Myocardial Work: a Systematic Review of Novel Echocardiography Method and Clinical Applications

Trabalho Miocárdio: uma Revisão Sistemática do Novo Método de Ecocardiografia e Aplicações Clínicas

Sidhi Laksono[1,2], Hillary Kusharsamita[3], Mefri Yanni[4], Astri Astuti[5]

[1]RS Pusat Pertamina, Department of Cardiology and Vascular Medicine, South Jakarta, Indonesia; [2]Universitas Muhammadiyah Prof Dr Hamka, Faculty of Medicine, Tangerang, Indonesia; [3]Universitas Diponegoro,Faculty of Medicine, Semarang, Indonesia; [4]University of Andalas, Medical Faculty, DR M Djamil Hospital, Department of Cardiology and Vascular Medicine, Padang, Indonesia; [5]Universitas Padjadjaran, Hasan Sadikin General Hospital, Department of Cardiology and Vascular Medicine, Bandung, Indonesia.

Abstract

Background: Myocardial work (MW) is a novel imaging modality that has emerged as a potential left ventricular (LV) function assessment in various clinical settings. MW calculates speckle-tracking echocardiography strain curves with an estimated LV pressure curve by non-invasively utilizing standard brachial blood pressure curves. Objective: This study aimed to provide a summary of current knowledge of non-invasive MW and its clinical applications, including in heart failure, coronary artery disease, cardiomyopathy, and hypertension. In addition, the limitations, and recommendations of MW in clinical practice are discussed. Methods: We searched the PubMed database using the following keywords: (myocardial constructive work) OR (wasted septal work) OR (global myocardial work) OR (myocardial work) OR (myocardial constructive work) OR (novel echocardiography). We further subjected 12 studies to full-text review and included them in this systematic review. Results: While MW indices, particularly global work index and global constructed work, have shown good correlations with ejection fraction (EF) and strain parameters, the opportunity of offering incremental information that is unaffected by loading conditions has made MW application particularly useful in a variety of clinical settings. Conclusion: Compared to EF and global longitudinal strain, MW is a promising test with higher sensitivity and accuracy for identifying individuals with cardiovascular disease. Clinicians should also evaluate symptoms and electrocardiographic findings until extensive multicenter studies validating this strategy are performed to establish the incremental value of MW in daily echocardiographic assessments.

Keywords

Myocardial Contraction, Left Ventricular Function, Echocardiography, Noninvasive Method.

Mailing Address: Sidhi Laksono •
Fakultas Kedokteran Universitas Muhammadiyah Prof Dr Hamka, Jl. Raden Patah No.01, RT.002/RW.006, Parung Serab, Kec. Ciledug, Kota Tangerang, Banten 13460.
E-mail: sidhilaksono@uhamka.ac.id
Manuscript received 4/29/2022; revised 6/15/2022; accepted 9/5/2022
Editor responsible for the review: Marco S. Lofrano Alves

DOI: 10.47593/2675-312X/20223504eabc299i

Introduction

The assessment of left ventricular (LV) systolic function is critical in all echocardiographic studies. The first-line method for describing LV systolic function is LV ejection fraction (LVEF). Despite its widespread usage, LVEF depends on geometric presumptions and is extremely load-dependent, resulting in substantial loss of reproducibility, and may be driven by changes in geometry and it is insufficiently sensitive at detecting decreasing ventricular function. All of these issues encouraged the exploration of novel myocardial function indicators.[1,2]

In the last decade, speckle-tracking echocardiography (STE) has transformed LV function evaluations. Peak global longitudinal strain (GLS), obtained from STE, has arisen as a highly sensitive method of detecting early LV dysfunction and has been utilized instead of LVEF in several clinical settings.[3] However, many studies have shown that GLS, similar to LVEF, has significant load dependency; hence, it is affected by elevated pre- or after-load.[4] In recent years, myocardial work (MW) has emerged as an alternative myocardial function assessment tool.

Russel et al. further evaluated MW non-invasively by coupling STE segmental strain curves with an estimated LV pressure curve in which systolic cuff pressure is employed as a substitute for LV peak pressure.[5] The method has been validated for many diseases, with high concordance to that of the invasive method.[6] This application is beneficial because it combines blood pressure measurements with a non-invasive approach using a simple brachial cuff, making the technology feasible in everyday practice in echocardiography facilities. As a result, MW is an alternate tool for assessing cardiac mechanics and a less load-dependent but non-invasive LV performance assessment method.[7,8]

Here we aimed to provide an up-to-date summary of the current understanding of non-invasive MW, its clinical application, future direction, limitation, and recommendation in clinical practice.

