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Evaluation of Myocardial Strain in Patients With Amyloidosis Using Cardiac Magnetic Resonance Feature Tracking

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A B S T R A C T

Purpose: To study the use of cardiac magnetic resonance (CMR) feature tracking technique in evaluation of myocardial amyloidosis.
Materials and Methods: CMR scans of 28 patients with biopsy proven myocardial amyloidosis and 35 controls were reviewed. Conventional short axis, vertical long axis, and 4-chamber cine steady-state free precession images from CMR scans were used to generate radial, circumferential, and longitudinal myocardial strain maps using feature tracking software. Global and regional peak radial, circumferential, and longitudinal strain values were computed.
Results: There were significant decreases in radial, circumferential, and longitudinal strains in patients with myocardial amyloidosis globally and across layers (all $P < 0.001$). Strain was relatively preserved for the apex and most affected for the basal level. The area under the receiver operating characteristic curve for base peak radial, circumferential, and longitudinal strain 0.899, 0.884, and 0.866 and cut offs of 22.9, −13.3, and −10.9, respectively, were determined by receiver operating characteristic analysis. CMR feature tracking strain analysis of base-level strain parameters was able to differentiate patients with myocardial amyloidosis from those without myocardial amyloid with high sensitivity (82.5%) and specificity (82.9%) particularly for radial strain. The maximum sensitivity (89.3%) was achieved if any of the 3 parameters were abnormal, and the maximum specificity (88.6%) when all 3 parameters were abnormal.
Conclusion: Myocardial amyloidosis produces significant changes in regional and global strain parameters, and the peak radial and circumferential strain are the most affected at the basal layer.

Introduction

Amyloidosis is the extracellular deposition of insoluble proteinaceous material in organs and tissues in the body. The main forms of amyloidosis that involve the heart are AL (immunoglobulin light chain), ATTR (familial), AApoA1, senile systemic, AA, and AANP (atrial natriuretic peptide); however, cardiac involvement is most common in AL type amyloidosis, which is associated with multiple myeloma and results in diffuse infiltration of the myocardium. In most patients, the disease may already be in its advanced stage at the time of diagnosis, and the mortality rate may reach up to 30%.[1,2] Endomyocardial biopsy is the current gold standard for the diagnosis of myocardial amyloidosis, which, however, is an invasive technique. For the noninvasive diagnosis of myocardial amyloidosis, late gadolinium enhancement (LGE) magnetic resonance imaging (MRI) is the modality of choice, which shows diffuse left ventricular thickening with characteristic subendocardial enhancement.[3] However, certain patient- and disease-related factors may not allow performance of the LGE images or render them nondiagnostic or both. Sometimes, the LGE images are technically limited owing to the patient's inability to sustain a long breath hold needed for the acquisition of these images. Also, a subset of patients cannot tolerate contrast owing to poor renal function. In addition, the myocardial involvement in amyloidosis can be patchy and LGE images may not be entirely diagnostic. Moreover, early myocardial involvement may not be apparent on LGE MRI. Thus, an alternative technique for evaluation of myocardial amyloidosis is needed that can supplement the current techniques.

Ideally, the novel technique should not be dependent on administration of contrast, relatively easy to perform, robust, and accurate in diagnosis of cardiac amyloidosis. One such technique is myocardial feature tracking (MFT) which depends on measurement of myocardial strain, that is defined as the percentage of shortening or lengthening of a small element of myocardium in relation to its original length.[4,5] The strain can be studied in 3 dimensions, radial, circumferential, and longitudinal corresponding to the contractility of the cardiac myocyte. Strain analysis allows objective assessment of the degree of myocardial

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deformation and its timing during the cardiac cycle. However, it is not dependent on administration of intravenous gadolinium contrast, which is easy to perform and provides multidimensional, load independent information of myocardial contractility. Echocardiography with Doppler imaging and cardiac magnetic resonance (CMR) tissue tagging technique has been widely used to measure myocardial strain.[5-8] Doppler echocardiography measures longitudinal, radial, and circumferential myocardial motion parameters. However, it lacks spatial resolution, is highly user dependent, and not infrequently limited by body habitus. Grid tagged CMR strain analysis technique involves magnetization of saturation bands in a grid format that are placed onto the myocardium at the start of the cardiac cycle.[5] Although CMR grid-tagging technique is the present reference standard for assessment of myocardial motion, it requires prospective acquisition of grid-tagged images and complex postprocessing analysis, which may be time consuming,[9] although advances in software and postprocessing techniques are being made. Moreover, the grid tags gradually fade during the cardiac cycle owing to tissue T1 relaxation and imaging radiofrequency pulses, which hampers the assessment of regional myocardial function, such as relaxation of heart during diastole.[5] On the contrary, CMR feature tracking (CMR-FT) strain analysis (2D Cardiac Performance Analysis, Tom Tec, Germany; CVI42-Tissue Tracking, Circle Cardiovascular Imaging, Canada) technique can use the routine multiplanar cine images for strain analysis, hence being easier to incorporate as part of routine cardiac protocol. There is no requirement of special tagged images. The software tracks the cardiac contour and its movement from frame-to-frame to quantify myocardial deformation over the cardiac cycle. CMR-FT technique has been used to measure global and regional myocardial strain in normal individuals.[9] It has also been used in other cardiac conditions, such as Wegener granulomatosis and ischemic cardiomyopathy[10-16]; however, to our knowledge, there are no published studies on the use of MFT for strain analysis in patients with amyloidosis.

