

Amylose à transthyrétine :

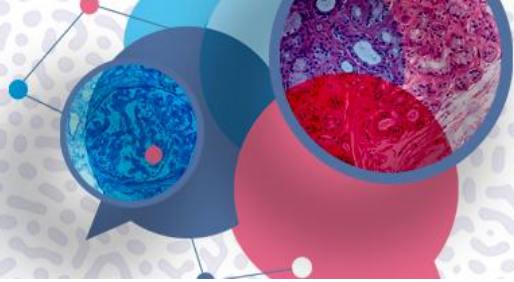
Organiser le bilan et le suivi des patients porteurs d'une amylose TTR rhumatologique



Dr Julien JEANNETEAU



CLINIQUE
ST-JOSEPH



Liens d'intérêts

Honoraires pour conférences : BMS, Astrazeneca, Novartis, Pfizer.

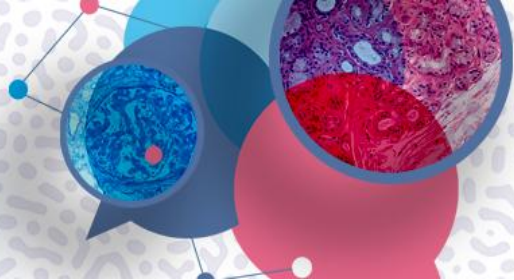
Honoraires pour consulting : Pfizer, Bayer

Défraiements pour congrès ou formations :

Hexacath, Biotronik, Abbott, Medtronic, Boston, Novartis, Astrazeneca, Amgen, Vitalaire, Bayer HealtCare, Terumo, Saint-Jude Médical, Genzyme, Siemens, Pfizer, Sanofi, Daiichi Sankyo, Boehringer, Cardinal Health France

8^e

MASTERCLASS AMYLOSES CARDIAQUES



ÉVÉNEMENT HYBRIDE



Jeudi 18 décembre 2025

Fondation Biermans-Lapôte ■ PARIS

www.masterclass-amylose.com

WHY



WHO?



HOW?



HOW OFTEN?



MONTH



Characteristics and natural history of early-stage cardiac transthyretin amyloidosis



Multi-centre retrospective study



ATTR-CM (wild-type or V122I TTR genotype)



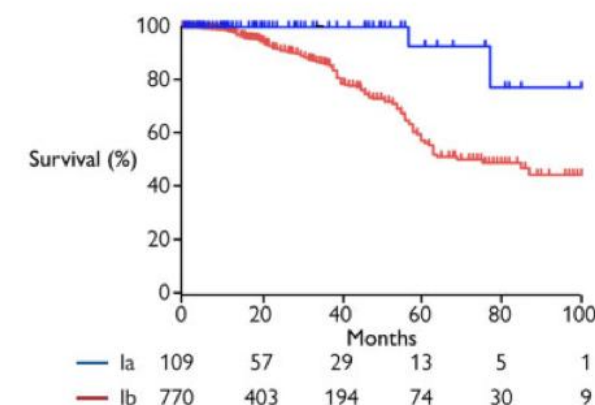
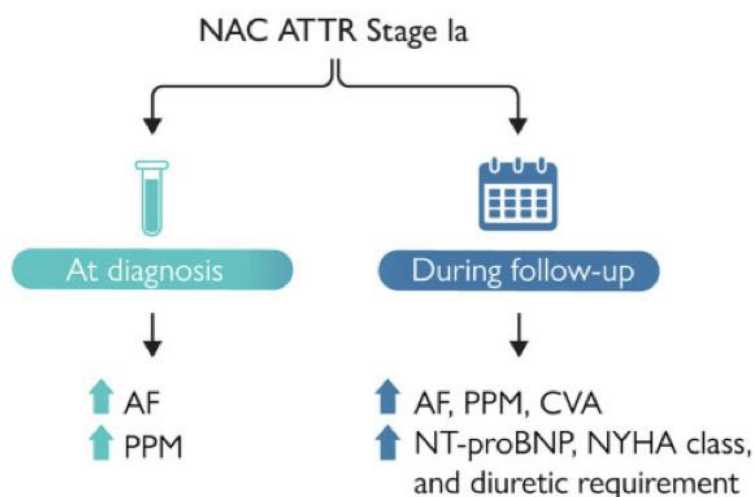
879 patients with NAC ATTR Stage I disease



Absence of disease modifying therapy

Stage Ia: NT-proBNP ≤ 500 ng/L (≤ 1000 ng/L with AF) and furosemide equivalent diuretic dose < 0.75 mg/kg.

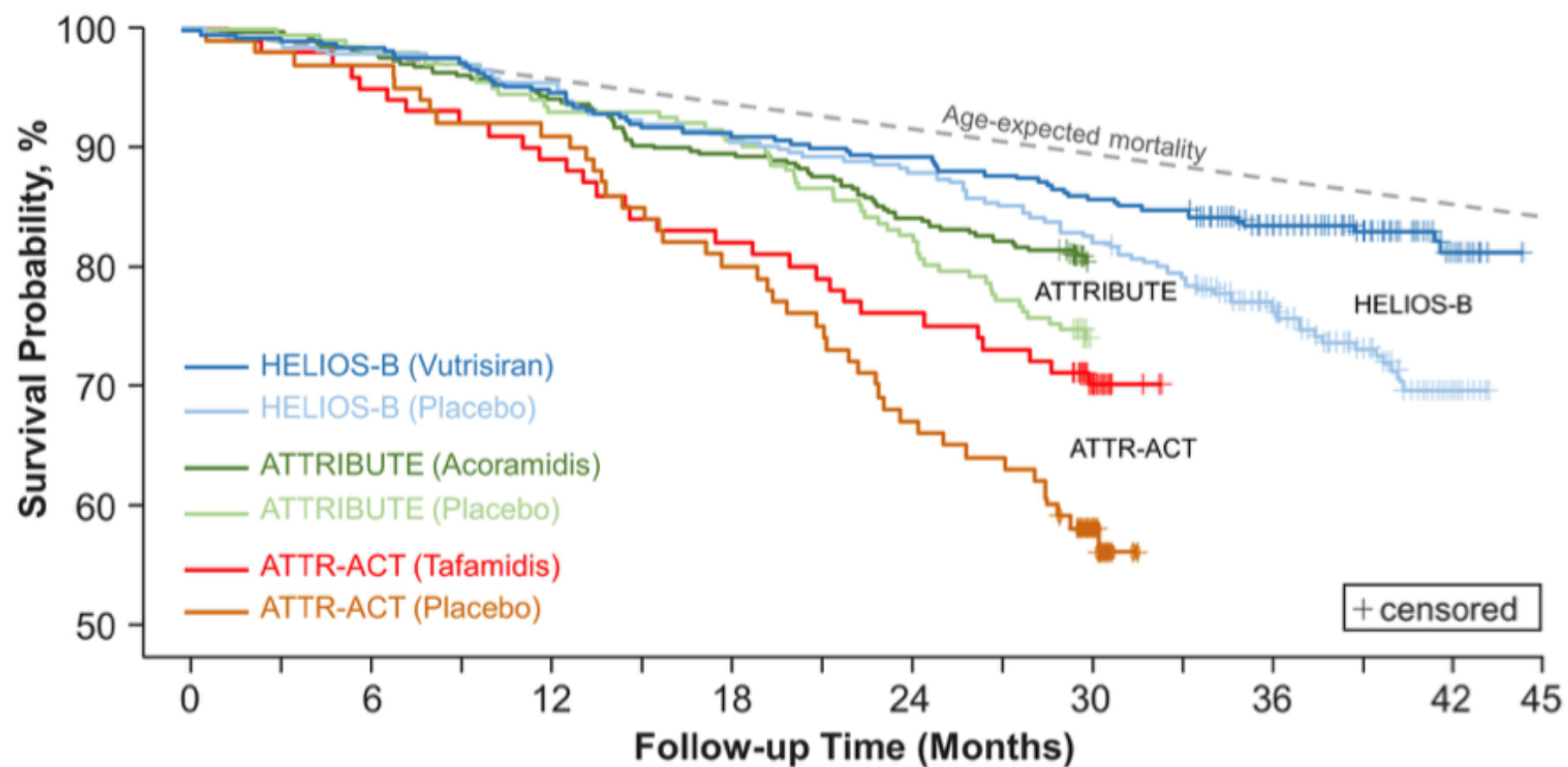
Stage Ib: NT-proBNP > 500 ng/L (> 1000 ng/L with AF) or furosemide equivalent diuretic dose ≥ 0.75 mg/kg



