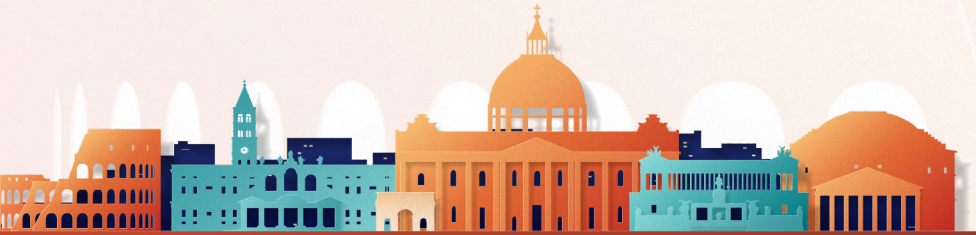
PLACE 2026
PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

CONGRESSO
ROMA, 25 - 27 Giugno 2026

INSUFFICIENZA CARDIACA: OLTRE …

L'antigene carboidratico 125 dalla diagnosi oncologica allo scompenso cardiaco. Può essere veramente un marker importante per il clinico?



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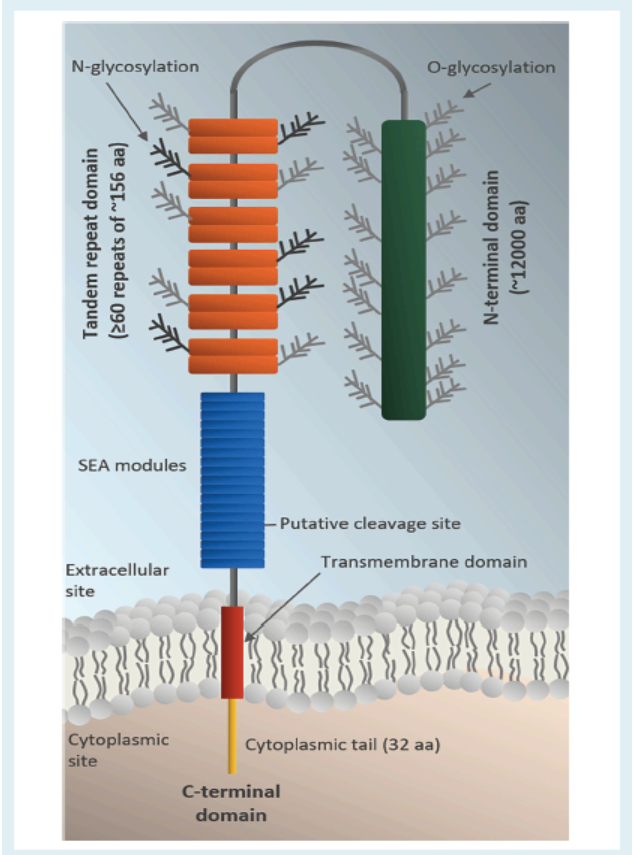
Definizione Ca125



Il **CA 125** è una glicoproteina complessa codificata dal gene MUC16 nell'uomo. Inizialmente riconosciuto nel 1981 dal 125° anticorpo monoclonale prodotto contro una linea cellulare di cancro ovarico

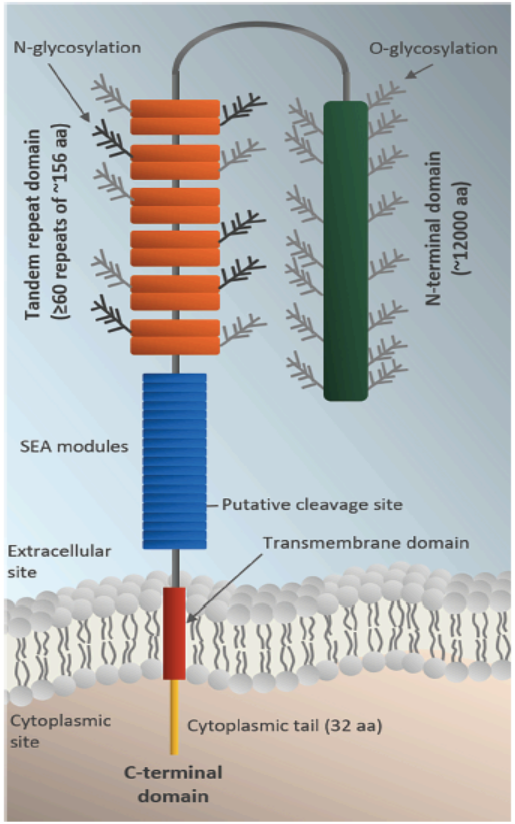
Contiene circa 22.000 amminoacidi, il che la rende la più grande mucina associata alla membrana

Il CA125 è sintetizzato principalmente dalle cellule mesoteliali del pericardio, della pleura o del peritoneo. Sembra essere coinvolto in molteplici processi, tra cui le risposte infiammatorie e immunitarie mediate dalle cellule.

Il CA125 è stato ampiamente studiato come biomarcatore circolante per il monitoraggio del cancro ovarico.

(European Journal of Heart Failure (2021) 23, 1445–1457)

Struttura Ca125

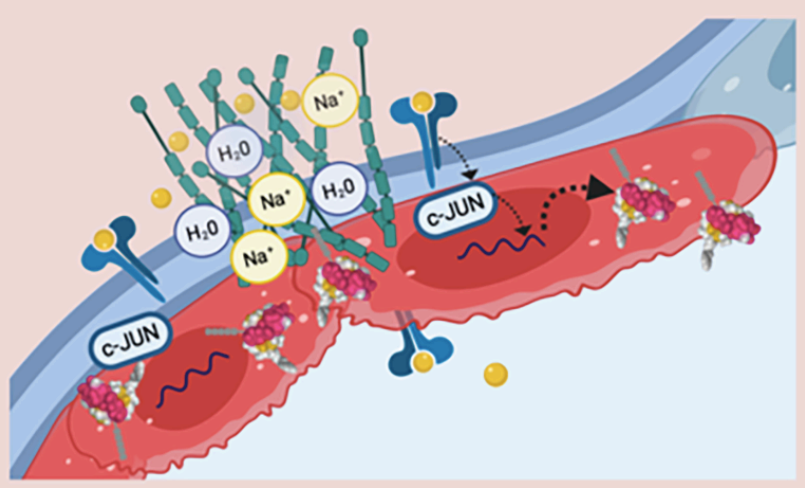


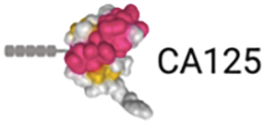
E' composta da tre differenti domini:

1) **Dominio extracellulare**
   Massiccia porzione rivolta all'esterno ricca di carboidrati e di sequenze di aminoacidi ripetute responsabile delle caratteristiche di idratazione e protezione delle mucose
2) **Dominio transmembrana**
   La regione che ancora la proteina alla superficie cellulare
3) **Dominio intracellulare**
   Una breve porzione citoplasmatica (coda) che interagisce con il citoscheletro cellulare

(European Journal of Heart Failure (2021) 23, 1445–1457)

