22è Congrés Societat Catalana de Geriatria i Gerontologia

Avenços a l'abordatge de la patologia de la serie vermella a la gent gran

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Barcelona

SOCIETAT CATALANA DE GERIATRIA I GERONTOLOGIA

Introducción

Recomendaciones-perspectivas EHA (European Hematology Association)

Age and aging in blood disorders: EHA theme of the year 2013-2014

Christine Chomienne, Shaun McCann, Tony Green, Anton Hagenbeek, Catherine Lacombe, Margarita Guenova, Irene Roberts, and Ineke van der Beek

Haematologica 2013; 98: 831-832.

"*The impact of demographic aging within the European Union is likely to become of major significance… The share of those aged 80 years or above is predicted to almost triple between 2011 and 2060".*

http://epp.eurostat.ec.europa.eu/statistics_explained/index.php/Population_structure_and_ageing.

461 millones en 2004 a 2.000 millones en 2050
USA 2050: 85 millones
España 35% de la población.

Aging and blood disorders: new perspectives, new challenges

Dominique Bron, Lionel Ades, Tamas Fulop, Valentin Goede and Reinhard Stauder

On behalf of the Elderly Task Force in Hematology EHA SWG

Haematologica 2015; 100: 415-417

60% of patients with malignant hemopathies are today older than 65 years and this proportion will continue to increase in the future.
Cancer, like chronic diseases, increases exponentially after the age of 50 years.

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Definición de anemia

Anemia: criterios de la OMS. 2011

Haemoglobin levels to diagnose anaemia at sea level (g/l)±

Population	Non -Anaemia*	Anaemia*		
		Mild[a]	Moderate	Severe
Children 6 - 59 months of age	110 or higher	100-109	70-99	lower than 70
Children 5 - 11 years of age	115 or higher	110-114	80-109	lower than 80
Children 12 - 14 years of age	120 or higher	110-119	80-109	lower than 80
Non-pregnant women (15 years of age and above)	120 or higher	110-119	80-109	lower than 80
Pregnant women	110 or higher	100-109	70-99	lower than 70
Men (15 years of age and above)	130 or higher	110-129	80-109	lower than 80

± Adapted from references 5 and 6

* Haemoglobin in grams per litre

a "Mild" is a misnomer: iron deficiency is already advanced by the time anaemia is detected. The deficiency has consequences even when no anaemia is clinically apparent.

Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. WHO/NMH/NHD/MNM/11.1
http://www.who.int/vmnis/indicators/haemoglobin.pdf

Anemia ferropénica: criterios de la OMS.

Table 1

Relative extent of iron stores on the basis of serum ferritin concentration

	Serum ferritin (µg/l)			
	Less than 5 years of age		5 years of age or older	
	Male	Female	Male	Female
Depleted iron stores	< 12	< 12	< 15	< 15
Depleted iron stores in the presence of infection	< 30	< 30	-	-
Severe risk of iron overload (adults)	-	-	> 200	> 150

http://www.who.int/nutrition/publications/micronutrients/anaemia_iron_deficiency/en/

Definición de anemia: ¿Se deben utilizar los límites de la OMS?

Table 1. Lower limits of normal of hemoglobin concentration of the blood of adult men and women, as assessed by various sources

Source	Men, g/dL	Women, g/dL	Percent normal below cutoff	Effect of race
WHO (Blanc et al[1])	13	12	Not provided	Not provided
Jandl[3]	14.2	12.2	2.5	Discussed
Williams (Beutler et al[4])	14.0	12.3	2.5	Not provided
Wintrobe (Lee et al[5])	13.2	11.6	Not provided	Not provided
Rapaport[6]	14	12	Not provided	Not provided
Goyette[7]	13.2	11.7	5	Blacks' hemoglobin 0.5 g/dL lower
Tietz[8]	13.2	11.7	Not provided	Not provided
Hoffman et al[9]	13.5	12.0	2.5	Not provided

To convert hemoglobin from grams per deciliter to grams per liter, multiply grams per deciliter by 10.

Table 3. Lower limits of normal for hemoglobin concentration of the blood in g/dL of younger (age 20-59 for men; 20-49 for women) and older white and black adults

	Scripps-Kaiser					NHANES-III				
	No.	2.5% actual	2.5% normal distribution	5% actual	5% normal distribution	No.	2.5% actual	2.5% normal distribution	5% actual	5% normal distribution
White men, y										
20-59	6709	13.4	13.4	13.7	13.7	1456	13.4	13.4	13.8	13.7
60+	5515	12.8	12.8	13.2	13.2	934	12.2	12.4	12.8	12.7
White women, y										
20-49	2966	11.9	11.9	12.2	12.2	1045	12.0	11.9	12.2	12.1
50+	8313	11.9	11.9	12.2	12.2	1395	11.5	11.6	12.0	11.9
Black men, y										
20-59	434	12.6	12.5	12.9	12.9	1253	12.3	12.4	12.8	12.8
60+	135	—	12.4	—	12.7	235	11.4	11.9	11.8	12.2
Black women, y										
20-49	205	11.2	11.2	11.5	11.5	904	10.9	10.8	11.3	11.1
50+	255	11.2	11.2	11.5	11.5	442	11.0	10.9	11.3	11.2

To convert hemoglobin from grams per deciliter to grams per liter, multiply grams per deciliter by 10.
— indicates insufficient numbers to determine.

Table 4. Proposed lower limits of normal for hemoglobin concentration of the blood for white and black adults

Group	Hemoglobin, g/dL
White men, y	
20-59	13.7
60+	13.2
White women, y	
20-49	12.2
50+	12.2
Black men, y	
20-59	12.9
60+	12.7
Black women, y	
20-49	11.5
50+	11.5

Based on Scripps-Kaiser data for the 5th percentiles given in Table 2. NHANES data are considered to be confirmatory.

To convert hemoglobin from grams per deciliter to grams per liter, multiply grams per deciliter by 10.

Beutler E, Waalen J. The definition of anemia: what is the lower limit of normal of the blood haemoglobin concentration? Blood 2006: 107, 1747–1760.

Epidemiología de la anemia de las personas mayores

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Prevalencia de anemia y otras patologías en personas mayores

Table 2 – Prevalence of anemia, diabetes and hypertension.

	Eldorado	Piraporinha	p-Value[a]
Anemia – n (%)	11 (11.5)	32 (11.6)	0.9802
Male:female ratio	4:1	11:21	0.9050
Hemoglobin – n (%)			
≥10 g/dL	94 (97.9)	270 (97.5)	0.8071
<10 g/dL	2 (2.1)	7 (2.5)	
Diabetes – n (%)	25 (52.1)	25 (30.5)	0.0241
Male:female ratio	10:15	11:14	0.7
Hypertension – n (%)	45 (81.8)	55 (69.6)	0.16
Male:female ratio	14:31	23:32	0.37

[a] Chi-square test. Value in bold-face indicate statistically significant differences.

Lacerda J. Rev Bras Hematol Hemoter 2 0 1 6;3 8:141–146

Prevalencia de Eventos clínicos intercurrentes en el ingreso

(estudio REPOSI) (34% de 1267, Milán, Italia).

Infecciones tracto urinario
Neumonía
Anemia
Arritmias
Trastornos electrolíticos.

Rossi PD. Eur J Intern Med 2016;32:38-42.

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Prevalencia de anemia

Fuente: Revisión MEDLINE y EMBASE

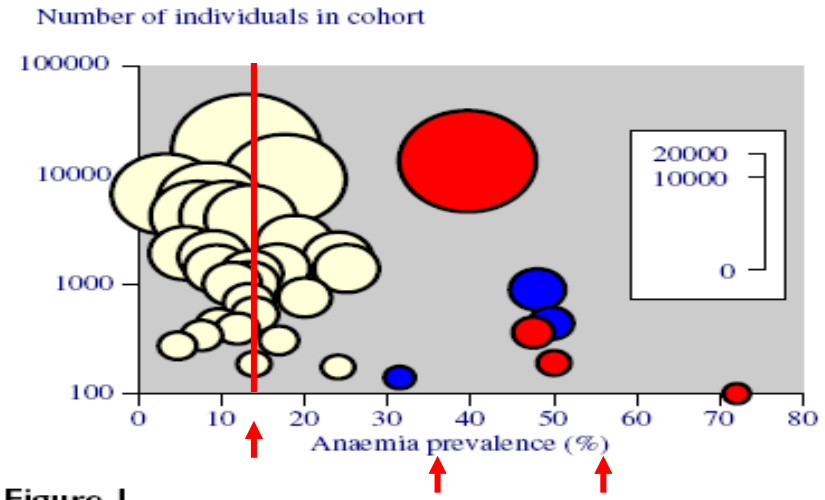

Figure 1
Anaemia prevalence according to the size of cohort (non-linear inset scale). Yellow symbols represent older people living in the community, blue those in nursing homes, and red admission to hospital.

Amarillo: comunidad
Rojo: hospitalizados.
Azul: residencias.

Table 1: Studies reporting anaemia in older persons using WHO criteria

Size range (individuals)	Number of		Percent of total	
	Studies	Patients	Studies	Patients
10,000–20,000	2	30,331	5.9	35.5
5,000–10,000	3	21,590	8.8	25.3
2,500–5,000	3	12,373	8.8	14.5
1,000–2,500	10	14,867	29.4	17.4
100–1,000	16	6,248	47.1	7.3

Table 2: Summary of results, including sensitivity analyses and use of alternative criteria for anaemia

	Number of studies	Number of individuals	Anaemia (weighted mean %)
WHO criteria			
All studies	34	85409	17
Community/Nursing Home	31	71456	13
Community only	27	69975	12
Nursing Homes only	4	1481	47
Hospital admissions only	3	13953	40
Sensitivity analyses			
Community/Nursing Home before 2000	12	19708	15
Community/Nursing Home 2000 and later	18	51748	12
Men	26	23856	15
Women	28	35781	14
Community only using Hb only	26	68912	12
Alternative criteria			
Community/Nursing Home Hb ≤ 120 g/L	3	2516	9
Community/Nursing Home Hb ≤ 110 g/L	4	21611	6

Note: Individual studies were weighted by number of individuals for calculation of overall mean rate of anaemia

Gaskell H. Prevalence of anaemia in older persons: systematic review. *BMC Geriatrics 2008, 8:1*
Patel KV. Epidemiology of anemia in older adults. Semin Hematol 2008:45, 210–217.

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Prevalencia de anemia

Fuente: Revisión MEDLINE y EMBASE

USA, Canada, EU.

Otros países:

China, Taipe, Korea, Japón, Australia, Perú, Brasil, Méjico, Polonia, Chequia,...

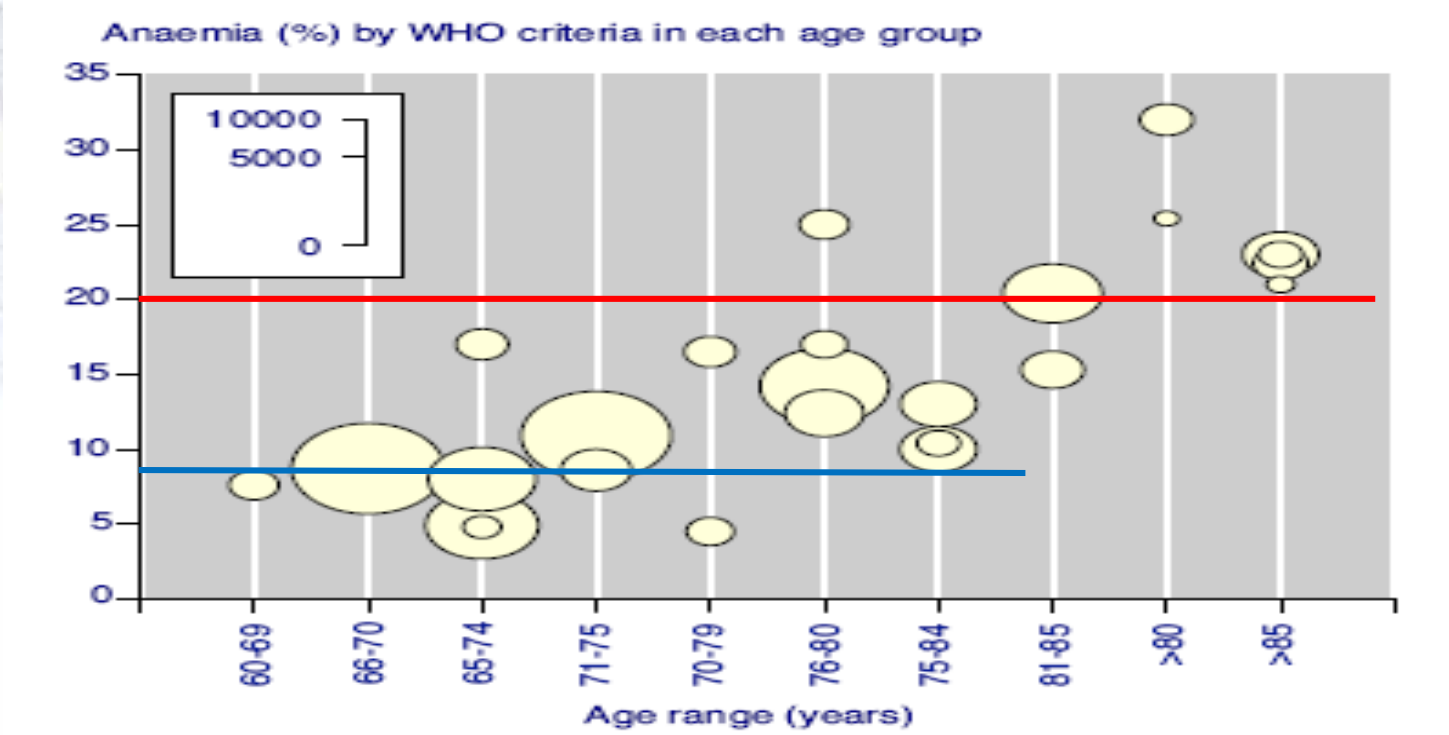
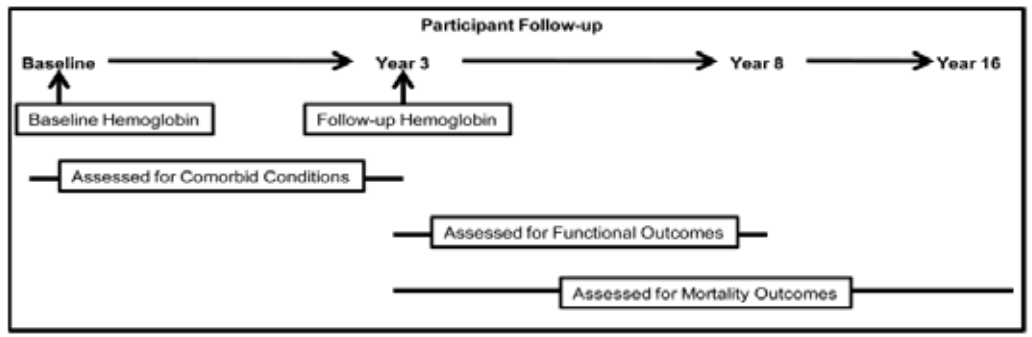


Figure 2
Anaemia prevalence by age range. Size of the symbol is proportional to the size of the cohort (inset scale)

Gaskell H. Prevalence of anaemia in older persons: systematic review. *BMC Geriatrics 2008, 8:1*
Patel KV. Epidemiology of anemia in older adults. Semin Hematol 2008:45, 210–217.

