Imaging nell'amiloidosi cardiaca

Prof. Gianluca Di Bella
Dir. UOC Cardiologia con UTIC
Resp. Centro Rif. Regionale malattie Cardiache Rare
AOU Policlinico Messina

PRESENTER DISCLOSURE INFORMATION

GIANLUCA DI BELLA

Dichiaro che negli ultimi due anni non ho avuto rapporti di finanziamento con soggetti portatori di interessi commerciali in campo sanitario.

OPPURE

Dichiaro che negli ultimi due anni ho avuto rapporti, anche di finanziamento, con i seguenti soggetti portatori di interessi commerciali in campo sanitario: ……

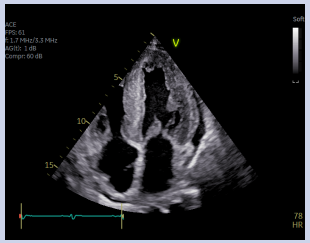
Alnylam, Pfizer, Bayer, AstraZeneca

Diagnosis

Differential Diagnosis

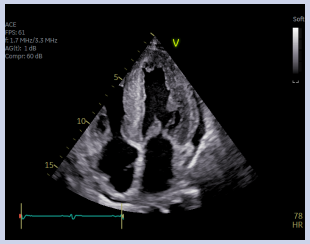
Progression of disease (therapies)

Imaging in TTR CA

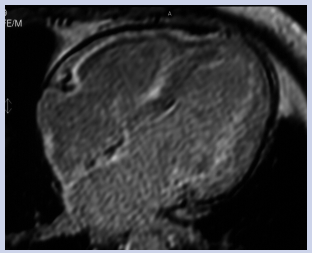


Echo : screening/suspect (red flags), confirming diagnosis, complications, FU stages

Imaging in TTR CA

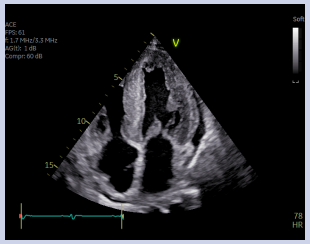


Echo : screening/suspect (red flags), confirming diagnosis, complications, FU stages

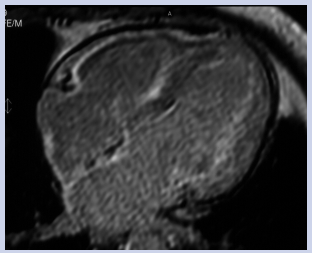


CMR: Suspected CA, differential diagnosis, FU stages and therapies,

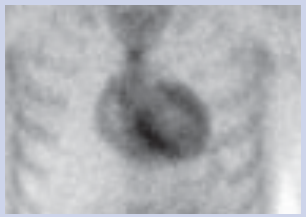
Imaging in TTR CA



Echo : screening/suspect (red flags), confirming diagnosis, complications, FU stages

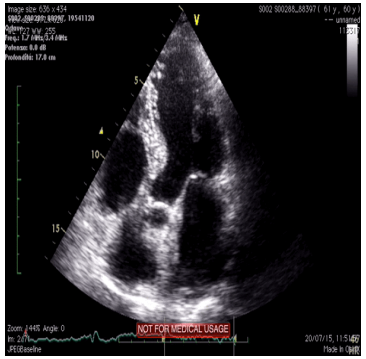


CMR: Suspected CA, differential diagnosis, FU stages and therapies,



SCINTI: definite non invasive diagnosis

Diagnosis and treatment of cardiac amyloidosis. A position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases



Signs & symptoms, ECG, echo or CMR suggestive of cardiac amyloidosis

^{99m}Tc-DPD/PYP/HMDP Scintigraphy with SPECT & **Haematologic tests** (serum free-light chain quantification & serum and urine immunofixation)

Scintigraphy grade 0 Haematologic tests -

AL/ATTR cardiac amyloidosis unlikely

If suspicion persists consider CMR followed by biopsy

Scintigraphy grade 1-3 Haematologic tests -

Grade 2-3

Cardiac ATTR amyloidosis

TTR genetic testing

ATTRwt / ATTRv

Grade 1

Histological confirmation (cardiac/extracardiac) **to diagnose**

Scintigraphy grade 0 Haematologic tests +

AL amyloidosis?

CMR negative

Amyloidosis unlikely

CMR + or inconclusive

Histological confirmation (cardiac/extracardiac) **to diagnose**

Scintigraphy grade 1-3 Haematologic tests +

Histological confirmation (usually cardiac) **to subtype**

European J of Heart Fail, Volume: 23, Issue: 4, Pages: 512-526, First published: 07 April 2021, DOI: (10.1002/ejhf.2140)

AMYLOID
https://doi.org/10.1080/13506129.2022.2064739

Taylor & Francis
Taylor & Francis Group

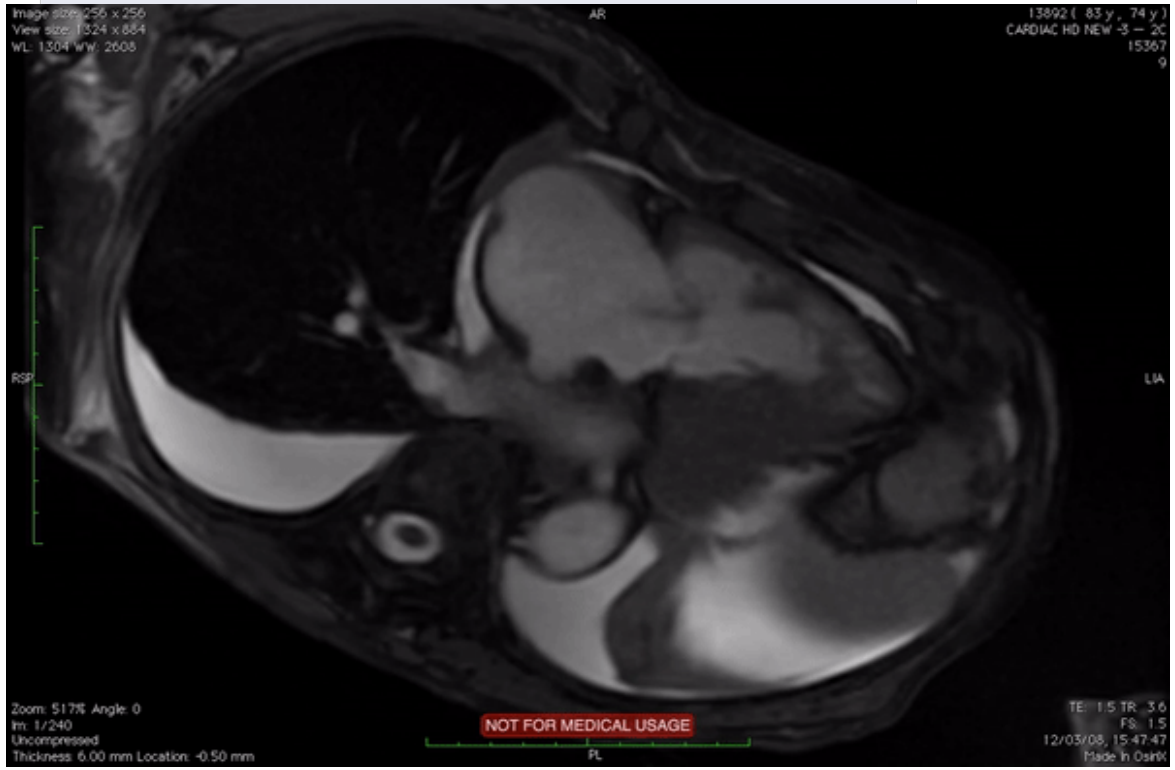
Check for updates

ARTICLE

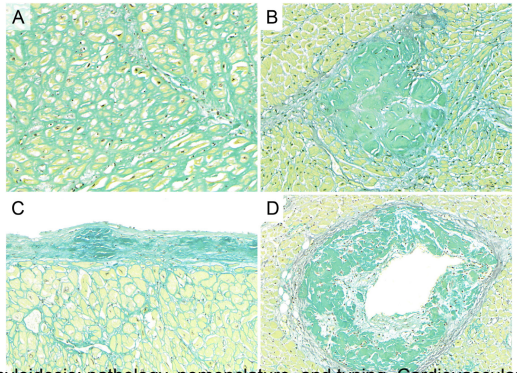
Prevalence and diagnostic value of extra-left ventricle echocardiographic findings in transthyretin-related cardiac amyloidosis

Gianluca Di Bella[a], Francesco Cappelli[b], Roberto Licordari[a], Paolo Piaggi[c], Mariapaola Campisi[a], Diego Bellavia[d], Fabio Minutoli[e], Luca Gentile[a], Massimo Russo[a], Cesare de Gregorio[a], Federico Perfetto[b], Anna Mazzeo[a], Calogero Falletta[d], Francesco Clemenza[d], Giuseppe Vita[a], Scipione Carerj[a] and Giovanni Donato Aquaro[f]

[a]Rare Cardiac Disease Centre, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy; [b]Tuscan Regional Amyloid Center, Careggi University Hospital, Firenze, Italy; [c]Department of Clinical and Experimental Medicine, Section of Endocrinology, University of Pisa, Pisa, Italy; [d]Division of Cardiovascular Diseases, Cardio-Thoracic Department, IRCCS-ISMETT, Palermo, Italy; [e]Department of Biomedical and Dental Sciences and Morphofunctional Imaging, University of Messina, Messina, Italy; [f]Gabriele Monasterio Foundation, Tuscan Region, Pisa, Italy



(A) Pericellular interstitial deposition;



(B) Nodular interstitial deposition;

(C) Endocardial deposition;

D) Obstructive vascular deposition;

AMYLOID

Cardiac amyloidosis: pathology, nomenclature, and typing. Cardiovascular Pathology Volume 24, Issue 6, November–December 2015, Pages 343-350

