Case Report

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대한영상의학회지

Treatment Response Evaluation of Cardiac Amyloidosis Using Serial T1- and T2-Mapping Cardiovascular Magnetic Resonance Imaging

T1 지도화 기법 심장 자기공명영상 추적 검사를 이용한 심장 아밀로이드증의 치료 반응 평가

Jinwoo Son, MD, Yoo Jin Hong, MD*

Department of Radiology and Research Institute of Radiological Science, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

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***Corresponding author**
Yoo Jin Hong, MD
Department of Radiology and Research Institute of Radiological Science, Severance Hospital, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.

Tel 82-2-2228-7400
Fax 82-2-2227-8337
E-mail uzzin@yuhs.ac

ORCID iDs
Jinwoo Son
https://orcid.org/0000-0002-0525-6828
Yoo Jin Hong
https://orcid.org/0000-0002-7276-0944

Amyloidosis is a multisystemic disease characterized by the accumulation of abnormal proteins in extracellular spaces in various organs, with frequent involvement of the myocardium. We report a case of a patient who had cardiac amyloidosis with a trend of reduction in native T1 and T2 values and extracellular volume fraction on serial cardiac magnetic resonance imaging after chemotherapy and stem cell transplantation. The native T1 value and the extracellular volume fraction are closely associated with tissue amyloid burden in amyloidosis patients. This case demonstrated that cardiac magnetic resonance imaging may be used as a non-invasive and quantitative biomarker in the treatment monitoring of amyloidosis.

Index terms Amyloidosis, Cardiac; Extracellular Matrix; Magnetic Resonance Imaging

INTRODUCTION

Amyloidosis is a multisystemic disease characterized by the extracellular accumulation of misfolded proteins in various tissues and organs throughout the body. Light-chain (AL) amyloidosis is derived from the abnormal breakdown of normal immunoglobulin light chains caused by an underlying plasma cell dyscrasia. Approximately 50% of patients with AL amyloidosis develop cardiac involvement, and cardiac amyloi-

dosis (CA) is a significant factor for morbidity and mortality (1).

Evaluation of prognosis and treatment response in cardiac involvement of AL amyloidosis is dependent on electrocardiography (ECG), echocardiography, and serum cardiac biomarkers such as N-terminal pro-brain natriuretic peptide (NT-pro-BNP) and troponin T levels.

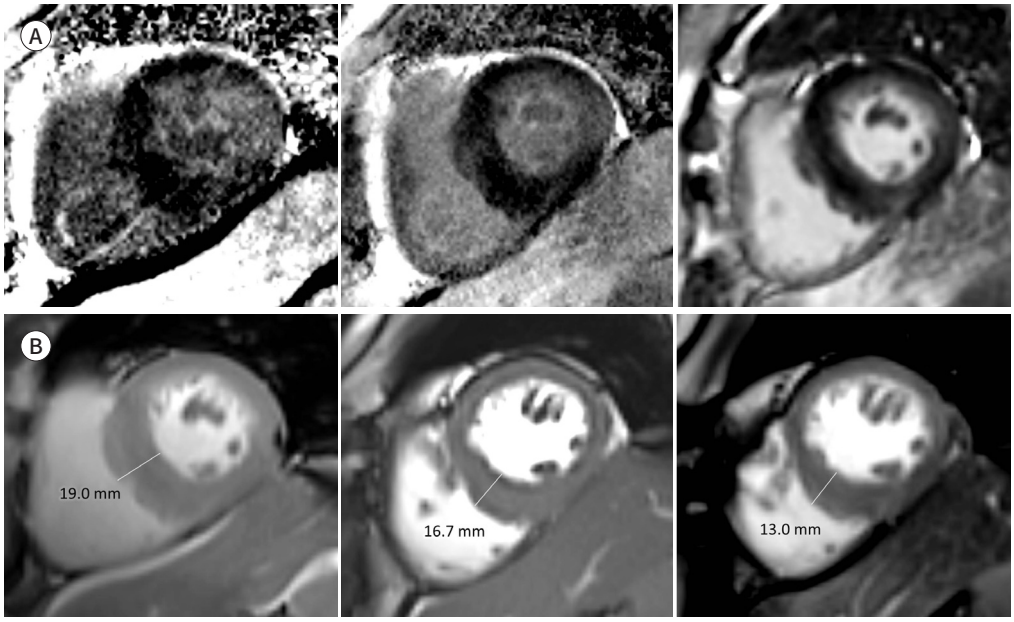
Native T1 value and extracellular volume fraction (ECV) using cardiac magnetic resonance imaging (MRI) have been used for the diagnosis and predicting prognosis of CA (2, 3) usually at a single point in time. Here, we present a case where cardiac treatment response was evaluated by the reduction of native T1 and T2 values and ECV in serial cardiac MRI after the treatment of amyloidosis.

