascular disease: multi-ethnic study of atherosclerosis (MESA). *J Card Fail*. 2014;20(12):905-911. doi:10.1016/j.cardfail.2014.09.002
2. Baig MK, Goldman JH, Caforio AL, Coonar AS, Keeling PJ, McKenna WJ. Familial dilated cardiomyopathy: cardiac abnormalities are common in asymptomatic relatives and may represent early disease. *J Am Coll Cardiol*. 1998;31:195-201.
3. McKenna CJ, Sugrue DD, Kwon HM, Sangiorgi G, Carlson PJ, Mahon N, McCann HA, Edwards WD, Holmes DR, Schwartz RS. Histopathologic changes in asymptomatic relatives of patients with idiopathic dilated cardiomyopathy. *Am J Cardiol*. 1999;83:281-283.