DIAGNOSTICO DIFERENCIAL Y MANEJO DE ERITROCITOSIS

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OBJETIVOS

- Conocer las causas principales de eritrocitosis / policitemia
- Conocer los principales elementos de ayuda diagnostica de eritrocitosis / policitemia
- Proponer un algoritmo diagnostico de eritrocitosis / policitemia
- Describir las opciones terapeuticas de eritrocitosis / policitemia

DEFINICION

- Eritrocitosis
  - Hto > 48% (mujer) o >52% (varón)
  - Hb > 16.5 g/dl (mujer) o >18.5 g/dl (varón)

- Incremento de masa eritrocitaria
  - Relativa: disminución de plasma
  - Verdadera: incremento de masa eritrocitaria

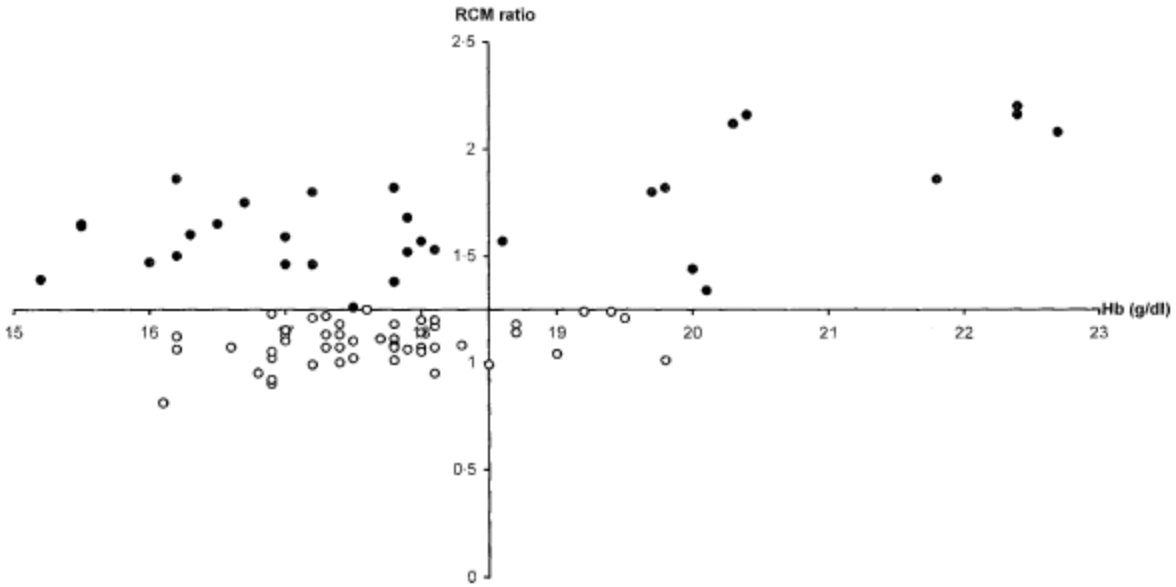


Fig 1. The relationship between haemoglobin (Hb) and the measured/predicted red cell mass (RCM) in 31 male polycythaemia vera (PV; ●) and 49 male apparent polycythaemia (AP; ○) patients. The abcissa (*x*-axis) intersects the ordinata (*y*-axis) at 1·25. The ordinata intersects the abcissa at 18·5 g/dl.

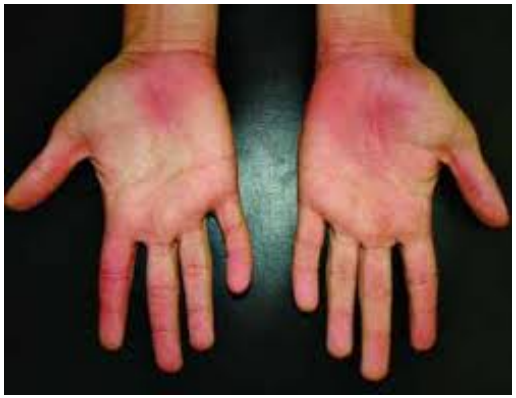
Un Hto > 60% siempre estará relacionado con eritrocitosis verdadera sean varones o mujeres.

