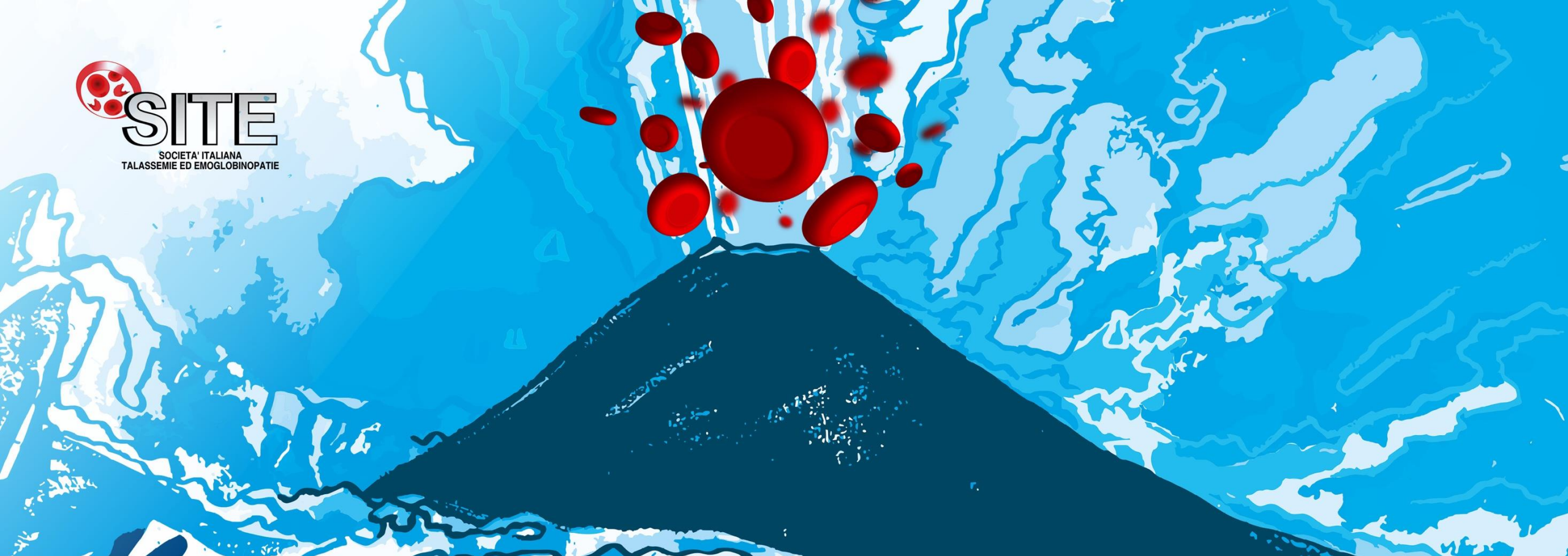




Prevalenza e rilevanza clinica dell'ematopoiesi clonale nella beta-talassemia

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Meeting del CLUB DEL

**Globulo
Rosso** 2026

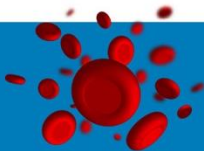
NAPOLI

28-29 SETTEMBRE 2026

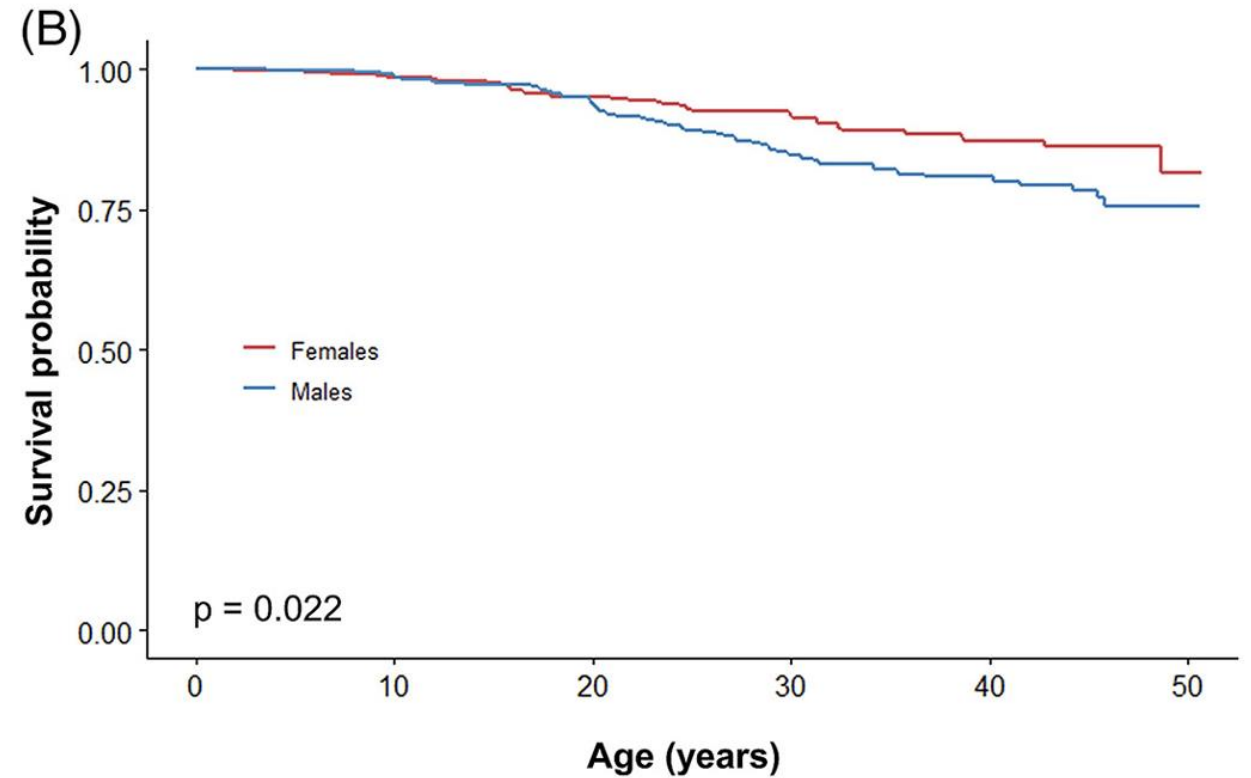
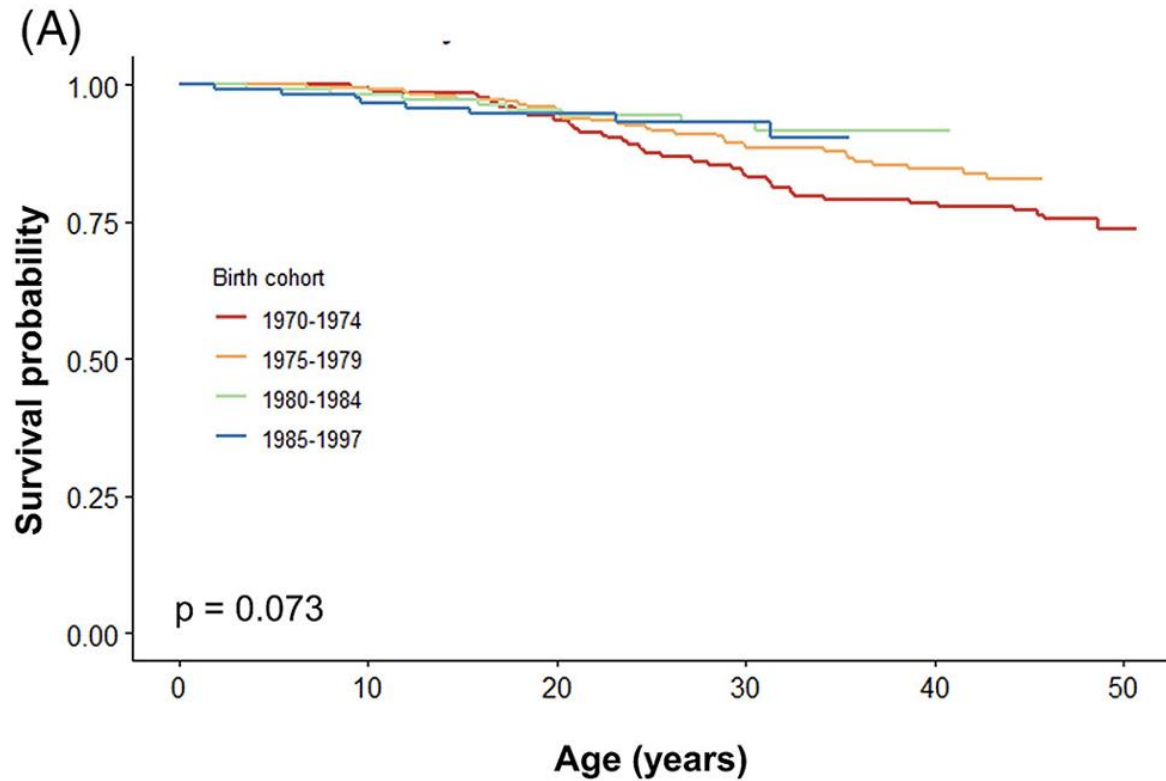
Complesso dei SS. Marcellino e Festo

