

Validation of Mitral Annular Plane Systolic Excursion & end Point Septal Separation for Rapid Assessment of Left Ventricular Systolic Function

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ABSTRACT:

BACKGROUND:

Assessment of LV systolic function is sometimes difficult because of obesity, chest wall deformities or in critically ill patients. We try to evaluate alternative methods for rapid assessment of LV systolic function.

OBJECTIVE:

In this study we try to evaluate mitral annular plane systolic excursion (MAPSE) (Since LV longitudinal shortening reflected by MAPSE is a sensitive marker of LV systolic function.) & E-point septal separation (EPSS) for rapid assessment of LV systolic function & as alternative way to assess ejection fraction (EF).

METHODS:

This is an observational case-control study enrolling 143 patients, 73 patients with LV dysfunction & 70 persons with normal LV function served as a control group.

LV EF (Left ventricle ejection fraction), MAPSE & EPSS all are measured for patients & the control groups. P-value ≤ 0.05 is considered as a statistically significant.

RESULTS:

A 73 patients with LV dysfunction & 70 patients with normal LV function (taken as a control) were enrolled in this study. There are significant LV dilatation, a decrease in LVEF, decrease in MAPSE & increase in EPSS in patients group in comparison with control groups, & all are statistically significant (P-value=0.0001). MAPSE less than 7 mm & EPSS more than 7 mm had a sensitivity of 34.24 % & 97.26% respectively & a specificity of 100% & 85.71% respectively.

CONCLUSION:

Both MAPSE & EPSS parameters are simple, easy to obtained & require no time especially in patients with poor acoustic window.

An average MAPSE of less than 7 mm & EPSS of more than 7 mm can be used as a surrogate of LV systolic dysfunction with acceptable sensitivity & specificity.

KEY WORD: MAPSE, EPSS, LV function.

INTRODUCTION:

Mitral annular plane systolic excursion (MAPSE) also known as mitral ring displacement & mitral annulus excursion (MAE), is obtained from M mode & it assesses LV longitudinal function ^(1,2,3). It can be get easily ^(5,6,7) even for the junior doctor ⁽⁷⁾ and in patients with poor acoustic windows ⁽³⁾. It has been suggested as a surrogate measurement for LVEF in cardiac patients ^(6,8). MAPSE may be reduced with increasing age & in patients with atrial fibrillation, myocardial infarction & heart failure ^(9,10,11) and to be more sensitive than

conventional echocardiographic markers in detecting abnormalities in LV systolic function at an early stage ^(2,12). MAPSE is known to be prognostic for major cardiac events and mortality in patients with cardiovascular disease ^(9,13,14,15).

Measurement of MAPSE

MAPSE can be measured using the M mode from the lateral & septal walls of the apical 4 chambers views & from the anterior & inferior walls of the apical 2 chambers views. The best is to obtain it from the lateral & septal walls.

Generally, the lateral MAPSE values are higher than that of septal walls. ⁽¹⁶⁾

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& during measurement always make the cursor parallel to the LV walls. The excursion in M mode should be measured from the lowest point to the highest point i.e. from end diastole to end systole. (Fig. 1). The post-systolic motion towards the apex

during the isovolumetric relaxation period, which is sometimes linked with ischaemia, fibrosis, or pressure overload,(17) should not be included in the measurement.

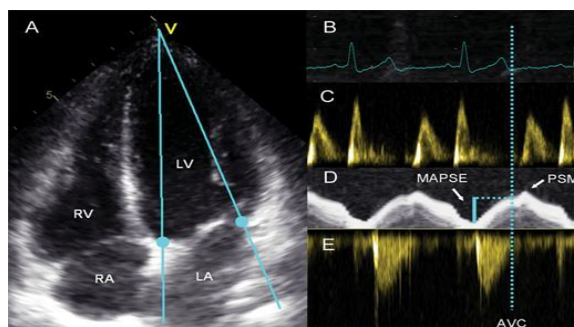


Figure 1

The average normal value of MAPSE derived from previous studies for the four annular regions (septal, anterior, lateral, and posterior) ranged between 12 and 15 mm (18, 9) and a value of MAPSE <8 mm was associated with a depressed LV EF (<50%)(18) . A mean value for MAPSE of ≥ 10 mm was linked with preserved EF ($\geq 55\%$) (1, 20). In addition, a mean value for MAPSE of <7 mm could be used to detect an EF <30% in dilated cardiomyopathy patients with severe congestive heart failure (9).

