ATRIAL FIBRILLATION

COMPLEX CASE STUDY

Cardiac Resynchronization Therapy and Atrial Fibrillation Management in the Elderly

TIFFANY C. RANDOLPH, MD and CAMILLE G. FRAZIER MILLS, MD, MHS

1Department of Medicine, Duke University Medical Center, Durham, NC
2Division of Cardiology, Duke University Medical Center, Durham, NC

ABSTRACT. RM is an 89-year-old man with ischemic cardiomyopathy, ejection fraction (EF) 25–30%, New York Heart Association class (NYHA) III symptoms, left bundle branch block with QRS of 163 ms, and atrial fibrillation (AF) who presented to clinic requesting AF management and possible device placement. RM’s symptoms had progressed despite optimal medical management, so initially his AF management was switched to rhythm control. Overall he felt better after this change but remained limited functionally. After a discussion regarding goals of care, he opted for cardiac resynchronization therapy (CRT) with pacemaker rather than CRT with defibrillator. His device was placed without complication and at 15-week follow up his EF improved to 50% with NYHA class I symptoms. The management of AF and heart failure in the elderly population is poorly studied. This article will review the management of both disease states and related data through case review.

KEYWORDS. atrial fibrillation, cardiac resynchronization therapy, elderly, heart failure, implantable cardiac-defibrillator.

Case

RM is a pleasant 89-year-old-gentleman with mixed ischemic and non-ischemic cardiomyopathy with an ejection fraction (EF) of 25–30%, New York Heart Association (NYHA) class III symptoms, longstanding left bundle branch block (LBBB) with QRS duration of 163 ms, atrial fibrillation (AF), and renal insufficiency who presented to clinic for evaluation regarding potential device and management of AF.

Over the past 8–12 months, he had increased fatigue, dyspnea on exertion, palpitations, and light-headedness. His echocardiogram demonstrated worsening ventricular function. His cardiologist adjusted his heart failure regimen but was limited due to symptomatic hypotension and bradycardia. A 24-h Holter monitor demonstrated atrial fibrillation with controlled ventricular response 40–91 bpm on beta-blockers. He had no pauses greater than 2 s. He continued to experience significant dyspnea on exertion and fatigue and had difficulty walking up a few steps.

RM meets the criteria for cardiac resynchronization therapy with defibrillator (CRT-D) with symptomatic class III heart failure (HF) <35% and LBBB. This was discussed with the patient and his family in clinic. RM had not thought about his end-of-life wishes, which would impact his decision regarding defibrillation therapy. They were asked to discuss his wishes and then decide between pacing versus pacing and defibrillation therapy. In the meantime, he was admitted for amiodarone initiation, adjustment of his beta-blocker, and direct current cardioversion for his AF (Figures 1 and 2).

RM reported feeling better in sinus rhythm than AF. His activity did remain limited, becoming dyspneic with minimal activity. He and his family decided on CRT with pacemaker (CRT-P) instead of CRT-D, which was consistent with his overall wishes. He was admitted for CRT-P. He underwent a successful procedure with lateral vein placement of the left ventricular (LV) lead (Figures 3 and 4).

RM returned to clinic 15 weeks after CRT-P and AF management. He denied any chest pain or palpitations.

The authors report no conflicts of interest for the published content. Manuscript received April 2, 2011, final version accepted April 14, 2011.

Address correspondence to: Dr. Camille G. Frazier-Mills, Duke University Medical Center, DUMC Box 3174, Durham, NC 27710. E-mail: frazi018@mc.duke.edu
His energy level had improved and he was quite active. He had recently gone hiking with his son and was able to walk uphill without difficulty. His echocardiogram was repeated and his EF was 50%.