Disclosures

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other



Aging nella talassemia

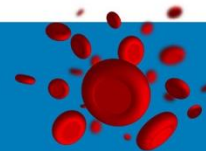


Incremento dell'aspettativa
di vita media dei pazienti
con talassemia

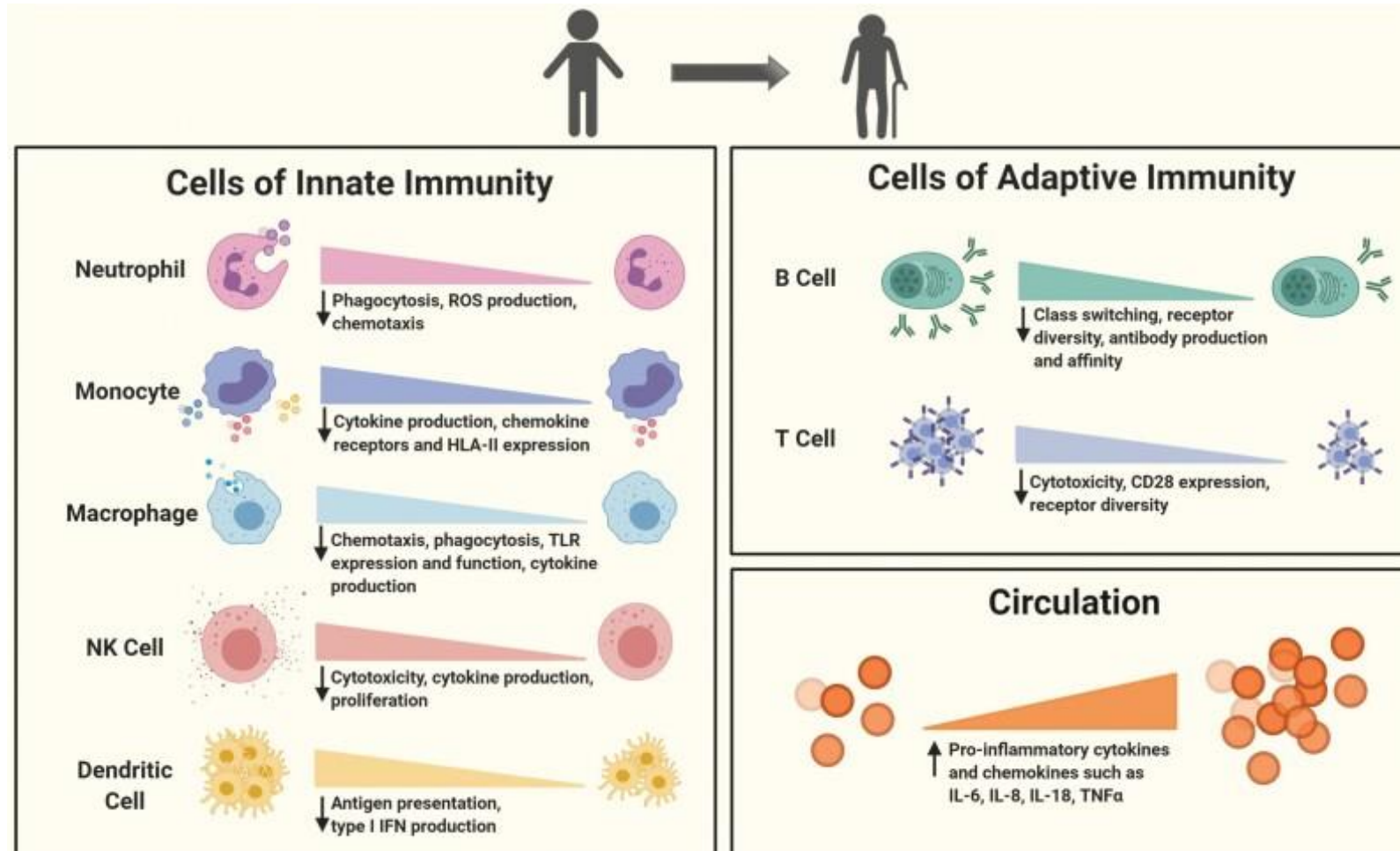


- Complicanze età-correlate
- Programmi di screening e prevenzione primaria

Forni GL, et al. Am J Hematol. 2023;98(3):381-387



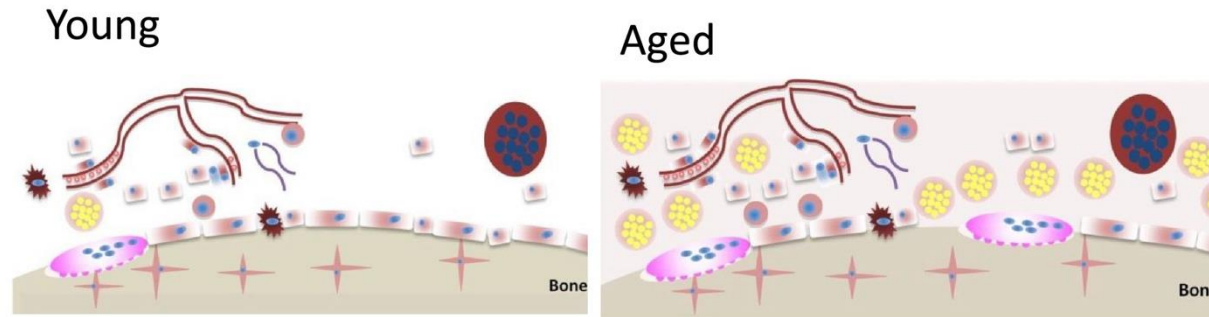
Inflammaging



Bulut O, et al, Int Immunol 2020;32(12):741–53 c

Inflammaging midollare

Modified from the *Primer on Metabolic Bone Diseases and Disorders of Mineral Metabolism, 8th Edition*