MW definition and analysis

The MW echocardiographic assessment procedure uses the same principle and practical approaches as the two-dimensional image capture process for GLS analysis by STE. The following are the MW and its component, namely global work index (GWI), global work efficiency (GWE), global constructed work (GCW), and global wasted work (GWW) presented in Table 1.

Using the same bull's-eye plot as for the GLS analysis, the

GWI bull's-eye canals are visually evaluated using a color scale, with red indicating high work, green indicating normal work, and blue indicating negative work. The shift from zero to a negative number on the color scale of wasted effort is shown in dark blue. As a result, lighter blue indicates decreased but still positive work, whereas deeper blue is used to code the transition to zero. On the other hand, GWE is also shown in a segmented bull's-eye format with numerical values and colored scaling. Green denotes locations with high efficiency (closer to 100%), while red denotes poor efficiency areas (closer to 0%).[9]

Table 1 - Definition of myocardial work components.[30]

Variable	Meaning
Global work index	Total work within the area of the left ventricular (LV) pressure-strain loop, from mitral valve closure to mitral valve opening
Global constructive work (GCW)	Myocardial work performed during LV shortening in systole and LV lengthening during the isovolumic relaxation phase
Global wasted work (GWW)	Myocardial work performed during LV lengthening in systole and LV shortening during the isovolumic relaxation phase
Global work efficiency	Calculated as the ratio of GCW/(GCW + GWW)

Method

This systematic review was designed and performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. We reviewed English-language studies published during the last 10 years that investigated the clinical application of MW in cardiovascular diseases, particularly heart failure (HF), coronary artery disease (CAD), cardiomyopathy (CMP), and hypertension (HTN).

Two independent authors searched the PubMed database on March 5, 2022, using the following keywords: (myocardial constructive work) OR (wasted septal work) OR (global myocardial work) OR (myocardial work) OR (myocardial constructive work) OR (novel echocardiography). Only studies that were previously peer-reviewed were considered for inclusion in our review. Reviews, case reports, editorials, comments, and letters were excluded. The study consort flowchart is shown in Figure 1.

Each abstract was examined separately by the authors. If at least one of the authors considered the research suitable, the full text was reviewed. In the event of disagreement, the authors discussed the reasons for their judgments before reaching a final resolution. Data were extracted from the studies, recorded in Microsoft Excel, and checked and confirmed by two authors (SL and HK). The extracted data of each study included the following: authors' names, outcome assessed, participants, and main result.