Incidencia de anemia

3.758 non-anemic from the Cardiovascular Health Study
≥65 years old at baseline and followed for up to 16 years.



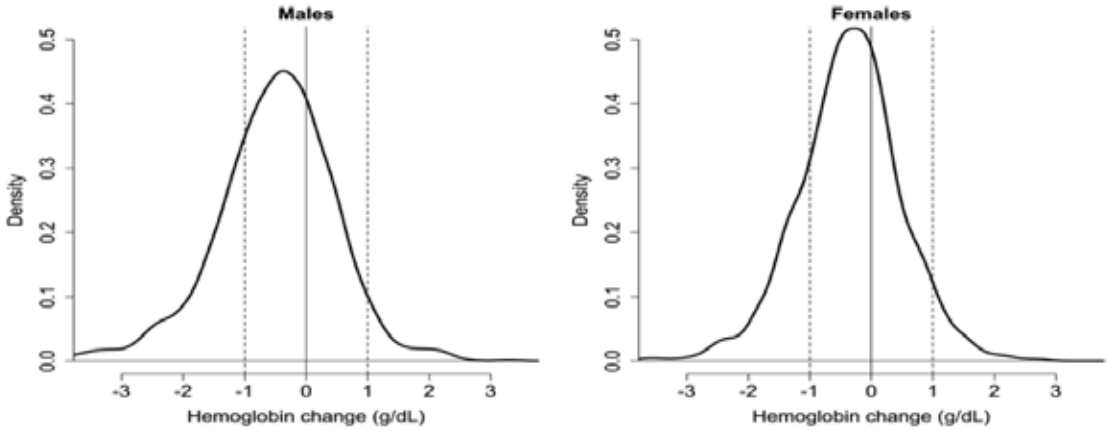


Figure 2.
Distribution of Change in Hemoglobin Concentration between Baseline and 3 Years Later Among Males and Females

InCHIANTI study Tuscany region of Italy. 1270 persons

274 male and 337 female participants free of anemia at baseline who were reevaluated after 3 years.

23 men (8.3%) and 26 women (7.7%) developed anemia

Ferrucci L. Low testosterone levels and the risk of anemia in older men and women. Arch Intern Med 2006;166:1380-8

Hb decreased by 0.4 g/dL and 9% developed anemia over 3 years. Factors: advanced age, afro-american, CKD.
Hb decrease related to worse cognitive function and mortality.

Zakai NA. Hemoglobin Decline, Function and Mortality in the Elderly: The Cardiovascular Health Study. *Am J Hematol 2013; 88: 5-9.*

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Incidencia de anemia

All residents 65 years or older in Biella, Italy. (46,000 inhabitants, Piedmont)

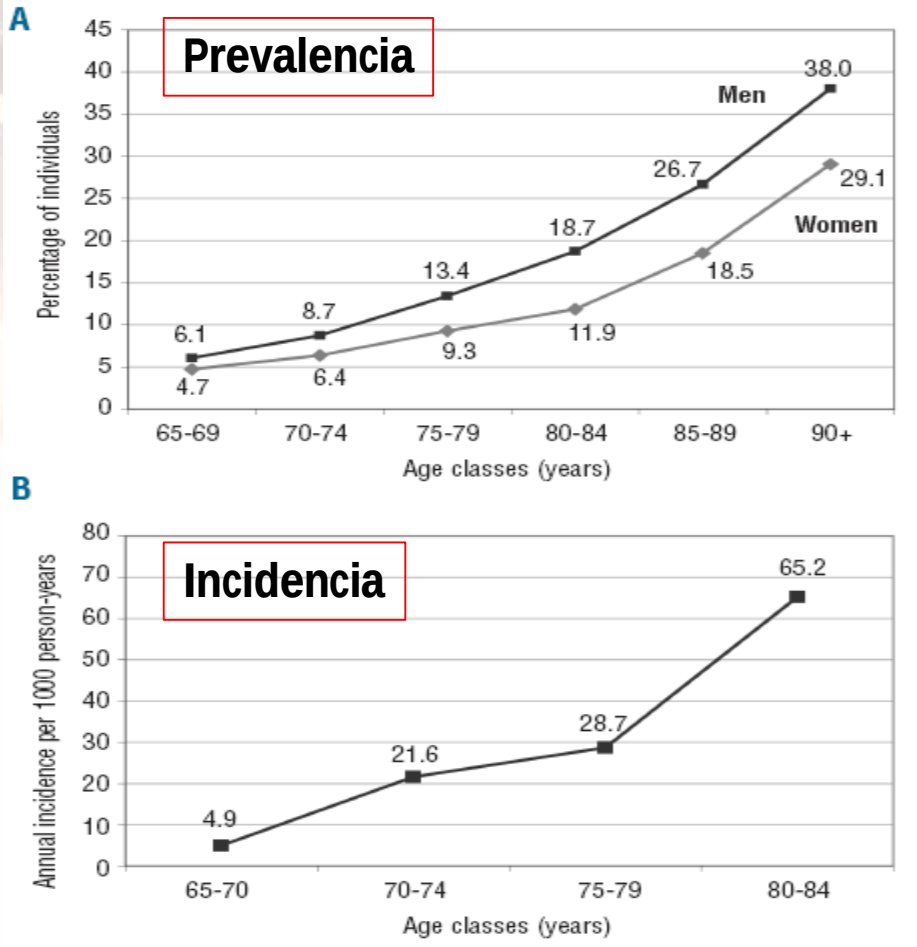

Figure 2. (A) Prevalence of mild anemia in the elderly population by sex. (B) Annual incidence of mild anemia in the elderly population.

Tettamanti M. Prevalence, incidence and types of mild anemia in the elderly: the "Health and Anemia" population-based study. Haematologica 2010;95(11):1849-1856.

All 618 Olmsted County Minnesota men and women aged 65 years

Olmsted County Minnesota
men (90.3 per 1000; 95% CI, 79.2-101.4)
women (69.1 per 1000; 95% CI, 62.3-75.8

Anía BJ. Incidence of anemia in older people: an epidemiologic study in a well defined population. J Am Geriatr Soc 1997;45:825-31.

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Impacto clínico

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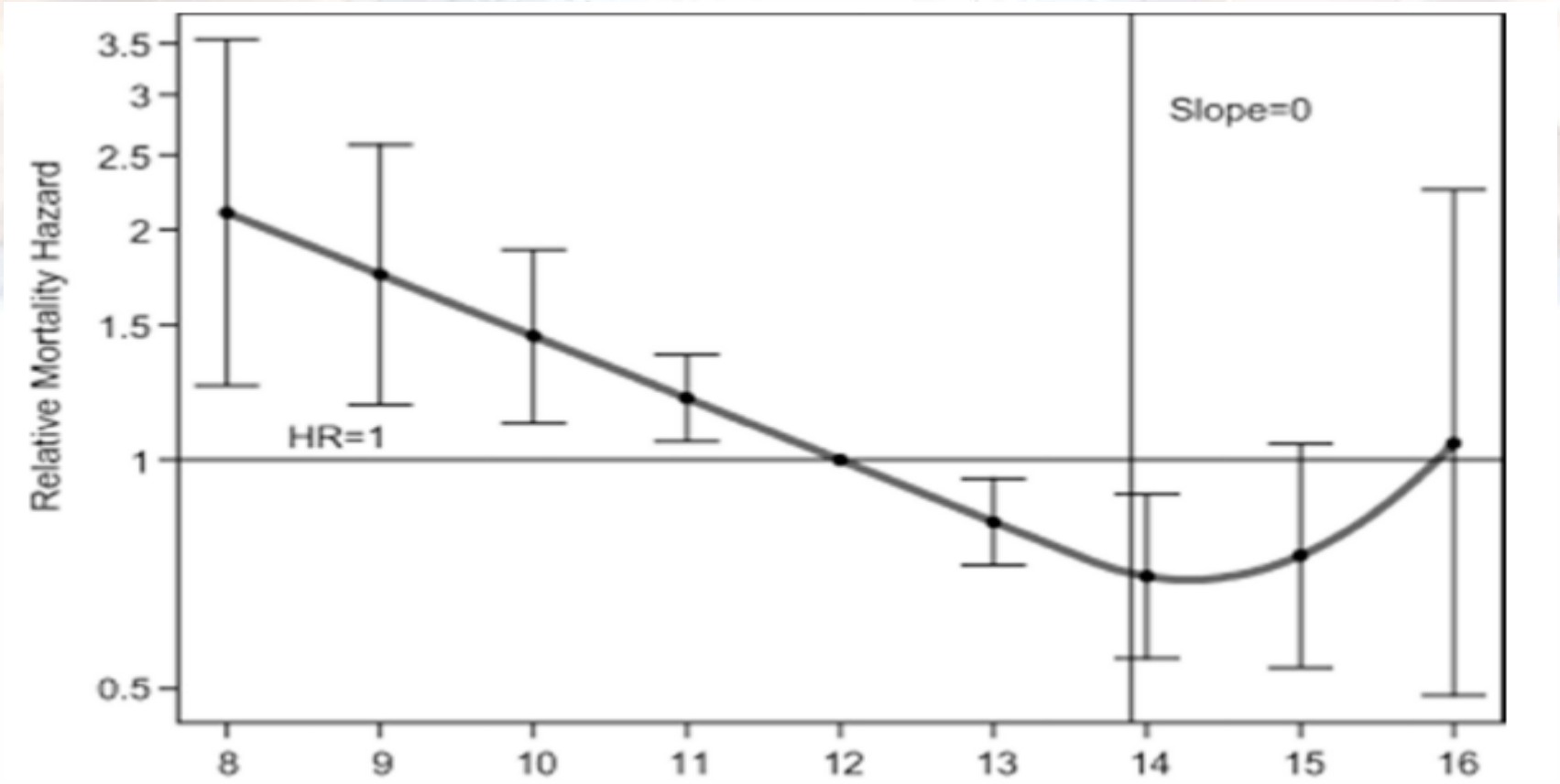
Consecuencias de la anemia: Aumento del riesgo

Table 1. Risks Associated with Anemia in Older Persons

Increased morbidity	Increased mortality
Decreased mobility in community-dwelling older persons[3,4]	Community-dwelling older persons[11,12]
Decreased quality of life[5]	Nursing home residents[13]
Increased risk of fatigue,[6] depression,[5] dementia,[7,8] delirium (in hospitalized patients),[9] and falls[10]	Persons with preexisting heart or kidney disease[14-16]
	Persons undergoing noncardiac surgery[17]

Bross MH. Anemia in Older Persons. Am Fam Physician. 2010;82:480-487.
Busti F, Campostrini N, Martinelli N, Girelli D. Iron deficiency in the elderly population, revisited in the hepcidin era. Front Pharmacol 2014;5:83.
Shi WH. The Status and Associated Factors of Successful Aging among Older Adults Residingin Longevity Areas in China. Biomed Environ Sci 2016;29:347-55
Cho J. Protective and Risk Factors for 5-Year Survival in the Oldest Veterans: Data fromthe Veterans Health Administration. J Am Geriatr Soc 2016;64:1250-7

Relación entre Hb y riesgo de mortalidad



5-year all-cause mortality in community-dwelling, disabled older women.

Chaves PH. J Am Geriatr Soc. 2004; 52:1811–1816.

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Relación entre Hb, riesgo de mortalidad y hospitalización

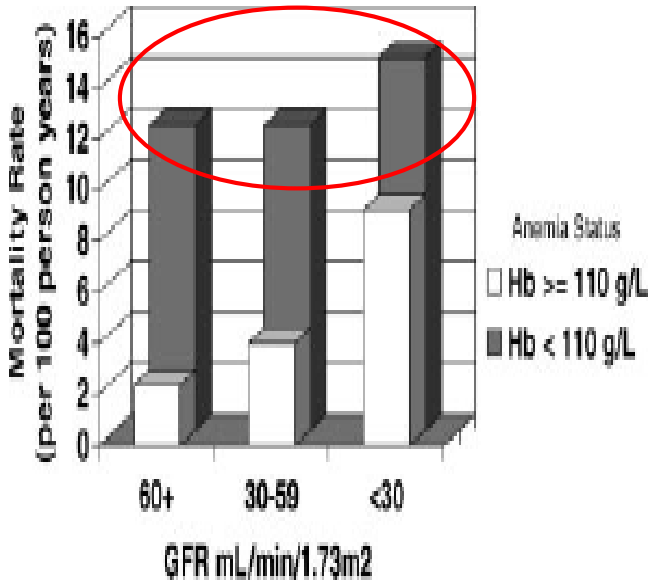

Figure 1. Mortality rate (per 100 person-years) by stage of kidney function and the presence or absence of anemia (adjusted for age and sex).

