The benefit of cardiac resynchronization therapy and QRS duration: a meta-analysis

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Introduction

- In patients with advanced HF symptoms (New York Heart Association [NYHA] class III or IV), despite optimal medical treatment, with a left ventricular ejection fraction (LVEF) ≤40%, and a wide QRS ≥120 ms, cardiac resynchronization therapy (CRT) has been shown to improve functional status and exercise capacity, and to reduce hospitalizations and mortality.
- More recently, in patients with mild to moderate HF, CRT resulted in left ventricular remodeling and prevention of disease progression, as well as a reduction in HF hospitalizations and mortality.
- Approximately 30% of the patients who are selected for therapy according to the current criteria do not benefit from CRT.
- Whether the benefit from CRT is consistent across all degrees of QRS widening remains unclear.
- We undertook a meta-analysis of subgroup data from published randomized clinical trials evaluating the efficacy of CRT with or without an implantable cardioverter defibrillator (ICD) to examine the impact of QRS duration on the efficacy of CRT.

Methods

- We searched MEDLINE and EMBASE databases for studies evaluating the efficacy of CRT with or without ICD, through January 2011. Our search included both Medical Subject Headings (MeSH) and keywords including: 1) Cardiac resynchronization therapy OR Cardiac pacing AND 2) HF AND 3) Randomized controlled trial. Bibliographies of the retrieved articles were screened to identify additional studies. We had no language restrictions.
- We selected randomized controlled trials that tested the efficacy of CRT with or without ICD versus standard medical therapy with or without ICD, respectively, in patients with HF with reduced left ventricular systolic function (LVEF ≤40%) and wide QRS complex (≥120ms). Studies that provided estimates of the risk for the primary outcome of the CRT group compared with the respective control group stratified by QRS duration were included.
- The extracted data included the inclusion criteria, the total number of patients enrolled in the study and their baseline characteristics (including medication use), the duration of follow-up, the number of patients stratified by QRS duration, the hazard ratio (HR) of the primary outcome with its 95% confidence interval of the CRT group compared with the control group, and any adverse effects.
- The quality of eligible studies was assessed using criteria that were previously published, including randomization, double blinding and description of withdrawals and drop outs.

Statistical Analysis:

- The natural log of the HR was pooled across studies using the inverse variance method. Estimates were combined using a random effects modeling approach.
- The I² index was used to summarize the proportion of the total variability in the estimates due to between-study variation.
- A sensitivity analysis was performed by estimating the pooled effect sizes after leaving each study out one by one.

Results

- 5 trials involving 6,501 patients (4,437 with QRS≥150ms and 2,064 with QRS<150ms) were included.

- 3 trials, enrolling patients with mild to moderate HF, compared CRT-ICD with CRT, whereas CRT vs. medical therapy was compared in the other 2 trials, which included patients with advanced HF.

Table 1. Summary of study design and subject characteristics

<table>
<thead>
<tr>
<th>Study name</th>
<th>Sample size</th>
<th>Study design</th>
<th>HR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAFT 2010</td>
<td>1,151</td>
<td>CRT-ICD vs. ICD (1:1)</td>
<td>0.83 (0.68-1.01)</td>
<td>0.06</td>
</tr>
<tr>
<td>MADIT-CRT 2009</td>
<td>448</td>
<td>CRT-ICD vs. ICD (1:1)</td>
<td>0.79 (0.64-0.98)</td>
<td>0.03</td>
</tr>
<tr>
<td>REVERSE 2000</td>
<td>1,000</td>
<td>CRT-ICD vs. ICD (1:1)</td>
<td>0.78 (0.65-0.94)</td>
<td>0.01</td>
</tr>
<tr>
<td>CARE-HF 2005</td>
<td>4,349</td>
<td>CRT-ICD vs. ICD (1:1)</td>
<td>0.82 (0.70-0.96)</td>
<td>0.01</td>
</tr>
<tr>
<td>COMPANION 2004</td>
<td>1,000</td>
<td>CRT-ICD vs. ICD (1:1)</td>
<td>0.80 (0.66-0.96)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

- 5 studies included in meta-analysis

- 24 studies included in meta-analysis

Figure 1. Flowchart of the search for eligible studies

- QRS ≥150ms

- QRS <150ms

Conclusions

- The benefit of CRT appears to be dependent on QRS duration.
- Available data suggest a significant benefit associated with CRT in patients with QRS≥150ms, but not in patients with QRS<150ms.
- Further studies are needed to identify patients with QRS<150ms who might benefit from CRT.

Disclosures: The authors have nothing to disclose.