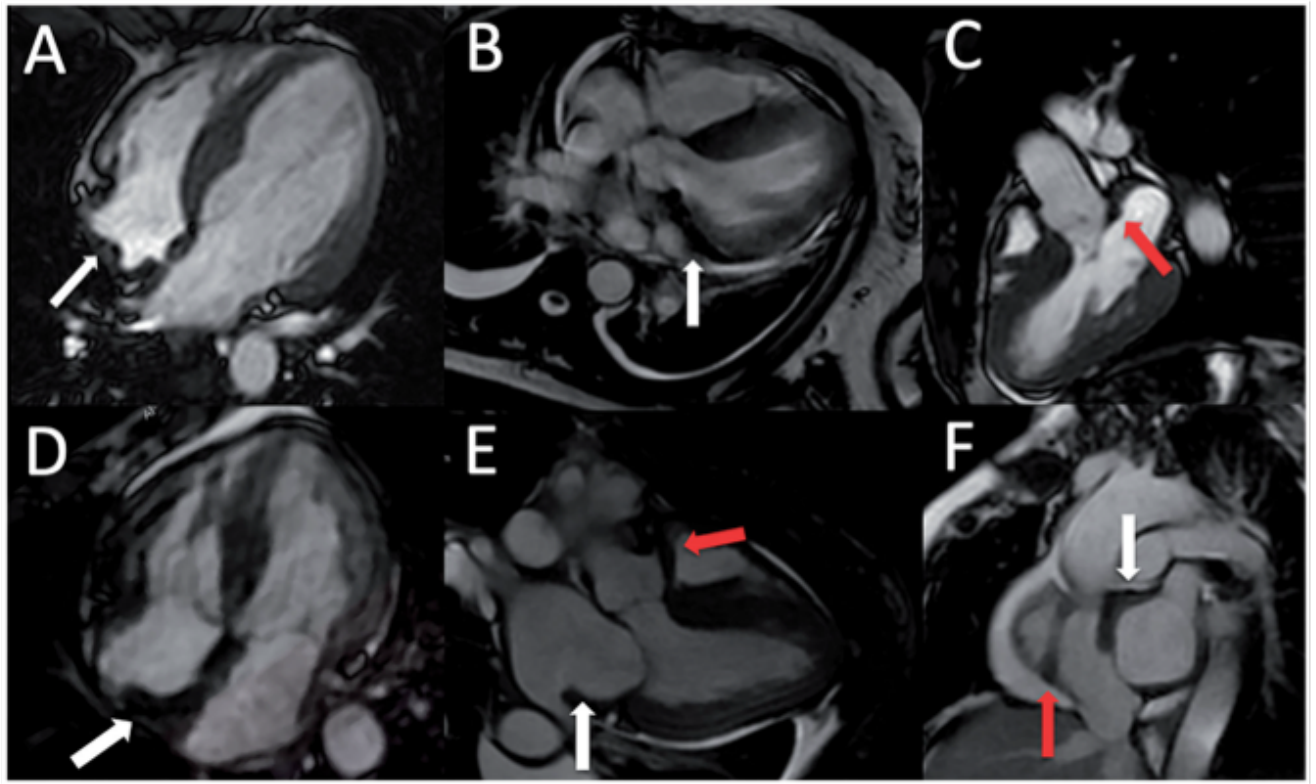


Figure 1. Examples of bSSFP CMR images of extra-LV amyloid deposition. Panel (A) and panel (D) show a thickened CriT (white arrow). Panel (B) shows a thickene atrioventricular plane (white arrow). Panel (C) shows a thickened mitro-aortic lamina (red arrow). Panel (E) shows an anterior ascending aortic wall (red arrow) an coumadin ridge (white arrow). Panel (F) shows Eustachian valve (red arrow) and a diffuse and circumferential involvement of amyloid deposition of the left atriu (white arrow).

Cardiac amyloidosis

AMYLOID
https://doi.org/10.1080/13506129.2022.2064739

ARTICLE

Prevalence and diagnostic value of extra-left ventricle echocardiographic findings in transthyretin-related cardiac amyloidosis

Gianluca Di Bella[a], Francesco Cappelli[b], Roberto Licordari[a], Paolo Piaggi[c], Mariapaola Campisi[a], Diego Bellavia[d], Fabio Minutoli[e], Luca Gentile[a], Massimo Russo[a], Cesare de Gregorio[a], Federico Perfetto[b], Anna Mazzeo[a], Calogero Falletta[d], Francesco Clemenza[d], Giuseppe Vita[a], Scipione Carerj[a] and Giovanni Donato Aquaro[f]

[a]Rare Cardiac Disease Centre, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy; [b]Tuscan Regional Amyloid Center, Careggi University Hospital, Firenze, Italy; [c]Department of Clinical and Experimental Medicine, Section of Endocrinology, University of Pisa, Pisa, Italy; [d]Division of Cardiovascular Diseases, Cardio-Thoracic Department, IRCCS-ISMETT, Palermo, Italy; [e]Department of Biomedical and Dental Sciences and Morphofunctional Imaging, University of Messina, Messina, Italy; [f]Gabriele Monasterio Foundation, Tuscan Region, Pisa, Italy

ABSTRACT

Background: Cardiac amyloidosis (CA) is cardiomyopathy with a hypertrophic phenotype characterised by diffuse deposition of anomalous fibrillar proteins in the extracellular matrix.

Objectives: To evaluate the prevalence and diagnostic value of extra left ventricle echocardiographic findings in patients with left ventricular (LV) hypertrophic phenotype and amyloid deposition.

Methods: A group of 146 patients with LV thickness ≥15 mm were enrolled: 70 patients who received a definite diagnosis of sarcomeric hypertrophic cardiomyopathy (HCM group) and 76 patients with transthyretin cardiac amyloidosis (CA group). Echocardiographic analysis of crista terminalis (CriT), atrio-ventricular plane (AVP), mitro-aortic lamina (MAL), anterior ascending aortic wall, interatrial septum (IAS), Eustachian valve (EusV) and coumadin ridge (CouR) was performed in all patients, and these structures were compared among the two groups.

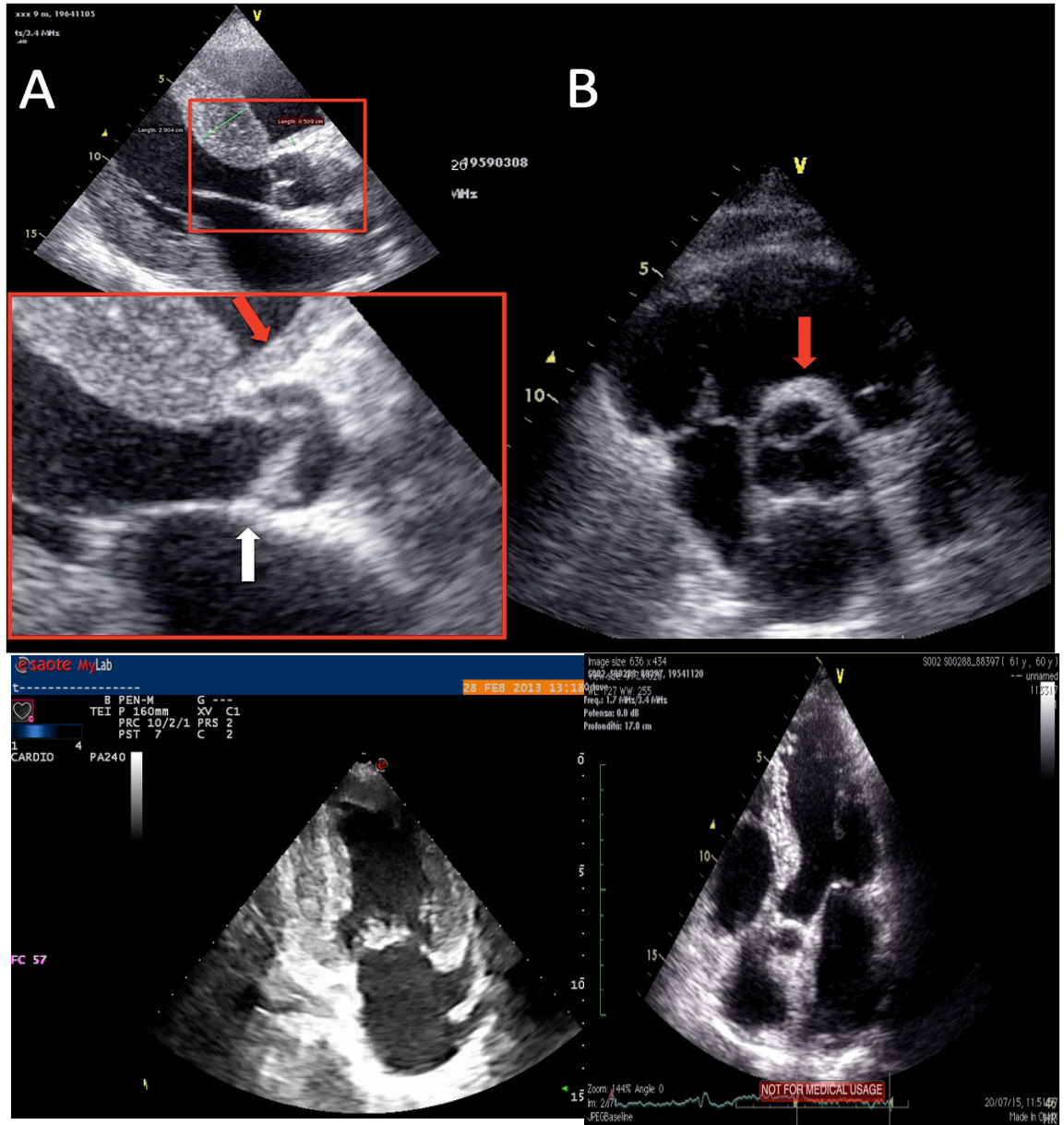
Results: CA group showed significantly higher dimensions of CriT, IAS, CouR, AVP, MAL and IAS compared to the HCM group. The logistic analysis showed that LV EF, LV septal thickness, CriT presence, CriT area, MAL and IAS were all predictors of CA in univariate analyses. The stepwise multivariate analysis showed independent predictors of CA: CriT area, MAL and LVEF. According to areas under the receiver operating characteristic curves the best cut-off values to determine CA were identified (IAS > 9 mm, MAL > 7 mm, CriT > 9 mm^2). Among these 3 independent predictors, IAS > 9 mm had the best specificity (96%) and positive predictive value (93%) in identifying CA.

Conclusions: evidence of extra left ventricle sites of amyloid deposition is a frequent finding in CA. In the context of hypertrophic phenocopies, an increased thickness of IAS, and/or CT and/or MAL should suggest a diagnosis of transthyretin CA.

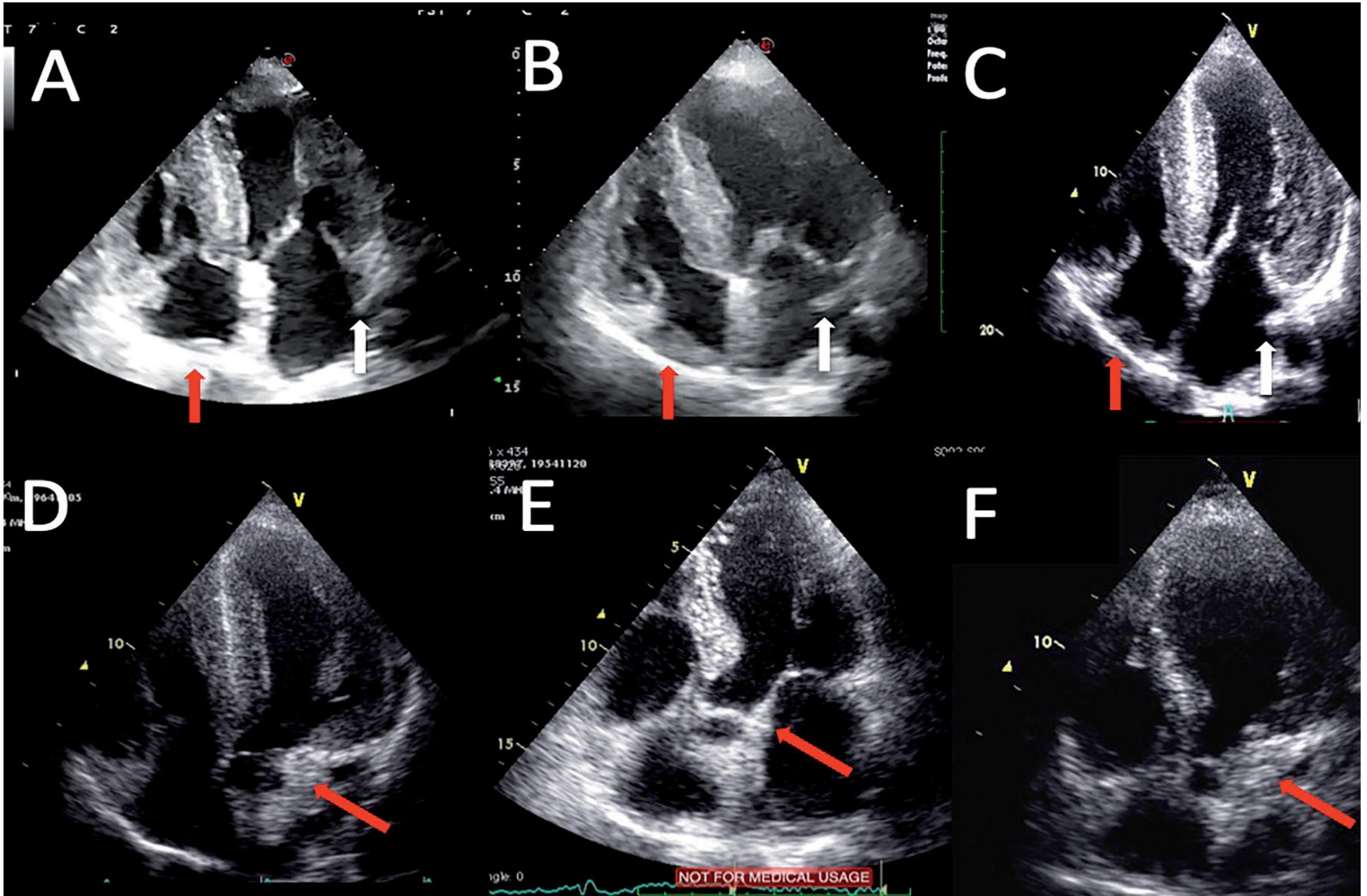
Abbreviations: AL: light chain amyloid; ATTRm: mutated transthyretin amyloid; ATTRwt: wild type transthyretin amyloid; AUC: area under the curve; AVP: atrio-ventricular plane; bSSFP: balanced Steady State Free Precession; CA: cardiac amyloidosis; CMR: cardiac magnetic resonance; CouR: Coumadin ridge; CriT: crista terminalis; ECHO: echocardiography; EusV: Eustachian valve; HCM: hypertrophic cardiomyopathy; IAS: interatrial septum; ICC: intraclass correlation coefficient; LV: left ventricle; LV-EDV: left ventricular end diastolic volume; LVEF: left ventricular ejection fraction; MAL: mitro-aortic lamina; NPV: negative predictive value; NYHA: New York Heart Association; PPV: positive predictive value; ROC: receiver operating characteristic

