

The Role of Echocardiography in Cardiac Structural and Functional Assessment in Dialysis Patients

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In recent decades, echocardiography has evolved into a useful tool in the assessment of cardiovascular anatomy, physiology, and pathology. Its use has enabled the measurement of structural parameters such as left ventricular mass, which has both diagnostic and prognostic value. Doppler measurements have allowed for accurate hemodynamic assessment that can help to guide therapy. Newer methods have also been used and proposed to evaluate systolic and diastolic function. Here, we review the use of echocardiography in cardiac structural and functional assessment, providing insights into the challenges and limitations of these techniques in dialysis patients.

Key words

Echocardiography, structural assessment, functional assessment, chronic kidney disease

Introduction

Despite considerable advances in medical care and in dialysis facilities, cardiovascular disease remains the major cause of death among patients with end-stage renal disease (ESRD) (1). Central to the evaluation and management of patients on dialysis is the knowledge that underlying cardiac pathology is the most likely cause of major episodes of morbidity and mortality. In recent decades, the role of echocardiography has transitioned from a purely anatomic and structural assessment of the heart to a critical and reproducible tool in the functional assessment of the heart. In 2008, this noninvasive role included assessment of hemodynamics when coupled with a careful physical examination.

The overview presented here provides the reader with guidelines and evidence for the use of echocardiography as it relates to cardiac structural and functional assessment.

Discussion

Structural assessment

Although left ventricular (LV) mass has received less attention in clinical cardiology than ejection fraction (EF) has, LV mass has important prognostic value. Data in heart failure patients from the SOLVD (Studies of Left Ventricular Dysfunction) Registry showed that an increase in LV mass is associated with increased mortality and hospital readmission independent of EF (2). In patients with ESRD on dialysis, LV mass is increased even in normotensive individuals and has been attributed to higher cardiac output and subclinical LV dysfunction (3). The normal LV mass index (indexed to body surface area) for women is 43 – 95 g/m². For men, it is 49 – 115 g/m² (2). Left ventricular mass increases in the setting of LV remodeling because of myocardial thinning, with increased volume or myocardial hypertrophy as a result of hypertension (4).

Assessment of LV mass is subject to the same limitations in reproducibility and accuracy as measurement of LV dimensions (5). These methods rely heavily on geometric assumptions and are furthermore subject to inaccuracies from image foreshortening.

Hemodynamic assessment

PRELOAD AND FLUID STATUS

In ESRD patients on intermittent dialysis, the maintenance of fluid status within an optimal range is critical to avoid circulatory complications. Failure to

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achieve true dry weight may result in chronic volume overload and contribute to overall cardiovascular mortality, and dialysis to below dry weight may produce symptoms of volume depletion. The evaluation of fluid status is generally approached from clinical observation of body weight change, edema, blood pressure, and chest radiograph. Methods that are more objective, such as biochemical markers, bioimpedance analysis, and inferior vena cava (IVC) diameter, have been developed for the assessment of fluid status in dialysis patients. However, no single method has emerged as a "gold standard," and the combination of these methods is generally needed to complement their respective limitations.

The mitral inflow Doppler spectrum reflects LV filling dynamics, and the pulmonary vein Doppler spectrum reflects the left atrium filling dynamics. Both spectra have been shown to be load-dependent in subjects with various cardiac diseases (6).

Wu *et al.* investigated the various Doppler parameters in hemodialysis patients as compared with healthy volunteers and prospectively analyzed parameters that may be used as markers of fluid status. From mitral inflow velocity tracings, they measured peak velocity (E) and deceleration time of the early inflow wave, peak velocity (A) of the late inflow wave at atrial contraction, and isovolumic relaxation time [Figure 1(A)]. The parameters evaluated for the pulmonary vein spectrum included the peak velocity of the systolic (S) and diastolic (D) forward spectra [Figure 1(B)]. The S/D ratio of the pulmonary vein spectrum and the E/A ratio of the mitral inflow spectrum were also used. The IVC diameter was measured on M-mode echocardiograms and indexed by body surface area in centimeters per square meter (2). The foregoing readings were then all correlated with references for fluid status: extracellular water as a percentage of body weight (measured by bioimpedance analysis) and pre-dialysis mean blood pressure. Among all of the pulmonary vein and mitral inflow velocity parameters, the S/D ratio correlated best with fluid status parameters. A ratio of above 1.33 has a 90% sensitivity and 77% specificity for identifying patients dialyzed to dry weight (7).

