Echocardiography

Assessment of Doppler-derived Aortic Flow in Atrial Fibrillation Using Beats with Equal Subsequent Cycles

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Background: Prior studies have demonstrated that during atrial fibrillation (AF), beats with equal preceding and pre-preceding R-R intervals, defined as intervals differing less than 5%, could be used to determine the mean values instead of measuring over 20 cardiac cycles. It is not known whether beats with interval difference less than 10% could be used in the same way.

Methods: In 120 patients with AF, Doppler aortic flow time-velocity integral was determined for at least 20 consecutive cardiac cycles. The values at beats with interval difference of less than 5% and less than 10% were chosen. These were then compared with the measured average values over all cardiac cycles.

Results: Agreement and mean percentage difference analyses revealed that the accuracy of measurements using inter-beat variability less than 10% was similar to that using less than 5% for 2- and 3-beat analyses provided the R-R intervals were longer than 500 milliseconds. The values at beats with cycle lengths shorter than 500 milliseconds were usually far below the average values. The mean percentage differences were not significantly different between methods using interval differences of less than 5% and less than 10% for 3-beat analysis (2.83% vs. 2.97%, $p = 0.269$). Moreover, it is relatively easy to obtain beats with interval difference less than 10%. The median numbers of beats required finding 3 beats with inter-beat variability of less than 10% and less than 5% were 9 and 16, respectively.

Conclusions: Averaging 3 beats with R-R interval difference less than 10% and cycle lengths longer than 500 milliseconds can be applied to accurately estimate Doppler-derived aortic flow for patients with AF.

Key Words: Atrial fibrillation • Left ventricle • Stroke volume • Systole • Ventricular function

INTRODUCTION

Assessment of left ventricular (LV) systolic function in atrial fibrillation (AF) has proved to be difficult because of beat-to-beat variation.[1,2] It is therefore necessary to average many beats to obtain an accurate evaluation during AF.[3] This method is usually suboptimal because the averaged value depends on a selected window of cardiac cycles. Moreover, in AF, the average number of beats required to determine LV systolic function with the same degree of accuracy is approximately three times that for sinus rhythm.[3]

Previous studies have demonstrated that during AF, the parameters of LV systolic function positively correlate with the ratio of the preceding R-R interval (RR_1) to the pre-preceding R-R interval (RR_2). The values at RR_1 to RR_2 ratio = 1 in the regression line is an excellent esti-

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mate of the average value over all cardiac cycles.[4,5] Sumida et al. further showed that in AF, a representative stroke volume (SV) could be obtained at a beat with equal RR_1 and RR_2 ($RR_1 = RR_2$), which was defined as R-R interval difference of less than 5% of mean.[6] However, Tabata et al. countered the use of single-beat determination because they found that substantial variability existed between the LV parameters determined from beats with $RR_1 = RR_2$.[5] Wang et al. refined the single-beat method and improved the accuracy by using 2 to 3 beats with $RR_1 = RR_2$ (R-R interval difference < 5% of mean) and cycle-length limits (> 500 milliseconds).[7] However, in patients with marked cycle-length irregularity, it is difficult to obtain 2 or more beats with interval difference between RR_1 and RR_2 less than 5% of mean.

This study was therefore planned to (1) evaluate the influence of the RR_1/RR_2 ratio and the R-R interval differences on the value of aortic Doppler-derived SV, and (2) to assess the accuracy and clinical feasibility of a proposed method to determine LV systolic function in AF using beats with interval difference between RR_1 and RR_2 less than 10% of mean.

METHODS

Study Population

The study population comprised consecutive adult patients with AF who were referred for echocardiographic examinations from Nov. 2003 to Oct. 2004. Patients were excluded if they had poor acoustic window, complete atrioventricular block, aortic stenosis, prosthetic aortic valve, or LV outflow obstruction. None were excluded on the basis of age, sex, or degree of hemodynamic impairment. Informed consent was obtained before the study from all patients, and the ethics committee approved the research.

