Original Article

Validation of "left ventricular early inflow-outflow index": A novel echocardiographic method for quantification of mitral regurgitation in an Indian population with special focus on rheumatic etiology

Charan Lanjewar, Aniruddha Pawar, Devendra Patil, Madivalaswami Dhavalagimath, Girish Sabnis[*], Hetan Shah, Prafulla Kerkar

Seth G S Medical College, K E M Hospital, Mumbai, India

ABSTRACT

Background: Quantification of mitral regurgitation (MR) has always required an "integrated approach" as there is no single gold-standard method. We investigated a new Doppler-derived parameter "left ventricular early inflow-outflow index (LVEIO)" for the quantification of MR and its likelihood to predict severe MR in correlation with already established parameters in an Indian population including a large subset of patients with rheumatic etiology.
Methods: A prospective study was performed at a major tertiary care center in western India over a 5-month period. Five hundred patients diagnosed with isolated MR including 260 (52%) patients with rheumatic etiology were included in the study after applying exclusion criteria. We analyzed MR using color flow jet, effective regurgitant orifice area (EROA), and vena contracta (VC) width. LVEIO is a simplification of the regurgitant volume (RV) method, which was calculated as "E velocity divided by LV outflow velocity integrated over the systolic ejection period left ventricular outflow tract velocity time integral" and compared with the established parameters.
Results: LVEIO was 4.65 ± 1.45, 6.56 ± 1.52, and 9.91 ± 3.70 among patients diagnosed with mild, moderate, and severe MR, respectively ($p < 0.001$). Those with LVEIO ≥8 were the most likely to have severe MR (positive likelihood ratio: 10.42). LVEIO had specificity of 93.25% for diagnosis of severe MR with positive predictive value of 86.36%. There was positive correlation observed between LVEIO and VC width ($r = 0.591$), RV ($r = 0.410$), and EROA ($r = 0.778$) (all $p < 0.001$) in the Pearson correlation test. The specificity of LVEIO remained consistent in diagnosing severe MR in patients with rheumatic etiology.
Conclusion: LVEIO is a simple yet specific Doppler echocardiographic parameter for estimation of severity of MR including that of rheumatic etiology.

1. Introduction

Valvular heart diseases constitute a major cardiovascular burden. Mitral regurgitation (MR) is the most commonly encountered valvular pathology in modern clinical practice.[1] Doppler echocardiography is an excellent tool for detecting the presence of MR and defining the underlying pathological cause. However, quantification of MR using a single parameter is difficult.

The American Society of Echocardiography (ASE) and European Society of Cardiology (ESC) guidelines for valvular heart diseases outline a number of validated semiquantitative and quantitative parameters for grading severity of MR including early diastolic mitral inflow (E) velocity, vena contracta (VC) width, and effective regurgitant orifice area (EROA) measured by the proximal iso-velocity surface area (PISA) method and regurgitant volume (RV) method.[2,3] However, an integrative approach is recommended because of the limitations specific to each parameter. In addition, measurement of each of the aforementioned parameters is time consuming. We focused on Doppler tracing measurements, which are more reproducible than anatomic measurements. The left ventricular early inflow-outflow index (LVEIO) has initially been described by Lee et al[4] and was calculated using a single-point measurement of E (instead of a tracing of the entire mitral inflow profile), divided by the left ventricular (LV) outflow velocity integrated over the systolic ejection period. We sought to study the

* Corresponding author.
E-mail address: girishsabnis@yahoo.co.in (G. Sabnis).

application of this appealing echocardiographic parameter to our patient population.

2. Methods

2.1. Study sample and design

All patients ($n = 5570$) referred for echocardiography in a major tertiary care center in western India during a 5-month period from January 2017 to May 2017 were screened for the presence of MR. Patients having other coexisting valvular heart diseases such as mitral stenosis, aortic stenosis, LV outflow tract obstruction, aortic regurgitation, prior valve replacement, or congenital cardiac diseases were excluded from the study. Patients with atrial fibrillation and heart rates beyond normal range (60–110 beats per minute) were excluded. However, patients having eccentric jets of MR and LV dysfunction were included. The examinations were performed using a S-3 probe of Vivid T8 (GE Healthcare, Chicago, Illinois, United States) echocardiography systems by a single operator (a clinical cardiologist having about 30-month experience in echocardiography). The imaging was supervised by a senior resident in cardiology with about 4-year experience in echocardiography.

