Accuracy of the Single Cycle Length Method for Calculation of Aortic Effective Orifice Area in Irregular Heart Rhythms

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Introduction: In irregular heart rhythms, echocardiographic calculation of aortic effective orifice area (EOA) requires averaging measurements from multiple cardiac cycles. Whether a single cycle length method can be used to calculate aortic EOA in aortic stenosis with nonsinus rhythms is not known.

Methods: Transthoracic echocardiograms of 100 patients with aortic stenosis and either atrial fibrillation (AF) or frequent ectopy (FE) were retrospectively reviewed. The aortic valve velocity time integral (VTI_{AV}) and the left ventricular outflow tract VTI (VTI_{LVOT}) were measured by two methods: the standard method (averaging multiple beats) and the single cycle length method. The latter matches the R-R intervals for VTI_{AV} and VTI_{LVOT}. Stroke volume, EOA, and Doppler velocity index were calculated by both methods in all patients. The single cycle length method was used for short and long R-R cycles in AF and for postectopic beats (long R-R cycles) in FE.

Results: In AF, long R-R cycles resulted in larger stroke volumes (73 ± 21 vs 63 ± 18 mL; $P \le .0001$) but no difference in EOA (0.84 ± 0.27 vs 0.82 ± 0.27 cm^2; $P = .11$), whereas short R-R cycles resulted in smaller stroke volumes (55 ± 18 vs 63 ± 18 mL, $P \le .0001$) but a larger EOA (0.86 ± 0.28 vs 0.82 ± 0.27 cm^2; $P = .01$). In FE, the postectopic beat led to larger stroke volumes (96.1 ± 28 vs 78 ± 23 mL; $P < .0001$) and a larger EOA (0.99 ± 0.32 vs 0.94 ± 0.32 cm^2; $P = .0006$) and Doppler velocity index (0.24 ± 0.07 vs 0.23 ± 0.07; $P < .001$).

Conclusions: In AF patients, the single, long cycle length method of calculating EOA can be used instead of averaging multiple cardiac cycles. The single cycle length method used on a postextrasystolic beat results in a larger EOA than a normal sinus beat and may have utility in clinical decision-making. (J Am Soc Echocardiogr 2019;32:344-50.)

Keywords: Aortic valve, Aortic stenosis, Echocardiography, Continuity equation, Atrial fibrillation, Transcatheter aortic valve replacement

The derivation of the continuity equation using echocardiographic parameters dramatically changed the approach to determining effective orifice area (EOA) of a stenotic orifice and thus the diagnosis and management of aortic stenosis (AS).[1-3] The most recent American College of Cardiology/American Heart Association guidelines give a class I recommendation to the use of echocardiography in determining the severity of AS.[4] In addition to clinical symptoms, the quantitative assessment of AS severity by Doppler-derived hemodynamics is a major determinant of patient prognosis and need for aortic valve (AV) replacement. Using the left ventricular outflow tract (LVOT) velocity time integral (VTI) obtained on spectral pulsed-wave Doppler tracings (VTI_{LVOT}) and the AV VTI from continuous-wave Doppler tracings (VTI_{AV}), the EOA can be calculated by the continuity equation, which has been shown to correlate well with values obtained by cardiac catheterization.[3,5-7] The Doppler velocity index (DVI) is an alternate measure of AS severity, using the ratio of the VTI_{LVOT} to the VTI_{AV}. Like EOA, the DVI takes into account beat-to-beat changes in left ventricular filling and stroke volume that occur with varying R-R intervals that are reflected in both LVOT and transaortic flow measurements. The DVI also avoids error that may be introduced with measurement of the LVOT diameter.

