

# Left ventricular performance by work and wasted energy: is strain not sufficient?

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Online publish-ahead-of-print 5 November 2021

**This editorial refers to ‘Novel insights into the athlete’s heart: is myocardial work the new champion of systolic function?’ by M. Tokodi et al. pp. 188–197.**

Almost 60 years ago, Folsø and Braunwald<sup>1</sup> introduced left ventricular (LV) ejection fraction (EF) as a method to measure LV pump function. Since then, EF has been the most important measure of LV function in clinical practice. An important limitation of EF, however, is that about 50% of all heart failure patients have normal or near-normal EF, a condition named heart failure with preserved EF (HFpEF). After a couple of decades with negative drug trials in HFpEF, it was recently shown that the sodium–glucose co-transporter 2 inhibitor empagliflozin reduced the combined risk of cardiovascular death or hospitalization for heart failure in HFpEF.<sup>2</sup> This therapeutic breakthrough holds strong promise for the future and gives motivation for developing new and more sensitive methods to identify HFpEF.

In the 1980’s myocardial strain by cardiovascular magnetic resonance tagging was introduced as a research tool.<sup>3</sup> In 1998, Heimdahl et al.<sup>4</sup> introduced myocardial strain rate by echocardiography as a clinical method to quantify LV function. Peak systolic myocardial strain is closely related to contractility but is somewhat limited by strong load dependency.<sup>5</sup> In spite of that, LV global longitudinal strain (GLS) by speckle-tracking echocardiography has become an important diagnostic tool and may also be used in the evaluation of patients suspected of HFpEF.<sup>6</sup> Importantly, nearly half of all HFpEF have normal GLS and therefore, additional methods are needed to make the diagnosis.<sup>7</sup>

An alternative and more fundamental approach to the assessment of LV function is quantification of the energetics of the ventricle, as proposed by Tyberg et al.,<sup>8</sup> who quantified regional myocardial work and energy waste by LV pressure–dimension loop analysis. The rationale behind this approach is that the quantity of energy expended on, or by, a material is proportional to the integral of stress with respect to strain. Similarly, the global LV pressure–volume loop provides a measure of work and energy consumption for the entire

ventricle, as shown by Suga.<sup>9</sup> More recently, when we introduced myocardial work by non-invasive LV pressure–strain analysis, this was a translation to clinical cardiology of the principles so nicely demonstrated in the experimental studies of Tyberg et al.<sup>8</sup> and Suga.<sup>9</sup> In addition to the estimates of work, we wanted to establish a measure of pump efficiency by quantifying the *energy waste*. We confirmed a relationship between non-invasively measured myocardial work and myocardial metabolism in the study by Russell et al.<sup>10</sup> and showed a potential clinical application of the method with measurement of wasted work in the study by Aalen et al.<sup>11</sup> When compared to GLS, which provides measurement at a single point on the strain curve, myocardial work takes into account the entire strain trace and in addition, incorporates systolic pressure. Many applications of the work method have been tested with promising results.<sup>12</sup> More research is needed, however, before it can be concluded regarding the clinical value of the method.

In a study by Tokodi et al.,<sup>13</sup> it was investigated if the myocardial work index is superior to GLS as parameter of LV contractility in the athlete’s heart. The studies were done at rest, in rats with physiological cardiac hypertrophy induced by swimming, and in human subjects, which included elite swimmers. In the rat model of the athlete’s heart, myocardial work was calculated from strain by speckle-tracking echocardiography and invasive LV pressure. The study showed a strong association between the myocardial work index and LV contractility measured as the slope of the LV end-systolic pressure–volume relationship. Similar to the work index, GLS was associated with contractility, but the dependency on afterload was stronger than for myocardial work.

In the elite swimmers, the myocardial work index was measured by non-invasive LV pressure–strain analysis.<sup>10</sup> The swimmers had increased myocardial work at rest. Furthermore, myocardial work correlated with peak myocardial oxygen uptake during exercise. In this population, there was essentially no wasted work and therefore myocardial work efficiency was normal.

The opinions expressed in this article are not necessarily those of the Editors of *EHJCI*, the European Heart Rhythm Association or the European Society of Cardiology.

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The authors should be acknowledged for including an advanced experimental model to obtain mechanistic insights into the relationship between indices of contractile function and exercise capacity. The experimental model, however, is influenced by anaesthesia and surgery, and its value is primarily as a method to study interactions between physiological parameters. Therefore, it was not surprising that the findings in trained rats differed somewhat from the observations in athlete swimmers.

In the elite swimmers, there was, as expected, a slower heart rate, larger LV volume, and GLS was subnormal, or in the lower normal range. Arterial blood pressure was higher than in controls, which the authors attribute to characteristics of swimmer athletes. The authors conclude that the myocardial work index at rest captured the super-normal systolic performance in human athletes, suggesting a role for the myocardial work index in the evaluation of the athlete's heart. As discussed by the authors, the finding of normal or increased myocardial work may be clinically useful as a sign of normal myocardial function when LV EF and GLS are reduced in athlete's heart.

In principle, the myocardial work index by non-invasive LV pressure-strain analysis can be further improved. The most obvious adjustment is to include LV geometry in the work estimates, which should be feasible by applying standard imaging technologies. Taking into account geometry may be important in particular when comparing hearts of different sizes. Since strain is a relative measure, whereas work by definition is calculated from absolute dimension, enlarged ventricles have a lower work index than smaller ventricles with similar contractility. In the study by Tokodi *et al.*,<sup>13</sup> different heart size was apparently not a major limitation when comparing athletes and controls, but this may be different when studying patients with heart failure and marked enlargement of the ventricle. When considering refining the work method from today's relatively simple approach, it will be a balance between the advantages of improved estimates and downsides of complexity in analysis.

In conclusion, the study by Tokodi *et al.*<sup>13</sup> is mechanistically interesting, but the number of individuals studied is too small to make definitive conclusions regarding contractility in the heart of elite swimmers. The value of the study is that it provides additional evidence in support of incorporating afterload when interpreting indices

of LV contractility. Potentially, the work method can be further improved by including parameters of geometry.

**Conflict of interest:** Otto A. Smiseth is co-inventor of Method for myocardial segment work analysis and has filed patent on Estimation of blood pressure in the heart.

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