Table 2. Primary and secondary outcomes by anemia status and CKD category

Outcome	No anemia		Anemia		
	No.	Age-* and sex-adjusted rate per 100 person-years (95% CI)	No.	Age-* and sex-adjusted rate per 100 person-years (95% CI)	Hazard ratios† (95% CI)
GFR, 60 mL/min per 1.73 m²					
All-cause mortality	999	2.39 (2.24-2.54)	122	11.92 (9.95-14.28)	4.29 (3.55-5.12)
All-cause hospitalization	4770	15.24 (14.81-15.67)	220	38.80 (33.98-44.36)	2.16 (1.88-2.48)
CVD-specific hospitalization	1318	4.18 (3.96-4.41)	83	13.44 (10.82-16.69)	2.49 (1.99-3.12)
GFR, 30 to 59 mL/min per 1.73 m²					
All-cause mortality	565	4.00 (3.65-4.38)	114	11.95 (9.90-14.42)	2.80 (2.28-3.43)
All-cause hospitalization	1747	20.05 (19.10-21.06)	202	42.46 (36.94-48.80)	1.87 (1.61-2.12)
CVD-specific hospitalization	717	7.38 (6.82-7.99)	102	18.38 (15.08-22.39)	2.15 (1.74-2.65)
GFR, less than 30 mL/min per 1.73 m²					
All-cause mortality	117	9.20 (7.64-11.07)	66	14.61 (11.43-18.67)	1.53 (1.12-2.07)
All-cause hospitalization	230	34.72 (30.48-39.55)	109	46.33 (38.36-55.97)	1.23 (0.97-1.56)
CVD-specific hospitalization	127	17.24 (14.44-20.59)	60	21.40 (16.56-27.65)	1.15 (0.84-1.59)

Absence of anemia is defined as Hb at or above 110 g/L; anemia was defined as Hb below 110 g/L.
*Age adjusted to the sample mean using Poisson regression.
†Adjusted for age, sex, diabetes mellitus, and comorbidity.

17 030 community dwelling (Calgary Health Region)

Culleton BF. Impact of anemia on hospitalization and mortality in older adults. Blood. 2006;107:3841-3846.

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Etiología

Causas de anemia en las personas mayores

Unexplained Anemia in the Elderly
Erythropoietin (CKD)

Nutrient Deficiencies (Fe, B12, Fo)
Chronic Inflammation or Disease

Endocrine dysfunction
Marrow toxic drugs
MDS

Busti F, Campostrini N, Martinelli N, Girelli D. Iron deficiency in the elderly population, revisited in the hepcidin era. Front Pharmacol 2014;5:83.
Merchant AA, Roy CN. Not so benign haematology: anaemia of the elderly. Br J Haematol. 2012; 156: 173–185.
Vanasse GJ, Berliner N. Anemia in elderly patients: an emerging problem for the 21st century. Hematology 2010;:271-5.

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Etiología

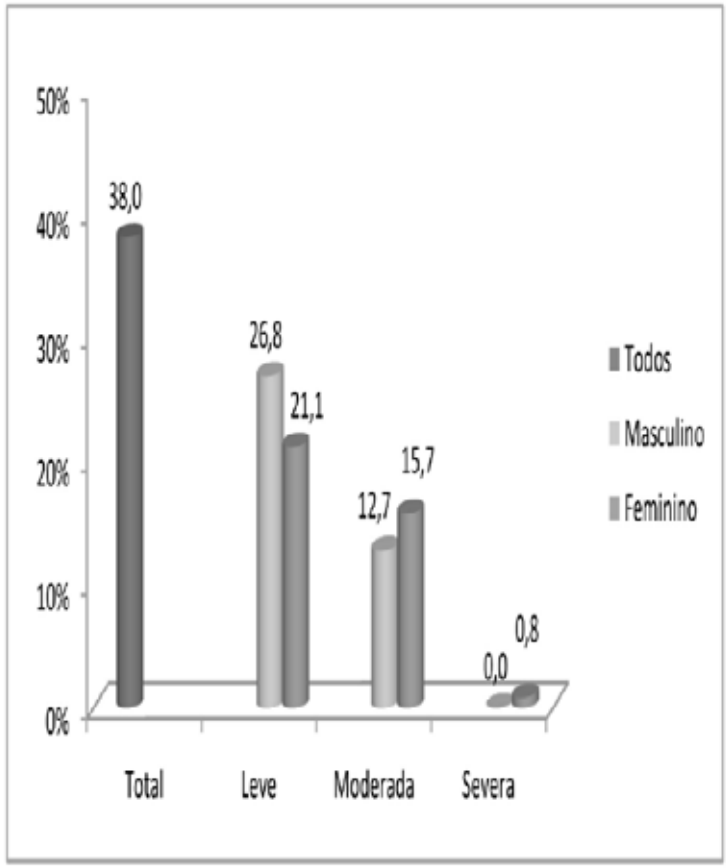

Fig 1. Total prevalence and degrees of anemia according to gender in the institutionalized elderly in Salvador, Bahia, Brazil.

Cruz da Silva E. PLOS ONE 2016: 0162240

Table 3 Age distribution of anemia

Age groups, years	Age distribution % (n)	Hb values (g/dL) Mean ± SD	Prevalence of anemia[a] % (n)	Prevalence of severe anemia[a] % (n)
Total	100 (19,758)	13.6±1.8	21.1 (4,177)	3.7 (722)
64–69	31.8 (6,290)	13.9±1.7	15.1 (949)	2.5 (155)
70–74	23.1 (4,573)	13.8±1.8	18.3 (835)	3.0 (135)
75–79	20.5 (4,056)	13.5±1.8	22.3 (903)	3.6 (148)
80–84	14.9 (2,943)	13.1±1.8	28.4 (837)	5.0 (148)
85–89	5.8 (1,155)	12.9±1.8	32.8 (379)	6.6 (76)
≥90	3.9 (741)	12.7±2.0	37.0 (274)	8.1 (60)

Notes: [a]Hb <12 g/dL in women and <13 g/dL in men; [b]Hb <10 g/dL. P-values for differences between age groups: *P<0.05; **P<0.001.
Abbreviations: Hb, hemoglobin; n, number positive; SD, standard deviation.

Anemia normocítica: 78.0%, Microcítica: 3.7%. Macrocítica: 18.4%.

Insuf Renal 45.1% con anemia

En 28.1% de las Insuf Renal tenían marcadores de inflamación.

ATC(definida por Prt C elevada) 62.1% de los anémicos.

AF en 14,1 %

Déficit de Folato 6.7% y de B12 en 2% de los anémicos.

Table 1 Classification of anemia based on laboratory parameters

Parameter	Overall		Nonanemic		Anemic	
	n/N	%	n/N	%	n/N	%
Total	19,758	100	15,581/19,758	79.0	4,117/19,758	21.1
Renal insufficiency						
GFR[a] <60 mL/min/1.73 m²	5,906/18,271	32.3	4,185/14,459	28.9	1,721/3,812	45.1
GFR[a] <30 mL/min/1.73 m²	728/18,271	4.0	297/14,459	2.1	431/3,812	11.3
Inflammation (CRP >0.7 mg/dL)	6,471/16,882	38.3	4,101/13,067	31.4	2,370/3,815	62.1
Absolute iron deficiency (SF <30 ng/mL)	360/3,826	9.4	193/2,668	7.2	167/1,158	14.4
Functional iron deficiency						
TSAT <16%, SF 30–100 ng/mL	219/3,715	5.9	98/2,581	3.8	121/1,134	10.7
TSAT <16%, SF >100 ng/mL	405/3,715	10.9	206/2,581	8.0	199/1,134	17.5
Folate deficiency (<3.8 ng/mL)	138/3,363	4.1	68/2,290	3.0	70/1,042	6.7
Vitamin B_{12} deficiency (<141 pmol/L)	51/3,302	1.5	31/2,298	1.3*	20/1,004	2.0*
Cytopenias						
Thrombopenia (<100 G/L)	373/19,758	1.9	145/15,581	0.9	228/4,177	5.5
Leukopenia (<4 G/L)	882/19,758	4.2	477/15,581	3.1	345/4,177	8.3
Leukopenia (<2 G/L)	54/19,758	0.3	9/15,581	0.1	45/4,177	1.1
Multifactorial anemia						
GFR[a] <60 mL/min/1.73 m² + CRP >0.7 mg/dL	2,417/15,995	15.1	1,417/12,440	11.4	1,000/3,555	28.1
GFR[a] <30 mL/min/1.73 m² + CRP >0.7 mg/dL	469/15,995	2.9	172/12,440	1.4	297/3,555	8.4
GFR[a] <60 mL/min/1.73 m² + CRP >0.7 mg/dL + FID	220/3,575	6.2	94/2,468	3.8	126/1,107	11.4
GFR[a] <30 mL/min/1.73 m² + CRP >0.7 mg/dL + FID	59/3,575	1.7	15/2,468	0.6	44/1,107	4.0
CRP >0.7 mg/dL + FID	462/3,585	12.9	214/2,475	8.6	248/1,110	22.3

Notes: Leukopenias as defined by Common Terminology Criteria for Adverse Events. P-values for anemic versus nonanemic: *P=0.170; all others P<0.001. (FID: TSAT <16%, SF ≥30 ng/mL). [a]According to the Modification of Diet Renal Disease study.[6]
Abbreviations: CRP, C-reactive protein; GFR, glomerular filtration rate; n, number positive; N, number evaluated; SF, serum ferritin; TSAT, transferrin saturation; FID, functional iron deficiency.

Bach V. Clinical Interventions in Aging 2014:9 1187–1196

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Valor del cociente TFR/Ft en el diagnóstico de la anemia ferropénica en el anciano.

Comparado con Gold standard Fe medular (49 IDA y 14 controles)
>80 años Rohovot, Israel.

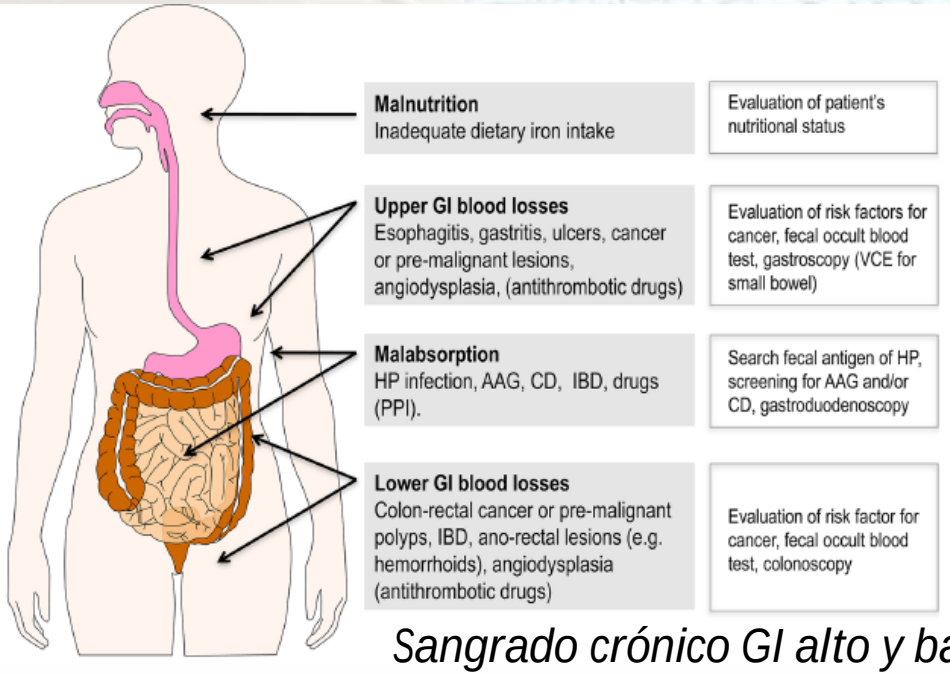
Otros índices eritrocitarios.

	FE/SAT/Ft	TFR-Ft
Especificidad %	100	**92.9**
Sensibilidad	16,3	**87,7**
VPP %	100	**97,7**
VPN%	22,2	**68,4**

El cociente TFR/Ft es el que permite un mejor diagnóstico de anemia ferropénica

Rimon E, Levy S, Sapir A, Gelzer G, Peled R, Ergas D, Sthoeger ZM. Diagnosis of iron deficiency anemia in the elderly by transferrin receptor-ferritin index. Arch Intern Med 2002; 162:445-9.
Buttarello M. Laboratory diagnosis of anemia: are the old and new red cell parameters useful inclassification and treatment, how? Int J Lab Hematol 2016;38 Suppl 1:123-32.,
Shin DH, Kim HS, Park MJ, Suh IB, Shin KS. Utility of Access Soluble Transferrin Receptor (sTfR) and sTfR/log Ferritin Index in Diagnosing Iron Deficiency Anemia. Ann Clin Lab Sci 2015;45:396-402.

Déficit de hierro en personas mayores



Sangrado crónico GI alto y bajo

Hernia de hiatus
Angiodisplasia
Neoplasia de colon
Fármacos (antitrombóticos)
50% Malabsorción digestiva

136 casos: adultos (N.=31, 40-64), entre 65-75 (N.=48) y > 75 (N=57).
Estudio digestivo demostró la causa en la mayoría

Lesiones sangrantes: menos frecuentes en adultos que en personas mayores (29% vs. 49.5%, P=0.0252).
Hernia de hiatus (15%) y c. colon (12.5%).

Malabsorción Fe: (HP, G. Autoinmune, CD) más frecuentes en adultos (80.6% vs. 56.2%, P=0.0367).

Papel de la cápsula endoscópica en personas mayores: erosiones, úlceras, angiodisplasia

Busti F. Iron deficiency in the elderly population, revisited in the hepcidin era. Front Pharmacol 2014;5:83
Vannella L. Upper and lower gastrointestinal causes of iron deficiency anemia in elderly compared with adult outpatients. Minerva Gastroenterol Dietol 2010;56:397-404..
Muhammad A. Evaluation of iron deficiency anemia in older adults: the role of Wireless capsule endoscopy. J Clin Gastroenterol. 2009; 43:627-31.

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Anemia inexplicada de las personas mayores

SOCIETAT CATALANA DE
GERIATRIA I GERONTOLOGIA

Anemia de causa desconocida de las personas mayores

Unexplained Anaemia in the Elderly

Table 1. Prevalence and subtypes of anemia in the elderly in selected studies.

