

Diagnosi differenziale tra amiloidosi AL e TTR

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CONGRESSO

ROMA, 25 - 27 Giugno 2026

SEDE DEI LAVORI

A. Roma Lifestyle Hotel
Via Giorgio Zoega 59, Roma



PROGRAMMA



PREMIER LEAGUE WIN
Leicester City make history

BREXIT



UK VOTES TO LEAVE
European Union referendum

2016



AI BREAKTHROUGH
AlphaGo defeats Lee Sedol

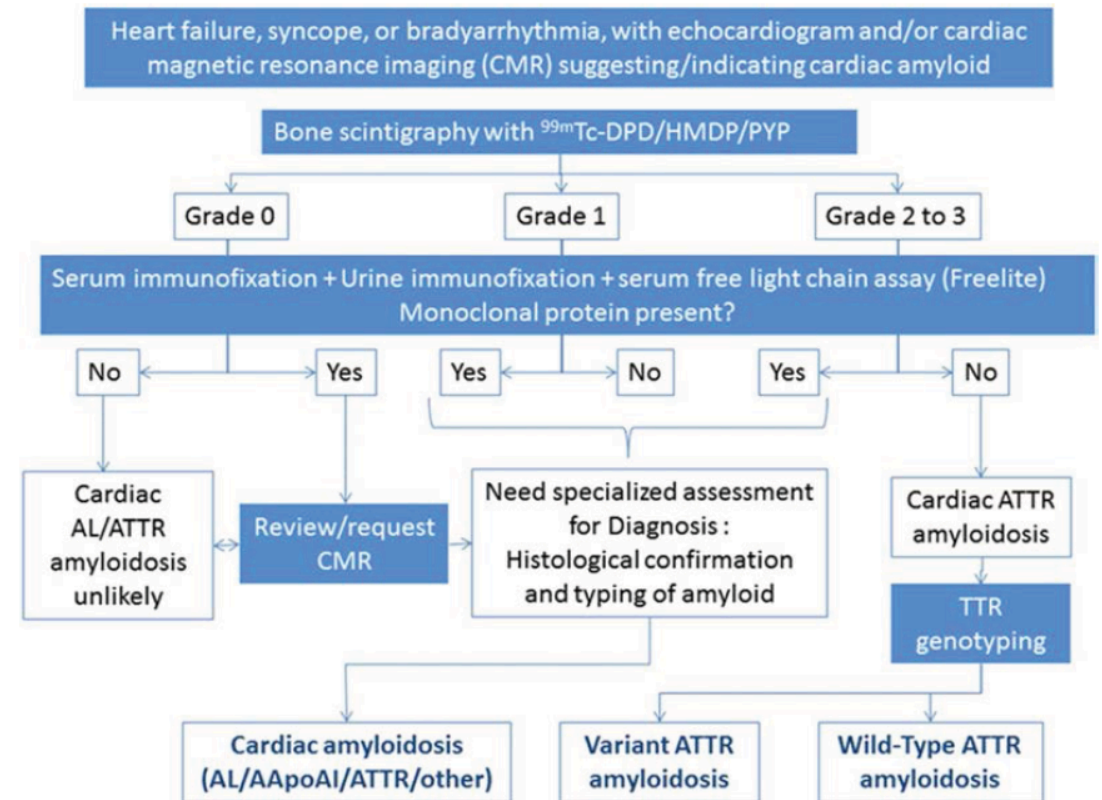


TRUMP ELECTED PRESIDENT
A new era in US politics

Heart Failure

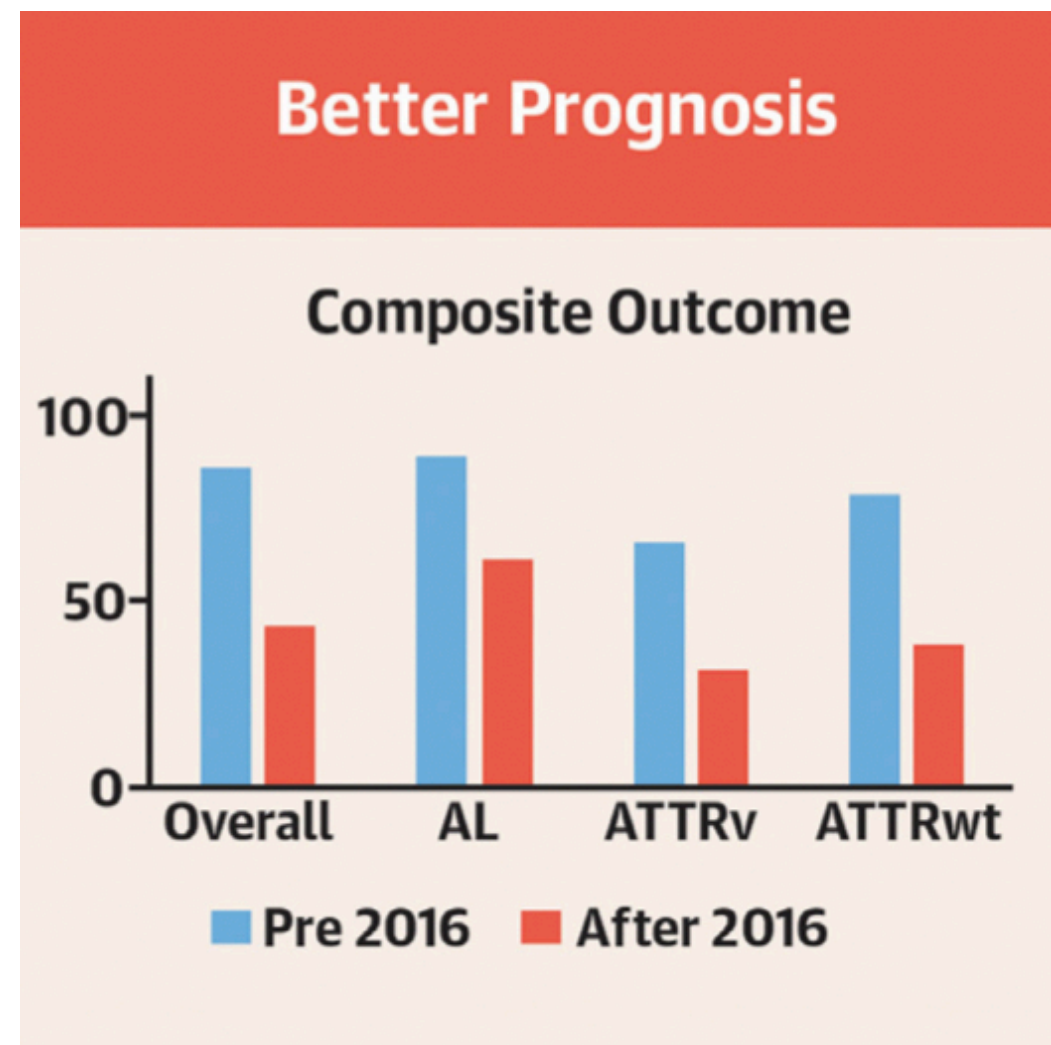
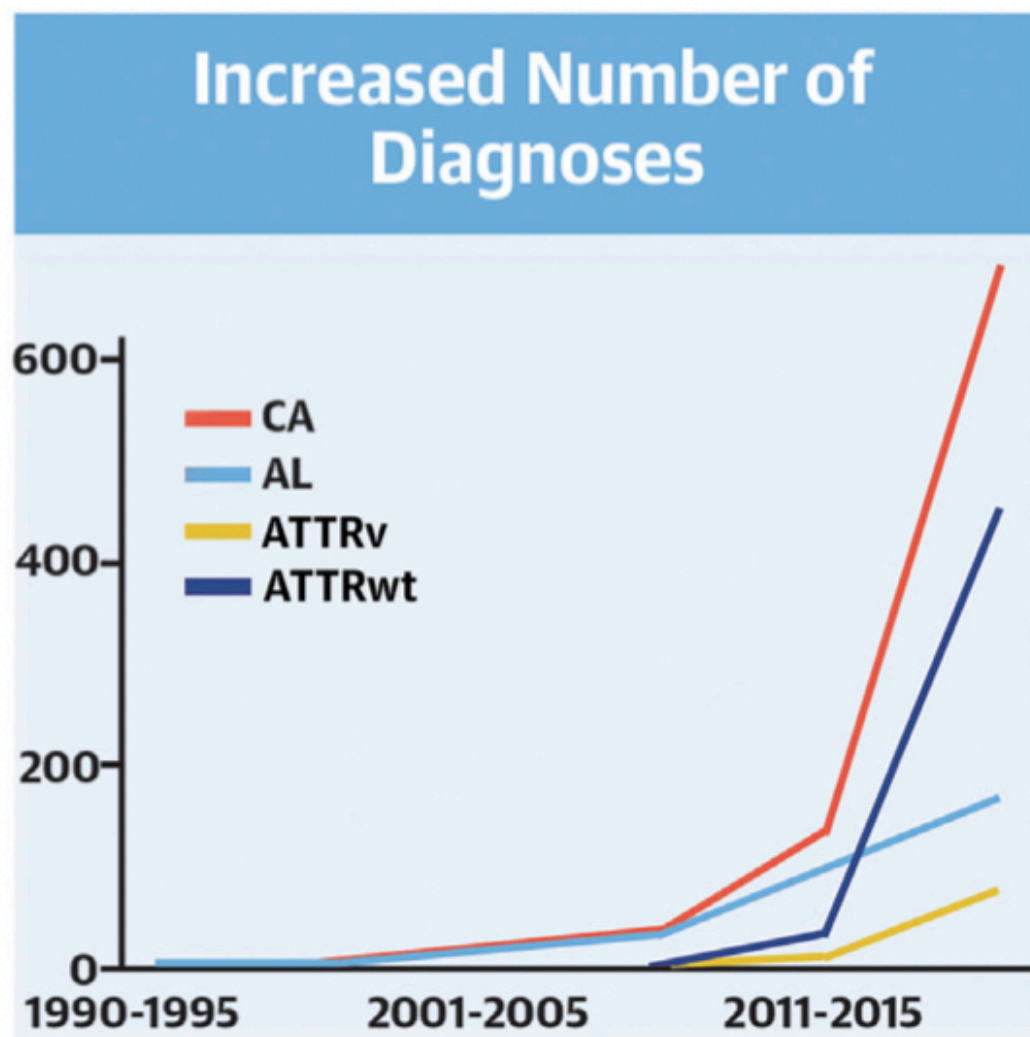
Nonbiopsy Diagnosis of Cardiac Transthyretin Amyloidosis

Julian D. Gillmore, MD, PhD; Mathew S. Maurer, MD; Rodney H. Falk, MD;
Giampaolo Merlini, MD; Thibaud Damy, MD; Angela Dispenzieri, MD;