Fisiologia del Ca125





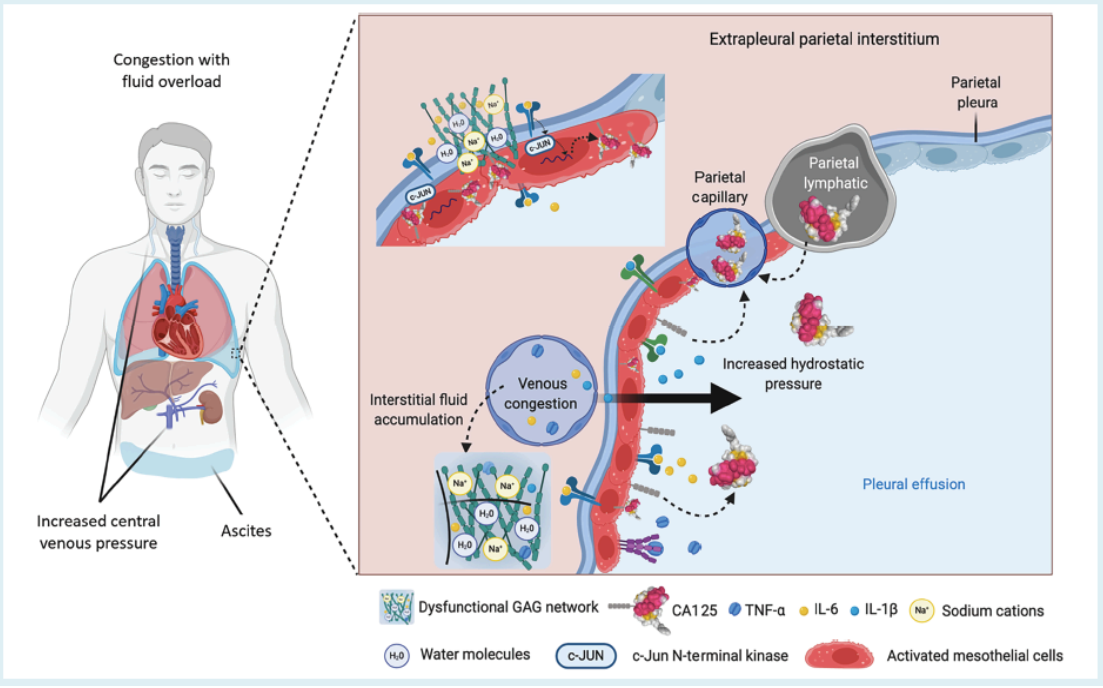
Cellule mesoteliali

Il ruolo biologico del CA125 è in gran parte sconosciuto.
È stato suggerito che il **CA125 protegga la superficie epiteliale** dallo stress meccanico agendo come lubrificante.

Inoltre, l'interazione tra le mucine trans-membrana e altre mucine mesoteliali/interstiziali proteiche sembrano supportare il ruolo del CA125 nei processi che coinvolgono **il trasporto di fluidi e cellule, l'infiammazione, la riparazione dei tessuti** e la disseminazione del tumore

Zeillemaker AM, et al J Clin Pathol 1994;47:263–265.
Huang F et al Med Hypotheses 2012;79:381–383.
Murphy SP et al . J Am Coll Cardiol 2020;75:1324–1340.
Nunez J et al European Journal of Heart Failure 2021 23, 1445

Pato-Fisiologia del Ca125



A differenza delle neoplasie che sovra-esprimono le mucine, **il miocardio non è una fonte di CA125**

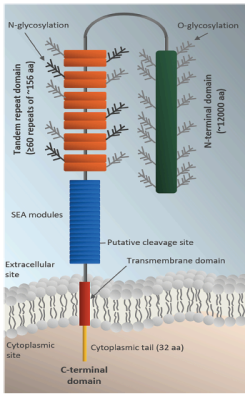
Sia gli **stimoli emodinamici che quelli infiammatori** sembrano svolgere un ruolo cruciale nei meccanismi che portano alla sovraregolazione del CA125 nell'insufficienza cardiaca con presenza di congestione.

L'attivazione delle cellule mesoteliali in risposta all'aumento della pressione idrostatica, allo stress meccanico e all'attivazione delle citochine è stata suggerita come il meccanismo cruciale che promuove la sintesi di CA125

Zeillemaker AM, et al J Clin Pathol 1994;47:263–265.
Huang F et al Med Hypotheses 2012;79:381–383.
Murphy SP et al . J Am Coll Cardiol 2020;75:1324–1340.
Nunez J et al European Journal of Heart Failure 2021 23, 1445

Ruolo Clinico del Ca125

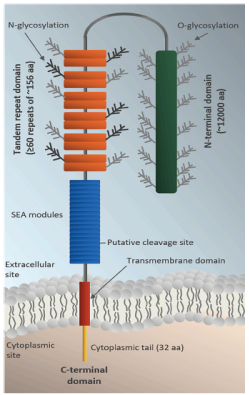
Ca125



- Ca125 e Stratificazione del Rischio
- Il monitoraggio dello Scompenso Cardiaco
- Ca 125 ed il ruolo della terapia

Ruolo Clinico del Ca125

Ca125



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Stratificazione del Rischio

Research article

CA 125 and its relation to cardiac function

H. Nagele, M. Bahlo, R Klapdor, D. Schaeperkoetter, W.Rodiger
Am Heart J 1999; 137: 1044

- CA 125 was **significantly correlated** with neurohormones and filling pressures.
- CA 125 **decreases** after HTx (401 +/- 259 U/L vs 33 +/- 22 U/L, P <.001, n = 25) stabilization (429 +/- 188 U/L vs 78 +/- 35 U/L, P <.001, n = 25)
- CA 125 **increases** during worsening of heart failure (42 +/- 25 U/L vs 89 +/- 32 U/L, P <.01, n = 9). In 4 patients after HTx, unexpected death was preceded by rising CA 125 levels.
- **CEA, CA 199, CA 153, TPS, or TPA** did not correlate with HF status.

Stratificazione del Rischio

SYSTEMATIC REVIEW Open Access

Carbohydrate antigen 125 and clinical outcomes in heart failure: systematic review and meta-analysis

Seyed Morteza Pourfaraji[1], Fatemeh Ojaghi Shirmard[1], Dorsa Salabat[1], Danyal Salabat[2], Zahra Mehdipournamdar[3], Toshiki Kuno[4], Anil Harrison[5], Marc Samsky[6] and Kaveh Hosseini[1*]

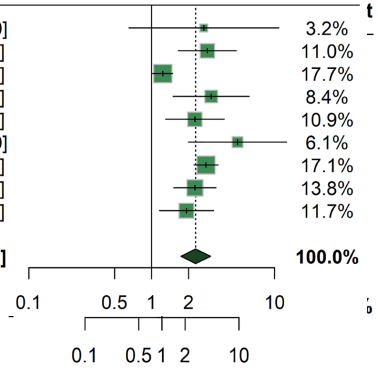
Cardiovascular Disorders (2025) 25:637

AHF and CHF
4570 pts, 9 studi
Ca125 > 35 U/ml

Hospitalization+C.Death

Study	HR	95%-CI	Weight
Monteiro et al. 2009	2.66	[0.66; 10.80]	3.2%
Mansour et al. 2010	2.84	[1.65; 4.88]	11.0%
Yoon et al. 2019	1.23	[1.02; 1.48]	17.7%
Chen et al. 2020	3.05	[1.50; 6.20]	8.4%
Lourenco et al. 2022	2.25	[1.30; 3.89]	10.9%
Nuenz et al. 2022	5.00	[2.00; 12.50]	6.1%
Docherty et al. 2023	2.77	[2.21; 3.47]	17.1%
Zhang et al. 2023	2.25	[1.52; 3.33]	13.8%
Menghoum et al. 2024	1.92	[1.16; 3.18]	11.7%
Random effects model	**2.28**	**[1.74; 3.01]**	**100.0%**

