Topographic mapping of left ventricular regional contractile injury in ischemic mitral regurgitation

Timothy S. Lancaster, MD, Julia Kar, PhD, Brian P. Cupps, PhD, Matthew C. Henn, MD, Kevin Kulshrestha, BS, Danielle J. Koerner, and Michael K. Pasque, MD

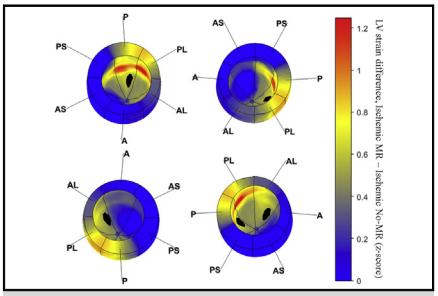
ABSTRACT

Objective: Restrictive leaflet tethering resulting from regional left ventricular (LV) contractile injury causes ischemic mitral regurgitation (MR). We hypothesized that 3-dimensional LV topographic mapping by MRI-based multiparametric strain analysis could characterize the regional contractile injury patterns that differentiate ischemic coronary artery disease patients who have ischemic MR from those who do not.

Methods: Magnetic resonance imaging-based multiparametric strain data were calculated for 15,300 LV grid points in 100 normal volunteers. Strain parameters from ischemic MR (n = 10) and ischemic no-MR (n = 36) patients were then normalized to this normal human strain database with z score quantification of standard deviation from the normal mean. Mean multiparametric strain z scores were calculated for 18 LV subregions (basilar/mid/apical levels; 6 LV regions). Mean strain z scores for papillary muscle-related (basilar/mid levels of anterolateral, posterolateral, and posterior) and nonpapillary muscle-related (all other) subregions were compared between ischemic MR and ischemic no-MR groups.

Results: Across all patients, contractile injury was greater in the papillary muscle-related regions compared with the nonpapillary regions ($P = .007$). In the papillary regions, contractile injury was greater in the ischemic MR group compared with the no-MR group (z scores, 1.91 ± 1.13 vs 1.20 ± 1.01, respectively; $P < .001$). Strain values in the nonpapillary muscle-related subregions were not different between the 2 groups (1.31 ± 1.04 vs 1.20 ± 1.03; $P = .301$).

Conclusions: Multiparametric strain analysis demonstrated severe normalized contractile injury in the papillary muscle-related LV subregions in patients with ischemic MR. The mean degree of normalized injury approached 2 standard deviations and was significantly worse than the levels seen in ischemic no-MR patients. (J Thorac Cardiovasc Surg 2017;154:149-158)



Contractile injury in the papillary regions distinguishes patients with ischemic mitral regurgitation from those without mitral regurgitation.

Central Message

MRI-based 3D topographic mapping of regional LV contractile injury patterns differentiates patients with ischemic MR from patients without ischemic MR.

Perspective

Because mitral leaflet tethering from regional left ventricular contractile injury is the root cause of ischemic mitral regurgitation, characterization of associated contractile injury distribution may affect management. The imaging and analytical capabilities necessary to perform a high-resolution topographic 3-dimensional mapping of regional contractile injury have only recently become clinically available.

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Ischemic mitral regurgitation (MR) is characterized by a structurally normal mitral valve (MV) with regurgitation due to left ventricular (LV) dysfunction.[1] The primary root cause of

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From the Division of Cardiothoracic Surgery, Washington University School of Medicine, Barnes-Jewish Hospital, St Louis, Mo.

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Address for reprints: Michael K. Pasque, MD, Washington University School of Medicine, 660 S Euclid Ave, Campus Box 8234, St Louis, MO 63110 (E-mail: pasquem@wudosis.wustl.edu).

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Abbreviations and Acronyms
3D = 3-dimensional
CAD = coronary artery disease
LV = left ventricle
MR = mitral regurgitation
MRI = magnetic resonance imaging
MV = mitral valve

ischemic MR is restrictive leaflet tethering resulting from regional LV ischemic contractile injury.[2] Displacement of the papillary muscles, especially the posteromedial papillary muscle, leads to restrictive tethering and deformation of the MV leaflets with impaired leaflet coaptation and resulting regurgitation.[3,4] The regional distribution of the ischemic contractile injury is key in determining the occurrence, severity, and exact mechanism of subsequent MR in patients with coronary artery disease (CAD) and myocardial infarction.[1,5]

