



SIMPOSIO

**CREAZIONE DI UN NETWORK PER
L'IDENTIFICAZIONE PRECOCE DELL'AMILOIDOSI
CARDIACA SENILE**

**Amiloidosi cardiaca senile: come
identificarla nei reparti di Geriatria ed
aspettativa di vita**

**Dott. Carlo Fumagalli
Università degli Studi della Campania –
L. Vanvitelli (Napoli)**

Giovedì 18 dicembre 2025

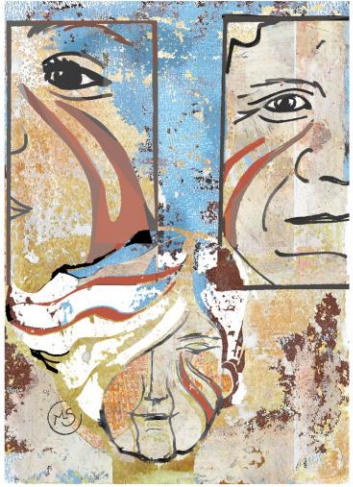
70^o CONGRESSO NAZIONALE SIGG LIBERI E LONGEVI

17-20
Dicembre
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Università degli
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SOCIETÀ ITALIANA
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E GERIATRIA



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No Conflict of Interest to disclose for the present work.

Left Ventricular Amyloid Deposition in Patients With Heart Failure and Preserved Ejection Fraction

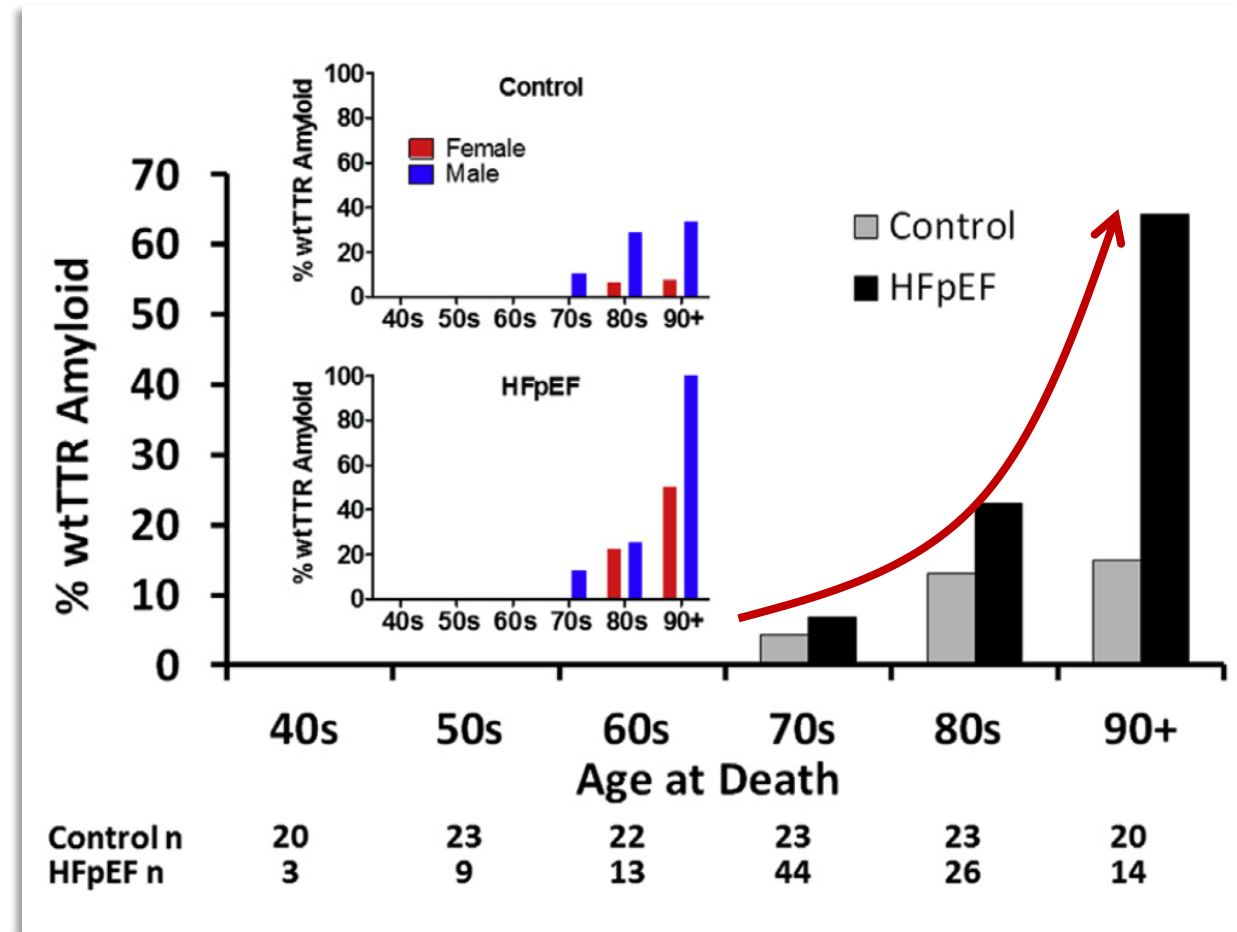
Selma F. Mohammed, MBBS,*† Sultan A. Mirzoyev,‡ William D. Edwards, MD,§ Ahmet Dogan, MD, PhD,|| Donna R. Grogan, MD,¶ Shannon M. Dunlay, MD,* Veronique L. Roger, MD,*# Morie A. Gertz, MD,|| Angela Dispenzieri, MD,|| Steven R. Zeldenrust, MD, PhD,|| Margaret M. Redfield, MD*

Rochester, Minnesota; and Montreal, Canada

Autopsy study on patients who had no suspicion of cardiac amyloidosis of any type antemortem.

