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Assessment of Mitral Valve Stenosis by Simplifying Proximal Isovelocity Surface Area in Iraqi Patients by Transthoracic Echocardiography

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ABSTRACT

Background: *Mitral Stenosis refers to narrowing of the mitral valve orifice, resulting in impairment of filling of the left ventricle in diastole. Proximal isovelocity surface area measurement, also known as the flow convergence method, can be used in transthoracic echocardiography to estimate the area of an orifice through which blood flows.* ***Objectives:*** *To compare simple PISA equation, created by combined fixing the angle to 1000 and the V_{al} to 33 cm/s, with mitral valve area measured by pressure half time and planimetry which was taken as reference method.* ***Patients and Methods:*** *A cross sectional prospective study was conducted in multi teaching centers. Total 104 patients were enrolled in this study from which 41 were excluded from the study. Transthoracic echocardiographic examination was used to analyze parameters selected by M-mode, 2D, and pulse doppler.* ***Results:*** *The patients enrolled in this study were with a mean age of 45.4 ± 7.1 years and 23.8% of them within the age group 30-39 years and the remaining 76.2% were >40 years. Female patients were the dominant represented 73.0% while males were 7.0% of the studied group (female: male ratio was 3:1); 61.9% were in sinus rhythm and 38.1% in atrial fibrillation. About 58.7% of the patients had Wilkin's score less than 8, the mean mitral valve area according to planimetry method was 1.14 ± 0.32 cm^2 and it was 1.12 ± 0.28 cm^2 by PISA while the mean mitral valve area by pressure half time method was 1.19 ± 0.30 cm^2. The agreement between PISA and planimetry revealed that PISA had good agreement with planimetry in diagnosis of mitral stenosis, (kappa=0.835, P<0.001). On the other hand, there was a fair significant agreement between pressure half time and planimetry.* ***Conclusion:*** *PISA method can effectively predict mitral valve area and severity of mitral stenosis by the equation: mitral valve area = 115 × r^2/V_{max}, provided that aliasing velocity is fixed at 33 cm/s, with the advantage of easy calculation over other methods used to evaluate mitral valve area by transthoracic echocardiography.*

Keywords: Mitral stenosis, Transthoracic echocardiography, PISA

INTRODUCTION

Mitral Stenosis (MS) refers to narrowing of the mitral valve orifice, resulting in impairment of filling of the left ventricle in diastole. It is usually caused by rheumatic heart disease. Less common causes include severe calcification of the mitral annulus, infective endocarditis, systemic lupus erythematous, rheumatoid arthritis, and carcinoid heart disease [1]. Both rheumatic fever and mitral stenosis remain common in developing countries. Mitral stenosis develops at an earlier age, progresses more quickly, and requires earlier intervention [2].

Proximal isovelocity surface area (PISA) measurement, also known as the "flow convergence" method, can be used in echocardiography to estimate the area of an orifice through which blood flows. Since its development in the early 1990s, the PISA method has been applied clinically to the evaluation of mitral regurgitation (MR), mitral stenosis, tricuspid regurgitation, aortic insufficiency, and intracardiac shunts with variable degrees of success [3].

The Basic Principles of PISA

The PISA method is based on: 1) The properties of flow dynamics; 2) The continuity principle.

The proximal isovelocity surface area method is based on the hemispherical shape of the convergence of diastolic mitral flow on the atrial side of the mitral valve, as shown by color doppler. It enables mitral volume flow to be assessed and, thus, to determine MVA by dividing mitral volume flow by the maximum velocity of diastolic mitral flow as assessed by CWD [3].

$MVA=2\pi r^2 \times (V_{al}/V_{mitral}) \times (\alpha/180) = 2 \times 3.14 \times r^2 \times (33/V_{max}) \times (100/180)$

Where r is the radius of the convergence hemisphere (in cm), V_{al} is the aliasing velocity (in cm/s), peak V_{mitral} the peak CWD velocity of mitral inflow (in cm/s), and α is the opening angle of mitral leaflets relative to flow direction [4].

Aim of the Study

To measure the MVA by simple PISA equation which was created by the combined fixing the angle to 1000 and the V_{al} to 33 cm/s and compare it with pressure half time and the planimetry (which was taken as reference method).

