Transthoracic bioimpedance and brain natriuretic peptide levels accurately indicate additional diastolic dysfunction in patients with chronic advanced systolic heart failure

Gabriella Malfatto1*, Giovanna Branzi 1, Alessia Giglio 1, Alessandra Villani1, Camilla Facchini1, Francesca Ciambellotti1, Mario Facchini1, and Gianfranco Parati1,2

1Divisione di Cardiologia, Istituto Scientifico Ospedale San Luca, Istituto Auxologico Italiano IRCCS via Spagnoletto, 3, 20149 Milano, Italy; and 2Dipartimento di Medicina Clinica, Prevenzione e Biotecnologie Sanitarie, Università di Milano-Bicocca, Milano, Italy

Aims
Diastolic dysfunction in patients with heart failure has prognostic relevance, possibly because of its relationship with worsening haemodynamic status. In the quest for simpler indexes of haemodynamic status in patients, brain natriuretic peptide (BNP) levels have been proposed as a surrogate of diastolic function. To date, the value of combining BNP levels with non-invasive haemodynamic monitoring by transthoracic electric bioimpedance (TEB) for the prediction of diastolic function has not been evaluated.

Methods and results
We compared left ventricular diastolic function measured by tissue Doppler imaging (TDI) with TEB results and BNP levels in 120 patients with chronic advanced systolic heart failure on optimal treatment (70 ± 9 years, NYHA 2.4 ± 0.8, ejection fraction 31 ± 5%). Of the TEB variables measured, we only considered thoracic fluid content (TFC). To describe diastolic function, we used the TDI of the velocity of displacement of the mitral annulus (E’) and the ratio E/E’. In all patients, E/E’ was significantly related to TFC and to BNP levels (P < 0.001). Moreover, the combination of BNP ≥ 350 pg/mL and TFC ≥ 35/kΩ identified patients with diastolic dysfunction (defined as E/E’ ≥ 15) with high sensitivity and specificity (95 and 94%, respectively).

Conclusion
The combination of transthoracic bioimpedance monitoring and BNP measurement accurately indicated the presence of diastolic dysfunction in most patients. These user-friendly and operator-independent tools may be useful as a screening assessment for diastolic dysfunction, and consequently abnormal central haemodynamic status, either in ambulatory patients or when an adequate echocardiographic evaluation is not readily available.

Keywords
Chronic heart failure • Diastolic dysfunction • Transthoracic bioimpedance monitoring • Brain natriuretic peptide

Introduction
As the burden of congestive heart failure as a cause of morbidity and mortality in Western countries increases,1–3 so does the need for useful prognostic indexes to facilitate risk stratification and the selection of appropriate therapeutic strategies.3,4 Although most patients with advanced chronic heart failure have some degree of left ventricular systolic dysfunction, left ventricular ejection fraction (EF) appears to be poorly related to individual prognosis.5 However, the finding of an associated abnormal diastolic function is related to a worse prognosis.3–7 This finding has been explained by the relationship between abnormal diastolic function and high left ventricular filling pressures, which are the main determinants of dyspnoea and fatigue in severely ill patients.7

Not surprisingly, Doppler echocardiography remains the gold standard for the non-invasive evaluation of patients with congestive heart failure,8,9 and many variables have been described for the evaluation of diastolic function. Among them, pulsed wave tissue
Doppler imaging (TDI) echocardiography directly measures myocardial velocities, the early diastolic mitral annular velocity (E') has been shown to be a relatively load-independent measure of myocardial relaxation in patients with cardiac disease. When TDI is combined with pulsed Doppler transmitral flow in early diastole (E), the resultant E/E' ratio has been shown to be correlated with left ventricular filling pressures measured invasively. However, Doppler echocardiography requires a comprehensive evaluation by a well-trained operator, and its high cost limits its use as a routine screening tool for diastolic dysfunction. Therefore, alternative markers of diastolic functional status could provide useful information for a first-step assessment of congestive heart failure patients.

