Accuracy of The Single Beat Method for Assessment of Mitral Valve Stenosis Severity in Atrial Fibrillation

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Abstract

Purpose: In mitral stenosis (MS) patients, determining stenosis severity in atrial fibrillation (AF) is time-consuming by averaging measurement by multiple cardiac cycles. Whether a single beat method can be used to measure the mitral valve area (MVA) and transmitral gradient for stenosis severity assessment in AF is still uncertain. **Methods**: Forty-eight MS patients with AF (mean age 46.8+8.6 years) underwent routine echocardiographic study. The MVA by pressure half time (PHT) and transmitral mean gradient were measured by four methods: the standard approach (averaging multiple beats), single short R-R cycle, single long R-R cycle, and single beat RRp/RRpp = 1. 2D and 3D planimetry MVA were measured at the mitral orifice. **Results**: The single beat RRp/RRpp = 1 showed no significant difference in MVA PHT measurement compared with standard approach (0.8 (0.3 – 2.7 vs 0.9 + 0.3 cm ^{2}) cm ^{2}, $P = 0.472$), whereas there was a significant difference in MVA by PHT when short R-R cycle (1.0 (0.4 – 2.7) cm ^{2}, $P = 0.0001$) and long R-R cycle (0.8 (0.3 – 1.7) cm ^{2}, $P = 0.013$) were selected. There was a significant difference in mean MVG measurement when short R-R cycle (12.1 + 3.9 mmHg, $P = 0.001$) , long R-R cycle (10.1 + 4.0 mmHg, $P = 0.007$), and single beat RRp/RRpp = 1 (12.2 + 4.4 mmHg, $P = 0.0001$) were selected. Correlation coefficients for MVA PHT calculated by single beat RRp/RRpp = 1 compared with MVA PHT measured by standard approach are $r = 0.87$ ($P < 0.001$). There is weak correlation in measurement MVA between PHT single beat RRp/RRpp = 1 and 3D planimetry ($r = 0.316$, $P = 0.044$). **Conclusion**: In AF, the single beat method RRp/RRpp = 1 for measurement MVA by PHT in MS has a high correlation with the current standard approach by averaging multiple beats. Compared with MVA by 3D planimetry as the reference measurement of MVA, measurement of MVA by PHT standard approach and single beat RRp/RRpp = 1 have a weak correlation in AF patients. MVA by planimetry especially 3D planimetry, is considered as a reference measurement, but MVA by PHT single beat RRp/RRpp =1 can be an alternative, especially when MVA by planimetry is not feasible.

TITLE PAGE

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INTRODUCTION

Echocardiography plays an important role in assessing valve anatomy, stenosis severity, and its consequences in mitral stenosis (MS) [1]. Doppler has a principal part in quantitation stenosis severity. In patients with atrial fibrillation (AF), Doppler assessment is limited by the variability in cycle length [2]. It should be calculated as the average of at least five cycles with the least variation of R–R intervals and as close as possible to normal heart rate[1]. This method of calculating stenosis severity in AF is time-consuming and may still lead to inaccurate area assessment depending on the R-R intervals included in the calculations [3].

In patients with MS and irregular ventricular rate due to AF, beat to beat variations in the filling of the left ventricle take place due to alterations in the duration of the filling period. It was considered that if Starling's law of the MS, the characteristic of each left ventricular (LV) contraction should appear to be a function of the previous end-diastolic fiber length [4]. Beat to beat variation in LV performance shows not only changes in contractility but changes in preload [5]. Previous end-diastolic fiber length defined as the preceding R-R interval (RRp) and pre-preceding R-R interval (RRpp). Previous studies reported a significant positive linear relationship between LV pressure and the ratio of preceding R-R to pre-preceding R-R (RRp/RRpp). Some studies reported the value at RRp/RRpp =1 has the linear regression line that could estimate stable LV performance [6-10]. Previous studies reported the single long cycle length method of calculating valvular stenosis could be used instead of averaging multiple cardiac cycles [3].

This study aims to determine whether a single beat method can be used for severity assessment of MS compared with averaging at least five cycle method as the standard approach and mitral valve area (MVA) by 3D planimetry as the reference measurement in MVA when the patients have AF.

