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The Contemporary Role of Echocardiography in Improving Patient Response to Cardiac Resynchronization Therapy

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Abstract

Cardiac resynchronization therapy (CRT) is an important therapy for heart failure patients with widened electrocardiographic QRS complexes and depressed ejection fractions, however, approximately one-third do not respond. This article presents a practical contemporary approach to the utility of echocardiography to improve CRT patient response by assessing mechanical dyssynchrony, optimizing left ventricular lead positioning, and performing appropriate echo-Doppler optimization, along with future potential roles. Specifically, recent long-term outcome data are presented that demonstrates that baseline dyssynchrony is a powerful marker associated with CRT response, in particular for patients with narrower QRS duration or non left bundle branch block morphology. Advances in speckle tracking echocardiography to tailor delivery of CRT by guiding LV lead position is discussed, including data from randomized clinical trials supporting targeting the LV lead toward the site of latest activation. In addition, an update on the current role of Doppler echocardiographic device optimization after CRT implantation is reviewed.

Keywords

echocardiography; heart failure; pacemaker; Doppler

Introduction

Cardiac resynchronization therapy (CRT) has become established as an important therapy for heart failure (HF) patients with a widened electrocardiographic QRS complex and depressed ejection fraction (EF).[1–3] The majority of patients who meet current guidelines for implantation receive benefit in terms of morbidity and mortality, however, approximately one-third of patients do not appear to respond. [4, 5] Echocardiography has played a variety of roles in attempting to improve the care of CRT recipients, including patient selection, guiding lead placement and device optimization after implantation. This article will present a practical contemporary approach of the utility of echocardiography to improve CRT patient response by assessing mechanical dyssynchrony, optimizing left ventricular (LV) lead positioning, performing appropriate echo-Doppler device optimization, and introduce future potential roles.

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Echocardiographic Evaluation of Dyssynchrony

Current CRT guidelines use electrocardiographic QRS widening as a marker for abnormalities in the timing of regional cardiac contraction, known as dyssynchrony. However, there is increasing evidence that mechanical dyssynchrony is the major pathologic entity that is associated with deleterious biological processes affecting myocardial function in HF patients, and the therapeutic effect of CRT is closely linked to improvement in dyssynchrony. Although there is an association of QRS widening with cardiac mechanical dyssynchrony, several studies have demonstrated that the surface 12 lead electrocardiogram (ECG) lacks the sensitivity and specificity to precisely quantify mechanical dyssynchrony, and that imaging approaches are superior. [6–14] Unfortunately, the field of echocardiographic dyssynchrony has been criticized largely because of a multi-center observational study, known as PROSPECT, which examined several baseline dyssynchrony measurements and determined CRT response at 6 months. [15] Although some interpreted PROSPECT as a completely negative study, routine pulsed Doppler measures predicted CRT response. Specifically, the pre-ejection interval 140 ms (n=239) predicted both clinical composite score response (p=0.013) and LV end-systolic volume reduction 15% response (p=0.012). Also, the interventricular mechanical delay (IVMD) 40 ms predicted both clinical composite score response (p=0.045) and LV end-systolic volume reduction 15% response (p=0.016) (Figure 1). In addition, the tissue Doppler longitudinal velocity delay from the septum to the lateral wall 60 ms was highly statistically associated with LV end-systolic volume response (p=0.005) (Figure 2). Legitimate criticisms of PROSPECT included an unusually low yield of high quality echo data available, for example only 50% of patients had 12-site standard deviation (Yu Index) tissue Doppler data that could be analyzed. Furthermore, the follow-up duration was short at 6 months and multiple vendors' software and three different echo core labs contributed as confounding variables. [16, 17]

