
REPLY
Dr. Leite-Moreira and colleagues raise important issues regarding relations between chamber loading, relaxation and end-diastolic pressure (EDP). They argue that load-induced relaxation changes importantly determine chamber EDP. Since the monoeponential-derived (ME) time constant better correlates with EDP than does an alternative hybrid-logistic (HL) parameter, they contend that this supports use of the former. Our study (1) also reported links between ME relaxation time constants and EDP; however, this was more attributable to mathematics, as changes in EDP for whatever reason (real or arbitrary) altered ME relaxation estimates even when the pressure decay waveform was unchanged. This was particularly true in depressed hearts due to systematic deviation of the ME model from actual pressure decline, and this same behavior largely explained apparent enhanced load-sensitivity of relaxation in such hearts.

There are many determinants of EDP: notably, intrinsic chamber stiffness and volume loading, extrinsic forces from the right heart and pericardium, atrial-ventricular interactions, and relaxation. However, for the last to affect EDP it must be very prolonged or the heart rate must be particularly fast, because otherwise there is sufficient time to complete relaxation during filling. Reported correlations between EDP and ME-relaxation rates do not imply a physiologic cause and effect dependence. For example, in one study (2) leg raising induced a 5 ms prolongation in relaxation, yet, relative to the constant heart rate of 90 min⁻¹, this change was small and hard to link to the EDP rise. On the other hand, preload increase with leg raising should elevate EDP and, thereby, raise the lower-range cutoff pressure for data subjected to relaxation analysis. As we showed (1) this alone can amplify apparent relaxation changes based on the ME model. Such behavior is particularly anticipated with depressed basal function observed in the prior study (2), but would be blunted by use of the HL model (1). In this sense, the improved EDP prediction by ME-tau changes noted by the authors may be more mathematical in origin.

In other studies of normal rabbit and canine hearts, coelevation of EDP with relaxation rate was observed only at very high afterloads from single-beat aortic clamping (3). Such nonphysiologic loading is different from the volume and pressure changes we and others employed (1,4,5). Here EDP rise could also be explained by increased end-systolic volumes with aortic occlusion, diminishing restoring forces that contribute to pressure decline (6). Also, the pressure at the onset of filling (that is, left atrial pressure) increases, which can elevate diastolic pressures at any relaxation rate (7). Similar maneuvers performed in isolated hearts in which the pressure at the onset-of-filling was constant revealed minimal EDP change (8).

Correlations between upward or downward diastolic PV-curve shifts or EDP and relaxation rate does not require physiologic causality. As we showed (1), this can largely stem from discrepancies between the decay-model indexing relaxation and actual pressure decline. These mathematical issues predict the stronger correlations between ME-decay and load-dependent changes in EDP that the authors note. Our analysis suggests caution when interpreting such data. Further studies testing these links with more targeted and selective manipulations are still needed to better separate the math from the physiology.

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REFERENCES