Ashutosh D. Wechalekar, MD, DM; John L. Berk, MD; Candida C. Quarta, MD, PhD;
Martha Grogan, MD; Helen J. Lachmann, MD; Sabahat Bokhari, MD; Adam Castano, MD;
Sharmila Dorbala, MD, MPH; Geoff B. Johnson, MD, PhD;
Andor W.J.M. Glaudemans, MD, PhD; Tamer Rezk, BSc; Marianna Fontana, MD;
Giovanni Palladini, MD, PhD; Paolo Milani, MD; Pierluigi L. Guidalotti, MD;
Katarina Flatman; Thirusha Lane, MSc; Frederick W. Vonberg, MBBS; Carol J. Whelan, MD;
James C. Moon, MD; Frederick L. Ruberg, MD; Edward J. Miller, MD, PhD;
David F. Hutt, BAPSc; Bouke P. Hazenberg, MD, PhD; Claudio Rapezzi, MD;
Philip N. Hawkins, PhD, FMedSci



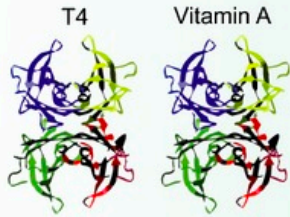
Circulation. 2016;133:2404-2412. DOI: 10.1161/CIRCULATIONAHA.116.021612.

