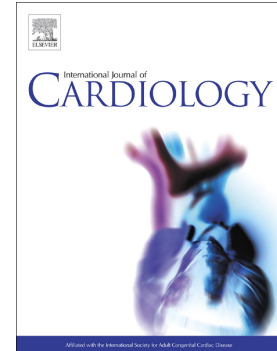


Journal Pre-proof

Characteristics of patients with suspected cardiac amyloidosis in Tuscany and Umbria: Insights from the cardiac amyloidosis RegistRY (CARRY)



Vincenzo Castiglione, Olena Chubuchna, Giulia Elena Mandoli, Yu Fu Ferrari Chen, Alberto Aimò, Giorgia Panichella, Alessandro Paoletti Perini, Francesco Grossi, Massimo Milli, Annamaria Traini, Francesco Bellandi, Alessio Lilli, Giancarlo Casolo, Maurizio Pieroni, Serena Poli, Chiara Chiriatti, Simone Bartolini, Federico Perfetto, Alberto Palazzuoli, Claudio Passino, Riccardo Liga, Alberto Giannoni, Marta Focardi, Erberto Carluccio, Cinzia Zuchi, Carlo Di Mario, Giuseppe Ambrosio, Francesco Cappelli, Michele Emdin, Matteo Cameli, Giuseppe Vergaro

PII: S0167-5273(25)00728-4

DOI: <https://doi.org/10.1016/j.ijcard.2025.133685>

Reference: IJCA 133685

To appear in: *International Journal of Cardiology*

Received date: 13 October 2024

Revised date: 28 April 2025

Accepted date: 30 July 2025

Please cite this article as: V. Castiglione, O. Chubuchna, G.E. Mandoli, et al., Characteristics of patients with suspected cardiac amyloidosis in Tuscany and Umbria: Insights from the cardiac amyloidosis RegistRY (CARRY), *International Journal of Cardiology* (2024), <https://doi.org/10.1016/j.ijcard.2025.133685>

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production

process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2025 Published by Elsevier B.V.

Characteristics of Patients with Suspected Cardiac Amyloidosis in Tuscany and Umbria: Insights from the Cardiac Amyloidosis RegistRY (CARRY)

Vincenzo Castiglione^{1,2*}, Olena Chubuchna^{1*}, Giulia Elena Mandoli³, Yu Fu Ferrari Chen², Alberto Aimo^{1,2}, Giorgia Panichella^{1,9}, Alessandro Paoletti Perini⁴, Francesco Grossi⁴, Massimo Milli⁴, Annamaria Traini⁵, Francesco Bellandi⁵, Alessio Lilli⁶, Giancarlo Casolo⁶, Maurizio Pieroni⁷, Serena Poli⁸, Chiara Chiriatti⁸, Simone Bartolini⁹, Federico Perfetto⁹, Alberto Palazzuoli³, Claudio Passino^{1,2}, Riccardo Liga¹⁰, Alberto Giannoni^{1,2}, Marta Focardi³, Erberto Carluccio¹¹, Cinzia Zuchi¹¹, Carlo Di Mario⁹, Giuseppe Ambrosio¹¹, Francesco Cappelli⁹, Michele Emdin^{1,2}, Matteo Cameli^{3*}, Giuseppe Vergaro^{1,2*}

1. Health Science Interdisciplinary Center, Scuola Superiore Sant'Anna, Pisa, Italy; 2. Fondazione Toscana Gabriele Monasterio, Pisa, Italy; 3. University Hospital of Siena, Siena, Italy; 4. Ospedale Santa Maria Nuova, Florence, Italy; 5. Ospedale Santo Stefano, Prato, Italy; 6. Ospedale Versilia, Lido di Camaiore, Italy; 7. Ospedale San Donato, Arezzo, Italy; 8. Ospedale del Mugello, Borgo San Lorenzo, Florence, Italy; 9. Careggi University Hospital, Florence, Italy; 10. University Hospital of Pisa, Pisa, Italy; 11. Cardiologia e Fisiopatologia Cardiovascolare and CERICLET, University of Perugia, Perugia, Italy.

*Vincenzo Castiglione and Olena Chubuchna contributed equally; Giuseppe Vergaro and Matteo Cameli share the last authorship.

Running title: Characteristics of Patients with Suspected Cardiac Amyloidosis

Keywords: amyloidosis; diagnosis; epidemiology.

