Cardiac Resynchronization Therapy: New Hope for Congestive Heart Failure

Bandar Al Ghamdi, MD and Andrew Ignaszewski, MD, FRCPC

Faye’s Fatigue

Faye, 73, presents with a three-year, progressive shortness of breath (New York Health Association [NYHA] Class III), chest discomfort upon walking short distances and fatigue.

Faye has a history of dyslipidemia, but no history of diabetes mellitus or hypertension. She is an ex-smoker and has no history of alcohol intake.

Three years earlier, myocardial perfusion scans showed mild anterior and septal ischemia. Subsequent cardiac catheterization showed diffuse but non-critical coronary artery disease. She was not a revascularization candidate.

Faye’s echocardiogram at that time showed a severely reduced left ventricular (LV) ejection fraction of 15% and regional LV wall abnormalities. The LV was dilated with an end-diastolic diameter of 63 mm (normal < 50 mm) and an end-systolic diameter of 57 mm (normal < 33 mm). A moderate mitral regurgitation (MR) was noted. The right ventricle (RV) was normal in diameter and function.

Faye was treated with aggressive medical therapy. Her medications at presentation included:

- Metoprolol SR, 100 mg, every day (qd)
- Candesartan 4 mg, qd (she could not tolerate an angiotensin-converting enzyme inhibitor because of cough)
- Spironolactone, 25 mg, qd
- Atorvastatin, 10 mg, qd
- Acetylsalicylic acid, 325 mg, qd
- Nitroglycerine patch, 0.4 mg/hour, qd
- Furosemide, 60 mg, qd

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About the authors...
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CardioCase presentation

Faye’s Fatigue continued...

Upon present-day examination, Faye was in no distress. Her blood pressure was 110/72 mmHg and her pulse was regular at 60/min. Her jugular venous pressure was not elevated. Her cardiac exam showed normal S₁ and S₂, with no S₃ or S₄. There were no chest crackles or peripheral edema. Her ECG is shown in Figure 1; a repeat echocardiogram and cardiac nuclear scan showed no changes from previous examinations.

How would you proceed? For the answer, see page 29.

Figure 1. Faye’s ECG demonstrated sinus rhythm and left bundle-branch block (LBBB) with a wide QRS (200 ms) consistent with ventricular dyssynchrony.

What’s your CardioCase diagnosis?

CardioCase discussion

What’s wrong with Faye?

In Canada, congestive heart failure (CHF) is a major public health problem associated with significant morbidity, mortality and health-care costs. CHF currently afflicts more than 350,000 Canadians, and mortality rates range from 25% to 40% one year postdiagnosis.¹ Despite advances in the treatment and prevention of cardiovascular disease, incidences of CHF have steadily increased in the past several years, making it the only major cardiovascular disorder that is increasing in both incidence and prevalence.

Optimal pharmacologic therapy (OPT) is mandated by all recent guidelines. There remain, however, a number of patients for whom a purely medical approach is insufficient, due to recurrent symptoms, a lack of effect on exercise tolerance and poor patient compliance with treatment.²

Cardiac resynchronization therapy (CRT) is one of the new modalities for treatment of medically
refractory cases of CHF that may relieve symptoms, improve patient quality of life and reduce rehospitalization.

**Cardiac dyssynchrony and the rationale for CRT**

CRT is usually accomplished with a pacing lead in the right atrium to sense the beginning of the cardiac cycle and two leads in the ventricles (biventricular pacing):
- one in the right ventricle and
- one placed on the left ventricle (LV) free wall, either directly by surgery via thoracotomy or laparoscopic thoracostomy or, more commonly, through the coronary sinus and cardiac veins (Figure 2).

About 15% to 30% of patients with CHF and LV systolic dysfunction have conduction system disease. The resulting conduction abnormalities alter the normal pattern of heart contraction, causing different parts of the heart to contract at different times. This dyssynchrony leads to abnormal wall stress, inefficient contraction and worsening CHF.

Electrophysiologic disturbances increase the risk of potentially serious ventricular arrhythmias and sudden cardiac death. For some patients, disturbances lead to chronic mechanical ventricular dyssynchrony, often clinically apparent on a surface ECG as a prolonged (> 120 ms) QRS interval, which further reduces cardiac efficiency.

An ECG is only an indirect measurement of mechanical dyssynchrony. Recent studies suggest that patients with dyssynchrony resulting from an incomplete bundle-branch block, manifested as a narrow QRS (< 120 ms) on an ECG, may also benefit from CRT.

**Indications**

Eligibility criteria for CRT treatment are adapted from published clinical trials. The two most important criteria for CRT are severe symptomatic CHF (despite OPT) and QRS duration more than 120 mm (Table 1). Current criteria may not be optimal, as the rate of non-responders is as high as 30%. Other variables, such as paradoxical septal motion or Doppler echocardiographic features of asynchrony, have been suggested by some authors as additional criteria.

