Amylose cardiaque et patients âgés

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- Liens d’intérêts

Société	Type d’affiliation	Période
Amgen	Orateur	2025
Novartis	Consulting, Formations	2019-2023
Vifor	Consulting	2020-2022
Pfizer	Consulting, Formations, Boards, Expertise	En cours
Astra Zeneca	Consulting, Formations, Boards	En cours
Boehringer	Orateur	2023
Bayer	Orateur	2024
Alnylam	Consulting	2025

Amylose

- Vaste groupe de maladies
- Précurseur protéique s'agrège dans la matrice extracellulaire des tissus sous forme de feuillets ß plissés, stabilisé par la SAP (*serum amyloid P*)
- Actuellement 36 protéines amyloïdogènes (ou précurseurs)
- En histologie : dépôts Rouge Congo + et biréfringents jaune-vert en lumière polarisée
- Conséquences fonctionnelles : Épaississement / Rigidité / Dysfonction d'organe par mort cellulaire

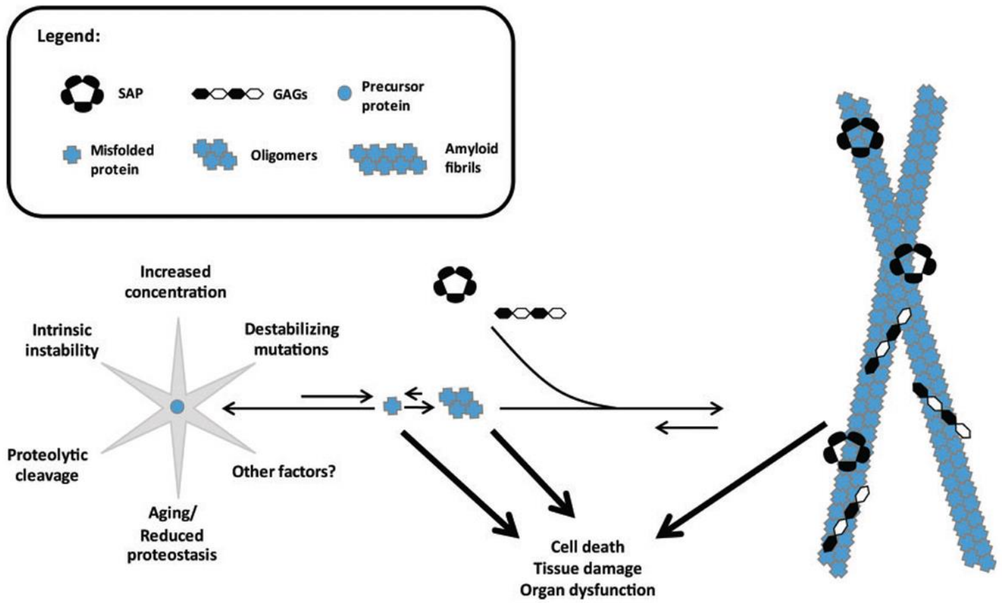

Table 1. Amyloid fibril proteins and their precursors in human[a].

Fibril protein	Precursor protein	Systemic and/or localised	Acquired or hereditary	Target organs
AL	Immunoglobulin light chain	S, L	A, H	All organs, usually except CNS
AH	Immunoglobulin heavy chain	S, L	A	All organs except CNS
AA	(Apo) serum amyloid A	S	A	All organs except CNS
ATTR	Transthyretin, wild type	S	A	Heart mainly in males, lung, ligaments, tenosynovium
	Transthyretin, variants	S	H	PNS, ANS, heart, eye, leptomeninges
Aβ2M	β2-microglobulin, wild type	S	A	Musculoskeletal system
	β2-microglobulin, variants	S	H	ANS
AApoAI	Apolipoprotein A I, variants	S	H	Heart, liver, kidney, PNS, testis, larynx (C terminal variants), skin (C terminal variants)
AApoAII	Apolipoprotein A II, variants	S	H	Kidney
AApoAIV	Apolipoprotein A IV, wild type	S	A	Kidney medulla and systemic
AApoCII	Apolipoprotein C II, variants	S	H	Kidney
AApoCIII	Apolipoprotein C III, variants	S	H	Kidney
AGel	Gelsolin, variants	S	H	Kidney PNS, cornea
ALys	Lysozyme, variants	S	H	Kidney
ALECT2	Leukocyte chemotactic factor-2	S	A	Kidney, primarily
AFib	Fibrinogen α, variants	S	H	Kidney, primarily
ACys	Cystatin C, variants	S	H	CNS, PNS, skin
ABri	ABriPP, variants	S	H	CNS
ADan[b]	ADanPP, variants	L	H	CNS
Aβ	Aβ protein precursor, wild type	L	A	CNS
	Aβ protein precursor, variant	L	H	CNS
AαSyn	α-Synuclein	L	A	CNS
ATau	Tau	L	A	CNS
APrP	Prion protein, wild type	L	A	CJD, fatal insomnia
	Prion protein variants	L	H	CJD, GSS syndrome, fatal insomnia
	Prion protein variant	S	H	PNS
ACal	(Pro)calcitonin	L	A	C-cell thyroid tumours
		S	A	Kidney
AIAPP	Islet amyloid polypeptide[c]	L	A	Islets of Langerhans, insulinomas
AANF	Atrial natriuretic factor	L	A	Cardiac atria
APro	Prolactin	L	A	Pituitary prolactinomas, aging pituitary
AIns	Insulin	L	A	Iatrogenic, local injection
ASPC[d]	Lung surfactant protein	L	A	Lung
ACor	Corneodesmosin	L	A	Cornified epithelia, hair follicles
AMed	Lactadherin	L	A	Senile aortic, media
AKer	Kerato-epithelin	L	A	Cornea, hereditary
ALac	Lactoferrin	L	A	Cornea
AOAAP	Odontogenic ameloblast-associated protein	L	A	Odontogenic tumours
ASem1	Semenogelin 1	L	A	Vesicula seminalis
AEnf	Enfurvitide	L	A	Iatrogenic
ACatK[e]	Cathepsin K	L	A	Tumour associated
AEFEMP1[e]	EGF-containing fibulin-like extracellular matrix protein 1 (EFEMP1	L	A	Portal veins Aging associated

Benson et al. Amyloid. 2020 Dec;27(4):217-222 ; Nuvolone et al. Nephrol Dial Transplant. 2017 May 1;32(5):770-780

Amylose

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Réseau Amylose

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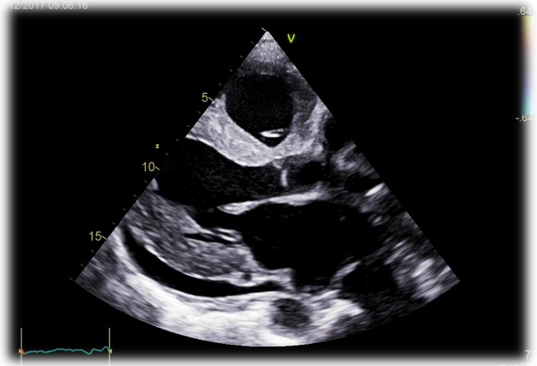


Benson et al. Amyloid. 2020 Dec;27(4):217-222

Epidémiologie

- En « vraie » vie (TTR ++ et AL)

- Dans les séries histologiques (AL et TTR)

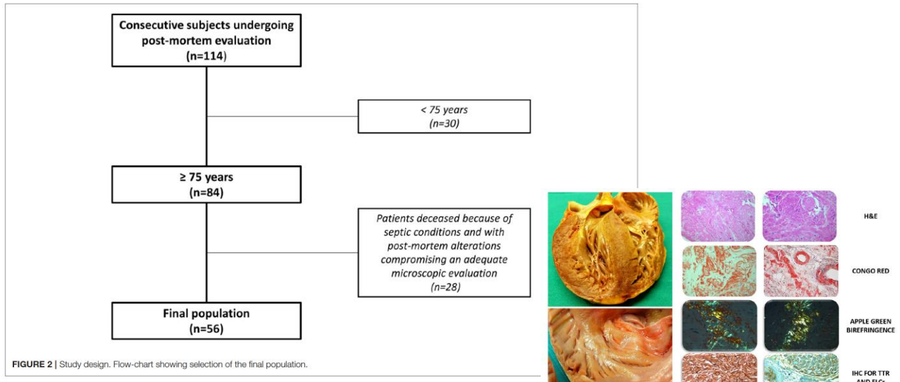


FIGURE 2 | Study design. Flow-chart showing selection of the final population.

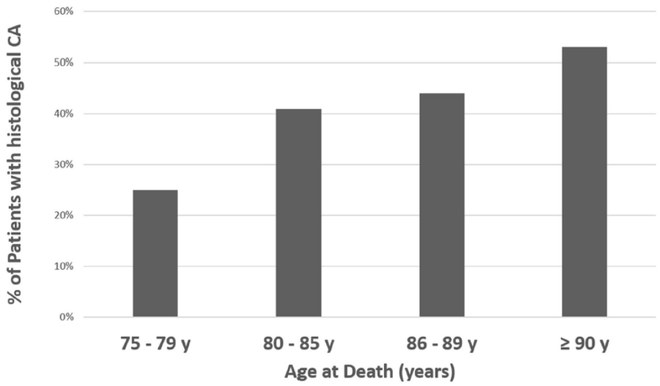


FIGURE 3 | Prevalence of CA (any site) at autopsy according to age at death. %, percentage; CA, Cardiac Amyloidosis.

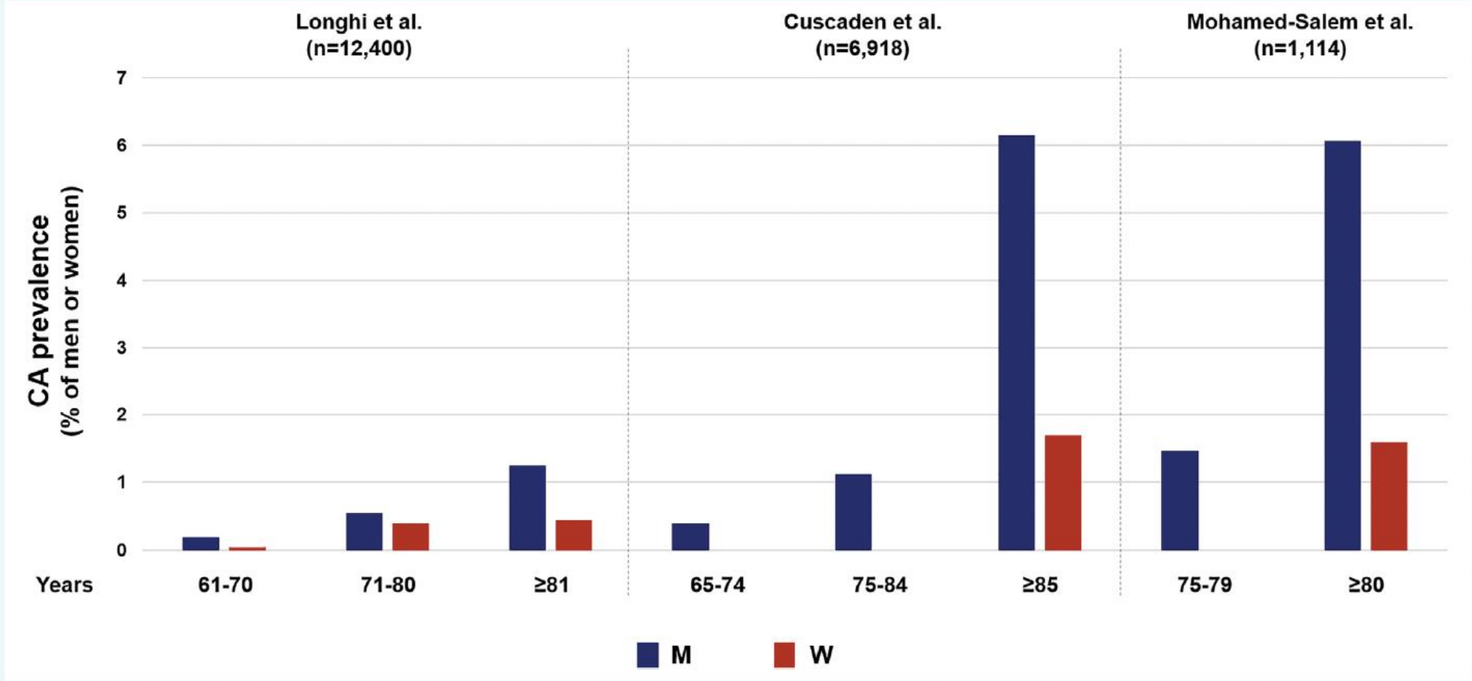


Figure 2 Prevalence of incidental myocardial uptake of bone tracers among men (M) and women (W) from the general population. See *Table 1* for details on the original studies. CA, cardiac amyloidosis.

Porcary et al., Front Cardiovasc Med. 2021 Nov 23;8:749523 ; Aimo et al. European Journal of Heart Failure (2022) 24, 2342-2351.

Journal of Clinical Medicine

MDPI

Article

Estimating the Prevalence of Cardiac Amyloidosis in Old Patients with Heart Failure—Barriers and Opportunities for Improvement: The PREVAMIC Study

- A total of 453 patients ≥ 65 years with HF and an interventricular septum or posterior wall thickness > 12 mm were included.
- All patients underwent a 99mTc-DPD/PYP/HMDP scintigraphy and monoclonal bands were studied, following the current criteria for non-invasive diagnosis.

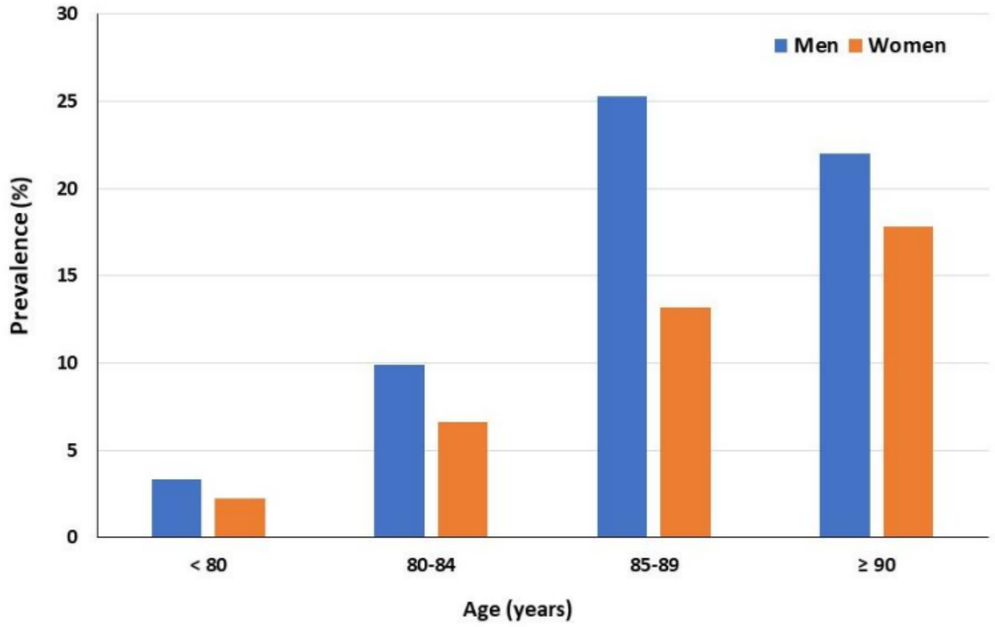


Figure 2. Cardiac amyloidosis prevalence according to age and sex.

