More is better with cardiac resynchronization therapy—but is it enough?

Leslie Anne Saxon

Division of Cardiology, Cardiac Electrophysiology, USC Keck School of Medicine, 1500 San Pablo Street, Los Angeles, CA 90033, USA

Online publish-ahead-of-print 7 July 2006

This editorial refers to 'Longer-term effects of cardiac resynchronization therapy on mortality in heart failure [The Cardiac REsynchronization-Heart Failure (CARE-HF) trial extension phase]' by J.G.F. Cleland et al., on page 1928

The extension phase of the CARE-HF trial results provide important data describing the chronic clinical course of the cardiac resynchronization therapy (CRT) recipient. After all, the device is implanted and, unlike a drug that can be stopped, is a relatively permanent part of a patient’s treatment. These new data also provide a unique perspective on the use of CRT devices alone, without defibrillating capability (CRT-D). This information, originating in the old world, has practice implications and relevance for the new world. In USA, in 2005, over 73% of CRT implants were CRT-D devices and this is expected to increase to 91% of CRT devices implanted in this calendar year. In Europe, CRT-D devices represent only 50–60% of all CRT implants.

The 7-month extension phase of the 813 patients’ CARE-HF trial, includes an additional 53 patient deaths. There were a total of 101 deaths observed in the original study over a mean follow-up of 30 months. In that publication, we learned that CRT alone, compared with drug therapy, improved survival by 36% (hazard ratio for death 0.64, \(P < 0.002\)). This appeared to be primarily due to a reduction in death because of progressive pump dysfunction, and sudden death accounted for 7% of CRT deaths (29 patients). With the follow-up extended to 37 months, the mortality reduction for CRT compared with medical therapy is still robust at 40% (hazard ratio for death 0.60, \(P < 0.0001\)) and the benefit appears to extend to reduced risk from both progressive pump dysfunction and sudden cardiac death (hazard ratio for sudden death 0.54, \(P = 0.005\)).

This data is encouraging and makes sense for a therapy that has been shown to improve symptom status, retard or reverse the remodeling response, and reduce morbidity and mortality in short-term studies. The relationship and relative risks between modes of death in CRT recipients is complex. We have learnt that if a patient responds to chronic CRT, risks of both modes of death are reduced. Although the predominant mode of death after CRT is progressive pump dysfunction, sudden death still accounts for a third of all deaths. Further, for those who benefit most from CRT, sudden death risk after CRT may actually increase proportionately, compared with the risk of a pump death.

Although the COMPANION (Comparison of Medical therapy, Pacing and Defibrillation in Heart Failure) trial was not designed to compare CRT with CRT-D therapy (each were compared separately with optimal drug therapy), it does provide the only comparative mortality and mode of death data to the CARE-HF study. Table 1 summarizes the mortality and mode of death events from the two trials. In COMPANION, a total of 595 patients received a CRT-D device, and when compared with both drug therapy and the CRT device, sudden death risk was reduced by 50% over a follow-up interval of only 16 months. The sudden death risk in COMPANION CRT-D patients was also exactly 50% less than the risk in CRT-only patients in the CARE-HF extension phase (16 vs. 32%). This strongly suggests that the ICD has added value for CRT recipients.

There are three other reasons that the CRT-D device is the preferred CRT device in USA. First and probably foremost, is that the devices are paid for by Medicare, the single largest third party payer in the U.S. Second, the primary prevention ICD trials such as the SCD-HeFT and MADIT trials include the CRT patient population. The third reason is practical in nature. At the time of implant, when one is assuming or hoping for a response to CRT, the tendency is to give the patient the benefit of the doubt and place a defibrillating lead in the RV instead of a pacing lead and an ICD instead of a CRT pacemaker. This avoids the need for a second operation or ‘upgrade’ in the event the patient responds and is, therefore, confronting a reduced risk for a pump death but a greater risk of a sudden death.

Regardless of geographic variations in type of CRT device implant and the factors that influence device selection, the CARE-HF Trial Extension Phase data impact all patients considered for CRT. For the majority of patients expected to survive at least 37 months, it means that the device continues to reduce the risk of death from all causes. For those patients with an anatomical limitation to CRT-D implantation, not expected to survive long enough to benefit from CRT-D therapy or not desirous of an ICD,
these data assure us that chronic CRT alone is an enduring and powerful therapy.

Conflict of interest: L.A.S. is a consultant for Guidant Corp. and Medtronic Inc., and has received research and training funds from Guidant Corp. and Medtronic Inc.

References


<table>
<thead>
<tr>
<th>Table 1</th>
<th>Mortality and mode of death analysis—CRT/CRT-D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean follow-up (months)</td>
<td>Total mortality (%)/pump death (%)/sudden death (%)</td>
</tr>
<tr>
<td></td>
<td>OPT</td>
</tr>
<tr>
<td>COMPANION 16</td>
<td>25/44/23</td>
</tr>
<tr>
<td>CARE-HF 30</td>
<td>30/47/32</td>
</tr>
<tr>
<td>CARE-HF extension 37</td>
<td>38/42/36</td>
</tr>
</tbody>
</table>

*Per cent of deaths within each treatment group.*