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The Role of Echocardiography in Cardiac Resynchronization Therapy

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Introduction

Systolic asynchrony, which illustrates discoordinated contraction of the heart, is relatively common in heart failure patients, in particular those with prolonged QRS complexes. It is caused by electromechanical delay in some regions of the failing heart and will result in further reduction of cardiac function. Cardiac resynchronization therapy(CRT) is a rapidly evolving pacing modality for advanced heart failure, characterized by implantation of the left ventricular(LV) lead through coronary sinus to the free wall region. It is recommended in patients with reduced ejection fraction (<35%) and prolonged QRS complex (≥120ms) who remain symptomatic (NYHA class III, IV) despite optimal medical therapy to improve symptoms (class of recommendation I, level of evidence A), hospitalization (class of recommendation I, level of evidence A) and mortality (class of recommendation I, level of evidence B).[1)2)]

Echocardiography has an prominent role in the era of CRT by virtue of its non-invasive nature with high feasibility and reproducibility. More importantly, it permits serial assessment after device implantation. The clinical applications include not only quantification of the change in systolic function, hemodynamics, LV volume, or mitral regurgitation, but also assessment of systolic asynchrony by a number of new echocardiographic technologies.

Assessment of Favorable Responses to CRT

A number of methods have been used to demonstrate the favorable responses after CRT, including hemodynamic, clinical and echocardiographic variables.[3)] However, acute hemodynamic improvement may not predict the long-term outcome, and some patients who have no or minimal acute changes in any assessment modality may show gradual and delayed improvement after a few months.[4)] Obviously, the limitation of clinical assessment at present is the lack of consensus on what clinical criteria should be selected. Furthermore, some clinical endpoints are subjected to a placebo effect.[5)6)]

Demonstration of reverse remodeling response

Another way to confirm a favorable response to CRT relies on the assessment of change in LV size and cardiac function by echocardiography. A commonly used description is LV reverse remodeling that signifies a reduction in LV volume, a less spherical LV shape, and improved systolic function assessed by the LV ejection fraction. In fact, LV reverse remodeling is the structural premise to reveal the improvement of cardiac function and ventricular hemodynamics.

Among various parameters, left ventricular end-systolic volume(LVESV) measured by biplane Simpson's method is particularly useful, as previous large clinical trials have observed that an increase in LVESV is the single best predictor of adverse prognosis in patients with LV dysfunction.[7)] The advantage of this method is that it is an objective endpoint based on cardiac structure and function, which can be assessed offline in a blinded fashion, and theoretically less subjected to placebo effect.

LV reverse remodeling consists of both structural and functional changes. It has been consistently shown in case series

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Table 1. Summary of major benefits in cardiac structure and function after CRT assessed by conventional echocardiography

Echocardiographic Parameters	Change after CRT
M-Mode	
LV end-diastolic diameter	↓
LV end-systolic diameter	↓
2D Echocardiography	
LV end-diastolic volume	↓
LV end-systolic volume	↓
LV ejection fraction	↑
LV end-diastolic sphericity index (LV length/width)	↑
LV end-systolic sphericity index (LV length/width)	↑
Doppler Echocardiography	
Mitral regurgitation	↓
Cardiac output	↑
+dp/dt	↑
LV diastolic filling time	↑
LV preejection period	↓
Myocardial performance index	↓

and multicenter trials.[8-11] Yu et al. demonstrated an onset as well as an offset of the favorable reverse remodeling effects of CRT in an early key study.[8]

This study not only confirmed the previous observation that biventricular pacing could result in reverse remodeling,[12)13] but also found that LV volume increased gradually over 4 weeks after cessation of biventricular pacing. In addition, other echocardiographic benefits were also lost with time. These observations provided strong evidence that pacing is the cause of LV reverse remodeling. In a recently published study,[14] it was illustrated that a small amplitude of reduction in LV volumes and increase in ejection fraction was observed within the first 24 hours after CRT, however LV mass and regional wall thickness in all measured sites were unchanged in the acute stage. In contrast, at the end of 3 months, there was a further reduction in LV volumes and gain in ejection fraction associated with a decrease in LV mass and LV wall thickness. Therefore, the true benefit of reverse remodeling has been suggested by the occurrence of structural change in LV at mediumterm follow up. In addition, a close correlation was found between the degree of reverse remodeling and reduction in LV mass. As a result, the decrease in LV mass that occurred over 3 months of treatment is probably due to a decrease in both wall thickness and overall chamber size. In MIRACLE study,[15] a reduction of LV mass in the CRT treatment group was also reported at the medium-term, as opposed to the significant increase in LV mass in the control group.