One important thing is that the association between MAPSE & EF is only true in case of a normal or dilated LV (20, 21), but this association is not applicable in case of left ventricular hypertrophy

(LVH) (22). This is because the LV longitudinal function represented by MAPSE is impaired in case of LVH while radial function represented by EF will remain normal or even increased (23). The same is also true with increasing age in which MAPSE is impaired while the EF remain normal or even increased.(24,25)

EPSS, Surrogate markers of LV systolic function:

EPSS refers to the distance between the anterior leaflet of the mitral valve and the interventricular septum during early diastole. This is easiest to measure using M-mode echocardiogram, and the measurement is taken when the anterior mitral leaflet is at its closest to the septum (Figure 2).

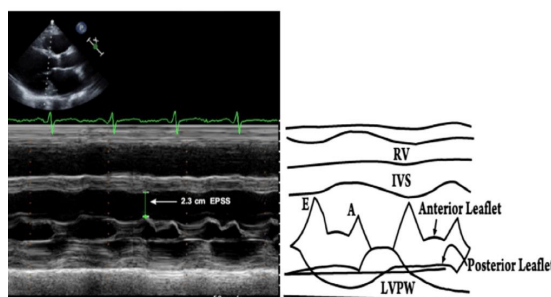


Figure 2

During diastole, the tip of the anterior MV leaflet move toward the septum & during M mode this is represented by E point as seen in fig. 2. The distance between E point & the septum is called E point septal separation (EPSS) & it does not only

assess LV dilatation & function but it has a strong negative correlation with EF i.e. the higher the distance the lower the EF (26,27).

Normally, the EPSS is no more than 6mm. The distance increases with worsening left ventricular

systolic function, and an EPSS >7mm is a sensitive marker for severely impaired systolic function.

METHODS:

Study design:

This was an observational case-control study evaluating the relationship of MAPSE & EPSS to LVEF in patients with LV dysfunction & in healthy population who attended the Echocardiogram department in Al-Yarmouk hospital for any indication.

Subjects:

73 patients with LV dysfunction as documented by an LVEF < 54 % in females or LVEF < 52% in males were enrolled during the period from 21ST of April 2016 to 25th of March 2017.

A 70 healthy individuals as documented by an LVEF ≥ 54 % in females & LVEF ≥ 52% in males were enrolled as a control during the period of 21st of April 2017 to 20th of April 2017.

Exclusion:

1. Patients with valvular cardiomyopathy (valve leading to LV dysfunction).
2. Patients with left ventricular hypertrophy.

Measures:

All echocardiographic examination were completed using S4 probe 2.5 Mhz phased-array. Comprehensive transthoracic echocardiogram was performed with Vivid E9 echocardiography system (GE).

After taking a consent, we asked about past medical history, current or past occupation, smoking status & presence or absence of ischemic heart disease.

By echocardiogram, we measure LV size (left ventricular internal diameter diastolic) (LVIDD), LVEF, EPSS & MAPSE.

Two-dimensional imaging examination was performed in the standard fashion in parasternal long- & short-axis views & apical 4-& 2- chamber views.

LVEF were calculated using cubed formula i.e. Teichholz methods.

Excursion of mitral annulus was measured using M mode from the apical 4 chambers view with beam

positioned to the lateral walls. The amount of excursion was measured in mm.

In M mode the longitudinal motion of MV annulus was recorded against time giving the appearance of a sine wave. The depth of the sine wave occurred in end diastole while the height occurred in end systole. Measurement of depth to height represent MAPSE

Regarding measurement of EPSS, an M-mode from parasternal long axis view was taken at the level of mitral valve leaflet tips.

Measurement was taken in early diastole (in mm), & EPSS was defined as the shortest distance from the E-point of mitral valve (the tip of the anterior mitral valve leaflet) to the ventricular septum.

Statistical analysis:

Data were coded & analyzed using the SPSS package program, version 24.0 (SPSS Inc, Chicago, IL, USA) & excel 2013 programs. Qualitative data were presented using the frequency & its related percentage, while quantitative data were presented using the mean & standard deviation. Continuous variables were compared between the two groups using student's t-test, while categorical variables were compared using Pearson Chi-square test. One-way analysis of variance (ANOVA) was used to compare three or more groups.