RIGHT ATRIAL PRESSURE

Estimation of right atrial pressure using two-dimensional echocardiographic measurement of IVC size (Figure 2), together with its respirophasic variation, is commonly

performed. An IVC size greater than 2.0 cm and optimal IVC collapsibility cutoff of less than 40% were found to predict a right atrial pressure above 10 mmHg (8).

RIGHT VENTRICULAR SYSTOLIC PRESSURE AND PULMONARY ARTERY SYSTOLIC PRESSURE

One method of measuring the right ventricular systolic pressure (RVSP) is to quantify the tricuspid regurgitation (TR) jet velocity. Using the Bernoulli equation, the systolic pressure gradient between the right atrium and the right ventricle can be calculated by squaring the maximum TR velocity and multiplying by 4. Adding the estimated right atrial pressure to this calculated pressure gradient results in the RVSP. Because the RVSP and pulmonary artery systolic pressure are similar in the absence of significant pulmonic stenosis, this method allows for a simple but accurate means of evaluating the presence and severity of pulmonary hypertension (9).

LEFT VENTRICULAR FILLING PRESSURE

The LV filling pressure can be expressed as LV end-diastolic pressure (LVEDP), left atrial mean pressure, or pulmonary capillary wedge pressure (9). Several methods have been used to measure these values. The size of the left atrium has been used as a marker of the severity and chronicity of left atrial pressure elevation. The mitral E-wave peak velocity corresponds to the pressure gradient between the left atrium and the left ventricle at the time of mitral opening, and it has been used as a marker of the severity of the increase in left atrial pressure. However, factors such as volume loading, atrial contractility, and ventricular relaxation properties influence both measurements, limiting their sensitivity and specificity. More recently, tissue Doppler imaging has been used to assess LV filling pressure. This technique measures E' , which is the velocity of the medial or lateral mitral annulus in the early or rapid filling phase of diastole. Studies have shown that a ratio of the mitral E-wave peak velocity to the annular E velocity (E/E') in excess of 15 has an 86% specificity in predicting an elevated LVEDP, defined as more than 15 mmHg (10).

Functional assessment

SYSTOLIC FUNCTION

The LVEF is the most commonly used measure of systolic function. Image quality in patients with poor

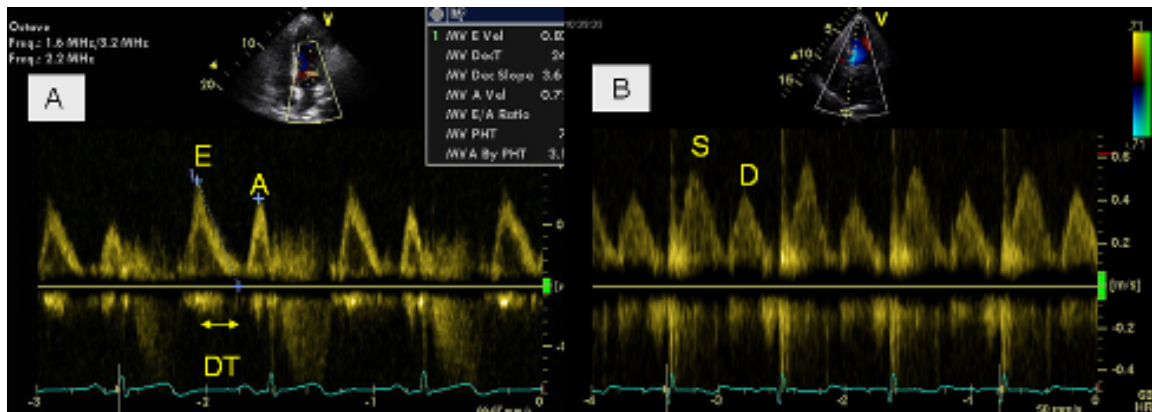


FIGURE 1 Echocardiography can be used to assess preload and volume status. (A) Mitral inflow velocity tracings show peak velocity [E] and deceleration time [DT] of the early inflow wave and peak velocity [A] of the late inflow wave at atrial contraction. (B) Pulmonary-vein Doppler image shows peak velocity of the systolic [S] and diastolic [D] forward spectrum.