Study population	N.	Age (years)	Prevalance (%)	Iron deficiency anemia (IDA) (%)	B12/ folate deficiency (%)	Anemia of chronic disease (ACD) (%)	Renal insufficiency (%)	Unexplained anemia (UA) (%)	Comments
NHANES III-Study[6] Non-institutionalized US population from 3rd National Health & Nutrition Examination Survey (1988-1994).	2096	≥ 65	10.6	16.6	B_{12}: 5.9 B_9: 6.4 both: 2.0	19.7	8.2	33.6	
NHANES III-Study[7] Cohort constituted as described in Guralnik *et al.*[8]	7171	≥ 50	12	24		26	11	39	Relevant negative impact of anemia on survival is shown (RR of 1.8; P<0.001)
Health / Anemia Study (Salute e Anemia)[9] Prospective, population-based study in all residents (including nursing or residential homes) in Biella, Italy	8744	≥ 65	14.2	16	10.1	17.4	15	26.4	Thalassemia trait in 14.4% Possible MDS in 8.5%
Community-dwelling older outpatients from hematology clinics at Stanford Hospital and Clinics (SHC) and Veterans Affairs Palo Alto Health Care System (VAPAHCS), USA[5] A comprehensive hematologic evaluation was performed	190	≥ 65	not applicable	12	nd	6	4	35	MDS 4% Suspected for MDS 16%
Cohort from Chicago, USA[10] *Racially diverse cohort (African Americans 69%)* from a single-institutional university referral anemia clinic; primarily community-dwelling adults aged 65 years. A comprehensive hematologic evaluation was performed	174	≥ 65	not applicable	25.3	4.6	9.8	3.4	43.7	Thalassemia trait in 4.6% Hematologic malignancy in 7.5%
InCHIANTI (Invecchiare in Chianti, "Aging in the Chianti Area") Population based study, Tuscany Region, Italy[11]	582	≥ 65	9.6	17.4	10.5	24.4	10.5	37.2	Patients with potentially associated bleeding source were excluded
Leiden 85+-Study[12] Population–based prospective study; Leiden, The Netherlands	490	≥ 85	23.3	11.4	5.3	20.2	7.0	25.4	
Innsbruck Medical University cohort, Austria[13] Cross-sectional, retrospective analysis of in- and outpatients	4117	≥ 64	21.1	AID: 14.4 FID: 28.2	B_{12}: 2.0 B_9: 6.7	62.1	11.3	-	Large proportion of multifactorial anemias detected; MDS is suspected in a substantial proportion

The definition of anemia in all studies cited is based on WHO-criteria.[1] The classification of the different types of anemia varies between the different studies particularly in ACD and in UA. RR: relative risk; AID: absolute iron deficiency; FID: functional iron deficiency.

Stauder R, Thein SL. Anemia in the elderly: clinical implications and new therapeutic concepts. Haematologica 2014;99:1127-30.

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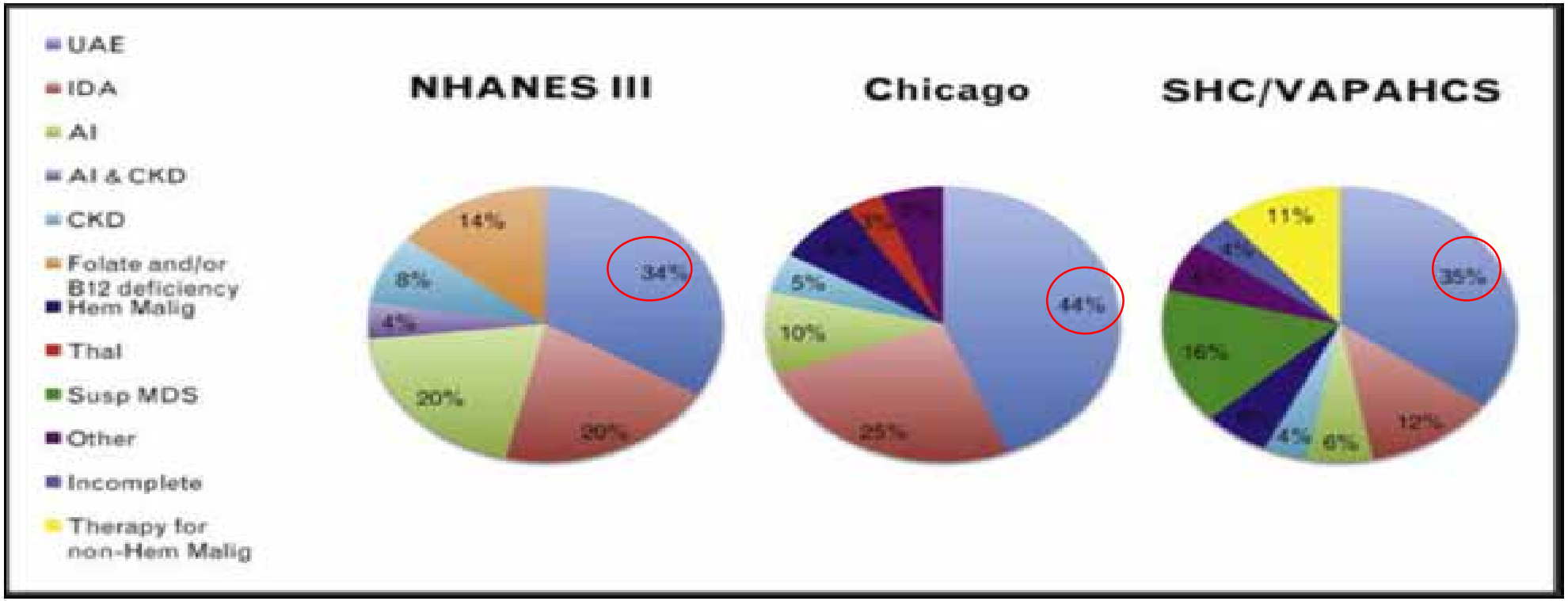
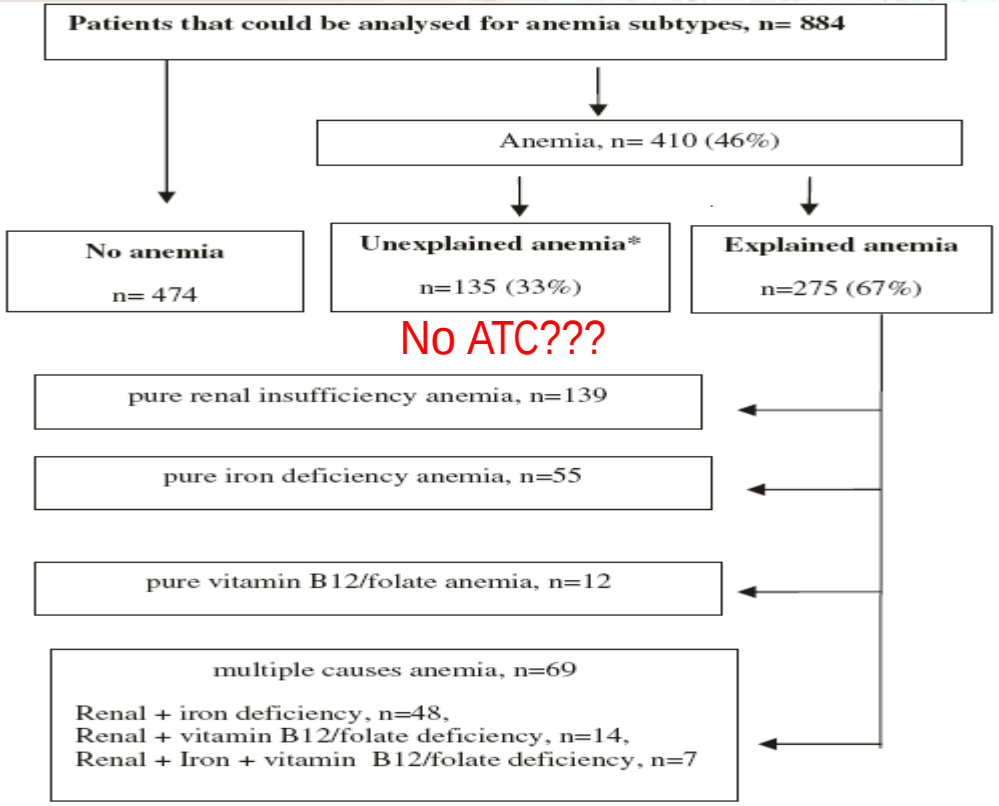
Anemia de causa desconocida de las personas mayores



Pang WW, Schrier SL. Anemia in the elderly. Curr Opin Hematol. 2012; 19:133–140.
Goodnough LT, Schrier SL. Evaluation and management of anemia in the elderly. Am J Hematol 2014; 89: 88–96.

Anemia de causa desconocida de las personas mayores



	No anemia	Unexplained anemia	Explained anemia	Unexplained vs explained anemia
	N=474	*N*=154	*N*=256	*p*-value
Demographics				
Age	84 (6.0)	84 (6.2)	85 (6.2)	0.08
Male sex	119 (25 %)	51 (38 %)**	114 (42 %)**	0.48
Receive home care	196 (41 %)	43 (32 %)	114 (42 %)	0.07
Admitted after a fall	177 (38 %)	73 (55 %)**	103 (38 %)	0.002
Diagnosis				
Hip fracture	15 (3 %)	30 (12 %)**	21 (8 %)*	0.001
Other acute trauma	144 (30 %)	51 (33 %)	63 (25 %)	0.06
nfection	116 (24 %)	36 (23 %)	66 (26 %)	0.63
heart disease	68 (14 %)	16 (10 %)	49 (19 %)	0.02
other medical	131 (28 %)	21 (14 %)**	57 (22 %)	0.03
Geriatric assessment				
More than 5 diagnosis	266 (56 %)	76 (60 %)	186 (71 %)**	0.02
Use > 5 drugs	361 (77 %)	100 (75 %)	244 (90 %)**	<0.001
Barthel index	80 (60–90)	70 (60–85)**	75 (60–85)*	0.37
MMSE	26 (23–28)	26 (23–28)	26 (23–28)	0.78
GDS	7 (4–12)	7 (3–11)	6 (4–11)	0.88
MNA-SF	10 (8–12)	10 (7–11)	10 (8–11)	0.42
Laboratory investigations				
Hb g/dl	13.6 (1.1)	11.0 (1.0)**	11.0 (0.9)**	0.22
Severe anemia (Hb < 10.6 g/L)[a]	0	38 (28 %)**	92 (36 %)**	0.29
MCV fL	94 (5.5)	95 (5.2)	93 (6.1)	0.001
Ferritin	179 (101–333)	204 (138–399)**	171 (93–336)	0.007
Transferrin Receptor (TfR)	3.3 (2.7–4.2)	3.0 (2.4–3.4)**	4.1 (3.0–5.5)**	<0.001
CRP mg/L	13 (5–30)	31 (10–63)**	27 (12–53)**	0.60
Pro-BnP > 225 pmol/L	90 (20 %)	21 (16 %)	110 (42 %)**	<0.001
Renal insufficiency[b]	157 (34 %)	0**	205 (75 %)**	<0.001
Iron deficiency[c]	91 (21 %)	0**	110 (43 %)**	<0.001
12 months follow up				
>2 hospital admissions	114 (31 %)	29 (27 %)	86 (39 %)*	0.03
Dead	74 (16 %)	21 (14 %)	55 (22 %)*	0.05

GDS Geriatric Depression scale 1–30, *MMS* Mini Mental Status Examination, *MNA-SF* Mini Nutritional Assessment- Short Form, *CRP* C-reactive protein, *NT pro- BnP* N-Terminal pro brain-type natriuretic peptide
[a]Severe anemia defined as Hb concentration in the lower anemia tertile
[b]Renal insufficiency was defined as e-GFR (described in methods) < 60 mL/min/1.73 m²
[c]Iron deficiency defined as anemi + ferritin < 35ug/l or TfR > 4.5 mg/L
Continous parameters are presented as mean (standard deviation), and median (interquartile range). Categorical data are presented as numbers (percentages)
*$p < 0.05$, **$p < 0.01$ when the group of patients with unexplained and explained anemias each were compared with patients without anemia

Table 2 Unadjusted and adjusted Odds Ratios for hospital readmission and death 12 months after acute hospitalization

	Hospital readmission[a]						Death[b]					
	Univariate			Multivariate			Univariate			Multivariate		
	OR	95 % CI	*p*	OR	95 % CI	*p*	OR	95 % CI	*p*	OR	95 % CI	*p*
Anemia[c]	1.20	0.87–1.65	0.26	1.42	0.96–2.09	0.08	1.24	0.88–1.77	0.22	1.24	0.83–1.84	0.30
Severe anemia[d]	0.92	0.59–1.44	0.73	1.13	0.66–1.94	0.66	1.88	1.21–2.93	0.005	1.89	1.11–3.22	0.02
Unexplained anemia[e]	0.83	0.51–1.34	0.44	0.95	0.55–1.64	0.83	0.74	0.41–1.31	0.30	1.04	0.54–2.02	0.90
Explained anemia[f]	1.42	1.00–2.01	0.05	1.54	1.05–2.25	0.03	1.53	1.04–2.23	0.03	1.07	0.63–1.83	0.79

OR odds ratio, *CI* confidence interval, *Hb* hemoglobin concentration
[a]Adjustment for age, > 5 diagnoses, Barthel index, influence of 5 different admission diagnoses
[b]Adjustment for age, > 5 diagnoses, Barthel index, influence of 5 different admission diagnoses, gender, MMSE, renal insufficiency
[c]Comparing patients with or without anemia, defined by WHO
[d]Comparing patients with and without severe anemia, defined as Hb in lowest gender –specific anemia tertile, (<10.6 g/dL)
[e]Comparing patients with unexplained anemia versus patients without anemia (WHO defined)
[f]Comparing patients with explained anemia versus patients without anemia (WHO defined)

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Abrahamsen JF. Readmission and mortality one year after acute hospitalization in older patients with explained and unexplained anemia – a prospective observational cohort study. BMC Geriatrics 2016; 16:109

Anemia de causa desconocida de las personas mayores

242 patients admitted to the **short-stay unit** during the study period, 190 were included. Age (70-103).

Anemia in in 83 (43.7%), 44.7% in women and 41.8% in men.

The laboratory screen detected at least one cause of anemia in 71 (85.5%) of the 83 patients.