We prospectively analyzed 500 patients with isolated MR, and assessment of severity was performed using color flow jet, left atrial (LA) size, E velocity, EROA by the PISA method, VC width, and RV method. Because there is no true gold standard for grading the severity of MR, the integrative assessment according to the ASE guidelines was used as a reference standard for this study (Fig. 1).[2] Efforts were taken by the operator to obtain the best possible measurements in every case. Unsuitable images were discarded, and reimaging was performed. LVEIO is a simplification of the RV method and uses only a single-point measurement of E and LV outflow velocity integrated over systolic period.

2.2. Echocardiographic evaluation of MR

The echocardiography preset of the echocardiography machine was kept fixed for the entire study duration. The settings included imaging at frequency of 3.3 MHz, pulse repetition frequency at 3.3 KHz, dynamic range set between 70 and 75 dB, and optimal gain and color flow sample volume at 1.2 mm. The Doppler assessment was performed at 2 MHz with a sample volume of 2–4 mm for pulsed-wave Doppler.

2.3. Color flow imaging

Color flow imaging was used to determine the presence of MR. With increasing severity, the size and the extent of the jet into the LA also increase.[2,5,6] However, color flow imaging as a sole method to assess MR severity was discouraged because of its dependence on multiple confounding variables such as instrument settings, jet eccentricity, and overall hemodynamics. It was used only for detecting MR. Integrative approach was followed when the MR grade was suspected to be mild or above on color flow imaging. Fig. 1 shows an integrated approach for MR quantification followed in our study. However, a large holosystolic jet imaged at optimum color gain wrapping around the LA was also considered as severe MR.
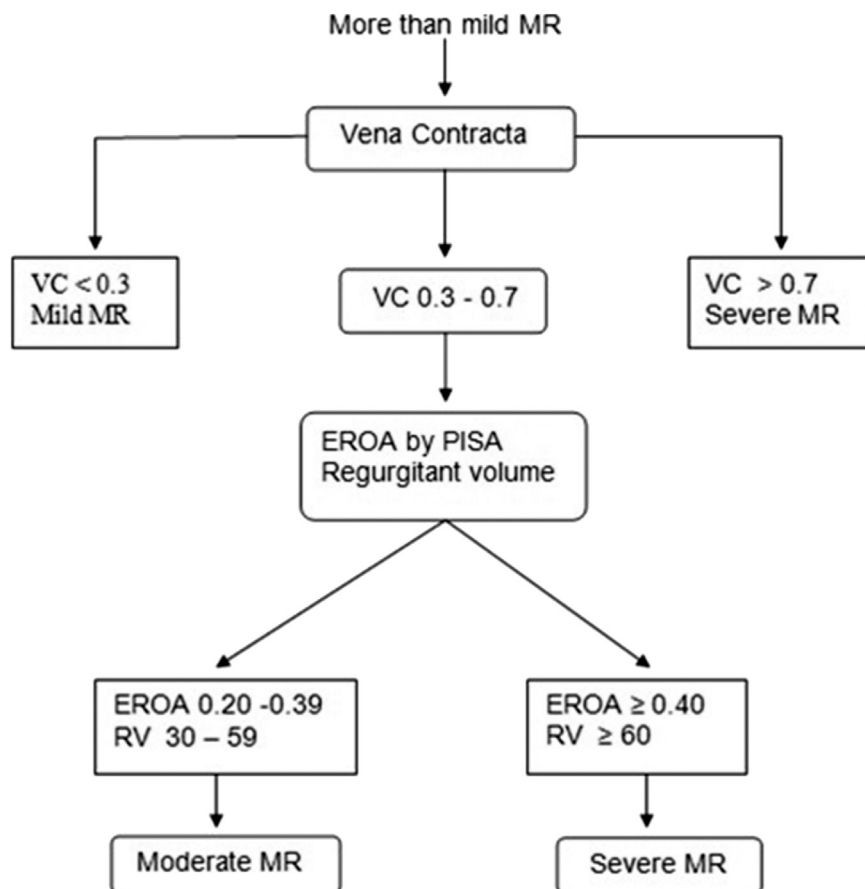

Fig. 1. Integrative approach for quantification of severity of mitral regurgitation (adapted from the study by Zoghbi et al[2]). EROA, effective regurgitant orifice area; MR, mitral regurgitation; PISA, proximal isovelocity surface area; RV, regurgitant volume; VC, vena contracta.