acoustic windows has traditionally played a major role in limiting the accuracy of LV volume and EF quantification. Tissue harmonic imaging with and without echocardiographic contrast for LV cavity opacification has improved the accuracy and reproducibility of EF measurements (11). Ejection fraction can be measured using qualitative and quantitative methods. Qualitatively, a visual interpretation of EF can be made. Quantitatively, EF can be calculated using geometric assumptions on M-mode echo or on biplane two-dimensional echo using Simpson's rule (the "method of discs"). With either two-dimensional method, the new American Society of Echocardiography guidelines define an abnormal EF as less than 55%, with the cut-offs for moderately abnormal and severely abnormal being 44% and 30% respectively (4).

DIASTOLIC FUNCTION

Myocardial fibrosis in uremic patients is a phenomenon thought to be mediated by angiotensin II, parathyroid hormone, aldosterone, endothelin, and increased plasma catecholamines (13). Refractory hypertension and volume expansion can cause LV hypertrophy. These factors contribute to decreased myocardial compliance and increased filling pressures. Abnormal diastolic parameters carry considerable prognostic value in symptomatic and asymptomatic patients with either preserved or abnormal LV systolic function (14).

A variety of echocardiographic techniques are used to evaluate diastolic function. Among these are

mitral inflow pulsed Doppler, pulmonary vein flow Doppler, color M-mode flow propagation velocity, and tissue Doppler. Increased left atrial volumes (32 mL/m^2 or more), although not a direct measure of diastolic function, are an indicator of chronically elevated LV filling pressures and have been shown to predict morbidity (15).

Diastolic dysfunction can be characterized according to severity (Figure 3). Mild diastolic dysfunction—abnormal LV relaxation—can be detected as a decrease in early diastolic flow velocity (E-wave) and a greater reliance on atrial contraction (A-wave) to fill the LV ($E/A < 1$). Moderate diastolic dysfunction—"pseudonormalization"—reflects increasing left atrial pressure at the onset of diastole and an increase in early diastolic flow velocity to a level near that of normal filling ($E/A = 1$ to 1.5). Reduction in preload with the Valsalva maneuver can change a pseudonormalized pattern to an abnormal relaxation pattern, or a restrictive pattern to a pseudonormalized one. Severe diastolic dysfunction—restrictive filling—occurs when left atrial pressure is further elevated such that early diastolic flow is extremely rapid, and left atrial and LV pressures equalize quickly during early diastole ($E/A > 2$) (12).

Pulsed Doppler and color M-mode techniques are mostly preload-dependent (15–19). Pulmonary vein Doppler flow velocities are thought to be less dependent on loading conditions and heart rate (20); however, these measures are limited by their inability to

