HEART FAILURE WITH PRESERVED EJECTION FRACTION

ASSESSMENT OF LEFT VENTRICULAR DIASTOLIC FUNCTION IS A MUST

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HEART FAILURE WITH PRESERVED EJECTION FRACTION

• At least 50% of the patients presenting with symptoms and signs of heart failure have a normal LV ejection fraction.

• The prevalence of HFPEF is increasing.

• The primary symptom of HFPEF is breathlessness on exercise.

• These patients are often hypertensive, obese, older and much more female.

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CRITERION

• Definitive evidence of CHF
  AND
• Objective evidence of normal LV systolic function in proximity to the CHF event
  AND
• Objective evidence of LV diastolic dysfunction

OBJECTIVE EVIDENCE

Clinical symptoms and signs, supporting laboratory tests and a typical clinical response to treatment, with or without documentation of elevated LV filling pressures, or a low cardiac index

LV EF ≥ 0.50 within 72h of CHF event

Abnormal LV relaxation/filling/distensibility indices on cardiac catheterization

Vasan, Levy, Circulation 2000
Mauer MS et al. **Diastolic dysfunction: can it be diagnosed by Doppler echocardiography?**

“Doppler-derived diastolic parameters do not provide specific information on intrinsic passive diastolic properties, thus, diastolic dysfunction cannot be diagnosed by Doppler echocardiography”

*J Am Coll Cardiol 2004;44:1543–9.*
IVRT

With the delay in relaxation, time from the closing of AoV to the opening of MV (IVRT) increases > 100msec.

Decrease in aortic pressure or increase in LA pressure can shorten IVRT

Therefore, it is safe to conclude that LA pressure is elevated if the IVRT is short (60 ms) in the presence of cardiac disease. However, it is difficult to estimate LA pressure when IVRT is relatively normal.
When myocardial relaxation is markedly abnormal, an early mitral diastolic flow velocity with rapid deceleration is followed by an increased mid-diastolic flow velocity as LV middiastolic pressure falls with continuing relaxation.

JK Oh, L Hatle et al. JACC 2006
When filling pressure is markedly elevated, there may be **diastolic mitral regurgitation**

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Mitral Valve blood flow Doppler

- E/A ratio + Deceleration Time prevalence of primary diastolic dysfunction of 3–5%.
- Isovolumic ventricular relaxation time prevalence of primary diastolic dysfunction of 27%.

- Poor overlap between the two different criteria, with only 2–3% when both indices were combined.

Caruana et al, Eur Heart J, 1999
When combining mitral valve blood flow Doppler with pulmonary vein blood flow Doppler, 93% of patients suspected of HFPEF showed evidence of diastolic LV dysfunction.
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TISSUE DOPPLER:

Normal E’ velocity is unusual in patients with diastolic dysfunction related to a myocardial abnormality or disease.

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TISSUE DOPPLER and progressive diastolic dysfunction

Lam et al, Circulation, 2007
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TISSUE DOPPLER and PCWP

- Ea behaves as a preload-independent index of LV relaxation. \( \frac{E}{E_a} \) ratio relates well to mean PCWP and may be used to estimate LV filling pressures.

[Graph showing relationship between Ea (cm/sec) and PCWP (mmHg) with normal, impaired relaxation, and pseudonormal states.

NL: normal
IR: impaired relaxation
PN: pseudonormal

Nagueh et al, J Am Coll Cardiol 1997]
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TISSUE DOPPLER and LV filling

- E/E' (septal) ratio was the single best predictor of LV filling pressure but did not have adequate discriminatory power to be used in isolation.

- E/E' < 8 accurately predicted normal M-LVDP,
- and E/E' > 15 identified increased M-LVDP.

Ommen et al, Circulation 2000
HEART FAILURE WITH PRESERVED EJECTION FRACTION
TISSUE DOPPLER and LV filling

Conclusions—Of all echocardiographic parameters investigated, the LV filling index $E/E'_\text{lat}$ was identified as the best index to detect diastolic dysfunction in HFNEF in which the diagnosis of diastolic dysfunction was confirmed by conductance catheter analysis.

Kasner et al, Circulation, 2007
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TISSUE DOPPLER

E depends on LA driving pressure, LV relaxation kinetics, and age

E' depends mostly on LV relaxation kinetics and age

E/E' eliminates the effects of age and relaxation kinetics and became a measure of LA driving pressure or LV filling pressure

- E' is the amount of blood entering the LV during early filling.
- E is the gradient necessary to make this blood enter the LV.
- A high E/E' represents a high gradient for a low shift in volume!

