doi- https://doi.org/10.3329/cardio.v16i1.68216

## Original Article

# Use of the Left Ventricular Internal Dimension at End-Diastole and the Mitral Valve E-Point Septal Separation Ratio in the Prediction of the Left Ventricular Systolic Function

**Rownak Jahan Tamanna[1], Shabnam Jahan Hoque[2], Faisal Mohammed Pasha[3]**

*[1]Department of Cardiology, Shaheed Mansur Ali Medical College Hospital, Dhaka, [2]Department of Cardiology, BIRDEM General Hospital, Dhaka, [3]Department of Community Medicine, Shaheed Mansur Ali Medical College, Hospital, Dhaka*

***Key Words :***
*E-point septal separation, Left Ventricular ejection fraction, Left Ventricular Internal Dimension at End-Diastole.*

**Abstract:**

***Background:*** *Rapid assessment of left ventricular ejection fraction (LVEF) may be critical among emergency department (ED) patients. This study examined the predictive relationship between bedside Left Ventricular Internal Dimension at End-Diastole and the Mitral Valve E-Point Septal Separation (EPSS) Ratio to the quantitative calculated LVEF.*

***Methods:*** *A prospective observational study was conducted on a sequential convenience sample of patients, receiving comprehensive Transthoracic Echocardiography (TTE). The current study recruited 100 patients who presented to the Cardiology Clinic of Lab Aid Cardiac Hospital. Echocardiographic examinations were performed to obtain 2D guided M-mode measurements of the LVIDd & EPSS in addition to calculation of conventional, quantitative LVEF. All the measurements were done in the Para-sternal long-axis view.*

***Results:*** *It was found that LVEF determined by EPSS has very significant negative correlation with Calculated LVEF (r=—.766, p<0.001). LVEF determined by LVIDd/EPSS has also very significant positive correlation with calculated LVEF (r=.806, p<0.001), but correlation of LVIDd/EPSS was significantly higher than correlation of LVEF with only EPSS. LVIDd/EPSS <7 is strongly predictive of reduced LVEF<50% (P<.001). An LVIDd/EPSS <6 mm is evidence of reduced LVEF < 40%, (P<.001). Of note LVIDd/ EPSS <4 mm correlates with severely decreased function, with an estimated LVEF of <30% (P <.001). As was shown by the results of the linear regression analysis, most significant determinant of LVEF was LVIDd/EPSS (R=.806, p<0.001) The results of the linear regression analysis indicated that the LVIDd/EPSS was an independent predictor of the LVEF (P<0.001). Measurements of LVIDd/EPSS were significantly associated with the calculated measurements of LVEF from comprehensive TTE.*

***Conclusion:*** *The LVIDd/EPSS may allow certain clinicians, especially beginners and emergency department physicians, to assess the LVEF when other methods are not available or questionable.*

***(Cardiovasc j 2023; 16(1): 24-31)***

### Introduction:

Transthoracic Echocardiography is the method of choice for the assessment of the LV myocardial systolic function. The best approach to evaluate the cardiac function in the emergency department setting has not been determined. Measures for the calculation of the LVEF are difficult to perform and time-consuming, which limits their use in the emergency department.[1] Most emergency department physicians are not trained in the quantitative calculation of the LVEF. A limited number of studies in the literature suggest that visual prediction by emergency department physicians correlates with the quantitative and semi quantitative methods of estimating the cardiac function.[2] The major limitations of visual prediction for evaluating the LVEF are observer dependency and subjectivity.[3] An alternate

**Address of correspondence:** Dr. Rownak Jahan Tamanna, Department of Cardiology, Shaheed Mansur Ali Medical College Hospital, Dhaka, Bangladesh. email-tamannarownak4@gmail.com

method for estimating the LVEF is the mitral valve E-point septal separation (EPSS). Similar to the left ventricular internal dimension at end-diastole (LVIDd), the EPSS is a simple linear M-mode measurement obtained from the parasternal long-axis view. The amount of separation between the valve leaflet and the septum in early diastole is defined as the EPSS.[4] The EPSS can generate a rapid quantitative measure of the LV function, especially when the acquisition of multiple breath-hold short-axis images proves difficult.[5] Previous studies have demonstrated a high negative correlation between the EPSS and the LVEF, with the EPSS measurements of >7 mm indicating a poor LV function.[6] A previous investigation revealed a significant correlation between the LV end-diastolic dimensions and the body surface area in patients with HF.[7] The same research also demonstrated that the basal LVIDd affected the EPSS, which was useful in predicting systolic dysfunction.

