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COMMENTARY

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Is myocardial work the piece of puzzle that we missed?

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This issue of the Journal brings an interesting study about the usefulness of novel echocardiographic set of parameters in a specific population that has been under investigation for a long time – pediatric patients after kidney transplantation.[1] The authors provided a short-term follow-up data regarding left ventricular (LV) structure, function, and myocardial work (MW) in a small population of children with kidney transplantation and found that LV MW was superior to LV global longitudinal strain (GLS) in evaluating of LV systolic function recovery in these specific patients.[1] Reported findings are of a clinical and research importance and therefore deserve further discussion and clarification.

LV ejection fraction (LVEF) has been used as a gold standard parameter for assessment of LV systolic function. However, the large number of studies conducted over the last decade showed that GLS is more reproducible and sensitive on subtle changes in LV systolic function than LVEF and a significant, if not even better, predictor of adverse events in the large number of cardiovascular conditions.[2,3] Nevertheless, GLS is not a perfect parameter, and it has its limitations. One of the most commonly cited limitation of GLS is load-dependence, which is certainly lower than for tissue-Doppler derived parameters and LVEF, but still not neglectable and particularly important in patients who incline to prompt changes in load condition such as patients with decompensated heart failure and those with end-stage renal disease who are on dialysis program.[4,5]

MW is not entirely novel set of parameters, as it was described for the first time more than a decade ago. It was evaluated by the pressure–volume relationship that represents the myocardial oxygen consumption and LV performance. Pressure–volume loop was measured with invasive methods, which explains why wider clinical usage is not feasible. More recently, MW was presented as a novel set of parameters that includes global work index (GWI), global constructed work (GCW), global wasted work (GWW), and global work efficiency (GWE).[6] These set of parameters incorporates both LV afterload, assessed by radial blood pressure (BP), and LV deformation.[6] GWI is a measure of the total amount of LV work performed by the sum of all LV segments. GCW represents myocyte shortening during systole and lengthening during isovolumic relaxation and GWW illustrates myocyte lengthening during systole and shortening during isovolumic relaxation. All these parameters are available at global and regional levels. GWE represents the ratio of GCW to the sum of GCW and GWW (GWE = GCW/[GCW + GWW]).

The increasing body of evidence shows the large importance of MW parameters and even higher sensitivity in the detection of subtle changes in LV systolic function in patients with normal LVEF and even GLS in normal ranges in wide range of cardiovascular conditions (heart failure, hypertension, cardiomyopathies, coronary artery disease, valvular heart diseases, etc.). MW provides an estimation of the contribution of every LV segment during the cardiac cycle. This work is affected by the contraction of myocardial fibers, LV loading conditions, as well as the wall stress applied on the LV segments. Loading conditions are very important, *as this is one of the main differences from GLS*, and include both preload and afterload. They have a significant role during LV contraction. MW involves afterload in its formula based on the presumption that aortic pressure is equal to systolic LV pressure, which eliminates the possibility of LV outflow tract (LVOT) and aortic valve gradients. In the condition of LVOT obstruction and aortic stenosis, MW parameters should not be used or evaluated cautiously. There are more limitations of this technique and one of the most important is large variability and lack of reference values, even though the efforts were made in this direction. Studies that aimed to provide normal values for MW indexes were not consistent regarding values that were suggested as normal and standard deviation for most of these parameters, except for GWW, is very high to provide accurate threshold values.[7] The values are also sex-specific and currently only one vendor (General Electric) provides possibility for noninvasive echocardiographic evaluation of MW.

