JACC: CARDIOVASCULAR IMAGING
VOL. 9, NO. 9, 2016

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcmg.2015.12.019

EDITORIAL COMMENT

A Remedy for the Achilles' Heel of Echocardiography?*

Jan D'hooge, PhD, Frank Rademakers, MD, PhD

Echocardiography remains the modality of choice for diagnosis and follow-up of heart disease, as it is relatively risk-free, mobile (even portable), and, importantly, inexpensive and therefore widely available. Although improvements in ultrasound technology have resulted in faster, more accurate, reproducible, and user friendly methodologies toward the morphologic and functional evaluation of the heart, to date, no robust ultrasonographic methodology is available for clinical routine to determine tissue viability. Because tissue viability is an important boundary condition for treatment options and treatment outcome, patients are often referred, for this reason, for other imaging modalities such as cardiac magnetic resonance or positron emission tomography. Viability imaging could therefore be considered the Achilles' heel of echocardiography.

Not surprisingly, it has thus been an active research topic for decades, and new approaches to assess viability were proposed hand-in-hand with evolutions in ultrasonographic imaging technology. Although it was demonstrated that irreversibly damaged, that is, nonviable, myocardium is thicker than dysfunctional but viable, that is, stunned, myocardium early after reperfusion of acute myocardial infarctions (1), most methodologies did not directly measure tissue properties but rather focused on assessing the variable functional reserve of stunned versus infarcted myocardium. For example, stress echocardiography has demonstrated that stunned segments show preserved contractile reserve, whereas infarcted segments do not (2). Similarly, Doppler myocardial imaging (3) and speckle tracking echocardiography (4) during stress echocardiography provide a similar differentiation but in a more quantitative manner. In the 1980s, it was demonstrated that the cyclic variation of the integrated backscatter could equally distinguish stunned from infarcted myocardium (5). Finally, the assessment of myocardial perfusion using ultrasound contrast echocardiography has been shown to differentiate between both of the ischemic substrates (6).

Without doubt, the major technological evolution of ultrasonographic imaging in the last decade has been fast imaging, and likely, this will be similar in the decade to come. Although the frame rate of echocardiography has always been adequate to look at the gross motion of the heart, it has not been until recently that imaging strategies were proposed that allow imaging the heart at very high temporal resolution with frame rates up to 10,000 Hz. Although it may seem unnecessary to image the heart at this time scale, it does allow extraction of new information that could be of (added) diagnostic value (7).

SEE PAGE 1023

In this issue of *iJACC*, Pernot et al. (8) report an experimental animal study demonstrating the potential use of one of these new parameters in distinguishing infarcted from stunned myocardium. More specifically, the authors used ultrafast imaging to measure the propagation speed of shear waves acoustically induced in the myocardium, thereby estimating local myocardial stiffness. Interestingly, this methodology characterizes the native tissue (mechanical) properties rather than the functional consequences of viability. The authors convincingly demonstrated that stunned myocardium returns to near normal elastic properties within minutes after reperfusion while infarcted myocardium continues to stiffen after reperfusion. Importantly, these findings were not only obtained with the novel ultrafast imaging approach but validated by an independent, invasive estimate of local stiffness.

*Editorials published in *JACC: Cardiovascular Imaging* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Imaging* or the American College of Cardiology.

From Cardiovascular Imaging and Dynamics, Department of Cardiovascular Sciences, KU Leuven–University of Leuven, Leuven, Belgium. Dr. D'hooge collaborates with Philips Healthcare and GE Healthcare. Dr. Rademakers has reported that he has no relationships relevant to the contents of this paper to disclose.

JACC: CARDIOVASCULAR IMAGING, VOL. 9, NO. 9, 2016
SEPTEMBER 2016:1031–3

The findings of Pernot et al. (8) are perfectly in line with those of Pislaru et al. (1). Indeed, on the one hand, Pislaru et al. (1) measured the response of ventricular wall thickness on changing left ventricular pressure as a result of vena cava occlusion; on the other hand, they measured the local tissue deformation (i.e., strain) as a result of left ventricular pressure increase during atrial contraction. Both of these approaches allowed estimating local tissue stiffness and demonstrated that nonviable myocardium is stiffer than viable myocardium early after reperfusion.

An important improvement of the ultrafast imaging methodology proposed by Pernot et al. (8) is that it provides absolute measurements of stiffness. Indeed, although strain induced by atrial contraction in stunned myocardium was different from that of infarcted myocardium in an experimental animal setting (1), translating their methodology to clinical practice is difficult as many confounding factors can result in equally low local strain values during atrial contraction: global left ventricular (LV) dilation; local LV shape and wall thickness changes that are in turn related to infarct size, location and transmurality; changed LV compliance; poor left atrial function; and other factors. Moreover, assessing myocardial stiffness using an absolute value (i.e., kPa), as done by Pernot et al. (8), implies not only that these confounding factors can be mostly neutralized but also that local myocardial stiffness can be compared between individuals. As such, it becomes possible to define clear threshold values to differentiate between viable and nonviable myocardium without the need to correct for confounders. In this context, it appears very promising that the stiffness of nonviable myocardium was an order of magnitude different from that of normal or viable myocardium (12.1 vs. 2.3 kPa, respectively) and that the range of normal values was very narrow (SD: 0.4 kPa).

