Assessment of ventricular dyssynchrony: global or regional function?

John E. Sanderson*

Department of Cardiology, University Hospital of North Staffordshire NHS Trust, Keele University Medical School, City General Hospital, Stoke-on-Trent ST4 6QG, UK

This editorial refers to 'Comparison of segmental and global markers of dyssynchrony in predicting clinical response to cardiac resynchronization'† by A.M. Duncan et al., on page 2426.

A common cliche states that if you stand still every 10 years, you will find yourself in the forefront of fashion. Thus it seems with the analysis of ventricular function. It has been recognized for many years that incoordinate or non-uniform contraction reduces global left ventricular (LV) function. Wiggers demonstrated in 1922 that stimulation from a ventricular focus rather than supraventricular produced a reduced pulse pressure, prolonged isometric contraction, and systolic ejection time in normal hearts. Although regional wall motion abnormalities were recognized early in ischaemic heart disease, it was also demonstrated later that it occurs in dilated or hypertrophic cardiomyopathy. However, the realization that asynchronous wall motion due to delayed activation such as in the presence of a left bundle branch block profoundly affected global function did not take place until more recently. Developments in cardiac imaging have allowed us to appreciate how common delayed activation and dyssynchronous mechanical contraction are and the degree to which they affect overall ventricular efficiency. Even in the normal heart, there is some degree of dyssynchrony; and the normal QRS duration reduces with sympathetic stimulation, implying greater synchrony so that some of the improvement in 'contractility' is actually due to a reduction in asynchrony. In the original studies on contractility, the possibility of incoordination was never considered. In disease states, asynchronous activation has marked deleterious effects on ventricular pump function due to both inter- and intra-ventricular asynchrony, leading to prolonged contraction, reduced ejection time, delayed and prolonged relaxation, and reduced diastolic filling time. Lack of coordination between the two papillary muscles also creates mitral regurgitation, and the overall result is LV remodelling with increasing ventricular cavity volumes and a shape change. Much of this can be reversed by biventricular or LV pacing [cardiac resynchronization therapy (CRT)].

The success of CRT has given great impetus to the assessment of ventricular asynchrony because it is clear that although CRT is highly effective therapy for the majority, it is not so for all patients. Therefore, it has become apparent that an 'index' of dyssynchrony is required on the assumption that this will improve patient selection and hence the outcome of CRT. Traditionally, QRS duration has been assumed to be a marker of delayed activation, and some concordance between it and impaired systolic and diastolic function has been found in some studies but not others. These inconsistent results probably reflect the fact that QRS duration is not related to the sequence of activation, nor the amount of myocardium that is affected by late activation. However, tissue Doppler imaging (TDI) has emerged as the most promising tool for detecting and more precisely quantifying the degree of intra- and inter-ventricular dyssynchrony. The standard deviation of the time to peak systolic contraction in 12 segments (Ts-SD12) obtained from three different axes from the apex, i.e. the longitudinal axis, has proved to be a robust measure of dyssynchrony. Several studies have shown that using a 6- or even better a 12-segment model can detect dyssynchrony, which can predict whether reverse remodelling of the ventricle will occur after CRT. Reverse remodelling is probably the best functional endpoint in heart failure and relates to mortality. Therefore, Ts-SD can be used to predict potential responders from non-responders. The advantage of TDI is excellent temporal resolution, but not all segments can be assessed accurately, particularly the apical segments, whereas MRI can image the entire heart from any axis. Dyssynchrony can be detected using MRI, and preliminary studies have found that when multiple segments (up to 60) are utilized, some degree of LV dyssynchrony is observed in all heart failure patients with either narrow or wide QRS complexes (F. Leyva, personal communication).

Duncan et al. from London take us back to a simple global measurement—the total isovolumic time (t-IVT). The t-IVT is essentially the time when the heart is neither ejecting nor filling. It is the combination of the isovolumic contraction and the isovolumic relaxation times, and it...
can be measured relatively easily by Doppler echocardiography and is derived as [60 – (total ejection time + total filling time)]. It is an interesting concept, as the percentage of wasted time when the heart is neither pumping nor filling during one cycle reflects the overall efficiency of the ventricle. To some, this may sound familiar to the Tei index, but the same group has demonstrated previously that although it also reflects abnormal activation, it appeared to be less sensitive than t-IVT, and the addition of the ejection time does not provide any additional discrimination. In the current study, a prolonged t-IVT was found more frequently in clinical responders than in non-responders after CRT, as was the difference between LV and RV pre-ejection periods (D-PEP). These two measurements were compared to TDI-derived time to onset and time to peak systolic contraction. Although in a univariate analysis both global and segmental indices could predict responders from non-responders, in a multivariable model only baseline values of cardiac output, t-IVT, and D-PEP remained. Combining t-IVT and D-PEP demonstrated almost complete separation between responders and non-responders. Of course, this study can be criticized for being retrospective, using only three basal segments for the TDI analysis, and pulse wave tissue Doppler rather than simultaneous colour TDI. Interestingly, in every non-responders, CRT produced further prolongation of t-IVT and D-PEP and worsened the segmental or regional measures of dyssynchrony, confirming that in some cases, CRT can induce dyssynchrony.

Which index, if any, is the cardiologist to use? Probably a combination of segmental and global would provide the best information on the degree and severity of mechanical dysynchrony and its consequences on global ventricular function. These indices are not mutually exclusive. It is useful to know where exactly the delayed segments are, especially if epicardial lead placement is being considered and to confirm that mechanical dyssynchrony is indeed the cause of the reduction in global LV function. However, it is right to use any mechanical index to decide on whether a patient should have CRT? The criteria used in the major trials such as CARE-HF were symptoms (NYHA class III/IV), LVEF <35%, a QRS duration >150 ms, and echocardiographic criteria for dysynchrony in only those with a QRS duration from 120 to 149 ms (two of three of the following: aortic pre-ejection delay >140 ms, an inter-ventricular mechanical delay of >40 ms, or delayed activation of the posterolateral LV wall defined as maximal posterolateral wall inward movement using M-mode or TDI occurring later than the start of LV filling using the transmitral Doppler flow signal). This view was endorsed in a recent review by Hawkins et al., who concluded that echocardiographic assessment was not necessary, that all patients should be considered for CRT if they meet the criteria used in the major clinical trials, and that indices of dyssynchrony will only become credible and applicable after they have been shown to be predictive in large prospective randomized trials. It is true that there are a number of other reasons for non-responders, such as lead position, poor thresholds, non-viable or infarcted myocardium in the lateral wall, and inadequate device optimization. However, the conclusion that only QRS duration should be used and that it is not essential to undertake any assessment of mechanical dyssynchrony flies in the face of the available evidence.

It is established that QRS duration correlates poorly with mechanical dyssynchrony and CRT can induce dyssynchrony in those without it with deleterious effects, and at least 25–30% of patients implanted with CRT devices do not clinically improve and typically these do not have evidence of significant mechanical dyssynchrony. For a comparison witness the recent awareness of the deleterious impact of apical RV pacing in a subset of a population where large clinical trials previously had demonstrated a definitive mortality benefit. There seems little doubt that selection of patients for CRT can be improved and to-date some index of dyssynchrony, whether this is a global measure or a segmental analysis of delayed activation or preferably both, would appear to be potentially useful. Although not perfect, the PROSPECT trial will provide some further evidence to support or refute this approach, although it is also clear that eventually a larger scale prospective trial will have to be done.

Conflict of interest: none declared.

References