Original Article

Impact of Valvular Event Time Assessment Methods on Myocardial Work Calculation by Echocardiography

Marcio Mendes Pereira,[1] *Francisco das Chagas Monteiro Júnior,*[2] *Sayuri Yamamura*[2]
UDI Hospital,[1] *São Luis, MA – Brazil*
Universidade Federal do Maranhão,[2] *São Luis, MA – Brazil*

Abstract

Background: Left ventricular ejection fraction (LVEF) is the traditional parameter for assessing cardiac function, but it has limitations in the early detection of dysfunction. Global Longitudinal Strain (GLS) and myocardial work (MW) are promising alternatives, the latter being less influenced by load conditions. The calculation of MW depends on valvular event times (VET), obtained by methods that may generate divergent results.

Objectives: To compare the impact of different methods of VET measurement – visual analysis (VA), tissue Doppler imaging (TDI) and pulsed Doppler (PD) – on global work index (GWI), global constructive work (GCW), global wasted work (GWW) and global work efficiency (GWE).

Method: Cross-sectional clinical study with 35 healthy patients who underwent echocardiography between October 2022 and March 2023. MW was assessed using the EchoPAC software, with VET measurement by VA, TDI and DP. The results were analyzed by ANOVA and Friedman tests, followed by post-hoc analyses with a significance level of 5%.

Results: GWI showed significant variation between the VET measurement methods, being lower by AV compared to TDI and DP (p<0.001). The GCW, GWW and GWE indexes did not demonstrate statistically significant differences between the methods.

Conclusions: The VET measurement method significantly impacts the GWI, but does not affect the other MW indexes.

Keywords: Echocardiography; Left Ventricular Dysfunction; Ventricular Function.

Introduction

Left ventricular ejection fraction (LVEF) has been widely used in the assessment of systolic function in several clinical conditions, especially cardiac diseases. However, studies have demonstrated that LVEF has limitations, particularly in the early detection of cardiac dysfunction in patients with preserved ejection fraction but with subclinical impairment. In this context, new echocardiographic techniques, like the global longitudinal strain (GLS) have gained importance, providing a more sensitive assessment of myocardial deformation.[1,2]

More recently, the introduction of the concept of myocardial work (MW) has enabled a more comprehensive evaluation of cardiac function, considering the interaction between myocardial strain and afterload during cardiac cycle. In contrast to GLS, MW is less influenced by preload and afterload conditions, which may provide a more robust estimate of myocardial function.[3,4]

For MW calculation, it is essential to precisely estimate valvular event times (VETs), particularly events related to the aortic valve opening and closure. The times may be obtained using different methods, including visual analysis (VA), tissue doppler imaging (TDI) and pulsed Doppler (PD) ultrasound. However, there is no consensus on the most accurate method, and implications on MW indexes – global work index (GWI), global constructive work (GCW), global wasted work (GWW) and global work efficiency (GWE) – are still little explored.[5-8]

The aim of the present study was to compare the methods used for VET estimation for differences in determining MW.

Methods

This was a cross-sectional study with 35 patients, conducted in a private hospital in Sao Luis, state of Maranhão, Brazil, between October 2022 and March 2023. Patients aged 18 years or older, without comorbidities underwent echocardiography. The echocardiographic studies were conducted following the American Society of Echocardiography (ASE) recommendations, with two-dimensional images recorded during three cardiac cycles, synchronized with the QRS complex, for offline analysis using the EchoPAC software (version 202, GE Vingmed Ultrasound). LVEF was determined by the Simpson method.