Other benefits of CRT assessedy by conventional echocardiography, including M-mode, 2-dimentional(2D) and Doppler, are listed in Table 1.

Differentiation between responders and non-responders

Despite consistent benefits in multiple clinical trials, a proportion of patients do not respond adequately to CRT. The MIRACLE study demonstrated that 35% of patients receiving CRT experienced no improvement in the “heart failure clinical composite score”.[15] Several echocardiographic case series observed no reverse remodeling in up to 40% of patients who underwent CRT.[9,16-18] Due to the lack of consensus on clinical definition of responders as well as the associated placebo effect in some parameters, reverse remodeling as reflected by reduction of LVESV has been adopted in many CRT studies. This method is fast and independent of preconceived ventricular shape. It is more accurate than assumptions based on M-mode or single plane 2D analysis. In CRT trials, using a vigorous definition of reduction of LVESV >15%, volumetric responders were found in about 55~60% of patients.[18,19]

Apart from the reduction in LVESV, responders also had a more favorable improvement in cardiac systolic function, and LV geometry as illustrated by the increase in sphericity indices.[20-22] Interestingly, only responders had a significant decrease in LV mass for a mean amplitude of over 15%, and reduction of wall thickness in all the regions which ranged from 7 to 11%. On the other hand, non-responders behaved in the opposite direction with increase in LV mass for 9% and regional wall thickness for the average of 10%.[14] In addition, responders showed a better improvement in all conventional clinical endpoints, whereas lack of clinical response was not uncommon in volumetric non-responders.[20-22] Therefore, LV reverse remodeling occurs in parallel with symptomatic and functional improvement, which suggests that volumetric assessment could be a useful tool for differentiating responders from non-responders and predicting other favorable responses after CRT.

Furthermore, chronic LV reverse remodeling response after CRT has been observed to be associated with a better prognosis, including a lower mortality as well as fewer heart failure hospitalizations.[15,21,23] It is likely a combined effects of improvement in intraventricular synchronicity,[8] hemodynamics,[24] atrioventricular synchronicity,[25] interventricular synchronicity[8)23)] and mitral regurgitation.[8)23)] In a recent clinical study which recruited 141 heart failure patients receiving CRT,[21)] volumetric responders showed a significantly lower all-cause mortality, cardiovascular mortality, heart failure events, and the composite endpoint of all-cause mortality or cardiovascular hospitalization. Therefore, LV reverse remodeling is not only an objective measure of beneficial responses after CRT, but also a strong prognosticator of better long-term outcomes.

Comprehensive Assessment of Systolic Asynchrony

Current guidelines for CRT recommend the prerequisite occurrence of prolonged QRS duration.[1)2)] This phenomenon occurred in only about 30% or less of the heart failure population according to large heart failure registries.[26)27)] Since the sensitivity and specificity of QRS duration to detect the presence or severity of electromechanical delay were challenged, other methods for direct measurement of mechanical asynchrony have been used to investigate heart failure patients.[28-30)]

Many studies that applied a variety of echocardiographic techniques to patients receiving CRT focus on the assessment of systolic asynchrony, because it is believed to be the primary abnormality in heart failure with prolonged QRS duration. Secondly, examination of regional asynchrony is now possible by advanced echocardiographic technology which helps to elucidate the mechanism of benefit from CRT. Thirdly, echocardiographic assessment of baseline asynchrony (before

Table 2. Summary of echocardiographic technologies for assessment of systolic asynchrony