PATIENTS AND METHODS

A cross sectional prospective study was conducted in multi teaching centers (Baghdad teaching hospital, Ibin AL Nafees hospital, Ibn AL Bitar hospital and Ghazi AL Harriry teaching hospital) from the June 2015 to the June 2016. 104 patients were enrolled in this study. 41 were excluded from the study (patients with mild MS, with AR, MR and those with poor window were excluded from the study). Transthoracic echocardiographic examination using the general electric vivid E9 equipped with a phase array transducer of 3.5 MHz frequency with TDI facilities.

M mode, 2D and doppler echocardiography parameters were averaged over 3 cardiac cycles if the patients have sinus rhythm and ≥ 5 cycles if the patient's rhythm was atrial fibrillation.

All echocardiographic measurement was performed according to the American society of Echocardiography guidelines. By color doppler radius of PISA were measured. From parasternal short axis view careful scanning from the apex to the base of the left ventricle to ensure that the CSA is measured at the leaflet tips. Continuous wave doppler was used for measurement of maximum velocity across the mitral valve, mean pressure gradient (mean PG), pressure half time ($T_{1/2}$). The proximal isovelocity surface area method without mitral valve angle correction ($PISA_{simple}$) [5-7]. Because the V_{al} was used as a constant in our study, and because it was previously reported that mitral valve angle can be fixed as 100° in the PISA equation, MVA calculated by PISA could be simplified as follows leaving only two variables to be calculated, namely, PISA radius and V_{max}:

$PISA_{simple}=2\pi r^2 \times (V_{al}/V_{max}) \times (\alpha/180) = 2 \times 3.14 \times r^2 \times (33/V_{max}) \times (100/180) = (2 \times 3.14 \times 33 \times 100/180) \times (r^2/V_{max}) = 115 \times r^2/V_{max}$

The Pressure Half-Time Method

MVA determined with the PHT method $T_{1/2}$ was calculated in the apical four-chamber view using color Doppler Echocardiography with clearly visible mitral inflow color flow mapping (Figure 1B) [6].

The cursor line was moved across the mitral valve tips to the most parallel alignment in relation to the color signal of the mitral inflow. Continuous wave Doppler was initiated, and a clear spectral tracing of the mitral inflow wave was acquired. The deceleration time of the early mitral filling phase spectrum was obtained and MVA by PHT was then calculated using the equation

$MVA = 220/ T_{1/2}$ (Figure 1B)

The Planimetry Method

The smallest orifice of the mitral valve was identified by scanning from the left atrium in the direction of the LV apex using basal-LV short-axis view (Figure 1C). The gain settings were adjusted until the lowest level was determined, at which the circumference of the mitral orifice was still visible. After identification of the frame with the orifice at its maximal opening in early diastole, MVA determined with the planimetry method (PLN) was measured by planimetry of its contours, and the result served as the gold standard for MVA calculation in this study (Figure 1C). The severity of MS measured with PLN, as well as $T_{1/2}$ and PISA, was defined as: moderate if MVA was more 1.0 and less than or equal to 1.5 cm^2, and severe if MVA was less than or equal to 1.0 cm^2 [6].