Doppler Echocardiography

Doppler echocardiography was performed using a Sonos 7500 machine (Philips Medical Systems, Andover, Massachusetts). Pulsed Doppler aortic flow velocity spectrum was obtained from the apical 5-chamber view. The sample volume was placed at the LV outflow tract 0.5 to 1 cm proximal to the aortic valve. The Doppler signals were recorded during at least 22 consecutive cardiac cycles and analyzed offline. The time-velocity integral (TVI) of aortic flow, that is proportional to stroke volume, was measured 3 times and averaged for analysis for at least 20 consecutive cardiac cycles. Simultaneous electrocardiograms were used to measure the R-R intervals. Figure 1 shows representative Doppler aortic flow velocity profile during AF. The variability of repeat measurements of TVI was evaluated for 20 cardiac cycles in 10 patients to represent the variations in the measurement process.

Influence of RR_1/RR_2 Ratio and R-R Interval Difference

The linear relation between the measured TVI at a given cardiac cycle and the RR_1/RR_2 ratio was examined. The influence of interval difference between RR_1 and RR_2 on the measured TVI was evaluated by calculating the mean percentage difference between the measured value and the average value over 20 cardiac cycles.

Beats with Interval Difference between RR_1 and RR_2 < 10% vs. < 5%

Prior studies have demonstrated that beats with $RR_1 = RR_2$ (R-R interval difference less than 5% of mean) can be used to determine the mean values by averaging 3 beats with cycle lengths longer than 500 milliseconds.[6,7] The accuracy and clinical feasibility of a proposed method using beats with a wider R-R interval difference (less than 10% of mean) were compared with those of the method using beats with R-R interval difference less than 5%. The value of TVI at a given cardiac cycle with

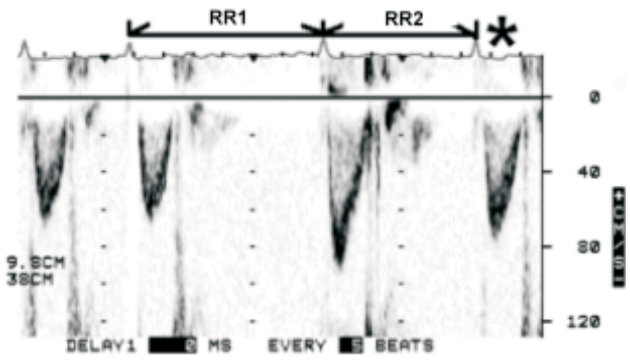

Figure 1. *Representative Doppler aortic flow recording for patient with atrial fibrillation. Aortic time-velocity integral at given cardiac beat (*) and ratio of preceding R-R interval (RR_1) to pre-preceding R-R interval (RR_2) were evaluated.*

R-R interval difference less than 10% of mean was chosen and compared with the measured average value over all cardiac cycles (single-beat method including all cycle lengths). To decrease the variability of the measurement of single-beat method, we averaged the values of 1 to 3 beats with $RR_1 = RR_2$ (interval difference < 5% or < 10% of mean) and cycle-length limits and compared them with the measured average values over all cardiac cycles. The influence of cycle-length variations on the values of TVI at beats with R-R interval difference less than 10% was examined from the plot of normalized TVI (measured value/average value over 20 cycles) against R-R intervals. Mean percentage difference between the calculated values by each method and the measured average values over all cardiac cycles was also evaluated.

Statistical Analysis

All analyses were performed using the Software Package for the Social Science (SPSS for Windows 10.0, SPSS Inc., Chicago, IL, USA). The results are expressed as mean ± SD. Linear regression analysis was applied to analyze the relation between the value of TVI at a given cardiac beat and the RR_1/RR_2 ratio. Bland-Altman agreement analysis[8,9] was used to evaluate agreement between the calculated values and the measured average values over all cardiac cycles. Student's *t*-test was used for analysis of continuous variables. All tests were two-tailed, and *p* values of < 0.05 were considered statistically significant.

RESULTS

Baseline Characteristics

Complete data were obtained from 120 patients with AF. Demographic and clinical characteristics are shown in Table 1. Their mean heart rate was 81 ± 16/min (range: 52 to 121), mean TVI was 16.2 ± 4.2 cm (range: 7.9 to 27.4), and mean ejection fraction was 57 ± 14% (range: 17 to 81). Of the 120 patients, 45 (37.5%) were female, and 28 (23.3%) patients' LV ejection fractions were less than 50%. The most common cardiac diagnosis was hypertension (46%). Most patients were in the first and second functional classifications according to the New York Heart Association's classification.