The prevalence was **20.1%.** Most of the CA were transthyretin (**ATTR-CM**, 84.6%), with a minority of cardiac light-chain amyloidosis (AL-CM, 2.2%).

Revista Española de Geriatría y Gerontología 58 (2023) 8–14

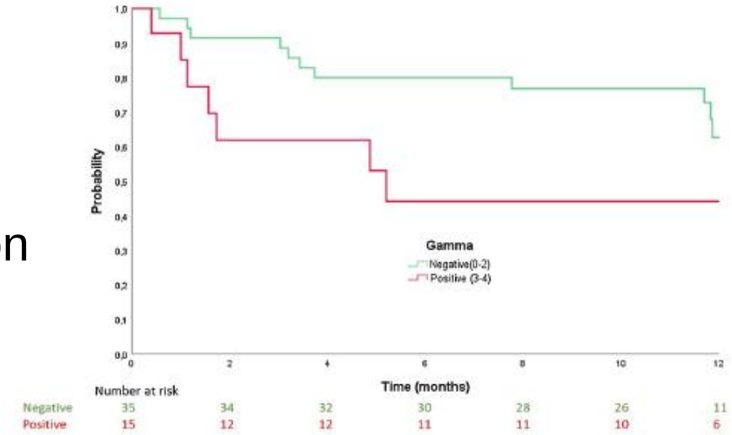
Revista Española de Geriatría y Gerontología

www.elsevier.es/regg

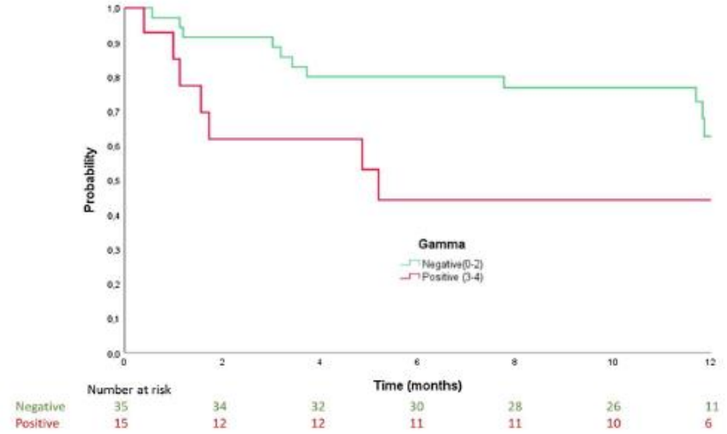
ORIGINAL ARTICLE

Prevalence of transthyretin cardiac amyloidosis in elderly patients diagnosed with heart failure

Death and HF Readmission



HF Readmission



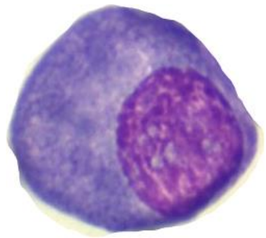
Ruiz-Hueso, JCM 2023

Jaramillo-Hidalgo et al. Revista Española de Geriatría y Gerontología 2023

Amylose(s) cardiaque(s)

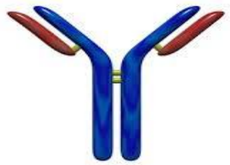
AP-HP. Hôpitaux universitaires Henri-Mondor

Réseau Amylose



Clone lympho ou plasmocytaire

MGUS, myélome, lymphome…

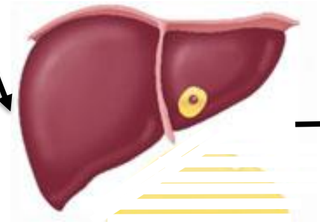


Chaînes légères d'Ig

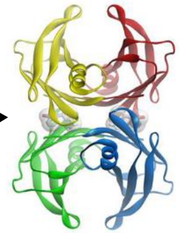
Lambda > kappa

Apolipoprotéine

AL



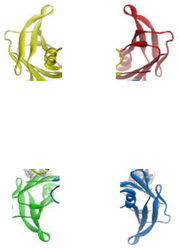
Foie



TTR

Tétramérique

Dissociation



TTR

monomérique

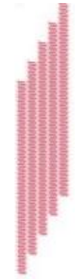
Mutation TTR -

Mutation TTR +

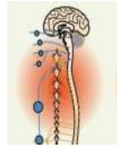
ATTR séniles

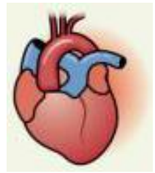
ATTR mutée

Dépôts de fibrilles amyloïdes



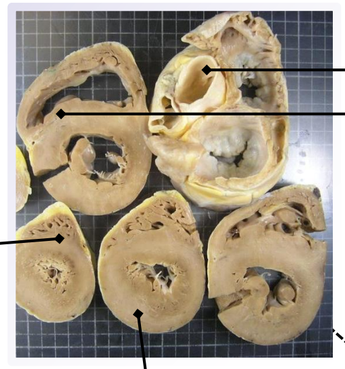
Cœur = pronostic





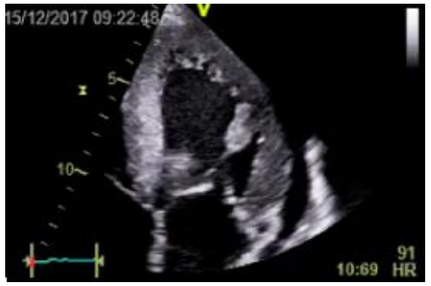
Conséquences cardiologiques

± Neuropathie périphérique sensitivo-motrice, symétrique et longueur dépendante



Myocarde

Ventriculaire

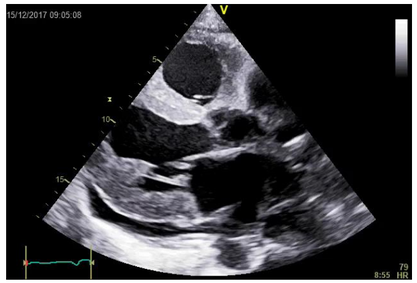


↗ Epaisseur
↗ Rigidité
Dysfct diastolique
Dysfct systolique
➔ **CMH** concentrique biventriculaire
➔ **CMR**
➔ **Insuffisance cardiaque**

Atrial

Dilatation bi-atriale
Infiltration SIA
↘ systole atriale
➔ **Emboles**, AVC ; AIT
➔ **TSV**

Péricarde

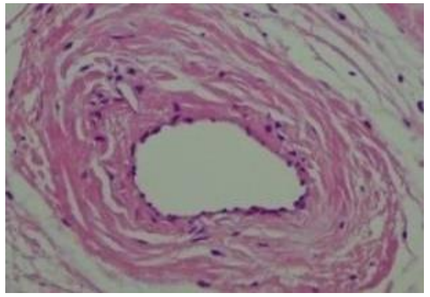


Ep. péricardique
Tamponnade

Endocarde

IM, IT
RAC

Vaisseaux



Ischémie
Nécrose
➔ DT atypique ; ↗ troponine

Tissus conductif

BAV, BSA, BB
➔ **Syncope**

SNA

↘ FC
hTOS
➔ Insuffisance chronotrope
➔ **Malaises** à l'orthostatisme

Conséquences cardiologiques – maladie des discordances

AP-HP. Hôpitaux universitaires Henri-Mondor

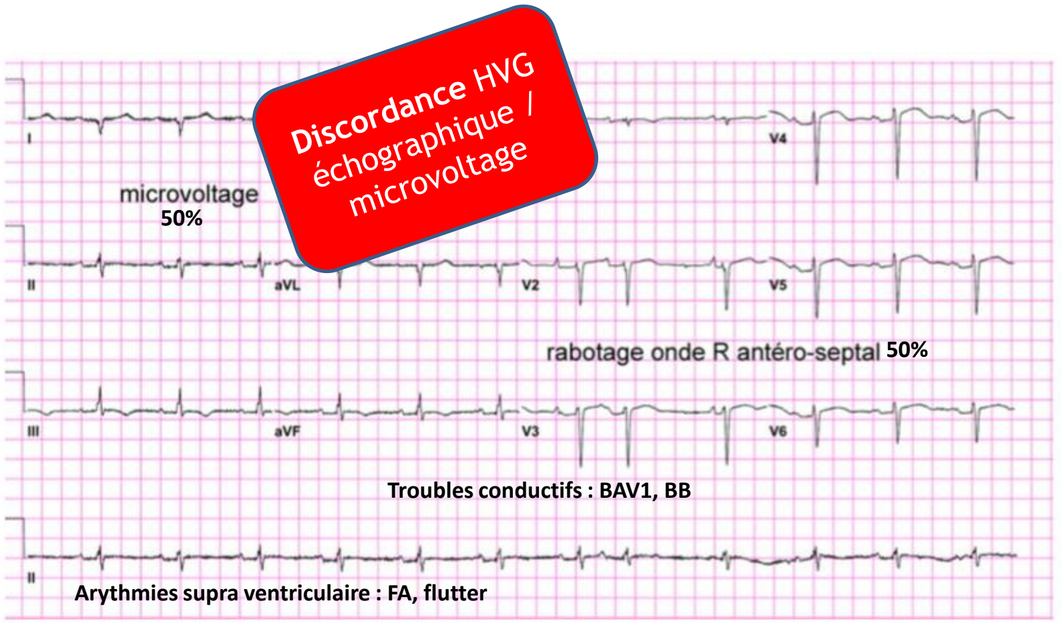
Réseau Amylose

En échocardiographie :

- CMH biventriculaire (> 12mm)
  - Homogène / concentrique
  - Epaississement des valves et du SIA
- Aspect brillant / granité du myocarde
- FEVG préservée (altéré à un stade tardif)
- Ventricule de taille normale / réduite
- Dilatation bi-atriale
- Epanchement péricardique de faible abondance
- Profil mitral restrictif (50% des cas)
- Diminution des vitesses du doppler tissulaire
- Altération du SGL avec épargne apicale (cocarde)

Discordance FEVG préservée / SGL altéré

A l'ECG :



A l'IRM cardiaque :

Morphologie : CMH concentrique biventriculaire
Rehaussement tardif : diffus, localisé, en rails
T1 mapping allongé (> 1,048 ms : différencie amylose vs autre CMH (Se 80% Sp 83%))
MAIS si normale, n'élimine pas le diagnostic

Biomarqueurs:

troponine et NTproBNP élevés

Discordance FEVG préservée / biomarqueurs élevés

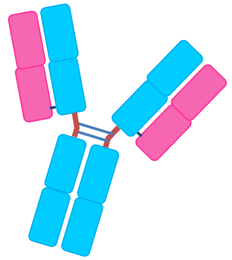
Fontana M et al, JACC Imaging, 2014

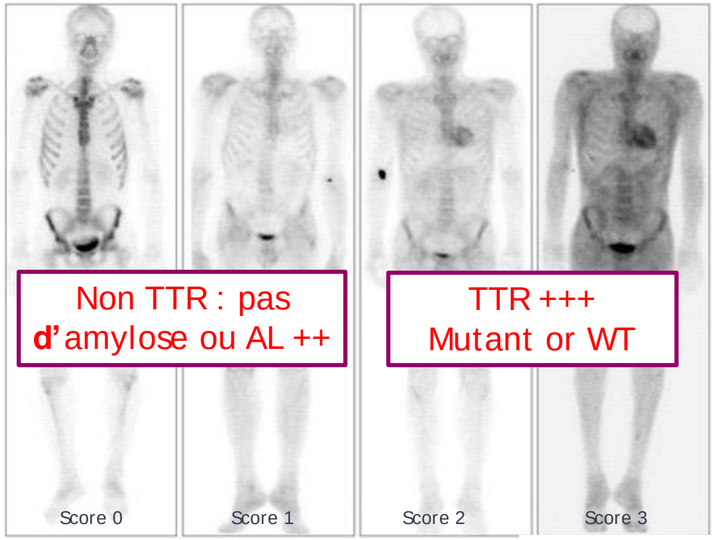
Examens morphologiques à la recherche d'arguments en faveur : ECG, ETT, IRM

Scintigraphie osseuse
(HMDP, DPD, PYP)

&

Bilan de gammapathie monoclonal complet
- EPP, IF
- EPU, IEPU (= Bence Jones)
- Dosage des chaînes légères libres circulantes





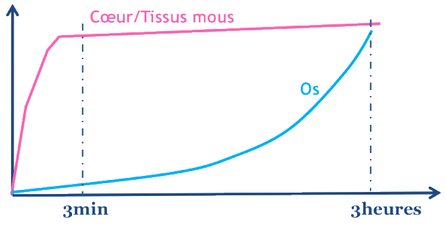
Non TTR : pas **d'**amylose ou AL ++

TTR +++
Mutant or WT

Pas de fixation cardiaque & fixation osseuse normale

Forte fixation cardiaque & extinction de la fixation osseuse

Score visuel de Perugini : en faveur d'une ATTR si ≥ 2



ou

Ratio (précoce) cœur / mediastin : en faveur d'une ATTR > 1,2

Electrophorèse des protides sériques : pic, hypogamma, normale

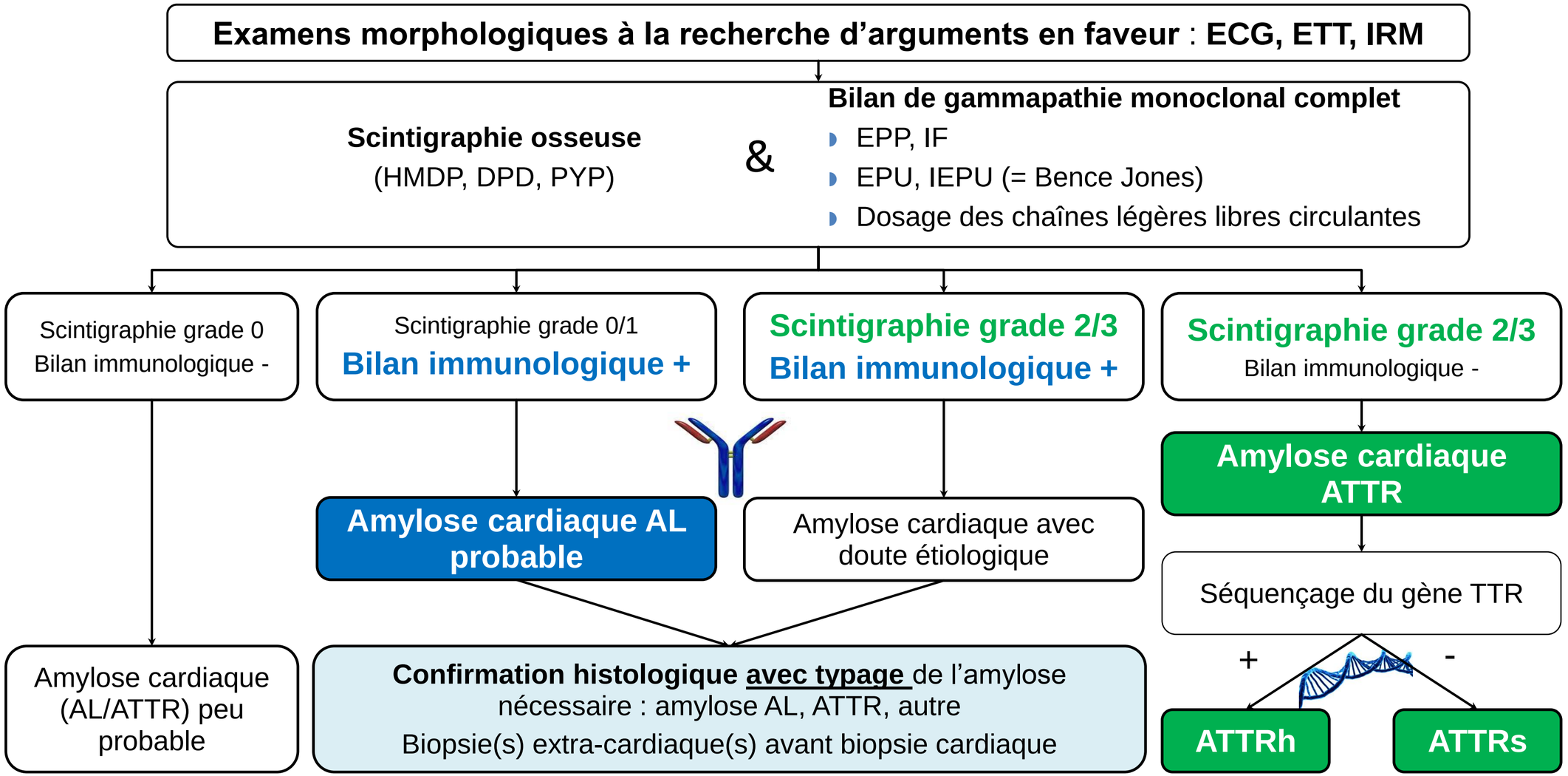
Immunofixation : plus sensible que l'électrophorèse

Dosage des chaines légères libres sériques : plus sensible que l'immunofixation. Dépend du niveau de production (plasmocyte) et d'élimination (rein)

Recherche d'une protéinurie de Bence Jones

Perugini et al., JACC 2005 Sep 20;46(6):1076-84 ; Galat A et al JACCardioVasc Imaging 2016

Comment poser le diagnostic ?



