THE POTENTIAL OF INTRA-OPERATIVE ECHOCARDIOGRAPHIC IMAGING DURING CARDIAC RESYNCHRONIZATION TREATMENT

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ABSTRACT

Cardiac resynchronization treatment (CRT) causes improvement in symptoms and reverse cardiac remodeling in patients with drug resistant congestive heart failure. Improvement of patient selection criteria by mechanical rather than electrical dyssynchrony has been proposed to decrease the number of non responders which may be as high as 50% when echocardiographic reverse remodeling is used as an improvement criterion. Use of echocardiography thus far has been limited to evaluation pre and post CRT. No imaging modality has been tested intra-operatively during device implantation to assist with selection of optimum site of lead implantation, to detect immediate effect of CRT on cardiac function and secondary parameters and for pacemaker optimization. This article evaluates current status and potential of imaging using echocardiography during CRT.

Key words: Echocardiography, cardiac resynchronization treatment, pacemaker optimization, mechanical dyssynchrony, intraoperative.

INTRODUCTION

Attempts are being made to improve the responder rate to cardiac resynchronization therapy (CRT) which is as high as 45-50% when echocardiographic reverse remodeling is used as the outcome criterion. These include assessment of mechanical dyssynchrony,[1,2,3] myocardial viability, site of the most delayed left ventricular (LV) segment, imaging of coronary sinus to determine its anatomy and that of its branches prior to CRT,[4] optimization of biventricular (biv) device post CRT,[5,6,7] and epicardial[8,9], lead placement instead of coronary sinus approach. Imaging during biv pacing treatment is an attractive option that can assist with several of these issues once the patient is selected for CRT. Echocardiography is particularly well suited for this purpose due to its portability and ability to perform online evaluation. While most of the evaluation stated above can be performed pre or post device implantation, practical constraints may sometimes not allow evaluation of mechanical asynchrony, scar or coronary sinus anatomy pre-procedurally such as patients referred from outside after having undergone diagnostic workup that may may not be available, supoptimal, incomplete or may not have evaluated asynchrony or coronary sinus anatomy. Repeat imaging pre procedure may be be feasible due to reimbursemet issues and imaging post procedure may not be feasible due to time constraints or lack of availability of appropriate skill.

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There are however no published studies that have evaluated the utility of echocardiography during cardiac resynchronization treatment (CRT). Logistic problems related to need for dedicated echo equipment, skilled echo-cardiographer and technical limitations of imaging in a supine patient along with lack of reimbursement are practical limitations that have precluded the use of echocardiography during CRT. This review will focus on the potential utility of echocardiography intraoperatively during CRT.

Transthoracic (TTE), transesophageal (TEE) as well as intra-cardiac echocardiography (ICE) can all be used during CRT. Echocardiography can provide technical assistance as well as provides specific anatomic and physiologic information.

Technical Assistance with Coronary Sinus Cannulation. All three echocardiographic modalities in particular TEE and ICE can assist with catheter navigation when there is failure of coronary sinus ostium cannulation. Figure 1 shows the views obtained by TEE showing the origin and the first few centimeters of coronary sinus. In fact TEE is used to guide and may replace fluoroscopy during coronary sinus venous cannula placement for minimally invasive and robotic heart surgeries.[10]

Specific Anatomic Information - *Presence and Extent of Myocardial Scar*

Echocardiography can assist with identification of location as well as the extent of myocardial scar and determine the site of maximum mechanical delay. Figure 2 shows parasternal long axis view in a patient with extensive posterior wall thinning and scarring which is identified by increased echogenicity and thinning. It is controversial whether left ventricular (LV) lead placement at the site of or adjoining an akinetic segment will reduce the efficacy of CRT. One study that evaluated the location of LV lead in vicinity or away from akinetic segment identified by TTE found that there was no difference in improvement in LV function whether or not LV lead site was placed at or adjoining an akinetic segment following CRT.[11] However what determined lack of improvement was actually whether the LV lead was placed in the posterior or lateral branch vs. anterior branch of coronary sinus. This study also did not find any difference in 12 month mortality or hospitalization for heart failure in groups with LV leads was in proximity or was away from an akinetic site. Other studies have suggested that presence of a transmural scar in the posterolateral wall despite presence of mechanical dyssynchrony is a predictor of poor response to CRT if the lead is placed at the posterolateral site.[12] Effect of lead placement away from this transmural scar has not been evaluated. Besides routine 2D echocardiography 2D speckled tracking can also assist with localization of presence and extent of myocardial scar.[13] In addition strain rate imaging by tissue Doppler imaging allows evaluation of infarct transmurality and presence of viable myocardium.[14]

