CLINICAL VIGNETTE

Optimizing Cardiac Resynchronization Therapy for Advanced Heart Failure

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Case Presentation

A 41-year-old female with a history of childhood neuroblastoma treated with chemotherapy and radiation was diagnosed with non-ischemic cardiomyopathy with a left ventricular ejection fraction of 10% to 20% at age 27. Her medical history was also notable for chronic hepatitis C contracted from multiple transfusions which was cured after successful antiviral treatment. She lived with her family and was self-sufficient with activities of daily living.

She was regularly followed by General Cardiology and Heart Failure and was compliant with all of her visits and medications. Her medical regimen included highest tolerated doses of beta-blocker, angiotensin receptor blocker, mineralocorticoid receptor antagonist, and a diuretic. She was eventually transitioned to an angiotensin receptor-neprilysin inhibitor and symptomatic hypotension did not allow increasing to goal doses. Despite optimal tolerated medical management, the patient continued to be symptomatic with New York Heart Association Class III symptoms, had a left ventricular ejection fraction of <35% and a left bundle branch block with a QRS complex duration of 160miliseconds. She met criteria for cardiac resynchronization therapy (CRT) and underwent placement of a biventricular pacemaker/defibrillator (CRT-D).[1,2] Despite biventricular pacing, she continued to have NYHA Class III symptoms with dyspnea on exertion while doing activities of daily living and constant abdominal bloating. Her objective weight measurements were also increasing (Figure 1). Due to her poor functional status despite medical and device therapy, she was referred for consideration of advanced therapies including cardiac transplantation and/or durable left ventricular assist device.

Intervention and Post-Intervention Course

Because she failed to improve clinically the patient was deemed to be a non-responder to CRT. Another attempt was made to optimize her CRT while waiting for advanced therapies. When placing CRT devices, the settings are usually empirically programmed, however, these settings may not be optimal for all patients. To optimize CRT the patient was taken to the cardiac catheterization laboratory where timing between the atrial and ventricular pacing (AV pacing delay) and ventricular pacing vectors were changed. Cardiac function was assessed during these changes via aortic valve velocity-time index (a measure of flow across the aortic valve) and cardiac output using transthoracic echocardiography and right heart catheterization respectively. Her CRT was reprogramed with the condition that led to the largest increase in aortic valve velocity-time index and cardiac output (Figure 2).

The patient's post-optimization course demonstrated a durable improvement in left ventricular outflow tract velocity-time integral from 12.8cm to 20cm on repeat transthoracic echocardiography. She also experienced objective weight loss without needing significant changes in diuretics (Figure 3). Subjectively, she was feeling well and has not required any emergency room visits or hospitalizations related to decompensated heart failure.

Discussion

Cardiac resynchronization therapy has improved outcomes in select patients with advance heart failure. However, among appropriately selected patients, some do not improve. In most studies to date, 30% to 50% of patients who undergo CRT fail to clinically improve and are deemed non-responders.[3] Non-responders have been found to have worse outcomes, including increased frequency and duration of hospitalization and a 5-year all-cause mortality of under 50%.[3] Characteristics that are predictive of non-responders include: 1) having a low percentage of biventricular pacing, 2) having ischemic cardiomyopathy, and 3) having a non-left bundle branch block.[3]

Relying solely on clinical evaluations in comparison to addition of echocardiographic or invasive hemodynamic assessment may incorrectly under-estimate non-responders by 35% and may contribute to the finding that approximately 44% of non-responders receive no additional treatment.[3] Treatments that have improved outcomes in non-responders include education, medication changes, pacing and device parameter changes, treatment for arrhythmias and comorbidities, and atrioventricular/interventricular re-optimization.[3] This patient was symptomatic despite attempts at optimizing each of these treatments, except for atrioventricular/intraventricular optimization of her CRT device.

When placing CRT devices empiric programming of atrio-ventricular delays and pacing vectors is common. However, there is evidence that optimizing these parameters may lead to improvement left ventricular filling and thus function, with improvement to patient symptoms and function. Although no large RCT have shown that routine optimization improves outcomes, optimization of CRT may be recommended in certain patients.[4-6]

Conclusion

Cardiologists have an extensive armamentarium to treat cardiomyopathy that includes CRT. However, there are a large group of patients that are non-responders. Such patients are underdiagnosed and undertreated which may contribute to their higher morbidity and mortality when compared to patients that respond to CRT. As this case demonstrates, multimodality optimization of resynchronization therapy may benefit heart failure patients who continue to be symptomatic despite optimal medical therapy and who have been identified as being a non-responder to CRT.