Echo Tools	Views	Asynchrony Indices	Cutoff	Advantage	Disadvantage
M-Mode[9)]	Parasternal short-axis	Septo-posterior delay in systole	130ms	• Easy to perform • Predict +ve response	• Not useful in “flat” or paradoxical septal motion • Less comprehensive
Doppler[46)]	LV & RV outflow	QRS to onset of aortic flow -QRS to onset of pulmonary flow*	40ms	• Easy to perform	• Less comprehensive
TDI (4 segments)[35)]	Apical 4-chamber	Septo-lateral delay in Ts (ejection phase)	65ms	• Predict +ve response • Robust as based on fundamental data	• Less comprehensive
TDI (12 segments)[19,20)]	Apical 4-, 2- & 3-chamber	Ts-SD of 6 basal, 6 mid LV segments (ejection phase)	>32ms	• Predict +ve response • Highly comprehensive • Robust	• Learning curve
DLC (by TDI & SRI)[39)]	Apical 4-, 2- & 3-chamber	DLC (or post-systolic shortening)	Not clear	• Correlates with gain in systolic function	• Semiquantitative • Time consuming • Learning curve
Strain[37,38,47)]	Apical views	Time to peak -ve strain, Peak negative strain	NIL	• Change in regional strain may reflect change in asynchrony	• Role of time to peak -ve strain unsure • Relatively large variability • Learning curve • Technically demanding
Strain rate[20,38,47)]	Apical views	Time to peak -ve strain rate	NIL	• Differentiate translational motion theoretically	• Time to peak -ve strain rate not confirmed • Relatively large variability • Learning curve • Strong technical demand
Tissue synchronization imaging[4,22)]	Apical views	Time to peak +ve myocardial velocity sampled automatically	Similar methods as TDI	• Quick visual appreciation of regional wall asynchrony • Faster than TDI “theoretically” • Both quantitative & qualitative	• Setting of beginning & end of TSI is critical • Intrinsic problems of automated sampling of Ts • Learning curve • Technically demanding
3D Echo[28,48)]	Apical window	Time to minimal regional volume of multiple segments	Not clear	• Accurate volumetric measurement • Potentially most comprehensive • Quantitative and qualitative	• Relatively low spatial resolution • Angle for capture not wide enough

* index for interventricular asynchrony; others for intraventricular asynchrony. DLC, delay longitudinal contraction