Does this methodology then finally solve the weak spot of echocardiography? Did we finally get a robust and reliable ultrasonographic methodology to predict functional recovery of segments after reperfusion of an acute myocardial infarction as a first application of viability imaging? Unfortunately, the answer to these questions remains negative for clinical as well as technological reasons. Indeed, in clinical practice, the range of ischemic substrates encountered is more diverse than the 2 extreme situations created in this animal study (i.e., stunned vs. transmural infarction). In particular, nontransmural infarctions will equally often be encountered, resulting in a more heterogeneous substrate that might lead to intermediate stiffness values when measured at the segmental level, thereby complicating the viability classification. Of course, one could hope that the spatial resolution of the ultrafast imaging approach is sufficiently high in order to make a stiffness estimate at different depths across the wall leading to a stiffness image that might be read very similar to a cardiac magnetic resonance delayed enhancement image. This might be the case as the team of Pernot et al. (9) previously demonstrated that the shear wave speed can be measured at different depths across the myocardial wall in order to determine local fiber orientation based on the fact that these shear waves travel faster along the fiber than across them. Unfortunately, this implies that a change in shear wave speed across the wall cannot simply be related to local stiffness as local fiber orientation should be considered. Although this confounder may be corrected for, it does complicate classification.

A more fundamental problem of the proposed methodology might be the technological challenges related to its translation to the clinical setting. Indeed, inducing shear waves in the anterior wall of an open-chest animal preparation and imaging their propagation at ultrahigh frame rate by a linear array transducer in direct contact with the heart is quite distinct from inducing a shear wave in any other wall of a closed-chest patient and imaging its propagation through a narrow acoustic window for the following 3 reasons. First, the induction of shear waves requires sonification of the tissue with sufficient acoustic energy to push the tissue away from the transducer by its acoustic radiation force; this is not obvious farther away from the transducer due to attenuation, particularly when a transducer with a small footprint is used (e.g., a transthoracic phased array), which limits focusing. Second, for the shear wave to be generated and detected using the same (2-dimensional) transducer position as required by the presented methodology, the only echocardiographic view that can be used is the parasternal one; this implies that stiffness can only be measured in the anterior and posterior wall segments. Third, ultrafast imaging is facilitated by linear arrays with a large footprint and therefore an intrinsically large field of view; translation to phased arrays is not straightforward, although solutions are being proposed.

Despite the challenges in translating the proposed methodology to the clinical setting, this study convincingly demonstrates the potential of stiffness imaging of the heart. Although it may not allow mapping local stiffness (changes) bedside in its present implementation, new technological advances may solve this. Moreover, even if local stiffness maps remain unfeasible, the technique presented may still be of great value for example to determine the

aetiology of diastolic heart failure by obtaining a quantitative estimate of (local) ventricular compliance. It is thus clear that this study is just the tip of the iceberg and that many exciting applications of ultrafast cardiac imaging are yet to come. Without doubt, ultrafast cardiac imaging will further strengthen ultrasonography as the cardiac imaging modality, and it is again Paris who finds the weak spot of Achilles; this time not to murder him but rather to help make him truly invincible.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Jan D'hooge, Department of Cardiovascular Sciences, Medical Imaging Research Centre (MIRC), KU Leuven–University of Leuven, Herestraat 49, Leuven 3000, Belgium. E-mail: jan.dhooge@uzleuven.be.

REFERENCES

1. Pislaru C, Bruce CJ, Anagnostopoulos PC, et al. Ultrasound strain imaging of altered myocardial stiffness stunned versus infarcted reperfused myocardium. Circulation 2004;109:2905–10.

2. Watada H, Ito H, Oh H, et al. Dobutamine stress echocardiography predicts reversible dysfunction and quantitates the extent of irreversibly damaged myocardium after reperfusion of anterior myocardial infarction. J Am Coll Cardiol 1994;243:624–30.

3. Bijnens B, Claus P, Weidemann F, Strotmann J, Sutherland GR. Investigating cardiac function using motion and deformation analysis in the setting of coronary artery disease. Circulation 2007;116:2453–64.

4. Gong L, Li D, Chen J, et al. Assessment of myocardial viability in patients with acute myocardial infarction by 2-dimensional speckle tracking echocardiography combined with low-dose dobutamine stress echocardiography. Int J Cardiovasc Imaging 2013;295:1017–28.

5. Milunski MR, Mohr GA, Wear KA, Sobel BE, Miller JG, Wickline SA. Early identification with ultrasonic integrated backscatter of viable but stunned myocardium in dogs. J Am Coll Cardiol 1989;142:462–71.

6. Dourado PM, Tsutsui JM, Mathias W Jr., Andrade JL, da Luz PL, Chagas AC. Evaluation of stunned and infarcted canine myocardium by real time myocardial contrast echocardiography. Braz J Med Biol Res 2003;36:1501–9.

7. Cikes M, Tong L, Sutherland GR, D'hooge J. Ultrafast cardiac ultrasound imaging: technical principles, applications, and clinical benefits. J Am Coll Cardiol Img 2014;7:812–23.

8. Pernot M, Lee W-N, Bel A, et al. Shear wave imaging of passive diastolic myocardial stiffness: stunned versus infarcted myocardium. J Am Coll Cardiol Img 2016;9:1023–30.

9. Lee WN, Pernot M, Couade M, et al. Mapping myocardial fiber orientation using echocardiography-based shear wave imaging. IEEE Trans Med Imaging 2012;31:554–62.

KEY WORDS elasticity, ischemia, myocardial stiffness, shear wave, ultrasonographic imaging