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ORIGINAL RESEARCH ARTICLE

Clinical characterization of patients with cardiac amyloidosis in a referral center of Colombia

Caracterización clínica de pacientes con amiloidosis cardíaca en un centro de referencia en Colombia

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Abstract

Objective: *The objective of the study is to describe the characteristics of our first cohort of amyloidosis in a Latin America cardiovascular reference center in Colombia.* **Methods:** *This is a historic cohort study and data were taken from the electronic records of the Fundación Cardioinfantil-Instituto de cardiología; adult patients with a diagnosis of cardiac amyloidosis were included and a descriptive analysis was presented.* **Results:** *A total of 31 patients with amyloidosis were included. 17 were Transthyretin Amyloidosis (ATTR) subtype and 14 were AL subtype. An overall mortality of 25% was found. The mean age at diagnosis was 74 years, male sex predominant. More frequent comorbidities were hypertension and atrial fibrillation. The most frequent clinical presentation was congestive heart failure (75%), with mildly reduced ejection fraction (41.94%), followed by reduced ejection fraction (32.26%), and preserved ejection fraction (25.81%). In the ATTR subtype, a reduced ejection fraction was found at 41.18% and a mildly reduced ejection fraction at 35.29%.* **Conclusion:** *These results provide information on the most frequent type of amyloidosis and the late timing to diagnose in our historic cohort study, we present some of the baseline characteristics and most frequent approaches to diagnose Cardiac Amyloidosis that represents all challenges in clinical practice. Improvements are needed in the diagnosis and early treatment of these patients.*

Keywords: *AL amyloidosis. Amyloidosis. Heart failure. Transthyretin amyloidosis.*

Resumen

Objetivo: *Describir las características de nuestra primera cohorte de amiloidosis en un centro de referencia cardiovascular de Latinoamérica en Colombia.* **Métodos:** *Los datos fueron tomados de los registros electrónicos de la Fundación Cardioinfantil-Instituto de cardiología; Se incluyeron pacientes adultos con diagnóstico de amiloidosis cardíaca y se presenta un análisis descriptivo.* **Resultados:** *Se incluyeron un total de 31 pacientes con amiloidosis. 17 eran ATTR y 14 eran AL. Se encontró una mortalidad global del 25%. La edad media al diagnóstico fue de 74 años, predominando el sexo masculino. Las comorbilidades más frecuentes fueron Hipertensión y Fibrilación auricular. La presentación clínica más frecuente fue insuficiencia cardíaca congestiva (75%), con fracción de eyección levemente reducida (41.94%), seguida de fracción de eyección reducida (32.26%) y fracción de eyección preservada (25.81%). En el subtipo ATTR, la fracción de eyección reducida se encontró en el 41.18% y la fracción de eyección levemente reducida en el 35.29%.*

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Conclusión: *Estos resultados brindan información sobre el tipo de amiloidosis más frecuente y el momento del diagnóstico, el cual fue tardío en nuestra cohorte, su prevalencia en el sexo masculino (61.29%), edad promedio al diagnóstico de 74 años, principal presentación clínica y abordaje más frecuente, mostrando el desafío que representa en la práctica clínica llegar al diagnóstico. Se necesitan mejoras en el diagnóstico y tratamiento precoz de estos pacientes.*

Palabras clave: *Amiloidosis AL. Amiloidosis. Falla cardiaca. Amiloidosis transtiretina.*

Introduction

Cardiac amyloidosis (CA) is caused by amyloid fiber deposition in the myocardium. The two most common types are light chain (AL) and transthyretin (TTR) accumulation; the latter may be due to inherited transthyretin amyloidosis (ATTRh) or acquired wild type transthyretin amyloidosis protein (ATTR-wt), as previously called senile amyloidosis[1,2]. The most frequent form of amyloidosis is transthyretin amyloidosis (ATTR), which was conceived previously as a rare disease and misdiagnosed as non-amyloid heart failure. Now, the evidence is moving forward to many targets and the outcomes have been improved with the TTR stabilizers[1,3-9].

The prevalence remains unknown worldwide and it is considered an underdiagnosed pathology. Recent studies have reported the prevalence of HF as a principal finding in developed countries as 11.8% in those aged > 65 years[10]. In another study, the prevalence of CA was higher among men (70/100 000 person-years) compared with women (44/100 000 person-years)[11,12]. A more recent trial documented an increased prevalence of hospitalizations for CA in the United States reporting 18-55/100,000 person-years, which suggests that CA should be considered during the initial work-up for heart failure with preserved ejection fraction, atrial fibrillation (AF), restrictive myocardiopathy, especially in those older than 75 years[11,13].