More recently, echocardiographic dyssynchrony has been shown to be convincingly associated with important long term clinical outcome and survival after CRT. One study of 229 patients with routine CRT indications showed that echocardiographic dyssynchrony before CRT was associated with a more favorable survival free from death, heart transplant or left ventricular assist device (LVAD). [10] Specific associations with favorable outcome over 4 years were IVMD 40 ms (p=0.019), Yu Index 32ms (p=0.003), and speckle tracking radial strain antero-septal to posterior wall delay 130ms (p=0.003) (Figure 3). When adjusted for confounding baseline variables of ischemic etiology and QRS duration, Yu Index and radial strain dyssynchrony remained independently associated with outcome (p<0.05). Lack of radial dyssynchrony was particularly associated with unfavorable outcome in those with a QRS duration of 120–150 ms (p=0.002). The STAR (Speckle Tracking and Resynchronization) used a prospective multi-center design on 132 consecutive CRT patients with class III and IV heart failure, ejection fraction (EF) 35% and QRS 120ms with similar primary end-points of death, transplant, or LVAD. [18] Baseline radial strain dyssynchrony, defined as 130 ms, had the highest sensitivity at 86% for predicting EF response with a specificity of 67% over 3.5 years. (Figure 4). Patients who lacked both radial and transverse dyssynchrony had unfavorable clinical events of death, transplant or LVAD occur in 53%, in contrast to events occurring in 12% of patients where baseline dyssynchrony was present (p<0.01). A third study by Delgado et al. examined speckle tracking radial dyssynchrony in 397 CRT patients with ischemic disease. [19] They observed that radial dyssynchrony 130 ms at baseline was an independent predictor of superior long-term survival after CRT over 3 years. (p=0.001). These three studies combine to 758 patients with similar results that echocardiographic dyssynchrony is favorably associated with long-term survival after CRT. Despite these cumulative supportive data, echocardiographic dyssynchrony has not yet been adopted by panels of experts for selecting patients for routine CRT.

Echocardiographic Dyssynchrony and Narrower QRS width or Non-LBBB Patients

Recent updated guidelines have summarized that the evidence of benefit from CRT is most convincing in patients whom have QRS duration > 150 ms and/or LBBB morphology, and is less convincing in patients with narrower QRS width < 150 ms when using electrocardiographic criteria alone. [4, 5, 20] Accordingly, it appears that the opportunity for echocardiographic dyssynchrony to play a potential adjunct role in refining patient selection for CRT is in subgroups where QRS width is < 150 ms or QRS morphology is not LBBB. Evidence exists of the additive value of echocardiographic dyssynchrony in improving patient selection with narrower QRS width in the CARE-HF trial where patients with a QRS interval of 120 to 149 ms were required to meet two of three echocardiographic criteria for dyssynchrony: an aortic preejection delay > 140 ms, an IVMD > 40 ms, or delayed activation of the posterolateral left ventricular wall. [3] In the pre-defined subgroup of patients with QRS width < 160 ms, CRT conferred a benefit in reducing death or cardiovascular hospitalizations compared to control with a hazard ratio of 0.74 (95% confidence interval of 0.54–1.02). This beneficial result of CRT in patients with narrower QRS from CARE-HF where echocardiographic dyssynchrony was required is in contrast to other clinical trials that did not require an assessment of mechanical dyssynchrony. [20]