Mailing Address: Marcio Mendes Pereira •
UDI Hospital. Av. Prof. Carlos Cunha, 2000. Postal code: 65076-820. Jaracati, São Luis, MA – Brazil
E-mail: marciomp50@hotmail.com
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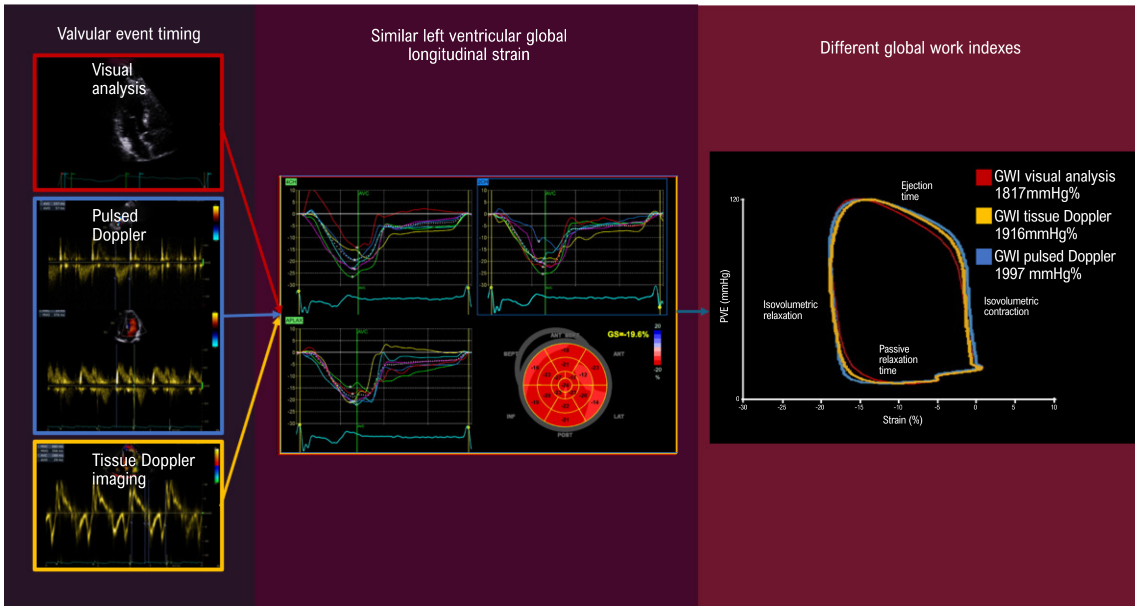
Central Illustration: Impact of Valvular Event Time Assessment Methods on Myocardial Work Calculation by Echocardiography



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Calculation of MW. Estimation of VET by VA, pulsed wave Doppler of mitral inflow and LV outflow and tissue doppler of the mitral annulus tissue. Using automated function imaging, the GLS is generated through the apical 2, 3 and 4-chamber views. GWI, calculated using the event markers obtained by VA is lower than GWI values obtained by tissue Doppler and PD. LVP: left ventricular pressure ; GWI: global work index

The GWI was estimated by calculating the segmental shortening rate by differentiation of the strain tracing and multiplying by instantaneous left ventricular (LV) pressure. This instantaneous measure was integrated over time to measure MW as a function of time during systole (time interval from mitral valve closure to mitral valve opening). During LV ejection, segments were analyzed for GWW and/or GCW, with global values determined as means of all segmental values and displayed on the LV pressure-strain loop diagram.

The main parameters calculated were the following: GWI (mmHg%), area within the LV pressure curve; GCW (mmHg%), estimated work performed by the LV segments; GWW (mmHg%), estimated negative work done by the LV segments; GWE (mmHg%) (defined as the ratio between GCW and the sum of GCW and GWW.

Categorical variables were expressed as absolute and relative frequencies, and continuous variables as mean and standard deviations, depending on data distribution. Normality of data distribution was assessed by the Shapiro-Wilk test ($p<0.05$).

Sample size was calculated to detect a difference of 123 mmHg% in GWI between the methods, with a power of 90% and level of significance of 5%. Comparisons of means were made by ANOVA for parametric data and the Friedman test for nonparametric data. Post-hoc tests, like pairwise comparisons of the marginal linear predictions and the Bonferroni test were applied to detect significant differences. The statistical analysis was performed using the Stata® Intercooled test, version 18.0.

The study was approved by the ethics committee of Sao Domingos hospital and maternity hospital (CAAE 71514222.1.0000.5085).

Results

Mean age of patients was 39.9 years (18-60 years), and most of them were men (57.1%). Clinical and echocardiographic parameters of participants are summarized in Table 1. Averages of echocardiographic measurements were within normal range.