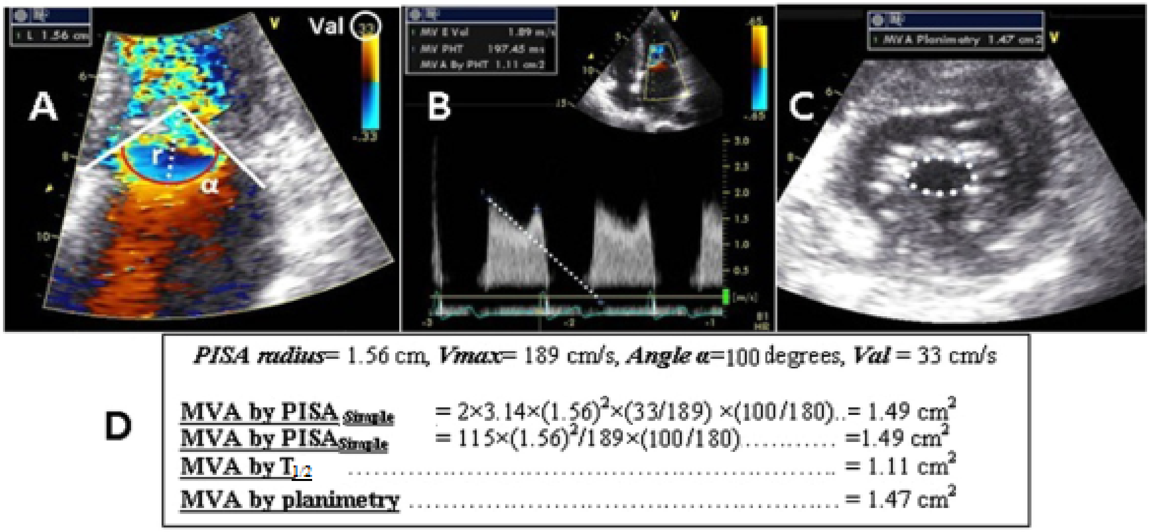

Figure 1 Calculation of mitral valve area (MVA) by different methods; A, proximal isovelcoity surface area method (PISA), B: pressure half time method ($T_{1/2}$), C, the planimetry method (PLN), which was taken as the reference method in our study, and D, an example of calculation of MVA by different methods showing good agreement between PLN, l and $PISA_{simple}$, which was not the case for ($T_{1/2}$) [6]

Statistical Analysis

Data of the 63 patients with MS were entered and analyzed using the statistical package for social sciences (SPSS) version 22, IBM Inc., Chicago, USA, 2013. Descriptive statistics were presented as mean, standard deviation, range, frequencies, and proportions according to the variable types. Analysis of variances (ANOVA) test was used to assess the significance of differences in mean values of MVA by different methods of measurement, post-hoc test (LSD) was used to compare between two methods. Pearson's correlation test (Bivariate analysis) and curve estimation regression analysis were used, the correlation coefficient (R) value indicated the strength of the correlation where: $R<0.4$=weak correlation, 0.4-0.7: moderate and > 0.7-1 strong correlation, the higher R value indicated the stronger correlation. Bland-Altman analysis was conducted for both PISA and $T_{1/2}$ methods to compare their agreement with PLN. Receiver operating characteristics (ROC) curve was used to assess the validity of PISA and $T_{1/2}$ in prediction of severity of MS in PLN. Level of significance was set at 0.05 to be significant difference or correlation. Finally results and findings were presented in tables, figures and explanatory paragraphs using Microsoft office (Word), 2013 software for windows.

RESULTS

There were 63 patients enrolled in this study with a mean age of 45.4. Figure 1 demonstrates calculation of mitral valve area (MVA) by different methods: a) proximal isovelcoity surface area method (PISA); b) pressure half time method; c) the planimetry method (PLN), which was taken as the reference method in our study, and D, an example of calculation of MVA by different methods showing good agreement between PLN, l and PISA simple, which was not the case for ($T_{1/2}$) [7].

7.1 (range: 31-58) years, on the other hand, 15 (23.8%) of the patients aged 30-39 years and the remaining 48 patients (76.2%) aged more than 40 years. Female were the dominant represented 73.0% while males were 17 (27.0%) of the studied group (female: male ratio was 3:1), (Table 1).

Table 1 Age and gender distribution of the studied group

Variable		No.	%
Age (year)	30 - 39	15	23.8
	40 - 49	32	50.8
	50 - 59	16	25.4
	Mean (SD*)	45.4 (7.1)	-
	Range	31 - 58	-
Gender	Male	17	27.00%
	Female	46	73.00%
Total number		63	100
*SD: standard deviation			

As it shown in Table 2, the mean MVA according to planimetry method was (1.14 ± 0.32) cm^2 and it was (1.12 ± 0.28) cm^2 according to PISA while the mean MVA according to ($T_{1/2}$) method was (1.19 ± 0.30) cm^2. Hence the difference between MVA according to planimetry and PISA was (0.02) which was lower than that between planimetry and ($T_{1/2}$) (0.05) and also lower than that between PISA and $T_{1/2}$ (0.07), nonetheless, ANOVA test analysis revealed that the differences in MVA between the different methods were statistically insignificant (P>0.05).