Presence and Location of Mechanical Delay

ICE has now become a routine tool that is used during trans-septal punctures and for pulmonary vein ablations as well as evaluation of pulmonary vein ostia during electrophysiologic studies.[15] However the device can be used to get views of mitral, aortic and tricuspid valves as well as left and right ventricles. The device can be placed in the right artrium, right ventricle (RV) across the tricuspid valve in the right ventricular outflow tract to get views of both right and left ventricles in great anatomic detail[16] (Figure 3). The device also has the capability of doing color Doppler as well as color tissue Doppler from which M mode and PW tissue Doppler can be derived for assessment of mechanical dyssynchrony. A recent study found the utility of ICE for patients undergoing CRT in 21 patients.[17] These patients underwent ICE guided atrioventricular and VV optimization by evaluating LV ejection fraction from M-mode. The study found that LV ejection fraction improved from 23±8 to 40±13% following CRT and optimization. Optimal AV delay was determined to be 150 to 200mm which is significantly longer than the conventional setting of 100- 120 ms. In addition, 18 patients required LV excitation first, one patient required right ventricular (RV) excitation first and 2 patients required simultaneous LV and RV excitation. The 10 month New Heart Association Class reduced from 3.1±0.2 to 1.7±0.6 and there was 92% survival at one year. This suggests that sequential Bi V pacing and longer atrioventricular delay programming is often necessary to obtain maximum optimization with CRT.

There have been recent studies that have suggested that improvement in mechanical dyssynchrony occurs acutely following CRT and predicts long term response of LV remodeling following CRT.[18] A recent study found that in 100 patients with Class III and Class IV heart failure with classic indication for CRT, septolateral delay reduced substantially in those patients whose systolic volume reduced more than 10% at 6 months vs. those classified as non responders.[19] The fact that LV resynchronization following CRT is an acute phenomenon suggests that imaging can be used intra-operatively to detect whether or not significant reduction in dyssynchrony occurs after CRT is turned ON and also to help determine the optimal LV lead placement site as well as to determine reduction in intraventricular dyssynchrony with sequential biventricular (biv) pacing. Conventionally dyssynchrony is assessed by offline processing using velocity based criteria which do not lend themselves to be used in an acute setting during device implantation. There are however several online color based tissue Doppler modalities available which can provide visual assessment of dyssynchrony by color coding the myocardium. These include tissue synchronization imaging where the time depicting systolic velocity data is color coded and overlayed on the moving 2-D myocardium.[20,21] Segments that contract early are shown in green color and segments that contract late are depicted in yellow to red color. This assists in gross evaluation of maximally delayed sites. Figure 4 shows tissue synchronization imaging examples of patients with delay in the lateral wall and right ventricle (4A), inferior wall (4B), and the posterior wall (Figure 4C). In tissue tracking tissue Doppler mode, the myocardium is color coded based on the amount of longitudinal systolic displacement. In particular color code appearing in a segment in diastole but not in systole suggests delayed longitudinal contraction of that segment[22] Similarly strain imaging displays negative systolic strain in shades of pink and red and positive systolic screen as blue. Timing of contraction in these segments in response to RV, or biv pacing can be rapid evaluated intraprocedurally. Effect of RV lead placement in RV apex vs. mid septum vs. RV outflow tract on inter and intraventricular dyssynchrony can be assessed.[23] In addition effect of LV lead placement high or low within a coronary sinus branch or in multiple coronary sinus branches when available can be evaluated acutely.

Determining the Optimal Site of LV Lead Placement

The standard method is to place the LV in the LV mid lateral or posterior wall and avoid the medial vein as well as the very posterior and the anterior interventricular veins. However, small studies that have looked at placement of LV lead in concordance vs. discordant site have found that placement of LV lead in the most delayed LV segment results in better improvement in LV function and more negative remodeling compared to when there is a discordance between LV lead site placement and maximally delayed segment. In one study comprising of 31 patients with ischemic cardiomyopathy who underwent CRT by conventional criteria and clinically based parameters found that in the 13 patients in whom the lead was concordant there was better improvement in the LV function including LV end diastolic and end systolic volumes and LV ejection fraction, New York Heart Association Class and six minute hall walk. Of these 13 patients, one each of the maximally delayed segments had the LV lead placement in the corresponding anterior, lateral, posterior and inferior vein, whereas 3 with lateral segment delay had the LV lead placed in the posterior vein and 5 with the posterior segment delay had the LV lead placed in the lateral vein.[24] Another study looked at the effect of LV lead placement and the most delayed segment in 54 patients who were followed for six months. This study found that in all the seven patients whose delay was located in the anterior wall and anterior septum, there was no response to CRT. However in all these 7 patients LV lead was placed in the posterior or lateral veins. In the 22 patients in whom there was a concordance between LV lead site placement and maximally delayed segment there was a 73% response, in the 13 patients in whom the LV lead was placed one segment adjacent to the maximally delayed site there was a 54% response rate and when the LV lead site was remote to the most delayed segment there was only a 5% response rate.[25] A recent study of 47 patients who were followed for 10 months, evaluated 2D circumferential strain to determine the effect of concordance on LV function. Twenty eight patients had concordance and 19 patients had discordant lead placement. The magnitude of LV ejection fraction improvement was greater as well as reduction in volumes was greater in the concordant group. Similarly, the VO2 max was higher in the concordant group.[26] However, a closer look at these studies suggests that the majority of these studies had LV lead placement in the postero-lateral territory. It remains unclear whether similar magnitude of improvement on LV function would occur if the mechanical delay occurred at a non-conventional site, such as anterior wall, anterior septum or inferior wall, and the LV lead was placed in the corresponding branch such as anterior interventricular vein or medial vein.

