The basic criteria for cardiac resynchronization therapy (CRT) is a patient who has refractory congestive heart failure with a left ventricular ejection fraction (EF) < 30%, a markedly dilated left ventricle, left bundle branch block with a QRS duration > 130 ms and continued symptoms despite maximally tolerated pharmacologic therapy. These are complex and expensive systems to implant in a group of patients who are very ill. As such, it has been a frustration to everyone when the therapy is ineffective. Based on published studies, the incidence of non-responders is in the range of 20-30%. There is an ongoing quest to determine who is likely to respond and who will not respond to CRT prior to implantation of the system. The initial screening criterion is a very wide QRS complex (usually left bundle branch block) based on the reasoning that a disordered electrical activation sequence will result in a disordered ventricular contraction pattern. Indeed, the objective of CRT is to restore synchronous mechanical contraction of the left ventricle using stimulation therapy.

Although LBBB has been used as an initial screening requirement, this is the group with a 20-30% non-responder rate presuming that the LV lead can be successfully positioned. As such, investigators have been looking for another marker that will separate responders from non-responders with the eventual goal of not subjecting a patient who is unlikely to respond to the implant procedure. A variety of complex technologies have been proposed, the basic limitation to general application being that these techniques are not generally available except in unique referral centers.

Pitzalis and coworkers in an initial paper in 2002 with a follow-up study published in 2005 have shown that a specific echocardiographic measurement associated with the “standard” 2D-echocardiogram and can be readily performed in virtually
every cardiology department and most cardiologists’ offices if they have an
echo machine is a superb discriminator. One of the standard echocardiographic
measurements is Left Ventricular End-Systolic and End-Diastolic diameter.
These are measured with the echo-beam aimed just below the mitral valve as
shown in the picture below:

Pitzalis and coworkers looked at all standard echocardiographic measurements
in addition to some that have been proposed to be specific and helpful in CRT
patients. These included:

- **Left Ventricular Electrical Mechanical Delay (LVEMD)** which is the
  interval from the onset of the QRS complex to the opening of the aortic
  valve and the start of effective forward ejection
- **Interventricular delay (IVD)** which is the difference between LVEMD
  and a similar measurement on the right side (RVEMD) with respect to
  pulmonary valve opening
- **LV Septal to posterior Wall Motion Delay (SPWMD)** measuring the
  delay between peak septal contraction of the posterior wall of the left
  ventricle.

Regardless of the pre-implant measurements, all patients received a CRT
system and then were followed with repeat testing at 6 month and correlating
the results of the echocardiographic study with the 6 minute walk test, NY Heart
Association Functional Classification, Quality of Life and other measurements.
In the authors’ initial study published in 2002, there were 21 patients of whom
17 received a CRT-P system and 4 received a CRT-D system. This first study
utilized Guidant and Medtronic devices. The second study included 72 patients of whom 65 provided data for the study because of either inability to implant the LV lead or poor echocardiographic image quality.
Of all the various measurements, the authors found that the SPWMD (septal posterior wall motion delay) proved to be highly specific and sensitive.

If the SPWMD was greater than or equal to 130 ms, there was a significant benefit of CRT and subsequent ventricular remodeling. Indeed, the wider the SPWMD, the greater the apparent benefit of CRT. If the SPWMD was less than 130 ms, there was a poor response with a very high incidence of continuing severe CHF.