Other more recent data have suggested that a potential application of echocardiographic dyssynchrony to assist in patient selection for CRT is in those with non-LBBB QRS morphology. The MADIT-CRT trial randomized New York Heart Association Class I–II HF patients with depressed EF to CRT with a defibrillator versus a defibrillator alone. [21] CRT afforded a significant reduction in heart failure hospitalizations or deaths as the primary endpoint overall, but important subgroup analysis revealed that patients with LBBB morphology received the greatest benefit. [22] Accordingly, only New York Heart Association Class I–II HF patients with LBBB are currently considered candidates for CRT. [4, 5] The impact of echocardiographic dyssynchrony for predicting response to CRT in class III–IV HF patients with widened QRS but non-LBBB morphology was recently studied in 248 CRT patients with QRS ≥ 120 ms and EF $\leq 35\%$. [23] Of these patients 124 with LBBB were compared to 80 who had intraventricular conduction delay and 44 with right bundle branch block (RBBB). LBBB patients had a more favorable long-term survival free from transplant or LVAD, than either intraventricular conduction delay or RBBB patients. However, when stratifying patients by the presence or absence of dyssynchrony, non-LBBB patients with radial dyssynchrony had a more favorable long term survival than those without dyssynchrony (hazard ratio 2.6; 95% confidence interval 1.47–4.53, $p=0.0008$). (Figure 5) Using routine pulsed Doppler as a less technically demanding dyssynchrony measure, non-LBBB patients with IVMD ≥ 40 ms had a much more favorable long term survival after CRT than those with lesser IVMD (hazard ratio (HR) 4.9; 95% confidence interval (CI) 2.60–9.16, $p=0.0007$). Using either method, RBBB patients who lacked dyssynchrony had the least favorable outcome. Accordingly, dyssynchrony appears to be a promising potential adjunct to improve patient selection for CRT with non-LBBB QRS morphologies.

Echocardiographic Dyssynchrony in Patients with Narrow QRS

Fundamental to current patient selection for CRT is QRS widening. An intriguing hypothesis is that mechanical dyssynchrony exists in a subset of HF patients with truly narrow QRS width (usually defined as < 130 ms). In other words, the concept is that abnormalities of regional mechanical activation in HF patients may not be evident by the 12-lead surface ECG, and that they may benefit from CRT. Accordingly, cardiac imaging is essential to detect mechanical dyssynchrony in patients with narrow QRS. There was one

completed randomized clinical trial known as ReThinQ that tested this hypothesis in CRT patients with QRS width < 130 ms with echocardiographic dyssynchrony by tissue Doppler or M-mode. [24] This study examined peak oxygen consumption at 6 months after CRT as the primary end point and showed no significant difference between treatment and control groups. However, significant improvements in HF functional class as a secondary end-point was observed in patients randomized to CRT. Furthermore, peak oxygen consumption significantly increased with CRT in a prespecified subgroup with a QRS interval of 120–129 ms ($p=0.02$). Although reported as negative, this trial may be considered inconclusive because of a relatively small sample of 156 randomized patients and a follow-up duration limited to 6 months. Accordingly, a much larger randomized clinical trial, known as EchoCRT, is underway to test the hypothesis that HF patients with reduced EF and QRS width < 130 ms may be helped by CRT if they have dyssynchrony detected by echocardiography. [25] This study defines dyssynchrony as a speckle tracking radial strain septal to posterior wall delay ≥ 130 ms and/or tissue Doppler longitudinal velocity opposing wall delay ≥ 80 ms. EchoCRT proposes to randomize approximately 1,200 patients with a primary end-point as time to first HF hospitalization or death, with a follow-up duration of 2 years. This currently on-going study will likely make a major contribution to our understanding of the potential of echocardiographic dyssynchrony to influence patient selection for CRT.

Echocardiographic Guided Left Ventricular Lead Positioning

The potential role of echocardiography in assisting placement of the LV lead for CRT was introduced several years ago [26–28], and recent emerging data have increased interest. The routine clinical approach currently to CRT is to place two pacemaker leads, one in the right ventricular apex and a second LV lead retrograde through the coronary sinus directing the tip into a posterior or lateral epicardial coronary vein. This is typically done with coronary venography under fluoroscopic guidance by selecting a coronary vein that is most accessible or that can offer a stable pacing position. Previous observational studies have shown that patients in whom the LV lead was at the site of latest mechanical activation may result in a greater resynchronization effect and clinical benefit. For example, Murphy et al. used color-coded tissue Doppler longitudinal velocities latest time to peak tissue velocity in the first half of the ejection phase to determine site of latest activation. [27] They observed in 54 patients that those with LV lead placement concurrent with the site of latest activation had significantly greater reverse remodeling 6 months after CRT than those with remote LV lead locations. Suffeetto et al. introduced speckle tracking radial strain echocardiography to identify the site of latest mechanical activation before CRT and also observed that patients with concordant LV lead placement had more favorable LV EF response. [28] Similar to Suffeetto, Ypenburg et al analyzed site of latest activation by speckle tracking radial strain in a larger cohort of 244 CRT patients. [29] Echocardiography was performed before CRT implantation and 6 months after. In 153 CRT patients with concordant LV lead position, they observed significant LV reverse remodeling at 6 months as well as greater improvements in long term all-cause mortality and HF hospitalizations, in comparison to patients with discordant LV leads. In the study by Delgado et al of 397 patients with ischemic cardiomyopathy, [19] speckle tracking radial strain was used to demonstrate independent and additive favorable effects of CRT associated with baseline dyssynchrony and lack of scar at lead position. They found lead concordance with site of latest activation to be associated with improved long-term survival and reduced HF hospitalizations.

