Heart failure (HF) is a major burden in almost all countries. The prevalence of symptomatic HF is still high. Despite our best understanding of its pathophysiologic mechanisms and the recent advances in pharmacologic therapy, it remains a high-mortality and morbidity disease. About 30-50% of patients with HF have concurrent electrical delay in the electrocardiogram (ECG), mainly in the form of LBBB.\(^1\) This kind of conduction delay commonly occurs in patients with idiopathic dilated cardiomyopathy and ischemic cardiomyopathy as well. The abnormality of left ventricle (LV) conduction will lead to a change in LV contraction pattern resulting dyssynchronous intraventricular (within the LV) and interventricular (in respect with right ventricle) contraction. Thus, a dyssynchronous LV contractile pattern usually manifested by late activation of the LV lateral wall which in turn impairs LV systolic function, reduces cardiac output, raises filling pressure and worsens mitral regurgitation\(^2\).
Cardiac resynchronization therapy (CRT) improves cardiac function and exercise capacity leading to an improved survival in patients with advanced heart failure and ventricular conduction delay. The underlying mechanisms of these beneficial effects are not fully understood, but they appear to be related to a restored coordination of the left (LV) and right ventricular (RV) contraction and relaxation. These effects may directly lead to augmented contractility and reduction of LV filling pressures.

Echocardiography has been widely used to identify patients who are candidates for CRT and to monitor the response in LV function at follow-up after device implantation. This review addresses the applications of CRT in patients with moderate–severe heart failure and the role of echocardiography in optimizing CRT including patient selection, risk and benefit of CRT and appropriate measures.

**Keywords:** cardiac resynchronization, heart failure, echocardiography.

CRT consists of pacing the atria and, after an appropriately timed atroventricular (AV) delay, stimulating both ventricles. The CRT device consists of a right atrial lead, a right ventricular (RV) lead, and a LV lead, usually inserted through a branch of the great cardiac vein over the left ventricle. When CRT is applied to patients with systolic heart failure, who have both electrical and mechanical delay manifested by a wide QRS complex, there is usually improvement in LV function. Resynchronization is the process of optimizing the electrical activation of the left ventricle, with shortening of the QRS duration or activation time.

CRT corrects dyssynchrony by synchronous pacing from transvenous pacing catheters implanted in the right atrium and
right ventricle, and in a left-sided vein via the coronary sinus. Because CRT improves left intraventricular synchrony more than biventricular synchrony, its main impact is on the left ventricle. The beauty of CRT is its capacity to improve cardiac performance without increasing myocardial energy expenditure. Pacing both RV and LV walls causes delayed septal systolic contraction and earlier LV lateral wall contraction, making overall LV contraction more uniform and efficient, thereby improving the energetic of LV contraction.6

**METHODS AND INDICATIONS OF CRT**

Intraventricular mechanical delay or intraventricular dyssynchrony has been defined as the difference in electrical-mechanical delay between different segments and walls of the LV. It is characterized by either premature contraction, or late contraction, of LV wall segments as a result of the delayed electrical conduction and results in impaired LV systolic performance. Various echocardiographic parameters can be used to determine the difference in timing of ventricular wall contraction.6

There are a number of maneuvers to perform with the CRT device to optimize cardiac performance. One is to optimize the AV delay. This can be done by optimizing the LV filling pattern. As seen in figure 1, LV filling volume is represented by velocity time integral (VTI) of transmitral flow velocity.7 Another is to measure the forward flow by adjusting the filling pattern to the maximum aortic VTI or cardiac stroke volume (Figure 2). Interventricular mechanical delay (IVMD) measured as the difference in pulmonary and aortic pre-ejection intervals. Other changes on the device include atrial sensing and biventricular pacing.8
Figure 1: VTI of trans-mitral flow (EA VTI) as diastolic filling at 2 consecutive sensed AV delays (SAV). Note the clear difference in EA VTI value with change in the sensed AV delay. Sensed AV delay 120 ms gives maximal EA-VTI value (in this example is 16.5 cm) (Ref.no:7).