Heterogeneity: I^2 = 80.5%, τ^2 = 0.1014, p < 0.0001
Meta-analysis for Risk of All-Cause Mortality
Heterogeneity: I^2 = 75.0%, τ^2 = 0.1202, p < 0.0001
Meta-analysis for Risk of End Point Outcomes



All cause Death

Study	HR	95%-CI	Weight
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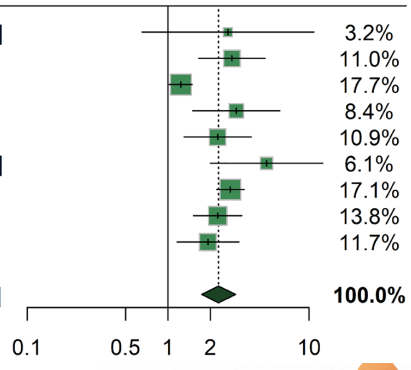
Meta-analysis for Risk of All-Cause Mortality



Stratificazione del Rischio

Original research

Cancer antigen-125 and outcomes in acute heart failure: a systematic review and meta-analysis

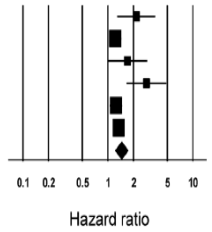
Ka Hou Christien Li,[1,2,3] Mengqi Gong,[4] Guangping Li,[4] Adrian Baranchuk,[5] Tong Liu,[4] Martin C S Wong,[6] Aaron Jesuthasan,[3] Rachel W C Lai,[1,2] Jenny Chi Ling Lai,[1,2] Alex Pui Wai Lee,[1,2] Antoni Bayés-Genis,[7,8] Rafael de la Espriella,[9,10,11] Juan Sanchis,[9,10,11] William K K Wu,[2,12,13] Gary Tse,[1,2,13] Julio Nuñez,[9,10] On behalf of International Health Informatics Study (IHIS) Network

Heart Asia 2018;10:e011044

High CA125 levels and mortality in acute heart failure

n	Event rate (High CA125)	Event rate (Low CA125)	Study name	Hazard ratio	Lower limit	Upper limit	Z-Value	p-Value
264	5.16 (10 patient years)	3.33 (10 patient years)	Nunez 2015 (Ca125 Gal3)	2.160	1.286	3.628	2.910	0.004
100	13/47	14/53	Dawutoglu 2010	1.222	1.038	1.438	2.413	0.016
1111	138/557	60/554	Nunez 2010	1.700	0.988	2.925	1.917	0.055
172	N/A	N/A	Mansour 2010	2.840	1.651	4.884	3.773	0.000
457	N/A	N/A	Jang 2017	1.241	1.051	1.465	2.548	0.011
946	N/A	N/A	Nunez 2015 (Ca125 BNP)	1.340	1.148	1.564	3.713	0.000
			Random-effects model	1.443	1.213	1.716	4.146	0.000

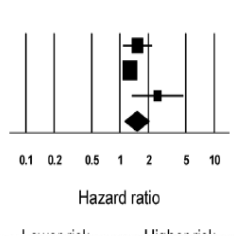
I^2 = 62%



High CA125 levels and HF readmission in acute heart failure

n	Event rate (High CA125)	Event rate (Low CA125)	Study name	Hazard ratio	Lower limit	Upper limit	Z-Value	p-Value
264	1.4 (per patient years)	1.49 (per patient years)	Nunez 2015 (Ca125 Gal3)	1.530	1.069	2.189	2.327	0.020
1111	208/557	200/554	Nunez 2010	1.271	1.119	1.444	3.699	0.000
95	N/A	N/A	Kouris 2006	2.500	1.330	4.700	2.845	0.004
			Random-effects model	1.506	1.113	2.037	2.655	0.008

I^2 = 59%



Stratificazione del Rischio

JACC: HEART FAILURE VOL. 8, NO. 5, 2020
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PUBLISHED BY ELSEVIER

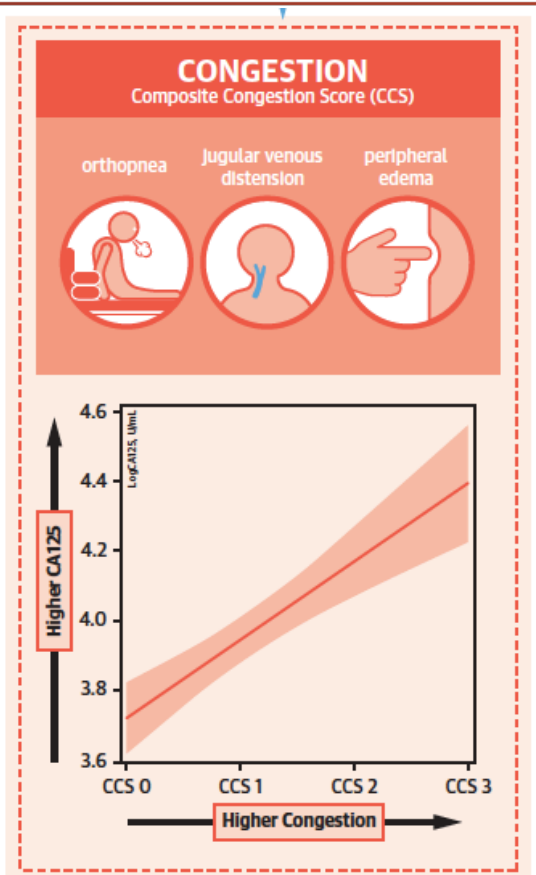
Clinical Role of CA125 in Worsening Heart Failure

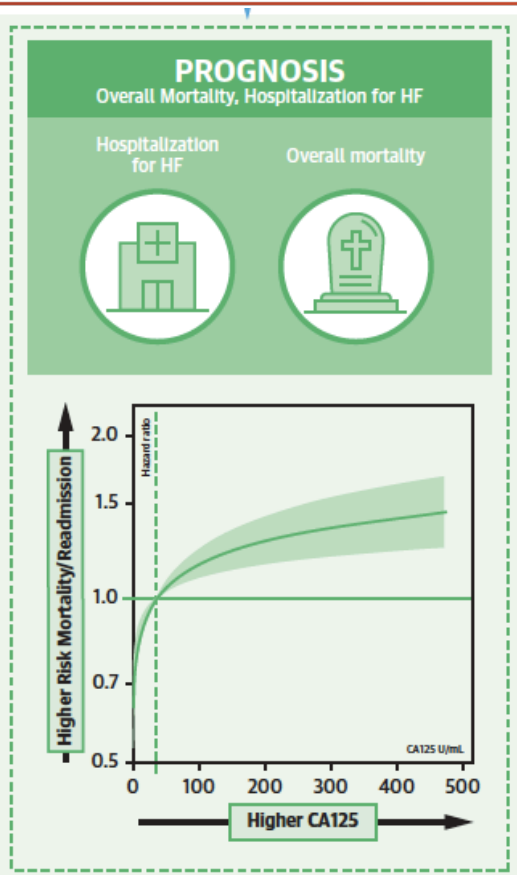
A BIOSTAT-CHF Study Subanalysis

Julio Núñez, MD, PhD,[a,b] Antoni Bayés-Genís, MD, PhD,[b,c] Elena Revuelta-López, PhD,[b,d] Jozine M. ter Maaten, MD, PhD,[e] Gema Miñana, MD, PhD,[a,b] Jaume Barallat, MD, PhD,[f] Adriana Cserkóová, PhD,[d] Vicent Bodi, MD, PhD,[a,b] Agustín Fernández-Cisnal, MD,[a] Eduardo Núñez, MD, MPH,[a] Juan Sanchis, MD, PhD,[a,b] Chim Lang, MD, PhD,[g] Leong L. Ng, MD, PhD,[h] Marco Metra, MD, PhD,[i] Adriaan A. Voors, MD, PhD[e]

