Left Ventricular Diastolic Dysfunction

I) Importance of Diastolic function:

Diastolic function is an important element of cardiac function. The ventricle must fill properly to eject enough stroke volume, required by the body. The assessment of left ventricular diastolic function non-invasively has become increasingly important for many reasons:

1- In most cardiac conditions that affect the myocardium, an impairment of active relaxation is often the first abnormality to occur. Therefore, early detection and assessment of the severity of this impairment may lead to application of preventive measures to delay or avoid the occurrence of clinical heart failure. (*Hunt, et al., 2005*)

2- Diastolic dysfunction may point to an early sign of myocardial involvement, when it is recognized as the earliest manifestation of ischemia.

3- Diastolic dysfunction is recognized in patients with congestive heart failure in whom normal systolic function is present as measured by ejection fraction. In addition, diastolic dysfunction is present in 44 percent of hypertensive, diabetic, obese patients. (*Poirier, et al., 2000*)

4- Lastly, the development of new treatments is reported to improve diastolic function and thus congestive heart failure, like calcium blockers, angiotensin converting enzyme inhibitors and beta-blockers. (*Poirier, et al., 2000*)
II) Epidemiology & Pathophysiology of diastolic dysfunction

In general, the prevalence of heart failure increases with age and is similar in women and men. The prevalence of heart failure with a decreased ejection fraction increase with age, but is more common in men than in women in any age group, unlike the prevalence of HFrEF which dramatically increase even with age (more than HF with depressed ejection fraction) and is less common in men than is women at any age. (Ceia, et al., 2002)

In the past, heart failure with preserved Ejection Fraction (HFrEF) was known as Diastolic heart failure. Although, this term was proved to be inaccurate, as the physiological abnormalities are not only restricted to Diastole e.g. many patients with symptoms and signs of HFrEF may have many causes rather than diastolic dysfunction, so diastolic heart failure more properly represents a group of patients with heart failure and preserved left ventricular ejection fraction. (Daly. 2009)

Due to the paucity of studies measuring diastolic function in patients with normal ejection fractions, some have agreed that both terms, heart failure with preserved ejection fraction (HFrEF) and heart failure with normal ejection fraction (HFnEF) can be used. But, HFnEF is the term that has been used in current heart failure management guidelines. (Adams, et al., 2006)

Ejection fraction is a variable with a fairly normal distribution within the population and the threshold value in order to define normal versus reduced ejection fraction is arbitrary although consensus towards an ejection fraction higher than 50% to designate HFrEF, but patient with
borderline reduction in ejection fraction (40-50%), making the definition more. (*Redfield et al., 2003*)

Finally, the European-working group defines HFpEF as:

- **a-** Symptoms and signs of congestive heart failure.
- **b-** Left ventricular ejection fraction (LVEF) > 50% and non-dilated left ventricle less than 97ml/m2.
- **c-** Evidence of increased left ventricular filling pressure.

The last criterion is fulfilled in one of the three ways:

1. Pulmonary capillary wedge pressure (PCWP) more than 12 mmHg or left ventricular end diastolic pressure more than 16 mmHg
2. Echocardiographic evidence of elevated left ventricular filling pressure (E/e’ > 15).
3. Echocardiographic evidence (E/e’ > 8 but < 15 and a positive B natriuretic peptide BNP > 200 pg /ml or NT-BNP > 220 pg /ml). (*Lau, et al., 2013*)

**Figure (1):** Algorithm helping for the diagnosis of elevated ventricular pressure in patients with normal ejection fraction.

**Figure (1):** Algorithm helping for the diagnosis of elevated ventricular pressure in patients with normal ejection fraction.
III) Pathophysiology of Diastolic dysfunction:

Understanding of the pathophysiologic mechanism of HFpEF necessitates an understanding of left ventricular diastolic and systolic function and the manner in which left ventricular function is affected by volume status (which determine preload together with left ventricular geometry) and arterial system (which determine afterload together with left ventricular geometry). Although abnormal diastolic function plays the most important role in the pathogenesis of HFpEF, many mechanisms also shares in the pathophysiological process in many patients. (Redfield. 2012)

Most pathophysiological evidence occurs during diastole, which is defined as the part of cardiac cycle that begins with closure of aortic valve and ends with equalization of left atrial and left ventricular pressure just before closure of mitral valve. In general, diastolic function relays on five important parameters:

1- Heart rate i.e. diastole is disproportionately shortened with faster heart rate.