Influence of RR_1/RR_2 Ratio and R-R Interval Difference

Figure 2 shows representative relation between TVI of aortic flow and the RR_1/RR_2 ratio. TVI was positively correlated with the RR_1/RR_2 ratio in all patients. The variability of repeat measurements of TVI was 3.0%. Table 2 lists the mean percentage difference between the values measured from beats with various R-R interval differences and the average values over 20 cardiac cycles. The mean percentage difference was lowest at beats with interval difference less than 5% of mean and in-

Table 1. Baseline characteristics

Age	63 ± 13 years
Male/female	75/45
LV ejection fraction	57 ± 14%
Time-velocity integral	16.2 ± 4.2 cm
Heart rate	81 ± 16/min
Predominant cardiac diagnosis	Patient number (percentage)
Hypertension	55 (46%)
Left ventricular hypertrophy	38 (32%)
Coronary artery disease	19 (16%)
Valvular heart disease	29 (24%)
Dilated cardiomyopathy	10 (8%)
NYHA functional class I/II	98 (82%)
NYHA functional class III/IV	22 (18%)

LV: Left ventricle; NYHA: New York Heart Association.

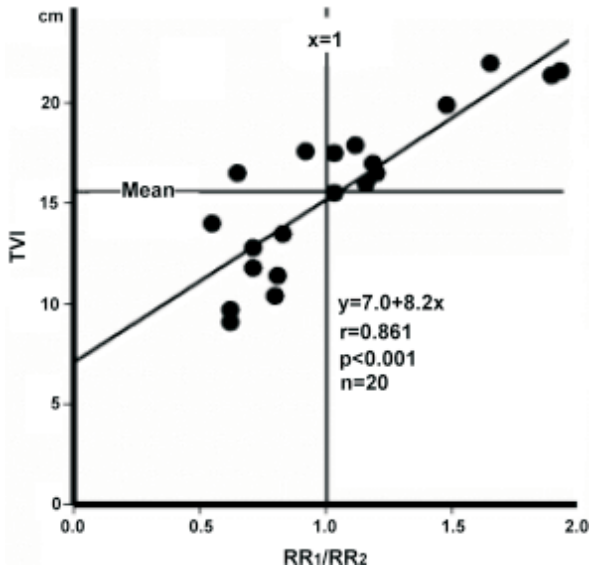

Figure 2. *Representative relation between aortic flow time-velocity integral (TVI) and ratio of preceding to pre-preceding R-R intervals (RR_1/RR_2) was evaluated using linear regression analysis for patient with atrial fibrillation.*

Table 2. Mean percentage difference between the measured average values of time-velocity integral over all cardiac cycles and the values measured from beats with various R-R interval differences (≦ 5%; 5-10%; 10-15%; 15-20%; and 20-25%) in patients with atrial fibrillation

R-R interval difference	Mean difference, %
≦ 5%	4.86
5-10%	6.83
10-15%	8.60
15-20%	12.21
20-25%	14.98

creased with the R-R interval differences.

Limits of Cardiac Cycle Intervals

Figure 3 shows the effect of cycle-length variations on the measured values of TVI at beats with interval difference between RR_1 and RR_2 less than 10% of mean. Similar to a previous report using beats with interval difference less than 5% of mean,[7] most of the normalized TVI were within the range of 0.9 to 1.1 except when the cycle lengths were short. When the cycle lengths were less than 500 milliseconds, the chance of underestimation was high.

Beats with Interval Difference between RR_1 and RR_2 Less than 10%

A total of 681 beats with interval difference between RR_1 and RR_2 less than 10% were selected for determining LV systolic function in AF. Agreement analysis revealed wide 95% limits of agreement (mean difference ± 2SD) between the measured values using the single-beat method including all cycle lengths (2.70 to -2.96 cm) (Figure 4A). To improve accuracy of measurements, we averaged the values of one to three beats with R-R interval difference less than 10% of mean and cycle lengths longer than 500 milliseconds and compared the mean values of one to three beats with the measured average values over all cardiac cycles. Agreement analysis revealed improved accuracy by gradually narrowing the range of the 95% limits of agreement when two or more beats were used for evaluation. The 95% limits of agreement for the single-, 2- and 3-beat analysis excluding cycle lengths shorter than 500 milliseconds were 2.45 to -2.49, 1.56 to -1.64 and 1.17 to -1.29 cm, respectively