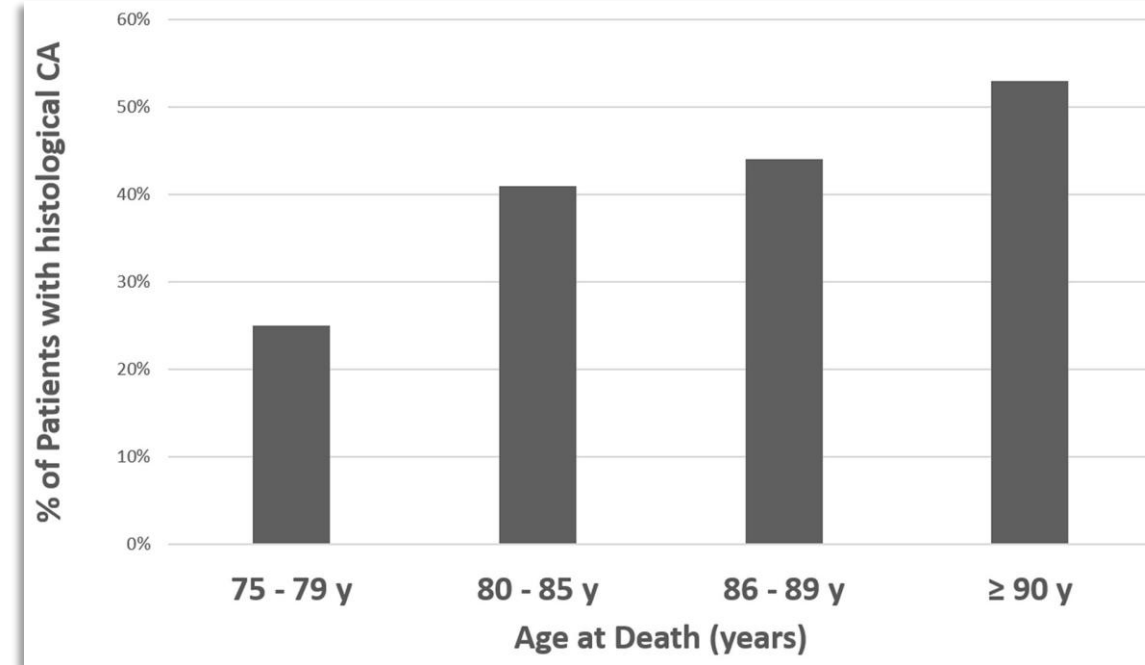
1. Controls without heart failure (HF) and not deceased due to cardiovascular (CV) disease.

2. HFpEF (>40%)



Incidence and Characterization of Concealed Cardiac Amyloidosis Among Unselected Elderly Patients Undergoing Post-mortem Examination

- **56** consecutive post-mortem examinations in individuals >75 years.
- **CA (TTR or AL) can be found in 43% of autopsied hearts** from unselected patients ≥ 75 years old, evenly distributed among ATTR and AL, **as long as cardiac samples are collected from multiple sites.**
- **Atria were involved in 96% of cases in patients with CA.**
- Individuals with **AF or HF had >3 times the probability of having CA** at autopsy.



Short communication

Prevalence of transthyretin-related amyloidosis in Tuscany: Data from the regional population-based registry

Francesco Cappelli^{a,b,1}, Annamaria Del Franco^{a,b,1}, Giuseppe Vergaro^{c,d}, Carlotta Mazzoni^{a,b,*}, Alessia Argirò^{a,b}, Maurizio Pieroni^c, Elisa Giacomini^f, Serena Poli^g, Marco Allinovi^h, Iacopo Olivetto^{a,b,i,j}, Federica Pieroni^k, Cristina Scaletti^{l,m,n}, Michele Emdin^{c,d}, Federico Perfetto^a



Registry: Tuscany (3.67 Mln People)