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Abbreviations

AF = Atrial fibrillation

AS = Aortic stenosis

AV = Aortic valve

DVI = Doppler velocity index

EOA = Effective orifice area

FE = Frequent ectopy (atrial and ventricular premature contractions)

ICC = Intraclass correlation coefficient

LVOT = Left ventricular outflow tract

R-R1 = Interval (in milliseconds) between beats for the preceding interval

R-R2 = Interval (in milliseconds) between beats for the prepreceding interval

TTE = Transthoracic echocardiogram

VTI_{AV} = Velocity time integral of the transaortic flow on continuous wave Doppler

VTI_{LVOT} = Velocity time integral of the left ventricular outflow tract flow on pulsed wave Doppler

The focused update of the assessment of AS by the European Association of Cardiovascular Imaging and the American Society of Echocardiography[8] continues to recommend averaging at least three consecutive beats in sinus rhythm to optimize the accuracy of EOA quantification. These same guidelines state that averaging at least five consecutive beats is mandatory with irregular rhythms, in part because the beat-to-beat variability of irregular heart rhythms is associated with changes in stroke volume with each cardiac cycle.[9,10] This method of calculating EOA in AF is time-consuming and may still lead to inaccurate area assessment depending on the R-R intervals included in the calculations. In patients with frequent ectopy (FE), it has been suggested that longer cardiac cycle lengths may lead to higher transaortic gradients; however, long R-R intervals are also associated with larger stroke volumes.[11] Therefore, calculation using the postectopic beat following an atrial or ventricular premature contraction may still lead to an accurate estimate of aortic EOA. The aim of this study was to determine whether a single cycle length method can be used for aortic EOA calculation compared with the standard approach to aortic EOA measurement in irregular rhythms.

METHODS

Patient Population

The database of transthoracic echocardiograms (TTEs) performed on patients undergoing evaluation for transcatheter AV replacement at Columbia University Medical Center in New York was retrospectively searched from October 2012 through September 2013. Patients in this database with R-R variability were identified and divided into two groups: those with atrial fibrillation (AF) and those with frequent atrial or ventricular premature contractions or FE. Baseline characteristics were recorded for all patients, including age, sex, body surface area, heart rate, ejection fraction, and EOA (Table 1). All patients signed informed consent, and the study was approved by the institutional review board on human research.

Study Protocol

The study protocol is shown in Figure 1. All studies were performed using a Philips iE33 xMATRIX echocardiography system (Andover, MA). Patients were evaluated according to a standard TTE protocol including two-dimensional, M-mode, and Doppler (pulsed wave, continuous wave, color) techniques. In all patients, the LVOT diameter was measured in midsystole, within 2-4 mm apical to the annulus.

Pulsed-wave Doppler interrogation of the LVOT was performed from apical windows. Continuous-wave Doppler across the AV for measurement of VTI_{AV} was obtained from multiple acoustic windows including apical, right parasternal, and suprasternal notch views to obtain the highest transaortic velocity profiles. The same acoustic window was used for both methods of VTI_{AV} measurement.

Aortic EOA and DVI Calculation: Standard Approach

VTI_{LVOT} and VTI_{AV} were measured and averaged over five to 10 consecutive beats in the AF group. In the FE group, the VTI_{LVOT} and VTI_{AV} were measured over three to five consecutive sinus beats. EOA and DVI were calculated from the values obtained.

Aortic EOA and DVI Calculation: Single Cycle Length Method

In patients in the AF group, a single VTI_{AV} was measured and then matched to a VTI_{LVOT} of similar cycle length (Figure 2). Similar cycle length was defined as R-R intervals within 10% of each other, such that the R-R interval immediately preceding the selected VTI_{AV} was matched to within 10% of the R-R interval that immediately preceded the selected VTI_{LVOT}. Short and long R-R cycles were defined relative to the average heart rate. EOA and DVI were then calculated for a short R-R cycle and for a long R-R cycle.

In patients in the FE group, only a long R-R cycle was measured: a VTI_{AV} following a postectopic beat was measured and matched to a VTI_{LVOT} following a postectopic beat of similar cycle length. EOA and DVI were calculated from the postectopic beat.

Statistical Analysis

All analyses were made using SPSS 20.0 (IBM, Armonk, NY). $P < .05$ was considered statistically significant, and all P values are two-sided. Categorical variables are presented as percentages and were compared with the χ^2 test or Fisher's exact test. The χ^2 test was used to calculate trend P values. Continuous variables are presented as mean and standard deviation and were compared using a paired Student's t-test. Intraclass correlation coefficients (ICCs) were used to assess interobserver (K.A.E. and Q.L.) and intraobserver (K.A.E.) variability. The intraobserver variability was assessed from 20 studies (10 AF; 10 FE) that were measured by the same operator 12 months apart. For interobserver variability 20 studies (10 AF; 10 FE) were used.