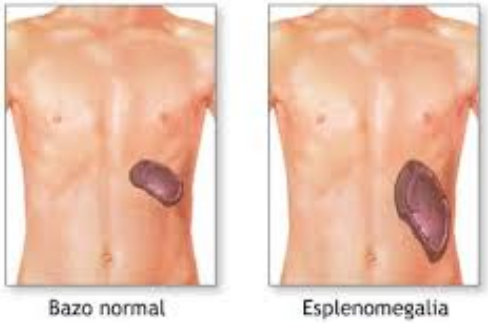
Johansson P. BJH. 2005; 129: 701-705

ANTECEDENTES

Mc Mullin M. Guidelines for the diagnosis, investigation and management of policytemia/erithrocytosis. BJH 2005
Keohane C. The diagnosis and management of erithrocytosis. BMJ. 2013

MANIFESTACIONES CLINICAS





Mc Mullin M. Guidelines for the diagnosis, investigation and management of policytemia/erithrocytosis. BJH 2005
Keohane C. The diagnosis and management of erithrocytosis. BMJ. 2013

AJUSTE SEGUN ALTURA

Nivel alustado = Nivel observado - Ajuste por altura

Ajuste por altura = $0{,}022 \times (alt)^2 - 0{,}032\ (alt)$

Donde (alt) = [(altura en metros)/1000] x 3,3

AJUSTE SEGUN ALTURA

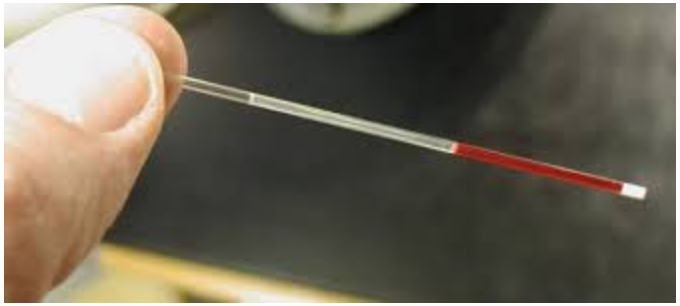
Tabla Nº 10

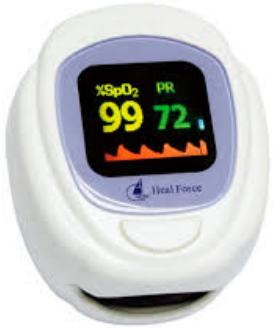
INCREMENTO DE HEMOGLOBINA Y HEMATOCRITO SEGÚN ALTITUD

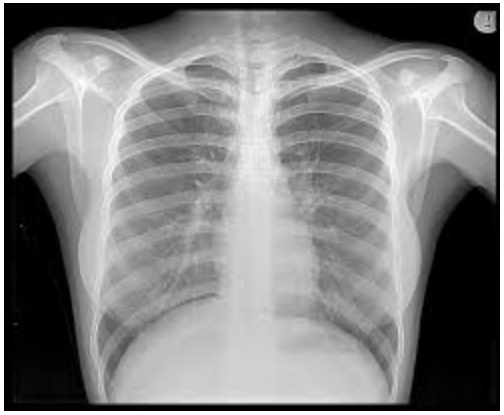
Altitud	Factor de Corrección Hemoglobina (g/100ml)	Factor de Corrección Hematocrito (%)
Menor a 1 000	0	0
1 000	0,2	0,5
1 500	0,5	1,5
2 000	0,8	2,5
2 500	1,3	4,0
3 000	1,9	6,0
3 500	2,7	8,5
4 000	3,5	11,0
4 500	4,5	14,0

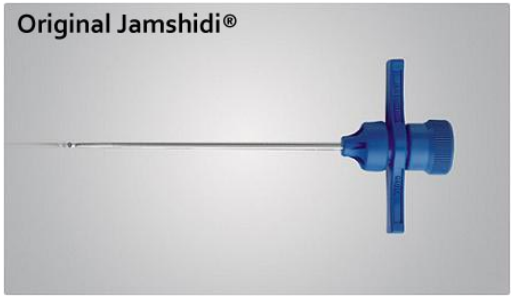
FUENTE: *INS. Manual de Procedimiento de Laboratorio, 1997.*