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TISSUE DOPPLER:
Time interval between onset of Ea and E

PCWP by Doppler:
\[ \text{LV end-systolic pressure} \times e^{-\text{IVRT/(TEa-E)}} \]

Rivas-Gotz et al, J Am Coll Cardiol 2003
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TISSUE DOPPLER:
Time interval between onset of Ea and E

\( T(Ea-E) \) may have an incremental value in the estimation of LVEDP in patients with normal systolic function and indeterminate E/Ea ratios (8 to 15).

Min et al, Am J Cardiol 2007
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Color M-Mode

Hemodynamics

- The early filling wave propagates rapidly towards the apex (pressure gradient between LV base and the apex)
- LV restoring forces, LV relaxation

Limitations

- Dependence on geometry, systolic function, contractile dyssynchrony
- Influence of preload on Vp in patients with normal EF
- E/Vp could be normal in patients with normal EF and abnormal filling pressures (low sensibility)
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Color M-Mode and wedge pressures

In patients with reduced EF, conventional and recent Doppler indexes can be used to predict the wedge pressure,

but in those with an EF >50%, the E/Ea ratio using lateral Ea has the best correlation with wedge pressure

Rivas-Gotz et al, Am J Cardiol 2003
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LEFT ATRIAL VOLUME and NTproBNP

- LAVi (ellipsoid formula) is a powerful independent predictor of diastolic heart failure in the presence of normal LVEF.
- This simple parameter may be used to rule out heart failure in patients with normal LVEF.

LAVi > 26 mL/m²

Lim TK et al, Eur J Heart Fail 2006
**HEART FAILURE WITH PRESERVED EJECTION FRACTION**

**LEFT ATRIAL VOLUME and diastole**

- LAVi (biplane area-length method), in patients without a history of atrial arrhythmias or valvular heart disease, expresses the severity of diastolic dysfunction and provides an index of cardiovascular risk and disease burden.

*Tsang et al, Am J Cardiol 2002*
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LAVi in addition to E/e’ in HFPEF

In patients with preserved LVEF, adding \( \text{LAVi} > 31 \, \text{mL/m}^2 \) to E/e’ (when E/e’ was in the gray zone) significantly increased the accuracy of E/e’ alone for the estimation of LV filling pressure.

Dokainish et al, J Am Soc Echocardiogr 2010
The purpose of this study was to identify cardiovascular features of patients with HFpEF that differ from those in individuals with HLVH of similar age, gender, and racial background but without failure. A cut-off value of 4,418 ml·g/m².7 separated both groups, with a sensitivity of 83.8% and a specificity of 82.5%.
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How to diagnose HFNEF

- Symptoms or signs of heart failure
- Normal or mildly reduced left ventricular systolic function
- LV EF ≥ 50%
- E/A > 0
- E/e’ > 15
- E/e’ > 0
- BNP > 200 pg/mL
- NT-proBNP > 220 pg/mL
- RI > 0.5
- MD > 140 g/m²
- Atrial fibrillation
- Evidence of abnormal LV relaxation, filling diastolic stiffness, and diastolic dysfunction

Practical Approach to Grade Diastolic Dysfunction

- Septal e’ > 8
- Lateral e’ > 10
- LA < 34 mm²
- LVMI > 122 g/m²
- A-Teal > 10 ms
- IVRT > 160 ms
- AOA > 10 ms
- Vel AE/A > 0.5

Estimation of Filling Pressures in Patients with Normal EF

- E/e’ > 8
- (Normal, Lat., or Av.)
- E/e’ > 14
- Sep. E/e’ > 16
- or La. E/e’ > 12
- or Av. E/e’ > 19
- LA volume < 34 mL/m²
- Ar-A < 6 ms
- Velodoe, A E/A > 0.5
- PAS <60 mmHg
- IVM/IVRT > 2

Paulus WJ, et al. EHJ 2007

Nagueh et al. JASE 2009
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Diastolic Strain Rate and filling pressures

Global $SR_{IVR}$ by 2-dimensional speckle tracking is strongly dependent on LV relaxation. $E/\text{SR}_{IVR}$ can predict LV filling pressures with reasonable accuracy, particularly in patients with normal ejection fraction and in those with regional dysfunction.
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Speckle Tracking and Diastolic Heart Failure

DHF patients: reduced LV longitudinal and radial strains, preserved circumferential deformation and twist

SHF patients: reduced longitudinal, radial, circumferential deformation and twist.