RESULTS

One hundred TTEs were identified that demonstrated either AF ($n = 55$) or FE ($n = 45$). Of the 100 patients, 51 were male and 49 were female. The mean age of the patients was 84.5 ± 6.4 years, with mean EOA of 0.88 ± 0.30 cm^2. Most patients had severe AS, although 15 of the 55 AF patients (27%) and 18 of the 45 FE patients (40%) had nonsevere AS. The mean ejection fraction was 54% ± 15% in the AF group (range, 20%-80%) and 50% ± 17% in the FE group (range, 17%-79%). The mean number of beats measured for the average VTI_{LVOT} was 9.6 ± 1.2 cm. The mean number of beats measured for the average VTI_{AV} was 9.7 ± 1.1 cm.

HIGHLIGHTS

- Aortic EOA was measured by matching RR intervals in irregular heart rhythms.
- AF: Aortic EOA can be measured with a single cycle length, a long cycle is preferred.
- FE: The postectopic beat results in a higher transaortic gradient, SV, DVI, and EOA.

R-R Cycle Matching

Figure 3 shows differences in RR cycle lengths between VTI LVOT and VTI AV for the standard and single cycle length methods (long and short cycles). In the AF group, the mean R-R interval for LVOT measured (RR_{LVOT}) by the standard approach was 823 ± 171 msec, while the mean R-R interval for AV (RR_{AV}) measured by the standard approach was 831 ± 165 msec ($P = .60$). By the single cycle length method for a short cardiac cycle, the mean RR_{LVOT} interval was 674 ± 136 msec and the RR_{AV} was 673 ± 134 msec ($P = .92$). For the long cardiac cycle, the mean RR_{LVOT} was 980 ± 195 msec and RR_{AV} was 983 ± 184 msec ($P = .52$). Using the single cycle length, short and long R-R cycle lengths were significantly different (RR_{LVOT} short = 674 ± 136 msec vs RR_{LVOT} long = 980 ± 195 msec; $P < .0001$; RR_{AV} short = 673 ± 134 msec vs RR_{AV} long = 983 ± 184 msec; $P < .0001$).

In the FE group, there was no significant difference in cycle lengths for sinus beats (RR_{LVOT} = 891 ± 151 msec vs RR_{AV} = 889 ± 150 msec; $P = .81$). Likewise, there was no significant difference in cycle lengths for long postectopic cycles (RR_{LVOT} 1,074 ± 211 msec vs $RR_{AV\,=}$ 1,057 ± 210 msec; $P = .61$). There was a significant difference, however, between sinus and ectopic RR_{LVOT} cycle length ($P < .001$) and ectopic RR_{AV} cycle length ($P < .001$).

Stroke Volume

In AF patients, the stroke volume calculated by the standard method (Table 1; 63.5 ± 17.6 mL) was significantly larger than the stroke volume calculated by the single cycle length short R-R cycle (55.1 ± 17.6 mL; $P < .0001$) and smaller than the stroke volume calculated by the single cycle length long RR cycle (72.8 ± 21.2 mL; $P < .0001$). In the FE group, stroke volume from the postectopic beat was significantly larger than stroke volume calculated from sinus rhythm (96.1 ± 28.2 mL vs 77.9 ± 23.2 mL; $P < .0001$).

Aortic EOA and DVI

The mean aortic EOA calculated by the standard approach was 0.82 ± 0.27 cm^2. By the single cycle length method, there was no difference in EOA when long R-R cycles were selected (0.84 ± 0.27 cm^2, $P = .11$). When short R-R cycles were used, EOA was larger than values calculated by the standard approach (0.86 ± 0.28 cm^2, $P = .01$). Likewise, there was no difference in DVI values obtained by the standard approach compared with the single cycle length using a long cycle; however, there was a significant difference in DVI when the short R-R cycle was used. There was no difference in EOA or DVI calculated by the single cycle length method comparing long and short R-R cycles (EOA: 0.84 ± 0.27 vs 0.86 ± 0.28, $P = .23$; DVI: 0.23 ± 0.07 vs 0.23 ± 0.07, $P = .28$). In the FE group, calculations from the postectopic beat led to larger EOA and DVI compared with measurement by the standard approach (0.99 ± 0.32 cm^2 vs 0.94 ± 0.32 cm^2, $P = .0006$; DVI: 0.24 ± 0.07 vs 0.23 ± 0.07, $P = .0002$).