There is a problem with diagnosis and lack of knowledge about the early detection of disease and search for some late findings called “red flags”. It probably delays diagnosis and makes physicians attribute increased thickness of the wall to other pathologies, such as high blood pressure, obesity, and other infiltrative diseases[11,14,15].

The objective of the study was to describe the characteristics of our first cohort of amyloidosis in a Latin America cardiovascular reference center in Colombia.

Methodology

A retrospective cohort of patients diagnosed with CA in the period 2013-2021 at the Fundación Cardioinfantil-Instituto de cardiología, Bogotá, Colombia, was described, following the international Consensus for the diagnosis of CA.

Inclusion criteria

- Patients diagnosed with CA both invasively and non-invasively in the case of ATTR, excluding other causes of left ventricular hypertrophy (LVH).
- Invasive diagnosis required histological confirmation of amyloid in a sample (intracardiac or extracardiac biopsy). When the biopsy is extracardiac, it must have associated cardiac involvement, given by LVH (≥ 12 mm) or restrictive pattern by echocardiogram or cardiac magnetic resonance imaging (CMR), having excluded other causes of LVH.
- Non-invasive diagnosis was made only in the case of ATTR amyloidosis, required LVH 12 mm or pattern restrictive by echocardiogram or CMR imaging, which was made by 99 mTc-pyrophosphates (PYP) scintigraphy or SPET with Perugini score 2 or 3; ruling out AL amyloidosis by concomitant analysis of light chains in serum, urine, and negative immunofixation in blood and urine.
- Monoclonal syndrome of uncertain significance (MGUS) or plasma cell dyscrasia diagnosis was made with the multidisciplinary help of the hematology team.

Exclusion criteria

- Patients under 18 years of age.
- Patients with missing data in the clinical history that did not allow making a diagnosis of CA.

The image interpretation was made for three experts in nuclear cardiology, several cardiologists cardiac imaging specialists.

Finally, a description of the qualitative variables in absolute and relative frequencies was made. Quantitative variables were described by means of central tendency and dispersion measurement, standard deviation, and interquartile range, as appropriate. SPSS was used for data analysis.

Results

Between January 1, 2013, and January 31, 2021, the data of 58 patients were recorded with suspected CA

at the Fundación Cardioinfantil-Instituto de Cardiología. 31 patients met the diagnostic criteria for CA. Of the 31 patients with a diagnosis of CA, 38.71% were women and 61.29% were men, with an average age of 74 years. 14 patients had AL amyloidosis, with an average age of 68 years, and 17 patients had ATTR amyloidosis with an average age of 79.35 (Table 1).

The most frequent comorbidity was AF. The most frequent extracardiac manifestations were lesions of the peripheral nervous system (12.90%) mainly in AL amyloidosis, three patients with neurological compromise were found in the ATTR group; one of them presented with sensorimotor axonal polyneuropathy, lumbar canal stenosis with loss of sphincter control, dysphagia, and dysautonomia, this patient has genetic study being an ATTRh carrier of the Val50Met mutation.

The most frequent clinical presentation was congestive heart failure (75%), with mildly reduced ejection fraction (41.94%), followed by reduced ejection fraction (32.26%) and preserved ejection fraction (25.81%). In the ATTR group, the most frequent clinical presentation was reduced ejection fraction (41.18%). Most of the patients were in the functional class of the New York Heart Association III (Tables 1 and 2).

The most frequent electrocardiographic findings were low voltage patterns in 11 patients (41.94%), being more frequent in the AL amyloidosis group 8/11 (72.73 %) compared to ATTR 3/11 (27.27%). One of the known features of CA is the mismatch between the wall thickness on echocardiogram and QRS voltage on electrocardiogram, either that the thickening is due to amyloid infiltration and not true hypertrophy of cardiomyocytes[1,16,17]. However, this feature has low sensitivity and the prevalence of low voltage varies according to the etiology, with greater frequency in patients with AL amyloidosis (60%) than in patients with ATTR amyloidosis (20%)[13,18,19]. Therefore, the absence of low voltage does not exclude disease, particularly in patients with ATTRwt amyloidosis[19].