AYUDA DIAGNOSTICA









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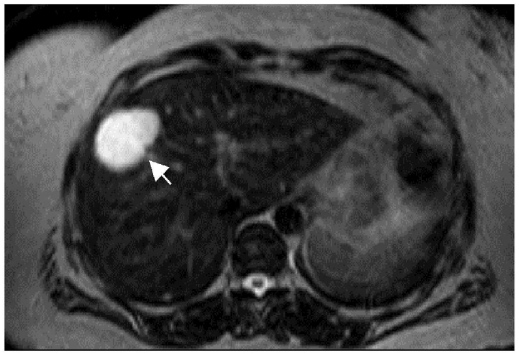
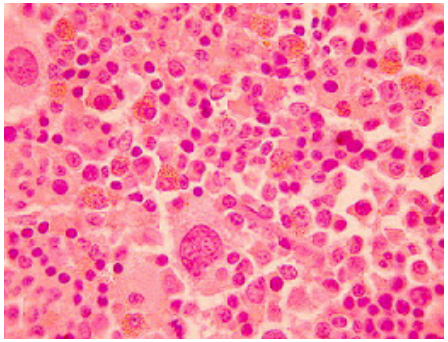
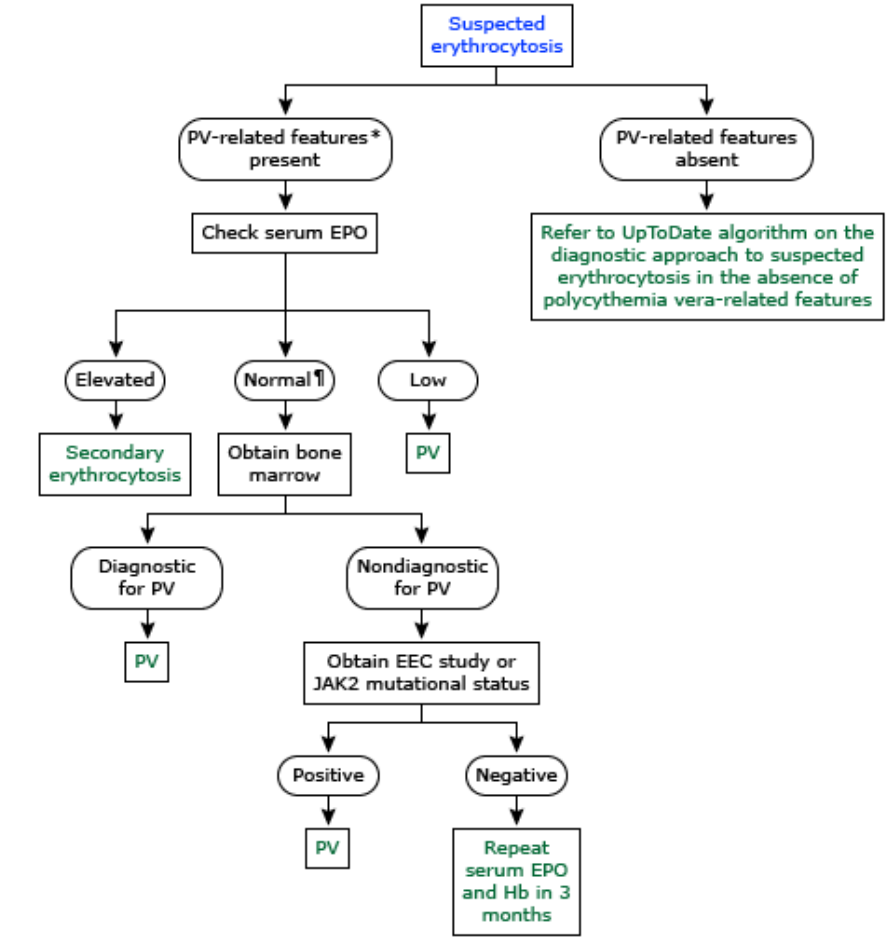
Major causes of erythrocytosis (polycythemia)