Role of Echocardiography in Providing Physiologic Information During CRT

Effect of RV Pacing

Echocardiography can assist with immediate evaluation of the effect of RV pacing on LV function, dyssynchrony and mitral regurgitation in those patients who are undergoing RV dual chamber pacing for conduction reasons and who are expected to have RV pacing most of the time. In these patients, pacemaker upgrade to biv pacemaker can be performed in the cath lab if the effect of RV pacing on LV dyssynchrony, LV function and mitral regurgitation could be evaluated acutely. Figure 5 is an example of an 80 year old patient who had moderate to severe mitral regurgitation at baseline who required a RV pacing for complete heart block. Subsequent to this the patient's mitral regurgitation became torrential along with an increase in pulmonary artery pressure to 55mmHg. Lack of mitral lead coaptation was seen on echocardiography (Figure 5, panel C). Significant mechanical dyssynchrony was found during paced RV rhythm. Placement of a biv device resulted in decrease in mitral regurgitation and RV only pacing led to worsening in MR instantaneously. Optimization with LV pre-excitation led to further decrease in MR.

Effect of Biventricular Pacing

Echocardiography can also assist with evaluation of effect of bi-v pacing on mechanical dyssynchrony, diastolic filling, cardiac function and mitral regurgitation acutely. Thus, in patients in whom no significant improvement in these parameters occurs, a change in RV lead placement or of LV coronary sinus lead placement could be performed on line. Figure 6 gives an example of a patient showing tissue synchronization images at baseline which showed delay in the entire lateral wall, basal to mid lateral and posterior wall and anterior interventricular septum that improved instantaneously after the bi-v device is turned ON. This same patient had significant MR during native rhythm which is improved instantly after the biv device was turned ON (Figure 7).

Role of Echocardiography in Biventricular Pacemaker Device Optimization

AV Optimization

In addition to assessment of mechanical dyssynchrony, optimization of AV delay can be performed at the time of pacemaker implantation. While conventionally an intermediate AV delay provides a maximum diastolic filling without premature mitral valve closure, there is significant individual variability so that the AV delay can range from as low as 30msec to as high as 300msec (in author's experience). Figure 8 is an example of a patient who had diastolic mitral regurgitation at an AV delay of 200 and even at 120msec which is only abolished when the AV delay is shortened down to 80msec. Diastolic tricuspid regurgitation seen at a long AV delay also was abolished at an AV delay of 80 ms along with an improvement in peak pulmonary artery systolic pressure.

Sequential Biventricular Pacing, VV Optimization

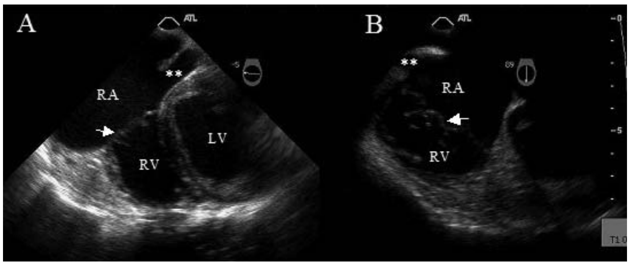
Online tissue synchronization imaging, tissue tracking and strain imaging can help evaluate mechanical delay during various LV and RV pre-excitation delays. Simple parameters such as septolateral delay and septoposterior wall delay by pulsed wave Doppler can be used to evaluate the effect of sequential ventricular excitation on mechanical dyssynchrony. Besides time delays, actual LV performance can be evaluated by strain imaging and peak negative systolic strain, maximum myocardial displacement, velocity times integral of LV outflow tract, myocardial performance index, mitral regurgitation severity, dp/dt from mitral regurgitation CW Doppler envelope and pulmonary vein flow profile. Figure 9 shows example of a patient who had RV and lateral wall delay at baseline which improved sequentially with increasing LV pre-excitation at 20 and 30msec.

Summary

Echocardiography can be used during biv implantation to locate the site of maximum mechanical delay, to evaluate the effect of RV pacing on dyssynchrony and MR, to evaluate the affect of biv pacing on mechanical dyssynchrony, cardiac performance and mitral regurgitation and to optimize AV and VV settings.