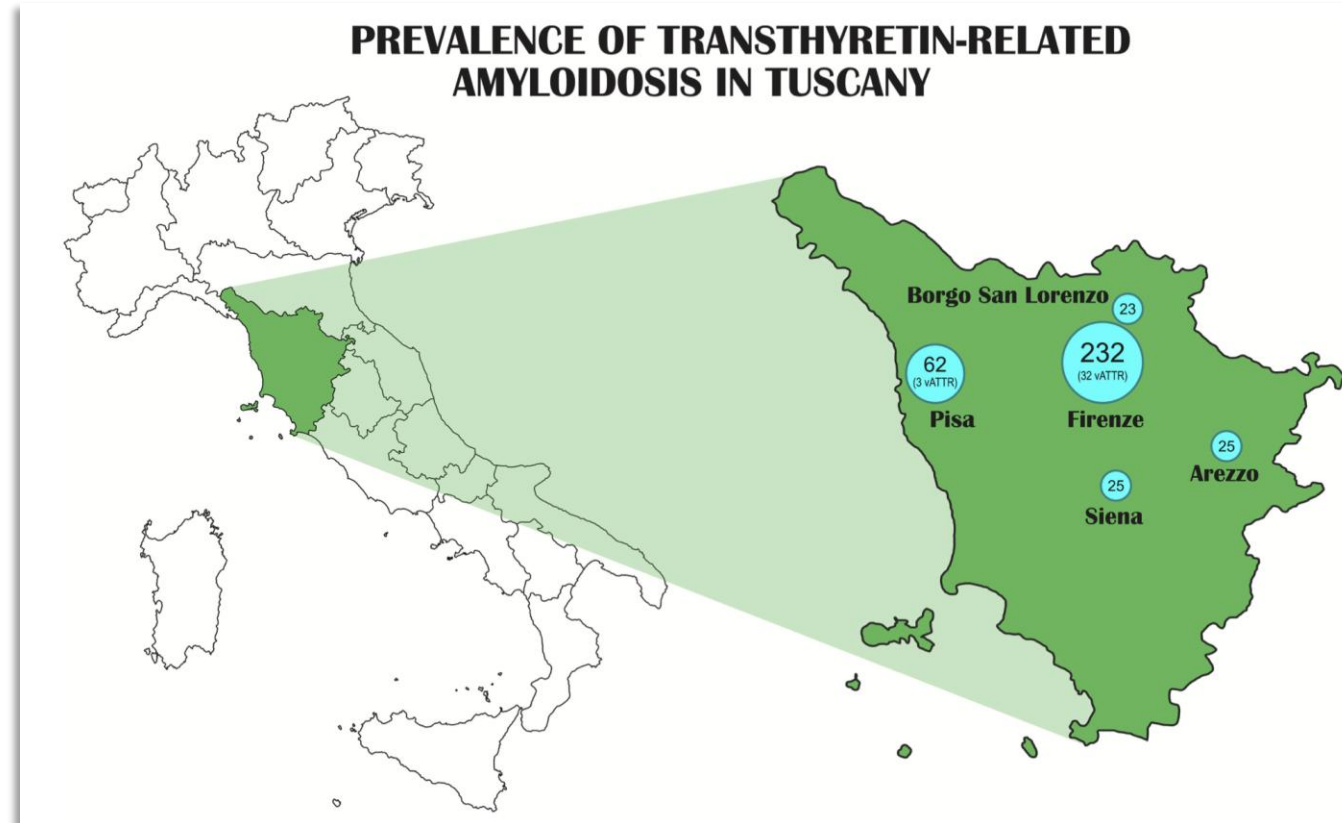
METHODS

Tuscan rare disease registry extraction

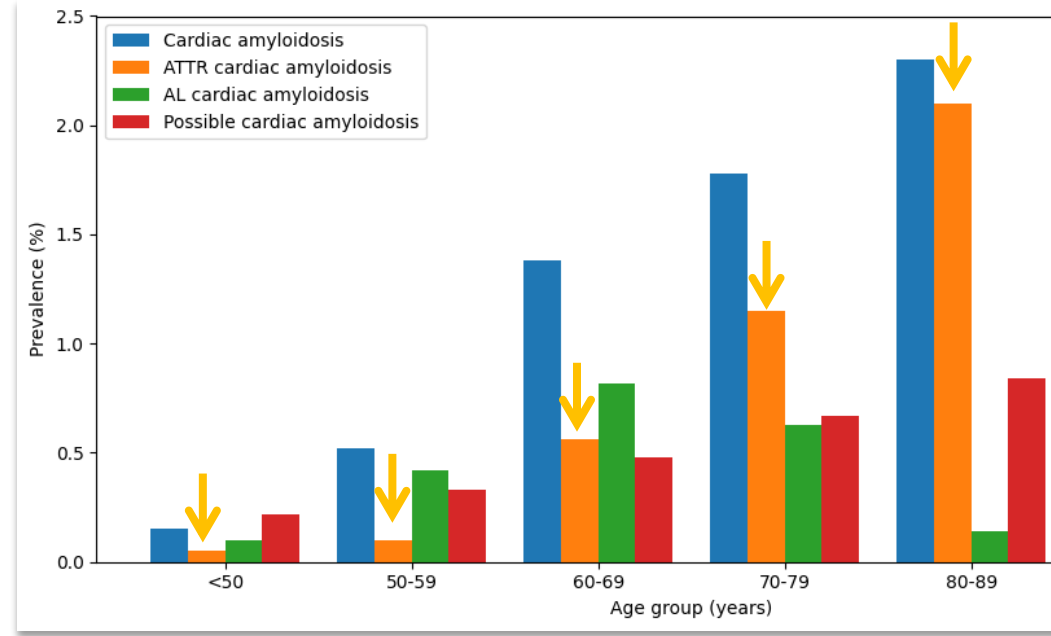
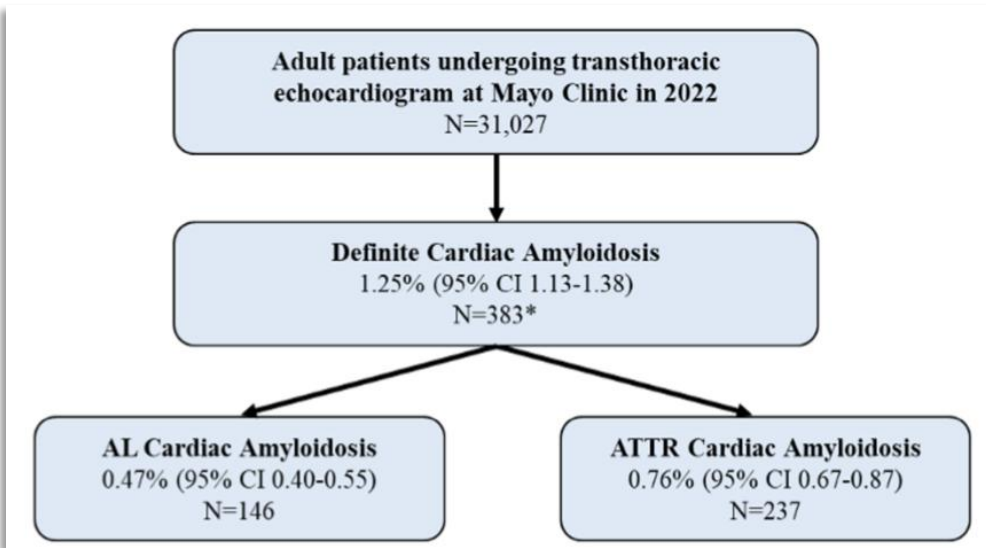
RESULTS (up to end 2022)

ATTRwt:Prevalence: **90.3 per 10⁶** (332 pts)Incidence: **26.7 per 10⁶** (95 new pts/2022)~66%pts: 80–99 y Male: Female 8:1

PREVALENCE OF TRANSTHYRETIN-RELATED AMYLOIDOSIS IN TUSCANY



Prevalence of Cardiac Amyloidosis in Patients Undergoing Echocardiography at a Tertiary Center



Redefining the epidemiology of cardiac amyloidosis. A systematic review and meta-analysis of screening studies


Alberto Aimo^{1,2}, Marco Merlo³, Aldostefano Porcari³, Georgios Georgiopoulos^{1,4,5}, Linda Pagura³, Giuseppe Vergaro^{1,2}, Gianfranco Sinagra³, Michele Emdin^{1,2}, and Claudio Rapezzi^{6,7*}


Aortic Stenosis
8-10%


HFpEF
12%

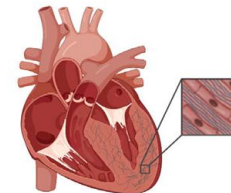
HFrEF
10%


 Bone scintigraphy
for non-cardiac reasons:
≥81 years: ~1.3% M, ~0.4% W

 Autopsy in unselected
elderly individuals: 21%
(95% CI 7-39%)

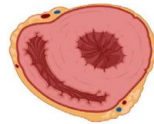
 HFpEF: 12%
(95% CI 6-20%)
M 73% (39-100%)
77 years (66-86)
AL-CA 10% (0-40%)


 Aortic stenosis: 8%
(95% CI 5-13%)
M 67% (50-89%)
84 years (75-88)
AL-CA 2% (0-6%)



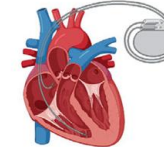
 HFrEF/HFmrEF: 10%
(95% CI 6-15%)
M 100%
81 years (76-85)
AL-CA 0%

Prevalence of cardiac amyloidosis in screening studies

 HCM: 7%
(95% CI 5-9%)
M 80% (73-87%)
74 years
AL-CA 0-9%

 Surgery for carpal tunnel
syndrome: 7%
(95% CI 5-10%)
M 64% (33-100%)
76 years (73-79)
AL-CA 18% (0-33%)

Conduction disorders: 2%
(95% CI 0-4%)
M 50%
90 years
AL-CA 0%



Il ritardo diagnostico e il suo impatto clinico

National Amyloidosis Centre, UK 2002 - 2017

- 711 pazienti diagnosticati con ATTR-CA
- 305 pazienti diagnosticati con V122I-hATTR-CA,
- 118 pazienti diagnosticati con non-V122I-hATTR-CA

ORIGINAL RESEARCH ARTICLE



Natural History, Quality of Life, and Outcome in Cardiac Transthyretin Amyloidosis

RESULTS: There was substantial diagnostic delay, with patients using hospital services a median (interquartile range) of 17 (9–27) times during the 3 years before diagnosis, by which time quality of life was poor; diagnosis of wild-type ATTR-CM was delayed >4 years after presentation with cardiac symptoms in 42% of cases. Patients with V122I-hATTR-CM were more impaired functionally ($P<0.001$) and had worse measures of cardiac disease ($P<0.001$) at the time of diagnosis, a greater decline in quality of life, and poorer survival ($P<0.001$) in comparison with the other subgroups.