Most recently, two independent randomized controlled clinical trials strengthened support for improving clinical response to CRT using an echocardiographic guided LV lead strategy. The TARGET trial (Targeted Left Ventricular Lead Placement to Guide Cardiac Resynchronization Therapy) randomized 220 patients with routine CRT indications to either

LV Lead targeted to site of latest activation determined by speckle tracking radial strain or routine LV lead positioning. [30] (Figure 6) In addition, speckle tracking radial strain amplitude data was used to avoid free-wall regions with less than 10% wall thickening felt representative of scar. They reported a more favorable effect of targeted LV lead placement in patients after 6 months of CRT on their primary end-points of LV volumes and EF. Favorable effects of targeted LV lead placement were also observed in the secondary endpoints of HF functional class, 6-min walk test, and HF hospitalizations combined with death. They used multivariate regression analyses to demonstrate important related effects on LV reverse remodeling at 6 months as follows: lack of scar at LV pacing site HR 3.06, 95% CI 1.01–9.26, $p=0.048$, concordant LV lead location with site of latest activation HR 4.43, 95% CI 2.09–9.40, $p=0.009$ and radial strain dyssynchrony HR 5.95, 95% CI of 2.78–12.7 $p=0.009$. The Speckle Tracking Assisted Resynchronization Therapy for Electrode Region (STARTER) trial was a similar but independent study that randomized 187 CRT patients to CRT to speckle-tracking echo guided vs. routine LV lead placement. [31] Basal and mid-LV short axis planes were analyzed by speckle tracking radial strain to determine the latest time to peak strain in 8 free-wall segments. Preliminary results were that patients with echo-guided LV lead position had significantly better outcome in the primary endpoint of death or HF hospitalization, as well as improvements in reverse remodeling. (Figure 7). STARTER also demonstrated that echoguided lead placement was associated with a comparatively better reduction of mechanical dyssynchrony as compared to routine lead placement and that reduction in mechanical dyssynchrony was strongly associated with long-term survival free from heart failure hospitalization. Although the STARTER results were only presented in preliminary abstract form at the time this was written, these two randomized controlled clinical trials combine with the previous body of observational data to provide evidence to support adopting an echo guided lead strategy to improve patient outcomes for CRT.

There have been technological advancements in three-dimensional (3D) speckle tracking echocardiography that has improved our understanding of mechanical dyssynchrony. [32, 33] Tanaka et al. showed in a pilot series of 54 HF patients for CRT that the distribution of site of latest activation may be plotted in a 3D format that enhanced our understanding of the spatial relationship of regional LV mechanics. This approach has promise to improve LV lead guidance and further study is underway, currently. (Figure 8)