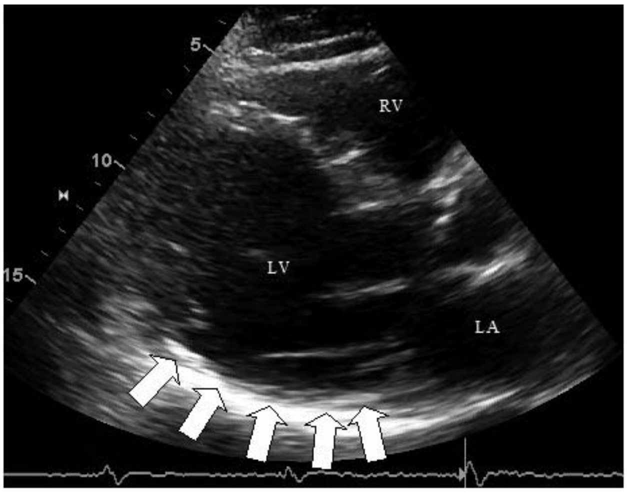
Figure Legends:

Figure 1. Low esophageal views at zero (A) and 90 degrees (B) showing right atrium, right ventricle, tricuspid valve (white arrow) and origin and proximal



part of coronary sinus (double asterisk). RA=right atrium, RV=right ventricle, LV=left ventricle.

Figure 2. Parasternal long axis view showing thin and echo dense basal to mid posterior myocardial segments (block arrows) due to a myocardial scar



from an old circumflex infarct. LA=left atrium, LV=left ventricle, RV=right ventricle.

Figure 3. View of left and right ventricles obtained by intracardiac echocardiography (ICE) in a swine model. ICE catheter was advanced from femoral vein into the right atrium, then across the tricuspid valve into the right ventricular outflow tract and main pulmonary artery. LA=left atrium, LV=left ventricle, RV=right ventricle

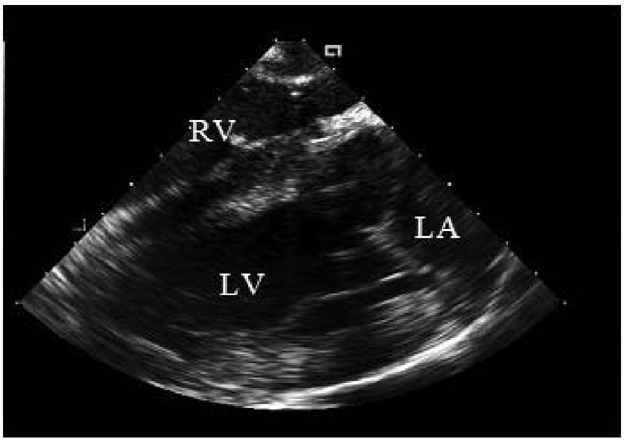
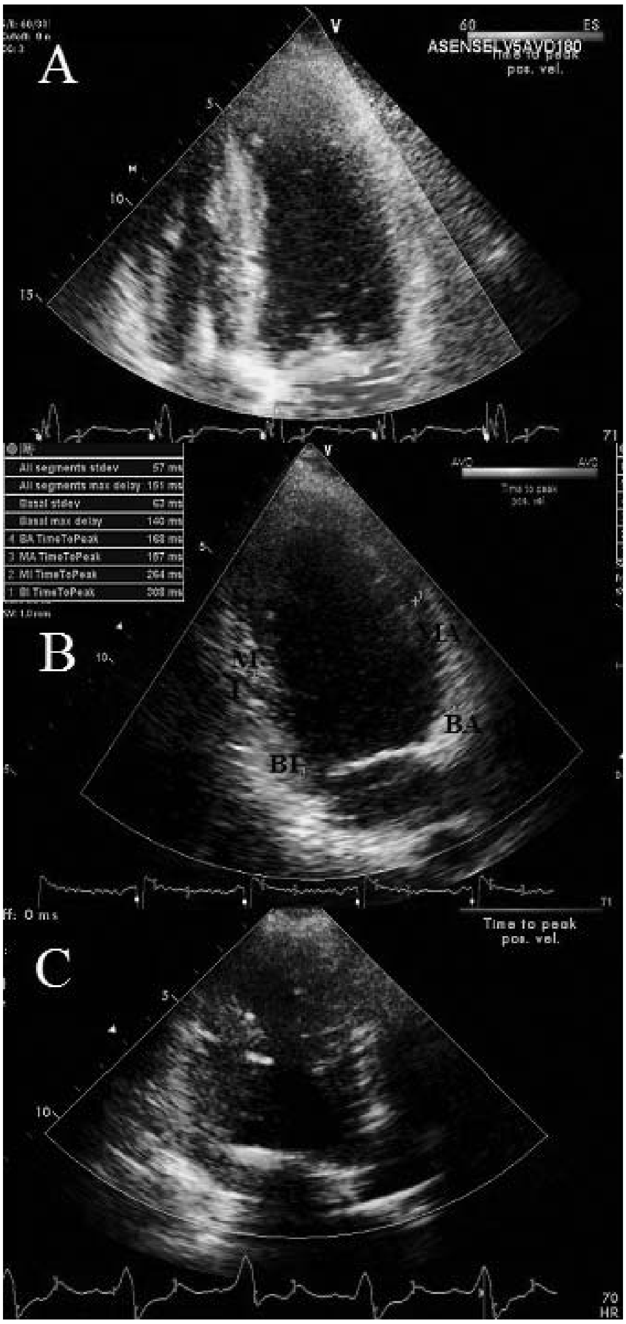