Autonomous (inappropriate) increase of Epo - inappropriately high serum Epo
Erythropoietin-producing neoplasms (most common)
Renal cell carcinoma
Hepatocellular carcinoma
Cerebellar hemangioblastoma
Pheochromocytoma
Uterine fibroids
Erythropoietin-producing renal lesions (eg, cysts, hydronephrosis, renal artery stenosis, distal renal tubular acidosis [rare])
Following renal transplantation (some cases are independent of erythropoietin)
Appropriate increases in erythropoietin - appropriately high serum erythropoietin
Hypoxemia secondary to:
Chronic pulmonary disease
Right-to-left cardiac shunts
Sleep apnea
Massive obesity (Pickwickian syndrome)
High altitude
Red cell defects
Some cases of congenital methemoglobinemia
Chronic carbon monoxide poisoning (including heavy smoking)
Cobalt
Germline and somatic mutational causes of polycythemia
Polycythemia vera (JAK2 mutation)
Activating mutations of the erythropoietin receptor (EPOR gene)
Chuvash polycythemia (VHL gene mutation)
Congenital methemoglobinemia
Idiopathic familial polycythemia
High oxygen affinity hemoglobins
2,3 bisphosphoglycerate (BPG) mutase deficiency
Other rare gene mutations (eg, PHD2, HIF2-alpha)
Miscellaneous causes
Use of androgens or anabolic steroids
Diuretics (reduced plasma volume rather than erythrocytosis)
Blood doping in athletes (ie, autologous blood transfusion)
Self-injection of erythropoietin
POEMS syndrome





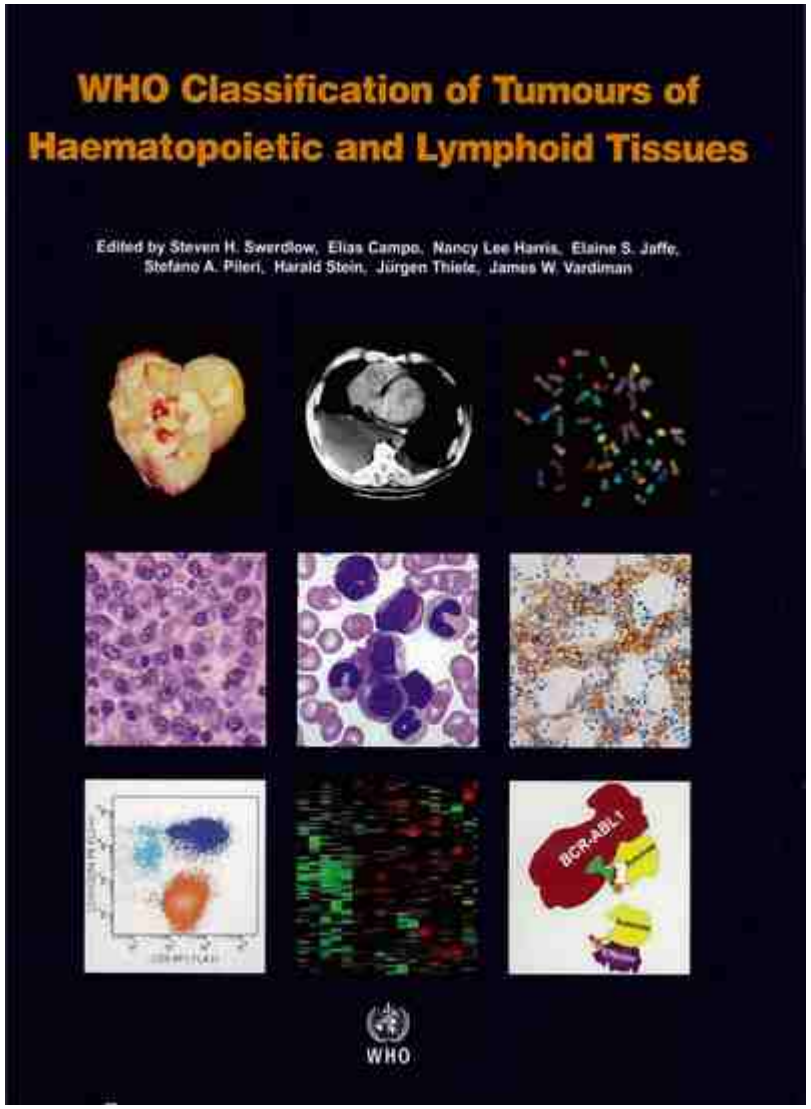
Diagnostic approach to suspected erythrocytosis in the presence of polycythemia vera-related features



Clinica sospechosa

- Hto elevado sin hipoxia
- Esplenomegalia
- Trombocitosis
- leucocitosis

Tefferi A. Diagnosis aproach to the patientwith policythemia. UpToDate. 2015



CRITERIO MAYOR

Hemoglobina > 18.5 g/dl (varones), 16.5 g/dl (mujeres)

