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Cardiac Resynchronization Therapy in Older Patients: Age Is Just a Number, and Yet ...

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Cardiac resynchronization therapy (CRT) is recommended for patients with severe left ventricular systolic dysfunction (ejection fraction < 35%), QRS duration > 120 ms, and symptomatic heart failure despite optimal medical therapy. CRT use in older adults is increasingly common; more than a third of all patients in the United States receiving implantable cardiac defibrillators (ICDs) also receive CRT.^{1,2} The proportion of devices that include CRT increases with age, from 15% among patients aged 18–39 years to 40% among those over age 80.^{3–5} Pivotal clinical trials in CRT did not set upper age limits for enrollment. However, due to enrollment of predominately younger patients, these studies were not specifically designed or powered to assess outcomes in elderly patients.^{3,4,6–8} Meta-analyses of CRT trials also have not examined outcomes specifically in older patients^{9,10} and are limited in their assessment of comorbid conditions. Thus, whether CRT is effective in an elderly population, and how CRT with or without defibrillator back-up (CRT-D versus CRT-P, respectively) influences outcomes is a pivotal concern greatly in need of additional data.¹¹

In this issue of *Journal of Cardiac Failure*, Mullens and colleagues present a single-center cohort study of 686 CRT recipients at an experienced referral center in Belgium, with the specific focus on mode of death among octogenarians (N = 178) at a mean follow-up of 38 months.¹² The octogenarian cohort was evenly divided between ischemic and non-ischemic substrates, included 21% receiving CRT-D systems, and was predominantly in New York Heart Association (NYHA) class II (31%) and III (64%) with left bundle branch block (78%). At six months, improvements in NYHA class, left ventricular ejection fraction, and left ventricular dimensions were similar between octogenarians and younger patients. Mode of death was ascertained in 100 patients predominantly from electronic health records. Deaths among octogenarians were largely non-cardiac (74%, compared with 50% among younger patients) and only 1 (3%) was tachy-arrhythmic, compared to 11% tachy-arrhythmic deaths in younger patients. From these findings, the authors conclude that CRT

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effectively provides functional and morphologic improvements in older patients, but that CRT-D may have little practical value compared with CRT-P given the low incidence of arrhythmic death.

This study has several strengths, including high rates of clinical and echocardiographic follow-up and vital status determination, and it provides useful data that will advance debate surrounding CRT utilization in older patients. Information about the modes of death support the more general observation that competing risks for mortality attenuate the benefits of ICDs in older patients.¹³ This study also supports the usefulness of CRT in heart failure populations where concerns about frailty or age alone may limit either patient or provider enthusiasm for implantation procedures. This cohort had relatively high rates of relevant medication usage and a high prevalence of left bundle branch block with QRS >150 ms, which are consistent with current guidelines.

Several considerations warrant caution in placing this study in context. First, the authors do not comment on observed device-related complications, a disappointing shortcoming given a study design in which identification of adverse events temporally removed from the implant procedure should be possible. This is important given lingering uncertainty about the “true” rate of device-related complications, which are likely underestimated by studies focused exclusively on the index hospital presentation. Second, information on inappropriate shocks for the CRT-D sub-cohort would be of interest, and the authors did not report whether standardized programming of tachy-therapy was employed (or changed during the course of the study). Third, the authors did not perform any statistical adjustment in assessing either the clinical or echocardiographic outcomes, yet observed significant differences between the older and younger patients according to key comorbidities such as renal failure. Modeling non-cardiac or non-arrhythmic deaths according to age alongside other simple covariates would more clearly delineate the associations between these factors and possible benefits of ICD therapy. A related problem is that while this study provides reassuring estimates of response rates between older and younger patients, the study may have been underpowered to detect differences in the primary morphologic outcomes between these groups. Fourth, the authors do not describe the manufacturer or model information for the CRT systems used. Developments such as algorithms to provide V-V timing based off of intrinsic conduction, vector optimization leveraging quadripolar left ventricular leads, and multipolar left ventricular pacing, as well as greater utilization of remote monitoring, have all demonstrated promise. Whether these technologies were employed at the study center would be of interest. Lastly, adjudicating modes of death by electronic records alone depends on the fidelity of clinical notes or other documentation from which these data are derived, faith perhaps mislaid.

It is also worth noting that, as a cohort emerging from routine clinical care, the Mullens study did not routinely measure quality of life (QoL). The major CRT studies assessed QoL using heart failure-specific instruments, but did not stratify their findings according to age or include other measures of functional status or independence that may be uniquely important to older patients. Similarly, though cognitive function has been recognized as an important concern for older patients,¹⁴ neither its prevalence among CRT recipients nor its subsequent trajectory have been described. This has important implications for fully characterizing the

health status and outcomes for older CRT patients, while also expanding our understanding of how likely these patients are to participate in a robust shared decision-making process.^{11,15}

Despite these limitations, the contribution from Mullens and colleagues admirably focuses attention on the critical and costly decision to select CRT-P or CRT-D for individual patients. As the authors note, CRT-D implantation dominates in the United States (US): One recent study of contemporary US CRT utilization based on claims (N = 17,780) found that only 15% of implants were CRT-P, though an increase from 12% to 20% was seen from 2008 to 2013.^{16,17} This contrasts to the current study (79% CRT-P in octogenarians) and other reports from Europe illustrating more judicious use of CRT-D systems.^{18,19} These observations collectively raise several questions: What matters most to older patients with heart failure? How do we select the device that best meets each patient's goals? Should the roughly four-fold difference in cost be considered when allocating CRT-P and CRT-D devices?²⁰ And, as we have asked before,¹⁵ are we any closer to a systematic approach to addressing these issues in the context of CRT use?

This study provides a step towards answering these difficult questions surrounding appropriate device selection for older patients, while reaffirming the physiologic effectiveness of resynchronization therapy in well-selected patients, regardless of age.

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