

# Diagnostic value of native T1 Mapping in patients with cardiac amyloidosis

## Valor diagnóstico del Mapeo T1 nativo en pacientes con amiloidosis cardiaca

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## Summary

***Introduction:*** Amyloidosis with cardiac involvement is often underdiagnosed and has a high mortality rate. Cardiac magnetic resonance imaging (MRI) with native T1 Mapping (without IV contrast) could serve as an early marker of the disease, but its diagnostic accuracy in our setting is unknown. ***Objectives:*** To determine the diagnostic value of native T1 Mapping in patients with cardiac light chain (AL) amyloidosis. ***Methods:*** Evaluation of Cardiac MRI as a diagnostc test in 8 patients with light chain amyloidosis (AL) with cardiac involvement and 18 healthy individuals. All patients underwent 3T (Tesla) CMR with native T1 Mapping sequence (MOLLI, Modified Look-Locker Inversion-recovery) and longitudinal and short-axis cine images. The T1 mapping mean with 95% CI was estimated and sensitivity and specificity were calculated. Inter and intra-observer agreement was evaluated. ***Results:*** Patients with AL amyloidosis demonstrated increased values of Native T1 Mapping compared to healthy ones (1,415 ms ± 69 vs. 1,214 ms ± 44; p <0.001). The value of the native T1 Mapping in patients with AL amyloidosis varied between 1,322 and 1,493 ms while in the healthy it varied between 1,098 and 1,285 ms. A native T1 Mapping value greater than 1,357 ms (3.25 standard deviations) achieves a sensitivity (S) of 87.5%, a specificity (E) of 100%, and an accuracy in the classification of sick or healthy of 96.2%. ***Conclusions:*** The native T1 Mapping CMR has adequate diagnostic performance and is a sensitive and specific tool for identifying patients with AL cardiac amyloidosis.

## Resumen

***Introducción:*** La amiloidosis con afectación cardiaca es frecuentemente subdiagnosticada y tiene alta mortalidad. La resonancia magnética cardiaca (RMC) con Mapeo T1 nativo (sin medio de contraste intravenoso) podría servir como marcador temprano de la enfermedad, pero se desconoce su precisión diagnóstica en Colombia. ***Objetivos:*** Determinar el valor diagnóstico del Mapeo T1 nativo en pacientes con amiloidosis cardiaca de cadenas livianas (AL). ***Métodos:*** Estudio de RMC como prueba diagnósticas en 8 pacientes con amiloidosis de cadenas livianas (AL) con afectación cardiaca y 18 individuos sanos. A todos los pacientes se les practicó RMC simple 3T (Teslas) con secuencia de Mapeo T1 nativo (MOLLI, Modified Look-Locker Inversion-recovery) e imágenes de cine longitudinales y en eje corto. Se estimó la media del Mapeo T1 con IC 95% y se calculó sensibilidad y especificidad. Se evaluó concordancia inter e intraobservador. ***Resultados:*** Los pacientes con amiloidosis AL presentaron valores aumentados de Mapeo T1 Nativo en comparación con los sanos (1.415 ms ± 69 vs. 1.214 ms ± 44; $p$ < 0,001). El valor del Mapeo T1 nativo en pacientes con amiloidosis AL varió entre 1.322 y 1.493 ms mientras que en los sanos varió entre 1.098 y 1.285 ms. Un valor del Mapeo T1 nativo mayor de 1.357 ms (3,25 Desviaciones Estándar) logra una sensibilidad (S) del 87,5%, una especificidad (E) del 100% y una precisión en la clasificación de enfermos o sanos del 96,2%. ***Conclusiones:*** La RMC con Mapeo T1 nativo tiene adecuado rendimiento diagnóstico y es una herramienta sensible y específica para la identificación de pacientes con amiloidosis cardiaca AL.

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## Introduction

Amyloidosis is a heterogeneous disease characterized by abnormal protein folding, in which one or more organs are infiltrated by insoluble amyloid protein deposits derived from multiple amyloidogenic precursors; the prognosis depends on the affected organ and the type of amyloid (1). More than 30 proteins involved in the pathogenesis have been identified, and the disease can affect the heart, kidneys, central nervous system, skin, liver, and gastrointestinal tract; however, cardiac involvement is associated with a poorer prognosis (1). It has an annual incidence of

6–10 cases per million people worldwide (2). Survival in patients with systemic amyloidosis varies, with an average of 12–18 months across different studies. This depends on the number of organs involved and the severity of the condition (3). It is a frequently underdiagnosed disease, and despite therapeutic advances, the rate of sudden death within 90 days of diagnosis remains between 25–30% (4).

