Review Article

My Approach to Myocardial Work: Why and for Whom?

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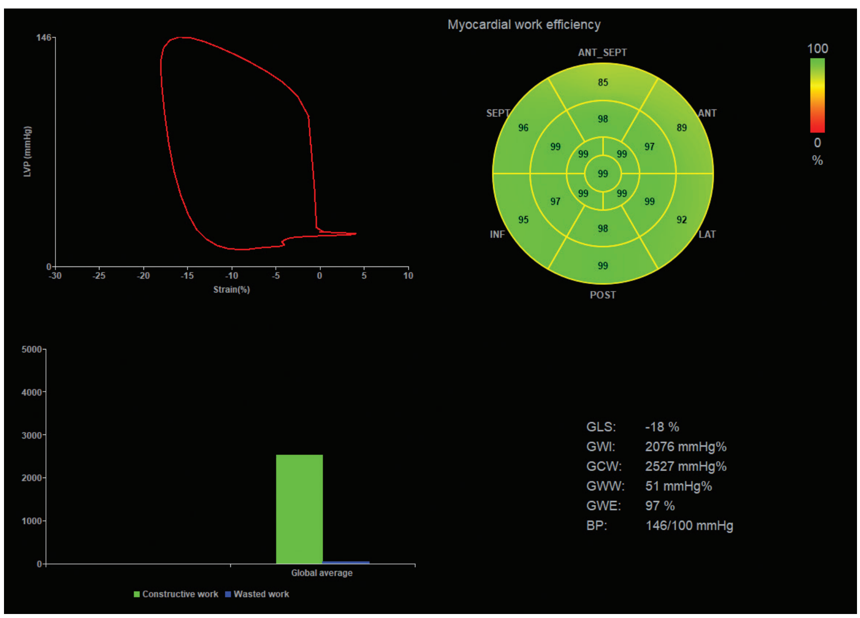
Central Illustration: My Approach to Myocardial Work: Why and for Whom?



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Calculation of left ventricular GWE, in a 17-segment model showing GWE segmental values. Preserved segmental GWE values are shown in green and expressed in %. The patient's GWI, GCW, GWW, GWE, and blood pressure values are shown in white. GCW: global constructive work; GWE: global work efficiency; GWI: global work index; GWW: global wasted work (Source: Author).

Abstract

The emergence of a new noninvasive tool known as myocardial work (MW) for assessing ventricular function, which is independent of load conditions, has been fundamental in advancing current imaging methods, such as myocardial strain. Strain is considered a sensitive technique in the detection of subclinical dysfunction, even though it is still dependent on load conditions, making it impossible to differentiate contractile alteration from interference caused by increased afterload alone. This new technology incorporated into myocardial strain will increase the sensitivity of the method.

Introduction

The concept of pressure-volume curves has been widely used in cardiovascular physiology and assessment of cardiac function.[1-3] Experimental studies have demonstrated that it is possible to assess the global performance of the ventricles by means of a contractility index that is independent of load conditions. This concept has not yet become the "gold standard" in clinical practice and research, because invasive techniques are still required to determine these curves. However, studies have shown that the noninvasive estimation

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of these curves is a strong predictor of events regardless of left ventricular ejection fraction (LVEF), as demonstrated in the study by Spevack et al.[4]

My approach

According to the same principle as pressure-volume curves, the concept of noninvasive evaluation of myocardial work (MW) was published by Russell et al. in 2012.[5] According to the authors, the determination of pressure-strain loop area by means of Doppler echocardiography would reflect MW and oxygen consumption. Currently, the calculation of MW by Doppler echocardiography is performed using commercially available software (EchoPac, GE Medical Systems). MW indices are estimated by combining noninvasive estimation of peak left ventricular (LV) pressure using blood pressure measurements with a sphygmomanometer (in which peak LV systolic pressure is assumed to be equal to systolic arterial pressure) associated with echocardiographic data from strain curves.

After calculating the strain and inserting the blood pressure values obtained by sphygmomanometer, the opening and closing times of the aortic and mitral valves are identified by echocardiogram in the apical 3-chamber view. A LV pressure-strain curve is then constructed with strain data from the entire cardiac cycle, according to the duration of relaxation and isovolumetric contraction, the ejection and filling phases defined by the opening and closing times of the aortic and mitral valves, and blood pressure values.[6]

LV work is calculated as a product of the segmental shortening rate and the instantaneous LV pressure. The following indices are derived from measurements of cardiac work by echocardiography (Central Figure):

Global work index (GWI): total work calculated from mitral valve closure to mitral valve opening, representing the area of the loop provided by the software (expressed in mmHg%);

Global constructive work (GCW): work performed by a segment during systolic shortening added to work performed during diastolic lengthening, representing the work that contributes to myocardial contractility (expressed in mmHg%);

Global wasted work (GWW): negative work performed by a segment during lengthening in systole added to the work performed during shortening in diastole, which represents the work that does not contribute to myocardial contractility (expressed in mmHg%);

Global work efficiency (GWE): GCW divided by the sum of GCW and GWW, representing the measure of LV performance (expressed in %).