B-type natriuretic peptide (BNP) is often used to estimate the presence and severity of heart failure. Initially, BNP was used for the diagnostic workout of acute dyspnoea, but levels are also closely related to NYHA functional class and to individual prognosis. Recently, a relationship between BNP levels and indexes of diastolic function has been described, both in patients with reduced and in those with preserved EF. Transthoracic electric bioimpedance (TEB) monitoring, also known as impedance cardiography (ICG), applies Ohm's law to the thorax, such that changes in voltage and impedance in patients are translated into haemodynamic parameters of cardiac function, such as cardiac output and thoracic fluid content (TFC). The value of TEB in the clinical assessment of heart failure patients is still under debate, but in a recent study, a combination of TEB and BNP levels has been used for improving the diagnosis and management of patients admitted to emergency units with acute heart failure.

There are currently no data on the relationship between TEB and the echocardiographic evaluation of diastolic dysfunction in patients with advanced heart failure. Therefore, we designed this study with a two-fold purpose. First, to determine the correlation between echocardiographic indexes of diastolic dysfunction, BNP levels, and a specific TEB variable (TFC). Second, to test the hypothesis that a combination of TEB and BNP levels may be a more accurate screening test than BNP alone for identifying patients with an abnormal diastolic phase in addition to reduced systolic function.

Methods

Patient population

We included 120 consecutive patients with chronic systolic heart failure followed in the Outpatient Heart Failure Centre, at the Ospedale San Luca, Milan, Italy. All patients fulfilled the entry criteria and were clinically stable under optimal treatment for at least 3 months before the study evaluation. We did not include patients presenting with any condition that would interfere either with the determination of diastolic function or with the accuracy of the BNP assay or TEB: severe chronic obstructive pulmonary disease, severe renal failure (creatinine clearance < 20 mL/min), mitral surgery (either repair or prosthetic valve insertion), moderate-to-severe aortic regurgitation, pleural or pericardial effusion, body weight < 50 and > 100 kg, left ventricular aneurism repair, recent (< 6 months) implantable cardioverter defibrillator, and/or biventricular pacemaker implantation. Table 1 shows the demographic and clinical characteristics of the patients. Overall, the patients were relatively old, a quarter of the patients were female, the majority had an ischaemic aetiology, and almost two-thirds of the patients had some degree of functional mitral regurgitation, which was severe in about 25%. Therapy for heart failure was appropriate in accordance with International Guidelines.

Study design

The study was approved by the local Ethics Committee. All patients gave written consent both for the anonymous use of their echocardiographic data (obtained during a routine clinical examination) and for the BNP assay and ICG test. Both TEB monitoring and BNP assay were performed during the morning, within 1 h of the scheduled clinical and echocardiographic examination. B-type natriuretic peptide was assessed by a point-of-care system (Triage BNP Test, Biosite Inc.): the average of two determinations was used, and the results were entered onto the database by a technician not involved in the study. Investigators performing the echocardiography and TEB were equally unaware of the results of the other tests and of the clinical examination. It was beyond the scope of this study to determine whether the results of the BNP and TEB assessment could modify clinical decisions regarding patient management, as has been shown in other studies. For this reason and in contrast with these previous reports, we did not analyse other TEB data such as indexes of systolic function or peripheral resistance.

Table 1  Demographic and clinical characteristics of the study population

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>71±9</td>
<td></td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>88/32</td>
<td></td>
</tr>
<tr>
<td>Ischaemic/non-ischaemic</td>
<td>75/45</td>
<td></td>
</tr>
<tr>
<td>NYHA class</td>
<td>2.4±0.8</td>
<td></td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>87±7</td>
<td></td>
</tr>
<tr>
<td>EF (%)</td>
<td>30.5±5.1</td>
<td></td>
</tr>
<tr>
<td>LVEDV (mL)</td>
<td>108±18</td>
<td></td>
</tr>
<tr>
<td>Functional mitral regurgitation any degree (%)</td>
<td>76 (64)</td>
<td></td>
</tr>
<tr>
<td>Significant mitral regurgitation (EROA &gt; 20 mm²) (%)</td>
<td>23 (20)</td>
<td></td>
</tr>
<tr>
<td>PAPs (mmHg)</td>
<td>39.1±12.4</td>
<td></td>
</tr>
<tr>
<td>Restrictive filling pattern (%)</td>
<td>47 (41)</td>
<td></td>
</tr>
<tr>
<td>E/E'</td>
<td>13.6±6.3</td>
<td></td>
</tr>
<tr>
<td>BNP (pg/mL)</td>
<td>419±256</td>
<td></td>
</tr>
<tr>
<td>TFC (1/kΩ)</td>
<td>39.3±8.7</td>
<td></td>
</tr>
<tr>
<td>VI (1/1000/s)</td>
<td>32.6±14.2</td>
<td></td>
</tr>
<tr>
<td>ICD ± biventricular pacing (yes/no)</td>
<td>44/76</td>
<td></td>
</tr>
</tbody>
</table>