2.4. Vena contracta width

The VC width is the area of the jet as it leaves the regurgitant orifice; it, thus, reflects the regurgitant orifice area.[7–10] The VC was imaged primarily in the parasternal long axis and apical four-chamber view. Multiple (3–4) readings in these orthogonal views were obtained. Measurements were obtained as perpendicular to the commissural line as possible. VC estimation was attempted even in eccentric jets. Zoom function was used for appropriate measurements of VC.

2.5. The flow convergence method

Measurements for calculations of EROA and RV by the PISA method were obtained as recommended in the apical four-chamber view.[5] For ease of calculations, the aliasing velocity (therefore the Nyquist limit) was fixed at 40 cm/s on both machines, and zoom function was used for accurate assessment of the PISA radius. Although known to be less accurate, efforts were taken to calculate the EROA and RV using the PISA method in eccentric jets too.

2.6. Volumetric assessment method

The RV was estimated as graphically depicted in Fig. 2. The mitral annular diastolic velocity time integral (VTI) was estimated by tracing the entire envelope obtained by pulsed Doppler interrogation at the tip of mitral leaflet in diastole. The mid diastolic mitral annular diameter was measured, and the LV inflow volume was calculated accordingly.[2] Similarly, LV stroke volume was assessed using the LV outflow systolic VTI in apical four-chamber view placing the sample volume just below the aortic valve and left ventricular outflow tract (LVOT) diameter in parasternal long-axis view (measurements calculated using zoom function).

2.7. LV early inflow-outflow index

LVEIO is modification of RV method (Fig. 2). The E velocity was measured from the pulsed-wave Doppler recording. A 2- to 4-mm sample volume was placed at the inlet of LV as parallel to the LV inflow as possible at the tip of mitral leaflets. Once a clean envelope was obtained after optimizing the filter and rejection limits, E velocity was obtained at near end expiration assessed clinically. Respiratory gating was not performed during the study. LVOT VTI was traced from the pulse-wave Doppler recording at the LV outflow tract assessed in the apical five-chamber view. As there was no aortic valvular pathology in the study population, the expected jets were low velocity, thereby minimizing errors due to Doppler angle malalignment. LVEIO was calculated using the following formula:

LVEIO = E velocity/LVOT VTI
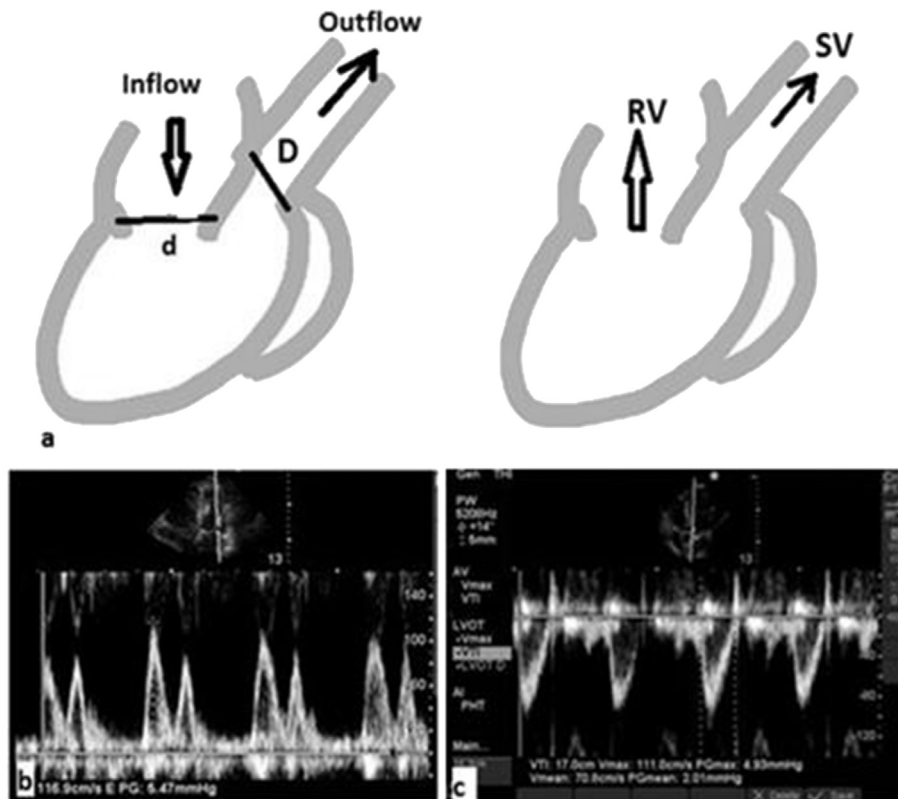
RV = LV Inflow − LV Outflow