NT-proBNP powerful independent predictor of mortality ($p=0.002$)
NAC ATTR Stage Ia median expected survival > 100 months

8^eMASTERCLASS
AMYLOSES
CARDIAQUES

ÉVÉNEMENT HYBRIDE

Jeudi 18 décembre 2025
Fondation Biermans-Lapôtre ■ PARISwww.masterclass-amylose.com*Heart Fail Rev.* 2025 January ; 30(1): 69–73.

8^e

MASTERCLASS AMYLOSES CARDIAQUES



ÉVÉNEMENT HYBRIDE



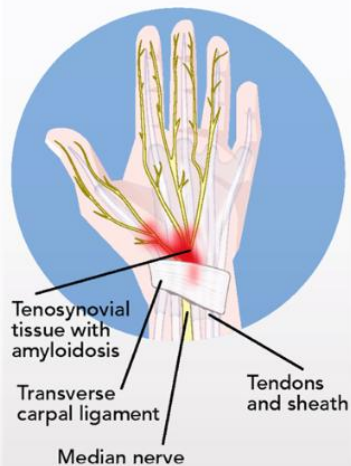
Jeudi 18 décembre 2025
Fondation Biermans-Lapôtre ■ PARIS

www.masterclass-amylose.com

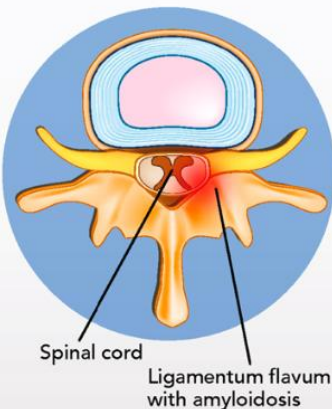
WHO?



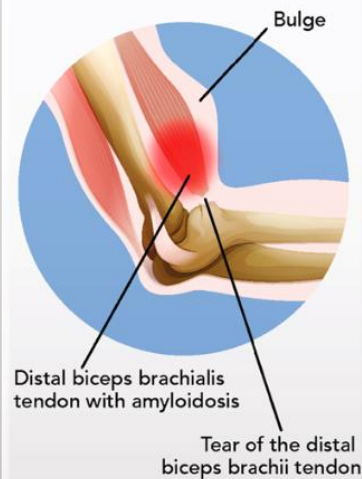
Carpal Tunnel Syndrome



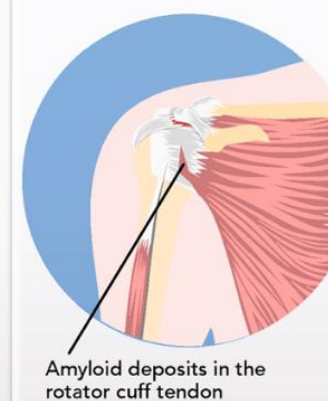
Back Pain/ Spinal Stenosis



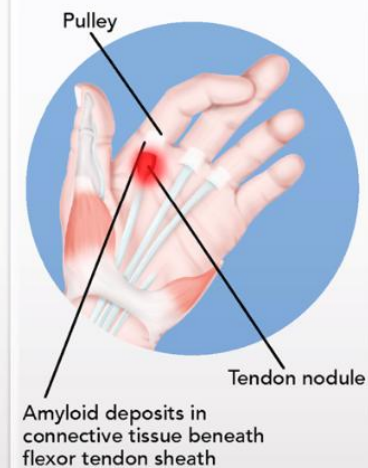
Distal Biceps Tendon Tear

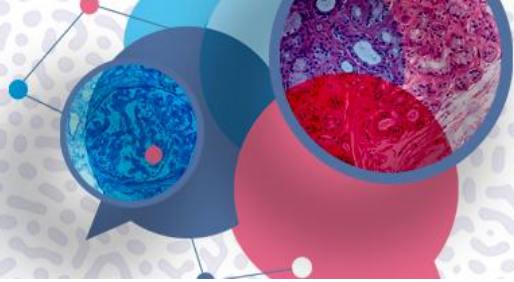


Shoulder, Knee and Hip Pain or Surgery



Trigger Finger





➤ Canal lombaire étroit : une autre occasion manquée ?

WHO?



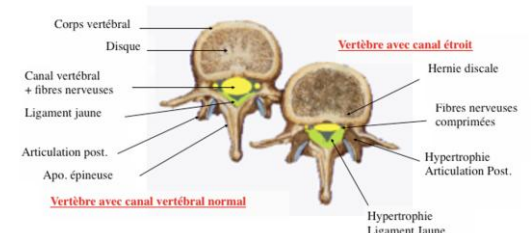
- Risque * par **2.29** de présenter une amylose en cas opération du CLE
- Sur une série rétrospective de 44500 patients danois
- Mais risque absolu faible 0.16% vs 0.08 % à 10 ans

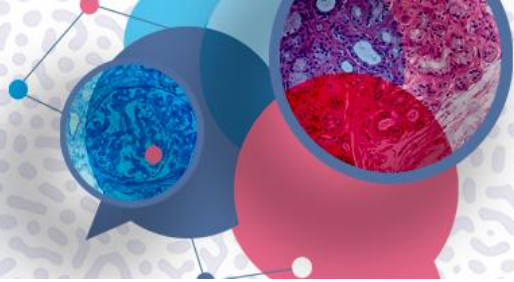
Noory et al Amyloid 2025 ; 32(3):154

- **37%** de dépôts d'amyloses TTR sur série anatomopathologique
- chez 250 patients suédois (n= 92)
- dont 17% (n =42) avec dépôts étendus

Eldhagen et al, J Intern Med 2021 Jun;289(6):895

- Optimisation par IRM lombaire pré-opératoire ?





➤ Canal lombaire étroit : une autre occasion manquée ?



Suivi prospectif des patients opérés d'un CLE avec anapath + :

- 0% atteinte cardiaque au diagnostic (n = 42)
- **16% à 6 ans**, tous NAC 1 et stade I NHYA (3 patients, n = 19, perdus de vue)
- Pourtant 48% avec d'autres localisations : CC bilat, doigt ressaut, ruptures tendineuses.

=> Rapport coût/efficacité ?

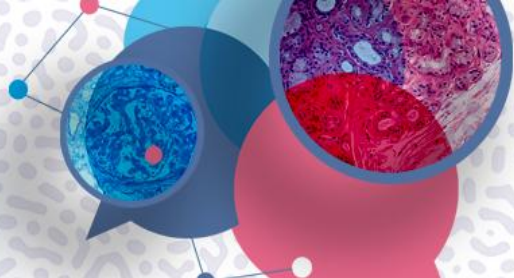
=> Quelle prise en charge de l'amylose TTRwt systémique sans atteinte cardiaque ?