Aging Hematopoiesis

Anemia

↓ Immune response

↑ Risk of leukemia

Myeloid skewing of HSCs

Megakaryocytic skewing of HSCs

↓ Regenerative capacity

↑ HSC pool

↑ Clonal hematopoiesis

Aging Marrow

↓ Wnt signaling

↓ Osteopontin

↑ Senescent cells

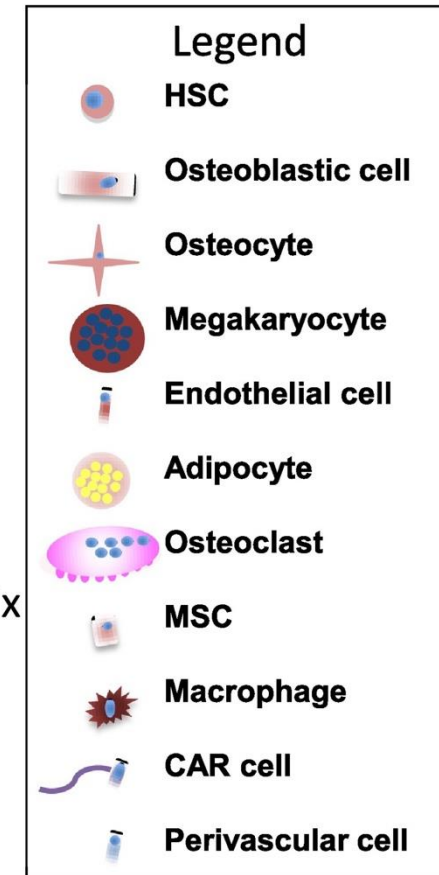
Aging Bone

↑ Fracture risk

Changes in matrix

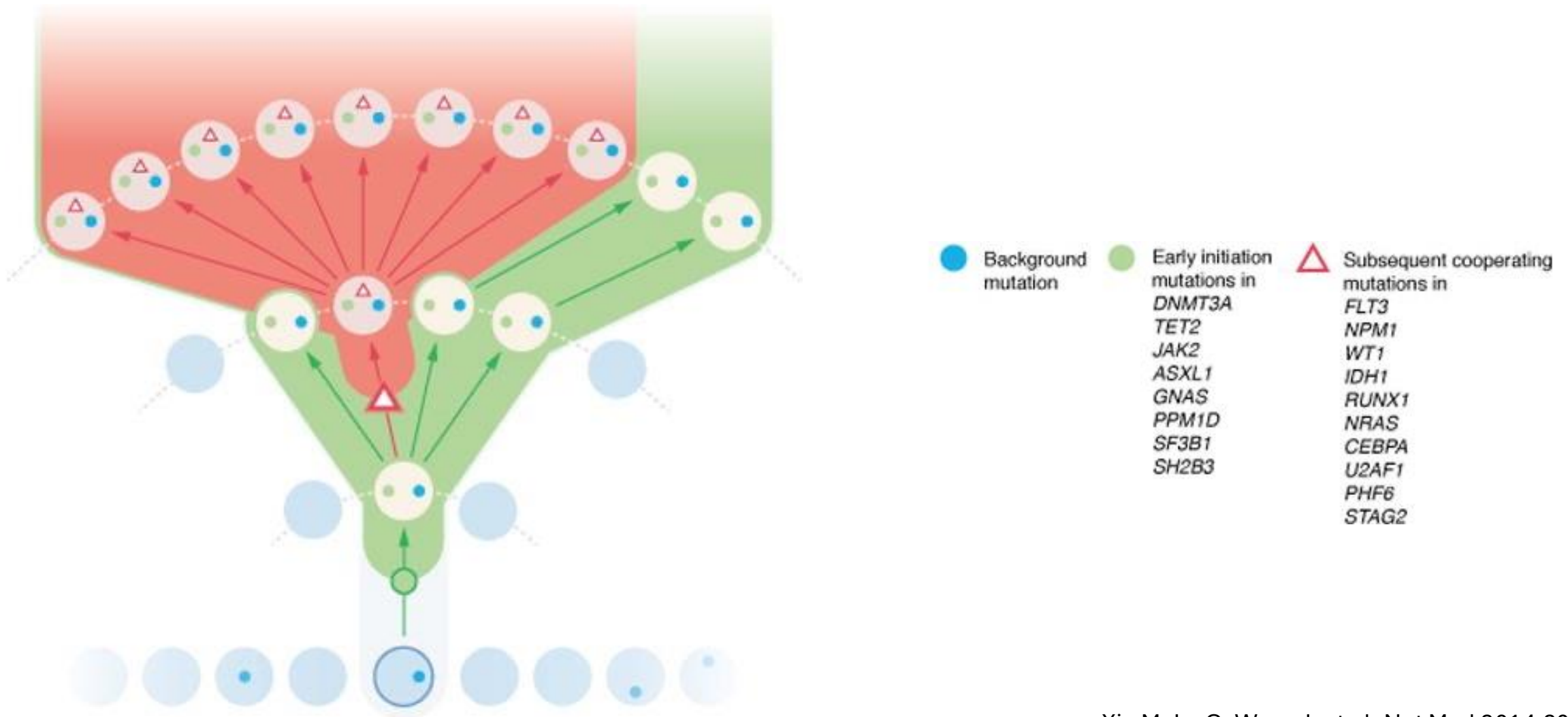
↓ Osteogenesis

↑ Adipogenesis



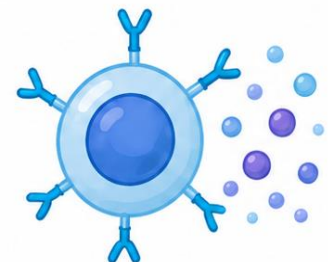
Hoffman CM, et al, Bone. 2019;119:1–7

Ematopoiesi clonale



Xie M, Lu C, Wang J, et al. Nat Med 2014;20(12):1472–8

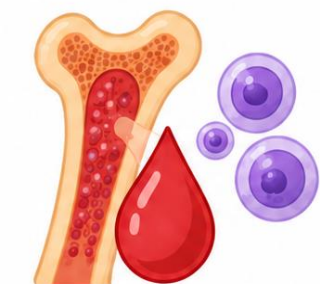
Cosa sappiamo nelle emoglobinopatie



Infiammazione cronica e immunosenescenza



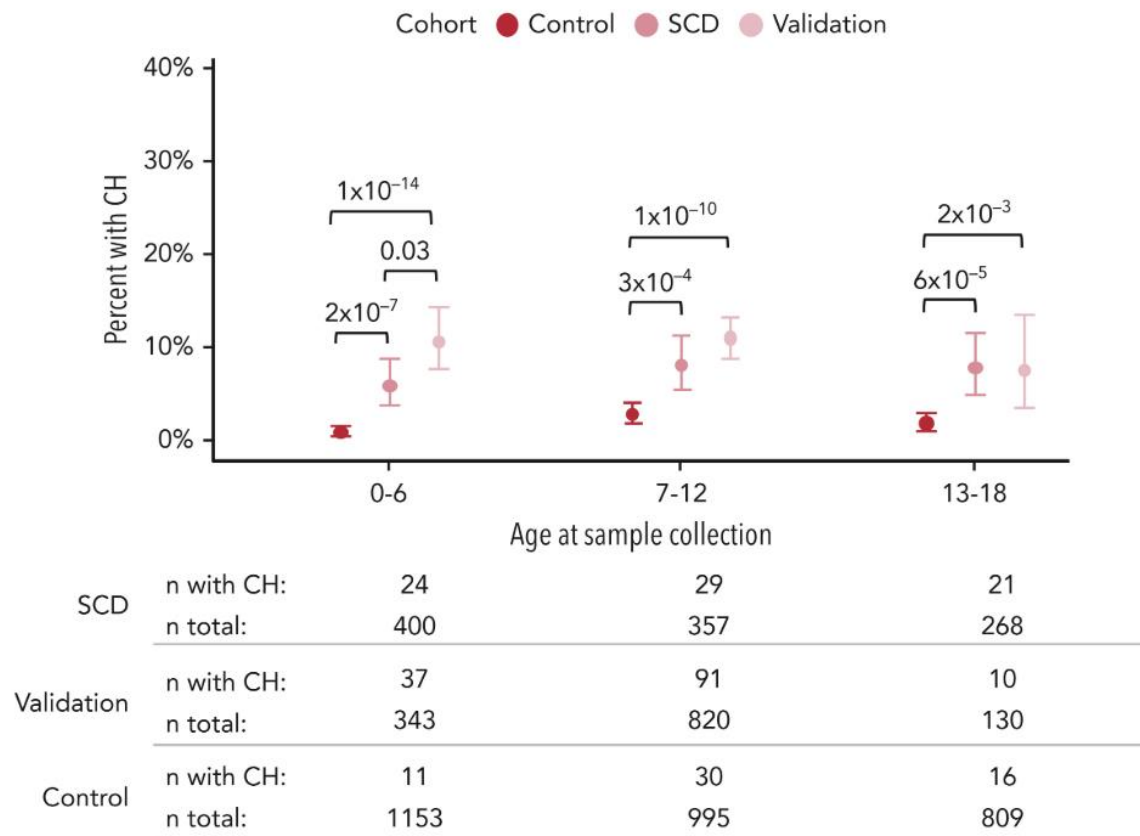
Sovraccarico marziale e stress ossidativo