Regurgitant fraction = RV / LV Inflow

LVEIO = E / LVOT VTI

Fig. 2. Graphical presentation of RV method (a), and measurement of E velocity (b) and LVOT VTI (c). d, mitral annulus diameter; D, LVOT diameter; E, mitral inflow velocity; LVEIO, left ventricular early inflow outflow index; LVOT, left ventricular outflow tract diameter; RV, regurgitant volume; SV, stroke volume; VTI, velocity time integral.

2.8. Statistical analysis

Descriptive and inferential statistical analysis was carried out using statistical software namely SPSS 15.0. Analysis of variance has been used to find the comparison of study parameters such as LA, VC, PISA, EROA, E velocity, LVOT VTI, and LVEIO and their significance with severity of MR. Chi-square/Fisher's exact test has been used to find the significance of study parameters on categorical scale between two or more groups. p values were considered significant if $p < 0.01$. Pearson correlation between study variables was performed to find the degree of relationship.

3. Results

Baseline characteristics of patients according to etiology of MR is shown in Table 1. There were 165 patients with mild MR, 146 patients with moderate MR, and 189 patients with severe MR. Significant increasing trends of values were demonstrated for E-wave velocity, LVOT VTI, VC width, PISA radius, EROA, RV, and LA dimension in end diastole in parasternal long-axis view across groups with increasing severity of MR (Table 2). The values found for each parameter were consistent with the ASE/ESC guidelines for grading MR.

3.1. LV early inflow-outflow index

LVEIO was 4.65 ± 1.45, 6.56 ± 1.52, and 9.91 ± 3.70 among patients diagnosed with mild, moderate, and severe MR, respectively ($p < 0.001$). Increasing trends were observed across groups with increasing severity of MR ($p < 0.001$) (Table 2). Those with LVEIO ≥ 8 were the most likely to have severe MR (positive likelihood ratio 10.42) and those with LVEIO ≤ 8 were unlikely to have severe MR (negative likelihood ratio 0.32). LVEIO had sensitivity of 70.37% and specificity of 93.25% for diagnosis of severe MR with positive predictive value of 86.36%. The area under the curve (AUC) using receiver-operating characteristic (ROC) analysis of each parameter for the detection of severe MR is shown in Table 3. LVEIO with an AUC = 0.908 was a significantly better discriminator of severe MR compared with E-wave velocity alone (AUC 0.847) ($p < 0.001$). LVEIO performed even better than VC width (AUC 0.879) and EROA (AUC 0.847) (both $p < 0.001$. Performance of most of the parameters was reduced when applied to patients in the reduced LV ejection fraction (left ventricular ejection fraction [LVEF] <40%) group in which LVEIO had an AUC of 0.894 (0.857–0.930) ($p < 0.001$). PISA performed better in the reduced LVEF group (Table 3). Pearson correlation test showed significant positive correlation between LVEIO and VC width ($r = 0.591$), RV and EROA ($r = 0.778$) (all $p < 0.001$); however, correlation with RV was only moderate ($r = 0.410$). Subgroup analysis of patients with rheumatic etiology ($n = 260$) (52%) of total study population was performed, which showed similar trends of various parameters across the severity of

Table 2
Distribution of various echocardiographic parameters according to grading of mitral regurgitation (MR) by color flow method and LVEIO according to severity of MR by the integrated approach.

Variables	Severity of MR			p value
	Mild	Moderate	Severe	
E (m/sec)	0.962 ± 0.195	1.100 ± 0.236	1.443 ± 0.408	<0.001
VC (cm)	0.29 ± 0.06	0.43 ± 0.12	0.60 ± 0.17	<0.001
PISA radius (cm)	0.32 ± 0.06	0.44 ± 0.09	0.70 ± 0.21	<0.001
EROA (cm^2)	0.04 ± 0.02	0.10 ± 0.14	0.21 ± 0.15	<0.001
LVEIO	4.65 ± 1.45	6.56 ± 1.52	9.91 ± 3.70	<0.001
RV (ml)	5.57 ± 3.10	15.43 ± 25.24	29.18 ± 21.70	<0.001
LA (mm)	26.06 ± 7.36	39.21 ± 8.39	50.48 ± 19.61	<0.001

E, early mitral inflow velocity; EROA, effective regurgitant orifice area; LA, left atrium; LVEIO, left ventricular early inflow outflow index; PISA, proximal isovelocity surface area; RV, regurgitant volume; VC, vena contracta.