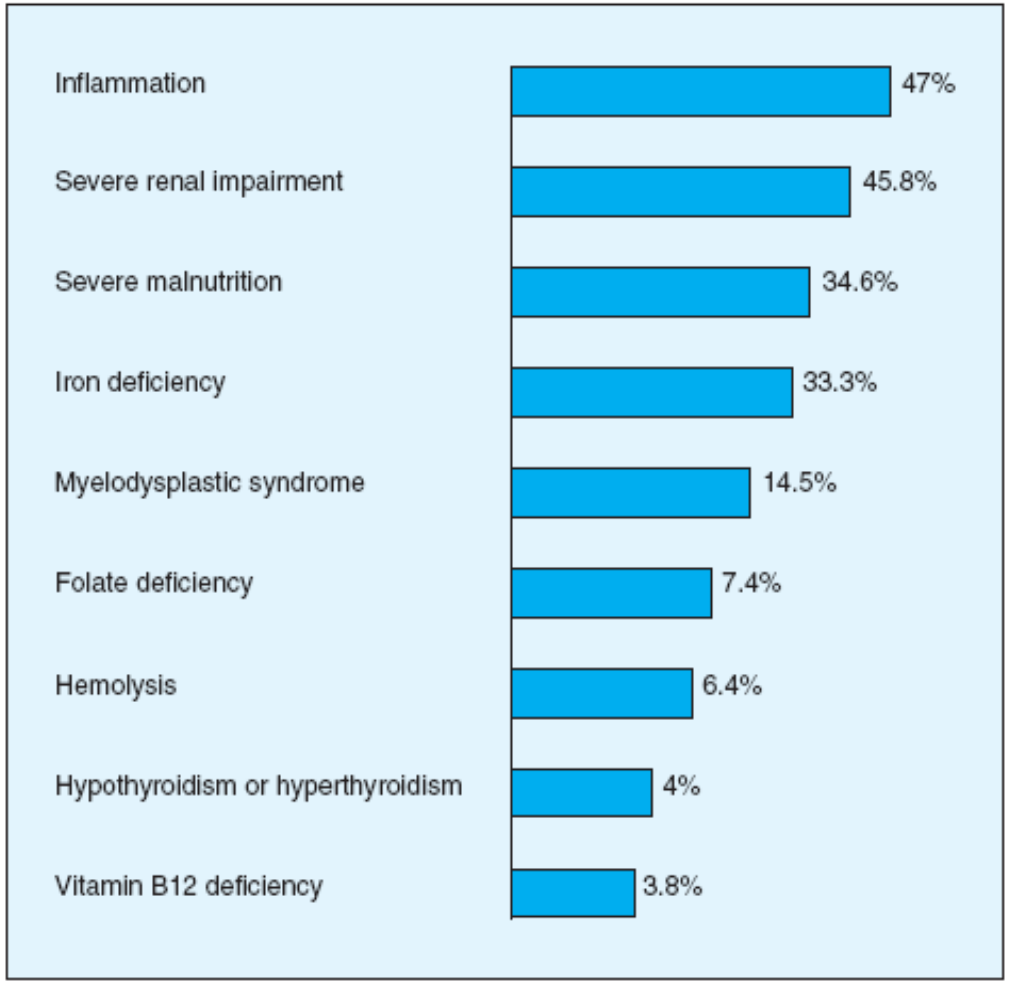

Figure 1. Causes of anemia in 83 patients.

Pautas E. Ann Biol Clin, 2012; 70:643-7

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Anemia de causa desconocida de las personas mayores

Prevalence of Anemia and Unexplained Anemia in the Elderly

	Population	% Anemic	% UA*
Joosten et al[55]	Geriatrics inpatient unit	24%	17%
Ania et al[2]	Community	7–9%	16%
Guralnik et al[1]	Community (NHANES III)	11%	33%
Ble et al[57]	Community (InCHIANTI)	10%	37%
Tecson J, IASIA, unpublished data	Community, internal medicine practices	21%	N/A
Artz et al[17,21]	Nursing home (NGRC)	49%	43%

Abbreviations: IASIA, Institute for Advanced Studies in Aging; NGRC, National Geriatrics Research Consortium; N/A, not available.

* Percent of anemic patients who fit UA criteria (see text).

País	Noruega	Usa	Usa	Bélgica	Usa
Procedencia	Centro de salud	Hospital comarcal	Institución	Hospital	Hospital
N	72	618	60	174	68
ATC	47	22	13	35	14
AF	18	14	23	15	1
Insuficiencia Renal	18	1	10		
B12/Fol	1	1			9
Sangrado(cirugía)		33			4
SMD					
Hemodilución				5	
Hepatopatía		6			
Miscelánea		1	9		
Múltiple	36	2		28	53
No causa	14	17	45	17	17

Makipour S. Unexplained anemia in the elderly. Semin Hematol 2008;45:250–254.

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Anemia de causa desconocida de las personas mayores

Features of Unexplained Anemia

Hemoglobin	10.5–12 g/dL
Reticulocyte index	Low
Mean corpuscular volume (MCV)	80–95 fL
Platelet and white blood cell counts	Normal
Peripheral smear	No dysplastic features
Serum iron	Mildly low or normal
Total iron binding capacity (TIBC)	Normal
% Iron saturation	Mildly low or normal
Serum levels of vitamin B_{12} and folic acid	Normal
Serum level of thyroid-stimulating hormone (TSH)	Normal
Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)	Normal
Serum erythropoietin level	Not elevated
Creatinine clearance	>30 to <90 mL/min

Anemia normocítica muy moderada hiporegenerativa

Makipour S. Unexplained anemia in the elderly. Semin Hematol 2008;45:250–254.

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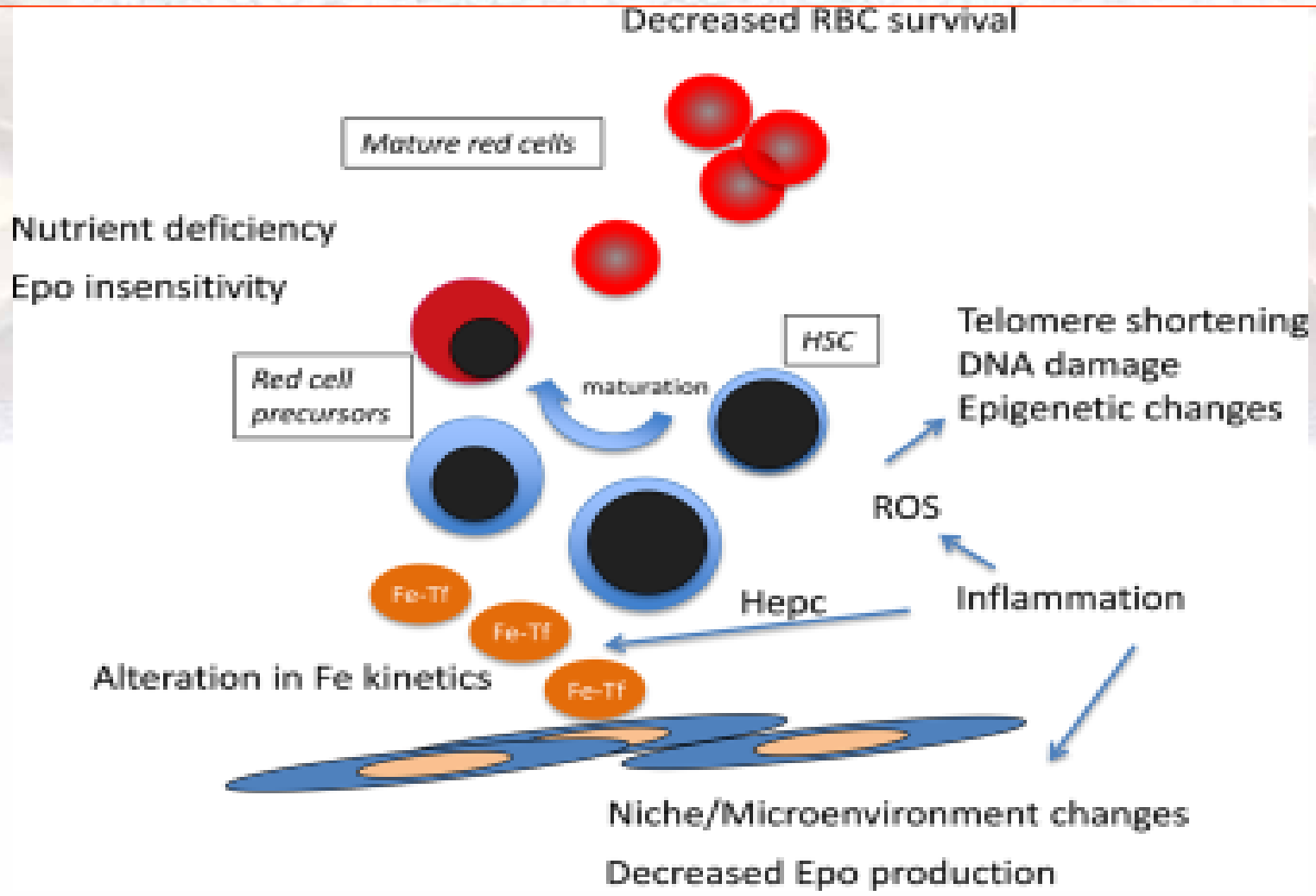
Anemia de causa desconocida de las personas mayores



Merchant AA. Br J Haematol. 2012; 156: 173–185.

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Anemia de causa desconocida de las personas mayores

Factores que contribuyen

Insuficiencia Renal asociada a la edad.

- Epo disminuida.
- Filtrado glomerular disminuido (la mitad 30-60 ml/min).
- GDF-15 y ERFE?

Envejecimiento de las HSC: especulativo.

Alteraciones endocrinas.

- Androgenos (hepcidina).
- Estrogen (aumenta actividad telomerase activity)(Hepcidina).
- Hipotiroidismo

Inflamación (INFLAMMAGING).

- La mitad: elevación PCR y VSG, Fe bajo y Ft elevada (> 100),elevación IL-6, hepcidina.

Mielodisplasia y toxicidad hematológica (MDS).

- **Tóxicos medulares:** Alcohol, fármacos (quimioterapia, inmunosupresores, inh folato, antivirales).
- Bicitopenia y anemia macrocítica (ICUS-CHIP).

Aspectos nutricionales

Busti F. Iron deficiency in the elderly population, revisited in the hepcidin era. Front Pharmacol 2014;5:83.
Merchant AA. Not so benign haematology: anaemia of the elderly. Br J Haematol. 2012; 156: 173–185.
Makipour S. Unexplained anemia in the elderly. Semin Hematol 2008;45:250–254.
Lewerin C. Serum Estradiol Associates With Blood Hemoglobin in Elderly Men: J Clin Endocrinol Metab 99: 2549–2556, 2014
Honda H. Associations among Erythroferrone and Biomarkers of Erythropoiesis and Iron Metabolism, and Treatment with Long-Term Erythropoiesis-Stimulating Agents in Patients on Hemodialysis. PLoS One 2016 ;11:e0151601
Carrero JJ. Testosterone deficiency is a cause of anaemia and reduced responsiveness to erythropoiesis-stimulating agents in men with chronic kidney disease. Nephrol Dial Transplant. 2012;27:709-15.
Waalen J. GDF15, IL6, hepcidin and testosterone levels in a large cohort ofelderly individuals with anaemia of known and unknown cause. Eur J Haematol 2011; 87:107-16.

Anemia de causa desconocida de las personas mayores

Aspectos nutricionales

Estudio Suizo (Geneve) con 392 participantes (< 80 años)
Estudiaron malnutrición como causa de anemia
Anemia 39,3% (Hb < 12).

14,3 % UA de ellos el 91% hipoalbuminemia
Relación entre Hb y albumina, independiente de FG.

Estudio en población China en Australia.
2009 China Health and Nutrition Survey data (2401, ≥60 años)
Estudia tipo de dieta y anemia

Relación entre dieta tradicional china y anemia 1.75 (95% CI: 1.33; 2.29)

Frangos E. Malnutrition in Very Old Hospitalized Patients: A New Etiologic Factor of Anemia? J Nutr Health Aging 2016;20:705-13.
Xu X. Dietary pattern, serum magnesium, ferritin, C-reactive protein and anaemia among older people. Clin Nutr 2015;pii: S0261-5614(15)00353-2.

Anemia de causa desconocida de las personas mayores

InCHIANTI (Invecchiare in Chianti, "Aging in the Chianti Area") Tuscany , Italy.

Table 1. Characteristics of the study population according to anemia and anemia type

Characteristic	No anemia	CKD anemia	Iron-deficiency anemia	Anemia of inflammation	Anemia with B_{12}/folate deficiency	Anemia unexplained
Total no.	496	9	15	21	9	32
Age, y	73.3 (69.9-77.9)	89.0‡ (84.0-90.8)	72.2 (68.8-90.7)	78.5‡ (74.7-83.1)	85.2† (73.6-87.9)	78.8† (73.8-85.5)
Male, %	46.5	44.4	73.3	61.9	33.3	27.3
Female, %	53.5	55.6	26.7	38.1	66.7	72.7
Years of education	5.0 (4.0-6.0)	4.0† (4.0-5.0)	5.0 (3.0-5.0)	5.0 (4.0-5.0)	5.0 (3.0-5.0)	5.0 (4.0-5.0)
Body mass index, %						
Less than 25 kg/m²	29.6	55.6‡	26.7	57.1‡	33.3	30.2
More than 25 kg/m²	70.4	44.4	73.3	42.9	66.7	69.7
Hepcidin, ng/mg creatinuria	60.7 (34.5-114.2)	64.0 (57.5-81.0)	15.0‡ (0.0-21.6)	50.9‡ (17.7-105.5)	49.4 (38.7-91.1)	80.0 (42.0-103.4)
Hemoglobin, g/dL	14.0 (13.3-14.8)	10.4‡ (8.8-11.3)	11.1‡ (9.9-12.2)	11.8‡ (11.0-11.9)	11.9‡ (11.4-12.5)	11.7‡ (11.4-12.0)
Ferritin, mg/L	118 (61-206)	108 (62-134)	8‡ (6-11)	67† (18-109)	106 (67-147)	103 (71-179)
Soluble transferrin receptor, nM/L	16.0 (13.6-19.2)	19.2 (16.8-28.8)	28.8‡ (19.2-38.4)	20.8‡ (17.4-27.2)	14.4 (13.6-16.0)	16.0 (14.4-18.4)
Iron, µg/dL	82 (67-99)	61 (38-68)	32 (18-41)	49 (38-55)	84 (73-95)	82 (73-97.0)
Erythropoietin, mU/mL	9.7 (7.4-12.5)	25‡ (19-34)	27‡ (19-58)	11.5‡ (9.5-23.4)	9.7 (8.7-11.0)	11.5 (9.7-14.2)
Vitamin B_{12}, pg/mL	374 (266-508.0)	340† (274-1108)	313 (194-404)	214‡ (175-376.0)	309 (157-362)	453 (318-567)
Folate, ng/mL	3.1 (2.4-4.2)	3.7 (2.8-6.0)	3.1 (2.1-4.8)	2.5 (2.2-4.1)	1.8‡ (1.7-2.1)	4.1‡ (3.0-5.3)
Creatinine clearance, mL/min	75.6 (58.6-93.8)	19.6‡ (13.6-24.1)	69.1 (42.2-102.7)	57.8 (45.2-83.6)	62.9 (48.9-69.5)	68.6 (47.9-87.4)
Presence of an inflammatory condition, %*	2.4	55.5‡	13.3	42.9‡	0.0	9.1
Interleukin-6, pg/mL	0.73 (0.37-1.43)	3.4‡ (3.4-5.4)	1.5‡ (0.8-2.6)	1.8‡ (1.1-2.1)	1.5† (1.2-2.7)	1.3† (0.8-2.0)
C-reactive protein, mg/L	1.3 (0.6-2.8)	9.2‡ (3.2-13.7)	3.5‡ (1.4-5.2)	3.6‡ (2.0-9.0)	2.3 (1.3-2.6)	1.5 (0.8-3.4)
Tumor necrosis factor-α, pg/mL	1.9 (1.4-3.2)	5.5‡ (3.3-7.2)	2.0 (1.7-3.4)	2.9‡ (1.8-5.2)	2.5 (1.9-3.0)	2.5 (1.9-3.6)
Interleukin-1β, pg/mL	0.01 (0.00-0.67)	0.08 (0.00-7.9)	0.00 (0.00-6.6)	0.00 (0.00-0.93)	0.00 (0.00-0.00)	0.00 (0.00-0.71)
Interleukin-1 receptor antagonist, pg/mL	130.0 (95.8-185.3)	193† (158-306)	136 (89.0-173.0)	124.7 (87.5-187.2)	154.1 (86.7-178.3)	128.0 (89.9-179.3)
Interleukin-18, µg/mL	382 (303-479)	545 (463-574)	410 (345-482)	376.6 (286.4-555)	343 (255-390.3)	337(268-518)