In this study, we aimed to investigate the ability of a new index, namely the LVIDd/EPSS, to predict the LV systolic function and to compare its performance with that of the EPSS using M-mode. Secondarily, we aimed to determine whether the LVIDd/EPSS measurements correlate with the calculated LVEF from comprehensive transthoracic echocardiography.

**Methods:**

This was an observational study of the association between the EPSS and the LVIDd/EPSS with the LVEF in patients undergoing comprehensive transthoracic echocardiography for any indication. The current study recruited 100 consecutive patients who presented to the Cardiology Outpatient Clinic of Lab Aid Cardiac Hospital, Dhaka in the period of March 2020 and April 2021. A normal left ventricular ejection fraction (LVEF) typically considered e"50%. An LVEF between 40% and 49% was considered heart failure with a midrange ejection fraction (HFmrEF), an LVEF<40% was classified as HFrEF, and an LVEFd"30% was defined as AHF. M-mode and 2D echocardiograms were recorded on a Vivid ™ E 95 with cSound ™ ultrasound system (GE Medical System) with M5sc-D ( GE) multifrequency transducer. To prevent systematic errors in obtaining or interpreting the echocardiograms, two different cardiologists performed the echocardiograms and the mean values were taken by at least 2 measurements for reducing interobserver and intraobserver variability. Echocardiographic examinations were performed to obtain two-dimensionally M-mode measurements of the LVIDd, LVIDs, septal and posterior wall thickness, all in the para-sternal long-axis view. The modified Simpson rule was used for calculating the LVEF. M-mode measurements of the LVIDd and quantitative, calculated LVEF was recorded.

In addition to routine echocardiographic measurements, EPSS was measured by M-mode in the para-sternal long axis view (PLAX) of the heart. EPSS was obtained by placing the M-mode tracer over the distal tip of the anterior leaflet of the mitral valve, as in the image below (Fig-1). The EPSS was measured in millimeters (mm) as the minimum separation distance between the mitral valve anterior leaflet and interventricular septum in M-mode echocardiography (Fig-2). Patients who had atrial fibrillation, asymmetric septal hypertrophy, severe LV hypertrophy, severe valve diseases were excluded from the study. This study was approved by the local institutional ethics committee and conducted in accordance with the Declaration of Helsinki.

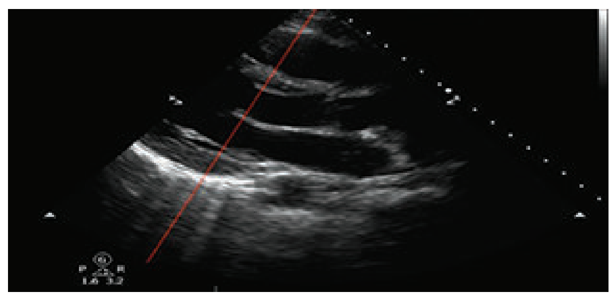

**Fig.-1:** *Red line showing correct M-mode cursor placement in PLAX view.*

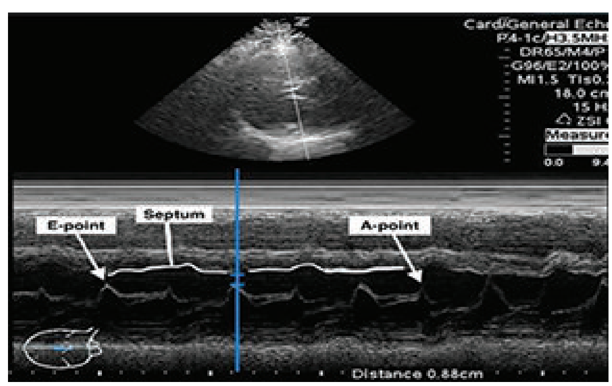


**Fig.-2:** *Measurement of EPSS (blue calipers) with labels of E-point, A-point and partial tracing of septal wall. In the image above EPSS is 8.8 mm, indicating abnormal systolic function.*

**Statistical Analysis:**
Numerical data obtained from the study were analyzed and significance of difference was estimated by using statistical method. The statistical data were analyzed using IBM SPSS 25.0. The continuous data were expressed as frequency, the mean±standard deviation, and the categorical data were expressed as percentages. Significance of difference between groups was evaluated by paired and unpaired student t test. Graphical representation, Correlation test & Pearson correlation coefficient were employed to analyze the relationship between EPSS, LVIDd/ EPSS & LVEF. Stepwise simple & multiple linear regression analysis was used to estimate the relation between Echocardiographic variables and calculated LVEF and also to identify best predictor of LVEF. Probability values ($P<0.05$) were considered statistically significant in the analyses.

