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RESEARCH LETTER

Prognostic Implications of Right Ventricular Size and Function in Patients Undergoing Cardiac Resynchronization Therapy

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Cardiac resynchronization therapy (CRT) is an established treatment for patients with symptomatic chronic heart failure, reduced left ventricular ejection fraction (≤35%), and a QRS duration ≥130 ms.[1] Furthermore, chronic left ventricular failure is the most frequent cause of right ventricular (RV) adverse remodeling, a complex process consisting of progressive RV dilatation and dysfunction.[2] Both parameters individually, RV dilatation and RV dysfunction, are important prognostic markers in CRT-recipients.[3,4] However, the prognostic value of both parameters in a single model has not been evaluated. Accordingly, this study evaluated the prognostic value of RV remodeling in CRT-recipients.

CRT-recipients with echocardiographic data on RV remodeling, before CRT implantation (both CRT-D and CRT-P), were identified from the departmental database of the Leiden University Medical Center (Leiden, The Netherlands). RV remodeling was assessed by RV size (measured by indexed RV end-diastolic area [right ventricular end-diastolic area—indexed for body surface area] using sex-specific cutoff values to define RV dilatation: right ventricular end-diastolic area—indexed for body surface area >12.6 cm^2/m^2 for men and right ventricular end-diastolic area—indexed for body surface area >11.5 cm^2/m^2 for women) and RV function (measured by tricuspid annular plane systolic excursion) with tricuspid annular plane systolic excursion <17 mm considered as a reduced RV function).[5] Subsequently, patients were classified into 4 remodeling patterns: (1) normal RV size and function; (2) RV dilatation and normal RV function; (3) normal RV size and RV dysfunction; (4) RV dilatation and RV dysfunction (Figure). The primary end point was all-cause mortality.

Cumulative survival rates were calculated using the Kaplan-Meier method. To investigate the association between RV size and RV function with all-cause mortality, multivariable Cox proportional hazards regression analysis was performed, adjusting for variables known to have an impact on prognosis. The incremental prognostic value of RV size and RV function was assessed by likelihood-ratio testing evaluating the change in global χ^2 values. This retrospective analysis was approved by the institutional review board of the Leiden University Medical Center, and the need for patient written informed consent was waived. The research reported in this article adhered to the Helsinki Declaration. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Of the 773 patients (mean age 66±10 years, 75% males) included, 264 (34%) patients had pattern 1, 101 (13%) had pattern 2, 256 (33%) had pattern 3, and 152 (20%) had pattern 4, prior to CRT implantation. A total of 414 (54%) patients had an ischemic cause of heart failure. A total of 739 (96%) patients received CRT-D, and only 34 (4%) patients had CRT-P with a comparable distribution among the 4 remodeling patterns. Overall, 130 (17%) patients had atrial fibrillation, and the mean QRS duration was 168±26 ms. Mean left ventricular ejection fraction was 27±8%, mean right ventricular end-diastolic area—indexed for body surface area was 11.5±3.5 cm^2/m^2, and mean tricuspid annular plane systolic excursion was 16±5 mm. When comparing the 4 RV remodeling patterns, ischemic cause varied significantly

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Nonstandard Abbreviations and Acronyms

CRT	cardiac resynchronization therapy
RV	right ventricle

(50%, 37%, 64%, and 54% in respectively patterns 1–4; P<0.001). Patients with patterns 2 to 4 more often had atrial fibrillation compared with patients with pattern 1 (8%, 22%, 18%, and 28%, in respectively patterns 1–4; P<0.001). Patients with pattern 4 had significantly less frequently left bundle branch block compared with the other patterns (70%, 64%, 60%, and 45%, in respectively patterns 1–4; P<0.05 for all comparisons). Inherent to the classification system used, significant differences among the RV remodeling patterns were observed about right-sided echocardiographic variables of size and function. Of note, patients with pattern 4 had more pronounced left ventricular systolic dysfunction.

During a median follow-up of 94 (IQR, 54–143) months after CRT implantation, 480 (62%) patients died. Cumulative 5-year survival rates after CRT implantation were significantly worse in patients with more advanced RV remodeling (83%, 73%, 71%, and 53% 5-year survival for patterns 1 to 4, respectively; P<0.001; Figure). Multivariable Cox regression analysis for all-cause mortality showed that RV size and RV function, assessed as continuous as well as categorical variables, were independently associated with all-cause mortality, both individually and in combination (Figure). In addition, the evaluation of RV size plus RV function provided incremental prognostic value over the evaluation of RV size or RV function individually (change in likelihood-ratio test P<0.05).

Our data show that a large proportion (66%) of CRT-recipients already present with extensive RV remodeling (defined by RV dilatation and/or RV dysfunction) at the time of implantation. The extent of RV remodeling prior to CRT implantation is strongly associated with worse survival. Furthermore, RV size and RV function were, both individually and in combination, independently associated with all-cause mortality. Noteworthy, this retrospective analysis included only CRT-recipients, and therefore the relative benefit of CRT among heart failure patients with RV adverse remodeling cannot be evaluated. Nevertheless, the current study underscores that in patients who receive CRT the combination of RV size and RV function conferred incremental prognostic value to assess all-cause mortality over a broad range of recognized prognostic parameters, emphasizing that risk assessment of CRT-recipients should systematically include comprehensive evaluation of RV size as well as RV function.