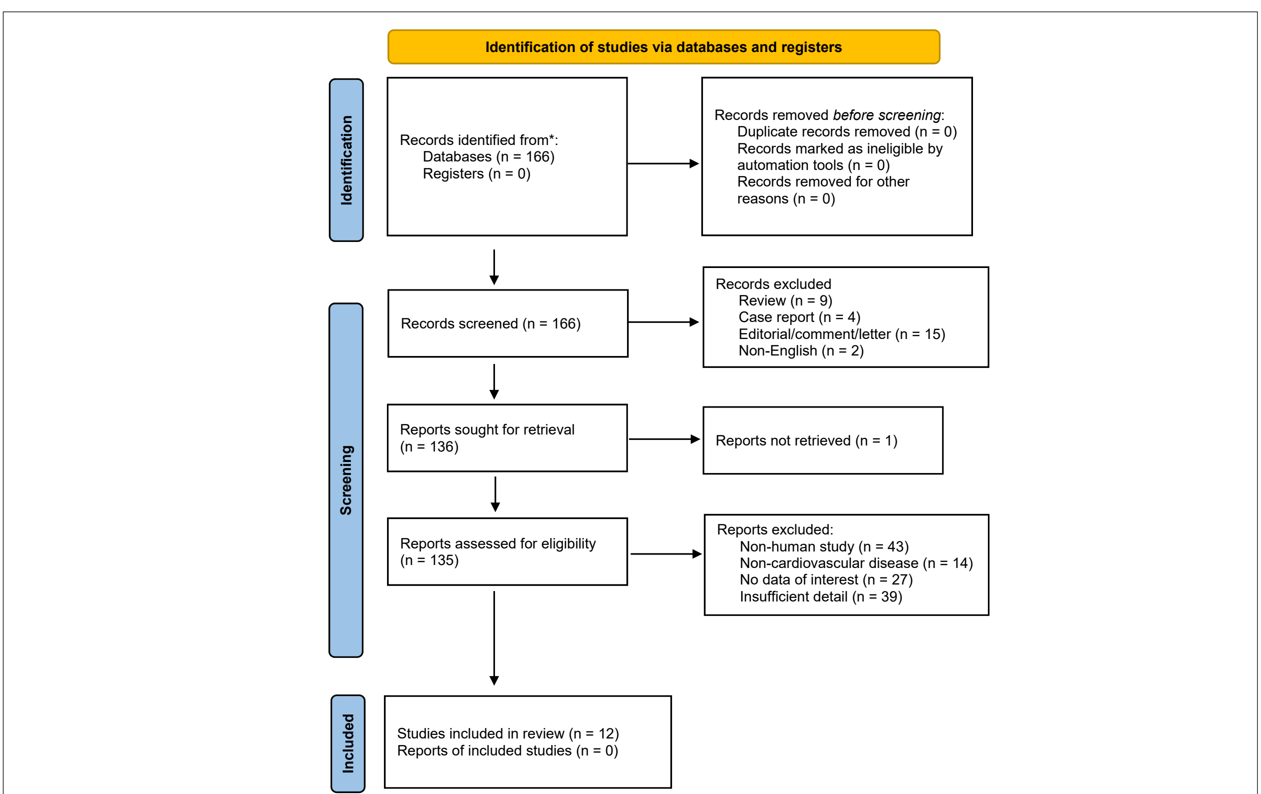

Figura 1 – *Fluxograma do consórcio de estudos da revisão sistemática.*

Results

A total of 166 were obtained from PubMed and subjected to title and abstract screening. Thereafter, 136 studies were subjected to full-text screening. One study was excluded because no full-text article was identified. After application of the inclusion and exclusion criteria, 12 studies were included in this systematic review.

The MW clinical applications in cardiovascular diseases assessed by the 12 studies differed: four assessed HF, two assessed CAD, five assessed CMP, and one assessed HTN. The baseline study information is shown in Table 2, while the baseline MW information in clinical applications is shown in Table 2.

Discussion

Clinical Application of MW

Heart failure

Predicting therapeutic advantages and outcomes in HF patients undergoing cardiac resynchronization therapy (CRT) was the first and most promising use of segmental MW. CRT is now used to treat symptomatic HF patients with an LVEF of 35% and a wide QRS complex.[10] MW appears to be capable of identifying patients who may benefit from cardiac resynchronization. According to a recent study, GWW

Table 2 - Baseline information of the myocardial work in clinical application.

No.	Study	Outcome assessed	Participants	Intervention	Main result
1	Vecera J, et al.[11]	HF	42 patients with HF (mean age, 72 ± 12 years;74% males) planned for CRT implantation	Clinical and echocardiographic data were collected before and at a median of 8 (IQR, 6–13) months after device implantation	GWW decreased from 39 ± 21% to 17 ± 7% with CRT (P,0.01) WW in the septum together with WMSI was a strong predictor of a CRT response
2	Galli E, et al.[8]	HF	97 patients with HF (ejection fraction: 27 ± 6%; QRS duration 164 ± 18 ms) underwent planned CRT implantation	STE was performed before CRT and at the 6-month follow-up. PSL analysis: calculation of CW and WW	>15% reduction in LV end-systolic volume at follow-up GCW was significantly increased in CRT responders
3	Wang CL, et al.[12]	HF	508 patients (mean age, 62.9 ± 15.8 years; 29.1% female) with LVEF ≤ 40%	Additional value of GMW for connection with composite outcome (all-cause death and HF hospitalization), clinical and echocardiographic variables	EF and GLS were not independent variables when GMW was included in the model Patients with a GMW < 750 mmHg% had a substantially higher risk of all-cause mortality and HF hospitalization (HR, 3.33; 95% CI, 2.31–4.80) than patients with a GMW > 750 mmHg%
4	Przewlocka-Kosmala M, et al.[31]	HF	114 patients (57 randomized to spironolactone, 57 to placebo)	At baseline and 6-month follow-up, resting and immediately post-exercise echocardiogram assessing GLS and MW indices	At follow-up, exercise intolerance in the spironolactone group was followed by a substantial improvement in GCW exertional rise (P = 0.002) but not GLS An increase in exercise capacity was independently linked with a change in exertional increase in GCW from baseline to follow-up (b = 0.24; P = 0.009) but not with GLS (P = 0.14) at 6 months. There was no significant interaction between spironolactone usage and peak VO_2 (P = 0.97).
5	Edwards NFA, et al.[15]	CAD	115 patients referred for coronary angiography who had an LVEF ≥ 55%, no resting regional wall motion abnormalities, and no chest pain	Three hours before cardiac catheterization, TTE was performed	Patients with significant CAD demonstrated a significantly reduced global MW (P < 0.001) versus those without CAD MW outperformed GLS (area under the curve = 0.693) as the most effective predictor of severe CAD (area under the curve = 0.786) The optimum global MW cut-off value for predicting substantial CAD was 1,810 mmHg% (sensitivity, 92%; specificity, 51%)
6	Lustosa RP, et al.[16]	CAD	600 STEMI patients divided according to the presence of LV remodeling	Non-invasive myocardial work indices were measured at 3 months after STEMI	The percentages of decreased GWI, GCW, and GWE as well as the percentage of increased GWW were found in patients with versus without LV remodeling: GWI (1,708 ± 522 mmHg% vs 1,979 ± 450 mmHg%; P < 0.001) GCW (1,941 ± 598 mmHg% vs 2,272 ± 519 mmHg%; P < 0.001) GWE (92% [range, 88–96%] vs 95% [range, 93–96%]; P < 0.001) GWW (116 mmHg% [range, 73–184 mmHg%] vs 91 mmHg% [range, 61–132 mmHg%]; P < 0.001).