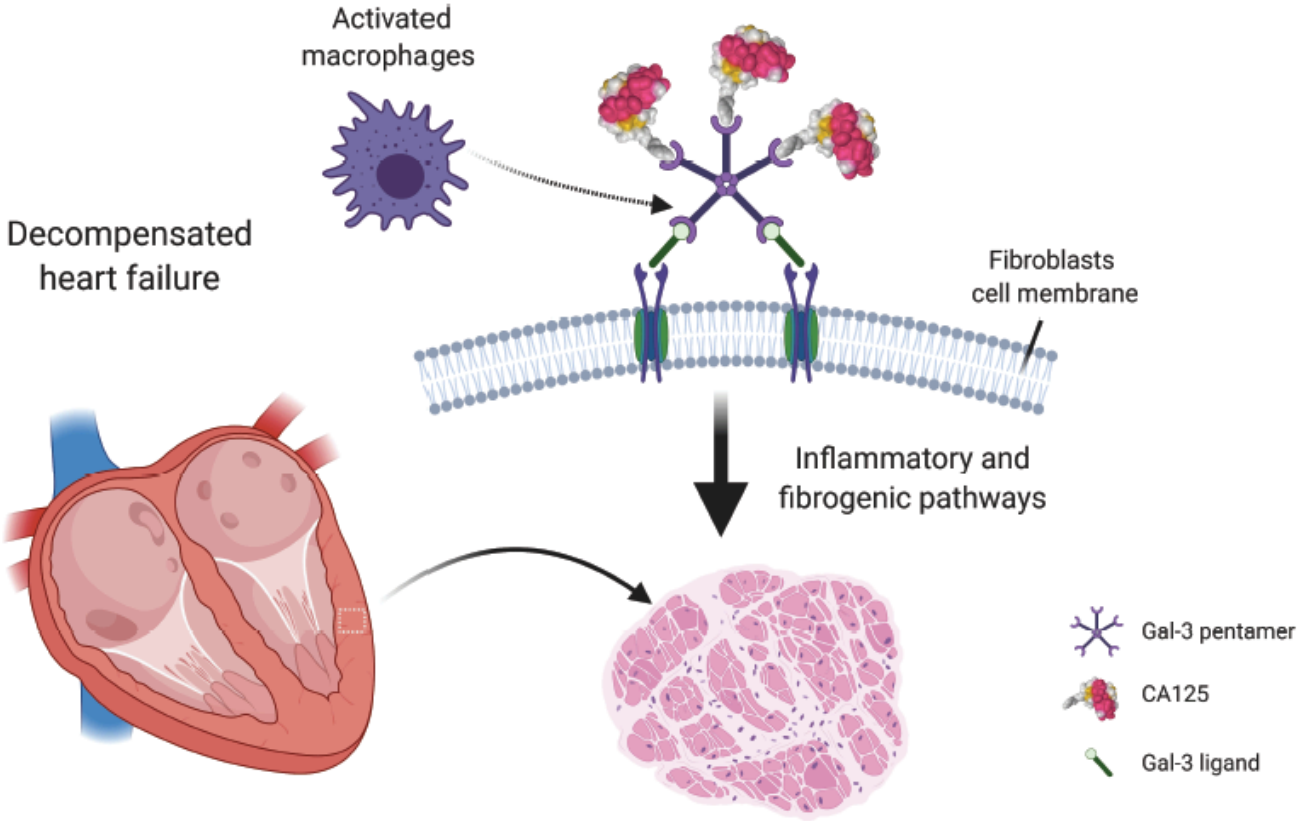
In a sensitivity analysis, **(N . 2,356)**, the prognostic implications of CA125 were tested and adjusted for a composite congestion score.

Data were validated in the BIOSTAT-CHF (Biology Study to Tailored Treatment in Chronic Heart Failure validation) cohort **(N . 1,630).**



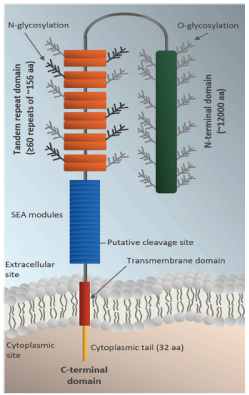


Stratificazione del Rischio: Possibile meccanismo



Ruolo Clinico del Ca125

Ca125



- Ca125 e Stratificazione del Rischio
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Relazione fra CA125 e Congestione nello SC

Il CA125 è un biomarcatore circolante con una **lunga emivita** **(media 5.1–12 giorni)**

Il CA125 fornisce informazioni sullo **stato dei fluidi nelle ultime settimane** e non riflette necessariamente le variazioni emodinamiche acute

Nei pazienti con insorgenza improvvisa di insufficienza cardiaca, il CA125 potrebbe non aver avuto il tempo di essere sovraregolato.

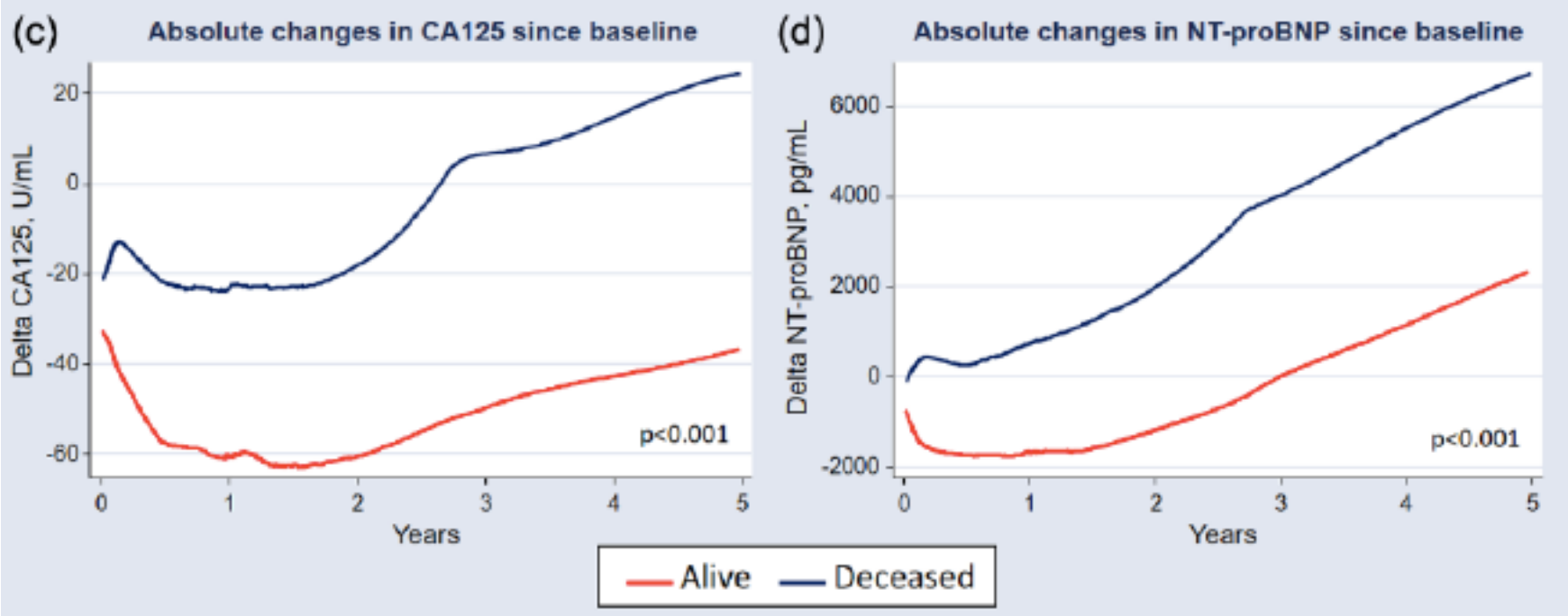
Nei giorni successivi ad una fase di scompenso, il **CA125 può rimanere stabile**, rendendo inutili le misurazioni seriali nei primi giorni successivi a un ricovero ospedaliero

Invece la cinetica del CA125 nelle **settimane-mesi successivi** ad una fase di SC si è rivelata un promettente strumento di monitoraggio.