Figure 2: Optimization of the VV interval by Doppler echocardiography. The optimal VV interval can be assessed by PW-Doppler at the aortic outflow VTI as a surrogate for improved stroke volume at different VV intervals. The IVMD is the difference in pulmonary and aortic pre-ejection intervals. The optimal VV interval was 20 ms LV before RV, which corresponded with an IVMD of 31 ms gives the maximal VTI.(ref.8.).
Electromechanical delay is the result of changed electrical conduction that affects mechanical activity within the RV and LV. The QRS duration is normally <120 ms and represents the electrical depolarization of the RV and LV that occurs before the onset of active contraction. Normal interventricular conduction time between the RV and LV, including intraventricular activation of the LV segments, is about 40 ms. In the presence of LBBB, there is delayed electrical activation of the LV by interruption of conduction through the anterior and/or posterior fascicle of the left bundle branch that results in dyssynchrony. This may be interventricular with discordance of contraction between the RV and LV, and/or intraventricular with premature and late activation of LV segments that results in discordant LV contraction. Physiologically, there seems to be an inherent interventricular dyssynchrony because LV contraction slightly precedes RV contraction by about 20-30 ms. Pathologic dyssynchrony has been described as RV preceding LV contraction by 40 to 56 ms.

The indication of patients for CRT varies among those with HF. However, recent trials with a total of more than 4000 patients have shown obvious benefit for CRT in the treatment of patients with end-stage, drug-refractory heart failure with wide QRS as an indicator of dyssynchrony. CRT improves NYHA functional class, quality of life and peak VO2, improves LVEF, reduces LVEDD and MR, reduces hospitalization and most importantly reduces mortality. Heart failure with wide QRS interval has higher morbidity and mortality compared to patients with normal QRS duration. Pharmacological treatment can improve the symptoms and clinical outcomes of HF but eventually does not affect the interventricular conduction delay. The application of CRT has developed into an adjunctive therapy for patient with refractory HF by synchronized biventricular activation and contraction and interventricular conduction delay.
Careful patient selection is vital for successful CRT. According to 2005 ACC/AHA heart failure guideline “Patients with LVEF (ejection fraction) less than or equal to 35%, sinus rhythm, and NYHA (New York Heart Association) functional class III or ambulatory class IV symptoms despite recommended, optimal medical therapy and who have cardiac dyssynchrony, which is currently defined as a QRS duration greater than 120 ms, should receive CRT unless contraindicated (Level of Evidence: A)”\textsuperscript{13}. Although these guidelines include the presence of sinus rhythm, data from Europe suggest that patients with atrial fibrillation may also benefit from CRT if the heart rate is controlled properly.\textsuperscript{1}

Identifying patients with significant ventricular dyssynchrony is very important since they are likely to respond to CRT. Traditionally, QRS duration determined from the ECG is the most commonly used predictor.\textsuperscript{13} In CARE-HF study, patients with QRS duration of 120–149 ms were required to meet two of three additional echocardiography criteria for dyssynchrony:\textsuperscript{3}

- Aortic preejection delay of more than 140 ms
- Interventricular mechanical delay of more than 40 ms
- Delayed activation of the posterolateral LV wall

Patients with prolonged QRS duration have a high prevalence of dyssynchrony, but some still have good cardiac synchronicity. Conversely, dyssynchrony also exists in a small percentage of heart failure patients with normal QRS duration. To identify the potential responders for CRT, both QRS duration and cardiac synchronicity should ideally be assessed. Mechanical dyssynchrony identified on echocardiography will play a more important role in selecting patients suitable for CRT.\textsuperscript{13}
ROLE OF ECHOCARDIOGRAPHY

Echocardiography is often the preferred method for evaluation of patients before CRT and for follow-up after device implantation. Echocardiography has emerged over recent years as the technique of choice to identify patients for the presence of mechanical dyssynchrony before CRT implantation. Echocardiographic evaluation of mechanical dyssynchrony uses the ECG as the indicator for timing of systole (often at onset of the QRS), and measures the time interval between different myocardial segments by a wide variety of structural or Doppler measurements. The major advantages of echocardiography include its excellent time resolution, low cost, broad availability, and ability to evaluate hemodynamic changes in a noninvasive and real-time manner.