Until recently, the standard of care in the surgical treatment of ischemic MR has been revascularization combined with undersized mitral ring annuloplasty. Unfortunately, recent randomized trial data have demonstrated recurrence of at least moderate MR in up to 59% of patients undergoing MV repair by 2 years of follow-up, in comparison to only 4% of patients undergoing MV replacement.[6,7] Although these results suggest that the long-term outcomes of MV replacement may be superior to MV repair, the higher perioperative mortality, sacrifice of the native valve apparatus, potential long-term prosthesis deterioration, and need for anticoagulation associated with MV replacement cannot be overlooked.[2,8-10] Given the considerable disadvantages of MV replacement, the remaining 40% of patients who may do well with MV repair should not be abandoned to valve replacement for a lack of clinically applicable prognostic metrics.

Because recurrent or persistent MR after annuloplasty repair is likely to occur by the same mechanism as primary ischemic MR (ie, leaflet tethering by ischemia-induced regional contractile injury and remodeling), regional contractile injury distribution patterns have potential to predict repair failure in ischemic MR. Whereas several echocardiographic features have been shown to correlate with MR recurrence after MV repair, including measures of leaflet and chordal geometry[11-14] and measures of LV remodeling,[15-18] these are all indirect surrogates of the regional ventricular contractile dysfunction responsible for ischemic MR. Logically, our first goal must be the full characterization of the ischemia-induced contractile injury distribution patterns that are associated with preoperative ischemic MR, because variants of these prognostic patterns have the highest likelihood of providing metrics to predict recurrent or persistent MR after repair.

Although speckle-tracking echocardiography can supply some degree of quantitative measurements of global and regional contractile function, cardiac MRI is widely regarded as the most accurate imaging modality for quantitative assessment of LV function.[19,20] A high-resolution, highly quantitative characterization of regional contractile function is necessary to uncover the complexities of the contractile injury distribution that causes ischemic MR. Only recently has a quantitative description of truly 3-dimensional (3D) regional LV contractile function by regional 3D strain calculation from MRI-derived LV displacement data become clinically available. We have demonstrated the high reliability of MRI-based multiparametric strain topographic mapping in the quantification and localization of regional LV contractile injury in patients with CAD.[21] As a first step in evaluating the clinical application of this technology to ischemic MV disease, we sought to fully map the associated distribution patterns of regional contractile injury in patients with ischemic MR. We hypothesized that topographic strain mapping of regional LV contractile function could characterize the regional contractile injury patterns that differentiate ischemic CAD patients who have MR from those who do not.

METHODS

Study Participants

The Institutional Review Board of Washington University School of Medicine approved this study, and all subjects gave written informed consent. One hundred forty-six total study participants were enrolled in the study and underwent cardiac MRI with radiofrequency tissue tagging. One hundred of these participants were normal, healthy volunteers with no historical, physical, or clinical evidence of heart disease who contributed complete strain parameter information to a normal human strain database. The remaining 46 participants were patients with ischemic CAD, 10 of whom had ischemic MR and 36 of whom had ischemic CAD without MR. CAD was defined as $\geq$ 1 lesion of $\geq$ 70% stenosis on coronary angiography as interpreted by an independent cardiac catheterization laboratory blinded to study results. MR was defined as moderate ($\geq$ 2) or greater MR as determined by an independent echocardiography laboratory blinded to study results. Restricted leaflet motion was the cause of the MR in all 10 patients with ischemic MR.

Cardiac MRI

All imaging studies were carried out using a 1.5T scanner (Siemens, Erlangen, Germany). Short-axis grid-tagged MR images were acquired in a stack starting at the level of the MV and extending to the apex of the LV, whereas long-axis line-tagged images were acquired in 4 radially oriented planes intersecting at the approximate center of the LV cavity (Figure 1, *A*). In each imaging plane, a spatial modulation of magnetization radiofrequency tissue-tagging preparation was applied, followed by a 2-dimensional balanced steady-state free precession cine image acquisition.[22,23] This process creates markers on the myocardium that deform with the tissue, which allows for quantification of wall motion. Typical imaging parameters were repetition time 32.4 ms, echo time 1.52 ms, field of view 350 $\times$ 350 mm, flip angle 20°, tag spacing 8 mm, and slice thickness 8 mm.

Strain Analysis

Strain measurements were obtained for all study participants using an established and validated method developed at our institution.[24-27] Clinical validation of this methodology has demonstrated resistance to interobserver variability.[28,29] Endocardial and epicardial wall boundaries were manually identified on each of the images. Tag lines were tracked