Zhang M et al Prog Mol Biol Transl Sci 2019;162:241–252
Sikaris KA. Heart Lung Circ 2011;20:634–640
Núñez J et al Heart Fail Rev 2014;19:575–584.

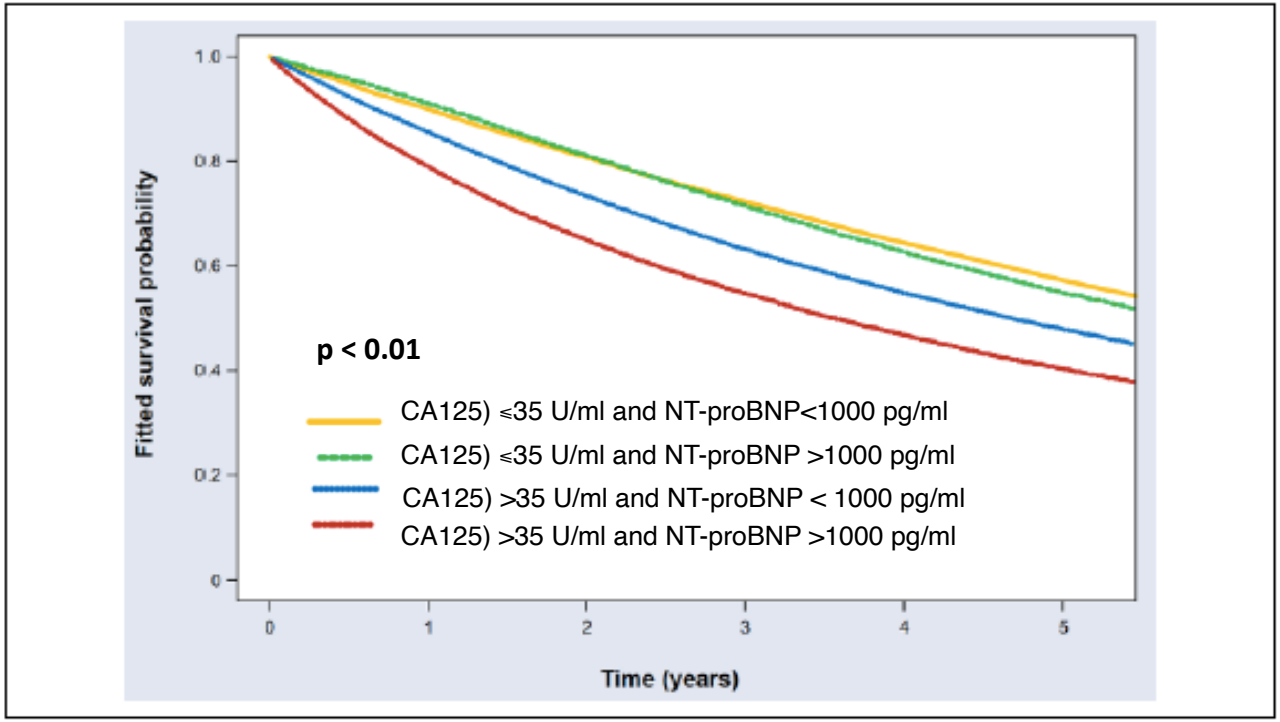
Il Monitoraggio nello Scompenso Cardiaco

Variazioni longitudinali di CA125 e di NT-proBNP dopo un evento di insufficienza cardiaca acuta in relazione alla sopravvivenza dei pazienti (3402 observations during a mean follow-up of 2.64 years)



Núñez J, et al Long-term serial kinetics of N-terminal pro B-type natriuretic peptide and carbohydrate antigen 125 Eur Heart J Acute Cardiovasc Care 2017;6:685–696.

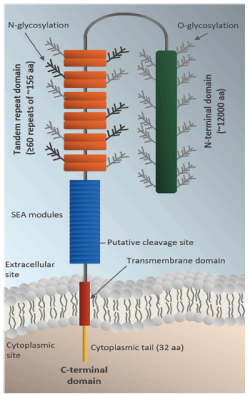
Ca125 e NTproBNP nello Scompenso Cardiaco



Núñez J, et al Long-term serial kinetics of N-terminal pro B-type natriuretic peptide and carbohydrate antigen 125 Eur Heart J Acute Cardiovasc Care 2017;6:685–696.

Ruolo Clinico del Ca125

Ca125



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Ca125 per guidare la Terapia Diuretica

Carbohydrate Antigen-125–Guided Therapy in Acute Heart Failure

CHANCE-HF: A Randomized Study

Julio Núñez, MD,[a] Pau Llàcer, MD,[b] Vicente Bertomeu-González, MD,[c] Maria José Bosch, MD,[d] Pilar Merlos, MD,[e] Sergio García-Blas, MD,[a] Vicente Montagud, MD,[f] Vicent Bodí, MD,[a] Vicente Bertomeu-Martínez, MD,[c] Valle Pedrosa, MD,[e] Andrea Mendizábal, MD,[b] Alberto Cordero, MD,[c] Jorge Gallego, MD,[d] Patricia Palau, MD,[d] Gema Miñana, MD,[a] Enrique Santas, MD,[a] Salvador Morell, MD,[f] Angel Llàcer, MD,[a] Francisco J. Chorro, MD,[a] Juan Sanchis, MD,[a] Lorenzo Fácila, MD,[f] for the CHANCE-HF Investigators

J Am Coll Cardiol HF 2016;4:833–43

	CA125-Guided Therapy (n = 187)	SOC (n = 193)	IRR	p Value
FED				
Randomization	186 (99.5)	187 (96.9)		0.12
End of the trial	180 (96.3)	184 (95.3)		0.80
FED at discharge, mg/24 h	94.0 ± 49.9 80 (60-120)	96.3 ± 56.2 80 (40-120)		0.67 0.73
FED at the end of the trial, mg/24 h	108.0 ± 89.9 80 (40-120)	97.3 ± 71.7 80 (40-80)		0.20 0.31
Dose adjustments*	2.91	1.47	1.98	<0.001
Dose increases*	1.30	0.83	1.57	<0.001
Dose decreases*	1.57	1.15	1.37	<0.001
IV furosemide				
Outpatient IV administration	40 (21.4)	21 (10.9)		0.01
Outpatient IV administration†	0.58	0.28	2.11	<0.001
Aldosterone receptor blockers				
Randomization	100 (53.5)	107 (55.4)		0.76
End of the trial	102 (54.6)	102 (52.9)		0.76
≥50% goal doses at baseline	93 (94.9)	98 (91.6)		0.41
≥50% goal doses at the end of trial	92 (92.0)	90 (89.1)		0.63
Dose adjustments*	0.32	0.22	1.50	0.05
Dose increases*	0.16	0.08	2.01	0.03
Dose decreases*	0.17	0.14	1.21	0.48