Table 2 Comparison of MVA by Planimetry, $T_{1/2}$, PISA

Assessment method	Mean	SD
MVA by planimetry (cm^2)	1.14	0.32
MVA by PISA (cm^2)	1.12	0.28
MVA by T1/2 (cm^2)	1.19	0.3
ANOVA and post hoc tests results		
Assessment method	**Mean Difference (cm^2)**	**P-value**
MVA by PLN vs. PISA	0.02	0.71
MVA by PLN vs. T1/2	0.05	0.37
MVA by PISA vs. T1/2	0.07	0.17

The bivariate analysis using Pearson's correlation test (Table 3) and curve estimation regression analysis (Figure 2), showed a statistically significant strong direct (positive) correlation between MVA by PISA equation and MVA by the planimetry method (PLN) (r=0.856, P<0.001).

Table 3 Correlations of MVA by PISA and $T_{1/2}$ with MVA by planimetry method of the studied group (N=63)

Method	Pearson's correlation test	
	Correlation coefficient (R)	P
PISA	0.856	<0.001
T1/2	0.441	<0.001

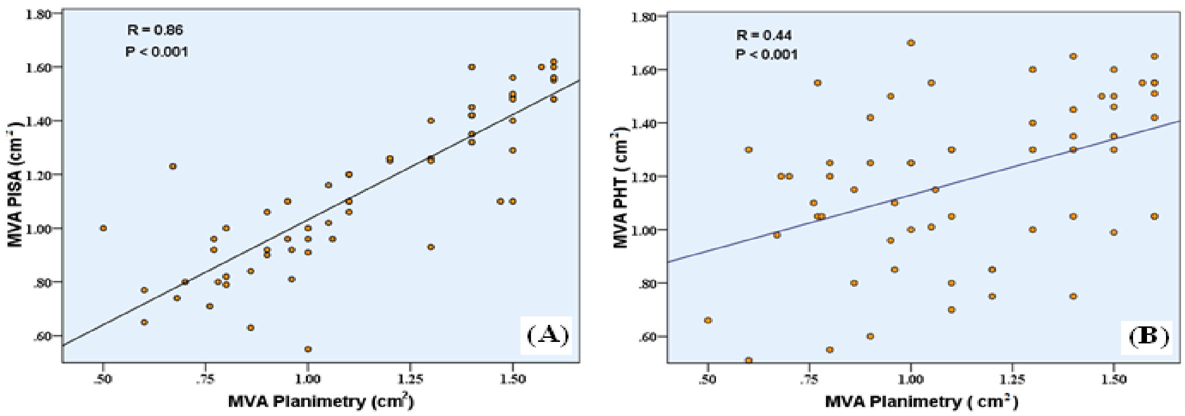

Figure 2 Linear correlations between planimetry versus different methods. (A) PISA, (B) $T_{1/2}$

Also, a statistically significant but moderate direct correlation was found between PLN and MVA by the pressure half time method ($T_{1/2}$) (r=0.441, P<0.001). However, despite both PISA and $T_{1/2}$ methods showed significant correlation with MVA by planimetry, it could be noticed that $T_{1/2}$ showed a weaker correlation than PISA.

Table 4 show the agreement between planimetry and each of PISA and $T_{1/2}$ methods the Bland-Altman analysis was performed to compare the differences between different methods against planimetry, it had been found that the limits of agreement for PISA (lower to upper limits: - 0.32 to 0.326) were better than that for $T_{1/2}$ (- 0.597 to 0.689), (Table 4 and Figure 3). It is worth mentioning that no bias was detected in any method.

Table 4 Bland-Altman analysis for agreement of different methods with planimetry

Method	Mean ± SD of differences	Bias ± SE	Lower limit of agreement (95%CI)	Upper limit of agreement (95%CI)
PISA	0.003 ± 0.165	0.003 ± 0.0208	-0.32 (-0.362 to – 0.278)	0.326 (0.285 to 0.368)
$T_{1/2}$	0.046 ± 0.328	0.046 ± 0.041	-0.597 (-0.633 to -0.468)	0.689 (0.652 to 0.817)

