Review of Literature
REVIEW OF LITERATURE

Even in the thrombolytic era, LV dysfunction remains the single most important predictor of mortality after AMI\textsuperscript{28}.

LV systolic function is reflected in the ability of LV to empty. This LV systolic function can be assessed at global as well as regional level. Global LV systolic function can be assessed as follows:

1) \textit{Fractional shortening}: It is the percentage change in LV cavity dimension with systolic contraction and relaxation and calculated as

\[
FS = \frac{LVEDD - LVESD}{LVEDD} \times 100\% 
\]

The normal value ranges from 25-50%.

2) \textit{Ejection fraction}: It is the stroke volume as percentage of end diastolic LV volume. The normal LVED volume averages 70±20(SD)ml/m\textsuperscript{2}. LV performance ordinarily is considered to be depressed when LVEDV is clearly elevated (i.e. >110ml/m\textsuperscript{2} or >2 SD, above the normal mean) and total stroke volume is either reduced or within normal limit. The LV stroke volume is the quantity of blood ejected with each beat and is the difference between EDV & ESV. Thus EF is
angiography. LV angiogram from 187 patients were suitable for analysis of systolic regional wall motion, 121 were found to be normal and 66 (35%) has a total of 115 hypokinetic segments. Patients with hypokinesia had significantly higher LVES volume and significantly lower EF and exercise capacity than those in whom regional wall motion was normal. There were more smokers in the patients in the group with hypokinetic segments. Thus patients with angina and normal coronary angiogram, 25% had evidence of LV systolic dysfunction, 20% had evidence of LV diastolic dysfunction and 11% had evidence of both systolic and diastolic dysfunction.

AU Goldersis M, et al (1992) studied 185 men and 147 women with CAD by 2-D echocardiography and followed for a mean of 3.9 years. At baseline, 37 men (18.4%) and 16 women (10.9%) had reduced fractional shortening, 43 men (23.2%) and 28 women (19%) had LV dilatation. During the follow up period new cardiovascular disease events (coronary disease, stroke, TIA, claudication, HF and death) occurred in 60 men (32%) and 58 women (39%). With the use of adjusted proportional hazards analysis LV end-dia-stolic diameter was predictor of new cardiovascular
disease events. Cardiovascular risk was also associated with LV end-systolic diameter in both sexes. Thus reduced fractional shortening alone in combination with LV dilatation was associated with the incidence of new cardiovascular disease outcomes in men.

Identifying patients with LV ejection fraction <35% in the absence of a recent acute event was the strategy in the SOLVD prevention trial\textsuperscript{32}. Patients who fulfilled this criteria in the absence of overt heart failure were randomised to receive either placebo or ACE-inhibitor. ACE-I significantly reduced the incidence of overt HF developing over the course of trial and produced a modest but statistically significant favourable trend on mortality.

Hammer Meister KE et al (1979)\textsuperscript{33} in a study of 733 patients showed that EF was the most important indicator of survival after MI, followed by age and extent of CAD.

In an angiographic study of 605 patients, long term follow-up after MI white et al\textsuperscript{34} showed that LV volume was the most important prognostic factor and LVES volume provides additional prognostic information to ejection fraction, when later was <50%.
Regional LV systolic function

The hyperkinesis of normal area may compensate for impaired function of an abnormal region, leaving global LV function normal or only minimally depressed. Thus assessment of regional function is more sensitive in detecting LV dysfunction in such patients than analysis of global LV function.

Regional wall motion abnormalities (RgWMA): Reduction of coronary blood flow secondary to intracoronary thrombus produces acute regional myocardial ischemia that may progress to acute infarction, if obstruction is not relieved. Experimental evidence indicates that the fall in ATP content in ischemic muscle decreases the transsarcolemmal inward calcium current, while the accumulation of hydrogen ion in ischemic muscle result in ionic competition with calcium for binding site on troponin-C, thereby impairing actin-myosin coupling. This result in abnormal wall motion.

Regional wall motion are characterized by abnormal endocardial motion, the failure of muscle to thicken during systolic contraction or even segmental bulging during systole\(^3^5\). The absence of wall thickening during systolic is
more suggestive of ischemia than endocardial wall motion alteration, since the latter alteration may be affected by cardiac rotation during contraction, cardiac motion during respiration and changes in ventricular pre or after load.

