Insights into Myocardial Microstructure During Infarct Healing and Remodeling
Pathologists Need Not Apply

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H
ing of acute myocardial infarction (MI) and subse-
quent increase in left ventricular (LV) cavity size or LV
remodeling\(^1\) is a complex process.\(^2\) LV remodeling depends
largely on infarct size\(^3\) and transmurality which in turn is
determined by the status of the epicardial infarct artery\(^4\) and
the microvasculature.\(^5\) Within a larger, near-transmural or
transmural infarction, there is myocyte loss, in part because
of apoptosis, and cellular slippag\(^6\) that leads to reduced
tensile strength within the infarct zone and subsequent infarct
expansion.\(^7\) Infarct expansion and wall thinning in the infarct
zone then leads to regional cavity dilatation and increased
wall stress throughout the LV. Elevated wall stress in turn
activates the renin-angiotensin system and other autocrine-
paracrine systems\(^8\) and cellular hypertrophy ensues.\(^9\) Cellular
hypertrophy occurs primarily in noninfarcted regions adja-
cent to the infarcted segment and is eccentric due to the laying
down of sarcomeres in series.\(^10,11\) Eccentric cellular hyper-

trophy in noninfarcted regions together with fibrosis\(^12\) con-
tribute to mechanical dysfunction in adjacent noninfarcted
regions that persists during remodeling.\(^13\) Remote nonin-
farcted regions are initially mildly dysfunctional in the first
few days after large MI,\(^14\) but these recover over the next
several weeks as global LV function improves.\(^15\) The sum
total of these events is a deleterious increase in end-diastolic
and -systolic cavity sizes. It is the latter that is the most
important determinant of outcome after acute MI.\(^16\)

Until very recently, studies of the structural events that
occur during LV remodeling have required painstaking hist-
opathology and have been performed primarily in animals.
With the advent of advanced cardiac imaging techniques,
similar observations can now be made in vivo. Diffusion
tensor cardiac magnetic resonance imaging (DT-CMR) was
developed more than a decade ago,\(^17\) but was initially applied
in MI only in animal studies.\(^18\) Its first application in patients
after MI was very recently and represents a technical
tour-de-force.\(^19\) DT-CMR enables delineation of the micro-
structure of the heart based on the principle that diffusion of
water within the myocardium parallels the orientation of
cardiac microstructure. Thus, DT-CMR can yield information
regarding not only the mean diffusivity of water molecules,
but also fractional anisotropy or the variability of the direc-
tion of water mobility and helix fiber angle of the myofibrillar
architecture. All these imaging parameters reflect myocardial
structural alterations during infarct healing and LV remodeling.

The article from this same group in this issue of *Circulation:*
Cardiovascular Imaging is a follow-up study of their original
study population.\(^20\) Twenty of the original 37 patients were
imaged for this study, but only 17, less than half of the original
and all male, had adequate data for analysis. The initial imaging
was performed 3 weeks after the index MI and follow-up on
average 7 months after MI. Five of the patients had received
percutaneous coronary intervention before the initial CMR,
whereas an additional 7 patients underwent percutaneous coro-


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certainly impact the findings because subsequent remodeling is distinctly different between subendocardial and transmural infarcts.

During the 6 months between DT-CMR studies, the infarct-adjacent region demonstrated wall thinning while the remote zone demonstrated hypertrophy and increased wall thickening relative to the infarcted segment. During infarct healing, the infarct-adjacent region demonstrated a decrease in mean diffusivity, toward normal, likely due to resolution of edema and further organization of scar. Similar findings were noted in remote. In addition, myofibrillar disarray as evidenced by fractional anisotropy tended to improve in the infarct zone and did improve in remote. The fiber angle became more right-handed helical with time in the infarct-adjacent region consistent with replacement with epicardial fibers whereas the remote region became more left-handed helical, likely due to relative hypertrophy of fibers with subendocardial orientation. Correlations were noted between mean diffusivity in the infarct-adjacent region and improved wall thickening. Similar correlations were noted in remote.

Despite all of these microstructural improvements, global ejection fraction did not improve over time in this patient population. This is a result of a relative decline in wall thickening in the infarct segment while remote regions improved. Wu et al did not include in their manuscript the changes in end-diastolic or -systolic volumes that may have occurred over time in this population of patients. Ejection fraction may not change, but if end-diastolic and -systolic volumes increase proportionally, this portends an adverse prognosis in the post-MI population.16

This study does not explain the wall thinning in the infarct zone as diffusivity and anisotropy improve. The wall thinning must still be in large part due to loss of myocytes and cell slippage. In addition, imaging doesn’t yet offer the kind of spatial resolution that can differentiate eccentric from concentric cellular hypertrophy. We must infer these changes from relationships between noninfarcted segment lengths, wall thickness, and cavity size. Despite these limitations, this study makes important contributions to our understanding of the process of scar healing and LV remodeling in vivo. Studies of this kind have previously not been possible in the living human heart. Wu et al should be congratulated for completing such technically challenging imaging as well as data analysis in this patient population. Only with similar studies in larger patient groups will investigators be able to tease out differences in infarct healing and LV remodeling based on infarct location, transmurality, and the presence or absence of microvascular obstruction in acute MI. As cardiovascular imagers become more proficient in such advanced techniques, the need for pathologists performing microstructural studies in small animals will dissipate.

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References

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