Post-Infarction LV Remodeling
Remote Changes Do Not Necessarily Occur Remotely From Time of Infarction*

Andrew J. Taylor, MBBS, PhD, William Chan, MBBS, PhD

Healing is a matter of time, but it is sometimes also a matter of opportunity.
—Hippocrates 460 BC to 377 BC

The prevailing theory of left ventricular (LV) remodeling post–acute myocardial infarction (MI) stems from experimental work and clinical observations dating back to the 1930s, proposing that structural changes in the infarct zone result in adverse LV wall stress in the noninfarct zone, and with time, progressive LV dilation and dysfunction develop as a compensatory response (2,3). Infarct expansion was thought to be the initial stimulus driving volume-overload hypertrophy contributing to LV enlargement, which is modified by infarct size, infarct healing, and LV wall stress (2). In spite of advances in timely mechanical reperfusion and adjunctive pharmacotherapy, a significant proportion of patients presenting with ST-segment elevation myocardial infarction (STEMI) still progress to pathological LV remodeling and experience adverse clinical outcomes (4).

In this context, cardiac magnetic resonance (CMR), with its high spatial resolution and ability to characterize tissue composition, has furthered our understanding of physiological processes occurring post-MI (5–7). Although interest in using CMR to quantify interstitial fibrosis by either post-contrast (8,9) or native T1 mapping (10) has recently garnered scientific debate about methodology (11), it has also stimulated scholarly pursuits into characterizing pathophysiological processes of different myocardial disease states that has not been previously possible, including the process of adverse LV remodeling post-MI (7).

Evolutionary changes in the remote myocardium distant to the infarct zone can now be assessed and quantified using novel CMR sequences. Because native T1 is influenced by water content and inflammatory cell infiltrate (12), prolonged native T1 times may represent areas of more severe myocardial injury or ischemia in the acute phase of injury (13,14). In the chronic phase, prolonged native T1 times correlate with the extent of interstitial myocardial fibrosis (10) and have been advocated as a sensitive test for the differentiation of cardiomyopathic from healthy myocardium (15). By performing native T1 mapping using an optimized modified look-locker inversion-recovery sequence, Carrick et al. (16) comprehensively assessed 300 patients with reperfused STEMI at approximately 2.2 days and 6 months post-MI and reported several interesting and provocative findings in this issue of iJACC. The upper tertile of remote zone native T1 values approximated infarct zone T1 times, suggestive of an acute pathological process in the remote myocardium occurring early in the course of MI in a significant number of patients. Secondly, remote T1 values were independently associated with markers of systemic inflammation and MI size. Finally, and perhaps most significantly, remote myocardial T1 was associated with adverse LV remodeling at 6 months after adjustment for MI size and LV end-diastolic volume on day 2. Although not powered for clinical endpoints, the researchers observed an association between remote native T1 and all-cause death and heart failure hospitalization during longer-term follow-up. In their post-hoc analysis, a native T1 value <969 ms had a high...
negative predictive value for adverse clinical outcomes, suggesting a potential clinical utility for native T1 mapping in post-MI risk stratification.

This is an important observational study on a large number of reperfused patients with MI, providing further insight into the pathophysiology of LV remodeling early post-MI. Changes in the remote myocardium occurred very early (within a few days of MI) and appeared to be intimately linked to the process of LV remodeling. Elucidating the exact mechanism of remote myocardial changes is problematic without histology, but the researchers provided several pieces of supporting data to suggest that remote zone changes likely reflect a diffuse myocardial inflammatory response triggered by myocyte death, as reflected by an association between remote T1 and markers of inflammation (monocyte numbers, C-reactive protein levels) and reperfusion injury (MI size, lower salvage index, ST-segment resolution) rather than with baseline N-terminal pro-B-type natriuretic peptide levels. This would suggest that LV wall stress alone is unlikely to be the principal contributor to remote native T1. Interestingly, there are also experimental data that support a diffuse inflammatory response throughout the myocardium (17). The findings of Carrick et al. (16) are broadly consistent with those of our prior study, in which we observed impaired regional systolic function associated with shortening of post-contrast myocardial T1 times in the remote myocardium among patients with acute MI imaged within a week post-MI (7). Together, these data support the concept that there are likely primary changes occurring in the remote myocardium acutely post-infarction that contribute to adverse LV remodeling.

To extrapolate exact changes occurring in the remote zone from changes in CMR T1 signals, be it native or post-contrast, is difficult. The results of the study of Carrick et al. (16) differ from prior literature suggesting an absence of myocardial edema in the remote zone (7,18), and certainly their native T1 values were not dissimilar to T1 values from their control cohort. Although the researchers argued that the upper tertile of remote zone native T1 overlapped with T1 values obtained from infarct zone and was suggestive of edema and increased cellularity, this assertion lacks rigorous supporting data. Perhaps the lack of difference in remote native T1 values between reperfused patients with MI and controls might be a function of sample size, but a more likely explanation might be that there is a spectrum of remote zone changes because the inflammatory response post-MI is heterogeneous and that different MI sizes might be associated with different degrees of remote zone changes. It would, therefore, be of significant interest to compare remote zone native T1 at 6 months or later to see if the changes observed acutely had regressed or were persistent. This would help clarify whether the observed changes in the remote zone from the outset may represent the initiation of interstitial fibrosis as suggested by prior animal studies (19,20).

So how do we interpret the findings from Carrick et al. (16)? Accumulating data now suggest that remote myocardial changes might be an important mediator to the overall process of MI healing and LV remodeling (7). Changes in the remote myocardium within days of MI may play an important pathophysiological role in determining the eventual fate of LV remodeling. That healing is a matter of time is a classical dogmatic observation, but healing is also sometimes a matter of opportunity. Further research evaluating what happens to the remote myocardium during MI is of significant importance because this may lead to the development of novel treatment strategies that target early changes in the remote myocardium to ameliorate longer-term adverse LV remodeling.

**REFERENCES**


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