AL vs ATTR: impatto dell'algoritmo diagnostico



ATTR

Normal function to transport



TTR composed of 4 identical subunits



Dissociated TTR monomers

This step occurs more readily in hereditary TTR amyloidosis

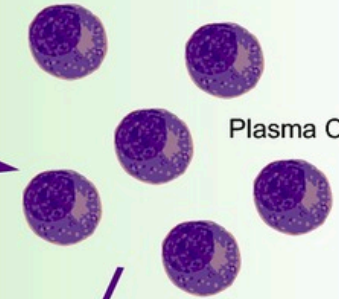
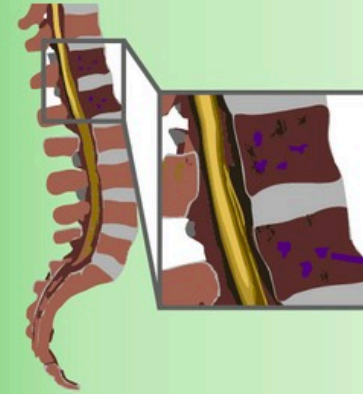


Amyloidogenic TTR intermediate

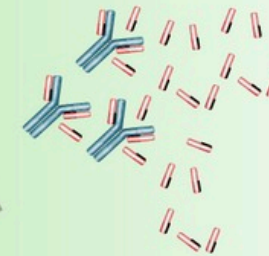


Restrictive Cardiomyopathy

AL



Plasma Cells



Amyloidogenic Light Chains

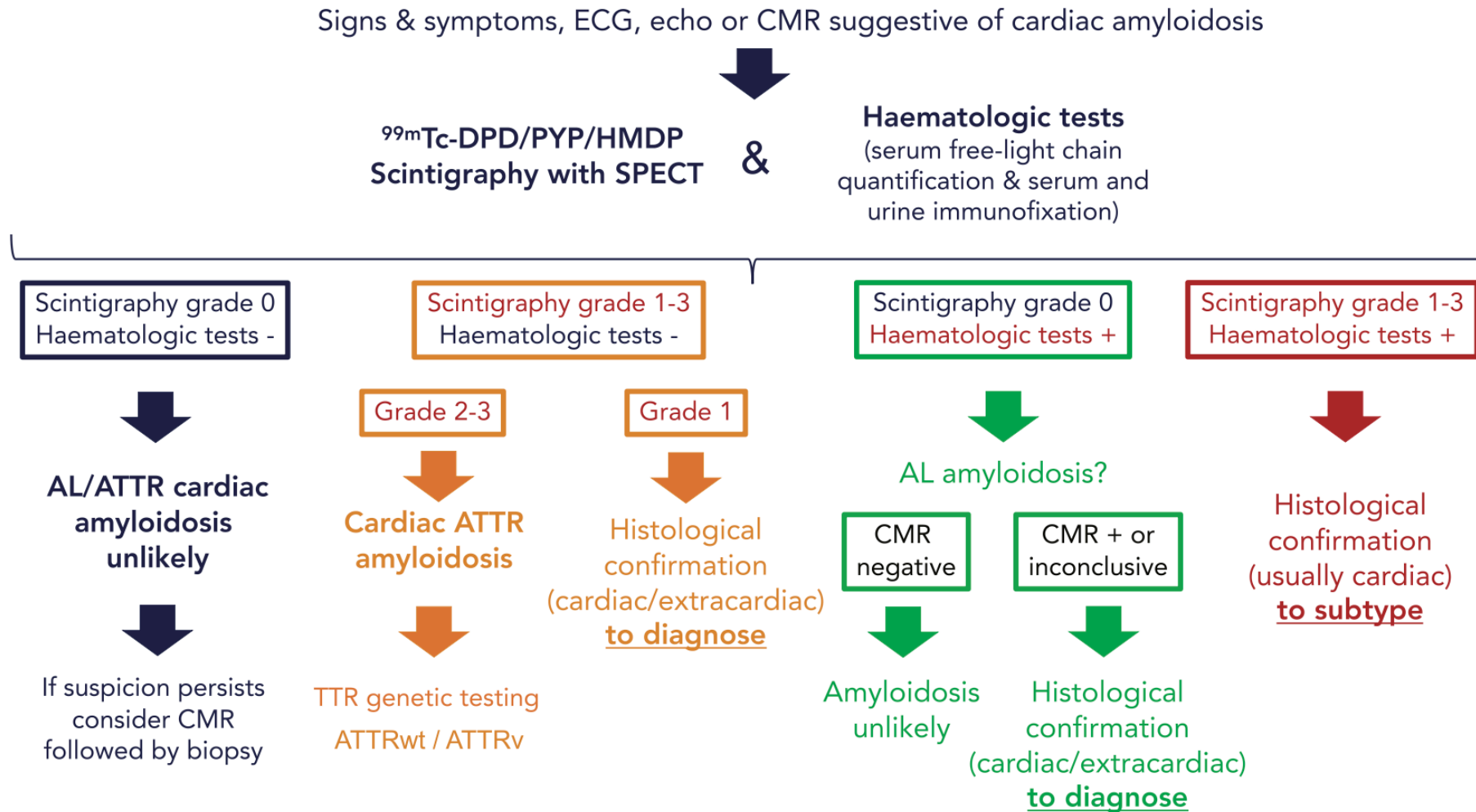


Progressione più lenta

Maggiore componente infiammatoria

Trattamento precoce migliora la prognosi

AL vs ATTR: procedimento diagnostico



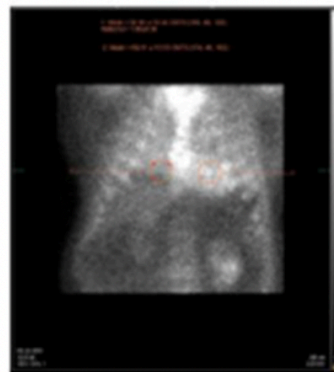
Planar ^{99m}Tc -PYP visual scoring:



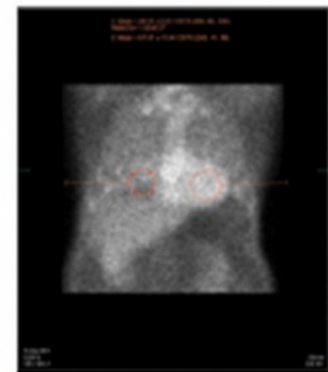
Grade 0



Grade 1



Grade 2

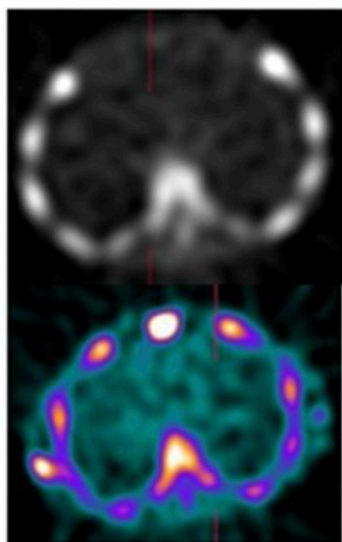


Grade 3

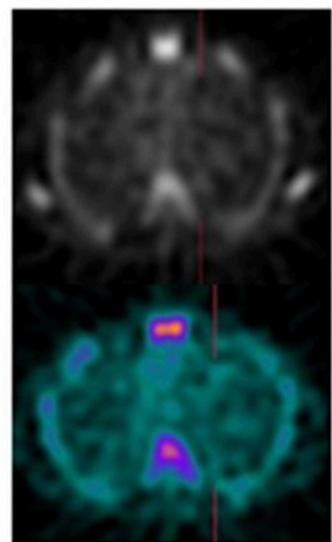
Heart-to-contralateral lung (H/CL) ratios:

$H/CL = 1.14 \pm 0.27$ $H/CL = 1.08 \pm 0.25$ $H/CL = 1.35 \pm 0.30$ $H/CL = 1.42 \pm 0.27$

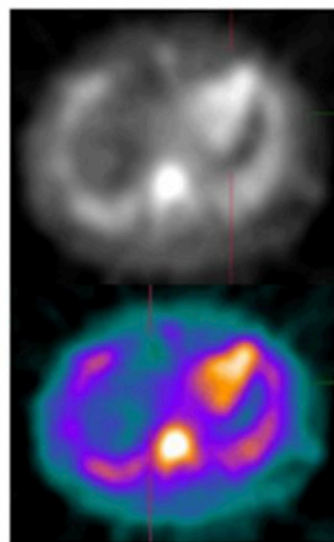
SPECT ^{99m}Tc -PYP visual scoring:



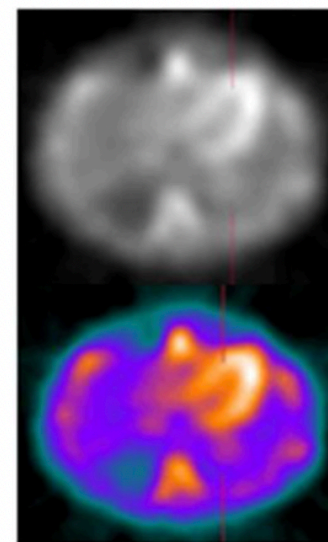
Grade 0



Grade 1



Grade 2



Grade 3

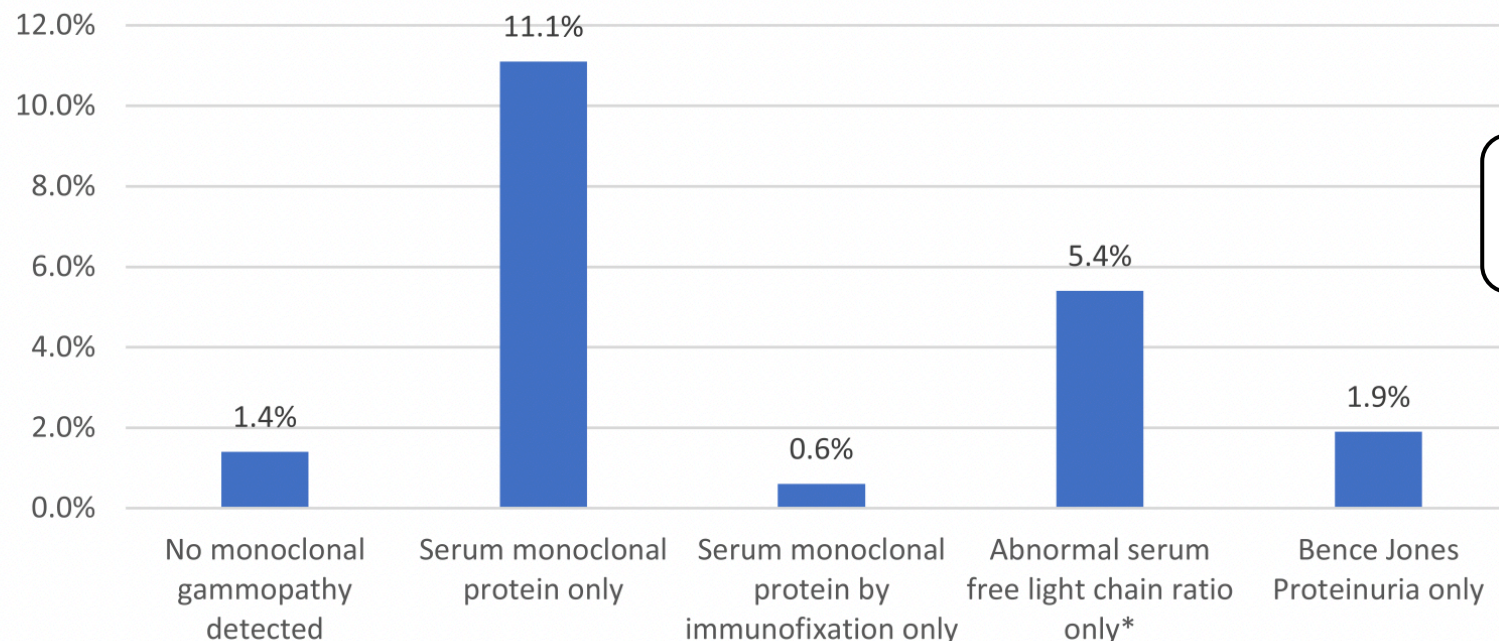
**Traccianti riconosciuti:
DPD – HMDP - PYP**