MATERIAL AND METHODS

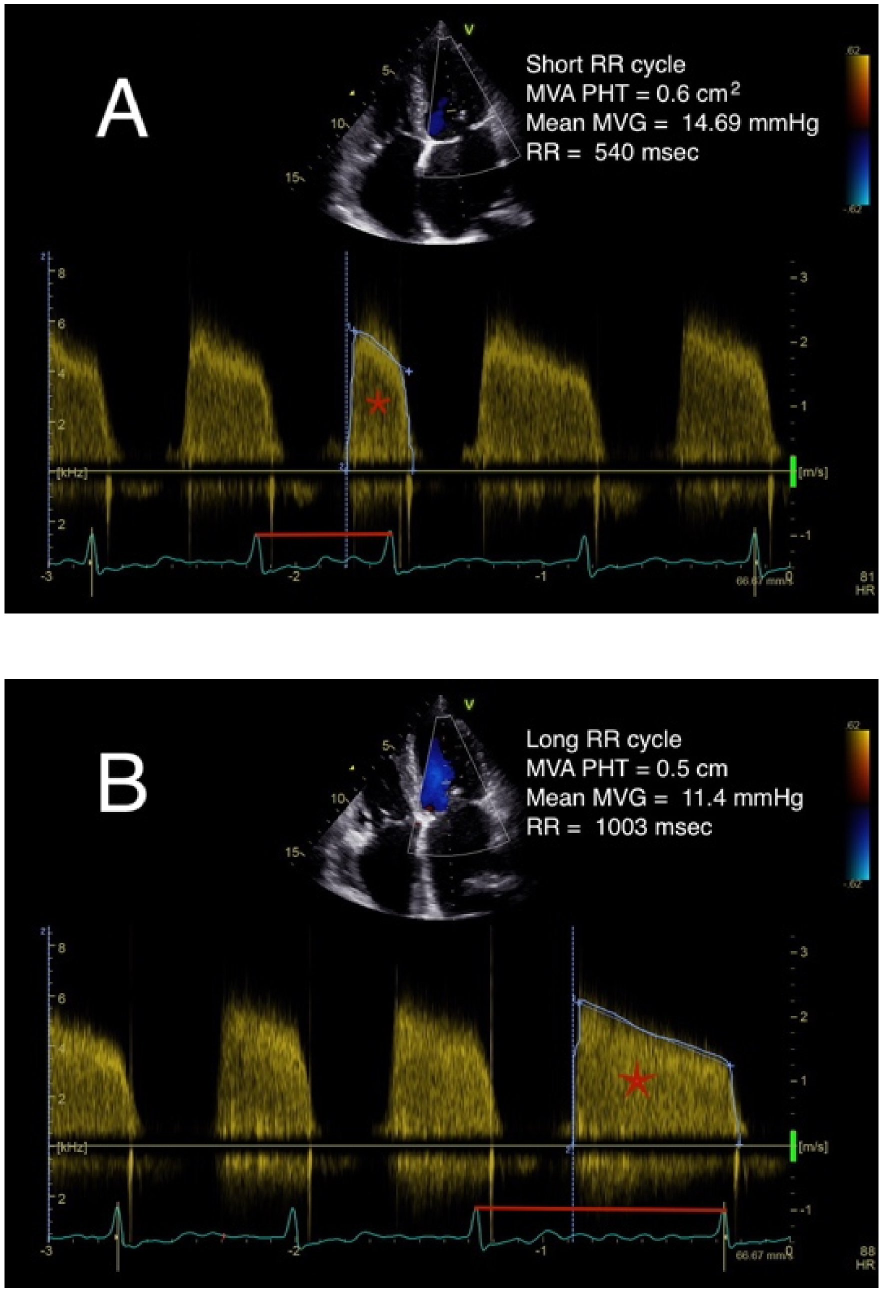
The study population consists of 48 patients with MS and AF, 18-55 years old, who were undergone transthoracic or transoesophageal echocardiography at National Cardiovascular Center Harapan Kita in Jakarta from September 2019 until January 2020. Baseline characteristics were recorded for all patients, including age, body surface area (BSA), heart rate, systolic and diastolic blood pressure, and echocardiography data (Table 1). The heart rate must be between 60 and 100 bpm. Patients were excluded if they had significant mitral regurgitation, significant aortic valve abnormality, and concomitant congenital heart disease. The study was approved by the institutional review board on human research.

Echocardiography Analysis

All patients underwent complete transthoracic and transesophageal echocardiographic evaluation using GE Vivid E9 system (GE Vingmed Ultrasound AS, Horten, Norway) with a 1.4-4.6 MHz for trans-thoracal and 3-8 MHz for transesophageal transducer. All data were analyzed in a workstation (EchoPAC PC; GE Vingmed Ultrasound AS). MS severity is evaluated based on the 2009 EAE/ASE Recommendations Echocardiographic of Assessment of Valve Stenosis for Clinical Practice and met the world heart federation criteria for diagnosis of rheumatic MS [1,11]. 2D and 3D planimetry MVA was measured at the mitral orifice.

