Artículo de investigación original

Implementation of a clinical algorithm and an institutional registry for the follow-up of patients with transthyretin amyloid cardiomyopathy.

Implementación de un algoritmo clínico y un registro institucional para el seguimiento de pacientes con miocardiopatía amiloide por transtiretina.

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CONFLICTO DE INTERESES
Los autores del artículo hacen constar que no existe, de manera directa o indirecta, ningún tipo de conflicto de intereses que pueda poner en peligro la validez de lo comunicado.

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ABSTRACT
Introduction: Transthyretin amyloid cardiomyopathy is an infiltrative disease caused by the deposition of extracellular proteins, considered an important and unrecognized cause of heart failure in people over 60 years of age. Despite advances in cardiac imaging, diagnosis remains a challenge for medical professionals, largely due to a lack of awareness regarding clinical manifestations and the diagnostic step-by-step process. Previously, few therapeutic alternatives existed for its treatment; however, pharmacological and interventional therapies are currently available with promising results in modifying the course of the disease. ***Objective:*** To describe the clinical and sociodemographic characteristics of patients with a confirmed diagnosis of transthyretin amyloid cardiomyopathy within an institutional registry at a fourth-level institution, including a multidisciplinary diagnostic approach for suspected cases and the clinical evolution of patients with this diagnosis. ***Materials and methods:*** The implementation of an institutional care algorithm allowed for the active follow-up of patients with transthyretin amyloid cardiomyopathy and the creation of the institutional registry to describe disease progression, evaluate the clinical outcomes of therapies, and promote multidisciplinary participation for patient treatment. ***Conclusions:*** An institutional registry for transthyretin cardiac amyloidosis contributes to the estimation of the incidence, clinical course, and impact of current therapies for the disease, favoring clinical decision-making across specialties in a healthcare institution that serves as a reference in the management of patients with heart failure secondary to this disease.

Keywords: Cardiac amyloidosis, diagnostic techniques and procedures, heart failure, genetic diseases, registries, survival rate, transthyretin.

RESUMEN
Introduction: La miocardiopatía amiloide por transtiretina es una enfermedad infiltrativa causada por el depósito de proteínas extracelulares, considerada una causa importante y no reconocida de insuficiencia cardíaca en mayores de 60 años. A pesar de los avances en imagenología cardíaca, el diagnóstico sigue siendo un reto para el profesional médico, en gran parte debido al desconocimiento sobre las manifestaciones clínicas y el paso a paso diagnóstico. Anteriormente existían pocas alternativas terapéuticas para su tratamiento; sin embargo, actualmente se cuenta con terapias farmacológicas y de intervención con resultados prometedores en la modificación del curso de la enfermedad. ***Objetivo:*** Describir las características clínicas y sociodemográficas de pacientes con diagnóstico confirmado de miocardiopatía amiloide por depósito de transtiretina en un registro institucional de una institución de cuarto nivel, que incluya un enfoque diagnóstico multidisciplinario de casos sospechosos y la evolución clínica de los pacientes con dicho diagnóstico. ***Materiales y métodos:*** La implementación de un algoritmo de atención institucional permitió el seguimiento activo de pacientes con miocardiopatía amiloide por transtiretina y la creación del registro institucional para describir la progresión de la enfermedad, evaluar los resultados clínicos de las terapias y promover la participación multidisciplinaria para el tratamiento de los pacientes. ***Conclusiones:*** Un registro institucional de amiloidosis cardíaca por transtiretina contribuye a la estimación de la incidencia, el curso clínico y el impacto de las terapias actuales de la enfermedad, favoreciendo la toma de decisiones clínicas entre especialidades en una institución de salud referente en el manejo de pacientes con falla cardíaca secundaria a dicha enfermedad.

Palabras clave: Amiloidosis cardíaca, enfermedades genéticas, insuficiencia cardíaca, registros, tasa de supervivencia, técnicas y procedimientos diagnósticos, transtiretina.