Presencia de JAK2 617V>F u otra mutación funcional (ej. JAK2 exon 12)

CRITERIO MENOR

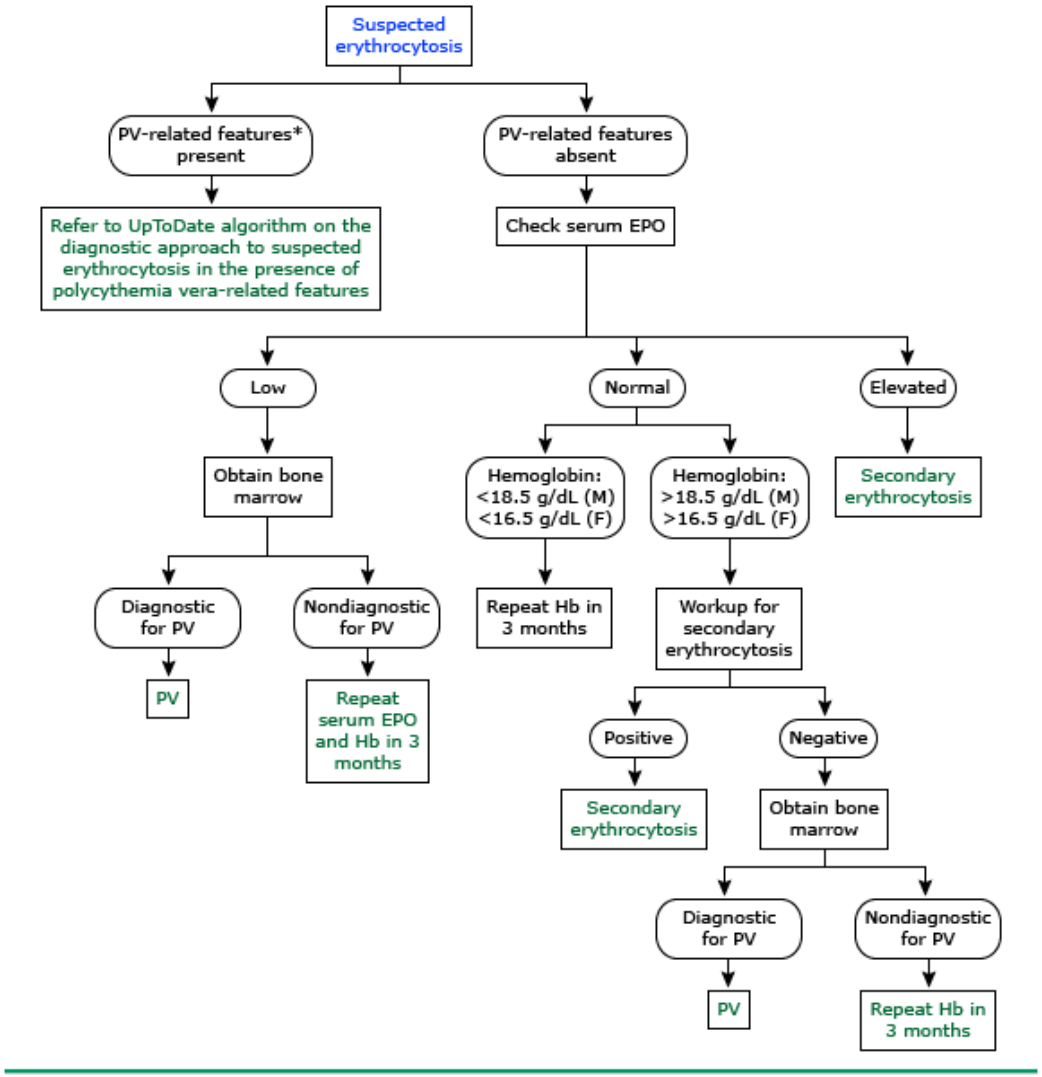
Biopsia de médula ósea que muestra hipercelularidad para la edad con crecimiento lineal (panmielosis) eritroide, granulocítico y megacariocítico