2- Active myocardial relaxation affecting left ventricular relaxation.

3- Left ventricular stiffness e.g. collagen composition and infiltration (pressure volume relationship). (Daly. 2009)

4- Circulating fluid volume.

5- Anatomic considerations e.g. left atrium- mitral valve- pericardium- left ventricular mass and pulmonary veins.
Although the complex mechanism of diastolic function, the most important component sharing in diastolic dysfunction are left ventricular diastolic stiffness and left ventricular relaxation, which leads to inability of the ventricles to fill properly during rest and exercise together with increase in diastolic pressure.\textit{(Redfield.2012)}

1) \textbf{Left ventricular relaxation:}

Left ventricular relaxation is a process demanding active energy that starts during ejection phase of systole and continues through iso-volumic relaxation and rapid filling phase. In healthy heart, enhancement of relaxation during exercise induced by catecholamines, lowers left ventricular pressure in early diastole, thus enhanced relaxation increase LA-LV pressure gradient without increase left atrial pressure and enhance filling during exercise without needing for increase LA pressure.\textit{(Lau, et al., 2013)}

Left ventricular relaxation is a complex mechanism related to the cellular mechanisms involved with actin myosin cross bridge detachment; this detachment needs intracellular calcium uptake (process requiring energy) into the sarcoplasmic reticulum.\textit{(Redfield.2012)}

Impaired calcium uptake or prolongation of the calcium transient may be caused by many mechanisms but mainly by decreased reuptake of calcium into sarcoplasmic reticulum as a result of reduce in the amount or activity of the sarcoplasmic reticulum calcium ATPase [SERCA]. \textit{(Redfield.2012)}

B adrenergic stimulation plays a significant role in calcium reuptake via activation of protein kinase A (PKA) which phosphorylate phospholamban removing its tonic inhibition of SERCA activity hastening calcium reuptake and left ventricular relaxation.\textit{(Bilchick, et al., 2007)}
Many studies revealed that there are increased levels of catecholamines in patients with HFpEF sharing in B adrenergic receptor down regulation and desensitization suggesting that defective B adrenergic signaling may share in relaxation impairment in HFpEF. (Kitzman, et al., 2002)

Another mechanism involved in impaired left ventricular relaxation is reduction of phospholamban phosphorylation through increased activity of proteinkinase C (PKC) through the effect on protein phosphatases impairing calcium reuptake impairing relaxation. (Braz et al., 2004)

Finally, impaired B adrenergic stimulation, protein kinase A signaling, reduced SERCA activity and amount and increase protein kinase C activity all might provide potential therapeutic targets for treatment of heart failure with normal ejection fraction. (Redfield. 2012)

2) **Left ventricular diastolic stiffness:**

Elastance or stiffness is defined as the relationship between the change in strain and stress. On the chamber level, the elastance of the left ventricle varies over the cardiac cycle and both the end systolic and end diastolic elastance, are defined by the changes in systolic or diastolic pressure accompanied with changes in end systolic or end diastolic volume. (Redfield.2012)

Increasing left ventricular diastolic stiffness mandates higher left atrial pressure to maintain filling with consequence of increase of pulmonary venous pressure and pulmonary congestion or reduction in cardiac output if left atrial pressure is not elevated. (Redfield.2012)

Left ventricular stiffness is affected by many factors that influence the cardiac extracellular matrix, cellular process or myocyte level and the myofibers themselves. (Kass, et al., 2004)
The increase in extracellular matrix is accompanied by impairment of relaxation and increase in diastolic stiffness. For example, increase in fibrosis and collagen deposition occurring in patients with hypertensive heart disease lead to increased stiffness. Also restrictive cardiomyopathies, have a similar pathophysiology but differ in the pathology underlying the change in ventricular compliance including either intracellular lysosomal engorgement with Sphingolipids (Fabry’s disease), extracellular amyloid deposition (Cardiac amyloidosis, endocardial fibrosis from eosinophilic injury {Löffler’s endocarditis}) or others. *(Lau, et al., 2013)*

On myofiber level, the change in the giant molecular structure such as titin also shares in myocardial diastolic tension; for example, titin isoform transforms into the less complaint N2B isoform or titinphosphorylation state can affect passive myofiber stiffness and perturbations in patient with heart failure with normal ejection fraction. *(Borbely, et al., 2009)*