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INTRODUCTION

Transthyretin amyloid cardiomyopathy (ATTR-CM) is an infiltrative disease caused by extracellular protein deposition and is a major and unrecognized cause of heart failure in people over 60 years of age. Among pro-amyloid proteins at the cardiac level, transthyretin produces one of the most common forms of cardiac amyloidosis, either through mutation (ATTRv-CM) or in its natural wild-type form (ATTRwt-CM), previously known as senile amyloidosis.[1] Historically, therapeutic options were limited. Advances in cardiac imaging and diagnostic strategies, including echocardiography and magnetic resonance imaging, have improved recognition, although these techniques cannot reliably differentiate ATTR-CM from other causes of hypertrophy or light-chain amyloidosis.[2,3] Delays and misdiagnoses have been common, with 10% to 15% of older adults with heart failure potentially having ATTR-CM. Clinical heterogeneity, limited access to specialized diagnostics, and its prior classification as a rare, untreatable disease have contributed to underdiagnosis.[4,5] Although primary amyloidosis dominated early data, ATTR-CM has become increasingly recognized and is now considered more prevalent. This shift reflects greater disease awareness and improved diagnostic processes, although targeted therapies were historically unavailable.[4,5] The complex clinical presentation of ATTR-CM, often involving heart failure with preserved or reduced ejection fraction and fatal arrhythmias, requires multidisciplinary attention.[6,7] If untreated, ATTR-CM is progressive and fatal within 5-15 years, with median survival often under 10 years.[8] Orthotopic liver transplantation has been used since 1990.[8,9] Patient registries are crucial to monitor outcomes and survival, helping address the challenges of data collection in rare diseases.[10,11] This study aims to describe an institutional, clinical, demographic, and genetic registry of patients with confirmed ATTR-CM, emphasizing clinical characteristics and diagnostic approaches.

METHODS

Dissemination strategy for ATTR identification

A knowledge appropriation campaign as an institutional strategy was implemented to ensure that the different services and specialties related to the disease could recognize these clinical conditions. Thematic webinars, flyers, and videos were disseminated through internal and institutional social networks (Figure 1).

Historical database review

Databases containing medical records of patients treated between 2015 and 2020 with heart failure (HF)-related diagnoses according to ICD-10 were pre-selected. Diagnoses included: I500, I509, G560, I350, I48X, E859, E85.4, and E85.82. Afterwards, clinical

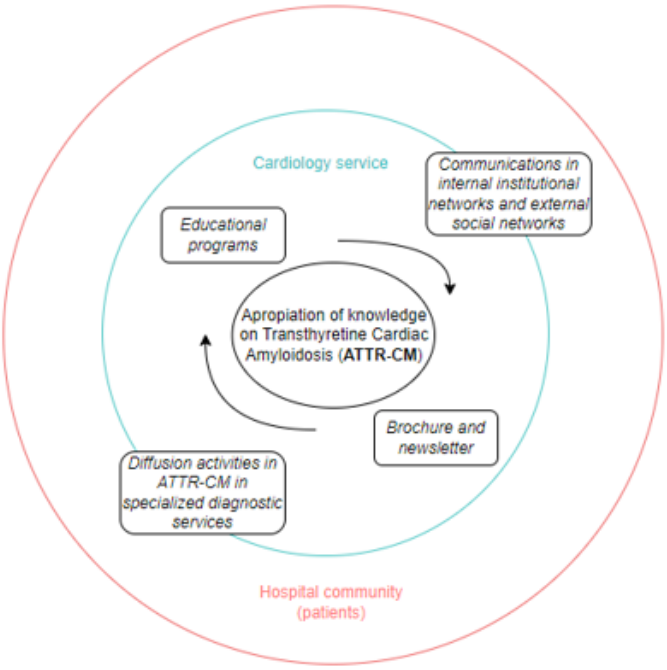

Figure 1. ATTR-CM knowledge appropriation institutional strategy.

conditions related to ATTR-CM were defined: left ventricular ejection fraction <45%, bilateral carpal tunnel syndrome, conduction disorders (atrial fibrillation, atrial flutter), biceps brachii rupture, aortic stenosis, dysautonomia, and peripheral neuropathy. A patient was considered suspicious for ATTR-CM if over 60 years old with heart failure, septal thickness ≥12 mm (transthoracic echocardiography), and at least one red flag identified through clinical record or questionnaire.Inclusion criteria were patients older than 18 years, with confirmed ATTR-CM diagnosis and signed informed consent. Exclusion criteria were patients under 18 years, those who refused participation, or those whose ATTR-CM diagnosis was ruled out.

