SSVQ Société des sciences vasculaires du Québec
Chef de file en santé vasculaire.

WEBINAIRE
AMYLOÏDOSE CARDIAQUE

18 MAI 2022 | 19 h | EN WEBDIFUSION

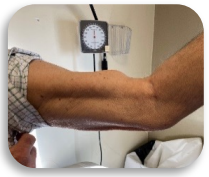
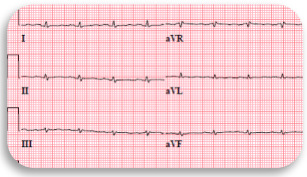
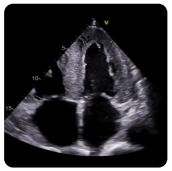
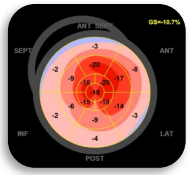
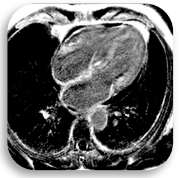
Amyloïdose cardiaque

Approche diagnostique et prise en charge

Francois Tournoux MD PhD
Directeur du programme AmyloCHUM, Centre Hospitalier de l'Université de Montréal
Professeur Agrégé de Clinique, Université de Montréal
Président, Société Québécoise d'Insuffisance Cardiaque
Chercheur Clinicien au Fonds de Recherche du Québec - Santé

Université de Montréal

CHUM


Consultant / Orateur / Recherche

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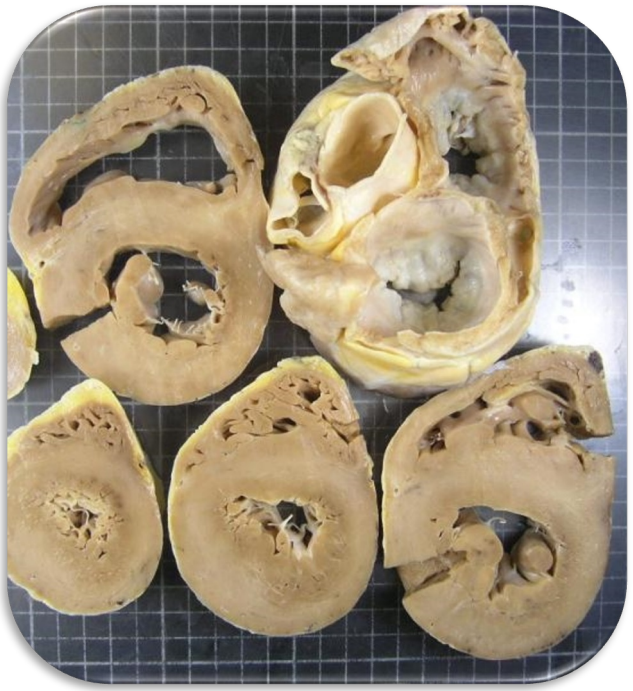
WEBINAIRE
AMYLOÏDOSE CARDIAQUE

18 MAI 2022 | 19 h | EN WEBDIFUSION

OBJECTIFS DE CETTE PRÉSENTATION

- Décrire la **pathophysiologie** et les **manifestations cliniques** de l'amylose à chaînes légères (AL) et de l'amylose à transthyrétine (ATTR)
- Savoir comment **faire le diagnostic** d'amyloïdose
- Connaître **quels traitements** sont possibles et pour quels patients

Rudolph Virchow, en 1854, a introduit et popularisé le terme de substance amyloïde



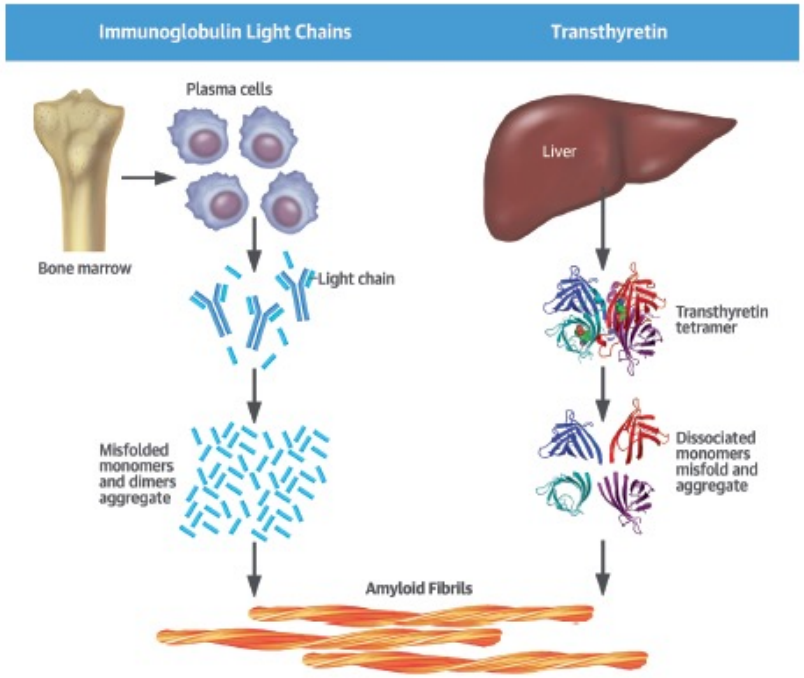
Courtesy of T Damy

Rudolf Virchow (1821–1902), photograph by J C Schaarwächter (1891)

Amyloidose, qu'est ce que c'est?

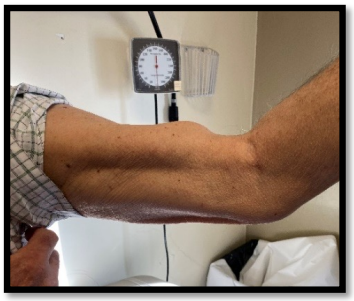
- Processus au cours duquel des protéines deviennent instables et changent de conformation → **fibrilles**
- **<u>Plusieurs types de protéines</u>** → l'amyloidose

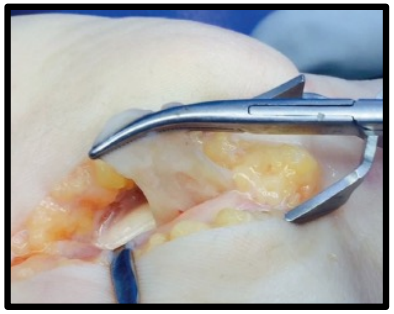
ACQUISES	HÉRÉDITAIRES
SENILE : WT-TTR Transthyrétine sauvage	**Transthyrétine mutée : mTTR**
AL Chaînes légères	**Fibrinogène**
	Gelsoline
	ApoA1
	ApoA2
AA Maladies inflammatoires	**Lysozyme**
	Cystatin C

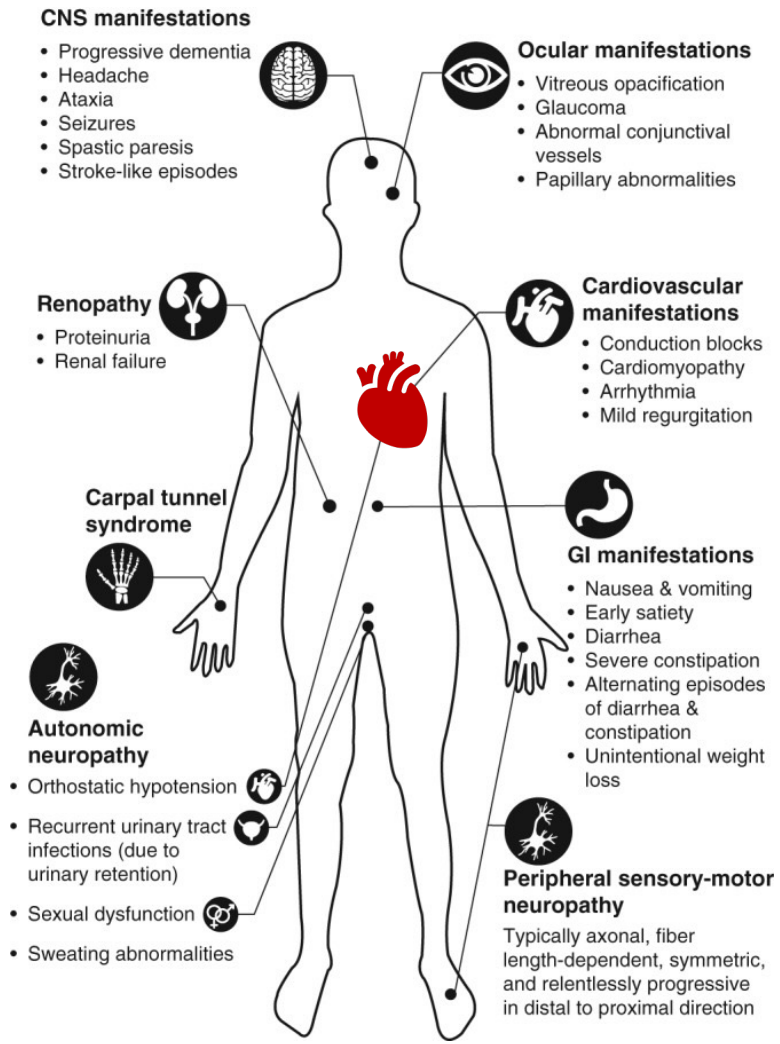


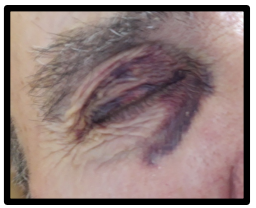
Et ces fibrilles vont précipiter dans ***<u>différents organes</u>***

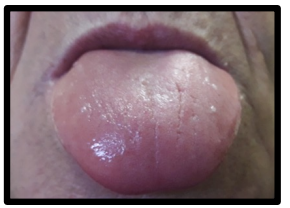
<u>Sperry, B.W., Reyes B.A., Ikram A. and al.</u>
<u>J Am Coll CardioL 2018;72(17):2040-50</u>
Accessible en ligne: 10.1016/j.jacc.2018.07.092

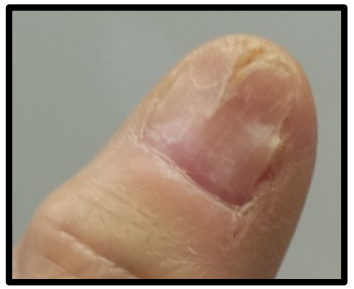










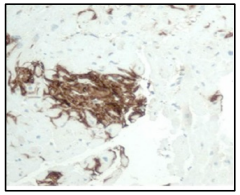


Conceição I., Gonzàlez-Duarte A., Obici L. and al. J Peripher Nerv Syst. 2016 Mar; 21(1): 5–9. Accessible en ligne: 10.1111/jns.12153

Courtesy of T Damy

MANIFESTATIONS CARDIAQUES

Myocardium

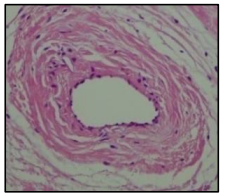


Hypertrophy
Ventricular dysfunction

Endocardium

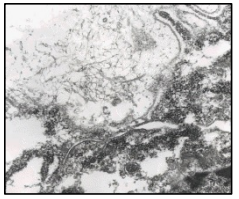
Valvular disease

Vascular



Ischemia

Pericardium



Pericardial effusion

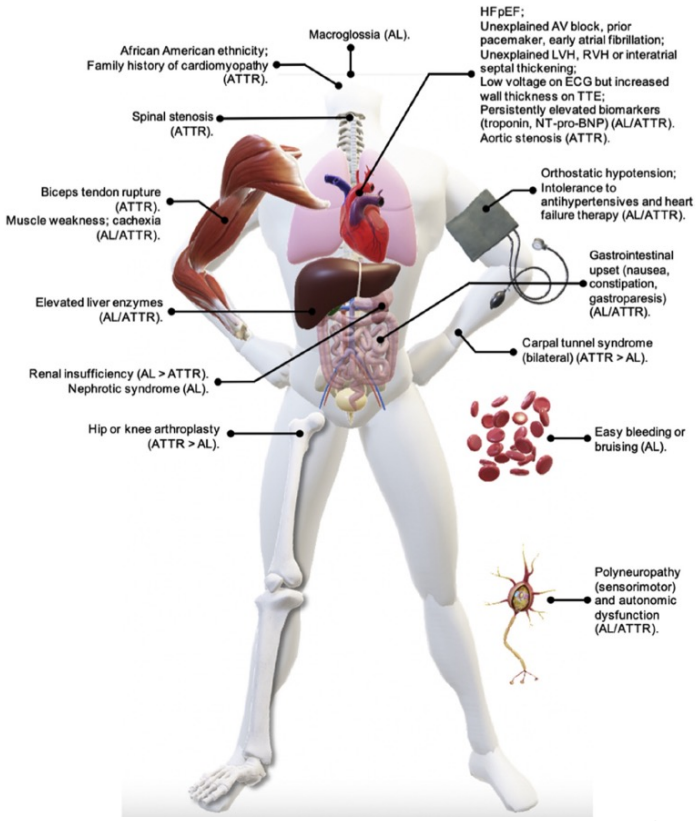
Conduction system

AV block

Courtesy of T Damy, adapted from Merlini, NEJM 2003

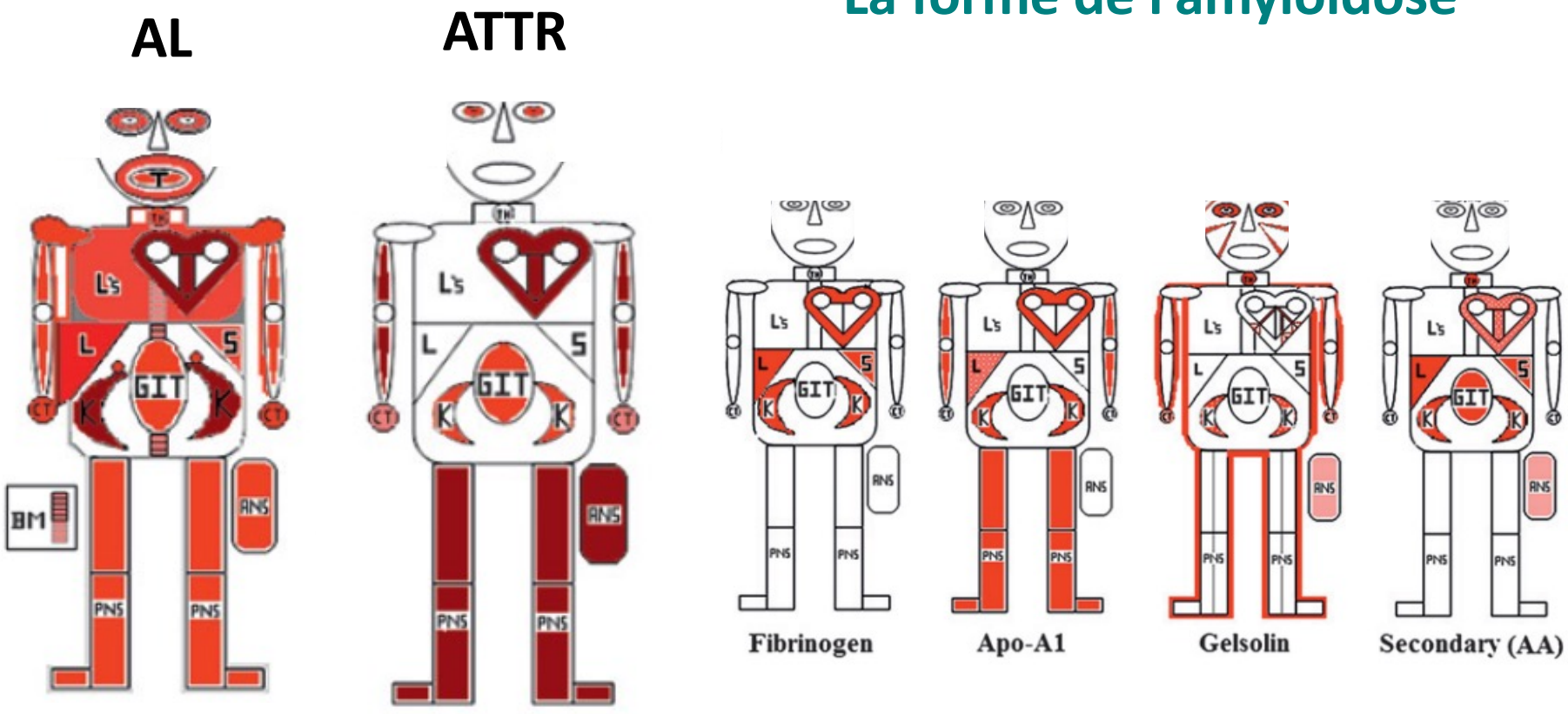
Quels sont les determinants du phenotype du patient?

1) La **forme** de l'amyloïdose : ATTR vs AL vs AA…
2) La **mutation génique impliquée** dans les formes hATTR
3) Le **moment du diagnostic** dans la vie du patient

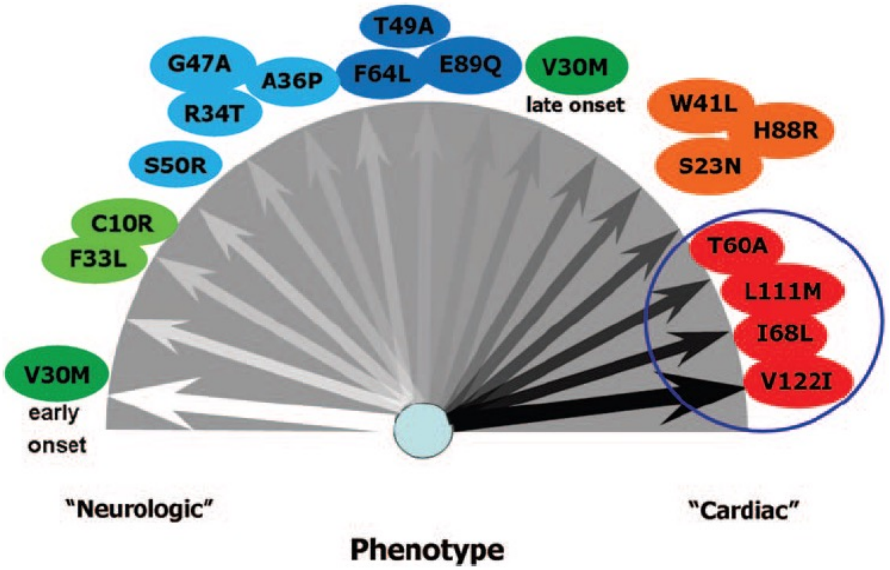


Music S and Coll. Canadian Journal of Cardiology 38 (2022) 384e388

La forme de l'amyloïdose

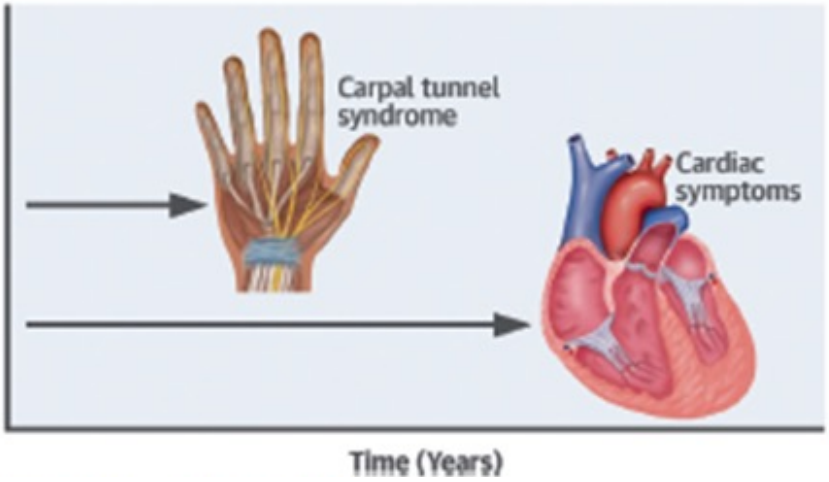


La mutation génique impliquée



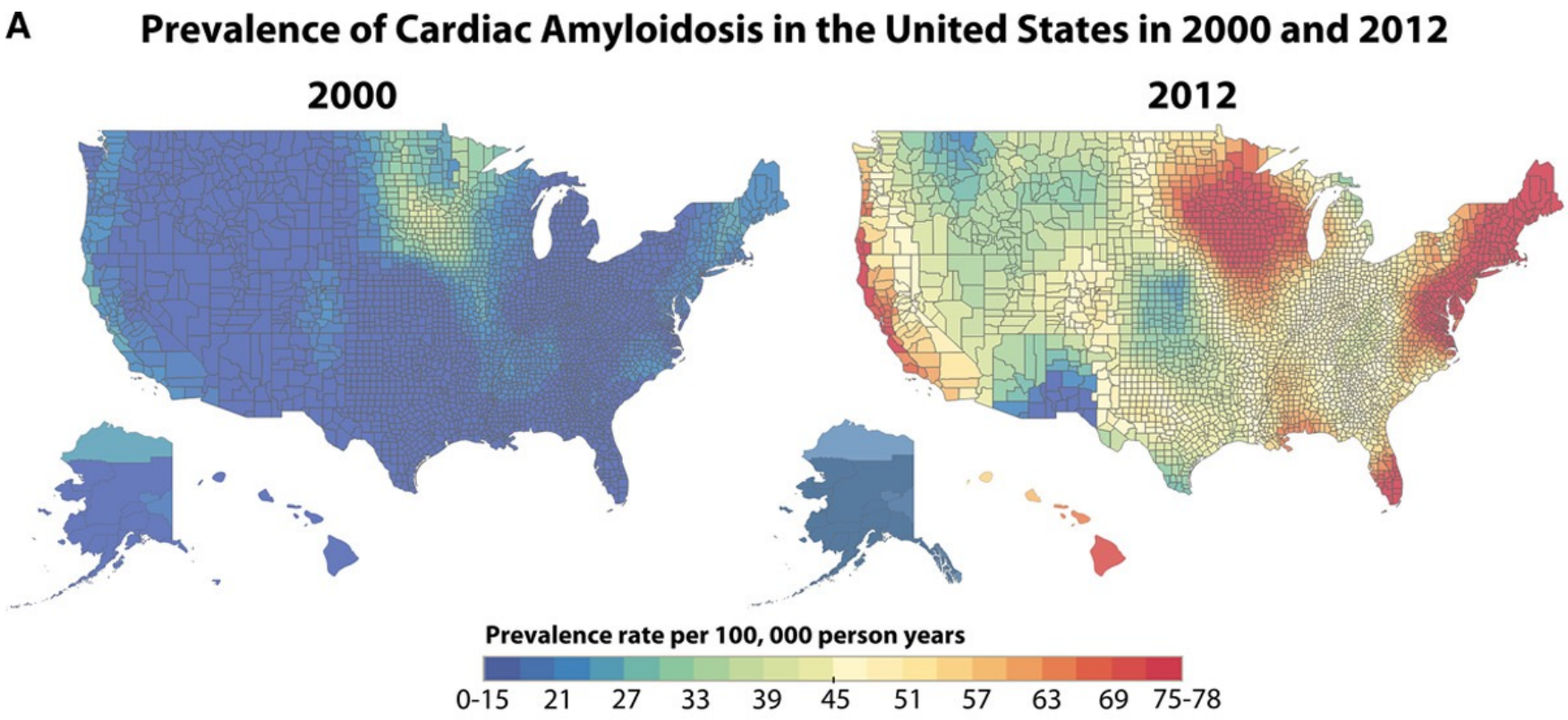
Rapezzi C. Arbustini E. Caforio A.L.P. and al. Eur Heart J 2013 May;34(19):1448-58