Table 2 describes the comparisons between MW indexes by the method used for VET estimation. The values obtained by VA were significantly different ($p<0.001$) than the Doppler (TDI and PD)-derived measurements. For example, mean GWI by VA was significantly lower than GWI estimated by TDI or PD. However, no significant differences were observed between the other myocardial indexes (Tables 2 and 3). These results were displayed in a Bland-Altman plot for a visual representation of the degree of agreement between the values obtained by different VET estimation methods. Figure 1 shows a more scattered distribution of points is observed in the plots A and B, indicating a lower degree of agreement between

Table 1 – General and echocardiographic characteristics of the study patients

Variables	TOTAL (n = 35)
Clinical profile	
Age	38.88 (18; 60)
Sex (%)	
Male	57.14
Female	42.86
Body surface (cm²)	1.87 ± 0.21
Height (m)	1.68 (1.50; 1.88)
Weight (kg):	77 (51; 124)
Systolic blood pressure (mmHg)	114 ± 9
Diastolic blood pressure (mmHg)	72 ± 7
Heart rate (bpm)	67 (47; 94)
Echocardiographic data	
End-diastolic diameter (mm)	4.84 ± 0.44
End-systolic diameter (mm)	2.98 ± 0.35
Septal thickness (mm):	0.82 ± 0.08
End-diastolic volume (mmHg):	90 ± 25
End-systolic volume (mmHg)	32 ± 12
Left atrial volume (mmHg)	24 ± 4
Ejection fraction (mmHg)	65 ± 3
LV mass index, (g/m²)	71 (48; 95.9)
Frame rate, (frames/s)	73 ± 52
GLS (%)	19 ± 1.8

GLS: Global Longitudinal Strain

the values. Figures 2, 3 and 4 corroborate the lack of statistical differences between the MW indexes calculated by different methods.

Table 4 describes relationships between the results, demonstrating a significant difference in the times of mitral valve closing and aortic opening between the three methods for VET estimation. According to both TDI and PD, mitral valve closing occurred at a later stage, whereas aortic valve opening at an earlier stage as compared with VA.

Discussion

The present study evaluated the impact of different methods of VET estimation on MW indexes. The results indicated that GWI was influenced by the method, with lower values obtained by VA as compared with TDI and PD, which demonstrated similar results. The Central Figure shows an example of GWI calculation using the three methods, reinforcing the significant difference observed with VA. However, no significant differences between the methods were found for estimation of other indexes such as GCW, GWW, or GWE, suggesting a lower sensitivity of these indexes to the method used.

These differences may be explained by the higher susceptibility of VA to errors, due to observer's subjectivity and lower temporal resolution, in contrast to the objective accuracy of TDI and PD, resulting in differences in VET values and ultimately in MW estimates. Changes in valvular times, such as in aortic valve opening time, may have influenced the GWI values obtained by VA, by reducing the time of ejection as compared with other methods. Since all other factors related to pressure-strain loop were maintained constant and the GLS was the same in all groups, differences in GWI obtained by the three methods may be attributed to differences in VETs. In the study by Russell et a.,[7] changes in aortic valve opening and closing times did not affect the GWI values, differently from our findings and those reported by Olsen et al.[6]

The study by Olsen et al.[6] was the only similar publication that included four subtypes of subjects – healthy subjects, subjects with atherosclerosis, subjects with atrial fibrillation during the echocardiographic examination, and subjects with reduced ejection fraction. The methods for VET estimation were VA, PD and TDI M-mode. Our results are in accordance with the results reported by these authors,[6] showing that GWI, when estimated by VA, was lower when compared with Doppler-based methods. These findings were similar in all subgroups of subjects evaluated, including the sample of healthy individuals.[6]

An important study on normal ranges for MW demonstrated an intra-observer and inter-observer variability for GWI of 42.2mmHg% and 34.6mmHg%, respectively.[9] In our study, GWI yielded by VA was significantly different from that estimated by both TDI and PD, with differences of 162mmHg% (9.2%) and 350mmHg% (20%), respectively. These differences were much higher than the intra-observer variation reported by Manganaro et al.,[9] which may be considered high enough to impact the clinical assessment of heart disease patients.[7,9] These findings highlight the importance of standardizing a single method, ideally a Doppler-based methods, due to its higher temporal resolution.