Identification of new cases of ATTR-CM

Related to historical database review:
Suspected patients were invited to participate in the registry after signing informed consent during follow-up appointments in the cardiology department. Patients followed a diagnostic algorithm (Figure 2), where physicians, based on clinical judgment, either ruled out ATTR-CM or requested further tests (NT-proBNP, free light chains, cardiac MRI). Confirmed cases underwent genetic counseling and molecular testing to classify ATTRv-CM or ATTRwt-CM.

Non-related to historical database:
Since 2021, after implementing the dissemination strategy, the

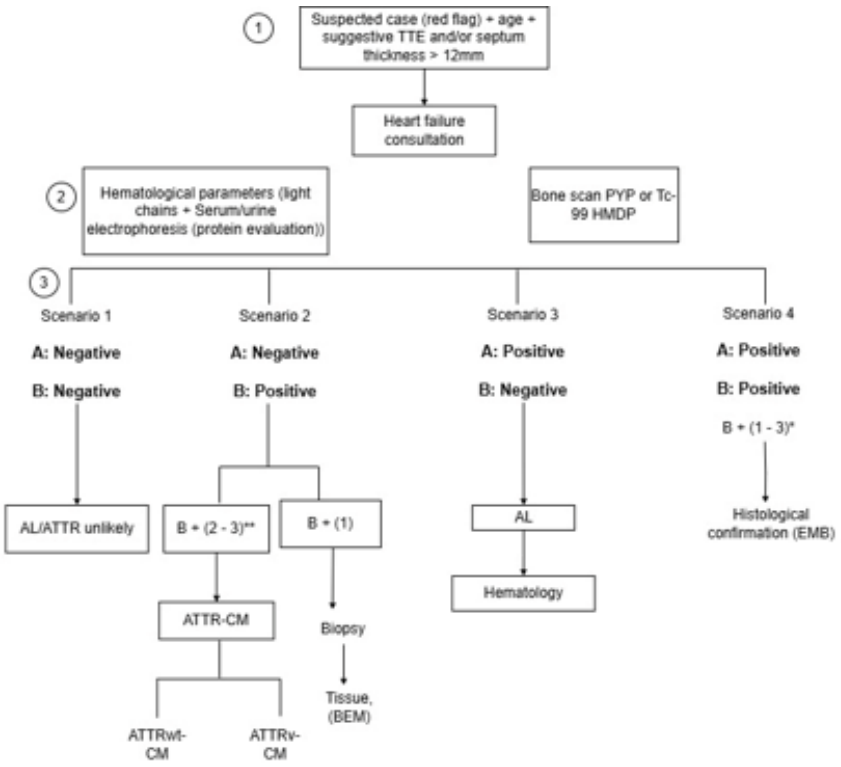

Figure 2. Clinical care algorithm for the classification and diagnosis of ATTR-CM patients (TTE: Transthoracic echocardiogram, PYP: Pyrophosphate, AL: Primary amyloidosis, wt: wild type, m: hereditary, EMB: Endomyocardial biopsy)**Uptake on Scintigraphy grade 2-3 * Uptake on Scintigraphy grade 1-3.

cardiology department and related services identified red flags in heart failure patients with septum thickness ≥12 mm and referred them to the heart failure program, where the diagnostic algorithm (Figure 2, Steps 1-3) was applied.

Registry procedures

Clinical information from confirmed patients was collected for the ATTR-CM registry through active search of institutional clinical records after obtaining informed consent. Collected data included: left ventricular ejection fraction, NYHA class, NT-proBNP, emergency consultations due to heart failure symptoms, septal thickness, medical treatment, ATTR-CM type, patient-reported outcome measures (EQ-5D), mortality, and clinical red flags. Patient information is continuously updated according to cardiology department follow-ups and the Colombian Integrated Social Protection Information System (SISPRO).

Patient-reported outcome measure analysis

Quality of life was assessed using the EQ-5D scale at 1, 3, and 6 months during the first year, and yearly thereafter.