In cardiac amyloidosis, the extracellular space of the heart is expanded by amyloid deposits, which produce a restrictive cardiac pattern in both ventricles and atrial infiltration that leads to atrial contractile dysfunction with valvular and perivascular involvement (5). This leads to infiltrative and restrictive cardiomyopathy, followed by the onset of heart failure, a reduced quality of life, and death (6). It has even been observed that survival after the onset of heart failure averages six months without treatment; however, current treatments increase the remission period and prolong survival (5).

There are several forms of amyloidosis, but the two most common—accounting for 95% of cases—are light-chain amyloidosis (AL) and transthyretin amyloidosis (ATTR) (7).

Light-chain amyloidosis (AL) is the type that most commonly affects the heart—in up to 50% of cases (8)—and occurs in people with an average age of 50; it does not show a preference for either sex and causes multiorgan damage. It can develop in up to 10–15% of patients with multiple myeloma or in 9% of patients with monoclonal gammopathy of undetermined significance (MGUS) (4). ATTR affects the heart less frequently, in approximately 8–10% of cases, and primarily encompasses senile or hereditary systemic amyloidosis; it is more common in people over 60 years of age and has a marked male predominance, with a male-to-female ratio of 15:1 (9).

Endomyocardial biopsy is the standard method for diagnosing cardiac involvement due to light-chain amyloidosis, with sensitivity and specificity close to 100% (6), but it is an invasive procedure with multiple adverse effects that occur in 0.6–0.8% of cases (10), such as hematoma at the puncture site, transient right bundle branch block, and transient arrhythmias (11). This has led to the replacement of biopsy with imaging, nuclear medicine, and serological studies, which, together with clinical suspicion, support the diagnosis (5).

Cardiac magnetic resonance imaging (CMR) is useful in the diagnosis and prognosis of patients with this condition because it allows for the evaluation of the anatomy, structure, and function of the myocardial tissue, as well as its characterization; it also detects changes that determine disease progression, regression, and therapeutic adjustments. Numerous studies have demonstrated its high performance, with a sensitivity of up to 90% (12). More recently, new diagnostic tools have been developed and implemented, such as native T1 mapping (without intravenous contrast); with this technique, the T1 value of each pixel in the myocardium can be determined without administering intravenous contrast, and subsequently, using post-processing software, a color is assigned to each T1 value, generating a color-coded map of the myocardium. Native T1 mapping values depend on factors related to the extracellular and intracellular components of the myocardium and are significantly elevated in patients with amyloidosis, due to an increase in extracellular space caused by infiltration of insoluble amyloid proteins and by edema; the latter appears to be more pronounced in patients with AL amyloidosis, as it is suggested that in these patients, amyloid proteins produce a toxic effect on the myocardium with secondary edema (13).

Native T1 mapping has been shown in various studies to have a diagnostic accuracy of approximately 92%, with a sensitivity of 92% and a specificity of 91% for amyloidosis, as reported by Karamitsos et al. when comparing patients with confirmed or suspected cardiac AL to healthy patients or those with aortic valve stenosis, in whom native T1 mapping values obtained with 1.5 T MRI were 1140 ms ± 61 for AL amyloidosis, 958 ms ± 20 for healthy patients, and 979 ms ± 51 for those with aortic valve stenosis ($p < 0.001$) (14).

Additionally, it has been shown to be an early marker of disease; it is also useful for follow-up, quantification, and monitoring changes over time; and its advantages include the fact that it does not require contrast media and is reproducible compared to other diagnostic methods (15).

In Colombia, the exact prevalence of cardiac amyloidosis is unknown; however, it has been observed that diagnosis is generally delayed, by which time changes and remodeling in the cardiac structure have already occurred, leading to symptoms and a decline in functional class. In a survey of patients with AL cardiac amyloidosis, it was found that in more than 30% of those affected, it took more than a year to obtain an accurate diagnosis, and they consulted at least five physicians (3). Therefore, given the advantages of cardiac MRI and the promising results shown by the use of native T1 mapping (without intravenous contrast), it is important to establish quantitative values for the population with cardiac amyloidosis that will allow for an earlier diagnosis of the cardiac condition, thereby enabling interventions to improve patients' quality of life. For this reason, the main objective of the study is to determine the diagnostic value of native T1 mapping in patients with AL cardiac amyloidosis at the study's host institution. Furthermore, there are few published research studies evaluating patients with cardiac AL using 3-Tesla (3T) using a native T1 mapping sequence (MOLLI, an acronym for Modified Look-Locker Inversion-recovery), and to our knowledge, there are no publications in the Spanish-language medical literature that assess the value of 3T MRI with native T1 mapping in patients with AL amyloidosis.