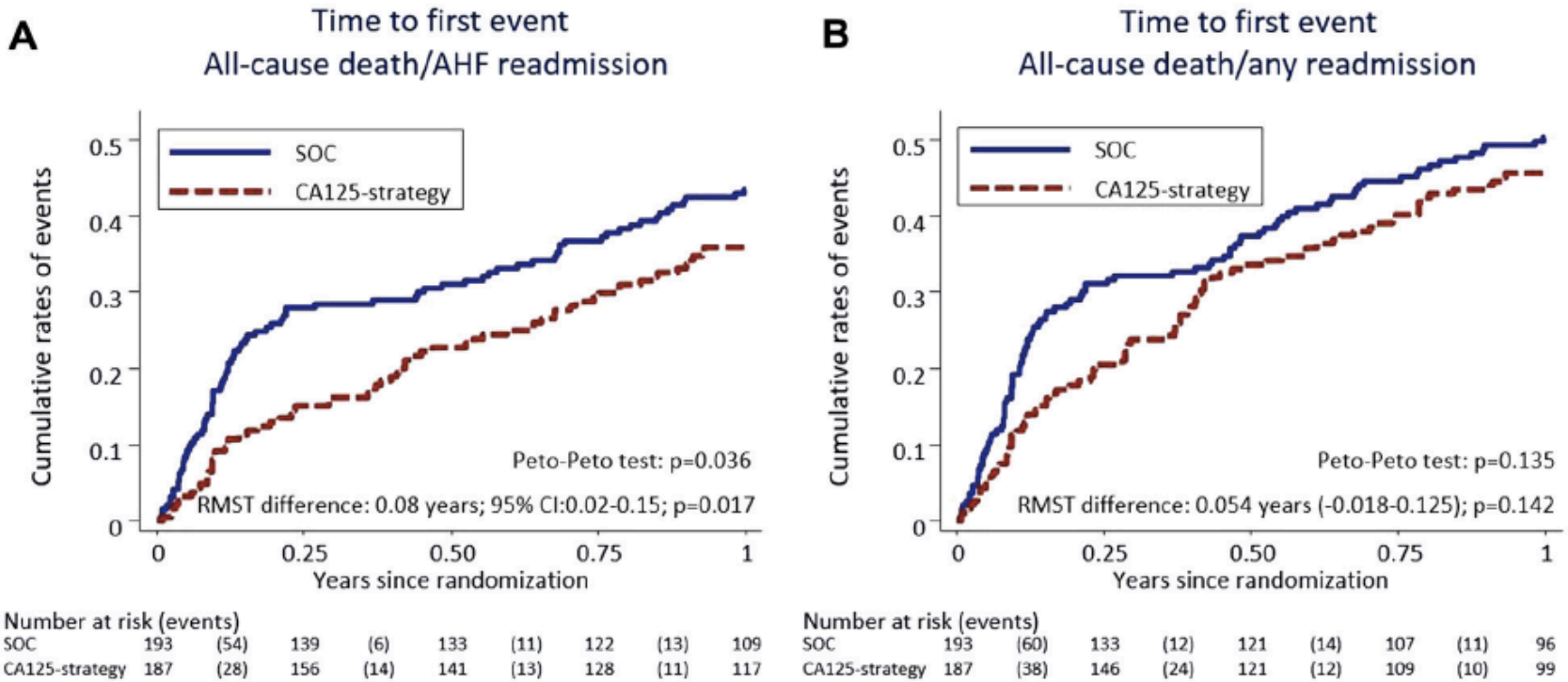
Inclusion Criteria

1) At least 1 episode of AHF in the last 180 days
2) NYHA ≥ 2 at the moment of enrollment
3) CA125 >35 U/ml
4) Echo evidence of structural Heart disease+
5) NTproBNP >1,000 pg/ml or BNP >100 pg/ml).

Randomization

1) Ca125 guided diuretic therapy
2) Standard of Care

Ca125 per guidare la Terapia Diuretica



Nunez et al J Am Coll Cardiol HF 2016;4:833–43

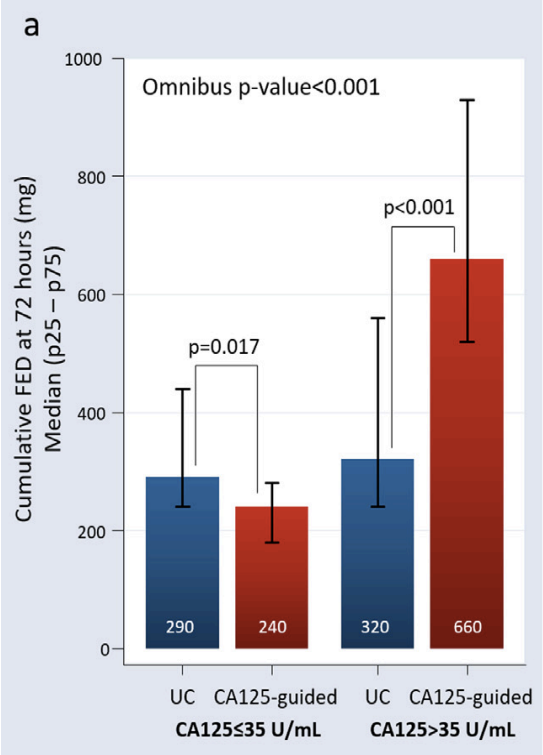
Ca125 e Terapia Diuretica in pazienti con SC e IRC

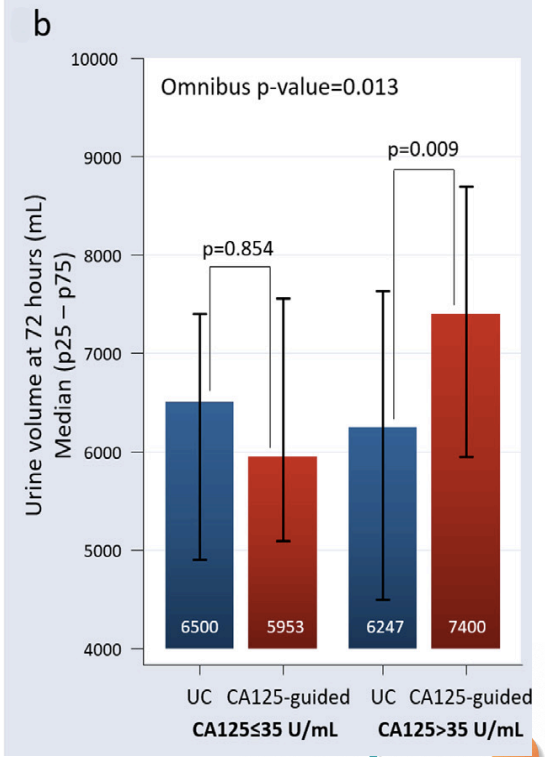
CA125-Guided Diuretic Treatment Versus Usual Care in Patients With Acute Heart Failure and Renal Dysfunction