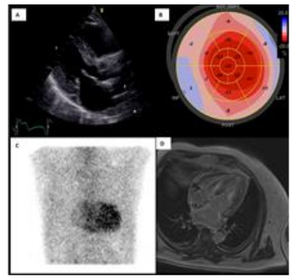
Adapté de Gillmore *et al.*, *Circulation*. 2016 Jun 14;133(24):2404-12.

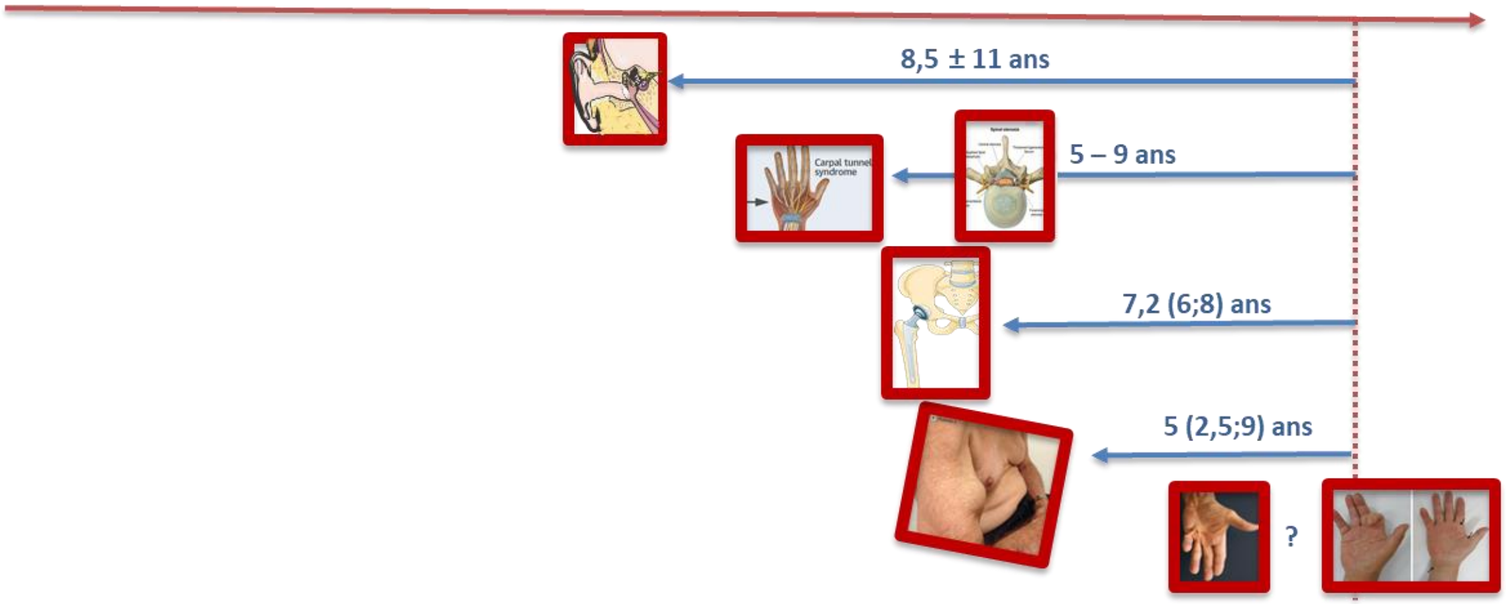
Amylose à transthyrétine sauvage

- Age d'apparition des symptomes cardiaques : 78 ans
- Symptômes extra-cardiaques (canal carpien ++) 5 à 10 ans avant
- Hommes 90%

- Prévalence sous-estimée
  - Dépôts d'amylose TTR sauvage ≈ 25% des plus de 80 ans (séries autopsiques)

- Mais de plus en plus reconnue





Tanskanen et al., Ann Med. 2008;40(3):232-9

Spécificités du traitement non spécifique

CHADS-TOP

Conduction

Mort subite : très fréquente quelque soit le type d'amylose : dissociation électro-mécanique, parfois TV/FV
Prévalence élevée des **troubles conductifs**
➔**Discussion implantation PM / DAI sur troubles conductifs de bas degré / sévérité**

Haute FC

Débit cardiaque = FC x VES
Cardiopathie restrictive donc VES constant : fréquence dependance pour augmenter le débit
➔ **Pas de bradycardisant (sauf amiodarone), PM pour insuffisance chronotrope**

Anticoagulation

Risque cardio-embolique élevé (même en rythme sinusal) ➔ **rechercher les indication à une anticoagulation (sd néphrotique, ATCD cardioembolique, profil mitral restrictif)**
Dosage facteur X pour pondérer le risque hémorragique

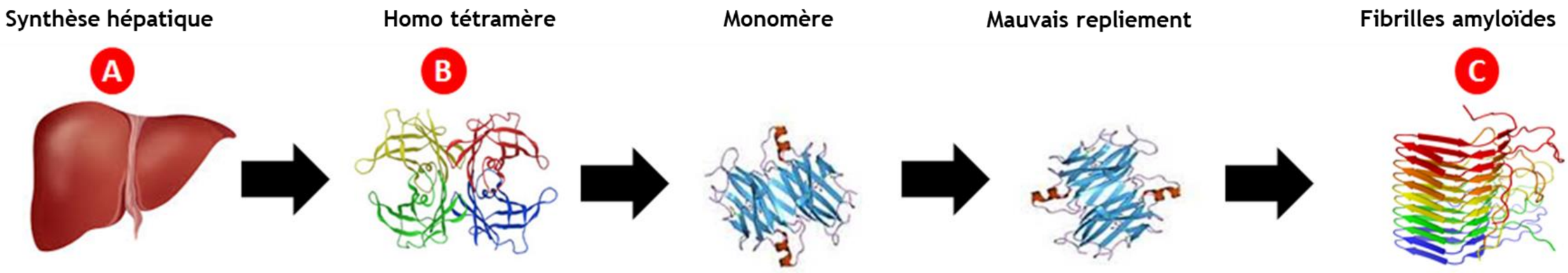
Diurétiques

Nécessaire pour la congestion mais marge thérapeutique étroite compte tenu du risque de dysautonomie

S-TOP BB, IEC, ….

Arrêt des traitements potentiellement délétères :
BB (bradycardie, inotrope -), Hypotenseurs (dysautonomie),
Digoxine (accumulation dans les fibrilles amyloïdes), Sacub/Valsartan

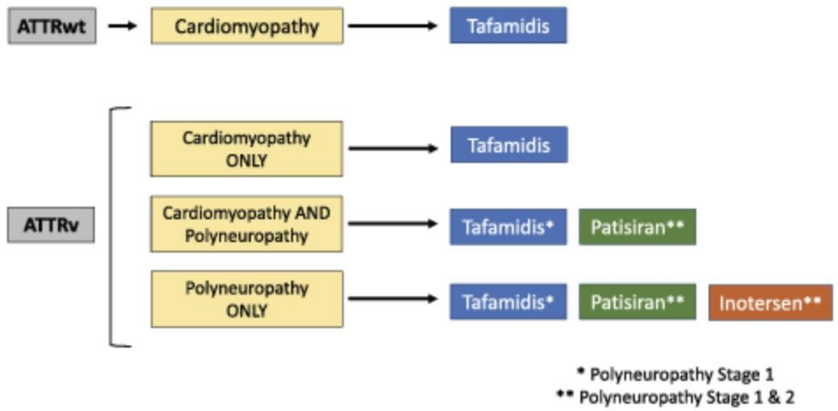
Traitement spécifique - amylose ATTR



A **Supprimer la TTR amyloidogénique** ⟹ siRNA : ARN interférant (ATTRwt et ATTRv) : APPOLLO B

B **Stabiliser le tétramère** ⟹ Stabilisateur du tétramère : tafamidis RTU initiale, AMM 06/2021

C **Dégrader les fibrilles amyloïdes** ⟹ AC anti TTR : études en cours



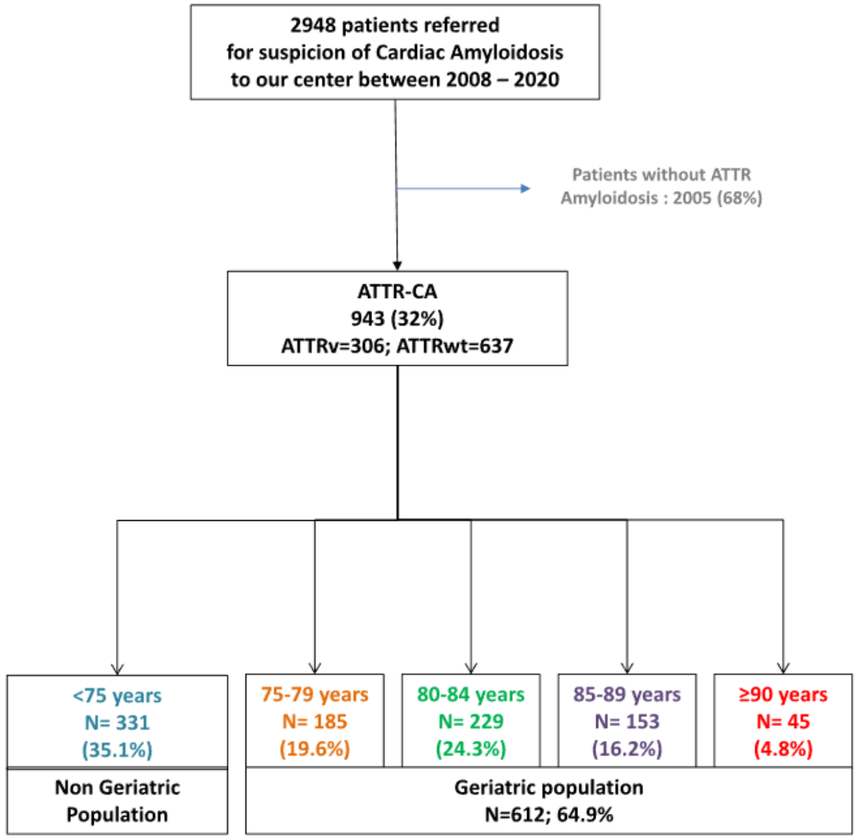
Garcia Pavia et al. Eur Heart J. 2021 Apr 21;42(16):1554-1568.

ESC HEART FAILURE
ESC Heart Failure (2024)
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.14793

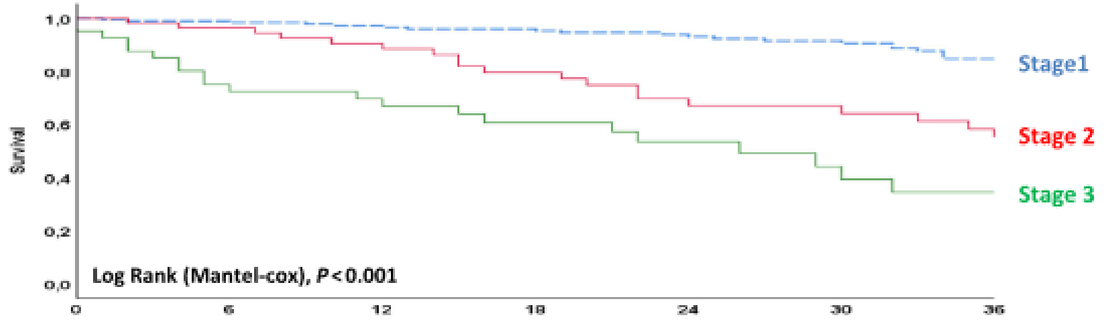
ORIGINAL ARTICLE

Phenotype and prognostic factors in geriatric and non-geriatric patients with transthyretin cardiomyopathy

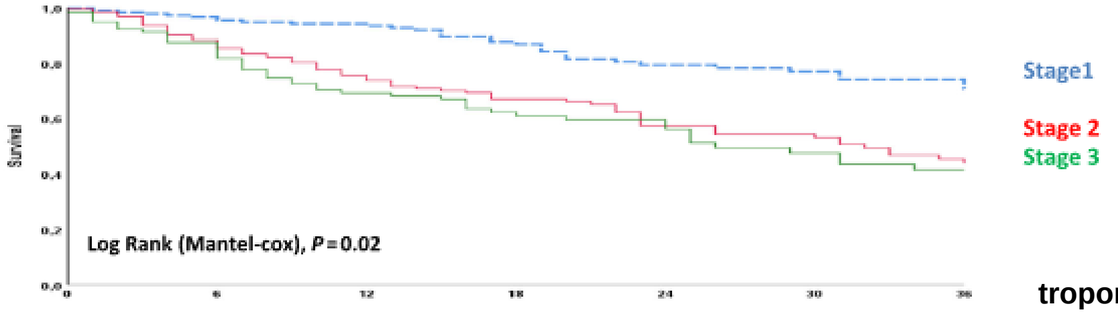
Eugenia Volpentesta[1,2], Mounira Kharoubi[3,4,5,6], Cristiano Donadio[2], Kahina Rebiai[3,4], Pascale Fanen[7], Benoit Funalot[5,7], Thierry Gendre[8,9], Vincent Audard[9,10], Florence Canoui-Poitrine[6,11,12], Emmanuel Itti[9,13,14], Emmanuel Teiger[3,4,5,6], Violaine Planté-Bordeneuve[8,9], Silvia Oghina[3,4], Denis Tixier[3,4], Sophie Mallet[3,4], Amaury Broussier[11,15], Thibaud Damy[3,4,5,6,11]* and Amira Zaroui[3,4,5,6,11]



