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## Review article

# Echocardiography and cardiac resynchronization therapy



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## ABSTRACT

Cardiac resynchronization therapy (CRT) is an effective therapeutic option in patients with congestive heart failure, left ventricular ejection fraction  $\leq 35\%$ , and a widened QRS complex. However, a significant proportion of individuals do not respond to CRT favorably. Understandably, a large number of studies have addressed various techniques to improve patient selection for CRT and to improve responder rate in patients with CRT devices. A large proportion of these approaches utilize echocardiography.

Techniques for improved patient selection include various metrics of dyssynchrony that could be associated with response to CRT and long-term outcome. Partly because of failure in the PROSPECT trial, these techniques have not been successfully translated into clinical practice thus far.

Novel echocardiographic approaches aiming to improve responder rate are based on selecting optimal placement for the left ventricular lead, using speckle-tracking echocardiography to avoid scarred tissue, and to guide the LV lead placement towards late-contracting segments. Single center randomized trials have shown positive results, but these need to be validated in multicenter studies.

Furthermore, several echocardiographic techniques have been developed for individual optimization of atrioventricular and interventricular delay settings, based on left ventricular filling patterns, stroke volume, and dyssynchrony. Again, despite encouraging single center studies, data from multicenter trials are presently lacking or inconclusive.

While these mixed results of studies using current echocardiographic techniques cannot warrant their routine clinical use, proper selection of patients for CRT and improving responder rate remains an important goal. Echocardiographic methods are continually evolving to address these issues. However, a meticulous approach including multicenter validation is needed to ensure clinical applicability in the future.

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## Introduction – the role of cardiac resynchronization therapy in heart failure patients

Cardiac resynchronization therapy (CRT) is a well-established method for heart failure patients with significantly reduced left ventricular (LV) ejection fraction (EF) and a widened QRS complex. Early randomized controlled trials have proven a beneficial effect on symptoms, heart failure hospitalizations, and even mortality in patients with class NYHA III–IV heart failure, EF  $\leq$  35%, and sinus rhythm with QRS duration over 120 ms [1–3].

Newer randomized studies have broadened the indications to include patients with less severe class NYHA II symptomatology [4–6]. On the other hand, efforts to identify a subset of patients with a narrow QRS who would benefit from CRT have been fruitless. EchoCRT, a randomized controlled trial, did not show benefit in patients with QRS duration  $\leq$  130 ms and echocardiographic signs of dyssynchrony [7]. On the contrary, it seems that CRT is directly harmful in these patients. Furthermore, data from newer randomized studies and metaanalyses support the conclusion that CRT is beneficial mainly in patients with QRS duration over 150 ms and/or left bundle branch block (LBBB) QRS morphology [8–10].

Based on these analyses, the European Society of Cardiology unequivocally recommends (class I indication) CRT in patients with symptomatic heart failure with NYHA classes II–IV, LV EF  $\leq$  35%, and LBBB QRS morphology with sinus rhythm. The indication for CRT implantation in patients with sinus rhythm and non-LBBB morphology is more equivocal: class IIa in patients with QRS duration  $>$  150 ms and class IIb in patients with QRS duration 120–150 ms. CRT is not indicated in patients with QRS duration  $<$  120 ms (class III).

In patients with atrial fibrillation, there is a class IIa indication for CRT in patients with LV EF  $\leq$  35%, QRS duration  $>$  120 ms, and NYHA III–IV symptoms, as well as for patients with decreased LV EF undergoing AV node ablation for uncontrollable ventricular rate [11].

## The mechanics of cardiac resynchronization

Despite significant research efforts, our understanding of the pathophysiology and mechanisms of CRT effects is still incomplete. The main postulated mechanism remains resynchronization of both electrical and mechanical activity of the heart, i.e., restoring the state where individual segments of left ventricle are contracting at the same moment [12].

This leads to improvement in stroke volume, but also improvement of contraction effectiveness. This means that the increase in cardiac output is not achieved by increased energy demands [13]. Achievement of mechanical resynchronization seems to be a necessary condition for good response to CRT [14]. However, other mechanisms of action, including AV synchronization or changes in interventricular dependence might also play a role [15].

## Echocardiographic quantification of mechanical dyssynchrony

### Prior to the PROSPECT study

In the field of echocardiography, significant effort has been put into development of methods that would identify patients with the greatest potential benefit from CRT implantation by

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