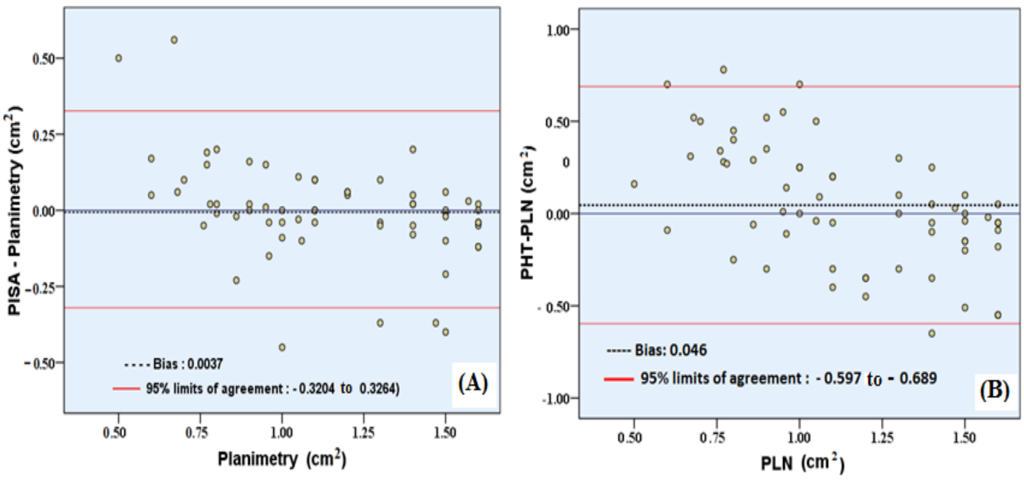

Figure 3 Bland-Altman analysis for the assessment of agreement between different methods and PLN: (A) PISA, (B) $T_{1/2}$

However, the limits of agreement in case of $T_{1/2}$ were worse than those of PISA method, which in turn, was very close to PLN.

As it shown in Table 5, the cross-tabulation and kappa statistics for the agreement between PISA and PLN revealed that PISA had good agreement with PLN in diagnosis of MS, (kappa=0.835, P<0.001).

On the other hand, there was a fair significant agreement between $PT_{1/2}$ and PLN (Table 6).

It had been significantly found that PISA was a good predictor for the sever MS as reported in PLN, (AUC=0.968, P<0.001) with a sensitivity, specificity, and accuracy of (94.6%, 88.5% and 92.1%), respectively. Also, PISA was a good predictor for moderate MS (AUC=0.968, P<0.001) with a sensitivity, specificity, and accuracy of (88.5%, 94.6% and 92.1%), respectively. Regarding $T_{1/2}$, it was a fair predictor with an (AUC of 0.673, P=0.020), for both severe and moderate MS in PLN, however, it had low sensitivity of 42.3%, fair specificity of 75.7% and accuracy of 61.9% in prediction of severe MS while in prediction of moderate MS the sensitivity, specificity and accuracy were 75.7%, 42.3% and 61.9%, respectively.

Table 5 Cross-tabulation for the severity of MS according to PLN and PISA

Severity by PISA	Severity by PLN				Total	
	Moderate		Severe			
	No.	%	No.	%	No.	%
Moderate	35	94.6	3	11.5	38	60.3
Severe	2	5.4	23	88.5	25	39.7
Total	37	100	26	100	63	100
Measure of Agreement: Kappa = 0.835 (Good), P<0.001						

Table 6 Cross-tabulation for the severity of MS according to PLN and $T_{1/2}$ methods

Severity by $T_{1/2}$	Severity by PLN				Total	
	Moderate		Severe			
	No.	%	No.	%	No.	%
Moderate	28	75.7	15	57.7	43	68.3
Severe	9	24.3	11	42.3	20	31.7
Total	37	100	26	100	63	100
Measure of Agreement: Kappa = 0.673 (Fair), P= 0.020						

DISCUSSION

In clinical practice, there is no real gold standard to estimate MVA or MS severity by transthoracic echocardiography. Planimetry method, despite being considered as the echocardiographic gold standard, carries some difficulties in being impossible in patients with bad echocardiographic views or severe mitral valve calcification, and being tedious, time consuming and expertise demanding in the instance of having mitral valve tunnel like structure. Compared to all that, PISA assessment by the simple equation in this study was found very easy to carry out, because it needs no special skill more than applying color and zoom on the mitral position and decreasing the V_{al} to 33 cm/s [4].