Continuous-wave Doppler (CWD) was used to derive transmitral velocity, and Doppler gradient was assessed using the apical window as it parallel alignment of the ultrasound beam and mitral inflow. Pressure half time (PHT) and mean mitral valve gradient (MVG) were measured and averaged over five beats as a standard method at speed 66.6 m/s.

R-R interval is measured immediately preceding (RRp) and pre-preceding (RRpp) the selected transmitral Doppler velocity. The short and long R-R cycle define relative to the average heart rate. Transmitral gradient and PHT was measured for a short R-R cycle and a long R-R cycle. Single beat transmitral gradient and PHT was measured when RRp/RRpp = 1 (Figure 1).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Short RR cycle
MVA PHT = 0.6 cm^2
Mean MVG = 14.69 mmHg
RR = 540 msec
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HR
B
Long RR cycle
MVA PHT = 0.5 cm
Mean MVG = 11.4 mmHg
RR = 1003 msec
[kHz]
[m/s]
88
HR

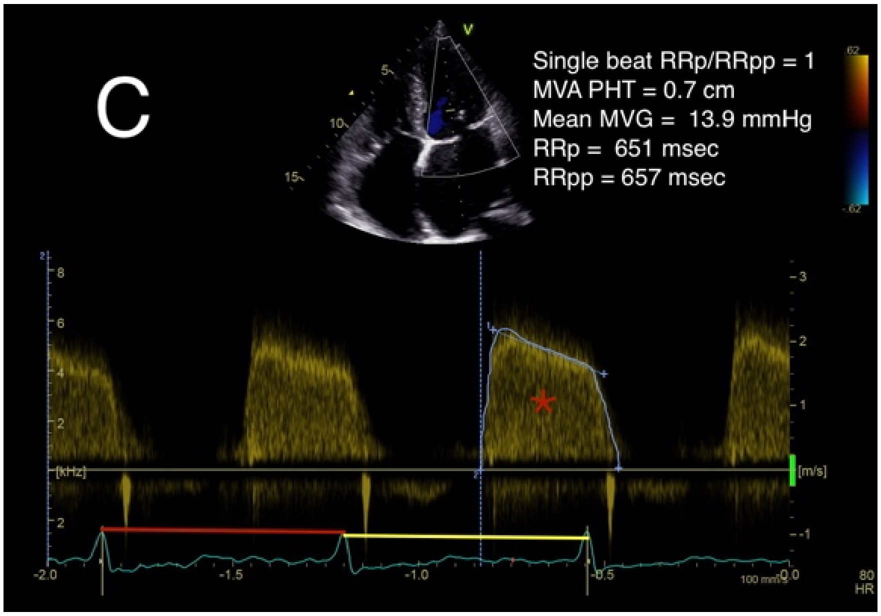

Fig. 1 . Measurement methods. Examples of measurement single continuous-wave Doppler across a stenotic mitral valve (*red asterisk*) are shown: short RR cycle (A), long RR cycle (B), single beat RRp/RRpp = 1 (C).

Statistical Analysis

Statistical analyses were made using IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, N.Y., USA). Normally distributed variables were expressed as mean ± standard deviation (SD). Shapiro-Wilk test was used for the normality test. For non-normally distributed variables, the Wilcoxon rank-sum test was used to calculate Pvalues. Spearman correlation coefficients calculated to determine correlations between MVA PHT standard approach and single beat methods. P values < 0.05 were considered statistically significant. Interclass correlation coefficients (ICCs) were used to assess interobserver and intraobserver variability. The interobserver and intraobserver variability was assessed from 18 studies.

RESULTS

Baseline characteristic

Forty-eight patients that have MS and AF, 18 were male, and 30 were female. The mean age of the patients was 46.8+ 8.6 years, with BSA 1.5+ 0.2 m^2. The median heart rate of the patients was 85 (60-100) beats/min. MVA by planimetry 0.7 (0.4-1.8) cm^2, MVA by PHT 0.8 (0.4-1.7) cm^2, and mean MVG 11 + 4.1 mmHg. Detail baseline characteristics and echocardiography data of 48 patients are shown in Table 1.

