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Evaluation of Delayed Enhancement Pattern of Cardiac Amyloidosis with Cardiac MRI in Patients with Subcutaneous Fat Biopsy Proven Amyloidosis

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Abstract

Background: Amyloidosis is an important infiltrative cardiac disease and recognition of imaging findings is crucial. This study was performed to determine the delayed enhancement pattern in patients with cardiac amyloidosis in Shahid Rajaei Heart Center. Materials and Methods: In this case series study, 30 patients with amyloidosis (confirmed by Subcutaneous Abdominal Fat biopsy) in ShahidRajaeiHeartCenter in Tehran, Iran in 2016 and 2017 were enrolled and the presence of delayed enhancement patterns of cardiac amyloidosis were determined in them. Results: Results showed that 46.7% had no enhancement, 40% had subendocardial, 3.3% subepicardial, 3.3% transmural, and 6.7% patchy pattern, respectively. The subendocardial pattern was significantly higher in amyloidosis cases (P=0.030). Conclusion: Overall, it may be concluded that subendocardial enhancement pattern is more common in patients with amyloidosis and it may be used as a diagnostic index.

Keywords: Amyloidosis, Enhancement, Subendocardial.

Introduction

Amyloidosis is an important infiltrative cardiac disease and early recognition by using cardiac imaging has an important role in the management, although, the prognosis is still poor and depends on the underlying disease (Murakami et al., 2014; Aster et al., 2009; Mohty et al., 2013). Imaging modalities such as trans-thoracic echocardiography, radionuclide scan, and cardiac magnetic resonance imaging (MRI) can be used to assess cardiac involvement (Mohty et al., 2013). MRI has the highest resolution and contrast demonstrates the function, morphology, and amyloid deposition in myocardial tissue simultaneously (Mohty et al., 2013; Syed et al., 2010).

Tissue characterization may be attained by late post-Gad enhancement which is due to substitution of myocytes with amyloid proteins leading to delayed absorption of contrast media seen as a bright high signal area (Maceira et al., 2005). This delay may be seen with different patterns useful to distinct various cardiac disorders (Syed et al., 2010; Maceira et al., 2005). If some types of late post-Gad enhancement found to be related to amyloidosis, the disease may be diagnosed and treated promptly. This study was performed to determine the delayed enhancement pattern in patients with cardiac amyloidosis. This matter would be useful in differentiation between various types of cardiac disease from amyloidosis.

Materials and Methods

In this case series, 30 consecutive patients with amyloidosis (confirmed by Subcutaneous Abdominal Fat biopsy) in Shahid Rajaei Heart Center, Tehran, Iran in 2016 and 2017 were enrolled and delayed enhancement patterns in them were determined. All patients signed a consent form and were informed about the study protocols and any probable harmful effects following the injection of contrast. This study was also approved by the local ethics committee of Iran University of Medical Science and there are no ethical issues to be declared.

Subcutaneous Abdominal Fat by biopsy was the gold-standard diagnostic method of amyloidosis in current study.

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MRI was done with 3 Plane 2Dimensional (2D) True-Fisp Localizer; 2 Chamber, 3 Chamber, 4 Chamber, Short-Axis, right ventricular outflow tract (RVOT) Retrospective Cine 2D True-Fisp MR Imaging; Pre-Gd T1w Turbo-Spin Echo MR Imaging; T2w Turbo-Spin Echo MR Imaging; 4 Chamber,2 Chamber, Short-Axis Short-Tau-Inversion-Recovery (STIR) MR Imaging; Dynamic T1w Fast-Low-Angle-Shot Contrast Enhanced Perfusion Short-Axis MR Imaging; Early True-Fisp post-Gd (Gadolinium) MR Imaging; Post-Gd T1w Turbo-Spin Echo MR Imaging; and Late phase-sensitive inversion recovery post-Gd MR Imaging (TI=200 to 500) performed after 2 and 20 minutes delay. Enlarged myocardial mass and atrial structure and also atrial and ventricular dysfunction and other morphological characteristics of restrictive cardiomyopathy were assessed and other presentations of amyloidosis on caridiac MR imaging were late gadolinium enhancement and also prolonged T1 times and the expansion in extracellular volume.

Data analysis was performed among 30 subjects by SPSS (version 20.0) software [Statistical Procedures for Social Sciences; Chicago, Illinois, USA]. Kolmogorov-Smirnov, Chi-Square, and analysis of variance (ANOVA) tests were used and were considered statistically significant at P values less than 0.05.

Results

Mean age was 56.57 ± 11.5 years. Twenty-two patients (73.3%) were male. As shown in Table 1, 46.7 % of patients had not any enhancement pattern. However, 40% of patients had sub-endocardial pattern, 3.3% had sub-epicardial pattern, 3.3% had transmural and 6.7% had patchy enhancement pattern (Figure 1).

Mitral regurgitation (MR), tricuspid regurgitation (TR), Aortic insufficiency (AI), and pulmonary insufficiency (PI) were seen in 53.3%, 53.3%, 23.3%, and 6.7%, respectively. Non-of subjects had valve stenosis. Imaging was high probability for cardiac amyloidosis in 18 cases (80%).

Valve regurgitation and insufficiency was not related to enhancement pattern. The age and gender were not related to enhancement pattern as shown in Table 2 and 3 ($P > 0.05$). The subendocardial pattern was related to amyloidosis ($P=0.030$) (Table 4).