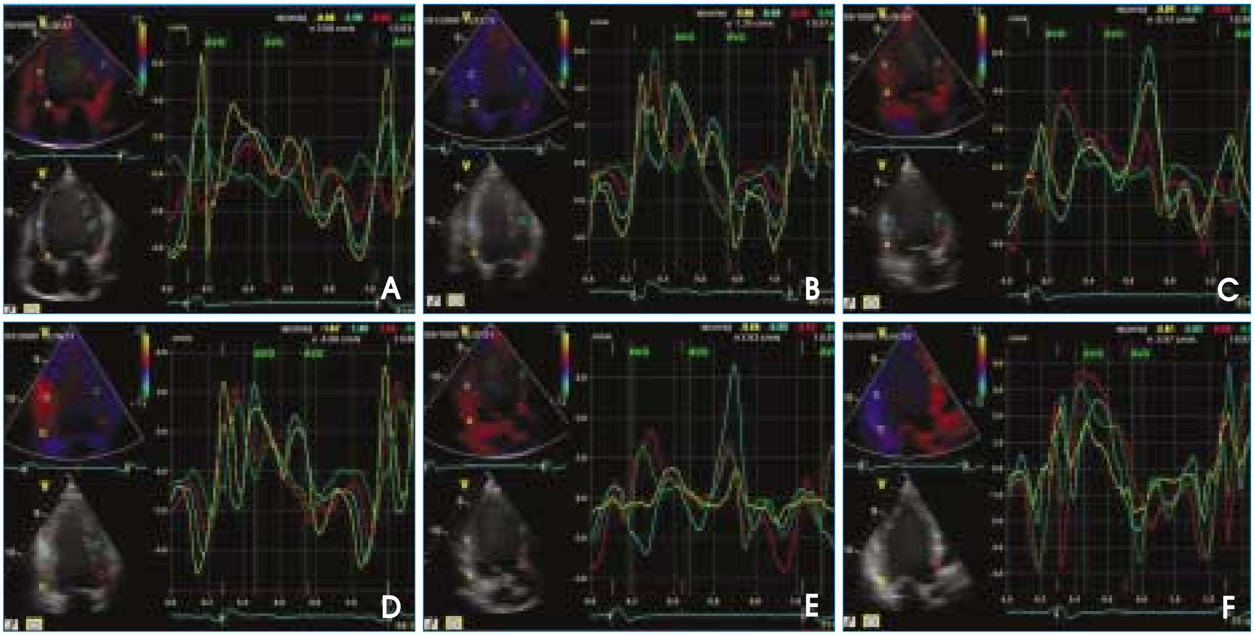

Fig. 1. An example of myocardial velocity curves reconstituted from 2-dimensional color tissue Doppler imaging(TDI) in apical 4-chamber (A and B), apical 2-chamber (C and D) and apical long-axis (E and F) views before (A, C and E) and after (B, D and F) CRT. Multiple sampling windows are placed at both basal and mid levels. During ejection phase between the opening (AVO) and closure (AVC) of aortic valve, the time to sustained systolic peak (Ts) was measured to assess systolic asynchrony. Before CRT, this patient had severe asynchrony as reflected by the dispersion of timing to systolic peak velocity (arrows), which was significantly reduced after the therapy.

the device implantation) has a vital role to predict who will exhibit a positive clinical or volumetric response after CRT. In addition, echocardiography is potentially helpful in selection of patients for CRT based on the presence of mechanical asynchrony, in particular when QRS complex is not so prolonged, or even normal.

In patients with advanced heart failure, the conduction system from the sinal node to the Purkinje fibers can be affected. Three different levels of asynchrony which are closely linked and appear commonly together, can be distinguished by echocardiography, namely atrioventricular asynchrony, interventricular asynchrony, intraventricular asynchrony.[31] Probably the most important level of asynchrony to be evaluated in the context of CRT is within the LV. It is speculated that when the culprit abnormal mechanical events are corrected by CRT, reversal of those abnormalities will result in the improvement of cardiac function, such as gain in ejection fraction, LV reverse remodeling and alleviation of mitral regurgitation.

A number of echocardiographic tools have been described in literatures for the assessment of systolic asynchrony in heart failure. These include conventional M-mode and Doppler echocardiography, as well as new technologies such as 3D echocardiography, tissue Doppler imaging(TDI) and its derived strain rate, strain, tissue tracking, displacement, tissue synchronization imaging(TSI). Table 2 summarizes the role, cutoff value, advantages and disadvantages of those available techniques.

High prevalence of systolic asynchrony in heart failure

Although the estimated prevalence of mechanical asynchrony for the heart failure population is not available from large cohort studies, several case registries observed that it was as high as 70% in wide QRS complexes and more than one-third in narrow QRS complexes.[28-30]

TDI is a robust and reproducible echocardiographic tool to detect regional function and timing of cardiac events in the myocardium. Yu et al. examined the prevalence of systolic asynchrony in 67 heart failure patients with QRS duration $>$120ms (in the form of LBBB or intraventricular conduction delay), 45 heart failure patients with QRS duration $\leq$120ms and 88 normal controls, which was the earliest report of this kind.[29] By the use of TDI, “Asynchrony Index” (or Ts-SD) was calculated as the standard deviation of the time to peak systolic velocity (Ts) in the 6-basal and 6-mid segmental LV model. When a cutoff value of $>$32.6ms that was derived from the normal subjects (mean+2SD) was used to define significant systolic asynchrony, it was present in 64% of heart failure patients with wide QRS and in 43% with narrow QRS complexes. The report by Ghio et al. examined 61 heart failure patients with normal QRS duration, 97 patients with LBBB where QRS width between 120~150ms in 21 and QRS duration ≥150ms in 76 patients.[30] Intraventricular asynchrony was assessed by apical 4- and 2-chamber views at basal and middle segments for maximal difference of the time to onset of systolic wave, with a cutoff value of >50ms. The prevalence of systolic intraventricular asynchrony in these three groups was 30%, 57%, and 71%, respectively. In another study, by using of septo-lateral delay >60ms at basal LV segments, 27% of heart failure patients with QRS duration ≤120 ms were reported to have systolic dyssynchrony, and these figures were 60% and 70% respectively in those with intermediate and wide QRS complex (>150ms).[32]