## Materials and methods

A study of diagnostic tests was conducted that included the collection of data from patients diagnosed with cardiac AL who were seen between January 2017 and December 2019 at a referral diagnostic imaging center with more than ten years of experience in cardiovascular imaging or at the private hematology clinic of another medical center. The study included patients diagnosed with amyloidosis involving the heart who had undergone CMR studies with or without native T1 mapping during the described period; patients who did not have native T1 mapping underwent the study at the aforementioned diagnostic center after signing an informed consent form. Patients with claustrophobia, clinical conditions precluding supine positioning, or those with devices incompatible with the MRI scanner—such as pacemakers or implantable cardioverter-defibrillators—were excluded. Additionally, a group of healthy individuals was randomly selected from the database of the same diagnostic center; these individuals agreed to undergo the CMR study with native T1 mapping using the

same MRI equipment and protocol, after verification of compliance with the inclusion and exclusion criteria (Appendix 1).

MRI images were acquired using a 3-T scanner (Skyra, Siemens Healthcare, Erlangen, Germany). The scan was performed with the patient in the supine position using a 30-channel cardiac coil. Longitudinal, four-camera, three-camera, and two-camera Steady-State Free Precession (SSFP) cine sequences, as well as short-axis sequences of the ventricles, were acquired to assess ventricular function. Native T1 mapping (without intravenous contrast) was performed using three short-axis images: basal, mid-third, and apical. The MOLLI T1 mapping sequence (Siemens MyoMaps software) was used. The T1 mapping value was calculated by delineating a region of interest (ROI) on the short-axis view of the interventricular septum where myocardial thickness was greatest, excluding the blood pool and epicardial fat to avoid false results. Postprocessing was performed using cardiovascular imaging postprocessing software (Circle CVI CMR 42, release 5.9.3-1130) to analyze function and native T1 mapping values.

The images were evaluated by two radiologists specializing in cardiac imaging with more than ten years of experience in the field, who interpreted the studies of patients with cardiac amyloidosis individually and independently at their respective workstations; in cases of discordant results, they reached a consensus. Subsequently, each radiologist, individually and independently, blinded to patient information and in a randomized manner, recalculated the native T1 mapping values in the affected patients to assess their validity and accuracy through inter- and intra-observer agreement.

## Statistical analysis

The native T1 mapping data were described using the range and mean with standard deviation (SD) for each population. The confidence interval (CI) for the mean T1 mapping value was estimated, since the values followed a normal distribution, as determined by the Kolmogorov-Smirnov test. The comparison of native T1 mapping values between patients with cardiac amyloidosis and healthy patients was performed using Student's t-test, and comparability by sex was assessed using the chi-square test.

The Bland-Altman method was used to determine inter- and intra-observer agreement, and the receiver operating characteristic (ROC) curve was used to estimate the diagnostic performance of native T1 mapping; the area under the curve (AUC) was estimated with a 95% confidence interval (CI). The cutoff point for native T1 mapping was identified based on maximizing specificity for the purpose of confirming the diagnosis of cardiac amyloidosis.

Analyses were performed using Stata 14.0 and Epidat 4.1. A two-sided significance level of 0.05 was used.