Stress midollare e aumento delle CD34+ circolanti e CFU-GM

→ Possibile rischio di sviluppare CH in età precoce

A



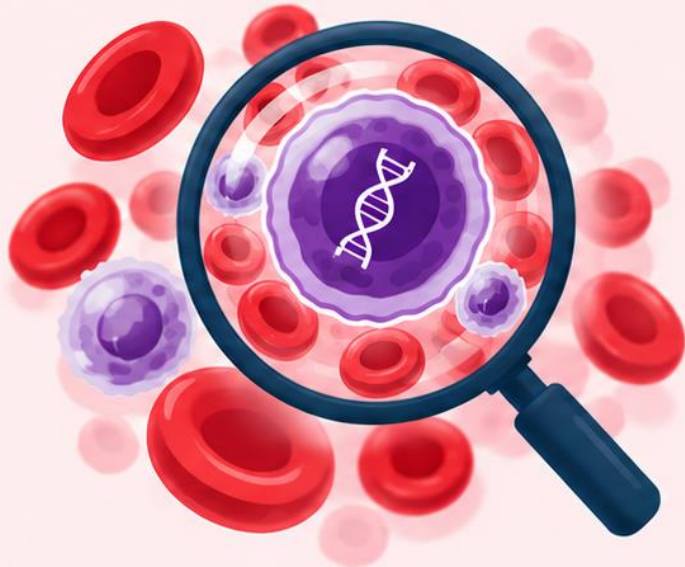
Ulloa J, et al. Blood. 2026;147(13):1447-1455