ACE-inhibitors 85
ARB 37
β-Blockers 80
Loop diuretics 70
Spirinolactone 50
Digitalis 6

MAP, mean arterial pressure; EF, ejection fraction; LVEDV, left ventricular end-diastolic volume; EROA, effective regurgitant orifice area; PAPs, estimated systolic pulmonary pressure; E/E', ratio between velocity of the E and A wave on Doppler transmitral flow; ARB, angiotensin receptor blockers; BNP, brain natriuretic peptide; TFC, thoracic fluid content; VI, velocity index.

Downloaded from eurjhf.oxfordjournals.org at European Society of Cardiology on August 25, 2010.
Echocardiographic measurements

Patients were imaged in the left lateral decubitus position using a commercially available system (Vingmed Vivid Seven, General Electric-Vingmed, Milwaukee, WI, USA). Images were obtained with a 3.5 MHz transducer, at a depth of 16 cm in the parasternal and apical views (standard long-axis and four-chamber images). Standard two-dimensional and colour Doppler data, triggered to the QRS complex, were saved in a cine-loop format. For each measurement, we averaged three cardiac cycles for patients in sinus rhythm and five for patients in atrial fibrillation. Measurements were obtained by two expert independent observers, with inter- and intra-observer coefficients of variation <5% for conventional echo and <10% for tissue Doppler variables and quantification of the effective regurgitant orifice area (EROA) and volumes: these coefficients are in agreement with the guidelines of the American Society of Echocardiography both for systolic and diastolic function assessment.26–29 End-diastolic and end-systolic left ventricular volumes and EF were determined by manual tracing of end-systolic and end-diastolic endocardial borders using apical four- and two-chamber views, employing the Simpson method for biplane assessment. Peak velocities of early (E) and late (A) diastolic filling and deceleration time were derived from transmitral Doppler recordings, as well as determination of pulmonary vein flow velocity. From the analysis of transmitral and pulmonary vein flow pattern, diastolic function was classified on a 1–4 scale, in which 1 is normal, 2 is abnormal relaxation, 3 is pseudonormal, and 4 is restrictive.27–29 Tissue Doppler imaging-derived peak systolic (S′), early (E′), and late (A′) diastolic velocities were derived from the septal and lateral mitral annulus and averaged for each patient and the mitral E/E′ ratio was calculated.12,27,30 Diastolic dysfunction was defined as E/E′ ≥ 15. The presence of mitral regurgitation was assessed by inspection of the colour Doppler jet area in the downstream chamber and the width of the vena contracta.31 The extent of mitral regurgitation (EROA) was calculated based on jet geometry, jet area, vena contracta width, and the area of regurgitant orifice with the proximal isovelocity area (PISA).31 Mitrut regurgitation was then rated on a 1–4 scale, on which 1 is mild, 2 is moderate, 3 is moderate/severe, and 4 is severe.

Bioimpedance cardiography

Transcutaneous electric bioimpedance cardiography was performed using machines with the same software (BioZ ICG Monitor: Cardio-Dynamics, San Diego, CA, USA; BioZed: NICCOMO, Germany).23,24 Patients were rested in the supine position for at least 15 min before TEB data were collected. Four dual ICG sensors were placed: above the base of the neck and under each ear, and one on either side of the thorax in the mid-axillary line at the level of the xiphoid. A cable with eight ICG lead wires was attached to the individual sensor sites. An integrated oscillometric blood pressure cuff was connected to the patient’s arm. The recording was performed for 10 min, and an average ICG status report was stored for analysis. Variables evaluated by TEB monitoring in this study have been described previously and include measurements of cardiac blood flow, vascular resistance, fluid status, and indices of electromechanical timing and contractility.21 For the present study, we took into account only TFC as an index of pulmonary congestion and velocity index (VI), i.e. the first time derivative of baseline impedance × 1000 as an index of contractility.23

