Ventricular arrhythmia risk after cardiac resynchronization therapy depends on myocardial scar but not on left ventricular remodeling. The GAUDI-Remod study

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Introduction
Ventricular arrhythmia risk estimation in patients with severe heart failure is challenging. Left ventricular (LV) ejection fraction (LVEF) is the most widely used parameter, however, its predictive value is limited. Myocardial scar in the LV as detected with delayed enhancement cardiac magnetic resonance (DE-CMR) is an emerging risk predictor and has been shown to be associated with malignant arrhythmic events and sudden cardiac death (SCD), both in ischemic (ICM) and non-ischemic cardiomyopathy. Patients qualifying for cardiac resynchronization therapy (CRT) are expected to improve LVEF and, surpassing the threshold of 35%, many of them abandon the ICD indication for primary prevention of SCD.

Purpose
The aim of this prospective international multi-center trial was to evaluate the association of myocardial scar with malignant arrhythmic events and mortality in function of the echocardiographic response in patients receiving CRT.

Methods
Decision between CRT-defibrillator (CRT-D) and CRT-pacemaker (CRT-P) was made clinically by the treating cardiologist. DE-CMR was performed in all patients before device implantation to determine presence and mass of LV scar. Transthoracic ecocardiography was performed at baseline and 12 months to determine response to CRT. Follow-up clinical evaluation and device interrogation was performed every 6 months.

Results
218 patients (158 (73%) male, mean LVEF 26±7%, 79 (36%) ICM) with indication for CRT were in included and followed for 54±37 months after device implantation (60 CRT-P (27.5%) vs. 158 CRT-ICD (72.5%)). LV myocardial scar was present in 135 (62%) patients (mean scar mass 22±23g). 126 (58%) patients were CRT responders, defined as showing a reduction in LV end-systolic volume (LVESV) of =15% within 12 months. The composite endpoint of sustained VT, appropriate ICD therapy and SCD was only reached in patients with myocardial scar and was independent of CRT response (HR 1.023 [1.016-1.030] for each 1g increase of scar mass and 1.002 [0.989-1.016] for each 1% of LVESV reduction in the multivariate analysis). With respect to cardiac mortality and heart transplantation, presence of myocardial scar and non-response to CRT had an additive effect. All-cause mortality was only significantly better in patients who did not have a myocardial scar and also were responders to CRT as compared to all other groups (Figure 1).
Conclusions
Malignant arrhythmic events and SCD depend on the presence of myocardial scar but not on the response to CRT. Only the absence of myocardial scar in combination with response to CRT was associated with improved all-cause mortality.