Does the heart really operate at ’isoefficiency’?

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In 1979, H. Suga revealed, using the isolated canine heart, a highly linear dependence of oxygen consumption (VO_2) on pressure-volume area (PVA). PVA is the area within the pressure-volume loop plus the area bounded by the end-systolic and the end-diastolic pressure-volume relations and the line denoting isovolumic relaxation of the trajectory of the pressure-volume loop. The former area denotes the external work (W) performed by the heart, whereas the latter is the so-called, but hitherto unexplained, ‘potential energy’ (U). Because the linear VO_2-PVA relation prevails under a wide variety of experimental conditions and across animal species, and because it relies on readily measureable mechanical variables: pressure and volume, its use as a predictor of cardiac function soon became widespread. Specifically, the inverse slope of the VO_2-PVA relation is now commonly used as an index of cardiac contractile efficiency (ε_{PVA}). Because the VO_2-PVA relation is independent of preload and afterload, ε_{PVA} is a constant, *i.e.* ‘isoefficiency’ (its typical value is 40%). In contrast, mechanical efficiency (ε_{mech}; the ratio of W to VO_2), the conventionally used definition of cardiac efficiency, is a complex function of both preload and afterload. It varies between 0% (for isovolumic contractions) and 15% (when the afterload is about one-third of the peak isovolumic pressure). The difference between these two indices of efficiency lies in ‘U’ (*i.e.*, it appears in the numerator of ε_{PVA} but it is absent in ε_{mech}). Hence, to answer the question ‘Does the heart really operate at isoefficiency?’, it is necessary to understand the meaning of ‘U’.

We thus performed experiments to gain insight into the meaning of ‘U’. We employed trabeculae, isolated from either ventricle of the rat heart. Using our unique work-loop calorimeter (Taberner *et al.*, 2011), we subjected them to both isometric contractions and force-length work-loop contractions (designed to mimic the pressure-volume work-loop of the heart) while simultaneously measuring their heat production (Q; derived from a temperature difference in the order of micro-Kelvin). We calculated force-time integral from the force-time trace, ‘U’ and W from the force-length relation, and change of enthalpy (ΔH; W + Q, equivalent to VO_2). Our results (the first from trabeculae) corroborated the linear relation between ΔH and force-length area (FLA; the 1-D equivalent of PVA), demonstrating that it was independent of the type of contraction. That is, isoefficiency obtained. We further made the observation that ‘U’ is proportional to the force-time integral, *i.e.*, to the area under the twitch, under both isometric and work-loop contractions.

Our experimental results allow us to consider three possible meanings of U. First, Suga had suggested that U is ‘potential energy’ which could be entirely converted into work. But, without resorting to an experimental manipulation in which work is performed by the apparatus on the muscle, it is improbable that a work-loop could be contrived to capture any proportion of U. Hence, U can not be regarded as ‘potential energy’. Second, since W is common to both ΔH and FLA, we transformed the ΔH-FLA relation into the Q-U relation, which provided incontrovertible evidence that U is related to Q (*i.e.* U is essentially a proxy for heat). This immediately abrogates its usefulness as a contributor to cardiac efficiency. Finally, we demonstrated that, under conditions where both isometric and work-loop contractions produce the same value of U, it is revealed to be merely a mathematical convenience – a chimera with no discernible physical interpretation. ‘U’ should not appear in the numerator of any index of cardiac efficiency. We conclude that inferring ‘isoefficiency’ from the inverse of the slope of the VO_2-PVA relation is thermodynamically untenable. The heart does not operate at isoefficiency.

Suga H. (1979) Total mechanical energy of a ventricle model and cardiac oxygen consumption. *American Journal of Physiology - Heart and Circulatory Physiology* **236:** H498-H505.

Taberner AJ, Han J-C, Loiselle DS, and Nielsen PMF. (2011) An innovative work-loop calorimeter for in vitro measurement of the mechanics and energetics of working cardiac trabeculae *Journal of Applied Physiology* **111:** 1798-1803.