CASE REPORT

A 59-year-old woman visited our hospital for the evaluation of an incidentally detected abnormal liver enzyme level during health screening. The patient had no specific clinical symptoms or past medical history. She underwent liver biopsy, and the pathologic report was AL amyloidosis. She was referred for cardiologic evaluation. ECG revealed low-voltage QRS complex. Transthoracic echocardiography revealed thick left ventricular (LV) myocardium (16 mm) and diastolic dysfunction. The LV ejection fraction was 77%, which was within the normal range. Her serum NT-pro-BNP level was 462 pg/mL (reference value: < 287 pg/mL) at initial evaluation. After 3 months, her serum NT-pro-BNP level increased to 2763 pg/mL. She received 6 cycles of chemotherapy (a combination of bortezomib, thalidomide, and dexamethasone) for 7 months and subsequently underwent autologous peripheral blood stem cell transplantation. Her serum NT-pro-BNP level gradually decreased to 329 pg/mL after chemotherapy and stem cell transplantation. After treatment, the low voltage QRS observed on the initial ECG disappeared. The LV ejection fraction on echocardiography remained in the normal range during and after treatment. She showed complete remission of amyloidosis and was undergoing regular outpatient follow-up.

The patient underwent 3 MRI studies, with baseline imaging at diagnosis and follow-up imaging at 1 month and 12 months after chemotherapy. MRI was performed using a 3.0-T scanner (MAGNETOM Trio Tim, Siemens AG Healthcare Sector, Erlangen, Germany). All MRI studies included a native T1 and T2 mapping and a post-contrast T1 mapping using a modified Look-Locker inversion recovery sequence. The initial MR image showed LV hypertrophy and diffuse circumferential subendocardial delayed hyperenhancement of the LV myocardium, which is a typical pattern of CA (Fig. 1A). The initial LV thickness was 19.0 mm, and the LV mass indexed to body surface area was 82.52 g/m^2 (Fig. 1B). Global native T1 and T2 values and the ECV of the myocardium were 1471.1 ms (reference value: 1213.9 ± 37.4 ms) and 53.7 ms (reference value: 48.5 ± 4.2 ms) and 41.1% (reference value: 25.8 ± 2.2 %), respectively. Based on the follow-up MRI at 1 month after chemotherapy, LV thickness and LV mass decreased to 16.7 mm and 79.10 g/m^2, respectively. Global native T1 and T2 values and the ECV of the myocardium were 1419.1 ms and 51.1 ms and 34.7%, respectively. Twelve months after chemotherapy, LV thickness and LV mass decreased to 13.0 mm and 68.04 g/m^2, respectively. Global native T1 and T2 values further decreased to 1343.1 ms and 42.1 ms, respectively, and the ECV was approximately 34.9% (Fig. 1C-E).

