

### Long-term outcome after adding an ICD to CRT in non-ischemic patients

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**Background:** There are limited and contradictory data on the long-term mortality benefit of cardiac resynchronization therapy with implantable cardioverter defibrillator (CRT-D) as compared to Cardiac resynchronization therapy with pacemaker.

**Purpose:** Our aim was to evaluate the long-term all-cause mortality benefit of CRT-D compared to CRT-P by ischemic aetiology.

**Methods:** Between 2000 and 2018, patients, who underwent successful CRT implantation were registered. From 2524 patients, 1366 (54%) had a CRT-D implantation and 1099 (44%) had CRT-P implantation. 59 (2%) patients were excluded from the current analysis, who had an ICD upgrade with a CRT-P device during the follow-up. The primary composite endpoint was all-cause mortality, LVAD implantation or heart transplantation. Kaplan-Meier and multivariate Cox regression analyses were used to assess all-cause mortality in the total cohort and by ischemic aetiology.

**Results:** The median follow-up time was 3.6 years. During this time 1389 patients died from any cause, 692 patients (50%) with a CRT-D device, and 697 patients (50%) with a CRT-P. Patients in the CRT-D group were younger (67 years vs. 70 years;  $p < 0.001$ ), had a less advanced functional class (NYHA III/IV, 52.2% vs. 61.4%;  $p < 0.001$ ), wider QRS [160ms (140/180) vs. 160ms (140/170);  $p = 0.03$ ] and less females (18.9% vs. 33.3%;  $p < 0.001$ ) with an ischemic aetiology (57.7% vs. 40.2%;  $p < 0.0001$ ).

CRT-D patients had a better renal function [eGFR, 60.5 (ml/min/1.73m<sup>2</sup>) vs. 57 (ml/min/1.73m<sup>2</sup>);  $p = 0.02$ ], decreased ejection fraction (28% vs. 30%;  $p = 0.002$ ), had more frequently ventricular arrhythmia (36% vs. 9.8%;  $p < 0.001$ ). CRT-D patients took more amount of beta-blockers (90.2% vs. 87.3%;  $p = 0.03$ ), MRA (72.2% vs. 61.6%;  $p < 0.001$ ) and amiodaron (32.2% vs. 20%;  $p < 0.001$ ). By multivariate analysis in the total cohort gender, renal function, functional class, aetiology, and the presence of ICD were independent predictors of all-cause mortality. By multivariate analysis, patients with a CRT-D device showed a 25% decreased risk of long-term mortality compared to CRT-P alone in the total cohort. (aHR 0.75; 95% CI 0.58–0.97;  $p = 0.03$ ). When patients were analysed by their etiology, those with non-ischemic cardiomyopathy showed a significant mortality benefit from ICD even after adjusting for relevant clinical variables (aHR 0.45; 95% CI 0.28–0.72;  $p < 0.01$ ). In ischemic patients despite of having a clear mid-term mortality benefit of ICD, it is decreasing after 5 years and less considerable after adjusting for clinical variables (aHR 0.92; 95% CI 0.67–1.27;  $p = 0.60$ ).

**Conclusions:** Although, CRT-D had a notable mid-term mortality benefit in ischemic patients compared to CRT-P alone, after 5 years it became less pronounced. While in non-ischemic patients, the benefit of adding an ICD to CRT lasts over 10 years.

**All-cause mortality in non-ischaemic patients with CRT-P vs CRT-D**