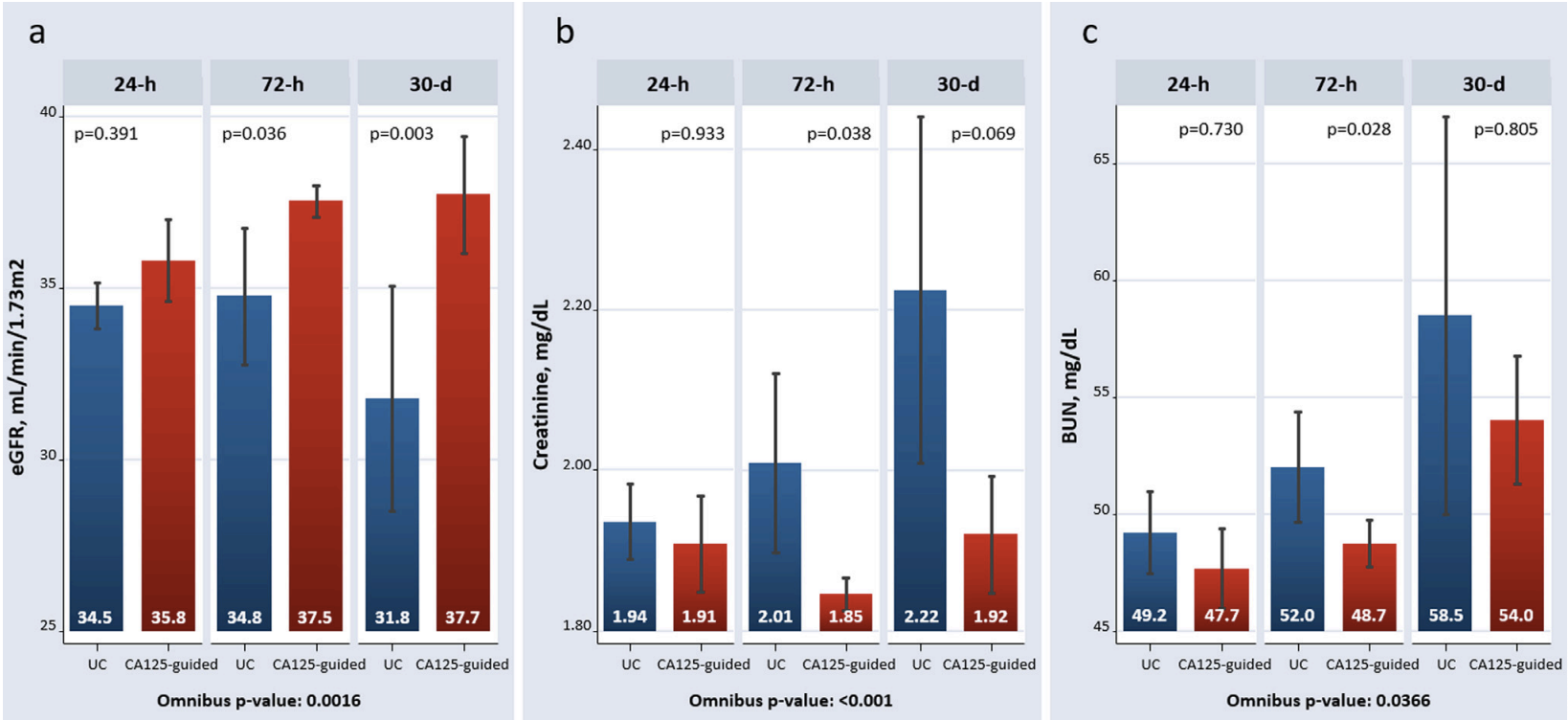
Julio Núñez, PhD,[a,b] Pau Llàcer, PhD,[c] Sergio García-Blas, MD,[a,b] Clara Bonanad, PhD,[a] Silvia Ventura, MD,[d] José María Núñez, MD,[e] Ruth Sánchez, MD,[f] Lorenzo Fácila, PhD,[g] Rafael de la Espriella, MD,[a] Juana María Vaquer, PhD,[h] Alberto Cordero, PhD,[i] Mercè Roqué, PhD,[j] Carlos Chamorro, PhD,[f] Vicent Bodi, PhD,[a,b] Ernesto Valero, MD,[a,b] Enrique Santas, PhD,[a] María del Carmen Moreno, MD,[c] Gema Miñana, PhD,[a,b] Arturo Carratalá, PhD,[h] Enrique Rodríguez, MD,[h] Anna Mollar, PhD,[a] Patricia Palau, PhD,[k] María José Bosch, PhD,[d] Vicente Bertomeu-González, PhD,[l] Josep Lupón, PhD,[b,l,m] Jorge Navarro, PhD,[n] Francisco J. Chorro, PhD,[a,b] Jose L. Górriz, PhD,[o] Juan Sanchis, PhD,[a,b] Adriaan A. Voors, PhD,[p] Antoni Bayés-Genís, PhD[b,l,m]

The American Journal of Medicine (2020) 133:370–380

- **Multicenter, open-label study**
- 160 patients with acute heart failure and renal dysfunction
- **Randomization into 2 groups (1:1):**
  a) Loop diuretics doses were established according to CA125 levels in the CA125-guided group (n = 79)
  b) usual-care group (n = 81).
- **Primary End-Point**
  Changes in estimated glomerular filtration rate (eGFR) at 72 and 24 hours.







The American Journal of Medicine (2020) 133:370–380

Ca125 e Terapia con Dapaglifozina dopo SC Acuto

Changes in Antigen Carbohydrate 125 in Patients Receiving Dapagliflozin following an Admission for Acute Heart Failure

