Survival prediction in patients undergoing cardiac resynchronization therapy: a machine learning based risk stratification system

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Background: Cardiac Resynchronization Therapy (CRT) has well-known beneficial effects in patients with advanced heart failure, reduced ejection fraction and wide QRS complex. However, mortality rates still remain high in this patient population. Therefore, precise risk stratification would be essential, nonetheless, the currently available risk scores have several shortcomings which hamper their utilization in the everyday clinical practice.

Purpose: Accordingly, our objective was to design and validate a machine learning based risk stratification system to predict 2-year and 5-year mortality from pre-implant parameters of patients undergoing CRT implantation.

Methods: We trained two models separately to predict 2-year (model 1) and 5-year mortality (model 2). As training cohort of model 1 we used 1678 patients (67±10 years, 1251 [75%] males) undergoing CRT implantation. From this population, 1320 patients (66±10 years, 1005 [76%] males) also completed 5-year follow-up and they served as the training cohort for model 2. Forty-seven pre-implant parameters (demographics, cardiovascular risk factors and clinical characteristics) were used to train the models. Our models were designed in a way to tolerate missing values. Among non-linear classifiers, random forest demonstrated the best performance. We validated our models, along with the Seattle Heart Failure Model (SHFM), VALID-CRT risk score and EAARN score on an independent cohort of 136 patients (66±10 years, 110 [81%] males). Based on the predicted probability of survival, patients were split into quartiles and survival was plotted via Kaplan-Meier (KM) curves.

Results: There were 358 (21%) deaths in the 2-year, 697 (53%) deaths in the 5-year training cohort. In the validation cohort, there were 30 (22%) deaths at 2 years and 58 (43%) deaths at 5 years after CRT implantation. For the prediction of 2-year mortality, the Area Under the Receiver-Operating Characteristic Curve (AUC) for model 1 was 0.77 (95% CI: 0.67–0.87; p=0.002), for SHFM was 0.54 (95% CI: 0.39–0.69; p=0.006), for EAARN was 0.57 (95% CI: 0.46–0.68, p=0.002), and for VALID-CRT was 0.62 (95% CI: 0.52–0.71; p=0.002). To predict 5-year mortality, the AUC for model 2 was 0.85 (95% CI: 0.78–0.91; p=0.001), for SHFM was 0.62 (95% CI: 0.51–0.74; p=0.003), for EAARN was 0.61 (95% CI: 0.51–0.70, p=0.002), for VALID-CRT was 0.65 (95% CI: 0.56–0.74; p=0.002). The AUCs of the machine learning based models were significantly higher than the AUCs of the pre-existing scores (DeLong test, all p<0.05). The KM curves of the quartiles were significantly separating in both models (Log-rank test, both p<0.001).

Conclusion: Our results indicate that machine learning algorithms can outperform the already existing linear model based scores. By capturing the non-linear association of predictors, the utilization of these state-of-the-art approaches may facilitate optimal candidate selection and prognostication of patients undergoing CRT implantation.
Abstract:
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