**Results:**
Echocardiographic tracings of sufficient quality for analysis were obtained in all patients.

Fig 3 showed age and sex distribution of study patients. In total, 100 patients were enrolled in the study. We examined 53 male (53%) and 47 female (47%). Age range: 30 - 103, majority of the cases (>60%), of are in between 41-to 70 yrs of age. Age - Mean ±SD (58.7±11.66 yrs), Male and Female ratio 1.1: 1. Majority male patient are in between 51-70 yrs of age and Majority of female patient are in between 61 to 70 yrs of age.

Table I showed Distribution of Echocardiography parameters. The LVEF ranged from 20% to 68% (mean ± SD 47.14±15.77), the EPSS ranged from 4 to 28 mm (mean ±SD 9.26±5.60), the LVIDd ranged from 30 to 72 mm (mean ± SD 50.43±8.97), LVIDd/EPSS ranged from 2.2 to 11 (mean ± SD 6.232 ± 2.097), LVIDs ranged from 12mm to 62 mm (mean ± SD 34.77 ± 12.32).

Fig 4 showed Distribution of LVEF in respect of LVIDd / EPSS. It has been shown that, there was a positive relationship of LVEF with LVIDd/EPSS. When LVIDd/EPSS was lower, ~ 2.7, LVEF was reduced, ~22%, but when LVIDd/EPSS was higher~ 8.4, LVEF was normal, ~66 %.

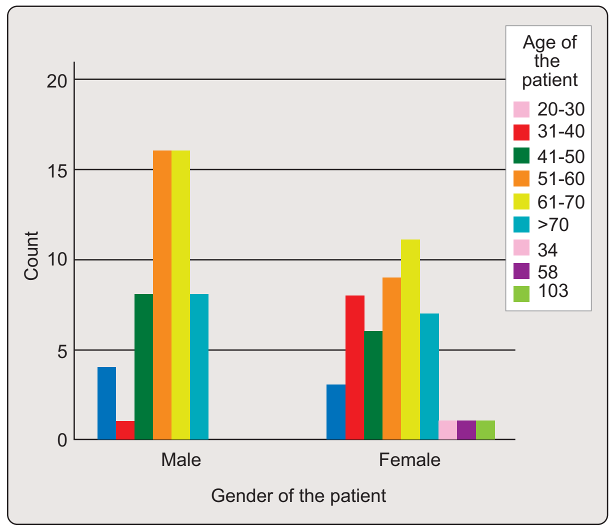


**Fig 3:** *Age and sex distribution of the study patients.*

**Table-I**
*Distribution of Echocardiography parameters.*

| *Echocardiographic Parameters* | N | Minimum | Maximum | Mean | Std Deviation |
|---|---|---|---|---|---|
| Left Ventricle Diastolic Dimension ( LVIDd) | 100 | 30 | 72 | 50.43 | 8.976 |
| Left Ventricle Systolic Dimension ( LVIDs) | 100 | 12 | 62 | 34.77 | 12.321 |
| Left Ventricular Ejection Fraction ( LVEF) | 100 | 20 | 68 | 47.14 | 15.777 |
| E Point Septal Seperation( EPSS) | 100 | 4 | 28 | 9.26 | 5.601 |
| LVIDd/EPSS | 100 | 2.2 | 11 | 6.232 | 2.097 |