3) Other Factors affecting diastolic function:

A) Vascular dysfunction:

Vascular stiffness or dysfunction increase with, hypertension, diabetes mellitus and age. Its incidence is lower in men. All of them are risk factors for heart failure with preserved ejection fraction. *(Redfield, et al., 2005)*

Vascular rarefaction results in decrease in micro vascular density with diabetes, hypertension and aging further impairing flow reserve of the heart and periphery, so the vascular dysfunction predisposes to impaired diastolic and systolic dysfunction in HFnEF. *(Redfield M.2012)*
Also, pulmonary vascular function has shown to be abnormal in patients with HFnEF as a result of presence of chronic pulmonary venous hypertension and aging related changes.\textit{(Tolle J, et al., 2008)}

\textbf{B) Impaired reserve function:}

Impaired vascular reserve (ability to vasodilate with exercise), ventricular systolic reserve, ventricular diastolic reserve and ventricular coupling reserve have been now documented in patients with HFP EF and shares in exercise intolerance\textit{(Tan et al., 2009)}.

\textbf{C) Atrial dysfunction:}

Although most studies have given attention to ventricular function in HFnlEF, atrial function may also have an important role in pathophysiological process of HFnlEF. Left atrial systolic function compensate for reduced early filling in the early stage of HFnlEF but on a late stage, atrial failure occur lead to heart failure decompensation\textit{(Phan, et al., 2009)}.

Reduced left atrial systolic function decrease left ventricular filling in the setting of impaired relaxation and needs higher mean left trial pressure to augments early diastolic filling, so enlarged and dysfunction atria may share in the pathophysiological process of HFnlEF\textit{(Redfield.2012)}.

\textbf{D) Neurohumeral activation:}

Neurohumeral activation play an important role in the progression of HFP EF. In general, the activation of sympathetic nervous system, aldosterone and the natriuretic peptide system occur in heart failure patients regardless of ejection fraction, is proven\textit{(Guder, et al., 2007)}.
E) Peripheral factors and Ergo Reflex Control:

Ventilatory drive and vascular tone are influenced by changes in mechanical and metabolic sensor. Stimulation in peripheral muscle during exercise and reflex control perturbations during exercise (ergo reflex) was been well described in heart failure with impaired ejection fraction in which the magnitude of the disruption is more in subjects with decreased muscle mass. (Piepoli, et al., 2006)

IV) Stages of diastolic dysfunction:

1) **Normal diastolic function:**

Generally, normal young individuals with normal cardiac function have normal E/A ratio > 1, Isovolumic relaxation time (IVRT) < 100 sec, Deceleration time (DT) 160 – 260 msec, pulmonary S/D ratio > 1, pulmonary Atrial reversal wave (AR) <35 cm/sec, tissue Doppler mitral annular velocity (E') > 8, E/e'<8. (Lau, et al., 2013)

2) **Stage I (Impaired relaxation):**

Characterized by a decrease in peak transmitral pressure gradient therefore E/A ratio <1, prolonged IVRT> 100 sec, prolongation of Deceleration time slope> 260 msec, normal pulmonary venous S/D ratio, TDI E' <8, E/e'>15 at rest or with exercise (Marwick, 2012).

3) **Stage II (Pseudonormal Filling pattern):**

When left atrial pressure increases with progressive left ventricular disease, transmitral flow pattern (E/A ratio, DT, IVRT) return to normal values.

Exception of this are patients with marked elevations of filling pressures and low heart rate who might show a mid-diastolic (L) wave. Pseudo normal pattern can’t be differentiated from normal one without the performance of other steps. The first step is suspicion of the
condition. Normal transmitral flow in the setting of LVH or systolic dysfunction is mostly pseudo normal. The second step is to estimate left atrial size followed by estimation of filling pressure (E/e’). Other surrogate markers that are only accepted in case of systolic dysfunction include effect of Valsalva maneuver, blunting of pulmonary venous S wave and the flow propagation velocity < 50 cm/sec. (Marwick, 2012)

4) **Stage III/IV (Restrictive pattern):**

Continued increase in filling pressure with marked decrease in left ventricular compliance leads to marked increase in E velocity, E/A ratio > 2, short DT time < 150 msec, short IVRT < 70 msec (Marwick, 2012).

The systolic forward flow velocity in pulmonary vein is decreased due to increased left atrial pressure and decreased compliance of left atrial. Tissue Doppler E’ is <8 with E/e’ ratio> 15 (Connolly and Oh, 2012).

