EDEMA DOES MATTER

To the Editor:

My colleagues and I read with great interest the recent article by Butler and colleagues titled, "Dysfunction Induced by Ischemia Versus Edema: Does Edema Matter?"¹ The authors demonstrated significant myocyte swelling after exposure to ischemia and hypotonic solutions (0.75 T) and reduced myocyte contractility after exposure to the ischemic solution but not the hypotonic solution. In an isolated rat heart model, they demonstrated a significant reduction in systolic function during exposure to hypotonic solution. The authors conclude that their data argue against edema as a major contributor to reduced cardiac performance.

Data from our laboratory using a different ischemic solution (metabolic inhibition) demonstrate that ischemia does result in isolated myocyte swelling and reduced contractility, similar to the authors' findings. However, when we evaluated changes in isolated myocytes exposed to isolated osmotic challenges, we found a *direct* relationship between volume change and contractility. This relationship was consistent after exposure to both hypotonic and hypertonic solutions.² Hypertonic solutions were associated with improved isolated myocyte contractility. Hypotonic solutions (0.9 T and 0.6 T) were associated with a reduction in myocyte contractility that was clearly related to the amount of myocyte swelling.² This is in contrast

to the authors' findings. We have also confirmed these findings in isolated human myocytes (after exposure to osmotic challenge as well as metabolic inhibition) (unpublished). We have thus proposed that during cardiac surgery, myocyte edema secondary to osmotic challenge (including exposure to commonly used cardioplegic solutions) does detrimentally affect contractility in a manner that is separate from, and additive to, the widely recognized "ischemia-based" edema and reduced contractility.³

Experimental differences between the two articles exist in that the authors used a shorter protocol (8 vs 20 minutes of exposure), different ischemic and hypotonic solutions, and a different species, all of which may make direct comparisons of data difficult. However, the relationship between isolated myocyte swelling and contractility has been consistently and repeatedly demonstrated in our laboratory after exposure to hyperkalemic cardioplegia, osmotic stress, and metabolic inhibition in myocytes obtained from two animal species and humans.

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References

- Butler TL, Egan JR, Graf FG, Au CG, McMahon AC, North KN, et al. Dysfunction induced by ischemia versus edema: does edema matter? *J Thorac Cardiovasc Surg*. 2009;138:141-6.
- Mizutani S, Prasad SM, Sellitto AD, Schuessler RB, Damiano RJ, Lawton JS. Myocyte volume and function in response to osmotic stress: observations in the presence of an adenosine triphosphate-sensitive potassium channel opener. *Circulation*. 2005; 112(Suppl 9):I219-23.
- Al-Dadah AS, Voeller RK, Schuessler RB, Damiano RJ, Lawton JS. Maintenance of myocyte volume homeostasis during stress by diazoxide is cardioprotective. *Ann Thorac Surg*. 2007;84:857-62.

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Reply to the Editor:

We thank Dr Lawton for her interest in our article¹ and the Editor for the

opportunity to respond. Our principal focus is postoperative low cardiac output syndrome (LCOS) in pediatric patients. By studying myocardial water content and function, we were expecting to scientifically validate the clinical dogma linking edema with dysfunction. However, use of three related models—isolated myocytes, Langendorff hearts,¹ and whole animals on cardiopulmonary bypass²—failed to implicate edema as a significant causal influence in LCOS.

We found that cells swelled in response to hypotonic stress (7%) more than they did in response to ischemia (2%). Cell function was not changed during or after swelling alone but severely affected by ischemia (reduced to 51% of baseline). When hypotonic stress followed the ischemic insult, we showed additional edema (from 2% to 6%) but no additional contractile dysfunction. From these findings, we assert that ischemia is the most important influence on contractile function.

We examined a single tonic change (0.75 T)¹ whereas the Lawton group (Mizutani and associates³) used both mild (0.9 T) and severe (0.6 T) hypotonic exposure. Cell shortening was identically reduced after recovery in both the 0.9 T and 0.6 T groups (~30%) and was also reduced in the 1.0 T isotonic control (15%–20%). Much of the impairment is simply temporal decline, also seen in our study by repeated measurement of isotonic controls and a characteristic of the model itself. In the Lawton study, statistical significance could only be shown by comparison of the 0.6 T and 0.9 T groups with a 2.6 T hypertonic group. No significant difference was shown in cell function between 0.6 T, 0.9 T, and isotonic buffers in agreement with our own work.

In the Lawton group's study, degree of swelling correlated well with severity of tonic change, but cell shortening was not affected to the same degree. For cells exposed to 0.6 T buffer, 30% swelling was seen, whereas cells

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