Correlation of EOA Calculated by Standard Method versus Single Cycle Length

In the AF group, correlation coefficients for EOA calculated by long and short R-R cycles compared with EOA calculated by the standard approach are $r = 0.96$ (95% CI, 0.93-0.98) and $r = 0.94$ (95% CI, 0.90-0.96), respectively (Figure 4). In the FE group, the correlation coefficient for EOA calculated by the long R-R cycle compared with EOA calculated by the standard approach is $r = 0.96$ (95% CI, 0.93-0.98).

Intra- and Interobserver Variability

The ICC for interobserver variability in the AF group was 0.95 (95% CI, 0.81-0.99) for short RR cycles and 0.94 (95% CI, 0.78-0.99) for long RR cycles. The ICC for interobserver variability in the FE group was 0.97 (95% CI, 0.86-0.99) for long RR cycles. The ICC for intraobserver variability in the AF group was 0.92 (95% CI, 0.69-0.98) for short RR cycles and 0.94 (95% CI, 0.78-0.99) for long RR cycles. The ICC for intraobserver variability in the FE group was 0.99 (95% CI, 0.95-1.0).

DISCUSSION

The main findings of this study are (1) matching cycle lengths for VTI_{LVOT} and VTI_{AV} results in a high correlation with standard methods of EOA calculation; (2) for patients in AF, the single cycle length method using a long R-R cycle is the most accurate method for assessing EOA for patients with AS; and (3) using a postsystolic beat in the setting of FE results in a higher peak transaortic gradient, larger stroke volume, and larger EOA compared with sinus beats.

Measuring multiple beats is a tedious task in a high-volume echocardiography laboratory, making the single cycle length method an attractive alternative to the standard method. In addition, the cycle lengths of the multiple LVOT VTI beats and AV VTI beats are unlikely to be the same, introducing significant error into this method. Current guidelines recommend averaging at least five consecutive beats in AF.[8] Averaging multiple beats attempts to approximate the mean heart rate; however, the number of cycle lengths measured tends to be arbitrary, and quantitation rarely includes more than 10 beats. As previous research has demonstrated, averaging 13-17 beats in AF may be required to approximate the true mean cardiac output for any individual patient.[12] The need for increasing numbers of R-R cycles may be explained by nonsimultaneous acquisition of VTI_{LVOT} and VTI_{AV} in irregular rhythms. In the present study using an average of between five and 10 consecutive beats, the VTI_{LVOT} and VTI_{AV} cycle lengths were not significantly different, validating this method.

Previous research has shown that when cycle lengths are matched, there is no significant change in EOA over a wide range of R-R intervals and stroke volumes in patients with spontaneous R-R variability and severe AS.[13] The current study confirms that matching cycle lengths for VTI_{LVOT} and VTI_{AV} results in a high correlation with standard methods of EOA calculation, and the correlation is highest with use of a long cycle length. Although EOA calculated from a short cycle length was statistically different from the standard method, the correlation coefficients achieved with the use of either short or long R-R cycles compared with the standard method are higher than those

Table 1 Doppler variables measured by different methods

Variable	Standard approach (a)	Single cycle long RR (b)	Single cycle short RR (c)	*P* value (a vs b)	*P* value (a vs c)	*P* value (b vs c)
VTI_{LVOT} (cm):						
AF	17 ± 4.9	20 ± 5.7	15 ± 5.0	<.0001	<.0001	<.0001
FE	19 ± 5.6	23 ± 6.4	N/A	<.0001	N/A	N/A
VTI_{AV} (cm):						
AF	81 ± 20	90 ± 22	68 ± 20	<.0001	<.0001	<.0001
FE	87 ± 21	101 ± 22	N/A	<.0001	N/A	N/A
Stroke volume (μg):						
AF	63 ± 18	73 ± 21	55 ± 18	<.0001	<.0001	<.0001
FE	78 ± 23	96 ± 28	N/A	<.0001	N/A	N/A
EOA (cm^2):						
AF	0.82 ± 0.27	0.84 ± 0.27	0.86 ± 0.28	.11	.01	.24
FE	0.94 ± 0.32	0.99 ± 0.32	N/A	.0006	N/A	N/A
DVI:						
AF	0.22 ± 0.07	0.23 ± 0.07	0.23 ± 0.07	.09	.01	.28
FE	0.23 ± 0.07	0.24 ± 0.07	N/A	.0002	N/A	N/A

