Amylose à transthyrétine : que faut-il optimiser ?

"Y-a-t-il des examens imageriques à privilégier ?«

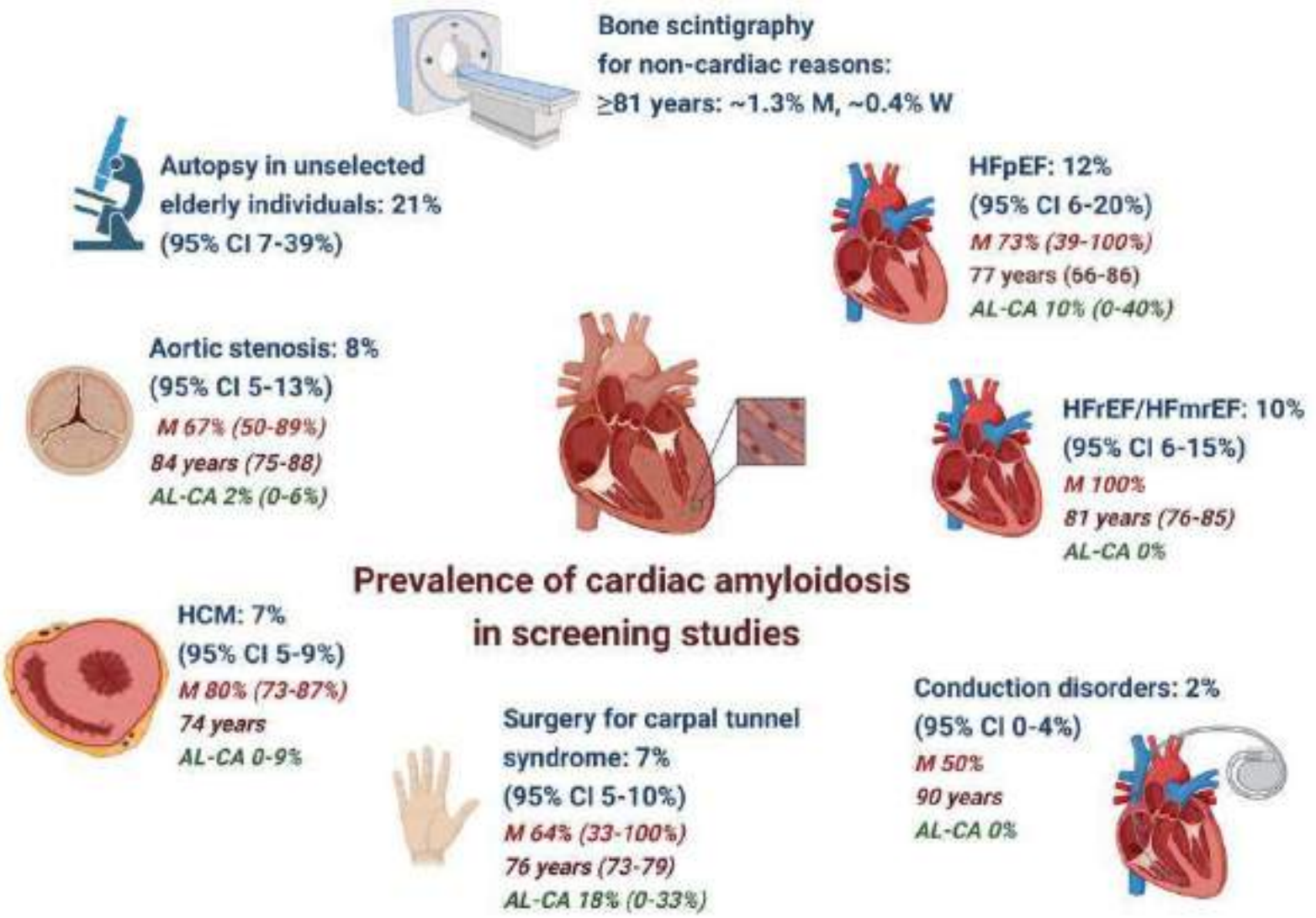
Pr L BIERE

CARDIOLOGIE
CHU ANGERS

Conflits d'intérêt

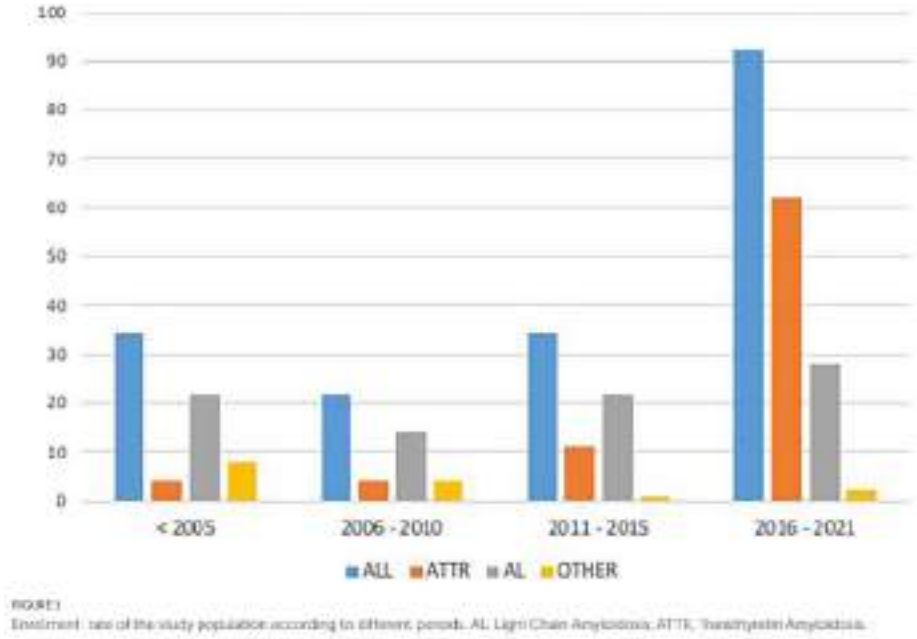
- Invitations congrès: BMS, Pfizer, MSD, Novartis
- Réunions scientifiques: Astrazeneca, Boehringer Ingelheim, Novartis

Une épidémie…

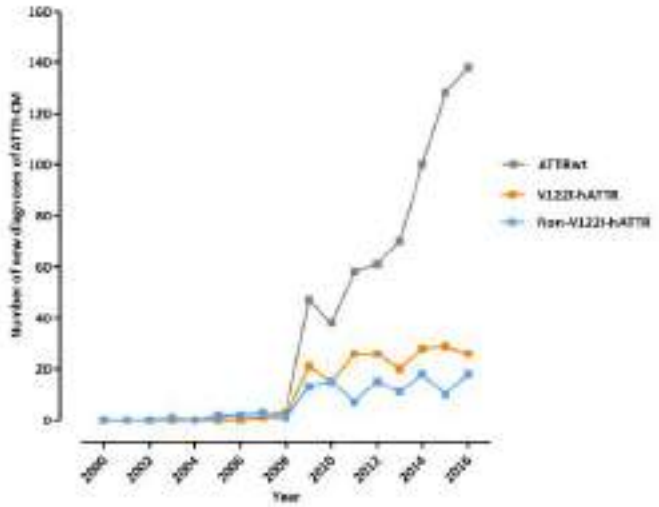


Aimo EHJ CV im 2022

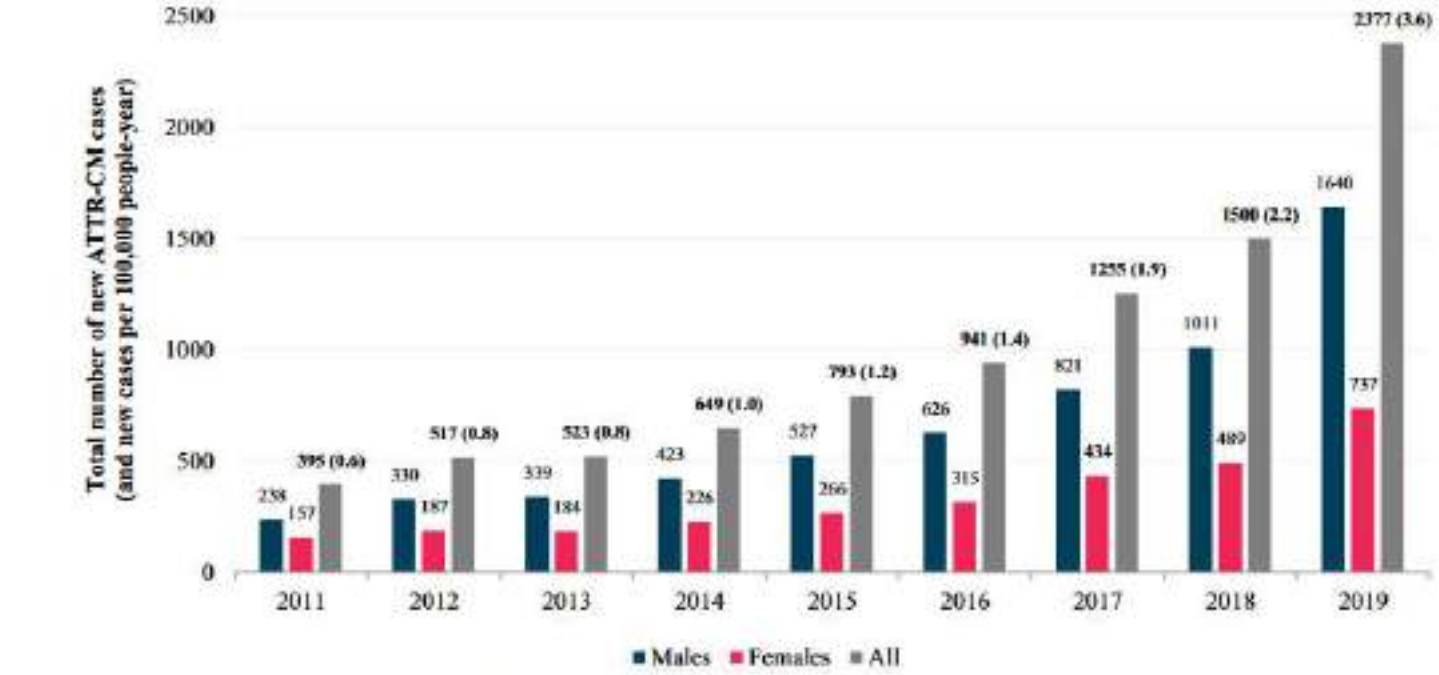
ve



Porcari 2023 ITA



Lane 2019 UK



ATTR-CM incidence overall and by gender between 2011 and 2019

Damy 2023 FR

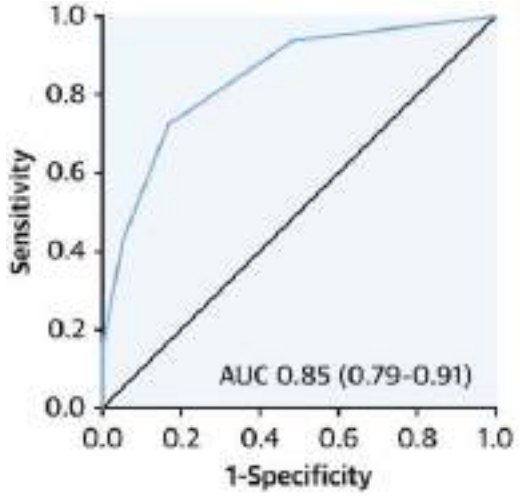
Imagerie de l’amylose TTR

- ETT – suspicion diagnostique
- IRM – caractérisation tissulaire, diagnostics différentiels
- SCINTIGRAPHIE BIPHOSPHONATES – l’essentiel

Specific populations

Aortic stenosis

- Prevalence and Outcomes of Concomitant Aortic Stenosis and Cardiac Amyloidosis
  J Am Coll Cardiol. 2021 Jan 19; 77(2): 128–139.