The presence of reversibility (reverse the filling pattern to grade 1 or 2 dysfunction with Valsalva maneuver or after diuresis) is very important indicating grade III dysfunction.

Failure of reversal means grade IV dysfunction (end stage diastolic dysfunction). (Marwick, 2012)

Although, if the restrictive filling pattern doesn't change with valsalva maneuver; reversibility can’t be excluded as valsalva maneuver may not be adequate or the filling pressure is too high to be changed by valsalva maneuver. (Connolly, et al., 2012)

V) **Evaluation of diastolic dysfunction:**

Heart failure with preserved ejection fraction is responsible for about 50 percent of all cases of heart failure and patients with a symptomatic diastolic dysfunction are at a higher risk for developing congestive symptoms and adverse outcomes irrespective of the cause (Aurigemma, et
Early identification of those patients is important to prevent progression of the disease. (Pirat, et al., 2007)

VI) Diagnosis of Diastolic dysfunction:

Diastolic function can be evaluated through laboratory measures (BNP and NT pro BNP), invasive methods (Catheterization) and non-invasive methods (Echocardiography). (Lau, et al., 2013)

A) Laboratory assessment (BNP and NT-pro BNP):

Brain natriuretic peptide (BNP) and N terminal pro BNP (NT pro BNP) are considered a reliable biochemical marker of cardiac function as well as good predictor of diastolic dysfunction when no systolic dysfunction happens. (Lubien, et al., 2002)

Normal plasma BNP concentration increase with age is lower in men than women and is lower in obese persons and increase in transmural wall stress is the main stimulus for increased BNP production. (Redfield, 2012)

According to this findings, BNP and NT pro BNP assay results are increased in patients with (HFnLEF) compared to those without heart failure but at the same time are lower than levels in patients with reduced ejection fraction, this is because most patients with (HFnLEF) are older, often female, usually obese, and there wall stress is much lower than in heart failure with impaired ejection fraction (due to small left ventricular cavity and thicker left ventricular wall). (Iwanaga, et al., 2006)

So, BNP level is less specific and less sensitive for diagnosing of HFnEF especially in its early or milder stages and the standard partition valve of 100 pg/ml suggested for the detecting heart failure may not be accurate in HFnLEF. (Redfield, 2012)
Lastly, in the last consensus stated by European working group stating that BNP level > 200 or NT Pro BNP > 220pg/mL with equivocal echocardiographic evidence (E/e’ > 8 but <15) is enough for diagnosis of HFnLEF. (Lau, et al., 2013)

B) Invasive assessment (Catheterization):

Left and right sided catheterization can be used to assess diastolic function and give the most accurate clinical assessment of left ventricular relaxation. It is not used routinely for evaluation of diastology as this modality is invasive and needs use of expensive catheters. So, it is preserved for differentiation between restrictive and constrictive physiologies when non-invasive modalities fail to do that. (Daly, 2009)

C) Echocardiography:

It is the best method to evaluate patients with clinical syndrome of congestive heart failure. It is considered the method of choice when evaluating left ventricular diastolic function. (McCray et al., 2009)

The most commonly used parameter in clinical practice is Doppler interrogation of transmitral flow pattern, pulmonary venous flow and tissue Doppler evaluation of annular velocity to determine E/e’ ratio. Other numerous 2D and Doppler findings are important to diagnose including chamber size and wall thickness. (Lau, et al., 2013)

1-Transmitral Flow Pattern:

Measuring of transmittal flow velocities (left ventricular filling) is the most important step of diastolic function evaluation (mainly E/A ratio) which is commonly refined with other Echo Doppler assessment for better evaluation. It is done by using pulsed wave (PW) Doppler sample volume placed over the mitral leaflet tips in the apical 4-chamber view. Color Doppler may be used if needed to optimize beam alignment with mitral inflow. (Marwick, 2012)
The transmitral velocity pattern recorded is formed mainly of 2 principal deflections; early peak (E wave) velocity occurring during rapid filling phase and later (A wave) velocity occurring secondary to atrial contraction. Measuring E/A ratio is an important parameter in assessing diastolic filling. (Nagarakanti, et al., 2008)

Figure (2): Echocardiogram showing measuring of Transmitral Flow Velocity Profile ('E' and ‘A’ Waves)

Normally in healthy people younger than 50 years, E is greater than A, therefore E/A ratio is > 1. With hypertension, ischemia, left ventricular hyper trophy or advancing age; the viscoelastic properties of ventricle decrease and E wave decrease in amplitude and the atrial kick increase causing E-A reversal (E/A ratio <1 donating grade I diastolic dysfunction). (Lau, et al., 2013)

With the progression of diastolic dysfunction, the left atrial pressure rises as a compensatory mechanism causing E wave to re-rise
and to be more prominent than A wave so E/A ratio become more than 1 donating (pseudo normalization or grade II diastolic dysfunction).