Variables calculated by the standard method and by the single cycle length method for the AF and FE groups for the following parameters: VTI_{LVOT}, VTI_{AV}, stroke volume, EOA, and DVI. N/A indicates that the parameters calculated for the single cycle short RR (c) were not applicable to the FE group.

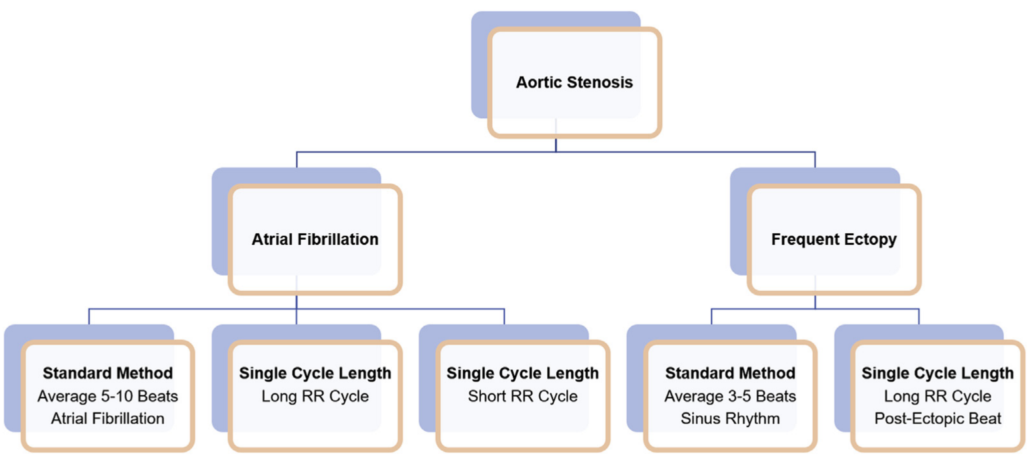

Figure 1 Study design. In the AF group, calculations were performed by the standard method and by the single cycle length with long and short cycle lengths. In the FE group, calculations were performed by the standard method and by the single cycle length using a long RR cycle.

achieved in studies that validated the use of the continuity equation for measurement of aortic EOA as compared with the Gorlin formula.[3,14] Further, while the numeric difference in EOA obtained by the single cycle length method versus the standard method is statistically significant when a short RR cycle is used, it is unlikely to be clinically significant. When comparing the single cycle length method using a short R-R cycle with the standard method, classification of severe AS by American College of Cardiology/American Heart Association guidelines changes in only two of 55 patients, with the change in classification due to a difference of 0.1 cm^2 in calculated EOA.

Nonetheless, the larger EOA calculated from short R-R intervals seems counterintuitive given the lower stroke volume. Despite the lower stroke volume with shorter R-R interval, there may be changes in contractility that could result in a larger EOA. Higher cardiac output is seen, for instance, with increasing regular heart rates achieved by pacing patients with AF.[15] Ventricular contractility and myocardial performance in AF are also affected by the relationship between the preceding and the prepreceding cycle lengths: myocardial contractility and left ventricular function are directly related to the preceding R-R interval (RR1) and the ratio of the preceding interval to the prepreceding interval (RR1/RR2).[16-20] Studies have also shown that rhythm irregularity has a greater effect on myocardial performance and contractility at faster heart rates, while myocardial performance is less dependent on RR1/RR2 at longer cycle lengths.[21,22] There may also be a systematic underestimating of the VTI_{AV} with short cycle lengths for indiscernible reasons. Given the very small numeric difference in EOA, particularly when a long RR