Table 1. Clinical Characteristics in All Patients (n = 48)

Variable	N = 48
Age (yrs)	46.8 + 8.6
BSA (m^2)	1.5 + 0.2
Sex (Male/Female)	18/30
HR (bpm)	85 (60 – 100)
Systolic blood pressure (mmHg)	120.3 + 16.9
Diastolic blood pressure (mmHg)	79.3 + 11.6
Echocardiography data	

Variable	N = 48
LV ejection fraction (%)	56.5 + 11.4
LVOT diameter (cm)	1.86 + 0.23
End diastolic LV dimension (mm)	46.9 + 6.1
End systolic LV dimension (mm)	33.2 + 6.1
LA volume index (ml/m^2)	110 (50 – 408)
MVA planimetry (cm^2)	0.7 (0.4 – 1.8)
TVG (mmHg)	51.3 + 24
TAPSE (mm)	15.4 + 3.4
Wilkins score	6 (4 – 13)
IVC dimension (mm)	17.6 + 5.4
MVA PHT (cm^2)	0.9 + 0.3
Mean MVG (mmHg)	11 + 4.1
LVOT VTI (cm)	14.3 + 3.0
Stroke Volume (ml)	39 + 12.1

BSA = body surface area; HR = heart rate; LV = left ventricle; LVOT = left ventricle outflow track; LA = left atrium; MVA = mitral valve area; TVG = tricuspid valve gradient; TAPSE = tricuspid annular plane systolic excursion; IVC = inferior vena cava; PHT = pressure half time; MVG = mitral valve gradient; VTI = velocity time integral.

MVA PHT and mean MVG

The average of MVA PHT measured by the standard approach was 0.9+ 0.3 cm^2. By the single beat method, there was a significant difference in MVA PHT when short R-R cycle (1.0 (0.4-2.7) cm^2, P = 0.0001) and long R-R cycle (0.8 (0.3-1.7) cm^2, P = 0.013) were selected. When single beat RRp/RRpp = 1 were used, there was no significant difference in MVA PHT measurement compared with the standard approach (0.8 (0.3-2.7) cm^2, P = 0.472). The average of mean MVG measured by the standard approach was 11.0+ 4.1 mmHg. There was a significant difference in mean MVG measurement when short R-R cycle (12.1+ 3.9 mmHg, P = 0.001) , long R-R cycle (10.1+ 4.0 mmHg, P = 0.007), and single beat RRp/RRpp = 1 (12.2+ 4.4 mmHg, P = 0.0001) were selected (Table 2).

Table 2. MVA PHT and mean MVG variables measured by different methods

Variable	Standard approach (a)	Single-cycle short RR (b)	Single-cycle long RR (c)	Single beat RRp/RRpp = 1
MVA PHT	0.9 + 0.3	1.0 (0.4 – 2.7)	0.8 (0.3 – 1.7)	0.8 (0.4 – 2)
Mean MVG	11.0 + 4.1	12.1 + 3.9	10.1 + 4.0	12.2 + 4.4

MVA = mitral valve area; PHT = pressure half time; MVG = mitral valve gradient.

Correlation of MVA PHT Measured by Standard Approach versus Single Beat RRp/RRpp =1

Correlation coefficients for MVA PHT calculated by single beat RRp/RRpp = 1 compared with MVA PHT measured by standard approach are $r = 0.87$ ($P < 0.001$). There was a strong positive correlation between MVA PHT standard approach and single beat RRp/RRpp = 1. Figure 2 shows a good agreement when comparing MVA PHT standard approach method with the single beat RRp/RRpp = 1 method.