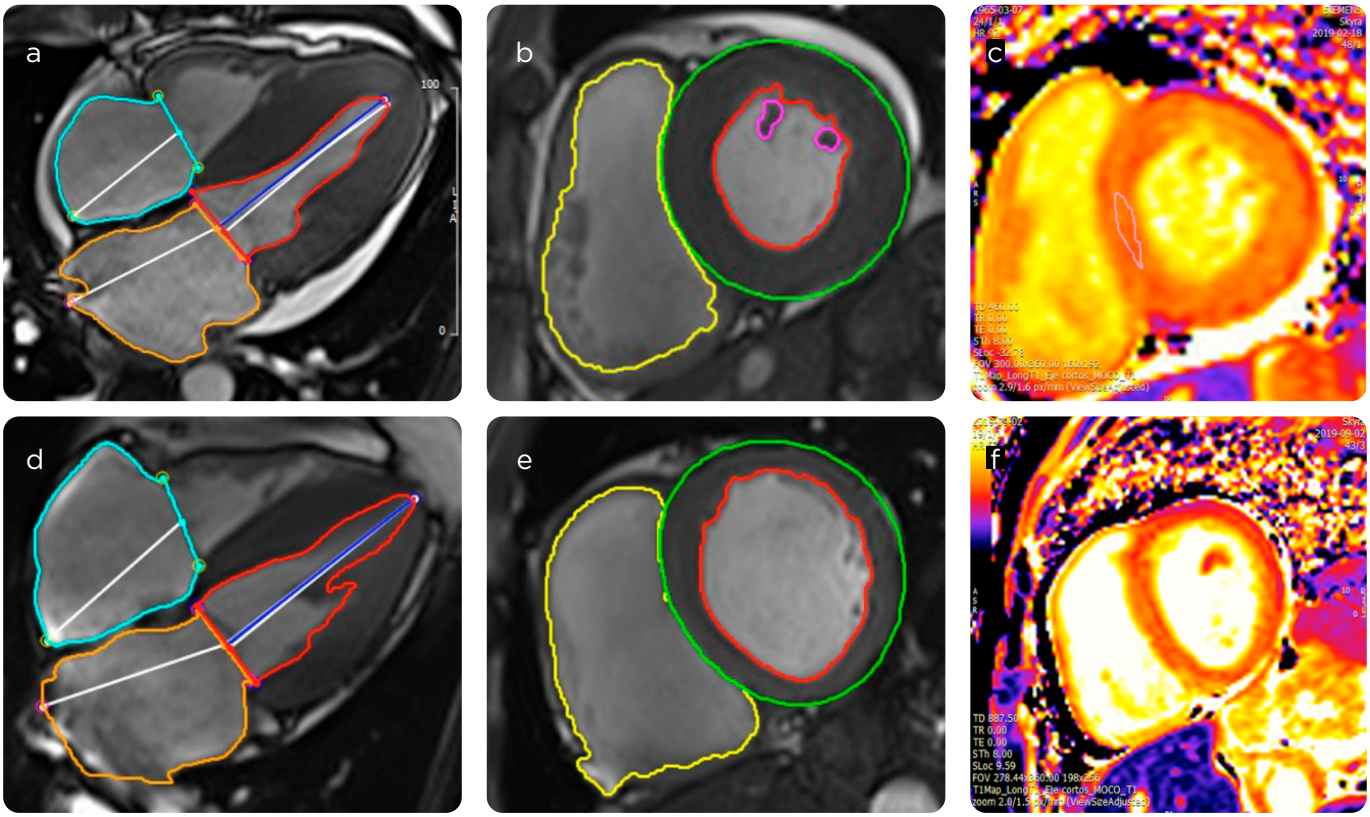



Figure 1. CMR in patients with AL cardiac amyloidosis. a and b) Longitudinal 4-chamber and short-axis SSFP cine sequences with segmentation of the ventricles and atria. Marked concentric biventricular hypertrophy; LV myocardial mass indexed at 148.7 g/m$^2$ (normal range 47–93). c) MOLLI T1 mapping sequence showing an ROI in the interventricular septum with elevated T1 mapping time of 1,493 ms. d and e) Longitudinal 4-chamber and short-axis SSFP cine sequences with ventricular and atrial segmentation. Left ventricular dilation and minimal hypertrophy; left ventricular myocardial mass indexed at 105 g/m$^2$ (normal range 34–80) compared to the case in the upper panel. f) MOLLI T1 mapping sequence showing an elevated T1 mapping time of 1,357 ms, to a lesser extent than in the previous case.

## Results

The study sample consisted of 26 patients, including 8 patients with AL-type cardiac amyloidosis and 18 healthy individuals. Among the patients with the disease, 5 were women (62.5%); the mean age was 66 years (SD: 11); and the diagnosis of systemic amyloidosis was made via biopsy of various regions and organs—abdominal fat in 3 cases, stomach in 2, kidney in 1, liver in 1, lung in 2, tongue in 1, and lymph nodes in 1, with some patients showing evidence of amyloid deposition in up to 2 organs—while cardiac involvement was established by CMR in conjunction with clinical findings for each case. Atrial dilation or thickening was the most common cardiac finding (7 cases, 87.5%). Left and right atrial size was assessed by measuring the area of the atria in the four-chamber view, with a normal area defined as less than 20 $cm^3$ for both atria and an atrial wall thickness of less than 3 mm.

Furthermore, regarding pleural effusion, extracardiac effusion was the most common and occurred in 5 individuals (62.5%) (Table 1). There were 18 healthy individuals, of whom 9 (50%) were women (p=0.683), and the mean age was 46 years (SD: 13.6) (p=0.001).

With regard to the native T1 mapping value, it was found that in patients with cardiac AL, this value ranged from 1322 to 1493 ms (Figure 1), while in healthy individuals it ranged from 1098 to 1285 ms (Figure 2). The mean T1 mapping value in patients with AL amyloidosis was significantly higher than that in healthy individuals (1,415 ms ± 69 vs. 1,214 ms ± 44; $p < 0.001$) (Figure 3).

To evaluate the validity of native T1 mapping in the diagnosis of cardiac amyloidosis, intra-radiologist and inter-radiologist precision were assessed using the Bland-Altman plots shown in Figure 2. Both radiologists showed little variation in their readings of native T1 mapping, and when their results were compared, the variation was even smaller, indicating a high ability to detect native T1 mapping values independently of the operator (Figure 4).

