Systolic and Diastolic Ventricular Dyssynchrony in Systolic and Diastolic Heart Failure*

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In 1952 Carl J. Wiggers gave the Henry Jackson Memorial Lecture before the Massachusetts Heart Association in which he reviewed his work over the previous 30 years (1). By analyzing ventricular pressure pulses, he demonstrated alterations in ventricular contraction patterns produced by pericardial effusion, hypervolemia, oligemia, arterial hypertension, aortic and pulmonary stenosis, idioventricular rhythms, ventricular alternation, coronary occlusion, myocardial ischemia, aortic regurgitation, and mitral insufficiency — a fairly comprehensive life's work by any standard. One of his early observations in 1922 was that stimulation from a ventricular focus rather than supraventricular produced a reduced pulse pressure, prolongation of both isometric contraction and systolic ejection time in normal hearts. However, after this, the effects of abnormal activation were relatively neglected, and the deleterious action of inco-ordination on myocardial contractility was not considered in the early studies on ventricular function. The full realization of the impact of a dysynchronous ventricular contraction such as produced by a left bundle branch block on global left ventricular (LV) function had to await the development of the newer imaging techniques (2).

Recently, using magnetic resonance imaging, it has been discovered that dyssynchrony can occur to some extent even in the normal heart (3). In heart disease, it is now clear that asynchronous activation, both intra- and inter-ventricular, has marked adverse consequence on ventricular pump function leading to prolonged contraction, reduced ejection time, delayed and prolonged relaxation, reduced diastolic filling time, and mitral regurgitation (4). The overall result is LV remodeling with increasing ventricular cavity volumes and a shape change (5). Most of these deleterious effects can be improved by biventricular or LV pacing or cardiac resynchronization therapy (CRT), and, indeed, the clinical success of CRT attests to the importance of dyssynchrony in the pathophysiology of heart failure (5,6). However, all these studies have been in heart failure patients with a low LV ejection fraction (LVEF) or systolic heart failure (SHF), and there is little data on whether dyssynchrony is a factor in that relatively common group of patients with heart failure and a normal ejection fraction (HFNEF or diastolic heart failure [DHF]). De Sutter et al. (7) found that, in 60 patients with heart failure and an LVEF >40% (a figure at the low end for DHF diagnosis), the prevalence of systolic intraventricular dyssynchrony by pulse-wave tissue Doppler velocity imaging was 18% compared with 36% in those with a low LVEF (7). However, in those with HFNEF and a QRS duration >120 ms, the prevalence of intraventricular dyssynchrony in systole was the same in both SHF and DHF (45%).

Now, in this issue of the Journal, we have 2 further publications on the same topic that have assessed the degree of ventricular dyssynchrony in both systole and diastole in HFNEF/DHF patient cohorts with interesting results (8,9).

Wang et al. (8) from Dr. Nagueh’s group compared 60 patients with DHF (LVEF >50%), 60 with SHF, and 35 control subjects. The LV intraventricular delay was calculated as the max time difference between 4 basal segments of the time to either peak or onset of the systolic myocardial velocity for systolic dyssynchrony, whereas only time to onset of the peak early diastolic velocity was used for diastolic dyssynchrony. Apparently, whether time to onset or peak systolic velocity was used, the same number of patients with dyssynchrony was identified (the normal range was derived from the control group, which was small). In those with DHF, 58% had evidence of dyssynchrony in diastole and, surprisingly, 33% also in systole. These results were very similar to those with SHF (60% with diastolic dyssynchrony and 40% with dyssynchrony during systole). In the second paper, by Yu et al. (9) from Hong Kong, the prevalence of diastolic and systolic dyssynchrony was similar in 92 patients with DHF (56% and 39%, respectively). However, they found much higher levels of dyssynchrony in the SHF group in both systole (57%) and diastole (43%) perhaps reflecting the larger numbers (n = 281) and the technique used to measure dyssynchrony. Yu et al. (9) used their established technique of SD of time to peak systolic and early diastolic velocities derived from a 6-basal and 6-mid-segmental model (i.e., 12 segments that increase the likelihood of detecting dyssynchrony) (10). Interestingly, 25% of the DHF patients had isolated systolic dyssynchrony, and the relationship between systolic and diastolic dyssynchrony was poor. This is in contrast to the tight curvilinear relationship between the absolute peak systolic and early diastolic veloc-

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LVEFs (11,17). As pointed out by Brutsaert and Sys (18), systolic and diastolic velocities across a wide range of dyssynchrony in systole and early diastole, which is surprising to have worse diastolic function although Yu et al. found that those DHF patients with systolic dyssynchrony as diabetes, hypertension, and LV hypertrophy (20–22).

In addition, incoordinate systolic contraction will prolong previous systole, which is the driver for ventricular suction. Diastolic filling is the strength and coordination of the part of a continuous cycle. The major determinant of early diastolic function in many of the precursor conditions to DHF such as diabetes, hypertension, and LV hypertrophy (20–22). Tissue Doppler velocity imaging and strain imaging isovolumic relaxation and further impair diastolic function.