(A-i) NAC - Non Geriatric population

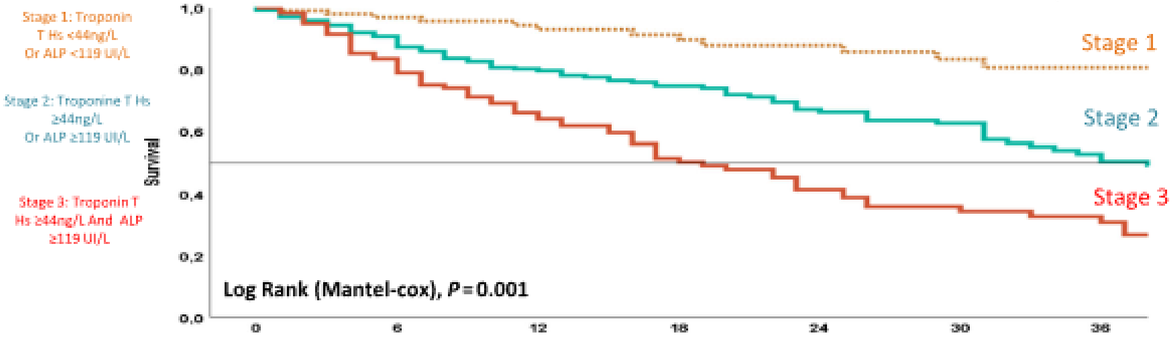


(A-ii) NAC - Geriatric population



troponin T hs (≥44 ng/L) and **ALP levels** (≥119 UI/L)

(B) New Geriatric cardiac amyloidosis staging (GCA) : for Geriatric pulation



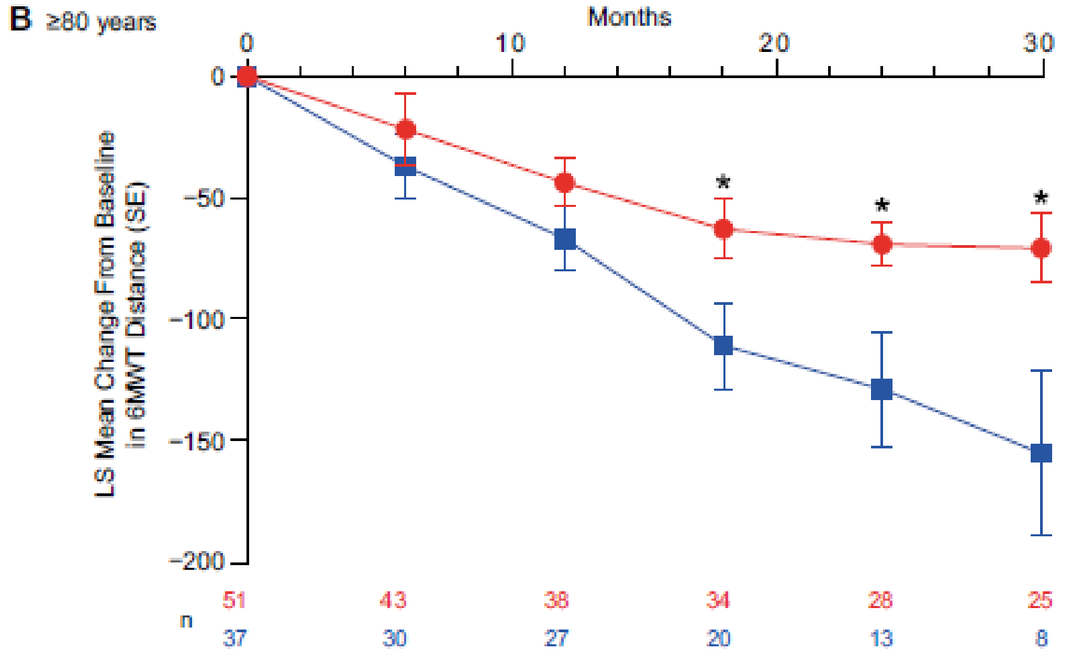
Volpentesta et al. 2024

JACC: HEART FAILURE VOL. ■, NO. ■, 2023

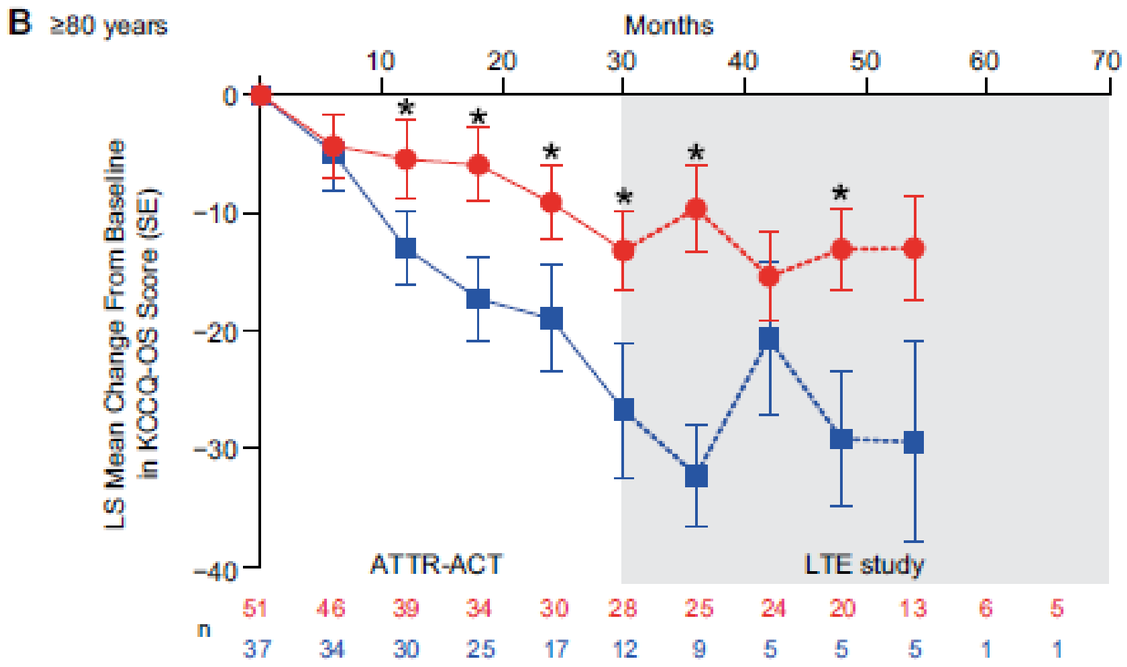
Tafamidis Efficacy Among Octogenarian Patients in the Phase 3 ATTR-ACT and Ongoing Long-Term Extension Study

Pablo Garcia-Pavia, MD, PhD,[a,b,c] Marla B. Sultan, MD, MBA,[d] Balarama Gundapaneni, MS,[e] Yoshiki Sekijima, MD,[f] Federico Perfetto, MD,[g] Mazen Hanna, MD,[h] Ronald Witteles, MD[i]

Patients aged ≥80 years
51 received tafamidis and 37 received placebo



6-MWT



Quality of life

Garcia Pavia et al. JACC HF 2023

JACC: HEART FAILURE VOL. ■, NO. ■, 2023

Tafamidis Efficacy Among Octogenarian Patients in the Phase 3 ATTR-ACT and Ongoing Long-Term Extension Study

Pablo Garcia-Pavia, MD, PhD,[a,b,c] Marla B. Sultan, MD, MBA,[d] Balarama Gundapaneni, MS,[e] Yoshiki Sekijima, MD,[f] Federico Perfetto, MD,[g] Mazen Hanna, MD,[h] Ronald Witteles, MD[i]

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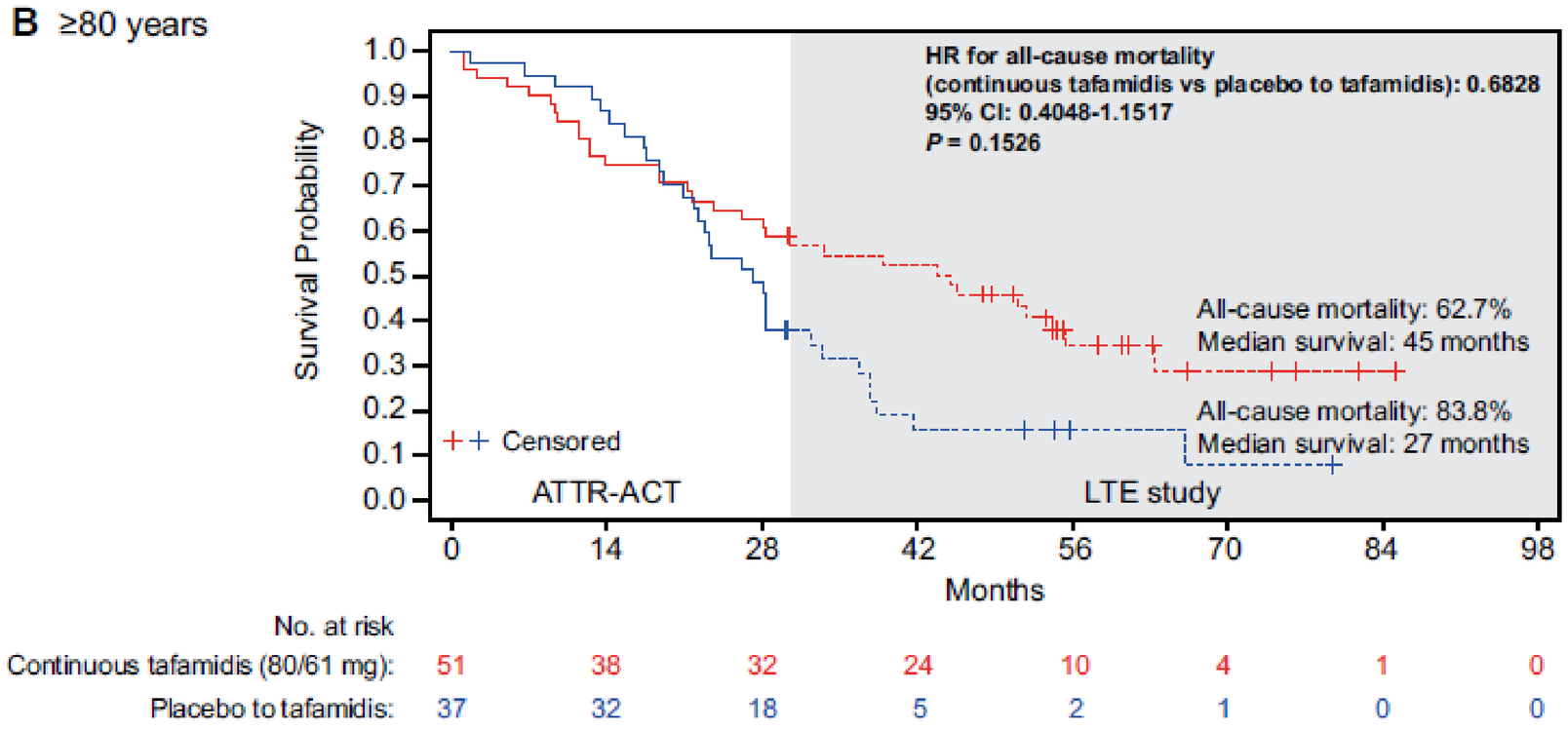


Garcia Pavia et al. JACC HF 2023

ESC European Society of Cardiology
European Heart Journal (2025) 46, 1057–1070
https://doi.org/10.1093/eurheartj/ehae923

CLINICAL RESEARCH
Heart failure and cardiomyopathies

Tafamidis in octogenarians with wild-type transthyretin cardiac amyloidosis: an international cohort study

	Overall cohort $n = 710$	Non-octogenarians $n = 295$	Octogenarians $n = 415$	*P*-value
Demographics				
Age, years	[710] 81 ± 7	[295] 74 ± 5	[415] 85 ± 4	<.001
Male	566/710 (79.7%)	258/295 (87.5%)	308/415 (74.2%)	<.001

- The impact of tafamidis treatment on mortality in real-world wild-type transthyretin cardiomyopathy octogenarians was studied.
- An international, multicentre cohort study of 710 consecutive wild-type transthyretin cardiomyopathy patients with mean follow-up of 2.2 ± 1.8 years for all-cause mortality endpoint was performed.
- 58.5% (415/710) octogenarians (85 ± 4 years, 74.2% male)

We demonstrated **poor overall survival** in untreated octogenarians with high 1- and 5-year mortality rates of 16% and 71%, respectively, and a median survival of 3.8 years

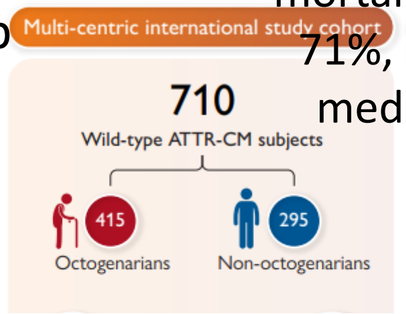
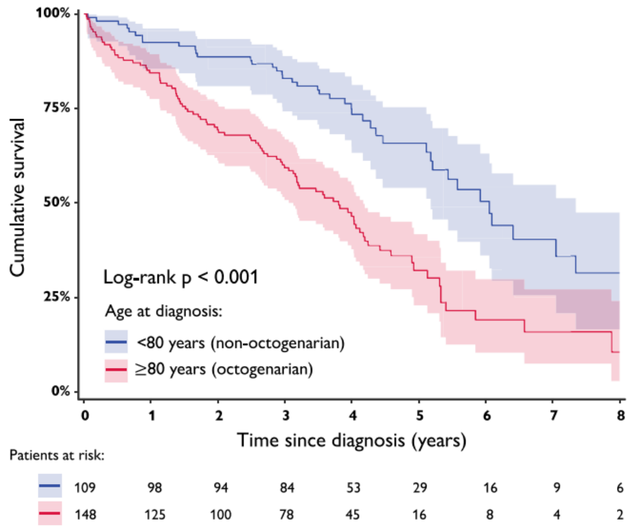


Table 3 Reasons for tafamidis discontinuation in treated patients

Principal reason	Overall $n = 43$	Non-octogenarians $n = 17$	Octogenarians $n = 26$
Progressive disease, advanced heart failure	17 (39.5%)	7 (41.2%)	10 (38.5%)
Undefined reason	8 (18.6%)	2 (11.8%)	6 (23.1%)
Comorbidities, cognitive decline and/or frailty	5 (11.6%)	2 (11.8%)	3 (11.5%)
Advanced age, presumed futility	3 (7.0%)	0 (0.0%)	3 (11.5%)
Side-effects	7 (16.3%)	4 (23.5%)	3 (11.5%)
Patient preference	2 (4.7%)	2 (11.8%)	0 (0%)
Early disease stage, no heart failure	1 (2.3%)	0 (0.0%)	1 (3.8%)



al course cohort cumulative survival, stratified by octogenarians and non-octogenarians

Debonnaire et al. EHJ 2025

ESC European Society of Cardiology
European Heart Journal (2025) 46, 1057–1070
https://doi.org/10.1093/eurheartj/ehae923

Tafamidis in octogenarians with wild-type transthyretin cardiac amyloidosis: an international cohort study