Figure 4. Tissue synchronization images in the apical 4 (A), 2 (B) and 3 (C) chamber views in a patient with dilated cardiomyopathy and congestive heart failure. Color bar denotes severity of delay in peak



contraction during ejection phase, recognized as time interval 80 ms after aortic valve opening and closure. In TSI, normal myocardium is coded in green. Presence of mechanical contraction delay is coded in progressive sequence of green, yellow, orange, and red colors. Moderate delay in present in the entire lateral wall and right ventricular free wall (A), moderate to severe delay in the basal (308 ms) and moderate delay in the mid inferior wall (264 ms) (B) and moderate delay is present in the posterior wall (C). ECG appears different due to display of different leads on the ultrasound screen during image acquistion.

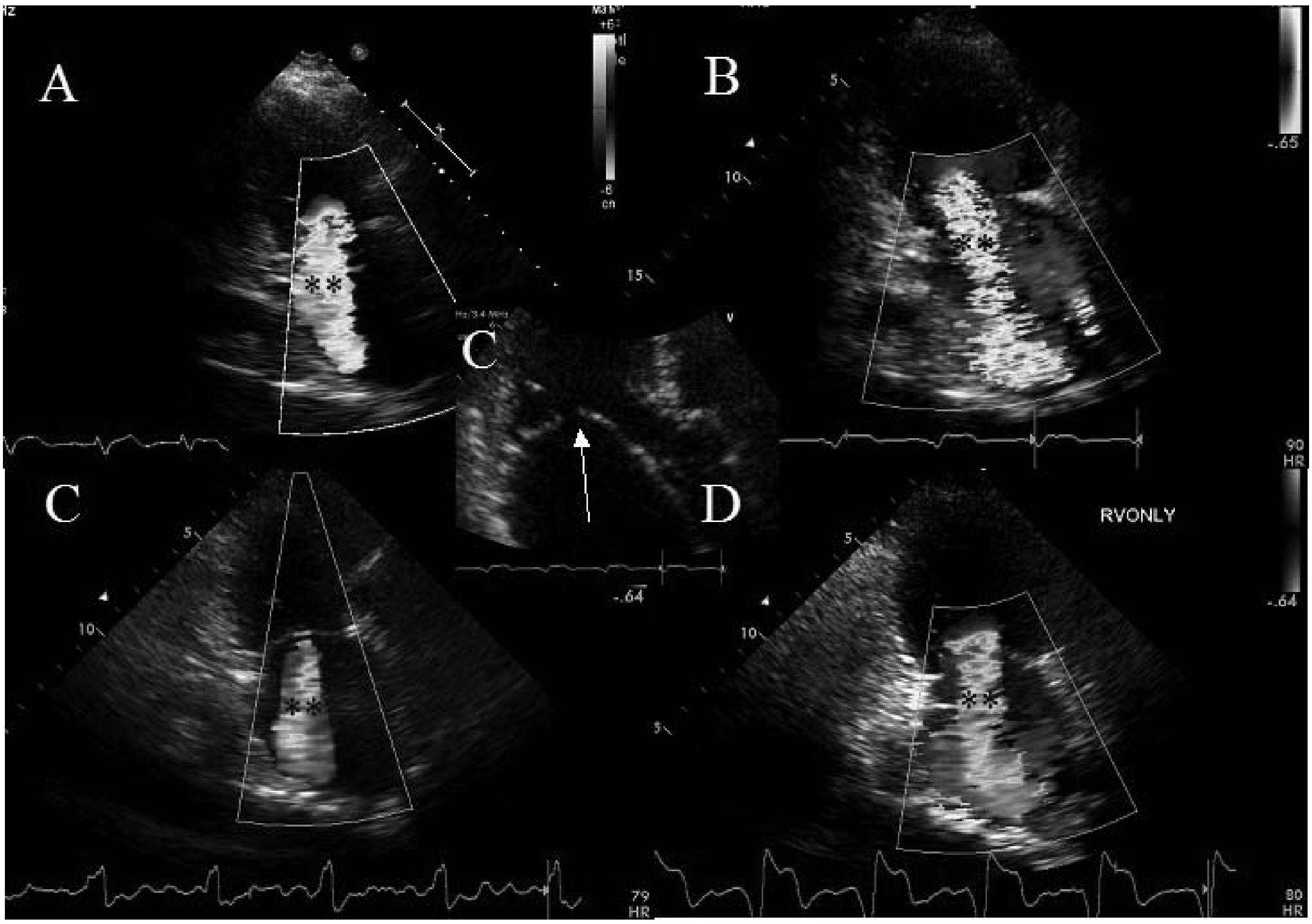


Figure 5. Mitral regurgitation (double black asterisks) in the apical 2 chamber view in an 80 year old female who had moderate to severe mitral regurgitation (A) who required right ventricular pacing for complete heart block. Image B was obtained a month later when patient presented with congestive heart failure. Mitral regurgitation is now severe. This was associated with pulmonary artery