LV lead placement in Relation to Scar

Complementary to guiding the LV lead to the site of latest mechanical activation is using imaging to guide LV leads to avoid scar. Bleeker et al originally demonstrated that LV lead position in a region of myocardial scar results in less favorable results in a pilot of 40 patients with ischemic cardiomyopathy undergoing CRT. [34] They used late gadolinium enhancement (LGE) cardiac magnetic resonance (CMR) imaging to define the location and transmural extent of scar (defined as extending >50% of LV wall thickness). They observed that patients with transmural scar in the posterolateral region had less improvements in LV remodeling compared to patients with LV leads positioned in regions without scar. Interestingly, they reported that posterior lateral scar was associated with non-response, regardless of dyssynchrony by tissue Doppler. Leyva et al reported a large investigation of scar characterization in CRT patients using LGE by CMR, comparing 209 patients where LV lead position was attempted to avoid scarred segments to 350 patients where LV lead placement was routine. [35] Among the CMR guided patients, those with successful LV lead placement away from scar had a more favorable clinical outcome after CRT than those where the implanter was unsuccessful and the LV lead was placed in a scarred region. LV lead in scar was associated with an increased risk of cardiovascular death (HR: 6.34), cardiovascular death or HF hospitalizations (HR: 5.57), death from pump failure (HR: 5.40),

compared to patients with LV lead not in scar (all $p < 0.0001$). Patients without LV guiding in whose scar and lead interaction was not reported, had intermediate outcome, with HRs of 1.51 ($p = 0.0726$), 1.61 ($p = 0.0169$) and 1.87 ($p = 0.0005$), respectively.

Although the majority of literature supports using CMR LGE for quantifying scar, echocardiography remains a more readily accessible imaging modality in most clinical environments and recent interest has emerged to use speckle tracking strain as a marker for scar. In the above mentioned seminal paper, Delgado et al used a $<16.5\%$ radial strain cutoff to relate LV lead position in scar as having a less favorable outcome in ischemic cardiomyopathy patients, which was of additive prognostic value to dyssynchrony and LV lead at site of latest activation. [19] Khan et al also used radial strain in a group of 140 CRT patients and observed that reverse remodeling response was significantly lower in those patients where low amplitude radial strain was $< 9.8\%$ at site of LV lead placement (62.7% vs. 31.3%, $p < 0.05$) with 92% specificity and 39% sensitivity. [36] These investigators went on to apply the combination of targeting LV lead position to avoiding scarred regions (radial strain $< 9.8\%$) while seeking the site of latest activation in the TARGET randomized trial previously discussed. [30] The targeted LV strategy was associated with more favorable LV reverse remodeling and superior clinical outcomes. In summary, there is growing evidence that avoiding scar is highly advisable when placing LV lead for CRT. A larger experience supports assessing transmural scar by CMR LGE, however, speckle tracking radial strain appears to be able to play a role in determine regions of likely scar. Further study is required to establish the radial strain cut-off most clinically useful in its association with scar.

Doppler Echocardiographic Device Optimization

The initial proposal of echocardiography for playing a role in improving response to CRT began with Doppler atrioventricular (AV) and ventricular-ventricular (VV) optimization. [37, 38] However, several subsequent studies have suggested that routine Doppler optimization may not be as important as originally thought. Kedia et al reported a large clinical experience of Doppler optimization using mitral inflow and LV outflow velocities in 215 CRT patients. [39] They reported a significant difference between AV delay pre- and post-optimization (120 ± 25 and 135 ± 40 ms, respectively, $p = 0.0001$). However, optimization achieved improvement in diastolic filling patterns by at least one stage in only 9%, and when comparing patients with AV delay $<$ or > 140 ms, no significant differences in clinical outcomes were observed. The FREEDOM trial randomized patients to a device-based AV and VV optimization algorithm (QuickOpt) employed frequently at 3 month intervals versus a routine clinical approach. [40] Of 1,647 patients enrolled, there were no differences after 1 year of CRT in the pre-specified clinical composite score between the treatment arms ($p=0.86$). Furthermore, there was no difference between frequent device-based optimization and standard care based on physicians discretion ($p = 0.8$ vs. standard care with AV/VV optimization and $p = 0.65$ vs. standard care with empirical settings).