7	Galli E, et al.[19]	CMP	82 patients with non-obstructive HCM and 20 age-matched healthy subjects (58 ± 7 years; P = 0.99) underwent STE	All HCM patients underwent clinical examination, standard and STE, 48-h Holter monitoring, and cardiopulmonary exercise test	GCW (1599 ± 423 vs 2248 ± 249 mmHg%; P < 0.0001) was significantly reduced in HCM versus control group No difference was observed in GWW (141 ± 125 mmHg% vs 101 ± 88 mmHg%; P = 0.18) and LVEF (63 ± 13% vs 66 ± 4%; P = 0.17) In HCM, GCW was the only predictor of LV fibrosis in the multivariable analysis (OR, 1.01; 95% CI, 0.99–1.08; P = 0.04). A cut-off value of 1,623 mmHg% was able to predict myocardial fibrosis with good sensitivity and fair specificity (82% and 67%, respectively)
8	Hiemstra YL, et al.[20]	CMP	110 patients with non-obstructive HCM and 35 healthy age- and sex-matched control subjects	Clinical data were collected from the department of cardiology information system and the first echocardiogram available was used	GCW (1,722 ± 602 vs 2,274 ± 574 mmHg%; P < 0.001) GWE (93% [89–95%] vs 96% [96–97%]; P < 0.001) GWI (1,534 ± 551 mmHg% vs 1,929 ± 473 mmHg%) were significantly reduced GWW (104 mmHg% [66–137 mmHg%] vs 71 mmHg% [49–92 mmHg%]; P < 0.001) was increased in patients with HCM versus control subjects Patients with a GCW > 1,730 mmHg% experienced better event-free survival than those with a GCW < 1,730 mmHg% (P < 0.001)
9	Chan J, et al.[21]	CMP	74 patients who underwent TTE and strain analysis before coronary angiography were divided into control, HTN, and CMP groups	TTE was performed immediately prior to coronary angiography	Increase in GCW and GWW. GLS, GWI, and GWE were significantly reduced in CMP (P < 0.05) GCW was elevated in HTN Grade1 but did not reach significant levels (P = 0.87; 2361 ± 377 mmHg%) and significantly elevated in HTN grade 2/3 (P = 0.0001; 3057 ± 403 mmHg%) when compared with controls (2184 ± 192 mmHg%) GWW was elevated in both HTN subgroups but not statistically significant
10	Cui C, et al.[22]	CMP	30 with DCM and 30 healthy patients as the control group	After 6 months of medical treatment, conventional echocardiography and MW were examined, and the measurements on the 6-min walk test were compared before and after therapy	GMW differences between controls and cases were significant (P < 0.05) The GWI and 6-min walking distance increased after treatment, while the LV ejection fraction and GLS did not change significantly GWI might be a marker of therapeutic efficacy
11	Clemmensen TS, et al.[24]	CMP	100 patients with CA	The patients were followed prospectively from the time of echocardiography until death or censoring on March 31, 2019; MACE and death during follow-up were registered	Patients with CA had significantly lower GWI and GWE than control subjects (P < 0.0001 for all) Patients with a GWI < 1,043 mmHg% had a higher MACE risk than patients with an LV myocardial work index > 1043 mmHg% (HR, 2.3; 95% CI, 1.2–4.3; P = 0.01) GWI <1039 mmHg% higher all-cause mortality risk than patients with LV GWI >1039 mmHg% (HR, 2.6; 95% CI, 1.2–5.5; P < 0.05).
12	Tadic M, et al.[26]	HTN	165 subjects (55 controls, 60 HTN patients without DM, and 50 HTN patients with DM)	This cross-sectional study performed a complete two-dimensional echocardiographic examination including two-dimensional STE	GWI gradually increased from controls to HTN patients to subjects with HTN and DM (1,887 ± 289 vs 2,073 ± 311 vs 2,144 ± 345 mmHg%, P = 0.001) DM demonstrated an additional negative effect on myocardial work in HTN patients