Obiettivi dello studio



Obiettivo primario

**Prevalenza di ematopoiesi clonale (CH)
nei pazienti adulti con β -talassemia
(TDT e NTDT)**



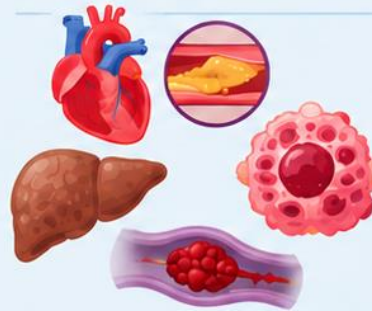
Obiettivi secondari



Caratterizzazione del
profilo mutazionale della CH

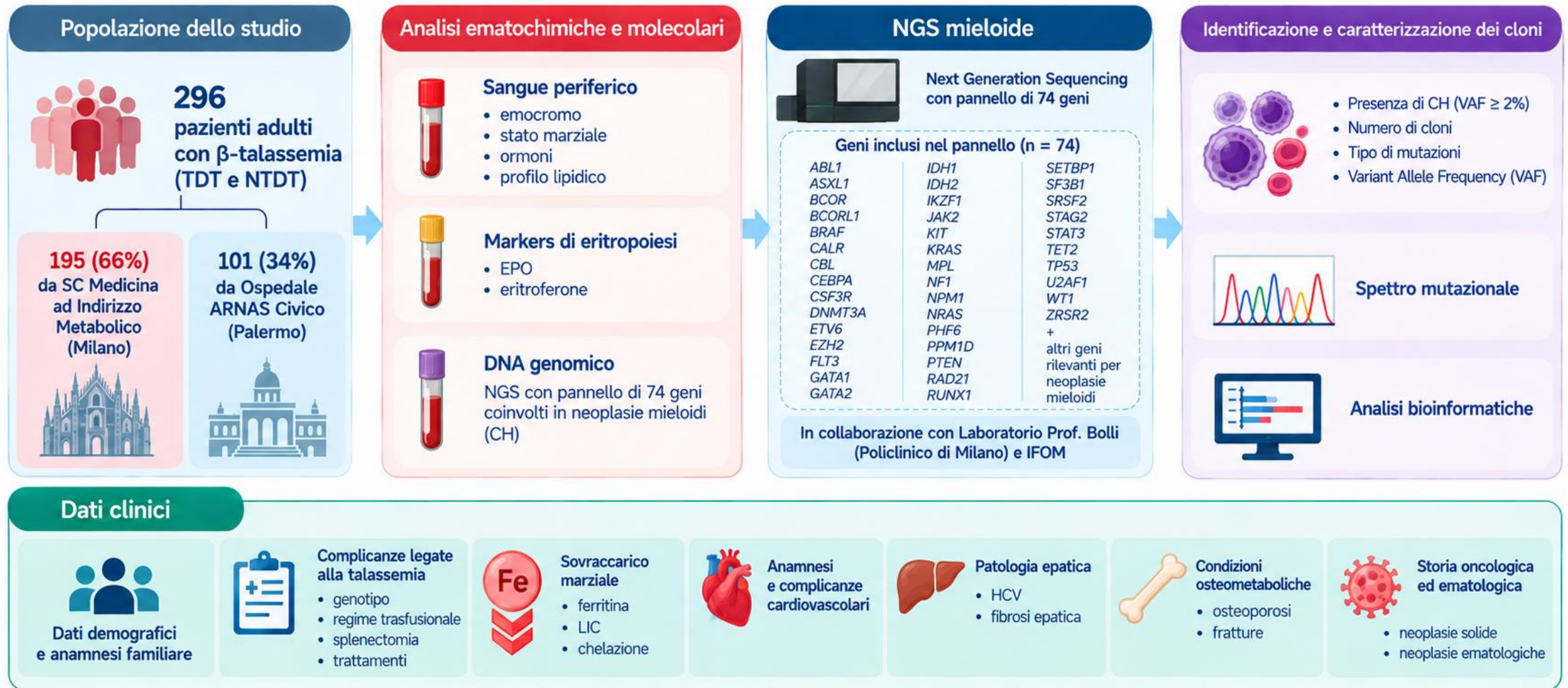