A P-value of < 0.05 was chosen as the level of significance.

RESULTS:

A 73 patients with LV dysfunction classified according to their EF (EF ≤ 54 % in females & ≤ 52 % in males) & 70 patients with normal LV function (EF > 54 in females & > 52 in males) (taken as a control) were enrolled in this study.

There were 47 (64.38 %) males & 26 (35.62%) females in patients group, & 31 (44.28%) males & 39 (55.72 %) females in the control groups. The mean age was 58.9 ±12.4 year of the patients group, the range was 6-77 years & the mean age of the control group was 45.8 ± 13.5 year, range 19-75 year. The rest of clinical data is demonstrated in table 1.

Table 1: Demographic & clinical data of patients with LV dysfunction & control groups.

	Patients	Controls	P-value
Number	73	70	
Age "Mean±SD (Range)"	58.9±12.4 (6-77)	45.8±13.5 (19-75)	0.0001*
Males	47	31	0.016#
Females	26	39	
Hypertension	36	26	0.142
Diabetes	33	12	0.0001#
IHD	33	8	0.0001#
Smoking	11	16	0.053

*Significant using Students-t-test for two independent means at 0.05 level

Significant using Pearson Chi-square test at 0.05 level.

Table 2 shows the echocardiographic parameters of patients & control groups, there are significant LV dilatation, a decrease in LVEF, decrease in MAPSE & increase in EPSS in patients group in comparison with control groups, & all are statistically significant (P-value=0.0001).

Table 2: Echocardiographic findings in patients with LV dysfunction & control groups.

Mean	Patients	Control	P-value
LV size (mm)	62.5±9.5 (41-90)	50.3±5.4 (40-68)	0.0001*
EF (%)	36.3±8.5 (17-53)	70.9±6.3 (57-83)	0.0001*
MAPSE (mm)	8.4±3.1 (4.2-17)	15.1±2.5 (11.3-22.1)	0.0001*
EPSS (mm)	16.3±5.9 (6-35)	4.0±2.5 (0-11.3)	0.0001*

*Significant using Students-t-test for two independent means at 0.05 level

Table 3 shows the echocardiographic parameters between males & females patients, there are significant LV dilatation, decrease in LVEF & decrease in MAPSE in male patients in comparison to the females (P-values: 0.001, 0.002, 0.001 respectively).

While there is no statistically significant deference between males & females regarding EPSS.

Table 3: Comparison of echocardiographic findings between males & females patients.

Mean	Male patients	Female patients	P-value
LV size (mm)	65.3±9.7 (41-90)	57.6±6.9 (44-70)	0.001*
EF (%)	34.1±7.9 (17-52)	40.4±8.2 (25-53)	0.002*
MAPSE (mm)	7.9±2.8 (4.2-17)	9.3±3.3 (5-16)	0.001*
EPSS (mm)	17.9±5.9 (6-35)	13.3±4.8 (6.8-22.7)	0.070

*Significant using Students-t-test for two independent means at 0.05 level

Table 4: Comparison of echocardiographic findings between ischemic & non-ischemic LV systolic dysfunction.

	Ischemic	Non-ischemic	P-value
LV size (mm)	61.6±8.4 (41-49)	67.0±12.9 (51-90)	0.061
EF (%)	36.6±8.2 (17-52)	35.2±10.3 (21-53)	0.587
MAPSE (mm)	8.4±2.9 (4.2-17)	8.5±3.7 (4.2-14.2)	0.919
EPSS (mm)	15.6±5.4 (6-27)	19.3±7.4 (8.3-35)	0.045*

*Significant using Students-t-test for two independent means at 0.05 level

Table 4 shows the echocardiographic parameters between ischemic & non-ischemic LV dysfunction patients. LV dilatation, LVEF & MAPSE all showed a non-statistically significant difference, while EPSS is significantly increased in non-ischemic patients in comparison to the ischemic ones (P-value: 0.045)

LEFT VENTRICULAR SYSTOLIC FUNCTION

Table 5 shows a statistically significant relation between MAPSE & LVEF in patients with LV dysfunction (LVD) (P-value: 0.0001)

Table 5: The relation between MAPSE & EF in patients with LV dysfunction.