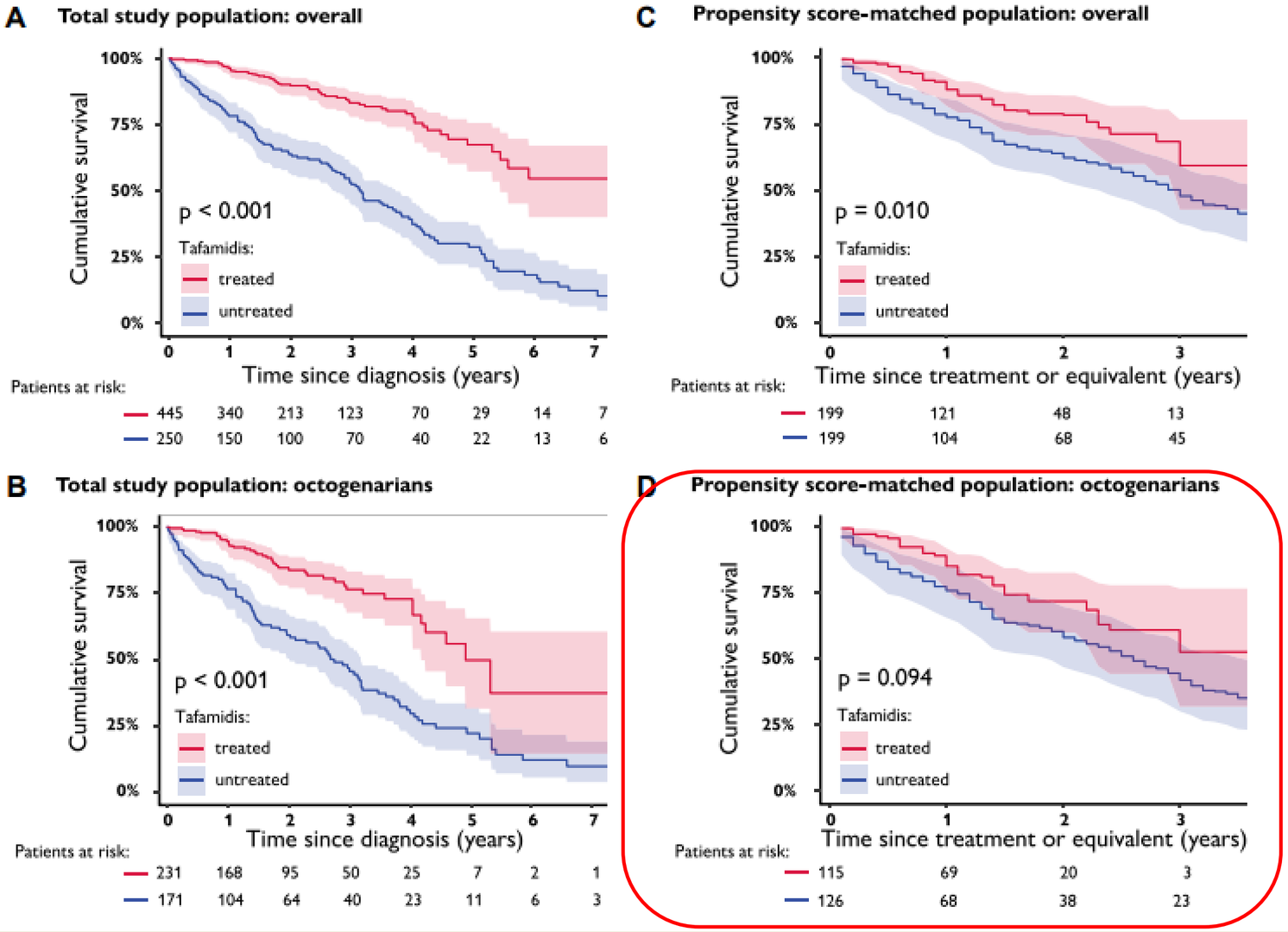


Figure 3 Cumulative survival in tafamidis treated vs. untreated patients. Total patient population. (*A*) Overall cohort. (*B*) Octogenarian cohort. Propensity score-matched population, with patients at risk from the first imputation. (*C*) Overall cohort. (*D*) Octogenarian cohort

Propensity score matching on baseline variables, including **age, National Amyloidosis Centre stage, and New York Heart Association class**

Debonnaire et al. EHJ 2025

International Journal of Cardiology 437 (2025) 133522

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Impact of Tafamidis on survival in elderly patients: Insights from the Healthcare European Amyloidosis Registry

- **Our aim** was to analyze clinical characteristics and survival of patients with ATTR-CM aged ≥80 years diagnosed after November 2018, treated with tafamidis 80/61 mg, and compare them with a non-treated group diagnosed before that date.
- Data from the two groups were extracted from the **Healthcare European Amyloidosis Registry (HEAR).** Propensity score matching was used to adjust for baseline differences between the groups

- Between June 2021 and June 2024, the HEAR cohort included **6051 patients with amyloidosis**, of whom 4310 were diagnosed with ATTR-CM. Among these, **1380 patients were over 80 years old**. Of the patients over 80 years old, **1194 were diagnosed after November 2018 and treated with tafamidis 80/61 mg, while 186 patients were diagnosed before November 2018 and were not treated.**

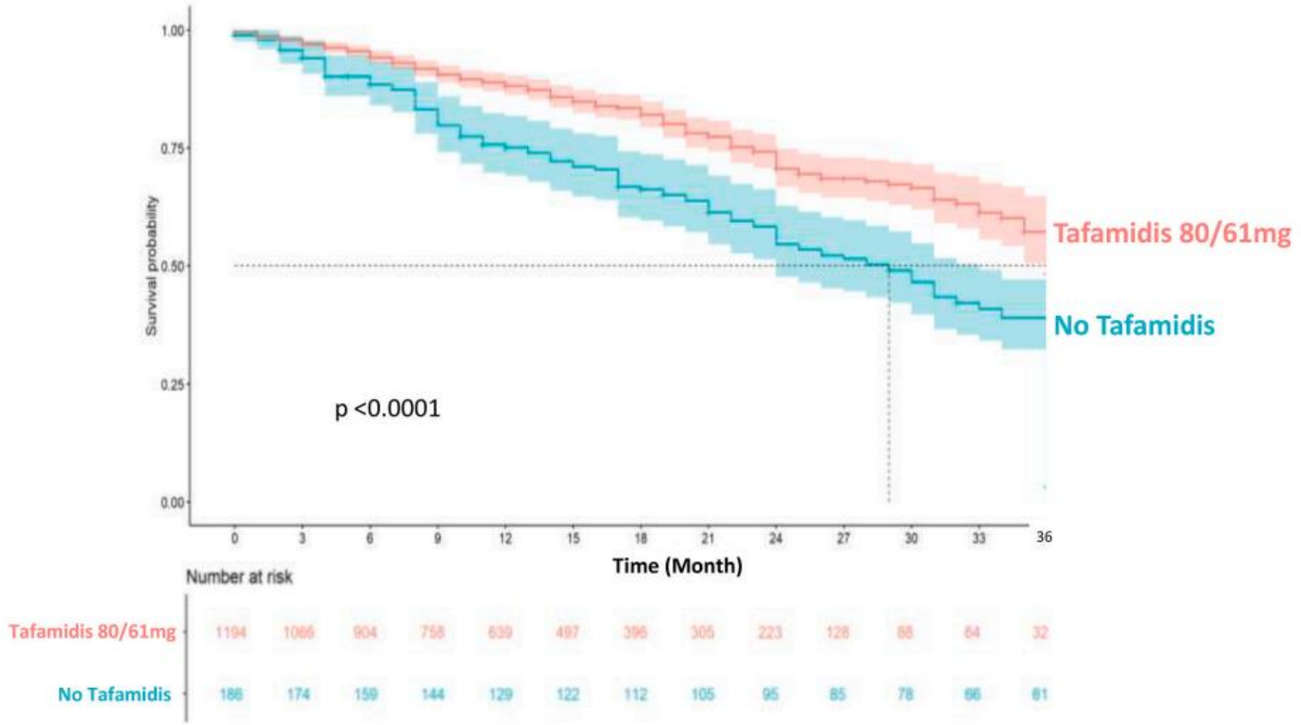


Fig. 1. Survival in patients over 80 years old treated with tafamidis 80/61mg versus no treatment: Kaplan-Meier curve.

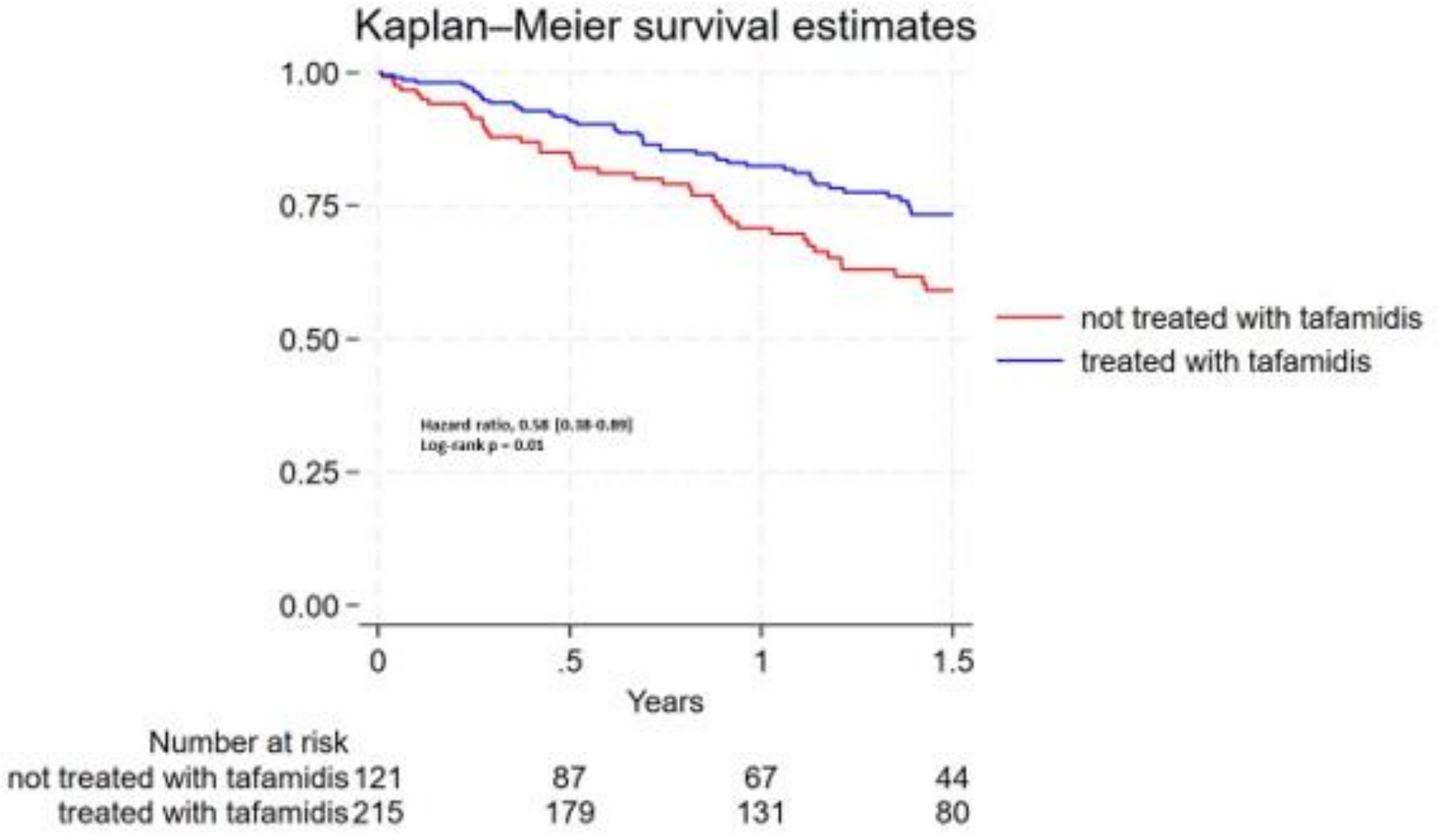
Jobbe-Duval et al. IJC 2025

ESC European Society of Cardiology
European Heart Journal (2025) 00, 1–2
https://doi.org/10.1093/eurheartj/ehaf482

Nonagenarian patients with ATTR cardiac amyloidosis: should they be treated with tafamidis?

Antoine Jobbé-Duval [1,*], Thibaud Damy [2,3,4], and Amaury Broussier [4,5]

- **336 patients over the age of 90**
- males: 69%; median hypertrophy: 16 mm, median ejection fraction: 55%; median ventricular strain: -11%; median serum level : median serum N-terminal prohormone of brain natriuretic peptide level: 3438 pg/ml; National Amyloidosis Centre (NAC) stage 2: 44%; NAC stage 3: 24%)

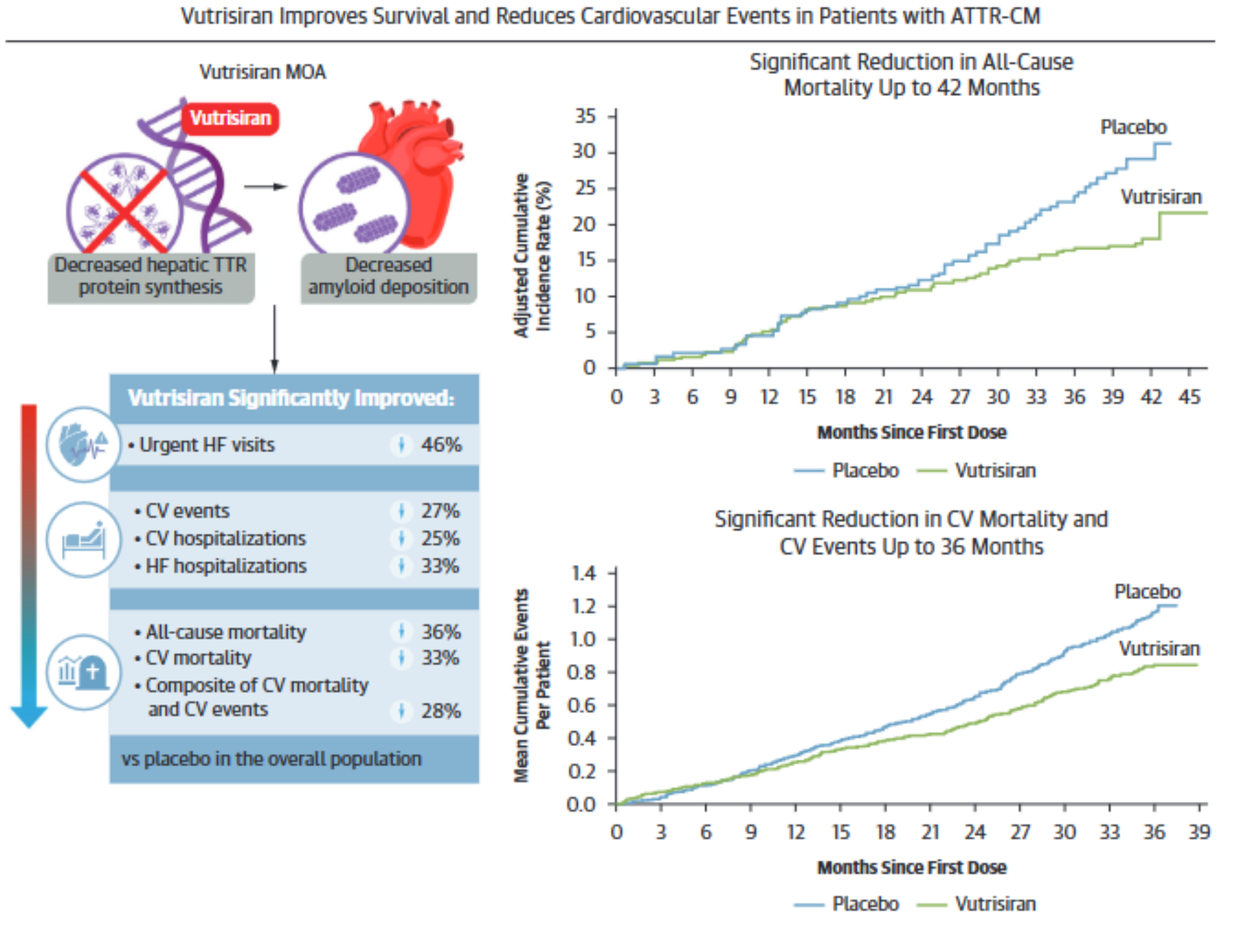


Jobbe-Duval et al. EHJ 2025

Vutrisiran Improves Survival and Reduces Cardiovascular Events in ATTR Amyloid Cardiomyopathy

HELIOS-B

CENTRAL ILLUSTRATION **Vutrisiran Reduces the Risk of Mortality and Cardiovascular Events Among Patients With Transthyretin Amyloidosis With Cardiomyopathy**



Witteles RM, et al. JACC. 2025;85(20):1959-1970.