Associazione della CH
con complicanze correlate
alla talassemia



Associazione della CH
con comorbidità e complicanze
età-correlate

Metodi

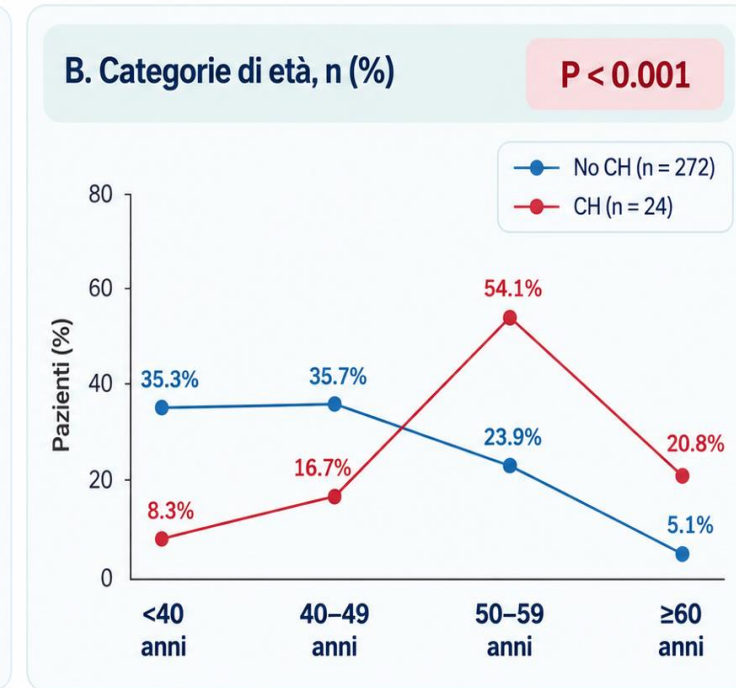
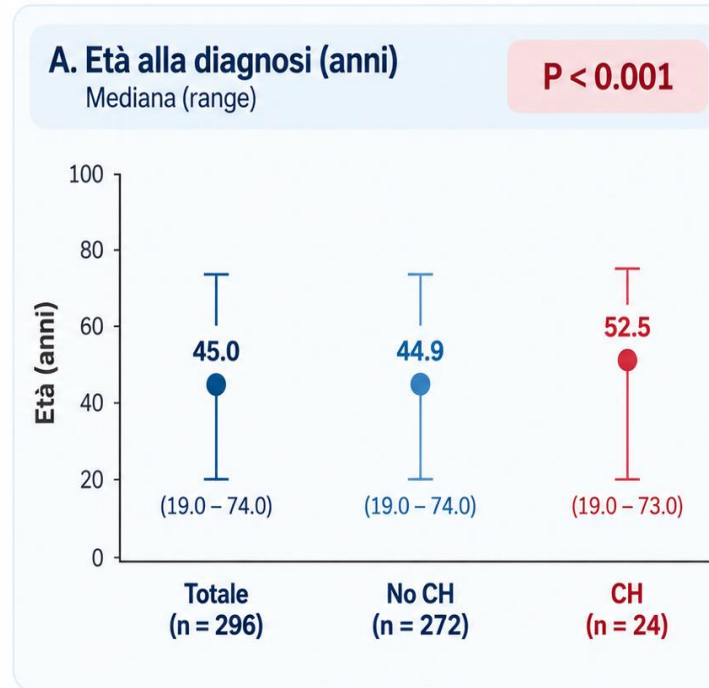
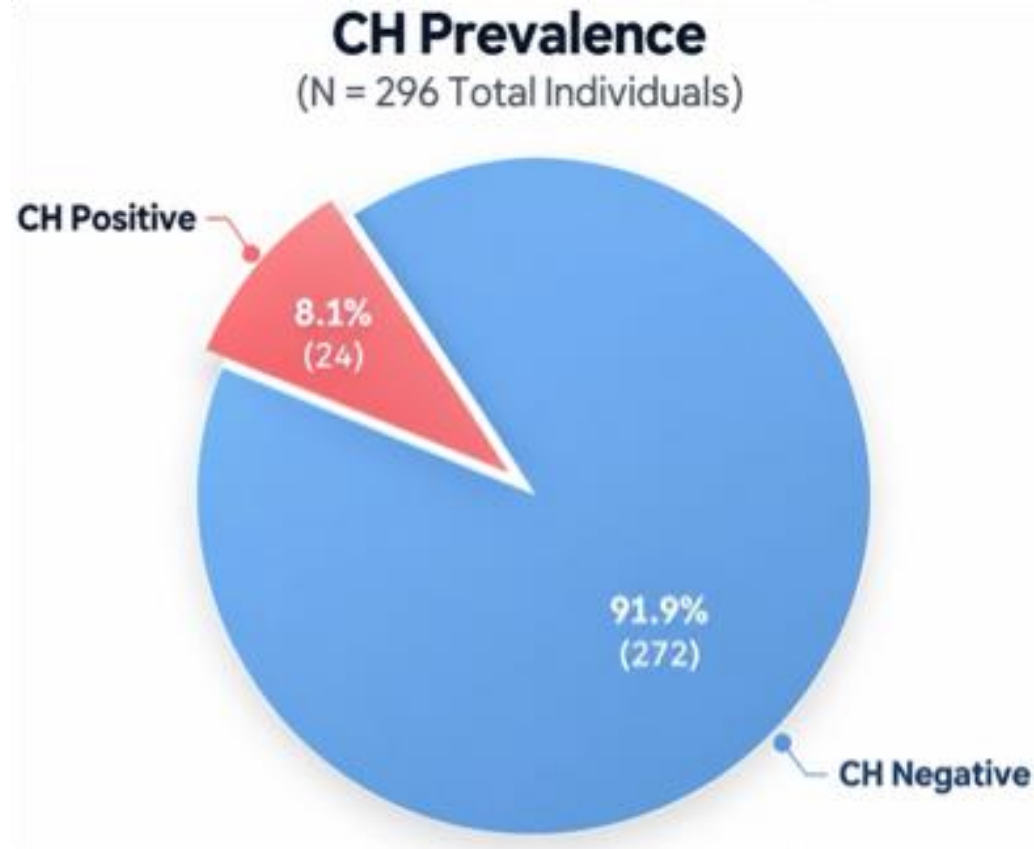