The mean reported normal values[7] for GWI and GCW are 2010 mmHg% (95% confidence interval [CI]: 1907 to 2113 mmHg%) and 2278 mmHg% (95% CI: 2186 to 2369 mmHg%), respectively. The mean for GWW is 80 mmHg% (95% CI: 73 to 87 mmHg%), and for GWE it is 96% (95% CI: 96% to 96%). The differences between men and women significantly contribute to the normal ranges for GWI, GWW and GWE.

Applicability

Ischemic heart disease

The use of MW in coronary artery disease can be divided into the context of acute coronary syndromes and chronic coronary artery disease. Moreover, global values are relevant, as are regional values derived from the software. In patients with acute ST-segment elevation myocardial infarction (STEMI), the study by El Mahdiui et al.[8] provided evidence that GWE was reduced in patients with heart failure with reduced ejection fraction (HFrEF) after STEMI, compared to healthy individuals and those with risk factors for cardiovascular disease. A study by Lustosa et al.[9] demonstrated, in a cohort of 600 patients after STEMI, that cardiac work indices were reduced 3 months after the index event in patients who had ventricular remodeling. The same author demonstrated that reduced GWE values (< 86%) measured by transthoracic Doppler echocardiography in the first 48 hours of STEMI admission would be associated with worse prognosis.[10] The study by Meimoun et al.[11] demonstrated that, in patients with STEMI previously treated with percutaneous coronary intervention, GCW was an independent factor for global and segmental LV recovery, and it was significantly reduced in patients who had in-hospital complications.

In the context of regional assessment of MW, the study by Boe et al.[12] demonstrated that the presence of reduced regional GWI values could identify coronary occlusion in patients with acute non-ST-segment elevation myocardial infarction (NSTEMI). A study by Lustosa et al.,[13] using regional GWI values, demonstrated that reduced regional GWI values in the territory of the culprit artery were independently associated with early cardiac remodeling.

MW has also been studied in chronic coronary artery disease. A study by Edwards et al.[14] evaluated 115 patients with normal LVEF referred for coronary angiography due to different indications and demonstrated that GWI values less than 1810 mmHg% were predictive of significant coronary artery disease (defined by stenosis above 70%), with a sensitivity of 92% and specificity of 51%. A study by Borrie et al.[15] demonstrated that MW indices can be used in stress echocardiography to identify myocardial ischemia.

Cardiomyopathies

The main role of MW analysis in clinical practice for evaluating patients with cardiomyopathies focuses on patients with dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), and cardiac amyloidosis. The study by Chan et al.[16] observed the difference between MW indices in patients with hypertension and DCM (19 non-ischemic and 10 ischemic). The authors reported that GWI, GCW, and GWE were significantly reduced, and GWW was significantly increased in patients with DCM compared to the control group. A study by Schrub et al.[17] investigated the relationship between MW analysis and exercise tolerance in 51 patients with DCM who underwent a cardiopulmonary exercise test to assess exercise performance and reported that, in patients with DCM and intraventricular dyssynchrony, septal work efficiency was the only predictor of exercise capacity in the multivariate analysis (β = 0.68, p = 0.03). A study by Cui et al.[18] compared MW indices in 30 patients with DCM and 30 healthy patients, finding significantly reduced values of MW indices in the DCM group compared to the control group ($p < 0.05$).

In 2019, Galli et al.[19] studied 82 patients with non-obstructive HCM who underwent MW assessment. Patients also underwent cardiac magnetic resonance imaging to estimate LV fibrosis with delayed gadolinium enhancement. The authors reported that GCW is significantly reduced in patients with HCM and normal LVEF, and a cutoff value of 1623 mmHg% demonstrated a sensitivity of 82% and specificity of 67% to predict LV fibrosis in this population (area under the curve [AUC] 0.80, 95% CI: 0.66 to 0.93, $p < 0.001$). A study by Hiemstra et al.[20] reported the prognostic role of MW analysis in 110 patients with non-obstructive HCM. Patients with GCW > 1730 mmHg% had better survival compared to those with GCW < 1730 mmHg% (log-rank 11.2, p = 0.001).