Data presented as Mean± SD

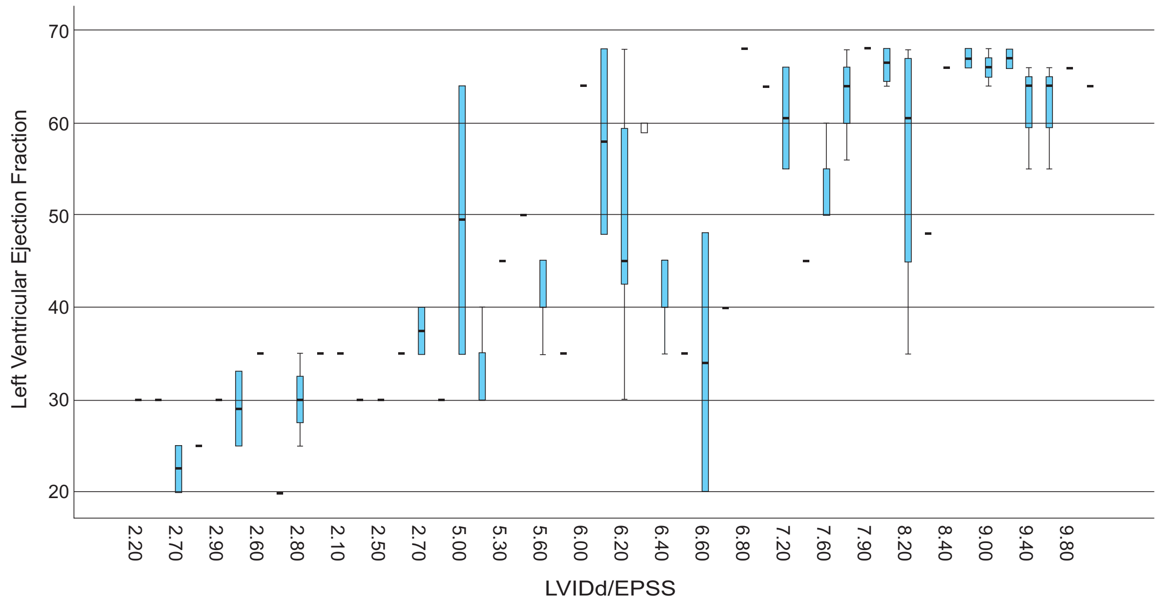


**Fig.-4:** *Stem-and-Leaf Plots of LVEF in relation to LVIDd/EPSS in the study patients.*

Table II showed significance of relation of LVEF with LVIDd/ EPSS. An LVIDd/EPSS <6 mm is evidence of reduced LVEF < 40%, (p<.001). Of note LVIDd/ EPSS <4 mm correlates with severely decreased function, with an estimated LVEF of <30%. (p<.001)

Table III showed correlation of mean LVIDd/EPSS & LVEF. The results of the analysis of the patients with an LVIDd/EPSS <7 revealed a significant association between the LVEF and the LVIDd/ EPSS (*r*=-0.806; p<0.001) and LVIDd/EPSS <7 is strongly predictive of reduced LVEF<50%.

Table IV showed Pearson Correlation between Calculated LVEF & EPSS. A statistically very significant negative correlation of EPSS (r=-.766, p<0.001) was found with calculated LVEF.

Table V showed Pearson Correlation between calculated LVEF & LVIDd/EPSS. A statistically very significant positive correlation of LVIDd/ EPSS (r=.806, p<0.001) was observed with calculated LVEF. But correlation of LVIDd/EPSS with LVEF was higher than the correlation of LVEF with only EPSS.

**Table-II**

*Significance of Relation of LVEF with LVIDd/ EPSS.*

| LVEF (%) | LVIDd/EPSS | Std Deviation | p value |
|---|---|---|---|
| 66 | 8.84 | .770 | .000$^{s}$ |
| 55 | 8.12 | 1.44 | .000 |
| 45 | 6.137 | .656 | .000$^{s}$ |
| 35 | 5.238 | 1.31 | .000$^{s}$ |
| 25 | 3.125 | .499 | .000$^{s}$ |

*p value reached from unpaired student t test/Independent sample t test,
S = significant, p<.001

**Table-III**

*Correlation of mean LVIDd/EPSS & LVEF.*

| Parameter | Mean | N | Std deviation | Correlation | p value |
|---|---|---|---|---|---|
| LVEF | 47.14 | 100 | 15.77 | .806 | .000$^{s}$ |
| LVIDd/EPSS | 6.232 | 100 | 2.097 | | |

p value reached from Paired sample t test, **.
Correlation is significant at the 0.01 level (2-tailed).

**Table-IV**

*Pearson Correlation between EPSS and Calculated LVEF.*

| LVEF | Pearson Correlation Co –efficient (r value)(N=100) | p value |
|---|---|---|
| EPSS | -.766** | .000s |

P value derived from Pearson correlation, S= significant, **. Correlation is significant at the 0.01 level (2-tailed).

**Table-V**

*Pearson Correlation between LVIDd/EPSS and Calculated LVEF.*

| LVEF | Pearson Correlation Co –efficient (r value) (N=100) | P value |
|---|---|---|
| LVIDd/EPSS | .806** | .000s |

P value derived from Pearson correlation, S= significant, ** Correlation is significant at the 0.01 level (2-tailed).