Le moment du diagnostic



Sperry, B.W., Reyes B.A., Ikram A. and al. JACC 2018;72(17):2040-50

EST-CE SI RARE QUE CELA?

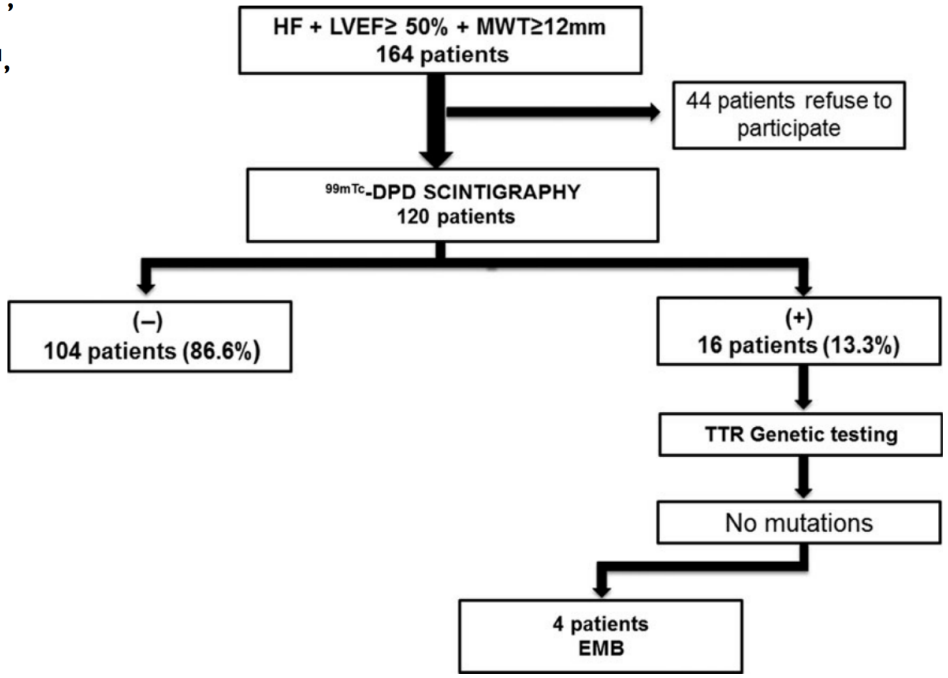


Circulation: Heart Failure. 2019;12:e005407

EST-CE SI RARE QUE CELA?

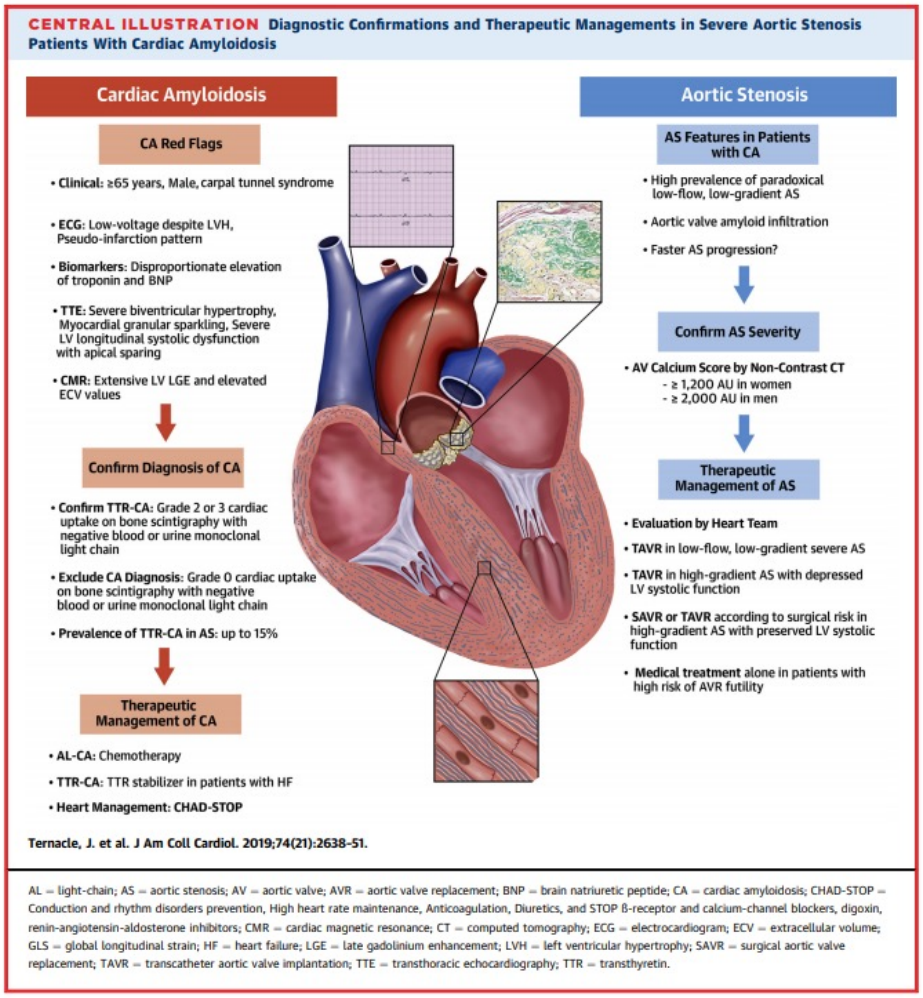
Wild-type transthyretin amyloidosis as a cause of heart failure with preserved ejection fraction

Esther González-López[1], Maria Gallego-Delgado[1], Gonzalo Guzzo-Merello[1], F. Javier de Haro-del Moral[2], Marta Cobo-Marcos[1], Carolina Robles[1], Belén Bornstein[3,4,5], Clara Salas[6], Enrique Lara-Pezzi[7], Luis Alonso-Pulpon[1], and Pablo Garcia-Pavia[1,7]*



13% HF-pEF

Eur Heart J. 2015 Oct 7;36(38):2585-94.



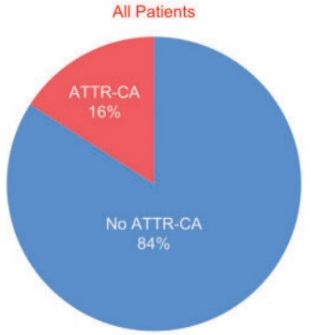
Aortic Stenosis and Cardiac Amyloidosis: Partners in Crime. Ternacle J et Coll. JACC. 2019.

EST-CE SI RARE QUE CELA?

~10-15% TAVI

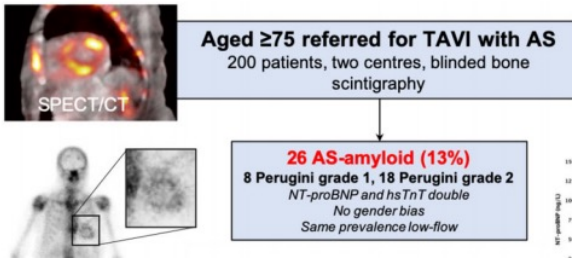
Unveiling transthyretin cardiac amyloidosis and its predictors among elderly patients with severe aortic stenosis undergoing transcatheter aortic valve replacement

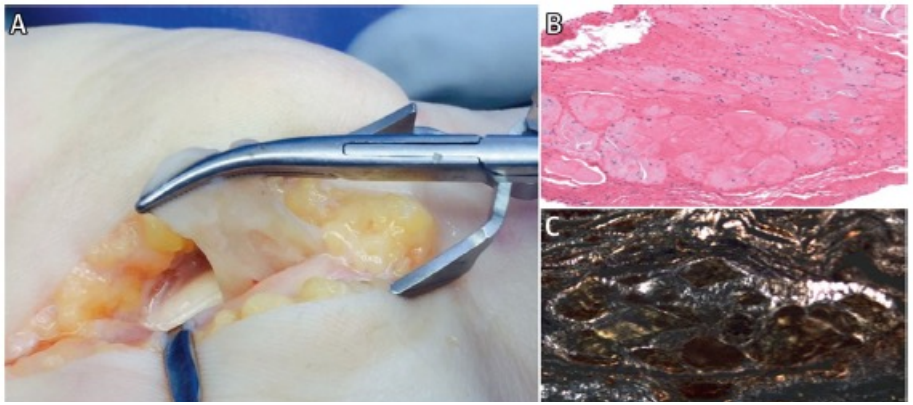
European Heart Journal (2017) 38, 2879–2887



Prevalence and outcome of dual aortic stenosis and cardiac amyloid pathology in patients referred for transcatheter aortic valve implantation

European Heart Journal (2020) 41, 2759–2767





EST-CE SI RARE QUE CELA?

≈10% canaux carpiens

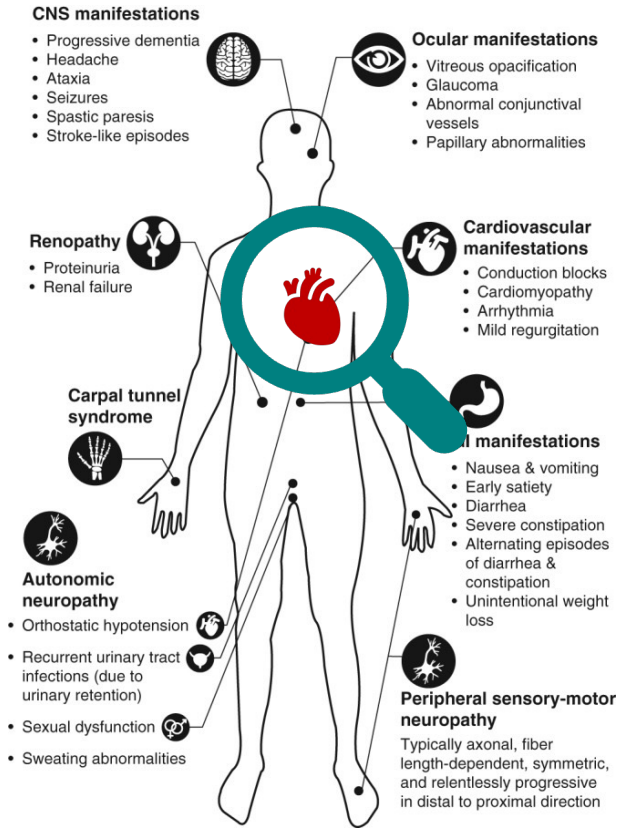
TABLE 2 Demographics and Diagnostic Criteria of Patients Diagnosed With Amyloidosis

Patient	Age, yrs	Sex	African American	Bilateral Symptoms	Prior CTS Release	Amyloid Type	Genetic Mutation	Kappa, mg/l	Lambda, mg/l	FLC Ratio	Monoclonal Protein
#1	73	F	No	Yes	Yes	ATTR	Ala81Thr	46.0	25.7	1.79	Yes
#2	82	F	No	Yes	Yes	ATTR	None	21.1	13.9	1.52	No
#3	85	M	No	Yes	Yes	AL	N/A	33.1	15.6	2.12	No
#4	78	F	No	Yes	Yes	AL	N/A	20.4	299.6	0.07	Yes
#5	67	M	No	Yes	Yes	ATTR	None	12.3	10.0	1.23	No
#6	56	M	No	Yes	Yes	ATTR	Leu58His	15.5	9.9	1.57	No
#7	62	M	No	Yes	No	ATTR	None	13.9	11.3	1.23	Yes
#8	72	F	No	Yes	Yes	Presumed ATTR*	None	20.9	11.2	1.87	No
#9	65	M	Yes	Yes	No	ATTR	None	29.7	26.3	1.13	Yes
#10	80	M	No	Yes	No	ATTR	None	14.7	18.6	0.79	Yes

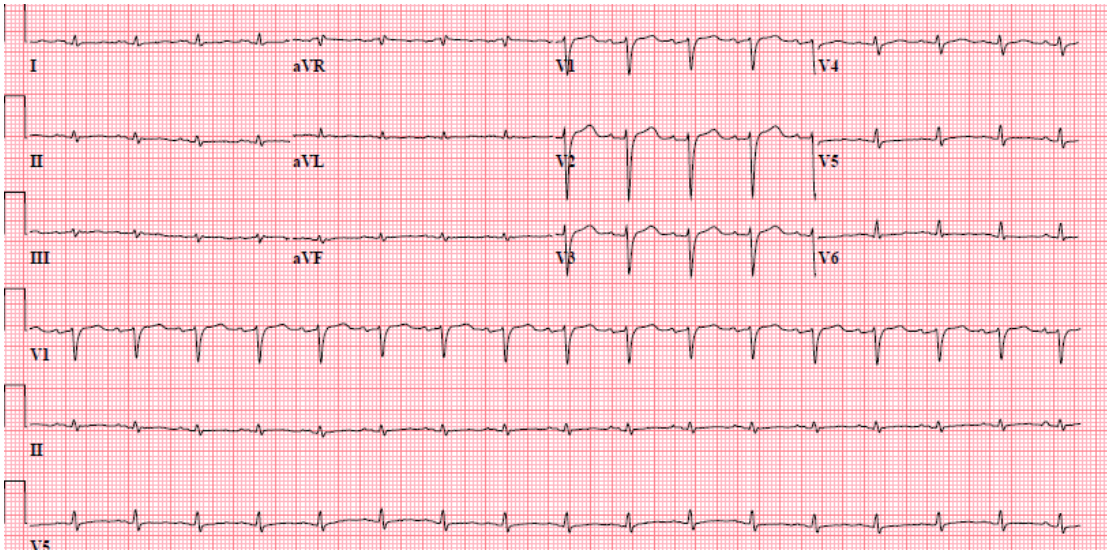
*Mass spectrometry and immunohistochemistry without sufficient tissue to accurately subtype sample.

CTS = carpal tunnel syndrome; FLC = free light chain ratio (kappa/lambda) with reference range 0.26 to 1.65.

QUELS OUTILS POUR ARRIVER AU DIAGNOSTIC?



ECG: **Micro-voltage / pseudo ondes q**

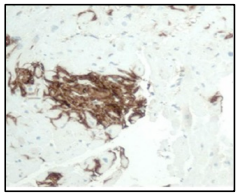


≤50% des cas d'ATTR avec CMP

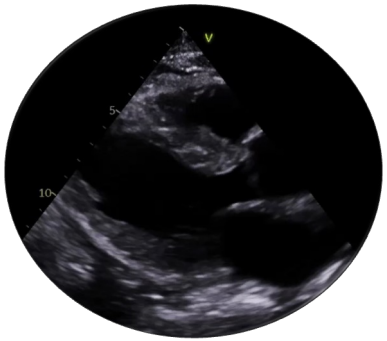
LABOS: **Troponine – NTproBNP**

ECHOCARDIOGRAPHIE

Myocarde

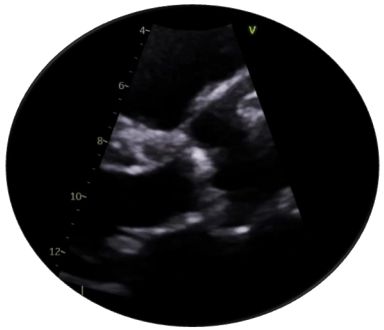


Hypertrophie
Dyfonction ventriculaire
Dilatation et dysfunction auriculaire

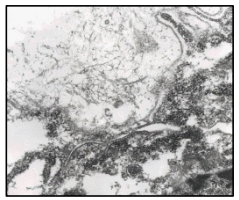


Endocarde

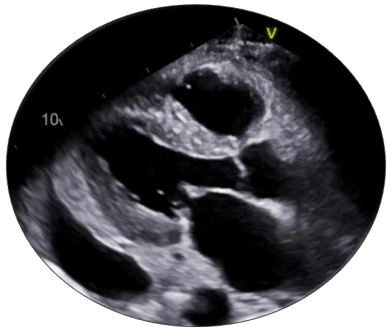
Sténose aortique
Fuites mitrale et tricuspide



Péricarde



Épanchement péricardique

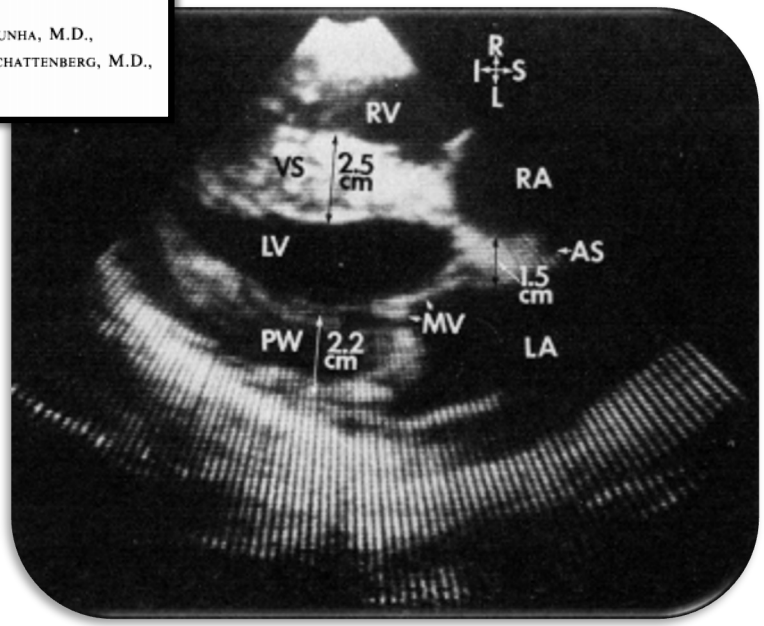


Merlini, NEJM 2003 – Chang JH, Korean J Med 2013

Apparence du myocarde

M-mode and Two-dimensional Echocardiographic Features in Cardiac Amyloidosis

ARISTARCO G. SIQUEIRA-FILHO, M.D., CLAUDIO L. P. CUNHA, M.D., ABDUL J. TAJIK, M.D., JAMES B. SEWARD, M.D., THOMAS T. SCHATTENBERG, M.D., AND EMILIO R. GIULIANI, M.D.