**CA, cardiac amyloidosis; CAD, coronary artery disease; CI, confidence interval; CMP, cardiomyopathy; DCM, dilated cardiomyopathy; DM, diabetes mellitus; EF, ejection fraction; GCW, global constructed work; GLS, global longitudinal strain; GWE, global work efficiency; GWI, global work index; HCM, hypertrophic cardiomyopathy; HF, heart failure; HR, hazard ratio; HTN, hypertension; LV, left ventricular; LVEF, LV ejection fraction; MACE, major adverse cardiac event; OR, odds ratio; STE, speckle-tracking echocardiography; STEMI, ST-elevated myocardial infarction; TTE, transthoracic echocardiography; WMSI, wall motion score index.*

evaluated at the septum was higher in CRT responders than non-responders, but these indices significantly dropped after CRT implantation, returning to normal cardiac values.[11] In a study of 97 patients, Galli et al. discovered that GCW is the sole predictor of CRT response at 6-month follow-up and closely associated with the idea of myocardial remodeling in ischemic and non-ischemic individuals.[8]

A recent study reported that MW was linked to HF hospitalizations and all-cause death. Patients with a GMW greater than 750 mmHg% had a significantly higher risk of all-cause mortality and HF hospitalization than patients with a GMW greater than 750 mmHg%. These results increase the use of MW in EF patients by 40% and provide a safe alternative to EF and GLS for evaluating patient survival and future hospitalization rates.[12]

Coronary artery disease

When wall motion abnormalities (WMA) are not seen in the coronary arteries, assessing individuals with coronary artery disease is difficult. GLS was previously shown to be a good predictor of stable ischemic cardiopathy in the absence of WMA.[13] However, agreement is lacking on the appropriate GLS diagnostic cut-off value, which differs widely among investigations due to clinical features, afterload dependency, and inter-evaluator variance. Furthermore, the contractile characteristics of the ischemic myocardium are substantially controlled by loading conditions, with fast transitions from hypokinesis to dyskinesis after an abrupt increase in afterload, which serves as the primary constraint.[14] MW indices demonstrated that it can overcome this constraint and provide diagnostic and prognostic information in chronic and acute settings. Edwards et al. observed that, in patients with suspected CAD but normal systolic function, GWI, GCW, and GWE all decreased dramatically in the presence of obstructive illness, although GWW increased modestly.[15]

At the 3-month follow-up, ST-elevation myocardial infarction (STEMI) patients who exhibited LV ischemia remodeling had significantly lower GWI, GCW, and GWE values but significantly higher GWW values.[16] These results imply that MW deficiency manifests in changed (permanently anaerobic) energy metabolism in the rebuilt myocardium.[17] The regional MW index is superior to all other echocardiographic markers (GLS and LVEF) at detecting acute coronary artery blockages in non-ST-segment acute coronary syndrome.[18]

Cardiomyopathy

GCW was the single predictor of LV fibrosis when late gadolinium enhancement was used, and values <1,730 mmHg% were related to a poorer long-term prognosis.[19,20] Chan et al. described a significant decrease in GWI, GCW, and GWE and an increase in GWW in a subgroup of patients with dilated cardiomyopathy (DCM).[21] This finding resulted from a significant deterioration of cardiomyocytes contractile performance in DCM patients, whether ischemic or non-ischemic. Moreover, another benefit of MW measurement may be its use an indication in the assessment of therapy benefits in DCM patients.[22] Another therapeutic use for MW indicators might be in predicting significant cardiovascular events among patients with cardiac amyloidosis (CA).[23] Study by Clemmensen et al. examined the impact of LV MW in predicting prognosis in individuals with CA. They discovered that individuals with a GWI <1,043 mmHg% were at an increased risk of severe adverse cardiac events, while those with a GWI of <1,039 mmHg% were at an increased risk of all-cause death.[24]