pressure of 55mmHg (not shown). Lack of mitral lead coaptation is shown in panel C (white arrow). Panel D was obtained 1 week after the patient underwent an upgrade to a biv pacemaker. Marked reduction in MR is shown compared to both A and B. During pacemaker optimization RV only pacing led to worsening of MR in the severe range (D). This case example illustrates that acute changes in MR can be seen during device placement and RV and biv pacing.

Figure 6. Panels A, B and C show tissue synchronization images in the apical 4 (A), 2 (B) and 3 chamber (C) views during native rhythm and panels D-F are corresponding views obtained immediately after biv pacing was turned ON in a 67 year old male with non-ischemic cardiomyopathy.. Note immediate improvement in lateral, basal to mid anterior, basal to mid inferior, basal to posterior and basal anterior interventricular septal segments with biv pacing. This example illustrates that correction of mechanical

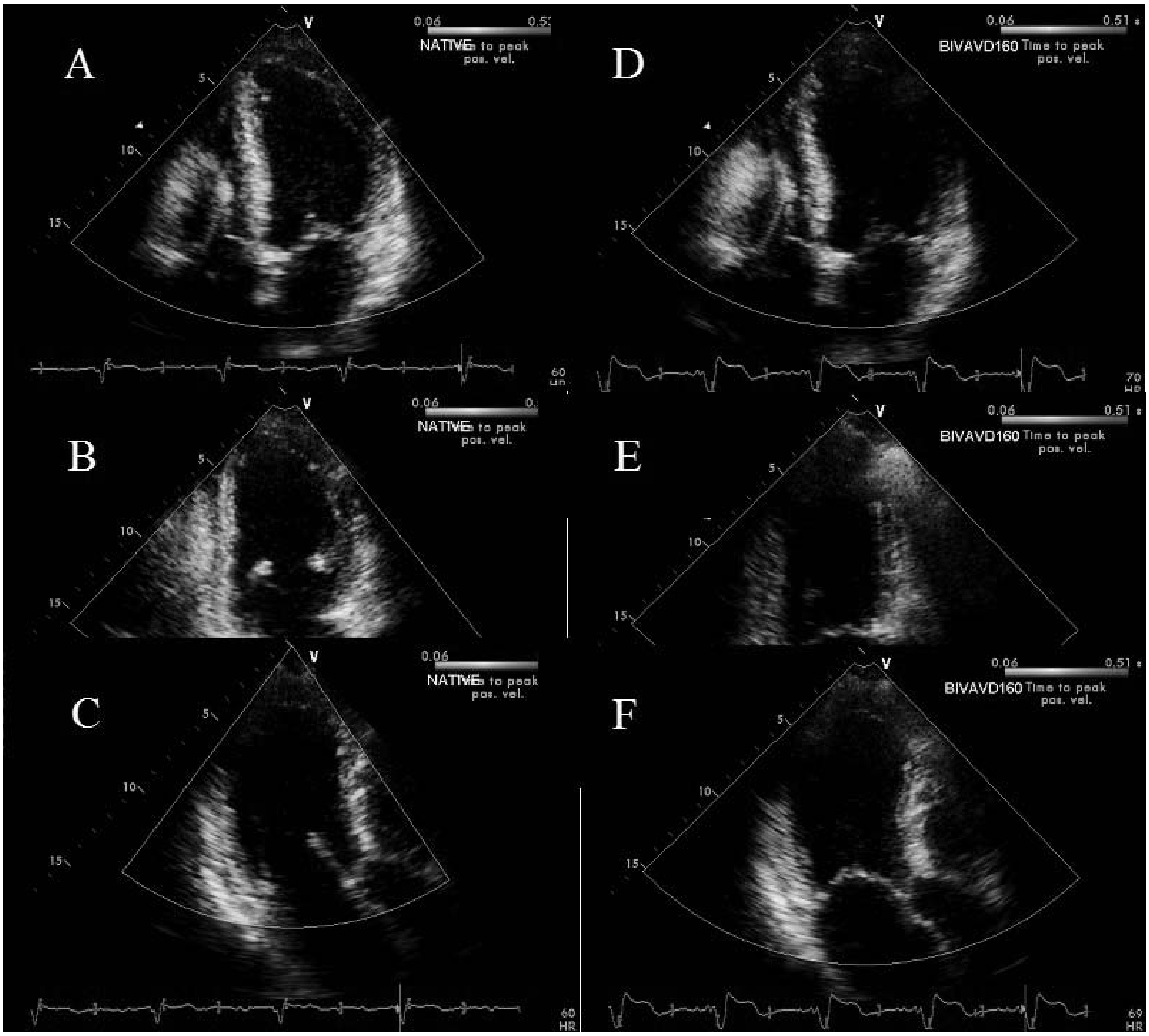


Figure 7. Color Doppler obtained in the same patient as in Figure 6 showing acute effect of biv pacing on mitral regurgitation. A was obtained during native rhythm showing moderate mitral regurgitation. MR reduces to mild immediately after biv pacing is turned ON.