Preserved LV twist and circumferential strain may contribute to normal EF in patients with DHF.

Wang et al, Eur Heart J 2008
• LAS relates significantly with LV diastolic pressures such that LAS decreases in the presence of increased LV filling pressures.

• It is possible to use LAS along with LA pressure or its Doppler echocardiographic surrogate (E/e) to calculate LA chamber stiffness.

• LA stiffness has good accuracy in identifying patients in DHF versus those with only D dysfunction when DHF is defined using invasive criteria.

Echocardiographic Indices Do Not Reliably Track Changes in Left-Sided Filling Pressure in Healthy Subjects or Patients With Heart Failure With Preserved Ejection Fraction

Paul S. Bhella, MD; Eric L. Pacini, MD; Anand Prasad, MD; Jeffrey L. Hastings, MD

Conclusions—Within individual subjects the noninvasive indices E/e’ and E/Vp do not reliably track changes in left-sided filling pressures as these pressures vary, precluding the use of these techniques in research studies with healthy volunteers or the titration of medical therapy in patients with HFpEF. (Circ Cardiovasc Imaging. 2011;4:482-489.)
Is this conclusion justified by the data? The astute reader will note that this editorial has until now conflated “diastolic function” with PCWP. However, these two are separate concepts, although interdependent. Echocardiography can distinguish systolic dysfunction from preserved ejection fraction (determined by LVEF ≥50%). The question is whether Doppler parameters can be used to further categorize patients with congestive heart failure into the 4 broad categories of systolic dysfunction with normal or elevated LA pressure and preserved systolic function with normal or elevated LA pressure. This is the clinically relevant issue. For example, it
In pts with clinical evidence of HF, normal EF on 2D-echo immediately suggests the potential diagnosis of DHF.

Doppler, color flow imaging, and TDI can confirm or exclude the diagnosis of DHF by assessing intrinsic diastolic function and estimating diastolic filling pressure.
It is our hope and recommendation that echocardiographic assessment of diastolic filling pressure can be used as “noninvasive Swan-Ganz catheter”
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Echocardiographic diastolic assessment in particular populations

<table>
<thead>
<tr>
<th>Disease</th>
<th>Echocardiographic measurements and cutoff values</th>
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<tbody>
<tr>
<td>Atrial fibrillation</td>
<td>Peak acceleration rate of mitral E velocity ($\geq 1.900$ cm/s$^2$), IVRT ($\leq 65$ ms), DT of pulmonary venous diastolic velocity ($\geq 220$ ms), E/Vp ratio ($\geq 1.4$), and septal E/e' ratio ($\geq 11$)</td>
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<td>Sinus tachycardia</td>
<td>Mitral inflow pattern with predominant early LV filling in patients with EFs $&lt;$ 50%, IVRT $\leq 70$ ms is specific (79%), systolic filling fraction $&lt;$ 40% is specific (88%), lateral E/e' $&gt;$ 10 (a ratio $&gt;$ 12 has highest the specificity of 96%)</td>
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<td>Hypertrophic cardiomyopathy</td>
<td>Lateral E/e' ($\geq 10$), Ar - A ($\geq 30$ ms), PA pressure ($\geq 35$ mm Hg), and LA volume ($\geq 34$ mL/m$^2$)</td>
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<tr>
<td>Restrictive cardiomyopathy</td>
<td>DT ($\geq 140$ ms), mitral E/A ($\geq 2.5$), IVRT ($\leq 50$ ms has high specificity), and septal E/e' ($\geq 15$)</td>
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<tr>
<td>Noncardiac pulmonary hypertension</td>
<td>Lateral E/e' can be applied to determine whether a cardiac etiology is the underlying reason for the increased PA pressures (cardiac etiology: E/e' $&gt; 10$; noncardiac etiology: E/e' $&lt; 8$)</td>
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<td>Mitral stenosis</td>
<td>IVRT ($\leq 60$ ms has high specificity), IVRT/T$_{E/e'}$ ($\leq 4.2$), mitral A velocity ($\geq 1.5$ m/s)</td>
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<tr>
<td>MR</td>
<td>Ar - A ($\geq 30$ ms), IVRT ($\leq 60$ ms has high specificity), and IVRT/T$_{E/e'}$ ($\leq 3$) may be applied for the prediction of LV filling pressures in patients with MR and normal EFs, whereas average E/e' ($\geq 15$) is applicable only in the presence of a depressed EF</td>
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Nagueh et al, J Am Soc Echocardiogr 2009
92% of pts with a history of HFpEF and evidence of LV concentric remodelling had an elevated LVEDP and all of them had at least one haemodynamic or Doppler echo index of abnormal LV relaxation, filling, or diastolic stiffness. In this group of patients, acquisition of data on diastolic LV dysfunction therefore provided no additional diagnostic information.