MR from mild to severe. LVEIO was 10.1 ± 3.84 in patients with severe MR. The AUC using ROC analysis of each parameter for the detection of severe MR in rheumatic subgroup is shown in Table 4. LVEIO with AUC 0.910 (0.877–0.942) showed similar specificity and better performance than VC in detecting severe MR when applied to rheumatic MR.

4. Discussion

LVEIO has been adapted as a simplification of RV method.[11,12] Our study demonstrates that this parameter can be used to assess the severity of MR. There is a positive correlation with other existing parameters used for assessing the severity of MR. There are multiple drawbacks noted with each method in assessing the severity of MR. The VC method though works well for both eccentric and central MR jets, difficulty in alignment of the imaging plane, computing in case of dynamic MR, and multiple MR jets remain its major drawback. As compared with the VC method, the LVEIO does not depend on the anatomical measurements, and the imaging angle can be easily aligned. The PISA method is cumbersome, time consuming, and less suitable in eccentric jets. In comparison, LVEIO method is based on Doppler velocities that are easily obtained. Both PISA and VC are snapshot of assessment of MR, while LVEIO takes into consideration an entire diastole. Although the LVEIO is a simplification of the RV method, the RV method itself tends to overestimate MR severity. The geometric error in assuming a circular orifice instead of an actual elliptical orifice at mitral annular level leads to overestimation of MR.[13–15] LVEIO omits this geometrical error and therefore is more accurate than the RV method as proven in our study too.[16,17]

Lee et al[4] were among the first to show the feasibility of assessing the severity of MR using LVEIO. Our study has tried assessing the applicability of this parameter in the Indian population where rheumatic heart disease forms the major etiology. As in their study, LVEIO >8 was associated with severe MR in our patient

Table 1
Baseline characteristics.

Etiology of MR	Patients (%) ($n = 500$)	Sex ratio, M (%)	Mean age (years)	Hypertensive, n (%)	Average blood pressure before examination (S/D) (mmHg)
RHD	260 (52.0)	66 (25.3)	32.5	17 (6.5)	135.5/68.7
DCMP	87 (17.4)	39 (44.8)	61.7	24 (27.5)	124.3/67.4
IHD	72 (14.4)	34 (47.2)	47.8	19 (26.3)	137.2/78. 5
Degenerative	46 (9.2)	20 (43.4)	59.4	13 (28.2)	129.6/75.4
MVP	28 (5.6)	11 (39.3)	23.3	0 (0%)	112.7/70.5
ARF	7 (1.4)	5 (71.4)	16.7	0 (0%)	115.2/75.7

ARF, acute rheumatic fever; DCMP, dilated cardiomyopathy; IHD, ischemic heart disease; MR, mitral regurgitation; MVP, mitral valve prolapse; RHD, rheumatic heart disease; S/D, systolic/diastolic.

Table 3
AUC by ROC analysis of LVEIO and other parameters in patients with severe mitral regurgitation in full study cohort as compared with cohort with reduced LVEF (below 40%).

Parameter	Entire study population	Reduced LVEF (less than 40%) group	p-value
PISA radius	0.912 (0.88—0.94)	0.914 (0.882—0.944)	<0.001
VC method	0.879 (0.84—0.91)	0.875 (0.837—0.912)	<0.001
E-velocity	0.847 (0.81—0.88)	0.843 (0.801—0.885)	<0.001
LVEIO	0.908 (0.878—0.938)	0.894 (0.857—0.930)	<0.001
EROA	0.847 (0.810—0.884)	0.852 (0.811—0.892)	<0.001
RV	0.882 (0.851—0.913)	0.890 (0.855—0.924)	<0.001

AUC, area under the curve; E, early mitral inflow velocity; EROA, effective regurgitant orifice area; LVEF, left ventricular ejection fraction; LVEIO, left ventricular early inflow-outflow index; PISA, proximal isovelocity surface area; ROC, receiver-operating characteristic; RV, regurgitant volume; VC, vena contracta.