Among the main limitations of the study, the fact that it has been conducted in a single center and by one investigator may cause selection bias, since the studied population may not be representative of other regions or health systems. In addition, the study included only patients without comorbidities, which restricts the extrapolation of the results to individuals with more complex cardiac diseases, like heart failure, hypertension and ischemic diseases. All measurements were made by one observer, which limits the evaluation of inter-observer variability, which is an important parameter to validate the reproducibility of the results.

Due to scarcity of data in the literature, further studies are needed to confirm or not our results, making it possible to standardize and to validate the best method to estimate VET, and strengthen the use of MW.

Conclusion

This study demonstrated that GWI is sensitive to VET estimates, with significant differences between VA, TGI and

Table 2 – Comparison of the MW indexes according to the method applied for valvular event time estimation

Myocardial indexes	VA	TDI	Pulsed-Doppler	p
GWI, mmHg%	1748 ± 258	1910 ± 264	2098 ± 279	<0,001*
TMCG, mmHg%	2072 ± 242	2098 ± 279	2087 ± 264	0,296*
TMDG, mmHg%	103 (38; 529)	79 (39;455)	75 (39; 375)	0,092†
ETMG, %	94 (80; 98)	96 (82; 98)	96 (84;98)	0,208†

**ANOVA. † Friedman's analysis of variance; TDI: tissue Doppler imaging; GWI: Global Work Index; GCW: Global Constructive Work; GWW: Global Wasted Work; GWE: Global Work Efficiency; VA: visual analysis*

Tabela 3 – Comparação das diferenças das médias entre os índices de TM de acordo com as formas diferentes de aferição dos eventos valvares, análise post-hoc

	Visual	TDI
GWI		
TDI	162 (p<0.001*)	---------------------------
PD	350 (p<0.001*)	168 (p=0.216*)
GCW		
TDI	26 (p=0.121*)	---------------------------
PD	15 (p=0.383*)	-11 (p=0.492*)
GWW		
TDI	-24 (p=0.202†)	---------------------------
PD	-28 (p=0.051†)	-4 (p=0.793†)
GWE		
TDI	2 (p=0.359†)	---------------------------
PD	2 (p=0.123†)	0 (p=0.862†)

**Pairwise comparison test of marginal linear predictions. †Bonferroni test.*
TDI: tissue Doppler imaging; GWI: Global Work Index; GCW: Global Constructive Work; GWW: Global Wasted Work; GWE: Global Work Efficiency; PD: pulsed Doppler

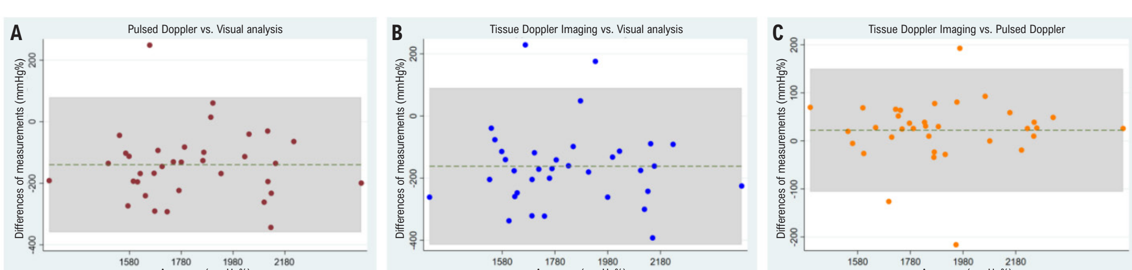

Figure 1 – *General agreement for GWI; Bland-Altman plots showing the agreement of GWI with PD versus VA (A), TDI versus VA (B) and TDI versus PD*

PD. VA resulted in underestimation of GWI as compared to Doppler-based methods, which showed higher agreement for VET estimation. However, other myocardial indexes (GCW, GWW and GWE) were not influenced by the methodology applied. The standardization of the methods used for VET estimation, preferably Doppler-based methods, is recommended to improve the accuracy of MW calculation, especially in studies that involve healthy populations and heart disease patients. Future studies are needed to confirm these findings and establish the most appropriate method.