Parameter	Points
CTS	3
RBBB	2
Age ≥85 years	1
Hs-TnT >20 ng/l	1
IVS ≥18 mm	1
If in SR*: E/A ratio >1.4	1
If no BBB or PM: Sokolow index <1.9 mV	1

* AUC for AFib sub-cohort: 0.83

Score	Specificity	Sensitivity
≥6 points	100%	14.9%
≥5 points	98.9%	23.4%
≥4 points	95.0%	42.6%
≥3 points	83.6%	72.3%
≥2 points	52.1%	93.6%
≥1 point	16.7%	97.9%

HFpEF

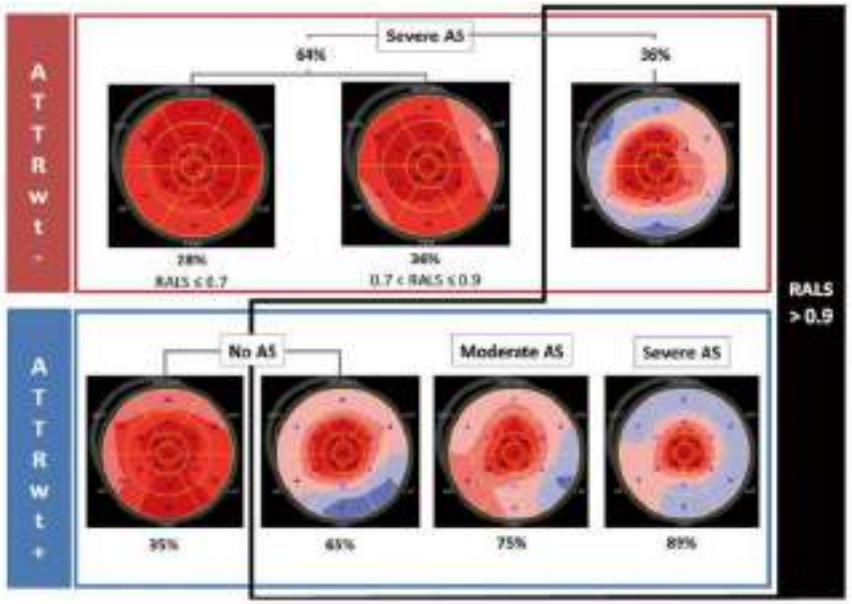
A Simple Score to Identify Increased Risk of Transthyretin Amyloid Cardiomyopathy in Heart Failure With Preserved Ejection Fraction
JAMA cardio 2022 Oct 1;7(10):1036-1044

Clinical variable	Value	Points[a]
Age, y	If 60-69	+2
	If 70-79	+3
	If ≥80	+4
Sex	Male	+2
Hypertension diagnosis	Present	-1
Ejection fraction	<60%	+1
Posterior wall thickness	≥12 mm	+1
Relative wall thickness[b]	>0.57	+2

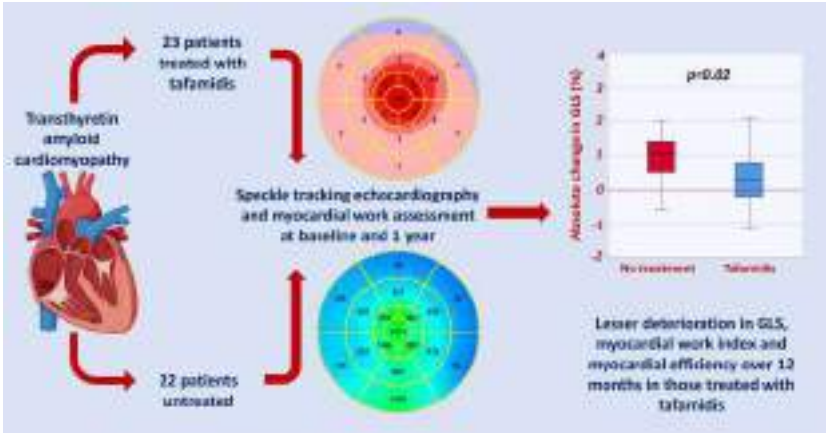
High-risk score ≥6

Transthoracic echocardiography

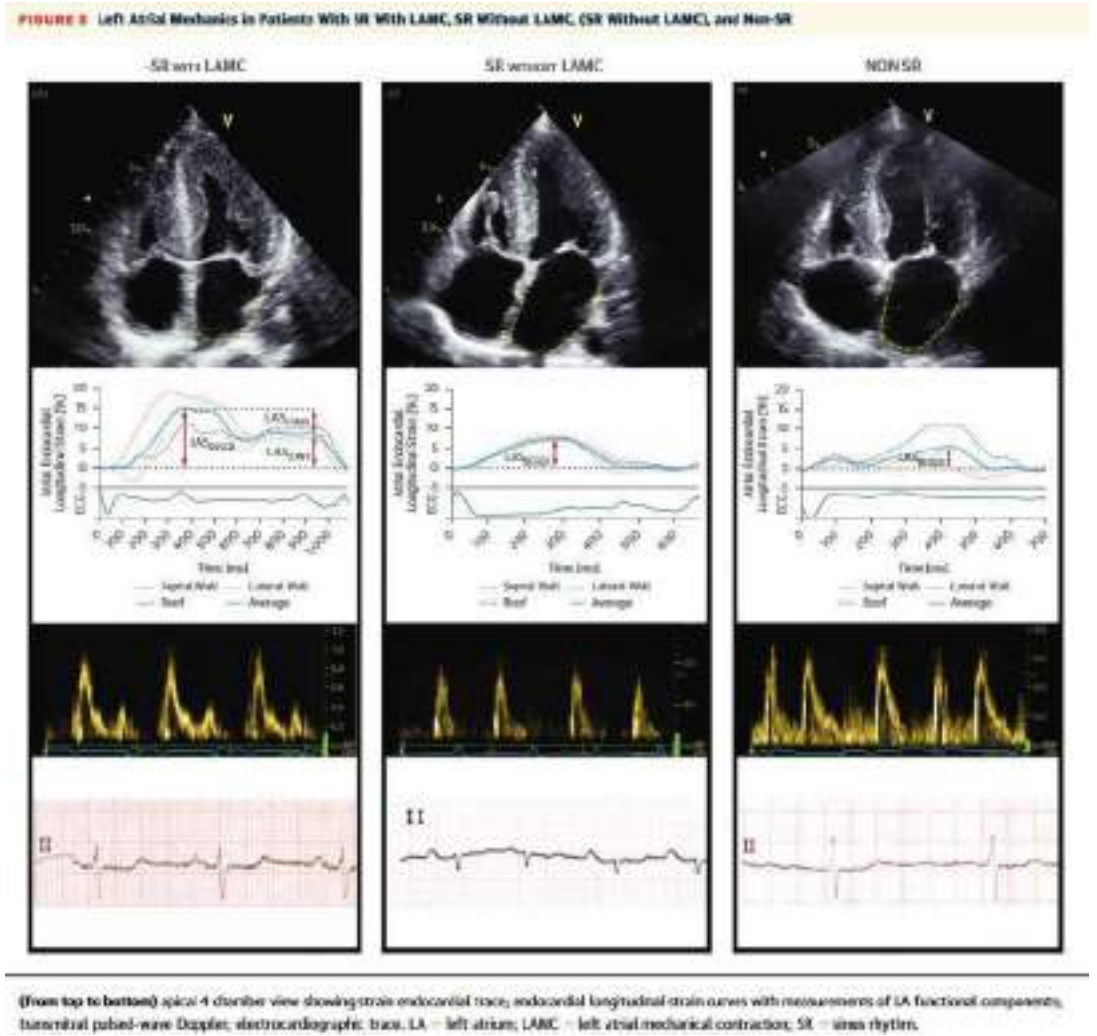
- apical sparring, LF/LG AS, atrial dysfunction



Robin Circ J 2021



Giblin EHJ CV im 2022



Attention à la FA
Bandera JACC CV im 2022

Echo = the screening for cardiac amyloidosis

Multiparametric echocardiographic score ≥8 points:

a. Relative LV wall thickness (IVS+PWT)/LVEDD >0.6
   3 points
b. Doppler E wave/e' wave velocities >11
   1 point
c. TAPSE ≤ 19 mm
   2 points
d. LV global longitudinal strain absolute value ≤ -13%
   1 point
e. Systolic longitudinal strain apex to base ratio > 2.9
   3 points

Boldrini J Am Coll Cardiol Img. 2020 Apr, 13 (4) 909–920

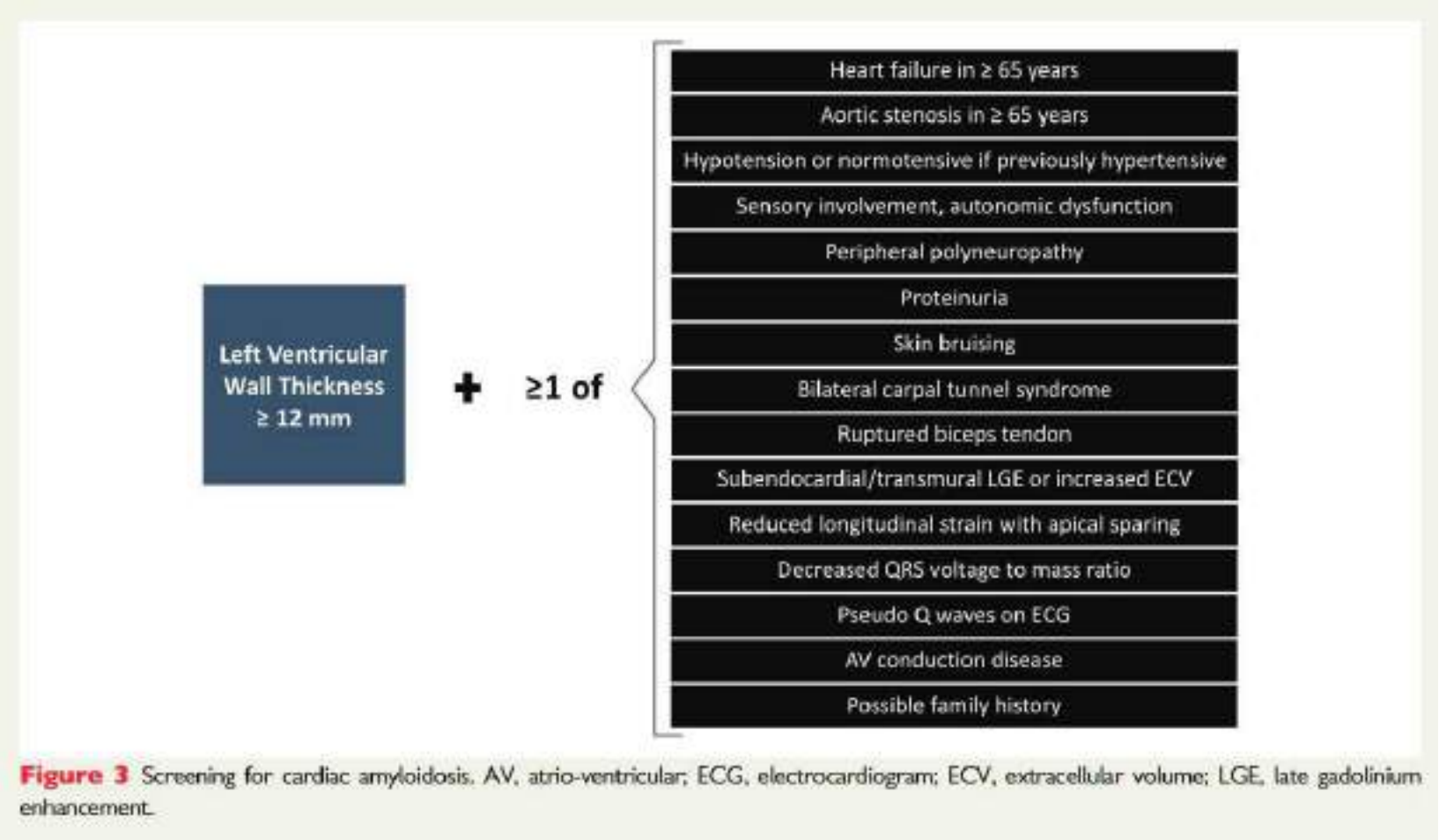
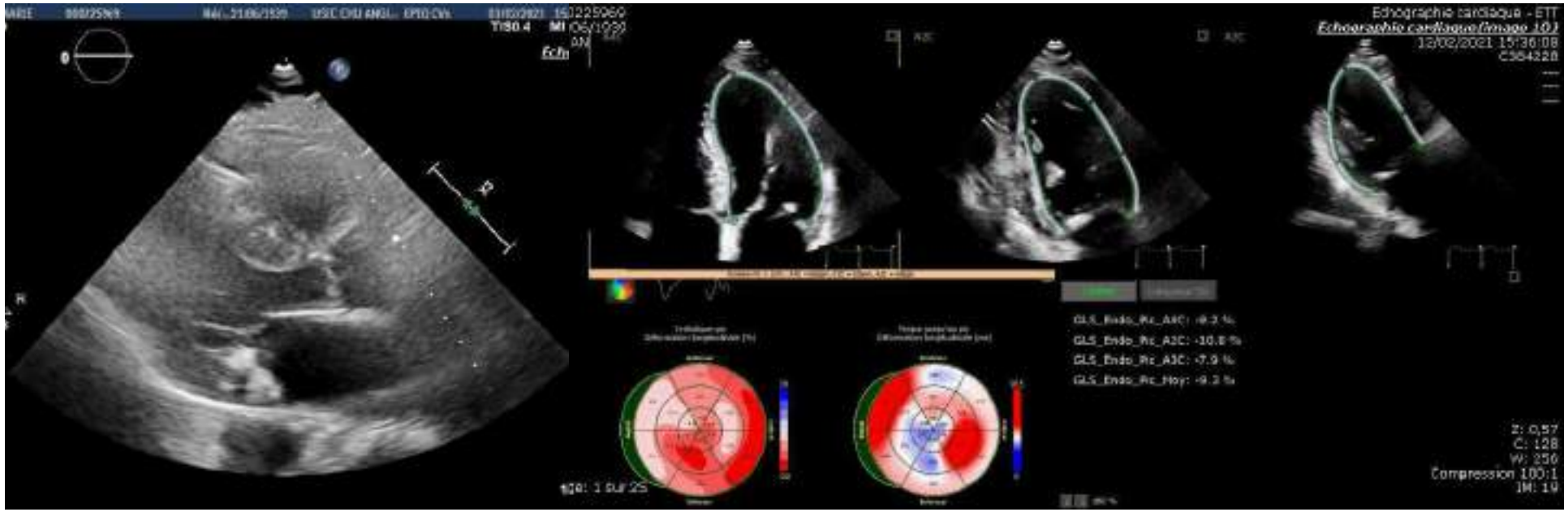


Figure 3 Screening for cardiac amyloidosis. AV, atrio-ventricular; ECG, electrocardiogram; ECV, extracellular volume; LGE, late gadolinium enhancement.

