Post-Systolic Shortening
A Functional Window Into Ischemic Memory?*

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The heart’s memory eliminates the bad and
magnifies the good; and thanks
to this artifice we manage to endure the
burdens of the past.
—Gabriel García Márquez (1)

Myocardial post-systolic shortening is characterized by a large variability in both duration and magnitude. Although typically occurring in a setting of ischemic heart disease, this regionally asynchronous myocardial contraction is considered a normal finding in approximately one-third of myocardial segments in healthy subjects, as long as the magnitude is low and the systolic strain is preserved (2). Post-systolic contraction takes place during an energetically demanding and vulnerable phase of the cardiac cycle.

Approximately 15% of overall myocardial energy consumption is required—within 5% of the cardiac cycle duration—to pump calcium ions (Ca^{2+}) against a concentration gradient and back into the sarcoplasmic reticulum. This allows myocyte relaxation and initiates diastolic reconstitution of the energy cycle (3). By comparison, the onset of myocardial contraction is initiated by a rapid entry of extracellular calcium followed by a passive release of large amounts of calcium from the sarcoplasmic reticulum, which is an energetically inexpensive process, although subsequent systolic contraction consumes approximately 60% of the cardiac cycle energy (3). Cellular electrical activity, protein synthesis, and restoration of Na^+ and K^+ gradients account for the remaining 25% of the energy consumption. As a result of the high energy dependence of myocardial relaxation, post-systolic contraction occurring in acute ischemia and reperfusion is closely coupled with the underlying mismatch between myocardial adenosine triphosphate (ATP) production and consumption. This mechanoe energetic coupling has been mathematically characterized and allows for an estimation of the myocardial energetic economy during acute ischemia and reperfusion using strain echocardiography (4).

Restoration of perfusion after transient myocardial ischemia is required for recovery of regional mechanical function and metabolism. Braunwald and Kloner (5) documented that brief or mild ischemia may “hit, run, and stun” and, in this way, form a temporary functional imprint (functional stunning) as a consequence of the antecedent ischemic event. Using iodinated fatty acid analogues, single-photon emission computed tomography (SPECT) imaging (6, 7) has demonstrated persistent alterations of regional myocardial metabolism shortly after chest pain at rest as an indicator of ischemic memory, or metabolic stunning. These SPECT studies have set the stage for investigations of cardiac ischemic memory as an indicator of antecedent ischemia.

In this issue of iJACC, Asanuma et al. (8) report the utility of post-systolic shortening and a strain imaging diastolic index for detection of ischemic memory. The study is an extension of previous work published by the same group (9). In their initial work, the investigators experimentally demonstrated that regional post-systolic contraction can persist for 30 min following restoration of blood flow to the related coronary artery, even with an immediate recovery of systolic function, and thus serve as a functional marker.
of ischemic memory. In their present study, Asanuma et al. (8) use a dog model of 2-min left circumflex coronary artery occlusion followed by a 1-h period of reperfusion. Speckle tracking echocardiography was used to measure radial and circumferential strains and strain rates at baseline, end of occlusion, and at several time points during the reperfusion period. Multiple quantitative parameters of regional systolic and post-systolic mechanical function were assessed, and their ability to identify ischemic memory was evaluated along with strain imaging diastolic index (10). This latter parameter, which was introduced by Ishii et al. in 2008 (11), incorporates strain changes during the first one-third of diastole duration (i.e., encompasses the highly energy-dependent period of relaxation).

In the current work by Asanuma et al. (8), the authors study which regional deformation parameters are the most useful functional markers of an earlier ischemic insult, if the initial data are obtained by speckle tracking echocardiography. The results imply that only post-systolic contraction-related parameters demonstrate ischemic memory. The cross-sectional experimental design maintains acceptable costs and supports a well-controlled study that minimizes confounding variables that may otherwise be unavoidable in a “real world” clinical setting. One could argue, however, that the current study design represents a scenario that has a low likelihood of occurring in a clinical setting. The design is limited to a 1-time, 2-min occlusion of a single coronary artery in an open-chest dog model with healthy hearts. Unlike human hearts, dog hearts that have never been exposed to an ischemic event already have abundant and readily available coronary collaterals (12). Therefore, the dog model may influence clinical implications of the study. Nonetheless, there is a good prospect for clinical detection of ischemic memory by analysis of post-systolic contraction with echocardiography, as Asanuma et al. (8) propose. Peak systolic strain occurring during the first one-third of diastole (i.e., post-systolic strain) in the clinical echocardiographic study by Ishii et al. (11) suggests that post-systolic contraction detects ischemic memory following elective percutaneous coronary angioplasty in patients with stable angina and normal resting cardiac function. In the context of brief antecedent ischemia, nonlethal ischemic stress can have a protective effect against subsequent lethal ischemic and reperfusion injuries (13). The mechanism of this well-established concept of ischemic preconditioning is at least in part due to reduced ATP depletion (13). One can speculate that post-systolic contraction may be a functional indicator of myocardium that has been conditioned for higher endurance against a lethal ischemia/reperfusion injury. However, the pathophysiological and clinical circumstances, under which post-systolic contraction acts as such an indicator, are questions that are yet to be answered.

In summary, there is growing evidence that post-systolic contraction provides a functional window into cardiac ischemic memory. In this issue, Asanuma et al. (8) present their experimental work introducing a potential niche for the clinical application of speckle tracking echocardiography as a non-ionizing technique for detecting functional ischemic memory. Translating these experimental findings into the clinical arena will provide information as to whether post-systolic contraction lasts long enough to be a reliable and practical diagnostic indicator of an antecedent ischemic insult, and whether this transient regional diastolic motion alteration can even be a marker of a more resilient heart that has been preconditioned to “manage to endure the burdens of the past” (1).

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