With more progression of diastolic dysfunction result in failure of compensatory mechanisms with marked increase in left ventricular stiffness causing E/A ratio to be more than 2 and the patient is considered to have restrictive diastolic pattern donating grade 3 or 4 diastolic dysfunction. *(Lau, et al., 2013)*

Although transmitral flow pattern is one of the primary way to estimate diastolic function, it has many limitations including difficulty to differentiate normal from pseudo-normal pattern because both have E/A ratio more than 1; in atrial fibrillation due to loss of atrial kick, during tachycardia where there is fusion of E and A wave, and in the case of mitral valve disease including moderate to severe mitral regurgitation, mitral stenosis and mitral prosthesis. So the American society of echocardiography guidelines have encouraged estimating other findings including tissue Doppler evaluation and left atrial chamber size. *(Lau, et al., 2013)*

**D) Other methods include:**

(I) Deceleration time:

Known as time interval between E wave peak and the point where descending limb touches baseline. Normally, it ranges between 160-260 msec. In stage I diastolic dysfunction, the value is increased (>260msec) then become normalized in stage II and decreased (< 160msec) in stage III and IV. *(Daly. 2009)*

(II) Isovolumic relaxation time.

Known as interval from closure of aortic valve till opening of mitral valve, estimated between end of ejection and onset of mitral flow. *(Daly. 2009)*
Normally requires two different Doppler recording (one of aortic outflow and other of mitral inflow) with timing taken relative to a fixed point on the ECG.

**Normal value is**

- For 21 years → 40 years 67 ± 8 msec
- For 41 years → 60 years 74 ± 7 msec
- Over 60 years, the valve is 87 ± 7 msec
- In general, 60-100 msec is considered normal. *(Marwick. 2012)*

Value is greater when ventricular relaxation is delayed donating grade I dysfunction and is decreased when no ventricular relaxation occurs donating grade III / IV dysfunction. *(Daly. 2009)*

**Figure (3)** Diagram showing different stages of diastolic dysfunction regarding E/A ratio and deceleration time.

**1- Pulmonary venous flow:**

Measured by placing PW Doppler in the right upper pulmonary vein in apical 4-chamber view. Placement can be optimized with color flow mapping to demonstrate pulmonary venous flow. *(Marwick. 2012)*

In normal pulmonary venous flow pattern is triphasic with 2 forward flow phases; systolic (S) and diastolic (D) and a retrograde flow
wave (AR) occur secondary to atrial contraction. (*Nagarakanti, et al., 2008*)

Normally the systolic wave is dominant or equal to the diastolic wave and valve of AR wave is less than 30 cm/sec.

**Figure (4):** Pulsed wave Doppler on pulmonary veins shows S wave, D wave and Ar wave

![Pulsed wave Doppler on pulmonary veins shows S wave, D wave and Ar wave](image)

Earlier stages of diastolic dysfunction, the S wave is bigger than D wave, but with the development of pseudonormal or the restrictive pattern (elevated LAP) the D wave become bigger than S wave (systolic blunting) and S/D ratio become <1. It is considered a good marker in patients with systolic dysfunction but not with normal functions (*Daly, 2009*).

A prominent atrial reversal (Ar) more than 35 cm/sec, and difference between peak Ar and peak A wave of the mitral inflow more than 20-30 is specific but not sensitive marker of elevated filling pressure. (*Marwick, 2012*)
2- **Tissue Doppler imaging of the mitral annular velocity:**

This new ultrasound technology is used now routinely in assessment of diastolic function with high sensitivity and specificity. It has now become an important part of evaluation of diastolic function by means of echocardiography. *(Daly, 2009)*

Tissue Doppler imaging is used to measure systolic and diastolic myocardial velocities by recording the velocity of tissue motion at either the lateral or septal annulus of mitral valve. *(Nagarakanti, et al., 2008)*