Eldhagen et al, J Intern Med 2021 Jun;289(6):895

Eldhagen et al, Amyloid 2025 ; 32(3):218

8^e

MASTERCLASS AMYLOSES CARDIAQUES



ÉVÉNEMENT HYBRIDE



Jeudi 18 décembre 2025
Fondation Biermans-Lapôtre ■ PARIS

www.masterclass-amylose.com



CLINIQUE
ST-JOSEPH

HOW?



Quelles performances pour nos outils du quotidien ?

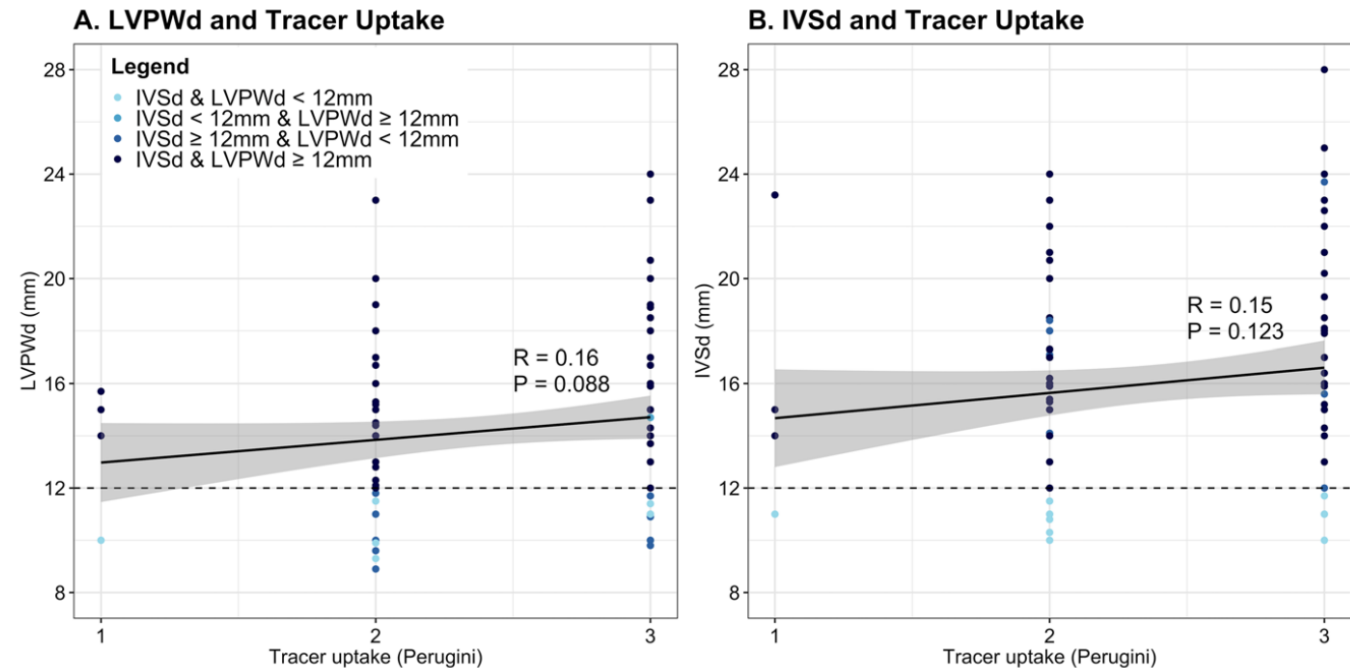
Electrocardiogramme
Echocardiographie
Biomarqueurs cardiaques



➤ L'épaisseur du VG seule ne suffit pas

HVG absente dans 11% des cas

- Sur population de 114 patients TTR.
- Raison du diagnostic :
 - IC inexpliquée (17%),
 - drapeaux rouges extracardiaque (8%),
 - combinaison des deux (67%).
- Pas HVG = ntprobNP significativement plus bas.
- Attention l'HVG peut être asymétrique.





➤ Le strain VG seul ne suffit pas



Circulation Journal
Circ J 2025; 89: 16–23
doi:10.1253/circj.CJ-24-0472

ORIGINAL ARTICLE
Cardiomyopathy

Diagnostic Accuracy and Prognostic Value of Relative Apical Sparing in Cardiac Amyloidosis — Systematic Review and Meta-Analysis —

Chung-Yen Lee, MS; Yosuke Nabeshima, MD, PhD; Tetsuji Kitano, MD, PhD;
Li-Tan Yang, MD; Masaaki Takeuchi, MD, PhD

- **Métaanalyse : 2872 patients, 37 études**
- **Se RASP = 61%**
- **Sp RASP = 83%**
- La valeur diagnostique varie selon le temps (baisse Se dans les études les plus récentes).
- La valeur diagnostique varie selon l'appareil (Philips > GE?).



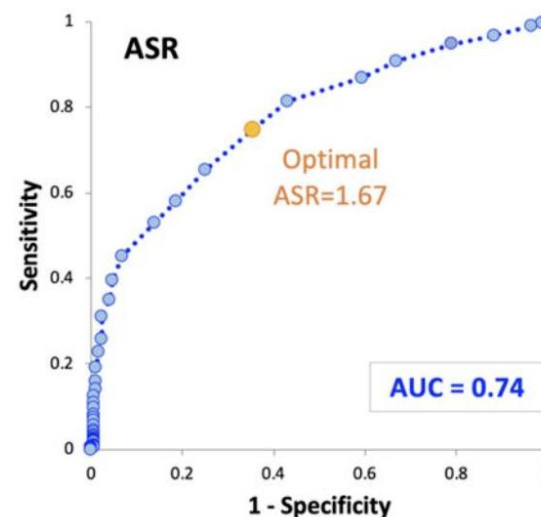
ESC

European Society
of Cardiology

European Heart Journal - Cardiovascular Imaging (2024) 25, 754–761
<https://doi.org/10.1093/ehjci/jeae021>

ORIGINAL PAPER

Limitations of apical sparing pattern in cardiac amyloidosis: a multicentre echocardiographic study



Avec le cut-off 1.67 :

- **Se RASP = 72%**
- **Sp RASP = 66%**
- Présent chez 32% des patients contrôles
- Présent chez 6% des contrôles sains.