**17 Visite in 3 anni
prima della diagnosi**

LE TRE FASI DEL PERCORSO DIAGNOSTICO

FASE 1

Il sospetto (*red flags*)

FASE 2

La diagnosi di certezza

FASE 3

La diagnosi eziologica



Clinical:

Cardiac:

Heart failure with preserved ejection fraction

Down-titration of anti-hypertensive medications

Intracardiac thrombosis, stroke and transient ischemic attack

Poor tolerance to heart failure therapy

Biohumoral:

Elevated BNP/NT-proBNP levels

Electrocardiography:

Discrepancy between QRS voltage and LV hypertrophy

Atrial fibrillation

AV conduction disorders

Pseudonecrosis pattern



Echocardiography:

Unexplained LV hypertrophy (>12 mm)

Right ventricular hypertrophy

Increased valve thickness

Pericardial effusion

Aortic regurgitation

Biatrial enlargement

Interventricular septal flattening

Dilated left atrium

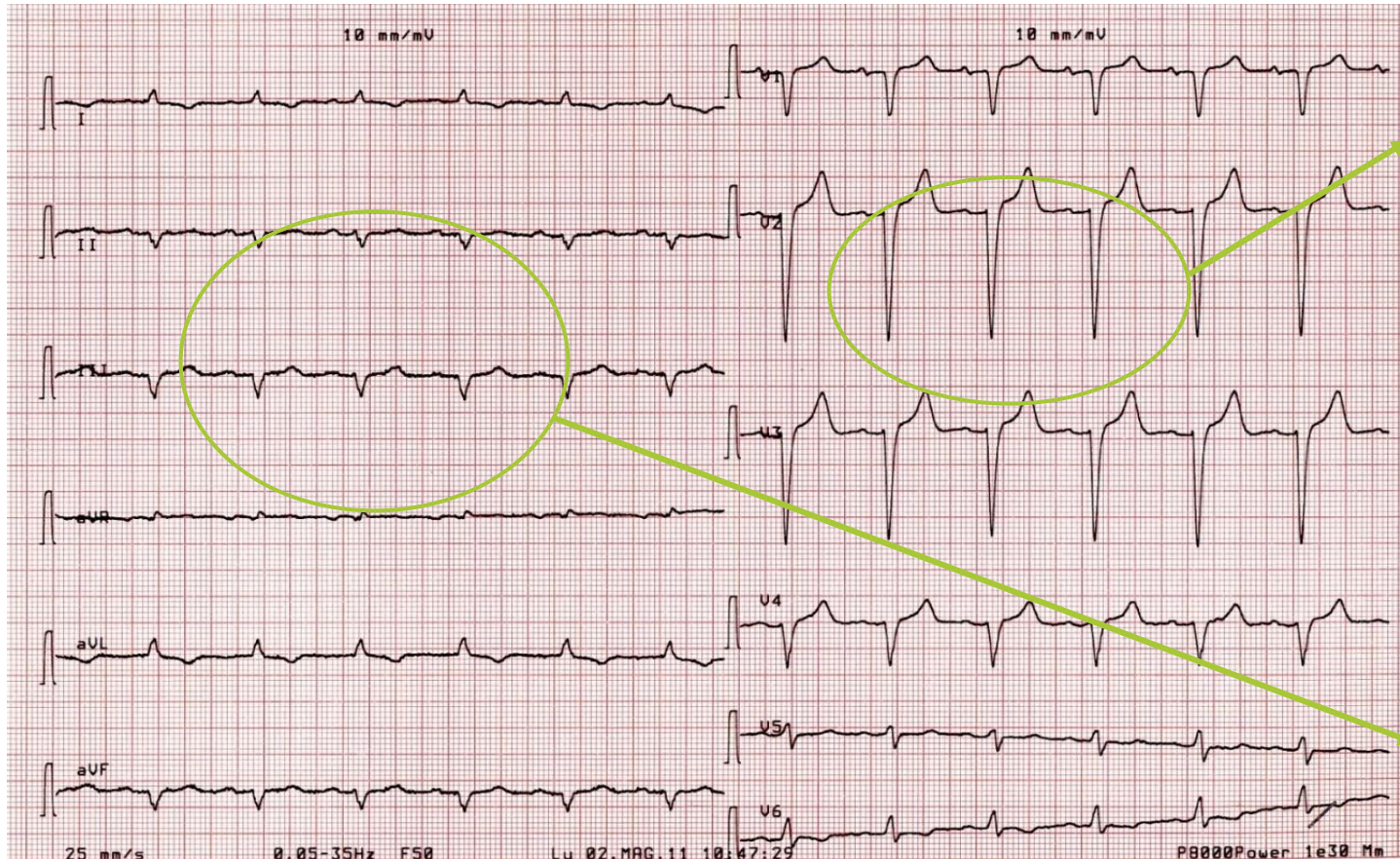
Cardiac Magnetic Resonance

Transmural or diffuse subendocardial late gadolinium enhancement

Abnormal gadolinium kinetics with difficulties in myocardial nulling in sensitive inversion recovery sequences

Elevated native T1 and extracellular volume (ECV>40%)

ECG



- Pseudoinfarction pattern
- Conduction abnormalities
- AV blocks
- Low voltages: 60%AL 20%ATTR

Discordance between LVH and QRS voltages!



Echocardiography

The image displays a 2x3 grid of echocardiogram panels. The top-left panel shows a longitudinal view of the left ventricle with a label 'Left ventricular hypertrophy' pointing to the thickened wall. The top-right panel shows a similar view of the right ventricle with a label 'Right ventricular hypertrophy'. The middle-left panel shows a cross-section of the heart with a label 'Granular Sparkling' pointing to the myocardium. The middle-right panel shows a cross-section with a label 'Pericardial effusion' pointing to the fluid-filled space around the heart. The bottom-left panel shows a cross-section of the atria with a label 'Biatrial dilation'. The bottom-right panel shows a cross-section with a label 'Interatrial septum thickening' pointing to the septum. A label 'Valvular thickening (less sensible but specific)' points to the mitral valve in the bottom-right panel.

Left ventricular hypertrophy

Right ventricular hypertrophy

Granular Sparkling

Pericardial effusion

Valvular thickening
(less sensible
but specific)

Biatrial dilation

Interatrial septum thickening

Bradi-, tachiaritmie, FA

Atrial Fibrillation

Atrial fibrillation is prevalent in up to 70% of patients and is often highly symptomatic and poorly tolerated.

Intracardiac Thrombus and Risk of Stroke

Atrial fibrillation with cardiac amyloidosis carries a high risk of intracardiac thrombus and stroke, regardless of CHA₂DS₂-VASc score.