Data are reported as median values and interquartile ranges or percentages.
Anemia was defined as hemoglobin < 12 g/dL in women and < 13 g/dL in men.
CKD indicates chronic kidney disease.
*Any of the following: recent or current infection, malignant cancer, rheumatoid arthritis, inflammatory bowel diseases, connective tissue disorders, or skin ulcer.
†$P < .05$ compared with the "no anemia" group, adjusted for age and sex.
‡$P < .01$ compared with the "no anemia" group, adjusted for age and sex.

Elevación de la hepcidina y de la ferritina, con disminución de la producción de Epo

Ferrucci L. Proinflammatory state, hepcidin, and anemia in older persons. Blood. 2010; 115: 3810-3816.

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Epo en la UA de las personas mayores

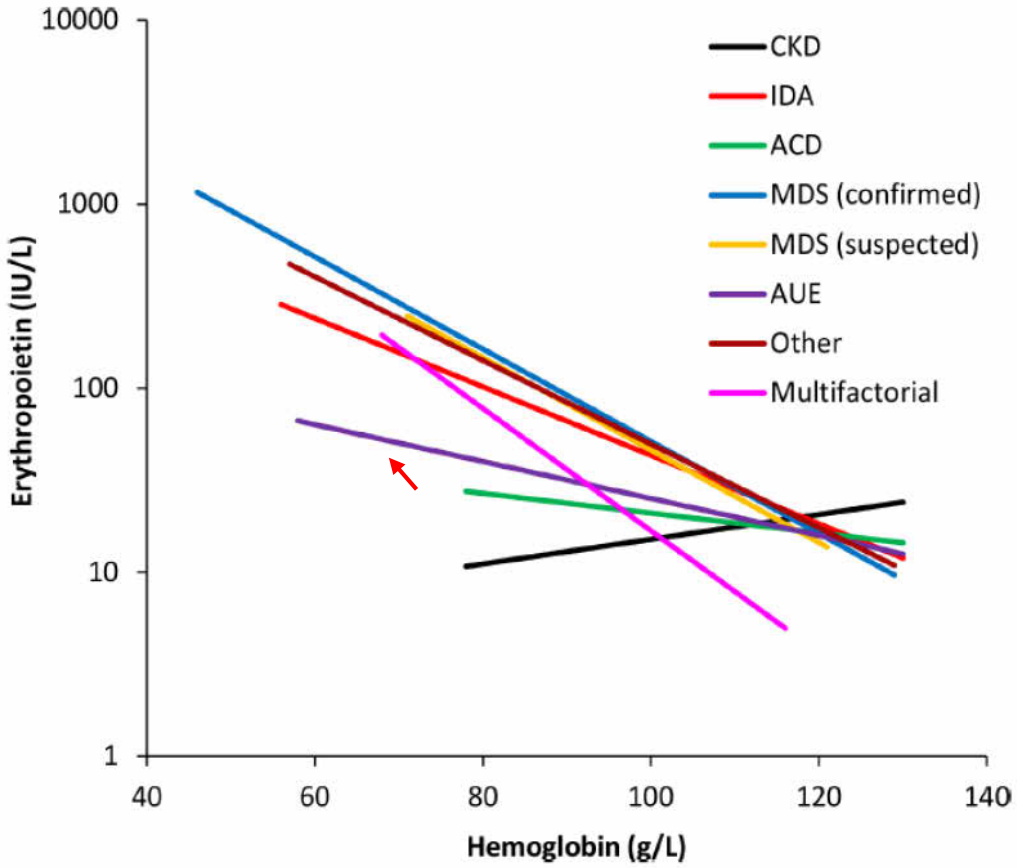
Etiology of the anemia	n	Erythropoietin, IU/L		Hemoglobin, g/L		eGFR (CKD-EPI), mL/min/1.73 m^2	
		Mean	p-value[a]	Mean	p-value[a]	Mean	p-value[a]
Iron deficiency	59	102.4	-	95.6	-	63.3	-
Chronic kidney disease	25	25.1	0.001[b]	96.6	0.794	20.2	<0.001[b]
Chronic disease	31	26.0	<0.001[b]	99.9	0.204	57.4	0.251
MDS (confirmed)	180	287.8	0.002[b]	91.1	0.044[b]	63.7	0.900
MDS (suspected)	19	148.1	0.425	97.0	0.739	61.6	0.732
Anemia of unknown etiology	117	39.1	0.003[b]	105.7	<0.001[b]	53.6	0.008[b]
Other etiology	118	271.4	0.002[b]	92.7	0.275	62.7	0.882
Multifactorial etiology	20	106.1	0.934	93.2	0.539	37.8	<0.001[b]

[a] The p-value is calculated using an unpaired t-test comparison against iron deficiency

[b] $p<0.05$

doi:10.1371/journal.pone.0157279.t002

EPO, Hb y la función renal en la anemia de las personas mayores según el tipo de anemia.



Curvas de correlación entre Epo vs Hb según los tipos de anemia en personas mayors (curvas exponenciales).

Gowanlock Z. Erythropoietin Levels in Elderly Patients with Anemia of Unknown Etiology. PLoS ONE 2016; 11: e0157279.

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Epo en la UA de las personas mayores

Metanálisis relación Epo y Hb en la anemia de las personas mayores

6 estudios:
EPO es significativamente inferior en la AUE comparada con:

Anemia Ferropénica (ROM 0.7210; 95% CI 0.7052 to 0.7372; P-value < 0.00001).
Anemia de tipo crónico: (ROM 0.8995; 95% CI 0.8362 to 0.9677; P = 0.004).

EPO era mayor en AUE que en la anemia asociada a insuficiencia renal (ROM 1.0940; 95% CI 1.0557, 1.1337; P < 0.00001

En la AUE los niveles de Epo están elevados, pero inapropiadamente comparado con otras anemias.
Los niveles de Epo se situán entre curvas de producción de Epo de bloqueo (como en la ATC) y falta de producción (IRenal).
Es decir, hay una déficit de producción o una respuesta bloqueada.

Sriram S. Erythropoietin in anemia of unknown etiology: A systematic review and meta-analysis. Hematology 2016; 21:234-40

Inflammaging, stress oxidativo y UEA

Inmunosenescencia: cambios del sistema inmune con la edad

Inflammaging es parte de ese proceso de inmunosenescencia, consiste en una respuesta inflamatoria aumentada asociada con la edad (estado proinflamatorio de bajo grado), se eleven las citokinas proinflamatorias (IL-6, IL-1, TNFα y IFNγ).

En las persona mayores la anemia y la fragilidad comparten patofisiología común asociada a procesos inflamatorios crónicos, inducidos por la inmunosenescencia y el stress oxidativo

Mecanismo de la anemia: Eriptosis y elevación de la hepcidina.

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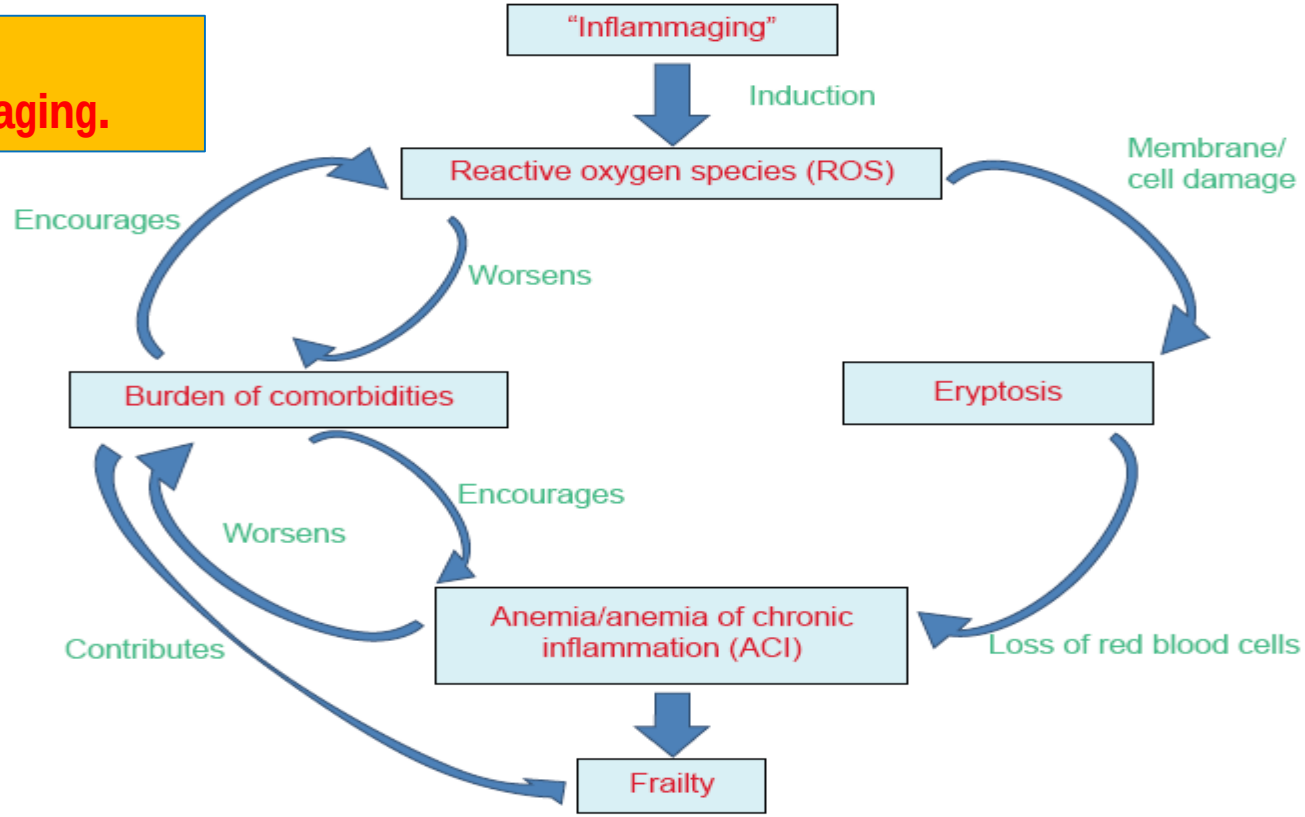
Röhrig G. Clinical Interventions in Aging 2016:11 319–326
Makipour S. Unexplained anemia in the elderly. Semin Hematol. 2008;45:250–254 Franceschi C. *Ann N Y Acad Sci. 2000; 908:244–254.*
Baylis D. Understanding how we age: insights into inflammaging. *Longev Healthspan. 2013;2(1):8.*
Macciò A. Management of anemia of inflammation in the elderly. *Anemia. 2012;2012:563251.*
Chang SS- Association between inflammatory-related disease burden and frailty: results from the Women's Health and Aging Studies (WHAS) I and II. *Arch Gerontol Geriatr. 2012;54:9–15.*

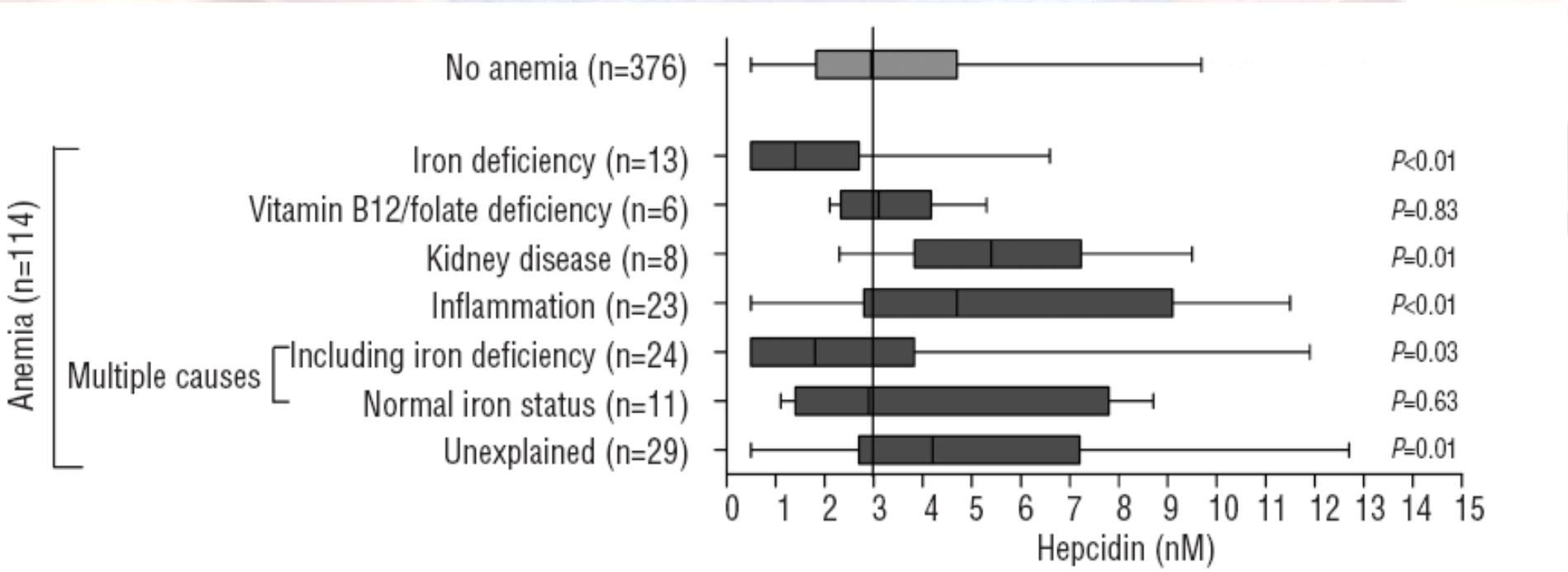
Hipótesis:
asociación entre fragilidad, ATC e inflammaging.