Tests ^a	What does it detect?	Most sensitive test for:	Normal range
SPIE	Clonal immunoglobulin and/or clonal light chain	Confirming clonal immunoglobulin production	No monoclonal protein present
UPIE	Clonal immunoglobulin and/or clonal light chain	Confirming clonal light chain production	No monoclonal protein present
Serum free light-chain assay	Ratio of serum kappa: lambda light chains	Detecting low-level clonal light chain production; clonality assumed if ratio is far from 1:1	Freelite: 0.26–1.65 ^b N Latex: 0.53–1.51

★★★ Valori di riferimento differenti secondo GFR

Biochemical triple testing to exclude monoclonal gammopathy for non-biopsy diagnosis of transthyretin amyloid cardiomyopathy

Detection of Monoclonal Gammopathy in AL Amyloidosis



4949 pz con AL confermata

Scenari clinici

**#1 scintigrafia ossea positiva
ed es.ematologici negativi**

**#2 scintigrafia ossea
negativa ed es.ematologici
positivi**

**#4 scintigrafia ossea positiva
ed es.ematologici positivi**

**#1 scintigrafia ossea
negativa ed es.ematologici
negativi**

**#1 scintigrafia ossea positiva
(Perugini 2-3) ed es.
ematologici negativi**

```
graph TD; A[Perugini 2-3] --> B[Test genetico];