Cardiac Amyloidosis

Amyloid fibers with apple-green birefringence under polarized light

Cardiac Conduction Disease

Conduction disease is common, most often involving His-Purkinje system. Placement of pacemaker is often required, although prophylactic pacing has not been shown to improve outcomes.

Ventricular Arrhythmias

Sudden death and ventricular arrhythmias are common in cardiac amyloidosis. Placement of an ICD for primary or secondary prevention has not been shown to improve outcomes.

Clinical Research

Prevalence of Cardiac Amyloidosis Among Elderly Patients With Recent-Onset Atrial Fibrillation: The PREVAL-ATTR Study

Screening population

n = 69 n = 49 n = 3

≥ 65 y Recent-onset AF (< 1 year) ≥ 1 red flag ATTR-CA

Key findings

Perugini 0 Perugini 2-3

8.3% (95% CI: 4-17%) CA prevalence

	No CA	CA	p
Basal characteristics			
Age (years)	76 ± 7	84 ± 4	< 0.001
Male sex, n (%)	65 (59%)	9 (90%)	0.047
Blood tests and echocardiography findings			
NTproBNP (pg/L)	1048 (427-3154)	3800 (1682-6101)	0.017
MWT at septum (mm)	12 (12-13)	14 (13-17)	0.003
Outcomes			
6 months AF, n (%)	45 (46%)	10 (100%)	< 0.001
Pacemaker, n (%)	8 (7.2%)	3 (30%)	0.049
Death, n (%)	12 (11%)	2 (20%)	0.326

^{99m}Tc-DPD scintigraphy

TTR gene test

Haematological tests
(serum FLC assay, SPIE & UPIE)

ATTR-CA screening may be considered in elderly patients with recent-onset AF, LVH ≥ 12 mm and an additional red flag sign suggestive of ATTR-CA.

Giancaterino, S. et al. J Am Coll Cardiol EP. 2020;6(4):351-61.



Cadute apparentemente **inspiegate** e intolleranza alla terapia antipertensiva



Syncope Unit (Neuromed Pozzilli, IS)

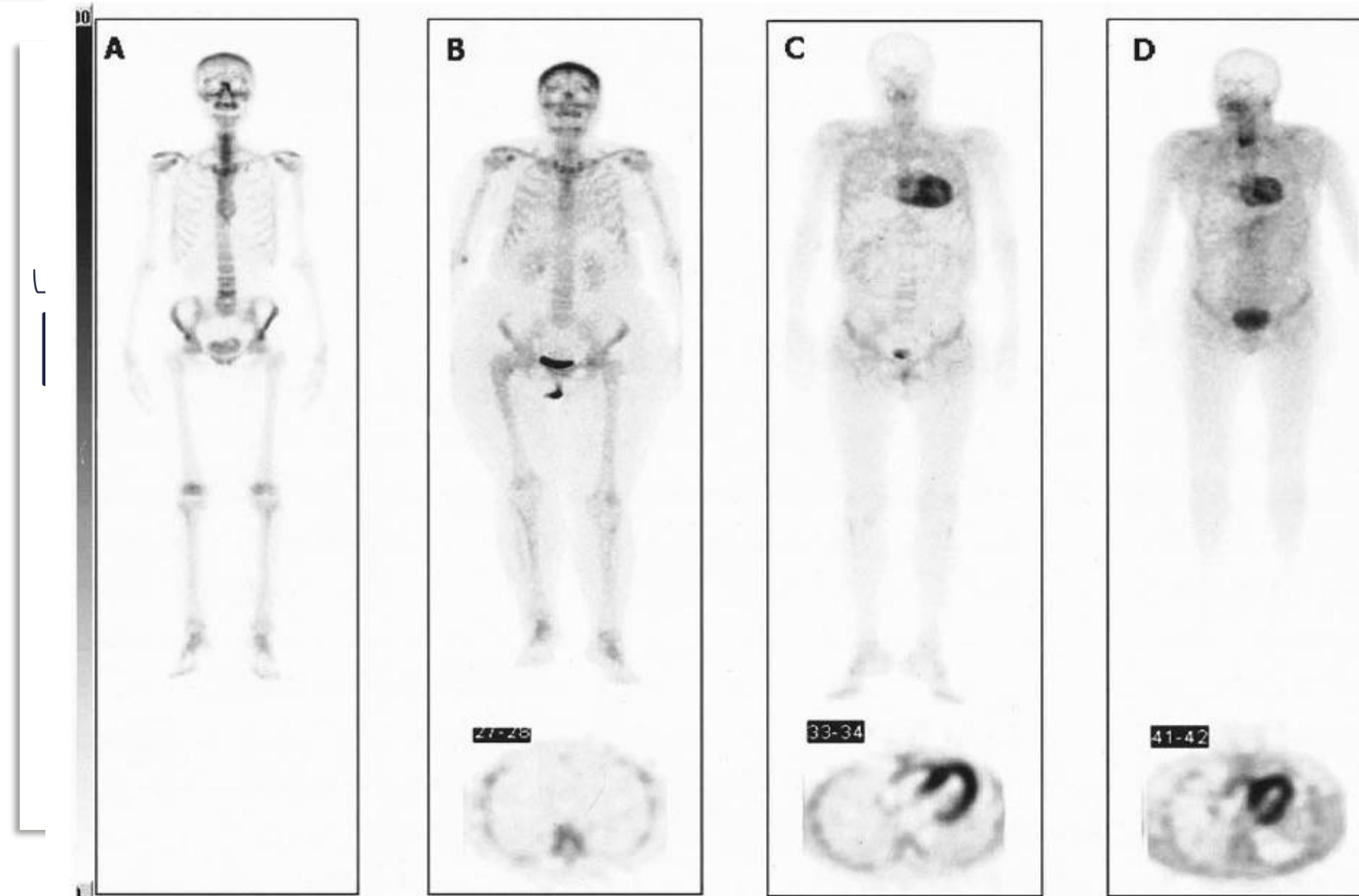
- 74 pazienti >75 anni ricoverati per sincope e indicazione a PM
- 32 con >1 red-flag per ATTR-CA
- Al momento 4 Casi ATTR-wt confermati