Concentric LV remodelling has important implications for the diagnosis of HFNEF and is a potential surrogate for direct evidence of diastolic LV dysfunction.

Yturralde RF et al. Prog Cardiovasc Dis 2005
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STRESS ECHO
A significant proportion of patients require exercise to diagnose HFNEF. 
Sa appears to be a significant independent predictor of HFNEF, which may increase the diagnostic value of models utilizing the variables recommended by the European Society of Cardiology guidelines.

30 patients with HFNEF:
- 24 (80%) by the combined resting echocardiography, electrocardiography, and NT-proBNP analysis
- 6 (20%) patients exclusively on the exercise Doppler echocardiography.

Meluzin et al, Eur J Echocardiogr 2011
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STRESS ECHO

Worsening of functional mitral regurgitation (MR) during dynamic exercise Doppler echocardiography in four female patients with HFPEF.

MR worsening during exercise
- increase in systolic mitral tenting area and in E/Ea ratio,
- local left ventricular (LV) remodelling was not aggravated.

Marechaux et al, Eur J Echocardiogr 2010
However, they demonstrate discordant findings in several of the subjects who are elderly or have HFrEF. In these cases, the PCWP decreased whereas the E/e’ increased. All but one of these discordant findings occurred with variations in the PCWP below 15 mm Hg, arguably not a hemodynamically significant finding if the goal is to categorize patients into the 4 broad hemodynamic presentations of congestive heart failure.
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Incapability of dilating the LV chambers (greater myocyte, stiffness).

Limitation in increasing stroke volume

Excessive elevation of LV filling pressures during exercise

Exercise intolerance
HEART FAILURE WITH PRESERVED EJECTION FRACTION

- Relaxation abnormalities
- ↑LV stiffness (fibrosis, myocyte hypertrophy)

Yamamoto et al, Circ J 2009
HEART FAILURE WITH PRESERVED EJECTION FRACTION

Mitral Valve blood flow Doppler

Survival free of hospital admission in patients with EF < 35%.

Giannuzzi et al, J Am Coll Cardiol, 1996
HEART FAILURE WITH PRESERVED EJECTION FRACTION

Mitral Valve blood flow and Pulmonary vein flow Doppler

Assessment of ARd-Ad (≥ 30 ms) exhibited an independent value in the prognostic evaluation of patients with LV systolic dysfunction.

Group 1: restrictive mitral flow
Group 2: Ard - Ad ≥ 30 ms
Group 3: Ard - Ad < 30 ms

A: survival free from cardiac mortality
B: cardiac event-free survival
C: freedom from heart failure

Dini et al, J Am Coll Cardiol 2000
Colour M-mode Doppler $V_p$ correlated significantly with invasive indices of LV relaxation, $dP/dt_{min}$, and $\tau$ during AF on the beat-by-beat basis.

*Kamiguchi et al, E J Echocard 2009*
HEART FAILURE WITH PRESERVED EJECTION FRACTION
TISSUE DOPPLER and PCWP

Dokainish et al, Circulation 2004
HEART FAILURE WITH PRESERVED EJECTION FRACTION

TISSUE DOPPLER and PCWP

- Both BNP and mitral E/Ea have high sensitivity for PCWP 15 mm Hg
- In patients without cardiac disease, BNP appears more accurate than E/Ea for PCWP 15 mm Hg
- E/Ea appears more accurate in patients with cardiac disease

Dokainish et al, Circulation 2004
Mitral annulus velocity is useful in the detection of impaired left ventricular relaxation and estimation of filling pressure even in patients with atrial fibrillation.

*Sohn et al, J Am Soc Echocardiogr 1999*
HEART FAILURE WITH PRESERVED EJECTION FRACTION

Prognostic value of TDI

E' gives incremental predictive power for cardiac mortality compared to clinical data and standard echocardiographic measurements.

Wang et al, J Am Coll Cardiol 2003
S’ and E’, particularly their combination, seem to be useful predictors of CV events in patients with HFPEF with AF.

