Furthermore, patients with acute MR showed less complete and slower recovery of LV function, occasionally associated with persistence of substantial regurgitation during follow-up.

The mechanism of acute MR during LVABS is likely due to complex and multiple mechanisms. Nevertheless, the main factor involved seems to lie in the altered spatial relationship between mitral leaflets and the subvalvular apparatus, caused by the apical ballooning. Indeed, papillary muscle displacement was a constant finding in all our patients with acute MR, leading to impaired leaflet coaptation secondary to tethering. In addition, SAM occurred in 36% of patients with MR and appeared to play a relevant role in determining the presence and degree of regurgitation during the acute phase of LVABS, as well as causing significant LV outflow obstruction (5). It is well known from studies on hypertrophic cardiomyopathy that SAM is almost constantly associated with variable degrees of MR, which may be severe (6,7). In patients with LVABS, SAM may originate from the combination of apical ballooning and distortion of the LV, abnormal papillary muscle tethering forces, mitral valve displacement, and proximity of midapical bulging and akinesia with hypercontractile basal LV segments (5).

In addition, we cannot exclude the contribution of other mechanisms to acute MR, such as reduced papillary muscle contraction and absolute or relative decrease in LV preload. Conversely, a key role for mitral annulus dilatation and structural leaflet abnormalities seems unlikely based on our findings. Finally, significant mitral leaflet sclerosis was found in the small number of patients with delayed or absent improvement of MR. This finding suggests that pre-existing degrees of valve degeneration or other structural abnormalities may be relevant in determining the extent and time-course of MR and its recovery in LVABS.

These observations imply that acute MR should be actively sought and carefully evaluated in patients with LVABS, as a potential marker of adverse clinical course requiring aggressive treatment. Likewise, LVABS should be systematically considered in the differential diagnosis of patients admitted for heart failure or cardiogenic shock associated with acute MR.

On the Mechanisms of Transmural Dispersion of Myocardial Mechanics

The study by Ashikaga et al. (1) in the February 27, 2007, issue of the Journal demonstrates left ventricular (LV) transmural gradient near the left anterior descending coronary artery (LAD) at the onset of shortening and relaxation of myocardial fibers with transmural break markers under biplane cineangiography. These anesthetized open-chest dog studies provide novel insight and help for a fuller understanding of what constitutes a normal cardiac electro-mechanical function. Such an understanding could be instrumental in developing optimal goals for therapy (i.e., cardiac resynchronization therapy) after a disease disrupts stability (i.e., heart failure). Of note in this study was the observation that transmural gradients in contraction and relaxation developed in the virtual absence of transmural gradient in electrical repolarization (shown by T-wave analysis of nearby transmural plunge bipolar electrodes). The authors suggest that the depth-dependent (transmural) differences in myocardial mechanics result solely from the complex interactions of myofiber mechanics within and between the layers due to myocardial cell architecture in the bundles ("tissue tethering") (1). Although tethering might influence regional mechanics and cause regional differences in the onset of contraction-relaxation of the LV, the potential role of transmural differences in intracellular calcium ion (Ca\(^{2+}\)) handling in the observed in vivo gradients of mechanics was dismissed (2). It is known that Ca\(^{2+}\) elevation is associated with the onset of contraction (shortening).
and the uptake of Ca$_{2+}$ by the sarcoplasmic reticulum (SR) with the onset of relaxation. For example, it has been shown in isolated canine LV wedge preparations near the LAD (same species and same site as in the in vivo studies of Ashikaga et al.) that whereas the onset of the epicardial and endocardial Ca$_{2+}$ transients are almost synchronous, the epicardial decline of the Ca$_{2+}$ transient (onset of relaxation) precedes the endocardial decline (3). Furthermore, the rate of Ca$_{2+}$ uptake by the SR is faster in the epicardium compared with endocardium (3). These effects mimic the in vivo canine observations made by Ashikaga et al. (1). Because the dynamics of Ca$_{2+}$ mirror that of contractility, changes in Ca$_{2+}$ are considered to be surrogate of myocardial contractility (4). Consequently, we think that the combined tissue tethering and transmural cellular differences in Ca$_{2+}$ handling need to be considered simultaneously as possible mechanisms for the in vivo observation of depth-dependent differences in myocardial mechanics in the canine mid-anterior LV.

*Hrayr S. Karagueuzian, PhD, FACC

*Division of Cardiology
Cedars-Sinai Medical Center
David Geffen School of Medicine at UCLA
Los Angeles, California 90048-1804
E-mail: karagueuzian@cshs.org

doi:10.1016/j.jacc.2007.03.061

REFERENCES


Reply

Our recent article (1) reported a new observation that there is discrepancy between cardiac electrical and mechanical behaviors by detecting relatively large mechanical dispersion with little electrical dispersion during both activation and relaxation in the canine mid-anterior left ventricle (LV). In his letter, Dr. Karaguezian logically and correctly points out the potential contribution of transmural dispersion in intracellular calcium handling (2) to the transmural mechanical gradients that we had described in the article. Given a slower decay of intracellular calcium to diastolic levels at the endocardium, due in part to significantly lower levels of sarcoplasmic reticulum Ca$_{2+}$ ATPase (SERCA2a) expression in endocardial cells than epicardial cells, the transmural differences in calcium handling likely contribute to the transmural dispersion of myofiber relaxation and should be added to the list of potential contributing factors, such as transmural dispersion of electrical repolarization, even if it is small at physiological heart rates, and tissue tethering. However, this does not seem to be the case with the transmural dispersion of myofiber shortening. Transmural differences in intracellular calcium during activation, where endocardial cells have a slower time to peak than epicardial cells, result in an earlier onset of myofiber shortening in the epicardium than in the endocardium by approximately 20 ms (3). This delay is close to the transmural conduction delay in the canine LV (1,4), thus allowing the impulse to traverse the LV wall to synchronize contraction across the ventricular myocardium; that is, the transmural differences in calcium handling do not contribute to but rather “negate” the transmural dispersion of myofiber shortening due to the delay in action potential propagation across the wall. Therefore, the transmural dispersion of myofiber shortening should be accounted for by other factors, including tethering.

*Hiroshi Ashikaga, MD, PhD
Elliot R. McVeigh, PhD
Jeffrey H. Omens, PhD

*Laboratory of Cardiac Energetics
National Heart, Lung, and Blood Institute
10 Center Drive, Building 10/B1D416
Bethesda, Maryland 20892
E-mail: ha8000@gmail.com

doi:10.1016/j.jacc.2007.05.013

REFERENCES


Immediate Coronary Imaging for Acute Chest Pain: Are We There Yet?

We read with great interest the elegant study by Goldstein et al. (1) suggesting the value of multislice coronary computed tomography (MSCT) in the evaluation of acute chest pain patients. The investigators should be commended for this landmark trial that constitutes one of the few studies assessing the value of an imaging diagnostic technique using a randomized design. As compared with patients managed in the emergency department with standard of care measures, those assigned to the MSCT arm not only had reduced diagnostic times and costs but also required less frequently repeated evaluations for recurrent chest pain (1). Considering the potential clinical implications of this provocative study, addressing some methodological issues would be appreciated.

First, in a randomized study defining the sample size calculation is critical. This is especially relevant considering the very-low-risk patient population included in the present study (none of the patients suffered an event after discharge). Likewise, the primary outcome measure of the study was not clearly stated. Therefore, the value and implications of the different study findings remain