ATTR-CM = transthyretin amyloidosis with cardiomyopathy; CV = cardiovascular; HF = heart failure; MOA = mechanism of action; TTR = transthyretin.

Witteles et al. JACC 2025

The NEW ENGLAND JOURNAL of MEDICINE

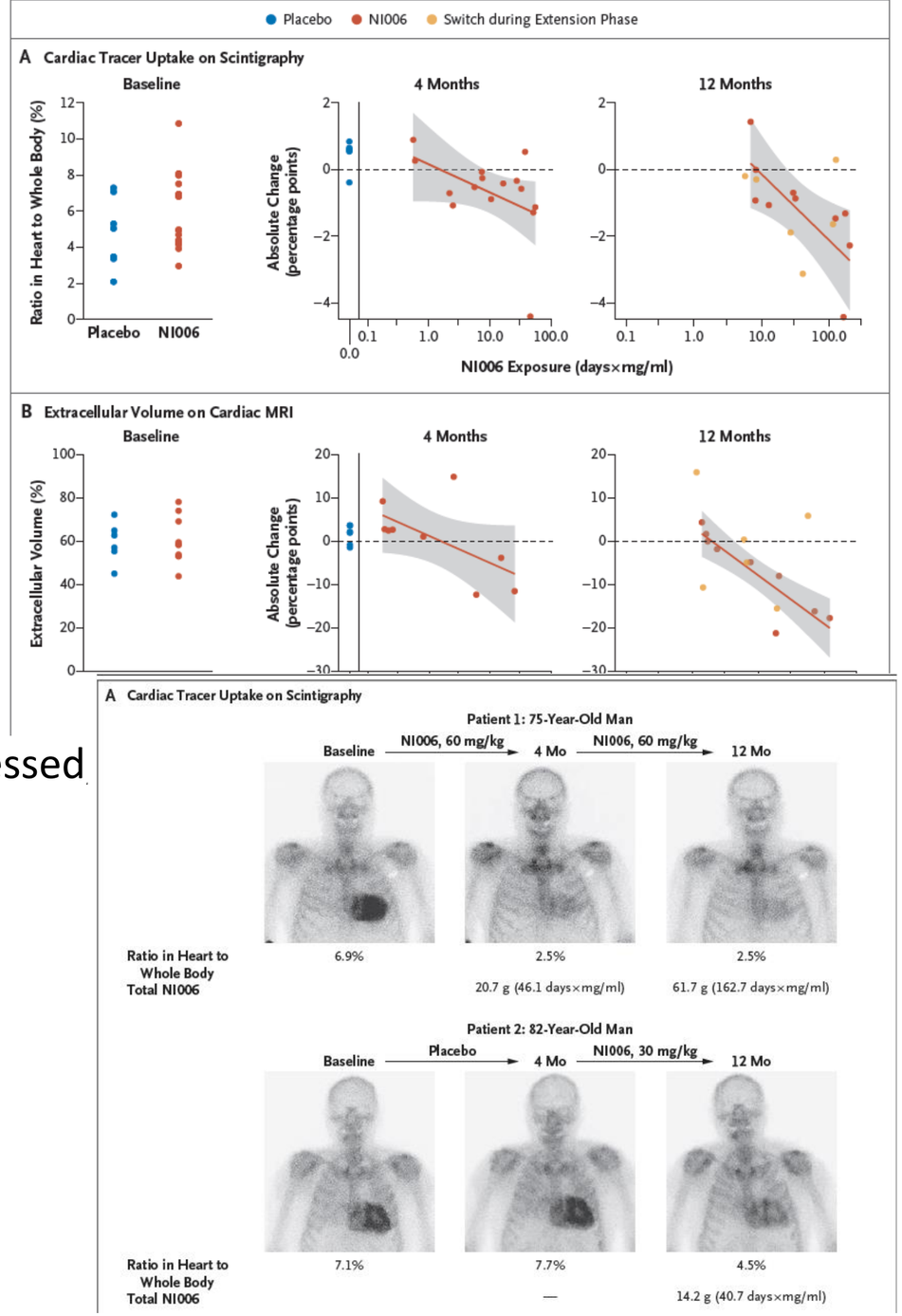
ORIGINAL ARTICLE

Phase 1 Trial of Antibody NI006 for Depletion of Cardiac Transthyretin Amyloid

Pablo Garcia-Pavia, M.D., Ph.D., Fabian aus dem Siepen, M.D., Erwan Donal, M.D., Ph.D., Olivier Lairez, M.D., Peter van der Meer, M.D., Ph.D., Arnt V. Kristen, M.D., Michele F. Mercuri, M.D., Ph.D., Aubin Michalon, Ph.D., Robert J.A. Frost, M.D., Ph.D., Jan Grimm, Ph.D., Roger M. Nitsch, M.D., Christoph Hock, M.D., Peter C. Kahr, M.D., and Thibaud Damy, M.D., Ph.D.

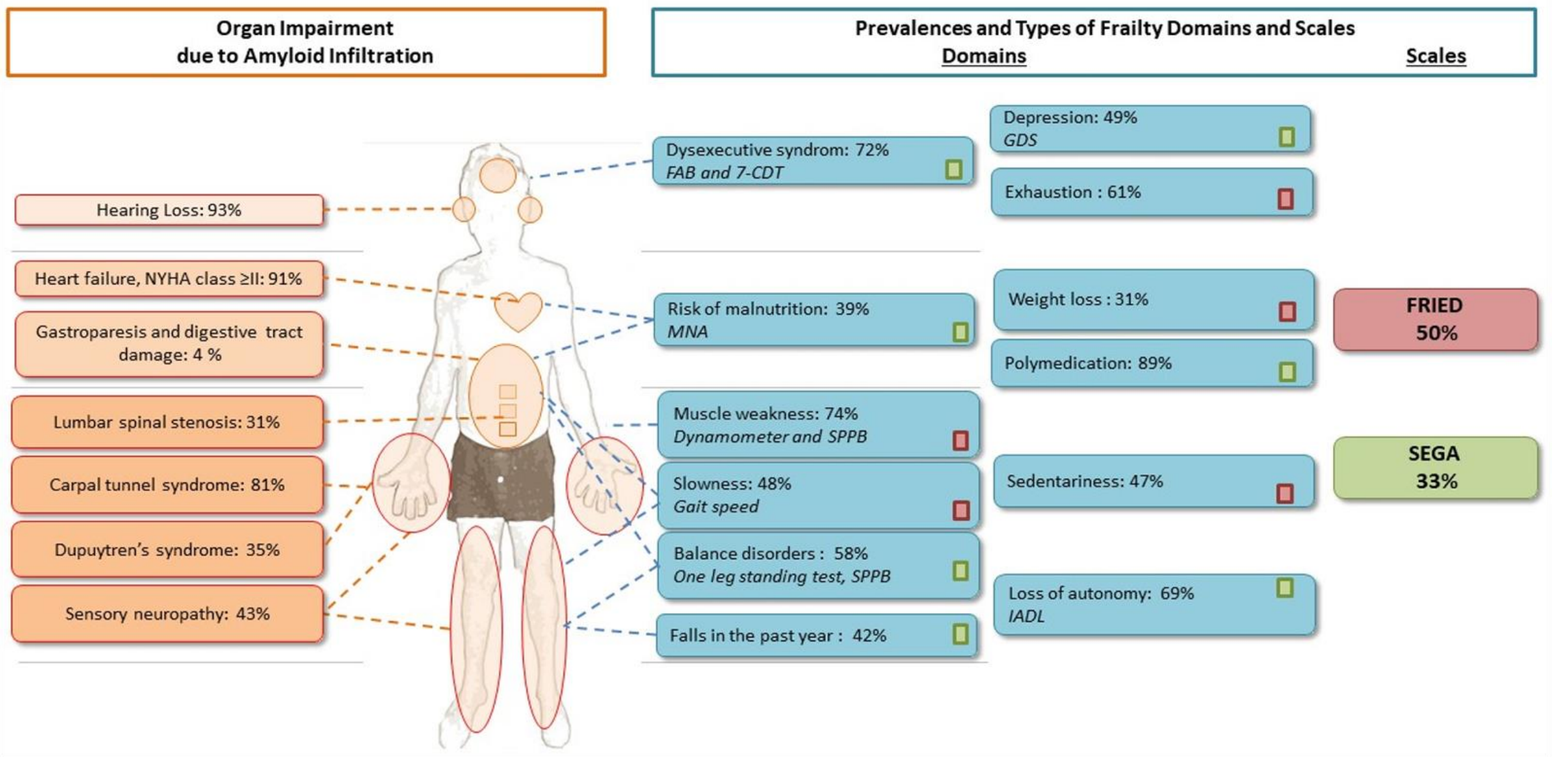
rial, we randomly assigned (ir
ATTR cardiomyopathy and chronic heart failure

- Intravenous infusions of either NI006 or placebo every 4 we kilogram of body weight).
- After four infusions, patients were enrolled in an open-labe infusions of NI006 with stepwise increases in the dose.
- The safety and pharmacokinetic profiles of NI006 were assessed performed.



Garcia-Pavia et al., NEJM 2023.

Fragilité et infiltrations amyloïdes



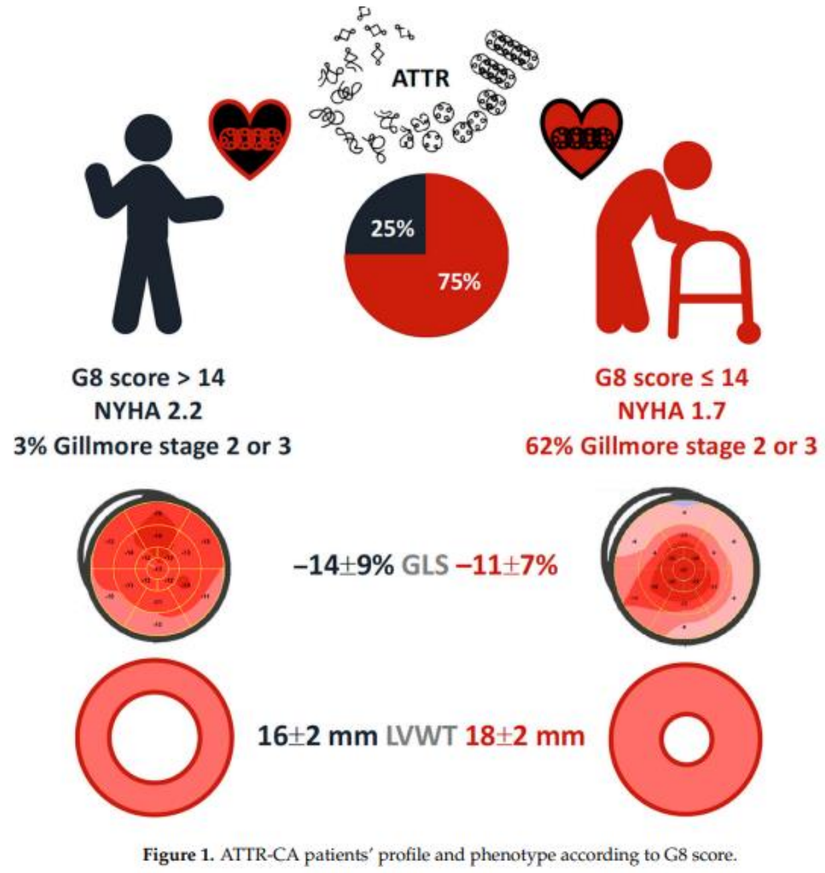


Figure 1. ATTR-CA patients' profile and phenotype according to G8 score.

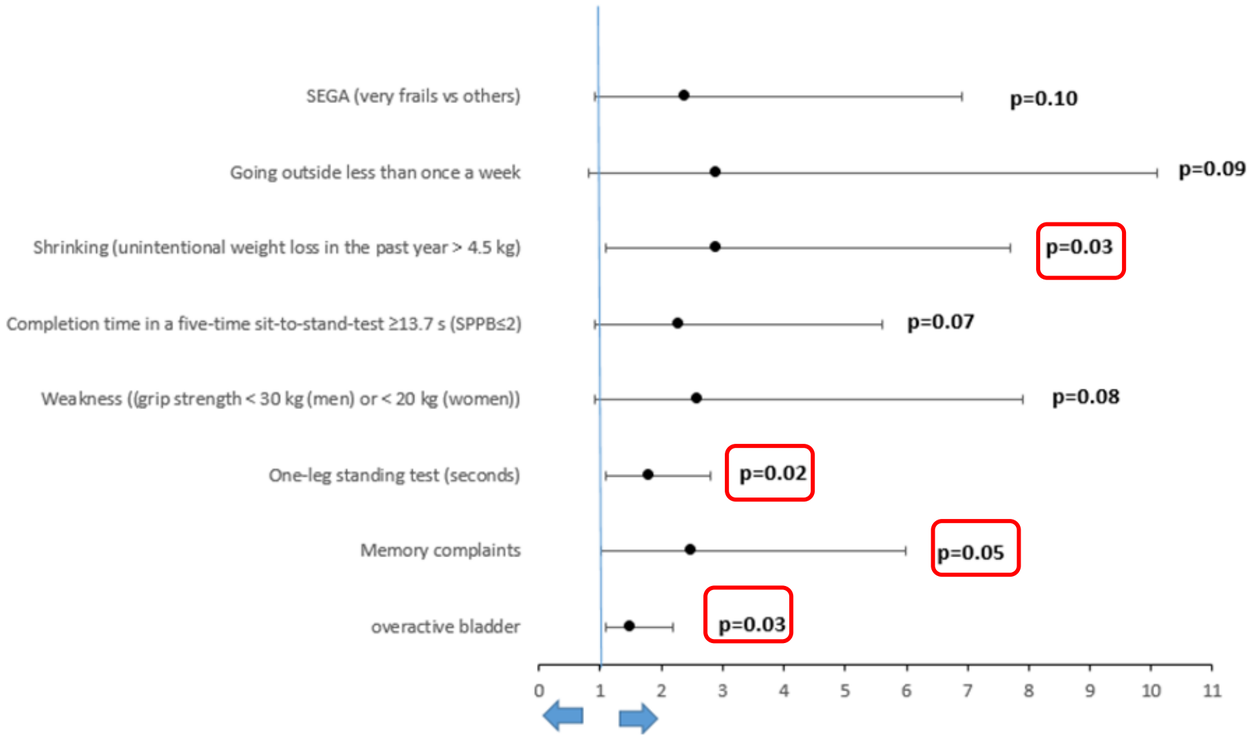
Broussier et al., JCM 2021
Cazalbou et al., JCM 2023

ESC HEART FAILURE
ESC Heart Failure 2025; **12**: 281–289
Published online 16 September 2024 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.15026

ORIGINAL ARTICLE

Un phénotype particulier

Frailty in heart failure according to the presence or absence of wild-type transthyretin cardiac amyloidosis



