

Trombofilias hereditarias y riesgo de recurrencia de la ETV

Factor V Leiden y PT20210A



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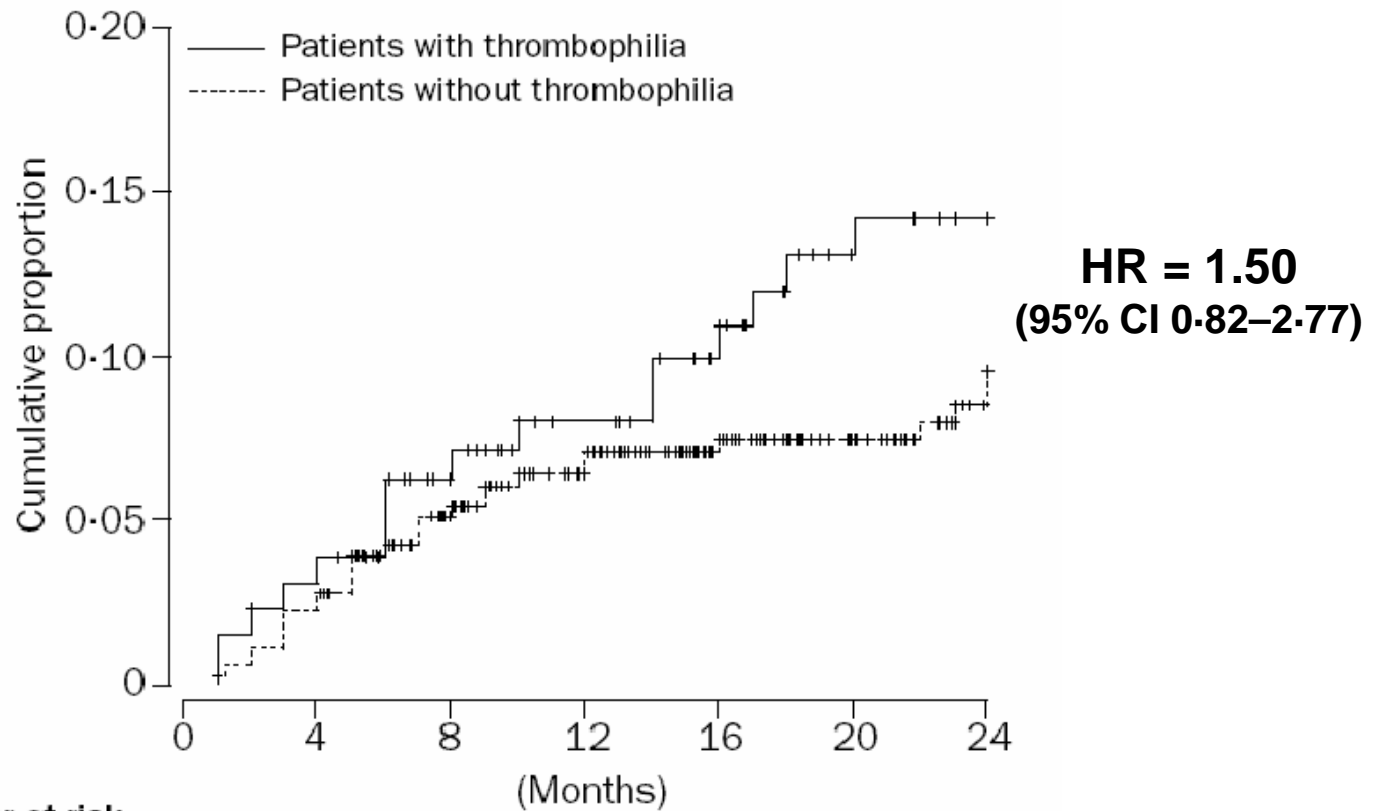


¿Cuándo investigar trombofilias?

- ¿Para qué saber la causa de la ETV?
- El estudio de trombofilia se justifica si el resultado va a influir en la conducta del paciente y/o familiares.
- ¿Es posible valorar el riesgo de recurrencia investigando la trombofilia hereditaria?

Cambridge Venous Thromboembolism Study

(E. prospectivo, 570 pacientes, sin cancer o SAF, seg. 2 años)



Testar para trombofilia no preve el riesgo de recurrencia

Leiden Thrombophilia Study (LETS)

(E. prospectivo, 474 pacientes, 18-70 años, sin cancer, seg. 7.3 años)

Table 4. Recurrence Rates for Prothrombotic Laboratory Abnormalities in 474 Patients

| Abnormality | No. of Recurrences | Incidence Rate (95% CI)* | Hazard Ratio (95% CI)† | Hazard Ratio (95% CI)‡ |
|---------------------------|--------------------|--------------------------|------------------------|------------------------|
| Factor V Leiden | 20 | 30 (18-46) | 1.2 (0.7-1.9) | 1.3 (0.8-2.1) |
| Prothrombin G20210A | 4 | 19 (5-48) | 0.7 (0.3-2.0) | 0.7 (0.3-2.0) |
| Anticoagulant deficiency§ | 8 | 45 (19-88) | 1.8 (0.9-3.7) | 1.8 (0.9-3.8) |

Mayor riesgo de recurrencia:

- En los primeros 2 años
- 2.7 x mayor en **hombres**
- 1.9 x mayor se 1º evento **idiopatico**
- 1.8 x mayor se **deficiencias de AT, PC e PS**
- **FV Leiden e PT 20210A** presentan pequeño riesgo

Factores clínicos son más importantes que los laboratoriales para determinar la duración del tratamiento

Is Thrombophilia Testing Useful?