Survival analysis

Survival analysis included diagnosed ATTR-CM patients. The survival period was calculated from diagnosis to death or last follow-up using the Kaplan-Meier method.The registry is hosted on an institutional platform and managed by the Institutional Research Center and the cardiology department. To ensure confidentiality, all registry members signed a confidentiality agreement. Platform access is restricted to authorized personnel with password protection. Qualified personnel collect information on new cases and update follow-up data on vital status and last contact.

RESULTS

The institutional socialization of this algorithm contributed to the involvement of cardiology, neurology, genetic and genomic medicine, geriatrics, and radiology services for the identification and management of patients with suspected ATTR-CM (Figure 3). The institutional historical database review strategy included an active recruitment search through an exhaustive medical record review process, allowing the identification of a cohort of 615 patients with a heart failure diagnosis. Thirty-seven of these patients

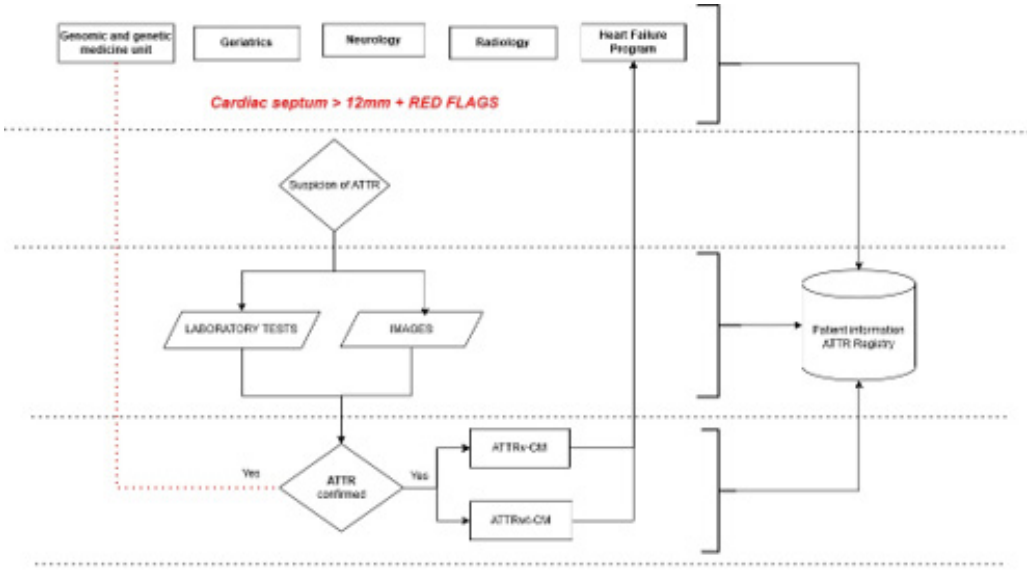

Figure 3. Diagnostic algorithm for Non-related to historical database for suspected ATTR-CM patients.

presented suspicious clinical characteristics (60 years or older, septum thickness ≥12 mm, and at least one confirmed red flag).

Of these 37 suspicious patients, the diagnostic algorithm (Figures 2-3) was applied in only three patients; because of local health system administration issues (lack of healthcare provider contracts, lack of authorization for diagnostic procedures), 34 patients could not follow the algorithm. Regarding the remaining three patients, one was confirmed and included in the registry, and two patients were ruled out for ATTR-CM.

Since 2021, the ATTR-CM knowledge appropriation institutional strategy allowed the implementation of the diagnostic algorithm. Eighteen new patients were diagnosed, five during the first year and thirteen over the following three years,of whom two refused to take part in the registry, resulting in sixteen additions to the registry (Table 1).

The estimated survival rate for patients diagnosed with ATTR after approximately 40 months of follow-up was 62% (Figure 4). The ATTR-CM registry includes the frequency of individuals for each level of quality of life measured across the five dimensions from the EQ-5D scale. The dimensions included are anxiety/depression, mobility, self-care, usual activities, and pain/discomfort (Table 2).