DHF. Systolic dyssynchrony in DHF was associated with poorer long-axis function (reduced peak basal myocardial velocities), lower stroke work, and even lower ejection fraction (although still within the “normal” range) than in those without dyssynchrony (8). This suggests that systolic dyssynchrony in DHF is part of a wider abnormality of systolic function in DHF. This observation is relevant to the ongoing debate about the role of systolic dysfunction in DHF. The orthodox view is that in DHF systolic function is completely normal (12).

However, in an early study, Yip et al. (13) showed that both peak annular systolic and peak early diastolic velocities and the respective excursions that are measures of ventricular long-axis function were reduced in HFNEF compared with that in age-matched controls. These findings have now been confirmed in 6 other studies (14). That systolic function is not entirely normal is perhaps expected as systole will be affected as much as diastole by the LV hypertrophy and the accompanying fibrosis due to hypertension, which is the most common etiologic risk factor for DHF (15). Shan et al. (16) showed that both peak annular systolic velocity and the early diastolic velocity are equally affected by interstitial fibrosis within the myocardium. Wang et al. (8) found that those DHF patients with systolic dyssynchrony tended to have worse diastolic function although Yu et al. (9) did not find a close relationship between the degree of dyssynchrony in systole and early diastole, which is surprising because physiologically systole and diastole are closely intertwined. There is a close relationship between annular systolic and diastolic velocities across a wide range of LVEFs (11,17). As pointed out by Brutsaert and Sys (18) many years ago, ventricular relaxation and contraction are part of a continuous cycle. The major determinant of early diastolic filling is the strength and coordination of the previous systole, which is the driver for ventricular suction. In addition, incoordinate systolic contraction will prolong isovolumic relaxation and further impair diastolic function (19). Tissue Doppler velocity imaging and strain imaging have demonstrated the presence of subclinical systolic dysfunction in many of the precursor conditions to DHF such as diabetes, hypertension, and LV hypertrophy (20–22). Even in hypertrophic cardiomyopathy, considered an example of isolated diastolic dysfunction, strain rate imaging has confirmed the presence of subclinical systolic dysfunction despite a normal ejection fraction (23). The demonstration of both systolic and diastolic dyssynchrony in DHF in these 2 studies adds further evidence that systolic function is not entirely normal in DHF as claimed. Thus, the term DHF is a misnomer; HFNEF is a more accurate description that does not imply a purely diastolic abnormality (14). Ultimately, the whole concept of dividing heart failure into 2 groups based on the ejection fraction, which is a continuously distributed variable in heart failure populations, seems to make less sense as more evidence accumulates for systolic abnormalities in those with a supposedly normal systolic function as defined by the LVEF. What really separates the 2 phenotypes of SHF and DHF is the degree of ventricular remodeling, and measuring volumes would be more useful than ejection fraction (14).

Could CRT have a role in DHF, or is medical therapy alone beneficial? Some evidence for a favorable effect of medical therapy on both systolic and diastolic dyssynchrony is given in the study by Wang et al. (8). In a non-randomized, open-label, non-blinded extension study, they assessed the effect of various standard therapies (diuretics, beta-blockers, calcium-channel blockers, and angiotensin-converting enzyme inhibitors or receptor blockers). Treatment significantly shortened the degree of diastole intraventricular dyssynchrony, and there was a non-significant trend to improving systolic intraventricular dyssynchrony. This was associated with a significant fall in blood pressure but not changes in LV mass, but the treatment period was very short (only 3 to 15 days). This implies that arterial pressure alone may be implicated in inducing dyssynchrony, perhaps part of a wider problem of arterial-ventricular stiffening. Cardiac resynchronization therapy has been used in patients with SHF and a normal QRS with some success in small trials (24). As yet, there is no evidence that CRT will improve systolic or diastolic function in DHF.

These 2 studies add new interesting data on the evolving analysis of the syndrome of heart failure with a normal ejection fraction or the DHF group of patients. It is still not entirely clear what precisely are the pathophysiological mechanisms and the underlying cause of symptoms. Interestingly, it seems that it is a mixture of systolic and diastolic abnormalities which will vary from patient to patient depending on the etiology and other cofactors such as arterial compliance and renal function. But one caveat to make about studies on HFNEF or DHF is the difficulty in being precise about the diagnosis and being certain that the symptoms are really due to cardiac disease. Criteria for diagnosis are still inadequate because there is no “gold standard” for measuring diastolic function (25). Many patients labelled as having HFNEF/DHF often have other possible reasons for breathlessness such as obesity, reduced respiratory function, transient arrhythmias, or ischemia. Here B-type natriuretic peptide measurements and, in particular, exercise testing with respiratory gas exchange and Doppler echocardiography for estimating filling pressures and dysynchrony on exercise have an important potential role (26–28). After all, heart failure is a disease of exercise (26).
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REFERENCES