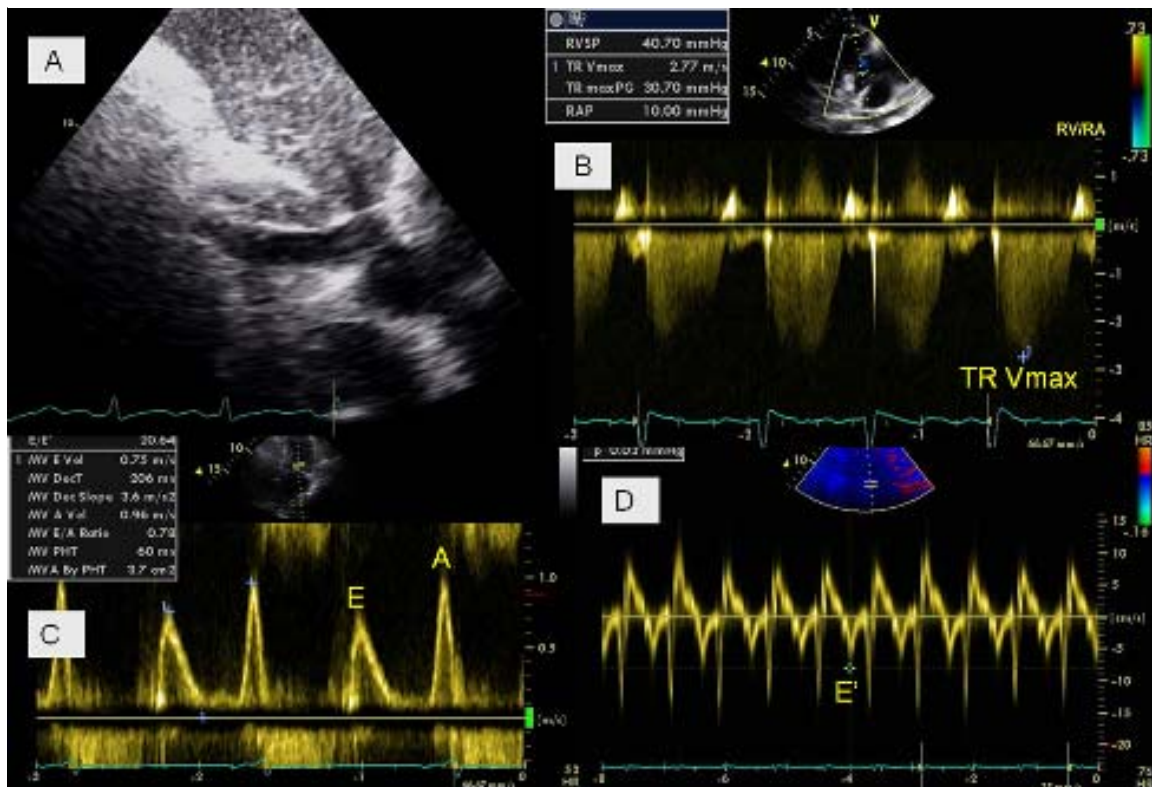


FIGURE 2 Two-dimensional and Doppler echocardiography is a powerful tool for hemodynamic assessment (see text for details). (A) Inferior vena cava (IVC) diameter. (B) Tricuspid regurgitation jet velocity ($TR V_{max}$), calculated pressure gradient, and estimated right ventricular systolic pressure. (C,D) Ratio of peak early mitral inflow velocity [E] and tissue Doppler velocity of the medial or lateral mitral annulus in the early phase of diastole [E'] provides an estimate of the left ventricular end diastolic pressure.

adequately image the pulmonary veins in some patients. Tissue Doppler imaging has been proposed as a preload-independent parameter of diastolic function (21). A ratio of peak early mitral inflow velocity (E) to peak early diastolic myocardial velocity (E') of 8 or more has been shown to predict an LVEDP of 15 mmHg or more (10). However, several later studies have shown that alterations in preload affect tissue Doppler measurements (17,22,23). These findings are particularly important in the ESRD population because of the volume fluctuations that occur during dialysis cycles. The timing of echocardiographic assessment will be important, because volume overload before dialysis may underestimate the degree of diastolic dysfunction.

Data suggest that, aside from affecting the diagnosis of diastolic dysfunction, the volume shifts

associated with hemodialysis may *per se* cause deterioration of diastolic function as assessed by tissue Doppler (24). The inference is that low ultrafiltration volumes or limited interdialytic weight gain (or both) are cardioprotective measures in hemodialysis patients. The route of dialysis—that is, peritoneal dialysis versus hemodialysis—and the dialysis frequency—that is, intermittent versus daily—may therefore affect the development of diastolic function. Data looking specifically into these issues are lacking, therefore opening a potential area of research.

New directions

The development of new methods of echocardiographic assessment may potentially be useful in the dialysis population. Myocardial strain, which is an index of change in myocardial length in response to

