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EDITORIAL

Predicting Heart Failure in Arrhythmogenic Right Ventricular Cardiomyopathy

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Since its recognition, arrhythmogenic right ventricular cardiomyopathy (ARVC) has been characterized as a heart muscle disease with high risk of ventricular arrhythmia. Much of the effort has been focused on the arrhythmogenic aspect of the disease, including the risk stratification for sudden death[1] and intervention to mitigate the risk for lethal arrhythmia such as exercise reduction,[2] medication,[3] and ablation.[4] The heart failure aspect of the disease had been largely neglected until Gilotra et al[5] reported that heart failure was present in 49% of patients with ARVC, with exertional dyspnea and fatigue being the most common symptoms. Also, classic left-sided heart failure signs such as orthopnea, paroxysmal nocturnal dyspnea, and pulmonary rales are usually absent. It was reported that patients with heart failure had higher odds of being a woman, having more severe right ventricular dysfunction, having hypertension, and having negative T waves in precordial leads V4 through V6. The predictors of end-stage heart failure remained unknown in ARVC. In this context, Chen et al drew our attention again to heart failure in ARVC by presenting a prediction model for adverse heart failure outcomes in ARVC in this issue of the *Journal of the American Heart Association* (*JAHA*).[6]

See Article by Chen et al.

This was a multicenter study with patients from ARVC registries in Fuwai Hospital, China (n=290) and University Heart Center, Switzerland (n=99). ARVC probands without end-stage heart failure at enrollment were included. The primary end point was heart transplant or death from heart failure. The least absolute shrinkage and selection operator method and Cox regression analysis was used to develop the model. The average age was 38 years with 65% being men. After ≈5 years of follow-up, 48 (12%) patients reached the primary end point (29 transplants, 19 heart failure deaths). The final model included 4 variables: left ventricular ejection fraction, tricuspid regurgitation, creatinine, and atrial fibrillation. The model performed well in internal bootstrap validation, with excellent discrimination (C-index of 0.92) and good calibration across high- and low-risk population as well as long and short follow-up. A user-friendly web-based calculator was also provided.

This is the first risk prediction model for heart failure adverse outcomes in ARVC. With the use of widely available clinical and laboratory data, this work enables clinicians to conveniently estimate the risk for development end-stage heart failure and need of transplant. This would remind providers to start or intensify neurohormonal therapies and facilitate early referral to heart failure providers. There are a few caveats to be kept in mind in the interpreting of the results. First, patients who met the study end point already had suffered advanced heart failure at enrollment (70% New York Heart Association class ≥3 at age 38, left ventricular ejection fraction 39.69±13.30%, NT-proBNP

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[N-terminal pro-B-type natriuretic peptide] 2289.5 pg/mL). It would be obvious that these individuals were at high risk for end-stage heart failure, which may explain the excellent model performance and the high incidence of end-stage heart failure observed. In practice, risk prediction would be most valuable for patients without heart failure symptoms to direct preventative interventions. Second, right ventricular dysfunction is a key feature of ARVC and has been associated with heart failure severity.[5] However, its prevalence was not reported. Right ventricular function was not included among the prespecified predictors. Prior ventricular arrhythmia (another disease feature of ARVC) was not included, despite repeated ventricular arrhythmia and defibrillator shocks having been which has been shown to worsen heart failure.[5] Both right ventricular function and recurrent ventricular arrhythmias would at least deserve exploration during model development. Third, it is notable that more than one-third of patients were not on a beta blocker, and no mention at all was made of how many patients, if any, were on an angiotensin-converting enzyme inhibitor. Fourth, although difference by genotype was observed (18% of *DSP* carriers reaching end point versus 3% of *PKP2* carriers), genotype was not included in the model because of the limited genetic testing rate. Furthermore, it is well known that exercise restriction after diagnosis of ARVC dramatically reduces the risk of heart failure and transplant.[7] But there was no mention as to whether the patients in this study restricted exercise. Finally, external validation would be required to be assess the generalizability of the model.

The authors are to be congratulated for this important work in risk-stratifying heart failure outcomes in ARVC and reminding us once again of the importance of heart failure in patients with ARVC. Future efforts need to be directed at better defining methods to reduce heart failure risk of patients with ARVC, and especially those determined to be at high risk of developing heart failure.

ARTICLE INFROMATION

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Disclosures

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