➤ Nécessité d'une évaluation échographique multiparamétrique

	AUC	Cut-Off	Sensitivity, %	Specificity, %	+Likelihood Ratio	–Likelihood Ratio
Increased wall thickness						
NT-proBNP, ng/ml	0.74 (0.70–0.77)	>1,452	76 (72–80)	62 (55–68)	1.98 (1.7–2.3)	0.39 (0.3–0.5)
IVSd, mm	0.77 (0.74–0.80)	>15	64 (60–68)	79 (74–83)	3.08 (2.5–3.8)	0.45 (0.4–0.5)
PWTd, mm	0.83 (0.81–0.85)	>13	82 (79–85)	73 (68–78)	3.02 (2.5–3.6)	0.25 (0.2–0.3)
LVEDD, mm	0.64 (0.61–0.67)	≤46	65 (61–69)	57 (52–63)	1.52 (1.3–1.7)	0.61 (0.5–0.7)
RWT	0.83 (0.80–0.85)	>0.6	79 (76–82)	72 (67–77)	2.84 (2.4–3.4)	0.29 (0.2–0.3)
LVEDV, ml	0.59 (0.55–0.63)	≤79	65 (61–69)	52 (46–59)	1.37 (1.2–1.6)	0.67 (0.6–0.8)
LVESV, ml	0.50 (0.47–0.54)	>52	17 (14–21)	73 (68–79)	0.64 (0.5–0.9)	1.13 (1.0–1.2)
LVMi, g/m ²	0.68 (0.64–0.71)	>141	64 (61–68)	65 (59–70)	1.84 (1.6–2.2)	0.55 (0.5–0.6)
MCF	0.74 (0.70–0.76)	≤0.13	62 (58–67)	75 (69–80)	2.45 (2.0–3.1)	0.51 (0.4–0.6)
LAA, cm ²	0.56 (0.52–0.59)	>23	68 (64–72)	45 (39–51)	1.24 (1.1–1.4)	0.71 (0.6–0.8)
LVEF, %	0.60 (0.57–0.63)	≤57	67 (63–71)	51 (46–57)	1.38 (1.2–1.6)	0.64 (0.5–0.7)
MAPSE, mm	0.70 (0.67–0.73)	≤11	72 (69–76)	60 (55–65)	1.82 (1.6–2.1)	0.46 (0.4–0.5)
TAPSE, mm	0.70 (0.67–0.73)	≤19	67 (64–71)	64 (58–69)	1.86 (1.6–2.2)	0.51 (0.4–0.6)
SV, ml	0.66 (0.62–0.69)	≤42	70 (66–74)	55 (49–62)	1.57 (1.3–1.8)	0.54 (0.5–0.6)
E/A	0.80 (0.77–0.83)	>1.1	74 (70–78)	75 (70–81)	3.01 (2.4–3.7)	0.35 (0.3–0.4)
DT, ms	0.57 (0.53–0.60)	≤210	70 (66–73)	48 (42–54)	1.34 (1.2–1.5)	0.63 (0.5–0.7)
E/e'	0.69 (0.66–0.72)	>11	70 (66–74)	61 (56–67)	1.81 (1.6–2.1)	0.49 (0.4–0.6)
LS, %	0.69 (0.66–0.72)	≥–13	67 (63–71)	63 (57–68)	1.79 (1.5–2.1)	0.53 (0.5–0.6)
SAB	0.77 (0.74–0.80)	>2.9	67 (63–71)	77 (72–81)	2.89 (2.4–3.5)	0.43 (0.4–0.5)
RALS	0.77 (0.75–0.80)	>0.9	71 (67–74)	73 (68–78)	2.67 (2.2–3.2)	0.40 (0.3–0.5)
EFSR	0.67 (0.64–0.70)	>4.3	62 (58–66)	65 (60–70)	1.77 (1.5–2.1)	0.59 (0.5–0.7)
IWT score	0.87 (0.85–0.90)	≥6	78 (75–81)	79 (74–84)	3.75 (3.0–4.7)	0.28 (0.2–0.3)

Epaisseur/cavité

Atteinte VD

Doppler tissulaire

Strain

SAB = systolic apex to base ratio

RALS, RASP = relative apical longitudinal sparing

EFSR = ejection fraction/longitudinal strain ratio



➤ Des marqueurs échographiques précoces ?

Strain OG

cutt off : fonction réservoir 20% ?

Doppler Tissulaire

cut-off : $e' < 12$ cm/s en latéral ?
 $e' < 10$ cm/s en septal ?

Rausch K et al, Int J Cardiovasc Imaging. 2021 Jan;37(1):81

Palka P et al. JASE. 2002; 15: 1353

➤ Rôle de l'IA ? ECG et Echographie



ESC

European Society
of Cardiology

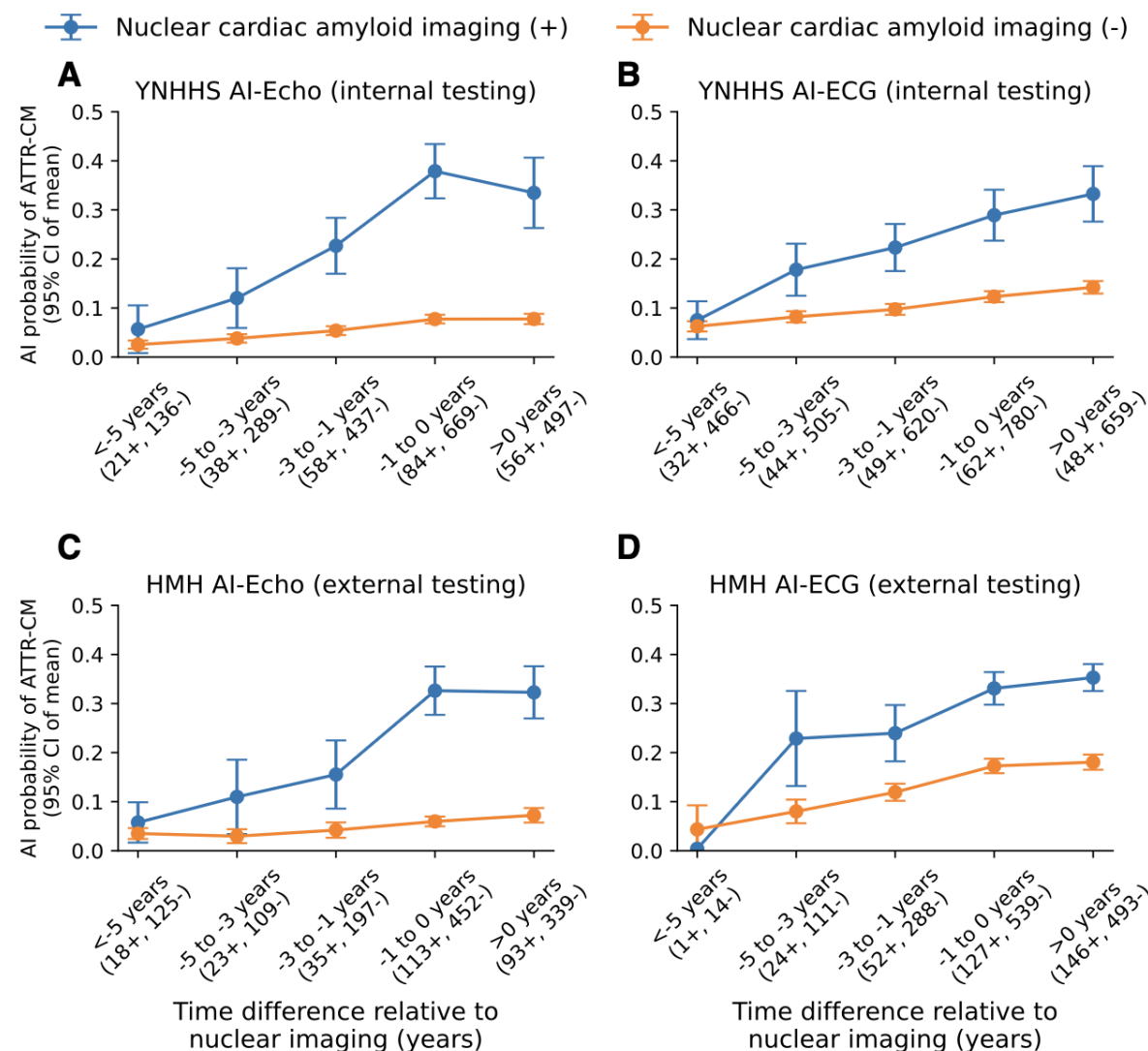
European Heart Journal (2025) 00, 1–12
<https://doi.org/10.1093/eurheartj/ehaf450>