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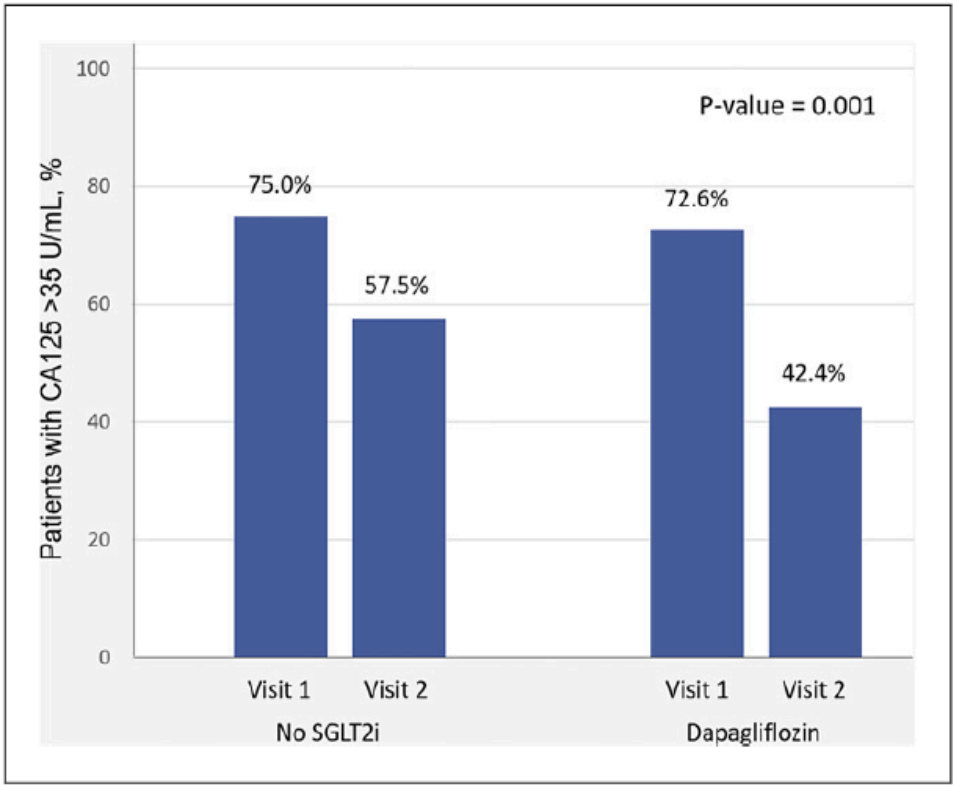
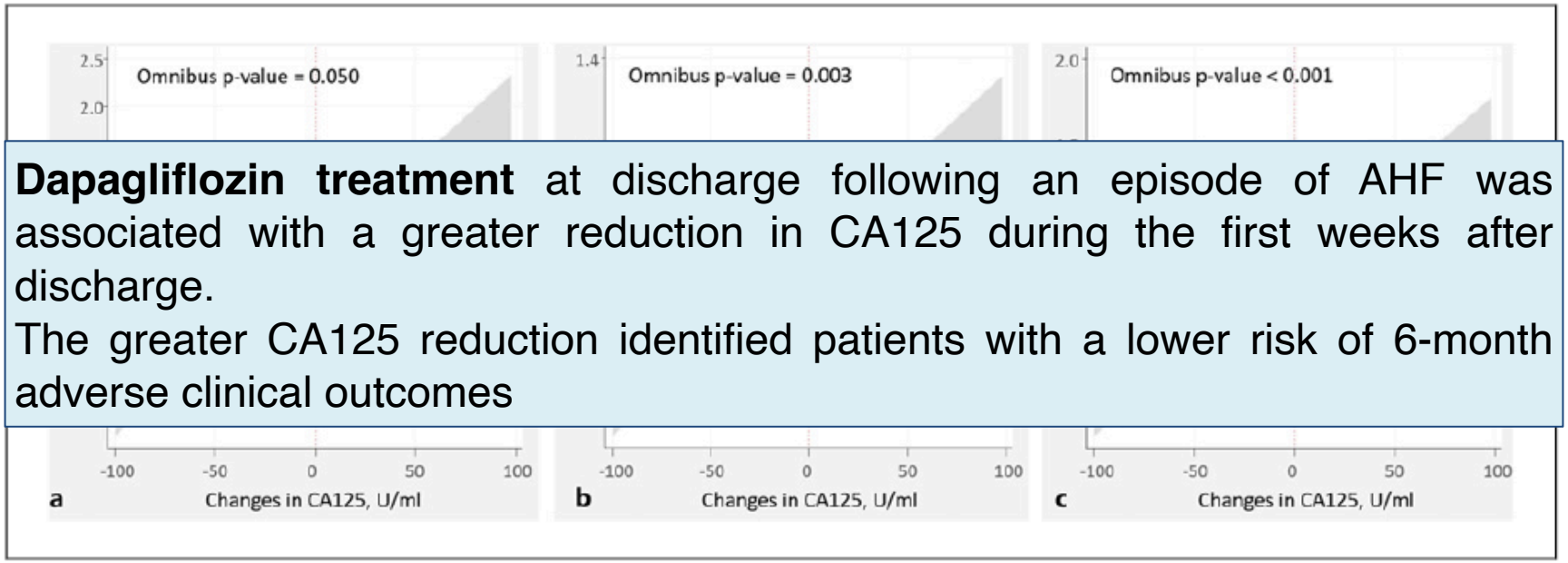
Cardiorenal Med 2025;15:122–132

- Retrospective observational study
- Data from 956 AHF patients
- CA125 assessed during the index admission (visit 1) and at a median of 26 (15–39) days after discharge (visit 2).
- The primary endpoint was changes in CA125 and its correlation with the risk of 6-month death and recurrent readmissions



Ca125 e Terapia con iSGLT2 dopo SC Acuto

All-cause mortality **All-cause rehospitalization** **HF-rehospitalization**

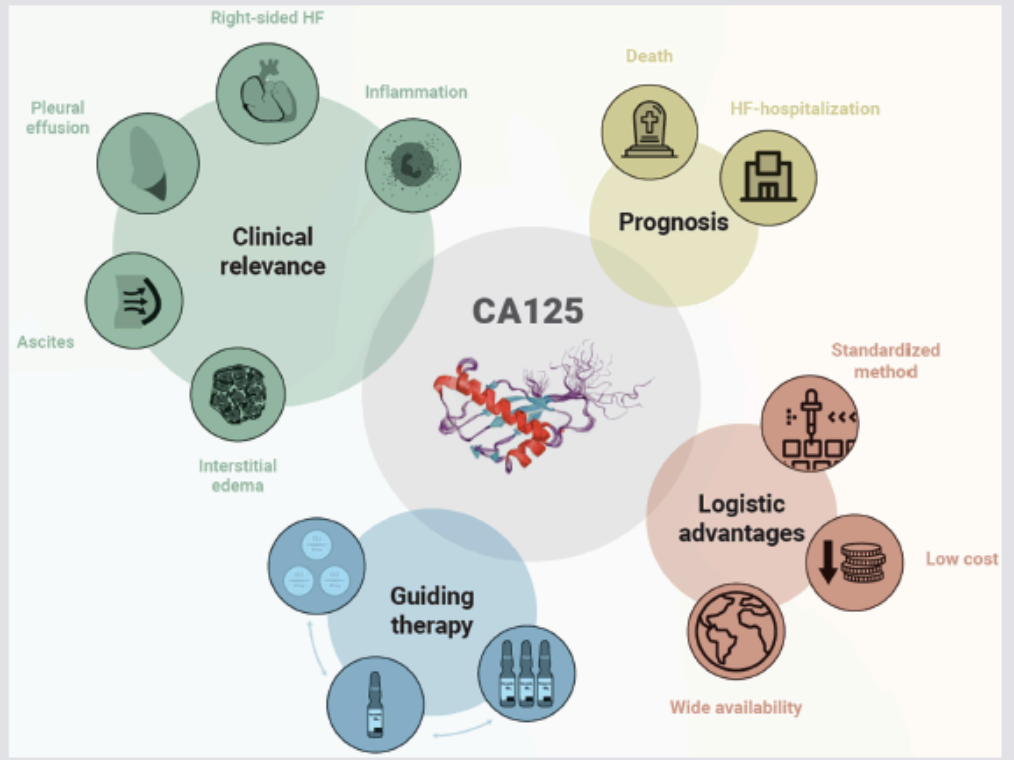


Dapagliflozin treatment at discharge following an episode of AHF was associated with a greater reduction in CA125 during the first weeks after discharge.

The greater CA125 reduction identified patients with a lower risk of 6-month adverse clinical outcomes

G. Minana et al, Cardiorenal Med 2025;15:122–132

Sintesi Conclusiva



Nunez J et al European Journal of Heart Failure (2021) 23, 1445–1457

Sintesi Conclusiva

Utilità Clinica	Descrizione
1) Ca125 per determinare la Congestione	Alti valori di Ca125 come indicatore di: - Congestione sub-clinica - Congestone predominante extra-vascolare - Scompenso del Vds predominante
2) Il Ca125 si aggiunge al pannello dei markers utilizzabili nello scompenso	Valore di un approccio multi-parametrico che include Peptide Natriuretico, NA+ urinario, ST2, Galactina-3 e Ca125
3) Guida alla terapia decongestionante	Due RCT di piccole dimensioni, dati da confermare in studi di maggiori dimensioni
3) Ca125 come potenziale target terapeutico	E' suggerito che il Ca125 puo' aiutare ad indirizzare la terapia nello SC

Grazie per l'attenzione