dyssynchrony after CRT is an acute phenomenon which can help during CRT device placement to determine the benefit of CRT and also help select the appropriate site of RV and LV pacing.

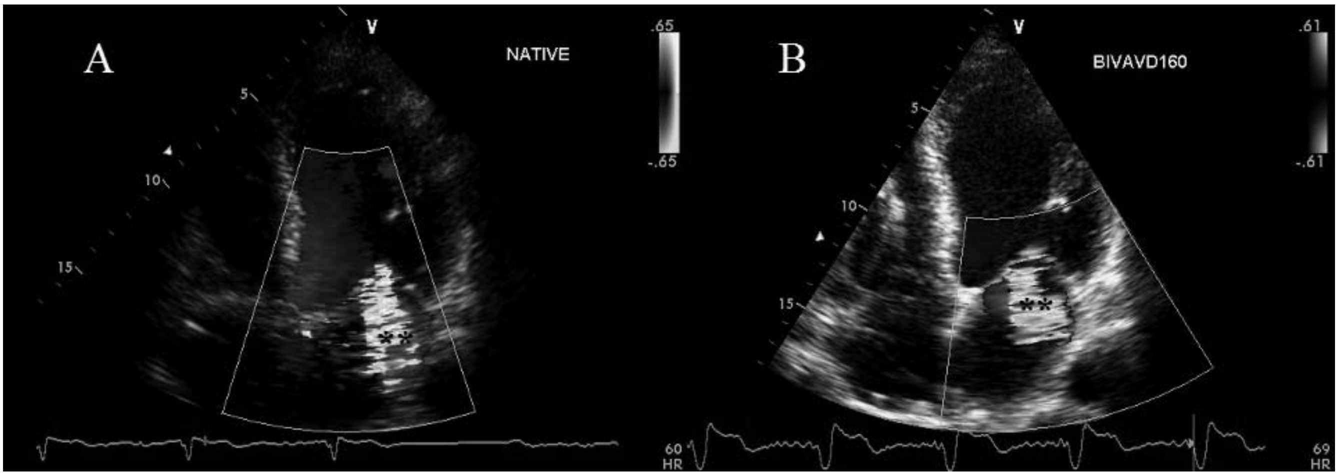
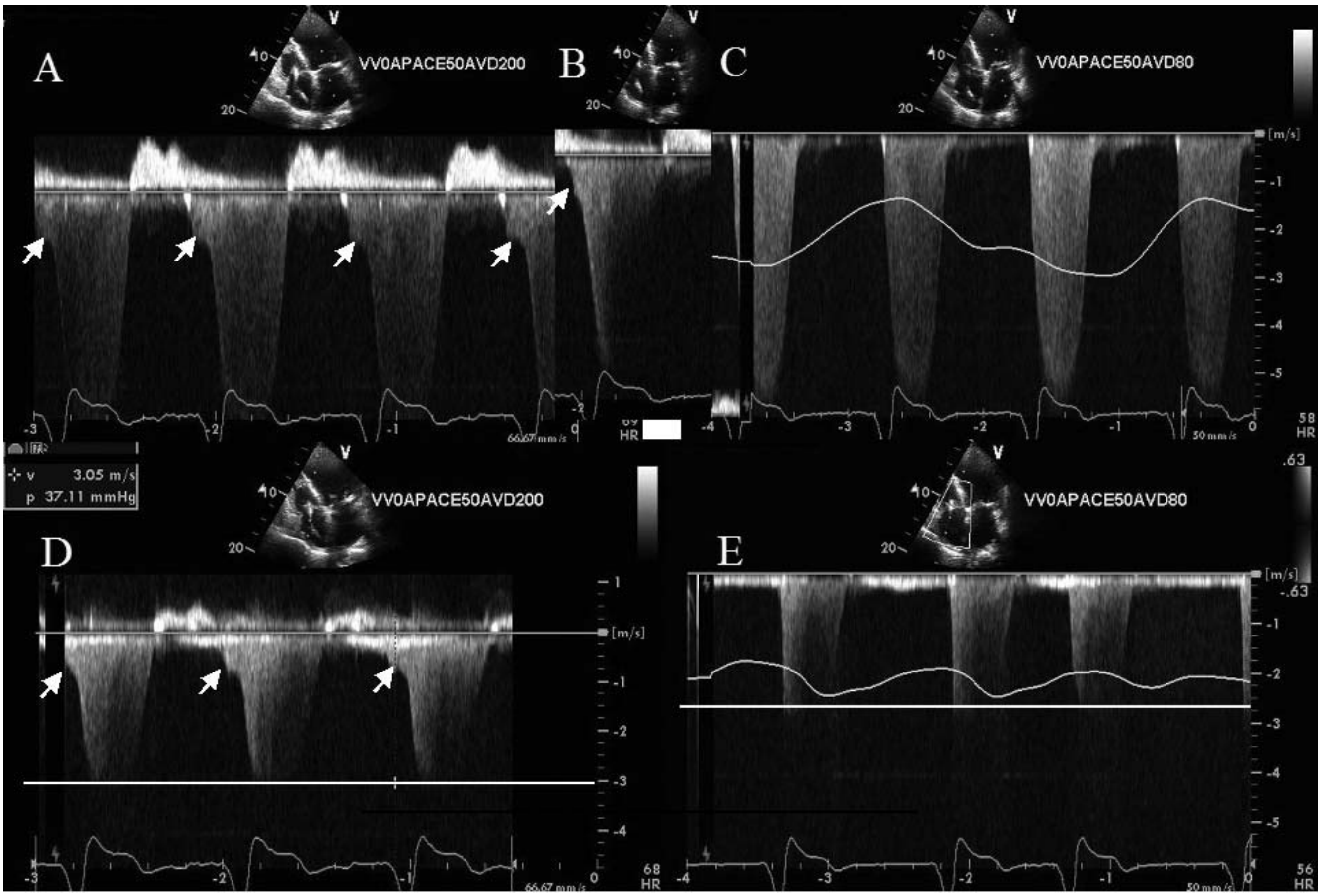