Prevalenza: 12.5%

Coinvolgimento muscolo-scheletrico

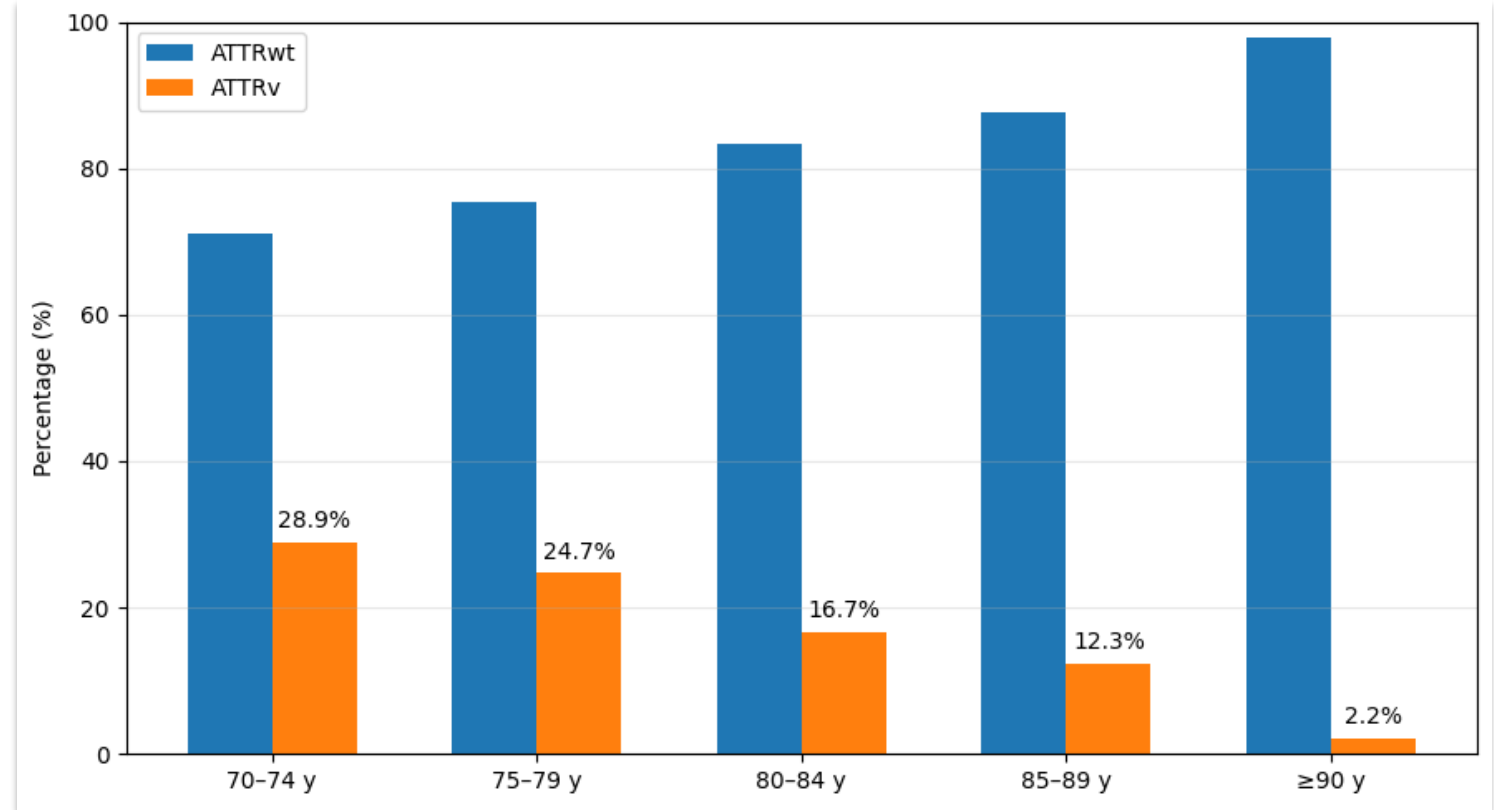


Diagnosis and treatment of cardiac amyloidosis: a position statement of the ESC Working Group on Myocardial and Pericardial Diseases





Amiloidosi cardiaca senile... wild-type o anche altro?





Stratificazione del rischio

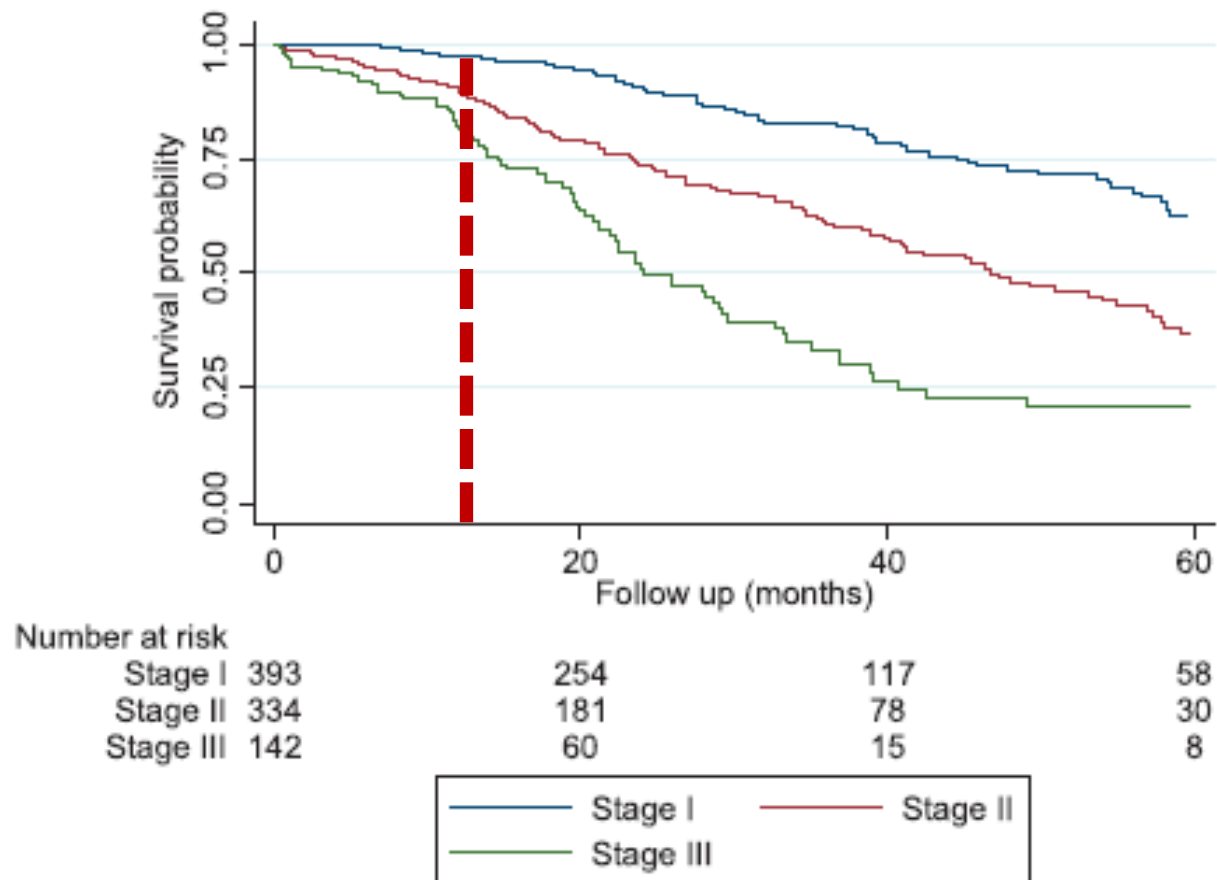
NT- pro BNP (cut off 3000 ng/L)

eGFR (cut off 45 ml/min/mq)