Eriptosis (erythrocyte suicidal death) es un mecanismo fisiológico para retirar los hematíes defectuosos de la circulación.
Se trasloca la fosfatidilserina a la superficie de la membrana.
Los macrófagos fagocitan y destruyen estos hematíes para evitar hemólisis.
Sus desencadenantes son el stress oxidativo y la multimorbilidad (diabetes mellitus, insuficiencia cardiaca, insuficiencia renal, deshidratación, Parkinson).
El incremento en la fosfatidilserina se relaciona con el incremento del stress oxidativo (ROS).

Lang E. Triggers, inhibitors, mechanisms, and significance of eryptosis: the suicidal erythrocyte death. *Biomed Res Int. 2015; 2015:513–518.*
Lupescu A. Enhanced suicidal erythrocyte death contributing to anemia in the elderly. *Cell Physiol Biochem. 2015;36:773–783.*
Röhrig G. Anemia in the frail, elderly patient. Clinical Interventions in Aging 2016:11 319–326

Inflammaging, stress oxidativo y UEA



Den Elzen WP. Plasma hepcidin levels and anemia in old age. The Leiden 85-Plus Study. Haematologica 2013; 98:448-54.

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Mielodisplasia-CHIP

SOCIETAT CATALANA DE
GERIATRIA I GERONTOLOGIA

Mielodisplasia

Table 4 Distribution of MCV subtypes as compared with the different causes of anemia

Parameter	Microcytic		Normocytic		Macrocytic	
	n/N	%	n/N	%	n/N	%
Total	153/4,177	3.7	3,257/4,177	78.0	767/4,177	18.4
Renal insufficiency						
GFR[a] <60 mL/min/1.73 m²	61/1,721	3.5	1,313/1,721	76.3	347/1,721	20.2
GFR[a] <30 mL/min/1.73 m²	16/431	3.7	324/431	75.2	91/431	21.1
Inflammation (CRP >0.7 mg/dL)	62/2,370	2.6	1,907/2,370	80.5*	401/2,370	16.9
Absolute iron deficiency (SF <30 ng/mL)	45/167	26.9**	115/167	68.9	7/167	4.2
Functional iron deficiency						
TSAT <16%, SF >100 ng/mL	12/121	10.0*	97/121	80.1	12/121	10.0
TSAT <16%, SF 30–100 ng/mL	4/199	2.0	164/199	82.4	31/199	15.6
Folate deficiency (<3.8 ng/mL)	3/70	4.3	48/70	68.6	19/70	27.1#
Vitamin B_{12} deficiency (<141 pmol/L)	4/20	20.0*	7/20	35.0	9/20	45.0*
Cytopenias						
Thrombopenia (<100 G/L)	5/228	2.2	143/228	62.7	80/228	35.1**
Leukopenia (<4 G/L)	7/345	2.0	224/345	64.9	114/345	33.1**
Leukopenia (<2 G/L)	1/45	2.3	29/45	64.4	15/45	33.3*

Notes: Leukopenias as defined by Common Terminology Criteria for Adverse Events. *P*-values: *$P<0.05$; **$P<0.001$; #$P=0.08$; all others not significant. [a]According to the Modification of Diet Renal Disease study.[45]

Abbreviations: CRP, C-reactive protein; GFR, glomerular filtration rate; n, number positive; N, number evaluated; SF, serum ferritin; TSAT, transferrin saturation; MCV, mean corpuscular volume.

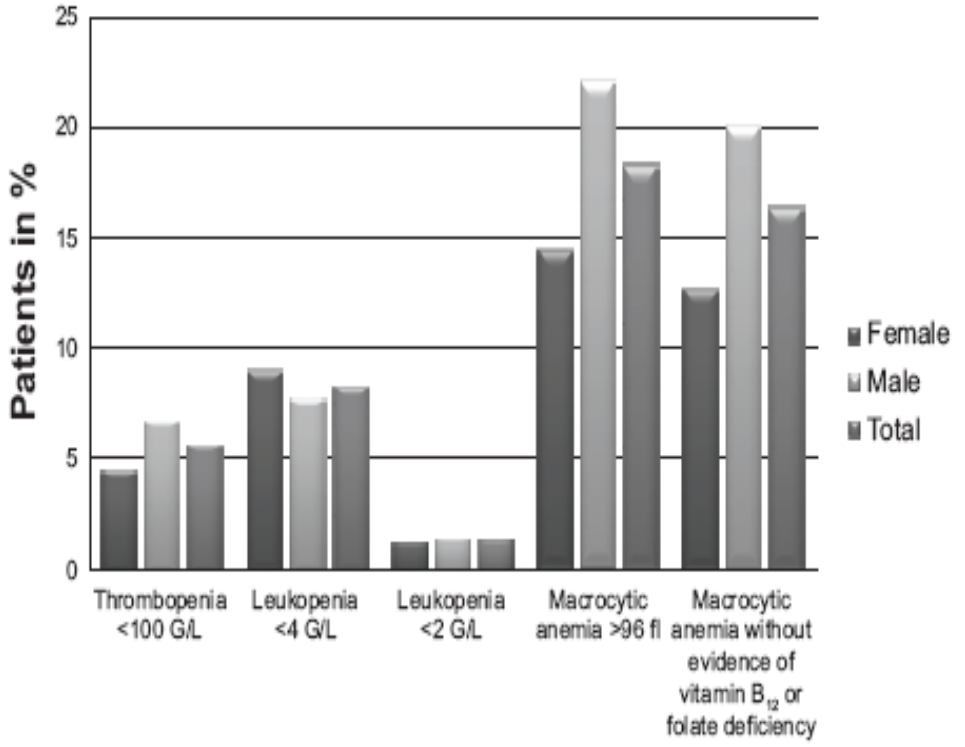

Figure 2 Evidence for possible underlying myelodysplastic syndromes in anemic patients (n=4,177).

Bach V. Clinical Interventions in Aging 2014:9 1187–1196

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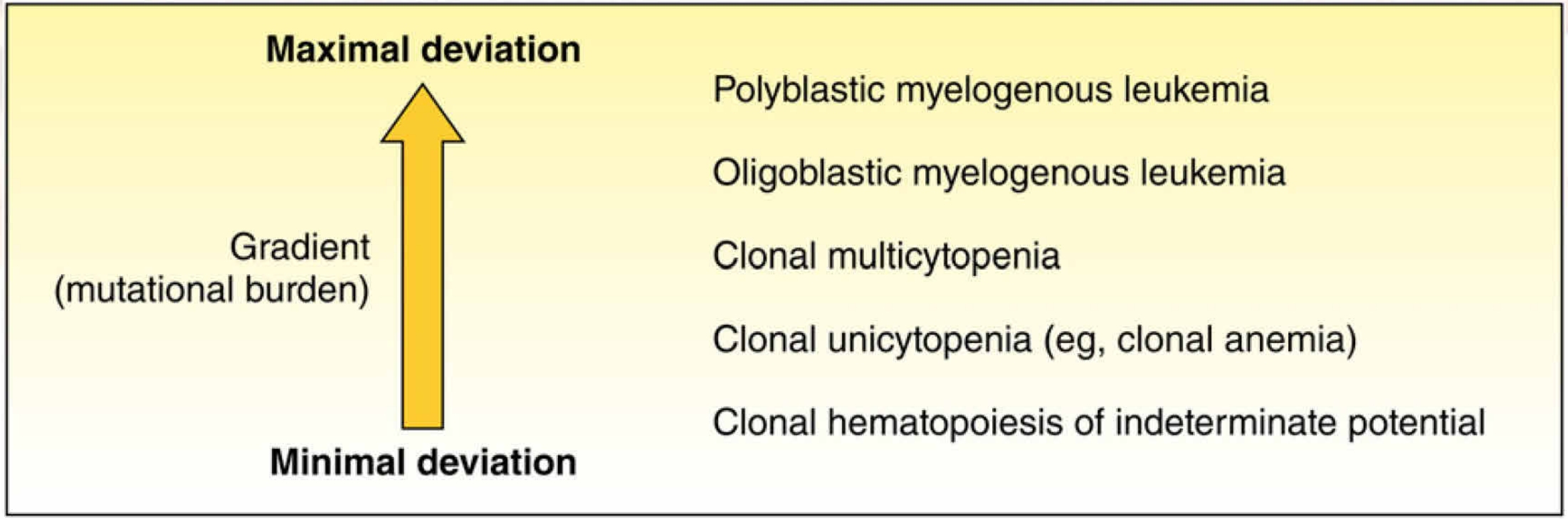
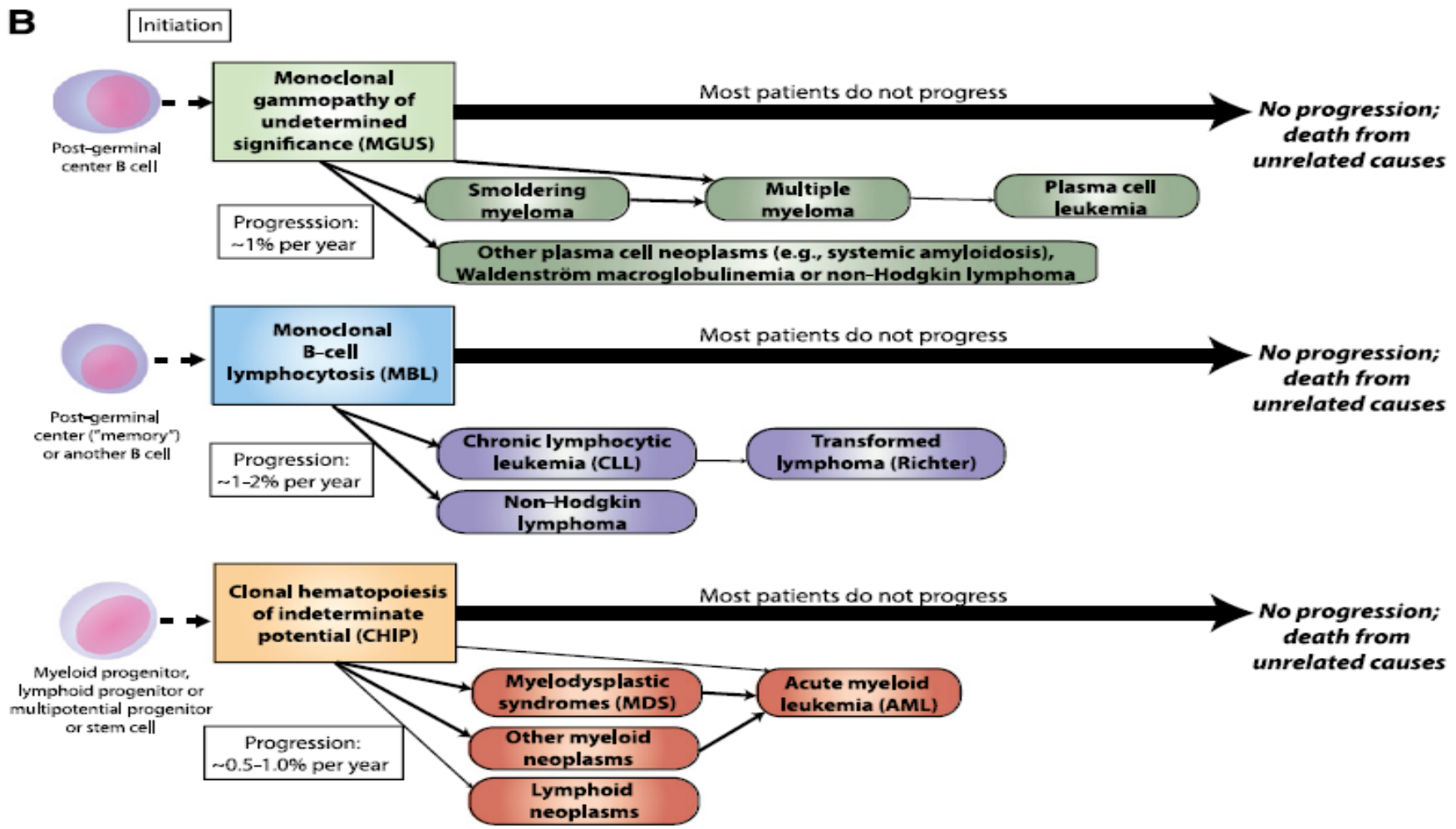
Mielodisplasia (CHIP)