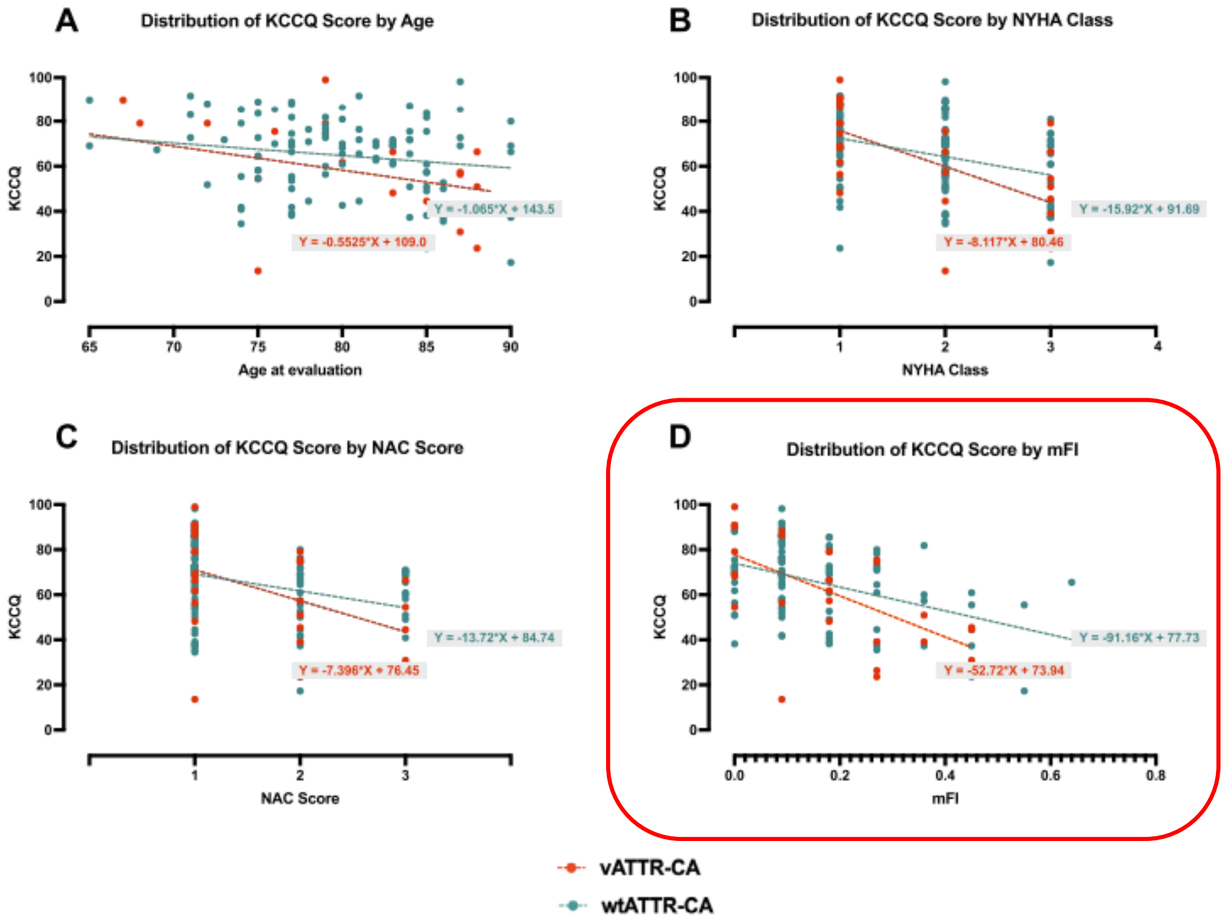
Aging Clinical and Experimental Research (2024) 36:89
https://doi.org/10.1007/s40520-024-02750-6

ORIGINAL ARTICLE

Determinants of health status in older patients with transthyretin cardiac amyloidosis: a prospective cohort study

Carlo Fumagalli[1,2,3] · Lucia Ponti[3,4] · Martina Smorti[5] · Francesca Pozza[3] · Alessia Argirò[2,5] · Mattia Zampieri[4] · Carlo Di Mario[7] · Raffaele Marfella[1] · Celestino Sardu[1] · Giuseppe Paolisso[1] · Iacopo Olivotto[2,9] · Federico Perfetto[5,6] · Andrea Ungar[10] · Niccolò Marchionni[8] · Francesco Cappelli[2,7,8]

Received: 12 March 2024 / Accepted: 27 March 2024



Broussier et al., ESC-HF 2024
Fumagalli et al. Aging Clinical and Experimental Research 2024

Clinical Phenotype and Prognostic Significance of Frailty in Transthyretin Cardiac Amyloidosis

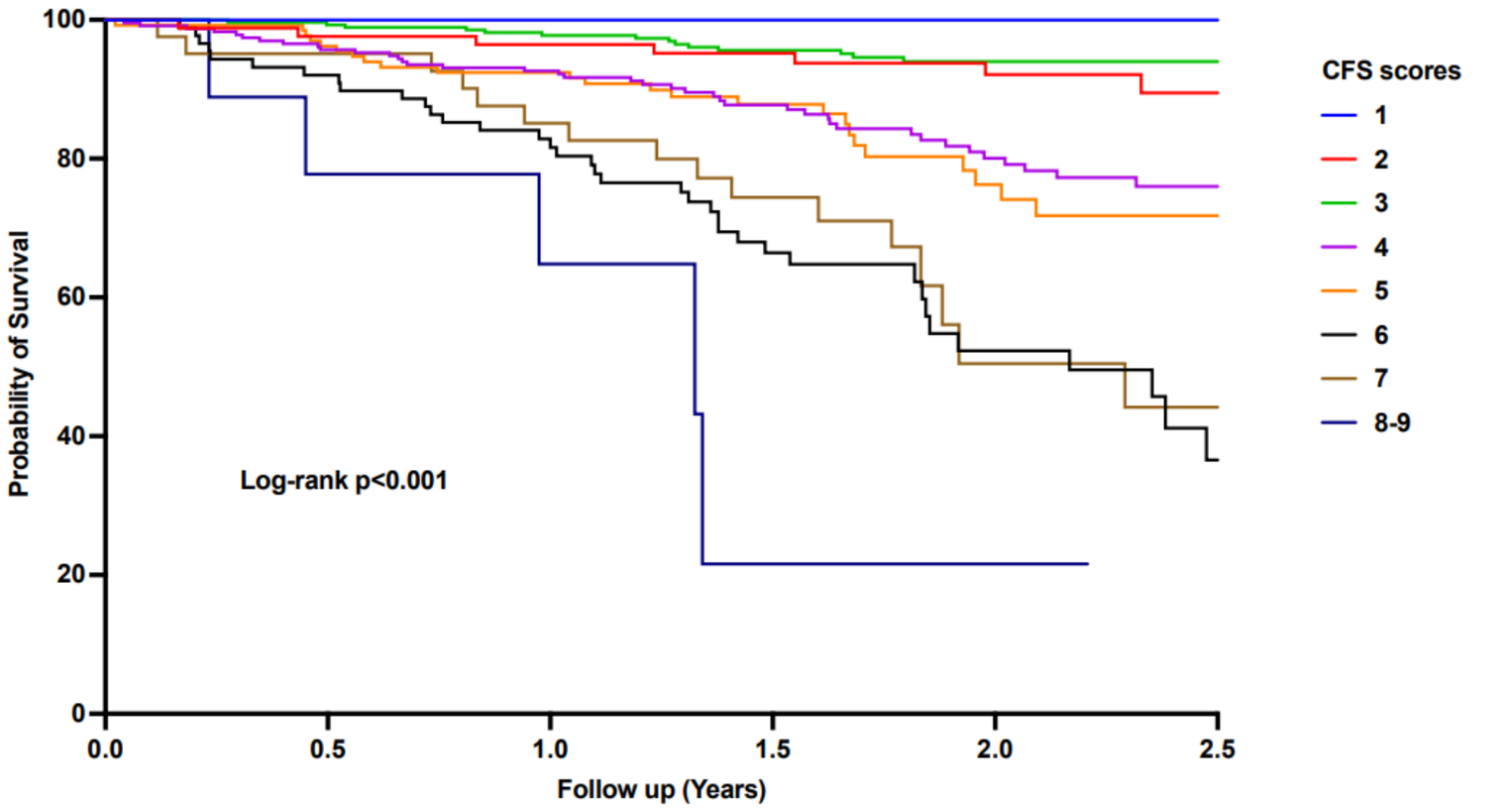
TABLE 1 Clinical and Imaging Characteristics of Patients Diagnosed With ATTR-CM at CFS Assessment

57.1 %

	CFS 1-3 (n = 378, 43.0%)	CFS 4 or 5 (n = 364, 41.4%)	CFS 6 or 7 (n = 129, 14.7%)	CFS 8 or 9 (n = 9, 1.0%)	*P* Value
Demographics					
Age, y	78 (74-82)	82 (77-85)	83 (78-88)	87 (84-90)	<0.001
>80 y	130 (34.3)	200 (55.2)	74 (57.4)	9 (100.0)	<0.001

- To evaluate the prevalence, clinical determinants, and prognostic significance of frailty in a large cohort of patients with ATTR-CA.
- Frailty was assessed in **880 patients with ATTR-CA** (median age 80 years [Q1-Q3: 75-84 years], 719 [81.7%] male) using the Clinical Frailty Scale (CFS).

FIGURE 2 Survival Analysis of Patients With ATTR-CA by Clinical Frailty Status



Fumagalli et al. JACC cardiooncol 2025

Clinical Phenotype and Prognostic Significance of Frailty in Transthyretin Cardiac Amyloidosis

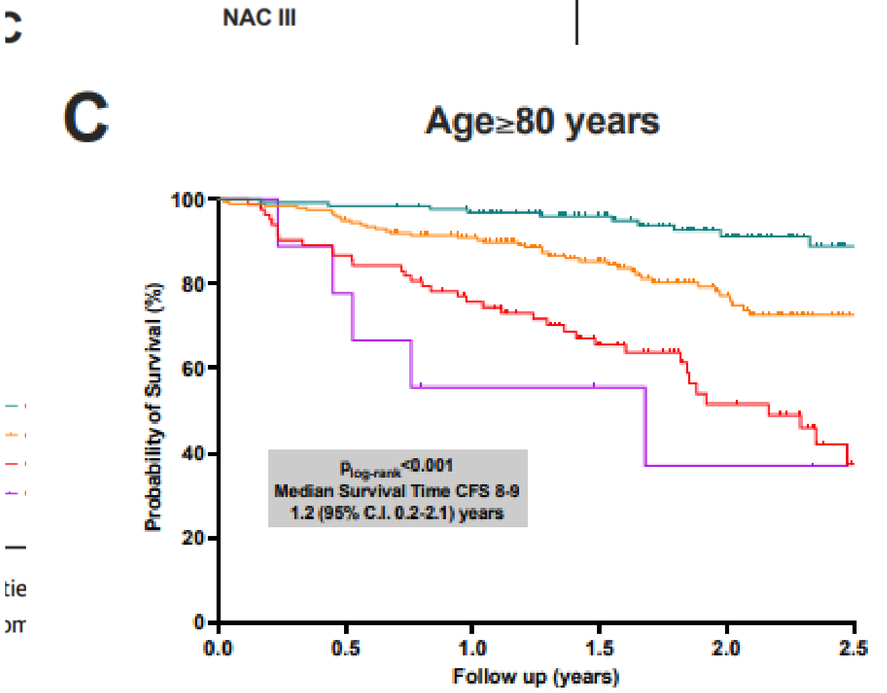
TABLE 3 Univariable and Multivariable Cox Regression Analysis to Determine Factors Associated With All-Cause Mortality

	Univariable			Multivariable		
	HR	95% CI	*P* value	HR	95% CI	*P* value
Age at evaluation (Δ year)	1.102	1.071-1.134	<0.001	1.029	0.998-1.061	0.063
Men	1.244	0.728-2.125	0.41			
NYHA functional class (III/IV)	3.162	2.226-4.493	<0.001	1.501	1.038-2.171	0.031
CFS (vs 1-3)			<0.001			<0.001
4 or 5	3.125	2.085-4.971	<0.001	2.941	1.774-4.867	<0.001
6 or 7	4.799	2.666-8.348	<0.001	4.123	2.423-7.015	<0.001
8 or 9	8.038	2.761-19.719	<0.001	9.716	3.340-28.266	<0.001
Log NT-proBNP	2.121	1.428-2.054	<0.001	1.897	1.512-2.379	<0.001
Log eGFR	0.491	0.301-0.894	0.015	0.533	0.311-0.915	0.022
Ischemic heart disease[a]	1.428	0.966-2.110	0.07	1.385	0.932-2.056	0.11
Diabetes mellitus[a]	1.404	0.946-2.082	0.09	1.067	0.719-1.592	0.84
Hypertension[a]	1.061	0.761-1.479	0.73			
Atrial fibrillation	1.330	0.951-1.860	0.09	0.815	0.578-1.152	0.25
Stroke/TIA[a]	1.134	0.653-1.970	0.66			
LV wall thickness (Δ mm)	1.071	1.007-1.138	0.029	1.052	0.966-1.099	0.36
LVEF (Δ %)	0.973	0.958-0.988	0.001	0.998	0.986-1.014	0.81
Loop diuretics[a]	1.381	0.980-1.946	0.07	1.050	0.734-1.509	0.78

The model was performed in 861 individuals. [a]At the time of assessment.

Abbreviations as in Table 1.