**Background**

The prevalence of HF continues to rise both among the general population and among elderly people, increasing from 5 million to 5.7 million Americans from 2004 to 2008.1 This disease is especially common in elderly people, who are disproportionately affected. For those aged 60–79 years, 9% of men and 5.4% of women have HF. In patients over 80 years, 11.5% of men and 11.8% of women have HF.1 Despite the fact that elderly people are most affected by HF, large clinical trials for device management in HF either exclude or enroll small percentages of very elderly patients.2–9

Each year, 20% of hospitalizations in patients over 65 years are attributable to HF exacerbations.10 In addition to targeted medical therapy, both implantable cardiac defibrillators (ICDs) and CRT devices have proven to benefit appropriately selected HF patients.2–9

---

**Figure 1:** Atrial fibrillation with left bundle branch block electrocardiogram.

**Figure 2:** Sinus rhythm with left bundle branch block electrocardiogram.
appropriate patients, studies have shown that these devices can decrease mortality, improve symptoms, and decrease hospitalizations. However, in practice, HF patients are often significantly older than the mean age of trial participants, which makes it difficult to interpret trial data regarding the placement of CRT-P and CRT-D devices in very elderly patients.

AF is the most common sustained cardiac arrhythmia among the general population. However, patients with HF have a 4.5- to sixfold increase in risk of developing AF. The development of concurrent AF in a patient with HF often leads to progression of HF symptoms due to tachycardia, decreased LV filling time, irregular ventricular rate, and loss of effective atrial contraction. In fact, AF and other tachyarrhythmias can lead to tachycardia-induced cardiomyopathy with depressed EF. Similarly, HF predisposes patients to the development and progression of AF, thus becoming a vicious cycle. Furthermore, the incidence of AF increases significantly with age, as each year roughly 14/100 000 people aged 15–44 years will develop it. This is contrasted with people ≥85 years, where approximately 1140/100 000 people develop AF yearly. Although this is predominantly a disease of elderly people, there are no randomized controlled trials (RCTs) focused on optimal management strategies in these patients. In this review...
we will analyze the data for management of AF as well as use of ICD, CRT-P, and CRT-D devices in the general HF population and we will evaluate how these data and smaller observational studies apply to the very elderly population.

Atrial fibrillation: rate vs rhythm

Several large, RCTs have evaluated whether a strategy of rate or rhythm control is optimal in the management of AF. Two of the largest trials, Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) and RAte Control versus Electrical cardioversion (RACE) trials both concluded no mortality benefit in a rhythm control strategy. AFFIRM enrolled 4060 participants, mean age 69.7 years, and randomized them to either pharmacologic rate or rhythm control. Although they found that there was no statistically significant difference in mortality between the two groups, they did note increased hospitalizations and adverse events (AEs) in the rhythm group. Also, a subgroup analysis of participants ≥65 years found a slightly higher risk of death with a rhythm control strategy than rate control.

Similarly, the RACE trial enrolled 522 AF patients, mean age 68 years, and randomized them to rate versus rhythm strategies. They also found no significant difference in mortality between the two groups, again noting an increase in adverse events with rhythm control. In a similar RCT, Roy et al. evaluated rate versus rhythm in HF patients (mean age 67 years) and found no difference in mortality, stroke, or progression of HF, but did find an increase in AEs with rhythm control. These trials and other similar trials among patients with and without HF conclude no mortality benefit with rhythm control, but are limited as they only enrolled a small number of participants ≥75 years.

Data for CRT in HF with depressed EF

Among patients newly diagnosed with HF, the 5-year mortality is nearly 50%, which is heavily attributable to sudden cardiac death (SCD) and progression of HF. The two largest ICD for primary prevention in heart failure trials, Multicenter Automatic Defibrillator Implantation Trial (MADIT-II) and Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) each enrolled patients, average age 60–64 years, and randomized them to conventional medical therapy alone or with ICD implantation. MADIT-II (1232 patients, ischemic cardiomyopathy, EF ≤30) showed a 31% reduction in risk of all-cause mortality in ICD patients compared with medical therapy alone. SCD-HeFT (2521 patients, ischemic and non-ischemic cardiomyopathy, EF ≤35%) also included a conventional therapy plus amiodarone arm. There was no significant difference in all-cause mortality between those treated with conventional therapy alone or with amiodarone. However, participants in whom an ICD was placed had a 23% reduction in relative risk compared with those treated with conventional therapy alone.