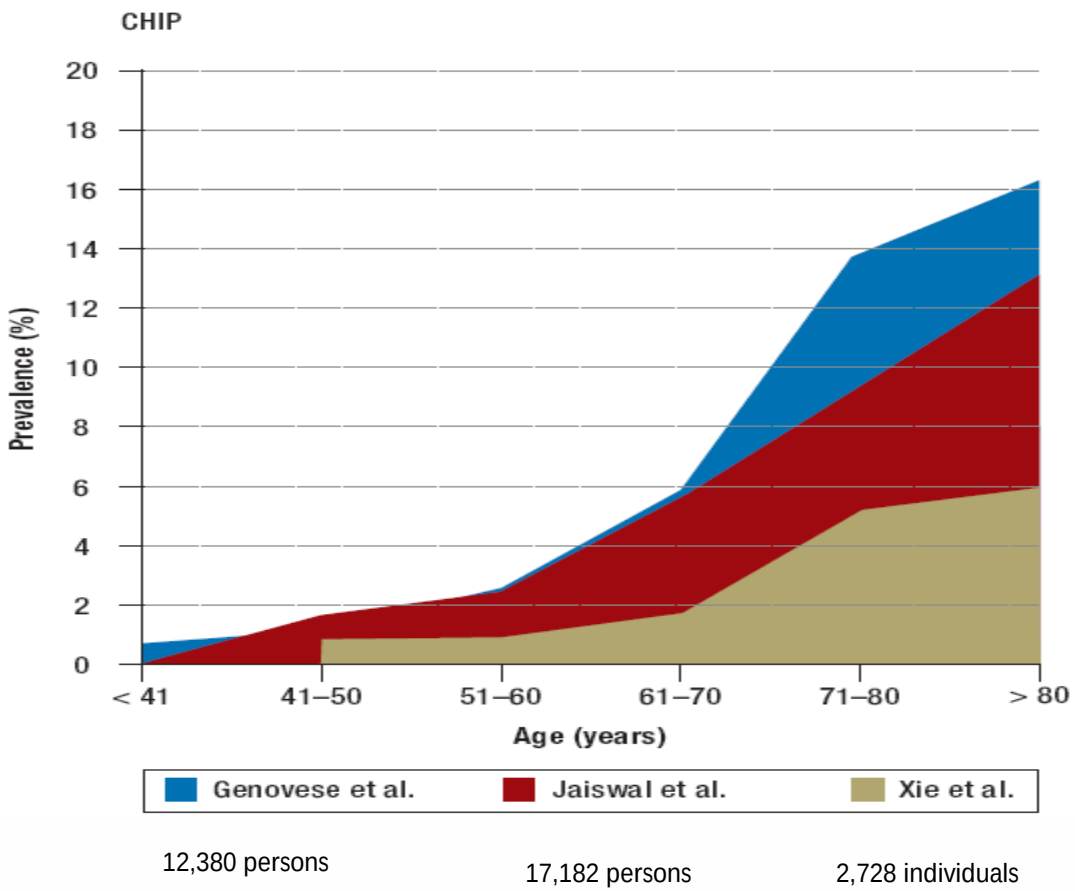
Lichtman MA. Clonal hematopoiesis: a “CHIP” off the old block Blood 2015; 126:1-2
Steensma DP. Clonal hematopoiesis of indeterminate potential and its distinction from myelodysplastic syndromes. Blood. 2015;126:9-16.

Mielodisplasia



Steensma DP. Blood. 2015;126:9-16.

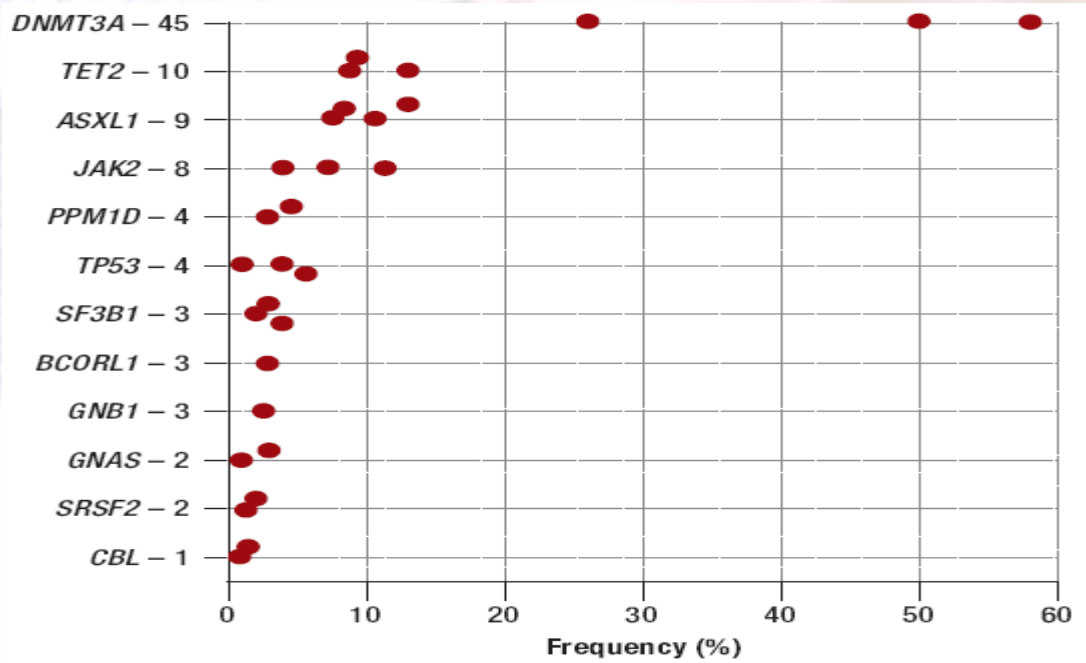
Mielodisplasia



12,380 persons

17,182 persons

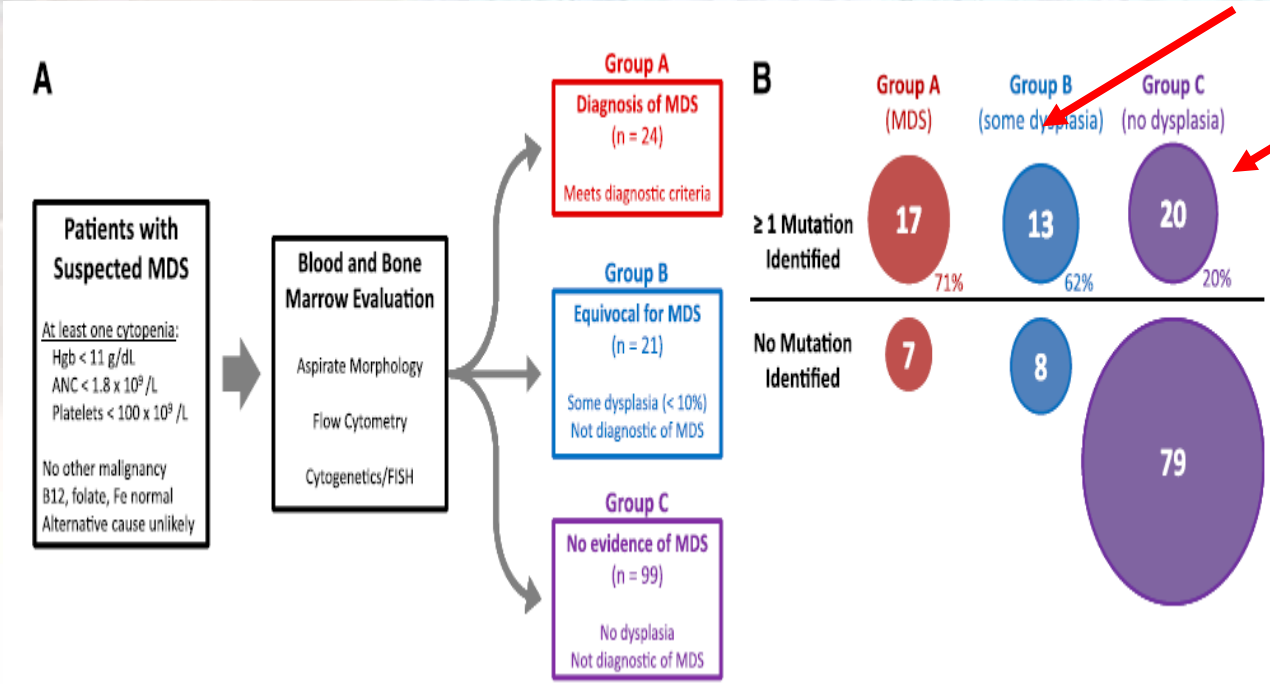
2,728 individuals



CHIP (Clonal hematopoiesis of indeterminate potential) es un fenómeno edad-dependiente y se asocia con hemopatías malignas. Ratio de transformación 0.5% a 1% por año (similar a GMSI y LBM)

Heuser M. Clonal hematopoiesis of indeterminate potential—a risk factor for hematological neoplasia. Dtsch Arztebl Int 2016; 113: 317–22.

Mielodisplasia



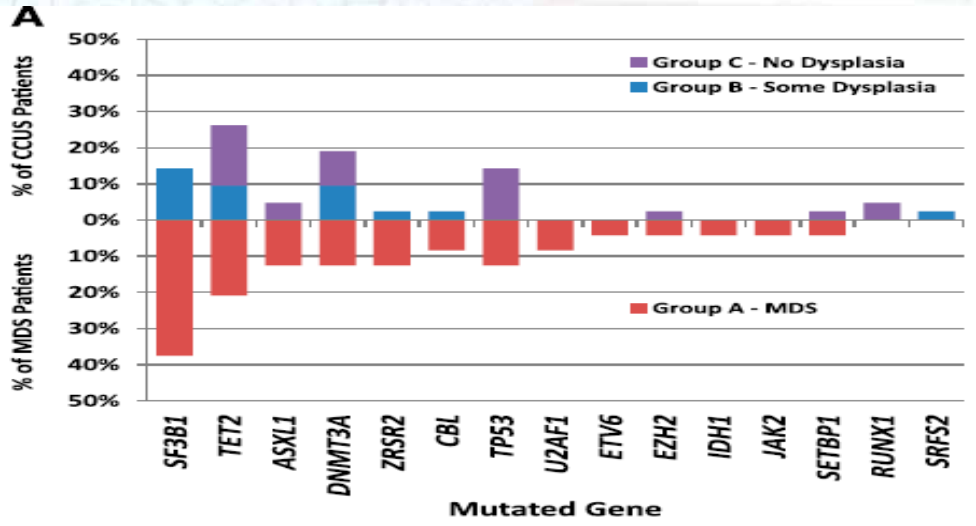


Table 1. Clinical measures by mutation status for both cohorts

	MDS	CCUS	Nonclonal ICUS	*P*
Group size, N	115	136	233	
Male:female ratio	1.0	1.65	0.68	.0003
Age, mean (SD), y	74.3 (10.4)	75.1 (12.5)	66.6 (13.6)	<.0001*
Hgb, mean (SD), g/dL	9.8 (1.8)	10.7 (1.8)	11.1 (2.0)	<.0001†
ANC, mean (SD), $\times 10^9$/L	3.2 (2.1)	3.5 (2.3)	3.4 (2.4)	.71
Platelets, mean (SD), $\times 10^9$/L	184 (110)	164 (104)	179 (101)	.27

ANC, absolute neutrophil count; SD, standard deviation.
*No difference between MDS and CCUS (*P* = .87).
†No difference between CCUS and ICUS (*P* = .21).

144 pacientes con citopenias no explicadadas.

17% con SMD
15% con ICUS y displasia
69% con ICUS sin displasia (20% mutaciones).

ICUS: Idiopathic cytopenia of undetermined sugnificance

Kwok B. Blood. 2015;126:2355-2361)

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Mielodisplasia

Definition of CHIP (modified from Steensma et al. 10)

- **A** No evidence of morphologic criteria for any hematologic neoplasm; especially, no dysplasia or blast increase (DD: MDS and AML)
- **B** PNH, MGUS, and MBL ruled out
- **C** Evidence of a somatic mutation that is associated with a hematologic neoplasm and has an allele frequency of at least 2% (= evidence of clonality)
- **D** Cytopenia in peripheral blood may be present but is not part of the definition of CHIP (DD: ICUS and MDS).
- **E** Annual risk of progression to hematologic neoplasm 0.5% to 1%

AML, acute myeloid leukemia; CHIP, clonal hematopoiesis of indeterminate potential; DD, differential diagnosis; ICUS, idiopathic cytopenia of indeterminate significance; MBL, monoclonal B-lymphocytosis; MDS, myelodysplastic syndrome; MGUS, monoclonal gammopathy of undetermined significance; PNH, paroxysmal nocturnal hemoglobinuria

IDUS: idiopathic dysplasia of undetermined significance
CCUS: Clonal cytopenia of undetermined significance.
ICUS: Idiopathic cytopenia of undetermined sugnificance.

Heuser M, Thol F, Ganser A: Clonal hematopoiesis of indeterminate potential—a risk factor for hematological neoplasia. Dtsch Arztebl Int 2016; 113: 317–22.
Malcovati L, Cazzola M. The shadowlands of MDS: idiopathic cytopenias of undetermined significance (ICUS) and clonal hematopoiesis of indeterminate potential (CHIP).Hematology Am Soc Hematol Educ Program. 2015;299-307.

Manejo terapéutico de la anemia en personas mayores

- Depende de las comorbilidades.
- Las personas mayores sanas no tiene porque presentar anemia, pero si niveles próximos al límite inferior de la normalidad.
- Es muy frecuente que sea de etiología mixta.
- Tratamiento etiológico, en su defecto fisiopatológico.

Anemia inexplicada de las personas mayores (características mixtas IR y ATC).

No siempre precisa tratamiento.

Con Hb < 11 considerarlo, Hb < 10 empeoran la morbi-mortalidad (aprox 5-10% de las anemias).

Opciones terapéuticas:

-Fe iv (pocos estudios, uso juicioso para evitar efectos secundarios), en contexto de AEE.
-AEE objetivo Hb entre 11 y 12 g/dl, evitar variaciones bruscas de la Hb, control de la TA.
-Transfusiones.
-Otras opciones en estudio (inhibición hepcidina).

Goodnough LT, Schrier SL. Evaluation and management of anemia in the elderly. Am J Hematol 2014; 89: 88–96.

Conclusión

Las anemias más frecuentes en los ancianos
ATC, AF, IRC.
Anemia de causa inexplicable de los ancianos (10-40%)

Predisposición a algunos tipos de anemia:
SMD.
No predisposición, pero características especiales:
Anemia ferropénica
Anemias más prevalentes en los ancianos.
ATC, Anemia por insuf renal, def B12/folato.

La etiología depende del lugar de procedencia
Hospitales: anemia por sangrado agudo (cirugía o traumatismo).