The value of the clinical application of MW indices in patients with cardiac amyloidosis has been reported by Clemmensen et al.[21] The authors' objective was to characterize resting and peak MW during exercise in patients with cardiac amyloidosis. They observed that patients with cardiac amyloidosis showed significantly reduced MW index values, and this difference was more evident during exercise compared to healthy subjects. In another study, the prognostic implications of MW analysis were demonstrated in 100 patients with cardiac amyloidosis.[22] Patients with GWI < 1043 mmHg% had a higher number of events than patients with GWI > 1043 mmHg% (hazard ratio [HR] 2.3, 95% CI: 1.2 to 4.3, p = 0.01). Furthermore, patients with GWI < 1039 mmHg% had a higher risk of all-cause mortality than patients with GWI > 1039 mmHg% (HR 2.6, 95% CI: 1.2 to 5.5, $p < 0.05$).

HFrEF and response to cardiac resynchronization therapy (CRT)

The first reports in clinical practice on the application of MW in patients with HFrEF were published in 2013. In an experimental study, Russell et al.[23] evaluated the WW ratio (WWR) in 6 anesthetized dogs with left bundle branch block (LBBB) and 28 patients with cardiomyopathy, including patients with LBBB and CRT. The study demonstrated a strong correlation between invasively and noninvasively estimated WWR in dogs (r = 0.94) and patients (r = 0.96), with higher global WWR values in patients with LBBB. The study by Galli et al.[24] estimated GCW and GWW in 97 patients before CRT and at 6-month follow-up. The authors showed that the addition of GCW > 1057 mmHg% and GWW > 384 mmHg% to a baseline model significantly increased the model's power to identify CRT responders. The authors reported good specificity (100%) and positive predictive value (100%), but low sensitivity (22%), negative predictive value (41%), and accuracy (49%). In another study,[25] the authors also showed, in 97 patients undergoing CRT implantation, that GCW > 1057 mmHg% (odds ratio [OR] 14.69, p = 0.005) and septal flash (OR 8.05, p = 0.004) were the only predictors of response to CRT. The study by Cvijic et al.[26] calculated segmental MW in 26 patients with sinus rhythm and non-ischemic cardiomyopathy. Before CRT, work was unevenly distributed with reduced work in the septal and anteroseptal walls and increased work in the lateral and posterior walls ($p < 0.001$). The authors showed that, after CRT, the segmental distribution of work was uniform. MW asymmetry between the septal segments and the lateral wall was also observed in a prospective multicenter study with 200 patients.[27] The authors showed that the lateral wall-septum work difference predicted the CRT response with an AUC of 0.77 (95% CI: 0.70 to 0.84); when combined with assessment of septal viability by cardiac magnetic resonance, the AUC increased to 0.88 (95% CI: 0.81 to 0.95). The prognostic importance of calculating MW in patients with heart failure was demonstrated by Van der Bijl et al.[28] in a cohort of patients with class I indications for CRT. The authors demonstrated that patients with lower energy efficiency (GWE < 75%) before CRT demonstrated a lower rate of events than patients with higher energy efficiency (GWE > 75%). Bouali et al.[29] investigated the effects of treatment with sacubitril/valsartan on MW indices in 79 patients with HFrEF and reported that the treatment significantly increased GCW (1023 ± 449 mmHg% to 1424 ± 484 mmHg%, $p < 0.001$) and GWE (87% [78% to 90%] to 90% [86% to 95%], $p < 0.001$). GCW was the only predictor of major adverse cardiovascular events (HR 0.99, 95% CI: 0.99 to 1.00, p = 0.04). Furthermore, GCW < 910 mmHg% was related to a high risk of major adverse cardiovascular events (HR 11.09, 95% CI: 1.45 to 98.94, p = 0.002, log-rank test $p < 0.001$). Another study by Wang et al.[30] investigated a cohort of 508 patients (62.9 ± 15.8 years, 29.1% women) with LVEF ≤ 40%. The authors showed that GWI < 750 mmHg% was associated with significantly higher mortality and heart failure hospitalization and significantly higher all-cause death (HR 3.33, 95% CI: 2.31 to 4.80) than in patients with GWI ≥ 750 mmHg%. Regarding observations from these studies, MW analysis in patients with HFrEF may be valuable to identify CRT responders and provide prognostic information in this population.