A ROC curve was used to identify the cutoff point for T1 mapping, and it was determined that a value of 1357 ms (3.25 standard deviations) yielded a sensitivity (S) of 87.5%, a specificity (E) of 100%, a classification accuracy of 96.2% for distinguishing between patients and healthy individuals, and an AUC of 1.0, with a positive predictive value of 100% and a negative predictive value of 94% (Figure 5). Additionally, it was found that a T1 mapping value of 1269 ms (1.25 standard deviations) has a positive predictive value of 80% and a negative predictive value of 100%.

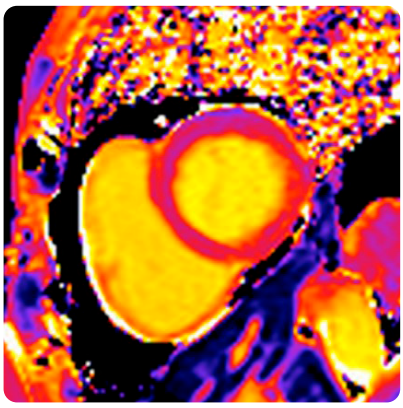


Figure 2. MOLLI T1 mapping sequence in a healthy patient, with no elevated T1 mapping time (1138 ms).

**Table 1. Sociodemographic and clinical characteristics of patients with cardiac amyloidosis. Medellín (2019)**

| Characteristic | Cardiac amyloidosis (*n*=8) |
|---|---|
| **Sex, *n* (%)** | |
| Female | 5 (62.5) |
| Male | 3 (37.5) |
| **Age, years** | |
| Mean (SD) | 65.9 (11) |
| **Time to diagnosis, *n* (%)** | |
| < 2 | 4 (50.0) |
| ≥2 | 4(50.0) |
| **Cardiac findings, *n* (%)*** | |
| Atrial dilation or thickening | 7 (87.5) |
| Ventricular hypertrophy | 6 (75.0) |
| Pericardial effusion | 6 (75.0) |
| Normal ventricular function | 4 (50.0) |
| Abnormal ventricular function | 4 (50.0) |
| Septal thickening | 4 (50.0) |
| **Extracardiac findings, *n* (%)*** | |
| Pleural effusion | 5 (62.5) |
| Atelectasis | 2 (25.0) |
| None | 3 (37.5) |
| **Comorbidities, *n* (%)*** | |
| Hypertension | 7 (87.5) |
| Diabetes mellitus | 1 (12.5) |
| Chronic kidney disease | 3 (37.5) |
| Other | 4 (50.0) |

* Patients had more than one condition; therefore, the sum of the percentages exceeds 100. SD: standard deviation.

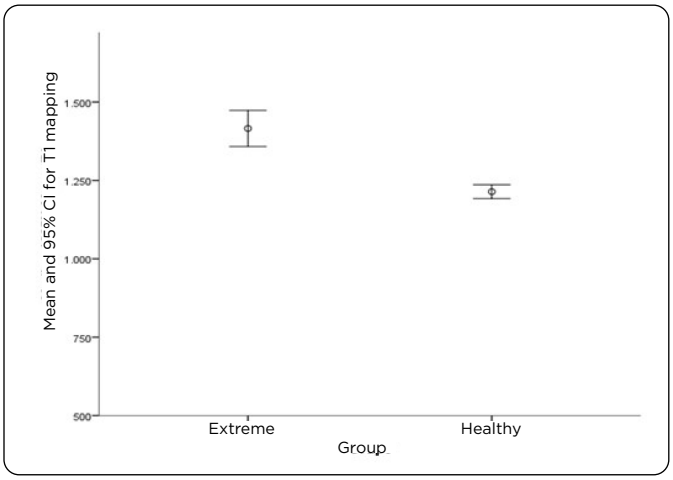



Figure 3. Native T1 mapping results in patients with and without cardiac amyloidosis. Medellín (2019). The values correspond to the 95% CI for the mean T1 mapping value: CI: 1358–1473 for patients with amyloidosis and CI: 1192–1236 for healthy individuals.