Nivel de eritropoyetina sérica debajo del rango normal referencial

Formación endógena de colonias eritroides in vitro

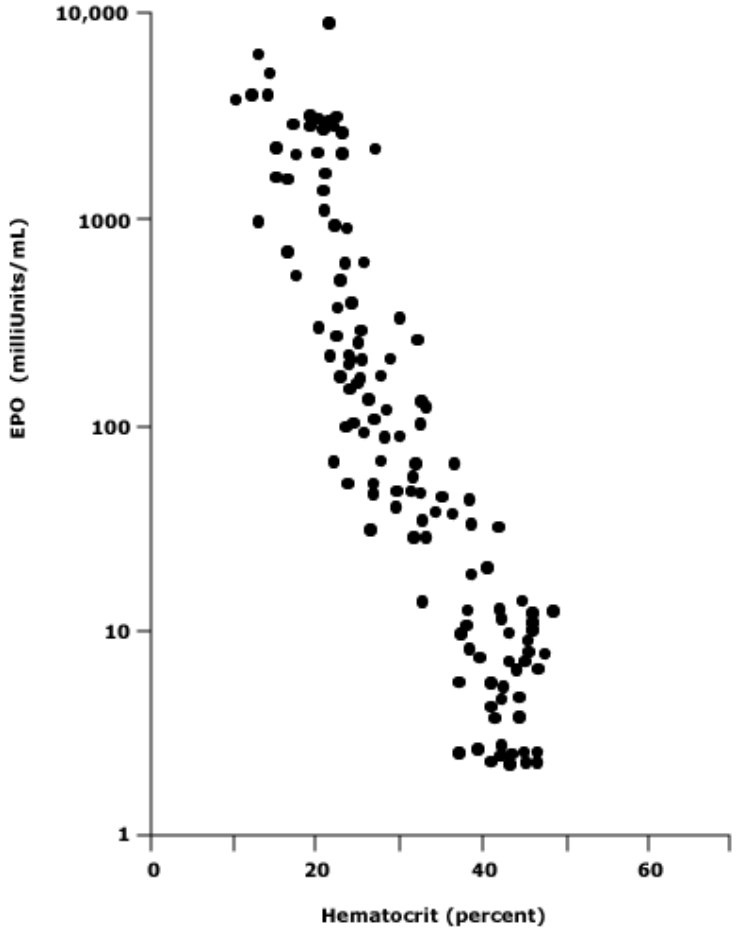
Diagnóstico requiere la presencia de ambos criterios mayores y un criterio menor o la presencia del primer criterio mayor junto a dos criterios menores

Diagnostic approach to suspected erythrocytosis in the absence of polycythemia vera-related features



Tefferi A. Diagnosis aproach to the patientwith policythemia. UpToDate. 2015

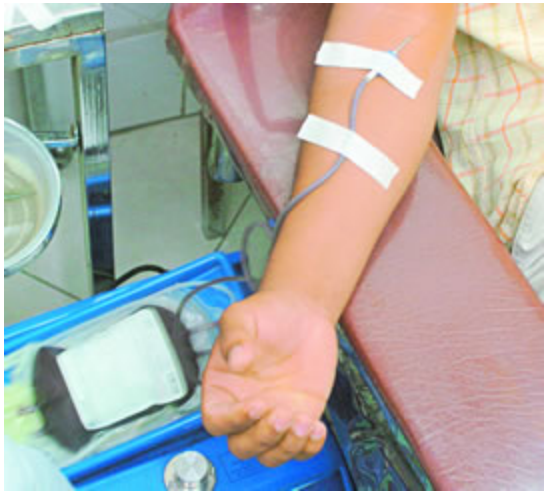
Serum erythropoietin levels in anemia



This graph indicates the exponential relationship between serum erythropoietin levels (EPO, milliUnits/mL, logarithmic scale) and venous hematocrit (percent, linear scale) in normal and anemic subjects without renal or chronic diseases. EPO was assayed by either bioassay or radioimmunoassay.

Data from: Erslev AJ, Wilson J, Caro J. Erythropoietin titers in anemic, nonuremic patients. J Lab Clin Med 1987; 109:429.

TRATAMIENTO



HTO
>
54%

Los pacientes con niveles de Hto > 50% tienen 2.4 veces (95% CI 1.6 - 3.5) riesgo de presentar un evento cardio-vascular fatal.

Mc Mullin M. BJH 2005. 130:174-195
Kunnas T. Preventive Medicine, 2009. 49(1):45-47

TRATAMIENTO

La tasa de mortalidad disminuye en 25% en aquellos pacientes con EPOC y terapia con oxigeno.