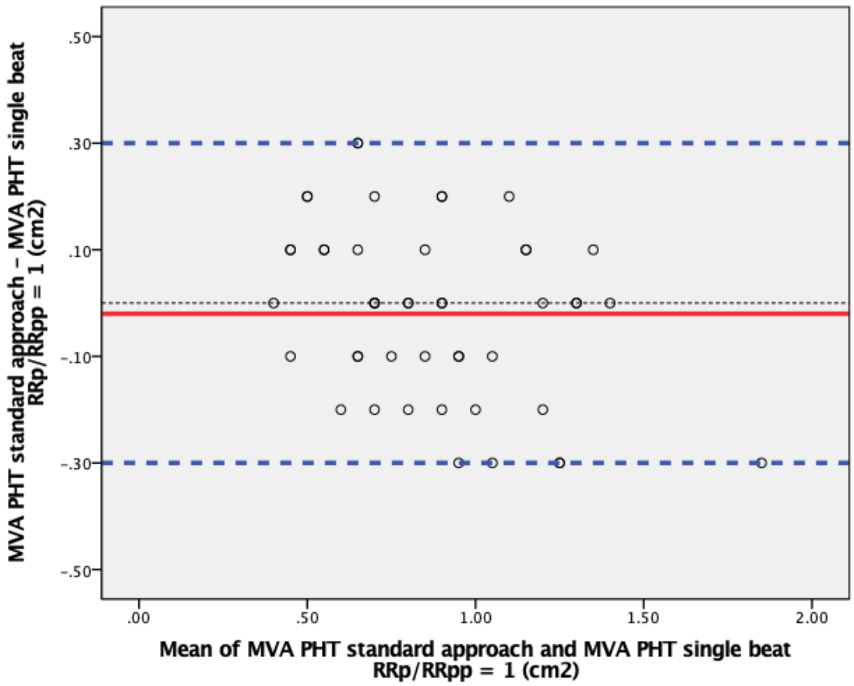

Fig. 2 . Bland-Altman plots assessing differences in MVA PHT measurement for standard approach method and single beat RRp/RRpp = 1 method.

MVA PHT Single Beat RRp/RRpp = 1 Method and MVA 3D Planimetry

Forty-one patients underwent 3D TEE MVA planimetry. There was a weak correlation between MVA PHT single beat RRp/RRpp = 1 and 3D planimetry (r = 0.316, P = 0.044). Figure 3 shows a good agreement when comparing MVA 3D planimetry with the PHT single beat RRp/RRpp = 1 method.

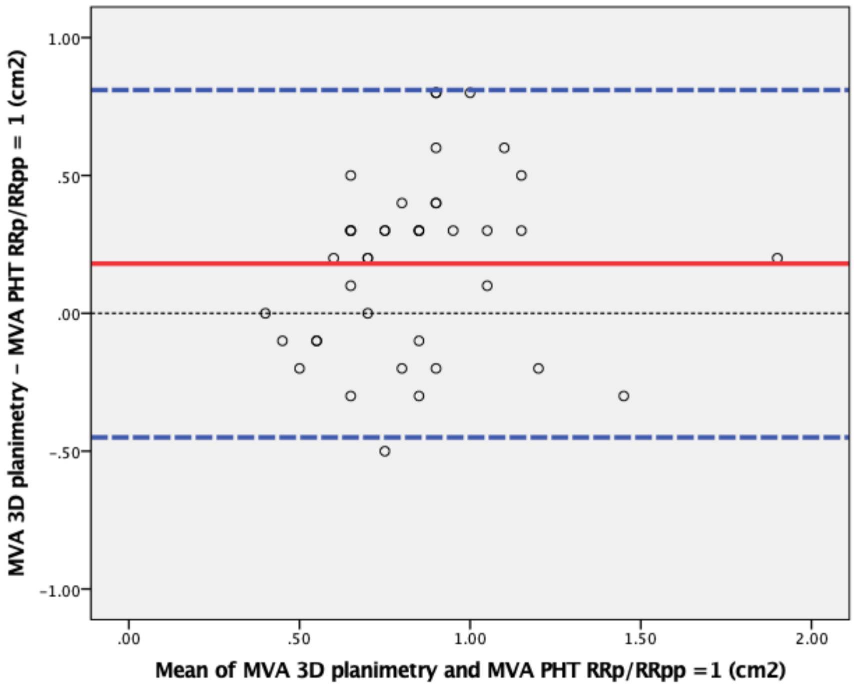

Fig. 3 . Bland-Altman plot assessed differences in MVA measurement for 3D planimetry and PHT single beat RRp/RRpp = 1 method.

Intra- and Interobserver Variability for MVA PHT Single Beat RRp/RRpp = 1 Method

The interclass correlation coefficients (ICC) for interobserver variability for MVA PHT single beat RRp/RRpp = 1 method was 0.94 (95% CI, 0.70 – 0.98). The ICC for intraobserver variability was 0.91 (95% CI, 0.56-0.97).

DISCUSSION

Multiple measurements in AF patients is a tedious task, especially in high volume echocardiography laboratory. The single beat measurement can be an alternative to the standard method by averaging at least five cycles. Esquitin et al. reported the use of a single long cycle length method that has the highest correlation with the current standard approach of averaging multiple beats for calculation of EOA (effective orifice area) in aortic stenosis and AF patients [3]. For transmitral flow, Kusunose et al. reported the single beat preceding RR interval (RRp)/pre-preceding RR interval (RRpp) = 1 has a good positive linear relationship compared with the standard method by averaging multiple beats for E/e' lateral measurement in AF and preserved systolic function patients [10]. Some studies reported the value at RRp/RRpp =1 has the linear regression line that could estimate stable LV performance [6-10]. In this study, we try to determine whether single short R-R cycle, long R-R cycle, and single beat RRp/RRp = 1 can be used for the severity assessment of MS.