Jen-fang Ren MD, et al\textsuperscript{37} assessed regional wall motion and wall thickening of the LV quantitatively in 9 normal subjects and in 21 patients with CAD, using 2-D echocardiography with a computerized light pen system. Eight equal sectors of cross sectional image from parasternal short axis, apical four chamber, & two chamber views were used for measuring sector area difference of endocardial motion and wall thickness between end diastole and end systole. In 13 patients with anterior wall motion abnormalities, area difference of wall thickening found by 2DE was abnormal in 12 of 13(92%) patients, and only in 6 of 13 (46%) patients by, endocardial wall motion. In 10 patients with dyskinetic regions in apex or ant. wall, dyskinesia by wall thickness was found in all patients, but only in 6 of 19(60%) by endocardial motion. Thus wall thickening assessed by 2DE is more sensitive technique than analysis of endocardial motion in evaluating RWMA in patients with CAD.
The American association of echocardiography has recommended standardization of various wall segments of left ventricle into 16 segments as follows:

**Basal level**: At the level of mitral valve.

1. Anterior septum  
2. Anterior wall
3. Anterolateral wall  
4. Posterolateral wall
5. Inferior wall  
6. Inferior septum

**Mid level**: At the level of papillary muscle

1. Anterior septum  
2. Anterior wall
3. Anterolateral wall  
4. Posterolateral wall
5. Inferior wall  
6. Inferior septum

**Apical level**: At the level of apex

1. Anterior wall  
2. Lateral wall
3. Inferior wall  
4. Septum

A revised grading system classifies formation as grade 1 to 5 as follows: Normal-1, Hypokinesis-2, Akinesis-3, Dyskinesis-4 and Aneurism-5.

And it is utilized to characterize wall motion in each segment. The composite score divided by the number of
segments provide semiqualitative evaluation of wall motion abnormality.

Lieberman AN et al (1975)\textsuperscript{38} studied that the sensitivity of echo in detection of alteration in RgWM depend upon two factors:

1) Reduction of resting coronary blood flow of at least 50% and

2) Involvement of transmyocardial ischemia or infarction of at least 20% of LV wall.

In patients with LV dysfunction associated with normal or dilated LV, RgWMA are highly sensitive in detecting significant CAD.

Media R et al (1985)\textsuperscript{39} study shows that the sensitivity, specificity and predictive accuracy of RgWMA in detecting significant CAD in patients with LV dysfunction and normal size LV were 95%, 100% and 95% respectively.

JG Nelson MA et al (1988)\textsuperscript{40} assessed the predictive value of abnormal regional wall motion by 90°2D Echocardiography in detecting coronary artery disease in 100 patients, all with 2D-evidence of diffuse hypokinesis or abnormal regional wall motion. Angiographically CAD was
seen in 81/84 (94%) patients with abnormal RgWM Vs 9/16(56%) with diffuse hypokinesia (p<0.001). Apical akinesis or dyskinesis plus diffuse hypokinesia occurred in 8/84 patients, all with CAD involving the left anterior descending. Abnormal regional wall motion predicted CAD in corresponding vessels as follows: Abnormal apex=LAD stenosis in 64/70(91%), abnormal anterior wall=LAD stenosis in 30/31 (94%); abnormal septum=LAD stenosis in 41/42 (98%), akinesis in upper septum=LAD stenosis to first septal in 4/6(67%), abnormal inferior wall=RCA stenosis in 29/36(81%); abnormal posterior wall=RCA stenosis in 18/24(75%). Thus abnormal RgWM by 2D Echocardiography is highly predictive. Abnormal apex, anterior wall or septum motion is 91-98% predictive of LAD stenosis. Abnormal inferior motion is 92% predictive of RCA and/or Cx-LAD stenosis while abnormal posterior or lateral wall motion predicts stenosis of either RCA or Cx.