Dati demografici

Variabile	Totale n = 296	Assenza di CH n = 272	CH n = 24	P value
 Sesso maschile, n (%)	136 (45.9%)	124 (45.6%)	12 (50.0%)	0.68
 Talassemia trasfusione-dipendente, n (%)	223/296 (75.3%)	204/272 (75.0%)	19/24 (79.2%)	0.62
 Regime trasfusionale, n (%)	n = 296	n = 272	n = 24	0.93
Mai	38 (13.3%)	36 (13.8%)	2 (8.3%)	
Saltuario	32 (10.2%)	29 (10.0%)	3 (12.5%)	
Regolare	226 (76.5%)	207 (76.2%)	19 (79.2%)	
 Trapianto di midollo osseo, n (%)	3/281 (1.1%)	3/258 (1.2%)	0/23 (0.0%)	0.61
 Splenectomia, n (%)	156/288 (54.2%)	142/264 (53.8%)	14/24 (58.3%)	0.67
 Storia di trattamento con ASA, n (%)	43/278 (15.5%)	37/255 (14.5%)	6/23 (26.1%)	0.14
 Storia di trattamento con idrossiurea, n (%)	24/159 (15.1%)	21/145 (14.5%)	3/14 (21.4%)	0.49
 Trattamento in corso con idrossiurea, n (%)	17/159 (10.7%)	14/145 (9.7%)	3/14 (21.4%)	0.17
 Storia di trattamento con luspatercept, n (%)	60/195 (30.8%)	55/179 (30.7%)	5/16 (31.3%)	0.96

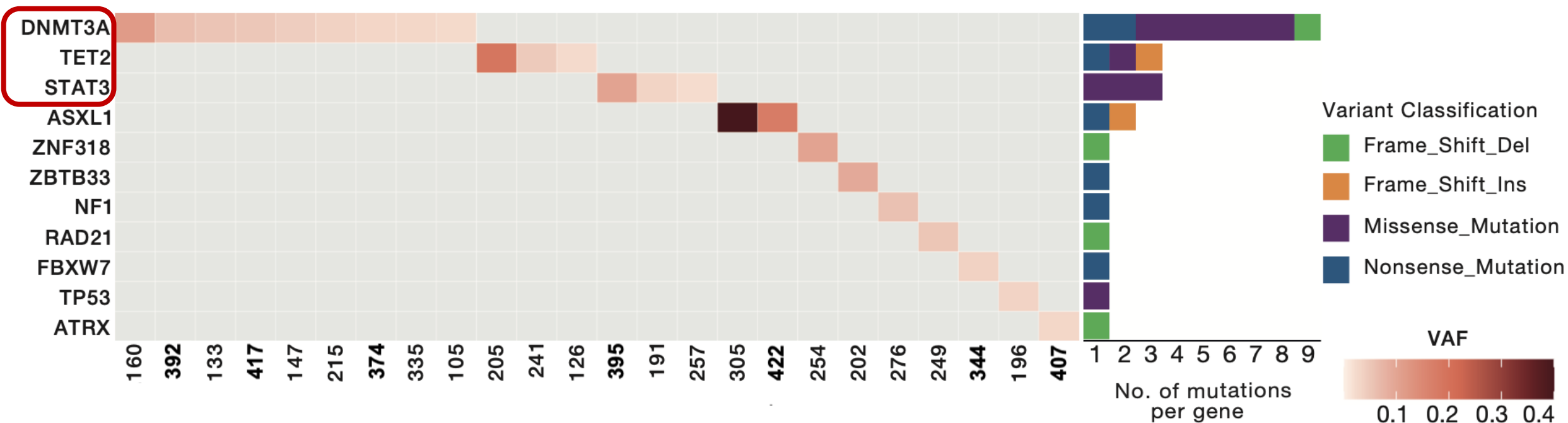
Leoni, et al, under revision

La prevalenza della CH aumenta con l'età



Leoni, et al, under revision

Profilo mutazionale



Leoni, et al, under revision

CH e complicanze patologia-correlate

Variabile	Totale n = 296	Assenza di CH n = 272	CH n = 24	P value
 Storia di sovraccarico di ferro, n (%)	207/265 (78.1%)	191/245 (78%)	16/20 (80.0%)	0.83
 Sovraccarico di ferro epatico, n (%)	179/268 (66.8%)	165/247 (66.8%)	14/21 (66.7%)	0.99
 LIC (mg Fe/g dw) n = 148	2.3 (1.0 - 28.1)	2.4 (1.0 - 28.1)	1.6 (1.1 - 10.6)	0.35
 Sovraccarico di ferro miocardico, n (%)	47/267 (17.6%)	43/246 (17.5%)	4/21 (19.0%)	0.86
 Splenomegalia, n (%)	151/276 (54.7%)	140/253 (55.3%)	11/23 (47.8%)	0.49
 EMH, n (%)	39/268 (14.6%)	35/246 (14.2%)	4/22 (18.1%)	0.61
 Endocrinopatia, n (%)	237/296 (80.1%)	216/272 (79.4%)	21/24 (87.5%)	0.34
 Alterato metabolismo glucidico, n (%)	n=296	n=272	n=24	0.22
Alterata tolleranza glucidica	40 (13.5%)	37 (13.6%)	3 (12.5%)	
Diabete	31 (10.5%)	26 (9.6%)	5 (20.8%)	
 Ipotiroidismo, n (%)	64/296 (21.6%)	58/272 (21.3%)	6/24 (25.0%)	0.67
 Ipoparatiroidismo, n (%)	19/296 (6.4%)	15/272 (5.5%)	4/24 (16.7%)	0.03
 Malattia minerale ossea, n (%)	210/296 (70.9%)	191/272 (70.2%)	19/24 (79.2%)	0.33
 Ipogonadismo, n (%)	107/296 (36.1%)	94/272 (34.6%)	13/24 (54.2%)	0.05
 Insufficienza surrenalica, n (%)	15/194 (7.7%)	13/178 (7.3%)	2/16 (12.5%)	0.46

