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T1 Mapping for Myocardial Extracellular Volume Measurement by CMR

Bolus Only Versus Primed Infusion Technique

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OBJECTIVES The aim of this study was to determine the accuracy of the contrast "bolus only" T1 mapping cardiac magnetic resonance (CMR) technique for measuring myocardial extracellular volume fraction (ECV).

BACKGROUND Myocardial ECV can be measured with T1 mapping before and after contrast agent if the contrast agent distribution between blood/myocardium is at equilibrium. Equilibrium distribution can be achieved with a primed contrast infusion (equilibrium contrast-CMR [EQ-CMR]) or might be approximated by the dynamic equilibration achieved by delayed post-bolus measurement. This bolus only approach is highly attractive, but currently limited data support its use. We compared the bolus only technique with 2 independent standards: collagen volume fraction (CVF) from myocardial biopsy in aortic stenosis (AS); and the infusion technique in 5 representative conditions.

METHODS One hundred forty-seven subjects were studied: healthy volunteers (n = 50); hypertrophic cardiomyopathy (n = 25); severe AS (n = 22); amyloid (n = 20); and chronic myocardial infarction (n = 30). Bolus only (at 15 min) and infusion ECV measurements were performed and compared. In 18 subjects with severe AS the results were compared with histological CVF.

RESULTS The ECV by both techniques correlated with histological CVF (n = 18, $r^2 = 0.69$, $p < 0.01$ vs. $r^2 = 0.71$, $p < 0.01$, $p = 0.42$ for comparison). Across health and disease, there was strong correlation between the techniques ($r^2 = 0.97$). However, in diseases of high ECV (amyloid, hypertrophic cardiomyopathy late gadolinium enhancement, and infarction), Bland-Altman analysis indicates the bolus only technique has a consistent and increasing offset, giving a higher value for ECVs above 0.4 (mean difference ± limit of agreement for ECV <0.4 = −0.004 ± 0.037 vs. ECV >0.4 = 0.040 ± 0.075, $p < 0.001$).

CONCLUSIONS Bolus only, T1 mapping-derived ECV measurement is sufficient for ECV measurement across a range of cardiac diseases, and this approach is histologically validated in AS. However, when ECV is >0.4, the bolus only technique consistently measures ECV higher compared with infusion. (J Am Coll Cardiol Img 2013;6:955–62) © 2013 by the American College of Cardiology Foundation

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Expansion of the myocardial extracellular volume is ubiquitous in cardiac disease, whether as focal scar, diffuse fibrosis, through infiltration in amyloidosis, or edema (1). Extracellular volume expansion might represent a key intermediate phenotype preceding cardiac morbidity and mortality. Recent developments in T1 mapping by cardiac magnetic resonance (CMR) have permitted its noninvasive quantification. This new biological parameter has the potential to provide new mechanistic insights into health and disease states (2,3) and might have the ability to detect early disease, guide therapy, and/or predict outcomes (4).

T1 mapping measures myocardial longitudinal magnetic relaxation, and this can be performed before and after a standard gadolinium-based contrast agent. The contrast agent distributes between cells embedded in the interstitium between cells (extracellular space) and blood plasma such that the relative pre- and post-contrast signal changes measure the myocardial extracellular volume fraction (ECV) (Fig. 1). However, this assumes that a steady-state equilibrium of gadolinium contrast agent exists between blood and myocardium. This can be established by the administration of a primed slow intravenous contrast infusion—a technique known as equilibrium contrast cardiac magnetic resonance (EQ-CMR) (5)—but it is time consuming and adds clinical complexity. One alternative is that at sufficient time after a single contrast bolus, a dynamic equilibrium might exist (6,7)—principally because contrast flux between tissue compartments is faster than renal excretion—allowing the equivalent ECV measurement. This clinically straightforward approach is highly attractive. However, concerns about the "bolus only" approach have been raised (8), and although the technique provides short-term prognostic information (4), it is not validated histologically and has not been tested in distinct disease groups.

We hypothesized that the bolus only technique would be good enough to measure ECV across a range of cardiac diseases. To achieve this we compared our results with 2 independent techniques: firstly, with histology, specifically collagen volume fraction (CVF) (%) in severe aortic stenosis (AS); and secondly, the infusion technique, EQ-CMR.

ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

CMR = cardiac magnetic resonance

CVF = collagen volume fraction (%)

ECV = extracellular volume fraction

EQ-CMR = equilibrium contrast cardiac magnetic resonance

HCM = hypertrophic cardiomyopathy

LGE = late gadolinium enhancement

ROI = region of interest

ShMOLLI = shortened modified look-locker inversion recovery

METHODS

Bolus only and infusion ECV measurements were performed and compared with histological CVF in 18 subjects with severe AS and in a population of 147 subjects with a range of different diseases. In conditions with late gadolinium enhancement (LGE) where the ECV is high, these areas were considered separately.

Patients with atrial fibrillation or a contraindication to contrast CMR examination were excluded from the study. The research received approval from the local research ethics committee, and all participants provided written informed consent.

The study population consisted of:

1. Normal healthy subjects (n = 50, median age 48 [range 24 to 88 years], 51% male) were recruited through advertising within the hospital, university, and general practitioner surgeries. All normal subjects had no history or symptoms of cardiovascular disease or diabetes. Four subjects had been prescribed statin therapy for hypercholesterolemia (primary cardiovascular prevention), but no other normal healthy subject was using any cardiovascular medication. All subjects had a normal blood pressure (defined as <140/90 mm Hg), 12-lead electrocardiogram, and clinical CMR scan.

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