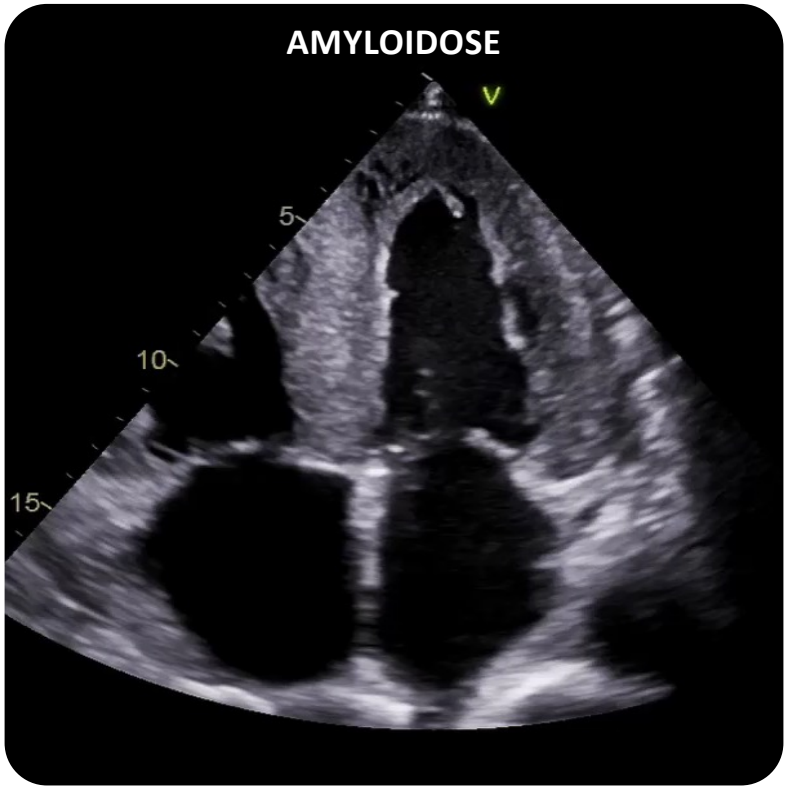


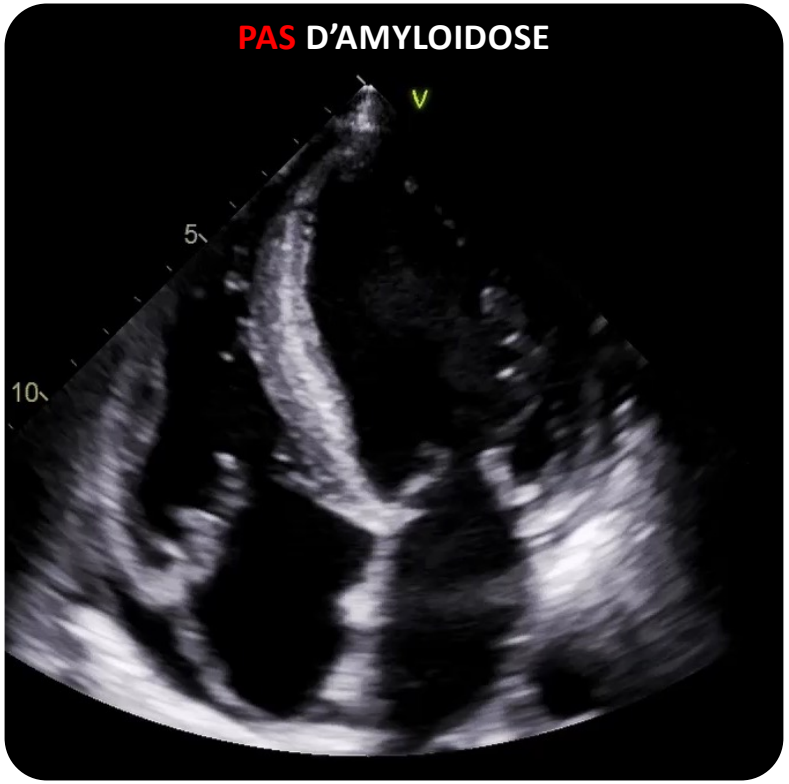
Circulation 63, No. 1, 1981.

« Granular sparkling »

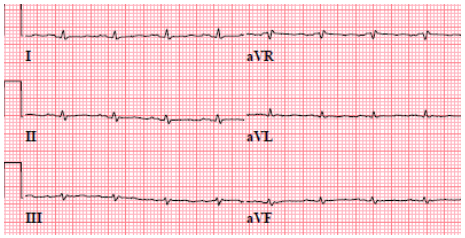
Siqueira-Filho A.G., Cunha C.L., Tajik A.J. and al. Circulation. 1981 Jan;63(1):188-96

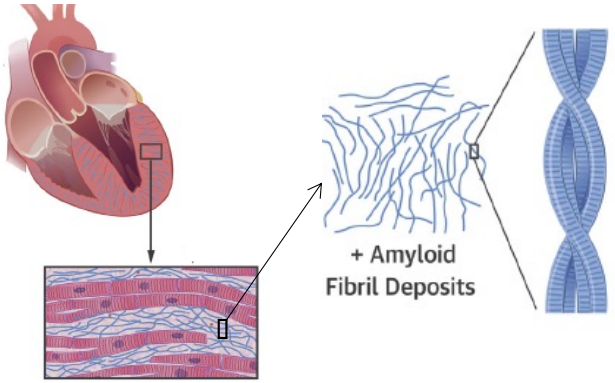
Apparence du myocarde en 2022



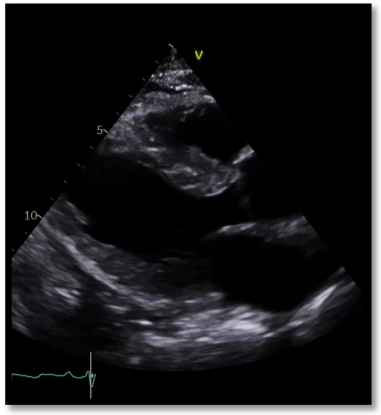


Hypertrophie ventriculaire gauche

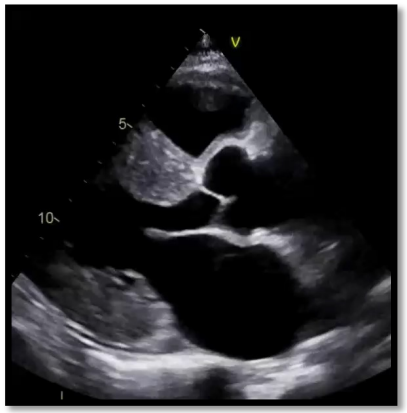




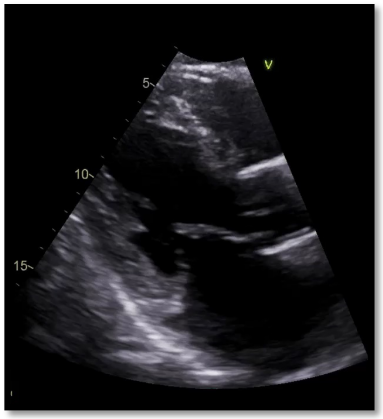
Dorbala, S. Cuddy S. and Falk R.H.
JACC Cardiovasc. Imaging. 2020 Jun;13(6):1368-83
Accessible en ligne: 10.1016/j.jcmg.2019.07.015



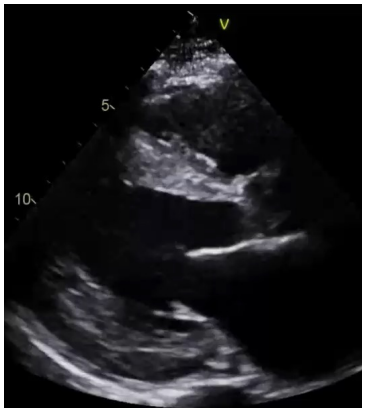
AL



mATTR

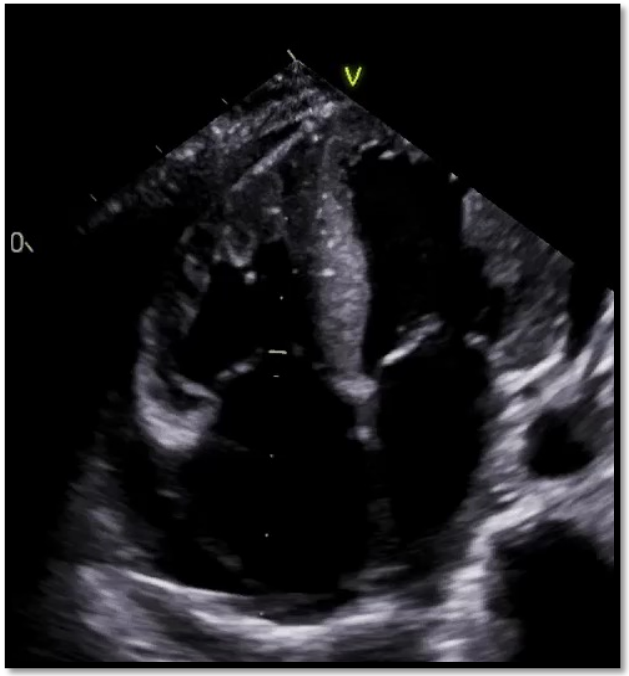


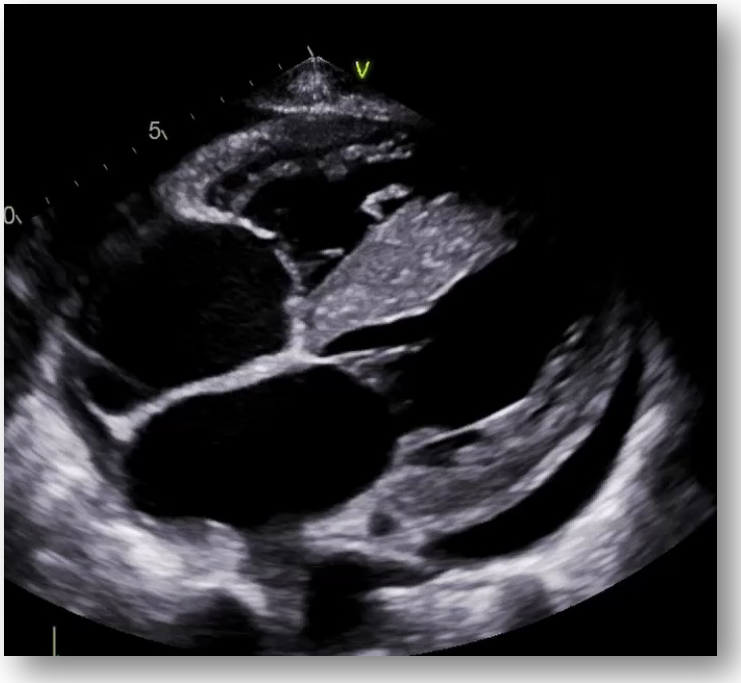
wtATTR



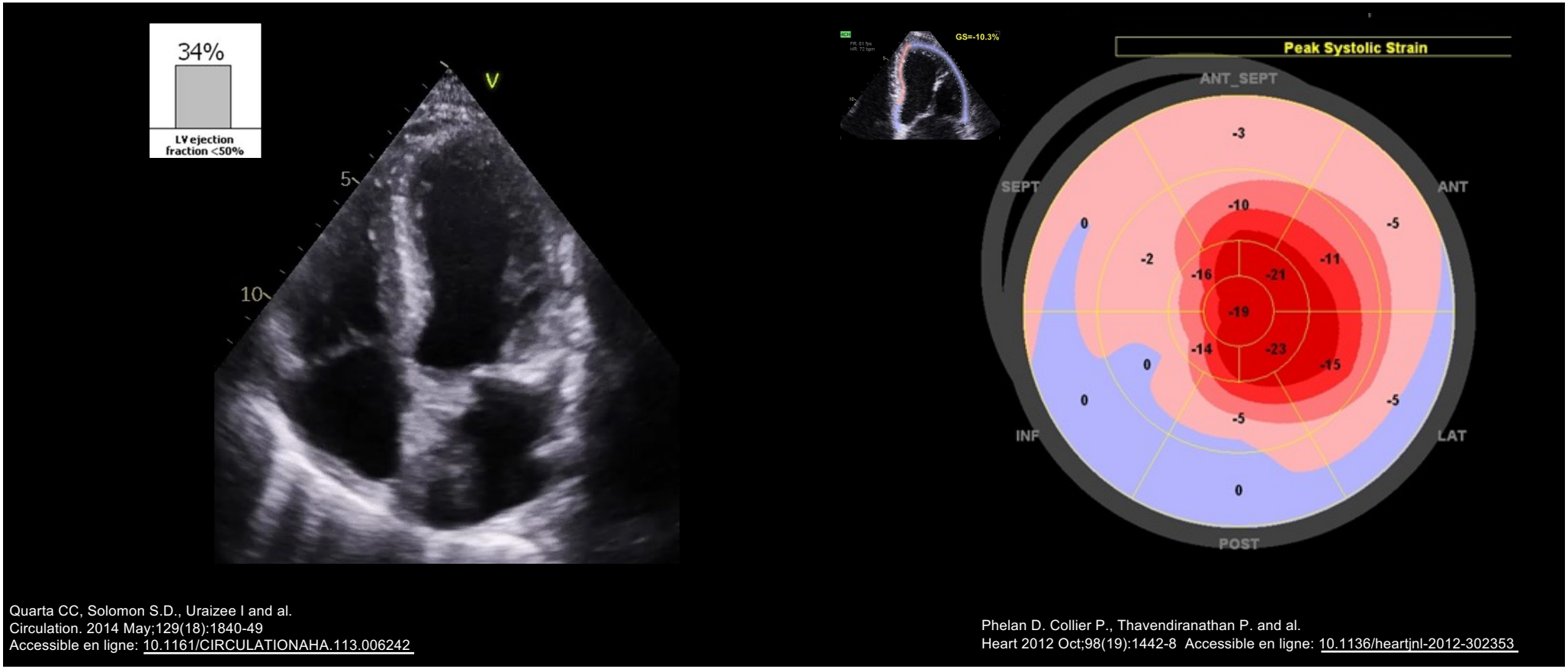
HCM

Hypertrophie Biventriculaire *est plus marquante ++*



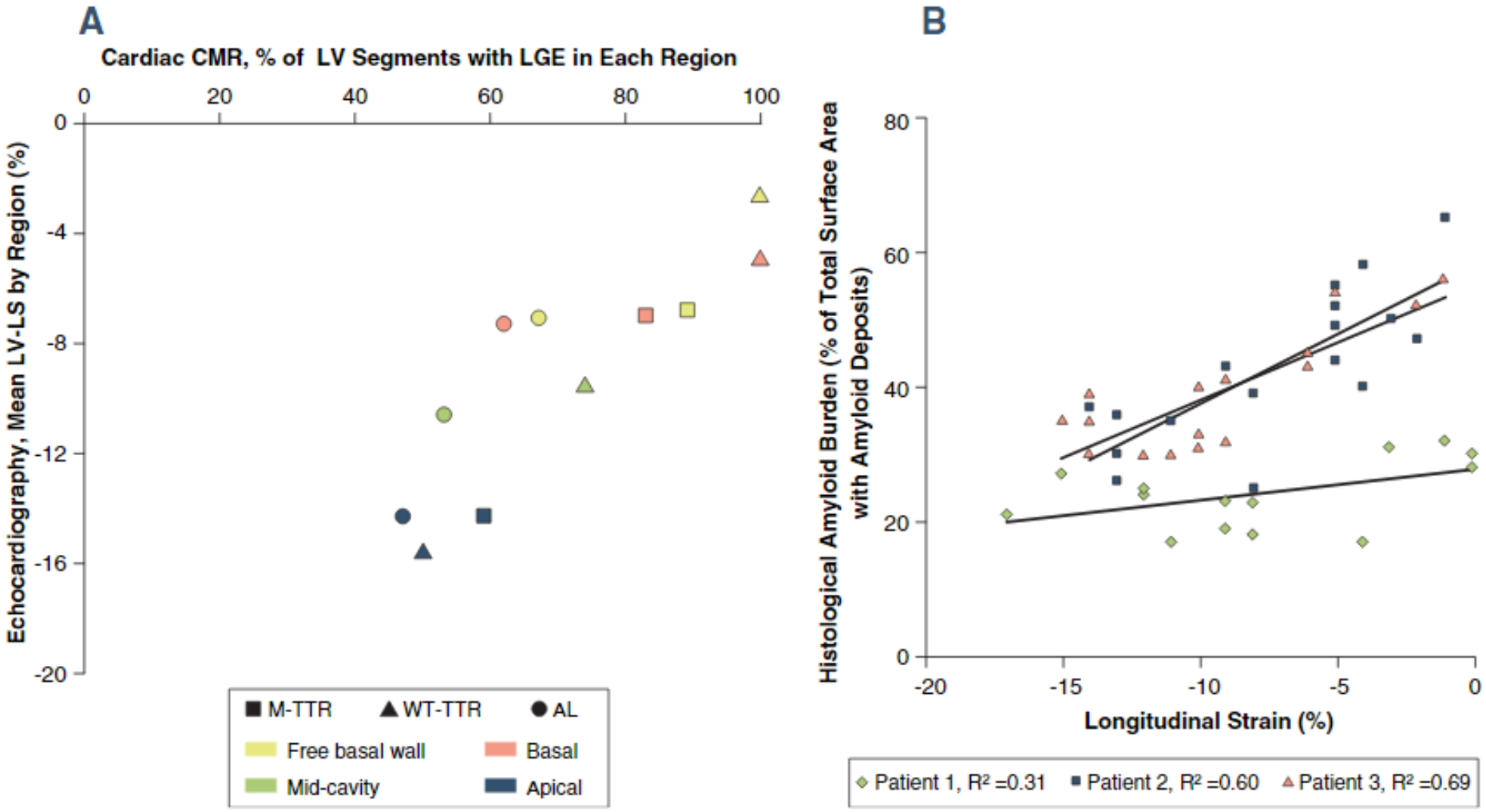


Fonction systolique



Quarta CC, Solomon S.D., Uraizee I and al.
Circulation. 2014 May;129(18):1840-49
Accessible en ligne: 10.1161/CIRCULATIONAHA.113.006242

Phelan D. Collier P., Thavendiranathan P. and al.
Heart 2012 Oct;98(19):1442-8 Accessible en ligne: 10.1136/heartjnl-2012-302353

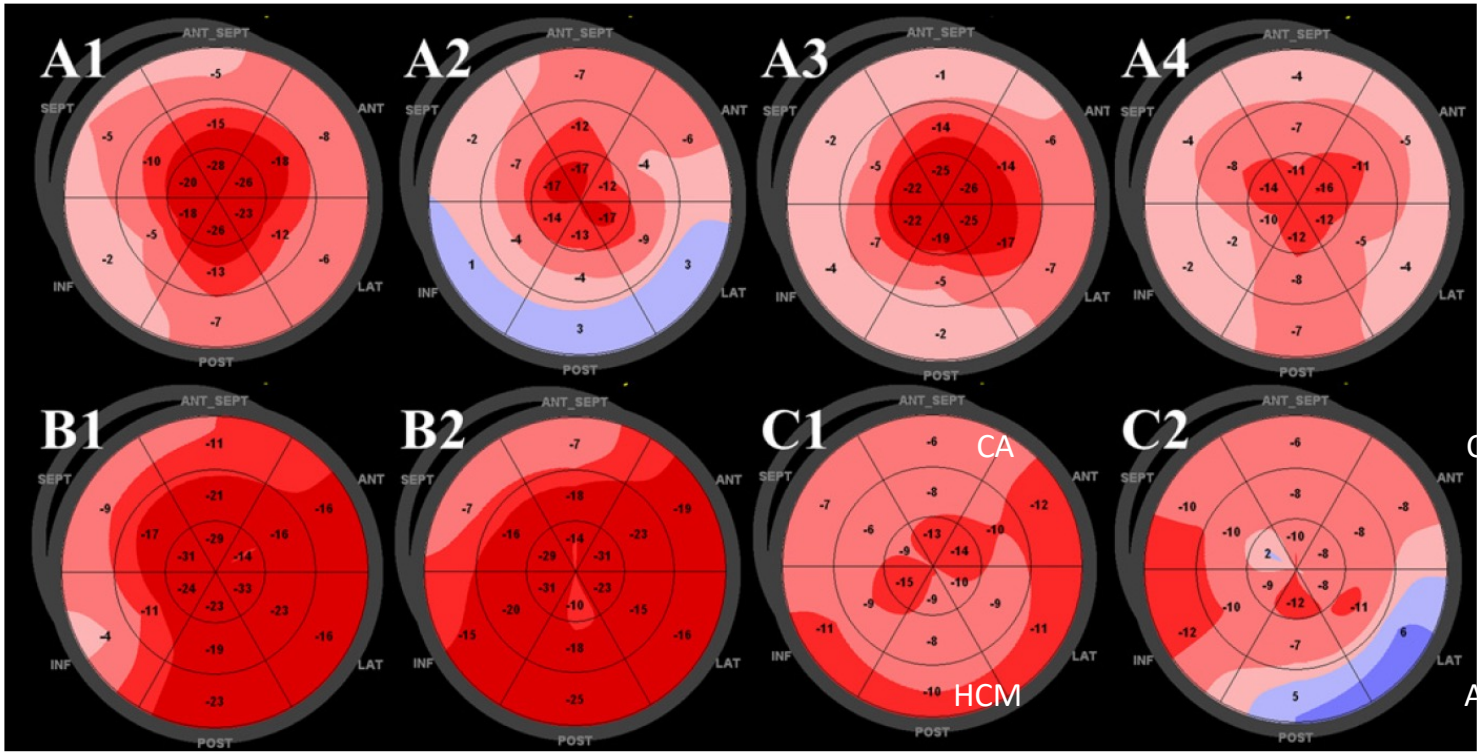


Ternacle J et Coll. JACC: Cardiovascular Imaging 2016

Relative apical sparing of longitudinal strain using two-dimensional speckle-tracking echocardiography is both sensitive and specific for the diagnosis of cardiac amyloidosis

Dermot Phelan, Patrick Collier, Paaladinesh Thavendiranathan, Zoran B Popović, Mazen Hanna, Juan Carlos Plana, Thomas H Marwick, James D Thomas

Se 93% - Sp 82%



Heart 2012;98:1442e1448.