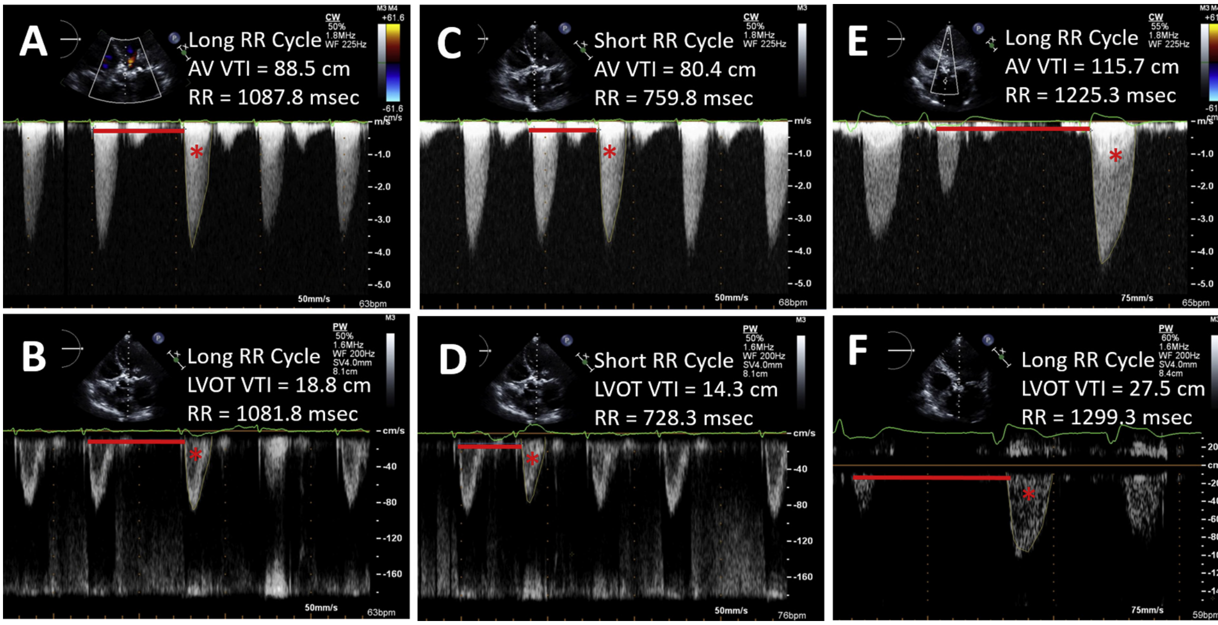

Figure 2 Measurement methods. Examples of matched cycles (*red asterisk*) chosen for measurements of EOA in patients with AF **(A-D)** and ectopic beats **(E-F)** are shown: a long RR cycle continuous-wave Doppler **(A)** and pulsed-wave Doppler **(B)** and a short RR cycle continuous-wave Doppler **(C)** and pulsed-wave Doppler **(D)**. Similar matching is performed on postextrasystolic beats **(E and F)**.

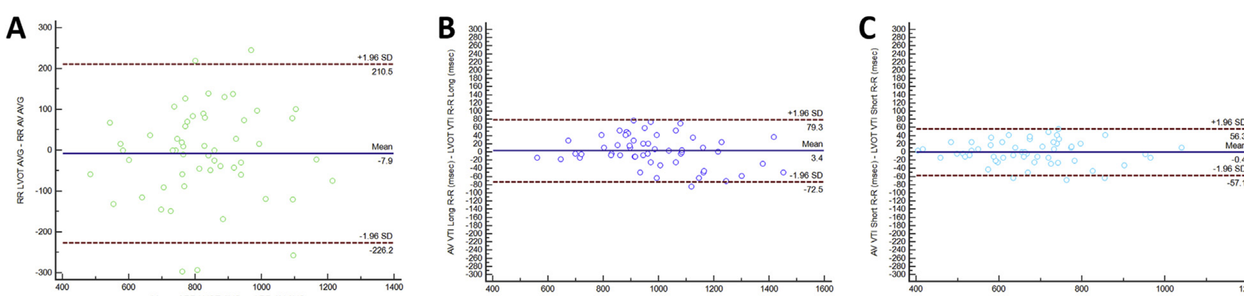

Figure 3 Differences in cycle lengths. Bland-Altman plots assessing differences in RR intervals for VTI_{LVOT} and VTI_{AV} by the **(A)** standard method and the single cycle length method for **(B)** long cycle lengths and (**C**) short RR cycle lengths.

