

EDITORIAL COMMENT

Risk Stratification After Myocardial Infarction

Toward Novel Quantitative Assessment of Left Ventricular Mechanics?*

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The prognosis of patients after acute myocardial infarction (AMI) depends on infarct size and left ventricular (LV) dysfunction. The extent of myocardial salvage relies on rapid and sustained myocardial tissue reperfusion. Preservation of myocardial viability can be followed by functional recovery, spontaneously when the myocardium is stunned, or after restoration of sufficient blood flow and flow reserve in the presence of hibernation (1). In contrast, transmural necrosis might lead to infarct expansion; progressive LV remodeling; and in turn, LV dysfunction, secondary mitral regurgitation, and heart failure, all associated with worse outcome.

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Echocardiography has become the technique of choice to evaluate LV function and stratify risk after AMI. Several parameters obtainable by Doppler echocardiography provide prognostic information: LV volumes, left ventricular ejection fraction (LVEF), wall motion score index (WMSI), mitral regurgitation, E/E' ratio, left atrial size, and right ventricular function (2). Both LVEF and WMSI are strong predictors of all-cause mortality after AMI. Mortality increases exponentially with decreasing LVEF, whereas it increases linearly with increasing WMSI.

Left ventricular ejection fraction is a marker of global LV systolic function, whereas WMSI allows better evaluation of LV regional dysfunction (3). However, low LVEF does not necessarily reflect the extent of reduced contractile function resulting from myocardial injury but can result from LV dilation and stretching of the myocardial scar. In contrast, LVEF might be almost normal,

despite extensive regional wall motion abnormalities due to compensatory regional hyperkinesis and/or ischemic mitral regurgitation. In addition, WMSI seems to better reflect the magnitude of myocardial damage and has been shown to be a powerful predictive parameter, particularly in the pre-thrombolytic era (4). Early after AMI, both LVEF and WMSI might be misleading, owing to the presence and extent of salvaged but still dyssynergic myocardium (3,4).

These classical parameters are limited by several drawbacks. Left ventricular ejection fraction is load dependent, and standard volumetric approaches to its measurement might be influenced by imaging quality, technical considerations such as off-axis imaging, and measurement errors. The assessment of regional function is more difficult, remains subjective, and requires training and experience.

Recently, new echocardiographic modalities providing new insights into cardiac mechanics have been developed. Speckle tracking is a recently validated method that is angle-independent (an advantage when compared with tissue Doppler imaging) and provides the assessment of strain and strain rate, which accurately reflect intrinsic measures of myocardial contractility and offer the opportunity of examining longitudinal and circumferential motion of the heart (5). The ventricular myocardium is known to exhibit a complex spatial organization, with fiber orientation varying as a function of transmural location. The subendocardial layer of fibers has an oblique clockwise orientation in the longitudinal direction and contributes mainly to the long-axis function. The middle layer is wrapped circumferentially, and the outer subepicardial layer is arranged in an oblique anticlockwise direction and contributes to thickening and short-axis function via cross-fiber shortening (6–8). Because the subendocardial fibers are the most sensitive to myocardial hypoperfusion, the longitudinal function is the first to be altered in the presence of ischemia. In the setting of AMI, the combined assessment of long-axis and short-axis function with 2-dimensional strain has demonstrated excellent ability to differentiate between different levels of infarct size. Subendocardial infarction is associated with a reduction in longitudinal strain, whereas radial and circumferential functions are relatively preserved or mildly impaired. In contrast, transmural infarction is associated with a severe reduction of both long- and short-axis function. Thus, the average strain from all myocardial regions, reflecting the total extent of the whole myocardial damage after AMI, provides a better surrogate for the assessment of global residual LV contractile performance. However, the independent prognostic value of strain imaging after AMI has not been fully examined (9,10). An advantage of the speckle tracking method is that it can be applied to previously stored grey-scale imaging and permits a retrospective

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analysis of prospectively recorded data. In this issue of the *Journal*, the VALIANT (Valsartan in Acute Myocardial Infarction Trial) investigators have applied this method in a series of patients from the VALIANT echocardiography study (11).

The VALIANT study was designed to test the efficacy and safety of long-term treatment with valsartan, captopril, or their combination after AMI in 14,703 patients with LV dysfunction (LVEF $\leq 35\%$ on echocardiography), clinical signs of heart failure, or both (12). The VALIANT echocardiography study enrolled 603 patients (with acceptable images) from the VALIANT population who underwent serial echocardiographic evaluation of LV function (11). Of these patients, 20% had LV dysfunction, 50% received a diagnosis of clinical heart failure, and 30% had both. Velocity vector imaging, a 2-dimensional image-based approach, was used to assess regional myocardial deformation. Longitudinal (assessable in 380 patients) and circumferential (assessable in 420 patients) strain and strain rate were measured; both were available in a total of 311 cases. A composite longitudinal strain rate value for each patient was derived from the mean value of 12 segments from the apical window, and the representative circumferential strain rate of each patient was composed of the mean value from 6 LV mid-wall short-axis segments. Both longitudinal and circumferential strain rate were predictive of death or hospital stay for heart failure. Longitudinal strain rate added significant incremental value in the prediction of all-cause mortality beyond clinical variables, LVEF, and WMSI. Lower strain rate values identified patients at increased risk of events, whereas the highest strain rate values were associated with very few events during the 2-year follow-up. These data reinforce the recent results reported by Park et al. (9) and Antoni et al. (10). The VALIANT echocardiography study also showed that circumferential strain rate but not longitudinal strain rate was strongly predictive of LV remodeling (defined as $\geq 15\%$ increase of LV end-systolic volume), suggesting that preserved circumferential function might serve to restrain ventricular enlargement after AMI. The limited value of long-axis function to predict LV remodeling reflects the complex interdependence among ventricular shape, infarct size, and myocardial deformation. In the acute phase, the decrease in long-axis function relates to both the subendocardial necrosis and the magnitude of post-AMI remodeling process. Thus, regardless of infarct size, longitudinal strain also decreases proportionally to the graded increase in end-systolic volume. Such a reduction in long-axis function is thus in part related to the more transverse alignment of both longitudinal counter-directional helical muscle fibers secondary to LV expansion (13). The short-axis function is less affected by the remodeling process. It is relatively preserved until severely enlarged and decreases gradually with the transmural extension of necrosis. It is well known that the

presence of residual viability in the infarct territory can favorably influence LV remodeling. Even if recovery of contractile function is not observed soon after reperfusion, the presence of viable myocardium in the outer layers of the ventricular wall might contribute to the maintenance of ventricular shape and size by preventing infarct expansion. The present VALIANT study confirms and extends these physiopathological considerations. With extensive necrosis, the short-axis function fails to overcome increased wall stress related to LV volume expansion, which in turn leads to a vicious remodeling process. Thus, a certain level of circumferential (mid-wall) function is required for maintaining LV structure and shape after AMI. The LV contractile pattern is fully characterized not by the amplitude of strain rate but also by its timing. Indeed, LV dyssynchrony is an independent predictor of poor prognosis in heart failure patients (14). The VALIANT echocardiography investigators have recently observed in the same population, with the similar speckle tracking with velocity vector imaging, that the SD between time to strain rate among LV segments was independently associated with increased risk of death or heart failure after AMI (15).

Practically, the results of the VALIANT echocardiography study clearly underscore the added value of quantifying LV systolic function by strain rate analysis after AMI.

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