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EDITORIAL COMMENT

Shortening Without Contraction: New Insights Into Hibernating Myocardium*

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It is well accepted that revascularization of patients with hibernating myocardium significantly improves their prognosis. The most convincing data were presented in a meta-analysis that pooled the data of 3,088 patients from 24 studies (1). Hibernation was determined using single-photon emission computed tomography (SPECT), positron emission tomography (PET), or dobutamine stress echocardiography (DSE), and patients were followed up for approximately 2 years. Analysis of the combined results demonstrated a strong association between myocardial hibernation identified with noninvasive testing and improved survival after revascularization. Revascularization was associated with a 79.6% reduction in mortality in patients with hibernation: mortality with medical therapy was 16% versus 3.2% with revascularization. Conversely, in the absence of hibernation, there was no significant difference in mortality with revascularization (7.7%) or medical therapy (6.2%). Indeed, selecting patients with residual ischemia or hibernation of the myocardium by pre-interventional noninvasive imaging or functional testing is important, if not a prerequisite to revascularization (2,3).

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In this issue, Gerber et al. (4) now add an additional layer of complexity. They analyzed the relation between the transmural extent of scar and regional improvement of strain parameters such as circumferential shortening (Ecc) at subendocardial, mid-myocardial, and subepicardial level as well as radial thickening strain (Err) at mid-myocardial level. Interestingly, after revascularization, mid-myocardial Ecc and Err improved only up to 25% transmurality, whereas subendocardial Ecc, global ejection fraction, and functional capacity improved up to 75% mean transmurality. Importantly, there is some correlation between mean transmurality of necrosis and recovery of mid-myocardial Ecc, but not with recovery of Err. The improvement of regional function in scar tissue after revascularization must be related to the rearrangement and shortening of fibers in the epicardium, which then influences the endocardial layer. The data need to be seen in relation to 2 major questions in hibernating myocardium.

What Is the Correct Definition of Hibernation?

Whereas different imaging strategies provide different definitions of hibernation (Table 1), the most accepted clinical definition of hibernation is a condition in which dysfunctional, but viable, myocardium is capable of improvement of function after revascularization. However, how do we assess recovery? Is it an improvement of regional wall motion as assessed by echocardiography or cardiac magnetic resonance (CMR) (5)? Or do we need to look at quantitative regional strain parameters such as Ecc and Err as shown by Gerber et al. (4)?

What Is the Optimal Parameter to Select Patients for Revascularization?

This is particularly relevant when complex percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) is undertaken in patients with ischemic cardiomyopathy and severely

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Table 1. Different Imaging Strategies and Surrogate Definitions of Hibernation

Metabolic Imaging	SCAR Imaging	Contractile Reserve
PET/SPECT	Delayed/late (hyper) enhancement	Low-dose DSE/low-dose DSMR
Assessment of functional integrity of myocardial cells	Exact localization + size of necrosis/fibrosis	Assessment of contractile function

DSE = dobutamine stress echocardiography; DSMR = dobutamine stress magnetic resonance; PET = positron emission tomography; SPECT = single-photon emission computed tomography.

impaired left ventricular function. The BCIS-1 (Balloon pump-assisted Coronary Intervention) study (6) recently reported a 6-month mortality of 6% in 301 patients with a mean ejection fraction of 24% and a jeopardy score of 10.5. The STICH (Surgical Treatment for Ischemic Heart Failure) trial showed that adding surgical ventricular reconstruction to CABG reduces left ventricular volume but is not associated with a greater improvement in symptoms or exercise tolerance, or with a reduction in the rate of death or hospitalization for cardiac causes (7). Among other trials, the OAT (Occluded Artery Trial) trial has shown that general revascularization of an infarct-related artery (IRA) by PCI in addition to optimal medical therapy (OMT) is not superior to OMT alone in stable patients in the subacute phase (8). The TOAT (The Open Artery Trial) trial even suggests an adverse effect on late ventricular remodeling when recanalizing occluded IRA in symptom-free patients approximately 1 month after acute myocardial infarction (9). These clinical studies in turn suggest a better selection of patients for a specific treatment to maximize the outcome and minimize the risk.