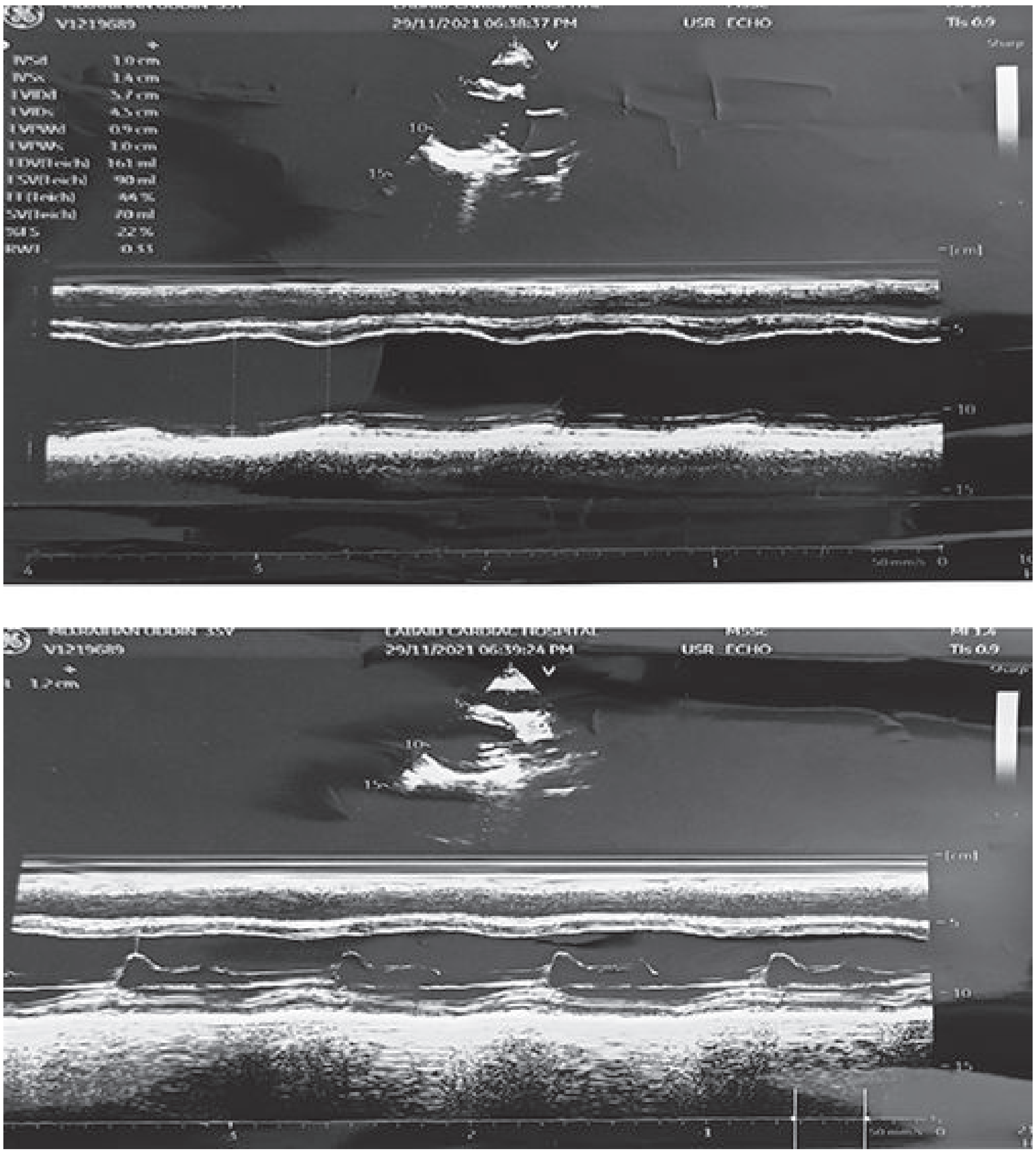


**Fig.-5a. & 5b:** *Measurement of LVEF In the image above (Fig 5a) & EPSS in the image below (Fig 5b). LVEF is ~44% and EPSS is ~12 mm, LVIDd~ 57 mm, LVIDd/EPSS ~4.75, indicating abnormal systolic function.*

Table VI showed Simple Linear Regression analysis. As was shown by the results of the linear regression analysis, the LVIDd/EPSS was significantly associated with the LVEF. Most significant determinant of LVEF was LVIDd/EPSS (r=.806, p<0.001) followed by LVIDs (r=.781, p<0.001), EPSS (r=.766, p<0.001)) & LVIDd (r=.613, p<0.001)

Table VII showed Stepwise Multiple linear regression analysis. By combining different Echocardiographic variables in stepwise multiple linear regression analysis an attempt for predicting LVEF was done. When other variables were included with the variable EPSS into multiple linear regression analysis the resultant correlation coefficient was ((r=.836, p= .001 s)