The baseline QRS duration significantly correlated ONLY with SPWMD ($r = 0.62, p<0.01$) while LVEMD and IVD did not correlate with QRS duration. There was also a statically significant and positive correlation between baseline QRS and SPWMD and reverse remodeling – the wider the QRS and the wider SPWMD, the greater degree of improvement with CRT. Another interesting observation was that patients with a longer PR interval (onset of the P wave to onset of the QRS duration) had a better response. In the first study involving 25
patients all of whom had “standard” implant indications, 12 were responders and these 12 had the longer PR interval and SPWMD. All of the responders had a baseline SPWMD > 130 ms, a QRS duration > 150 ms and PR interval > 180 ms. Using these cut-off values, the specificity of SPWMD was 63% with a positive predictive value of 80% and an accuracy of 85%. The specificity of both the QRS duration and PR interval was 13% with a positive predictive value of 63% and an accuracy of 65%. In the follow-up study published in 2005, effectively involving 65 patients, the mean follow-up was 14 months during which 4 patients died of progressive CHF and 12 were hospitalized. At the 6 month post-implant measurements, improvement in EF was evident in 22 of 28 patients with SPWMD > 130 ms and in only 2 of 23 patients with a SPWMD < 130 ms (p < 0.0001). There was also a significant linear correlation between SPWMD and EF improvement (r = 0.69, p < 0.001). NYHA functional class improved at least 1 grade in 22 of the 28 patients with SPWMD > 130 ms and in only 9 of 23 patients with SPWMD < 130 ms.

Septal to posterior Wall Motion Delay is an easy measurement to obtain. It only requires a standard 2D echo obtained in a standard view that can be effectively performed by virtually any echo lab. As valuable as this measurement appears to be, there were clearly responders among patients with the SPWMD < 130 ms and non-responders in the group with SPWMD > 130 ms. The major criticism of this and similar studies is that the echo study identifies two focal points within the heart and compares the relative contraction between these two points. Perhaps there may be a significant delay between two different portions of the LV wall and if those respective sites could be stimulated, either intentionally or inadvertently, there will be a good response; even though this specific measurement (SPWMD) would predict a lack of response. By the same token, with respect to the non-responders in those who had a SPWMD > 130 ms, the authors did not attempt to correlate actual lead location with these results. Not all of the leads could be placed on the posterior or lateral wall. A practical reality of CRT therapy is that one does not have total control over where the lead will be placed – this depends on venous anatomy as well as LV and phrenic nerve capture thresholds. The LV sensing threshold, while important, is not a practical issue with many systems where sensing is limited to the RV signal. An inability to pace from a particular location or induction of phrenic nerve stimulation means that the lead cannot be left in that position and must be moved. Adjustments in V-V timing, based on other studies, suggests that this might be able to compensate for the LV lead not being located at the site of latest LV contraction but its impact on the response to CRT has not been correlated with the SPWMD measurement. In this particular series of studies, the V-V interval was effectively simultaneous. Initially, this was a limitation of the available devices while in the second studies, devices were utilized that allowed V-V
timing but to maintain consistency, this parameter was kept as simultaneous. It is not known whether these investigators are looking at the impact of V-V timing on the responders (to further improve the results) or non-responders and its impact on SPWMD. Perhaps this will be reported in a future paper.

W long-term improvement in post-CRT clinical outcomes in patients with severe HF and LBBB" and they have “proposed (this) as a method of screening candidate patients,” it is not perfect. There are patients with a short SPWMD who respond and those with a long SPWMD who do not respond. Given that CRT is only indicated (based on current criteria) for patients with pharmacologically refractory CHF with continued symptomatic (NYHA Functional Class III, IV) with a marked LBBB and a dilated LV (left ventricular end-diastolic diameter of 55 mm), there are not a lot of options for these patients. Hence, while each of these patients will have had an echocardiogram and one can specifically look at SPWMD, I would use this data in a manner that was not proposed by the authors. IF this measurement shows a significant delay (> 130 ms), attempts should be made to place the CS lead on the posterior or postero-lateral wall. If that attempt is NOT successful, either abandon the approach and proceed with placement of an epicardial lead via thoracotomy (this may mean that the full implant procedure will be need to be completed at a second procedure) or use another imaging technique, perhaps radionuclide studies that can provide a more global view of the heart, to identify the area of latest contraction. Then, based on that other study, attempt to place the transvenous LV epicardial (coronary sinus) lead in the area of latest contraction. By the same token, the RV lead should not necessarily be placed in the RV apex (this was the standard RV lead position in the two studies by Pitzalis and colleagues) but in the area of the RV septum with the earliest contraction with respect to the LV site with the latest contraction.

Indexing Terms:
Cardiac Resynchronization Therapy
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