Pseudonormal or Intermediate Pattern?*

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In 1988, Appleton et al. (1) investigated the relation between transmitral Doppler flow dynamics and invasively determined measurements of pressure and flow in a variety of heart diseases. Based on their findings, three abnormal transmitral flow patterns by Doppler echocardiography have been proposed: 1) impaired relaxation, 2) pseudonormal and 3) restrictive patterns that reflect the pathophysiology of left ventricular (LV) diastolic dysfunction (2,3) (Fig. 1).

The impaired relaxation pattern is characterized by a long isovolumic relaxation time, slow deceleration of early filling (E) and high atrial filling (A) velocities, with a decreased E/A ratio. In this type of filling pattern, intracardiac pressures are unaffected, but less effective suction from LV relaxation results in a delayed and diminished left atrial (LA) to LV early diastolic pressure gradient, leading to a decreased E velocity and a prolonged E deceleration time.

The pseudonormal pattern appears normal in terms of E/A ratio and E deceleration time. In this setting, increased LA pressure offsets the reduced flow related to impaired relaxation and results in relatively normal E and A velocities and E deceleration time.

In the past decade, a number of studies have demonstrated that the Doppler transmitral flow pattern plays an important role in predicting prognosis in patients with congestive heart failure (CHF) (4–7). These studies have included cardiac amyloidosis, dilated cardiomyopathy and chronic coronary artery disease as etiologies. In all these studies, diastolic dysfunction was more predictive of prognosis than systolic dysfunction, since the restrictive filling pattern consistently and independently predicted cardiac mortality better than LV ejection fraction. These findings have added to our body of knowledge about the clinical usefulness of Doppler transmitral flow variables in assessing prognosis in various patient groups.

Interestingly, since early in this experience, the transmitral flow patterns were divided into restrictive and nonrestrictive groups. The pseudonormal pattern may have been included in the “nonrestrictive” group due to lack of the knowledge of its clinical implications. Recently, loading manipulations have been applied to further stratify the restrictive pattern into “reversible” and “irreversible” subgroups, resulting in incremental prognostic value in chronic heart failure (8,9). In this issue of the Journal, Whalley et al. (10) report on an attempt to further distinguish pseudonormal filling pattern from the nonrestrictive group in an elderly CHF population and to examine whether this pattern conveys a distinct prognosis compared with the restrictive and impaired relaxation patterns.

In the article, Whalley et al. (10) investigated 115 CHF patients (mean age of 73 years) who had adequate Doppler echocardiographic recordings before hospital discharge. The etiology for CHF was composed of ischemic and nonischemic heart diseases (54% vs. 46%). The patients were followed up for 12 months and all-cause mortality and hospital readmission data were analyzed. In patients with E/A ratio of 1 to 2, the Valsalva maneuver was employed as preload reduction to differentiate pseudonormal pattern from true normal pattern (11). In 42 patients with E/A between 1 to 2, the filling pattern was found to revert to one resembling impaired relaxation after a Valsalva maneuver. Therefore, this group was confirmed to be pseudonormal instead of true normal. The one-year follow-up results showed the following: 1) all-cause mortality in restrictive (27 patients), pseudonormal (42 patients) and impaired relaxation (46 patients) patterns was 37.5%, 23.4% and 17.4%, respectively; 2) hospital readmission for CHF in the three patterns was 40.7%, 30.9% and 15.2%, respectively; and 3) death/CHF hospital readmission was 62.9%, 47.6% and 26.1%, respectively. Therefore, for the follow-up endpoints, the patients with pseudonormal pattern were intermediate between restrictive and impaired relaxation patterns.

Previous investigators have used pulmonary venous Doppler recordings to stratify the nonrestrictive group. Dini et al. (12) reported that the difference in duration (ms) of pulmonary venous flow and mitral flow at atrial contraction (ARd-Ad) provided an incremental prognostic value to predict outcome in CHF patients. The index of ARd-Ad has been shown to directly reflect LV diastolic pressure (13). They found that patients with nonrestrictive pattern and ARd-Ad ≥30 ms had an intermediate prognosis between

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patents with restrictive pattern (worse) and those with nonrestrictive and ARd-Ad < 30 ms (better) in terms of survival and event rates. In that study, the E/A ratio of 1 to 2 and ≤ 1 was also used to group the nonrestrictive patients. However, the results failed to show any differences of clinical end points between those two groups. We suspect that if the Valsalva maneuver had been applied to the patients with E/A between 1 to 2, the true normal patients could be eliminated and the results might have been different. However, in the current study (10), the time duration from pulmonary venous flow Doppler was not reported. Therefore, it is difficult to comment on which approach may be more effective and reliable to further stratify the nonrestrictive group, even though these two studies have reached very similar conclusions.

In daily echo practice, the Valsalva maneuver would be easily used as a method for preload reduction. However, it is sometimes difficult to perform the Valsalva maneuver properly and one should be cautious about the results in these cases. In the future, it would be helpful to design a study in which Valsalva and pulmonary vein approaches are compared in the same patients, with regard to methodology and prognosis.

Color M-mode Doppler echocardiography has also been used to investigate the pseudonormal pattern in patients with acute myocardial infarction (14). The results showed that patients with a pseudonormal pattern and reduced color M-mode flow propagation velocity fell between those with restrictive and impaired relaxation patterns in terms of future risk for cardiac death and LV dilation.

The patients with restrictive filling pattern may also be a heterogeneous group. Pozzoli et al. (8) have clearly delineated that loading manipulations in CHF patients can induce dramatic alterations in the restrictive pattern. After infusion of nitroprusside, the Doppler filling pattern reverted to impaired relaxation in some patients, which was referred to as “reversible restrictive”; whereas in others it remained unchanged, referred to as “irreversible restrictive”. Patients who had reversible patterns had lower cardiac event rates than those who had irreversible patterns (19% vs. 51%). The authors also challenged patients with impaired relaxation by leg lifting (increase in preload) to find an “unstable” nonrestrictive subgroup (which reverted to restrictive pattern). This subgroup had worse prognosis than stable “nonrestrictive” (which remained as impaired relaxation), with cardiac event rates of 33% versus 6%. Considering the filling hemodynamics, the reversible restrictive pattern may be similar to the pseudonormal pattern. The nature of unstable nonrestrictive pattern has not been well elucidated, but the prognosis of this pattern seems to be even worse than reversible restrictive pattern (8,9). Currently, the number of study subjects remains small.

Transmitral filling dynamics are affected by many variables (15). Specifically, loading conditions may mask the
true LV diastolic properties. Therefore, it may be essential to utilize loading manipulations or additional modalities (pulmonary venous flow or color M-mode) to stratify LV filling patterns and to provide incremental prognostic value. The Valsalva maneuver proposed in the study by Whalley et al. (10) should be considered as a simple preload reduction tool to challenge all CHF patients with E/A > 1, including the restrictive pattern (Fig. 1). If the filling patterns revert to impaired relaxation, we might term these patients as having “intermediate” pattern rather than pseudonormal or reversible restrictive, because they represent an intermediate stage of filling dynamics. Further, their prognosis falls between impaired relaxation and restrictive patterns. As illustrated in Figure 1, abnormal Doppler transmitral filling in CHF patients could be classified into three patterns: 1) impaired relaxation, 2) intermediate and 3) restrictive to better define prognostic categories.

Clearly, the evaluation of LV diastolic properties remains an important area of clinical research. Doppler echocardiographic techniques provide a readily available tool for assessing bedside hemodynamics noninvasively. Further knowledge may help with planning medical management and selecting candidates for heart transplant in the CHF population.

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