The presence of systolic asynchrony in heart failure was also confirmed recently by another complementary technology, 3D echocardiography. The study by Kapetanakis et al. examined 83 patients with LV systolic dysfunction, of whom 40 patients (48%) had a QRS duration of ≥120ms.[28] Systolic asynchrony index was derived from 3D echocardiography by calculating the standard deviation of % time to minimal regional volume of 16 LV segments, and a cutoff value of 8.3% was defined from normal subjects (mean+3SD). Among those with moderate to severe LV dysfunction (ejection fraction <40%), 37% of patients had evidence of systolic asynchrony. Therefore, irrespective of QRS duration, patients with heart failure could develop systolic mechanical asynchrony. Although the condition is more prevalent in the wide QRS group, it is also a common feature in patients with narrow QRS complexes.

Understanding the mechanism of CRT benefits

Reverse remodeling response induced by CRT has been consistently demonstrated in all randomized prospective studies and in smaller mechanistic studies.[5)8)10-13] It might act through several mechanisms, including redistribution of regional ventricular loading, reduction of mitral regurgitation, reduction of sympathetic activity and others, as a result of improvement in systolic mechanical asynchrony.[11]

In an early study, 25 patients who underwent CRT were studied sequentially for three months by echocardiography with TDI.[8] Measurement of Ts was performed at six basal and six mid LV segments and the two RV segments. LV asynchrony before CRT was illustrated by the widespread regional variation of Ts among various segments, whereas systolic synchronicity was achieved 3 months after CRT by homogeneously delaying those early contracting segments to a timing similar to the delayed segments. As a result, not only septolateral delay was abolished, other patterns of intraventricular delay as well as the septal to RV free wall delay were also corrected. Furthermore, echocardiographic improvement was pacing dependent.[8]

Improvement of mitral regurgitation is another cardinal echocardiographic feature in CRT, which are likely related to the improvement of systolic dyssynchrony. Kanzaki et al.[33] demonstrated that interpapillary muscle delay was present in heart failure patients to distort the normal timing in closure of mitral valve, using the time to peak strain in short-axis view. Such delay was greatly reduced after CRT, which correlated with reduction in mitral regurgitant fraction ($r=0.77$, $p<0.001$). With reduction of regurgitant volume into the left atrium, atrial filling pressure is reduced and LV volume overload is decreased. It enhances the process of LV reverse remodeling.

Predicting responders to CRT

Despite the benefits of CRT improving clinical status, cardiac function, reverse remodeling and prognosis, non-responders have been consistently observed in up to 40% of patients receiving CRT.[9)16-19] A number of factors could result in failure to response, however, the absence of significant mechanical asynchrony before implantation to allow the therapy to target on could be one of the major reasons. Reported in previous studies,[20)34] only responders suffered from sufficient systolic asynchrony which was improved after CRT. On the other hand, non-responders had less obvious systolic asynchrony in whom CRT actually worsened mechanical synchronicity. In addition, suboptimal location of LV lead, loss of LV pacing due to lead dislodgement, as well as incorrect programming of the device would also lead to the lack of response

A number of echocardiographic techniques and their derived indices of systolic asynchrony have been proposed to predict favorable responses after CRT. However, to apply an echocardiographic index in clinical practice, a cutoff value needs to be identified objectively to determine if systolic asynchrony is clinically relevant. Furthermore, a good index needs to be able to predict a favorable response with a high sensitivity in order to be incorporated as a "screening test"; and a high specificity as a "rule in" test to ascertain the presence of systolic dyssynchrony.