Statistical analysis

Results are expressed as mean value ± 1 SD. Differences between patient groups for discrete variables (such as prevalence of mitral regurgitation) were assessed by χ² test. Differences between continuous variables were analysed by ANOVA (among groups of patients). Post hoc comparisons were analysed by t-test with Bonferroni’s correction. Linear regression analysis between variables was performed with a least square fitting routine (OriginPro 7.0, Microcal, USA). A value of P < 0.05 was considered significant. Finally, receiver-operating characteristic (ROC) curves were constructed to determine optimal sensitivity and specificity.

Results

The majority of patients in this population of chronic heart failure subjects had an abnormal diastolic phase. Table 2 shows that patients with abnormal diastole (either measured through the assessment of transmitral and pulmonary vein flow or by the determination of E/E′) had worse NYHA class, more severe mitral regurgitation, higher pulmonary pressure, higher levels of BNP, and higher TFC. In contrast, in patients with a normal diastolic phase, EF and ventricular volumes were similar, and contractility, as assessed by VI, was not different. The aetiology of heart failure did not influence any of the variables under study (Table 3).

The progression of the severity of functional mitral regurgitation was associated with a worsening of diastolic function, higher levels of BNP, and a greater TFC (Table 4), whereas inotropism, indicated by the value of VI, did not vary significantly. In the 23 patients with moderate-to-severe mitral regurgitation, i.e. those in whom EROA was >20 mm², a significant relationship between E/E′, BNP, TFC, and EROA was observed (Figure 1).

The severity of diastolic dysfunction was accurately indicated by the determination of both BNP levels and TFC values. We choose E/E′ values as a simple numerical index of diastolic function: as shown in Figure 2A and B, a significant relationship was present between E/E′ and both BNP levels and TFC values. In addition, the latter variables were also reciprocally correlated, as shown in Figure 3.

Once a significant relationship between the variables was confirmed, we determined whether the measurement of BNP and TFC could be used as a preliminary screening for the diagnosis of diastolic dysfunction. Figure 4 shows the ROC curves of BNP and TFC for the prediction of an E/E′ of >15. In all 120 patients, the optimal cut-off for BNP was 350 pg/mL (sensitivity 77%; specificity 75%), whereas the optimal cut-off for TFC was 35/kΩ (sensitivity 81%; specificity 70%). A significant improvement in the diagnostic likelihood of abnormal diastolic function, nonetheless, was obtained by combining a BNP level of >350 pg/mL with a TFC value of >35/kΩ, which increased the sensitivity and specificity for the prediction of E/E′ > 15 to 95 and 94%, respectively (positive predictive value of 88% and negative predictive value of 96%). Very similar results were obtained when diastolic dysfunction was evaluated by Doppler echocardiography. In this case, a BNP level of >350 pg/mL with a TFC value of >35/kΩ had a sensitivity of 89% and a specificity of 94% for the prediction of restrictive mitral and pulmonary vein flow pattern (positive predictive value of 86% and negative predictive value of 93%). In 23 patients (20%), we observed a discordant result, i.e. TFC > 35/kΩ and BNP < 350 pg/mL or vice versa. Only two of these patients had a normal diastolic function, while the majority had E/E′ between...
8 and 15 and an abnormal relaxation/pseudonormal transmitral and pulmonary vein flow pattern.

**Discussion**

In this study, by combining the assessment of serum BNP levels and the determination of transthoracic impedance by non-invasive haemodynamic monitoring, we were able to accurately predict the presence of diastolic dysfunction in an outpatient population with chronic systolic heart failure.

