Cardiac resynchronisation may reduce all-cause mortality: meta-analysis of preliminary COMPANION data with CONTAK-CD, InSync ICD, MIRACLE and MUSTIC

Abstract

Landmark trials have demonstrated that biventricular pacing (also called cardiac resynchronisation therapy or CRT) in chronic heart failure due to left ventricular dysfunction improves symptomatic status, exercise capacity and quality of life. Yet critically, all-cause mortality has not been demonstrated to be reduced in any of the four randomised controlled trials with mortality data (CONTAK-CD, InSync implantable-cardioverter defibrillator (ICD), MIRACLE and MUSTIC). With the much larger COMPANION study now terminated, however, the currently available pooled data from all five trials shows a significant reduction in all-cause mortality, odds ratio (OR), 0.74: 95% confidence interval (CI) 0.56–0.97. This may now establish biventricular pacing as a standard therapy for a specific subset of patients with chronic heart failure and LBBB.

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Keywords: Cardiac resynchronisation; All-cause mortality; COMPANION data
Mortality is also not immune to unintended bias if it is limited to any particular subtype (for example, cardiovascular) since even if the final decision panel is blinded to treatment allocation, the physicians treating the patient and providing information to the decision panel will not be blinded.

All-cause mortality is uniquely incontrovertible and not open to question. It has been a weakness in the evidence base for biventricular pacemakers that no individual trial demonstrates significant reduction in all-cause mortality. A meta-analysis [13], prepared before the largest study (COMPANION) was available, also showed no significant reduction in all-cause mortality.

If the preliminary COMPANION data are included, however, all-cause mortality is now seen to be significantly reduced (see figure below) with odds ratio 0.74, 95% confidence interval 0.56–0.97.

This meta-analysis demonstrates, for the first time, that cardiac resynchronisation therapy with biventricular pacing may reduce all-cause mortality in a selected group of patients with chronic heart failure. This may now propel biventricular pacing into a similar league to ACE inhibitors and beta blockers, namely routine therapy, albeit for a restricted subset of patients with chronic heart failure and LBBB.

### Odds ratios (OR) of all-cause mortality among patients randomised to cardiac resynchronisation therapy (CRT) or no CRT. Confidence interval, CI: Comparison of medical therapy, pacing and defibrillation in heart failure COMPANION: Multicentre InSync Randomized Clinical Evaluation, MIRACLE: Multisite stimulation in Cardiomyopathies, MUSTIC.

<table>
<thead>
<tr>
<th>Trial</th>
<th>CRT N</th>
<th>No CRT N</th>
<th>Favours CRT</th>
<th>Favours No CRT</th>
<th>Weight %</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>COMPANION</td>
<td>617</td>
<td>308</td>
<td></td>
<td></td>
<td>57.7</td>
<td>0.71 (0.5-1.02)</td>
</tr>
<tr>
<td>CONTAK CD</td>
<td>245</td>
<td>245</td>
<td></td>
<td></td>
<td>13.09</td>
<td>0.67 (0.31-1.48)</td>
</tr>
<tr>
<td>InSync ICD</td>
<td>272</td>
<td>282</td>
<td></td>
<td></td>
<td>13.56</td>
<td>0.85 (0.41-1.75)</td>
</tr>
<tr>
<td>MIRACLE</td>
<td>263</td>
<td>269</td>
<td></td>
<td></td>
<td>15.34</td>
<td>0.74 (0.36-1.51)</td>
</tr>
<tr>
<td>MUSTIC</td>
<td>29</td>
<td>29</td>
<td></td>
<td></td>
<td>0.41</td>
<td>3.11 (0.12-79.43)</td>
</tr>
<tr>
<td>Overall</td>
<td>1426</td>
<td>1133</td>
<td></td>
<td></td>
<td>100</td>
<td>0.74 (0.66-0.97)</td>
</tr>
</tbody>
</table>

Odds ratios (OR) of all-cause mortality among patients randomised to cardiac resynchronisation therapy (CRT) or no CRT. Confidence interval, CI: Comparison of medical therapy, pacing and defibrillation in heart failure COMPANION: Multicentre InSync Randomized Clinical Evaluation, MIRACLE: Multisite stimulation in Cardiomyopathies, MUSTIC.

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### References

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