CH e complicanze età-correlate

Variabile	Totale n = 296	Assenza di CH n = 272	CH n = 24	P value
 Ipertensione arteriosa, n (%)	12/294 (4.1%)	11/271 (4.1%)	1/23 (4.3%)	0.95
 Storia di malattia cardiovascolare, n (%)	119/296 (40.2%)	105/272 (38.6%)	14/24 (58.3%)	0.06
 Fibrillazione atriale, n (%)	28/295 (9.5%)	23/271 (8.5%)	5/24 (20.8%)	0.048
 TIA e/o ictus ischemico, n (%)	6/294 (2.0%)	5/270 (1.9%)	1/24 (4.2%)	0.44
 Tromboembolismo venoso, n (%)	n = 269 Spontaneo Provocato	n = 247 13 (5.3%) 3 (1.2%)	n = 22 4 (18.2%) 0 (0.0%)	0.05
 Ipertensione polmonare, n (%)	10/293 (3.4%)	10/269 (3.7%)	0/24 (0.0%)	0.34
 Malattia aterosclerotica, n (%)	77/195 (39.5%)	66/179 (36.9%)	11/16 (68.8%)	0.01
 Dislipidemia, n (%)	7/296 (2.4%)	7/252 (2.8%)	0/24 (0.0%)	0.41
 Ipertrigliceridemia, n (%)	6/181 (3.3%)	6/165 (3.6%)	0/16 (0.0%)	0.44
 Fibrosi epatica, n (%)	48/186 (25.8%)	40/170 (23.5%)	8/16 (50.0%)	0.02
 Elastografia epatica transitoria (kPa)* n = 189	4.8 (0.0 – 34.3)	4.7 (0.0 – 34.3)	6.2 (3.4 – 12.1)	0.03
 Storia di infezione da HCV, n (%)	120/296 (40.5%)	105/272 (38.6%)	15/24 (62.5%)	0.02
 Infezione da HIV, n (%)	2/296 (0.7%)	2/272 (0.7%)	0/24 (0.0%)	0.67
 Neoplasia ematologica, n (%)	0/296 (0.0%)	0/272 (0.0%)	0/24 (0.0%)	--
 Tumori solidi, n (%)	13/296 (4.4%)	9/272 (3.3%)	4/24 (16.7%)	0.01

CH e profilo metabolico

Parametro	Totale n = 296	Assenza di CH n = 272	CH n = 24	P value
 Hb (g/dL) n = 295	9.6 (3.5 – 15.9)	9.6 (3.5 – 15.9)	9.2 (8.4 – 14.2)	0.16
 Hct (%) n = 174	27.8 (20.8 – 49.8)	27.9 (20.8 – 49.8)	26.1 (23.1 – 42.4)	0.18
 RBC (10 ⁶ /mm ³) n = 295	3.5 (2.6 – 8.1)	3.5 (2.6 – 8.1)	3.5 (2.9 – 4.9)	0.37
 MCV (fL) n = 295	81.6 (52.1 – 91.6)	81.5 (52.1 – 91.6)	81.5 (60.4 – 87.7)	0.57
 RDW (%) n = 293	17.0 (2.4 – 36.3)	17.0 (12.4 – 36.3)	16.0 (13.1 – 32.6)	0.40
 PLT (x10 ³ /mm ³) n = 290	341 (75 – 1263)	344 (75 – 1263)	264 (134 – 771)	0.27
 WBC (x10 ³ /mm ³) n = 294	9.2 (2.9 – 32.7)	9.1 (3.2 – 32.7)	7.9 (2.9 – 16.2)	0.03
 Eritroblasti (x10 ³ /mm ³) n = 289	0.4 (0 – 120)	0.4 (0 – 120)	0.9 (0 – 67)	0.82
 Reticolociti (x10 ⁹ /mm ³) n = 182	0.08 (0 – 1.8)	0.08 (0 – 1.8)	0.01 (0 – 0.73)	0.80

Parametro	Totale n = 296	Assenza di CH n = 272	CH n = 24	P value
 Colesterolo totale (mg/dL) n = 173	114 (15 – 215)	113 (15 – 215)	132 (77 – 174)	0.03
 LDL (mg/dL) n = 187	53 (12 – 151)	49 (12 – 151)	64 (25 – 106)	0.01
 HDL (mg/dL) n = 173	40 (13 – 93)	41 (13 – 93)	40 (27 – 63)	0.60
 Trigliceridi (mg/dL) n = 170	97 (31 – 403)	96 (31 – 403)	112 (47 – 177)	0.36
 Glicemia a digiuno (mg/dL) n = 220	88 (43.0 – 250)	86 (43.0 – 250)	98.5 (62.0 – 151.0)	0.03
 AST (U/L) n = 147	24 (12 – 179)	24 (12 – 179)	24 (12 – 44)	0.36
 ALT (U/L) n = 220	17 (6 – 279)	17 (6 – 279)	18 (8 – 73)	0.70
 Gamma-GT (U/L) n = 208	13 (4 – 170)	13 (4 – 170)	17 (7 – 104)	0.08
 Ferritina (ng/mL) n = 220	583 (18 – 10112)	582 (18 – 10112)	582.5 (8 – 4412)	0.87
 Eritropoietina (IU/L) n = 151	60.6 (8.3 – 921)	59.2 (8.3 – 617.0)	69.4 (31.1 – 921.0)	0.31
 Epcidina (ng/mL) n = 105	15.1 (0.4 – 200)	15.8 (0.4 – 200.0)	12.2 (3.1 – 97.2)	0.61
Erfe (ng/mL) n = 102	22.8 (0.2 – 266.0)	23.6 (0.2 – 266.0)	17.0 (2.8 – 70.8)	0.63

Conclusioni

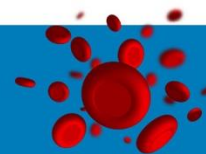
Primo studio a valutare la prevalenza della CH nella talassemia

La prevalenza della CH è maggiore e compare ad un'età più precoce nella talassemia

Come nella popolazione generale, c'è un'associazione con eventi cardiovascolari, dislipidemia e fibrosi epatica

Per la prima volta viene evidenziata un'associazione tra CH e infezione da HCV

Sono necessari ulteriori studi per definire le implicazioni cliniche di questi risultati e poter creare programmi di prevenzione dedicati



Ringraziamenti

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