Not all that hibernates necessarily wakes up

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After validating their superb laboratory model of surgical revascularization of hibernating myocardium, Stone and colleagues¹ have used it to characterize the completeness (or lack thereof) of regional contractile recovery 3 months after coronary artery bypass grafting. This important investigation must be viewed from the proper perspective. It is, after all, precisely this revascularization-based recovery of contractile function in chronically ischemic myocardium that relieves symptoms, improves functional recovery, and prolongs life in our patients undergoing coronary artery bypass grafting. We must remember that first and foremost, the heart is *a pump*. Both the disease processes themselves and their targeted therapeutic interventions (such as coronary artery bypass grafting), gain importance primarily from their effects on the contractile function of the heart.

To move toward perfection in the laboratory modeling of surgical revascularization of hibernating myocardium, the model must first be clinically relevant. This important attribute is not only what renders so many previously reported laboratory models of hibernating myocardium irrelevant, but also what moves the model developed by Dr Rosemary Kelly and associates into the very forefront of this investigative field. To obtain clinical relevance, the laboratory model must accurately reproduce what we know about the surgical revascularization of hibernating myocardium in the clinical setting. The target hibernating myocardium must proven (1) to be viable and noninfarcted, (2) to have an associated coronary artery stenosis with reduced blood flow, (3) to have regionally reduced contractile function, and (4) to have contractile reserve. The experimental model described in this manuscript by Dr Kelly and associates meets all these requirements. Their work is indeed a testament to the fact that hard work accomplishes good science. There have been many attempts at creating animal models of hibernating myocardium. I would argue that none are more clinically applicable to what we cardiothoracic surgeons do than is the swine model that Kelly's laboratory team has designed and is in the process of validating and perfecting.

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Central Message

A superb laboratory model of surgical revascularization of hibernating myocardium demonstrates that full recovery of regional contractile dysfunction takes longer than most of us would have guessed.

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The take-home message from this study seems to be that full recovery of the regional contractile dysfunction that characterizes hibernating myocardium takes longer than most of us would have guessed. As Stone and colleagues¹ point out in their article, this finding opens the gate to an endless list of questions. The biggest question—one that I previously never would have even considered—is whether long-duration chronically ischemic hibernating myocardium *ever* returns to normal. Is there a point beyond which the changes of chronic myocardial ischemia become irreversible? Is it possible that it mimics the myocardial dysfunction associated with long-standing valvular heart disease with which we are all so very familiar? *Duration* and *severity* of myocardial exposure to chronic valvular disease are clearly correlated with the degree of irreversibility of the associated fibrotic myocardial scar formation and contractile injury. Could it be the same with hibernating myocardium? Does all hibernating myocardium ultimately recover, or does hibernating myocardium also lie on a duration and severity-based spectrum of reversibility to irreversibility? When we think of *irreversibility* in the setting of coronary artery disease, we think of myocardial infarction as a result of coronary artery occlusion. Maybe Dr Kelly and her colleagues have

proven that a paradigm shift in our thinking is long overdue. Perhaps the classic model of infarction is not enough to explain *all* the *irreversible* contractile injury that may be associated with chronic myocardial ischemia in the setting of ischemic cardiomyopathy.

What a great spectrum of investigative opportunities has been opened by this study! The testing of adjuvant therapeutic interventions to speed up, or bring to 100% completion, the recovery of the contractile injury of the chronically ischemic myocardium is an obvious avenue that Dr Kelly and her colleagues are well positioned to investigate. Kelly's laboratory has already produced notable work regarding delays in recovery of mitochondrial bioenergetics that may contribute to the delays in contractile recovery in even well-revascularized hibernating myocardium.²⁻⁵ Our subspecialty eagerly awaits their future work to identify the culprit in this delay and determine possible adjuvant interventions to

facilitate the early and *complete* recovery that so many of us have previously assumed happens every time we revascularize chronically ischemic myocardium.

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