EDITORIAL COMMENT

Cardiac Resynchronization Therapy in the Autumn of Life*

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To implant or not to implant a primary prevention implantable-cardioverter defibrillator (ICD) in older patients is a question that has challenged clinicians for years. On the one hand, the ICD is a highly effective therapy for the prevention of sudden cardiac death. On the other hand, there are no definitive data regarding the benefit of the ICD in older patients. Indeed, in the pivotal randomized clinical trials that demonstrated the efficacy of the ICD, the mean or median age of enrolled patients was well below 75 years of age (1–4). There are reasons why older patients may not derive survival benefit from the ICD. Such patients typically have heart failure along with other comorbidities that may attenuate the efficacy of the ICD. Older patients may also be frail, and this, along with the coexisting diseases, may make the device implantation risky and negatively impact their quality of life, raising concerns about therapies, like the ICD, that prolong life but do not necessarily improve its quality. However, when the ICD is coupled with cardiac resynchronization therapy (CRT), there is potential for improved quality of life and reduced heart failure hospitalizations, 2 important goals in the care of heart failure patients.

In the main randomized clinical trials of CRT-defibrillator (CRT-D) or CRT-pacemaker (CRT-P), the relatively young age of enrolled patients is noticeable, with a mean age ranging from 64 to 68 years (5–8). As expected, their level of comorbidity was lower than that seen in the average older patient. As such, it is reasonable to wonder whether the results of those trials can be extrapolated to older patients. Although several investigations suggested an association between CRT and improved echocardiographic and/or clinical outcomes in older patients (9-13), most results were limited by the relatively small sample of older patients (9-12), and some results were limited by the retrospective analysis (10-12). Those studies were not a priori designed to examine survival or heart failure hospitalization in older patients nor were they statistically powered to do so (9-13). Therefore, in those studies, the similar survival observed between older patients and that of their younger counterparts is possibly due to the lack of adequate statistical power and should not be interpreted as a proof of survival benefit of CRT in the elderly. Although some of these studies examined New York Heart Association (NYHA) functional class before and after CRT (10-13), only a minority used robust and validated tools to assess quality of life (13).

Several of the knowledge gaps regarding the outcomes of CRT in older patients were highlighted in a 2014 report to the Agency for Healthcare Research and Quality (14). Relevant questions included: what are the clinical predictors of response in Medicare-eligible patients who are deemed appropriate candidates for CRT-D devices? What are the adverse effects or complications associated with CRT-D implantation in the Medicare population? What are the clinical predictors of response in Medicare-eligible patients who are deemed appropriate candidates for CRT-P devices? What are the adverse effects or complications associated with CRT-P implantation in the Medicare population? What is the effectiveness of CRT-D versus that of CRT-P in reducing heart failure symptoms, improving myocardial function, reducing hospitalization, and/or improving survival in patients with a left ventricular ejection fraction (LVEF) of ≤35% and a QRS duration of ≥120 ms? What are the adverse effects or complications associated with

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Intriguing in older patients for whom quality of life outcomes associated with CRT-P are especially important. What are some patient-centered outcomes like functional status and inappropriate ICD shocks; and most important, like short- and long-term complications, appropriate practice. What about other important endpoints and criteria: LVEF of ≥35%, a QRS interval of ≥120 ms, and NYHA functional class III or IV. Importantly, 22,686 of their patients were 75 to 84 years of age, and 4,613 patients were ≥85 years of age, making this study the largest study ever of CRT-D in older patients. Compared with ICD only, CRT-D was associated with better survival at 1 and 4 years of follow-up across all age groups.

Despite the important clinical data that Heidenreich et al. (15) provide, their study leaves several questions unanswered. What would the results look like if the authors used the updated criteria for CRT implantation that are largely based on QRS duration and morphology and include patients with NYHA functional class II symptoms (16)? Such results would be more relevant to today’s clinical practice. What about other important endpoints like short- and long-term complications, appropriate and inappropriate ICD shocks; and most important, patient-centered outcomes like functional status and quality of life? What about outcomes of CRT-P? Outcomes associated with CRT-P are especially intriguing in older patients for whom quality of life may be far more important than its duration. What is the impact of frailty and the burden and severity of comorbidities on various outcomes? A robust 80-year-old patient with 1 to 2 comorbidities may fare much better than a frail 60-year-old patient with multiple comorbidities. Although the authors’ statement that “[a]dditional studies are needed to determine the age threshold at which the life years gained from CRT become too small to justify the use of the device” is correct, this statement should be revised to also incorporate thresholds for frailty and burden of comorbidities. Finally, what were the effects of confounding and selection bias on the results of this study? Using even the most robust statistical methods, residual confounding cannot be totally avoided in observational studies. Therefore, a randomized clinical trial is the best study design to examine the effect of CRT-D versus that of CRT-P on different patient outcomes while accounting for frailty and comorbidities and examining complex interactions between different factors like race, sex, age, CRT, and outcomes.

An important goal of any related future initiative should be to enhance the knowledge of CRT-D and CRT-P outcomes in older patients and, as a result, improve the effectiveness of clinical decision making. The ultimate vision is to be able to provide patients with all the information they need to make the best decision for themselves based on what is most important to them.

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REFERENCES


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