Other findings in both subgroups (AL and ATTR) in the electrocardiogram and in the Holter test were supraventricular extrasystoles (SVE) in 16.36% of patients. All in the ATTR group presented SVE. Ventricular extrasystoles were found in 19.35%, mainly in the ATTR group. It was also evaluated who were carriers of an implantable device, finding only two patients with pacemakers, one of whom developed symptomatic sinus dysfunction in the ATTR group and another of the patients with atrioventricular block of high degree in the AL amyloidosis group[8,20].

Table 1. Sociodemographic variables and comorbidities

	ATTR (n = 17)	AL (n = 14)	General (n = 31)
Age	79.35	68.53	74.28
Sex (female)	23.53%	57.14%	38.71%
Sex (male)	82.35%	35.71%	61.29%
Congestive heart failure	64.71%	92.86%	75.00%
Atrial fibrillation	41.18%	42.86%	48.39%
Stroke	11.76%	28.57%	19.35%
Chronic kidney disease (CKD)	11.76%	28.57%	25.81%
Hemodialysis in (CKD)	0.00%	21.43%	9.68%
Valve repair or replacement	0.00%	14.29%	6.45%
Biological prosthesis	0.00%	14.29%	6.45%
Multiple myeloma	0.00%	21.43%	9.68%
MGUS	5.88%	0.00%	3.23%
Chronic medication			
	(n = 17)	(n = 14)	(n = 31)
Chronic use of beta blockers	52.94%	78.57%	64.52%
Chronic use of diuretics	41.00%	57.14%	80.65%
Chronic use of chemotherapy	0.00%	42.86%	19.35%

Regarding the biomarkers, the average proBNP was 1200 pg/mL, being higher in the AL amyloidosis group compared to ATTR (Table S1). On echocardiographic evaluation, the average mass of the wall of the left ventricle was 137.93 G/m^2. When performing the analysis by subgroups, it showed greater ventricular hypertrophy in the ATTR group with an average ventricular mass of 146 G/m^2 (Tables 2 and 3).

The majority of patients analyzed had diastolic dysfunction type 3 (35.48%). In the analysis by subgroup, ATTR amyloidosis presented the highest number of cases of diastolic dysfunction type 3 (Table 2); 51.61% of the patients had an abnormal strain, of which 37.50% showed longitudinal alterations in the basal and mid-ventricular segments with preservation of the apical segments, known with the cherry on top pattern that is characteristic of amyloidosis (Table 2).

CMR is not a test that we routinely performed on all patients with suspected amyloidosis[21]. Among the patients analyzed by CMR (N: 23), 43,48% had preserved LVEF, 82.61% had late gadolinium enhancement, and the main pattern of enhancement found was

Table 2. Echocardiographic variables

	ATTR (n = 17)	AL (n = 14)	n = 31
Preserved ejection fraction	23.53%	28.57%	25.81%
Mildly reduced ejection fraction	35.29%	50.00%	41.94%
Reduced ejection fraction	41.18%	21.43%	32.26%
Relative wall thickness (RWT) > 0.4	94.12%	78.57%	87.10%
Left ventricular (LV) mass (G/m^2)	146.2	128.4	137.93
End systolic volume (mL/m^2)	30.42	28.81	29.72
End diastolic volume (mL/m^2)	57.81	52	55.32
Intracavitary thrombus	0.00%	7.14%	3.23%
Left atrial diameter (mL/m^2)	78.33	57.15	68.5
Diastolic dysfunction (Grade I)	29.41%	0.00%	15.63%
Diastolic dysfunction (Grade II)	23.53%	50.00%	32.26%
Diastolic dysfunction (Grade III)	41.18%	28.57%	35.48%
Heart valve disease	11.76%	28.57%	19.35%
Abnormal global longitudinal strain	64.71%	35.71%	51.61%
Strain with "cherry on top" pattern	29.41%	7.14%	37.50%

Table 3. Gammagraphy with pyrophosphates

	n = 16	n = 7	n = 23
99mTc-PYP Scintigraphy (Perugini score 0)	0.00%	85.71%	26.09%
99mTc-PYP Scintigraphy (Perugini score I)	0.00%	14.29%	4.35%
99mTc-PYP Scintigraphy (Perugini score II)	12.50%	0.00%	8.70%
99mTc-PYP Scintigraphy (Perugini score III)	87.50%	0.00%	60.87%

subendocardial in 28.13% followed by transmural enhancement in 12.5% (Table 4). 13 of the patients had studies of ischemia with myocardial perfusion (Table S2).