ARTICLE HISTORY
Received 19 June 2021
Accepted 6 April 2022

KEYWORDS
Transthyretin cardiac amyloidosis; hypertrophic cardiomyopathy; Interatrial septum; crista terminalis; mitro-aortic lamina



Cardiac amyloidosis



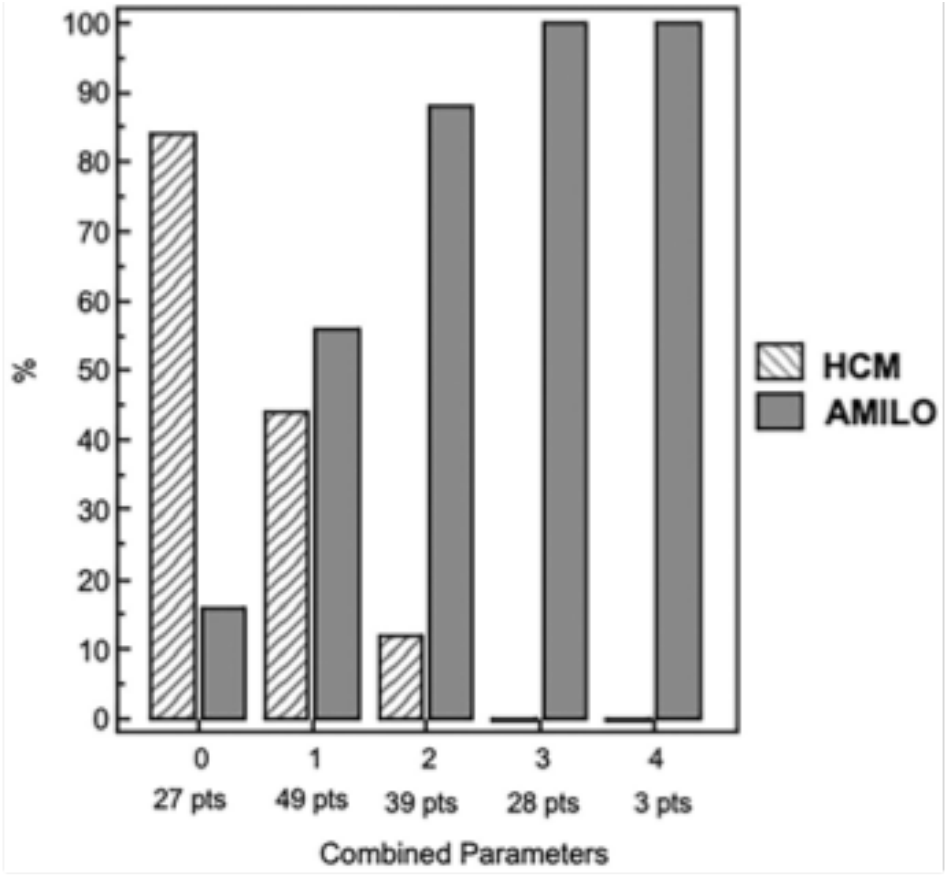


Figure 4. Quantitative distribution of extra-left ventricle parameters (0–4) in HCM and CA patients.

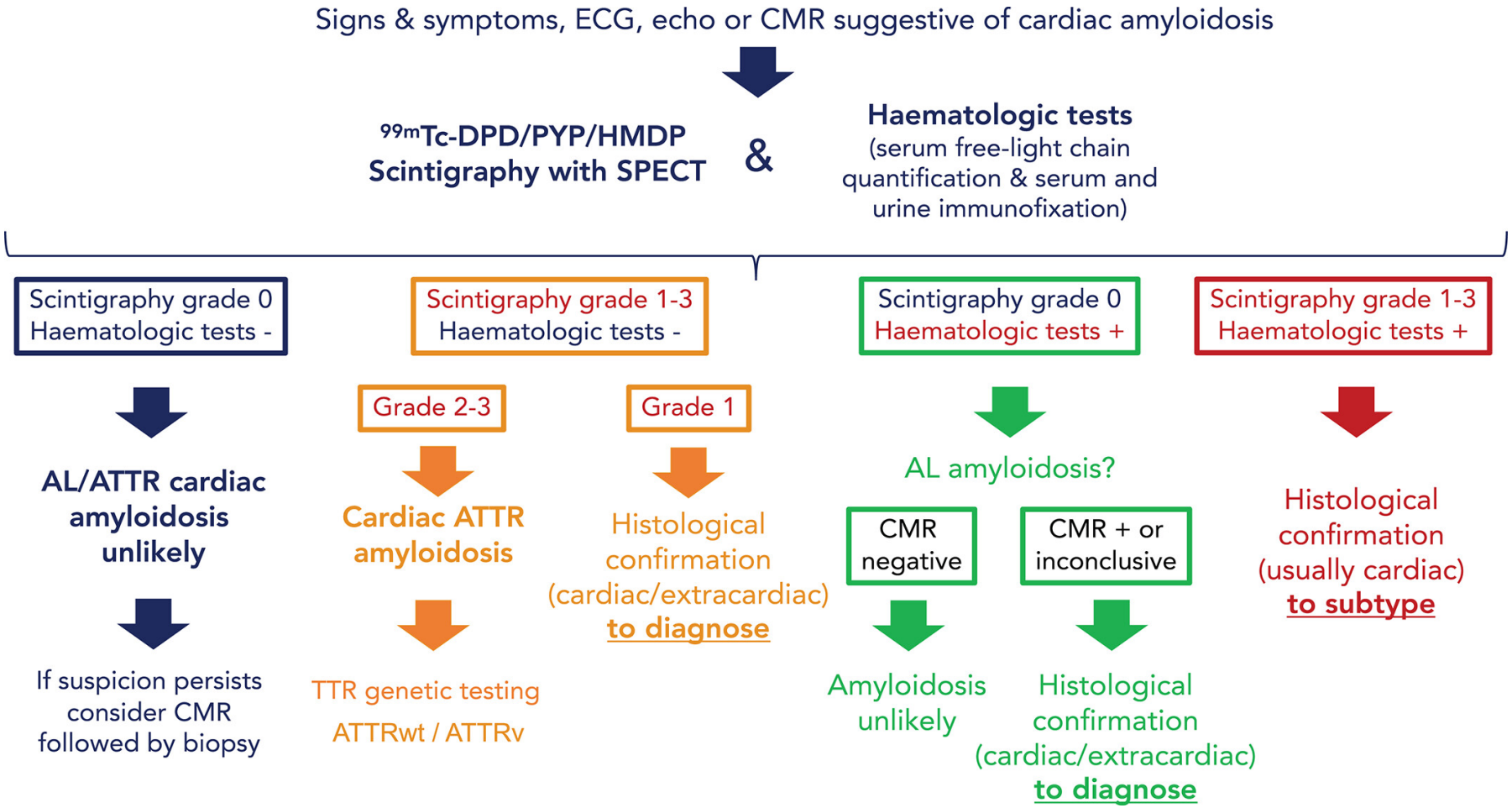
Table 3. Prevalence and dimensions of non-LV echocardiographic findings.

	HCM group ($n = 70$ patients)	CA group ($n = 76$ patients)	p-Value
Crista terminalis – CriT (prevalence, %)	24	57	**.003**
Eustachian valve – EusV (prevalence, %)	21	26	.452
Crista terminalis – CriT (mm^2)	80 (50–83)	110 (76–140)	**<.001**
Coumadin ridge – CouR (mm^2)	75 (60–93)	110 (86–140)	**<.001**
Atrio-ventricular plane – AVP (mm)	7 (6–9)	9 (7–10)	**<.001**
Mitro-aortic lamina – MAL (mm)	6 (6–7)	8 (6–9)	**<.001**
Anterior ascending aortic wall (mm)	8 (7–9)	8 (7–9)	.57
Interatrial septrum – IAS (mm)	7 (6–8)	8 (7–9)	**<.001**

CA: cardiac amyloidosis; HCM: hypertrophic cardiomyopathy.