In this study, we evaluate the CMR-FT technique for strain evaluation in patients with amyloidosis. The goals of this pilot project are 2-fold. We aim to demonstrate the feasibility of this technique in the diagnosis of cardiac amyloidosis using global radial, circumferential, and longitudinal strain values. We also evaluate the regional pattern of myocardial strain in the base, mid, and apical ventricular levels in patients with cardiac amyloidosis. Our hypothesis is that MFTtechnique would be able to differentiate patients with cardiac amyloidosis compared with normal cases based on differences in global systolic strain, and we would be able to delineate a regional pattern of strain values specific to amyloidosis.

Materials and Methods

Institutional review board approval was obtained for this Health Insurance Portability and Accountability Act compliant retrospective study.

Study Population and Image Acquisition

A retrospective review of CMR scans done at our institution over the past 5 years was performed. Overall, 28 patients (19 males and 9 females; mean age 62.3 years) with biopsy proven myocardial amyloidosis and 35 controls (20 males and 15 females; mean age = 61 years) were included in the study group. All patients in the cardiac amyloidosis group had evidence of amyloidosis on late gadolinium enhanced (LGE) images. The control group consisted of all patients who were referred for MRI and had normal LGE MRI. For myocardial strain analysis conventional short axis, vertical long axis, and 4-chamber cine images using steady-state free precession (SSFP) sequences on a 1.5T clinical CMR scanner (Avanto, Siemens, Erlangen, Germany) were reviewed. The SSFP sequence had the following parameters TR: 35-40 ms, TE = 1.3 ms, flip angle = 80°, number of excitations (NEX) = 1, slice thickness = 8 mm, 256 × 232 matrix, and 25 cardiac phases. These scans were used to generate radial, circumferential, and longitudinal myocardial strain maps using MFTsoftware (CVI42-Tissue Tracking, Circle Cardiovascular Imaging, Canada).

Image Analysis

All images were interpreted by a cardiac radiologist with 20 years of experience in radiology on a PACS workstation (Sectra PACS, Sectra AB Inc, Linköping, Sweden). After the strain mapping, separate radial; circumferential; and longitudinal strain parameters were generated.

Image Selection

To generate the strain maps the short-axis stacks, 2-chamber and 4-chamber SSFP images were imported into the feature tracking software. For the 4-chamber long axis, we chose image most central to the tricuspid valve and which had the clearest myocardium The series composer tool was used to create a full short-axis stack. Any slices, which had replacements taken, are checked and replaced with the newer images if they are of a better quality. The short axis stack and the long-axis 4-chamber stack were then loaded into the tissue tracking module. For the short axis, all trackable images between the base and apex were used. Basally, images that had significant tricuspid or pulmonic systolic presence were not used. Apically, slices that contained too much through-plane motion were also not used.

Contouring

The myocardial valvular plane and left ventricle (LV) apex were identified in long-axis views and the anterior-posterior insertion points of the right ventricle were defined on the cine short-axis stacks. A long axis LV extent contour was also used to define the systolic excursion of the mitral valve. The FT software identified and generated the endocardial and epicardial contours automatically. The septum was included in the endocardial and epicardial contours. All images were contoured at end diastole, unless the LV wall was not visible at this phase owing to artifacts (eg, brightening from surrounding fat). In these cases, the phase with the best free wall visualization was used, typically a phase closer to systole.

Quality Control

The contours were checked for adequacy by the cardiac radiologist, with ability to perform manual override if needed, after which the software performed the strain analysis. It involves refining the contours to optimize their tracking. We used the cine loop and turned on the boundary points overlay to ensure adequate quality control of the tracking software. The boundary points reflect the movement of the tracking algorithm, and any time this does not appear to reflect the actual motion of the myocardium, the contours are adjusted to improve the tracking. If the boundary points move too far in, and end up in the blood pool at systole, then the contours must be adjusted outwardly. If the boundary points are too far out and ending up extracardiac during systole, then the contours were adjusted inwardly. If large artifacts such as from the bright epicardial fat were present that obscured entire portions of myocardium, yielding nondiagnostic results, then these portions were to be excluded from analysis. This exclusion was considered acceptable for this study, as the LV segments were not broken up individually in each short-axis plane, but only as layers (basal, mid, and apex).