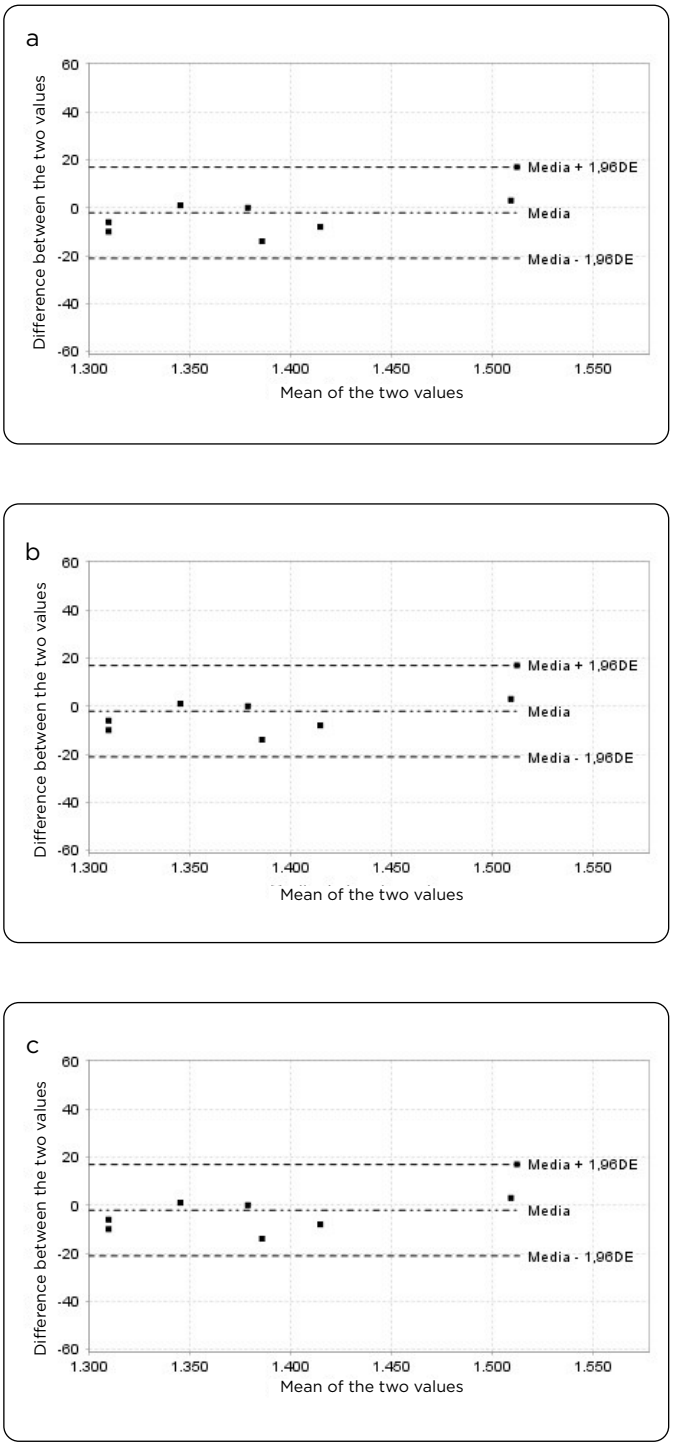



Figure 4. Intra- and inter-observer agreement in the interpretation of native T1 mapping in patients with cardiac amyloidosis. Medellín (2019). Intra-observer precision is shown in panels a and b, and inter-observer precision in panel c. SD: Standard deviation.

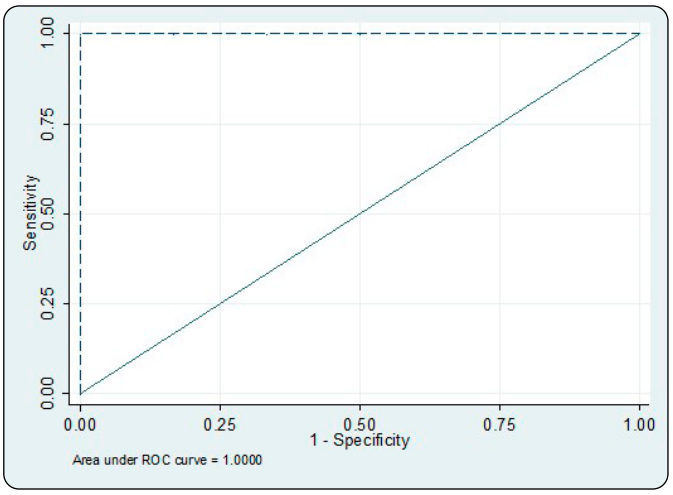



Figure 5. ROC curve for native T1 mapping in patients with AL cardiac amyloidosis. Medellín (2019). Ability to detect cardiac amyloidosis with a T1 mapping value of 1357 ms (3.25 standard deviations) compared to healthy patients. AUC: Area Under the Curve. CI: Confidence Interval

## Discussion

This is the first study in the country and in the region to examine the value of native T1 mapping in patients with AL amyloidosis using 3T MRI. Elevated native T1 mapping values were found using a 3T scanner (Skyra, Siemens) with the MOLLI sequence in patients with AL cardiac amyloidosis compared to healthy individuals. Native T1 mapping is an accurate and valid tool with adequate diagnostic performance. These findings are consistent with other studies that have shown similar results when comparing these patient groups and have found significant differences in T1 mapping values.