No conflict of interest to declare.

Funding: None.

Address for correspondence:

Giuseppe Vergaro, MD, PhD

Scuola Superiore Sant'Anna and Fondazione Toscana Gabriele Monasterio

Via G. Moruzzi 1, 56124 Pisa, Italy.

Email: vergaro@ftgm.it

ABSTRACT

Background: Cardiac amyloidosis (CA) involves the deposition of misfolded proteins in the heart, most commonly light-chains (AL) or transthyretin (ATTR). Advancements in non-invasive diagnostics have challenged the classification of CA as a rare disease. The Cardiac Amyloidosis Registry (CARRY) provides updated insights into CA's epidemiology, diagnosis, and clinical features.

Methods: CARRY is a prospective, multicenter study across 20 hospitals in Tuscany and Umbria. All patients aged ≥ 18 years with suspected CA were enrolled between January and December 2022. Baseline demographic, clinical, laboratory, and imaging data were collected, including all tests required to confirm or rule out CA diagnosis.

Results: Among 553 patients with complete data (median age 79 years [interquartile range, IQR, 74-84], 70% male), 87% reported mild dyspnea, 32% had a history of heart failure, and one-third reported carpal tunnel syndrome. Elevated cardiac biomarkers were prevalent, with a median NT-proBNP of 1015 ng/L (IQR 275-3198). Most patients exhibited a heart failure with preserved ejection fraction phenotype. No significant differences in clinical features were found between patients from university (referral centers) and non-university hospitals, though referral centers more often reported patients with hematologic disorders. Echocardiographic signs of overt CA were more frequent in non-university centers.

Conclusions: The CARRY registry highlights the clinical characteristics of patients with suspected CA, revealing that despite educational efforts, suspicion remains biased towards older patients with advanced disease. Increased awareness and earlier diagnosis, particularly with available disease-modifying therapies, are critical for improving outcomes.

Word count: 237

ABBREVIATIONS AND ACRONYMS

AL: amyloid light-chain

ATTRwt/v: wild type/variant amyloid transthyretin

CA: cardiac amyloidosis

ECG: electrocardiogram

HF: heart failure

HFpEF: heart failure with preserved ejection fraction

IQR: interquartile range

Journal Pre-proof

INTRODUCTION

Cardiac amyloidosis (CA) is characterized by the pathological deposition of misfolded proteins in the heart. Most causes of CA are caused by the accumulation of light-chains (AL) or transthyretin (ATTR), the latter either wild-type (ATTRwt) or hereditary (variant, ATTRv). Advances in non-invasive diagnostics, particularly bone tracer scintigraphy, have redefined the epidemiology of ATTRwt-CA, challenging its previous classification as a rare condition.¹

Over the past years, both the incidence and prevalence of cardiac amyloidosis (CA) have increased. Among Medicare beneficiaries aged ≥ 65 years in the United States, a significant rise has been observed in the prevalence rate (from 8 to 17 per 100,000 person-years) and incidence rate (from 18 to 55 per 100,000 person-years) of hospitalizations for all types of CA.² Regarding amyloidosis subtypes, data from the Olmsted County Project in Minnesota indicated an incidence rate of AL amyloidosis of 8.9 cases per million annually from 1950-1989,³ which increased to 12 cases per million person-years from 1990-2015.⁴ The global incidence of AL amyloidosis is estimated at 1 case per 95,800 individuals, with a male predominance and a median diagnosis age of 64 years.⁵ Cardiac involvement occurs $>75\%$ of patients with AL amyloidosis.⁵ In contrast, the epidemiology of ATTR-CA has been harder to define due to diagnostic challenges.

Nearly all epidemiological data on CA are retrospective and collected from administrative registries, leading to possible underestimation of the true incidence and prevalence of CA. Nonetheless, new disease-modifying therapies with prognostic benefit, such as tafamidis for ATTR amyloidosis, and their associated costs - often relying on the notion of CA as a rare disease - highlight the need for updated disease epidemiology.⁶ Interestingly, the CATCH study, the first prospective screening for ATTR-CA in the general population in Tuscany, Italy, recently found a prevalence of 0.46% for ATTR-CA among non-selected individuals aged ≥ 65 years.⁷ Although these numbers may seem high, the true prevalence is likely even underestimated, given that a significant proportion of initially eligible participants did not ultimately undergo dedicated screening. Additionally, the ACTIVE study reported a 29% prevalence of CA (51 ATTR-CA, 11 AL-CA) among 381 patients with

echocardiographic findings suggestive of the disease.⁸ Importantly, these findings reinforce the notion that, even within the general population, CA can be identified and may not be as rare as previously thought.