Of the total number of patients, 23 underwent scintigraphy with bone tracers. The radiopharmaceuticals used were 99Tc-HMPD in 16/23 patients and 99Tc-PYP in 7/23 patients. No patient underwent a study with 99Tc-MDP. The average dose used was 740 MBq (20 mCi) between 555 and 1110 MBq. Of the total scintigraphies, 6/23 (26%) had Perugini 0, 1/23 (4%) Perugini 1, 2/23 (9% Perugini 2 and 14/23 (61%) Perugini 3. Furthermore, 16/23 (70%) were finally classified as ATTR amyloidosis and 7/23 (30%) as AL amyloidosis. Of the patients classified with ATTR amyloidosis, 0/16 had Perugini 0, 0/16 Perugini 1, 2/16 Perugini 2, and 14/16 Perugini 3. Of the patients classified as having AL amyloidosis, 6/7 had Perugini 0, 1/7 Perugini 1, 0/7 Perugini 2, and 0/7 Perugini 3 (Table 3).

The evaluation of free light chains together with immunofixation electrophoresis in serum and urine completes the algorithm of blood dyscrasia[1,2,22]. The evaluation was carried out with the ratio of kappa and lambda-free light chains, adjusting to kidney function. It was found that 14 patients had an abnormal kappa/lambda free light chain ratio (Table S1). The presence of immunofixation electrophoresis in serum and urine was performed in 93.75% and 78% respectively, being positive in 46.8% in serum and 12.5% in urine (Table S1). Monoclonal gammopathy of uncertain significance was found in 3.23% of patients and 9.68% had multiple myeloma associated with AL amyloidosis (Table 1).

A total of 21 biopsies were performed, 8 in the ATTR amyloidosis group and 13 in the AL amyloidosis group, the most common biopsy site was bone marrow biopsies (Table S3). Seven patients with extracardiac involvement were found, mainly due to neurological involvement, 4 of them were found with AL amyloidosis with the affection of the peripheral nervous system mainly. Three patients with neurological compromise were found in the ATTR group; one of them presented with sensorimotor axonal polyneuropathy, lumbar canal stenosis with loss of sphincter control, dysphagia, and dysautonomia, which the neurology group performed sural nerve biopsy finding amyloid deposit, this patient has genetic study being an ATTRh carrier of the Val-50Met mutation.

In our cohort, no ATTR patient received genetic stabilizers or silencers because they were not authorized in Colombia at the time of data collection. Regarding patients with AL amyloidosis, 42.86% received antineoplastic treatment by the hemato-oncology group. The patients who did not receive the treatment died. In our cohort, we had three positive pathogenic variants in the TTR gene. Two patients were carriers of Val142Ile, and one patient was a carrier of Val50Met.

The mortality found was 25.81%, from which, 19.35 % in the AL group and 6.45% in the ATTR group (Table S4). When analyzing the time between the moment of diagnosis and the date of death, it was shorter in the AL amyloidosis group with an average of 259 days compared to 922 days in the ATTR amyloidosis group as shown in other registries.

Table 4. Cardiac magnetic resonance

	n = 14	n = 9	n = 23
LVEF (preserved)	64.29%	33.33%	43.48%
LVEF (mildy reduced)	21.43%	44.44%	26.09%
LVEF (reduced)	14.29%	22.22%	17.39%
Teledyastolic volume (mL/m^2)	99.9	102	100.89
Telesystolic volume (mL/m^2)	51.02	58.46	54.54
Septum thickness (mm)	15.1	12.88	14.05
Late gadolinium enhancement	78.57%	100.00%	82.61%
Subendocardic enhancement	45.45%	44.44%	28.13%
Transmural enhancement	18.18%	33.33%	12.50%
Subepicardic enhancement	0.00%	0.00%	0.00%
Difuse cardiac enhancement	36.36%	22.22%	18.75%
Myocardial perfusion by c-MRI	27.27%	33.33%	26.09%
Pericardial disease	45.45%	77.78%	52.17%
Pericardial enhancement	0.00%	11.11%	4.35%

Discussion

The main forms of amyloidosis are AL and ATTR, the latter being the most frequent in our cohort. Regarding the sociodemographic characteristics, most of the patients analyzed were men. The average age was 74 years and ATTR was the principal type of cardiac amyloid in patients over 60 years which agrees with some previous reports[1,4,15,23,24].

Among the comorbidities to be highlighted, it is known that AF is common in patients with CA, either due to atrial amyloid infiltration or left atrial dilatation secondary to increased pressure in the context of diastolic dysfunction, mainly in the pseudonormalized pattern and restrictive[25].