Diastole is a complex phase in the cardiac cycle: it is a sequence of interrelated events influenced by changes in loading conditions, intrinsic myocardial properties, and heart rate. In the natural history of chronic heart failure, a close relationship exists between progressive ventricular remodelling leading to fibrosis, high levels of circulating BNP, increased left atrial and capillary wedge pressures, and deterioration of the diastolic phase. In fact, it is difficult to discern which phenomenon leads the cascade of events eventually resulting in dyspnoea, fatigue, and worsening of the haemodynamic status. Diastolic heart failure with preserved systolic function may be regarded as a prevalent ventricular disease, whereas in the setting of pre-existing systolic dysfunction, an abnormal diastolic phase is likely a combination of anatomical and haemodynamic derangements since unloading of the ventricles and reduction of pulmonary congestion in decompensated Class-IV heart failure patients is often associated with improvement of diastolic function. As current guidelines recommend the use of pulmonary artery catheterization only in decompen­sated advanced heart failure, a hint to the haemodynamic status of the patient—a target for tailoring more aggressive and effective treatments—may come only from clinical findings, experience, and the aid of indirect, non-invasive strategies.

The analysis of diastole by means of echocardiography, using both Doppler measurements of transmitral and pulmonary vein blood flow velocities and TDI, is widely accepted for clinical purposes. However, such assessment is costly because it
requires complex equipment, is time-consuming because it involves the analysis of many variables, and is difficult because it must be performed by a skilled and trained operator. For these reasons, echocardiography has limited use in the routine periodic assessment of patients in Heart Failure Clinics. In our study, BNP determination and analysis of thoracic impedance could effectively indicate the presence of an abnormal diastolic phase in the vast majority of ambulatory patients. In particular, we confirmed previously reported observations on the presence of a more severe diastolic dysfunction in patients with relevant mitral regurgitation, in whom a clear relationship between EROA and all the parameters under study (E', BNP levels, and TFC values) was observed. In these patients, the presence of a significant regurgitant volume could have induced a further increase in filling pressures besides that attributable to the increased haemodynamic load, leading to higher levels of BNP and to thoracic congestion.

The relationship between abnormal diastolic phase, high BNP levels, elevated TFC, and the presence of high ventricular filling pressures derives from correlation studies and should not be always taken for granted. In a recent study of patients with severe cardiac dysfunction, enlarged left ventricles, and worsening clinical status before both evaluations, tissue Doppler-derived mitral E/E' ratio alone was not reliable in predicting intra-cardiac filling pressures. Indeed, as stated above, at least part of the diastolic dysfunction observed in patients with reduced EF is due to an irreversible left ventricular stiffness. Also, BNP levels per se have a significant but sometimes weak connection with pulmonary wedge pressure. Finally, even though intrathoracic impedance offers a reliable index of fluid overload in ambulatory patients, the ability of transthoracic impedance to assess pulmonary congestion has been challenged in acute heart failure. As a matter of fact, the patients in the current report had severe left ventricular dysfunction but were ambulatory patients and were in a stable clinical condition, with no need for cardiac catheterization at the time of the echocardiographic evaluation. Moreover, compared with the patients studied by Mullens et al. and by Sandeep et al., they had smaller ventricles; thus, a comparison between these populations would be inappropriate.

Owing to the complex nature of diastole, in patients with advanced heart failure and very large ventricles, severe left ventricular fibrosis and low cardiac output may irreversibly modify diastolic function, making the echocardiographic indexes (among them E/E') insensitive to loading conditions and discordant with invasively measured pulmonary wedge pressures. In fact, even though further studies are needed to elucidate its correspondence with ventricular filling pressures, left ventricular diastolic dysfunction retains powerful prognostic significance, because in patients with long-term disease, it indicates the transition to a more severe stage. In our report, two simple, non-operator-dependent

---

### Table 3 Classification of patients according to the aetiology of heart failure

<table>
<thead>
<tr>
<th></th>
<th>Ischaemic, n = 75</th>
<th>Non-ischaemic, n = 45</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>70 ± 8</td>
<td>69 ± 8</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>55/20</td>
<td>32/13</td>
</tr>
<tr>
<td>NYHA class</td>
<td>2.4 ± 0.4</td>
<td>2.6 ± 0.5</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>88 ± 9</td>
<td>87 ± 8</td>
</tr>
<tr>
<td>EF (%)</td>
<td>31.3 ± 6.1</td>
<td>28.7 ± 5.9</td>
</tr>
<tr>
<td>LVEDV (mL)</td>
<td>183.8 ± 48.2</td>
<td>190.6 ± 40.3</td>
</tr>
<tr>
<td>Functional mitral regurgitation (%)</td>
<td>49 (65)</td>
<td>27 (60)</td>
</tr>
<tr>
<td>Severe mitral regurgitation (%)</td>
<td>15 (20)</td>
<td>8 (18)</td>
</tr>
<tr>
<td>PAPs (mmHg)</td>
<td>40.2 ± 12.8</td>
<td>36.9 ± 11.8</td>
</tr>
<tr>
<td>BNP (pg/mL)</td>
<td>450 ± 120.6</td>
<td>363 ± 241.9</td>
</tr>
<tr>
<td>TFC (1/k')</td>
<td>39.8 ± 8.0</td>
<td>38.3 ± 10.1</td>
</tr>
<tr>
<td>VI (/1,000/s)</td>
<td>32.1 ± 9.2</td>
<td>30.5 ± 11.9</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.