Another large controlled trial (SMART-AV) randomized 980 patients to three AV optimization strategies: a device-based electrocardiogram algorithm (SmartDelay), echo-Doppler optimization, or empiric “out of the box” settings with AV delay = 120 ms, and VV delay = 0. [42] This was uniquely important because it included comparing echo-Doppler optimization to a control strategy of no optimization at all. Overall, no significant differences between 3 treatment arms were observed in the primary end point of LV end-systolic volume reduction or secondary clinical end points at 6 months. Interestingly, echocardiographic AV optimization was similar to the empiric AV delay of 120 ms. An unexpected finding from sub-group analysis was that female CRT patients benefited from optimization by either device-based or echo-Doppler approaches, compared to empiric control, even after adjusting for covariates of age, QRS width or baseline LV end-systolic

volume index. [42] Beneficial effects of optimization appeared to be entirely concentrated in women with nonischemic cardiomyopathy. Interestingly, optimization in females with nonischemic cardiomyopathy resulted in a shorter median programmed AV delay of 100 ms for both the SmartDelay and echo-optimized groups ($p < 0.003$ vs. the empiric AV delay of 120 ms). This observation suggests that females with nonischemic cardiomyopathy may be a subgroup of individuals who may benefit from routine optimization after CRT, or at least that an empiric AV delay setting of 120 ms is too long in these individuals. Further prospective study is needed to draw a definitive conclusion.

Although not yet directly tested in a randomized clinical trial, Mullens et al reported the important utility of echo Doppler optimization in the subgroup of patients deemed as CRT nonresponders. [43] After 75 CRT patients underwent a comprehensive protocol-driven evaluation to determine the potential reasons for non-response, 47% appeared to benefit from echo-Doppler AV optimization. Overall, multidisciplinary recommendations led to changes in device settings and/or other therapeutic modifications in 74% of patients and were associated with fewer adverse events (13% vs. 50%, odds ratio: 0.2 [95% confidence interval: 0.07 to 0.56], $p = 0.002$) compared with those in which no recommendation could be made. Patients with a favorable outcome of intervention had more often changes in device settings including AV timing reprogramming (20% vs. 69%, $p < 0.001$). These data suggest that a comprehensive evaluation of non-response, including echo-Doppler optimization is appropriate in the subgroup of HF patients who do not seem to be benefiting from CRT.

Conclusion

CRT has been a major clinical advance in the treatment of HF patients. A high level of interest in the utility of echocardiographic approaches to improve patient benefit remains. (Table 1) Long-term outcome data have emerged demonstrating that baseline echocardiographic dyssynchrony is a powerful marker associated with response. Because response rates are much higher in patients with QRS duration > 150 ms or LBBB morphology, the opportunity for echocardiographic dyssynchrony to positively influence CRT patient selection appears to be in those with narrower QRS and with non-LBBB morphology, where the ECG is a less robust surrogate for dyssynchrony. One of the most exciting recent advances for echocardiography to tailor delivery of CRT has been in guiding LV lead position. Two randomized clinical trials have supported the use of positioning the LV lead toward speckle tracking radial strain site of latest activation to improve clinical outcomes after CRT. In addition, data are emerging that diminished radial strain indicating a likely scarred segment may be used to avoid LV lead positioning. Finally, the sum of existing data suggest that routine echo-Doppler device optimization is not required in all patients after CRT, but the subgroups of non-responders and possibly females with nonischemic cardiomyopathy are those who may benefit the most from optimization. This is an exciting and evolving field where new indications and refinements in the utility of echocardiography for improving patient response to CRT are advancing.

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Figure 1.

Routine pulsed Doppler examples from the right ventricular (RV) outflow track (top panels) and left ventricular (LV) outflow track (bottom panels) from a patient with dyssynchrony before cardiac resynchronization therapy. The calculation of interventricular mechanical delay (IVMD) is the difference from between LV pre-ejection period (PEP) and RV PEP (arrows).

Figure 2.