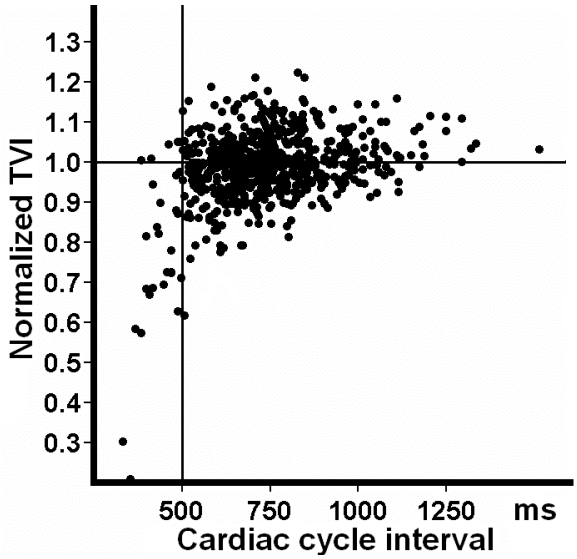

Figure 3. *Influence of cycle-length variations on values of time-velocity integral (TVI) at beats with interval difference less than 10% was examined from plot of normalized values of TVI against cycle lengths. Normalized TVI was calculated as ratio of measured average values over all cardiac cycles.*

(Figure 4B).

Comparison between Methods Using Beats with Different Interval Differences (< 5% vs. < 10%)

The accuracy of assessment was compared between the two methods using beats with different interval differences between RR_1 and RR_2 (< 5% vs. < 10% of mean). A total of 360 beats with interval difference between RR_1 and RR_2 less than 5% of mean was selected. Agreement analysis revealed wide 95% limits of agreement between the measured values using the single-beat method including all cycle lengths (2.29 to -2.45 cm) (Figure 4C). The 95% limits of agreement for the single-, 2- and 3-beat analysis excluding cycle lengths shorter than 500 milliseconds were 2.01 to -2.04, 1.47 to -1.58 and 1.13 to -1.26, respectively (Figure 4D). The mean percentage difference of the method using beats with interval difference less than 5% of mean was smaller than that using beats with interval difference less than 10% of mean for single-beat analysis with or without cycle-length limits, but was not significantly different for 2- and 3-beat analysis with cycle-length limits (Table 3). As the variation of 3-beat analysis with interval difference of less than 5% or 10% of mean was no greater than that of repeat measurement, both methods were

