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Scar Detection by Pulse-Cancellation Echocardiography

Validation by CMR in Patients With Recent STEMI

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ABSTRACT

OBJECTIVES This study sought to assess an echocardiographic approach (scar imaging echocardiography with ultrasound multipulse scheme [eSCAR]), based on existing multipulse ultrasound scheme, as a marker of myocardial scar in humans, compared with cardiac magnetic resonance assessing late gadolinium enhancement (CMR-LGE).

BACKGROUND The detection of myocardial scar impacts patient prognosis and management in coronary artery disease and other types of cardiac disease. The clinical experience with echocardiography suggests that the reflected ultrasound signal is often significantly enhanced in infarcted myocardial segments.

METHODS Twenty patients with a recent ST-segment elevation myocardial infarction (STEMI) (cases) and fifteen patients with absent CMR-LGE (negative controls) were imaged with both the eSCAR pulse-cancellation echo and CMR-LGE to assess their potential association.

RESULTS Scar was detectable at CMR-LGE in 19 of 20 STEMI patients (91%), whereas all (100%) demonstrated eSCAR at echocardiography. In the 19 STEMI patients in whom CMR-LGE was detected, regional matching between eSCAR and CMR-LGE was total, although the segmental extent of detected scar was not always superimposable, particularly in the most apical segments, a region in which eSCAR demonstrated undersensitivity for the true extent of scar.

CONCLUSIONS A 2-dimensional multipulse echocardiography allows detection of myocardial scar, reliably matching the presence and site of CMR-LGE at 30 days after STEMI, or its absence in negative controls. (J Am Coll Cardiol Img 2016;■:■–■) © 2016 by the American College of Cardiology Foundation.

The detection of myocardial scar or severely fibrotic areas profoundly impacts patient management and prognostic stratification, both in coronary artery disease and other cardiac conditions (1–5). Myocardial scar detection currently requires nuclear medicine techniques or cardiac magnetic resonance assessing late gadolinium enhancement (CMR-LGE). These methods are costly, time consuming, and unfit for wide population studies; in addition, CMR-LGE is generally contraindicated in patients with cardiac devices. All of these factors limit the widespread clinical use of scar imaging. Clinical experience with echocardiography suggests that patients with a prior myocardial infarction not only demonstrate wall motion abnormalities, but the reflected echo signal is often enhanced significantly in the infarcted myocardial segments (6–8).

We tested a pulse cancellation ultrasound technique (scar imaging echocardiography with ultrasound multipulse scheme [eSCAR]) to differentiate normal from scarred myocardium; the technique is in principle not different from CMR-LGE pulse-inversion technique: 2 ultrasound signals—phase or amplitude shifted—are transmitted and cancel each other when reflected by normal myocardium, but not

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ABBREVIATIONS AND ACRONYMS

2D = 2-dimensional

3D = 3-dimensional

CMR-LGE = cardiac magnetic resonance assessing late gadolinium enhancement

eSCAR = scar imaging echocardiography with ultrasound multipulse scheme

LVO = left ventricle opacification

STEMI = ST-segment elevation myocardial infarction

in case of abnormally fibrotic or disarrayed myocardium, which returns a measurable, nonzero signal, due to nonlinear ultrasound response. In time, eSCAR would bring scar detection to the bedside, potentially expanding scar assessment to any type of patient.

We aimed to establish whether eSCAR is an accurate surrogate for the presence of CMR-LGE in humans, testing patients with a recent ST-segment elevation myocardial infarction (STEMI), versus patients with nonischemic suspect cardiomyopathies and absence of CMR-LGE, who were chosen as negative controls.

METHODS

STUDY DESIGN AND POPULATION. This prospective pilot study enrolled 21 consecutive patients with recent STEMI treated with coronary angiography and primary percutaneous angioplasty (if required), who consented to participate (group A, cases), and 15 patients who underwent CMR-LGE during the same study period for a clinical indication of suspect cardiomyopathy with known normal coronary arteries (or <30% coronary artery stenosis) at recent coronary angiogram performed <6 months before (group B, negative controls). Exclusion criteria were common to both groups and were the presence of prior history of acute coronary syndrome, prior coronary revascularization, severe chronic kidney disease, intracardiac pacing leads or other devices precluding CMR-LGE, hemodynamic instability, or known claustrophobia. The study was performed at the Parma University Tertiary Medical Center, Parma, Italy. Demographic data, clinical characteristics, and concomitant drug therapy were recorded. In the STEMI group, echocardiography was performed between 28 and 32 days after STEMI and CMR-LGE was performed within 72 h after echocardiogram.

In group B (negative controls) the absence of scar at CMR-LGE was part of inclusion criteria, so that echocardiography was performed after their CMR study, within 72 h. Echocardiography was performed using both standard 2-dimensional (2D) and the newly devised eSCAR ultrasound setting, which is detailed below. The same echocardiography imaging protocol was used for both STEMI cases (group A) and control patients (group B). The ultrasound eSCAR data were compared with CMR-LGE results in both groups. The study complies with the Declaration of Helsinki and the locally appointed ethics committee has approved the research protocol and informed consent has been obtained from the subjects.

IMAGING PROTOCOLS. Scar imaging echocardiography with ultrasound multipulse scheme. A standard echocardiography machine (Philips ie33, Philips Medical Systems, Best, the Netherlands), equipped with standard S5 phased array 2D transthoracic probe was used for ultrasound examinations. Although the built-in setting for left ventricle opacification (LVO) is provided by vendors to be used in conjunction with ultrasound contrast, thanks to cancellation of "linear" signals back from normal myocardium, it is incidentally very efficient to enhance signals from abnormal myocardial tissue, such as fibrotic (or calcified) tissues, which on the contrary show "nonlinear" response (similarly to the nonlinear acoustic behavior of microbubbles) (**Figure 1**).

Starting from the 2D standard setting, the "iscan button" on the machine panel was pushed once (set at 0 dB) to automatically normalize gains, and then the built-in 2D LVO setting, originally devised for left ventricle contrast opacification, was activated, exploiting power-modulation/pulse inversion harmonic imaging (transmit 1.6 MHz/receive 3.2 MHz). The LVO setting was tuned to an intermediate mechanical index, between 0.40 and 0.47, and general gain between 70% and 77%, depending on individual patient echogenicity.

This eSCAR setting enhances exponentially contrast between scar and normal myocardium (**Figures 1** and **2**, Online Figure 1, Online Videos 1 and 2).

Each echocardiographic examination comprised at least 2 clips of apical 4-, 2-, and 3-chamber views, which were saved on a hard disk as DICOM and AVI files for offline reading.

CMR-LGE. Patients were examined supine in a 1.5-T imaging unit (Achieva, Philips Medical Systems) equipped with master gradients (30 mT/m peak gradients; 150 mT/m/ms slew rate) and a 5-element cardiac phased-array receiver coil. Images were acquired with the use of electrocardiographic gating and expiratory breath holds. All data were acquired in the true LV short axis, with 10 to 12 contiguous sections as required to cover the entire LV. A dose of 0.2 mmol/kg of body weight of gadopentetate dimeglumine (Magnevist; Bayer Schering Health Care, Cambridge, United Kingdom) was administered intravenously at a rate of 5 ml/s with a power injector. Ten minutes after contrast agent injection, a Look-Locker sequence was performed to obtain the most appropriate inversion time to null the signal intensity of normal myocardium. This was immediately followed by acquisition of LGE images, with an inversion-recovery prepared T1-weighted gradient-echo