MAPSE (mm)	No.	EF (%) (Mean)	P-Value
≥10	24	40.2±6.4 (29-53)	0.0001*
9.9-8 borderline	17	40.0±8.0 (28-52)	
<8 LVD	7	37.9±7.5 (28-47)	
<7 Severe LVD	25	29.7±7.2 (17-51)	

*Significant using ANOVA test at 0.05 level

Table 6 shows a non-statistically significant relation between EPSS & LVEF in patients with LV dysfunction (LVD) (P-value: 0.380)

Table 6: The relation between EPSS & EF in patients with LV dysfunction (LVD).

EPSS (mm)	No.	EF (%) (Mean)	P-Value
≥7	71	36.1±8.4 (17-53)	0.380
<7	2	45.5±9.2 (39-52)	

*Significant using Students-t-test for two independent means at 0.05 level

Table 7: The sensitivity and specificity of different echocardiographic parameters for diagnosing LVD.

		Diagnosis of LVD by EF (Male ≤52; Female ≤54)	
		LVD (n=73)	Control (n=70)
MAPSE	Severe LVD (<7)	25	-
	LVD (<8)	7	-
	Borderline (10-8)	17	-
	Normal (≥10)	24	70
EPSS	LVD (≥7)	71	10
	Normal (< 7 mm)	2	60

EPSS:

Sensitivity = $71/(71+2) \times 100 = 97.26\%$; False negative = $2/71 \times 100 = 2.74\%$; Positive predictive value = $71/(71+10) \times 100 = 87.65\%$

Specificity = $60/(10+60) \times 100 = 85.71\%$; False positive = 14.29% ; Negative predictive value = $60/(60+2) \times 100 = 96.77\%$

Accuracy rate = $(71+60)/143 \times 100 = 91.61\%$

MAPSE:

1. For MAPSE less than 8 for the detection of LV dysfunction

Sensitivity = $(25+7)/73 \times 100 = 43.84\%$; False negative % = 56.16% ; Positive predictive value = $32/32 \times 100 = 100\%$

Specificity = $70/70 \times 100 = 100\%$; False positive % = 0% ; Negative predictive value = $70/(24+17+70) \times 100 = 63.06\%$

Accuracy rate = $(7+25+70)/143 \times 100 = 71.33\%$

2. For MAPSE less than 7 for the detection of LV dysfunction

Sensitivity = $25/73 \times 100 = 34.24\%$; False negative % = 65.76% ; Positive predictive value = $25/25 \times 100 = 100\%$

Specificity = $70/70 \times 100 = 100\%$; False positive % = 0% ; Negative predictive value = $70/(24+17+7+70) \times 100 = 59.23\%$

Accuracy rate = $(25+70)/143 \times 100 = 66.43\%$

DISCUSSION:

Assessment of LV systolic function & obtaining LV EF is sometimes difficult because of obesity, chest wall deformities, and poor window or in critically ill patients. So we have to look for other parameters, compare these parameters with EF & trying to know their sensitivity & specificity. Longitudinal shorting of the left ventricle is a sensitive marker reflecting heart function & can be obtained by measuring MAPSE. Measurement of MAPSE doesn't require high imaging quality nor highly specialized personnel.

Although MAPSE & EF are strongly positively related, they are not completely related. MAPSE is more likely to assess longitudinal function of the LV i.e. subendocardial fibers & is more sensitive to subtle LV function changes while EF is more likely to assess radial LV function i.e. subepicardial (circumferential) fibers.⁽²⁹⁾ i.e. the longitudinal function could be impaired while the radial function can be preserved or even increased.

The other method for assessment of left ventricular function is by measuring the distance between anterior MV leaflet & ventricular septum in diastole (EPSS) which can roughly assess LV EF.

In diastole, the anterior MV leaflet should approach or even touch the septum. In LVD, the dilated LV with increased preload will pull valve away from the septum.

It is easy to obtain, fast as it is a simple linear m-mode measurement obtained from parasternal long axis view.