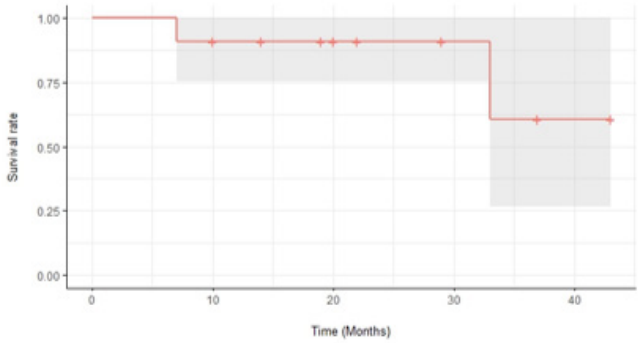

Figure 4. Survival rate for ATTR registry patients.

DISCUSSION

The creation of an institutional ATTR-CM registry has become a useful tool to study the etiology and progression of this rare disease. In addition, it could serve as a regional and local pioneer study for establishing diagnostic algorithms in orphan diseases. The benefits of using global patient registries for rare diseases are well established. Creating this tool is often the initial step in charting the natural history of a rare disease, with the information gathered describing its progression, including patient-reported outcomes. Registries also unite an international community of physicians from different disciplines, whose collective clinical experience can lead to recommendations for clinical management.[11]

In this fourth-level clinic, there were multiple challenges for follow-up. To address them, strategies based on patient education and evidence-based medicine were proposed, contributing

to the systematization and structuring of the information.[11] One challenge was the awareness and education about ATTR-CM across clinical services. As a rare disease, paradigms and myths surrounding its diagnosis are common; thus, focusing on education with other specialties enhances active patient searching. Multidisciplinary work with clinical specialties contributed to timely diagnosis; communication channels included academic webinars and care algorithm dissemination.[12,13]

Identifying red flags for ATTR-CM diagnosis through historical database reviews of heart failure patients proved effective for establishing suspicion criteria. Prior to the registry's implementation and the limited dissemination of clinical criteria, delays hindered timely ATTR-CM diagnosis.[1] Classical clinical manifestations of ATTR-CM vary between wild-type and hereditary forms, yet most patients experience a mixed phenotype with heart failure symptoms as well as neuropathic and cardiac manifestations. Heart dysfunction is primarily characterized by restrictive cardiomyopathy, arrhythmias like atrial fibrillation, and sensorimotor and autonomic neuropathies, alongside histories of carpal tunnel syndrome, spinal stenosis, and distal biceps tendon rupture. Other extracardiac manifestations include orthostatic hypotension, erectile dysfunction, gastrointestinal abnormalities, and unexplained weight loss.[14-16]

Patients with ATTR-CM are known to have high morbidity and mortality rates (up to 15% mortality in hospitalized heart failure patients with preserved ejection fraction). Tafamidis has shown promising results by reducing all-cause mortality and cardiovascular hospitalizations in ATTRwt-CM and ATTRv-CM patients in phase 3 trials.[16] In our study, the mortality rate increased to 35.29%. This can be explained by a lack of efficient healthcare provision, associated comorbidities worsening clinical condition, or patients not seeking timely medical attention, as all deaths occurred outside this institution. Notably, none of these deceased patients received tafamidis or underwent heart transplantation. The six patients receiving tafamidis are alive and show favorable clinical evolution, and only one underwent a heart transplant, currently experiencing complications likely related to chronic rejection. Major comorbidities seen included hypertension, diabetes mellitus, aortic stenosis, arrhythmias, chronic kidney disease, and prostate cancer, though not all are among the most frequent. The p.Val142Ile variant, a single amino acid substitution of valine to isoleucine at position 142, is the most common cause of ATTRv-CM and predominates among individuals of African descent. Reported prevalence ranges from 1.1% to 9.8% in African-descent populations.[17] The prevalence in a region depends on the proportion of individuals of African descent; Cali, having Colombia's largest Afro-descendant population,[18] may explain why all cohort patients with ATTRv-CM had the p.Val142Ile variant. This amyloidosis typically manifests in the seventh to eighth decades of life, more commonly in men, with 25-38% presenting atrial fibrillation. This variant correlates with worse quality of life and lower adjusted survival rates compared to other ATTR-CM types, findings also observed in our cohort.[19]

Table 1. Sociodemographic, Clinical and Treatment Characteristics.