Figure 8. Mitral inflow continuous wave Doppler in a 93 year old Caucasian female showing diastolic mitral regurgitation (white arrows – A) at long AV delays of 200 (A). Diastolic MR persists at an AVD of 120 ms (white arrow - B) and only abolished at an AVD of 80 ms (C). D shows tricuspid regurgitation CW Doppler in the same patient showing diastolic tricuspid regurgitation (white arrows - D) at a long AV delay of 200 which is abolished at an AV delay of 80 ms (E). There is concomitant reduction in right atrial-RV gradient from 36 mm Hg (A) to 25 mm Hg (B). Left ventricular outflow tract PW Doppler showing reduced ejection duration at an AV delay of 200 ms (C) which improved at an AV delay of 80 ms (D). Green tracing in the middle of panels in C and E represent the respirogram.



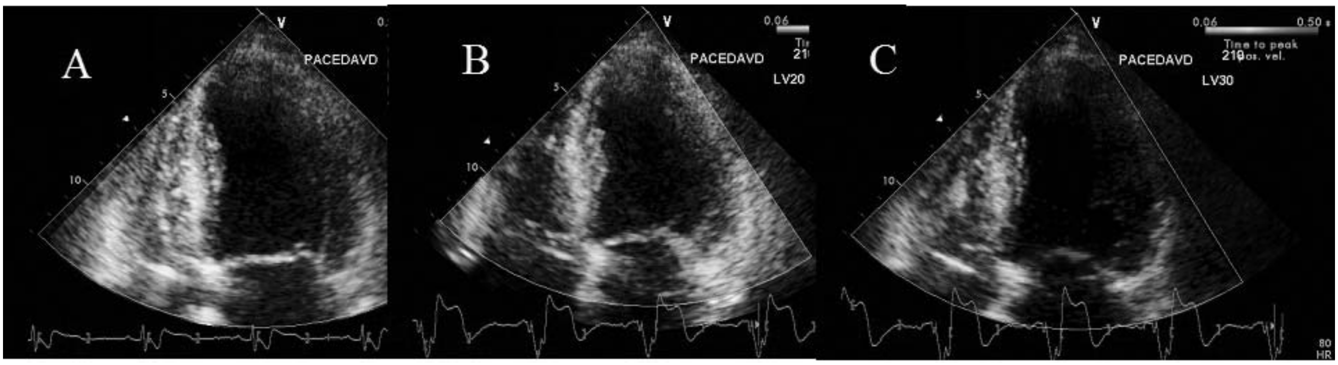


Figure 9. Tissue synchronization images in the four chamber view showing moderate delay in systolic displacement at the basal and mid lateral wall, basal interventricular septum and right ventricular free wall during simultaneous left and right ventricular pre-excitation (A). Normalization in right ventricular and septal delay as well as a marked improvement in basal to mid lateral wall delay is noted at LV pre-excitation of 20 ms (B). LV pre-excitation of 30 ms results in normalization of all left and right myocardial segmental displacement (C). This example illustrates that optimization of interventricular delays can be performed acutely during device placement.

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