Haiveys et al assessed 36 patients with CAD and suspected wall motion abnormalities by equilibrium radionuclide angiography (RA) in the left ant. oblique and by cross-sectional echocardiography (CSE) in apical four & two chamber views. 12 segments were independently
analysed; two each for the septum, ant., Inf., posterolateral and two for the apex in each view. Wall motion in each area was classified as either normal/hypokinetic or akinetic/dyskinetic. Of 156 areas, 109 (70%) had the same classification by RA and CSE (P < 0.001). 63 were normal/hypokinetic and 46 were akinetic/dyskinetic. The agreement for each area was: Apex-85%, posterolateral-78, septum-64%, anterior-63% and inferior-54%. In summary, there was significantly agreement in the evaluation of segmental left ventricular wall motion between RA and CSE.

Nixon JV, et al (1980)\textsuperscript{41} studied that in patient with unstable angina responding to medical treatment, transient RgWMA are associated with a favourable prognosis. In contrast, the persistence or progression of RgWMA in patients with unstable angina often correlates with an adverse clinical prognosis at 3 month post hospital discharge. Patients with extensive RgWMA are especially prone to develop CHF, hypotension and sudden cardiac death.

Horowitz and Morganroth et al (1982)\textsuperscript{42} found that echo had a sensitivity of 83% and a specificity of 85% in
detecting patients in hospital complications. In contrast, the Killip classification was found to be relatively insensitive in detecting in-hospital complication during MI\textsuperscript{13}.

**Diastolic function**

Little WC et al, firstly evaluated the LV diastolic performance and defined the normal LV diastolic function as “filling of LV sufficient to produce a cardiac output commensurate with body’s need with a normal pulmonary venous pressure (<12mmHg)”.

Gressman W et al (1993)\textsuperscript{44} recognize that in 30% of patient with CHF, the CHF is secondary to LV diastolic dysfunction.

Warner JG, et al (1998)\textsuperscript{45} evaluated LV diastolic filling profile by Doppler echocardiography using transmitral flow and recorded four phases of LV filling:

i) Isovolumetric relaxation phase

ii) Rapid filling phase (E-wave)

iii) Diastasis phase

iv) Atrial filling phase (A-wave)
The normal pattern of LV filling is characterized by rapid filling early(E) in diastole with some additional filling during atrial contraction(A). The relative contribution of early and late filling is commonly expressed as the E/A ratio. Normally the E>A ratio is greater than 1.0. The time required for deceleration of the early diastolic flow is another important parameter of the filling pattern. The normal values are:

\[ \text{IVRT}= 100 \text{msec (70 – 100 msec)} \]

\[ \text{E-wave velocity} = 76 \pm 13 \text{cm/sec} \]

\[ \text{DT}= <220 \text{ msec (184±24)} \]

\[ \text{A-wave velocity} = 56\pm13 \text{ cm/sec} \]

\[ \text{E/A} = >1 \]

**Abnormal pattern of LV filling**

*Delayed relaxation pattern:* When myocardial relaxation is the predominant diastolic abnormality, IVRT is prolonged and the initial decline in LV pressure is slow. Hence early filling (E-wave) is reduced and there is a longer compensatory filling with atrial contraction (A-wave). The ventricle continue to relax even after the opening of mitral valve, and it takes longer to equilize ventricular pressure
with atrial pressure, resulting in prolongation of E-wave deceleration time (DT). Therefore delayed relaxation pattern characterized by:

1. Prolonged IVRT >100msec
2. Prolonged DT >220msec
3. Reversed E/A ratio <1cm/sec

_Pseudonormalized pattern_: This pattern in which the E/A ratio is greater than 1.0 (as occurs in normal pattern) is seen in patients with more severe impairment of diastolic performance then pattern of delayed relaxation. The pseudonormalized pattern is due to restoration of the normal early diastolic LV pressure gradient due to an increase in LA pressure that compensates for the slowed rate of LV relaxation. Thus pseudonormalised pattern is distinguished from normal by a more rapid rate of early diastolic flow deceleration, a faster deceleration time (<150msec) and alteration in pulmonary valve flow velocity.