Clinical significance of the relative apical sparing pattern of longitudinal strain in patients with cardiac amyloidosis

[a]Makoto Saito, [a,b]Yasuhisa Nakao, [a]Rieko Higaki, [c]Yuki Yokomoto, [c]Akiyoshi Ogimoto, [d]Moeko Suzuki, [d]Hideo Kawakami, [e]Go Hiasa, [e]Hideki Okayama, [b]Katsuji Inoue, [b]Shuntaro Ikeda, [b]Osamu Yamaguchi

[a]Department of Cardiology, Kitaishikai Hospital, Ozu, Japan; [b]Department of Cardiology, Pulmonology, Nephrology and Hypertension, Ehime University Graduate School of Medicine, Toon, Japan; [c]Department of Cardiology, Uwajima City Hospital, Uwajima Japan
[d]Department of Cardiology, Ehime Prefectural Imabari Hospital, Imabari, Japan; [e]Department of Cardiology, Ehime Prefectural Central Hospital, Matsuyama, Japan

The authors have no conflicts of interest to disclose concerning the presentation.

Abstract

Background: The relative apical sparing pattern (RASP) of left ventricular (LV) longitudinal strain (LS) is frequently associated with cardiac amyloidosis (CA). However, some patients with CA do not show the RASP, and their clinical characteristics have not been fully clarified. We sought to investigate the clinical significance of RASP in patients with CA.
Methods: One hundred consecutive CA patients who were diagnosed by biopsy or myocardial pyrophosphate scintigraphy and evaluated for RASP (mean age: 76 years, male: 77%, LV mean wall thickness: 13.5 mm, light-chain [AL] type: 33 cases, transthyretin [TTR] type: 67 cases) were retrospectively enrolled. The RASP was semi-quantitatively and quantitatively assessed. Semi-quantitative RASP was defined as reduction of LS (≥-10%) in ≥5 (of 6) basal segments relative to preserved LS (<-15%) in ≥1 apical segment. Quantitative RASP was calculated according to the following formula: Quantitative RASP = [Average apical LS] / [Average basal LS + Average mid LS]. We adapted three validated thresholds (>1.00, >0.90, and >0.87) according to the literature.
Results: Semi-quantitative and binalized quantitative RASP (>1.00, >0.90, and >0.87) were observed in 55, 55, 63, and 65 patients, respectively. RASP in each definition was more prevalent in the TTR group than in the AL group. Additionally, RASP was significantly associated with higher LV wall thickness (all, p<0.05). After the RASP assessment, 35 all-cause deaths and 26 cardiac deaths were observed during the follow-up period (median, 1.1 years). No association was found with RASP.
Conclusions: The incidence of RASP is low in the case of thin LV wall thickness in CA patients, which may indicate the difficulty of early diagnosis of CA using RASP in patients with mild LV hypertrophy. The prognostic prediction using RASP may be challenging in this cohort.

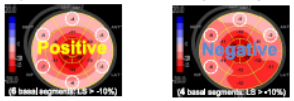
Background

- The relative apical sparing pattern (RASP) of left ventricular longitudinal strain (LS) is determined on the strain polar map, while global longitudinal strain (GLS) is

Methods

- **Study design:** Retrospective cohort study
- **Study parameters:**
  - Demographic data
  - Comorbidity
  - Laboratory data
  - ECG data
  - Routine echo data
  - Follow-up data
  (**All-cause death/Cardiac death** after the index echo exam)
- **Echo:** Vivid 7 or Vivid E9 or Vivid E95 (GE Healthcare)
- **Speckle tracking:** EchoPAC PC BT13 (GE Healthcare)
- **RASP**

1, Semi-quantitative assessment (sRASP)



- **sRASP** was defined as reduction of LS (> −10%), showing pink or blue in **≥5** segments out of the basal six segments, relative to apical LS (<−15%) showing red.

Saito M, et al. IJCHV 2020.

Methods

- **Subjects:**

100 consecutive **CA** patients who were diagnosed by **biopsy** (n=65) or **^{99m}Tc-PYP scintigraphy*** (n=61) and **evaluated for RASP**

light-chain [**AL**] type: **33** cases
transthyretin [**TTR**] type: **67** cases

*The cases with Perugini score ≥ 2 (moderate uptake equal to bone) using 99mTc-PYP scintigraphy were expediently defined as TTR-CA in the present study.

*The cases with Perugini score ≥ 2 (moderate uptake equal to bone) using 99mTc-PYP scintigraphy were expediently defined as TTR-CA in the present study.

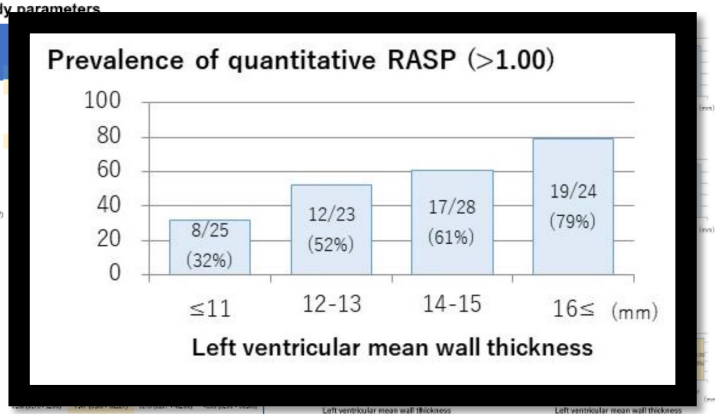
Results

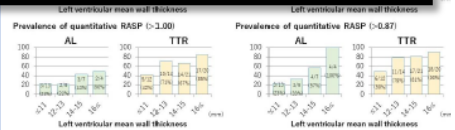
- **Table 2: Baseline patients' characteristics and associations between RASPs and study parameters**

Variables	Values
Age (years)	76 (71, 80)
Male, n (%)	77 (77)
Body mass index (kg/m²)	22.0 (20.1, 24.1)
Systolic blood pressure (mmHg)	113 (102, 126)
Heart rate (/min)	72 (63, 79)
NYHA functional class at discharge I/II/III, n (%)	18/31/34/17 (18/31/34/17)
Comorbidities	
Hypertension, n (%)	31 (31)
Diabetes, n (%)	16 (16)
Atrial fibrillation (Non-Paroxysmal/Paroxysmal), n (%)	61/22/17 (61/22/17)
Serum markers	
B-type natriuretic peptide (pg/mL)	309 (169, 707)
Hemoglobin (g/L)	13.8 (11.4, 14.2)
Blood urea nitrogen (mg/dL)	22.0 (17.0, 27.0)
Creatinine (mg/dL)	1.0 (0.8, 1.4)
Troponin I (pg/mL)	80 (34, 186)
Electrocardiographic variables	
SV_1+RV_5 voltage (mm)	1.9 (1.2, 2.8)
Low voltage, n (%)	19 (20)
PQ duration (ms)	160 (153, 233)
QRS duration (ms)	105 (90, 138)
QTc (ms)	443 (424, 466)
Right bundle branch block, n (%)	17 (18)
Left bundle branch block, n (%)	10 (11)
Pseudoinfarct pattern, n (%)	22 (23)
Echocardiographic variables	
Interventricular septal thickness (mm)	14.0 (12.0, 15.7)
LV posterior wall thickness (mm)	13.0 (11.0, 15.0)
LV mean wall thickness (mm)	13.5 (11.4, 15.1)
LV end-diastolic diameter (mm)	44.0 (40.0, 48.7)
LV end-systolic diameter (mm)	31.2 (27.2, 36.0)
LV ejection fraction (%)	54.8 (44.1, 62.6)
Relative wall thickness	0.58 (0.50, 0.70)
LV mass index (g/m²)	199.0 (112.0, 180.1)
e'-wave velocity (cm/s)	3.6 (3.7, 4.4)
E/e'	21.9 (17.1, 29.4)
E velocity deceleration time (ms)	171 (149, 201)
LA volume index (mL/m²)	52.6 (40.7, 64.3)
RV wall thickness (mm)	3.7 (3.3, 4.5)
Anterior mitral valve leaflet thickness (mm)	3.0 (2.4, 3.6)
Pericardial effusion (>5mm), n (%)	19 (19)
Granular sparkling, n (%)	23 (23)
LV global longitudinal strain (%)	-9.8 (-13.5, -7.8)
EF/SR	5.4 (4.4, 6.7)
LA longitudinal strain (reservoir phase) (%)	7.7 (5.4, 11.4)
LA longitudinal strain (booster phase) (%)	3.7 (1.9, 5.6)

- Data are expressed as the median (interquartile range), or number (percentage).
- Variables highlighted with pink show the variables with significant associations with all RASP measurements.
- Significant associations (p<0.05) was highlighted with orange and bold style.
- Weak associations (p<0.10) was highlighted with yellow.

- **Figure 1: Associations between RASPs and LVMWT**





- **Table 3: Associations between RASPs and mortality**

Variables	All-cause death (n=35) Hazard ratio (95% CI), p	Cardiac death (n=26) Hazard ratio (95% CI), p
Semi-quantitative RASP	1.37 (0.65-2.62), p=0.45	1.41 (0.62-3.22), p=0.41
Quantitative RASP (>1.00)	1.31 (0.65-2.64), p=0.46	0.97 (0.43-2.18), p=0.94
Quantitative RASP (>0.90)	0.82 (0.41-1.61), p=0.57	0.61 (0.28-1.32), p=0.21
Quantitative RASP (>0.87)	0.81 (0.41-1.59), p=0.54	0.60 (0.28-1.30), p=0.20
Quantitative RASP	1.80 (0.84-3.87), p=0.13	1.53 (0.60-3.92), p=0.37

- After the RASP assessment, 35 all-cause deaths and 26 cardiac deaths were observed during the follow-up period (median, 1.1 years).
- All-cause death was significantly associated with lower blood pressure, higher New York Heart Association class, higher BNP, longer QTc, lower LV diastolic diameter, and lower e'.
- Cardiac death was significantly associated with AL subtype, higher New York Heart Association class, higher BNP, longer QTc, and lower LV diastolic diameter.

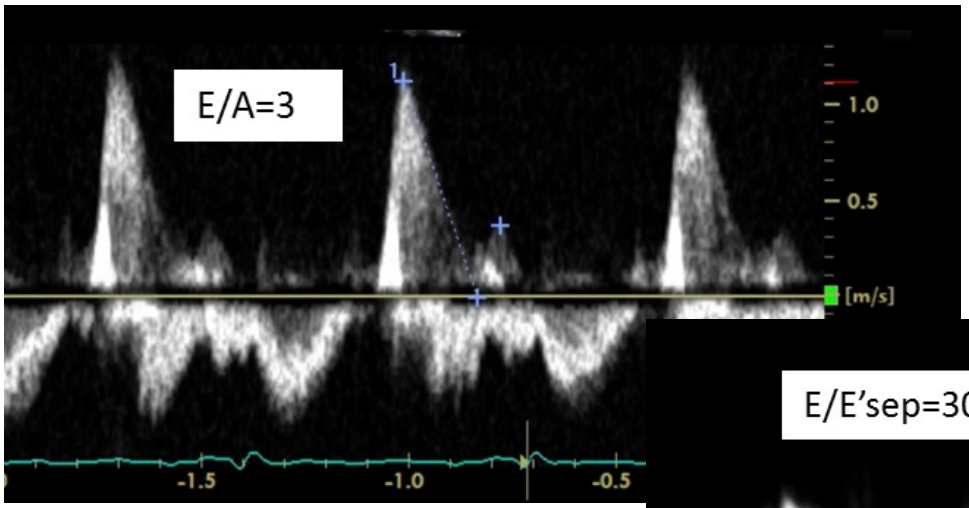
Conclusion

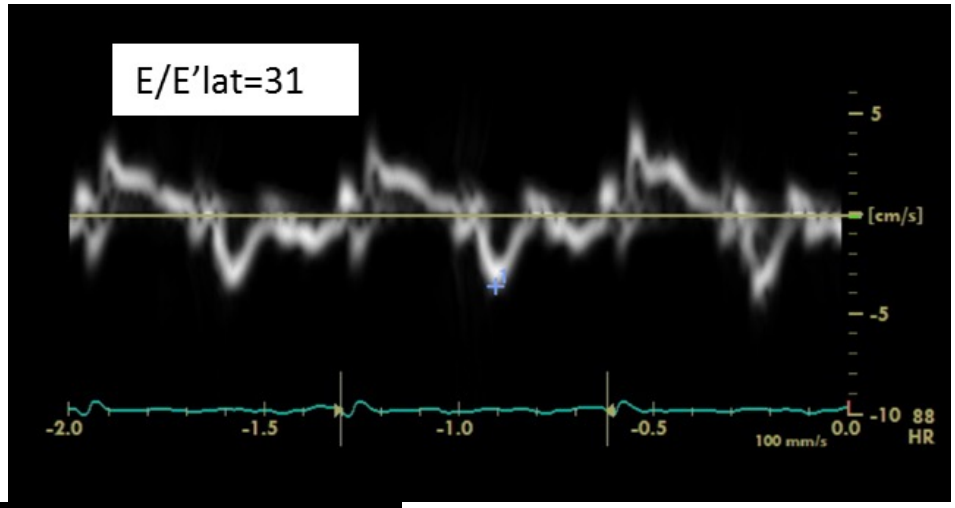
The incidence of RASP is low in the case of thin LV wall thickness in CA patients, which may indicate the difficulty of early diagnosis of CA using RASP in patients with mild LV hypertrophy. The prognostic prediction using RASP may be challenging in this cohort.

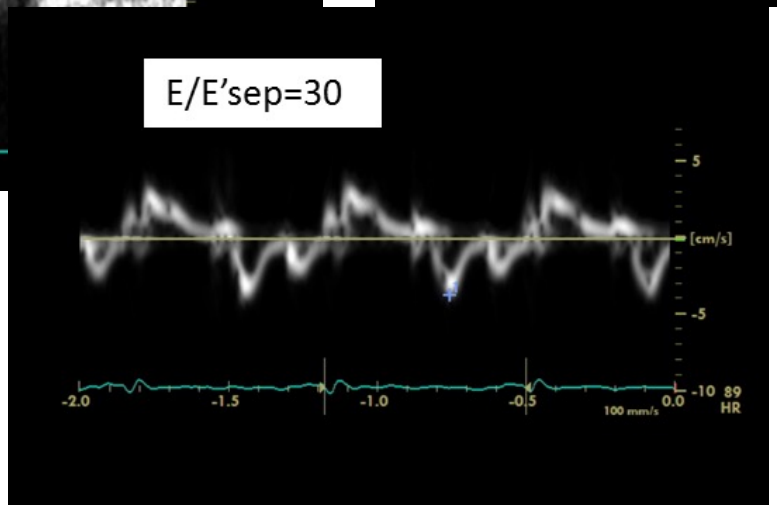
Zhang K.W., Sadhu J.S., Miller B.W. and al.
JACC: Case reports 2020 May;2(5):1-5
Accessible en ligne: 10.1016/j.jaccas.2020.02.018

ESC 2020

Dysfonction diastolique







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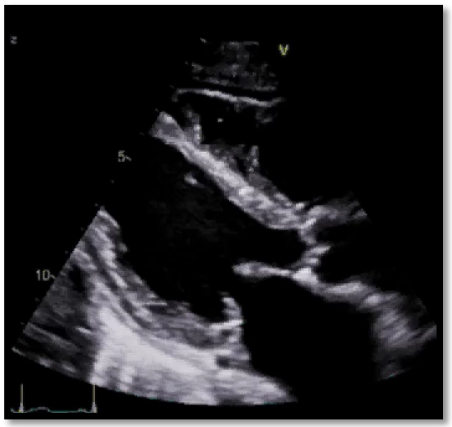
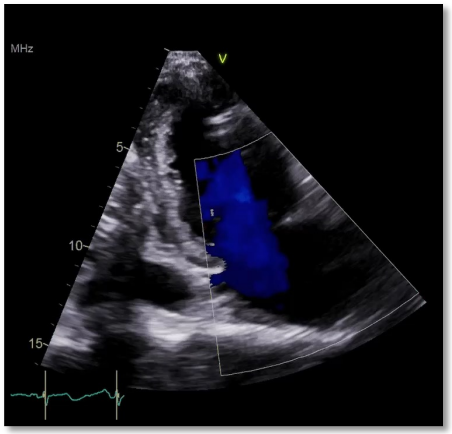
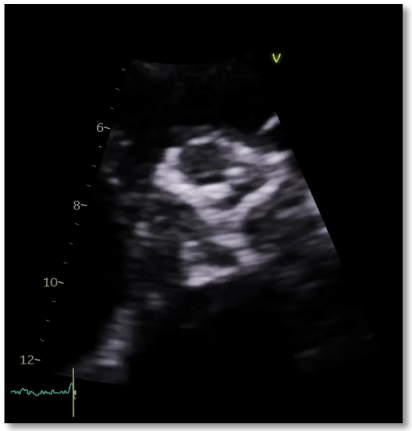
Accessible en ligne: 10.1161/CIRCULATIONAHA.113.006242

Valves







ESC European Society of Cardiology
European Heart Journal (2017) 38, 2879–2887
doi:10.1093/eurheartj/ehx350

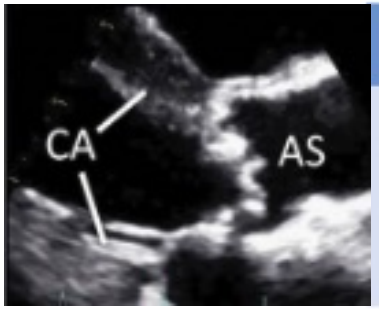
CLINICAL RESEARCH
Heart failure/cardiomyopathy

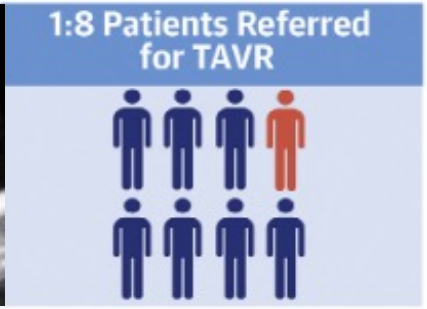
Unveiling transthyretin cardiac amyloidosis and its predictors among elderly patients with severe aortic stenosis undergoing transcatheter aortic valve replacement