**Table-VI**

*Simple Linear Regression.*

| Simple Linear Regression analysis | r value | r Square | Standardized Co-efficient Beta | p value |
|---|---|---|---|---|
| LVIDs | .781 | .611 | - .781 | .000s |
| EPSS | .766 | .586 | -.766 | .000s |
| LVIDd | .613 | .376 | - .613 | .000s |
| LVIDd/EPSS | .806 | .650 | .806 | .000s |

p value derived from Pearson correlation, S= significant, **
Correlation is significant at the 0.01 level (2- tailed).

**Table-VII**

Stepwise Multiple linear regression analysis

| Stepwise Multiple Linear regression analysis | r value | r Square | p value |
|---|---|---|---|
| LVIDs | .781 | .611 | .000s |
| LVIDs+EPSS | .812 | .660 | .000 s |
| LVIDs+EPSS+LVIDd | .836 | .699 | .001 s |

P value derived from Pearson correlation, S= significant, **. Correlation is significant at the 0.01 level (2-tailed). *a)Predictor s (Constant): Left Ventricle Systolic Dimension, E Point Septal Separation, Left ventricle Diastolic Dimension. b) Dependent variable : Left Ventricular Ejection Fraction*

Fig 6 depicts the scatter plot of the LVEF versus the EPSS with a regression line. There was a highly significant negative correlation between the LVEF and the EPSS (*r*= -.766; P<0.001).
LVEF, Left ventricular ejection fraction; EPSS, mitral valve E-point septal separation.

Figure 6b depicts the scatter plot of the LVEF versus the LVIDd/EPSS with a regression line. There was a highly significant positive correlation between the LVEF and the LVIDd/EPSS (*r*= .806; p<0.001). *LVEF, Left ventricular ejection fraction; EPSS, mitral valve E-point septal separation, LVIDd-Left ventricular internal dimension in diastole.*

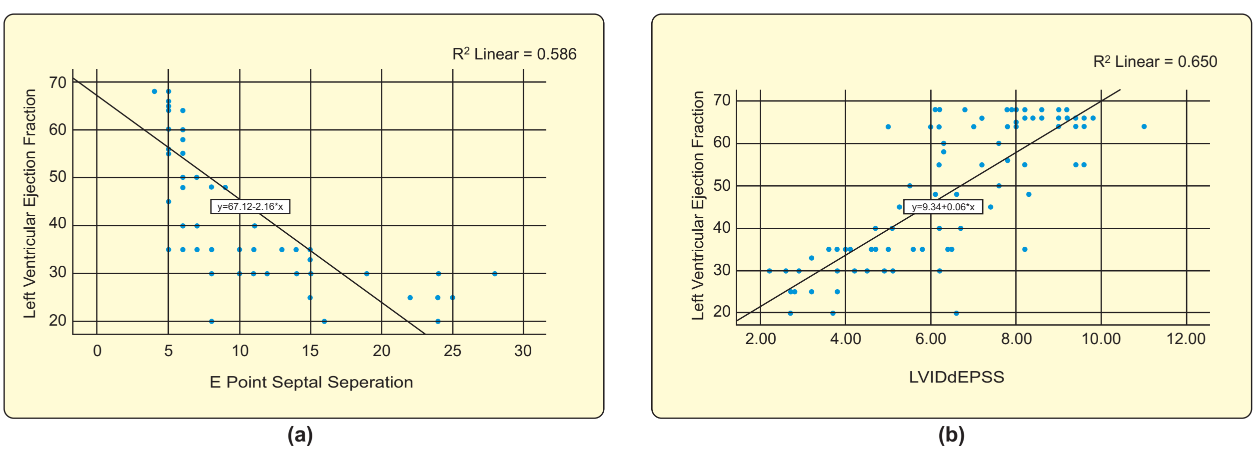


**Fig-6:** *(a) Scatter plot showing correlation between Calculated LVEF & EPSS. (b) Scatter plot showing correlation between Calculated LVEF & LVIDd/EPSS*

## Discussion

The visual estimation of the LVEF is commonplace and correlates well with ventriculography.[8] Emergency physicians have been shown to be accurate at visual estimation of the LVEF without quantitative measurements.[9,10] However, there is still value in a quick and easy quantitative measurement of the LVEF. Objective measurements can be helpful for early learners who aren't yet confident in visual LVEF estimation. The E-Point Septal Separation (EPSS) is an easy measurement to obtain that is accurate in estimating the LVEF.