Table 4
AUC by ROC analysis of LVEIO and other parameters in patients with severe mitral regurgitation in full study cohort as compared with cohort with rheumatic MR.

Parameter	Entire study population	Rheumatic MR group	p value
PISA radius	0.912 (0.88—0.94)	0.920 (0.893—0.954)	<0.001
VC method	0.879 (0.84—0.91)	0.869 (0.839—0.922)	<0.001
E-velocity	0.847 (0.81—0.88)	0.847 (0.804—0.890)	<0.001
LVEIO	0.908 (0.878—0.938)	0.910 (0.877—0.942)	<0.001
EROA	0.847 (0.810—0.884)	0.862 (0.818—0.901)	<0.001
RV	0.882 (0.851—0.913)	0.894 (0.862—0.931)	<0.001

AUC, area under the curve; E, early mitral inflow velocity; EROA, effective regurgitant orifice area; LVEF, left ventricular ejection fraction; LVEIO, left ventricular early inflow-outflow index; PISA, proximal isovelocity surface area; ROC, receiver-operating characteristic; RV, regurgitant volume; VC, vena contracta.

cohort too. Subgroup analysis of rheumatic MR was also performed, which showed similar accuracy results to whole study population analysis. When analyzed, isolated assessment of E velocity >1.5 m/sec has also been suggested as a semiquantitative assessment of MR severity. However, when this is corrected to the outflow VTI, the accuracy of LVEIO as shown in our study improves with rise in the AUC. The alignment of Doppler line is very important during Doppler interrogation. Malalignment leads to significant error in estimation. However, alignment of the Doppler line across the LV inflow is usually feasible in almost all cases in the apical 4-chamber view. Also, as there was no associated aortic valvular pathology, the expected velocities across the aortic valve were less than 3 m/sec; and therefore, minor malalignment in Doppler line were expected to have less significant error in estimating the LVOT VTI. We, therefore, feel that LVEIO is less dependent on alignment of the Doppler line as compared with other parameters to quantify the severity of MR.

This study parameter has several important limitations. LVEIO is not applicable for multivalvular diseases. In patients with multivalvular pathology, measurement of E velocity (eg, in case of mitral stenosis) and LVOT VTI (eg, in case of aortic regurgitation) may introduce significant error in estimating LVEIO. Considering the high prevalence of rheumatic disease in Indian population, mixed valvular pathology is very frequently encountered. Decisions on management of MR, therefore, rely heavily on the quantification of MR in such situations. Quantification of MR using the LVEIO parameter faces a major limitation in such situation because of confounding factors that tend to alter both the E-velocity and LVOT VTI. Also, measurement of E velocity and therefore LVEIO will be difficult in patients with rhythm abnormalities such as atrial fibrillation or tachycardia. Mitral E-wave velocity primarily reflects the LA-LV pressure gradient during early diastole. The contribution of atrial systole to LV filling is minimal (<10%) in majority of patients. Therefore, the A-velocity in the LV inflow pulsed Doppler interrogation is neglected while calculating LVEIO. Exclusion of A-velocity tends to reduce errors while tracing the

envelope. However, E velocity is affected by preload and alterations in LV relaxation as seen in patients with diastolic dysfunction. Atrial systolic contraction contributes more significantly to LV filling when diastolic dysfunction is present. Since reduced LVEF is associated with lower stroke volume and are also likely to have inherent diastolic dysfunction of LV myocardium, the quantification of MR using LVEIO was expectedly less accurate in those with reduced LVEF compared with those with normal LVEF (AUC 0.908 vs. 0.894). The behavior of LVEIO in patients with heart failure with preserved ejection fraction was not assessed separately in our study. LVEIO is expected to be higher in patients with reduced LVEF and result in overestimation in MR severity. Ventricular dilatation in patients with reduced LVEF may alter the size of the LV inflow and outflow. The subsequent changes in the velocity profile affect the LVEIO and thereby its reliability. Despite this, we found that LVEIO has a good overall clinical reliability in assessing severity of MR. Although the sensitivity of LVEIO was low for detection of severe MR (70.37%), considering high prevalence of MR in valvular diseases, LVEIO can be used as an index of severity of MR with high specificity (93.25%).

5. Conclusion

LVEIO is a simple yet specific Doppler echocardiographic parameter for estimation of severity of isolated MR. It can be considered as a stand-alone parameter in patients with isolated severe MR. The specificity of LVEIO remained consistent in diagnosing severe MR in patients with rheumatic etiology. Larger studies will be needed to assess its reliability in patients with significant diastolic dysfunction and patients with associated mixed valvular heart diseases.