Beat to beat variation in ventricular performance associates with variations in the length of the preceding heart period. It was consistent with the Frank-Starling mechanism. During regular rhythm, there is a simple relationship between the constant ventricular cycle length (VCL) and the heart rate (HR), namely HR (bpm) = 60.000/VCL (ms). According to the equation, a prolongation of VCL is equivalent to a slower heart rate. Otherwise, the shortening of VCL is equivalent to a faster heart rate. Previous study has shown that faster AF or short R-R cycle correlates with less maximum LV power, dP/dtmin, and the time constant of relaxation (t). Otherwise, slower AF or long R-R cycle showed an increase in maximum LV power and dP/dtmin, while t decreased i.e. the relaxation improved [6]. It was consistent with MVA by PHT measurement. It was smaller when the long R-R cycle, and larger when short R-R cycle. A short time interval makes a shorter PHT due to a faster decline of the velocity of diastolic transmitral blood flow. The long-time-interval makes a longer PHT due to the slower decline of the transmitral flow. PHT is inversely proportional to MVA [1]. This explanation applies to the transmitral gradient; the short R-R cycle has an association with a higher gradient and long R-R cycle with a lower gradient. Shortened diastole in faster AF has an association with a higher transmitral gradient [12].

The main finding of this study is the measurement of MVA PHT by single beat RRp/RRpp = 1 method results in a high correlation and good agreement with the standard method of MVA by PHT for AF patients whereas short R-R cycle and long R-R cycle have a significant difference compared with the standard method. The previous study reported that using a long R-R cycle in AF patients is the most accurate method for assessing EOA [3]. EOA calculation using left ventricular outflow tract (LVOT) velocity time integral (VTI) measurement reflects stroke volume in systolic phase that influenced by previous end-diastolic fiber length or preceding R-R cycle [4]. Studies have shown that myocardial contractility and LV function are also directly related to the ratio of preceding interval (RRp) to the pre-preceding interval (RRp/RRpp). Different from AS severity calculation, measuring MVA by PHT is from transmitral inflow in diastolic phase. Kusunose et al., reported clinical utility single beat RRp/RRpp = 1 of transmitral flow for the evaluation of LV diastolic function [10]. This is the first study that evaluated the usefulness of the single beat RRp/RRpp = 1 MVA PHT compared with standard approach in MS and AF patients.

The severity assessment of rheumatic MS should rely mostly on the valve area. MVA by PHT and MVA by planimetry have level 1 recommendation to assess stenosis severity. MVA by planimetry is a direct measurement of MVA, unlike other methods, does not involve any hypothesis regarding flow conditions, cardiac chamber compliance, or associated valvular lesion. It has been shown to have the best correlation with the anatomical valve area [1]. Real-time three-dimensional (3D) echocardiography reported as a feasible, accurate, and highly reproducible technique for assessing MVA in MS patients [13]. This study also analyzed the correlation between MVA PHT single beat RRp/RRpp =1 method with MVA 3D planimetry as reference measurement. There was a weak correlation in measurement MVA between PHT single beat RRp/RRpp = 1 and 3D planimetry. Since MVA planimetry has the best correlation with anatomical MVA and does not influence by multiple factors, measurement of MVA PHT single beat RRp/RRpp = 1 should not be the decisive parameter when assessing MVA in MS and AF patients. MVA by planimetry, especially 3D planimetry, is considered as reference measurement of MVA. In some conditions, planimetry measurement may not be feasible when there is a poor acoustic window or severe distortion of valve anatomy, in particular with severe valve calcifications of the leaflet tips [1]. Especially in an industrialized country like Indonesia, the percentage of significant elderly MS patients might be higher in whom planimetry is not feasible. This method can be an alternative when planimetry MVA is not feasible.

The mean gradient of transmitral flow is the relevant hemodynamic findings. Although reliably assessed by Doppler, it is not the best marker for MS severity [1]. In this study, there was a significant difference in mean MVG measurement for single short R-R cycle, long R-R cycle, and single beat RRp/RRpp = 1 compared with the standard approach by averaging multiple beats (Table 2). The values of mean gradient influenced by multiple factors and only a supportive sign and cannot be considered as a surrogate indicator of the severity of MS. Mean gradient can be a supportive sign at heart rates between 60 and 80 bpm in sinus rhythm patients, and considered cannot be a supportive sign in AF patients [1]. Sabbagh et al. reported low flow low gradient MS which define as mean MVA planimetry less than 1.5 cm^2 but mean transmitral gradient <10 mmHg and stroke volume index <35 mL/m^2. Presence of low gradient MS in patients with severe MS associated with high arterial afterload, prevalent AF, and decreased LV compliance [14].