Recent studies have documented that asynchronous contraction can be present without substantially increasing the QRS duration on the ECG. The possible role of echocardiography to identify and quantify mechanical asynchrony has been studied. These include M-mode and Doppler echocardiography, Doppler tissue imaging (DTI), strain and strain rate, tissue tracking, real-time 3-dimensional echocardiography. Today, some of echo Doppler parameters have clearly been shown to be able to predict response to CRT.

Echocardiography may play an important role in titrating the optimal “pacing configuration” for these patients, because the atrio-ventricular (AV) and ventriculo-ventricular (VV) device settings closely interact with each other and changes in their settings may result in immediate hemodynamic alterations in a small percentage of patients, which could be detected by echocardiography on a beat-to-beat analysis in a noninvasive setting. The primary goal of using echocardiography before implantation are:
to confirm the presence of an impaired LV systolic function,

to assess other significant cardiac structural abnormalities
that may contribute to technical difficulties during
implantation, and

to assess the presence or absence and location of
dyssynchrony.8

Several new and sophisticated echocardiographic
techniques are evolving, trying to overcome some limitations
present in several conventional parameters.

DOPPLER TISSUE IMAGING

Tissue Doppler Imaging is one of the most promising techniques
for guiding patient selection. Ventricular asynchrony has a high
prevalence in patients with LV dysfunction but there is poor
agreement among the different methods available for detecting
asynchrony.14 In this light, Doppler parameters can play a
helpful additional role for patient selection. Doppler analysis
can and should serve as the first line optimization tool that is
easily applicable, reflects impaired filling and ejection of the
asynchronous ventricle, and helps to achieve the optimal benefit
for the patient.

DTI can be used for determination of strain and strain rate
in patients before and after CRT (Fig.3). During systole,
myocardial strain reflects segmental tissue deformation and the
relationship to shortening. Strain rate is derived from regional
myocardial strain measurements by the time integral of Doppler
velocity gradients to determine the degree of systolic segmental
shortening. TDI technique appears to be the most promising
method of asynchrony detection and preoperative patient
selection.11,12 But conventional Doppler echocardiography can
be expected to serve as a useful tool for the definition of the
best individual CRT setting with regard to atrioventricular (AV)
delay and pacing mode (left vs. biventricular pacing). It reflects the partial restoration of cardiac cycle timing, and thus can provide a relatively simple and readily applicable method of haemodynamic optimization.\textsuperscript{15}

**CONCLUSIONS**

CRT is a welcome addition to optimal medical therapy for patients with HF, severe LV systolic dysfunction, and ventricular dyssynchrony. It significantly provides symptomatic, haemodynamic, and survival benefits to these patients, including those with AF. The role for echocardiography in patient selection, guiding lead placement, and optimization of CRT following the procedure is increasing. At present, there is still no “gold standard” or general consensus, which makes evaluation and

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**Figure 3:** The tissue synchronization imaging (TSI) of LV segments was taken before and after CRT implantation in patient with severe HF. Before CRT (A) a dysuniformity of green color suggesting dyssynchronous with delay RV contraction (A). There was also delay in the onset and peak sustained systolic contraction in the septal (yellow curve) compared with lateral wall (red curve). After CRT (B), tissue synchronization became homogeneous or uniformity where as the nearly overlapping of myocardial velocity curve representing left and right ventricular systolic contraction (arrows).
management of patients with CRT challenging. With the expanding knowledge of echocardiographic dyssynchrony, ongoing clinical trials will also be testing their clinical use in patient selection and optimization beyond subjects with traditional indications of wide QRS complex.

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**REFERENCES**