The assessment of MW indices in heart failure with preserved ejection fraction (HFpEF) was reported in 2019 by Przewlocka-Kosmala et al.[31] In the STRUCTURE (Spironolactone in Myocardial Dysfunction with Reduced Exercise Capacity) study, with 57 patients randomized to spironolactone and 57 to placebo, the authors measured MW indices at rest and immediately after exercise at baseline and at 6-month follow-up and reported GCW as a better determinant of exercise capacity than strain in HFpEF.

Valve disease

Previous studies have also explored the clinical application of MW analysis in valve disease. Hubert et al.[32] studied LV mechanics using MW analysis in 37 patients with heart failure and important functional mitral regurgitation who underwent percutaneous mitral valve repair, compared with 19 patients with functional mitral regurgitation in optimal clinical treatment. The authors reported that GCW significantly improved in both groups and demonstrated that GWI identifies patients with worse evolution (AUC = 0.882, p = 0.009), mainly patients with GWI < 482 mmHg%. Papadopoulos et al.[33] investigated echocardiographic predictors of clinical response and LV reverse remodeling in 86 patients with severe functional mitral regurgitation and high surgical risk, including MW indices. The authors reported that baseline GWI and GCW were associated with a reduction in LV end-diastolic volume 1 year after the MitraClip intervention, and GCW was the only variable associated with a reduction in LV end-systolic volume. The MitraClip procedure was associated with significant improvement in GWI ($p = 0.045$) and GCW ($p < 0.001$). Yedidya et al.[34] evaluated the prognostic impact of MW indices in functional mitral regurgitation. In 143 patients with functional mitral regurgitation, worse GWI and GCW values and better GWW and GWE values independently reflected worse prognosis in this population.

Jain et al.[35] explored the relationship between severe aortic stenosis and MW analysis in a cohort of 35 patients undergoing transcatheter aortic valve replacement (TAVR). The authors evaluated MW indices in severe aortic stenosis with the addition of the mean aortic gradient to noninvasive systolic blood pressure. Based on this method, which showed a high correlation ($r = 0.92$), the authors demonstrated that GWI reduced between the pre-TAVR and post-TAVR periods (1856.2 mmHg% ± 704.6 versus 1534.8 mmHg% ± 385). The study by Fortuni et al.[36] used the same calculation of MW indices in severe aortic stenosis that were shown to be independently associated with symptoms of heart failure. D'Andrea et al.[37] recruited 115 asymptomatic patients with severe aortic insufficiency and 55 controls. GWE was significantly reduced in patients with aortic insufficiency compared to controls (87.1% ± 3.3% versus 94.4% ± 4.1%, $p < 0.01$), and strain and GWE were strong independent predictors of contractile reserve, suggesting early subclinical damage in this population. In a recent review by Muthukumar et al.[38] on the association between malignant mitral valve prolapse and sudden cardiac death, the authors reported that patients with mitral valve prolapse and mitral annulus disjunction had higher MW regional index values in the posterolateral region of LV segments, suggesting the hypothesis that more work due to repeated traction causes greater energy demand and stress in these segments.

Limitations and future directions

As with any new technology, MW needs to be disseminated for widespread knowledge of the protocol, with a learning curve and improved expertise. New software that has come to replace the invasive gold-standard method is the objective that researchers always seek to reduce the complications inherent to invasive methods, in this case, cardiac catheterization. For the time being, there is only one software product available from a single company.

The technical limitations are mostly related to the classic limitations of strain. For example, it requires an adequate acoustic window and frame rate, absence of tachycardia, and regular rhythm. Regarding blood pressure measurements, they need to be taken correctly, and patients with aortic stenosis or fixed LV outflow tract obstruction should be excluded, as noninvasively measured systolic pressure is not equivalent to invasive measurement. Blood pressure measurement needs to be adequate.

Moreover, MW is not useful for evaluating cases with important cardiac remodeling. It is a promising technique still under development.

Conclusion

The development of new software associated with strain that presents good sensitivity and specificity, inserting only blood pressure measurements in a noninvasive manner will be important in the assessment of subclinical alterations that ejection fraction is not able to detect, assisting in the early treatment of several diseases that affect the myocardium, such as infiltrative, valvular, and ischemic diseases, thus changing their prognosis.

Author Contributions

Conception and design of the research, writing of the manuscript and critical revision of the manuscript for intellectual content: Lustosa RP, Rabischoffsky A, Gripp EA.

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 article does not contain any studies with human participants or animals performed by any of the authors.

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