Review

Table 1. Prevalence of thrombophilia and relative risk estimates for various clinical manifestations

| | Antithrombin deficiency | Protein C deficiency | Protein S deficiency | Factor V Leiden | Prothrombin 20210A mutation | Lupus anticoagulant* | Anti-cardiolipin antibodies* | Anti-β2 GPI antibodies |
|---|-------------------------|----------------------|----------------------|-----------------|-----------------------------|----------------------|------------------------------|------------------------|
| Prevalence in the general population | 0.02% | 0.2% | 0.03%-0.13% | 3-7% | 0.7%-4% | 1%-8 % | 5 | 3.4 |
| Relative risk for a first venous thrombosis | 5-10 | 4-6.5 | 1-10 | 3-5 | 2-3 | 3-10 | 0.7 | 2.4 |
| Relative risk for recurrent venous thrombosis | 1.9-2.6 | 1.4-1.8 | 1.0-1.4 | 1.4 | 1.4 | 2-6 | 1-6 | |

Pacientes con ETV y trombofilia tienen un ligero aumento en el riesgo de recurrencia.

Son todavía necesarios estudios comparando el tratamiento de rutina con tratamiento más prolongado.

RIETE

Tasa de recurrencia de los pacientes
con FV Leiden, PT 20210A

Hospitales con seguimiento > 1 año
1.676 pacientes

Tasa de recurrencia durante el tratamiento

| | Negative thrombophilia | Factor V Leiden heterozygous | PT 20 210 A heterozygous |
|--|-------------------------|------------------------------|--------------------------|
| Patients, N | 1,112 | 154 | 136 |
| Length of anticoagulation (months) | 11.4±11.5 | 18±21[‡] | 16±17[‡] |
| Median | 8.0 | 11.8 | 10.8 |
| % recurrence rate / 100 patients year | | | |
| DVT recurrences | 1.70 (1.04-2.64) | 0.42 (0.21-2.09) | 1.12 (0.19-3.71) |
| PE recurrences | 0.85 (0.41-1.56) | 0.85 (0.14-2.79) | 0 |
| VTE recurrences | 2.55 (1.72-3.66) | 1.27 (0.32-3.45) | 1.12 (0.19-3.71) |

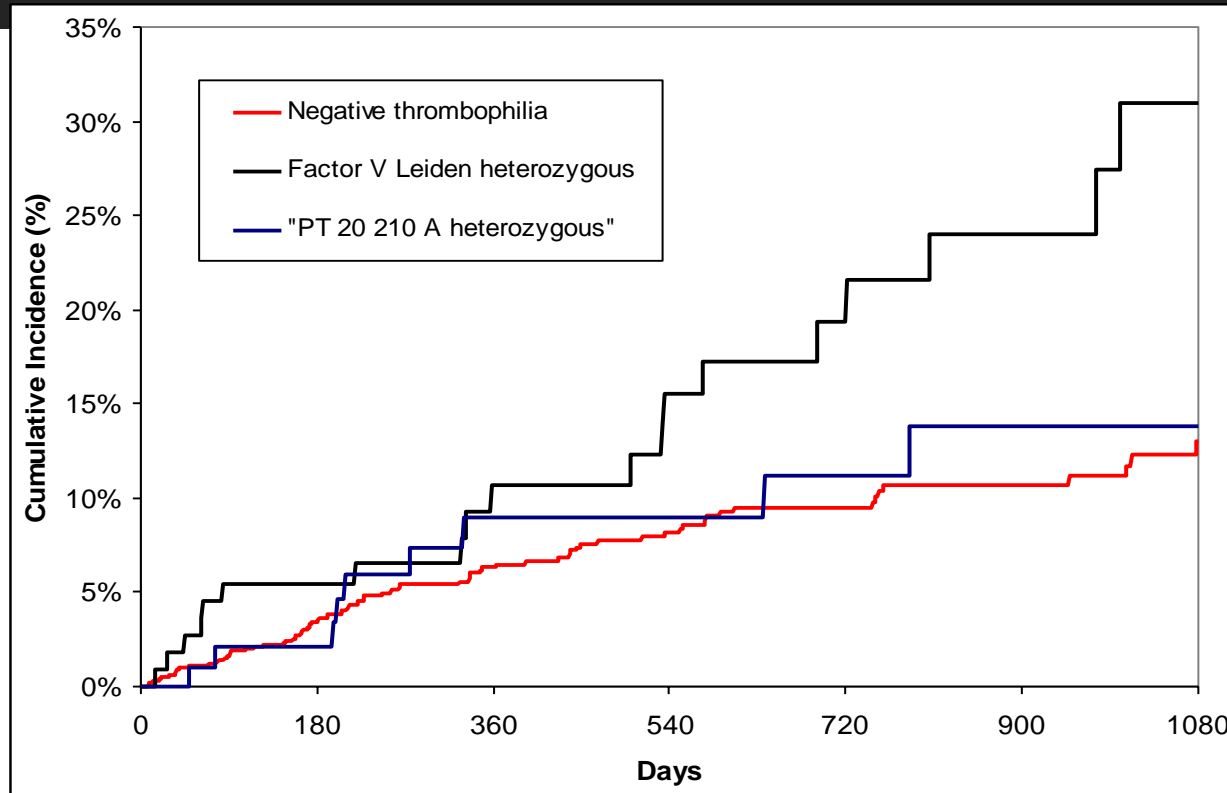
Tras discontinuación del tratamiento anticoagulante

