New risk prediction score for life-threatening ventricular tachyarrhythmias in laminopathies

Authors:
K Wahbi¹, R Ben Yaou², E Gandjbakheh², F Anselme³, T Gossios⁴, N Lakdawala⁵, C Stalens¹, F Sacher⁶, D Babuty⁷, P Charron², C Vigouroux⁸, G Bonne², S Kumar⁹, P Elliott⁴, D Duboc¹, ¹Hospital Cochin - Paris - France, ²AP-HP - Hospital Pitie-Salpetriere - Paris - France, ³Rouen University Medical School - Rouen - France, ⁴Barts Health NHS Trust - London - United Kingdom of Great Britain & Northern Ireland, ⁵Brigham and Women’s Hospital - Boston - United States of America, ⁶Hospital Haut Leveque - Bordeaux-Pessac - France, ⁷University Hospital of Tours - Tours - France, ⁸Hospital Saint-Antoine - Paris - France, ⁹Westmead Hospital - Sydney - Australia,

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Background: An accurate estimation of the risk of life-threatening (LT) ventricular tachyarrhythmia (VTA) in patients with LMNA mutations is crucial to select candidates for implantable cardioverter defibrillator (ICD) implantation.

Methods: We included 839 adult patients with LMNA mutations, including 660 from a French nationwide registry in the development sample, and 179 from other countries, referred to 5 tertiary centers for cardiomyopathies, in the validation sample. LTVTA was defined as a) sudden cardiac death or b) ICD-treated or hemodynamically unstable VTA. The prognostic model was derived using Fine-Gray’s regression model. The net reclassification was compared with current clinical practice guidelines. The results are presented as means (standard deviation) or medians [interquartile range].

Results: We included 444 patients 40.6 (14.1) years of age in the derivation sample and 145 patients 38.2 (15.0) years in the validation sample, of whom 86 (19.3%) and 34 (23.4%) suffered LTVTA over 3.6 [1.0-7.2] and 5.1 [2.0-9.3] years of follow-up, respectively. Predictors of LTVTA in the derivation sample were: male sex, non-missense LMNA mutation, 1st degree and higher atrioventricular block, non-sustained ventricular tachycardia, and left ventricular ejection fraction. In the derivation sample, C-index (95% CI) of the model was 0.776 (0.711-0.842). In the external validation sample, the C-index was 0.800 (0.642-0.959) and calibration slope 1.082 (95% CI, 0.643-1.522). A 5-year estimated risk threshold =7% predicted 96.2% of LTVTA and net reclassified 28.8% of patients with LTVTA compared with the guidelines-based approach.

Conclusions: Compared to the current standard of care, this risk prediction model for LTVTA in laminopathies facilitated significantly the choice of ICD candidates.