The present study showed a significant correlation between the LVEF and the EPSS. But the study at the same time revealed a more significant correlation between the LVEF and the LVIDd/ EPSS.

The mitral valve EPSS is easy-to-obtain echocardiographic parameter that correlates inversely with the LVEF. Secko et al.[11] showed that junior emergency physicians could readily obtain the EPSS measurements that correlated with the visual estimates of the LVEF. By contrast, we used a quantitative calculation of the LVEF. Our results demonstrated a highly significant negative correlation between the LVEF and the EPSS (r=-.766, p<0.001). In this study, we investigated whether the LVIDd/EPSS could serve as a substitute for the EPSS index and whether it could augment the sensitivity of this index. In all the study groups, the LVIDd/EPSS showed highly significant positive correlation with the LVEF (r=.806, p<0.001) and correlation was stronger than that with the EPSS. The results of the analysis of the patients with an LVIDd/EPSS <7 revealed a significant association between the LVEF and the LVIDd/EPSS (*r*=-0.806; P<0.001) and LVIDd/EPSS <7 is strongly predictive of reduced LVEF<50%. In our study an LVIDd/EPSS <6 is evidence of reduced LVEF < 40% (P<.001). Of note LVIDd/ EPSS <4 mm correlates with severely decreased function, with an estimated LVEF of <30% (p<.001)· Another study demonstrated that an EPSS > 7 mm is evidence of reduced LVEF. Of note, EPSS e" 13 mm correlates with severely decreased function, with an estimated LVEF of d" 35%.[12] For most patients, EPSS gives a good estimation of Cardiac function.

One study derived the following equation: LVEF = 75.5 – (2.5 x EPSS) with a correlation of (r= 0.80).[13] A second study derived a similar equation and correlation and demonstrated 100% sensitivity of an EPSS measurement > 7mm for detecting severely reduced EF (<30%).[6]

This is the study to suggest that the LVIDd/EPSS may predict the LVEF using linear regression. As was shown by the results of the linear regression analysis, the LVIDd/EPSS was significantly associated with the LVEF. Most significant determinant of LVEF was LVIDd/EPSS (r=.806, p<0.001) followed by LVIDs (r=.781, p<0.001), EPSS (r=.766, p<0.001)) & LVIDd (r=.613, p<0.001). The LVIDd/EPSS was an independent predictive marker of LVEF. Our results demonstrated a significant positive correlation between the LVEF and the LVIDd/EPSS in patients with HFmrEF and HFrEF & AHF.

There are some patient populations in which EPSS may give an inaccurate estimate of cardiac function. Patients with mitral stenosis have poor opening of their mitral valve even with otherwise adequate cardiac function, and may have a falsely high EPSS measurement despite normal function. Similarly, patients with aortic regurgitation may also have poor forward anterior leaflet movement and will have a falsely high EPSS measurement while possibly having a preserved LVEF. Patients with atrial fibrillation will lack an A-point due to lack of coordinated atrial contraction, and will have beat-to-beat variability in EPSS due to the same discoordination.[14] To improve estimations in these patients averaging several measurements of EPSS is required. In dilated cardiomyopathy or other non-ischemic diseases that cause AHF, ventricular dilatation develops and the chamber becomes rounder (spherical) as the disease progresses. Holler et al., [15] showed that the sphericity index, which is calculated by dividing the length of the LV through the width of the LV, does not appear to be more sensitive than the EPSS. We did not use this index in our study. The EPSS was more affected by the basal LVIDd. Therefore, a smaller basal LVIDd may result in a smaller EPSS increase. The LVIDd/EPSS accurately distinguished individuals with a normal LV function from those with an abnormal LV function, irrespective of the LV size.

**Limitations:**

This study was based on data from a single centre. Another weakness of this study is its relatively small sample size. In future studies, it may be more appropriate to include healthy individuals as well as patients suffering from HF (HFrEF, HFmrEF, and HFpEF) in wide spectrum and multicentre. In addition, the associations between the LVIDd/EPSS and the LVEF in each category of the LV geometry (normal, concentric remodeling, concentric hypertrophy, and eccentric hypertrophy) merit further research.

**Conclusion:**

LVIDd/EPSS was significantly & more strongly correlated with calculated measurements of LVEF from comprehensive TTE than it was with the EPSS. An LVIDd/EPSS measurement less than <7 mm was uniformly sensitive at identifying patients with reduced LVEF<50%. The LVIDd/EPSS, which can easily be calculated, appears to be quite useful for the prediction of systolic dysfunction. The role of the LVIDd/EPSS in the prediction of systolic dysfunction requires further investigation in studies with a larger patient population.