Our center is a national referral center whose patients from all regions in Indonesia. Most patients in our center have significant to severe MS, which is prepared for percutaneous balloon mitral valvuloplasty or mitral valve surgery. Non-significant or mild MS were not represented in this study.

CONCLUSION

In AF, the single beat method RRp/RRpp = 1 for measurement MVA by PHT in MS has a high correlation with the current standard approach by averaging multiple beats. Compared with MVA by 3D planimetry as the reference measurement of MVA, measurement of MVA by PHT standard approach and single beat RRp/RRpp = 1 have a weak correlation in AF patients. MVA by planimetry, especially 3D planimetry, is considered as a reference measurement, but MVA by PHT single beat RRp/RRpp =1 can be an alternative, especially when MVA by planimetry is not feasible.

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ABSTRACT

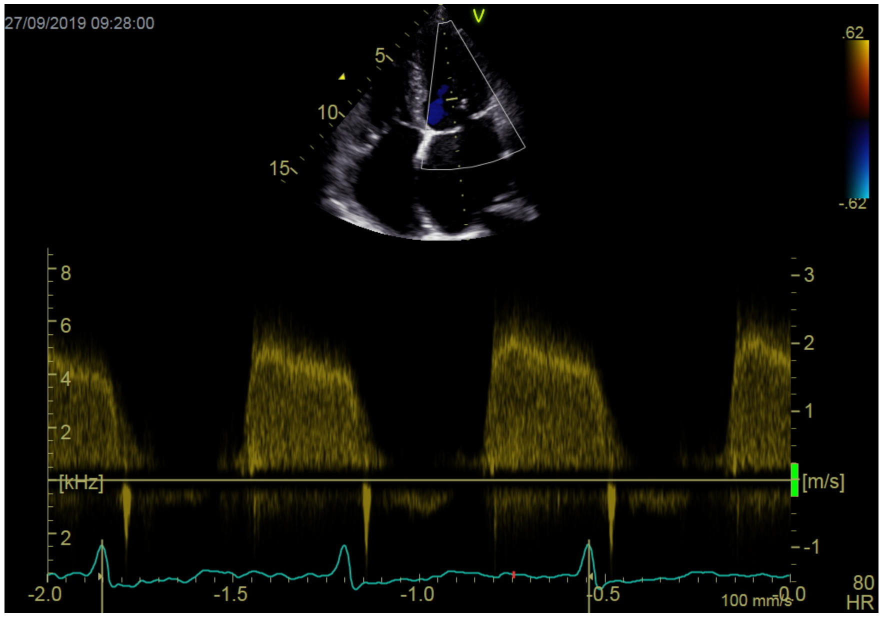
Purpose : In mitral stenosis (MS) patients, determining stenosis severity in atrial fibrillation (AF) is time-consuming by averaging measurement by multiple cardiac cycles. Whether a single beat method can be used to measure the mitral valve area (MVA) and transmitral gradient for stenosis severity assessment in AF is still uncertain.

Methods : Forty-eight MS patients with AF (mean age 46.8+ 8.6 years) underwent routine echocardiographic study. The MVA by pressure half time (PHT) and transmitral mean gradient were measured by four methods: the standard approach (averaging multiple beats), single short R-R cycle, single long R-R cycle, and single beat RRp/RRpp = 1. 2D and 3D planimetry MVA were measured at the mitral orifice.

Results : The single beat RRp/RRpp = 1 showed no significant difference in MVA PHT measurement compared with standard approach (0.8 (0.3 – 2.7 vs 0.9 + 0.3 cm^2) cm^2, $P = 0.472$), whereas there was a significant difference in MVA by PHT when short R-R cycle (1.0 (0.4 – 2.7) cm^2, $P = 0.0001$) and long R-R cycle (0.8 (0.3 – 1.7) cm^2, $P = 0.013$) were selected. There was a significant difference in mean MVG measurement when short R-R cycle (12.1 + 3.9 mmHg, $P = 0.001$) , long R-R cycle (10.1 + 4.0 mmHg, $P = 0.007$), and single beat RRp/RRpp = 1 (12.2 + 4.4 mmHg, $P = 0.0001$) were selected. Correlation coefficients for MVA PHT calculated by single beat RRp/RRpp = 1 compared with MVA PHT measured by standard approach are $r = 0.87$ ($P< 0.001$). There is weak correlation in measurement MVA between PHT single beat RRp/RRpp = 1 and 3D planimetry ($r = 0.316$,$P = 0.044$).