Variable	Total (N=17)
Sociodemographic	
Age (Years) Me, (min-max)	76 (35-88)
Male gender (n, %)	11 (64.71%)
Race/Ethnicity (n, %)	Hispanic 10 (58.82%)
	Afro-American 7 (41.18%)
Mortality	6 (35.29 %)
Medical History	
Hypertension (n, %)	12 (70.59%)
Carpal Tunnel Syndrome (n, %)	8 (47.06%)
Atrial Fibrillation (n, %)	8 (47.06%)
Peripheral Neuropathy (n, %)	4 (23.53%)
Diabetes Mellitus (n, %)	4 (23.53%)
Aortic Stenosis (n, %)	4 (23.53%)
Gastrointestinal Affection (n, %)	4 (23.53%)
Biceps Brachii Rupture (n, %)	1 (5.88%)
Clinical Characteristics	
ATTR-CM Type (n, %)	ATTRv-CM 10 (58.82%)
	ATTRwt-CM 7 (41.18%)
Hereditary ATTR-CM Mutation	Val142Ile 10 (100%)
NYHA Scale at Onset (n, %)	NYHA III 7 (41.18%)
	NYHA II 6 (35.29%)
Diagnostic Tests	
Interventricular Septal Thickness Me, (min-max)	16 (12-28)
Initial Ejection Fraction (%) Me, (min-max)	45% (26-68)
Treatment	
Tafamidis n (%)	6 (35.29%)
Cardiac Transplant n (%)	1 (5.88%)

Finally, the institutional ATTR-CM registry collects clinically relevant variables, serving as a complementary tool to the heart failure program for patient follow-up. Beyond being a structured digital tool, it consists of specialized professionals dedicated to providing personalized, timely care, where each health professional contributes to expanding knowledge and improving life expectancy and quality of life for these patients.[20] This study is limited by administrative barriers in the healthcare system, as patients often face impediments in accessing medical appointments, procedures, and treatments, hindering continuous follow-up and clinical outcome supervision.

Table 2. Patient Reported Outcomes for Quality of Life (EQ-5D) in ATTR-CM after inclusion.

	Anxiety and depression n (%)	Day-to-day activities n (%)	Pain n (%)	Independence n (%)	Mobility n (%)
No problem	20 (50%)	20 (50%)	21 (52.5%)	32 (80%)	21 (52.5%)
Minor problem	12 (30%)	13 (32.5%)	10 (25%)	6 (15%)	11 (27.5%)
Moderate problem	6 (15%)	5 (12.5%)	7 (17.5%)	2 (5%)	7 (17.5%)
Severe problem	1 (2.5%)	2 (5%)	2 (5%)	0 (0%)	1 (2.5%)
Extreme problem	1 (2.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

N= 40 surveys realized, last updated March 10, 2025

ETHICAL DISCLOSURES AND ACKNOWLEDGEMENTS

The study was carried out in accordance with the ethical standards of the Declaration of Helsinki of 1975 and was approved by the Research Ethics Committee under registration number IRB00008539. The participating patients all signed the informed consent document.This study received unrestricted funding and support from Pfizer's Global Medical Grants (ID #62972511).

GENERATIVE ARTIFICIAL INTELLIGENCE (AI) USE DECLARATION

The authors declare that no Generative Artificial Intelligence (GAI) tools, Large Language Models (LLMs), or Artificial Intelligence (AI)-assisted technologies were used in any of the stages of conceptualization, writing, data processing, or image creation of this manuscript

