Cardiac Resynchronization for Heart Failure

Cardiac conduction abnormalities may worsen heart failure by disrupting the coordination of left ventricular contraction, making it even less effective. This pathophysiologic insight suggests that judiciously applied electrical stimuli could improve the coordination and efficiency of left ventricular contraction (1). The clinical value of this new approach, called cardiac resynchronization therapy (CRT), has been evaluated in several randomized, controlled clinical trials. This evidence is summarized in a systematic review by McAlister and associates in this issue (2), which also contains a companion article by Nichol and coworkers (3) analyzing the cost-effectiveness of using CRT in patients with heart failure.

Randomized trials are essential tests of the effect of therapy on clinical outcomes, but trials of implanted devices are particularly challenging. Most of the studies of CRT have been small, which limits the conclusions that can be drawn. Another challenge is that the technology is rapidly evolving. Current CRT devices are combined with an implantable cardioverter defibrillator (ICD), but only a few trials with limited outcome data have directly tested the value of adding CRT capability to an ICD. The evidence about use of CRT in heart failure is therefore relatively thin, especially in comparison with the solid evidence about pharmacologic treatments such as angiotensin-converting enzyme inhibitors and β-blockers.

Two major goals of heart failure treatment are to improve either the length or quality of the patient's life. As reviewed by McAlister and associates, trials of CRT have shown improvements in functional status, the distance patients can walk in 6 minutes, and hospital admissions for heart failure (2). The evidence is therefore pretty convincing that CRT can meaningfully improve patient quality of life.

The evidence about the effect of CRT on mortality is less clear, however, since none of the individual clinical trials found a statistically significant reduction. McAlister and associates used meta-analysis to combine the results from 9 trials of CRT and reported a statistically significant 21% reduction in mortality (2). While this result is suggestive, it is not definitive. Meta-analyses based only on small trials often yield lower relative risk reductions than definitive large trials (4), perhaps because small positive studies are more likely to be published than small negative studies. All of the randomized trials used in McAlister and associates' meta-analysis have flaws that limit inferences about the effect of CRT on mortality. Eight of the 9 trials required successful device implantation before patients were randomly assigned to have the CRT function turned on or off. This design caused the results to overstate the effect of CRT on mortality by omitting all of the implantation failures (10% or more) and procedural deaths (0.4% or more) while exposing all of the controls to the adverse effects of an implanted device. A more serious limitation is that CRT was combined with an ICD in some studies but not in others, making it tricky to isolate the effect of CRT on mortality. The Comparison of Medical Therapy, Pacing, and Defibrillation in Chronic Heart Failure (COMPANION) trial (5) poses particular problems because of its unbalanced, 3-arm design (medical therapy, CRT, and CRT combined with an ICD) and the weight it was given in the meta-analysis because of its large enrollment and high mortality rates. We think that McAlister and associates should have omitted the CRT-ICD arm of the COMPANION trial, since including it inappropriately credited CRT with the mortality reduction that was due to the ICD. With omission of this unpaired arm of the COMPANION trial, the estimated effect of CRT on mortality would certainly be much less favorable and, if so, no longer statistically significant. Thus, while CRT improves functional status and quality of life, there is not yet significant evidence that it reduces mortality.

Introduction of new medical technologies is a major reason that health care costs continue to increase. The economic outcomes of a new treatment are therefore of great interest, especially as we attempt to weigh whether a new treatment is worth the added cost. The initial cost of implanting a CRT device is about $34 000, but the total cost may be either higher or lower depending on its effect on the cost of heart failure treatment and the additional costs of treating device complications. Nichol and coworkers used the limited economic data from the randomized trials and some reasonable assumptions based on other data sources to project the economic impact of using CRT in patients with heart failure (3). Their analysis strongly suggests that CRT does not "pay for itself" but has a net lifetime cost of roughly $30 000.

Cardiac resynchronization therapy may be worth its high cost if it substantially improves patient survival, quality of life, or both. Cost-effectiveness analysis provides a quantitative measure of clinical value by computing the dollars spent per quality-adjusted life-year added by a treatment. Nichol and coworkers estimated the cost-effectiveness of CRT at $107 800 per life-year gained (3), which is not economically attractive when compared against the standard benchmark of $50 000 per life-year gained. However, their analysis also showed that the cost-effectiveness of CRT is exquisitely sensitive to variations in clinical efficacy. This suggests that if clinicians can prospectively identify patients whose quality of life would be greatly improved by CRT, use of the device in such patients would be far more economically attractive. Routine use of CRT is not cost-effective, but properly targeted use may well be.

Nichol and coworkers did not examine the cost-effectiveness of combined CRT-ICD devices. The recently completed Sudden Cardiac Death in Heart Failure Trial

(SCD-HeFT) adds to the evidence that ICDs reduce overall mortality, and the COMPANION trial suggests that CRT-ICD devices do so as well. Most future CRT devices will probably include ICD capability, but the cost-effectiveness of these more costly and complex combined devices has not been examined. More data are needed on the clinical and economic outcomes of combined CRT-ICD devices to develop evidence-based recommendations for their appropriate use in patients with heart failure.

The weight of evidence suggests that CRT improves functional status and quality of life in selected patients with heart failure. Cardiac resynchronization therapy can be considered in patients with heart failure, an ejection fraction of 0.35 or less, and a QRS duration of 120 ms or greater who remain symptomatic despite meticulous fluid management with diet and diuretics and adherence to appropriate doses of angiotensin-converting enzyme inhibitors and β-blockers.

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