Little WC, et al (1995)\(^{46}\) recognised that the deceleration time (DT) is proportionate to the inverse of the square root of the LV chamber stiffness, thus the pseudonormalized pattern is characterized by:
IVRT = <100msec

DT = <150msec

E/A ratio =1-2cm/sec

**Restricted pattern:** When ventricular compliance is decreased, the rise in ventricular diastolic pressure is very rapid during the early filling phase (short DT) and the elevated LVED pressure minimize ventricular filling due to atrial contraction (decrease or absent A-wave). With the resultant high LA pressure, the IVRT becomes short and the E-velocity is high. Thus restricted pattern of LV filling is characterized by

Shortened IVRT =<60msec

Shortened DT = 150msec

E/A Ratio = ≥2.0cm/sec

The three abnormal patterns of LV filling represent a continuum of increasing severity of diastolic abnormalities. The pattern of delayed relaxation may be observed in asymptomatic individual with only impaired diastolic reserve, whereas the psuedonormalised and restrictive pattern occur in patients with progressively more severe
diastolic dysfunction, these patients almost always have pulmonary congestion.

*Effect of ischemia on diastolic function:* The process of myocardial relaxation is energy dependent. Therefore MI impairs the rate and extent of relaxation and causes the slowing of early diastolic filling.

MC Laurin LP et al (1973)⁴⁷ and various other workers studied the effect of transient ischemia on diastolic function in patients with CAD undergoing cardiac catheterization. In whom angina pectoris was induced by exercise or by pacing tachycardia. They demonstrated that demand ischemia result in an abrupt and reversible increase in LV diastolic pressure which is related to the prolongation of IVRT. The ischemic changes in diastolic function can occur in the presence of variable degree of depression of global and regional systolic function. The magnitude of the acute depression of diastolic as well as systolic function are related to the extent of ischemic territory.

Pouleur and coworkers (1984)⁴⁸ studied that demand ischemia profoundly depresses the diastolic relaxation in
ischemic region compared with non ischemic segment in patient with demand ischemia.

MA Garcia Fernandez et al (1999)\(^49\) assessed 30 normal subjects and 43 patients with IHD. Doppler tissue imaging was performed in each of the 16 segments of the myocardium. The following parameters were obtained for each segments: Early diastolic filling peak velocity (E-wave cm/s), Late diastolic filling peak velocity (A-wave cm/s), Diastolic transmitral E/A velocity ratio and LV isovolumnic relaxation time (IVRT).

Each of the parameters were evaluated and compared in ischemic and normally perfused segments, based on the presence or absence of obstructing lesion in coronary arteries supplying these regions. In patients with CAD several differences were observed between diseased and normal wall segments: the mean segmental early peak diastolic velocity (E-wave) was reduced (mean±SD±2.1 cm/s Vs 8.5±2.8 cm/s P<0.01), the E/A Diastolic velocity ratio was decreased (0.95±0.3 Vs 1.5±0.6 respectively P<0.01), and the regional isovolumic relaxation time was prolonged, (104±36.7 ms Vs 69.6±30ms, P<0.01). No difference were
observed in any of these parameter between the normally perfused segment of ischemic patient and normal subjects.

Rahintoola SH et al (1988)\textsuperscript{50} studied transmitral flow velocity echocardiography in 15 patients with CAD and 14 age and heart rate matched normal subjects. Statistically significant differences (p<0.05) in acceleration half time (55.3±8.2 Vs 70.4±14.9ms), deceleration half time (83.1±17.9 Vs 109.5±18.1ms), peak velocity of early diastolic left ventricular inflow (E-wave) (0.78±0.13 Vs 0.61±0.13ms) and A/E ratio (0.74±0.20 Vs 0.98±0.31) between normal subjects and patients were noted. There was no significant difference in peak velocity of atrial systolic flow (A-wave) between normal subjects and patients. Significant correlation between deceleration rate versus maximal isovolumic left ventricular pressure were found (0.53 & 0.65) respectively.

Grossman W et al (1993)\textsuperscript{44} recognised that in approximately 30% of patient with CHF, the CHF is secondary to LV diastolic dysfunction.

SE Jensen et al (1997)\textsuperscript{51} assessed 65 consecutive patients with first MI within one hour of arrival in CCU and
concluded that [1] LV diastolic dysfunction is present early after onset of symptoms of a first AMI [2] Most patients with heart failure had early systolic dysfunction with decreased EF, but 23% had an abnormal filling pattern with preserved EF.