During the recent years, various echocardiographic parameters has been adopted in single-center, small-scaled studies by different investigators to assess systolic asynchrony and predict responses after CRT. The study by Yu et al., for the first time, examined systematically for the potential predictor(s) of LV reverse remodeling in 30 patients who had undergone CRT.[19] Improvement of NYHA class was observed in all the responders of LV reverse remodelling, but only in

54% of non-responders. Improvement of peak oxygen uptake, maximal metabolic equivalent achieved during treadmill exercise test, and six minute hall-walk test distance were only observed in the responders. It confirmed that electrocardiographic criteria, patient characteristics, clinical investigations and noninvasive hemodynamic parameters did not predict the reverse remodeling response. In contrast, the baseline "Asynchrony Index" was observed to correlate with the degree of LV reverse remodelling closely, and a cutoff value of $>$ 32.6ms was able to segregate volumetric responders from non-responders. The study by Bax et al. examined 85 patients receiving CRT for one year to determine the non-responder rate and the value of septo-lateral delay by TDI velocity modality in assessment of systolic asynchrony.[35] Chronic responders were found in 73% of the patients, defined as an improvement in NYHA functional class of $\geq$1 score and a gain of $\geq$25% in 6-Minute Hall-Walk distance. In addition, it was observed that a septo-lateral delay $\geq$65ms predicted the clinical response with a sensitivity and specificity of 80%. More importantly, patients who were above this cutoff value had a lower mortality than those who were below, illustrating the more severe systolic asynchrony at baseline, the better response after CRT. Notobartolo et al. evaluated 49 patients with color TDI by a six-basal segmental model in a follow up study. The index of systolic asynchrony was calculated from the maximal difference in time to highest peak velocity in either ejection phase or post-systolic shortening(PSS) among the six segments, so called "peak velocity difference". The cutoff value of $\geq$110ms at baseline predicted LV reverse remodeling at 3 months after CRT with a sensitivity of 97%, though the specificity was only 55%.[16]

Furthermore, other post-processing modalities of TDI technology have also been questioned on its ability to quantify systolic asynchrony and predict a favorable response to CRT, in particular TSI, strain rate, strain and displacement mapping.[20][22][36][37] Gorcsan and colleagues applied TSI in 29 patients, and observed that 15 patients with greater differences in baseline Ts of opposing ventricular walls showed an acute hemodynamic improvement.[4] A cutoff value of $\geq$65ms in anterior septum to posterior wall delay had a sensitivity of 87% and a specificity of 100% for predicting an acute response. Whereas, in another study when patterns of regional wall delay by 2D TSI color-coding were investigated, it was observed that the presence of most severe delay in lateral wall gave a sensitivity of 47% and specificity of 89% to predict LV reverse remodeling. However, the "Asynchrony Index", which calculated by TSI and hence made an equivalent to that by TDI, was the best predictor of LV reverse remodeling. A cutoff value of $>$34.4ms was obtained from the receiver operating characteristic(ROC) curve with a sensitivity of 87% and a specificity of 81%. It has been suggested that the improvement of peak displacement, strain and strain rate can serve as a surrogate marker of reduced systolic asynchrony.[38][39] Strain rate and strain mappings have the theoretical advantage of being less affected by translational cardiac movement, however, their superiority to tissue Doppler velocity in assessing patients with CRT has not been confirmed.[20][37] The role of displacement mapping in predicting a reverse remodeling response was found inferior to myocardial velocity mapping.[37]

Real-time 3D echocardiography used in predicting favorable responses has the advantages of allowing a comparison of synchrony between all segments in the left ventricle together. It also provides an intuitive display of ventricular synchronicity which appears to be attractive to non-echocardiographers, in particular electrophysiologists. The study by Kapetanakis et al. examined 26 patients before and after CRT for a mean duration of 10 $\pm$1 months.[28] It was observed that patients with long-term clinical response had significantly larger values of baseline Systolic Dyssynchrony Index, which was derived from the standard deviation of % time to minimal regional volume of 16 LV segments. However, prospective, multicenter, large scale trials are urged to test the ablility of a variety of echocardiographic measures of LV systolic asynchrony to predict clinical and echocardiographic outcomes.