Diagnosis and treatment of cardiac amyloidosis: a position statement of the ESC Working Group on Myocardial and Pericardial Diseases. EHJ 2021

81 yrs old female
Dyspnea
2023 Feb: TTE

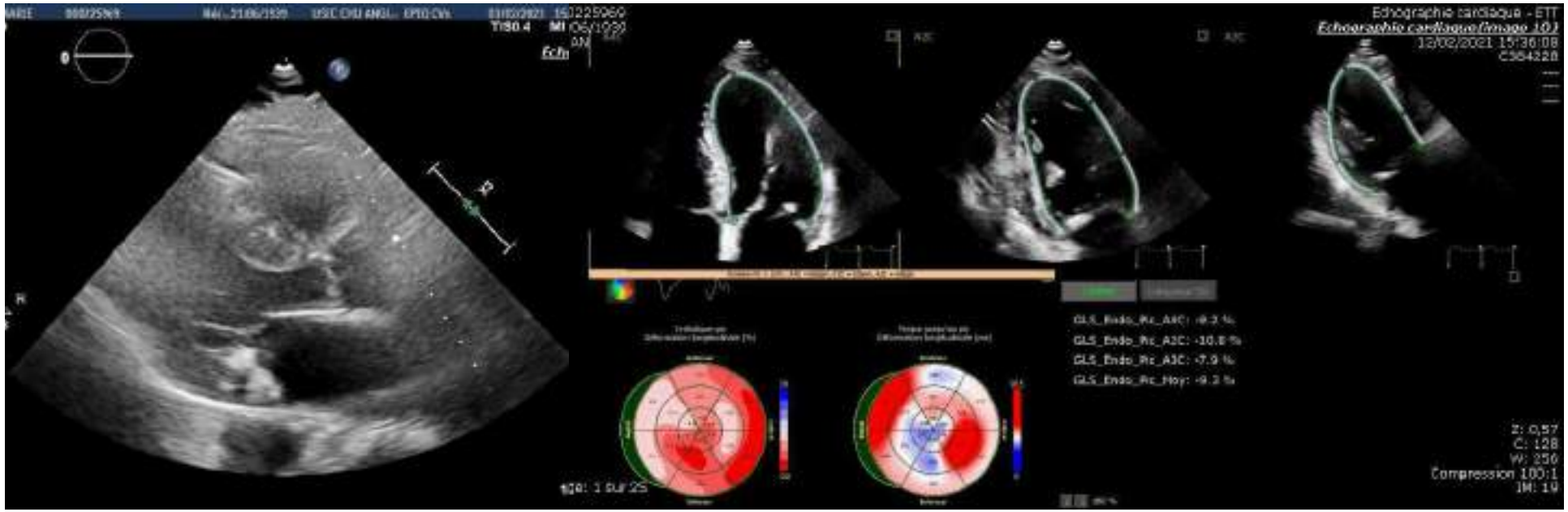


Cardiac Magnetic Resonance

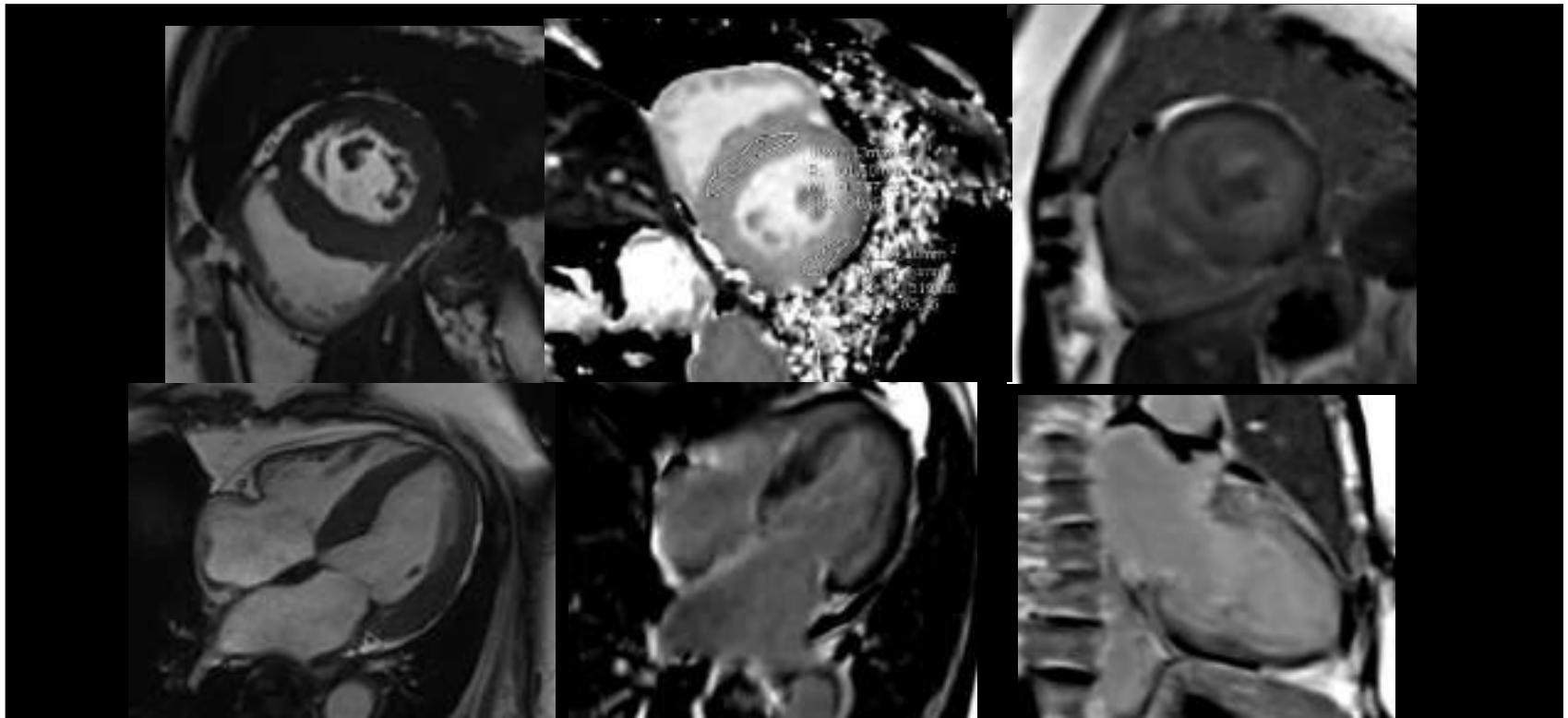
« Une bonne echo vaut une IRM pour le morpho… », « L'IRM c'est une super écho… »

- Morphology, hypertrophy, atrial septum, strain
- Gadolinum kinetics
- Late gadolinium enhancement µ (5 to 10 min)
- T1 mapping (T2 mapping)
- Extra-cellular volume
- Atrial fibrillation
- Contra-indications to gadolinium or MRI
- LGE is not 100% sensitive
- T1 mapping: magnetic fields, MOCO, spatial definition
- ECV : hematocrit