Stuart-Harris C. Lancet, 1981. 317:681-6

TRATAMIENTO

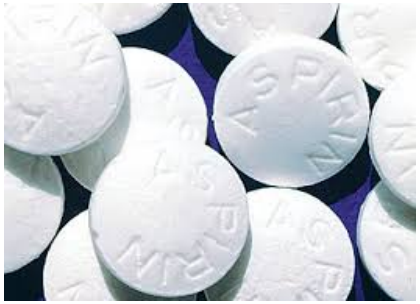
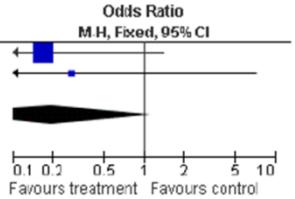


Figure 1. Forest plot of comparison: 1 Polycythaemia vera, outcome: 1.1 Mortality for thrombotic events.

Study or Subgroup	Aspirin Events	Aspirin Total	Placebo Events	Placebo Total	Weight	Odds Ratio M-H, Fixed, 95% CI
ECLAP 2004	1	253	6	265	78.6%	0.17 [0.02, 1.43]
GISP 1997	0	60	1	52	21.4%	0.28 [0.01, 7.12]
Total (95% CI)		**313**		**317**	**100.0%**	**0.20 [0.03, 1.14]**
Total events	1		7			

Heterogeneity: Chi² = 0.07, df = 1 (P = 0.80); I² = 0%
Test for overall effect: Z = 1.81 (P = 0.07)



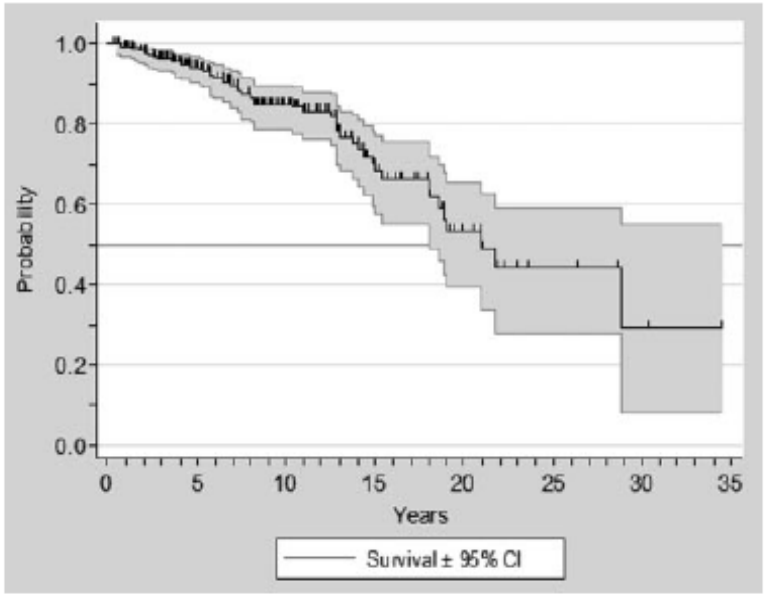


Figure 1. Overall survival from diagnosis in 261 patients with PV treated with HU.

Squizzato A. Cochrane Database Syst Rev 2011
Alvarez-Larrán A. Blood 2012.

REFENCIAS

- Mc Mullin M. Guidelines for the diagnosis, investigation and management of policytemia/erithrocytosis. BJH 2005. 130:174-195
- Keohane C. The diagnosis and management of erithrocytosis. BMJ. 2013; 347: f6667
- McMullin M. The clasiffication and diagnosis of erythrocytosis. Int J Lab Hemat. 2008; 30:447-459
- Tefferi A. Diagnosis aproach to the patientwith policythemia. UpToDate. 2015.
- Ferrant A. What clinical and laboratory data are indicative of polycythemia and when are blood volume studies needed? Nouv Rev Fr Hematol. 1994;36:151-154
- Johansson P. An elevated venous haemoglobin concentration cannot be used as a surrogate marker for absolute erythrocytosis: a study of patients with polycythaemia vera and apparent polycythaemia. BJH. 2005; 129: 701-705
- Mossuz P. Diagnostic value of serum erythropoietin level in patients with absolute erythrocytosis. Haematologica. 2004;89:1194-1198
- Silver R. Evaluation of WHO criteria for diagnosis of polycythemia vera: a prospective analysis. Blood. 2013; 122:1881-1886