**The benefits of CRT**

Several recent, large, well-designed trials have demonstrated that adding CRT for patients on existing OPT results in hemodynamic and clinical improvements above and beyond those observed in patients treated with OPT alone. These studies have further shown that CRT can reduce CHF hospitalizations in carefully selected patients, which could contribute to overall healthcare cost savings. Benefits include:
- improved quality of life,
- improved New York Heart Association (NYHA) class,
- improved exercise tolerance (six-minute walk),
- reduced rehospitalization for worsening CHF,
- improved cardiac contractility and ejection fraction and
- reduced mitral regurgitation.

The role of CRT in reducing CHF mortality is still unresolved. A meta-analysis of four randomized studies—two trials using CRT alone and two using CRT-Implantable Cardioverter Defibrillator—suggests that CRT reduces mortality from progressive CHF by about 51%. The addition of a defibrillator appears to confer significant improvement in survival.

The effect of CARdial REsynchronization on
More about Faye

Despite medical therapy at its maximum toleration, Faye continued to be symptomatic at NYHA Class III. She met the research inclusion criteria for biventricular pacing. There was no indication for defibrillator implantation at that time.

She underwent implantation of a biventricular device, with an LV lead implantation in the mid-lateral position, an RV lead to the RV apex and a right atrium (RA) lead to the lateral RA wall. There were no complications (Figure 3).

See page 30 for Faye’s followup.

### Table 1

<table>
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<th>Indications for CRT</th>
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<tr>
<td>Symptomatic NYHA Class III or IV (moderate to severe) CHF, despite optimal therapy</td>
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<tr>
<td>Systolic CHF with LV ejection fraction &lt; 35%</td>
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<td>LV end-diastolic dimension &gt; 55 mm</td>
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<td>QRS duration &gt; 120 ms</td>
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**COMMENTS:**

**CRT:** Cardiac resynchronization therapy

**CHF:** Congestive heart failure

**NYHA:** New York Heart Association

**LV:** Left ventricle

And technical issues related to LV lead position and atrioventricular interval delay. Improving patient selection criteria, lead placement and pacemaker programming will hopefully maximize patient benefit from CRT.

### Complications

CRT is not without risk (Table 2). In addition to those complications associated with conventional pacing, there are also problems with LV lead insertion using the preferred transvenous approach.

### A final note

CRT offers a new and promising approach for treating patients with moderate to severe CHF and dyssynchrony. Clinical trials have shown positive clinical effects of CRT, including improvements in functional class and exercise capacity, reduced rehospitalization for CHF exacerbations and reduced mortality.

### References


morbidity and mortality in Heart Failure (CARE-HF) study is the first study to show the benefits of CRT with respect to survival, demonstrating a 37% relative risk reduction of death (P < 0.002), as well as benefits and continued improvement for a period of over two years.\(^{10}\)

### Limitations

Although the cost involved is a limiting factor, the major limitation of CRT is the high rate of non-responders, which may represent suboptimal patient selection and technical issues related to LV lead position and atrioventricular interval delay. Improving patient selection criteria, lead placement and pacemaker programming will hopefully maximize patient benefit from CRT.

### Complications

**Peri-implant complications**

- Cardiac perforation/coronary sinus dissection (0.8% / 3%)
- Inability to position LV lead (4% to 10%)
- Electrical trauma occurs in up to 5% of all implantations (e.g., RBBB)
- Dislodgement of the LV lead
- Haematoma
- Pneumothorax or Haemothorax
- Pulmonary edema

**Complications during followup**

- LV lead dislodgement
- Infection of ICD and/or lead
- Stimulation of the diaphragm
- Device migrations
- Right atrial lead dislodgement

**Table 2 Complications of CRT**

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**CRT:** Cardiac resynchronization Therapy

**LV:** Left ventricle

**RBBB:** Right bundle-branch block

**ICD:** Implantable cardioverter defibrillator

**Table 2 Complications of CRT**

**Symptomatic NYHA Class III or IV (moderate to severe) CHF, despite optimal therapy**

**Systolic CHF with LV ejection fraction < 35%**

**LV end-diastolic dimension > 55 mm**

**QRS duration > 120 ms**

**CRT:** Cardiac resynchronization therapy

**CHF:** Congestive heart failure

**NYHA:** New York Heart Association

**LV:** Left ventricle
Faye's Follow up

Following implantation, Faye reported a significant improvement in physical activities, sleep and general quality of life. After three months, she was able to walk eight to 10 blocks without shortness of breath or chest pain, but she would stop because of leg fatigue (NYHA Class I).

Faye's repeated echocardiograms showed gradual, but steady, improvement in LV systolic function and diameters. Her last echocardiogram, three years after implantation, revealed an LV ejection fraction of 60% and an LV end-diastolic diameter of 49 mm and end-systolic diameter of 34 mm. Her MR was graded as mild.

Figure 3. Faye’s ECG following implantation. The QRS duration was reduced to 136 ms with biventricular pacing.