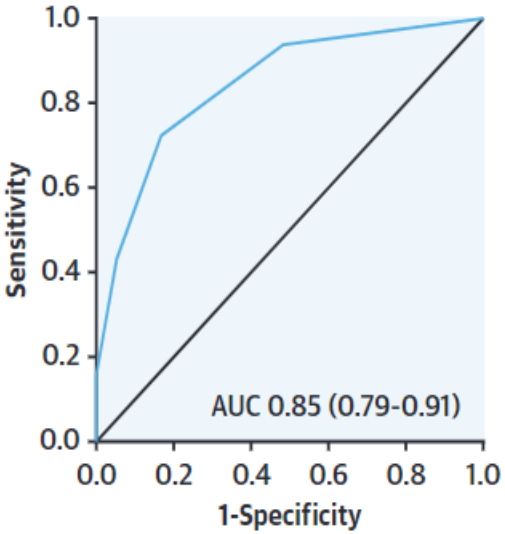
Adam Castaño[1,2]*, David L. Narotsky[1], Nadira Hamid[3], Omar K. Khalique[3], Rachelle Morgenstern[2], Albert DeLuca[2], Jonah Rubin[1], Codruta Chiuzan[4], Tamim Nazif[3], Torsten Vahl[3], Isaac George[3], Susheel Kodali[3], Martin B. Leon[3], Rebecca Hahn[3], Sabahat Bokhari[2], and Mathew S. Maurer[1]

	No ATTR-CA ($n = 127$)	ATTR-CA ($n = 24$)
Severe symptomatic AS stage		
D1: High gradient AS	102 (82.2%)	15 (62.5%)
D2: Low-flow, low-gradient AS with reduced LVEF	13 (10.5%)	7 (29.2%)
D3: Low-flow, low-gradient AS with normal LVEF	9 (7.3%)	2 (8.3%)

Castaño A., Narotsky D.L., Hamid N. and al. Eur Heart J. 2017 Oct;38(38):2879-87
Accessible en ligne: 10.1093/eurheartj/ehx350

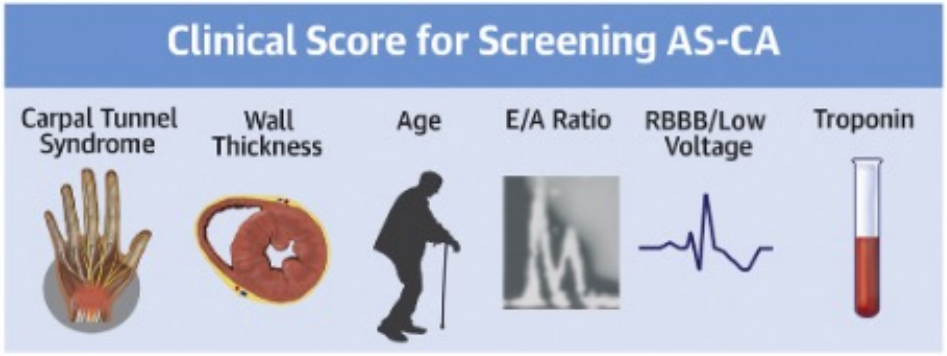






Parameter	Points
CTS	3
RBBB	2
Age ≥85 years	1
Hs-TnT >20 ng/l	1
IVS ≥18 mm	1
If in SR*: E/A ratio >1.4	1
If no BBB or PM: Sokolow index <1.9 mV	1

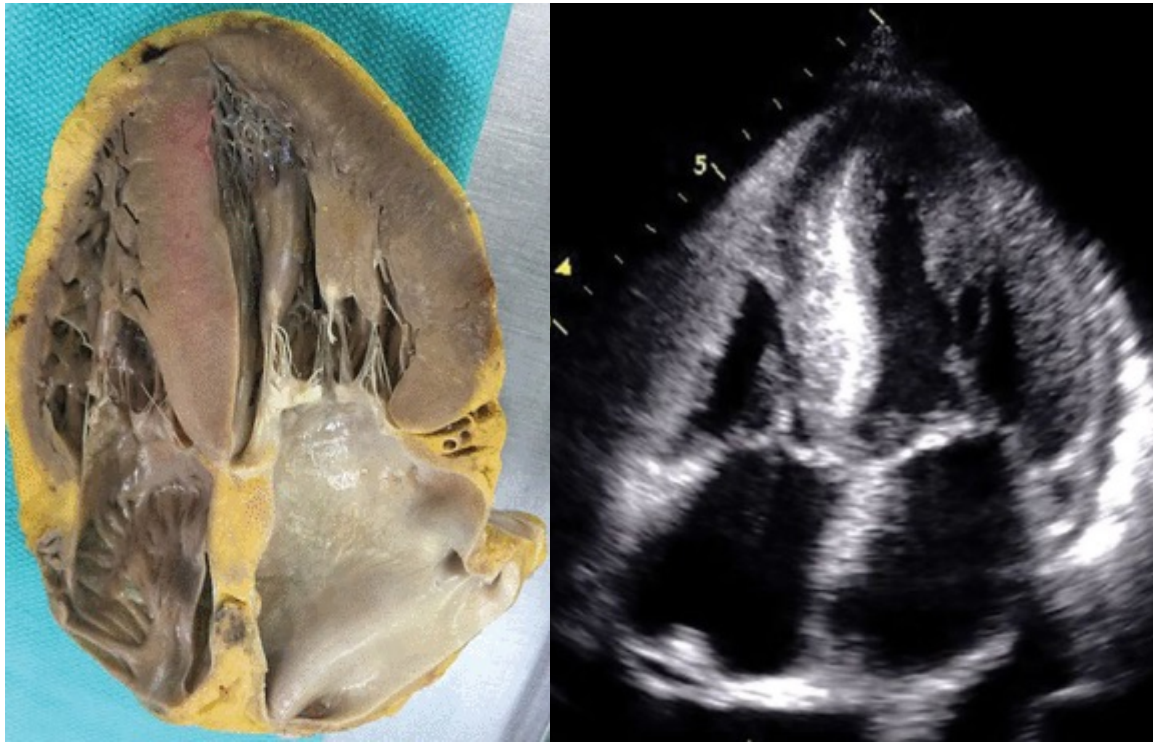
* AUC for AFib sub-cohort: 0.83



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%

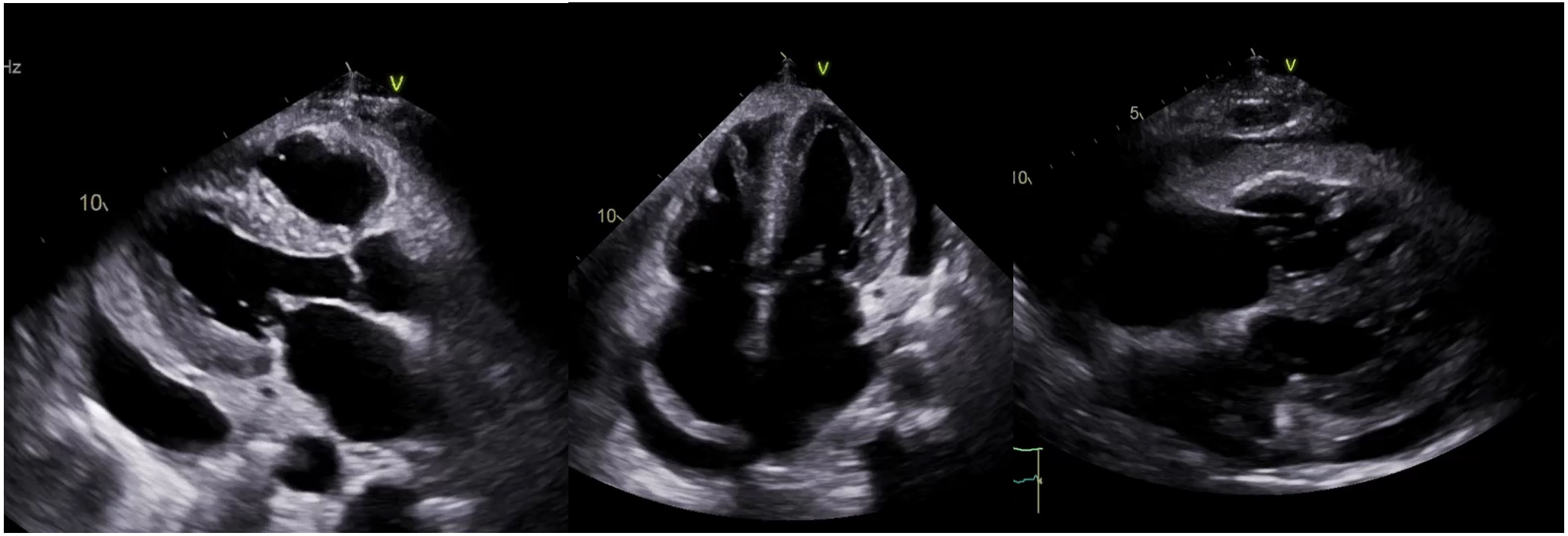
Nitsche, C. et al. J Am Coll Cardiol. 2021;77(2):128–39.

Oreillettes



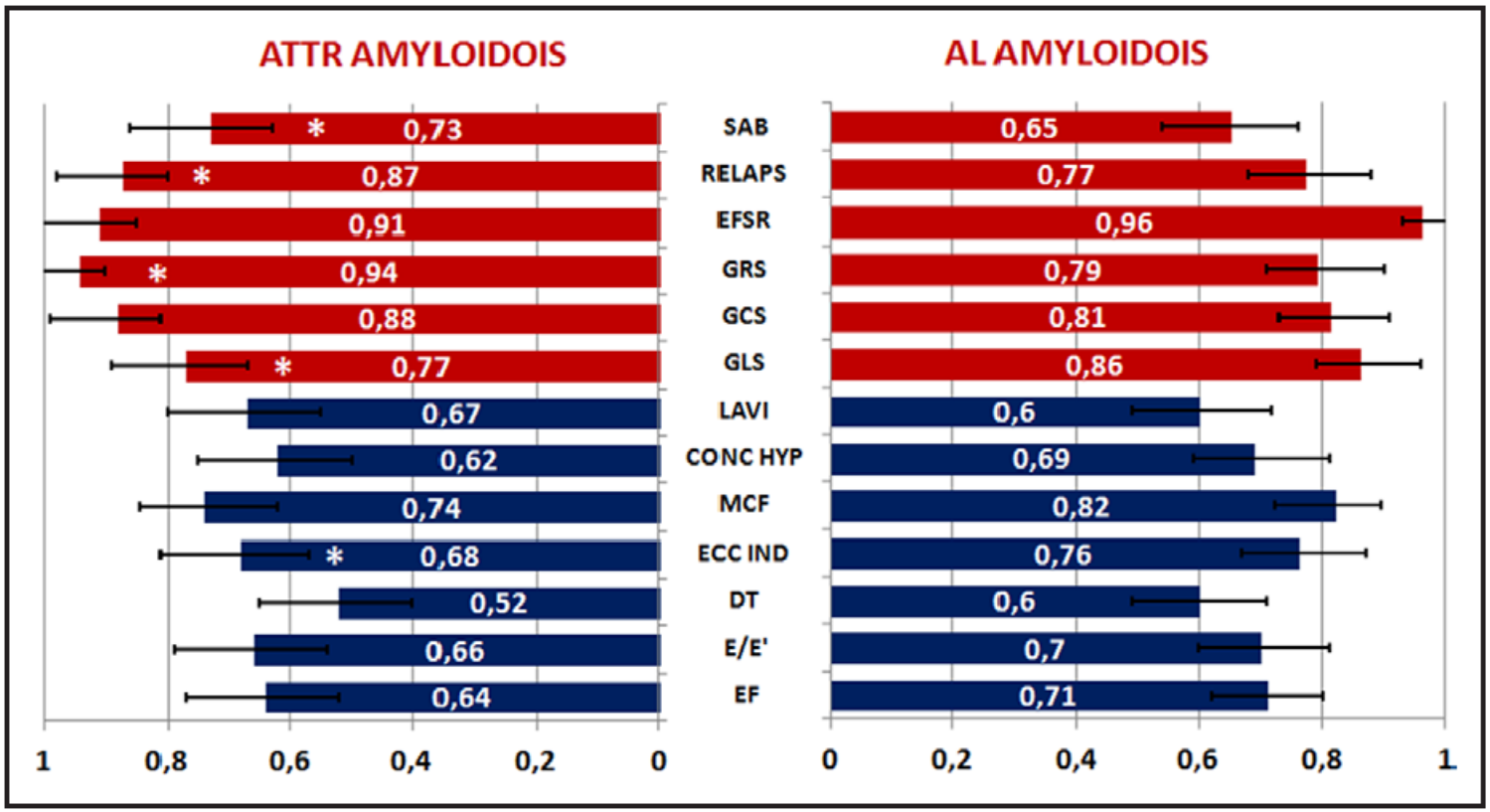
Cleveland Clinic Journal of Medicine December 2017, 84 (12 suppl 3) 12-26

Épanchement péricardique >50%



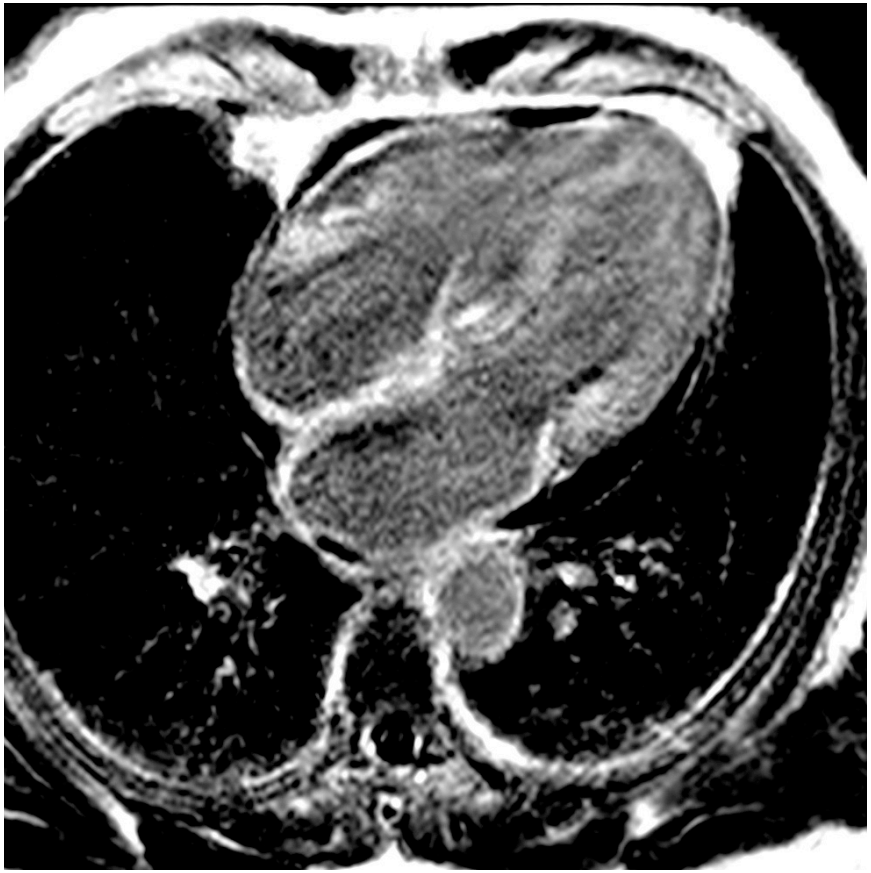
Quarta CC et Coll. Circulation. 2014 May 6;129(18):1840-9.

Différence en écho AL vs ATTR ?



Pagourelias ED et Al. Circ Cardiovasc Imaging. 2017

Quels outils pour arriver au diagnostic? IRM



Recommendations	Class[a]	Level[b]	Ref.[c]
It is recommended that CMR studies be performed and interpreted by teams experienced in cardiac imaging and in the evaluation of heart muscle disease.	I	C	148,149
In the absence of contraindications, CMR with LGE is recommended in patients with suspected HCM who have inadequate echocardiographic windows, in order to confirm the diagnosis.	I	B	126,127
In the absence of contraindications, CMR with LGE should be considered in patients fulfilling diagnostic criteria for HCM, to assess cardiac anatomy, ventricular function, and the presence and extent of myocardial fibrosis.	IIa	B	124,126,127,130 136,138–143
CMR with LGE imaging should be considered in patients with suspected apical hypertrophy or aneurysm.	IIa	C	127,129
CMR with LGE imaging should be considered in patients with suspected cardiac amyloidosis.	IIa	C	22,147
CMR with LGE may be considered before septal alcohol ablation or myectomy, to assess the extent and distribution of hypertrophy and myocardial fibrosis.	IIb	C	150,151

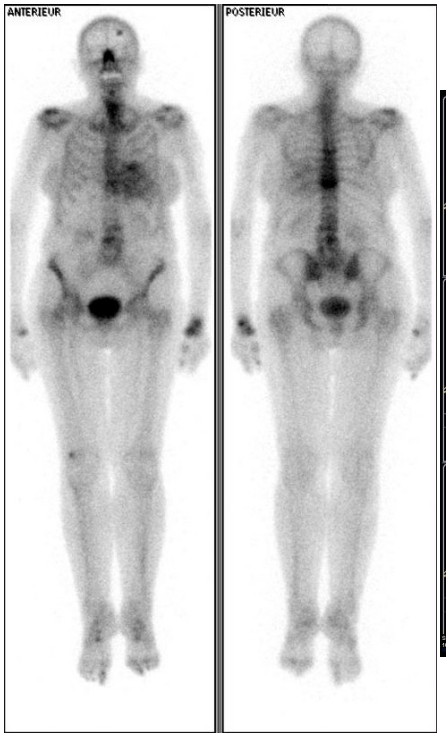
Influence of centre expertise on the diagnosis and management of hypertrophic cardiomyopathy: A study from the French register of hypertrophic cardiomyopathy (REMY)

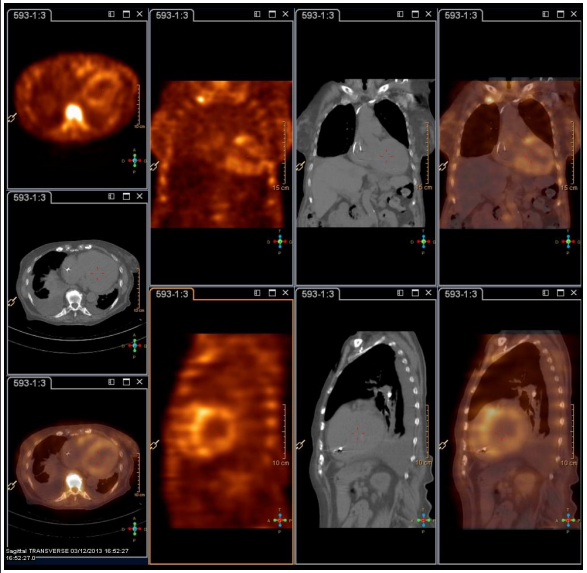
67 patients → amyloïdose ≈ 5%

All patients	Gene positive sarcomeric HCM	Gene negative suspected sarcomeric HCM	Suspected Sarcomeric: no genotype or missing data	Non-sarcomeric HCM	Missing data or not confirmed
N = 1431	N = 261	N = 242	N = 781	N = 107	N = 40
Age: mean (SD), years	46.47 (15.99)	56.41 (16.40)	53.16 (15.05)	63.23 (14.66)	59.53 (12.96)
Male sex, N (%)	169 (64.75)	516 (66.07)	171 (70.66)	82 (76.64)	34 (85.00)
NYHA class, N (%)*					
I	119 (45.77)	273 (35.97)	96 (40)	23 (22.33)	14 (38.89)
II	108 (41.54)	324 (42.69)	101 (42.08)	39 (37.86)	14 (38.89)
III	31 (11.92)	142 (18.71)	41 (17.08)	35 (33.98)	6 (16.67)
IV	2 (0.77)	20 (2.64)	2 (0.83)	6 (5.83)	2 (5.56)

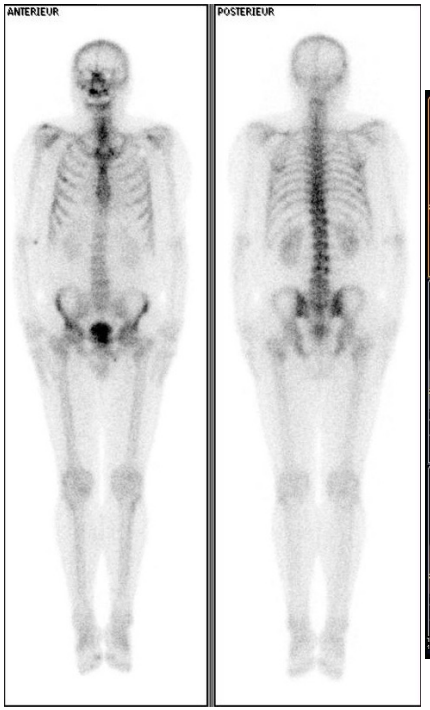
Quels outils pour arriver au diagnostic?