This study show that the mean age of the patients was 45.4 ± 7.1 years and the female patients were the dominant and represented 73.0% of the studied group, moreover 61.9% were in sinus rhythm and 38.1% in atrial fibrillation. Which is consistent with that mentioned by Omar, et al. [4] in which the mean age group was 48 ± 19 and 59% of the patients was with sinus rhythm. Also, it is similar to that found by Ghazi, et al. in 2015 [6] in which patients who had sinus rhythm was 58% and 42% had atrial fibrillation and the female was dominant than men but the mean age group was less (40.5 ± 11.3 years) than this study.

This study is not concordant with that found by Manjunath, et al. [6] were the Female to male ratio was 1.93:1 and the main age group was in between 30-39 years old, this might be attributed to the large sample size in the Manjunath, et al. study was included.

This study show that the radius of the PISA was 1.44 ± 0.16 which is within range agreement with that registered by Ikawa [7] study when the radius of the PISA was ranged from 0.8-1.9 cm.

The mean PG, max velocity was increase and EF (%) was with in normal, which is same that revealed by Uzun, et al. [8]. The measurement of MVA by PHT is an inaccurate measure if the patients suffer from MS with moderate or severe AR, MR and tachycardia, or conditions associated with changes in atrial or ventricular compliance [9-14]. In this study the difference between planimetry and PHT was 0.05 cm^2 which is similar to that found by many studies Kim, et al. in 2008 and Messika-Zeitoun [15,16] where the difference was more than 0.03.

This difference between $T_{1/2}$ and planimetry might be due to extreme values of net atrioventricular compliance [7,8].

The PISA method, on the other hand, has been validated in almost all conditions that tend to render $T_{1/2}$ inaccurate [17-20], and moreover, in this study, differences between MVA calculated by planimetry and PISA were not affected by the changes in the net atrioventricular compliance values that render $T_{1/2}$ inaccurate as a measure of MVA. Pearson's correlation test and curve estimation regression analysis, showed a statistically significant strong direct (positive) correlation between MVA by PISA equation and MVA by the planimetry method (PLN). Also, a statistically significant but moderate direct correlation was found between PLN and MVA by the pressure half time method. However, despite both PISA and PHT methods showed significant correlation with MVA by planimetry, it could be noticed that $T_{1/2}$ showed a weaker correlation than PISA.

It had been significantly found in this study that PISA was a good predictor for the sever MS as reported in PLN, with a sensitivity, specificity, and accuracy of (94.6%, 88.5% and 92.1%), respectively. Also, PISA was a good predictor for moderate with a sensitivity, specificity, and accuracy of (88.5%, 94.6% and 92.1%), respectively. Regarding $T_{1/2}$, it was a fair predictor with an (AUC of 0.673, P=0.020), for both severe and moderate MS in PLN, however, it had low sensitivity of (42.3%), fair specificity of (75.7%) and accuracy of (61.9%) in prediction of severe MS while in prediction of moderate MS the sensitivity, specificity and accuracy were 75.7%, 42.3% and 61.9%, respectively. Same finding was reported by Omar, et al. [4]. Moreover it's concordant with that revealed by Ghazi, et al. [5] in 2015 and with Ural, et al. study in which MVAs measured by PISA are closely correlated to classical echocardiographic methods, especially to planimetry [20]. Analysis for the validity of PISA and $T_{1/2}$ in prediction of severity of MS in compares with PLN method, was performed using the Receiver operating characteristics curve (ROC) it had been significantly found that PISA was a good predictor for the sever MS as reported in PLN, (AUC=0.968, P<0.001) with a sensitivity, specificity and accuracy of (94.6%, 88.5% and 92.1%), respectively. Also, PISA was a good predictor for moderate MS with a sensitivity, specificity, and accuracy of (88.5%, 94.6% and 92.1%), respectively.

Limitations of the Study

Small sample size was included in this study. Moreover, we use the planimetry method as the gold standard; it has some limitations in that it may be influenced by severe leaflet or subvalvular calcification, asymmetrical leaflet affection, imaging technique or poor image quality.

CONCLUSION

The measurement of the MVA by simple PISA equation which was created by the combined fixing the angle to1000 and the V_{al} to 33 cm/s, was superior to the pressure half time method with the advantage of easy calculation in evaluation of MVA by transthoracic echocardiography.

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