The Cardiac Amyloidosis Registry (CARRY) aims to determine the current incidence, diagnostic approaches, and clinical features of CA in Tuscany and Umbria.

METHODS

Study design

The CARRY is a prospective multicenter registry, endorsed by the Italian Society of Cardiology, collected data from in- and outpatients with suspected CA across 20 centers in Tuscany and Umbria, encompassing both cardiology and internal medicine departments from 5 amyloidosis referral (University) and 15 non-referral (non-University) hospitals. Recruitment occurred between January 1st and December 31st, 2022. Ethical approval was granted by the local Regional Institutional Review Board. The study adhered to the European Medicines Agency Guidelines for Good Clinical Practice and the 1975 Declaration of Helsinki principles.

All patients aged ≥ 18 years with suspected CA could be enrolled. Exclusion criteria were a prior diagnosis of amyloidosis or refusal/inability to provide informed consent. The study was divided into two phases: data collection of baseline characteristics and follow-up of patients diagnosed with CA (**Figure 1**). This article presents the study design and baseline characteristics of the enrolled population. At enrollment, comprehensive clinical, laboratory, electrocardiographic (ECG), and echocardiographic data were collected (**Supplementary table 1**). The initial visit involved gathering demographic data, medical therapy, vital parameters, and conducting ECG, echocardiography, and biohumoral tests. Detailed information on timing and results of each diagnostic procedure, including scintigraphy, cardiac magnetic resonance imaging, histology, and genetic testing leading to a final diagnosis of CA or alternative conditions, was documented. CA diagnosis was established according to the European Society of Cardiology position statement.⁹

Initial disease suspicion was raised by cardiology or internal medicine physicians at participating hospitals. The index physician performed the first clinical assessment. Echocardiographic measurements were performed by sub-investigators at each center. Given the study's real-world design, some heterogeneity in assessments between different hospitals was expected. Diagnostic confirmation occurred either at the same hospital or at a referral center. Patients were enrolled from both outpatient and inpatient settings. In case of hospital transfers, the center where suspicion first arose was considered the enrolling site, and a unique code ensured no duplication of participants.

The primary objective was to estimate the current incidence of CA in Tuscany and Umbria, which will be the subject of a forthcoming publication. Another objective of the CARRY registry was to elucidate the current diagnostic pathways for CA patients and assess the clinical characteristics of patients with suspected CA.

Statistical analysis

Statistical analyses were conducted utilizing IBM SPSS Statistics version 22 (IBM, Armonk, NY, USA). Normality of data distributions was evaluated through the Kolmogorov-Smirnov test. Data adhering to a normal distribution are presented as mean \pm standard deviation, while non-normally distributed data are reported using the median and interquartile range. Group comparisons were performed through either the Student's t-test or the Mann-Whitney U test, contingent on the distribution of the data. For comparisons between more than two groups, ANOVA or Kruskal–Wallis tests were employed, depending on the distribution of the data. Comparisons of categorical data were conducted using the Chi-square test with Yates correction. A two-tailed p-value <0.05 was deemed statistically significant.

RESULTS

Patients with complete baseline data were 553 (out of 564 initially enrolled), with a median age of 79 years (interquartile range, IQR, 74-84) and male predominance (70%) (**Table 1**). Most patients (87%)

reported mild effort dyspnea (New York Heart Association class I or II), and 18% experienced paresthesia. One third had a history of heart failure (HF), and 15% had a diagnosed hematologic disease at baseline, mainly monoclonal gammopathy of unknown significance. Musculoskeletal red flags of amyloidosis, particularly carpal tunnel syndrome, were reported by 33% of patients. Cardiac biomarkers were elevated in almost all patients, with median N-terminal pro-B-type natriuretic peptide of 1,015 ng/L (IQR 275-3,198) and high sensitivity troponin T 29 ng/L (17-58). Most patients had a HF with preserved ejection fraction (HFpEF) phenotype, with increased left ventricular wall thickness, diastolic dysfunction, and an enlarged left atrium.