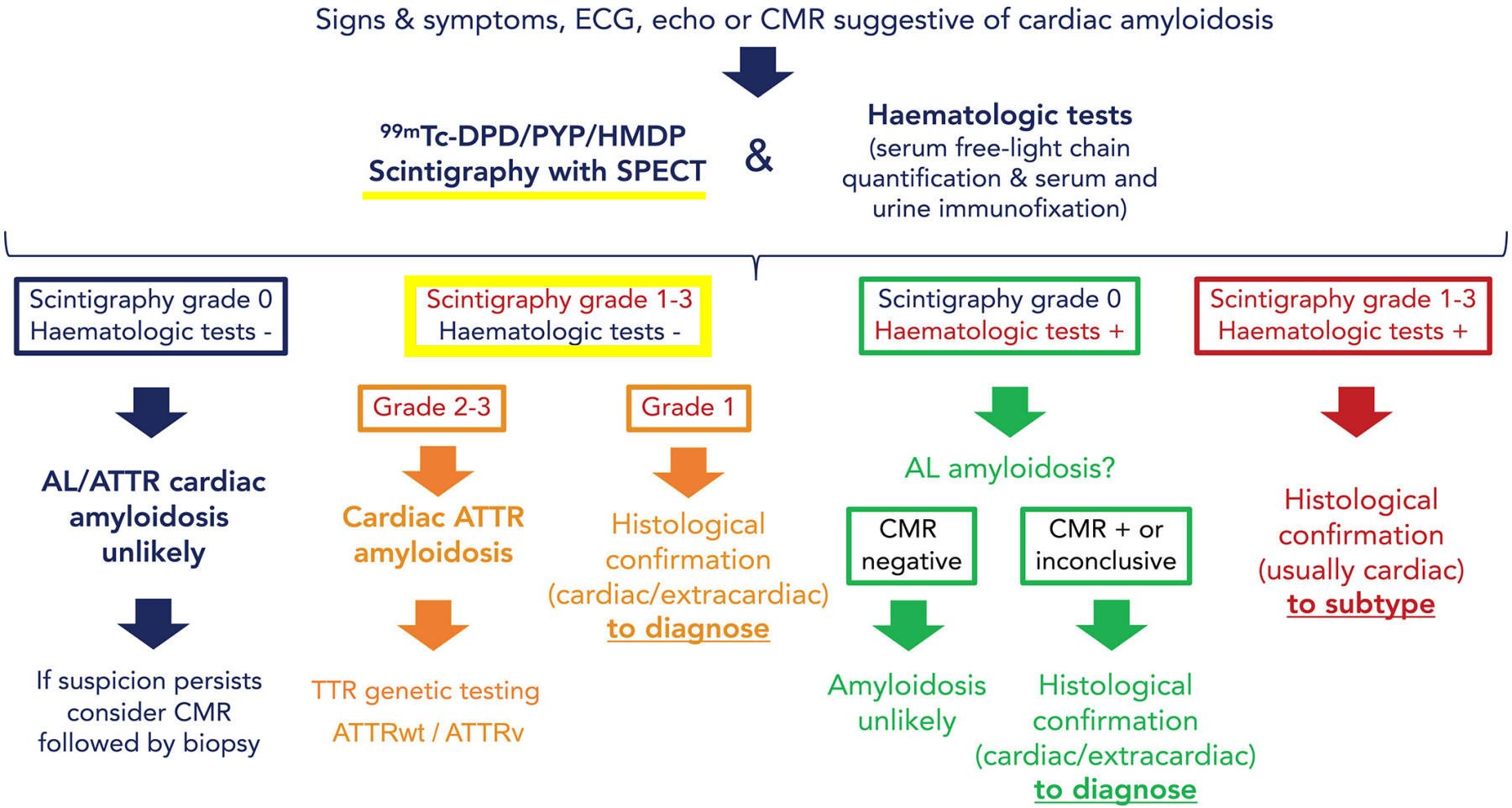
Di Bella, Gianluca, et al. "Prevalence and diagnostic value of extra-left ventricle echocardiographic findings in transthyretin-related cardiac amyloidosis." *Amyloid* 29.3 (2022): 197-204.

Diagnosis and treatment of cardiac amyloidosis. A position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases



European J of Heart Fail, Volume: 23, Issue: 4, Pages: 512-526, First published: 07 April 2021, DOI: (10.1002/ejhf.2140)

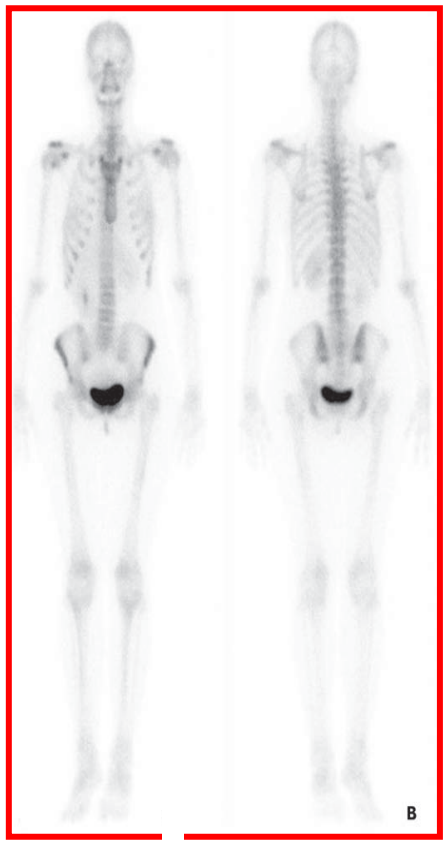
Diagnosis and treatment of cardiac amyloidosis. A position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases



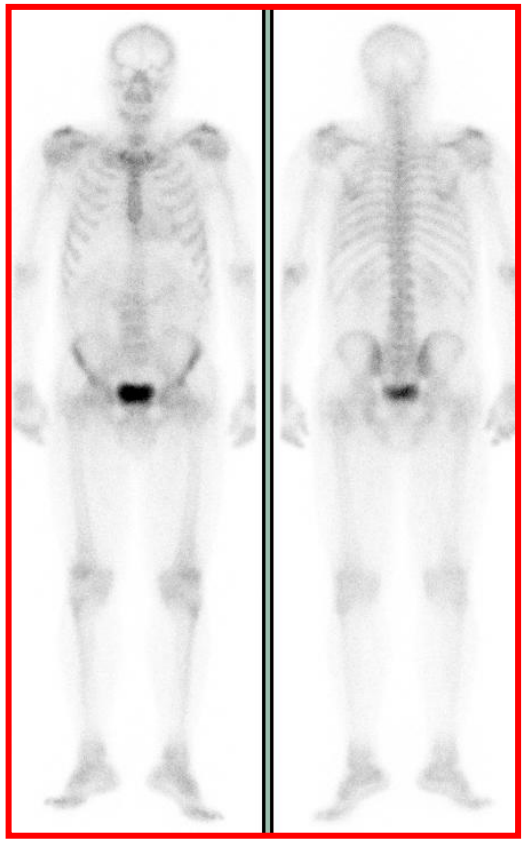
Perugini 2–3 + assenza di monoclonalità → diagnosi non invasiva di ATTR-CM con specificità/PPV 100%

European J of Heart Fail, Volume: 23, Issue: 4, Pages: 512-526, First published: 07 April 2021, DOI: (10.1002/ejhf.2140)

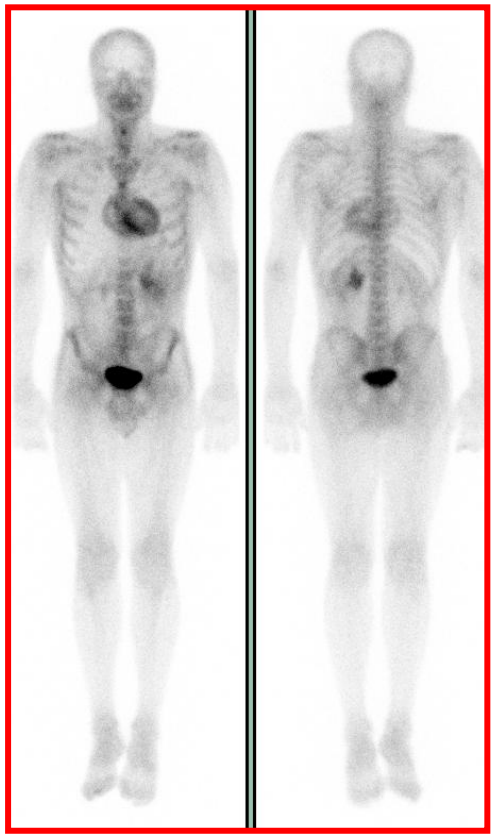
Visual analysis



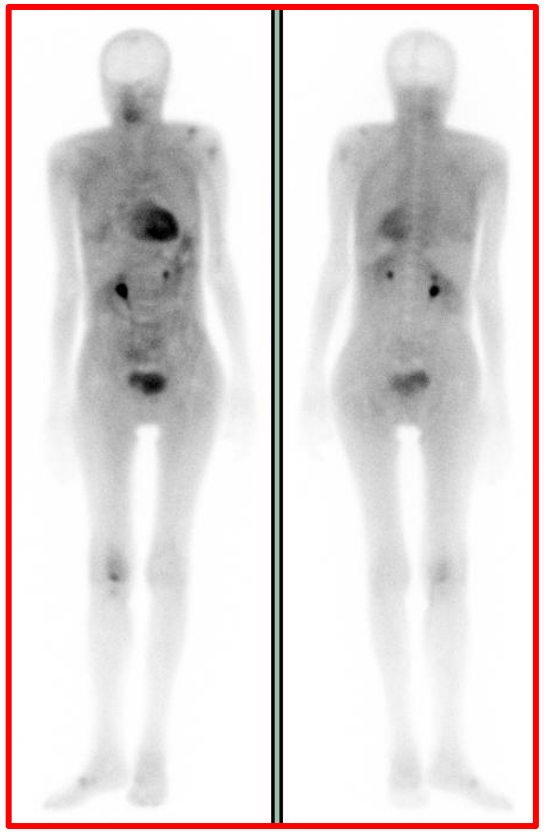
Score 0: absent cardiac uptake and normal bone uptake



Score 1: mild cardiac uptake, inferior to bone uptake



Score 2: moderate cardiac uptake accompanied by attenuated bone uptake



Score 3: strong cardiac uptake with mild/absent bone uptake.

ESC European Society of Cardiology
European Journal of Heart Failure (2021) 23, 512–526
doi:10.1002/ejhf.2140
POSITION PAPER

Diagnosis and treatment of cardiac amyloidosis. A position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases

Pablo Garcia-Pavia[1,2,3]*, Claudio Rapezzi[4,5], Yehuda Adler[6], Michael Arad[7], Cristina Basso[3,8], Antonio Brucato[9], Ivana Burazor[10], Alida L.P. Caforio[3,11], Thibaud Damy[12], Urs Eriksson[13], Marianna Fontana[14], Julian D. Gillmore[14], Esther Gonzalez-Lopez[1,3], Martha Grogan[15], Stephane Heymans[16,17,18], Massimo Imazio[19], Ingrid Kindermann[20], Arnt V. Kristen[21,22], Mathew S. Maurer[23], Giampaolo Merlini[24,25], Antonis Pantazis[26], Sabine Pankuweit[27], Angelos G. Rigopoulos[28], and Ales Linhart[29]

Table 4 Possible false positives and false negatives of bisphosphonate scintigraphy for detecting transthyretin cardiac amyloidosis

	Situation	How to suspect and confirm?
False positive	AL amyloidosis	Abnormal SPIE, UPIE or serum free light ratio. Requires histologic confirmation.
	Hydroxychloroquine cardiac toxicity	Interrogation. Requires histologic confirmation.
	AApoAI and AApoAII amyloidosis	Concomitant kidney disease present. Genetic testing.
	ApoAIV amyloidosis	Concomitant kidney disease present. Requires histologic confirmation.
	Aβ2M amyloidosis	Long-term dialysis (>9 years). Requires histologic confirmation.
	Blood pool	Cardiac dysfunction could be present. Use SPECT to detect uptake in myocardium. Delay acquisition.
	Rib fractures, valvular/annular calcifications	Use SPECT to detect uptake in myocardium.
	Recent myocardial infarction (<4 weeks)	Interrogation. Use SPECT to detect diffuse uptake in myocardium.
False negative	Phe84Leu ATTRv, Ser97Tyr ATTRv	Concomitant neuropathy. Familial disease. Genetic testing.
	Very mild disease	Requires histologic confirmation
	Delayed acquisition	Shorter acquisition time interval
	Premature acquisition	Prolong acquisition time interval