---

### Table 4 Classification of patients according to the severity of mitral regurgitation

<table>
<thead>
<tr>
<th>Grades 0–1, EROA &lt; 10 mm², n = 62</th>
<th>Grades 2–3, EROA 10–20 mm², n = 35</th>
<th>Grades 3–4, EROA &gt;20 mm², n = 23</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>69 ± 8</td>
<td>69 ± 11</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>47/15</td>
<td>25/10</td>
</tr>
<tr>
<td>NYHA class</td>
<td>2.0 ± 0.4</td>
<td>2.4 ± 0.5</td>
</tr>
<tr>
<td>Ischaemic/non-ischaemic</td>
<td>50/12</td>
<td>24/11</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>90 ± 6</td>
<td>90 ± 10</td>
</tr>
<tr>
<td>EF (%)</td>
<td>32.3 ± 5.2</td>
<td>30.5 ± 6.6</td>
</tr>
<tr>
<td>LVEDV (mL)</td>
<td>182 ± 46</td>
<td>191 ± 50</td>
</tr>
<tr>
<td>E/E'</td>
<td>10.7 ± 4.8</td>
<td>12.9 ± 6.1</td>
</tr>
<tr>
<td>PAPs (mmHg)</td>
<td>32.4 ± 7.9</td>
<td>38.8 ± 12.7</td>
</tr>
<tr>
<td>BNP (pg/mL)</td>
<td>231 ± 109</td>
<td>449 ± 207</td>
</tr>
<tr>
<td>TFC (1/k')</td>
<td>35.5 ± 6.2</td>
<td>40.3 ± 9.1</td>
</tr>
<tr>
<td>VI (/1,000/s)</td>
<td>32.4 ± 10.1</td>
<td>31.5 ± 13.7</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.

*P < 0.05 vs. other groups, ANOVA or χ² test.
and relatively inexpensive tools were used as a screening evaluation for left ventricular diastolic dysfunction in the ambulatory setting, and echocardiography was only required in those patients in whom a discordance between BNP levels and TFC values was present. An intriguing future development would be the introduction of simple and non-invasive markers of haemodynamic status other than right heart catheterization to help stratify the prognosis of the patients and to verify the hypothesis that an improvement in haemodynamic status could effectively modify the outcome of patients. Such studies are now warranted.

**Figure 1** Significant relationship of the effective regurgitant volume (effective regurgitant orifice area assessed by the PISA method) with $E/E'$ (A), B-type natriuretic peptide levels (B), and thoracic fluid content value (C) in the subset of 23 patients with moderate-to-severe functional mitral regurgitation.

**Figure 2** Significant relationship of $E/E'$ with B-type natriuretic peptide levels (A) and thoracic fluid content value (B) in the whole population of 120 patients.

**Figure 3** Significant relationship between B-type natriuretic peptide levels and thoracic fluid content values ($R = 0.64, P < 0.0001$).
Acknowledgements

We are grateful to Ada Spiezia, RN, and Cosetta Corapi, RN, for their valuable help in data collection.

Conflict of interest: none declared.

References


11. Sohn DI, Chai IH, Lee DJ, Kim HC, Kim HS, Oh BH, Lee MM, Park YB, Choi YS, Seo JD, Lee YW. Assessment of mitral annulus velocity by Doppler tissue imaging in the evaluation of left ventricular diastolic function. J Am Coll Cardiol 1997;30:995–1000.


27. Naguef SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, Waggoner AD, Flachskampf FA. Recommendations for the evaluation of left