ARTICLE INFORMATION

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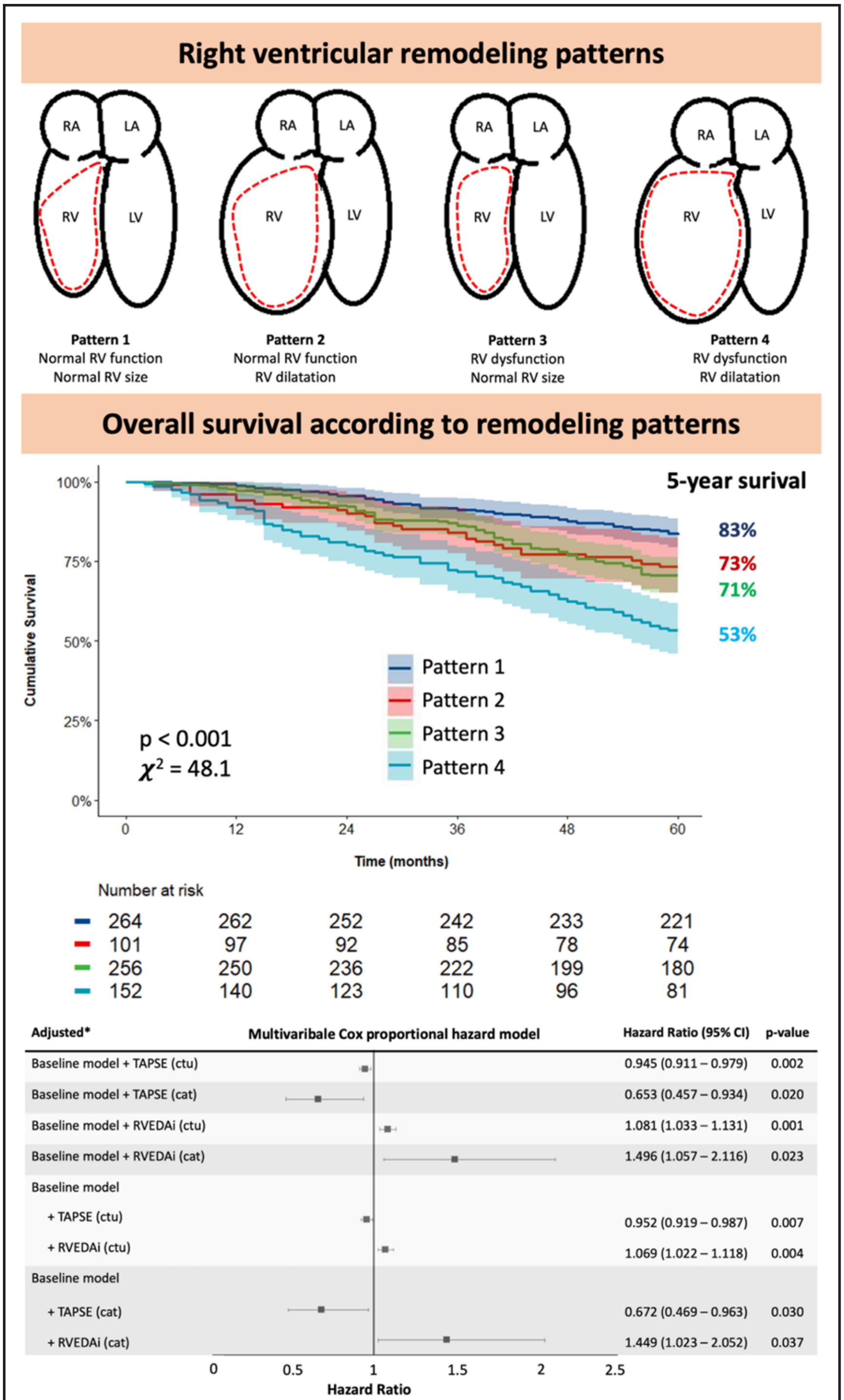

Figure. Right ventricular (RV) remodeling patterns based on RV size and RV systolic function with overall survival according to the RV remodeling patterns.
Four patterns of RV remodeling were defined according to the presence or absence of RV dilation and RV systolic dysfunction. The Kaplan-Meier curves show significantly lower 5-year survival rates for patients with more advanced RV remodeling patterns. Shaded areas represent 95% CIs. *Adjusted for baseline model including the following variables: age, sex, ischemic cause, diabetes, New York Heart Association class III/IV, atrial fibrillation, QRS duration, left bundle branch block, presence of a defibrillator, hemoglobin, kidney function (eGFR-MDRD), left ventricular (LV) end-diastolic volume-indexed, LV ejection fraction, left atrial (LA) volume-indexed, and maximal tricuspid regurgitation gradient. Categorical variables were defined as follows: tricuspid annular plane systolic excursion (TAPSE) ≥17 mm and dilated right ventricle end-diastolic area-indexed for body surface area (RVEDAi) according to sex-specific cutoff values: RVEDAi >12.6 cm²/m² for men and RVEDAi >11.5 cm²/m² for women. Cat indicates categorical variable; Ctu, continuous variable; RV, right ventricle; and TAPSE, tricuspid annular plane systolic excursion.