The Management of Heart Failure after Biventricular Pacing

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Approximately 271,000 heart failure (HF) patients in the U.S. have received cardiac resynchronization therapy (CRT) since the Food and Drug Administration approved this therapy in 2001 for moderate to severe HF (1). Indications for CRT are based on the American College of Cardiology, American Heart Association, and Heart Rhythm Society guidelines, which recommend CRT for New York Heart Association (NYHA) functional class III or IV HF patients who are refractory to pharmacologic therapy and have QRS durations ≥130 ms, ejection fractions ≤35%, and left ventricular (LV) end-diastolic dimensions ≤55 mm (level of evidence IIA) (2). These guidelines reflect the results of several large clinical trials that randomized over 2,500 HF patients to CRT versus placebo and demonstrated the benefit of CRT in measurements of functional capacity, exercise tolerance, ventricular remodeling, and reduction in hospitalizations and mortality over a six-month period (3–8). How best to manage patients after CRT and what to do with the nonresponder remain difficult challenges.

After successful implantation of a CRT device, a series of clinical events can be expected over the next several months. Immediately after implant, assuming adequate LV lead position and thresholds, systolic blood pressure, cardiac output, and stroke work usually increase, whereas end systolic volumes and pulmonary capillary wedge pressure decrease (9,10). The change in hemodynamic profile is the result of immediate correction of ventricular dyssynchrony resulting in direct improvement of LV systolic dysfunction. Some patients may feel the effects as early as one month after implant though others may require a longer period of time for symptom relief (3). The change in hemodynamic profile (increased cardiac output, systolic blood pressure, and decreased

pulmonary capillary wedge pressure) is important to recognize because it may require reduction in diuretic dose.

Beta-blockers may also be increased after CRT. Pharmacologic therapy with beta-blockers has dramatically reduced HF mortality, sudden death, and hospitalizations (11–13). Despite these established benefits, use of beta-blockers in recent randomized clinical HF trials is somewhere between 30% and 62% (3,14). Many physicians hesitate starting beta-blocker therapy or increasing beta-blocker dose because of potential worsening HF, hypotension, and bradycardia (15). Cardiac resynchronization therapy improves HF symptoms and blood pressure while restoring synchrony by pacing both ventricles (3,7,9). Therefore, some of the clinical problems for which beta-blocker therapy is abandoned or not aggressively pursued are stabilized with CRT. CRT offers a unique opportunity to optimize beta-blocker therapy to therapeutic doses that have been shown to be of benefit in clinical trials (16).

There is no clear consensus or standardized definition of what is considered to be an adequate response to this therapy or when a patient should be considered a nonresponder. Some would consider improvement in NYHA functional class or increased distance walked in 6 minutes as an adequate response; however, these improvements may be influenced by spontaneous changes as well as by a placebo effect. Based on current CRT data, we believe that re-evaluation of a CRT device should be considered if there is no improvement in symptoms after six months of CRT or there is worsening heart failure with increased ventricular remodeling within the first several months after initiation of CRT.

Figure 1 represents a potential troubleshooting algorithm for HF patients who are not responding to CRT (17). This algorithm may or may not improve clinical outcomes and has not been prospectively validated. It does suggest a strategy to manage common problems found in this heart failure population, and it combines that strategy with adequate device optimization and function.