81 yrs old female
Dyspnea
2023 Feb: TTE



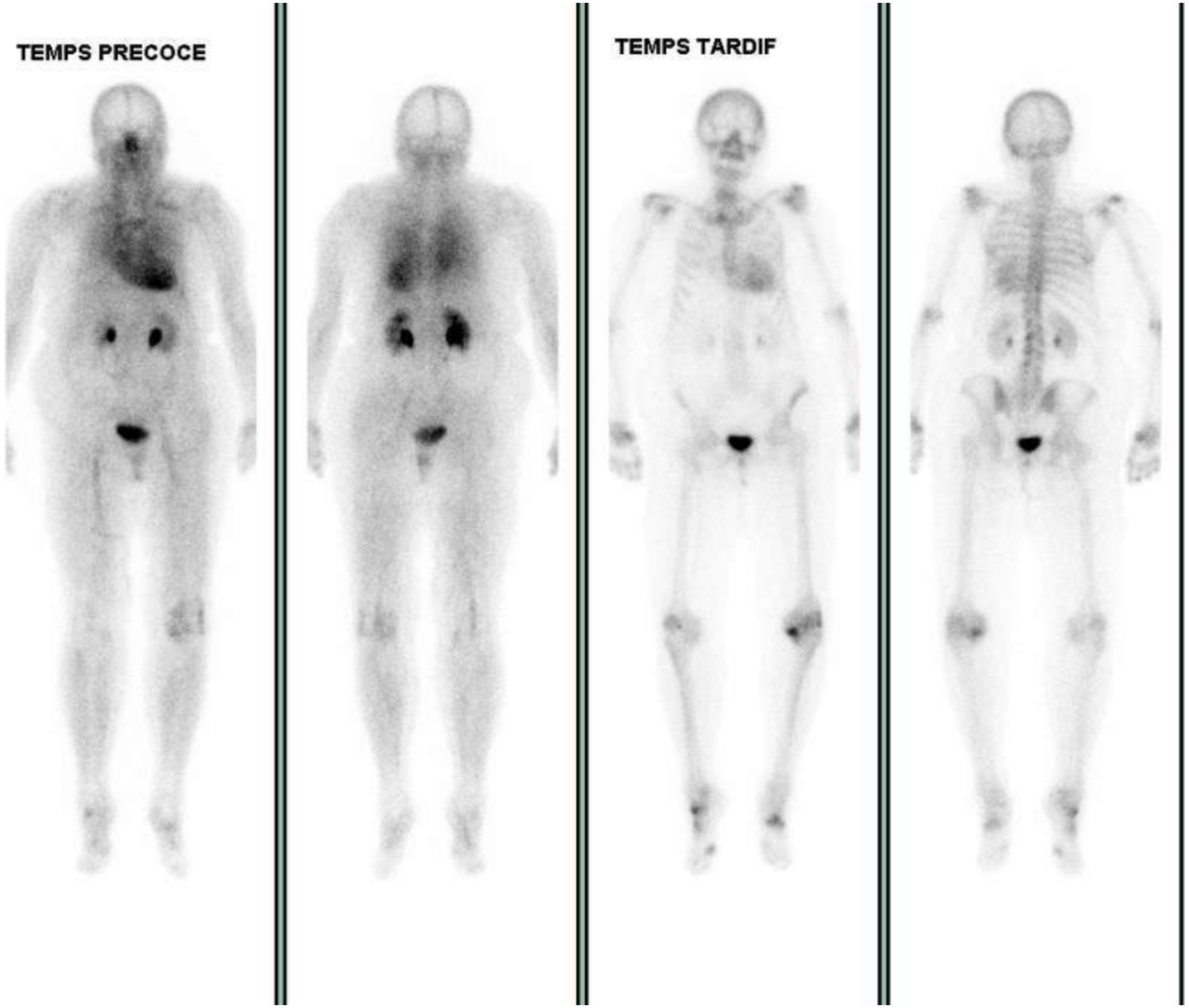
2023 Apr: CMR

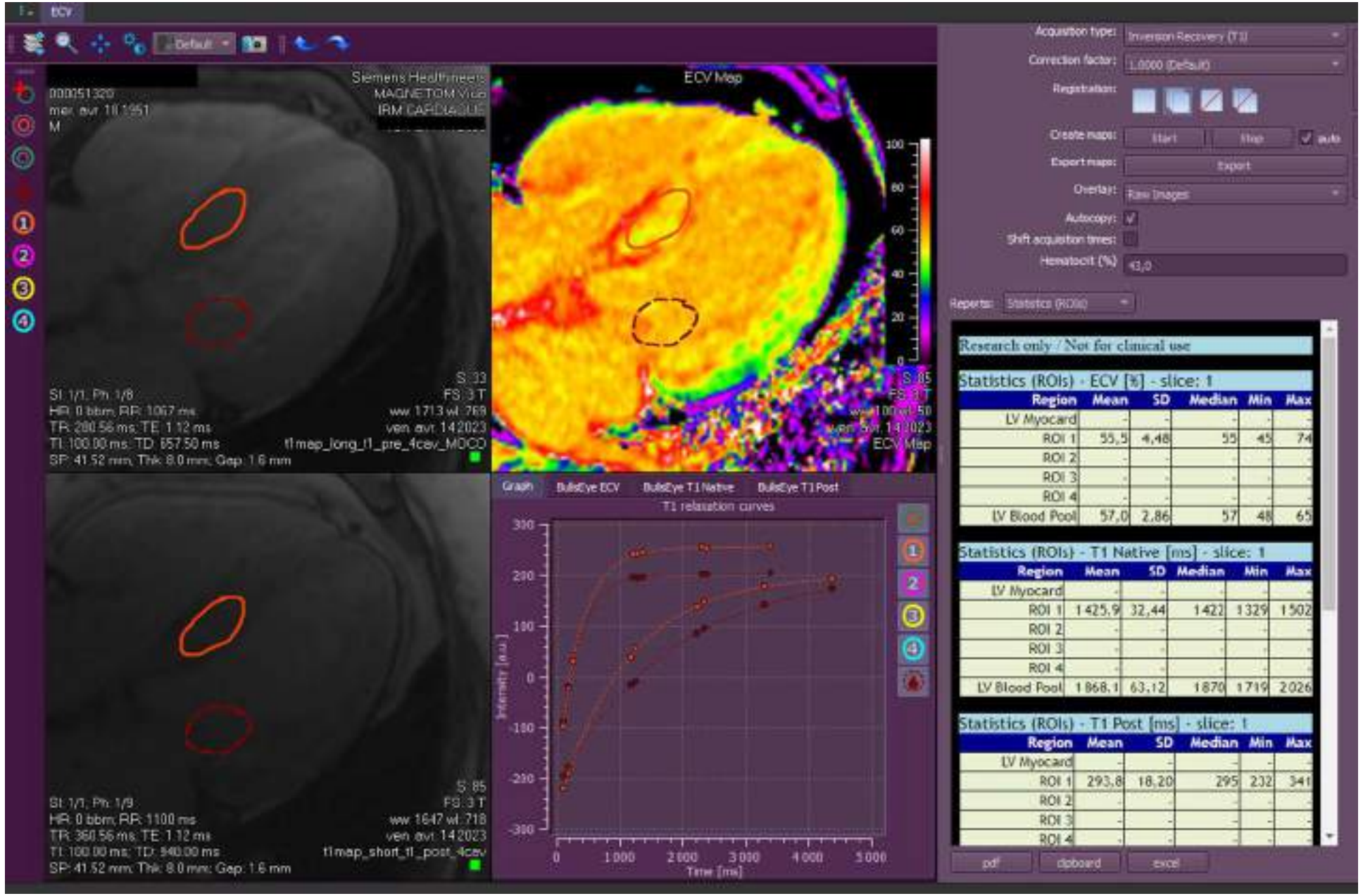


81 yrs old female
Dyspnea
2023 Feb: TTE

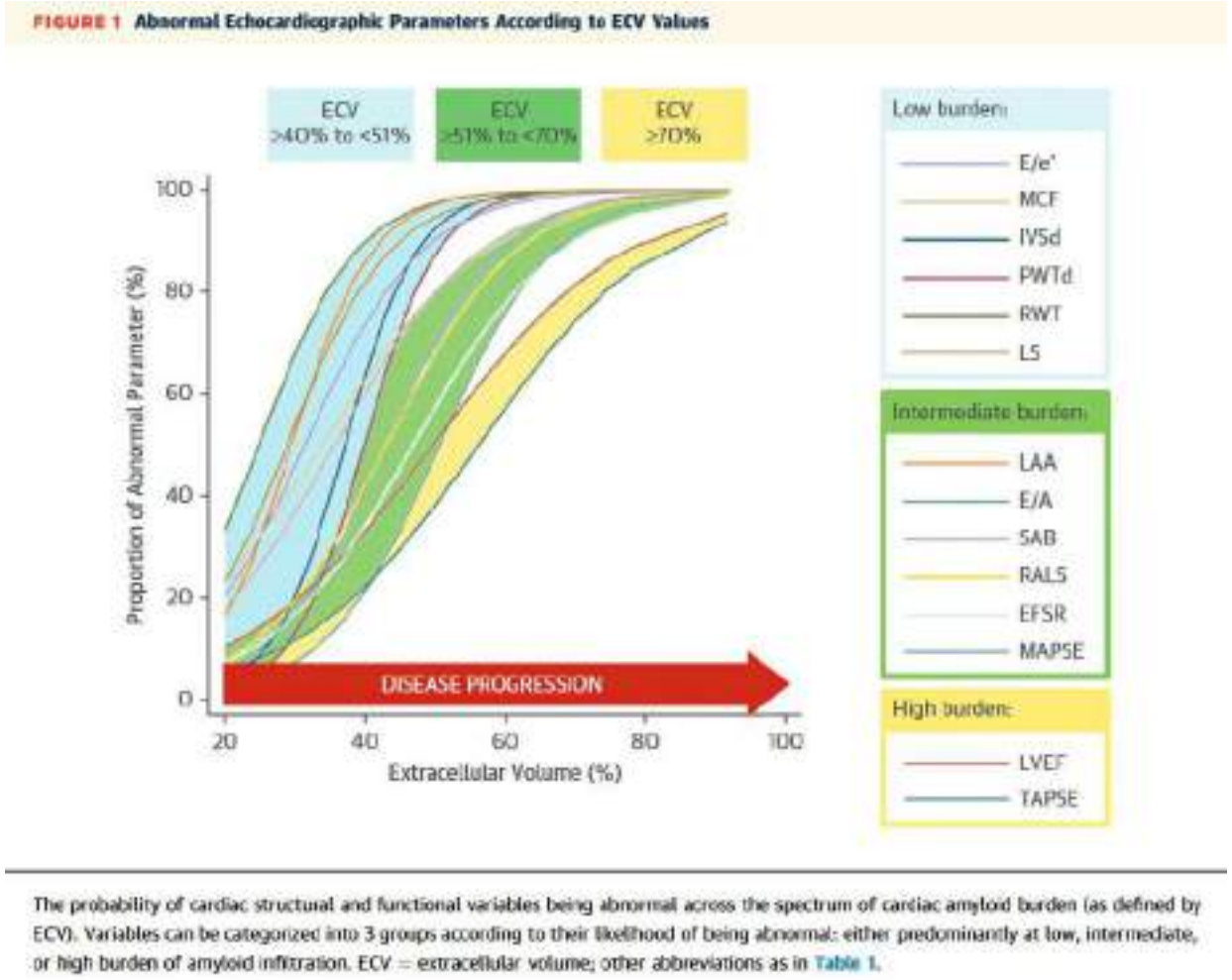
2023 Apr: CMR

2023 May: HMDP…




ECV
Siemens Healthineers
MAGNETOM Vida
IRM CARDIAQUE
ECV Map
Graph
BullsEye ECV
BullsEye T1 Native
BullsEye T1 Post
T1 relaxation curves
Intensity [a.u.]
Time [ms]
Acquisition type:
Inversion Recovery (T1)
Correction factor:
1.0000 (Default)
Registration:
Create maps:
Start
Stop
auto
Export maps:
Export
Overlay:
Raw Images
Autocopy:
Shift acquisition times:
Hematocrit (%)
43,0
Reports:
Statistics (ROIs)
Research only / Not for clinical use
Statistics (ROIs) - ECV [%] - slice: 1
Region | Mean | SD | Median | Min | Max
LV Myocard | - | - | - | - | -
ROI 1 | 55,5 | 4,48 | 55 | 45 | 74
ROI 2 | - | - | - | - | -
ROI 3 | - | - | - | - | -
ROI 4 | - | - | - | - | -
LV Blood Pool | 57,0 | 2,86 | 57 | 48 | 65
Statistics (ROIs) - T1 Native [ms] - slice: 1
Region | Mean | SD | Median | Min | Max
LV Myocard | - | - | - | - | -
ROI 1 | 1425,9 | 32,44 | 1422 | 1329 | 1502
ROI 2 | - | - | - | - | -
ROI 3 | - | - | - | - | -
ROI 4 | - | - | - | - | -
LV Blood Pool | 1868,1 | 63,12 | 1870 | 1719 | 2026
Statistics (ROIs) - T1 Post [ms] - slice: 1
Region | Mean | SD | Median | Min | Max
LV Myocard | - | - | - | - | -
ROI 1 | 293,8 | 18,20 | 295 | 232 | 341
ROI 2 | - | - | - | - | -
ROI 3 | - | - | - | - | -
ROI 4 | - | - | - | - | -
pdf
clipboard
excel

Extracellular volume

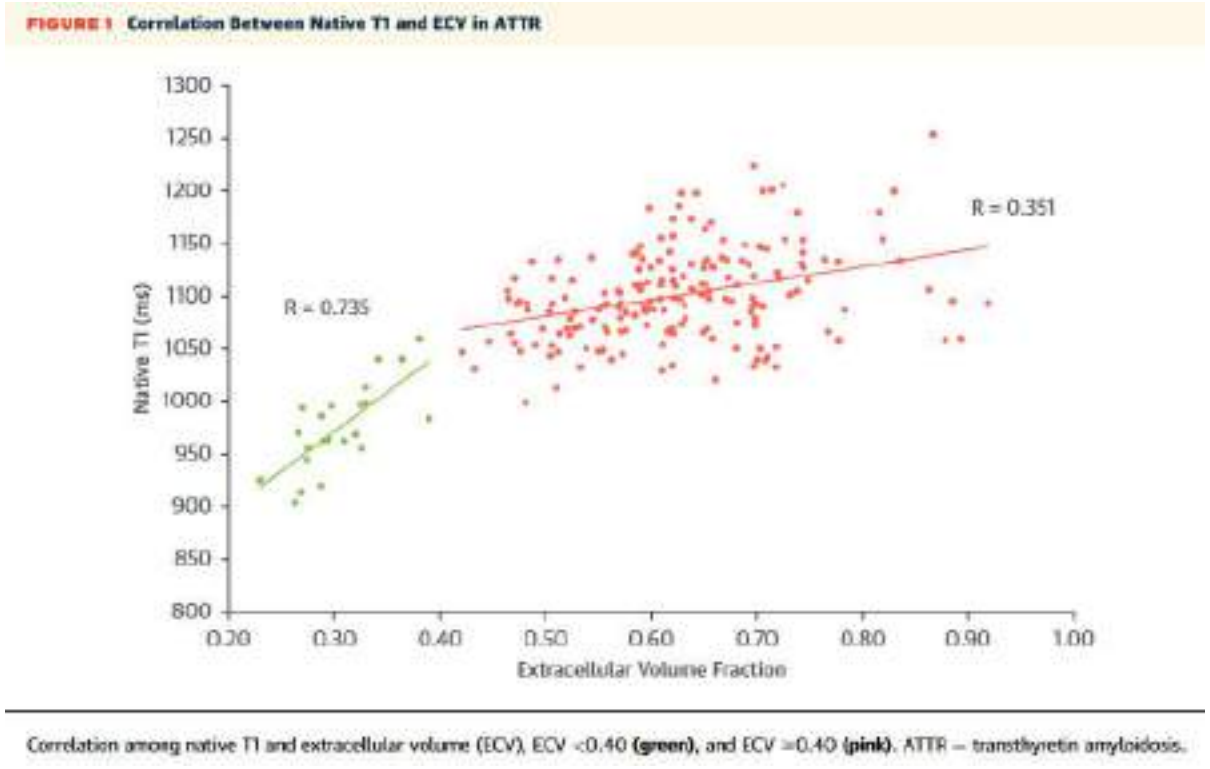


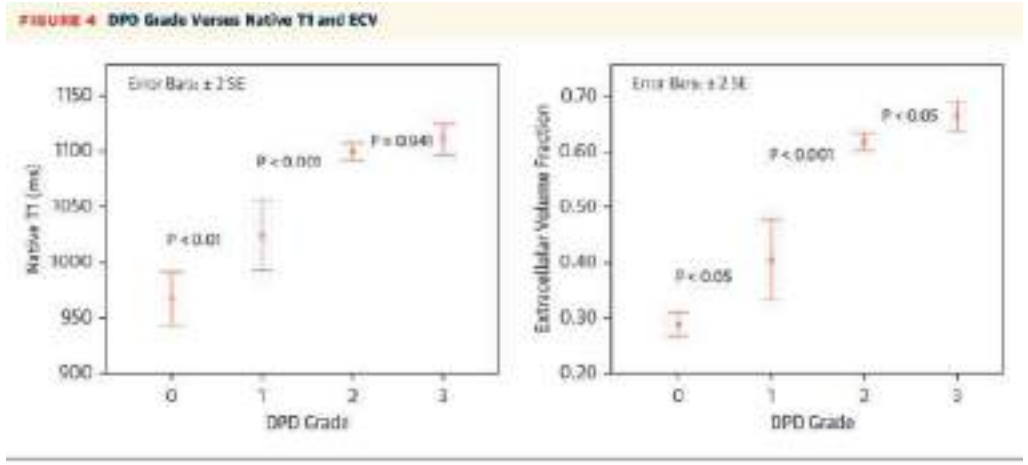
AUC = 0.87
(95% CI: 0.85-0.90)