Shin et al, J Am Soc Echocardiogr 2010
HEART FAILURE WITH PRESERVED EJECTION FRACTION

Myocardial Performance Index and HFNEF

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<tr>
<th>Variables</th>
<th>Univariate</th>
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<td>HR (95% CI)</td>
<td>P Value</td>
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<td>Age</td>
<td></td>
<td>1.05 (1.01–1.08)</td>
<td>0.010</td>
<td>1.01 (0.94–1.04)</td>
<td>0.919</td>
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<td>CAD</td>
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<td>6.70 (3.29–13.62)</td>
<td>&lt;0.001</td>
<td>2.27 (0.97–5.30)</td>
<td>0.058</td>
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<td>Heart failure</td>
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<td>3.01 (1.15–7.92)</td>
<td>0.025</td>
<td>1.20 (0.38–3.74)</td>
<td>0.757</td>
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<td>Diabetes</td>
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<td>3.61 (1.78–7.32)</td>
<td>&lt;0.001</td>
<td>2.91 (1.25–6.83)</td>
<td>0.014</td>
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<td>Log NT-ProBNP</td>
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<td>1.70 (1.10–2.29)</td>
<td>&lt;0.001</td>
<td>1.45 (1.05–2.00)</td>
<td>0.025</td>
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<td>BUN</td>
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<td>1.03 (1.00–1.05)</td>
<td>0.038</td>
<td>0.99 (0.98–1.13)</td>
<td>0.543</td>
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<td>Diuretics</td>
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<td>3.11 (1.53–6.30)</td>
<td>0.002</td>
<td>0.81 (0.33–1.99)</td>
<td>0.640</td>
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<td>Ejection fraction</td>
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<td>0.90 (0.86–0.94)</td>
<td>&lt;0.001</td>
<td>0.95 (0.88–1.01)</td>
<td>0.115</td>
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<td>LVESD</td>
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<td>2.15 (1.15–4.03)</td>
<td>0.016</td>
<td>0.94 (0.85–1.04)</td>
<td>0.214</td>
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<td>LAVI</td>
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<td>1.02 (1.01–1.03)</td>
<td>&lt;0.001</td>
<td>1.04 (0.97–1.12)</td>
<td>0.229</td>
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<td>IVSTd</td>
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<td>1.27 (1.11–1.44)</td>
<td>&lt;0.001</td>
<td>1.19 (0.91–1.56)</td>
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<td>PWTd</td>
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<td>1.24 (1.00–1.54)</td>
<td>&lt;0.001</td>
<td>0.74 (0.52–1.04)</td>
<td>0.085</td>
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<td>LVMI</td>
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<td>1.01 (1.01–1.02)</td>
<td>&lt;0.001</td>
<td>1.01 (0.97–1.13)</td>
<td>0.235</td>
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<td>s′</td>
<td></td>
<td>0.53 (0.40–0.69)</td>
<td>&lt;0.001</td>
<td>0.72 (0.47–1.12)</td>
<td>0.134</td>
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<td>e′</td>
<td></td>
<td>0.61 (0.46–0.80)</td>
<td>&lt;0.001</td>
<td>1.10 (0.72–1.67)</td>
<td>0.666</td>
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<td>a′</td>
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<td>0.71 (0.59–0.86)</td>
<td>&lt;0.001</td>
<td>1.19 (0.91–1.57)</td>
<td>0.201</td>
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<td>E/e′</td>
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<td>1.15 (1.01–1.23)</td>
<td>0.032</td>
<td>0.99 (0.91–1.07)</td>
<td>0.763</td>
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<tr>
<td>TDI-MPI &gt; 0.66</td>
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<td>10.11 (4.52–22.6)</td>
<td>&lt;0.001</td>
<td>2.90 (1.01–8.28)</td>
<td>0.030</td>
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</table>

Kim et al, Clin Cardiol 2011
HEART FAILURE WITH PRESERVED EJECTION FRACTION

LA STI in HFPEF

In patients with HFNEF, LA subendocardial systolic and diastolic dysfunction is common and possibly associated with the same fibrotic processes that affect the subendocardial fibers of the left ventricle and to a lesser extent with elevated LV filling pressures.