Most patients (87%) were enrolled at University Hospitals. No significant differences were noted between patients enrolled at University versus non-University Hospitals regarding biometric characteristics, symptoms, comorbidities, musculoskeletal indicators, treatment, and ECG features. However, patients at non-University Hospitals displayed more overt CA echocardiographic features, such as greater hypertrophy/pseudohypertrophy and smaller left ventricular chamber size. Hematologic diseases were more frequently reported among patients enrolled at University Hospitals, likely due to referral bias of patients with suspected AL amyloidosis to tertiary referral Centers.

Supplementary table 2 shown patient characteristic stratified by age group (<70, 70-79, 80-89, ≥90 years). Older patients were more likely to report a higher NYHA class, but less likely to report paresthesia. The burden of comorbidities increased with age, except for hematologic diseases. Musculoskeletal and ECG indicators of CA did not show significant age-related differences. However, cardiac biomarker levels and prevalence of tachyarrhythmias or conduction disturbances increased with age. Older patients more frequently had a history of HF and exhibited echocardiographic phenotypes typical of overt CA.

DISCUSSION

This is a comprehensive report on the clinical characteristics of a contemporary cohort of individuals undergoing a diagnostic workup due to suspected CA. The baseline characteristics align with those

reported in contemporary retrospective studies.¹⁰ Specifically, the echocardiographic data are consistent with those from the AC-TIVE study, aimed at determining the prevalence of CA among subjects with suggestive echocardiograms.¹¹

Despite recent educational activities have increased awareness about CA even among general cardiologists, CA is less frequently suspected in non-referral hospitals. Nonetheless, the similarity in patient characteristics from referral and non-referral centers suggests that suspicion of disease, whenever is raised, occurs at similar stage. Moreover, the suspicion of CA remains age-biased, with older subjects suspected of having the disease only when exhibiting a more advanced phenotype, limiting the potential prognostic impact of therapy. With the recent introduction and effectiveness of disease-modifying treatments, awareness of CA among healthcare professionals needs to be further increased. Due to its progressive nature and potential for more effective intervention at earlier stages, there is imperative clear need to actively seek out and diagnose CA in a broader patient population, including the elderly. Besides providing more information about the epidemiology of CA, the results of the CARRY registry may help identify some clinical, educational and organizational barriers to the timely diagnosis of CA.

FUNDING

None.

DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

Journal Pre-proof

REFERENCES

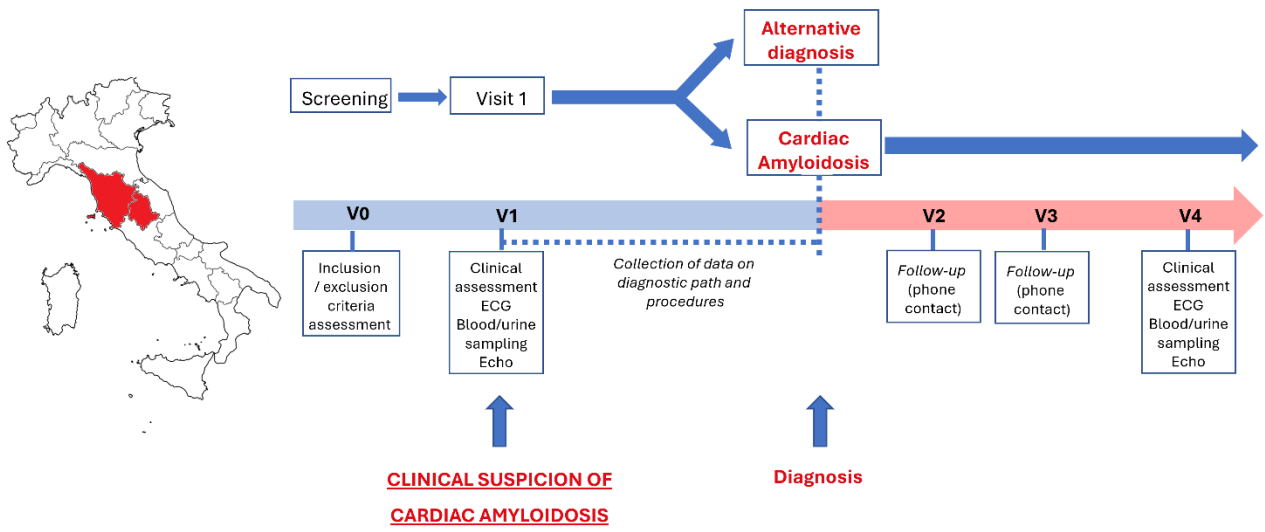
1. Aimo A, Merlo M, Porcari A, Georgiopoulos G, Pagura L, Vergaro G, Sinagra G, Emdin M, Rapezzi C. Redefining the epidemiology of cardiac amyloidosis. A systematic review and meta-analysis of screening studies. *Eur J Heart Fail* 2022;**24**:2342–2351.
2. Gilstrap LG, Dominici F, Wang Y, El-Sady MS, Singh A, Di Carli MF, Falk RH, Dorbala S. Epidemiology of Cardiac Amyloidosis-Associated Heart Failure Hospitalizations Among Fee-for-Service Medicare Beneficiaries in the United States. *Circ Heart Fail* 2019;**12**:e005407.
3. Kyle RA, Linos A, Beard CM, Linke RP, Gertz MA, O'Fallon WM, Kurland LT. Incidence and natural history of primary systemic amyloidosis in Olmsted County, Minnesota, 1950 through 1989. *Blood* 1992;**79**:1817–1822.
4. Kyle RA, Larson DR, Kurtin PJ, Kumar S, Cerhan JR, Therneau TM, Rajkumar SV, Vachon CM, Dispenzieri A. Incidence of AL Amyloidosis in Olmsted County, Minnesota, 1990 through 2015. *Mayo Clin Proc* 2019;**94**:465–471.
5. Orphanet: Amyloidosis <https://www.orpha.net/en/disease/detail/69> (10 March 2024)
6. Castiglione V, Aimo A, Vergaro G. Cost-effectiveness of transthyretin cardiac amyloidosis screening and treatment: A Dilemma for the clinician. *Int J Cardiol* 2024:131855.
7. Aimo A, Vergaro G, Castiglione V, Fabiani I, Barison A, Gentile F, Ferrari Chen YF, Giorgetti A, Genovesi D, Buda G, Franzini M, Piepoli M, Moscardini S, Rapezzi C, Fontana M, Passino C, Emdin M. Wild-type transthyretin cardiac amyloidosis is not rare in elderly subjects: the CATCH screening study. *Eur J Prev Cardiol* 2024;**31**:1410–1417.
8. Merlo M, Pagura L, Porcari A, Cameli M, Vergaro G, Musumeci B, Biagini E, Canepa M, Crotti L, Imazio M, Forleo C, Cappelli F, Perfetto F, Favale S, Di Bella G, Dore F, Girardi F, Tomasoni D, Pavasini R, Rella V, Palmiero G, Caiazza M, Carella MC, Igoren Guaricci A, Branzi G,

- Caponetti AG, Saturi G, La Malfa G, Merlo AC, Andreis A, Bruno F, Longo F, Rossi M, Varrà GG, Saro R, Di Ienno L, De Carli G, Giacomini E, Arzilli C, Limongelli G, Autore C, Olivotto I, Badano L, Parati G, Perlini S, Metra M, Emdin M, Rapezzi C, Sinagra G. Unmasking the prevalence of amyloid cardiomyopathy in the real world: results from Phase 2 of the AC-TIVE study, an Italian nationwide survey. *Eur J Heart Fail* 2022;**24**:1377–1386.
9. Garcia-Pavia P, Rapezzi C, Adler Y, Arad M, Basso C, Brucato A, Burazor I, Caforio ALP, Damy T, Eriksson U, Fontana M, Gillmore JD, Gonzalez-Lopez E, Grogan M, Heymans S, Imazio M, Kindermann I, Kristen AV, Maurer MS, Merlini G, Pantazis A, Pankuweit S, Rigopoulos AG, Linhart A. Diagnosis and treatment of cardiac amyloidosis: a position statement of the ESC Working Group on Myocardial and Pericardial Diseases. *Eur Heart J* 2021;**42**:1554–1568.
10. Vergaro G, Castiglione V, Aimo A, Prontera C, Masotti S, Musetti V, Nicol M, Cohen Solal A, Logeart D, Georgiopoulos G, Chubuchny V, Giannoni A, Clerico A, Buda G, Patel KN, Razvi Y, Patel R, Wechalekar A, Lachmann H, Hawkins PN, Passino C, Gillmore J, Emdin M, Fontana M. N-terminal pro-B-type natriuretic peptide and high-sensitivity troponin T hold diagnostic value in cardiac amyloidosis. *Eur J Heart Fail* 2023;**25**:335–346.
11. Merlo M, Porcari A, Pagura L, Cameli M, Vergaro G, Musumeci B, Biagini E, Canepa M, Crotti L, Imazio M, Forleo C, Cappelli F, Favale S, Di Bella G, Dore F, Lombardi CM, Pavasini R, Rella V, Palmiero G, Caiazza M, Albanese M, Guaricci AI, Branzi G, Caponetti AG, Saturi G, La Malfa G, Merlo AC, Andreis A, Bruno F, Longo F, Sfriso E, Di Ienno L, De Carli G, Giacomini E, Spini V, Milidoni A, Limongelli G, Autore C, Olivotto I, Badano L, Parati G, Perlini S, Metra M, Emdin M, Rapezzi C, Sinagra G. A national survey on prevalence of possible echocardiographic red flags of amyloid cardiomyopathy in consecutive patients undergoing routine echocardiography: study design and patients characterization - the first insight from the AC-TIVE Study. *Eur J Prev Cardiol* 2022;**29**:e173–e177.