The current study showed that there are significant LV dilatation, a decrease in LVEF, decrease in MAPSE & increase in EPSS in patients group in comparison with control groups, & all are statistically significant (P-value=0.0001), Matos et al. (7) reported that the average systolic excursion of the mitral annulus correlated excellently with LVEF. Previous studies also stated that chronic heart failure patients showed a significant reduction of MAPSE, and there was a good correlation between MAPSE and EF (9). Qin et al.⁽³⁰⁾ have shown that MAPSE measurement correlate well with other techniques for LV functional assessment including 3D echocardiogram & cardiac MRI imaging. Also, Tsang et al.⁽³¹⁾ studied the correlation of MAPSE, as derived from speckle-tracking echocardiography, with MRI-derived LVEF. They found a very strong correlation using this alternative MAPSE technique, suggesting a strong relation between MAPSE & LVEF.

The current study showed that there are significant LV dilatation, decrease in LVEF & decrease in MAPSE in male patients in comparison to the females (P-values: 0.001, 0.002, 0.001 respectively). While there is no statistically significant difference between males & females regarding EPSS. The explanation is that women's hearts are typically smaller than men's, this could account (at least partially) for the observed differences between men and women. Matos et al.⁽⁷⁾ showed that although average MAPSE values did not differ significantly between men and women, EFs did (P-values 0.33 & < 0.001 respectively). For a given MAPSE value, the

correlating EF was higher for women than for men. No other study to date has been published that evaluated gender specifically as a factor that affects the correlation between MAPSE and EF.

The current study showed that LV dilatation, LVEF & MAPSE all showed a non-statistically significant difference between ischemic & non-ischemic (dilated cardiomyopathy) LV systolic dysfunction, while EPSS is statistically significant in non-ischemic (dilated cardiomyopathy) patients in comparison to the ischemic ones (P-value: 0.045). The explanation is that the LV takes on a more spherical geometry in dilated cardiomyopathy than ischemic LV systolic dysfunction & with progressive dilatation, the minor axis increases disproportionately, & the ratio of long to minor axis decreases i.e. sphericity index less than 1.5:1 implies marked pathological remodeling. There is no published data to date comparing MAPSE & EPSS between ischemic LV dysfunction & dilated cardiomyopathy.

In this current study there is strong relation between MAPSE & EF (measured by M-mode), P-value:0.0001. In Walaa et al (32) study they found a significant positive correlation between average MAPSE & EF measured by M-mode ($p < 0.001$), EF measured by Simpson's rule ($p < 0.001$), & EF measured by visual inspection ($p < 0.001$). Our study failed to find a relation between EPSS & EF measured by M-mode (P value: 0.38). While in Conor et al study⁽³³⁾ they found that a prediction of LVEF from linear regression equation using EPSS measurement could theoretically be used to generate a quantitative prediction of LVEF, while in Abdalla Elghaha et al⁽³⁴⁾ study they found that Correlation coefficient revealed to be very strong between Mitral EPSS measured by CMR & LVEF ($r = -0.92$; 95% Confidence interval for $r = -0.95$ to -0.87) with high significant level ($P < 0.0001$).

The current study showed that a MAPSE less than 8 had a sensitivity of 43.84%, a specificity of 100% & accuracy rate of 71.33% for the detection of LV systolic dysfunction & a MAPSE less than 7 had a sensitivity of 34.24%, a specificity of 100% & accuracy rate of 66.43% for the detection of severe LV systolic dysfunction. While in Walaa et al⁽³²⁾ study showed that an average MAPSE cutoff value of less than or equal to 5 provided the best balanced sensitivity (67.1%) and specificity (76.5%) to predict $EF < 30\%$. A cutoff value of less than or equal to 3.9 could determine $EF < 30\%$ in 100% of the patients. Matos et al.⁽⁷⁾ study stated that a MAPSE cutoff point of < 6 served as an appropriate

cutoff point to predict severely depressed EF less than or equal to 30%. Elnoamany et al.[5] demonstrated that a MAPSE value of <7 mm had 92% sensitivity and 67% specificity for the detection of severe left ventricular dysfunction. Alam et al.⁽⁹⁾ demonstrated that a mean MAPSE < 7 mm could detect an EF < 30% with sensitivity of 92% and specificity of 67% in patients with dilated cardiomyopathy with severe congestive heart failure.

Our study showed that EPSS ≥ 7 had a sensitivity of 97.26%, a specificity of 85.71% & accuracy rate of 91.61% for the detection of LV systolic dysfunction. In Conor et al.⁽³³⁾ study they found that an EPSS greater than 7 may be used to predict patients with severely reduced LVEF. In another study, EPSS of 7 mm would determine severe left ventricular dysfunction (EF <30%) with 100% sensitivity.