<table>
<thead>
<tr>
<th>Variable</th>
<th>HFNEF (n = 119)</th>
<th>Asymptomatic LVDD (n = 301)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA volumes</td>
<td></td>
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</tr>
<tr>
<td>LA Vol\textsubscript{max} (mL)</td>
<td>64.8 ± 24</td>
<td>45 ± 16</td>
<td>&lt;.0001</td>
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<tr>
<td>LA Vol\textsubscript{min} (mL)</td>
<td>27.8 ± 18.3</td>
<td>15.3 ± 9.5</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>LA Vol\textsubscript{p} (mL)</td>
<td>48.8 ± 21.1</td>
<td>33.5 ± 12.9</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>LA total emptying volume (mL)</td>
<td>37 ± 11</td>
<td>29.7 ± 9.5</td>
<td>.0006</td>
</tr>
<tr>
<td>LA active emptying volume (mL)</td>
<td>21 ± 7.5</td>
<td>18.2 ± 6.4</td>
<td>.0885</td>
</tr>
<tr>
<td>LA Doppler parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A mitral inflow peak velocity (cm/s)</td>
<td>65.5 ± 26.8</td>
<td>76.6 ± 19.8</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Septal a’ mitral annular peak velocity (cm/s)</td>
<td>6.8 ± 2.3</td>
<td>9.1 ± 2</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Lateral a’ mitral annular peak velocity (cm/s)</td>
<td>8.3 ± 2.9</td>
<td>10.6 ± 2.4</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Septal-lateral a’ mitral annular peak velocity (cm/s)</td>
<td>7.5 ± 2.4</td>
<td>9.8 ± 2</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>LA remodeling</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA Vol\textsubscript{max} index (mL/m\textsuperscript{2})</td>
<td>325 ± 13</td>
<td>235 ± 8</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>LA Vol\textsubscript{max} index ≥ 34 mL/m\textsuperscript{2}</td>
<td>78%</td>
<td>19.6%</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>LA systolic function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA total emptying fraction (%)</td>
<td>57 ± 14.7</td>
<td>66 ± 10.6</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>LA active emptying fraction (%)</td>
<td>43 ± 16.2</td>
<td>54.3 ± 13</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>LA systolic dysfunction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA total emptying fraction &lt; 50%</td>
<td>31%</td>
<td>5.6%</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>LA active emptying fraction &lt; 35%</td>
<td>26%</td>
<td>9.3%</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

Morris et al, J Am Soc Echocardiogr 2011
Global $\text{SR}_{\text{IVR}}$ by 2-dimensional speckle tracking is strongly dependent on LV relaxation. $\text{E}/\text{SR}_{\text{IVR}}$ can predict LV filling pressures with reasonable accuracy, particularly in patients with normal ejection fraction and in those with regional dysfunction.

Open circles: normal EF
Closed circles: depressed EF

Wang et al, Circulation 2007
HEART FAILURE WITH PRESERVED EJECTION FRACTION

Untwisting Rate and Heart Failure

Wang et al, Eur Heart J 2008
HEART FAILURE WITH PRESERVED EJECTION FRACTION

LA longitudinal systolic and diastolic dysfunction could be related to reduced functional capacity during effort in patients with HFNEF.

<table>
<thead>
<tr>
<th>Variable</th>
<th>HFNEF (n = 119)</th>
<th>Asymptomatic LVDD (n = 301)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA longitudinal diastolic function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA-Strain (%)</td>
<td>19.9 ± 7.3</td>
<td>30.8 ± 11.4</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>LA-SR (s⁻¹)</td>
<td>1.17 ± 0.46</td>
<td>1.67 ± 0.59</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>LA longitudinal systolic function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA-SRa (s⁻¹)</td>
<td>−1.17 ± 0.63</td>
<td>−1.80 ± 0.70</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>LA longitudinal diastolic dysfunction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA-SR &lt; 0.82 s⁻¹</td>
<td>28.5%</td>
<td>1.3%</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>LA longitudinal systolic dysfunction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA-SRa &gt; −1.32 s⁻¹</td>
<td>65.5%</td>
<td>30%</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

*Morris et al, J Am Soc Echocardiogr 2011*
Exercise with shortened diastole

- Arterial Stiffness
- Diabetes & LVH
- Myocardial fibrosis

↓ Systolic function
↓ Long axis function
↓ Strain

↓ LV Rotation
↓ Delayed untwisting

↓ Ventricular suction
↓ Recoil of annulus

↓ Early diastolic filling
↓ Late diastolic filling

↑ End-diastolic pressure (E/E’)

↑ Breathlessness
HEART FAILURE WITH PRESERVED EJECTION FRACTION

LA STI in HFPEF

Morris et al, J Am Soc Echocardiogr 2011
HEART FAILURE WITH PRESERVED EJECTION FRACTION
Right ventricular STI in HFPEF

In patients with HFNEF, RV subendocardial systolic and diastolic dysfunction are common and possibly associated with the same fibrotic processes that affect the subendocardial layer of the LV and to a lesser extent with RV pressure overload.