Patient selection for implantation of CRT

Based on the current inclusion criteria, echocardiography is the very first step to confirm and assess the severity of LV systolic function, in particular identify patients with low ejection fraction (typically $<$35%) and dilated LV.[1][2] However, recent studies have suggested that the effectiveness of CRT depends heavily on whether systolic asynchrony is present before the device implantation.[16][39-41] Although at present the QRS duration remains the only marker for the presence of systolic dyssynchrony in clinical practice and available guidelines,[1][2] it appears not to be sensitive in predicting the presence or absence of electrical activation delay in the LV. Therefore, selection of patients based on the direct assessment of mechanical asynchrony is potentially helpful to increase response rate where its clinical utility needs to be examined by prospective studies.[18][31][40]

Optimization of Device Programming after CRT

Improvement of atrioventricular asynchrony is one of the mechanisms of benefit from CRT.[31] This is particularly helpful in those patients with first degree atrioventricular block where diastolic filling time will be in further jeopardy.[31] About half of heart failure patients who have prolonged QRS duration also have accompanied first degree atrioventricular block. Optimzation of atrioventricular interval (AV interval) is in attempt to ensure atrioventricular synchrony and near 100% ventricular pacing in individual patients. It allows a longest LV filling time and maximal cardiac output, but abolishes the "wasted" pre-systolic time after completion of atrial contraction hence reduces the diastolic mitral regurgitation.[42)43)] Usually, AV interval optimization is performed shortly after the device implantation, ie. at the pre-discharge period. However, re-optimization of AV interval at intermediate (eg. 3 months) and long-term (eg.12~18 months) follow up may be necessary to further improvement in cardiac performance.[44]

The two commonly employed methods of AV interval optimization by Doppler echocardiography are based on the principles of optimal LV diastolic filling or maximal cardiac output. The former principle can be achieved by the methods described by Ritter or Ishikawa.[42)43)] For either method, it aims at enforcing mitral valve closure to occur right after atrial filling is completed in order to reverse the aforementioned deleterious effect of prolonged AV interval. When a discernible completion of the A wave is got from the transmitral inflow at apical 4-chamber view by pulse Doppler echocardiography, Ritter's method[43] is preferred. It is based only on the programmed "long" and "short" AV intervals and their corresponding Q-A intervals (from the onset of QRS complex to the completion of A wave). The optimal AV interval is calculated as followed, where $Q\text{-}A_{long}$ represents for the Q-A interval at the programmed "long" AV interval and $Q\text{-}A_{short}$ for that at the "short" AV interval:

$$\text{Optimal AV interval} = \text{Short AV interval} + [(\text{Long AV interval} + Q\text{-}A_{long}) - (\text{Short AV interval} + Q\text{-}A_{short})]$$

In the situation where the A wave was too small or too noisy that its completion were not apparent, the AV interval can be optimized based on reiterative cardiac output method. Cardiac output is calculated by pulse Doppler echocardiography at the LV outflow tract by the continuity equation. Starting from 30ms, AV interval is programmed at incremental steps of 20ms until the ventricular sensing occurs. The AV interval with the largest cardiac output is regarded as the optimal one.

Optimization of interventricular interval (V-V interval) after CRT may further improve intraventricular asynchrony, although it has not effect on interventricular asynchrony.[45] However, this may further enhance systolic function and reduces mitral regurgitation. Currently, the reiterative cardiac output method is the most commonly used. As a number of V-V interval settings with LV or RV pre-excitation need to be programmed where cardiac output are measured, it is quite time consuming. It is recommended to optimize the AV interval before the V-V interval so that the AV synchrony in the LV will remain unchanged when different V-V intervals are tested.

Summary

Systolic asynchrony is common in heart failure patients, especially those with prolonged QRS complexes. It can be corrected by CRT, with demonstrated improvement of cardiac function, reverse remodeling and benefit in prognosis. Since QRS duration is not an accurate marker of systolic mechanical dyssynchrony and hence not a determinant of favorable responses after CRT, a number of new echocardiographic technologies have been studied and proven to be useful. Many indices have been succefully developed to assess systolic dyssynchrony, which helps to decode the mechanism of this promising therapy, differentiate and predict the clinical or echocardiographic responders, and select patients with significant pre-existing mechanical dyssynchrony to receive CRT. With evolving new techniques, improvement in image quality, acquisition capability, as well as speed and accuracy of offline analysis, assessment of systolic asynchrony by echocardiography has a good potential to be applied widely in CRT era. Therefore, more accurate identification of responders to CRT would be expected so as to reduce the number of non-responders and improve the cost effectiveness of the therapy.

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