Discussion

In this study, the enhancement pattern in amyloidosis cases was assessed and it was found that subendocardial pattern was related to amyloidosis disease. Different research studies have beenconductedin this matter worldwide ((Mesquita et al., 2013; Slaughter & Strugnell, 2006; Hashimura et al., 2016; Fikrle et al., 2016; Gillmore et al., 1997; Wechalekar et al., 2016; Pepys, 2006; Falk et al., 2016; Georgiades et al., 2004; Loizos et al., 2014). Alicia Maria Maceiraand collegues (Maceira et al., 2005). assessed 30 patients with amyloidosis and 16 control subjects with late Post-Gad enhancementand T1 mapping. They found that subendocardial regions had higher contrast media accumulation versus mid-wall and subpericardium regions. It was seen in 69 percent of their study subjects. They declaimed 97% accuracy rate for simultaneous use of two methods. However, a single method was also useful in our study. Mesquita and co-workers (Mesquita et al., 2013) reported that late post-Gad was a good diagnostic tool for amyloidosis.

(Mohty et al., 2013). reported in a review article that cardiac MRI and late post-Gad enhancement roles are controversial and further studies should be performed in this topicWhich indicates the importance of our study. (Slaughter & Strugnell, 2006). Reported high-signal in relatively all patients with amyloidosis but there was no significant pattern. However, they only assessed ten patients and reported no especial enhancement pattern for the patients with amyloidosis (Slaughter & Strugnell, 2006;Zhao et al., 2016) reported that cardiac MR with late gadolinium enhancement as well as our study would provide high diagnostic accuracy for disgnosis of amyloidosis with possible cardiac involvement. As reported by (El Issa et al., 2018) cardiac MR may be considered a good diagnosis method for amyloidosis especially because the biopsies are not easy and routine measures.

As reported by (Oda et al., 2017) myocardial strain analysis by cardiac MR would help to detect amyloidosis with late gadolinium enhancement without the need to contrast medium. The importance of cardiac MR would be more emphasized with consideration of some studies such as those by (Magesh et al. 2017) that presented a case of amyloidosis with negative congo red staining, manifesting with mainly cardiac features. Fikrle et al., 2016) assessed 20 amyloidosis patients and found that transmural and subendocardial enhancement patterns were the most common ones totally seen in 77 percent of cases. We also found that subendocardial pattern was the most common enhancement pattern in amyloidosis patients. Among our limitations, small sample size and lack of consideration of some variables such as the types of amyloidosis due to lack of definite diagnostic assessment by genetic counseling may be mentioned.

Conclusion

Overall, we have investigated the CMR features of cardiac amyloidosis in patients with subcutaneous fat biopsy proven amyloidosis. It may be concluded that subendocardial enhancement pattern is more common in amyloidosis patients and it may be used as a diagnostic index. However, an endomyocardial biopsy which is a gold standard diagnosis for cardiac amyloidosis is needed in order to confirm these findings as a diagnostic marker. Forasmuch as we did not use endomyocardial biopsy for our patients, this can be considered as another limitation of this study. Further studies with larger sample size and multi-center sampling would develop more definite results in this topic of research with more generalization ability.

Table 1- Enhancement pattern in the patients.

Enhancement pattern	Frequency	Percent
None	14	46.7
Subendocardial	12	40
Subepicardial	1	3.3
Trans-mural	1	3.3
Patchy	2	6.7
Total	30	100

the most common enhancement pattern in patients was subendocardial

Table 2- Enhancement pattern in the patients according to age.

Enhancement pattern	Mean age	Standard deviation
None	56.7	9.3
Subendocardial	57.4	11
Subepicardial	56.0	---
Trans-mural	76.0	---
Patchy	41.0	22.6
Total	56.6	11.5

There was not any significant difference between different enhancement patterns and age of patients ($P \geq 0.05$)

Table 3- Enhancement pattern in the patients according to gender.

Enhancement pattern	Male	Female
None	7 (31.8%)	7 (87.5%)
Subendocardial	11 (50%)	1 (12.5%)
Subepicardial	1 (4.5%)	---
Trans-mural	1 (4.5%)	---
Patchy	2 (9.1%)	---
Total	22 (100%)	8 (100%)

There was no significant difference between different enhancement patterns and gender of patients ($P \geq 0.05$)

Table 4- Enhancement pattern in the patients according to amyloidosis.

Enhancement pattern in cardiac MRI	With high probability of cardiac amyloidosis	Without probability of cardiac amyloidosis
None	5 (27.8%)	9 (75%)
Subendocardial	11 (61.1%)	1 (8.3%)
Subepicardial	1 (5.6%)	---
Trans-mural	---	1 (8.3%)
Patchy	1 (5.6%)	1 (8.3%)
Total	18 (100%)	12 (100%)

Subendocardial enhancement pattern were significantly higher in patients with amyloidosis ($P = 0.03$)

Financial Disclosure and conflict of interest:

Authors have no financial interests and conflict of interest related to the material in the manuscript to be declared.

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Fig. 1. Three differen enhancement patterns in patients with cardiac amyloidosis in this study. A: Transmural pattern, B: Patchy enhancement pattern and C: Subendocardial patter

Fig. 2. Three different enhancement patterns in patients with cardiac amyloidosis in this study. A: Transmural pattern, B: Patchy enhancement pattern and C: Subendocardial pattern