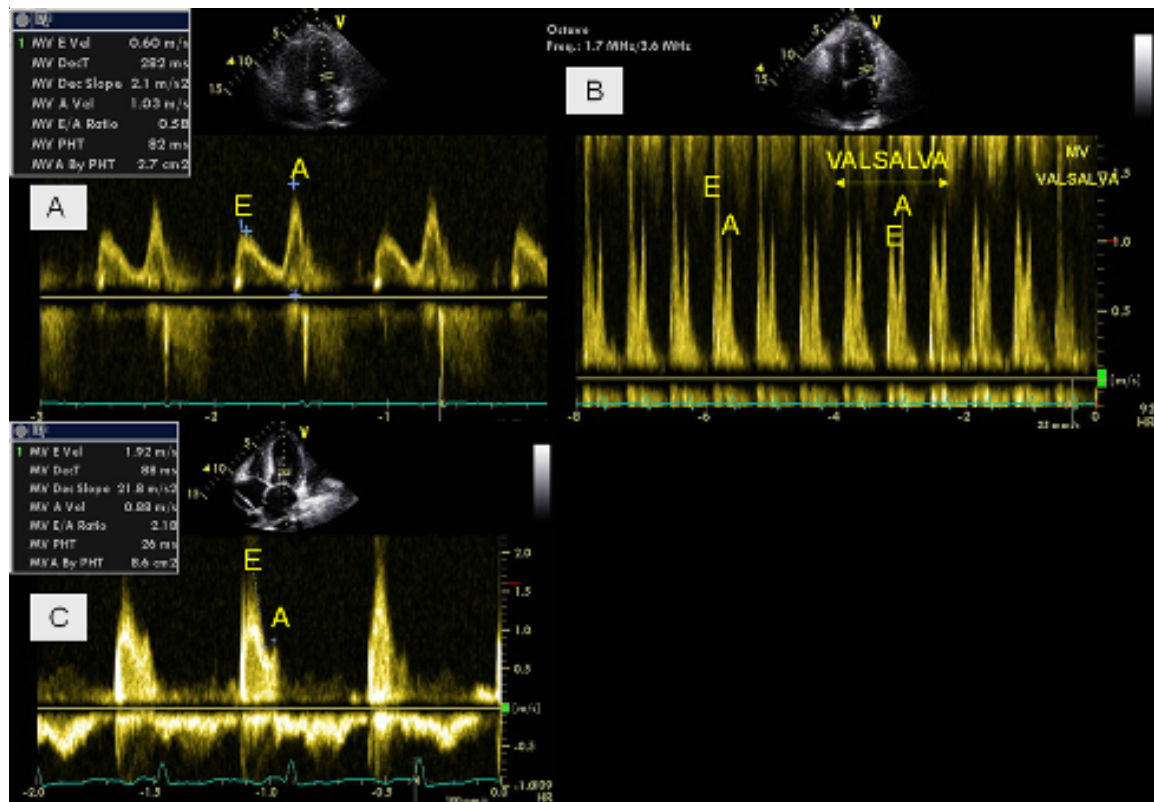


FIGURE 3 The severity of diastolic dysfunction can be assessed using Doppler and tissue Doppler imaging echocardiography. (A) Mild diastolic dysfunction or abnormal left ventricular relaxation, where there is reversal of the ratio of early diastolic flow velocity (E wave), atrial contraction (A wave) ($E/A < 1$). (B) Moderate diastolic dysfunction or “pseudonormalization” occurs with an E/A of 1:1.5; a reduction in preload with the Valsalva maneuver can change a pseudonormalized pattern to an abnormal relaxation pattern, or a restrictive pattern to a pseudonormalized one. (C) Severe diastolic dysfunction or restrictive filling is defined when $E/A > 2$.

an applied force, can be measured using color two-dimensional tissue Doppler imaging. It allows for an assessment of regional myocardial systolic and diastolic function and has a theoretic advantage over Doppler tissue imaging by being relatively immune to cardiac translational motion and tethering (25). Using this technology, patients on dialysis were shown to have impairment in longitudinal myocardial function despite an absence of symptoms as compared with normal control subjects (26).

Real-time three-dimensional echocardiography is another technological advance that may improve structural and functional assessment, because it provides a rapid and easy way of calculating LV volumes and EF, overcoming the limitation of relying on geometric assumptions (27). One study measured

LV volumes and EF using three-dimensional echocardiography during hemodialysis and showed the method's feasibility and good correlation with two-dimensional techniques (28). Moreover, *post hoc* analysis showed the tendency for two-dimensional methods to underestimate volume and overestimate EF. Three-dimensional echocardiography may therefore provide an accurate assessment of acute changes in cardiac function during dialysis and may contribute to an understanding of the pathogenesis and mechanics of intradialytic hypotension.

Summary

Echocardiography is a powerful tool for the non-invasive evaluation of cardiac structure and function. The technique is widely available and without known

risks. It is generally quick and painless for patients. Despite these great attributes, sophisticated measures of LV function during systole and diastole have limitations. Further, little work has been done in populations of dialysis patients, using these parameters to provide powerful outcomes data with regard to mortality and morbidity. Given the high rate of cardiovascular morbidity and mortality in the dialysis population, further investigations into methods of obtaining prognostic information are critical.

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