Lin Lu et al. evaluated 82 patients with AL cardiac amyloidosis (55.5 ± 8.5 years; 52 women) and 20 healthy individuals (53.2 ± 11.7 years; 10 women) using 3T MRI (Siemens, SKYRA) with the native T1 mapping (MOLLI) sequence. These authors found elevated native T1 mapping values in patients with AL amyloidosis compared with healthy individuals (1438 ± 120 ms vs. 1283 ± 46 ms, p = 0.001) (16). Similarly, Cui et al., using 3T MRI (Phillips), evaluated 9 patients with AL amyloidosis and 12 healthy individuals, and also found elevated native T1 mapping values in patients with cardiac AL amyloidosis (1497.3 ± 22.0 ms vs. 1273.3 ± 30.1 ms) (17). This trend and these native T1 mapping values, which are similar to those in the present study, indicate that the protocol and sequence used in this study can yield results equivalent to those described in the literature using similar protocols.

It is important to note that native T1 mapping values are higher on 3T MRI systems compared to 1.5T systems (18). Fontana et al. compared four groups of patients using 1.5T MRI (Avanto, Siemens) and the ShMOLLI sequence (shortened modified look-locker inversion recovery) and found significant differences in T1 mapping values between the comparison groups, with values of 967 ms ± 34 in healthy individuals and 1130 ms ± 68 in patients with AL amyloidosis, with p < 0.0001 (9). Similarly, Banypersad et al., using 1.5T MRI (Avanto, Siemens) with the ShMOLLI sequence, found a T1 mapping value of 1080 ± 87 ms in 100 patients with AL amyloidosis compared with 54 healthy volunteers with values of 954 ± 34 ms, p < 0.001 (19), reflecting

T1 mapping values lower than those obtained with 3T MRI systems, as evidenced in this study and others (16, 17). This suggests that T1 mapping values depend on the MRI system used and, therefore, normal values for native T1 mapping must be validated locally according to the type of MRI scanner (1.5 vs. 3T), the type of native T1 mapping sequence (e.g., MOLLI vs. ShMOLLI), the population, and the protocol, before this diagnostic tool is used clinically.

It is therefore possible to establish clinically validated normal ranges of native T1 mapping values specific to each MRI scanner to detect and distinguish patients with cardiac amyloidosis from those without it, which could reduce the future use of traditionally employed invasive diagnostic methods such as endomyocardial biopsy, which—in addition to the potential to cause adverse events such as those mentioned in the introduction—requires specific expertise on the part of pathologists for its performance and interpretation, and in many cases leads to diagnostic delays (6).

In this study, with a T1 mapping value of 1357 ms (3.25 standard deviations), a sensitivity (S) of 87.5%, a specificity (E) of 100%, and an accuracy in classifying patients as diseased or healthy of 96.2% were achieved, along with an area under the curve (AUC) of 1, results comparable to those observed in previous studies, such as that by Karamitsos et al., who compared patients with confirmed (n = 28) or suspected (n = 11) AL cardiac amyloidosis with healthy individuals (n = 36) and with aortic valve stenosis (n=17) using 1.5 T MRI and the ShMOLLI sequence, in which they found a diagnostic accuracy with a T1 mapping value of 1020 ms (3.1 standard deviations) of nearly 92%, a sensitivity of 92%, and a specificity of 91%, with an area under the curve (AUC) of 0.97 (14). These data support the role of native T1 mapping as a sensitive and specific diagnostic tool for identifying amyloid in cardiac tissue, with the added advantage that it does not require contrast agents, given the relatively high incidence of chronic kidney disease in the population with amyloidosis (20).

In a recent prospective study using 1.5 T MRI and the MOLLI sequence, Baggiano et al. examined 222 patients with AL cardiac amyloidosis (214 patients) and ATTR cardiac amyloidosis (427 patients), as well as 30 healthy individuals, and found that a value greater than 1091 ms (1.7 standard deviations) has high diagnostic accuracy, with a positive predictive value (PPV) of 87%, a negative predictive value (NPV) of 85%, and an area under the curve (AUC) of 0.93 (21). This study highlights the utility of native T1 mapping (without intravenous contrast) for the diagnosis of cardiac amyloidosis in patients with renal failure, a common comorbidity in this population. According to these authors, native T1 mapping can confirm the diagnosis of both AL and ATTR cardiac amyloidosis with a T1 mapping value greater than 1164 ms—equivalent to 3.5 standard deviations—and a PPV of 98%; conversely, cardiac amyloidosis can be ruled out with a native T1 mapping value of 1036—equivalent to 0. 4 standard deviations, with a NPV of 98%. They also emphasize that there is an intermediate "gray zone" of native T1 mapping values in which cardiac amyloidosis cannot be ruled out or confirmed; in these cases, based on a risk-benefit analysis, a contrast-enhanced CMR should be considered in order to calculate the myocardial extracellular volume (ECV). According to this study, an ECV value greater than 37% on CMR has high diagnostic accuracy in this group with intermediate native T1 mapping values (AUC: 0.976). This approach is highly appealing, as native T1 mapping without contrast can confirm or rule out the diagnosis of cardiac amyloidosis in 42% of this cohort using a short, 15-minute CMR protocol.