Hypertension

In hypertensive individuals, the LV pumps against higher arterial pressure, reducing the LV stroke volume and increasing the energy required for LV pump function, hence elevating the global MW index.[25] Chan et al. discovered that patients with a systolic blood pressure (SBP) > 160 mmHg had substantially elevated GWI and GCW values. GWW steadily rose in patients with an SBP of 140–159 mmHg, peaking at 160 mmHg in those with an SBP > 160 mmHg.[21]

Additionally, Tadic et al. discovered that hypertension patients' MW values worsened compared to normotensive controls, but these values were considerably worse in hypertensive patients with concurrent diabetes mellitus. Only GCW was significantly greater in individuals with concurrent hypertension and diabetes mellitus than those with hypertension alone.[26] Moreover, Sahiti et al. investigated the correlation between MW with CV risk factors and sex and discovered that the link between hypertension and obesity and GWI was greater in women.[27]

Limitation and recommendation

Although an MW analysis may be conducted on a large proportion of patients, there are several limitations to consider. Because MW is based on the estimated non-invasive LV pressure from SBP measured with a cuff manometer, its use was not highly recommended for evaluation in pathologic situations such as aortic stenosis (AS) in which SBP is not reflective of LV peak systolic pressure due to the fixed obstruction caused by a stenotic valve. Jain et al. recently recommended that the total of the transaortic mean gradient and SBP be used to estimate the LV peak systolic pressure in a group of severe AS patients undergoing transcatheter aortic valve replacement (TAVR). When MW indicators were compared before and after TAVR, a substantial decrease in GWI and GCW was seen, contributing to the rapid relief of the increased oxygen demand associated with increased afterload.[28] These findings suggest that MW correction by the addition of a transaortic mean gradient to SBP is both possible and dependable. However, validation in larger AS patients undergoing TAVR is required before it can be used consistently.

Finally, MW is vendor platform–dependent and requires specialized software that is presently solely supported by General Electric and cannot be tested using other software. This fact restricts the number of patients whose data may be analyzed using this strategy and limits the comparison of the same patient's findings with items from multiple vendors.[9,29]

Conclusion

MW is a reasonable, feasible, and dependable method of non-invasive LV function assessment enabling the widespread use of MW measurement in the diagnostic and treatment evaluation of various cardiovascular diseases. MW improves LVEF and GLS assessments by minimizing their load dependence. While current information on MW alone is insufficient to guide further interventions, the development of an integrated method offering incremental value to conventional echocardiographic measures is expected. Clinicians also must rely on symptoms and electrocardiographic data until multicentered well-designed research validating this strategy in large populations is undertaken to establish its added value and MW indices are included in routine echocardiographic assessments.

Acknowledgments

The authors thank all who supported this systematic review.

Authors' contributions

Research conception and design: Laksono S, Kusharsamita H; data collection: Yanni M, Astuti A; data analysis and interpretation: Laksono S, Kusharsamita H; statistical analysis: Yanni M, Astuti A; obtaining funding: Yanni M, Astuti A; manuscript writing: Laksono S, Kusharsamita H; critical review of the manuscript for important intellectual content: Laksono S.

Conflict of interest

The authors have declared that they have no conflict of interest.

References

1. Marwick TH. Ejection Fraction Pros and Cons: JACC State-of-the-Art Review. J Am Coll Cardiol. 2018;72(19):2360-2379. doi: 10.1016/j.jacc.2018.08.2162.

2. Konstam MA, Abboud FM. Ejection Fraction: Misunderstood and Overrated (Changing the Paradigm in Categorizing Heart Failure). Circulation. 2017;135(8):717-719. doi: 10.1161/CIRCULATIONAHA.116.025795.

3. Zito C, Longobardo L, Citro R, Galderisi M, Oreto L, Carerj ML, et al. Ten Years of 2D Longitudinal Strain for Early Myocardial Dysfunction Detection: A Clinical Overview. Biomed Res Int. 2018;2018:8979407. doi: 10.1155/2018/8979407.

4. Reant P, Metras A, Detaille D, Reynaud A, Diolez P, Jaspard-Vinassa B, et al. Impact of Afterload Increase on Left Ventricular Myocardial Deformation Indices. J Am Soc Echocardiogr. 2016;29(12):1217-1228. doi: 10.1016/j.echo.2016.09.006.

