Noninvasive Diagnosis of Cardiac Amyloidosis by MRI and Echocardiography

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Summary: This study described the radiological features on echocardiography and MRI specific to cardiac amyloidosis confirmed on biopsy. Eleven cases of biopsy-proven cardiac amyloidosis were retrospectively reviewed in this study. All patients underwent biopsy, cardiac MRI and echocardiography. The main echocardiography and MRI findings were as follows: diffuse ventricular and septum wall thickening, atrial enlargement, pericardial effusion, restricted left ventricular (LV) systolic and diastolic function, characteristic granular sparkling of myocardium. MRI revealed a characteristic pattern of global subendocardial late enhancement, extending in varying degrees into the neighboring myocardium. The findings agreed with the infiltration distribution of amyloid protein. Typical abnormalities seen on echocardiography and MRI should have important diagnostic and prognostic value of cardiac amyloidosis. MRI should be considered in the diagnosis of cardiac amyloidosis if echocardiographic features are suspicious.

Key words: amyloidosis; cardiomyopathy; cardiac MRI; echocardiography; diagnosis

1 MATERIALS AND METHODS

1.1 Patients and Controls

We retrospectively studied 11 patients (eight males, three females) from the Centre of Cardiology of the Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (China) between 1993 and 2008. All patients had histological confirmation of amyloidosis by tissue biopsies, who ranged in age from 37 to 75 (mean 56.5). All patients had clinical assessment, electrocardiograph, echocardiography as well as cardiac MRI, in addition, 9 of them had been assessed by delayed contrast enhancement cardiac magnetic resonance (DCE-CMR). Of the 11 patients, 9 had low voltage QRS, and 4 had pseudoinfarct (acute or old) pattern, abnormal Q wave and ST-T changes. Coronary angiography and coronary CT angiography demonstrated normal coronaries. Seven of the patients died after the study data was collected (ranged in age from 37 to 68 years), and one lost to follow-up. Because this study was a retrospective review of clinical cases, no ethics committee approval was required.

1.2 CMR and CMR Analysis

Electrocardiographically gated CMR was performed on a 1.5T Magnetom Avanto (Siemens Medical Systems, Germany). Cine MR images were acquired using a steady state free precession (SSFP) acquisition in the vertical long-axis, horizontal long-axis, and short-axis orientations with following parameters: TR 270 ms, TE 1.12 ms, flip angle 80°, slice thickness 6-8 mm, FOV 360 mm. Left ventricular function was obtained with cine images in short-axis slices covering the ventricles and in 4-chamber, 2-chamber orientations. Late gadolinium enhancement images were obtained in the same slice location using inversion recovery Truefisp sequence with magnitude and phase sensitive reconstruction (PSIR) 10−15 min after intravenous administration of a gadolinium-DTPA bolus (0.2 mmol/kg, Bayer-Schering, Germany) with the following parameters: TR 270 ms, TE 3.36 ms, flip angle 80°, slice thickness 6−8 mm, FOV 360 mm. Left ventricular end-diastolic volumes, end-systolic volume, left ventricular ejection fraction, and left ventricular mass were analyzed by using
Syngo Argus software on a workstation. Contrast images were used to evaluate the distribution pattern. Images were interpreted independently by two radiologists with training and experience in cardiac MRI.

### 1.3 Echocardiography

Echocardiography was performed on a HP Sonos 7500, Siemens Sequoia 256, GE Vivid7, Philips iE33 ultrasound system with a phased array transducer (2-5 MHz) where standard two-dimensional and Doppler echocardiography were used as well as pulsed and color myocardial TDI. A parasternal 4-chamber, apical 4-chamber, and long-axis view was used for the following M-mode echocardiographic measurements: biventricular and biatrial internal diameter, left ventricular wall thickness, interventricular and atrial septal thickness all measured at end diastole. Left ventricular ejection fraction was calculated by Simpson’s modified biplane method. Peak early (E) and late (A) diastolic velocities were measured from pulsed wave Doppler recordings of the mitral and the tricuspid flow velocities respectively, and E/A ratio was calculated. Left ventricular early (E) wave deceleration time (DT) was measured from the peak to the zero velocity of the E-wave.

### 2 RESULTS

#### 2.1 CMR Results

The thickness of the left ventricular wall and/or interventricular septum was increased in all patients (thickness at end diastole >1.5 cm; range 1.5-2.7 cm). In 5 of the patients, increased thickness of the atrial septum was also evident (thickness at end diastole >0.6 cm). CMR also confirmed left atrial enlargement in 7 patients, right atrial enlargement in 4 patients, the pleural effusion in all patients and pericardial effusion in 9 patients. Seven of the patients had increased left ventricular mass index, 2 had increased left ventricular systolic volume, and 6 had impaired left ventricular ejection fraction (<50%). Myocardial delayed contrast enhancement was present in 8 of the 9 patients. In 4 of them, DCE was distributed over the global subendocardial circumference, as well as the papillary muscles and valve leaflets in one case(fig. 1A, B, C and D). In 2 cases, DCE was affected in areas of transmural left ventricular wall. In other 2 cases, DCE was demonstrated in areas of subendocardium and midwall.

![Fig. 1 MRI images in a 51-year-old man with CA](image)

Cine MRI (A, C) and DCE-MRI (B, D) in the cardiac long-axis and short-axis plane. A thickened left ventricular wall can be clearly seen, as well as atrial and ventricular septal wall thickening(A). Note the presence of thickening of the papillary muscles, as well as the presence of a right pleural effusion and a small pericardial effusion (C). A diffuse, global, subendocardial enhancement with a dark subepicardial and mid-wall layers, involving biventricular, atrial septal wall (B), the valve leaflets and the thickening papillary muscles (D)

#### 2.2 Echocardiography Results

All patients tested on echocardiography showed increased interventricular septum thickness (>1.3 cm) and/or left ventricular lateral wall thickness (>1.1 cm). Increased thickness of the atrial septum was also found (thickness at end diastole >0.6 cm) in 5 patients, and 7 patients had enlarged atrial internal diameter. Myocardial echoes of interventricular septum and free wall of left ventricle were enhanced, and 6 had “ground glass” or “sparkling” appearance of walls (fig. 2 A and B). Mild-moderate hydropericardium was found in 9 patients, and pleural effusion in 10 patients. Five patients had depressed left ventricular systolic function (LVEF<50%), and 10 had a restrictive left ventricular filling pattern (The Doppler transmitral flow showed the peak E velocity and E/A ratio were decreased, whereas the peak A velocity and deceleration time of E velocity were increased).

#### 2.3 Histopathological Results

All patients had histological confirmation of amyloidosis by tissue biopsies. In 3 cases, the diagnosis was proven by endomyocardial biopsy. Two patients were proven by both endomyocardial biopsy and tongue muscle biopsy. One patient was proven by endomyocardial biopsy and gastrocnemius skeletal muscle biopsy. Five cases had histological confirmation of amyloidosis by tongue muscle biopsy. Histological assessment of these patients was indicated by interstitial expansion with amyloid protein of apple-green birefringence when stained with Congo red and viewed under a polarizing microscope (fig. 3A and B). Gastrocnemius skeletal muscle biopsy demonstrated deposits composed of non-branching fibrils viewed under the electron microscopy with a diameter of 7.5 to 10 nm (fig. 4).

![Fig. 2 Echocardiography in a 53-year-old man with CA](image)

Echocardiographic showing left ventricular thickening and biatrial enlargement. The mitral valve leaflets are thickened (A). The echoes presented as ground glass-like images, with spotty hyperechoes in ventricular septal wall (B).