<table>
<thead>
<tr>
<th></th>
<th>HFNEF (n = 201)</th>
<th>Asymptomatic LVDD (n = 364)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV systolic function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV global longitudinal systolic strain, %</td>
<td>-14.41 ± 3.80</td>
<td>-16.90 ± 4.28</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>TAPSE, mm</td>
<td>16.5 ± 3.5</td>
<td>18.7 ± 4.0</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>RV fractional area change, %</td>
<td>40.1 ± 9.2</td>
<td>44.0 ± 8.7</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Lateral s’ tricuspid annular peak velocity by TDI, cm/s</td>
<td>11.0 ± 1.9</td>
<td>13.0 ± 2.8</td>
<td>.0005</td>
</tr>
<tr>
<td>RV diastolic function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV global longitudinal diastolic SRe, s⁻¹</td>
<td>0.86 ± 0.33</td>
<td>1.02 ± 0.34</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Lateral e’ tricuspid annular peak velocity by TDI, cm/s</td>
<td>9.3 ± 2.8</td>
<td>13.2 ± 4.2</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>RV wall thickness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV free wall, mm</td>
<td>5.5 ± 0.9</td>
<td>4.9 ± 0.9</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>RV chamber dimensions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV basal diameter, mm</td>
<td>30.2 ± 5</td>
<td>27.1 ± 4</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>RV mid cavity diameter, mm</td>
<td>24.5 ± 6</td>
<td>23.2 ± 5</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>RV longitudinal dimension, mm</td>
<td>69.2 ± 10</td>
<td>65.5 ± 8</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

Morris et al, J Am Soc Echocardiogr 2011
HEART FAILURE WITH PRESERVED EJECTION FRACTION

Right ventricular STI in HFPEF

RV longitudinal systolic and diastolic dysfunction could contribute to the symptomatology of patients with HFNEF.

Morris et al, J Am Soc Echocardiogr 2011
HEART FAILURE WITH PRESERVED EJECTION FRACTION

Right ventricular STI in HFPEF

Morris et al, J Am Soc Echocardiogr 2011
HEART FAILURE WITH PRESERVED EJECTION FRACTION
LEFT MECHANICAL DYSSYNCHRONY

<table>
<thead>
<tr>
<th>Grades of Diastolic Dysfunction</th>
<th>Normal (n = 11)</th>
<th>Grade 1 (n = 29)</th>
<th>Grade 2 (n = 37)</th>
<th>Grade 3 (n = 15)</th>
<th>ANOVA p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF, %</td>
<td>64 ± 8</td>
<td>62 ± 9</td>
<td>61 ± 7</td>
<td>60 ± 9</td>
<td>NS</td>
</tr>
<tr>
<td>WMSI</td>
<td>1.1 ± 0.2</td>
<td>1.1 ± 0.1</td>
<td>1.1 ± 0.1</td>
<td>1.2 ± 0.2</td>
<td>NS</td>
</tr>
<tr>
<td>Mean Em, cm/s</td>
<td>8.1 ± 0.9</td>
<td>6.3 ± 0.4*</td>
<td>4.8 ± 0.9*†</td>
<td>3.6 ± 1.2††</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean Sm, cm/s</td>
<td>6.6 ± 1.6</td>
<td>5.1 ± 1.1*</td>
<td>5.0 ± 1.2*</td>
<td>4.6 ± 1.1*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E/A</td>
<td>1.27 ± 0.18</td>
<td>0.69 ± 0.07*</td>
<td>0.94 ± 0.19*†</td>
<td>2.27 ± 0.13††</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DT, ms</td>
<td>181 ± 27</td>
<td>254 ± 44*</td>
<td>200 ± 36†</td>
<td>134 ± 10††</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E/Em</td>
<td>8.1 ± 1.8</td>
<td>10.2 ± 2.9*</td>
<td>14.8 ± 5.5*†</td>
<td>24.7 ± 4.6††</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Te-SD, ms</td>
<td>16 ± 3</td>
<td>21 ± 5*</td>
<td>28 ± 9*†</td>
<td>41 ± 17††</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ts-SD, ms</td>
<td>29 ± 14</td>
<td>33 ± 18</td>
<td>37 ± 17</td>
<td>29 ± 17</td>
<td>NS</td>
</tr>
</tbody>
</table>

Pui-Wai Lee et al, J Am Coll Cardiol 2011
LV diastolic mechanical dyssynchrony may impair diastolic function and contribute to the pathophysiology of HFPEF, complicating ACS.