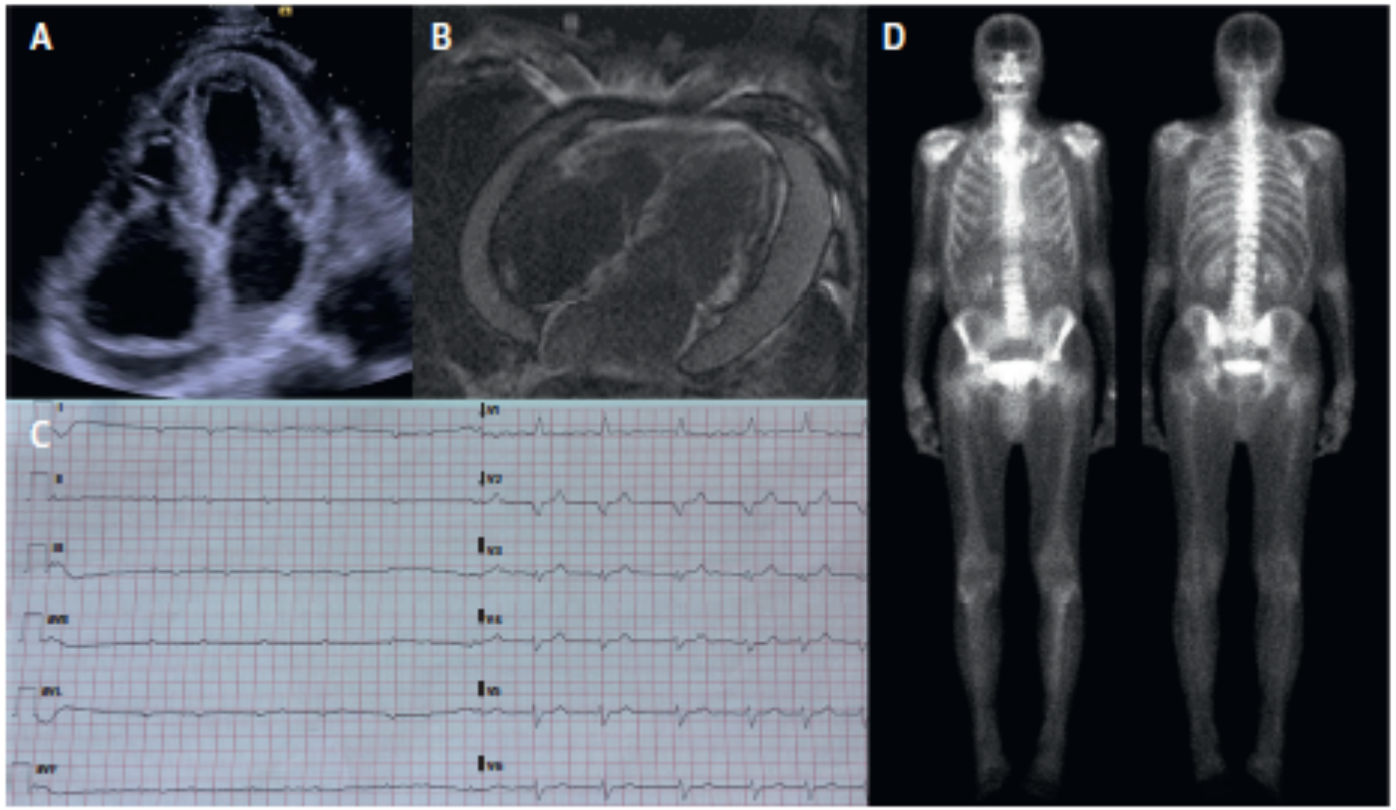
AApoAI, apolipoprotein A-I amyloidosis; AApoAII, apolipoprotein A-II amyloidosis; AApoAIV, apolipoprotein A-IV amyloidosis; Aβ2M, β2-microglobulin amyloidosis; AL, light-chain amyloidosis; ATTRv, hereditary transthyretin amyloidosis; SPIE, serum protein electrophoresis with immunofixation; SPECT, single photon emission computed tomography; UPIE, urine protein electrophoresis with immunofixation.

Grade 0	**No cardiac uptake**	**Negative**
Grade 1	**Cardiac uptake < Bone (rib) uptake**	**Equivocal / Early / Possible AL**
Grade 2	**Cardiac uptake = Bone (rib) uptake**	**Positive for ATTR**
Grade 3	**Cardiac uptake > Bone (rib) uptake**	**Positive for ATTR**

L'imaging SPECT può essere utile per

1. Evitare la sovrapposizione dell'assorbimento osseo
2. Distinguere l'attività della cavità ventricolare da quella miocardica
3. Valutare la distribuzione dell'assorbimento miocardico negli individui con scansioni planari positive
   Identificare l'assorbimento nel setto interventricolare (comunemente coinvolto nell'amiloidosi)
4. Quantificare il grado di assorbimento miocardico confrontandolo con quello delle costole

FIGURE 1 Representative Case of a Phe64Leu TTR Patient With Cardiac Involvement and Negative Bone Scintigraphy



(A) Echocardiography showed symmetric left ventricular hypertrophy, severe biatrial dilatation, and circumferential pericardial effusion. (B) Cardiac magnetic resonance showed diffuse LGE. (C) Electrocardiogram demonstrated atrial fibrillation and diffuse low voltages. (D) Tc99-HMDP bone scintigraphy did not show myocardial bone tracer uptake.

ORIGINAL RESEARCH

Low Sensitivity of Bone Scintigraphy in Detecting Phe64Leu Mutation-Related Transthyretin Cardiac Amyloidosis

Maria Beatrice Musumeci, MD,[a,*] Francesco Cappelli, MD,[b,*] Domitilla Russo, MD,[a] Giacomo Tini, MD,[c] Marco Canepa, MD, PhD,[c] Agnese Milandri, MD,[d] Rachele Bonfiglioli, MD,[e] Gianluca Di Bella, MD, PhD,[f] Filomena My, MD,[g] Marco Luigetti, MD,[h,i] Marina Grandis, MD,[i,k] Camillo Autore, MD,[a] Stefano Perlini, MD,[l] Federico Perfetto, MD, PhD,[b] Claudio Rapezzi, MD[d]

ABSTRACT

OBJECTIVES The aim of this study was to assess the diagnostic accuracy of bone scintigraphy in a large multicenter cohort of patients with cardiac amyloidotic involvement and Phe64Leu transthyretin (TTR) mutation.

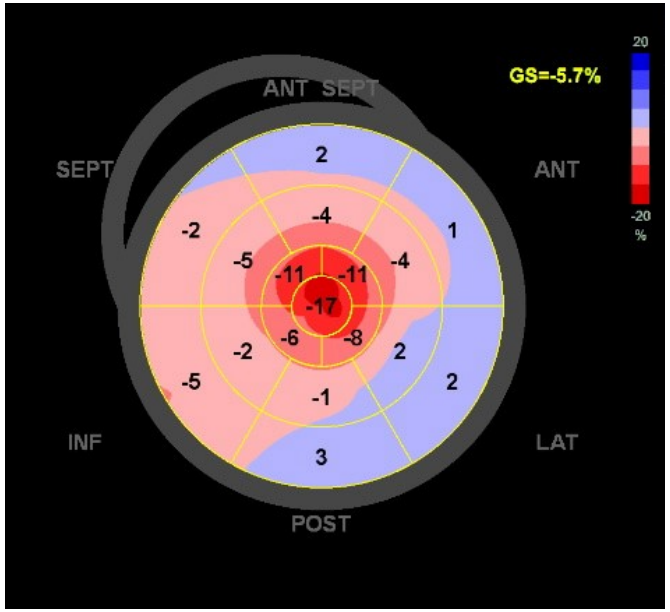
BACKGROUND Diagnostic accuracy of bone scintigraphy for transthyretin-related cardiac amyloidosis (TTR-CA) is considered extremely high, enabling this technique to be the noninvasive diagnostic standard for TTR-CA. Nevertheless, this approach has not been systematically validated across the entire spectrum of TTR mutations.

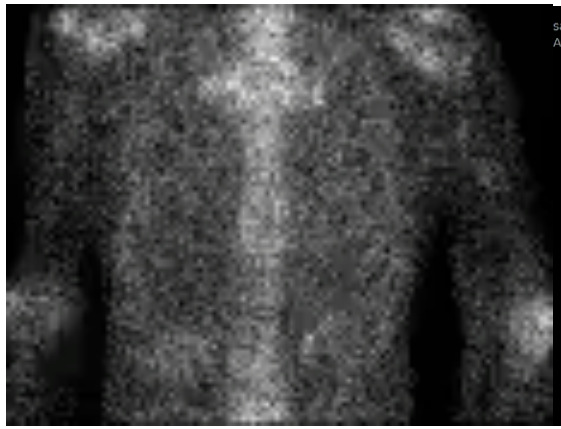
METHODS A total of 55 patients with Phe64Leu TTR mutation were retrospectively analyzed and evaluated between 1993 and 2018 at 7 specialized Italian tertiary centers. Cardiac involvement was defined as presence of an end-diastolic interventricular septum thickness ≥12 mm, without other possible causes of left ventricular hypertrophy (i.e., arterial hypertension or valvulopathies). A technetium-99m (99mTc)-diphosphonate (DPD) or 99mTc-hydroxyl-methylene-diphosphonate (HMDP) bone scintigraphy was reviewed, and visual scoring was evaluated according to Perugini's method.

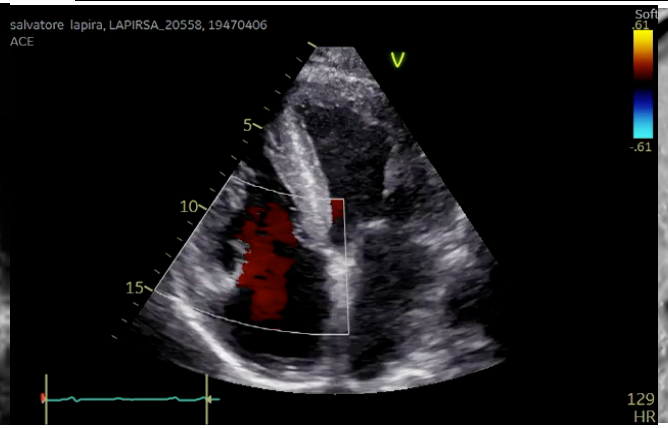
RESULTS Among 26 patients with definite cardiac involvement, 19 underwent 99mTc-DPD or 99mTc-HMDP bone scintigraphy. Of them, 17 (89.5%) patients had low or absent myocardial bone tracer uptake, whereas only 2 (10.5%) showed high-grade myocardial uptake. The sensitivity and the accuracy of bone scintigraphy in detecting TTR-CA were 10.5% and 37%, respectively. Patients with cardiac involvement and low or absent bone tracer uptake were similar to those with high-grade myocardial uptake in terms of age, sex, and electrocardiographic and echocardiographic findings.

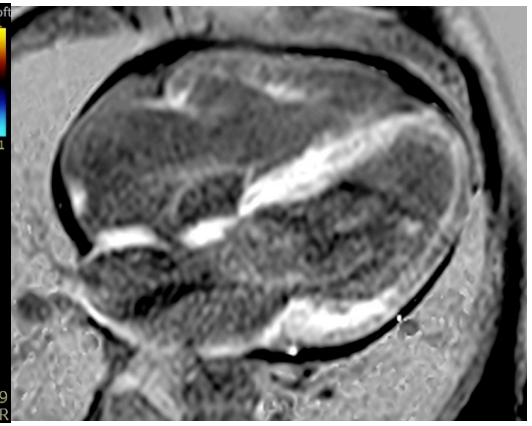
CONCLUSIONS The sensitivity of bone scintigraphy (DPD and HMDP) in detecting TTR-CA is extremely low in patients with Phe64Leu TTR mutation, suggesting the need to assess diagnostic accuracy of bone scintigraphy to identify cardiac involvement across a wider spectrum of TTR mutations. (J Am Coll Cardiol Img 2019;■:■–■) © 2019 by the American College of Cardiology Foundation.