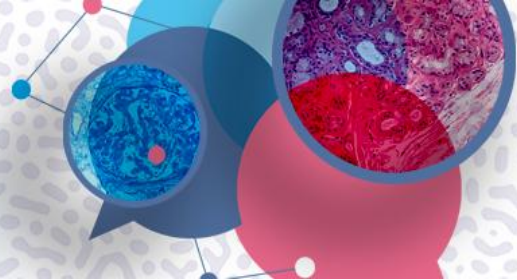
CLINICAL RESEARCH

Digital health and innovation

Artificial intelligence-enabled electrocardiography and echocardiography to track preclinical progression of transthyretin amyloid cardiomyopathy

Evangelos K. Oikonomou^{1,2}, Veer Sangha^{1,2,3}, Sumukh Vasisht Shankar^{1,2}, Andreas Coppi^{2,4}, Harlan M. Krumholz^{1,4}, Khurram Nasir^{5,6,7,8}, Edward J. Miller¹, Cesia Gallegos Kattan¹, Mouaz H. Al-Mallah⁷, Sadeer Al-Kindi^{7,8}, and Rohan Khera^{1,2,4,9,10,*}





➤ Place des biomarqueurs

Chez des patients avec suspicion d'amylose (n = 1149)

derivation cohort

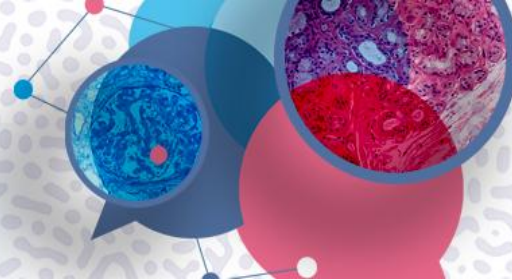
Rule-out cut-offs

Biomarker	Optimal cut-off (ng/L)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+	LR-	TN, n (%)	FN, n (%)
NT-proBNP	180	100 (98–100)	11 (6–18)	69 (63–74)	100 (75–100)	1.13	0.00	13 (4)	0 (0)
hs-TnT	14	100 (98–100)	11 (6–18)	69 (63–74)	100 (75–100)	1.13	0.00	13 (4)	0 (0)
Either NT-proBNP <180 ng/L or hs-TnT <14 ng/L								23 (7)	0 (0)
Combined NT-proBNP <180 ng/L and hs-TnT <14 ng/L								3 (1)	0 (0)

validation cohort

Rule-out cut-offs

Biomarker	Optimal cut-off (ng/L)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+	LR-	TN, n (%)	FN, n (%)
NT-proBNP	180	98 (97–99)	35 (30–41)	71 (67–74)	92 (86–96)	1.51	0.05	109 (14)	9 (1)
hs-TnT	14	98 (96–99)	35 (30–41)	71 (67–74)	91 (84–95)	1.51	0.06	110 (14)	11 (1)
Either NT-proBNP <180 ng/L or hs-TnT <14 ng/L								145 (18)	16 (2)
Combined NT-proBNP <180 ng/L and hs-TnT <14 ng/L								74 (9)	4 (0.5)



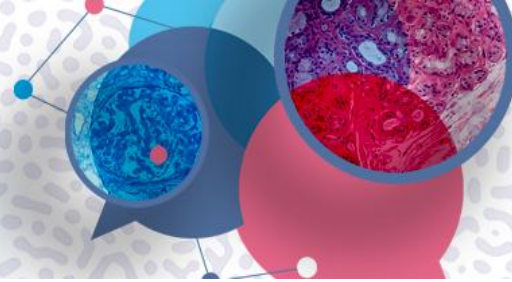
➤ **Place des biomarqueurs**

Série rétrospective chez 250 patients
spécifiquement en cas d'antécédents de canal carpien.

The diagnostic value of ^aNT-ProBNP and Troponin-T as indicative biomarkers in diagnosis of cardiac amyloidosis in 250 patients with previous surgery for bilateral carpal tunnel syndrome.

	N (%)	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
^b TnT ≥ 13 ng/L	62 (26.1)	100 [74–100]	74 [70–79]	16.2 (14–19]	100 [98–100]	3.8 [3.1–4.8]	0
NTproBNP >Age dependent (ng//L)	141 (56)	91.7 [61.5–99.8.]	45.4 [39–52]	7.8 [6.4–9.4]	99.1 (94.3–99.9]	1.68 [1.4–2.1]	0.18 [0.03–1.2]
NT proBNP (age dependent) increase ng/L <u>AND</u> TnT ≥13 ng/L combined	47 (18.8%)	91.7 (61.5–99.8)	84.5 (79.7–89.2)	23.4 (17.4–30.2)	99.5 (96.8–99.9)	6.1 (4.3–8.6)	0.1 (0.02–0.6)

Seuil ntproBNP <50 years: 50 ng/L: 50–75 years: 75 ng/L: ≥75 years: 250 ng/L

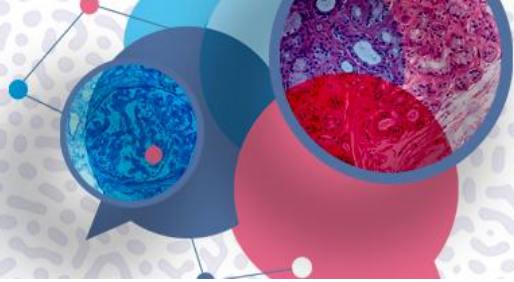


➤ Place des biomarqueurs

Dans une série prospective : problématique de la détection précoce.

Table 4. Individual characteristics of the patients with myocardial uptake and the echocardiogram parameters.

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13
Age	83	84	81	82	92	66	77	83	86	82	85	72	73
Gender	Female	Male	Female	Female	Male	Male	Male	Female	Male	Female	Male	Female	Male
Cardiac biomarkers													
Pro Bnp	235	157	448	444	2846	105	286	200	2788	67	1263	69	206
Troponin	20	11	24	20	56	12	34	11	62	10	32	15	17
EKG													
Rhythm	Sinus	Sinus	Sinus	Sinus	AF	Sinus	Sinus	sinus	Sinus	Sinus	Sinus	AF	Sinus
Altered conduction	No	No	No	No	RBBB	No	No	No	LBBB	No	No	No	No
ECHO parameters													
VST (mm)	1.22	1.03	1.07	1.03	1.62	1.15	1.25	1.01	1.47	1.15	1.48	1.09	1.33
LVPW (mm)	1.20	0.92	0.98	0.96	1.48	0.88	0.93	0.93	1	0.89	1.34	1.16	1.27
LVEF (%)	60	60.4	60	60	55	65	60	60	32	63	65	65	63
Diastolic stage	1	Normal	2	2	NA	Normal	2	2	3	NA	2	NA	Normal
LAV (L/m ²)	38.6	27.9	48.5	49.5	43.7	30.2	45.7	42.2	51.2	27.2	34.5	37.4	18.8
E/A VM	0.77	0.60	0.71	0.70	0.73	0.82	0.70	1.26	2.5	0.56	0.81	0.73	0.61
Average E/e'	12.65	6.6	13.2	13.4	17.75	6.35	14.6	14.15	20.7	13.25	14.05	10.9	8.05
Overall strain value	-18	-19.4	-21.7	-21.9	-12.5	-21	-21.9	-23	-5	NA	-18.8	-15	-21
Valvular involvement	No	No	No	No	No	Aortic stenosis	No	Aortic stenosis	Aortic stenosis	No	Aortic stenosis	No	No
Scintigraphy (Grade of uptake)	3	1	1	1	3	3	3	2	2	1	3	2	1

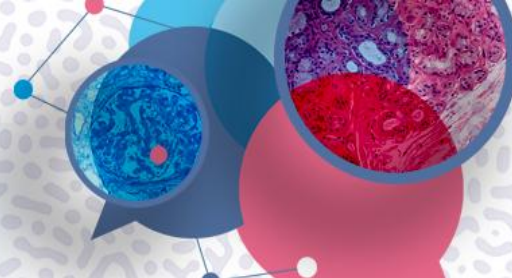


➤ **Place des biomarqueurs**

Dans notre série prospective : problématique de la détection précoce

- 8 patients diagnostiqués ATTR
 - 2 patients avec troponines < norme (tropo I).
 - 1 patient avec ntproBNP < 180 ng/l (83 ng/l à 78 ans).
 - 1 patient avec ntproBNP < 180 ng/l et troponine nle.