Pui-Wai Lee et al, J Am Coll Cardiol 2011
HEART FAILURE WITH PRESERVED EJECTION FRACTION

Conclusions

• Echocardiography provides important information noninvasively.

• Echocardiographic Doppler evaluation of LV filling in patients with heart failure has an important role in the individuation of abnormalities, in the management and in the prognosis assessment.
**Normal Diastolic Function**

- E
- A
- DT

0.75 < E/A < 1.5
DT > 140 ms

**Mild Diastolic Dysfunction**

- E/A ≤ 0.75
DT ≥ 230 ms
(Age > 40)

**Moderate Diastolic Dysfunction** (Pseudonormal)

- 0.75 < E/A < 1.5
DT > 140 ms

**Severe Diastolic Dysfunction** (Restrictive)

- E/A > 1.5
DT < 160 ms
(Age > 40)

---

**DIASTOLIC DYSFUNCTION CLASSIFICATION**

- Normal Diastolic Function Pattern
- Relaxation Deficit Pattern
- Pseudonormal Pattern
- Restrictive Pattern

---

**Mitral Flow**

- 0.75 < E/A < 1.5
DTE > 140 ms

- E/A ≤ 0.75

- 0.75 < E/A < 1.5
DTE > 140 ms

- E/A > 1.5
DTE < 140 ms

---

**Pulmonary Flow**

- S > D
ARdur < Adur

- S > D
ARdur > Adur + 30 ms

- S < D or ARdur > Adur + 30 ms

---

**Tissue Doppler**

- E/E' < 10

- E/E' ≥ 10

---

Source: J Am Board Fam Pract © 2005 American Board of Family Practitioners
Mid-diastolic “L” velocity also is evident in the mitral annulus velocity recording by TDI.
Diastolic Heart Failure Can Be Diagnosed by Comprehensive Two-Dimensional and Doppler Echocardiography

Jae K. Oh, MD,* Liv Hatle, MD,* A. Jamil Tajik, MD,* William C. Little, MD†

Rochester, Minnesota; and Winston-Salem, North Carolina
Constriction

Predominant Diastolic Revers flow during Esp

Insp

Esp

12 cm/sec
Relaxation abnormality  →  Pseudonormal  →  Restricted physiology

Increased filling pressure
HEART FAILURE WITH PRESERVED EJECTION FRACTION

Diastolic dysfunction, as assessed by echocardiography, is a powerful predictor of adverse prognosis in the community.

Redfield et al, JAMA 2003
At the end of systole, left ventricular (LV) relaxation begins as an initial diastolic process, and LV pressure falls rapidly as the LV expands. This relaxation phase is accompanied by active movement of the mitral annulus away from the apex. The velocity of LV dilatation and mitral annular movement during early diastole correlates well with how fast the LV fills and relaxes, respectively.
Heart as a Roller-Pump

A cardiac cycle consists of systolic (contraction) and diastolic (relaxation and filling) phases that are linked closely together for optimal function of the heart.

Normal diastolic function allows adequate filling of the heart without an excessive increase in diastolic filling pressure both in the resting state and with stress or exertion.
Abnormal Fx of the Tube

- **Sticky tube**
- **Stiff tube**

Sticky tube cannot expand quickly in the early phase of expansion but can still expand further when the pressure is imposed on the tube. (Abnormal relaxation)

Stiff tube can expand at a near normal rate during the early phase but excessive pressure is needed for adequate expansion (increase stiffness)
HEART FAILURE WITH PRESERVED EJECTION FRACTION

Prognostic value of TDI in HFPEF and AF

- $S'$ and $E'$, particularly their combination, seem to be useful predictors of CV events in patients with HFPEF with AF.

Shin et al, J Am Soc Echocardiogr 2010
HEART FAILURE WITH PRESERVED EJECTION FRACTION

Mitral Valve blood flow and Pulmonary vein flow Doppler

$A' - A$ has the highest accuracy in identifying pseudonormal mitral pattern in an unselected population.

Rossi et al, Echocardiography 2001
HEART FAILURE WITH PRESERVED EJECTION FRACTION

TISSUE DOPPLER

- The mitral E wave is augmented when there is an increased LA-to-LV pressure gradient. The E’ is reduced and delayed in the presence of slow relaxation.

- Thus increased E/E’ ratio indicates that the increased E was due to an elevation of LA pressure or impairment in LV filling pressure, not a fall in LV diastolic pressure.
HEART FAILURE WITH PRESERVED EJECTION FRACTION

STI and progressive severity of diastolic dysfunction

Park et al, J Am Soc Echocardiogr 2007