Study limitation:

1. This is a small observational case-control study, a large randomized multicenter study for extended period is required
2. Inclusion of diastolic function assessment
3. Inclusion of patients with Valve diseases
4. Comparing MAPSE & EPSS with Speckle tracking derived-, MRI derived- or 4 D echocardiogram derived EF.

CONCLUSION:

Despite the introduction of a sophisticated echocardiogram methods like 4D echocardiogram, Speckle tracking derived strain & CMR for the assessment of LVEF, we believe that both MAPSE & EPSS parameters are simple, easy to obtained & require no time especially in patients with poor acoustic window.

An average MAPSE of less than 7 mm & EPSS of more than 7 mm can be used as a surrogate of LV systolic dysfunction with acceptable sensitivity & specificity.

So we believe that both MAPSE & EPSS should be acquired routinely in all studies, & be used as an alternative method for assessing LV systolic function.

REFERENCES:

1. Alam M, Hoglund C, Thorstrand C: Longitudinal systolic shortening of the left ventricle: an echocardiographic study in subjects with and without preserved global function. *Clin Physiol.* 1992;12: 443-52.
2. Jones CJ, Raposo L, Gibson DG: Functional importance of the long axis dynamics of the human left ventricle. *Br Heart J.* 1990;63:215-20.
3. Hu K, Liu D, Herrmann S, Niemann M, Gaudron PD, Voelker W, Ertl G, Bijmens B, Weidemann F: Clinical implication of mitral annular plane systolic excursion for patients with cardiovascular disease. *Eur Heart J Cardiovasc Imaging.* 2013;14:205-12.
4. Willenheimer R, Israelsson B, Cline C, Rydberg E, Broms K, Erhardt L: Left atrioventricular plane displacement is related to both systolic and diastolic left ventricular performance in patients with chronic heart failure. *Eur Heart J.* 1999;20: 612-18.
5. Elnoamany MF, Abdelhameed AK: Mitral annular motion as a surrogate for left ventricular function: correlation with brain natriuretic peptide levels. *Eur J Echocardiogr.* 2006;7: 187-98.
6. Willenheimer R: Assessment of left ventricular dysfunction and remodeling by determination of atrioventricular plane displacement and simplified echocardiography. *Scand Cardiovasc J Suppl.* 1998;48:1-31.
7. Matos J, Kronzon I, Panagopoulos G, Perk G: Mitral annular plane systolic excursion as a surrogate for left ventricular ejection fraction. *J Am Soc Echocardiogr.* 2012;25: 969-74.
8. Bergenzaun L, Gudmundsson P, Ohlin H, During J, Ersson A, Ihrman L, Willenheimer R, Chew M: Assessing left ventricular systolic function in shock: evaluation of echocardiographic parameters in intensive care. *Crit Care.* 2011;15: R200-
9. Alam M, Hoglund C, Thorstrand C, Philip A: Atrioventricular plane displacement in severe congestive heart failure following dilated cardiomyopathy or myocardial infarction. *J Intern Med.* 1990;228: 569-75.
10. Willenheimer R, Cline C, Erhardt L, Israelsson B: Left ventricular atrioventricular plane displacement: an echocardiographic technique for rapid assessment of prognosis in heart failure. *Heart.* 1997;78:230-36.
11. Emilsson K, Wandt B: The relation between ejection fraction and mitral annulus motion before and after direct-current electrical cardioversion. *Clin Physiol.* 2000;20: 218-24.
12. Emilsson K, Wandt B: The relation between mitral annulus motion and ejection fraction changes with age and heart size. *Clin Physiol.* 2000;20: 38-43.
13. Höglund C, Alam M, Thostrand C: Atrioventricular Valve Plane Displacement in Healthy Persons. *Acta Med Scand.* 1988;224:557-62.