**Conflict of Interest - None.**

**References**


1. Pershad J, Myers S, Plouman C, et al. Bedside limited echocardiography by the emergency physician is accurate during evaluation of the critically ill patient. *Pediatrics*. 2004;114(6):e667-e671. doi:10.1542/peds.2004-0881
2. Randazzo MR, Snoey ER, Levitt MA, Binder K. Accuracy of emergency physician assessment of left ventricular ejection fraction and central venous pressure using echocardiography. *Acad Emerg Med*. 2003;10(9):973-977. doi:10.1111/j.1553-2712.2003.tb00654.x
3. Darbar D, Gillespie N, Byrd BF. Can qualitative echocardiography be used to select patients for angiotensin-converting enzyme inhibitors following acute myocardial infarction?. *Eur Heart J*. 1996;17(12):1783-1786. doi:10.1093/oxfordjournals.eurheartj.a014791
4. Weekes AJ, Reddy A, Lewis MR, Norton HJ. E-point septal separation compared to fractional shortening measurements of systolic function in emergency department patients: prospective randomized study. *J Ultrasound Med*. 2012;31(12):1891-1897. doi:10.7863/jum.2012.31.12.1891
5. Lew W, Henning H, Schelbert H, Karliner JS. Assessment of mitral valve E point-septal separation as an index of left ventricular performance in patients with acute and previous myocardial infarction. *Am J Cardiol*. 1978;41(5):836-845. doi:10.1016/0002-9149(78)90722-1
6. McKaigney CJ, Krantz MJ, La Rocque CL, Hurst ND, Buchanan MS, Kendall JL. E-point septal separation: a bedside tool for emergency physician assessment of left ventricular ejection fraction. *Am J Emerg Med*. 2014;32(6):493-497. doi:10.1016/j.ajem.2014.01.045
7. Andersson B, Caidahl K, Waagstein F. An echocardiographic evaluation of patients with idiopathic heart failure. *Chest*. 1995;107(3):680-689. doi:10.1378/chest.107.3.680
8. CHEITLIN M, ARMSTRONG W, AURIGEMMA G, et al. ACC/AHA/ASE 2003 guideline update for the clinical application of echocardiography: Summary article*1a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASE Committee to update the 1997 guidelines for the clinical application of echocardiography). *Journal of the American Society of Echocardiography*. 2003;16(10):1091-1110. doi:10.1016/s0894-7317(03)00685-0
9. Ünlüer E, Karagöz A, Akoðlu H, Bayata S. Visual estimation of bedside echocardiographic ejection fraction by emergency physicians. *Western Journal of Emergency Medicine*. 2014;15(2):221-226. doi:10.5811/westjem.2013.9.16185
10. Moore CL, Rose GA, Tayal VS, Sullivan DM, Arrowood JA, Kline JA. Determination of left ventricular function by emergency physician echocardiography of hypotensive patients [published correction appears in Acad Emerg Med 2002 Jun;9(6):642]. *Acad Emerg Med*. 2002;9(3):186-193. doi:10.1111/j.1553-2712.2002.tb00242.x
11. Secko MA, Lazar JM, Salciccioli LA, Stone MB. Can junior emergency physicians use E-point septal separation to accurately estimate left ventricular function in acutely dyspneic patients?. *Acad Emerg Med*. 2011;18(11):1223-1226. doi:10.1111/j.1553-2712.2011.01196.x
12. Ma O, Mateer JR, Reardon RF, Joing SA. Emergency Ultrasound, Third Edition. McGraw Hill Education. 2014.
13. Silverstein JR, Laffely NH, Rifkin RD. Quantitative estimation of left ventricular ejection fraction from mitral valve E-point to septal separation and comparison to magnetic resonance imaging. *Am J Cardiol*. 2006;97(1):137-140. doi:10.1016/j.amjcard.2005.07.118
14. Massie BM, Schiller NB, Ratshin RA, Parmley WW. Mitral-septal separation: new echocardiographic index of left ventricular function. *Am J Cardiol*. 1977;39(7):1008-1016. doi:10.1016/s0002-9149(77)80215-4
15. Holler PJ, Wess G. Sphericity index and E-point-to-septal-separation (EPSS) to diagnose dilated cardiomyopathy in Doberman Pinschers. *J Vet Intern Med*. 2014;28(1):123-129. doi:10.1111/jvim.12242