- **STADIO 1: NT-proBNP ≤ 3000 e eGFR ≥ 45**
- **STADIO 2: NT-proBNP < 3000 e eGFR < 45 oppure NT-proBNP > 3000 e eGFR > 45**
- **STADIO 3: NT-proBNP > 3000 e eGFR < 45**

Stratificazione del rischio

Staging of cardiac ATTR amyloidosis at diagnosis using NT-proBNP and eGFR



Sopravvivenza mediana:

69 mesi al I stadio

47 mesi al II stadio

24 mesi al III stadio



- Coorte 'storica'
- Ritardo diagnostico
- Assenza di terapia

Nuova (?) Stratificazione del rischio



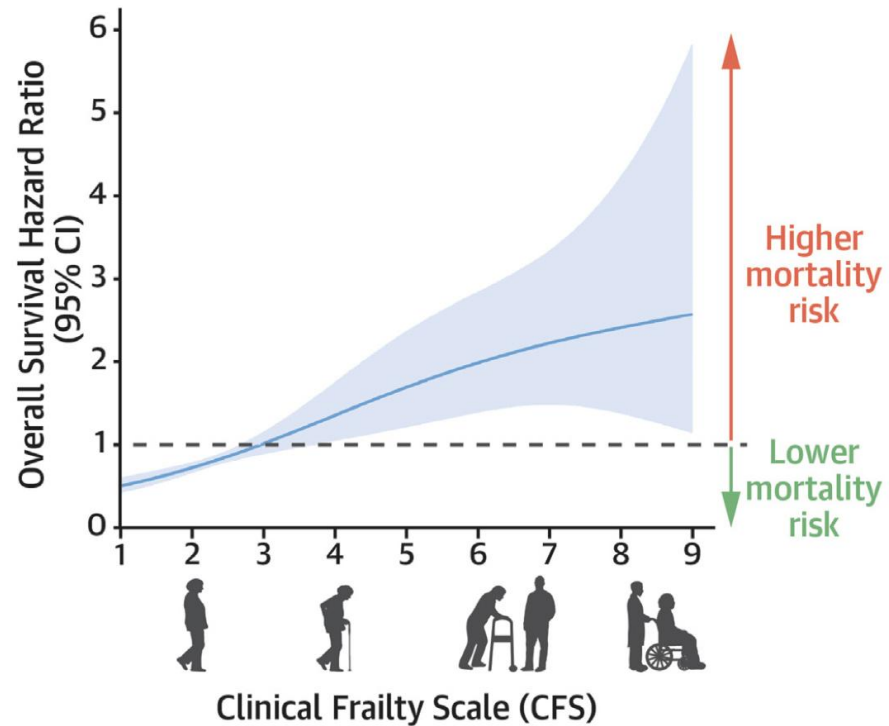
Clinical Phenotype and Prognostic Significance of Frailty in Transthyretin Cardiac Amyloidosis (ATTR-CA)

880 Patients With ATTR-CA Stratified by Clinical Frailty Scale (CFS)

- CFS 1-3: 378 (43.0%)
- CFS 4-5: 364 (41.4%)
- CFS 6-7: 129 (14.7%)
- CFS 8-9: 9 (1.0%)