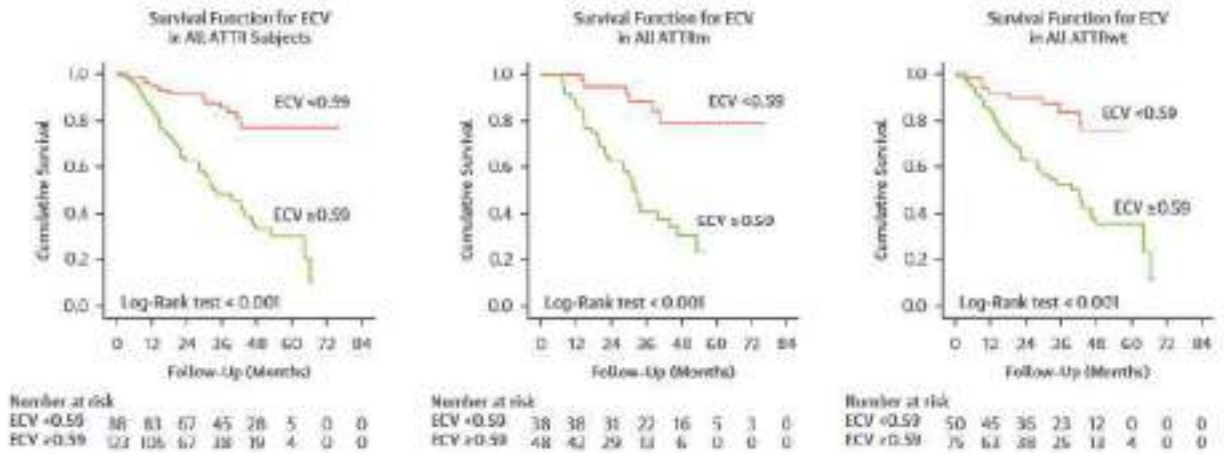
PARAMETERS	RWT >0.6	3 points
	E/e' >11	1 point
	TAPSE ≤19 mm	2 points
	LS ≥ -13%	1 point
	SAB> 2.9	3 points

Boldrini J Am Coll Cardiol Img. 2020 Apr, 13 (4) 909–920

Extracellular volume







Martinez-Naharro, J Am Coll Cardiol Img 2019;12:810–9

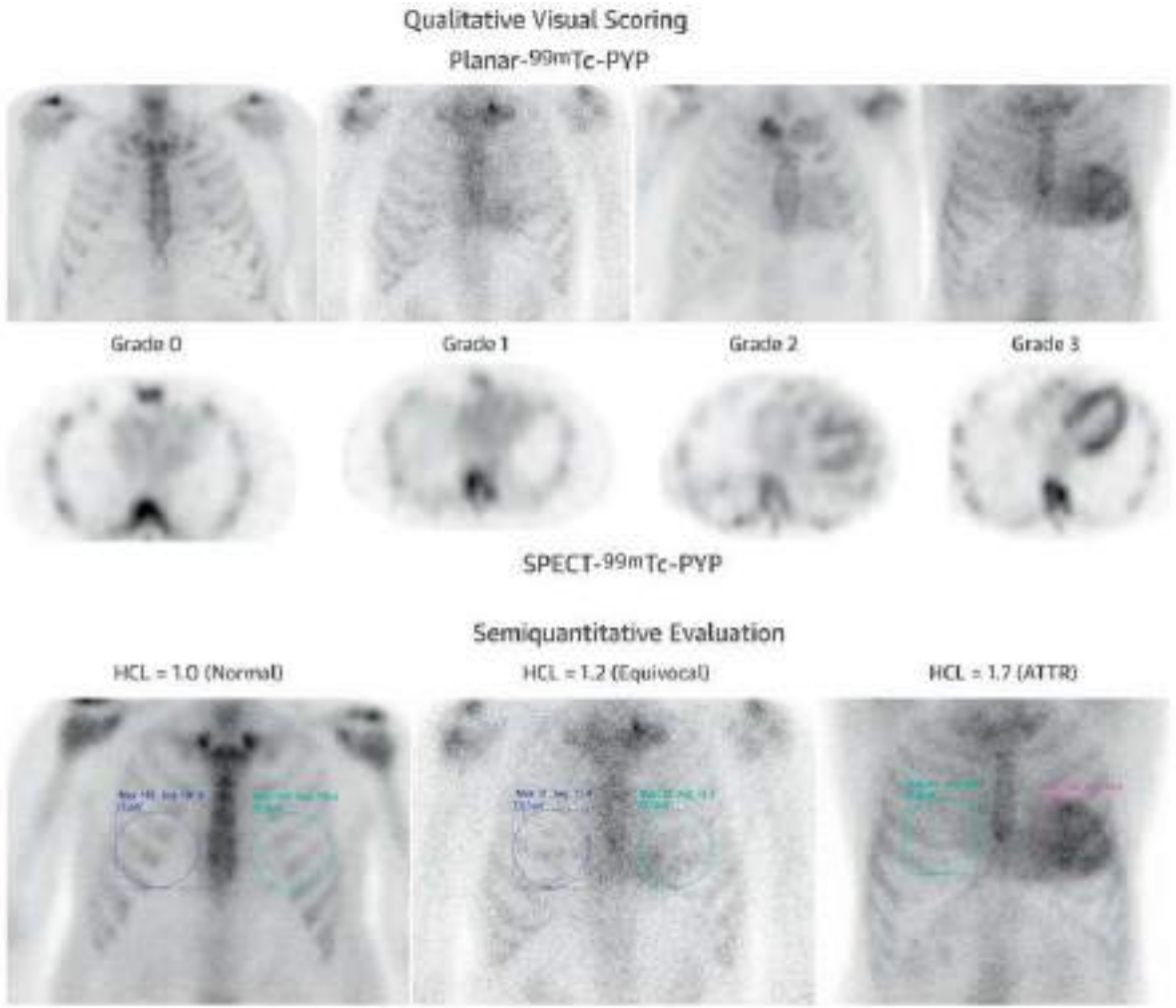
(BONE) SCINTIGRAPHY

- Tracers: DPD, HMDP
- early (10 min) vs late (3 hrs)
- SPECT
- !39% des amyloses AL sont perugini 1
  Quarto EHJ Cvim 2021
- !10% des ATTRv n'ont pas de fixation

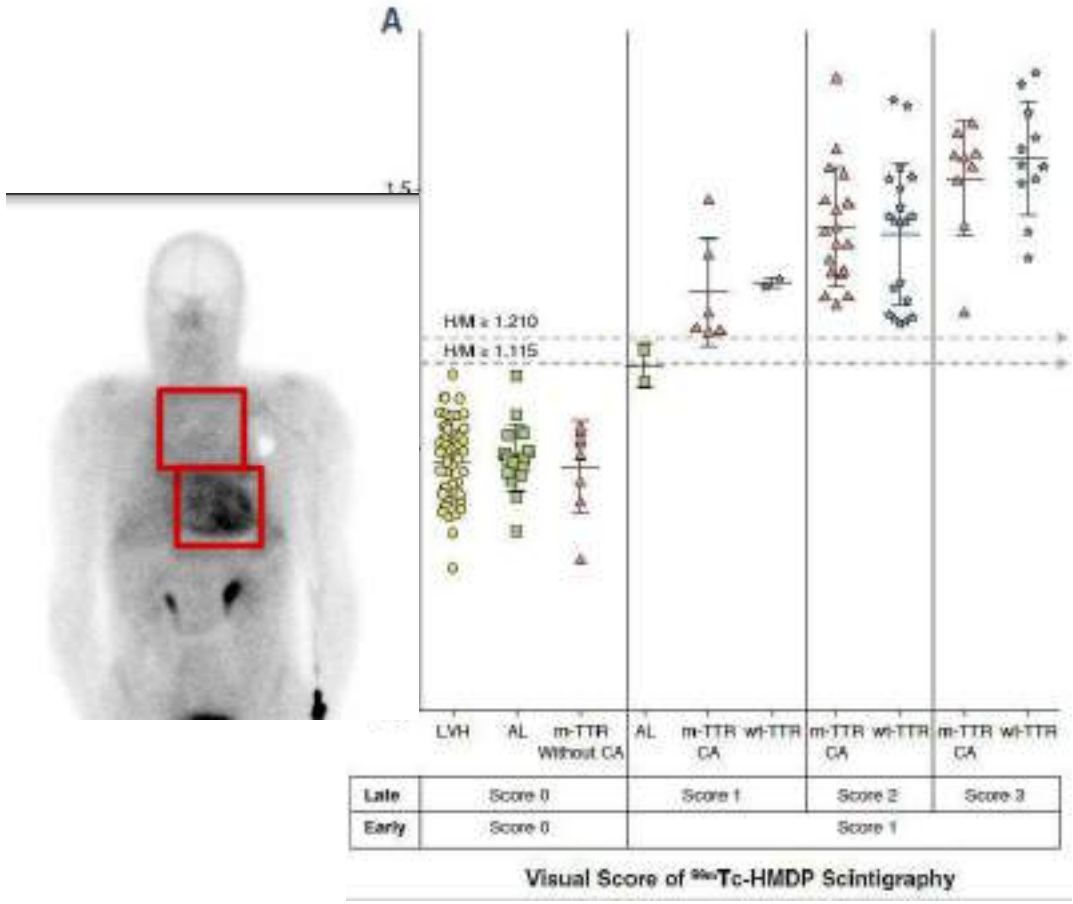
Table 4 **Possible false positives and false negatives of bisphosphonate scintigraphy for detecting transthyretin cardiac amyloidosis**

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



Dorbala JACC im 2020 Perugini qual et quant



Early
Ratio H/M
Gallat JACC 2017

Algorithme diagnostic

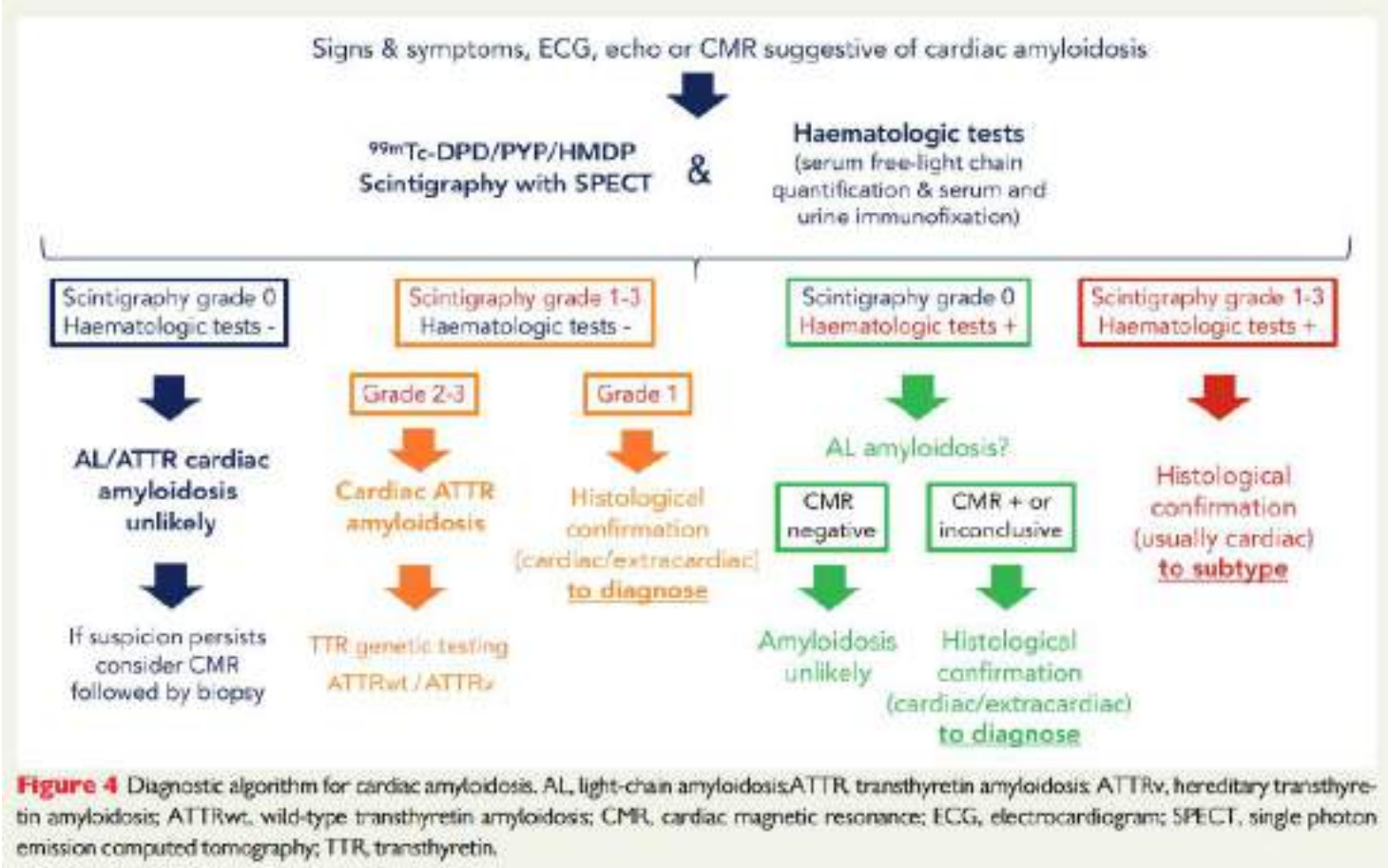
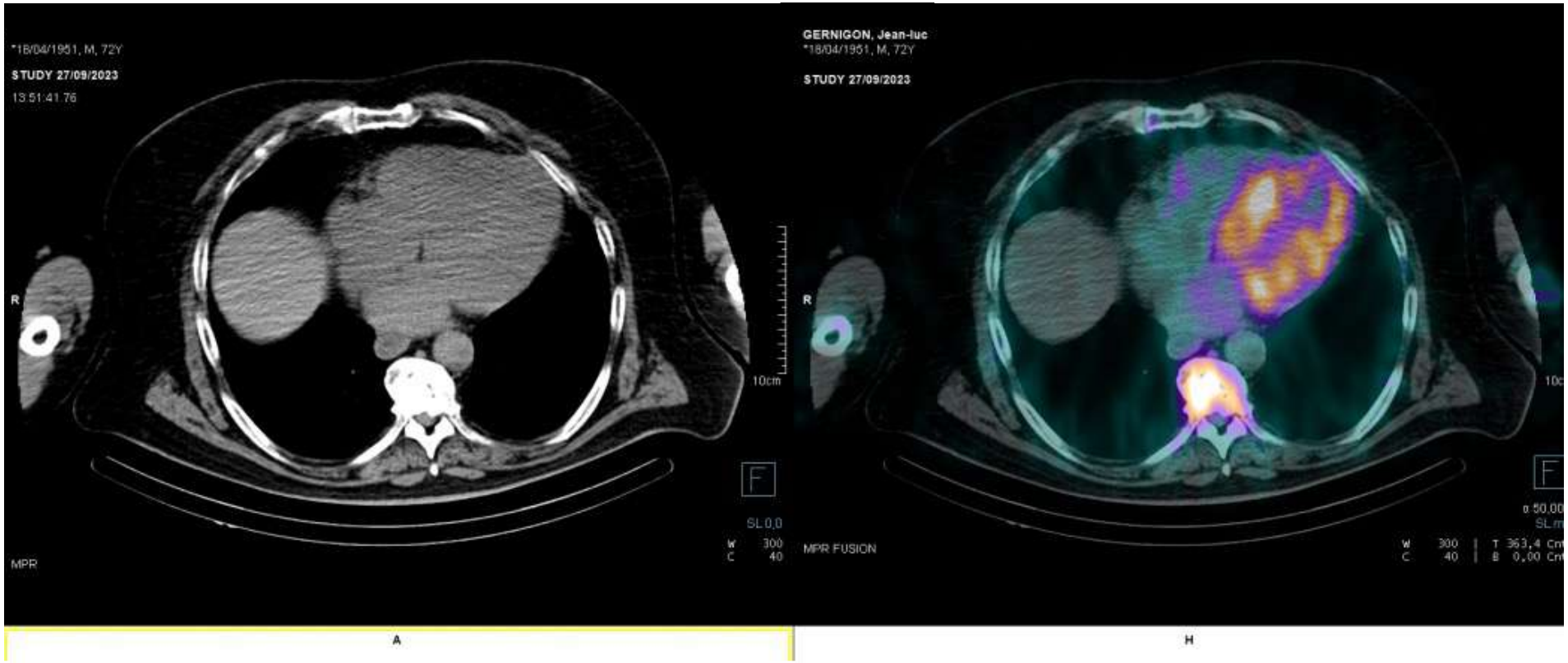