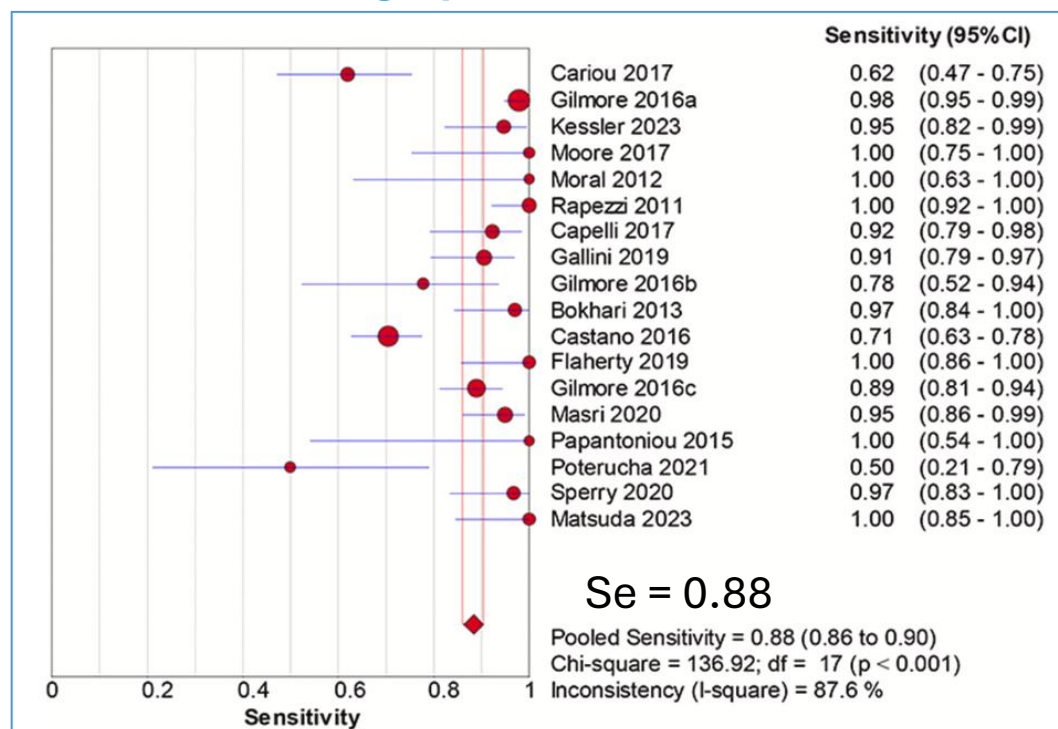
Année	2025
Âge	78 ans
NYHA	I
ECG	BBD axe G
Holter	RAS
SIV (mm)	13
FEVG (%)	65
SLG (%)	-13
NtproBNP (pg/ml)	83
Tropo I ng/l (N<53)	13
Scintigraphie	2 perugini
Poso lasilix (mg)	0
SF extra cardiaque	+++ Amylo-affect 21



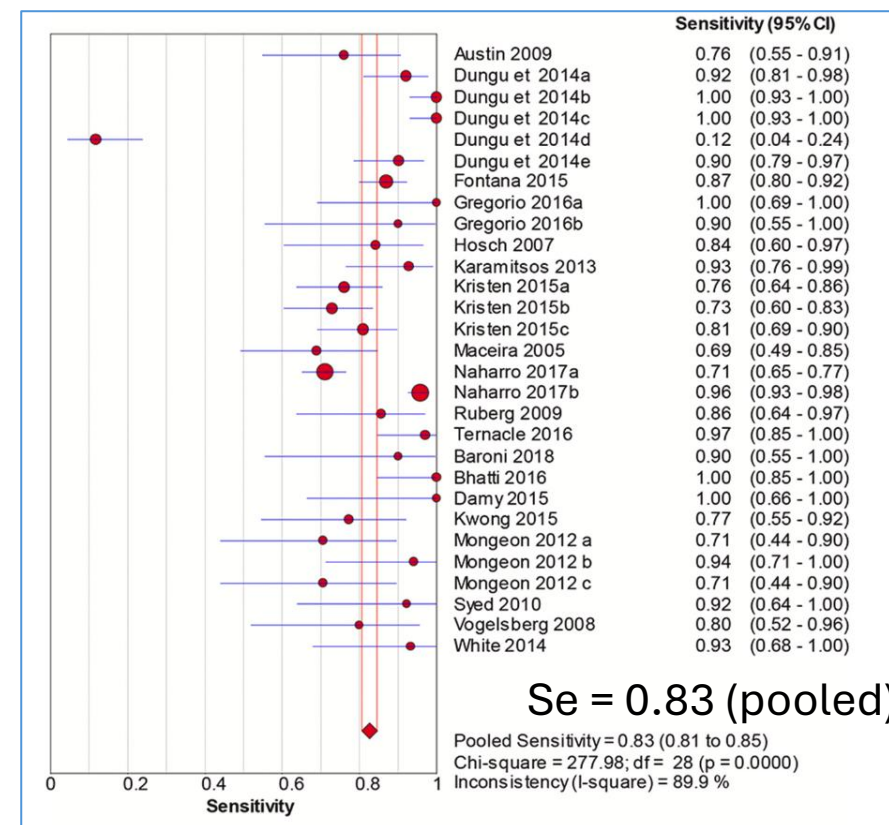
➤ IRM et scintigraphie, en cas de premiers examens douteux

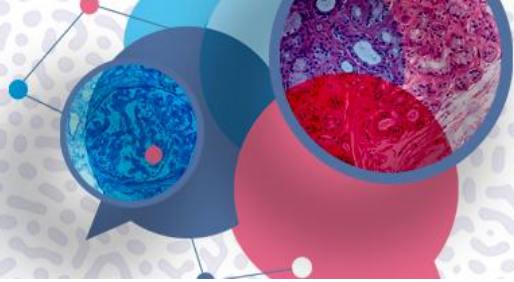
- les plus sensibles, mais moins accessibles et plus coûteux.

Scintigraphie osseuse



IRM





➤ Pas de recommandation / Pas de consensus d'experts

- sur le modèle des porteurs de mutation TTR ?