M Schofield et al (1986)\textsuperscript{30} study shows that in patient of angina pectoris the evidence of isolated diastolic dysfunction was 20% and isolated systolic dysfunction was 25% while 11% patient had combined systolic & diastolic dysfunction.

AV Knowalska A et al (1999)\textsuperscript{52} studied 107 patients and showed that in patients of CAD diastolic dysfunction preceeds the systolic dysfunction.

Jacob E et al (2000)\textsuperscript{53} recognized that pseudonormalised and restrictive filling pattern predict LV dilatation and cardiac death after a first MI. They studied 125 patients and found that LV filling was normal in 38 (30%) patients, impaired relaxation in 38(30%) patient, pseudonormalised in 23(18%) and restrictive in 26(21%). ESV &EDV indeces were significantly increased during the first 3 month after MI in patients with pseudonormalized or restrictive filling
(37±15 VS 47±19 ml/m², P<0.0005 and 76±20 VS 88±24 ml/m², P<0.005 respectively). During a follow up period of 12±7 months 33 patients died. Mortality was significantly higher in patients with impaired relaxation (p=0.02), pseudonormalized filling (p<0.0005) and restrictive filling (p<0.0005), compared with patients with normal LV filling.

Nijland F, et al (1997)⁵⁴ performed Doppler echocardiography in 95 patients on days 1, 3 and 7 and 3 months after acute myocardial infarction. Patients were classified into two groups: a restrictive group (n=12) with a peak velocity of early diastolic filling wave (E), peak velocity of late filling wave (A) ratio ≥2 or between 1&2 and a deceleration time (DT) ≥140 ms during at least one echocardiographic study; and a nonrestrictive group (n=83) with an E/A ratio≤1 or between 1&2 and a DT >140 ms at all examination. Results: cardiac death occurred in 10 patients during a mean follow up interval of 32±17 months. The survival rate at 1 year was 100% in the nonrestrictive group and only 50% in the restrictive group. After one year, there was a continuing divergence of mortality, resulting in a 3 year survival rate of 100% and 22% respectively.
SH Paulson et al (1997)\textsuperscript{55} studied the prognostic significance of LV diastolic function evaluated by transmitral flow velocity obtained in early phase of AMI in relation to later development of CHF. They studied 65 patients on the basis of presence of clinical heart failure during first week of hospitalization. The patients were divided in two groups. Group A had no signs of HF and group B had signs of HF. Study were assigned to the following 3 groups Gr-I with DT>140ms, IVRT <100ms respectively, a normal filling pattern (24 patients-38%), Gr-II= DT>140, IVRT≥100ms considered to be an expression of impaired relaxation (23 patients-37%) Gr-III with a DT≥140ms which may signify a pseudonormal or restrictive filling pattern (16 patients-25%). Patients in group III had a significantly higher ESV index, lower EF than patients of Gr-I & II. Patients in Gr-III more commonly had anterior Q-wave MI than in Gr I&II.

Bodi Peris V et al (1997)\textsuperscript{56} showed that the E-wave deceleration time (DT) predict LV diastolic pressure in AMI, in patients with systolic dysfunction. Here 89 patients with first AMI treated with thrombolytic agents were studied. Doppler-echocardiography at 29±3 days and cardiac
catheterization at 30±4 days postinfarction were performed. According to the ejection fraction (EF), the patients were divided into group I (n=17) with EF <45% and group 2 (n=72) with EF >45%. The E/A ratio showed a weak correlation with LVEDP (r=0.32; P=0.007), and E-DT did not correlate with LVEDP. When patients from group 2 were analyzed, no correlation was found between LVEDP and either E/A or E-DT. However, in patients from group 1, LVEDP strongly correlated with both E-DI (r=-0.83; P=0.00001) and E/A (r=0.70; P 0.003). Moreover, the sensitivity and specificity of an E-DT of less than 150 msec in predicting a LVEDP >20mmHg was 100%. This conclude that at the first month after a myocardial infarction E-DT provides a non-invasive and useful parameter for estimating LVEDP in patients with systolic dysfunction.

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