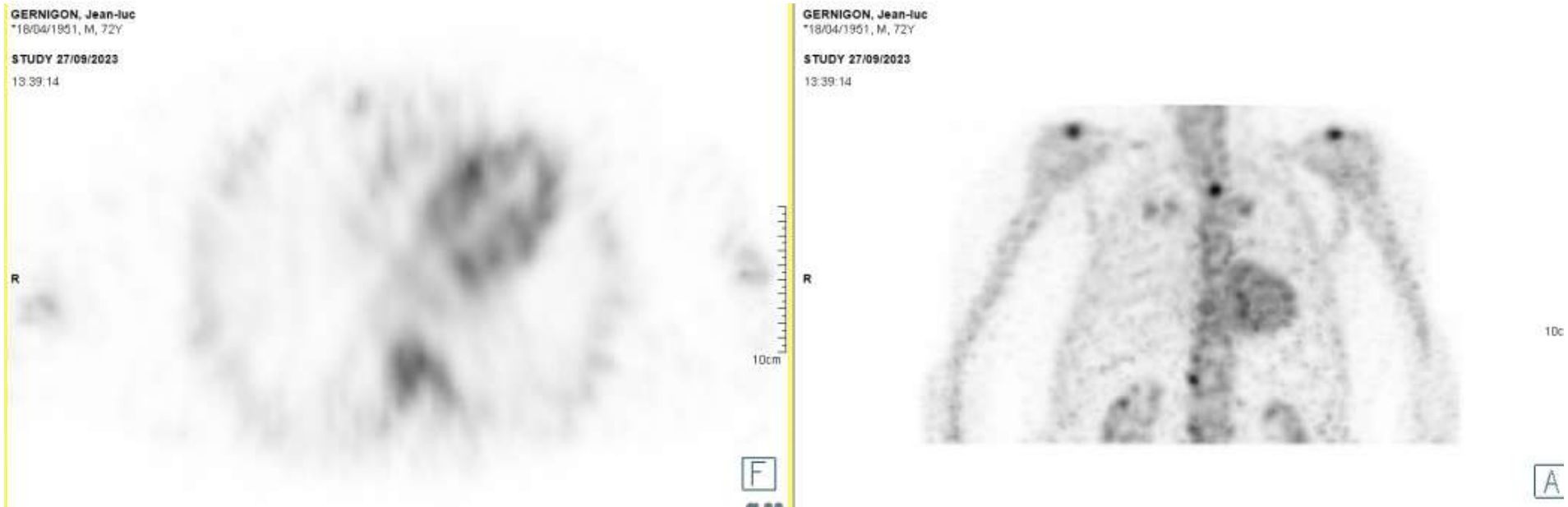
Figure 4 Diagnostic algorithm for cardiac amyloidosis. AL, light-chain amyloidosis;ATTR transthyretin amyloidosis ATTRv, hereditary transthyretin amyloidosis; ATTRwt, wild-type transthyretin amyloidosis; CMR, cardiac magnetic resonance; ECG, electrocardiogram; SPECT, single photon emission computed tomography; TTR, transthyretin.