FIGURE 3 Survival Analysis of Patients With ATTR-CA by NAC Stage and CFS



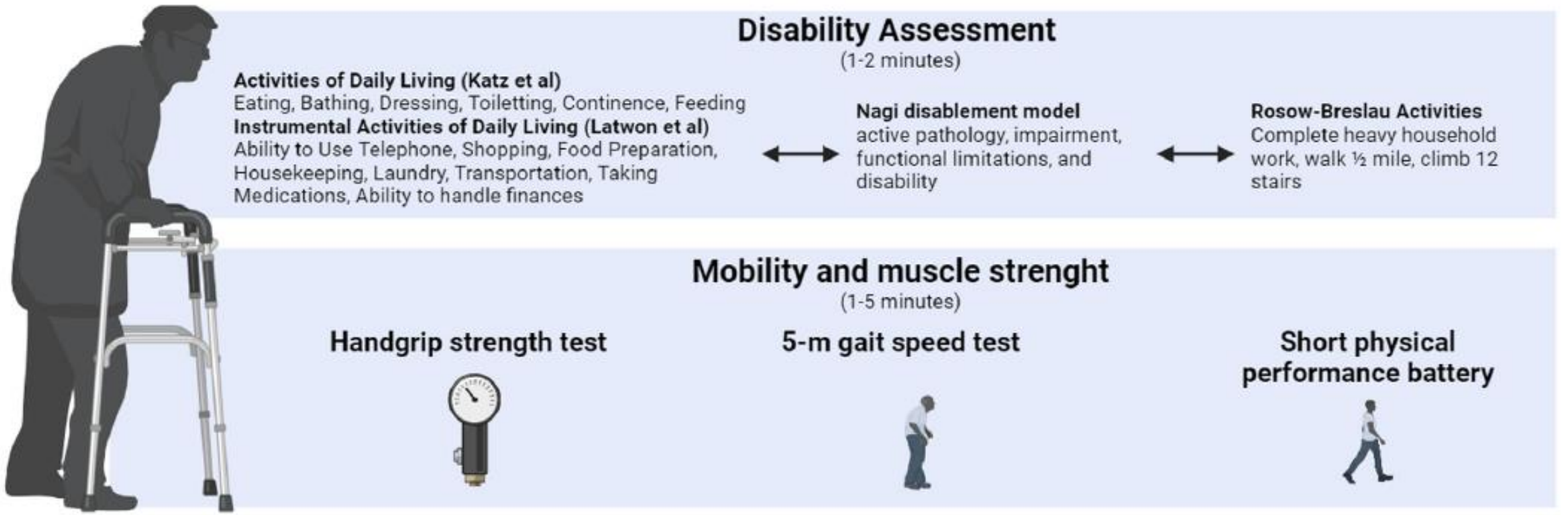
Fumagalli et al. JACC cardiooncol 2025

JACC: ADVANCES
VOL. 3, NO. 9, 2024

EXPERT PANEL

Comprehensive Geriatric Assessment to Optimize the Management of Older Patients With Transthyretin Cardiac Amyloidosis

FIGURE 1 Functional and Disability Assessment in Older Patients Diagnosed With ATTR-CA



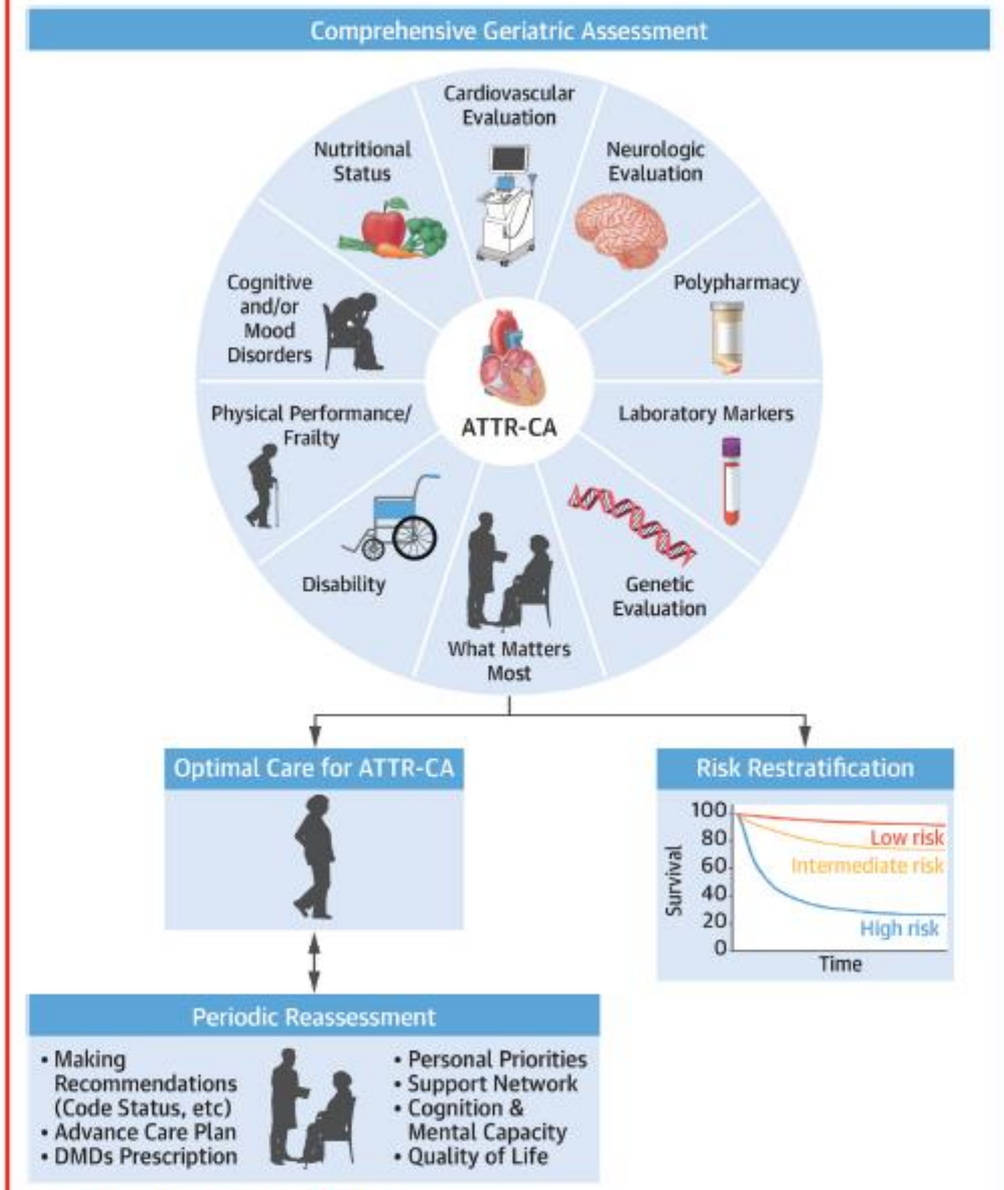
The figure illustrates the components of functional and disability assessment for older patients diagnosed with transthyretin cardiac amyloidosis (ATTR-CA). The assessment is divided into 2 main categories: disability assessment and physical performance. Created with BioRender.com.

HIGHLIGHTS

- Patients with ATTR-CA are almost exclusively older adults at diagnosis with multiple chronic conditions.
- A routine CGA is useful to delineate the clinical complexity (ie geriatric syndromes) of older ATTR-CA patients.
- A CGA that incorporates the expertise of geriatricians, cardiologists, neurologists, palliative care specialists, and others may help reduce ageism and futility and could be integrated in future clinical trials.

Fumagalli et al. JACC 2024

CENTRAL ILLUSTRATION Providing Optimal Medical Care for Patients With ATTR-CA From Diagnosis, to Risk Stratification, and Follow-Up



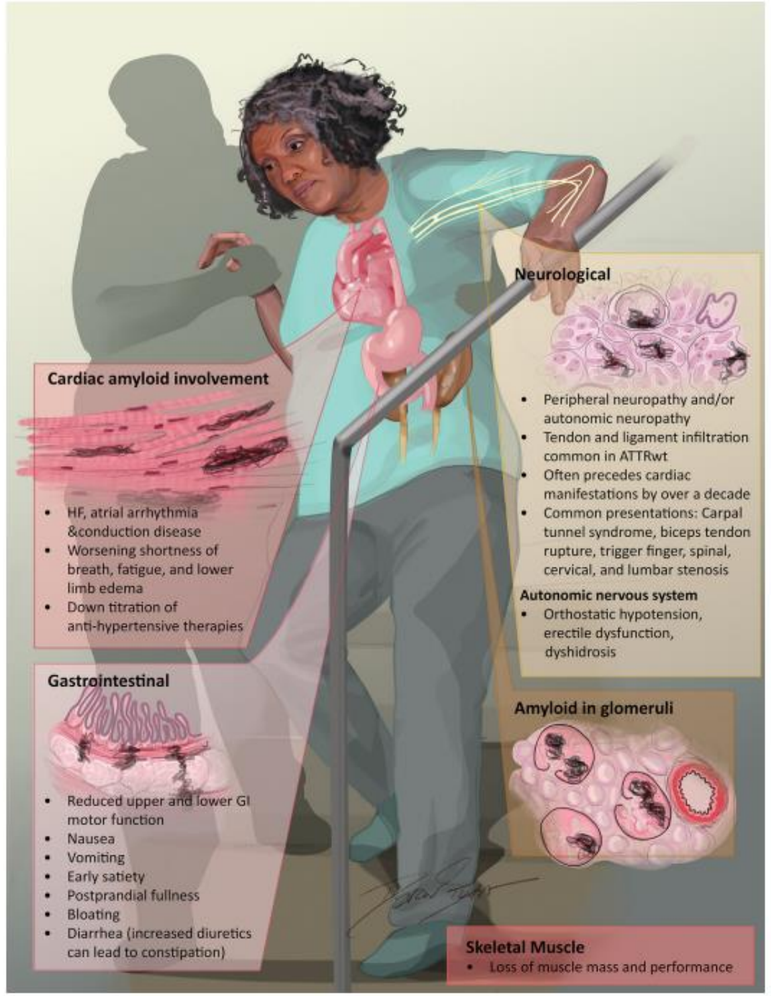
Fumagalli C, et al. JACC Adv. 2024;3(9):101123.

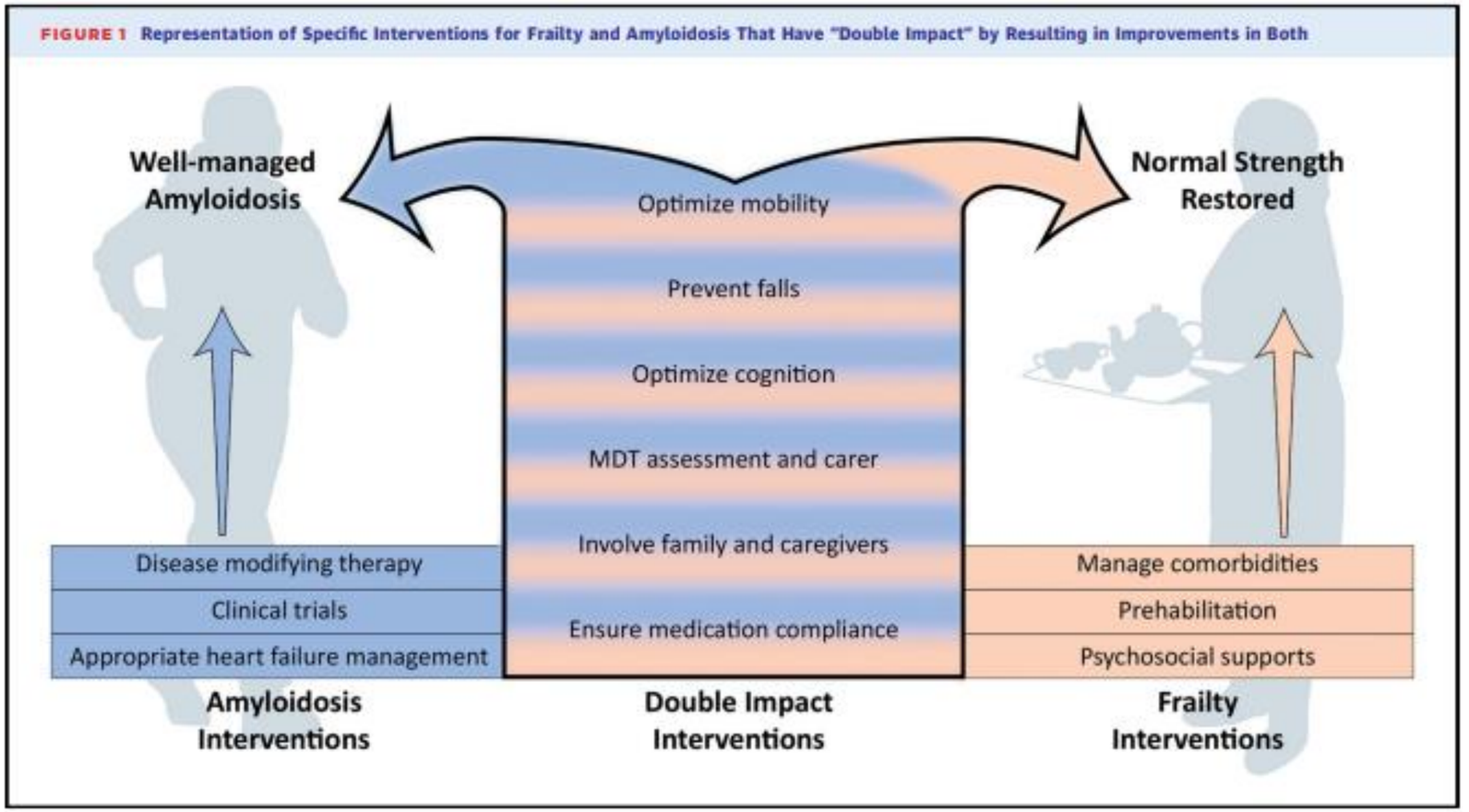
Includes key elements of the multidisciplinary evaluation with the comprehensive geriatric assessment (CGA). DMD = disease-modifying drug.

Fumagalli et al. JACC 2024

Cardiac Amyloidosis in Older Adults With a Focus on Frailty

JACC: Advances Expert Consensus





Bart et al. JACC Advances 2025

Mme B, 88 ans

Plainte de la patient : **DYSPNEE**

Mode de vie

- Secrétaire retraitée
- ADL 4.5/6 IADL 3/4

> Besoin d'aide dans déplacements, toilette, habillage ; et transports

- Sort de chez elle uniquement accompagnée pour faire les courses
- Pas de troubles cognitifs : MMS 29/30
- Marié, 2 filles

Echocardiographie :

- Ventricule gauche non dilatée, **hypertrophié de manière concentrique, SIV 15 mm**
- **FEVG 60 %, Strain -12 %** altéré en cocarde
- Insuffisance aortique minime, RAC lâche
- Insuffisance mitrale grade I/IV
- **Insuffisance tricuspide sévère avec dilatation modérée des cavités droites**
- **Ventricule droit hypertrophié. Altération sévère de la fonction systolique du VD**
- **Dilatation bi-atriale**
- VCI dilatée et compliante

- Adaptation du **traitement non spécifique** : Augmentation de la dose de diurétiques de l'anse
- Décision de ne pas mettre en place de traitement spécifique
- Dépistage génétique

Mme B, 83 ans

Mode de vie

- Institutionnalisée depuis 2 ans
- ADL 4.5/6, IADL 1/4
- Troubles neuro cognitifs majeurs ; MMS 24/30, 5 mots de Dubois 8/10
- Participe à l'ensembles des activités en EHPAD

Traitement habituel

- Apixaban 2.5 mg
- Furosemide 120 mg/jour
- Chlorure de potassium 600 mg
- Bisoprolol 2.5 mg
- Dapagliflozine 10 mg
- Amlodipine 10 mg
- Ramipril 2.5 mg
- Metformine 10 mg
- Paracetamol 500 mg
- Levothyrox 75 microg

Histoire de la maladie :

3 Hospitalisations pour IC dans les 12 derniers mois
Evolution favorable sous traitement diurétique IV
Réévaluation de l'autonomie, avec l'entourage
Etat moteur et nutritionnel satisfaisant.
Pas de trouble thymique

Scintigraphie HMDP :

Fixation myocardique du traceur Perugini III

Echocardiographie :

- Ventricule gauche non dilatée, **HVG concentrique**
- **FEVG 64 %, Strain -14 %** altéré en cocarde, **SIV 14 mm**
- Insuffisance aortique minime, pas de sténose aortique
- Insuffisance mitrale grade II/IV
- IT grade II/IV, HTAP modérée avec PAPs estimées à 46 mmHg
- Ventricule droit non hypertrophié de fonction systolique normale
- OG dilatée
- VCI dilatée et compliante

- Décision introduction **traitement spécifique** stabilisateur de transthyrétine par Tafamidis 61 mg, avec information de réévaluation
- Recherche de mutation génétique TTR
- Adaptation du traitement non spécifique

Take home messages

- Une **prévalence significative** dans l'IC du sujet âgé
- Une **explosion thérapeutique** avec différentes voies, différentes molécules
- Des **données de vraie vie** chez le sujet âgé
- **Place grandissante de l'EGA** chez ces patients : aide à la déci thérapeutique, management des comorbidités / fragilités / Syndromes gériatriques
- https://reseau-amylose.org/

Le **triple rôle du gériatre** dans la prise en charge de l'amylose cardiaque du sujet âgé :

1 : **Dépister et Diagnostiquer**
2 : **Orienter** vers le centre de référence
3 : **Évaluer la fragilité** des patients pour optimiser leur prise en charge

Merci de votre attention

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