It is notable that in our cohort, we only had one patient who required transcatheter aortic valve implantation due to low flow and low-gradient aortic stenosis. These findings raise the hypothesis that a search for amyloidosis is probably not being performed in patients with aortic stenosis mainly of low flow and low gradient since ventricular hypertrophy can be attributed only to the valve disease[1,26].

There are other cardiac findings considered as red flag signs, such as they are the disproportionate elevation of natriuretic peptides and a troponin persistently positive. In our study, we found that both troponin and proBNP have significant elevations, with higher elevations in the amyloidosis group AL compared to ATTR[1,2]. Regarding the echocardiographic findings, CA occurs in most cases as heart failure with preserved ejection fraction[2,16,18]. In our cohort, it was more frequent to find mildly reduced ejection fraction, followed by reduced and finally preserved. This may be secondary to late diagnosis, where there is already burnout phase[1,2]. AL amyloidosis produces greater impairment of ejection fraction with less hypertrophy and ATTR amyloidosis generates less drop in ejection fraction with greater ventricular hypertrophy[1,2,18,27]. When performing the analysis by subgroups, we observed contrary results, patients with ATTR amyloidosis presented with a worse ejection fraction compared to AL amyloidosis group. The results could be explained by late diagnosis of ATTR amyloidosis.

Another of the diagnostic methods that we have in our institution is the possibility of performing CMR. The indication is mainly in patients with negative hematological testing and negative scintigraphy but that persist with the suspicion diagnosis of amyloidosis since the scintigraphy can be negative in some certain of ATTRh[1,2,15]. In our study, CMR was performed on 23 patients, finding that a very high percentage of patients had late gadolinium enhancement mainly at the subendocardial and transmural. These findings have already been described previously in the literature[1,16,28,29].

Diffuse transmural LGE is more common in ATTR than in AL, while a pattern subendocardial is more common in AL amyloidosis, we found greater enhancement transmural in the AL amyloidosis group and the subendocardial pattern was similar in both groups, which differs from what was previously described by some descriptive studies and in a systematic review of studies that compared GTR with endomyocardial biopsy and/or echocardiography[28].

Late gadolinium enhancement has several limitations, including that gadolinium-based contrast agents have a relative contraindication in patients with reduced renal function, mainly filtration rates below 35 mL/min/1.73 m^2, which is common in patients with AL amyloidosis. Therefore, there are other findings in the diagnosis of amyloidosis such as elevated extracellular volume (ECV $\geq$ 0.40%). ECV in CA is higher compared to other heart diseases, except for infarct areas[1,21,28,29].

Native T1 increases and it may be abnormal before there is LVH and because it does not require contrast administration, this technique can be used in renal

disease. In addition, native T1 values are higher in ATTR than in other hypertrophic phenotypes[1,16,21,28,30]. Another sign considered a red flag and that we can see in the CMR, as well as in the echocardiogram is pericardial effusion, which is more frequently found in AL amyloidosis. In our cohort, we found that 52.17% of the population studied had mainly mild pericardial effusion and on subgroup analysis, this finding was found more frequently in AL amyloidosis compared to the ATTR group[1,16].

The initial diagnostic algorithm includes 99mTc-PYP scintigraphy or SPET together with the hematological test[1,2]. In our study, seven patients in the AL amyloidosis group did not have the complete algorithm since when hematological alterations were found, a biopsy of the affected organ was performed directly.

Elevated free serum or urine chains or immunofixation are not markers of specific AL, in some cases, can be seen in ATTRwt and in monoclonal gammopathy of uncertain meaning[1,2,27,31]. In our population, a patient with amyloidosis was found to have ATTR and MGUS.

One of the characteristics of AL amyloidosis is that the free light chains lambda predominated over the kappa light chains[16] and this behavior was observed in our AL amyloidosis cohort immunofixation in serum and urine should always be performed together with the chains, which increases diagnostic sensitivity[1,2,16,27] which we were able to observe in our study is that most of the patients had serum immunofixation, but this was not the case with the immunofixation in urine which was not performed in 21.88% of the patients.