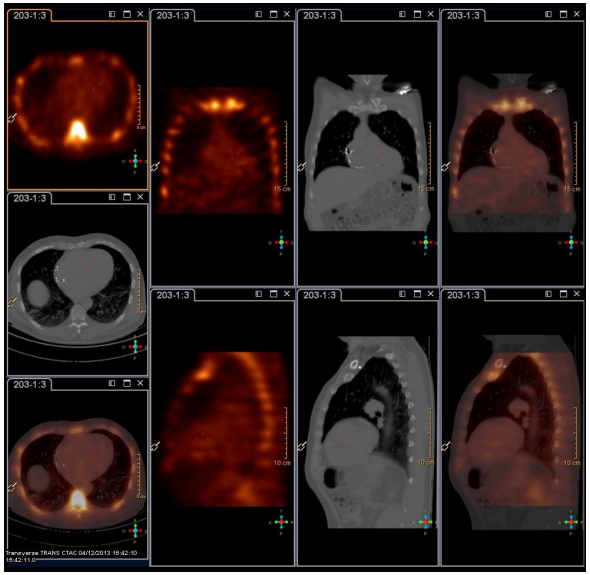
Scintigraphie ^{99m}*Tc-PYP/DPD/HMDP*





ATTR +++





AL +/-

ASNC/AHA/ASE/EANM/HFSA/ISA/SCMR/SNMMI Expert Consensus Recommendations for Multimodality Imaging in Cardiac Amyloidosis: Part 1 of 2—Evidence Base and Standardized Methods of Imaging

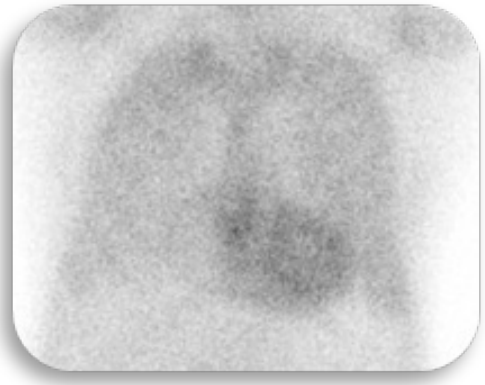
1-Hour Approach (validated for ^{99m}Tc-PYP):

- An elliptical/circular ROI should be drawn over the heart on the anterior planar images with care to avoid sternal overlap and with size adjusted to maximize coverage of the heart without inclusion of adjacent lung. This ROI (same size) should be mirrored over the contralateral chest to adjust for background and rib uptake (see Figure 6).
- A H/CL ratio is calculated as the fraction of heart ROI mean counts to contralateral chest ROI mean counts.
- **H/CL ratios of ≥ 1.5 at one hour can accurately identify ATTR cardiac amyloidosis if systemic AL amyloidosis is excluded.[113]**

3-Hour Approach:

- Examine 3-hour images for relative tracer uptake in the myocardium relative to ribs and grade using the following scale:

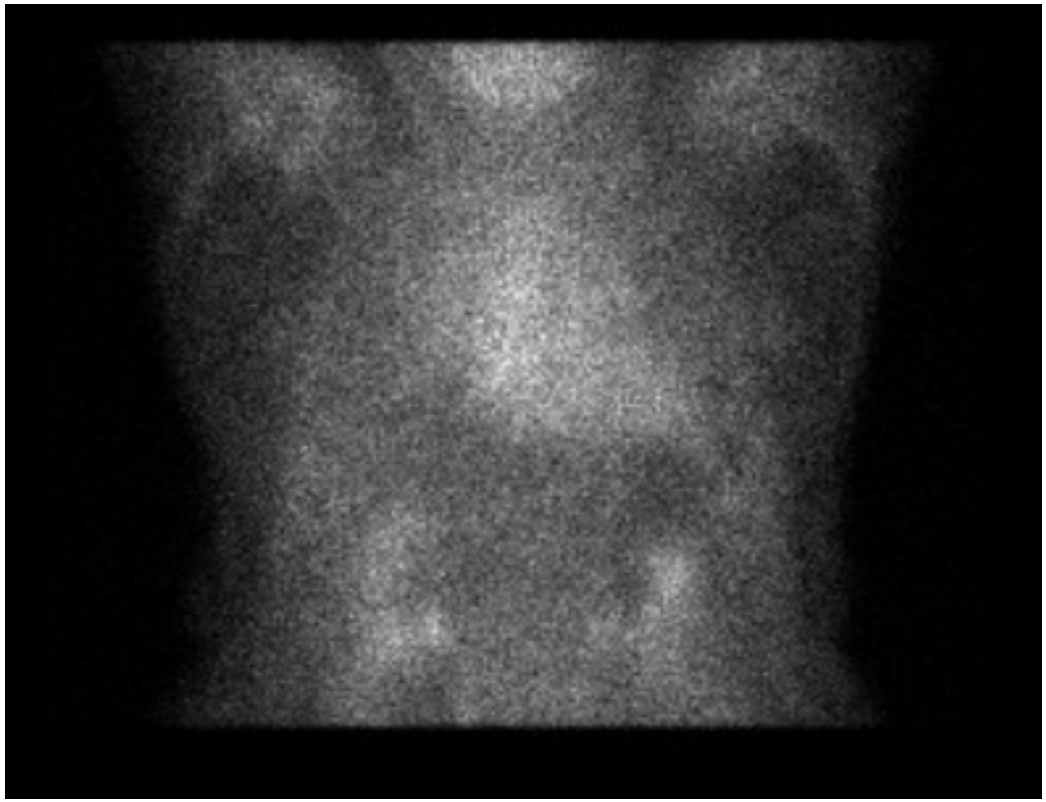
Grade 0	No myocardial uptake and normal bone uptake
Grade 1	Myocardial uptake less than rib uptake
Grade 2	Myocardial uptake equal to rib uptake
Grade 3	Myocardial uptake greater than rib uptake with mild/absent rib uptake



OBSERVATIONS ASSOCIÉES À L'ATTR-CM

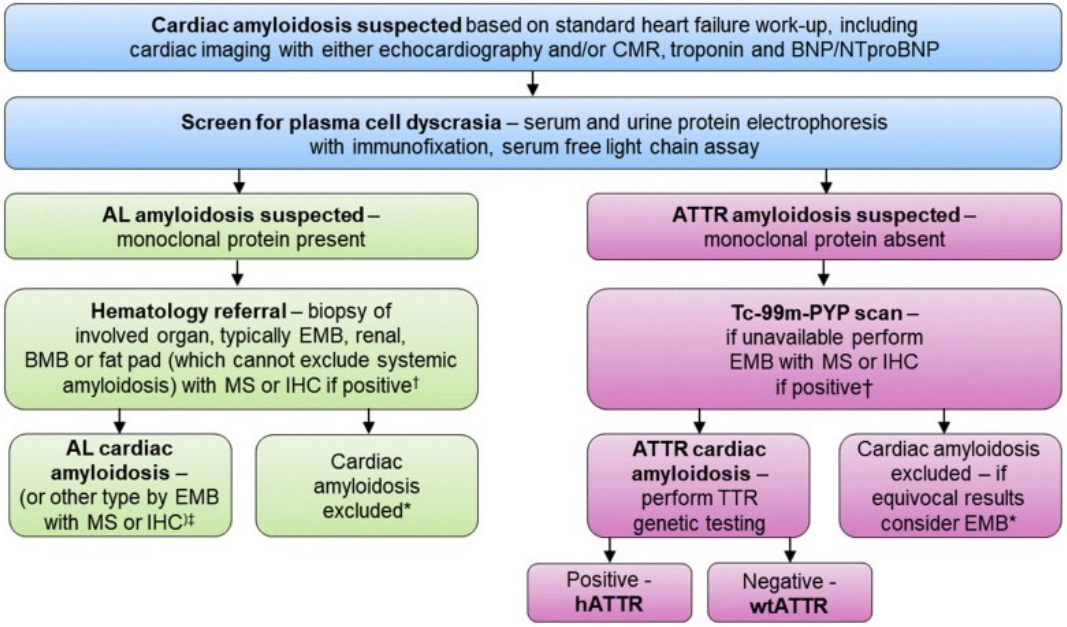
- augmentation de la fixation myocardique du radiotraceur, qui est ≥ à la fixation osseuse (grade ≥ 2)
- comparaison quantitative avec la fixation sur le poumon controlatéral (rapport h/cl ≥ 1,5)

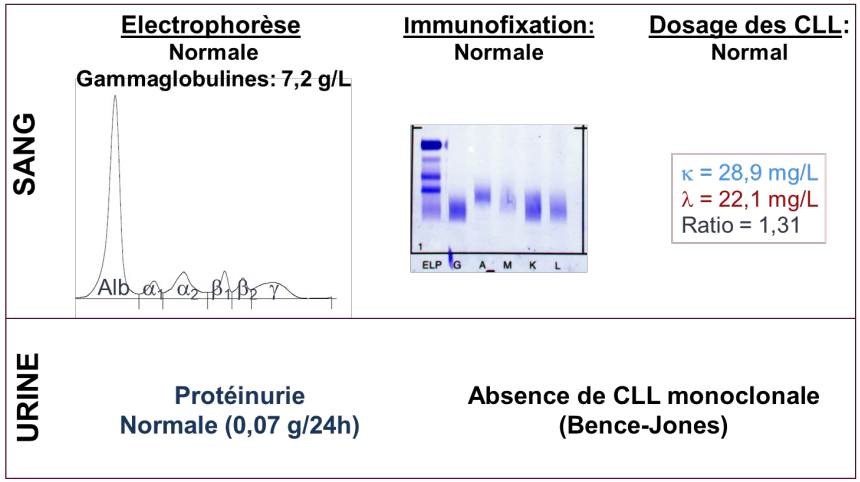
GRADE 2 OR 3 POSITIF = **SPECIFICITÉ ET VPP >98%**



ATTENTION AUX FAUX GRADE 1 !

ALGORITHME DÉCISIONNEL

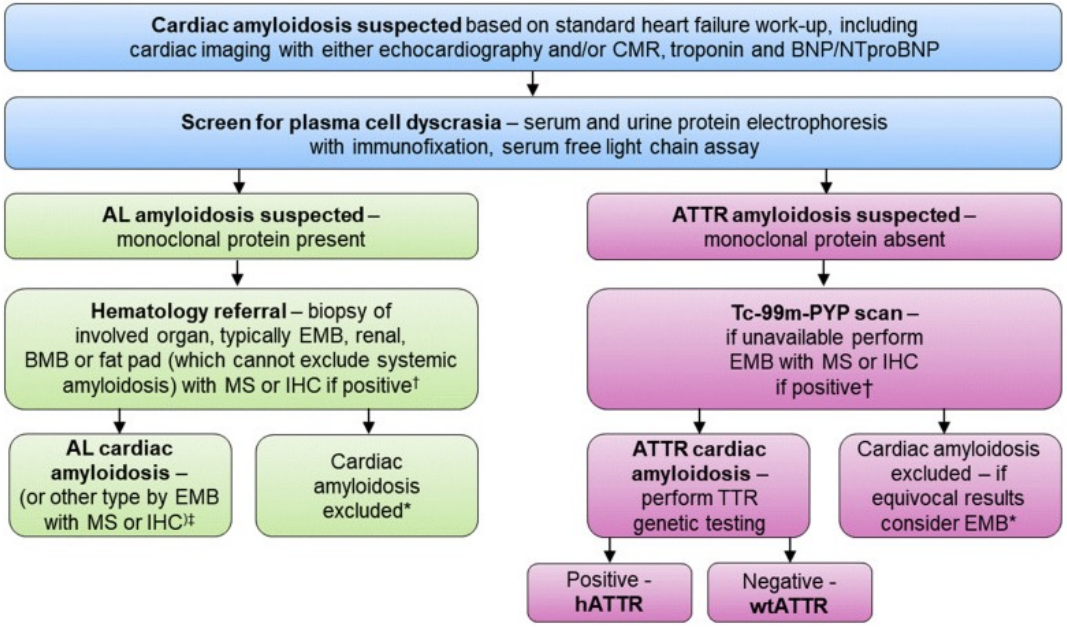




CCS guidelines 2020
Fine N.M., Davis M.K., Anderson K. and al.
CJC 2020 March;36(3):322-34
Accessible en ligne: https://doi.org/10.1016/j.cjca.2019.12.034

Courtesy of T Damy

ALGORITHME DÉCISIONNEL



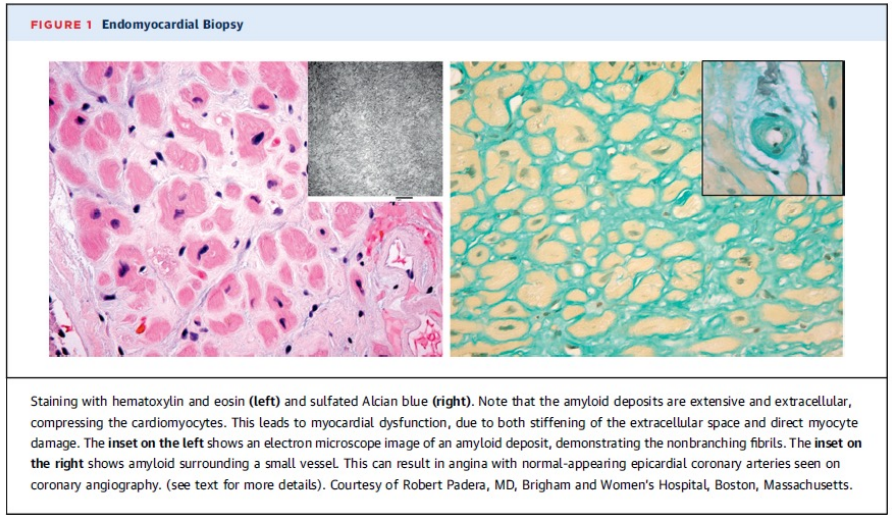


FIGURE 1 Endomyocardial Biopsy

Staining with hematoxylin and eosin **(left)** and sulfated Alcian blue **(right)**. Note that the amyloid deposits are extensive and extracellular, compressing the cardiomyocytes. This leads to myocardial dysfunction, due to both stiffening of the extracellular space and direct myocyte damage. The **inset on the left** shows an electron microscope image of an amyloid deposit, demonstrating the nonbranching fibrils. The **inset on the right** shows amyloid surrounding a small vessel. This can result in angina with normal-appearing epicardial coronary arteries seen on coronary angiography. (see text for more details). Courtesy of Robert Padera, MD, Brigham and Women's Hospital, Boston, Massachusetts.

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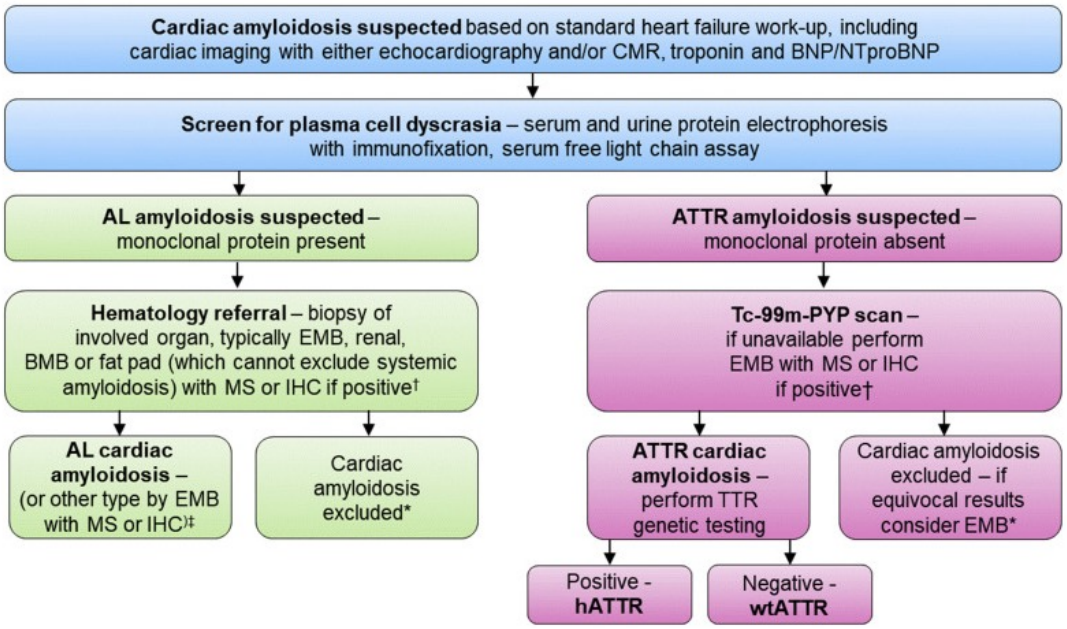
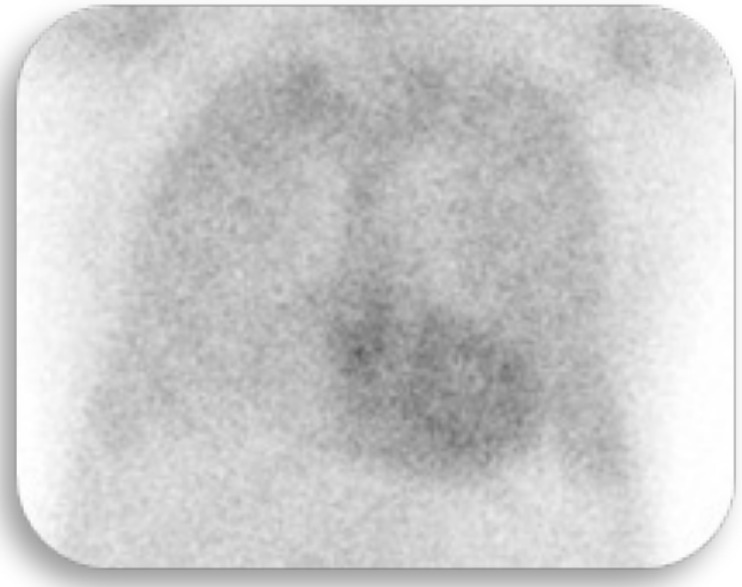
J Am Coll Cardiol 2016;68:1323–41

ALGORITHME DÉCISIONNEL





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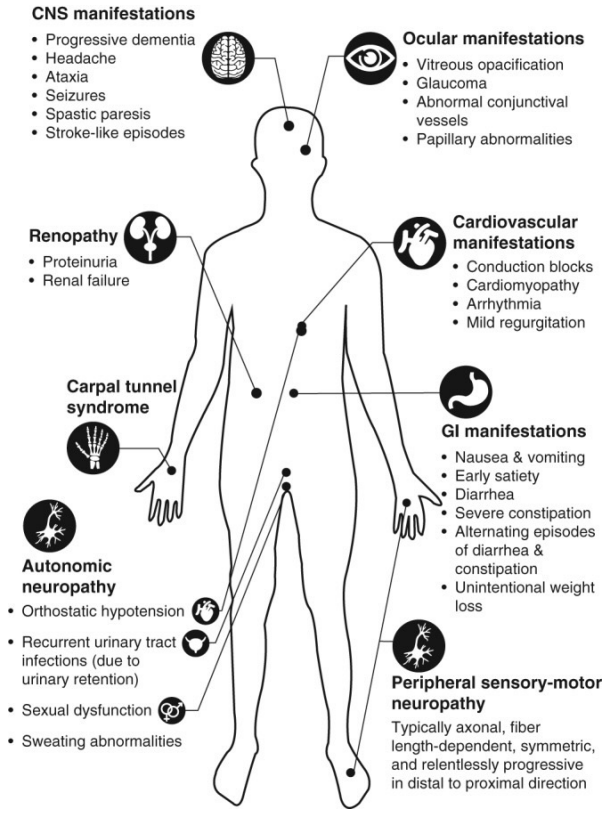
J Am Coll Cardiol 2016;68:1323–41