In the present study, Xiao et al. reported that GLS was significantly lower in children before and after kidney transplantation in comparison with the control group, whereas no difference was found between patients before and after transplantation.[1] Similar results were obtained for GWE, whereas only GWW was different between all observed groups (pre-transplantation vs. controls; post-transplantation vs. controls; pre-transplantation vs. post-transplantation). Interestingly, GWI and GCW were different between pre-transplantation versus controls and pre-transplantation versus post-transplantation. It should be also emphasized that LVEF followed changes in GWI and GCW, whereas LV mass index (LVMI) gradually and significantly reduced from pre-transplantation, across post-transplantation, to children in the control group. LV hypertrophy (LVH) has a crucial role in GLS reduction, but also in changes of MW parameters that have been already studied in patients with arterial hypertension.[8] Zhan et al. have recently reported that GWI and GCW were increased in hypertensive children comparing with normotensive controls, while LVEF and GLS were not impaired and were similar between these groups.[9] LVMI was obviously higher in the hypertensive group. Considering the large effect of LVH, Xiao et al. in the present study compared children with and without LVH before kidney transplantation and revealed significantly lower GLS and GWE, but significantly higher values of GWW in those with LVH.[1] GWI and GCW did not significantly differ between children with and without LVH, even though there was a trend of higher values among those with LVH.[1] One should also notice that (BP) was significantly higher among children with LVH, but authors did not perform adjustment while comparing those with and without LVH. This might be a significant confounding factor that was not taken into account. The authors also compared changes in LV function and mechanics among children with and without LVH before and after kidney transplantation and found a significant improvement in GWE and GWW, while there was no significant difference in GWI and GCW despite evident trend of improvement after transplantation.[1] There was also a significant improvement in systolic BP and LVMI after transplantation in patients with LVH, but this was not considered as a potential confounding factor during comparison analysis. The authors considered only the potential effect of clinical parameters and biomarkers on MW indices. The improvement of systolic and diastolic BP after transplantation correlated with all parameters of MW, while glucose change correlated only with GCW and GWI improvement.[1] Multivariate analysis showed that decline in systolic BP was independently related to change in GWW, GCW and GWI that was found after transplantation.[1] It should be noticed that brachial BP was used for evaluation of MW indexes, as widely accepted from the other authors. Even though radial BP would be a more appropriate measurement of afterload, it is considered that difference in afterload at the level of brachial and radial artery is negligible in children. Glucose change was also independently of other biomarkers and clinical characteristics (systolic and diastolic BP, eGFR, NT-pro-BNP, hemoglobin) related with GCW and GWI improvement.

In the light of above-mentioned results, some important limitations should be also stressed. Some of these limitations are evident, such as small population (n = 43 children with kidney transplantation and 28 in the control group). It would be also useful to have more clinical data that include therapy, cause of renal failure, and duration of dialysis. It is also not clear how much LVH and LVMI impacted on the differences in MW parameters as these variables were not included in multivariable analysis and difference between LVH and non-LVH patients revealed significant differences. Moreover, the authors provided only longitudinal mechanics, whereas circumferential and radial strains were not determined, which would be useful in determination of multidirectional strain changes in this particular group of patients and especially enlighten the role of kidney transplantation. The follow-up period of 3 months is potentially too short to reveal more pronounced changes, but it is certainly interesting that even this short time was enough to detect subclinical and subtle alterations that might be useful in prediction of more important clinical endpoints including survival. This short follow-up might be also put in the context of lack of data regarding outcome and association between MW parameters with some endpoints (rehospitalization, complications, mortality, etc.).

This study fulfilled some gaps in knowledge about specific population that has not been widely investigated. MW certainly provides some new information about LV function that have not been measurable with conventional echocardiographic index such as LVEF or even more sophisticated parameter as GLS. GWI and GCW can be clinically used for more detailed evaluation of LV systolic function, GWE may help in better assessment of functional capacity and LV diastolic function, while GWW reflects the improvement in function after cardiac resynchronization therapy or normalization of overall LV function after revascularization. However, it is evident that larger studies with longer follow-up that would include more clinical data and additional echocardiographic data are necessary to provide more relevant clinical data regarding the predictive value of GLS and MW parameters in pediatric patients with renal failure before and after kidney transplantation.

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CONFLICT OF INTEREST

The authors have nothing to disclose.

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