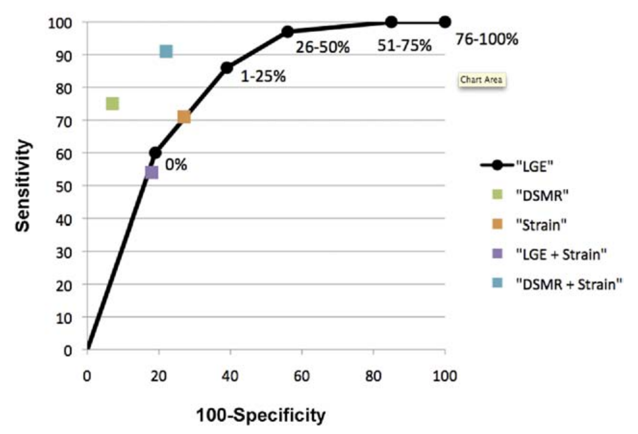

Figure 1. ROC of Different CMR Studies

Receiver-operator characteristics (ROC) of different cardiac magnetic resonance (CMR) studies using either late gadolinium enhancement (LGE) or low-dose dobutamine stress magnetic resonance (DSMR) with or without strain analysis for the assessment of myocardial hibernation. Adapted from Gerber et al. (4), Kim et al. (10), Wellnhofer et al. (13), and Bree et al. (16). Percentage terms refer to the transmural extent of LGE.

Major work, most notably from Kim et al. (10), has shown that late gadolinium enhancement (LGE) can be used to predict functional recovery by distinguishing scarred tissue from nonscarred tissue in different myocardial layers. If patients with dysfunctional myocardium without any or with a low amount of subendocardial scarred tissue were revascularized, regional function improved and global ejection fraction increased. However, even though LGE shows unprecedented sensitivity for the detection of subendocardial infarction due to its excellent spatial resolution (11), it does not provide information on the functional status of the remaining myocardium. This is of special importance for infarction of 1% to 50% transmurality where the likelihood of functional recovery is approximately 50% if only based on scar imaging (Fig. 1). To further discriminate this functional status of the remaining nonscarred myocardium, assessment of contractile reserve is useful. Kaandorp et al. (12) performed a head-to-head comparison between LGE and low-dose dobutamine stress magnetic resonance (DSMR) in 48 patients with chronic myocardial infarction and observed that in segments with an intermediate amount of scar tissue, an intermediate proportion of the segments (42%) showed contractile reserve during low-dose DSMR, suggesting additional value of low-dose DSMR for prediction of functional recovery in these segments. Wellnhofer et al. (13) studied 29 patients with chronic myocardial infarction before and after revascularization and demonstrated that assessment of contractile reserve with low-dose DSMR was superior to scar quantification for the prediction of functional recovery in segments with nontransmural scar tissue.

Recently, Kelle et al. (14) showed that scar tissue (LGE) is more important than contractile reserve (low-dose DSMR) for the prediction of events in medically treated patients with chronic myocardial infarction. However, in patients with large myocardial scar (≥6 segments with scar), contractile reserve is a better predictor of events than scar tissue on LGE CMR.

The main criticism of these studies remains the nonquantitative nature of the functional analysis with high interobserver variability. Assessment of myocardial strain has already been shown to be superior to visual analysis for the detection of ischemia during high-dose dobutamine stress (15). Interestingly, the utilization of strain parameters at rest does not change the predictive value of functional improvement after revascularization (Fig. 1) (16). In contrast, by adding quantitative parameters of regional contraction to low-dose stress testing, a higher accuracy can be reached (Fig. 1) (13,16).

At the current time, it remains elusive whether one of the tests or a combined approach is most suited to predict functional recovery. Also, other parameters, such as ischemia of the peri-infarct zone, might become available and further improve our ability to select the appropriate patient for revascularization (17).

Even though there is strong evidence supporting revascularization of patients with hibernating myocardium, randomized, prospective data on the value of LGE, low-dose DSMR, and strain and their prognostic implications are lacking.

An outcome study, preferably in a multicenter setting, with a thorough definition of hibernation is needed to address which patients to select for revascularization.

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