Garcia-Pavia European Heart Journal (2021) 42, 1554–1568

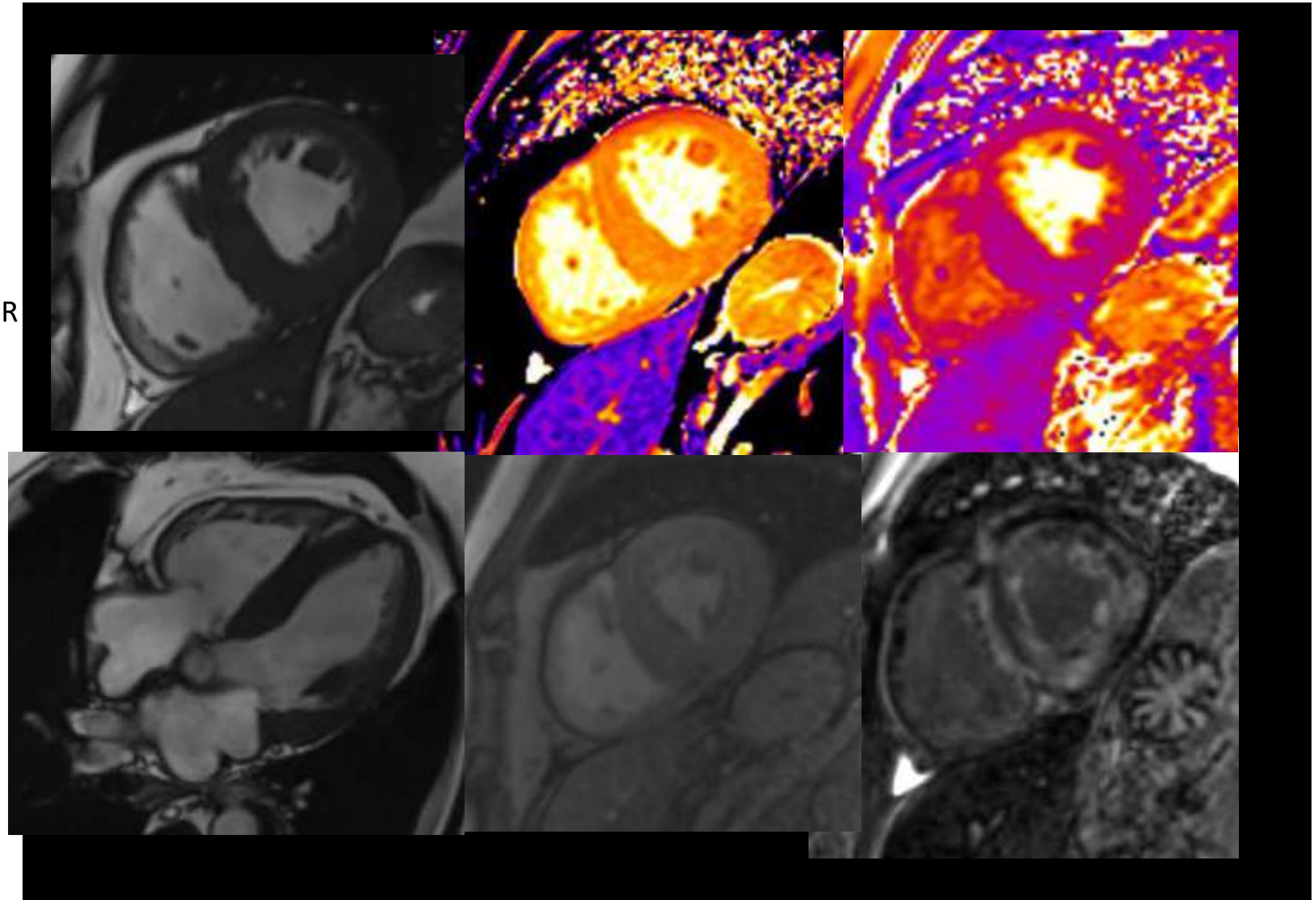
71 yrs old male
HF
LVH
2023 sept

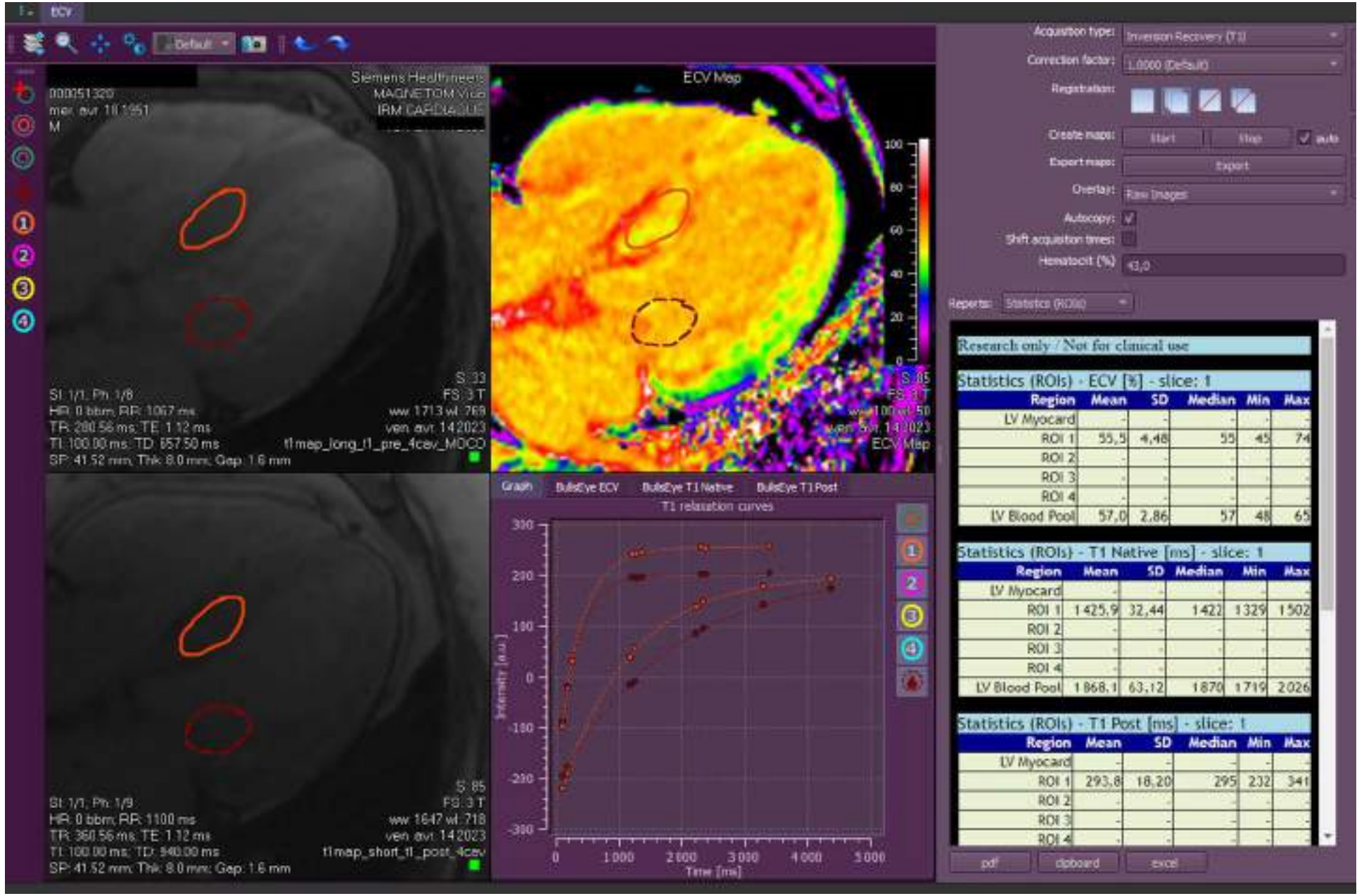
2023 sept HMDP





2023 oct : CMR




ECV
Siemens Healthineers
MAGNETOM Vida
IRM CARDIAQUE
000051320
mer. avr. 19 1951
M
SI: 1/1; Ph: 1/8
HR: 0 bbm; RR: 1067 ms
TR: 280.56 ms; TE: 1.12 ms
TI: 100.00 ms; TD: 857.50 ms
SP: 41.52 mm; Thk: 8.0 mm; Gap: 1.6 mm
S: 33
FS: 3 T
ww: 1713 wl: 768
ven. avr. 14 2023
t1map_long_t1_pre_4cav_MOCO
ECV Map
S: 85
FS: 3 T
ven. avr. 14 2023
ECV Map
SI: 1/1; Ph: 1/9
HR: 0 bbm; RR: 1100 ms
TR: 360.56 ms; TE: 1.12 ms
TI: 100.00 ms; TD: 940.00 ms
SP: 41.52 mm; Thk: 8.0 mm; Gap: 1.6 mm
S: 85
FS: 3 T
ww: 1647 wl: 718
ven. avr. 14 2023
t1map_short_t1_post_4cav
Graph
BullsEye ECV
BullsEye T1 Native
BullsEye T1 Post
T1 relaxation curves
Intensity [a.u.]
Time [ms]
Acquisition type:
Inversion Recovery (T1)
Correction factor:
1.0000 (Default)
Registration:
Create maps:
Start
Stop
auto
Export maps:
Export
Overlay:
Raw Images
Autocopy:
Shift acquisition times:
Hematocrit (%)
43,0
Reports:
Statistics (ROIs)
Research only / Not for clinical use
Statistics (ROIs) - ECV [%] - slice: 1
Region | Mean | SD | Median | Min | Max
LV Myocard | - | - | - | - | -
ROI 1 | 55,5 | 4,48 | 55 | 45 | 74
ROI 2 | - | - | - | - | -
ROI 3 | - | - | - | - | -
ROI 4 | - | - | - | - | -
LV Blood Pool | 57,0 | 2,86 | 57 | 48 | 65
Statistics (ROIs) - T1 Native [ms] - slice: 1
Region | Mean | SD | Median | Min | Max
LV Myocard | - | - | - | - | -
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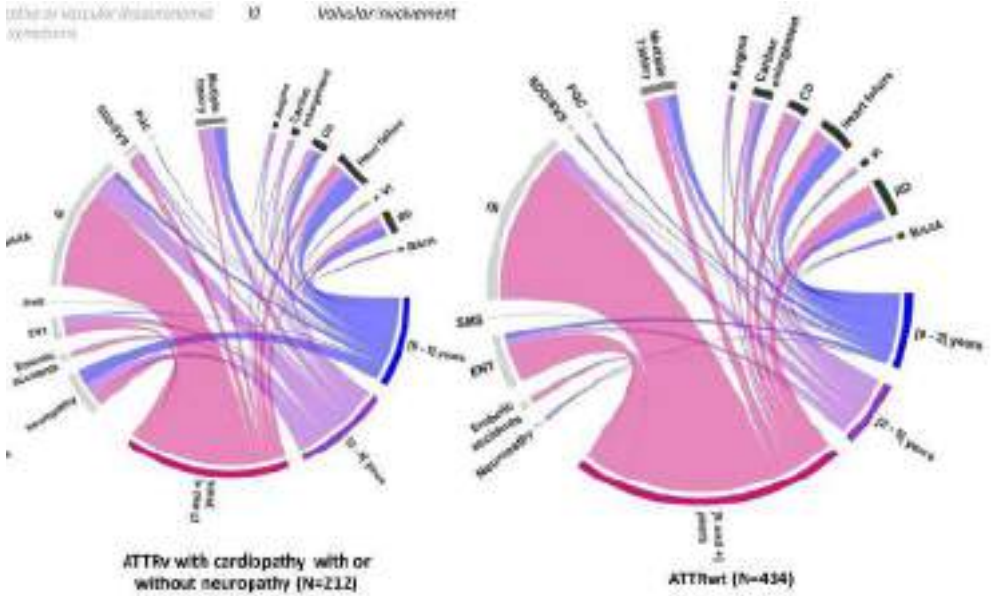
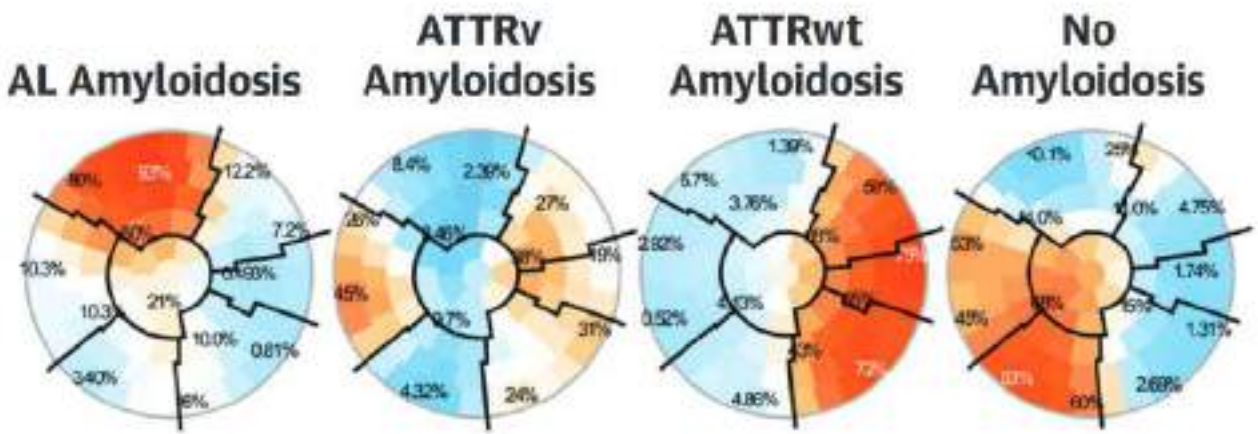
ROI 2 | - | - | - | - | -
ROI 3 | - | - | - | - | -
ROI 4 | - | - | - | - | -
LV Blood Pool | 1868,1 | 63,12 | 1870 | 1719 | 2026
Statistics (ROIs) - T1 Post [ms] - slice: 1
Region | Mean | SD | Median | Min | Max
LV Myocard | - | - | - | - | -
ROI 1 | 293,8 | 18,20 | 295 | 232 | 341
ROI 2 | - | - | - | - | -
ROI 3 | - | - | - | - | -
ROI 4 | - | - | - | - | -
pdf
dpboard
excel

Imaging to distinguish wild type from variant ATTR?



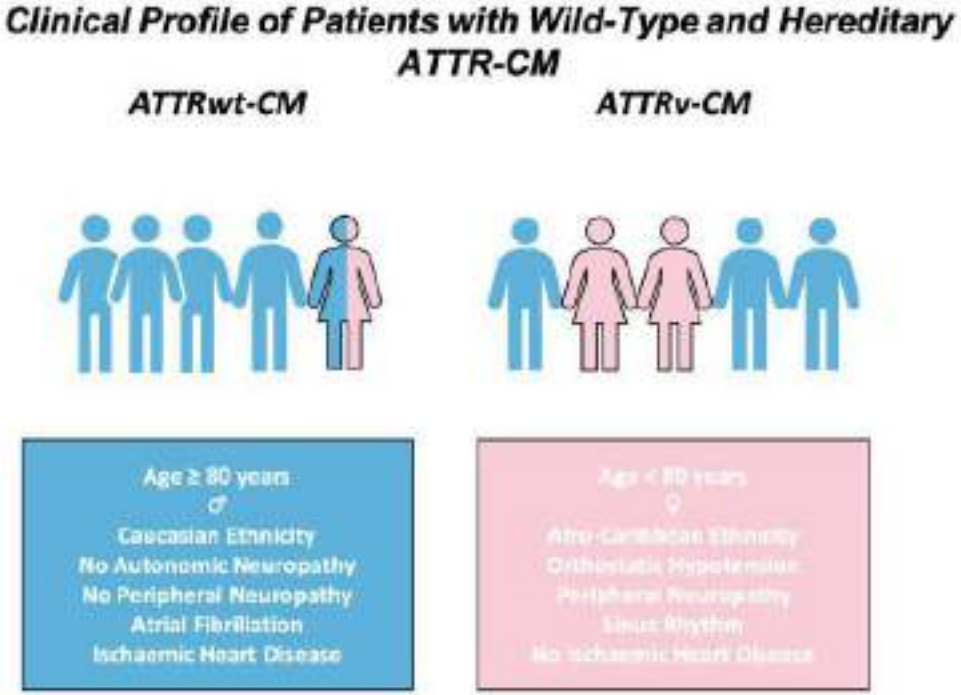
n=983

Kharoubi, ESC Heart Failure 2021; 8: 5501–5512



n=1394

Bonnefous, J Am Coll Cardiol 2021;78:2177–2192



n=2029

Porcari, European Journal of Heart Failure (2023) 25,515–524

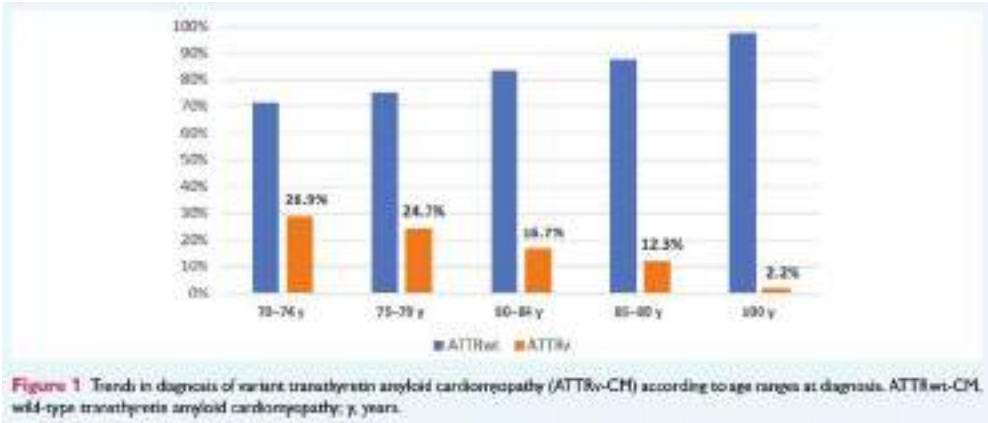
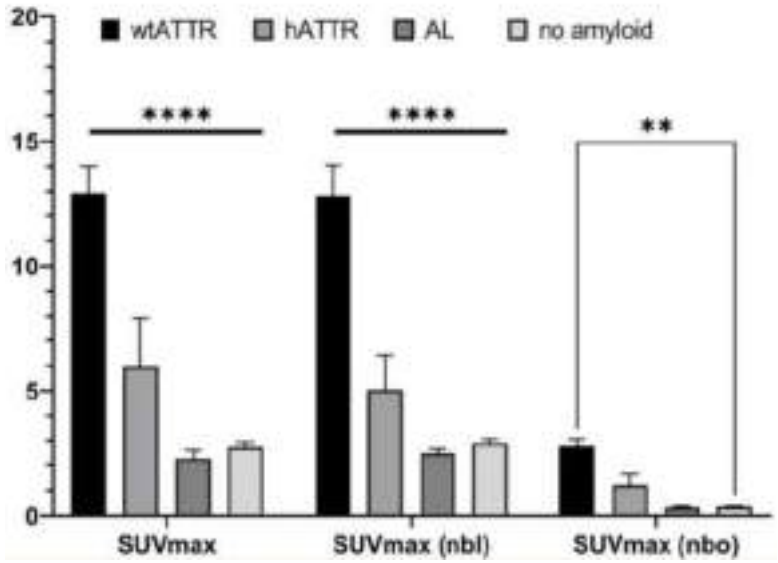


Figure 1 Trends in diagnosis of variant transthyretin amyloid cardiomyopathy (ATTRv-CM) according to age ranges at diagnosis. ATTRwt-CM, wild-type transthyretin amyloid cardiomyopathy; y, years.