➔ Biologie + ECG + Echographie tous les ans

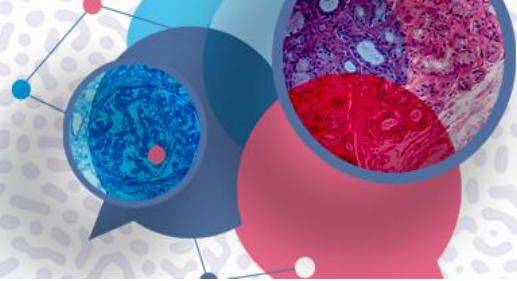
➔ Scintigraphie et/ou IRM au moindre doute et tous les 3 ans

1/ *Evaluation of the 2021 **ESC recommendations** for family screening in hereditary transthyretin cardiac amyloidosis. European Journal of Heart Failure (2024) 26:2025.*

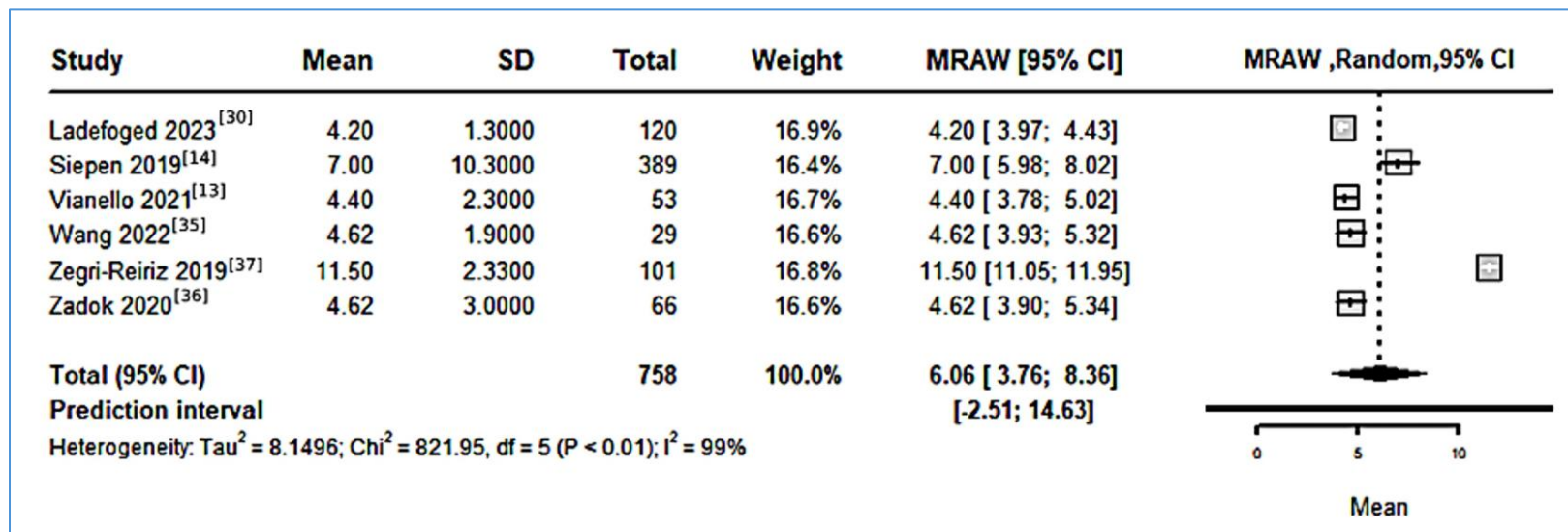
2/ **PNDS** amylose cardiaque, filière cardiogen, 2021

3/ 2023 **ACC expert** consensus decision Pathway on Cardiac Amyloidosis JACC
2023 ; 81(11):1076

4/ Ueda et al, Journal of the neurological sciences 414 (2020):116813



➤ Les délais entre la chirurgie de canal carpien et le diagnostic (+- précoce)

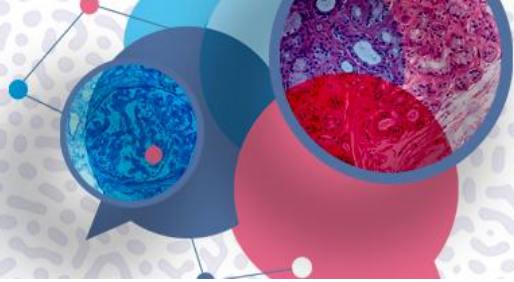


2024 Elghouneimy et al. Cureus 16(12): e75582. DOI 10.7759/cureus.75582

Table 2

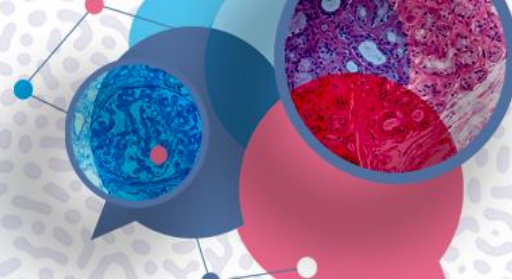
Time from inclusion since surgery for bilateral carpal tunnel syndrome in patients diagnosed with cardiac amyloidosis.

	1	2	3	4	5	6	7	8	9	10	11	12
Years since CTS surgery, yrs	5.8	5.9	6.9	7.1	7.0	7.1	8.3	6.4	8.1	9.1	NA	7.3

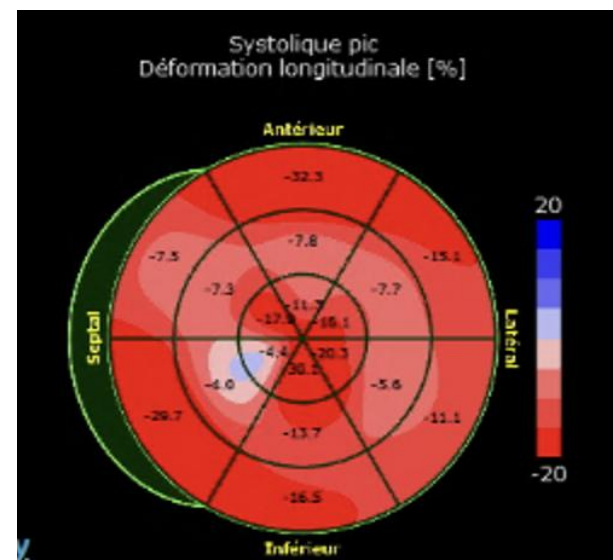
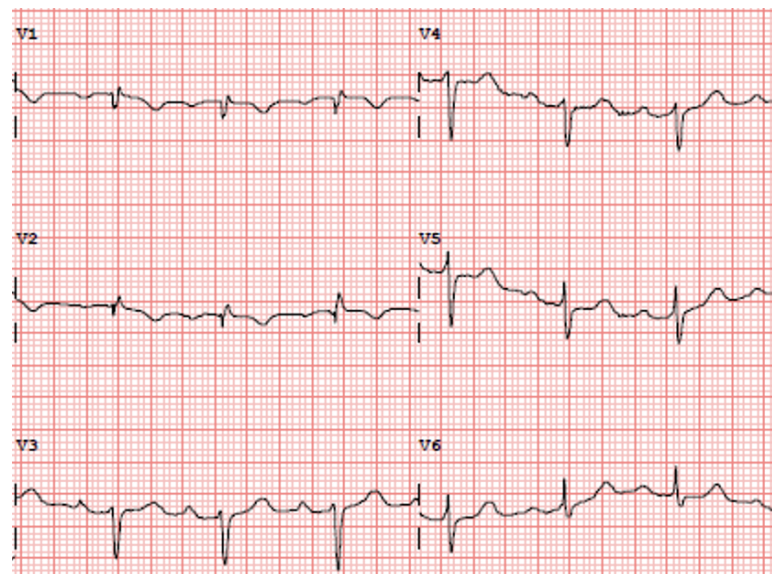