14. Rydberg E, Arlbrandt M, Gudmundsson P, Erhardt L, Willenheimer R: Left atrioventricular plane displacement predicts cardiac mortality in patients with chronic atrial fibrillation. *Int J Cardiol.* 2003;91:1-7.
15. Brand B, Rydberg E, Ericsson G, Gudmundsson P, Willenheimer R: Prognostication and risk stratification by assessment of left atrioventricular plane displacement in patients with myocardial infarction. *Int J Cardiol.* 2002;83: 35-41.
16. Carlhäll C, Wigström L, Heiberg E, Karlsson M, Bolger AF, Nylander E. Contribution of mitral annular excursion and shape dynamics to total left ventricular volume change, *Am J Physiol Heart Circ Physiol* , 2004; 287: H1836-41.
17. Claus P, Weidemann F, Dommke C, Bito V, Heinzl FR, D'Hooge J, et al. . Mechanisms of postsystolic thickening in ischemic myocardium: mathematical modelling and comparison with experimental ischemic substrates, *Ultrasound Med Biol* , 2007;33:1963-70.
18. Simonson JS, Schiller NB. Descent of the base of the left ventricle: an echocardiographic index of left ventricular function, *J Am Soc Echocardiogr* , 1989; 2: 25-35.
19. Silva JA, Khuri B, Barbee W, Fontenot D, Cheirif J. Systolic excursion of the mitral annulus to assess septal function in paradoxical septal motion, *Am Heart J* , 1996;131:138-45.
20. Hoffman EA, Ritman EL. Invariant total heart volume in the intact thorax, *Am J Physiol* , 1985; 249 : H883-90.
21. Carlhäll CJ, Lindstrom L, Wranne B, Nylander E. Atrioventricular plane displacement correlates closely to circulatory dimensions but not to ejection fraction in normal young subjects, *Clin Physiol* , 2001;21:621-8.
22. Wandt B, Bojö L, Tolagen K, Wranne B. Echocardiographic assessment of ejection fraction in left ventricular hypertrophy, *Heart* , 1999; 82:192-8.
23. Aurigemma GP, Silver KH, Priest MA, Gaasch WH. Geometric changes allow normal ejection fraction despite depressed myocardial shortening in hypertensive left ventricular hypertrophy, *J Am Coll Cardiol* , 1995;26:195-202.
24. Wandt B, Bojö L, Wranne B. Influence of body size and age on mitral ring motion, *Clin Physiol* , 1997;17:635-46.
25. Wandt B, Bojö L, Hatle L, Wranne B. Left ventricular contraction pattern changes with age in normal adults, *J Am Soc Echocardiogr* , 1998;11:857-63.
26. Lew W, Henning H, Schelbert H, Karliner J. Assessment of mitral valve E point-septal separation as an index of left ventricular performance in subjects with acute and previous myocardial infarction. *Am J Cardiol* 1978;41:836-45.
27. Engle SJ, Disessa T, Perloff J, Isabel-Jones J, Leighton J, Gross K, et al. Mitral valve E point to ventricular septal separation in infants and children. *Am J Cardiol* 1983;52:1084-7.
28. Emilsson K, Wandt B: The relation between ejection fraction and mitral annulus motion before and after direct-current electrical cardioversion. *Clin Physiol* 2000;20:218-24.
29. Emilsson K, Wandt B: The relation between mitral annulus motion and ejection fraction changes with age and heart size. *Clin Physiol* 2000;20:38-43.
30. QinQin J, Shiota T, Tsujino H. al.e. Mitral annular motion as a surrogate for left ventricular ejection fraction: real-time three-dimensional echocardiography & magnetic resonance imaging studies. *Eur j Echocardiogr* 2004;5:407-15.
31. Tsang W, Ahmad H, Patel A. al. e. Rapid estimation of left ventricular function using echocardiographic speckle tracking of mitral annular displacement. *J Am Soc Echocardiogr* 2010;23:511-15.
32. Walaa A, Alaa M, Mohamed Nabil. Mitral annular plane systolic excursion-derived ejection fraction: A simple & valid tool in adult males with left ventricular systolic dysfunction. *Echocardiography* 2016;33:179-84.
33. Conor J. McKaigney, Mori J. Krantz, Cherie L. La Rocque et al. E-point septal separation: a bedside tool for emergency physician assessment of left ventricular ejection fraction. *j.ajem.*2014.01.045
34. Abdalla Elagha, Anthon Fuisz. Mitral valve E-Point to Septal Separation (EPSS) measurement by cardiac magnetic resonance Imaging as a quantitative surrogate of Left Ventricular Ejection Fraction (LVEF). *J Cardiovasc Magn Reson.* 2012;14(Suppl 1):154.