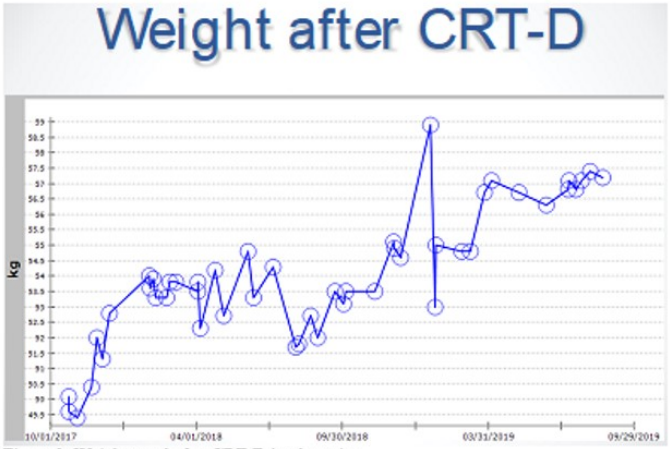

Figure 1: Weight trend after CRT-D implantation

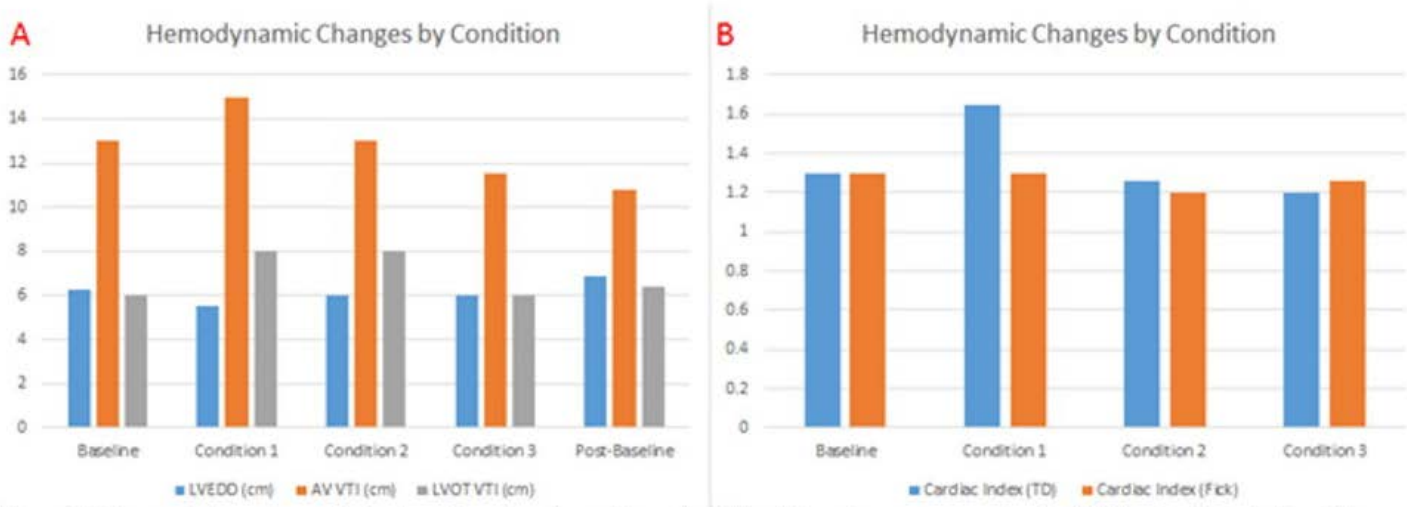

Figure 2. Changes in hemodynamics by transthoracic echocardiography (A) and invasive measurements via right heart catheterization (B).
Condition 1: Adaptive cardiac resynchronization therapy, sensed AV (SAV) delay 140ms, left ventricular – right ventricular (LV-RV) delay 0
Condition 2: SAV delay 170ms, LV0RV delay – 30ms
Condition 3: Multipoint pacing, SAV delay 140ms, LV-RV delay 0

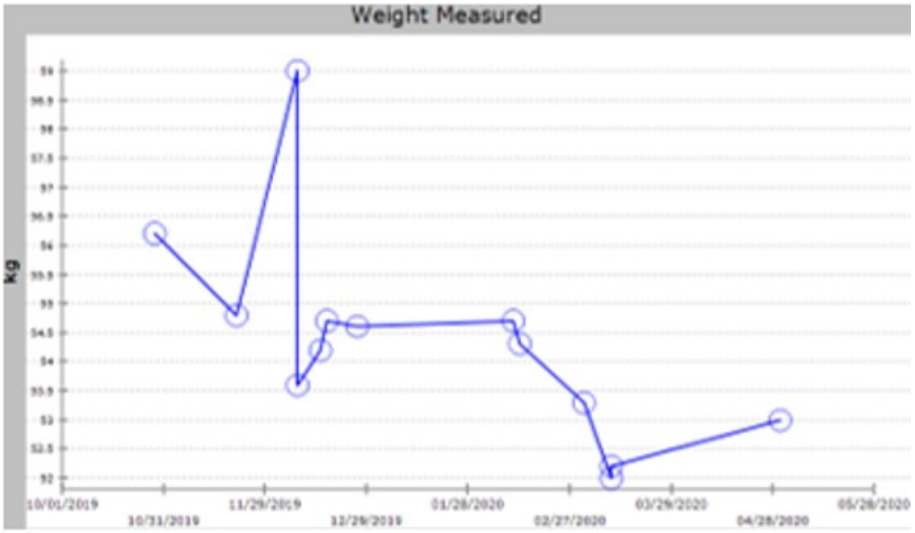

Figure 3: Weight trend after optimization of CRT-D

Disclosures: None.

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