This study found that a native T1 mapping cutoff greater than 1357 ms—equivalent to 3.25 standard deviations—can confirm the diagnosis of AL cardiac amyloidosis with a positive predictive value (PPV) of 100%, and that with a T1 mapping value of 1269 ms—equivalent to 1, 25 standard deviations, cardiac involvement can be ruled out with a NPV of 100%. Patients with native T1 mapping values between 1269 ms and 1357 ms require, based on a risk-benefit assessment, supplementary intravenous contrast-enhanced cardiac MRI to calculate the ECV and confirm the diagnosis of AL cardiac amyloidosis. This is clinically relevant, as these values can be used to create institutional algorithms that allow for an appropriate diagnostic approach, utilizing the necessary tools for each patient, avoiding the use of intravenous contrast or unnecessary lengthy studies, and prescribing them only when required in each individual case.

T1 mapping was found to be a valid and accurate tool with adequate inter-observer and intra-observer agreement, indicating a high ability to detect T1 mapping values regardless of the operator. Comparable findings were reported in previous studies, such as that by Kai Lin et al., who found good reproducibility with intraclass correlation coefficients (ICCs) for intra- and inter-observer reproducibility of 0.988 and 0.899, respectively (22). This demonstrates that native T1 mapping without intravenous contrast is a reliable method for follow-up, quantification, and assessment of changes over time, a finding that has been further supported by the study by Aus dem Siepen et al., who found that T1 mapping and ECV values remained stable over time in healthy patients, with baseline T1 mapping at 1017±24 ms vs. follow-up at 1015±21 ms; p=0.6 (study repeated at 3.6±0.5 years under the same conditions and using the same protocol) (23). These characteristics show promise for the evaluation of patients with this condition, as they could be decisive in assessing the effect of behavioral interventions and treatments in this population, as well as for prognosis and early diagnosis (24, 25).

Finally, this study also demonstrated the most common morphological and functional cardiac findings in this condition, which is consistent with what has been reported in the literature regarding this disease (13). The most common cardiac findings are atrial wall dilation and/or thickening, followed by left ventricular hypertrophy (myocardial thickness greater than 12 mm in the short-axis view at end-diastole) and pericardial effusion; while the most common extracardiac finding was pleural effusion; therefore, these features, when observed in an appropriate clinical context, raise suspicion of this condition, which would reduce delays in reaching a diagnosis.

In the patient group of this study, 3 (37.5%) had chronic kidney disease. In the past, it was believed that in patients with amyloidosis, native T1 mapping values could be altered by underlying comorbidities such as renal failure, anemia, or proteinuria. However, in the study by Baggiano et al., the authors found that the performance of native T1 mapping does not differ in patients with amyloidosis and these comorbidities, and that the severity of these comorbidities does not alter the results either (21). In the present study, there was insufficient statistical power to analyze this subgroup.

The authors acknowledge that this study has some limitations. First, it is a small sample that includes only eight patients diagnosed with AL amyloidosis; however, this sample is reliable given that the

results—in terms of native T1 mapping values—are similar to those found in two recent studies conducted using 3T scanners in patients with AL amyloidosis, with findings described in the discussion (16, 17). Second, this study did not evaluate patients with ATTR amyloidosis, and the T1 mapping results cannot be extrapolated to this population, since native T1 mapping values tend to be lower in this group, as described by Baggiano et al. using 1.5 T MRI: Native T1 mapping in AL cardiac amyloidosis: 1,166 ms ± 64; in ATTR amyloidosis: 1,133 ms ± 58; in healthy individuals: 1,020 ms ± 41 (21). Finally, the imaging studies were conducted at a single advanced diagnostic imaging center using specific equipment and protocols; therefore, the applicability of the T1 mapping values to centers with different equipment and protocols is limited. However, it is recognized that this is an inherent limitation of the T1 mapping technique, as each institution must determine the normal values for its own equipment before implementing this tool. Previous studies have found that these values can vary depending on these factors. Dabir et al. found significantly higher T1 mapping values in healthy individuals when the scans were performed on a 3T scanner compared to a 1.5T scanner, with average values of 950 ± 21 ms (1.5T) and 1052 ± 23 ms (3T) (18). This poses an obstacle to implementation in clinical practice; therefore, it is hoped that normal values, protocols, acquisition techniques, and analysis tools will be standardized in the future.

## Conclusion

This study shows that native T1 mapping has high diagnostic accuracy and is a sensitive and specific tool for identifying patients with AL cardiac amyloidosis. It is also a reliable, safe, rapid, reproducible, and non-invasive method that does not require the use of intravenous contrast agents, which could allow for its use in patients with renal failure as well.

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