

Prognostic value of collagen turnover biomarkers in cardiac resynchronization therapy: A subanalysis of the TRUST CRT randomized trial population.

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Abstract

BACKGROUND:

A substantial proportion of patients do not respond to cardiac resynchronization therapy (CRT). Various echocardiographic and biochemical markers including collagen turnover biomarkers were suggested to predict CRT results. However, pathological significance of collagen turnover biomarkers in CRT remains controversial.

OBJECTIVE:

The aim of the present study was to evaluate the relationship between levels of collagen turnover biomarkers (amino-terminal propeptide of procollagen type I and amino-terminal propeptide of procollagen type III [PIIINP]), N-terminal of the prohormone brain natriuretic peptide (NT-proBNP), high-sensitivity C-reactive protein, and matrix metalloproteinases (metalloproteinase-2 and metalloproteinase-9) and echocardiographic response to CRT and clinical outcomes.

METHODS:

The study population consisted of patients enrolled in the Triple Site Versus Standard Cardiac Resynchronization Therapy trial. Blood samples were obtained before implantation of a CRT with defibrillator. The levels of PIIINP, amino-terminal propeptide of procollagen type I, metalloproteinase-2, and metalloproteinase-9 were determined using commercially available ELISA kits. High-sensitivity C-reactive protein and NT-proBNP levels were determined in a standard way.

RESULTS:

Samples were collected from 74 of 100 enrolled patients. The multivariate logistic regression analysis demonstrated that low PIIINP levels (odds ratio [OR] 3.56; 95% confidence interval [CI] 1.23-10.24; P = .017) and baseline ejection fraction (OR 2.14; 95% CI 1.11-4.11; P = .02) were favorably associated with echocardiographic response. PIIINP and NT-proBNP

levels appeared to be independent predictors of all-cause mortality (PIIINP: OR 3.11; 95% CI 1.21-7.89; P = .033; NT-proBNP: OR 2.05; 95% CI 1.11-4.96; P = .039) and risk of major cardiac adverse event (PIIINP: OR 3.56; 95% CI 1.53-9.15; P = .007; NT-proBNP: OR 4.51; 95% CI 1.75-11.6; P = .001). PIIINP levels showed significant additive value in predicting mortality as compared with NT-proBNP levels, but they were not superior to ejection fraction in predicting response. Survival analysis with cutoff values identified by receiver operating characteristic analysis confirmed a significant benefit associated with low baseline PIIINP levels.

CONCLUSION:

Low PIIINP levels are associated with favorable echocardiographic response and long-term survival in CRT recipients.

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KEYWORDS:

Biomarkers; Cardiac resynchronization; Collagen turnover; Heart failure; Heart remodeling