What is already known?

- Echocardiography is the gold standard for diagnosis of MR, but quantification still remains a challenge
- Integrative approach with various semiquantitative and quantitative parameters is advised in guidelines

What this study adds?

- LVEIO is the modification of RV method and is a simple and accurate tool for the diagnosis of severe MR
- Dynamicity of MR is better represented by Doppler-derived LVEIO than anatomic measurements.
- Interpretation of LVEIO needs caution in patients with mixed valvular disease and diastolic dysfunction

Conflicts of interest

All authors have none to declare.

References

1. Jones EC, Devereux RB, Roman MJ, et al. Prevalence and correlates of mitral regurgitation in a population-based sample (the strong heart study). *Am J Cardiol.* 2001;87:298–304.
2. Zoghbi WA, Enriquez-Sarano M, Foster E, et al. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. *J Am Soc Echocardiogr.* 2003;16:777–802.
3. Falk V, Baumgartner H, Bax JJ, et al. 2017 ESC/EACTS guidelines for the management of valvular heart disease. *J Cardiothorac Surg.* 2017;52:616–664.
4. Lee MM, Salahuddin A, Garcia MJ, et al. Left ventricular early inflow–outflow index: a novel echocardiographic indicator of mitral regurgitation severity. *J Am Heart Assoc.* 2015;4:e000781.
5. Chaliki HP, Nishimura RA, Enriquez-Sarano M, et al. A simplified, practical approach to assessment of severity of mitral regurgitation by Doppler color flow imaging with proximal convergence: validation with concomitant cardiac catheterization. *Mayo Clin Proc.* 1998;73:929–935.
6. Sahn DJ. Instrumentation and physical factors related to visualization of stenotic and regurgitant jets by Doppler color flow mapping. *J Am Coll Cardiol.* 1988;12:1354–1365.
7. Vahanian A, Baumgartner H, Bax JA, et al. Guidelines on the management of valvular heart disease: the task force on the management of valvular heart disease of the European Society of Cardiology. *Eur Heart J.* 2007;28:230–268.
8. Irvine T, Li XK, Sahn DJ, et al. Assessment of mitral regurgitation. *Heart.* 2002;88(Suppl IV):iv11–iv19.
9. Yoshida K, Yoshikawa J, Shakudo M, et al. Color Doppler evaluation of valvular regurgitation in normal subjects. *Circulation.* 1988;78:840–847.
10. Biava G, Delfino M, Lagana B, et al. Prevalence of valvular regurgitation in structurally normal hearts: a colour-Doppler study. *Coron Artery Dis.* 1997;8:559–563.
11. Rokey R, Sterling LL, Zoghbi WA, et al. Determination of regurgitant fraction in isolated mitral or aortic regurgitation by pulsed Doppler two-dimensional echocardiography. *J Am Coll Cardiol.* 1986;7:1273–1278.
12. Enriquez-Sarano M, Bailey KR, Seward JB, et al. Quantitative Doppler assessment of valvular regurgitation. *Circulation.* 1993;87:841–848.
13. Doddamani S, Bello R, Friedman MA, et al. Demonstration of left ventricular outflow tract eccentricity by real time 3Dechocardiography: implications for the determination of aortic valve area. *Echocardiography.* 2007;24:860–866.
14. Doddamani S, Grushko MJ, Makaryus AN, et al. Demonstration of left ventricular outflow tract eccentricity by 64-slice multi-detector CT. *Int J Cardiovasc Imag.* 2009;25:175–181.
15. Ren B, de Groot-de Laat LE, McGhie J, et al. Geometric errors of the pulsed-wave Doppler flow method in quantifying degenerative mitral valve regurgitation: a three- dimensional echocardiography study. *J Am Soc Echocardiogr.* 2013;26:261–269.
16. Buck T, Plicht B, Kahlert P, et al. Effect of dynamic flow rate and orifice area on mitral regurgitation strove volume quantification using the proximal iso-velocity surface area method. *J Am Coll Cardiol.* 2008;52:767–778.
17. Hall SA, Brickner ME, Willett DL, et al. Assessment of mitral regurgitation severity by Doppler color flow mapping of the vena contracta. *Circulation.* 1997;95:636–642.