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Perugini 2-3

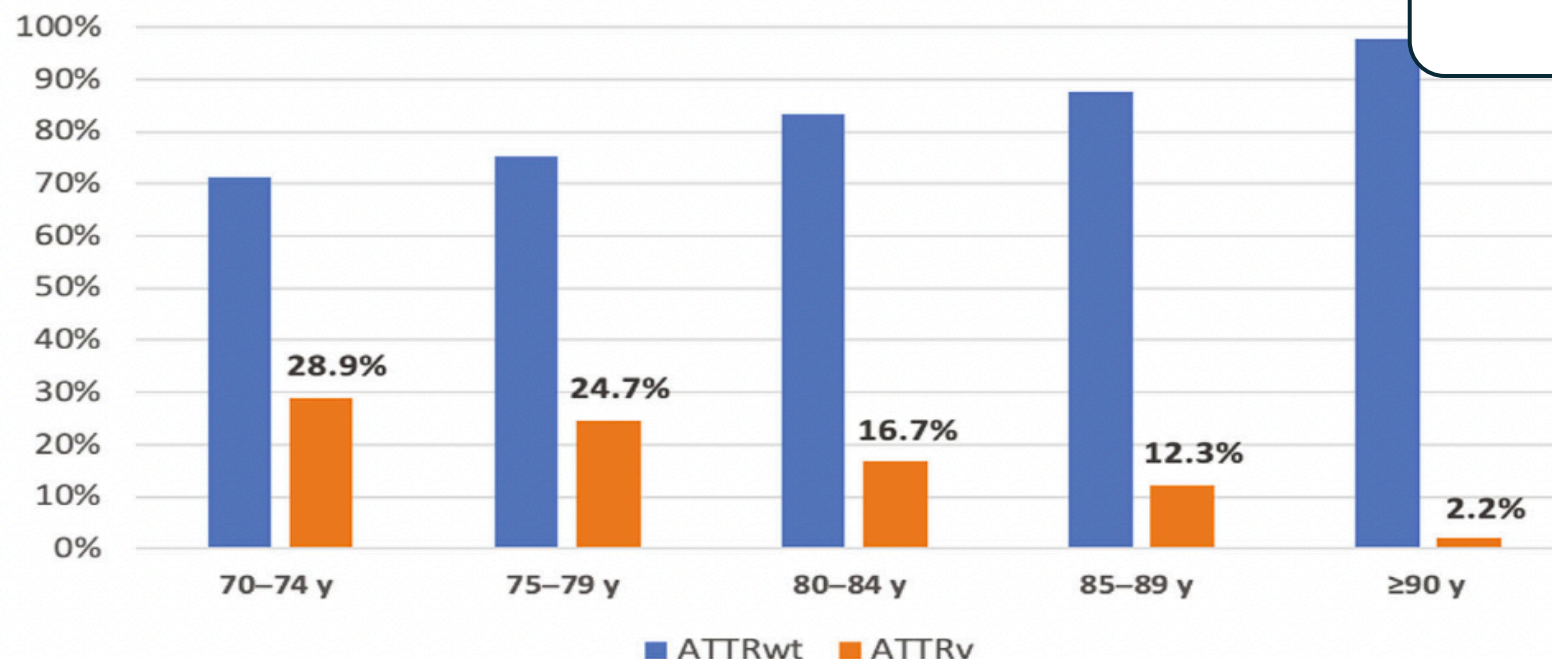
Test genetico

Prevalence, characteristics and outcomes of older patients with hereditary versus wild-type transthyretin amyloid cardiomyopathy

Aldostefano Porcari^{1,2,3†}, Yousuf Razvi^{1†}, Ambra Masi¹, Rishi Patel¹, Adam Ioannou¹, Muhammad U. Rauf¹, David F. Hutt¹, Dorota Rowczenio¹, Janet Gilbertson¹, Ana Martinez-Naharro¹, Lucia Venneri¹, Carol Whelan¹, Helen Lachmann¹, Ashutosh Wechalekar¹, Candida Cristina Quarta¹, Marco Merlo^{2,3}, Gianfranco Sinagra^{2,3}, Philip N. Hawkins¹, Marianna Fontana¹ and Julian D. Gillmore^{1*}

2029 patients with
ATTR-CM
(median age 79 years at
diagnosis)

20%.7% ATTRv-CM



Possibile sottodiagnosi della patologia in individui > 70 yrs

**#2 scintigrafia ossea
negativa (Perugini 0-1) ed es.
ematologici positivi**

Quadro cardiologico sospetto

Non sospetto cardiologico

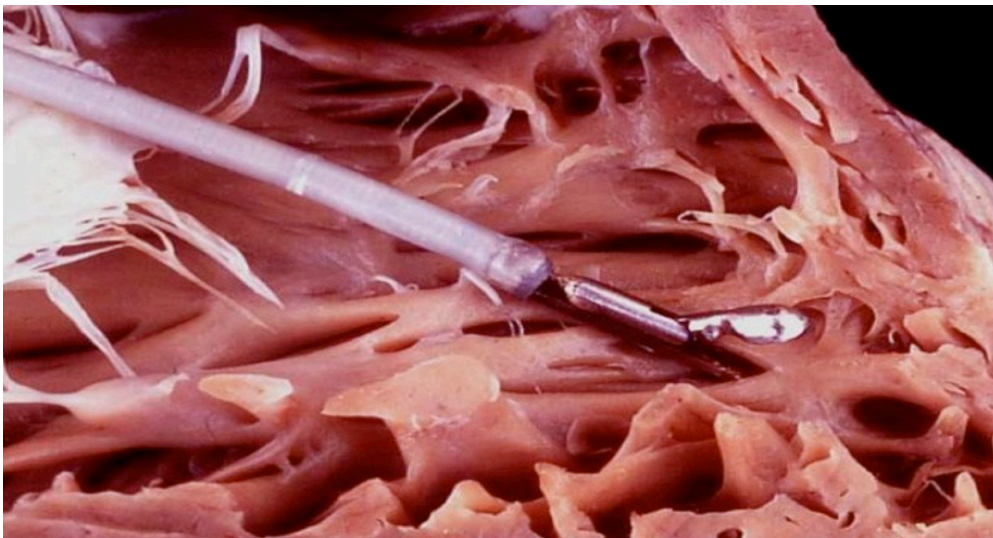
Risonanza magnetica cardiaca

Biopsia tissutale

Dove biopsizzare?

BIOPSIA ENDOMIOCARDICA

- Necessaria quando solo il cuore è coinvolto
- Maggiore invasività (1-3% complicanze)