All patients diagnosed with AL amyloidosis have a biopsy demonstrating the amyloid deposition, mainly bone marrow biopsy, followed by a cardiac biopsy, kidney, and finally, three cases of positive abdominal fat biopsy. Abdominal fat biopsy has a sensitivity of 84% to detect AL amyloidosis but has a low sensitivity in cases of ATTRh and ATTRwt (sensitivity 45% and 15%, respectively), for which it is not recommended for diagnosis but as we could see that it is still used, which demonstrates that continuous education should be carried out for health personnel from doctors to specialists, mainly hematologists, neurologists, and cardiologists for correctly apply diagnostic algorithms[22,32].

Extracardiac manifestations such as carpal tunnel syndrome, hematomas in the skin, cutis laxa, macroglossia, rupture of the biceps tendon, dysautonomia, deafness, lumbar spinal stenosis, vitreous deposits, corneal lattice dystrophy that are also considered red flag signs[1,16,33] were not reported in history at the time of the data collection, the hypothesis is that these findings were not found probably because they were not searched or recorded in the clinical history, which if we could observe is that the extracardiac manifestations found with greater frequency were at the level of the peripheral nervous system with small fiber neuropathy mainly in the group of AL amyloidosis[16,33].

Regarding the treatment in the group of patients with ATTR, none of them received any type of medication for the disease because it was not available in Colombia during the time of data collection.

The prognosis of ATTR amyloidosis without treatment is poor with a median survival between 2.5 years and 3.6 years[1,2,34,35].

Patients with AL amyloidosis with cardiac involvement without treatment for the disease have a median survival of approximately 6 months, the mortality in our cohort of patients with AL amyloidosis was 42.86%, of patients who died, none were undergoing chemotherapy.

Finally, if ATTR amyloidosis is identified, screening should be performed. Genetic sequencing of the TRR gene to define ATTRwt versus ATTRh since the confirmation of the latter should lead the patient to genetic counseling and the detection of family members[2]. A genetic study was performed on patients with ATTR amyloidosis, finding at the time of analysis, three patients with the results of the genetic study, two patients' carriers of the Val142Ile gene, and one carrier of the Val50Met gene.

Limitations

This is a descriptive and retrospective study, carried out in a single center.

We could not include all samples collected, since not everyone had the complete diagnostic algorithm, despite there being a high suspicion of CA.

Extracardiac manifestations that are considered red flag signs were not reported in history at the time of the data collection, the hypothesis is that these findings were not found probably because they were not searched or recorded in the clinical history.

Extracellular volume measurement was not performed in CMR, which can detect amyloidosis early even before the development of LV hypertrophy.

As a retrospective study, inherent biases related to the study type, such as data availability within medical records, may exist. However, the database was audited, and only records with over 90% of the data present were included to minimize data loss and prevent

interference with the proposed analysis. In addition, the data collection and audit process were conducted by two different experienced individuals, ensuring greater uniformity in the provided data.

Due to the lack of prevalence data for this disease in the country, convenience sampling was employed. Nevertheless, this is considered a limitation as it may affect the external validity of the study, as its generalizability to other areas may vary depending on the local prevalence of the disease.

A bivariate analysis was not performed because it is a case series with few patients, we consider an error with a high probability of bias.

Take home message

This study describes the first cohort of patients with CA in Colombia, developed in a center of high complexity and reference. Globally, few Published series describe the characteristics of patients with AC. The information obtained gives us an approach to the natural history and mortality of amyloidosis in our country. However, a big interrogation arises; are the diagnostic algorithms being applied correctly?

It is important to know the algorithms since there may be a coexistence of AL and ATTR amyloidosis or it may also be ATTR amyloidosis with concomitant MGUS or any hematological disorder, also the number of diagnoses made invasively decreases, hence the importance of all patients have 99mTc-DPD/PYP/HDMDP scintigraphy with SPECT at baseline. Even the greatest interest in the disease; it is still important to continue the awareness in the active search through red flags and to implement the use of diagnostic algorithms.

Conclusions

These results provided important information about the heterogeneous clinical presentation of patients with CA. Problems were found with late referrals, frequent hospitalizations, and lack of specific treatment. Most of the patients had reduced ventricular function, which translates into a delay in their diagnosis, with a higher mortality in the AL group, compared to ATTR.

There is an educational need for the knowledge of the disease, the use of diagnostic algorithms, and efficient diagnostic evaluations. An important part of patients with ATTR is that they can be diagnosed non-invasively, but it requires an increased level of suspicion and timely referral since early diagnosis has prognostic and therapeutic implications.

Supplementary data

Supplementary data are available at DOI: 10.24875/ACM.23000236. These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

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Conflicts of interest

None.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

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