CHARGE

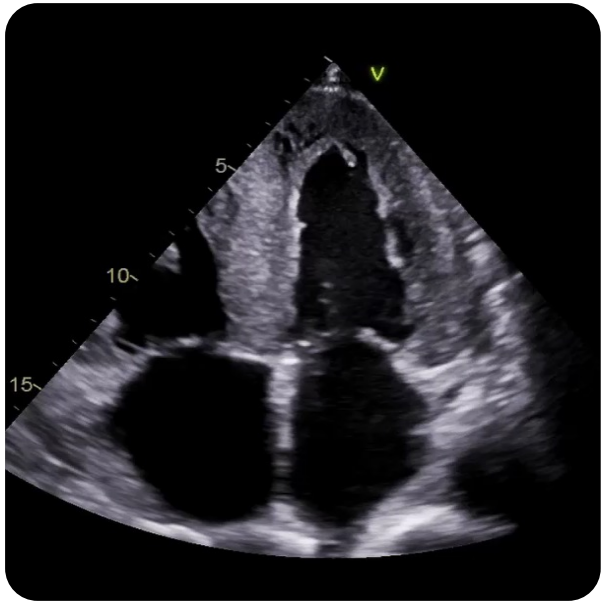


> 12 spécialités

- Cardiologie, Hémato-oncologie
- Médecine Interne, Neurologie, Néphrologie, Gériatrie
- Gastro-entérologie, Hépatologie, Chirurgie de la main
- Radiologie, Médecine Nucléaire, Anatomo-Pathologie, Génétique
- Psychologie, Pharamacie…

Importance de la multi- disciplinarité +++

LES TRAITEMENTS SPÉCIFIQUES EN AL



BORTEZOMIB, CYCLOPHOSPHAMIDE ET DEXAMETHASONE

TRANSPLANTATION DE CELLULES SOUCHES AUTOLOGUES

DARATUMUBAB

TABLE 5 Common Chemotherapy/Immunotherapy Agents in AL Amyloidosis

	Examples	First Line?	Notable Toxicities
Steroids	Dexamethasone, prednisone	Yes	Hyperglycemia, neuropsychiatric effects, edema, immunosuppression
Alkylators	Melphalan, cyclophosphamide	Commonly	Myelosuppression, stomatitis
Proteasome inhibitors	Bortezomib, carfilzomib, ixazomib	Commonly	Neuropathy, thrombocytopenia, shingles reactivation, thrombosis/hypertension/cardiotoxicity (carfilzomib)
Immunomodulators	Lenalidomide, pomalidomide	Occasionally	Myelosuppression, rash, neuropathy, thrombosis, birth defects
Anti-CD38 Antibody	Daratumumab	No (ANDROMEDA trial investigating) (66)	Infusion reaction, hypogammaglobulinemia
Anti-SLAMF7 antibody	Elotuzumab	No	Infusion reaction, hypogammaglobulinemia

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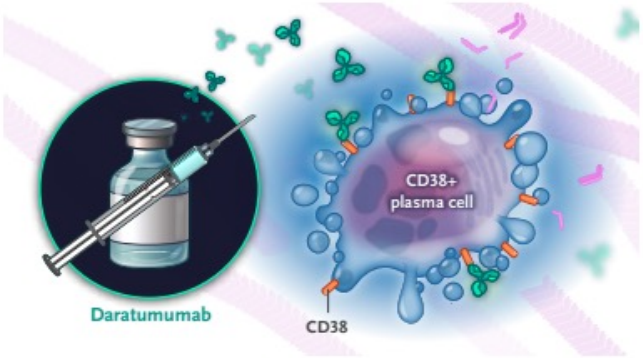
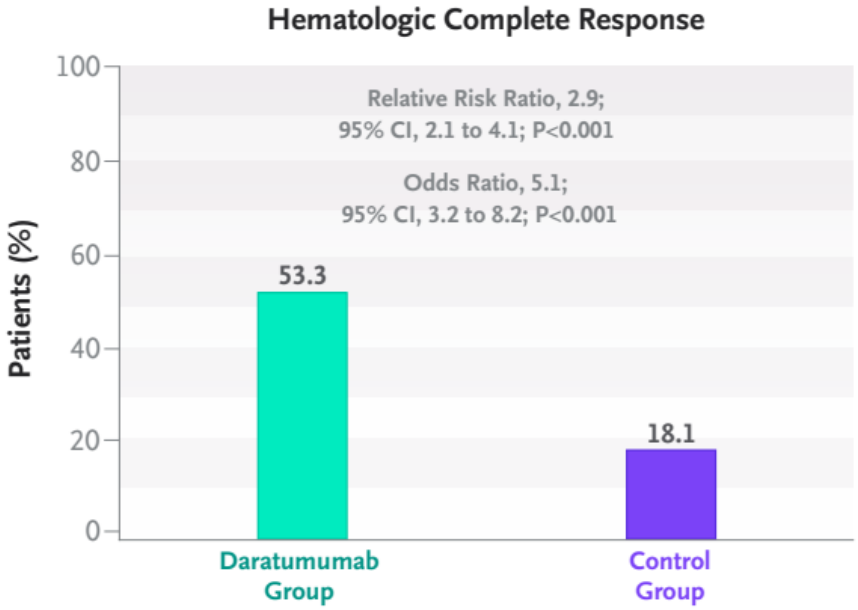


Daratumumab-Based Treatment for Immunoglobulin Light-Chain Amyloidosis

Kastritis E et al. DOI: 10.1056/NEJMoa2028631



Most Common Adverse Events of Grade 3 or 4

	Daratumumab Group (N=193)	Control Group (N=188)
Lymphopenia	13.0%	10.1%
Pneumonia	7.8%	4.3%
Cardiac Failure	6.2%	4.8%
Diarrhea	5.7%	3.7%

LES TRAITEMENTS USUELS DE LA CARDIOLOGIE

MANAGEMENT OF CARDIAC SEQUELAE

- Cautious use or avoidance of β-blockers, calcium channel blockers, ACEI/ARBs and digoxin
- Diuresis
- Anticoagulation for atrial fibrillation/flutter
- Pacemaker implantation for symptomatic bradycardia
- Defibrillator implantation for secondary prevention in appropriate patients
- Consideration of heart transplantation for highly selected patients

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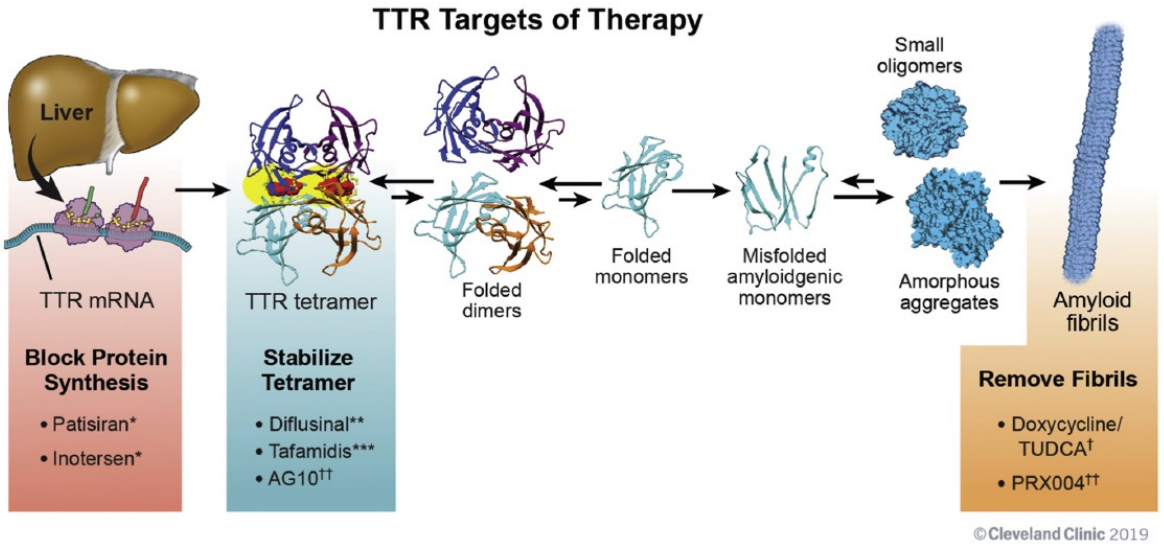
LES TRAITEMENTS SPÉCIFIQUES EN ATTR



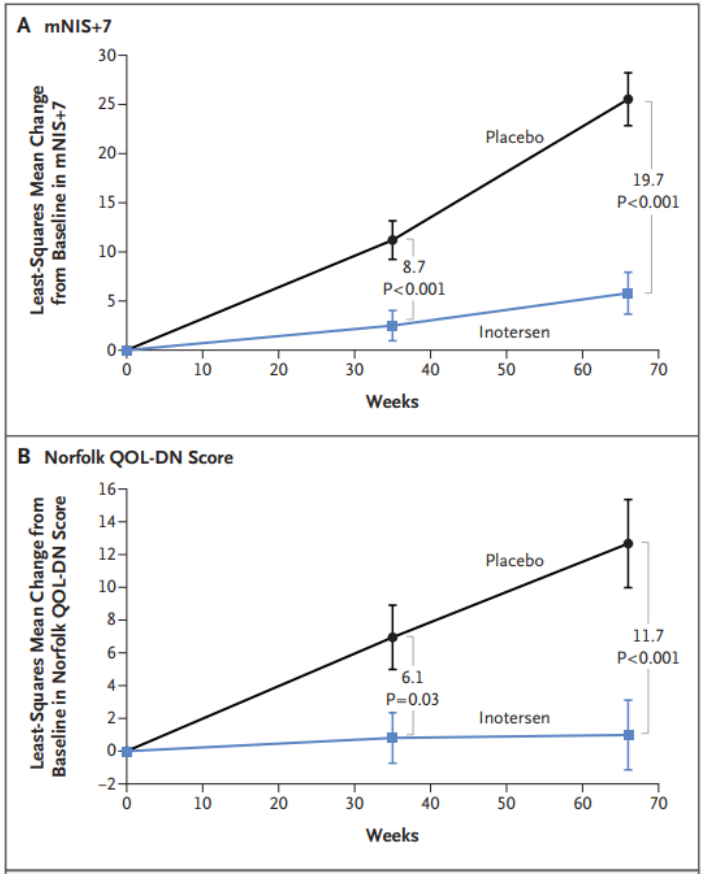
Ruberg, F.L., Grogan M., Hanna M. and al. J Am Coll Cardiol. 2019;73(22):2872–91.
Accessible en ligne: 10.1016/j.jacc.2019.04.003

ORIGINAL ARTICLE

Inotersen Treatment for Patients with Hereditary Transthyretin Amyloidosis

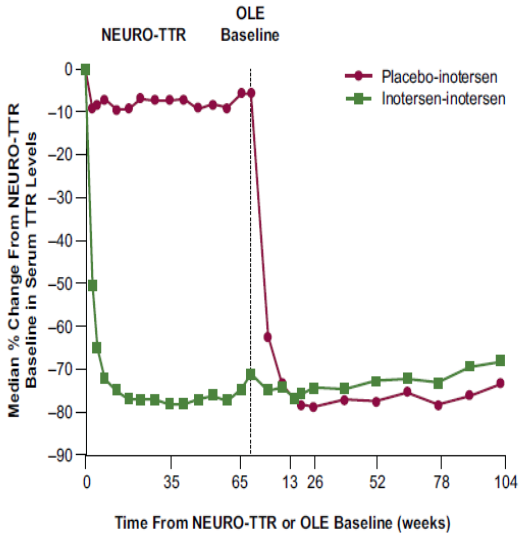
NEURO-TTR *- N Engl J Med 2018;379:22-31.*

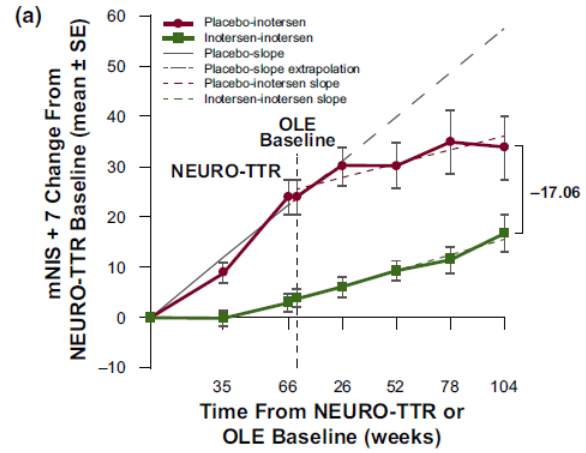
N=178 patients, R 2:1, mATTR, avec atteinte neurologique



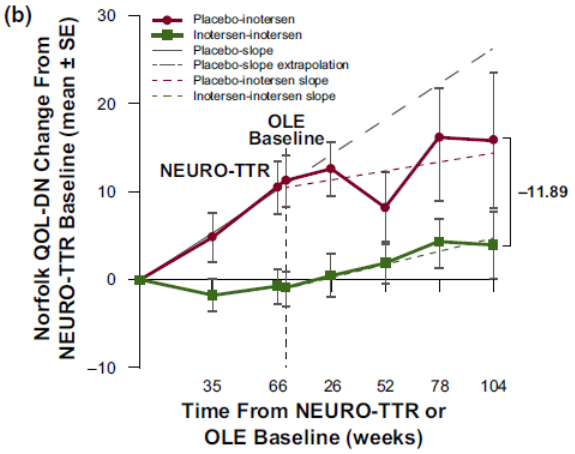
NEURO-TTR open-label extension

Brannagan et Al. 2020





Placebo-inotersen, *n*	49	50	49	47	34	22	19
Inotersen-inotersen, *n*	80	79	80	78	70	53	39



Benson M.D., Waddington-Cruz M., Berk J.L. and al.
N Engl J Med. 2018 Jul;379(1):22-31
Accessible en ligne: 10.1056/NEJMoa1716793

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JULY 5, 2018 VOL. 379 NO. 1

Patisiran, an RNAi Therapeutic, for Hereditary Transthyretin Amyloidosis

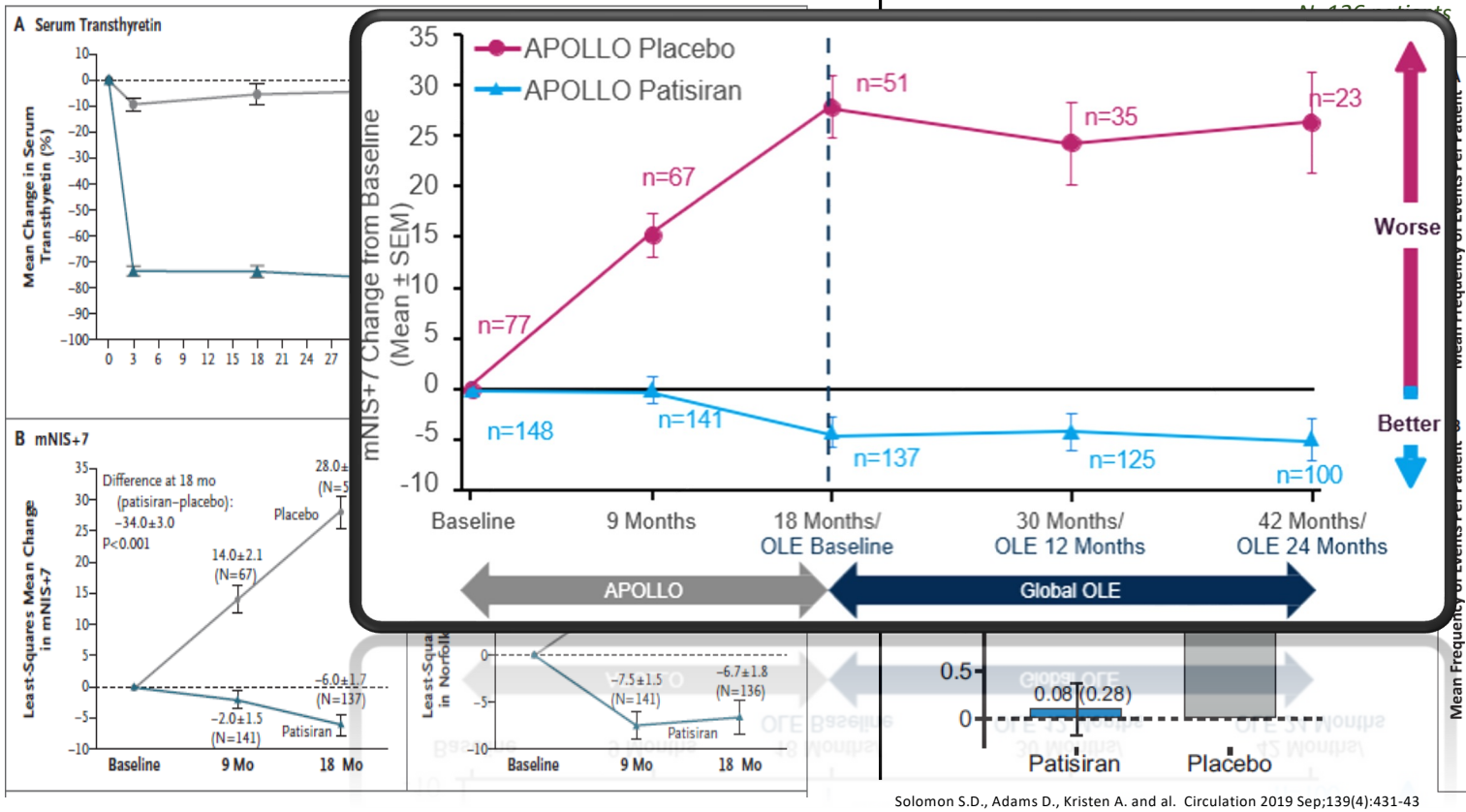
ORIGINAL RESEARCH ARTICLE

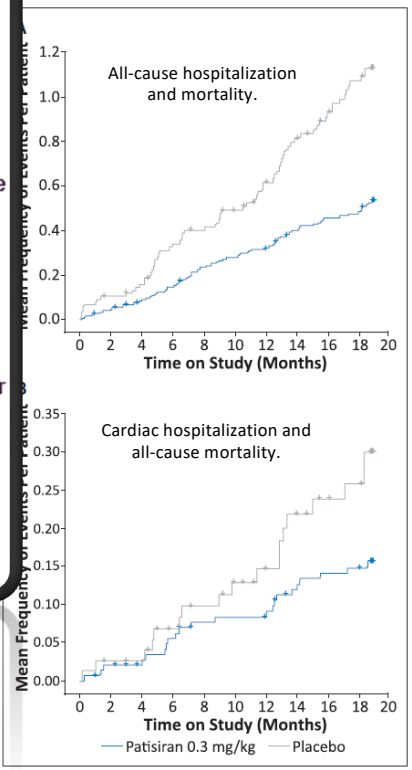
Effects of Patisiran, an RNA Interference Therapeutic, on Cardiac Parameters in Patients With Hereditary Transthyretin-Mediated Amyloidosis

Analysis of the APOLLO Study

N=225 patients, R 2:1, mATTR, avec neuropathie périphérique

Baseline LV wall thickness ≥13 mm and no history of aortic valve disease or hypertension.