- Va effettuata in centri esperti



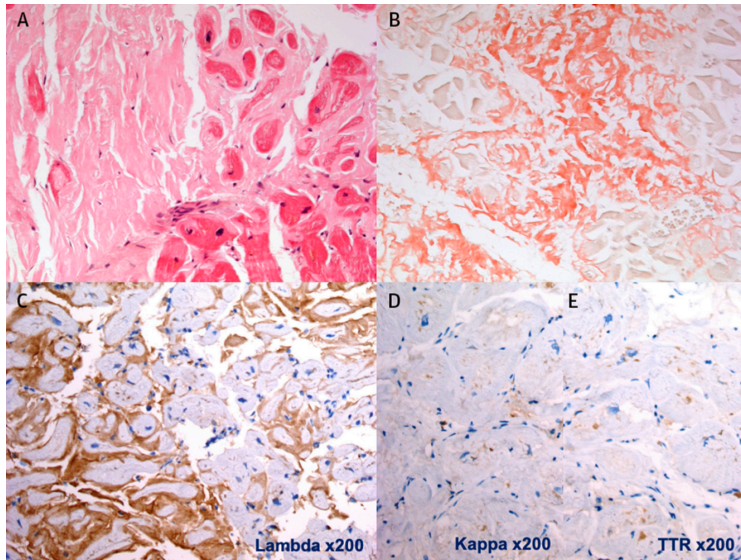
BIOPSIA EXTRACARDIACA

- Grasso periombelicale o ghiandole salivari
- Sensibilità alta per AL (84%) ma bassa per TTR (45% vTTR -15% wt-TTR)

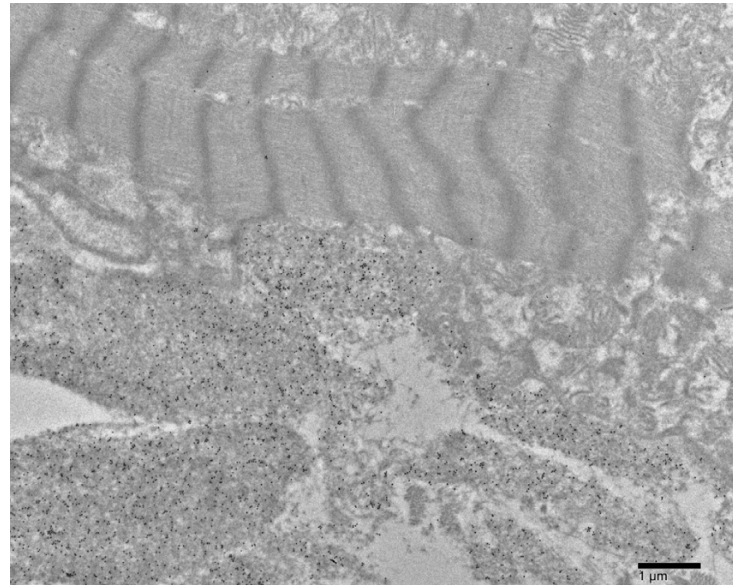


Come leggere la biopsia

Immunoistochimica con microscopia ottica



Immunoistochimica con microscopia elettronica



Spettrometria di massa

		Probability Legend:					
		≥95%					
		80% to 94%					
		50% to 79%					
		20% to 49%					
		0% to 19%					
#	Visible? Starred?	Bio View: Identified Proteins (56/61) Including 0 Decoys	Accession Number	Molecular Weight	Sample #1	Sample #2	
1	✓	★ Transthyretin	TTHY_HUMAN	16 kDa	227	198	
2	✓	★ Transthyretin with V122I mutation (p.Val142Ile) ...	MUT-TTHY_V122I_HUMAN	2 kDa	35	38	
3	✓	★ Apolipoprotein E	APOE_HUMAN (+1)	36 kDa	118	117	
4	✓	★ Apolipoprotein A-IV	APOA4_HUMAN	45 kDa	115	113	
5	✓	★ Serum amyloid P-component	SAMP_HUMAN	25 kDa	107	103	
6	✓	★ Vitronectin	VTNC_HUMAN	54 kDa	106	96	
7	✓	★ Serum albumin	ALBU_HUMAN	69 kDa	74	107	
8	✓	★ Myosin-7	MYH7_HUMAN	223 kDa	40	120	
9	✓	★ Clusterin	CLUS_HUMAN	52 kDa	62	60	
10	✓	★ Complement C3	CO3_HUMAN	187 kDa	48	45	