New patogenic mutation: Glu81Al









Unpublished

Grade 1
Perugini

Grade 1 Perugini

Table 2. Radionuclide 'Bone' Scintigraphy Findings Among 374 Patients With EMBs

	^{99m}Tc-DPD Scan Findings, n				
EMB Findings	Perugini 0	Perugini 1	Perugini 2	Perugini 3	n
No cardiac amyloid	31	3	0	1	35
Cardiac ATTR amyloid deposits	1	8	130	23	162
Cardiac AL amyloid deposits	21	13	7	2	43
Cardiac ApoAI amyloid deposits	0	2	0	0	2
Cardiac amyloid deposits of unknown type	1	1	0	0	2
Total	54	27	137	26	244
		^{99m}Tc-PYP can Findings			
	Grade 0	Grade 1	Grade 2	Grade 3	n
No cardiac amyloid	7	1	1	0	9
Cardiac ATTR amyloid	1	10	7	67	85
Cardiac AL amyloid deposits	10	1	3	1	15
Cardiac ApoAI amyloid deposits	0	0	0	0	0
Cardiac amyloid deposits of unknown type	0	0	0	0	0
Total	18	12	11	68	109
		^{99m}Tc-HMDP Scan Findings			
	Grade 0	Grade 1	Grade 2	Grade 3	n
No cardiac amyloid	3	0	0	0	3
Cardiac ATTR amyloid deposits	0	3	4	7	14
Cardiac AL amyloid deposits	4	0	0	0	4
Cardiac ApoAI amyloid deposits	0	0	0	0	0
Cardiac amyloid deposits of unknown type	0	0	0	0	0
Total	7	3	4	7	21

ApoAI indicates apolipoprotein A-I; DPD, 3,3-diphosphono-1,2-propanodicarboxylic acid; EMB, endomyocardial biopsy; HDMP, hydroxymethylene diphosphonate; and PYP, pyrophosphate.

8/27 CA

11/12 CA

3/3 CA

TOT 21/52 (50%)
Perugini 1 had TTR-CA

Grade 1 scans in patients with CA and no MG are strongly suggestive of early ATTR-type, but require urgent histologic corroboration.

Table 5 Patients with Perugini grade 1 radionuclide bone scan

	N	Amyloid type by histology +/– proteomics					
		ATTR amyloid	AL amyloid	AApoAIV amyloid	AApoAI amyloid	No amyloid	No biopsy taken
Patients with no monoclonal gammopathy	61	44	25	0	0	0	19	17
Endomyocardial biopsy	1	1	0	0	0	0	-
Extra-cardiac biopsy	43	24	0	0	0	19	-
Patients with monoclonal gammopathy	122	9	83	1	0	14	15
Endomyocardial biopsy	20	3	15	0	0	2*	-
Extra-cardiac biopsy	87	6	68	1	0	12	-
Total	**183**	**34**	**83**	**1**	**0**	**33**	**32**

Bold values are indicative of major groups which are further broken down in subgroups.
*Possible false positive radionuclide scan or false negative EMB; one patient was felt to have a false positive radionuclide scan due to cardiac sarcoidosis and/or ESRD; the other was felt to have a false negative EMB on the basis of a scanty tissue sample and characteristic cardiac imaging for amyloid and was treated with chemotherapy for cardiac AL amyloidosis.

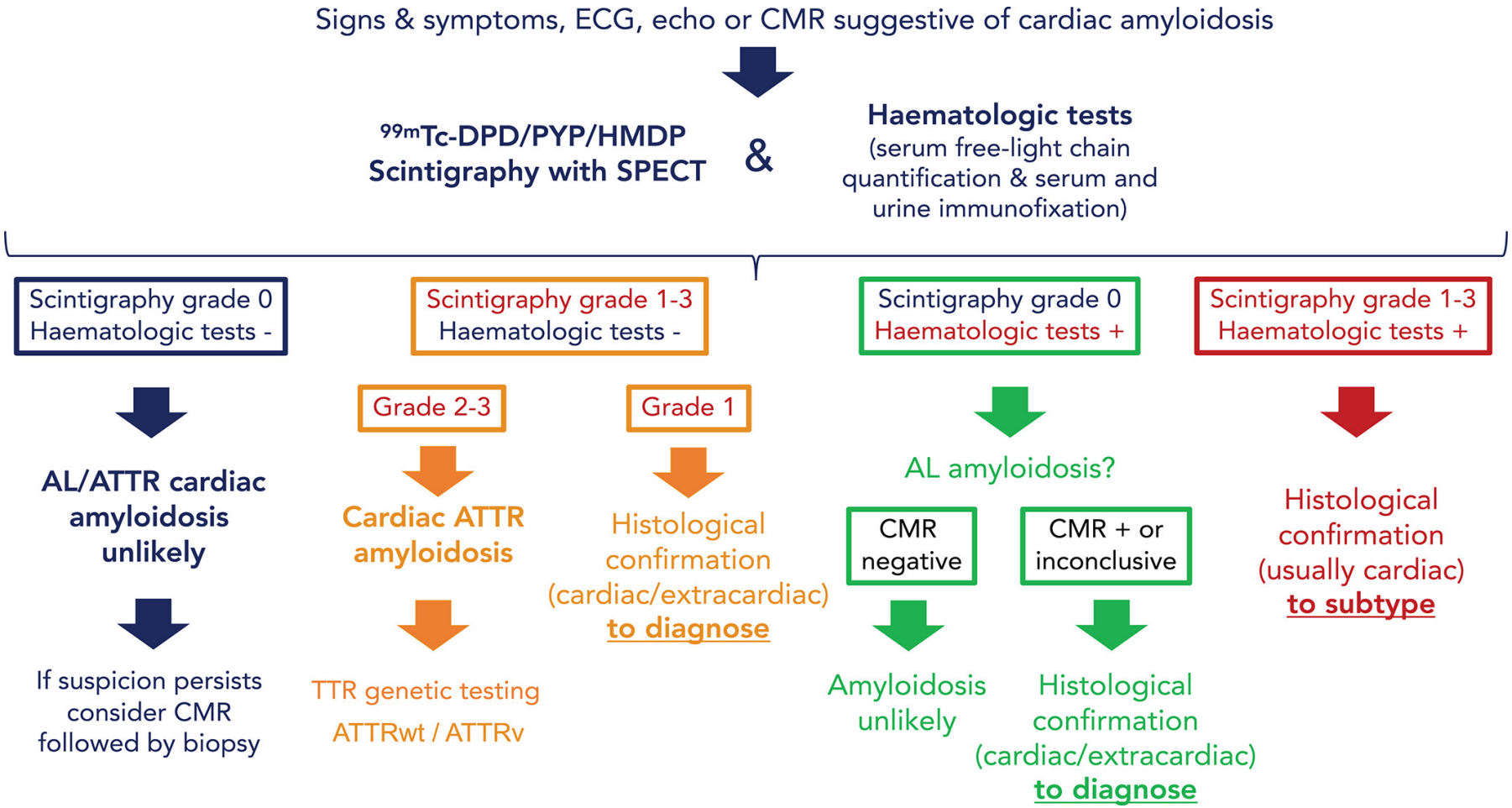
Conclusion

The NBDC for ATTR-CM are highly specific [97% (95% CI 0.91-0.99)] in clinical setting, and diagnostic performance was further refined here using new cut-offs for sFLC ratio in patients with CKD. A grade 0 radionuclide scan all but excludes ATTR-CM but occurs in most patients with AL-CA. Grade 1 scans in patients with CA and no MG are strongly suggestive of early ATTR-type, but require urgent histologic corroboration.

61 mg capsules

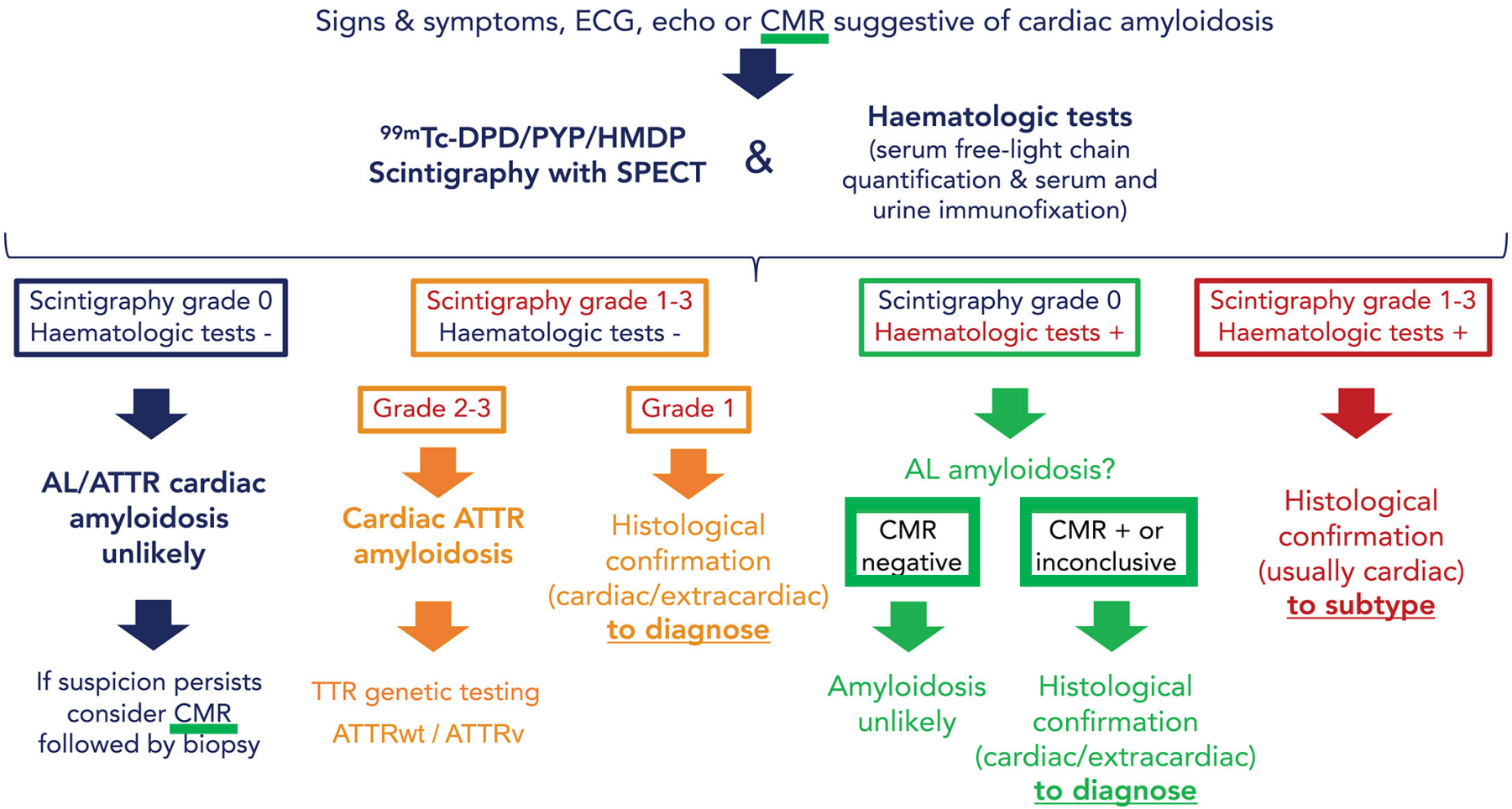
Rauf et al. Eur Heart Journal 2023

Diagnosis and treatment of cardiac amyloidosis. A position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases



European J of Heart Fail, Volume: 23, Issue: 4, Pages: 512-526, First published: 07 April 2021, DOI: (10.1002/ejhf.2140)