It is proved that the longitudinal motion of the mitral annulus correlates with rate of myocardial relaxation and the velocity of mitral annulus could be detected by tissue Doppler giving an idea about the rate of myocardial relaxation. *(Connolly, et al., 2012)*

Normally the Doppler pattern should be identical to the mitral valve inflow with an E wave and A wave (but below the base line away from the probe) known as e’ or Ea and a’ or Aa. *(Marwick, 2012)*

**Figure (5)** Tissue Doppler imaging on septal mitral annulus shows Sa wave, Ea wave and Aa wave.

![Figure 5](image)

**Figure (5)** Tissue Doppler imaging on septal mitral annulus shows Sa wave, Ea wave and Aa wave.

With the beginning of diastolic dysfunction (even in the earliest stage), the diastolic velocity of annular motion slows. Normally the
lateral annulus tends to have more velocity than the septal annulus so septal e' < 8 cm/sec or lateral e' < 10cm/sec suggests the presence of diastolic dysfunction. Unlike transmitral flow pattern, e' is relatively not preload dependent, not affected by LAP so there is no pseudo-normalization pattern, therefore it is easier to differentiate normal from abnormal diastolic function. (*Lau, et al., 2013*)

Correlating transmitral E wave with the effect of myocardial relaxation e' (E/e' ratio) improve the specificity and sensitivity in assessing filling pressure. (*Nagarakanti, et al., 2008*)

This correlation is better in patient with impaired ejection fraction (Systolic dysfunction) as well as reasonable in patient with normal ejection fraction. (*Kasner, et al., 2007*)

For all grades of left ventricular ejection fraction (LVEF) E/e' is the best parameter to assess filling pressure, e.g. if E/e' is 15 or more than the pulmonary capillary wedge pressure (PCWP) is 20 mmHg or more and PCWP is normal if E/e' is less than 8. (*Nagueh, et al., 2009*)

So, E/e' < 8 reflects normal filling pressure and normal diastolic function, while E/e' > 15 suggests elevated filling pressures donating diastolic dysfunction. (*Marwick, 2012*)

The limitation only happens in patients that fall in the intermediate zone (E/e' > 8 but less has 15). For these patients the presence of elevated filling pressures cannot be assessed by this method alone and Echocardiography guidelines suggest the use of other parameters; e.g. plasma BNP or left atrial enlargement (LAV index > 34 nl/n2) may be helpful in this equivocal cases. (*Lau, et al., 2013*)

3- Other measures:

a. Left atrial size:

Measuring left atrial size by standard methods (area – length formula, ellipsoid method and Simpson’s method) can help to assess filling
pressure. Increased left atrial size means raised left atrial pressure \textit{(Marwick.2012)}

b. \textbf{Flow propagation velocity (VP) by color M-mode:}

That index is directly related to the base to apex diastolic intracavitary pressure gradient that occur as the ventricle relax promoting mitral inflow into left ventricular cavity; color M mode can measure the velocity of the flow propagation forming a color wave front, the slope of the outer edge of this wave front represent VP (Flow propagation velocity).\textit{(Daly.2009)}

Normal VP is 45 – 50 cm/s or more and values less than 50 cm/s is an indication of impaired relaxation and diastolic dysfunction.\textit{(Connolly, et al.,2012)}

VP may be wrong or non-reliable in case of small left ventricular cavity and preserved ejection fraction, it also cannot be used in the presence of inflow obstruction like mitral stenosis(MS).\textit{(Lau, et al., 2013)}

4- \textbf{Recent Methods:}

\textbf{Strain rate and speckle tracking imaging}

These new methods have been recently used in assessment of both systolic and diastolic dysfunctions with higher sensitivity and specificity. Strain is a dimensionless index obtained by integrating strain rate over time, representing the force needed to produce a deformation of the myocardium expressed as the percent change from the original dimension.\textit{(Daly.2009)}

A newer invention to strain analysis is speckle tracking involving a computer algorithm that uses routine greyscale imaging containing unique speckle patterns. Within a user-defined area on the myocardial wall, the image-processing algorithm to track frame by frame differences in the speckle pattern to velocity vectors.\textit{(Pirat, et al., 2007)}
Strain and strain rate have been found to correlate with myocardial relaxation and are used to assess the response of the ventricles to treatment in case of AS, HCM and HTN hence has an additional prognostic rule. (Connolly, et al., 2012)