Journal Pre-proof

FIGURE LEGENDS

Figure 1. Flow chart of the CARRY registry.



Journal Pre-proof

Table 1. Baseline characteristics according to site of enrolment.

	All (n=553)	University Hospital (n=482)	Non-University Hospitals (n=71)	p value
Men, n (%)	385 (70)	341 (71)	44 (62)	0.133
Age (years)	79 (74-84)	79 (73-84)	80 (76-85)	0.211
BMI (kg/m ²)	26 (23-28)	26 (23-29)	25 (23-28)	0.077
SAP (mmHg)	135 (120-150)	135 (120-150)	130 (120-140)	0.081
DAP (mmHg)	80 (70-85)	80 (70-85)	70 (70-80)	0.026
NYHA class:				0.514
I, n (%)	179 (32)	156 (32)	23 (32)	0.968
II, n (%)	306 (55)	270 (56)	36 (51)	0.419
III, n (%)	66 (12)	54 (11)	12 (17)	0.167
IV, n (%)	2 (1)	2 (1)	-	-
Paraesthesia, n (%)	99 (18)	85 (18)	14 (20)	0.472
<i>Comorbidities</i>				
Hypertension, n (%)	434 (79)	374 (78)	60 (85)	0.186
Diabetes, n (%)	122 (22)	110 (23)	12 (17)	0.261
COPD, n (%)	70 (13)	63 (13)	7 (9)	0.447
Ischaemic heart disease, n (%) ^a	110 (20)	97 (20)	13 (18)	0.721
Heart failure, n (%)	176 (32)	157 (33)	19 (27)	0.326
Haematologic disease, n (%) ^b	84 (15)	76 (16)	8 (11)	0.324
Multiple myeloma, n (%)	13 (2)	13 (3)	-	-
Smouldering myeloma, n (%)	6 (1)	5 (1)	1 (1)	0.563
MGUS, n (%)	42 (8)	36 (8)	6 (9)	0.771
<i>Musculoskeletal red flags</i>				
Carpal tunnel syndrome, n (%)	181 (33)	157 (33)	24 (34)	0.837
Monolateral, n (%)	51 (9)	44 (9)	7 (10)	0.843
Bilateral, n (%)	130 (24)	113 (23)	17 (24)	0.926