Data for CRT in HF

In patients with NYHA class II–IV symptoms, up to 30% have ventricular dyssynchrony as evidenced by QRS duration greater than 120 ms. This intraventricular conduction delay is associated with higher end-systolic volumes and worsened symptoms. CRT decreases the electromechanical delay and allows for biventricular stimulation, thereby restoring ventricular synchrony, which ultimately enhances LV function by facilitating more coordinated contraction and relaxation.

Two key trials have evaluated the use of CRT in patients with advanced HF and cardiac dyssynchrony. The Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial (average age 65 years, NYHA class III–IV ischemic or non-ischemic cardiomyopathy, EF ≤35%, QRS≥120 ms) assigned 1520 participants to conventional therapy alone or conventional therapy plus CRT-P or CRT-D. CRT-P and CRT-D decreased the relative risk of the composite endpoint of all-cause mortality and hospitalization by 34%, p<0.002 and 40% (p<0.001), respectively. CRT-D was also associated with a 36% reduction in all-cause mortality (p=0.003) and both types of CRT devices were associated with improved quality of life (QOL), decreased symptoms from HF, improved exercise tolerance and reversal of cardiac remodeling.

The Cardiac Resynchronization-Heart Failure trial (CARE-HF) (average age 66 years, NYHA class III–IV HF, EF ≤35%, QRS≥120 ms) randomized 813 participants to standard medical care or standard care plus CRT. Similar to the COMPANION trial, they found that CRT reduced the risk of all-cause mortality and hospitalization due to cardiovascular events (HR 0.63, 95% CI 0.51–0.77, p<0.001). This study also found that CRT was associated with increased EF, improved QOL, decreased intraventricular conduction delay, decreased end systolic volume, and less mitral regurgitation.

It is thought that cardiac resynchronization improves QOL and decreases both mortality and hospitalization by improving LV function and decreasing mitral regurgitation. This effectively improves EF, increases perfusion pressure and improves ventricular remodeling. Therefore, the progression of HF can be slowed in many of these patients as demonstrated in MADIT CRT.

Data for ICD and CRT-P/CRT-D in elderly people

Despite HF prevalence increasing with age, the data for the use of ICD, CRT-P, and CRT-D devices in very elderly patients are limited. In the above-mentioned landmark trials, a small percentage of enrolled patients are over age 75. To date, there have not been any prospective RCTs to evaluate this issue specifically in very elderly people, although retrospective subgroup analyses of RCTs and several observational studies suggest that elderly patients can receive as much benefit from these therapies as their younger counterparts.

A subgroup analysis of MADIT-II showed that in patients ≥75 years, placement of an ICD for primary prevention was associated with a greater reduction in
all-cause mortality (44%) than the reduction demonstrated in all study participants (37%).8,30 This is especially significant since the very elderly population had more comorbidities such as cardiac conduction abnormalities and renal dysfunction, yet less diabetes and tobacco use, at baseline than their younger counterparts. A subgroup analysis of SCD-HeFT showed a trend towards reduced RR of all-cause mortality in those ≥65 years, but was not statistically significant.

Similar to the ICD trials, there have not been RCTs designed specifically addressing CRT for the elderly HF population. An analogous subgroup analysis was performed in both the CARE-HF trial and COMPANION trials. In CARE-HF, patients <66.4 and ≥66.4 years showed reductions in primary endpoint of all-cause mortality and hospitalization due to a cardiovascular event.6 In a retrospective subgroup analysis from COMPANION comparing ≤65 to >65 years, CRT-P was associated with a decrease in the primary endpoint for those ≤65 but not in those >65 years. Conversely, CRT-D was associated with a statistically significant decrease in the primary endpoint among those >65, but not those ≤65 years.9 A retrospective subgroup analysis of the MIRACLE ICD trial was performed in which patients were stratified by age <65, 65–75, and >75 years. Participants in each age class showed similar improvement in EF and functional class. Those >75 years did not show statistically significant improved exercise capacity.9,31