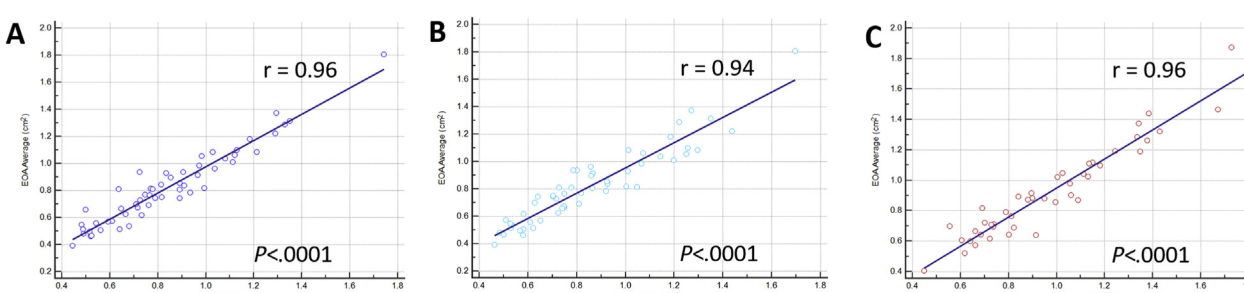

Figure 4 Differences in aortic EOA. Differences in aortic EOA calculated by the standard approach and the single cycle length method in the AF group using **(A)** long and **(B)** short RR cycles and **(C)** the FE group using long RR cycles.

cycle is used, it is unlikely that misclassification is related to an inherent flaw in the method, but rather to small differences in actual valve area measurement that occur with changes in flow. It thus seems reasonable to recommend using a long R-R cycle as an alternative to averaging multiple beats to calculate the EOA in patients with AF and AS.

In patients with FE, measurement of the postectopic beat (long R-R) by the single cycle length method in subjects in sinus rhythm led to significantly higher transaortic gradients and larger stroke volumes compared with average values obtained from sinus beats. This is likely related to the effect of postextrasystolic potentiation. Since valve opening may be flow dependent,[23-25] this postextrasystolic increase in stroke volume resulted in a larger EOA as compared with averaging sinus beats. In the current study, both atrial and ventricular premature contractions were included in the FE cohort. Previous research has demonstrated potentiation of contractility following atrial premature contractions, although the degree to which postextrasystolic potentiation varies following atrial or ventricular premature contractions has not been demonstrated.[26] Investigators have shown that postextrasystolic potentiation following premature atrial or ventricular contractions at baseline leads to peak aortic velocities and mean aortic gradients similar to those achieved with the use of dobutamine stress echocardiography performed for evaluation of low-flow, low-gradient AS.[27] Not only could postectopic beats identify true AS in patients with low baseline gradients, but they could also diagnose pseudosevere or moderate AS. We now know that low-flow, low-gradient severe AS may benefit from intervention.[28] Moderate AS might also benefit from intervention.[29] The Transcatheter Aortic Valve Replacement to UNload the Left Ventricle in Patients With ADvanced Heart Failure (TAVR UNLOAD) trial (ClinicalTrials.gov identifier: NCT02661451) is enrolling patients with moderate AS and reduced ejection fraction to determine the safety and efficacy of transcatheter AV replacement.

Limitations

Most patients in the current study undergoing evaluation for transcatheter AV replacement had severe AS. Future research may further substantiate the accuracy of the single cycle length method and its application to the measurement of EOA in a larger population of patients with nonsevere AS. Correlation with invasive hemodynamic data would also serve to validate the findings of the single cycle length method as an accurate measure of true transvalvular flow hemodynamics.

CONCLUSION

The single cycle length method matches R-R intervals of the preceding cardiac cycle for measurement of VTI_{LVOT} and VTI_{AV} in irregular heart rhythms. In AF, the use of a long cycle length is preferred to achieve the highest correlation with the current standard approach of averaging multiple beats. Calculation of EOA using a postectopic beat results in the highest transaortic gradient, stroke volume, DVI, and EOA and may have utility in clinical decision-making.

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