Author Contributions

Conception and design of the research and writing of the manuscript: Pereira MM, Monteiro Júnior FC, Yamamura S; acquisition of data and statistical analysis: Pereira MM; analysis

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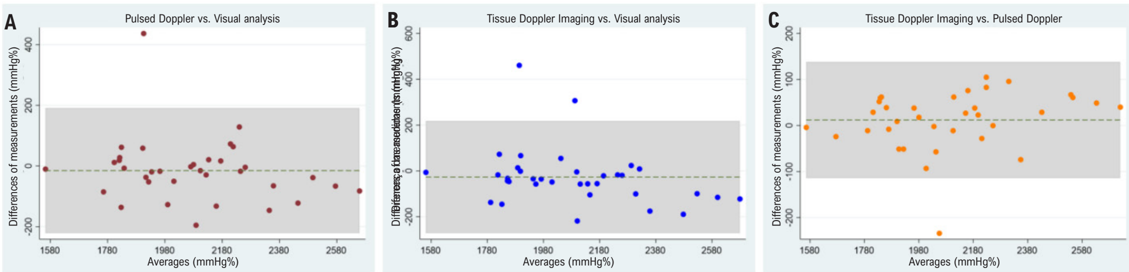

Figure 2 – *General agreement for GCW; Bland-Altman plots showing the agreement of GCW with PD versus VA (A), TDI versus VA (B) and TDI versus PD.*

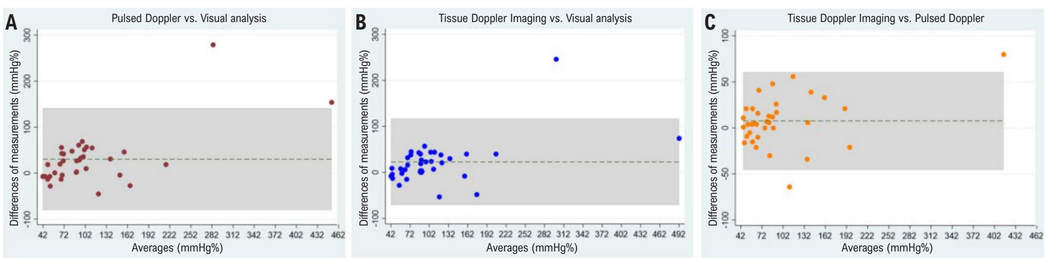

Figure 3 – *General agreement for GWW; Bland-Altman plots showing the agreement of GWW with PD versus VA (A), TDI versus VA (B) and TDI versus PD*

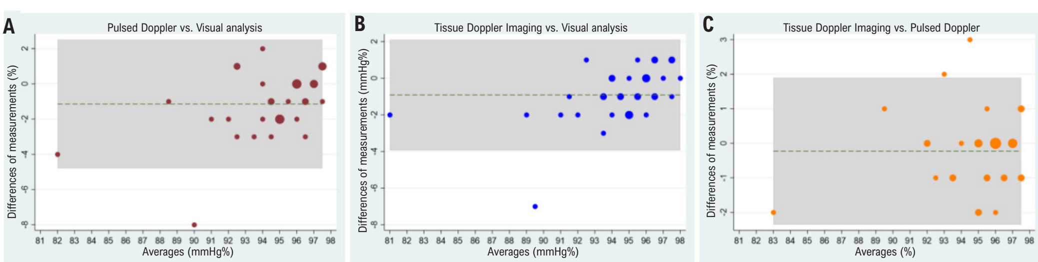

Figure 4 – *General agreement for GWE; Bland-Altman plots showing the agreement of GWE with PD versus VA (A), TDI versus VA (B) and TDI versus PD*

Table 4 - Comparison of VET according to the method applied to estimate VET

VET (ms)	VA	TDI	PD	p
Mitral valve opening	462 (363;529)	416 (326;537)	434 (358;492)	0.979*
Mitral valve closing	3 (0;33)	20 (1;45)	15 (0;43)	0.021*
Aortic valve opening	93 (36;128)	48 (11;98)	53 (13;358)	<0.001*
Aortic valve closing	370 (274;449)	347 (277;402)	342 (65;389)	0.989*

**Friedman's analysis of variance; TDI: tissue Doppler imaging. VET: valvular event times; VA: visual analysis; PD: pulsed Doppler; TDI: tissue Doppler imaging* and interpretation of the data: Pereira MM, Yamamura S; critical revision of the manuscript for intellectual content: Pereira MM, Monteiro Júnior FC.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the São Domingos under the protocol number 6.777.966. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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