Observational studies investigating the use of CRT in elderly patients have yielded similar beneficial findings. One study investigated the effectiveness of CRT in patients with NYHA class III–IV HF, EF ≤35, and QRS >120 ms. They examined patients <70 and ≥70 years and found improvement in NYHA class, QOL score, 6-min walk distance, EF, and LV remodeling in both populations.32

Finally, Delnoy et al.33 examined in a prospective, observational study 266 patients with NYHA class III–IV HF, EF ≤35 and QRS >120 ms and stratified them by age <75 or ≥75 years. At 2 years they found comparable improvement in NYHA class, QOL, and LVEF between both groups. Furthermore, a subgroup analysis of patients ≥80 years showed statistically significant improvement in NYHA class and EF.

Discussion

Many patients similar to RM present with a combination of AF and systolic HF, and it can be difficult to assess how symptomatic they are from each individual process. Given that large trials fail to demonstrate a mortality benefit in initiating a rhythm control strategy in atrial fibrillation, RM was initially well rate controlled.13,18,19 His NYHA class III HF symptoms and EF of 25–30% persisted despite optimal HR management on beta-blocker therapy, making it unlikely that his HF was tachycardia induced. However, this remains an important diagnosis to consider in all patients with HF and tachyarrhythmias, as both rate and rhythm control can improve or restore systolic function.14,23,34

In patients whose symptoms persist after optimal rate control, rhythm control is often employed for symptom management. Given that RM remained symptomatic, he was converted to sinus rhythm. Although AFFIRM and RACE did not find any mortality benefit to a rhythm control strategy, it is important to note that only 39% of patients treated with this strategy were actually in sinus rhythm at the end of the study.19 In clinical practice, there are some patients, like RM, who if able to maintain sinus rhythm symptomatically feel better.

Convincing studies have demonstrated a benefit in both mortality and hospitalization with the use of CRT devices in HF patients.5,6 However, no large, randomized controlled trials have been dedicated to studying the use of CRT in very elderly HF patients. Retrospective subgroup analyses of very elderly patients enrolled in RCTs evaluating the use of ICD and CRT in HF patients as well as observational studies dedicated to answering this question have both demonstrated that very elderly patients can benefit from CRT-P and CRT-D placement.2,3,6,9,26,30,31

Given that appropriately selected very elderly patients can benefit from these devices, it is our opinion that no patient should be denied CRT-P or CRT-D implantation based upon age alone. However, in clinical practice, the decision of whether to place a device for symptom improvement (CRT-P) or symptom improvement and primary prevention (CRT-D) in an elderly patient should be based on an evaluation of their baseline comorbidities, a conversation with the patient, and an understanding of their goals of care. Among the general population, 80% of CRT devices placed are CRT-D.35 However, especially in the very elderly population, it is important to evaluate whether the patient would desire defibrillation in the event of a ventricular arrhythmia. Although both CRT-P and CRT-D devices are associated with decreased all-cause mortality, it is thought that the CRT-P’s effect is mostly attributed to slowing the progression of HF and ventricular remodeling, rather than a reduction in sudden cardiac death (SCD). CRT-D does this as well as decrease SCD.2,3,6

In practice, we find that some of our very elderly patients, such as RM, who are not interested in defibrillator therapy or life-prolonging interventions, may choose to pursue CRT-P in an effort to improve QOL and decrease hospitalizations. Conversely, some patients may desire those benefits as well as any possible attempt at preservation of life. Similar to patients in any age demographic, in very elderly patients who have the cognitive ability to make such decisions and reasonable baseline functional status, age should not be a deterrent in placement of CRT-P or CRT-D devices.

References

CRT and AF in Elderly People