Fig. 1. A 59-year-old woman with baseline MRI and 1 month and 12 months follow up MRI after treatment of cardiac amyloidosis.
A. The initial late gadolinium enhancement image shows an extensive circumferential subendocardial delayed hyperenhancement, which decreases in serial images.
B. LV wall thickness on cine image decreases from 19.0 mm to 16.7 mm and 13.0 mm at 1-month and 12-month follow-ups, respectively; LV mass indexed to body surface area also decreases from 82.52 g/m^2 to 79.10 g/m^2 and 68.04 g/m^2, respectively.
LV = left ventricular

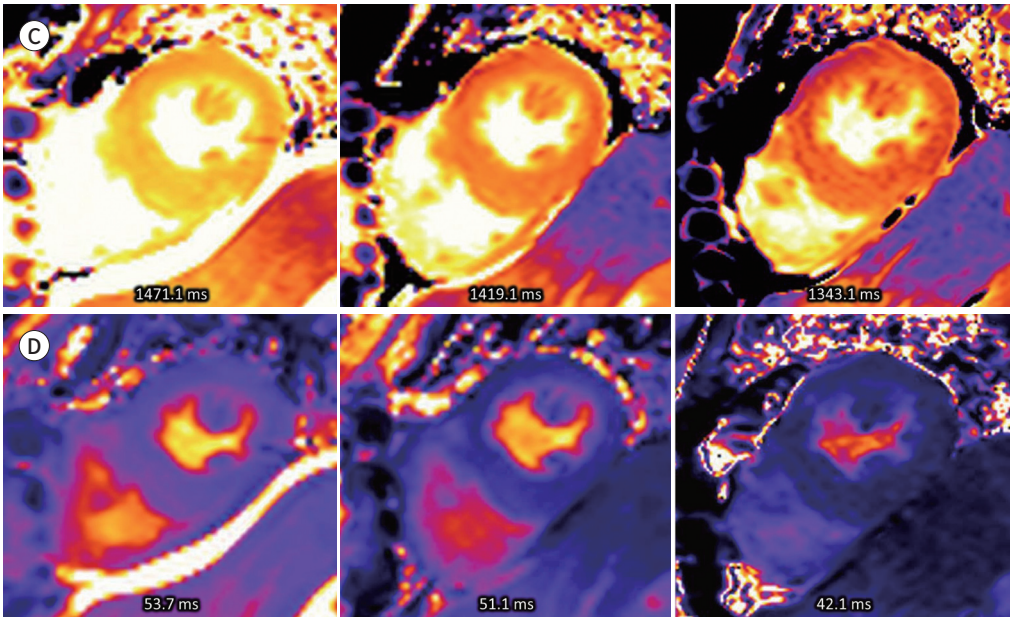


DISCUSSION

AL amyloidosis is a multisystemic disease characterized by the extracellular accumulation of misfolded proteins from dyscrasic plasma cells in the extracellular spaces of various organs. These insoluble deposits lead to interstitial expansion and disruption of structure and function, and cardiac involvement is a significant factor for morbidity and mortality. The median survival of amyloidosis patients decreased from 26 months to 10 months when NT-pro-BNP or troponin T levels increased according to the Mayo staging system (4, 5).

Cardiac MRI is a significantly useful tool used to establish the diagnosis of CA. Native T1 relaxation time is a composite measure of the interstitial and myocardial cells. ECV is a direct measure of the myocardial interstitium calculated from the relative changes in T1 relaxation time of the myocardium and blood pools after gadolinium administration. The accumulation of substances in the interstitial space of the myocardium causes a significant increase of the native T1 and ECV values in CA (2). Previous studies have confirmed that myocardial native T1 value and ECV are considered surrogate markers of cardiac amyloid burden (2, 3, 6). Cardiac amyloid load quantified with native T1 and ECV are important prognostic and predictive biomarkers of CA (3, 7). An increased native T1 value is associated with an approximately sixfold increase of mortality in CA (3), and ECV greater than 45% has an approximately fourfold increase of mortality in CA (3). Moreover, an increased native T1 value is also significantly associated with diastolic dysfunction, and several cardiac biomarkers reflect disease severity (3).