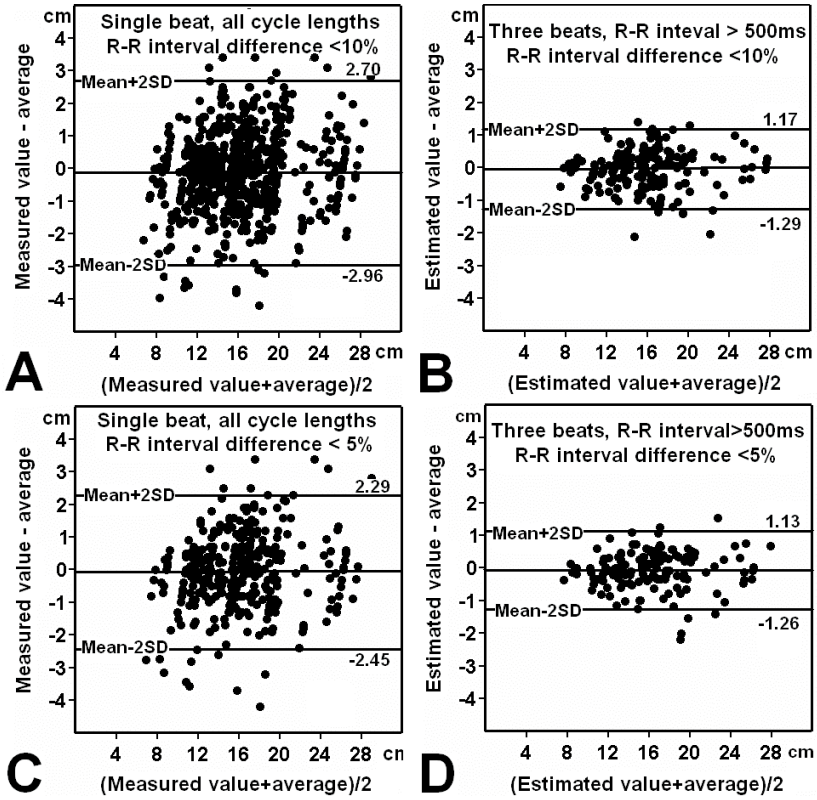

Figure 4. Agreement analysis between measured average values of time-velocity integral (TVI) over all cardiac cycles and estimated values using beats with different R-R interval differences (< 5% vs. < 10%) for patients with atrial fibrillation. A and C: single-beat analysis including all cycle lengths; B and D: Three-beat analysis excluding cycle lengths shorter than 500 milliseconds.

equally good.

Number of Beats Required to Find Three Beats with Equal RR_1 and RR_2

It is relatively easier to find a beat with interval difference between RR_1 and RR_2 less than 10% of mean than to find one with difference less than 5% of mean. Figure 5 shows the percentage of individual subjects in whom three or more beats with interval difference less

Table 3. Mean percentage difference between the measured average values of time-velocity integral over all cardiac cycles and the calculated values by different methods in patients with atrial fibrillation

	Mean difference, %		
Methods	Interval difference < 5%	Interval difference < 10%	*p* value
Single-beat*	5.62	6.65	0.013
Single-beat†	4.86	5.87	0.001
Two-beat†	3.62	3.80	0.527
Three-beat†	2.83	2.97	0.269

*Including all cycle lengths.
†Excluding cycle lengths < 500 milliseconds.

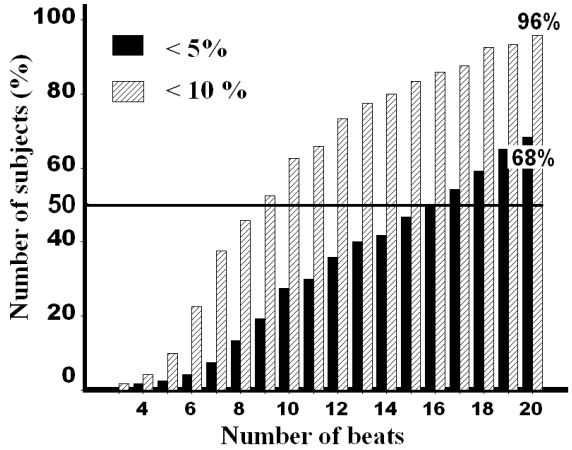

Figure 5. Percentage of individual subjects in whom three or more beats with interval difference less than 5% vs. less than 10% could be obtained by the acquisition of 20 beats for patients with atrial fibrillation.

than 5% vs. 10% of mean could be found by the acquisition of 20 beats. Of the 120 patients, 32% could not get three beats with interval difference between RR_1 and RR_2 less than 5% of mean by the acquisition of 20 beats, but only 4% could not get three beats with interval difference less than 10% of mean. The median number of beats required to find 3 beats with interval difference between RR_1 and RR_2 less than 10% of mean was 9, and the number was 16 for interval difference less than 5% of mean.

DISCUSSION

The measurement of LV SV or cardiac output by Doppler echocardiography is a noninvasive and reproducible technique that has been shown to correlate well with invasive methods of assessing LV SV and cardiac output.[10,11] In AF, marked variability exists in the Doppler aortic flow similar to the intrinsic beat-to-beat variation in LV SV. This beat-to-beat variation has always presented difficulty in estimating a true LV function in patients with AF.[1-3] Therefore, it would be very useful to have an accurate and fast method available by which one could estimate LV function during AF in patients undergoing routine cardiac evaluations. In this study, we have demonstrated that beats with interval difference between RR_1 and RR_2 less than 10% could be applied for determining the mean values over 20 cardiac cycles by averaging 2 to 3 beats with cycle lengths longer than 500 milliseconds.

AF is characterized by marked beat-to-beat variation.[1,2,12] With such beat-to-beat variation, it has been necessary to average many beats to obtain representative values of LV systolic function. Dubrey et al. showed that for patients with AF, a mean of 13 beats was required to achieve an estimation of cardiac output with the same level of variability in sinus rhythm.[3] It is time-consuming and not realistic to measure more than 10 beats for patients undergoing routine cardiac evaluation.