Spontaneous tendon rupture, n (%)	74 (13)	68 (14)	6 (9)	0.178
Lumbar spinal stenosis, n (%)	24 (4)	22 (5)	2 (3)	0.489
<i>Therapy</i>				
Beta-blocker, n (%)	301 (54)	268 (56)	33 (47)	0.150
ACEi/ARB/ARNI, n (%)	317 (57)	278 (58)	39 (55)	0.662
MRA, n (%)	104 (19)	93 (19)	11 (16)	0.444
Loop diuretic, n (%)	248 (45)	217 (45)	31 (44)	0.830
Antiplatelet, n (%)	174 (32)	151 (31)	23 (32)	0.857
Anticoagulant, n (%)	215 (39)	187 (39)	28 (39)	0.918
<i>Laboratory data</i>				
Haemoglobin (g/dL)	13 (12-14)	13 (12-14)	13 (12-14)	0.353
eGFR (mL/min/1.73 m ²)	48 (37-60)	48 (38-59)	48 (35-62)	0.959
NT-proBNP (ng/L) ^c	1015 (275-3198)	1105 (266-3235)	708 (405-2699)	0.820
hs-TnT (ng/L) ^d	29 (17-58)	27 (16-54)	68 (40-81)	0.008
<i>Electrocardiogram^e</i>				
Heart rate (bpm)	70 (61-80)	70 (62-80)	70 (60-80)	0.786
Sinus rhythm, n (%)	346 (63)	305 (63)	41 (58)	0.224
Atrial fibrillation/flutter, n (%)	135 (24)	115 (24)	20 (28)	0.515
Paced rhythm, n (%)	58 (11)	48 (10)	10 (14)	0.332
Low voltages – peripheral leads, n (%) ^f	104 (19)	91 (19)	13 (18)	0.774
Low voltages – diffuse, n (%) ^g	29 (5)	18 (4)	11 (16)	<0.001
Pseudo-infarct pattern, n (%) ^h	62 (11)	54 (11)	8 (11)	0.911
<i>Echocardiogram</i>				
IVSd (mm)	14 (12-16)	14 (12-16)	15 (13-16)	0.002
PWTd (mm)	12 (11-14)	12 (10-14)	14 (12-15)	<0.001
LVEDd (mm)	47 (42-52)	47 (43-52)	45 (42-50)	0.222
LVEDVi (mL/m ²)	54 (42-67)	55 (44-67)	36 (24-53)	<0.001

LVMi (g/m ²)	123 (101-154)	119 (99-149)	163 (127-174)	0.003
LVEF, n (%)	56 (50-62)	57 (50-62)	55 (46-60)	0.313
LVEF ≥50, 40-49%, ≤40%%, n (%)	419, 65, 69 (76, 12, 12)	368, 57, 57 (76, 12, 12)	51, 8, 12 (72, 11, 17)	0.482
E/e' ratio	13 (10-17)	12 (10-16)	14 (10-20)	0.192
LAd (mm)	43 (40-48)	43 (40-48)	44 (40-48)	0.820
TAPSE (mm)	20 (16-23)	20 (16-22)	21 (18-23)	0.034

a) Ischaemic heart disease: history of acute coronary syndrome, previous percutaneous coronary intervention or coronary artery bypass graft, or documentation of >50% stenosis in at least one epicardial vessel. b) Other or unspecified haematologic disease type: 23 (4%) cases. c) Available for 480 (87%) patients (428 [89%] from UH; 52 [73%] from GH). d) Available for 297 (54%) patients (286 [59%] from UH; 11 [16%] from GH). e) Unavailable/undetermined rhythm: 14 (3%) cases. f) QRS amplitude ≤5 mm in each peripheral lead. g) QRS amplitude ≤5 mm in each peripheral and ≤10 mm in each precordial lead. h) pathological Q waves (1/4 R amplitude) or QS waves on 2 consecutive leads in the absence of previous ischemic heart disease, left bundle branch block, and/or evidence of akinetic/dyskinetic wall segments.

ACEi, angiotensin-converting enzyme inhibitor; ARNI, angiotensin receptor-neprilysin inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; COPD, chronic obstructive pulmonary disease; DAP, diastolic arterial pressure; eGFR, estimated glomerular filtration rate; hs-TnT, high-sensitivity troponin T; IVSd, end-diastolic interventricular septum; LAd, left atrial diameter; LVEDd, left ventricular end-diastolic diameter; LVEDVi, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LVMi, left ventricular mass index; MGUS, monoclonal gammopathy of unknown significance; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; PWTd, end-diastolic posterior wall thickness; SAP, systolic arterial pressure; TAPSE, tricuspid annular plane systolic excursion.

HIGHLIGHTS

- The prospective CARRY registry provides updated data on the clinical characteristics and diagnostic pathways for suspected cardiac amyloidosis (CA) patients.
- There is an increased awareness of CA among cardiologists, including those at non-referral centers, aligning with recent retrospective studies.
- Despite advancements in diagnostics, suspicion of CA remains age-biased, underscoring the need for earlier detection to leverage disease-modifying therapies effectively.