Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT)

The results of the MADIT-CRT trial were published in the landmark paper, *Cardiac Resynchronization Therapy for the Prevention of Heart-Failure Events* in NEJM in 2009. The study set out to evaluate the benefit of cardiac resynchronization (CRT) via placement of a coronary sinus left ventricular pacing lead in patients with ventricular dyssynchrony (widened QRS) and only mild (NYHA I or II) symptoms. The benefit of CRT in a "sicker" population (NYHA III or IV) had already previously been established.

The study enrolled patients who met guideline indications for a primary prevention ICD and then were randomized (in a 3:2 fashion) to either receive a CRT-D (ICD + CRT) or an ICD alone. Over 1800 patients with ischemic or non-ischemic cardiomyopathy, LVEF≤30%, and QRS>130ms were enrolled. The primary end point in the patients was either death or any cause nonfatal heart-failure event (essentially patients being diagnosed with a heart failure exacerbation and responding to appropriate intervention like diuresis).

The trial was stopped early given the safety monitoring board noted a clear improvement in outcomes in patients treated with CRT. During a mean follow up of 2.4 years, the incidence of the primary end point was 17.2% in the ICD + CRT patients and 25.3% in the ICD only patients (P<0.001) or an overall 41% relative reduction in the primary endpoint. It is important to note that this difference was driven primarily from nonfatal heart-failure events. Basically that means that with this patient population and sample size, the addition of CRT decreased HF exacerbations but did not appear to reduce risk of death (at least not with statistical significance). Subgroup analysis was performed (we need to take some caution interpreting this information given the trial was not necessarily powered to conclude a difference between these groups) which showed that women compared to men as well as a very wide QRS (>150ms) were associated with better outcomes with CRT. Also, while not the primary endpoint, both LV volume and LVEF were statistically improved in CRT + ICD when compared to ICD alone.

This trial has had significant implications in the field of electrophysiology, heart failure, and cardiology in general. While clinicians were aware of the detrimental impact of LV dyssynchrony, these results showed how providing resynchronization (even to a group of "not as sick" heart failure patients) could dramatically improve a patient’s clinical outcome. There were criticisms of the trial which included lack of true blinding (providers at follow up knew if the patient had CRT or not), unclear cost effectiveness, and a lack of reduction in overall death (though future trials have eventually demonstrated mortality reduction in patients with LBBB). Overall, the findings were adopted into clinical practice and guidelines. Due largely to the MADIT-CRT trial, the updated 2013 ACC/AHA guidelines recommended that in addition to NYHA III and IV patients, CRT should be recommended or considered for NYHA II patients (class I if LBBB >150ms, class IIa if LBBB <150ms) as well as NYHA I and LBBB >150ms (class IIb).

While CRT has clearly helped many patients, there are still many patients who do not respond for unclear reasons. More recent and future trials hope to address which specific patients will ultimately benefit.

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