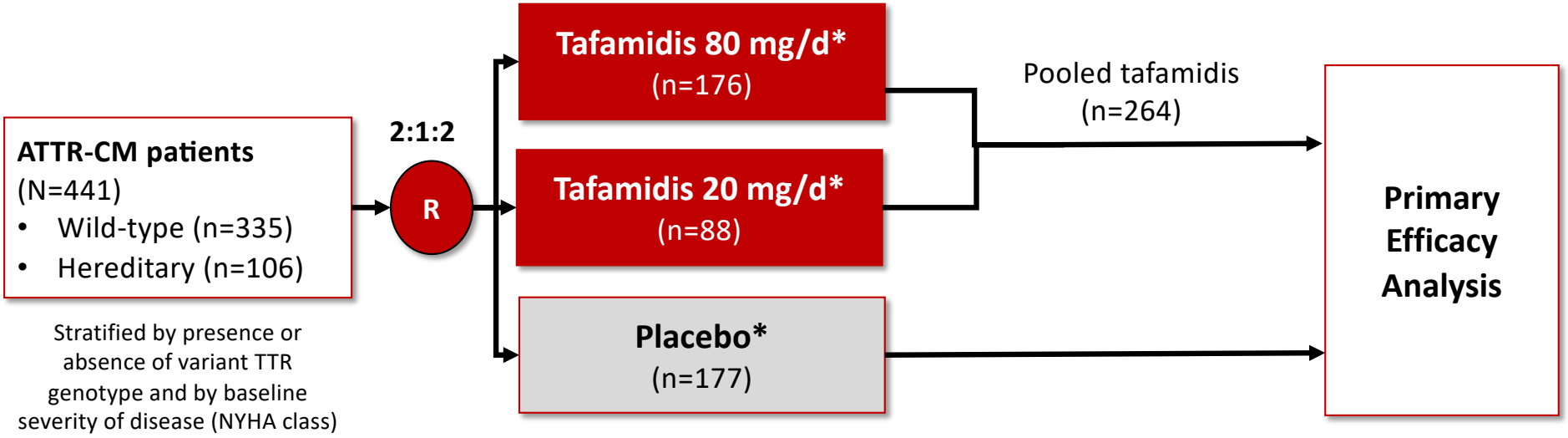
Solomon S.D., Adams D., Kristen A. and al. Circulation 2019 Sep;139(4):431-43
Accessible en ligne: https://doi.org/10.1161/CIRCULATIONAHA.118.035831

The NEW ENGLAND JOURNAL of MEDICINE

Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy

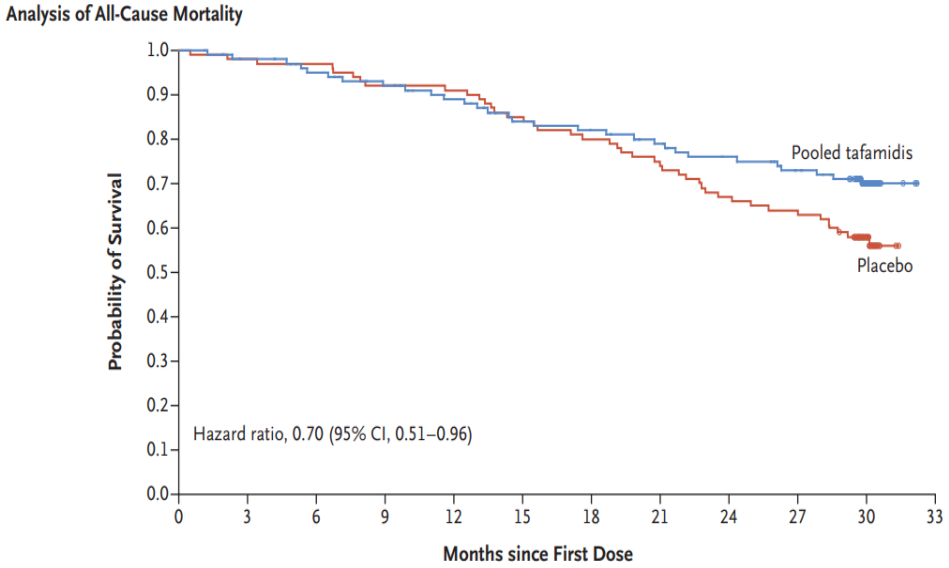
the ATTR-ACT Study

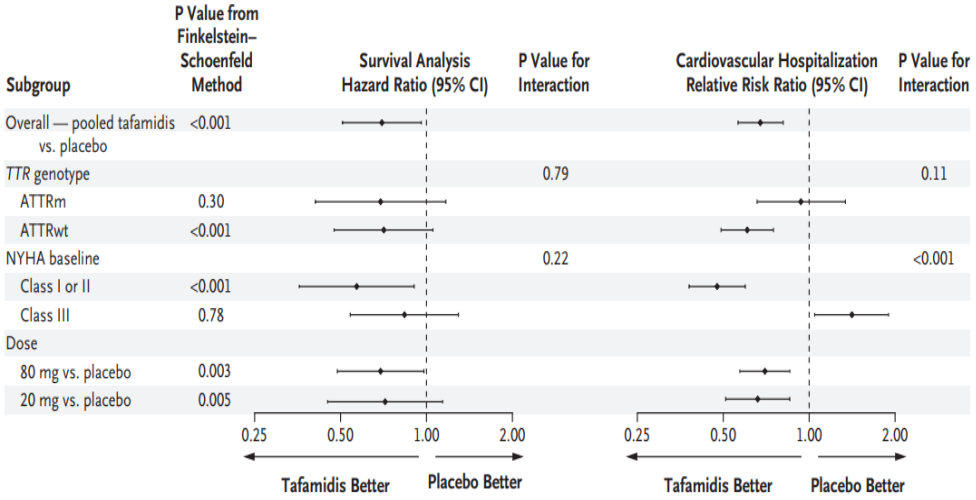
18 to 90 years of age
Medical history of HF with at least 1 prior hospitalization for HF or clinical evidence of HF (without hospitalization) manifested by signs or symptoms of volume overload or elevated intracardiac pressures that required/requires treatment with a diuretic for improvement
Evidence of cardiac involvement by echocardiography with an end-diastolic interventricular septal wall thickness > 12 mm
Presence of amyloid deposits in biopsy tissue and presence of a variant TTR genotype and/or TTR precursor protein identification by immunohistochemistry, scintigraphy or mass spectrometry

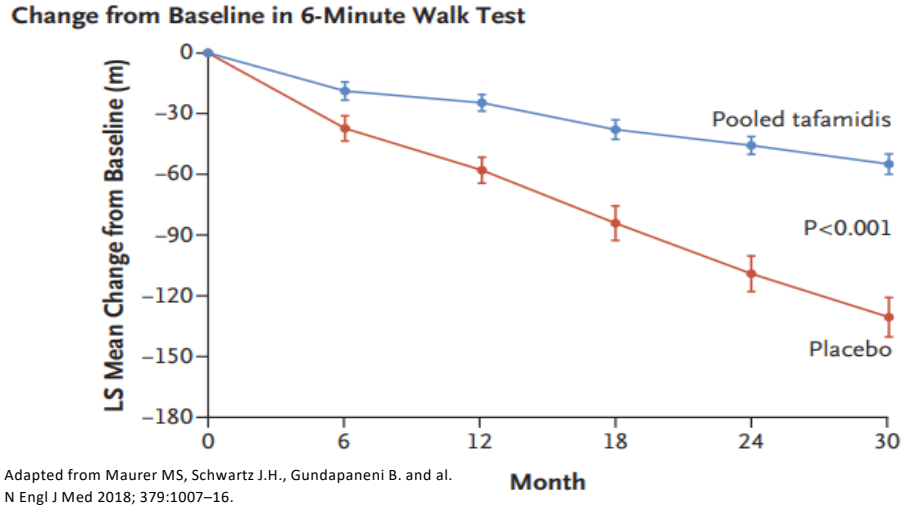


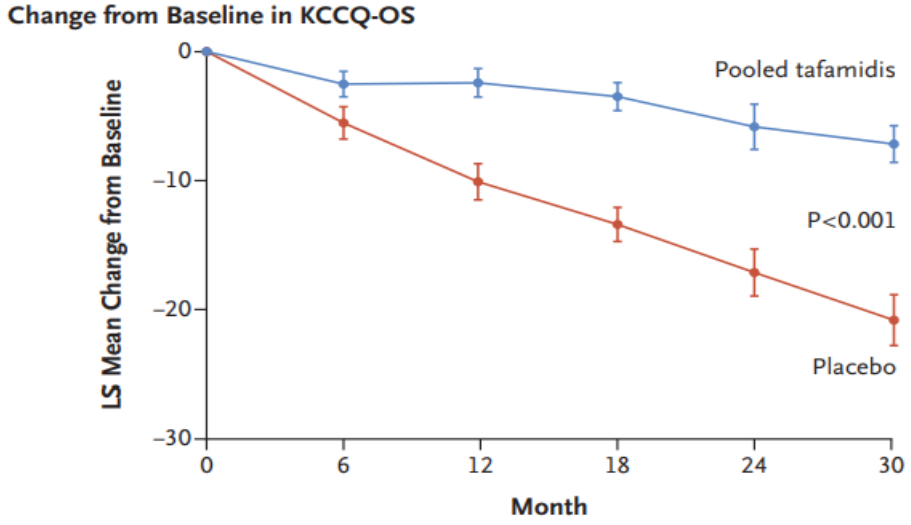
*each + standard of care (e.g., diuretics)

Adapted from Maurer MS, Schwartz J.H., Gundapaneni B. and al.
N Engl J Med 2018; 379:1007–16.
Accessible en ligne: 10.1056/NEJMoa1805689









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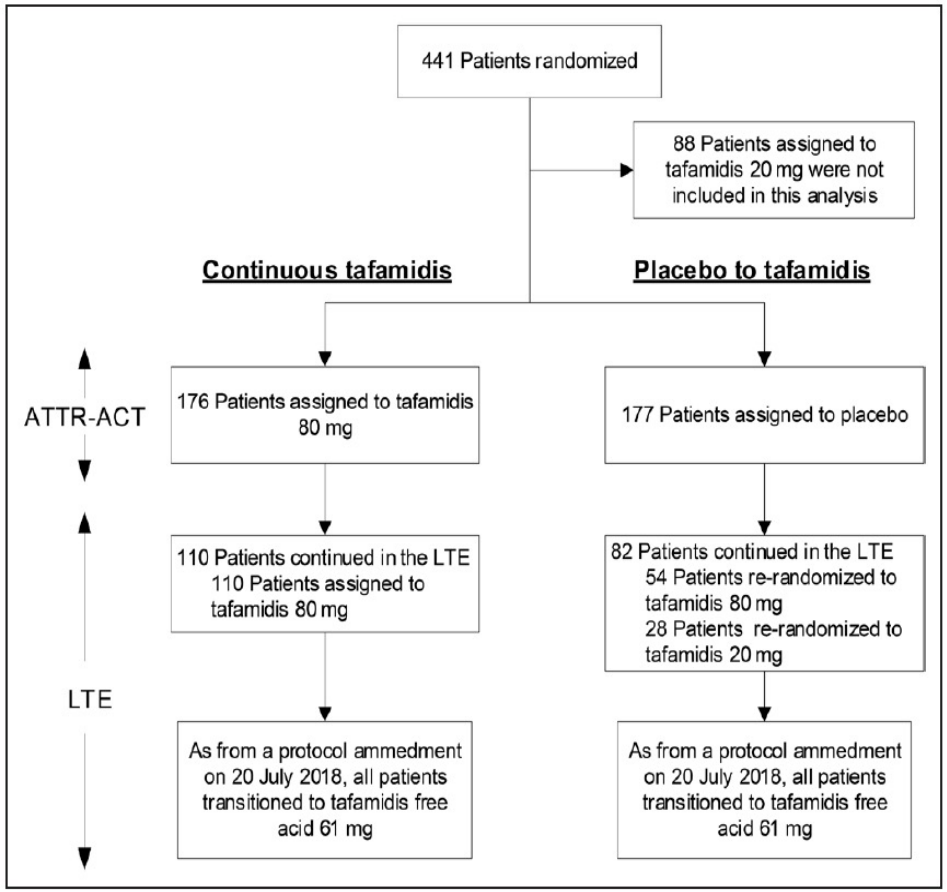
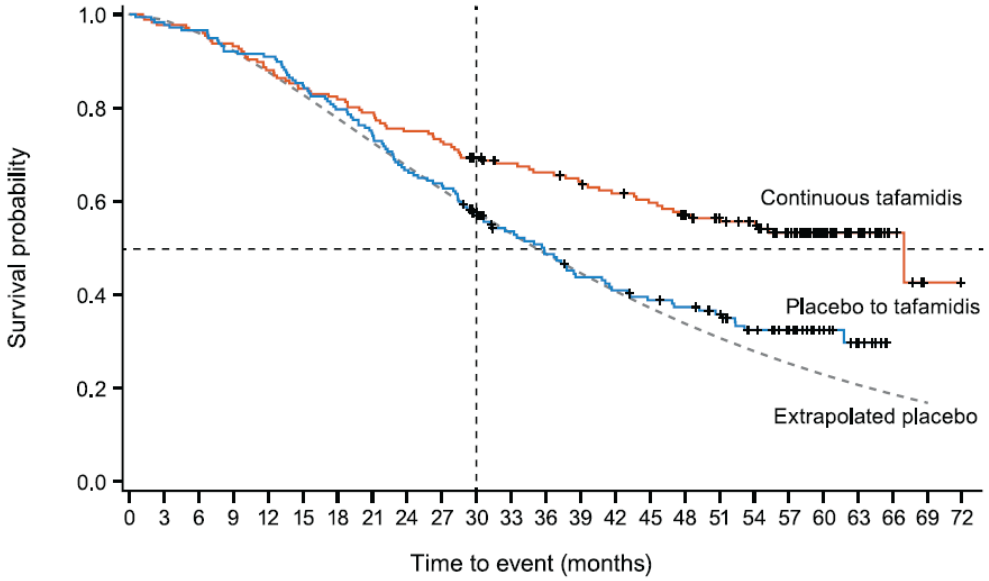


Circulation: Heart Failure

ORIGINAL ARTICLE

Long-Term Survival With Tafamidis in Patients With Transthyretin Amyloid Cardiomyopathy

Perry Elliott, MD; Brian M. Drachman, MD; Stephen S. Gottlieb, MD; James E. Hoffman, MD; Scott L. Hummel, MD; Daniel J. Lenihan, MD; Ben Ebede, MS, MBA; Balarama Gundapaneni, MS; Benjamin Li, MS; Marla B. Sultan, MD, MBA; Sanjiv J. Shah, MD



LES TRAITEMENTS USUELS DE LA CARDIOLOGIE

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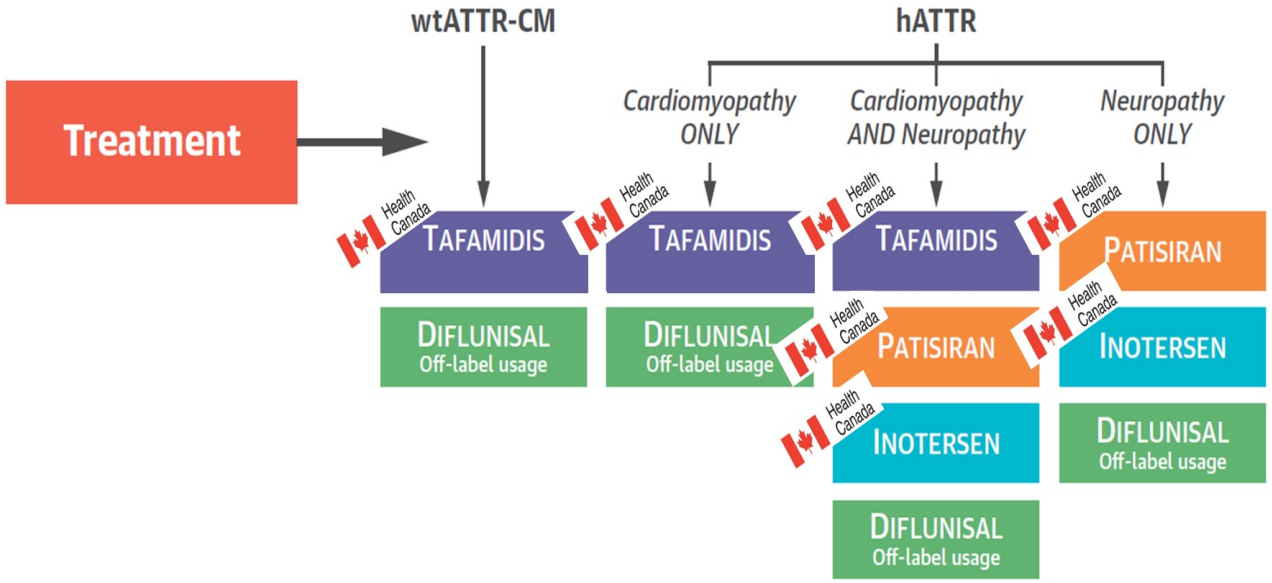


Ruberg, F.L., Grogan M., Hanna M. and al. J Am Coll Cardiol. 2019;73(22):2872–91.
Accessible en ligne: 10.1016/j.jacc.2019.04.003

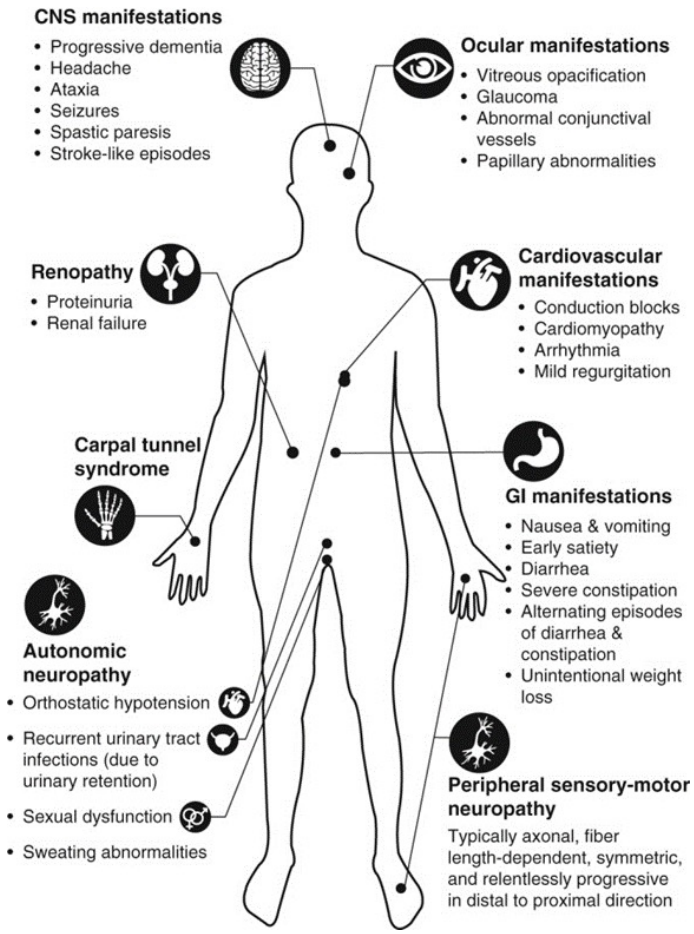
EN CONCLUSION, **I'AMYLOIDOSE…**

1) C'est d'abord y penser ! savoir porter notre regard partout

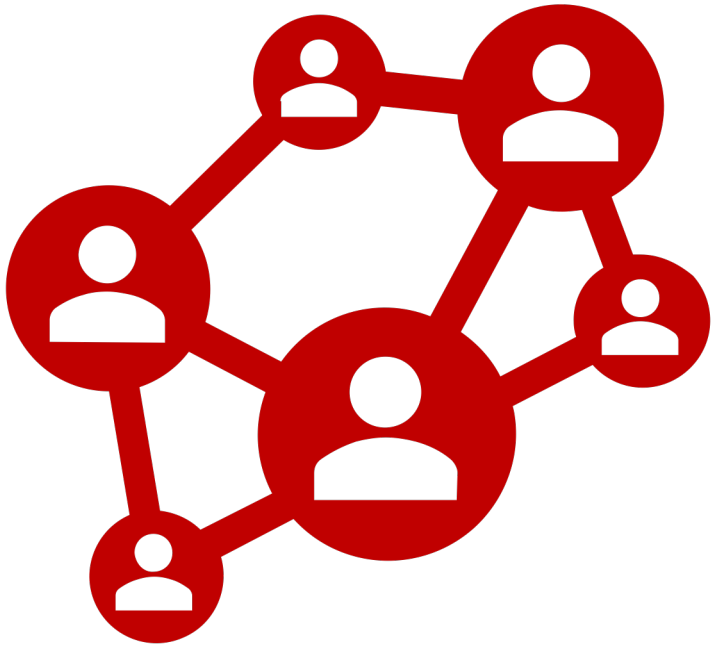
2) Structurer sa démarche diagnostique et savoir quel examen demander, quand et pour qui!

3) Avoir une trajectoire de soins bien définie, idéalement **multi-disciplinaire**

4) Avancées thérapeutiques majeures aussi bien en AL qu'en ATTR



Communauté de pratique au Québec en amyloïdose cardiaque



SQIC
SOCIÉTÉ QUÉBÉCOISE D'INSUFFISANCE CARDIAQUE

PROJET D'ÉDUCATION AMYLOÏDOSE

PROJET AMYLOÏDOSE

PROJET
Développer un programme provincial de formation pour PFS et un d'éducation pour les patients souffrant d'amyloïdose ainsi qu'un registre provincial de données permettant d'améliorer les connaissances en lien avec cette maladie

MANDAT

MANDAT
Élaborer différentes modalités de formation multidisciplinaire pour les professionnels de la santé
Développer un guide pratique de prise en charge de l'amyloïdose pour les professionnels
Produire un guide d'éducation pour les patients atteints d'amyloïdose
Élaborer différentes modalités d'éducation pour les patients
Proposer les éléments déterminants pour créer un registre québécois de données en amyloïdose

PROFESSIONNELS DE LA SANTÉ

- 3 Webinaires
- 3 Capsules cliniques — Amyloïdose AL-ATTR, Dépistage génétique
- Podcast
- Guide pratique

PATIENTS ET PROCHES

- Livret d'éducation
- 3 Capsules cliniques
- Témoignage de patients
- Conférence virtuelle

REGISTRE DE DONNÉES PROVINCIAL

Consensus d'experts pour développer une interface de données