REFERENCES

1. González-López E, López-Sainza A. Diagnostico y tratamiento de la amiloidosis cardiaca por transtiretina. Progreso y esperanza. 2017;70(11):991-1004. DOI: 10.1016/j.rec.2017.05.036
2. Gertz MA, Benson MD, Dyck PJ, Grogan M, Coelho T, Cruz M, *et al*. Diagnosis, Prognosis, and Therapy of Transthyretin Amyloidosis. J Am Coll Cardiol. 2015; 66(21):2451-66. DOI: 10.1016/j.jacc.2015.09.075
3. Jain H, Reddy MMRK, Dey RC, Jain J, Shakhatreh Z, Manandhar S, *et al*. Exploring Transthyretin Amyloid Cardiomyopathy: A Comprehensive Review of the Disease and Upcoming Treatments. Curr Probl Cardiol. 2024; 49(1):102057. DOI: 10.1016/j.cpcardiol.2023.102057
4. Wilches EC, López E, Arango GP. Rehabilitación funcional del paciente neurológico en la UCI. Fisioterapia en la UCI: Teoría, experiencia y evidencia. 2012;119-23.
5. Rapezzi C, Lorenzini M, Longhi S, Milandri A, Gagliardi C, Bartolomei I, *et al*. Cardiac amyloidosis: the great pretender. Heart Fail Rev. 2015; 20(2):117-24. DOI: 10.1007/s10741-015-9480-0
6. van der Meer P, Gaggin HK, Dec GW. ACC/AHA Versus ESC Guidelines on Heart Failure: JACC Guideline Comparison. J Am Coll Cardiol. 2019; 73(21):2756-68. DOI: 10.1016/j.jacc.2019.03.478
7. Saour B, Smith B, Yancy CW. Heart Failure and Sudden Cardiac Death. Card Electrophysiol Clin. 2017; 9(4):709-23. DOI: 10.1016/j.ccep.2017.07.010
8. Hund E, Linke RP, Willig F, Grau A. Transthyretin-associated neuropathic amyloidosis: Pathogenesis and treatment. Neurology. 2001; 56(4):431-5. DOI: 10.1212/wnl.56.4.431
9. Sekijima Y, Kelly J, Ikeda S ichi. Pathogenesis of and Therapeutic Strategies to Ameliorate the Transthyretin Amyloidoses. Curr Pharm Des. 2008; 14(30):3219-30. DOI: 10.2174/138161208786404155
10. Herlenius G, Wilczek HE, Larsson M, Ericzon BG. Ten years of international experience with liver transplantation for familial amyloidotic polyneuropathy: Results from the Familial Amyloidotic Polyneuropathy World Transplant Registry. Transplantation. 2004; 77(1):64-71. DOI: 10.1097/01.TP.0000092307.98347.CB
11. Planté-Bordeneuve V, Suhr OB, Maurer MS, White B, Grogan DR, Coelho T. The Transthyretin Amyloidosis Outcomes Survey (THAOS) registry: Design and methodology. Curr Med Res Opin. 2013; 29(1):77-84. DOI: 10.1185/03007995.2012.754349
12. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, *et al*. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2022; 79(17):e263-421. DOI: 10.1016/j.jacc.2021.12.012

13. Vanerio G. Síncope 2018: ¿qué hay de nuevo en las guías europeas? Revista Uruguaya de Cardiología. 2018; 33(3):295-302. DOI: 10.29277/cardio.33.3.9
14. Nativi-Nicolau JN, Karam C, Khella S, Maurer MS. Screening for ATTR amyloidosis in the clinic: overlapping disorders, misdiagnosis, and multiorgan awareness. Heart Fail Rev. 2022; 27(3):785-93. DOI: 10.1007/s10741-021-10080-2
15. Ruberg FL, Grogan M, Hanna M, Kelly JW, Maurer MS. HHS Public Access. 2020; 73(22):2872-91. DOI: 10.1016/j.jacc.2019.04.003
16. Porcari A, Fontana M, Gillmore JD. Transthyretin cardiac amyloidosis. Cardiovasc Res. 2022; 118(18):3517-35. DOI: 10.1093/cvr/cvac119
17. Jacobson DR, Alexander AA, Tagoe C, Buxbaum JN. Prevalence of the amyloidogenic transthyretin (TTR) V122I allele in 14 333 African-Americans. Amyloid. 2015; 22(3):171-4. DOI: 10.3109/13506129.2015.1051219
18. Secretaria de Salud Pública. ASIS Cali. 2022;1-274.
19. Chandrashekar P, Alhuneafat L, Mannello M, Al-Rashdan L, Kim MM, Dungu J, *et al*. Prevalence and Outcomes of p.Val142Ile TTR Amyloidosis Cardiomyopathy: A Systematic Review. Circ Genom Precis Med. 2021; 14(5):E003356. DOI: 10.1161/CIRCGEN.121.003356
20. Stern LK, Grodin JL, Maurer MS, Ruberg FL, Patel ARr, Khouri MG, *et al*. The Cardiac Amyloidosis Registry Study (CARS): Rationale, Design and Methodology. J Card Fail. 2023; 0(0). DOI: 10.1016/j.cardfail.2023.09.016