Risk Factors for Worsening Frailty

- Female
- Non-p.(V142I)
- Age
- Diabetes Mellitus

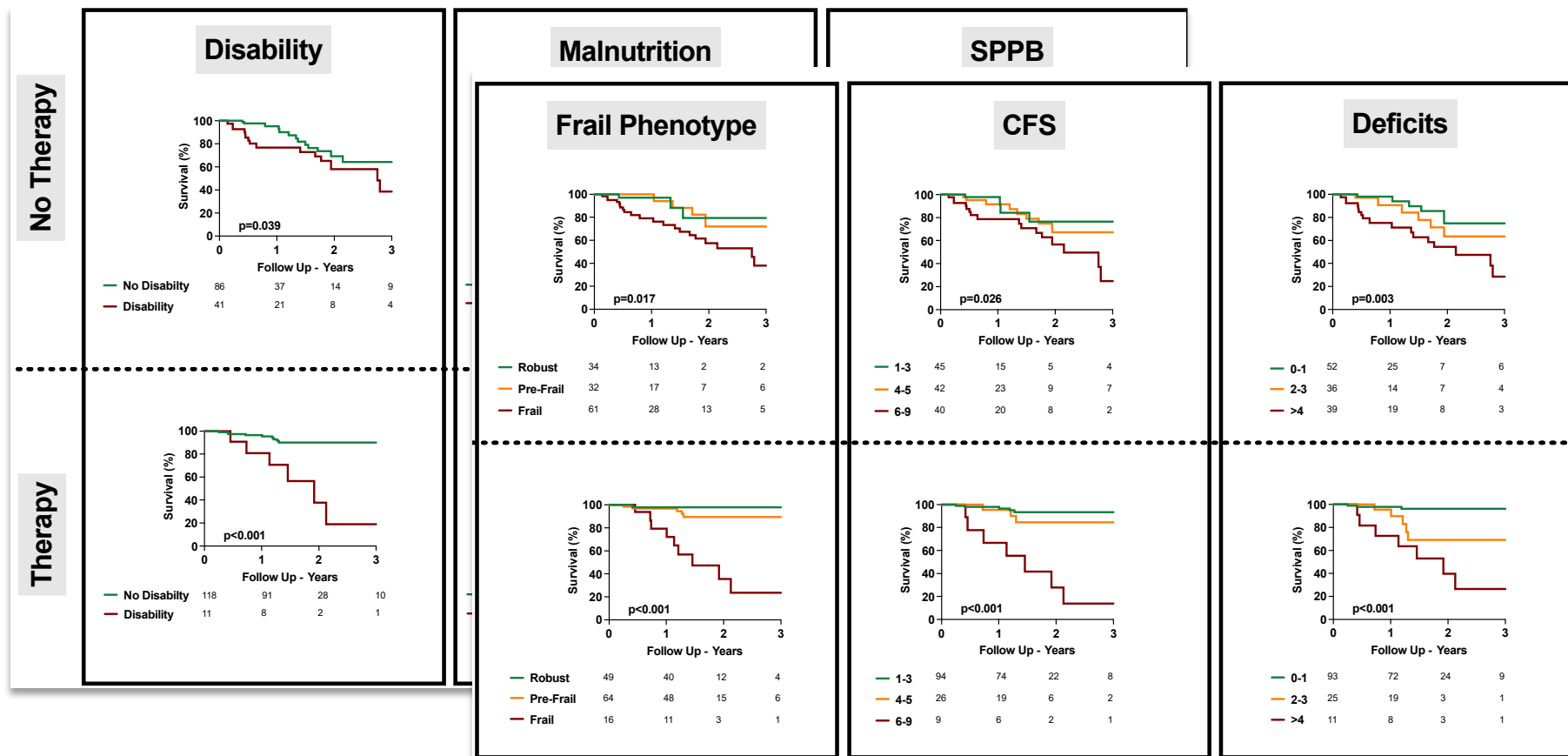




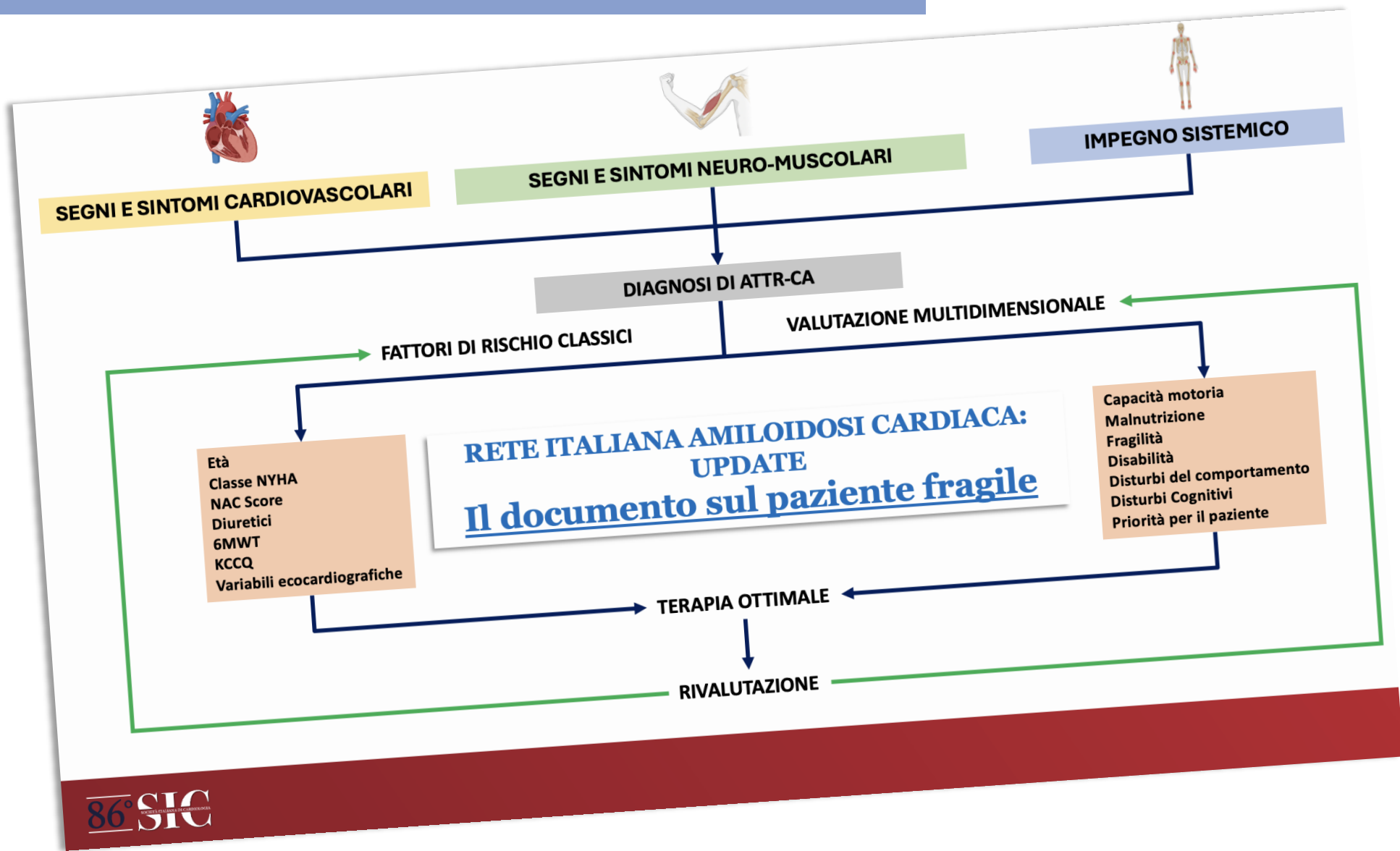
Nuova (?) Stratificazione del rischio

Prognostic Value of Malnutrition, Frailty, and Physical Performance in Transthyretin Cardiac Amyloidosis: Insights From a Prospective Multicenter Cohort Study

Carlo Fumagalli¹, MD; Mattia Zampieri², MD; Roberto Presta, MD; Greta Pini³, MD; Giulia Vetere⁴, MD; Alessia Argirò⁵, MD; Simone Longhi⁶, MD, PhD; Giacomo Tini⁷, MD, PhD; Beatrice Musumeci⁸, MD, PhD; Giuseppe Limongelli⁹, MD, PhD; Giuseppe Palmiero¹⁰, MD, PhD; Federica Verrillo, MD; Matteo Beltrami¹¹, MD, PhD; Mario Bo¹², MD, PhD; Gaetano De Ferrari, MD, PhD; Lorenzo Tofani¹³, BS, PhD; Celestino Sardu¹⁴, MD, PhD; Raffaele Marfella¹⁵, MD, PhD; Niccolò Marchionni¹⁶, MD; Federico Perletto¹⁷, MD, PhD; Iacopo Olivetto¹⁸, MD; Stefano Fumagalli¹⁹, MD, PhD; Mathew S. Maurer²⁰, MD; Marianna Fontana²¹, MD, PhD; Andrea Ungar²², MD, PhD; Francesco Cappelli²³, MD, PhD



Documento intersocietario SIGG – SICGe - SIC



CONCLUSIONI

- La **ATTR-CA** (soprattutto quando wt) è *la forma di scompenso* per eccellenza del **paziente anziano**.
- Il **sospetto** e una **diagnosi precoce** sono due elementi chiave per migliorare la prognosi dei pazienti.
- La **prognosi** del paziente con ATTR-CA è stratificata con **NTproBNP**, **funzione renale** e **terapia diuretica**.
- Oltre ad una precisa **caratterizzazione fenotipica** della malattia potrebbe essere utile, ai fini della riclassificazione prognostica, descrivere il compenso funzionale globale:
 - ✓ **Fragilità**
 - ✓ **Malnutrizione**
 - ✓ **Performance motoria**
- Nel paziente **grande anziano** dobbiamo capire quando eseguire un intervento terapeutico, per evitare di essere o “**ageisti**” (escludere un individuo solo per il criterio anagrafico) oppure “**futili**” (pazienti che hanno una prognosi limitata).
- La **valutazione multidimensionale** potrebbe essere uno strumento utile per riclassificare i pazienti.