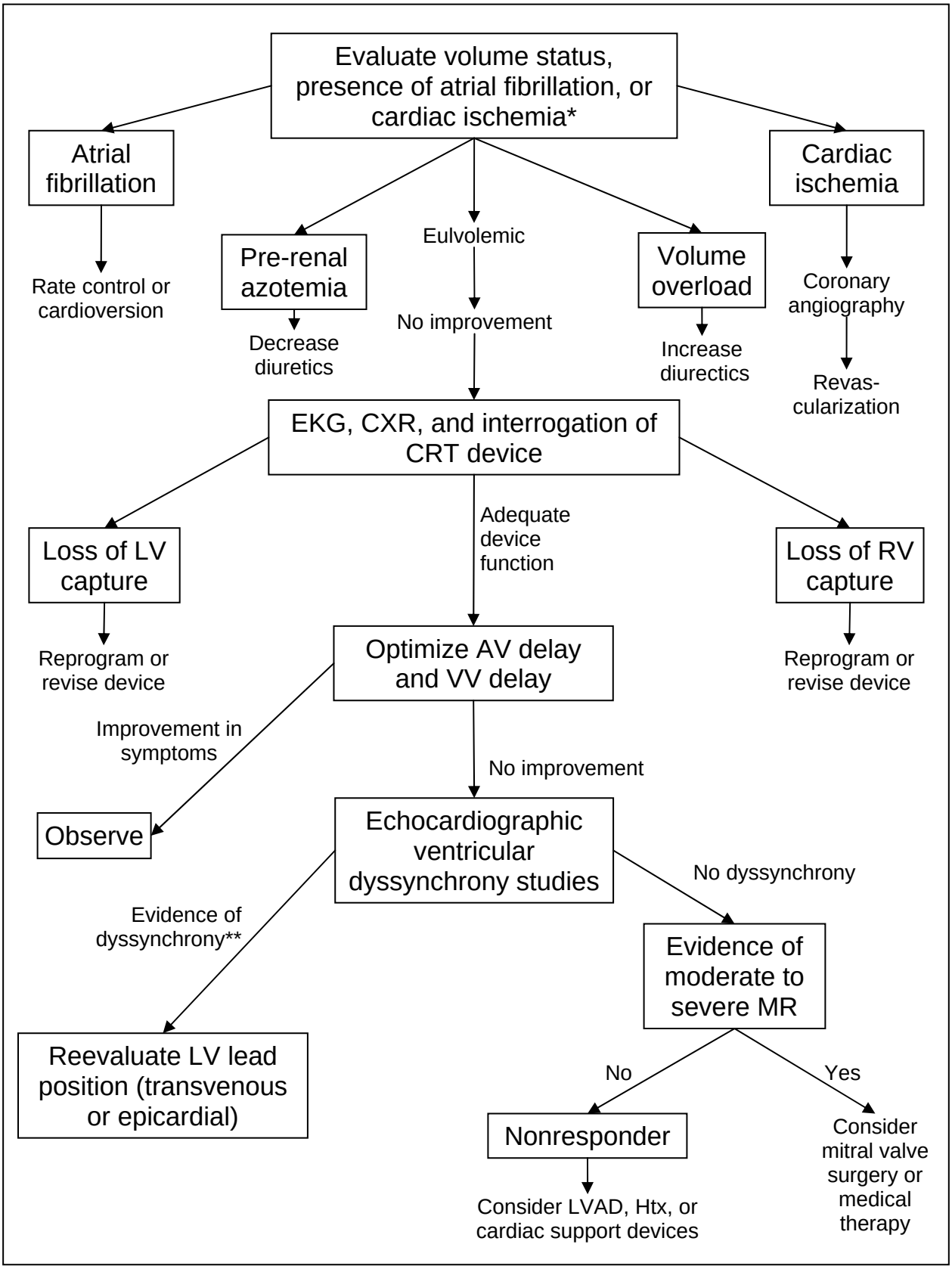
Evaluate volume status, presence of atrial fibrillation, or cardiac ischemia*
Atrial fibrillation
Rate control or cardioversion
Pre-renal azotemia
Decrease diuretics
Eulvolemic
No improvement
Volume overload
Increase diurectics
Cardiac ischemia
Coronary angiography
Revas-cularization
EKG, CXR, and interrogation of CRT device
Loss of LV capture
Reprogram or revise device
Adequate device function
Loss of RV capture
Reprogram or revise device
Optimize AV delay and VV delay
Improvement in symptoms
Observe
No improvement
Echocardiographic ventricular dyssynchrony studies
Evidence of dyssynchrony**
Reevaluate LV lead position (transvenous or epicardial)
No dyssynchrony
Evidence of moderate to severe MR
No
Nonresponder
Consider LVAD, Htx, or cardiac support devices
Yes
Consider mitral valve surgery or medical therapy

Figure 1. Troubleshooting algorithm for heart failure patients with worsening symptoms, progressive ventricular remodeling, or no improvement in New York Heart Association functional class despite one to six months of cardiac resynchronization therapy (CRT). AV = atrioventricular; CXR = chest X-ray; EKG = electrocardiogram; Htx = heart transplant; LV = left ventricular; LVAD = left ventricular assist device; MR = mitral regurgitation; RV = right ventricular; VV = interventricular. *Cardiac ischemia is evaluated in patients with ischemic cardiomyopathy. **Evidence of dyssynchrony includes septal to posterior wall motion delay ≥130 ms, intraventricular mechanical delay ≥40 ms, and tissue Doppler imaging ≥65 ms.

Key features of the algorithm beyond checking for adequate device function include making sure that there is no prerenal azotemia or developing atrial fibrillation, which can potentially decrease the amount of biventricular pacing that is present. One of the most important concepts that the algorithm emphasizes is the absence of ventricular dyssynchrony after a series of troubleshooting steps in a patient that is not responding to this therapy. If there is appropriate biventricular pacing, there should be minimal ventricular dyssynchrony. The presence of ventricular dyssynchrony in a patient who is not responding to biventricular pacing suggests that the coronary sinus lead is not in the proper position. In this case, lead revision should be considered.

Cardiac resynchronization therapy is now considered for severe heart failure refractory to pharmacologic therapy in patients with prolonged QRS intervals. As the number of patients receiving CRT continues to grow, a new, more uniform approach between heart failure and electrophysiology specialists will be needed to maintain and improve clinical results that are achievable through this therapy (18). This standardized approach will need to address issues of patient selection, changes in pharmacologic therapy after CRT, and appropriate treatment strategies for the nonresponder. It is the combination of these three factors that will further improve outcomes in the field of CRT.

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