5. Russell K, Eriksen M, Aaberge L, Wilhelmsen N, Skulstad H, Remme EW, et al. A novel clinical method for quantification of regional left ventricular pressure-strain loop area: a non-invasive index of myocardial work. Eur Heart J. 2012;33(6):724-33. doi: 10.1093/eurheartj/ehs016.

6. Hubert A, Le Rolle V, Leclercq C, Galli E, Samset E, Casset C, et al. Estimation of myocardial work from pressure-strain loops analysis: an experimental evaluation. Eur Heart J Cardiovasc Imaging. 2018;19(12):1372-1379. doi: 10.1093/ehjci/jey024.

7. Qin Y, Wu X, Wang J, Li Y, Ding X, Guo D, et al. Value of territorial work efficiency estimation in non-ST-segment-elevation acute coronary syndrome: a study with non-invasive left ventricular pressure-strain loops. Int J Cardiovasc Imaging. 2021 Apr;37(4):1255-1265. doi: 10.1007/s10554-020-02110-1.

8. Galli E, Leclercq C, Hubert A, Bernard A, Smiseth OA, et al. Role of myocardial constructive work in the identification of responders to CRT. Eur Heart J Cardiovasc Imaging. 2018;19(9):1010-1018. doi: 10.1093/ehjci/jex191.

9. Samset E. Evaluation of segmental myocardial work in the left ventricle. 2017. [Access on Sept 09, 2022]. Available from: https://www.gehealthcare.com/-/media/8cab29682ace4ed7841505f813001e33.pdf

10. Brignole M, Auricchio A, Baron-Esquivias G, Bordachar P, Boriani G, Breithardt OA, et al. ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: the Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). Eur Heart J. 2013;34(29):2281-329. doi: 10.1093/eurheartj/eht150.

11. Vecera J, Penicka M, Eriksen M, Russell K, Bartunek J, Vanderheyden M, et al. Wasted septal work in left ventricular dyssynchrony: a novel principle to predict response to cardiac resynchronization therapy. Eur Heart J Cardiovasc Imaging. 2016;17(6):624-32. doi: 10.1093/ehjci/jew019.

12. Wang CL, Chan YH, Wu VC, Lee HF, Hsiao FC, Chu PH. Incremental prognostic value of global myocardial work over ejection fraction and global longitudinal strain in patients with heart failure and reduced ejection fraction. Eur Heart J Cardiovasc Imaging. 2021;22(3):348-356. doi: 10.1093/ehjci/jeaa162.

13. Choi JO, Cho SW, Song YB, Cho SJ, Song BG, Lee SC, et al. Longitudinal 2D strain at rest predicts the presence of left main and three vessel coronary artery disease in patients without regional wall motion abnormality. Eur J Echocardiogr. 2009;10(5):695-701. doi: 10.1093/ejechocard/jep041.

14. Skulstad H, Edvardsen T, Urheim S, Rabben SI, Stugaard M, Lyseggen E, Ihlen H, Smiseth OA. Postsystolic shortening in ischemic myocardium: active contraction or passive recoil? Circulation. 2002;106(6):718-24. doi: 10.1161/01.cir.0000024102.55150.b6.

15. Edwards NFA, Scalia GM, Shiino K, Sabapathy S, Anderson B, Chamberlain R, et al. Global Myocardial Work Is Superior to Global Longitudinal Strain to Predict Significant Coronary Artery Disease in Patients With Normal Left Ventricular Function and Wall Motion. J Am Soc Echocardiogr. 2019;32(8):947-957. doi: 10.1016/j.echo.2019.02.014.

16. Lustosa RP, van der Bijl P, El Mahdiui M, Montero-Cabezas JM, Kostyukevich MV, Ajmone Marsan N, et al. Noninvasive Myocardial Work Indices 3 Months after ST-Segment Elevation Myocardial Infarction: Prevalence and Characteristics of Patients with Postinfarction Cardiac Remodeling. J Am Soc Echocardiogr. 2020;33(10):1172-1179. doi: 10.1016/j.echo.2020.05.001.

17. Azevedo PS, Minicucci MF, Santos PP, Paiva SA, Zornoff LA. Energy metabolism in cardiac remodeling and heart failure. Cardiol Rev. 2013;21(3):135-40. doi: 10.1097/CRD.0b013e318274956d.