Fig. 1. A 59-year-old woman with baseline MRI and 1 month and 12 months follow up MRI after treatment of cardiac amyloidosis.
C. The global native T1 values of the myocardium on native T1 map decreases from 1471.1 ms to 1419.1 ms and 1343.1 ms after 1 month and 12 months after chemotherapy, respectively; ECV also decreases from 41.1% to 34.7% and 34.9%, respectively.
D. The global T2 value of the myocardium on native T2 map gradually decreases from 53.7 ms to 51.1 ms and 42.1 ms after 1 month and 12 months after chemotherapy, respectively.
E. Timeline of the clinical course represents the changes in serum cardiac biomarkers, native T1 value, ECV, T2 value, and LV mass. Native T1 value, ECV, T2 value, and LV mass decreased after treatment, which correlated with the changes in serum biomarkers.
ECV = extracellular volume fraction, LV = left ventricular, NT-pro-BNP = N-terminal pro-brain natriuretic peptide



E

Timeline (month)	NT-pro-BNP (pg/mL)	Native T1 value (ms)	ECV (%)	T2 value	LV mass (g/m²)
0	462	1471.1	41.1	53.7	82.52
1					
2					
3	2763				
4	1094				
5	627				
6	549				
	946				
7	538				
8	329	1419.1	34.7	51.1	79.10
	414				
9					
⋮					
19		1343.1	34.9	42.1	68.04

Treatment

A previous study reported that myocardial T2 value significantly increased in CA, suggesting myocardial edema, specifically in AL patients. However, myocardial T2 was not a predictor of survival in CA (8).

This case report provides insight into the potential role of serial T1 mapping MRI assessment in the treatment of AL amyloidosis. Decreasing trend of myocardial native T1 and T2 values, ECV, LV mass [suggesting the reduction of the cardiac amyloid burden, not atrophy of the myocardium (9)], and NT-pro-BNP level after the treatment of AL amyloidosis patient were observed in this case report. A previous study reported a case of monitoring cardiac response of AL amyloidosis using myocardial native T1 values (10). The study presented the possibility of using cardiac MRI without contrast media in patients with renal failure. Our study suggested that not only native T1 but also ECV is an indicator of amyloid burden, and ECV accurately measures interstitial burden. Additionally, T2 value also showed serial decrement after treatment, suggesting the improvement of myocardial edema. Therefore, a follow-up assessment of these indicators is considered beneficial in the evaluation of treatment response.

In conclusion, measurement of native T1 and T2 values and ECV using cardiac MRI is considered as a noninvasive and quantitative biomarker for assessing the treatment response of AL amyloidosis patients with cardiac involvement. Considering that CA is a significant factor for morbidity and mortality in AL amyloidosis patients, it plays an important role in clinical practice.

Author Contributions

Conceptualization, H.Y.J.; data curation, all authors; formal analysis, all authors; investigation, S.J.; methodology, H.Y.J.; project administration, H.Y.J.; supervision, H.Y.J.; visualization, S.J.; writing—original draft, S.J.; and writing—review & editing, H.Y.J.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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T1 지도화 기법 심장 자기공명영상 추적 검사를 이용한 심장 아밀로이드증의 치료 반응 평가

손진우 · 홍유진*

아밀로이드증은 세포 외 공간에 비정상적인 단백질이 축적되는 것을 특징으로 하는 전신 질환이며, 심근을 포함한 다양한 기관을 침범한다. 저자들은 심장 아밀로이드증 환자에서 항암화학 요법 및 줄기세포 이식 후 심장 자기공명영상의 추적검사에서 조영 전 T1 및 T2 수치와 세포 외 부피 분율의 감소를 보인 사례를 보고한다. 조영 전 T1 이완시간 및 세포 외 부피 분율은 아밀로이드증 환자에서 조직의 아밀로이드 축적 정도와 밀접한 관련이 있다. 이 사례를 통해 T1 지도화 심장 자기공명영상 기법이 심장 아밀로이드증의 치료 반응 모니터링에 비침습적이며 정량적인 도구로서 큰 역할을 할 수 있는 가능성을 확인할 수 있다.

연세대학교 의과대학 세브란스병원 영상의학과