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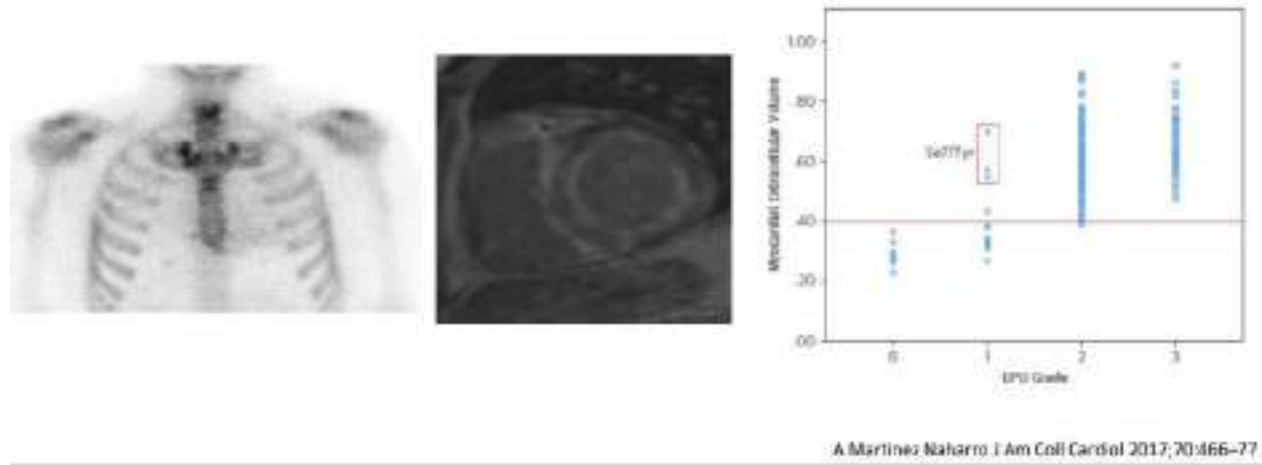
Kessler, J Nucl Cardiol. 2023; 30(1): 101–111



Diag précoce de l’atteinte amyloide

Prognostic staging

Table 6 Prognostic staging scores in light-chain and transthyretin amyloidoses

Kumar *et al.*[15] (Mayo)		Lilleness *et al.*[16] (BU)		Grogan *et al.*[17] (Mayo)		Gillmore *et al.*[18] (NAC)		Cheng *et al.*[19] (Columbia)	
AL		**AL**		**ATTRwt**		**ATTRv and ATTRwt**		**ATTRv and ATTRwt**	
Staging parameters: FLC-diff ≥ 18 mg/dL Troponin T ≥ 0.025 ng/mL NT-proBNP ≥ 1800 pg/mL		**Staging parameters:** Troponin I > 0.1 ng/mL BNP > 81 pg/mL		**Staging parameters:** Troponin T > 0.05 ng/mL NT-proBNP > 3000 pg/mL		**Staging parameters:** eGFR < 45 mL/min/1.73 m^2 NT-proBNP > 3000 pg/mL		**Scoring parameters:** Mayo or NAC score (0–2 points) Daily dose of furosemide or equivalent: 0 mg/kg (0 points), >0–0.5 mg/kg (1 point), >0.5–1 mg/kg (2 points), and > 1 mg/kg (3 points) NYHA class I-IV (1 to 4 points)	
Stage	**5-year survival**	**Stage**	**Median survival**	**Stage**	**4-year survival/ median survival**	**Stage**	**Median survival**	**Score**	**Median survival**
Stage I (0 parameters)	68%	Stage I (0 parameters)	Not reached	Stage I (0 parameters)	57% 66 months	Stage I (0 parameters)	69.2 months	Score 1–3	90.5 months
Stage II (1 parameter)	60%	Stage II (1 parameter)	112.8 months	Stage II (1 parameter)	42% 40 months	Stage II (1 parameter)	46.7 months	Score 4–6	38.5 months (Mayo) 36 months (NAC)
Stage III (2 parameters)	28%	Stage III (2 parameters)	51.6 months	Stage III (2 parameters)	18% 20 months	Stage III (2 parameters)	24.1 months	Score 7–9	20.3 months (Mayo) 19.8 months (NAC)
Stage IV (3 parameters)	14%	Stage IIIb (2 parameters and BNP > 700 pg/mL)	12 months						

AL, light-chain amyloidosis; ATTRv, hereditary transthyretin amyloidosis; ATTRwt, wild-type transthyretin amyloidosis; BU, Boston University School of Medicine; eGFR, estimated glomerular filtration rate calculated by the Modification of Diet in Renal Disease formula; FLC-diff, difference between involved and uninvolved free light chain; NAC, UK National Amyloidosis Centre; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association.

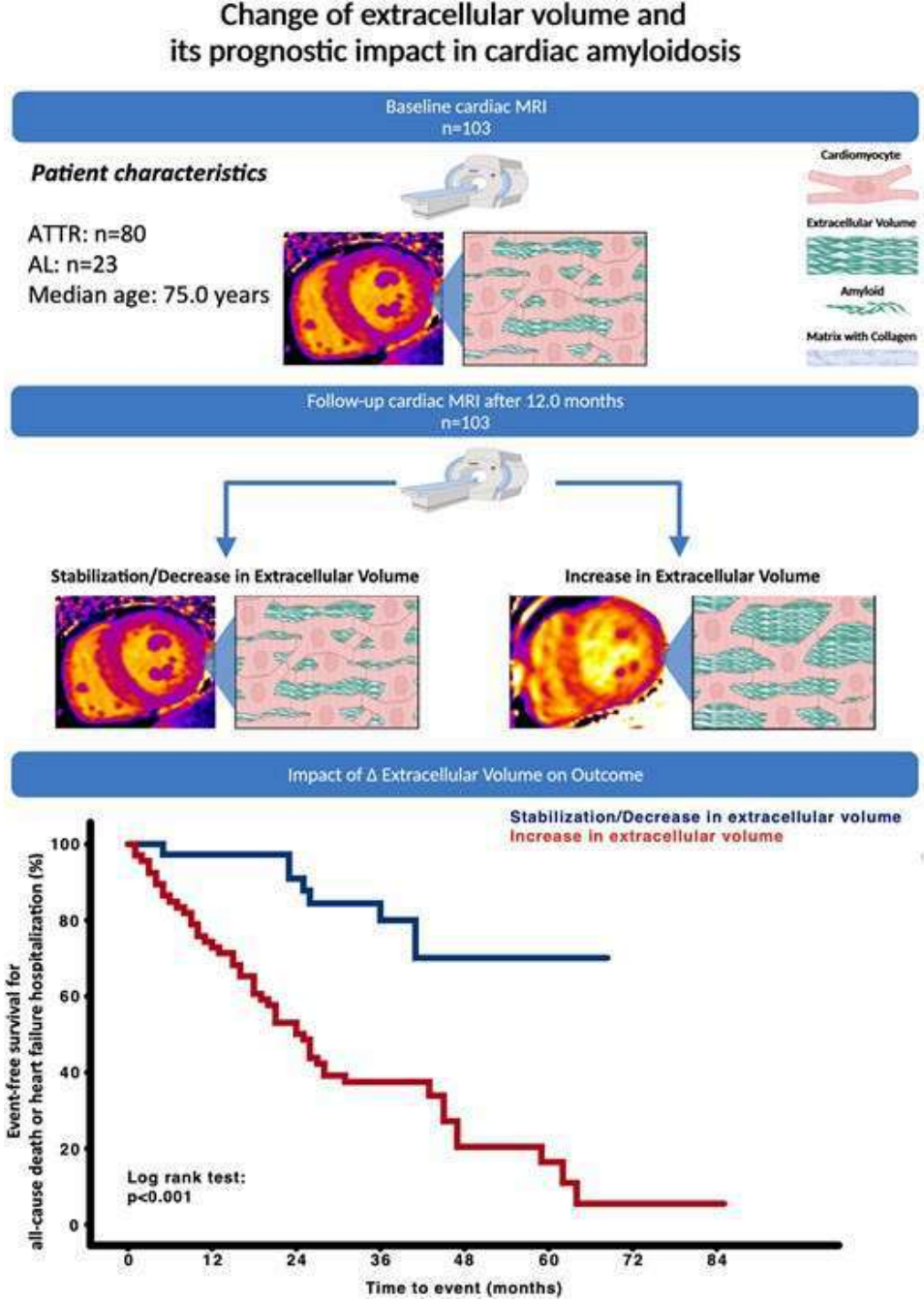


Table 7 Proposed follow-up scheme in cardiac amyloidosis

	AL	ATTR
Patients with cardiac amyloidosis	*Every month (during initial haematological treatment):* • Complete blood count, basic biochemistry, NT-proBNP, and troponin • Serum free light chain quantification • Clinical evaluation by Haematology • Evaluation by Cardiology if clinically indicated *Every 3–4 months (after completing initial haematological treatment):* • Complete blood count, basic biochemistry, NT-proBNP, and troponin • Serum free light chain quantification • Clinical evaluation by Haematology *Every 6 months:* • ECG • Echocardiography/CMR • Evaluation by Cardiology *Every 12 months:* • 24-h Holter ECG	*Every 6 months:* • ECG • Blood tests including NT-proBNP and troponin • Neurological evaluation (if ATTRv) • 6MWD (optional) • KCCQ (optional) *Every 12 months:* • Echocardiography/CMR • 24-h Holter ECG • Ophthalmological evaluation (if ATTRv)
ATTRv asymptomatic genetic carriers[a]		*Yearly:* • ECG • Blood tests including NT-proBNP and troponin • Echocardiography • Neurological and ophthalmological evaluation *Every 2 years:* • Holter ECG *Every 3 years or if any of above complementary tests is abnormal:* • Scintigraphy • CMR

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Take home messages

- Echo for screening
- CMR for differential diagnosis
- SCINTIGRAPHY is mandatory

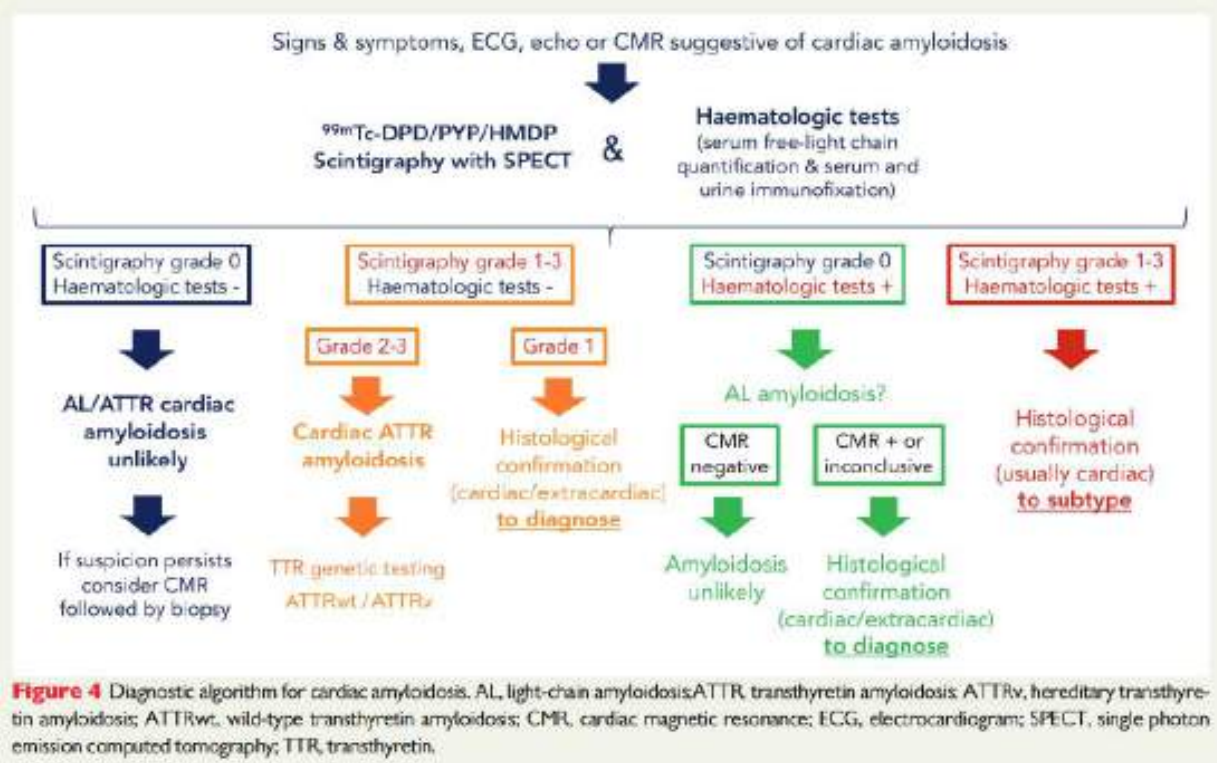

Figure 4 Diagnostic algorithm for cardiac amyloidosis. AL, light-chain amyloidosis;ATTR, transthyretin amyloidosis; ATTRv, hereditary transthyretin amyloidosis; ATTRwt, wild-type transthyretin amyloidosis; CMR, cardiac magnetic resonance; ECG, electrocardiogram; SPECT, single photon emission computed tomography; TTR, transthyretin.

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