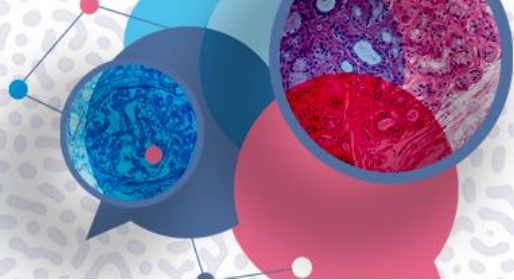
Cas clinique

Un homme de 72 ans
adressé par le Centre de la Main
pour biopsie + TTR dans la synovia du CC



Année	2020
NYHA	II
ECG	PR 216 ms
Holter	
SIV (mm)	11
FEVG (%)	60
SLG (%)	-16
NtproBNP (pg/ml)	326
Tropo ng/l (N<14)	24
Poso lasilix (mg)	0
SF extra cardiaque	CC





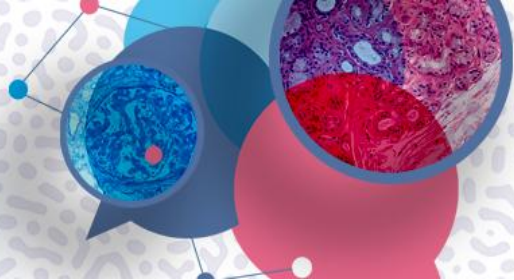
Année	2020
NYHA	II
ECG	PR 216 ms
Holter	
SIV (mm)	11
FEVG (%)	60
SLG (%)	-16
NtproBNP (pg/ml)	326
Tropo ng/l (N<14)	24
Poso lasilix (mg)	0
SF extra cardiaque	CC

IRM cardiaque :

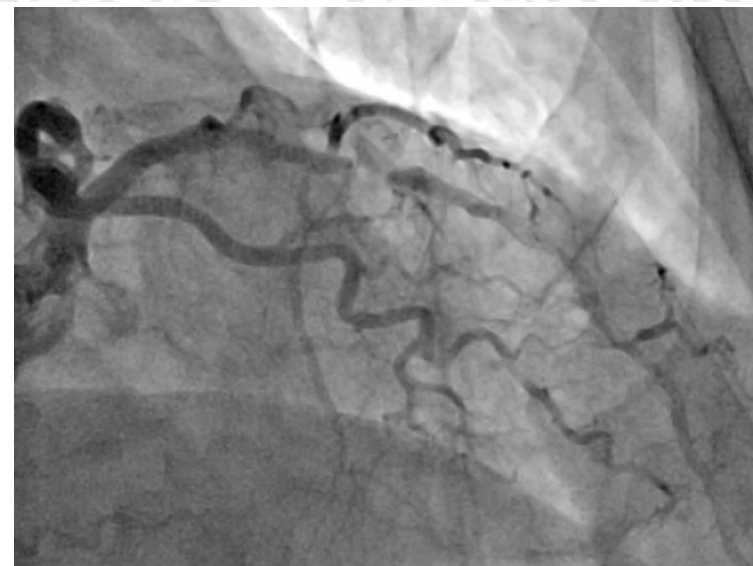
- Ti scout normal
- Pas de réhaussement tardif
- SIV = 10 mm
- T1 mapping = 990 ms
- ECV non fait

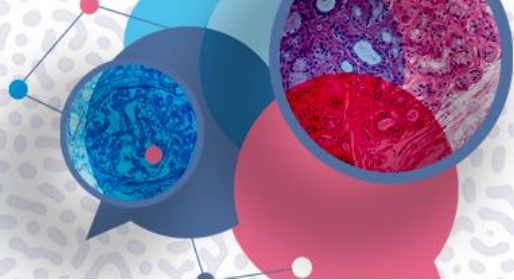
Scintigraphie osseuse :

- Grade 0 Perugini



Année	2020	2021
NYHA	II	II
ECG	PR 216 ms	PR 210 ms
Holter		RAS
SIV (mm)	11	11
FEVG (%)	60	60
SLG (%)	-16	
NtproBNP (pg/ml)	326	748
Tropo ng/l (N<14)	24	97
Poso lasilix (mg)	0	0
SF extra cardiaque	CC	0

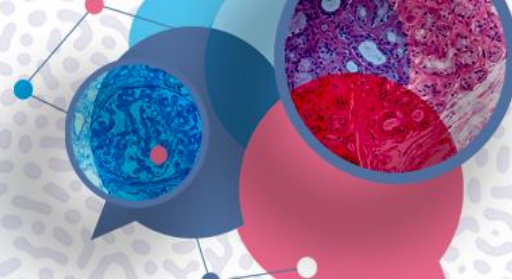




Année	2020	2021	2022	2023
NYHA	II	II	I	I
ECG	PR 216 ms	PR 210 ms	PR 210 ms	PR 220 ms
Holter		RAS		RAS
SIV (mm)	11	11	11	11
FEVG (%)	60	60	65	65
SLG (%)	-16		-15	-15
NtproBNP (pg/ml)	326	748	361	706
Tropo ng/l (N<14)	24	97	23	22
Poso lasilix (mg)	0	0	0	0
SF extra cardiaque	CC	0	0	0

Scintigraphie :
Grade 1 Perugini

=> tafamidis



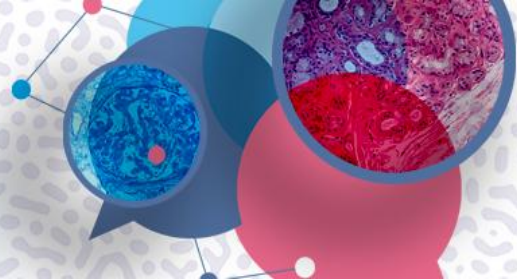
Année	2020	2021	2022	2023	2024	2025
NYHA	II	II	I	I	I	I
ECG	PR 216 ms	PR 210 ms	PR 210 ms	PR 220 ms	PR 220 ms	PR 220 ms
Holter		RAS		RAS		RAS
SIV (mm)	11	11	11	11	11	11
FEVG (%)	60	60	65	65	65	65
SLG (%)	-16		-15	-15	-15	-15
NtproBNP (pg/ml)	326	748	361	706	401	330
Tropo ng/l (N<14)	24	97	23	22	22	23
Poso lasilix (mg)	0	0	0	0	0	0
SF extra cardiaque	CC	0	0	0	0	0



Angioplastie



Tafamidis



En conclusion



ESC

European Society
of Cardiology

European Heart Journal (2022) **43**, 2633–2635

<https://doi.org/10.1093/eurheartj/ehac261>

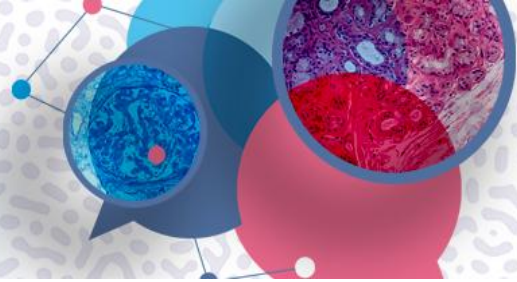
EDITORIAL

Early-stage amyloid transthyretin cardiomyopathy: uncertainties and opportunities

Claudio Rapezzi^{1,2*}, Matteo Serenelli¹, and Alberto Aimo ^{3,4}

¹Cardiologic Centre, University of Ferrara, Ospedale di Cona, Via Aldo Moro 8, 44124 Cona (Ferrara), Italy; ²Maria Cecilia Hospital, GVM Care & Research, Cotignola (Ravenna), Italy;

³Institute of Life Sciences, Scuola Superiore Sant'Anna, Pisa, Italy; and ⁴Cardiology Division, Fondazione Toscana Gabriele Monasterio, Pisa, Italy



What happens after a positive biopsy...

