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

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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 probabilistic 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.

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.

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. However, many studies have shown that GLS, similar to LVEF, has significant load dependency; hence, it is affected by elevated pre- or after-load. 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. The method has been validated for many diseases, with high concordance to that of the invasive method. 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.

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%).

Table 1 - Definition of myocardial work components.

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

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.
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.

<table>
<thead>
<tr>
<th>No.</th>
<th>Study</th>
<th>Outcome assessed</th>
<th>Participants</th>
<th>Intervention</th>
<th>Main result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Vecera J, et al.11</td>
<td>HF</td>
<td>42 patients with HF (mean age, 72 ± 12 years; 74% males) planned for CRT implantation</td>
<td>Clinical and echocardiographic data were collected before and at a median of 8 (IQR, 6–13) months after device implantation</td>
<td>GWW decreased from 39 ± 21% to 17 ± 7% with CRT (P&lt;0.01). WW in the septum together with WMSI was a strong predictor of a CRT response</td>
</tr>
<tr>
<td>2</td>
<td>Galli E, et al.8</td>
<td>HF</td>
<td>97 patients with HF (ejection fraction: 27 ± 6%; QRS duration 164 ± 18 ms) underwent planned CRT implantation</td>
<td>STE was performed before CRT and at the 6-month follow-up. PSL analysis: calculation of CW and WW</td>
<td>&gt;15% reduction in LV end-systolic volume at follow-up GCW was significantly increased in CRT responders</td>
</tr>
<tr>
<td>3</td>
<td>Wang CL, et al.12</td>
<td>HF</td>
<td>508 patients (mean age, 62.9 ± 15.6 years; 29.1% female) with LVEF ≤ 40%</td>
<td>Additional value of GMW for connection with composite outcome (all-cause death and HF hospitalization), clinical and echocardiographic variables</td>
<td>EF and GLS were not independent variables when GMW was included in the model. Patients with a GMW &lt; 750 mmHg% had a substantially higher risk of all-cause mortality and HF hospitalization (HR, 3.33; 95% CI, 2.31–4.88) than patients with a GMW &gt; 750 mmHg%</td>
</tr>
<tr>
<td>4</td>
<td>Przewlocka-Kosmala M, et al.21</td>
<td>HF</td>
<td>114 patients (57 randomized to spironolactone, 57 to placebo)</td>
<td>At baseline and 6-month follow-up, resting and immediately post-exercise echocardiogram assessing GLS and MW indices</td>
<td>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 VO2 (P = 0.97). Patients with significant CAD demonstrated a significantly reduced global MW (P &lt; 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%).</td>
</tr>
<tr>
<td>5</td>
<td>Edwards NFA, et al.15</td>
<td>CAD</td>
<td>115 patients referred for coronary angiography who had an LVEF ≥ 55%, no resting regional wall motion abnormalities, and no chest pain</td>
<td>Three hours before cardiac catheterization, TTE was performed</td>
<td>Three hours before cardiac catheterization, TTE was performed</td>
</tr>
<tr>
<td>6</td>
<td>Lustosa RP, et al.16</td>
<td>CAD</td>
<td>600 STEMI patients divided according to the presence of LV remodeling</td>
<td>Non-invasive myocardial work indices were measured at 3 months after STEMI</td>
<td>Non-invasive myocardial work indices were measured at 3 months after STEMI</td>
</tr>
</tbody>
</table>
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. 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.

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.

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

**Table 1**

<table>
<thead>
<tr>
<th>Study</th>
<th>Group</th>
<th>Population</th>
<th>Outcome Measure</th>
<th>Methodology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gallo E, et al.</td>
<td>CMP</td>
<td>82 patients with non-obstructive HCM and 20 age-matched healthy subjects (58 ± 7 years; P = 0.99)</td>
<td>GWI, GWE</td>
<td>Clinical examination, standard and STE, 48-h Holter monitoring, and cardiopulmonary exercise test</td>
</tr>
<tr>
<td>Hiemstra YL, et al.</td>
<td>CMP</td>
<td>110 patients with non-obstructive HCM and 35 healthy age- and sex-matched control subjects</td>
<td>GWI, GWE</td>
<td>Clinical data were collected from the department of cardiology information system and the first echocardiogram available was used</td>
</tr>
<tr>
<td>Chan J, et al.</td>
<td>CMP</td>
<td>74 patients who underwent TTE and strain analysis before coronary angiography were divided into control, HTN, and CMP groups</td>
<td>TTE</td>
<td>TTE was performed immediately prior to coronary angiography</td>
</tr>
<tr>
<td>Cui C, et al.</td>
<td>CMP</td>
<td>30 with DCM and 30 healthy patients as the control group</td>
<td>GWI, GWE</td>
<td>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</td>
</tr>
<tr>
<td>Clemmensen TS, et al.</td>
<td>CMP</td>
<td>100 patients with CA</td>
<td>GMW differences between controls and cases were significant (P &lt; 0.05)</td>
<td>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</td>
</tr>
<tr>
<td>Tadic M, et al.</td>
<td>HTN</td>
<td>165 subjects (55 controls, 60 HTN patients without DM, and 50 HTN patients with DM)</td>
<td>GWI, GWE</td>
<td>This cross-sectional study performed a complete two-dimensional echocardiographic examination including two-dimensional STE</td>
</tr>
</tbody>
</table>

*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.*
be a good predictor of stable ischemic cardiopathy in the absence of WMA. 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. 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.

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. These results imply that MW deficiency manifests in changed (permanently anaerobic) energy metabolism in the rebuilt myocardium. 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.

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. 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). 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 indicator in the assessment of therapy for DCM patients. Another therapeutic use for MW measurement is in detecting acute coronary artery blockages in patients with non-ST-segment acute coronary syndrome.

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. 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. 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. 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.

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. 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.

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, Ihlen H; data collection: 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