Examples of color-coded tissue Doppler images from the 4-chamber views (left) and corresponding septal and lateral time-velocity plots (right). The top panels are from a normal subject with similar septal and lateral time-velocity curves. The bottom panels are from a patient with left bundle branch block dyssynchrony before cardiac resynchronization therapy, demonstrating early septal and late lateral wall peak systolic velocities.

Figure 3.

Examples of speckle tracking radial strain images from the mid-ventricular short axis plane with corresponding time-strain plots from 6 segments. The top panels are from a normal subject with 6 synchronous time-strain curves. The bottom panels are from a patient with left bundle branch block dyssynchrony before cardiac resynchronization therapy, demonstrating early septal and late posterior and lateral wall peak strain.

Figure 4.

Kaplan Meier plots of probability of event free survival free from heart transplant or left ventricular assist device in cardiac resynchronization therapy (CRT) patients with and without radial dyssynchrony by speckle tracking radial strain from the STAR study. The cut-off defined as significant dyssynchrony was a septal to posterior wall delay of at least 130 ms. Significant radial dyssynchrony before CRT was associated with a more favorable clinical outcome.

Figure 5.

Kaplan Meier plots of probability of event free survival free from heart transplant or left ventricular assist device in cardiac resynchronization therapy (CRT) patients grouped by those with left bundle branch block (LBBB) and those non-LBBB and with and without radial dyssynchrony. The cut-off defined as significant dyssynchrony was a septal to posterior wall delay of at least 130 ms. Non-LBBB patients with significant radial dyssynchrony before CRT had a more favorable clinical outcome, similar to those with LBBB.

Figure 6.

An example of a speckle tracking radial strain image from the mid-ventricular short axis plane with corresponding time-strain plots from 6 segments. The right arrow indicates the posterior wall segment having the latest time to peak strain. The left arrow indicates the corresponding anatomical segment with the latest peak strain for LV lead targeting.

Figure 7.

Kaplan Meier plots of freedom from heart failure hospitalization or death from the STARTER trial showing 6 month data extracted as preliminary results. Cardiac resynchronization therapy patients were randomized to either LV lead positioning toward the site of latest activation by speckle tracking radial strain, or routine empiric lead placement as a control. The echo-guided strategy was associated with a significant reduction in heart failure hospitalizations or death.

Figure 8.

An example of color-coded three-dimensional speckle tracking strain in a patient with widened QRS who was referred for cardiac resynchronization therapy. The apex down three-dimensional map is on the left and the polar map is on the right. The latest site of peak radial strain, color-coded as red, appears in the mid ventricular inferior-posterior region. This representation has potential to assist in guiding left ventricular lead positioning.

Table 1**Potential Roles of Echocardiography to Improve Patient Response to CRT**

	Methods most Widely Supported	Evidence for Clinical Applications
Echocardiographic Dyssynchrony at Baseline	<ul style="list-style-type: none"> • Pre-Ejection Delay 140 ms • IVMD 40 ms • TDI Opposing Wall Delay 80 ms • TDI Yu Index 32 ms • Radial strain delay 130 ms 	<ul style="list-style-type: none"> • Prognostic Value for all with routine CRT indications • Borderline QRS width (110–130 ms) as adjunct • Non-LBBB QRS morphology as adjunct • Narrow QRS width (< 130 ms): further studies on-going.
Echo Guided Lead Positioning to Site of Latest Activation	Speckle Tracking Radial Strain site of latest activation	Patients with routine CRT indications
Echo Guided Lead Positioning to Avoid Sites of Regional Scar	Avoid segments with < 10% radial strain amplitude	Patients with ischemic disease: emerging support, further studies on-going.
Atrioventricular and Ventricular-Ventricular Optimization	<ul style="list-style-type: none"> • Mitral inflow velocity analysis • LV Outflow tract time velocity integral 	<ul style="list-style-type: none"> • Non-Responders • Female patients with non-ischemic disease

CRT = cardiac resynchronization therapy, IVMD = interventricular mechanical delay, TDI = tissue Doppler imaging, LBBB = left bundle branch block, LV = left ventricular.