Minore costo
Bassa specificità per AL
Cross-reakzione tra anticorpi

Costo intermedio
Necessità di buona tecnica di
fissazione del tessuto ed
esperienza del patologo

Costo elevato
GOLD STANDARD!

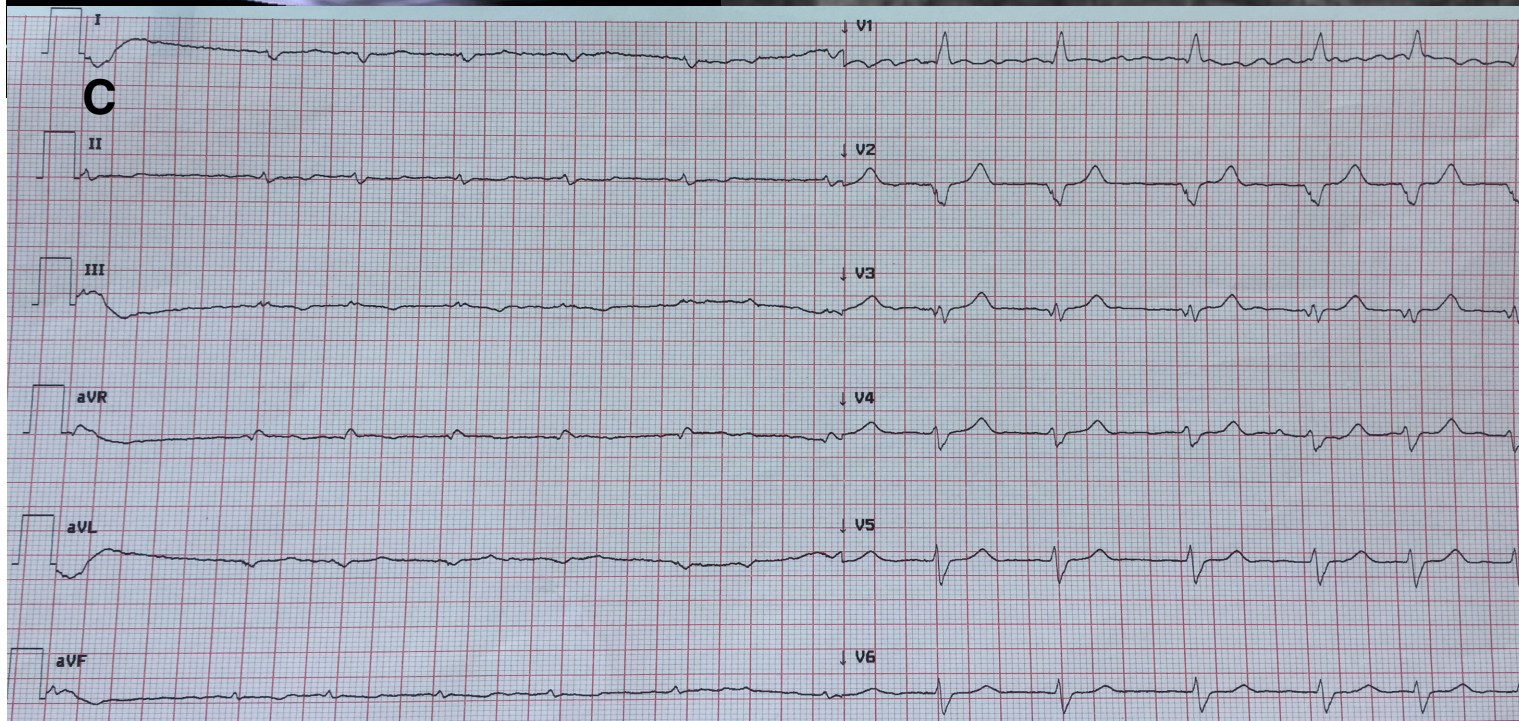
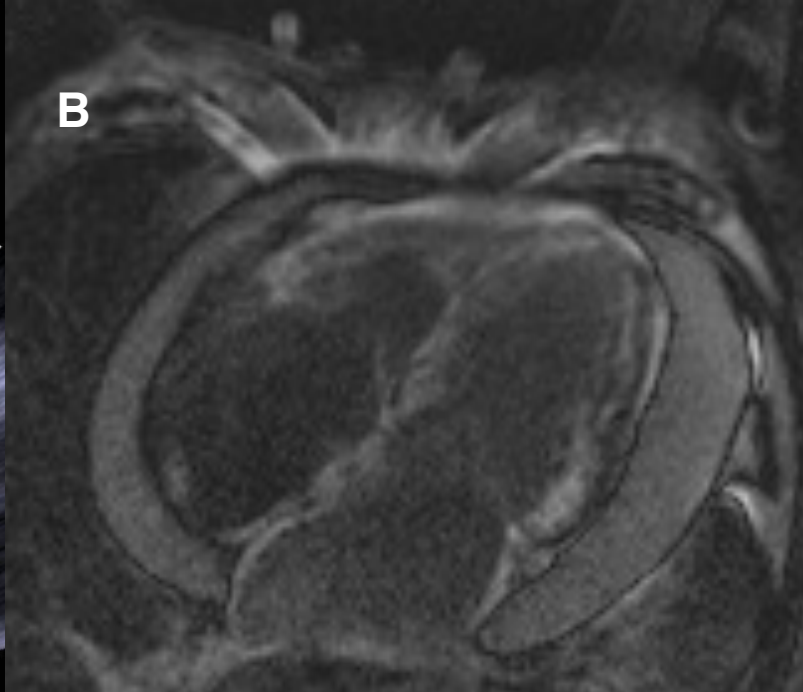
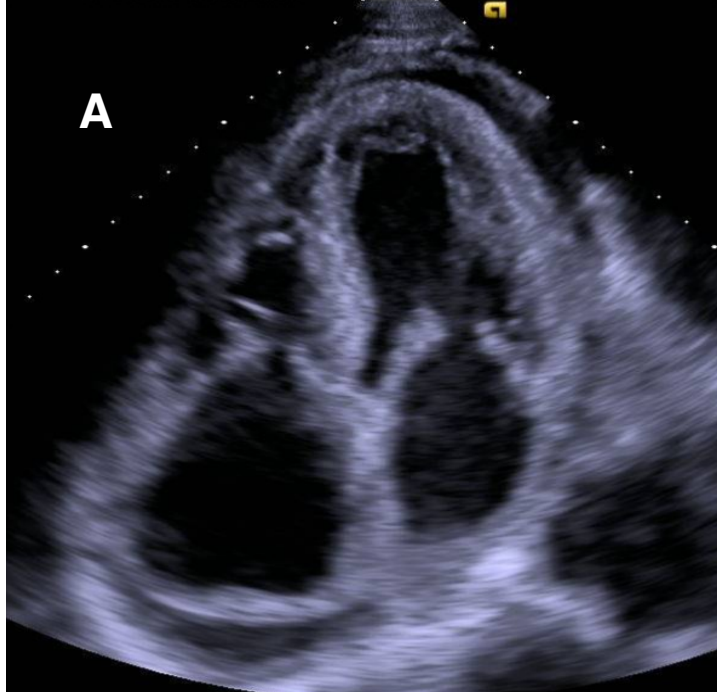
**#3 scintigrafia ossea
negativa (Perugini 0-1) ed es.
ematologici negativi**

Quadro estremamente suggestivo

Non è un'amiloidosi

Risonanza magnetica cardiaca

Biopsia tissutale (cuore)



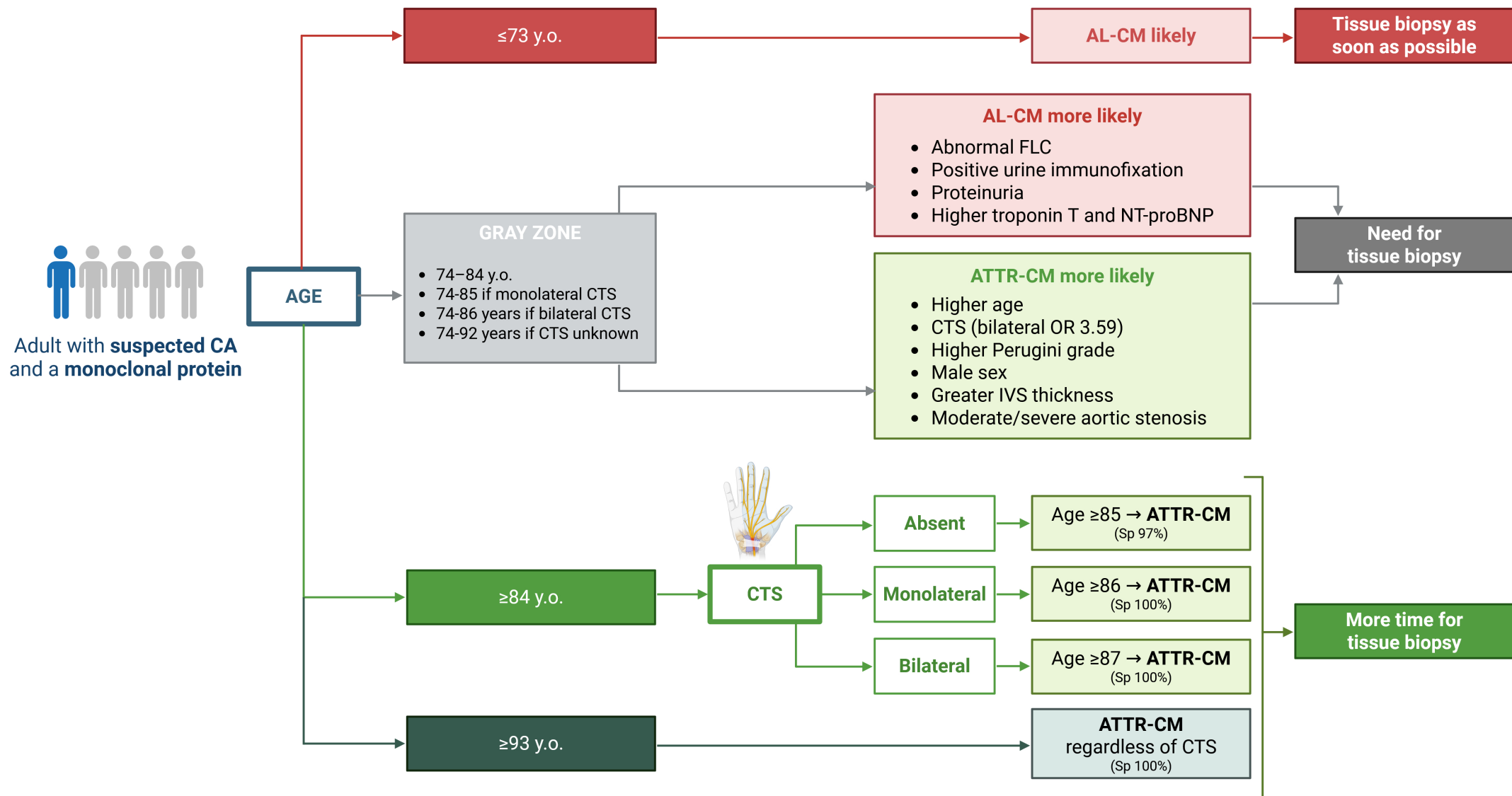
Phe64Leu

**#4 scintigrafia ossea positiva
(Perugini 2-3) ed es.
ematologici positivi**

***Biopsia tissutale cardiaca/
extracardiaca***

Amiloidosi TTR

Coesistenza AL/TTR



TAKE HOME MESSAGES

- ✓ ATTR ≠ AL: stessa infiltrazione, diversa malattia
- ✓ Scintigrafia + triple testing sono il cardine della diagnosi moderna
- ✓ ATTR: Perugini 2-3 + es. ematologici negativi. Negli altri casi la conferma istologia è necessaria
- ✓ La tipizzazione corretta dell'amiloide guida la terapia e cambia la prognosi

ROMA CARDIOMIOPATIE

2^A EDIZIONE • 2026



CENTRO CONGRESSI ROMA EVENTI • PIAZZA DI SPAGNA | 1-2 OTTOBRE 2026