Exploring sex-specific patterns of mortality predictors among patients undergoing cardiac resynchronization therapy: a machine learning approach

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Background: The relative importance of variables explaining sex differences in outcomes is scarcely explored in patients undergoing cardiac resynchronization therapy (CRT).

Purpose: We sought to implement and evaluate machine learning (ML) algorithms for the prediction of 1- and 3-year all-cause mortality in patients undergoing CRT implantation. We also aimed to assess the sex-specific differences and similarities in the predictors of mortality using ML approaches.

Methods: A retrospective registry of 2191 CRT patients (75% males) was used in the current analysis. ML models were implemented in 6 partially overlapping patient subsets (all patients, females or males with 1- or 3-year follow-up data available). Each cohort was randomly split into a training (80%) and a test set (20%). After hyperparameter tuning with 10-fold cross-validation in the training set, the best performing algorithm was also evaluated in the test set. Model discrimination was quantified using the area under the receiver-operating characteristic curves (AUC) and the associated 95% confidence intervals. The most important predictors were identified using the permutation feature importances method.

Results: Conditional inference random forest exhibited the best performance with AUCs of 0.728 [0.645–0.802] and 0.732 [0.681–0.784] for the prediction of 1- and 3-year mortality, respectively. Etiology of heart failure, NYHA class, left ventricular ejection fraction and QRS morphology had higher predictive power in females, whereas hemoglobin was less important than in males. The importance of atrial fibrillation and age increased, whereas the relevance of serum creatinine decreased from 1- to 3-year follow-up in both sexes.

Conclusions: Using advanced ML techniques in combination with easily obtainable clinical features, our models effectively predicted 1- and 3-year all-cause mortality in patients undergoing CRT implantation. The in-depth analysis of features has revealed marked sex differences in mortality predictors. These results support the use of ML-based approaches for the risk stratification of patients undergoing CRT implantation.

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