18. Boe E, Russell K, Eek C, Eriksen M, Remme EW, Smiseth OA, et al. Non-invasive myocardial work index identifies acute coronary occlusion in patients with non-ST-segment elevation-acute coronary syndrome. Eur Heart J Cardiovasc Imaging. 2015;16(11):1247-55. doi: 10.1093/ehjci/jev078.

19. Galli E, Vitel E, Schnell F, Le Rolle V, Hubert A, Lederlin M, et al. Myocardial constructive work is impaired in hypertrophic cardiomyopathy and predicts left ventricular fibrosis. Echocardiography. 2019;36(1):74-82. doi: 10.1111/echo.14210.

20. Hiemstra YL, van der Bijl P, El Mahdiui M, Bax JJ, Delgado V, Marsan NA. Myocardial Work in Nonobstructive Hypertrophic Cardiomyopathy: Implications for Outcome. J Am Soc Echocardiogr. 2020;33(10):1201-1208. doi: 10.1016/j.echo.2020.05.010.

21. Chan J, Edwards NFA, Khandheria BK, Shiino K, Sabapathy S, Anderson B, et al. A new approach to assess myocardial work by non-invasive left ventricular pressure-strain relations in hypertension and dilated cardiomyopathy. Eur Heart J Cardiovasc Imaging. 2019;20(1):31-39. doi: 10.1093/ehjci/jey131.

22. Cui C, Liu L, Li Y, Liu Y, Huang D, Hu Y, et al. Left Ventricular Pressure-Strain Loop-Based Quantitative Examination of the Global and Regional Myocardial Work of Patients with Dilated Cardiomyopathy. Ultrasound Med Biol. 2020;46(10):2834-2845. doi: 10.1016/j.ultrasmedbio.2020.06.008.

23. Roger-Rollé A, Cariou E, Rguez K, Fournier P, Lavie-Badie Y, Blanchard V, et al; Toulouse Amyloidosis Research Network collaborators. Can myocardial work indices contribute to the exploration of patients with cardiac amyloidosis? Open Heart. 2020;7(2):e001346. doi: 10.1136/openhrt-2020-001346.

24. Clemmensen TS, Eiskjær H, Ladefoged B, Mikkelsen F, Sørensen J, Granstam SO, et al. Prognostic implications of left ventricular myocardial work indices in cardiac amyloidosis. Eur Heart J Cardiovasc Imaging. 2021;22(6):695-704. doi: 10.1093/ehjci/jeaa097.

25. Kuznetsova T, Nijs E, Cauwenberghs N, Knez J, Thijs L, Haddad F, et al. Temporal changes in left ventricular longitudinal strain in general population: Clinical correlates and impact on cardiac remodeling. Echocardiography. 2019;36(3):458-468. doi: 10.1111/echo.14246.

26. Tadic M, Cuspidi C, Pencic B, Grassi G, Celic V. Myocardial work in hypertensive patients with and without diabetes: An echocardiographic study. J Clin Hypertens (Greenwich). 2020;22(11):2121-2127. doi: 10.1111/jch.14053.

27. Sahiti F, Morbach C, Cejka V, Tiffe T, Wagner M, Eichner FA, et al. Impact of cardiovascular risk factors on myocardial work-insights from the STAAB cohort study. J Hum Hypertens. 2022;36(3):235-245. doi: 10.1038/s41371-021-00509-4.

28. Jain R, Bajwa T, Roemer S, Huisheree H, Allaqaband SQ, Kroboth S, et al. Myocardial work assessment in severe aortic stenosis undergoing transcatheter aortic valve replacement. Eur Heart J Cardiovasc Imaging. 2021;22(6):715-721. doi: 10.1093/ehjci/jeaa257.

29. Papadopoulos K, Özden Tok Ö, Mitrousi K, Ikonomidis I. Myocardial Work: Methodology and Clinical Applications. Diagnostics (Basel). 2021;11(3):573. doi: 10.3390/diagnostics11030573.

30. Galli E, John-Matthwes B, Rousseau C, Schnell F, Leclercq C, Donal E. Echocardiographic reference ranges for myocardial work in healthy subjects: A preliminary study. Echocardiography. 2019;36(10):1814-1824. doi: 10.1111/echo.14494.

31. Przewlocka-Kosmala M, Marwick TH, Mysiak A, Kosowski W, Kosmala W. Usefulness of myocardial work measurement in the assessment of left ventricular systolic reserve response to spironolactone in heart failure with preserved ejection fraction. Eur Heart J Cardiovasc Imaging. 2019;20(10):1138-1146. doi: 10.1093/ehjci/jez027.