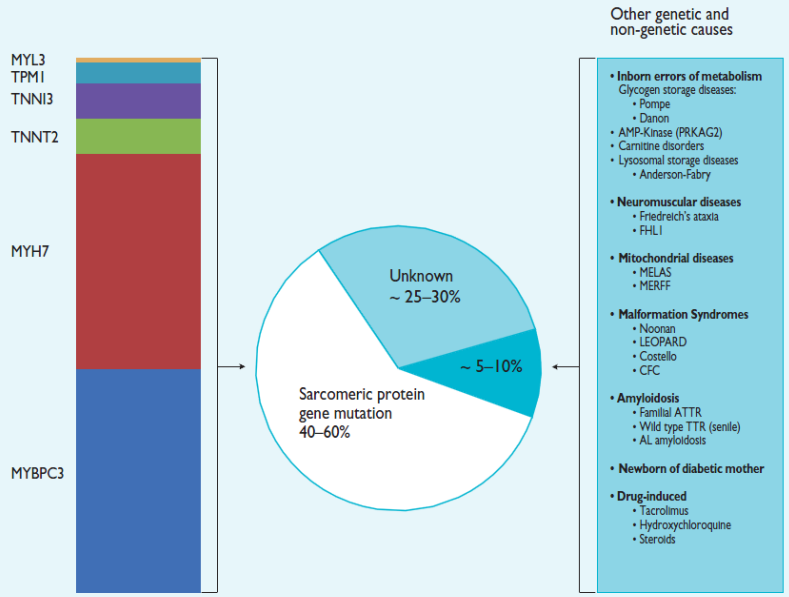
Diagnosis and treatment of cardiac amyloidosis. A position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases



European J of Heart Fail, Volume: 23, Issue: 4, Pages: 512-526, First published: 07 April 2021, DOI: (10.1002/ejhf.2140)

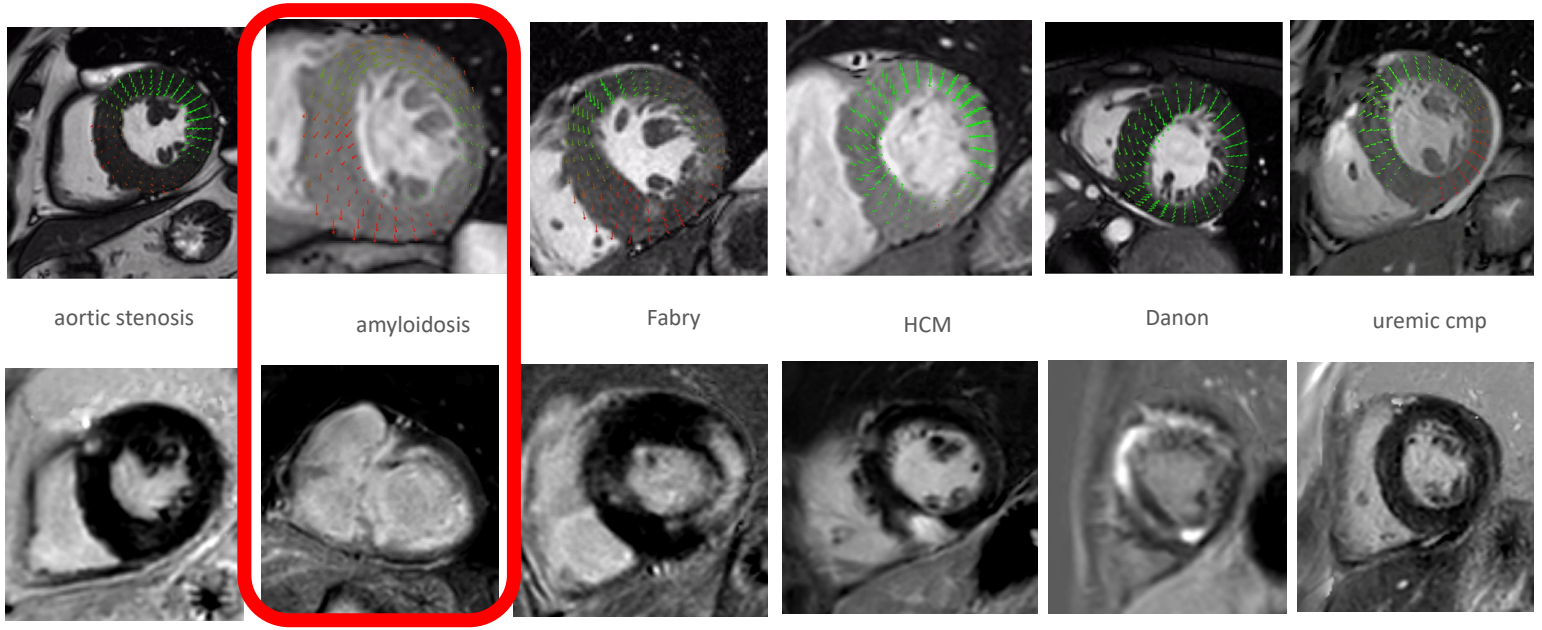
Advantages and limits of CMR in TTR CA

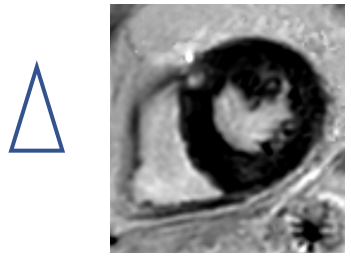
Phenotyping in 'Thick-Walled' Ventricles

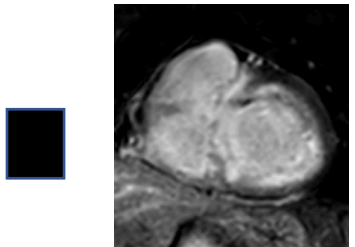


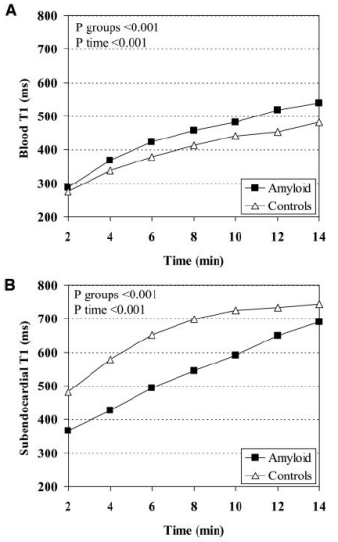
The majority of cases in adolescents and adults are caused by mutations in sarcomere protein genes. AL = amyloid light chain; ATTR=amyloidosis, transthyretin type. CFC = cardiofaciocutaneous; FHL-1=Four and a half LIM domains protein 1; LEOPARD = lentigines, ECG abnormalities, ocular hypertelorism, pulmonary stenosis, abnormal genitalia, retardation of growth, and sensorineural deafness; MELAS = mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes; MERFF = myoclonic epilepsy with ragged red fibres; MYL3 = myosin light chain 3; MYBPC3 = myosin-binding protein C, cardiac-type; MYH7 = myosin, heavy chain 7; TNNI3 = troponin I, cardiac; TNNT2 = troponin T, cardiac: TPM1 = tropomyosin 1 alpha chain; TTR = transthyretin.

CARDIOLOGY









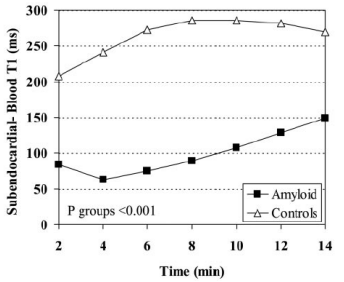
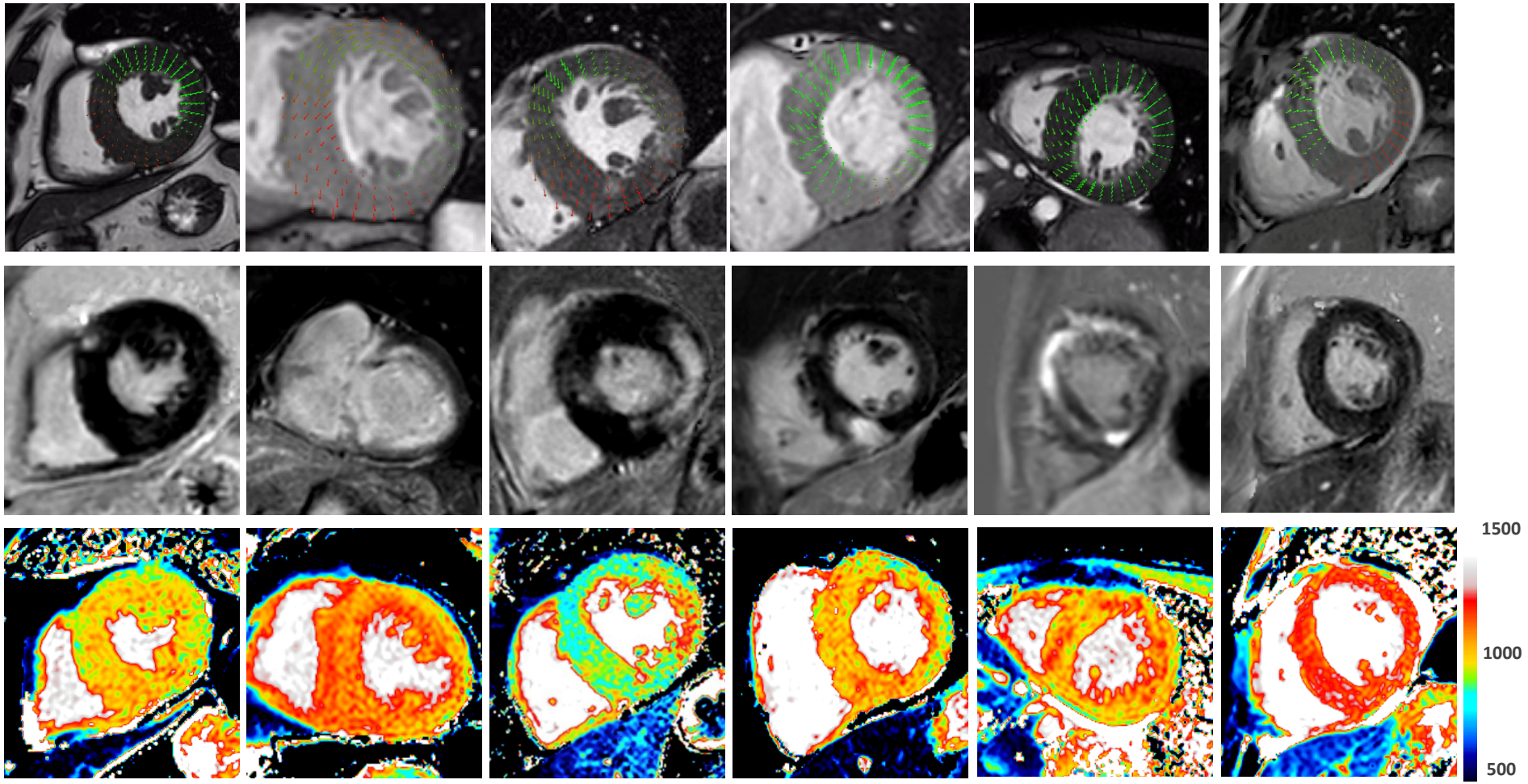


Figure 3. As a result of the abnormal blood and myocardium gadolinium kinetics, the difference between subendocardial T_1 and blood T_1 is substantially lower in the amyloidosis group than in controls.