Conclusion : In AF, the single beat method RRp/RRpp = 1 for measurement MVA by PHT in MS has a high correlation with the current standard approach by averaging multiple beats. Compared with MVA by 3D planimetry as the reference measurement of MVA, measurement of MVA by PHT standard approach and single beat RRp/RRpp = 1 have a weak correlation in AF patients. MVA by planimetry especially 3D planimetry, is considered as a reference measurement, but MVA by PHT single beat RRp/RRpp =1 can be an alternative, especially when MVA by planimetry is not feasible.

Keywords : Mitral stenosis, mitral valve area, pressure half time, planimetry, mean gradient, atrial fibrillation.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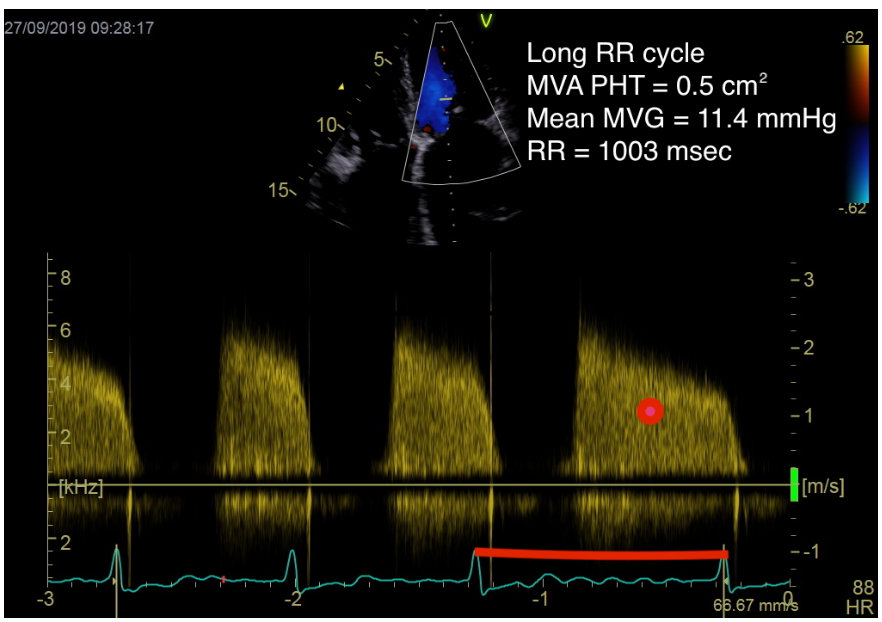
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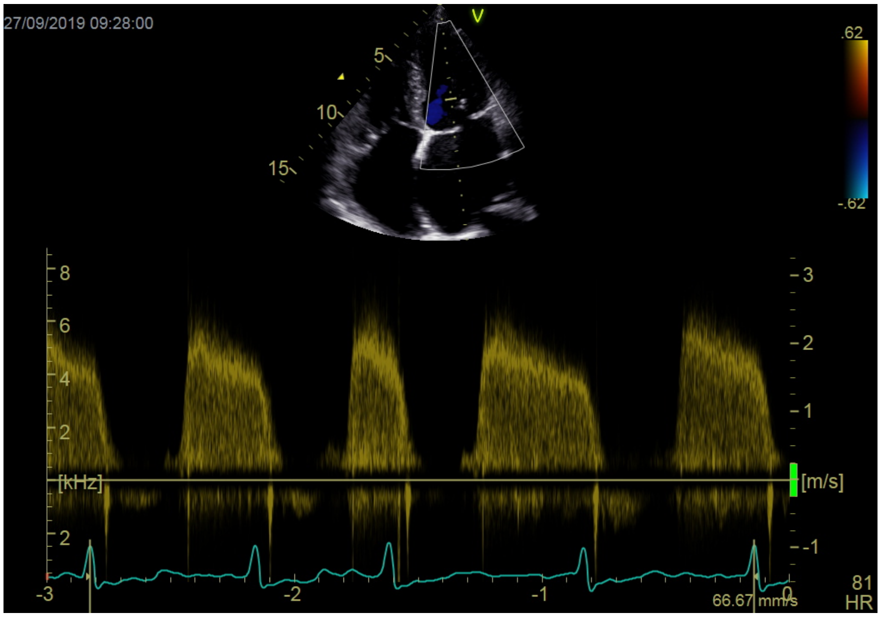
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2
[kHz]
2
3
2
1
[m/s]
-1
-3
-2
-1
0
66.67 mm/s
81
HR