In AF, the impact of RR_1 and RR_2 on the LV systolic parameters has been widely studied and reported.[4-7,13,14] Specifically, the parameters of LV systolic function show positive and negative linear relations with RR_1 and RR_2, respectively.[15,16] These phenomena were explained by interaction of the interval-force relationships: mechanical restitution determined by RR_1 and post-extrasystolic potentiation governed by RR_2, as well as by the Frank-Starling mechanism.[16-20] Several investigators have noted that in addition to RR_1 and RR_2, the ratio RR_1/RR_2 is a strong predictor of LV performance during AF.[4-7,21,22] Prior studies have demonstrated that in AF, several LV systolic parameters positively correlate with the ratio RR_1/RR_2 and the value at the ratio = 1 in the regression line is an excellent estimate of the measured average value over all cardiac cycles.[4-7] However, the correct estimation still requires a large number of beats to obtain the regression line. The minimum number of beats required to get a representative regression line has not been decided yet.

Single-beat determination at a beat with equal subsequent cycles (interval difference < 5% of mean) has been proposed as a good estimate of the measured average value over all cardiac cycles.[6,14] However, in the canine study of Tabata et al. where a large number (> 100) consecutive beats were evaluated, a substantial scattering of data points for each of the systolic parameters at the ratio $RR_1/RR_2 = 1$ was observed.[5] Their finding precludes the use of just one given beat with equal subsequent cycles for assessing LV function in AF. We have shown that the variability of single-beat method could be decreased to an acceptable level just by measuring and averaging 2 to 3 beats with equal subsequent cycles and cycle-length limits. We also compared the accuracy of two methods using beats with different interval differences between RR_1 and RR_2 (< 5% vs. < 10%) and found no significant difference between these two methods after averaging 2 or more beats. It is easier to obtain three beats with interval difference between RR_1 and RR_2 less than 10% of mean, and clinically practical.

One of the limitations of our proposed method may exist in its application to rapid AF, in which the cycle lengths of the selected cardiac cycles will usually be shorter than 500 milliseconds. For such an application, one may need a long recording of consecutive cardiac cycles. An additional limitation is that to find cardiac cycles with intervals difference less than 10% of mean, it may require measuring many R-R intervals in which the ratio RR_1/RR_2 is likely to be one.

In conclusion, substantial variability exists between the values of LV systolic function measured at beats with equal subsequent cycles during AF. Averaging 2 to 3 beats with equal subsequent cycles and cycle lengths

longer than 500 milliseconds can be applied to estimate accurately the LV systolic function in AF. The accuracy of measurements using 2 to 3 beats with interval difference between RR_1 and RR_2 less than 10% of mean was similar to that using beats with interval difference less than 5% of mean. This method is easier to be applied in clinical practice by obtaining 2 to 3 beats with interval difference less than 10% of mean, particularly for patients with marked cycle-length variations.

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應用前兩心跳週期相同之心跳評估心房纖維顫動時的經主動脈瓣杜普勒血流量

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背景 先前的研究發現前兩心跳週期相同 (定義為心跳週期誤差在百分之五以內) 之心跳，取二至三個心跳平均可運用於預測心房纖維顫動病患 20 個心跳週期的平均值。而取心跳週期誤差在百分之十以內之心跳是否可以運用來預測，目前並不清楚。

方法 我們收集了 120 位心房纖維顫動患者的資料，於每一個患者分析及測量流經主動脈瓣杜普勒血流量至少連續 20 個心跳週期，比較取心跳週期誤差在百分之五以內及取心跳週期誤差在百分之十以內來預測之兩種方法之間，是否有所不同。

結果 於心跳週期小於 0.5 秒的心跳其數值容易低估 20 個心跳的平均值，在分析時須加以排除。而相符性分析及平均差比較分析顯示，取心跳週期誤差在百分之五以內及取心跳週期誤差在百分之十以內來預測之兩種方法，於排除小於 0.5 秒的心跳及取二至三個心跳平均後，準確度並無不同。在臨床運用上取心跳週期誤差在百分之十以內之心跳來預測 20 個心跳的平均值，相對容易許多。

結論 在臨床上可以取三個心跳週期誤差在百分之十以內及排除週期小於 0.5 秒的心跳，準確地評估心房纖維顫動患者之經主動脈瓣杜普勒血流量。

關鍵詞：心房纖維顫動、左心室、心搏出量、收縮期、心室功能。