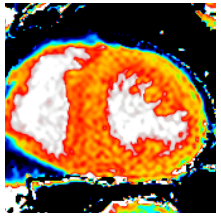
Courtesy of J Bogaert

Cardiac MRI in Cardiac Amyloidosis

2 main approach

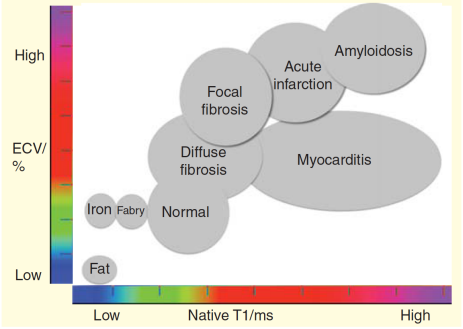
- (1) LGE (conventional and available in all CMR lab) – diagnosis

- (2) T1-Mapping
  - Native (msec)

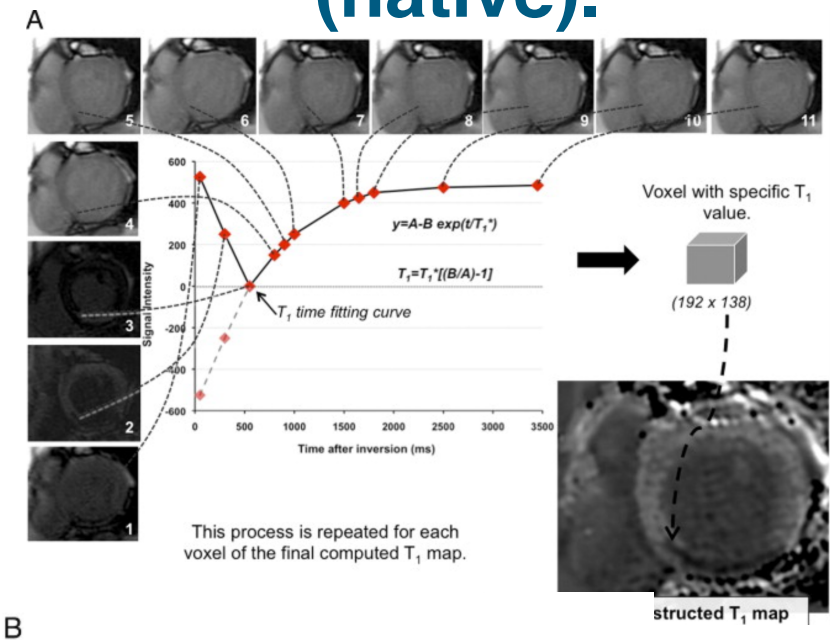


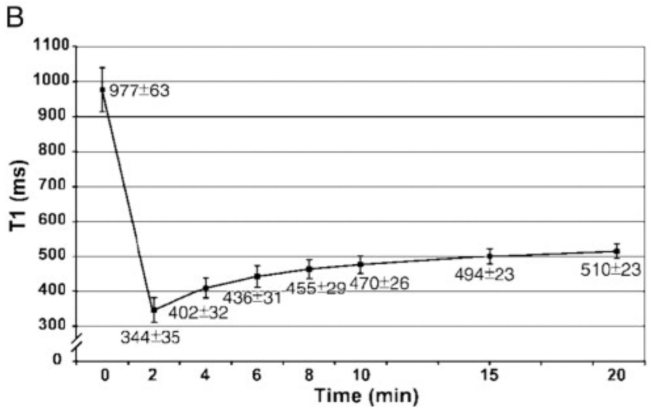
T1 elevato: edema, infiammazione, fibrosi o infiltrazione (soprattutto amiloidosi)
T1 ridotto: principalmente Fabry e sovraccarico di ferro

  - ECV (%)



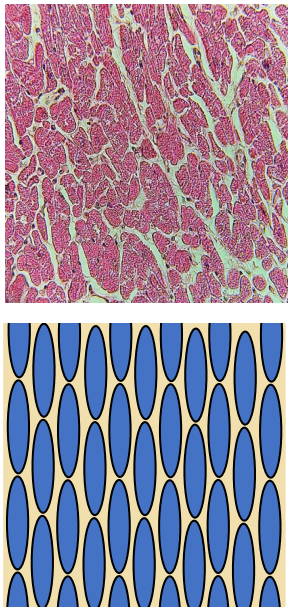
the mapping methods (native).





J Am Coll Cardiol. 2011;57(8):891-903. doi:10.1016/j.jacc.2010.11.013

Extra Cellular Volume



T1 myocardium

- single value for entire myocardium
- T1 can be increased or decreased

extracellular compartment

2 Differential Diagnosis AL vs TTR

Forty-four patients with CA (24 AL; 20 ATTR) and 40 healthy subjects

ESC European Society of Cardiology
European Heart Journal (2022) **43**, 4722–4735
https://doi.org/10.1093/eurheartj/ehac363

CLINICAL RESEARCH
Imaging

Cardiovascular magnetic resonance in light-chain amyloidosis to guide treatment

Ana Martinez-Naharro [1†], Rishi Patel [1†], Tushar Kotecha [1,2], Nina Karia [1,2], Adam Ioannou[1], Aviva Petrie [3], Liza A. Chacko[1], Yousuf Razvi [1], Sriram Ravichandran [1], James Brown[1,2], Steven Law [1], Cristina Quarta [1], Shameem Mahmood[1], Brendan Wisniowski[1], Silvia Pica[1], Sajitha Sachchithanantham[1], Helen J. Lachmann[1], James C. Moon [2,4], Daniel S Knight [1,2], Carol Whelan[1], Lucia Venneri[1], Hui Xue [5], Peter Kellman [5], Julian D. Gillmore [1], Philip N. Hawkins [1], Ashutosh D. Wechalekar[1‡], and Marianna Fontana [1*‡]

[1]National Amyloidosis Centre, Division of Medicine, University College London, Royal Free Hospital, London, UK; [2]Institute of Cardiovascular Science, University College London, London, UK; [3]UCL Eastman Dental Institute, London, UK; [4]Barts Heart Centre, West Smithfield, London, UK; and [5]National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, MD, USA

Received 27 October 2021; revised 26 May 2022; accepted 14 June 2022; online publish-ahead-of-print 26 July 2022

See the editorial comment for this article 'The challenge of managing patients with light-chain cardiac amyloidosis: the value of cardiac magnetic resonance as a guide to the treatment response', by Thibaud Damy *et al.*, https://doi.org/10.1093/eurheartj/ehac526.

Abstract

Aims To assess the ability of cardiovascular magnetic resonance (CMR) to (i) measure changes in response to chemotherapy; (ii) assess the correlation between haematological response and changes in extracellular volume (ECV); and (iii) assess the association between changes in ECV and prognosis over and above existing predictors.

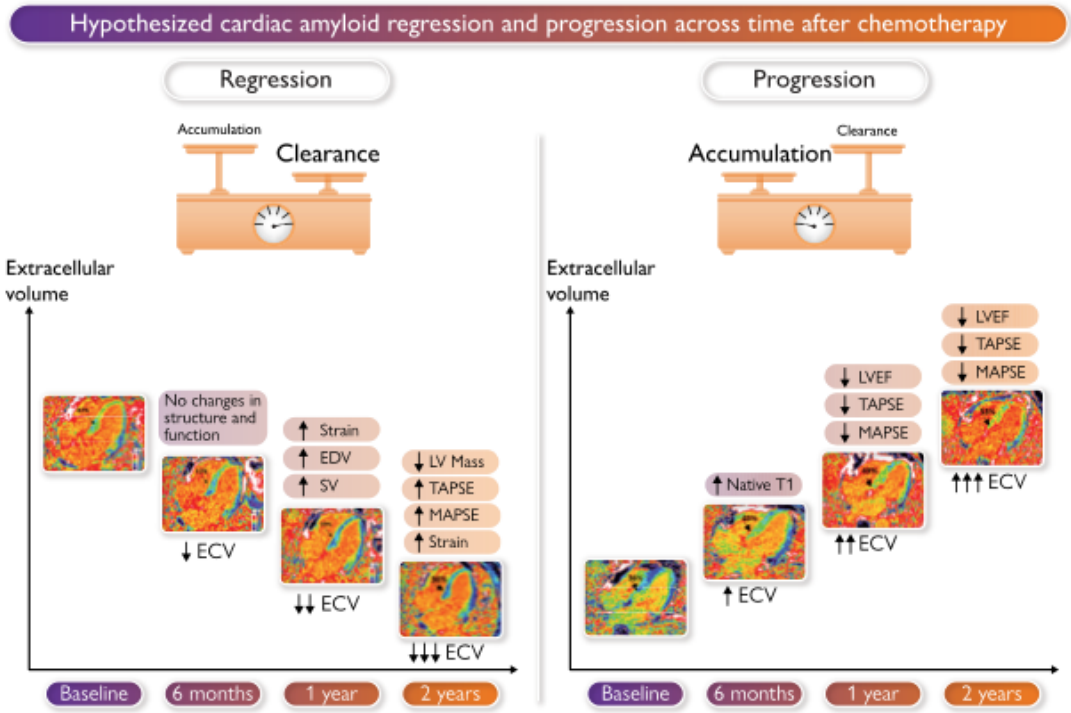
Methods and results In total, 176 patients with cardiac AL amyloidosis were assessed using serial N-terminal pro-B-type natriuretic peptide (NT-proBNP), echocardiography, free light chains and CMR with T1 and ECV mapping at diagnosis and subsequently 6, 12, and 24 months after starting chemotherapy. Haematological response was graded as complete response (CR), very good partial response (VGPR), partial response (PR), or no response (NR). CMR response was graded by changes in ECV as progression (≥0.05 increase), stable (<0.05 change), or regression (≥0.05 decrease). At 6 months, CMR regression was observed in 3% (all CR/VGPR) and CMR progression in 32% (61% in PR/NR; 39% CR/VGPR). After 1 year, 22% had regression (all CR/VGPR), and 22% had progression (63% in PR/NR; 37% CR/VGPR). At 2 years, 38% had regression (all CR/VGPR), and 14% had progression (80% in PR/NR; 20% CR/VGPR). Thirty-six (25%) patients died during follow-up (40 ± 15 months); CMR response at 6 months predicted death (progression hazard ratio 3.82; 95% confidence interval 1.95–7.49; $P < 0.001$) and remained prognostic after adjusting for haematological response, NT-proBNP and longitudinal strain ($P < 0.01$).

Conclusions Cardiac amyloid deposits frequently regress following chemotherapy, but only in patients who achieve CR or VGPR. Changes in ECV predict outcome after adjusting for known predictors.

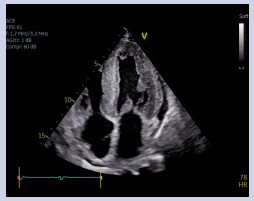
Can CMR be used to follow the effects of therapies?

Take Home Message

CMR demonstrates that cardiac amyloid deposits often regress following chemotherapy, but only in patients achieving a deep and rapid haematological response. Changes in ECV are independently associated with prognosis, supporting the unique role of CMR in assessing treatment response.

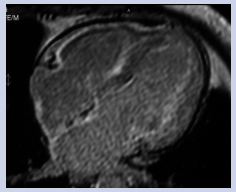


Conclusion of Cardiac Imaging in TTR CA

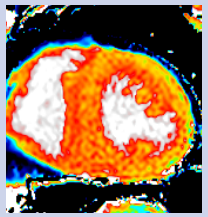


Echo : screening/suspect (red flags), confirming diagnosis, complications, FU stages

See the entire heart (RV, atria, CR, IAS, ….)

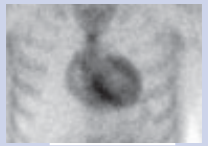


CMR: Suspected CA, differential diagnosis*, FU stages* and therapies*



*

Mapping quantitative data … increasing data in false negative scinti and grade 1 perugini (personal opinion) to FU therapies



SCINTI: definite non invasive diagnosis – ATTENTION FN in vTTR !!!!

Open questions in Imaging and TTR CA?

- Advantages and limits of CMR in TTR CA
- Is there a diagnostic role of CMR for a «Nonbiopsy Diagnosis of Cardiac Transthyretin Amyloidosis» in grade 1 of Perugini Score?
- Can CMR be used to follow the effects of therapies?