| | Negative thrombophilia | Factor V Leiden heterozygous | PT 20 210 A heterozygous |
|--|-------------------------------|-------------------------------------|---------------------------------|
| Patients, N | 993 | 114 | 99 |
| Follow-up (months) | 21±18 | 22±21 | 24±25 |
| Median | 16.4 | 16.3 | 14.9 |
| % recurrence rate / 100 patients year | | | |
| DVT recurrences | 3.31 (2.51-4.30) | 7.21 (4.19-11.6) | 3.03 (1.23-6.31) |
| PE recurrences | 1.69 (1.14-2.42) | 2.41 (0.88-5.33) | 2.02 (0.64-4.88) |
| VTE recurrences | 4.97 (3.96-6.15) | 10.1 (6.36-15.4) | 5.12 (2.60-9.12) |

Tras discontinuación del tratamiento anticoagulante

| | Number of recurrences | % recurrence rate/100 patients year (95% CI) | Hazard Ratio (95% CI) | P-Value |
|-------------------------------|-----------------------|--|-----------------------|---------|
| Negative Thrombophilia (Ref.) | 80 | 4.97 (3.96-6.15) (Reference) | 1 (Ref.) | - |
| Factor V Leiden heterozygous | 20 | 10.1 (6.36-15.4) | 2.11 (1.29-3.44) | 0.003 |
| PT 20 210 A heterozygous | 10 | 5.12 (2.60-9.12) | 1.14 (0.59-2.20) | 0.705 |

Tras discontinuación del tratamiento



| Recurrent VTE | Days | | | | | | |
|-------------------------------------|------|---------------|---------------|---------------|---------------|---------------|---------------|
| | 0 | 180 | 360 | 540 | 720 | 900 | 1080 |
| <i>Negative thrombophilia</i> | 0 | 30 (3.42%) | 51 (6.34%) | 61 (8.17%) | 67 (9.49%) | 71 (10.7%) | 75 (13.0%) |
| <i>Factor V Leiden Heterozygous</i> | 0 | 6 (5.46%) | 10 (10.7%) | 13 (15.5%) | 15 (19.4%) | 17 (24.0%) | 19 (30.9%) |
| <i>PT 20 210 A heterozygous</i> | 0 | 2 (2.13%) | 7 (8.94%) | 7 (8.94%) | 8 (11.2%) | 9 (13.8%) | 9 (13.8%) |

Factores de riesgo y recurrencia tras discontinuación del tratamiento anticoagulante

| | Patients with recurrences | Patients with no recurrences | Hazard ratio (95% CI) | P-Value |
|-------------------|---------------------------|------------------------------|-----------------------|---------|
| Surgery | 15 (13%) | 153(15%) | 0.85 (0.49-1.47) | 0.562 |
| Immobility | 19 (17%) | 212 (20%) | 0.81 (0.50-1.33) | 0.415 |
| Cancer | 12 (11%) | 112 (11%) | 1.03 (0.57-1.88) | 0.915 |
| Long term travel | 5 (4.5%) | 41 (4%) | 1.14 (0.47-2.8) | 0.771 |
| Estrogens | 6 (5.4%) | 145 (14%) | 0.33 (0.14-0.74) | 0.008 |
| Pregnancy | 1 (0.9%) | 32 (3.1%) | 0.28 (0.04-1.99) | 0.202 |
| None of the above | 65 (58%) | 437(42%) | 1.97 (1.35-2.87) | <0.001 |

Multivariate analysis. Cox regression for recurrent VTE after discontinuing anticoagulation

| | HR (95% IC) | p-value |
|--|-------------------------|------------------|
| Thrombophilia testing, | | 0.039 |
| Negative | 1 (ref.) | |
| Factor V Leiden | 2.02 (1.23-3.30) | 0.005 |
| PT 20 210 A | 1.23 (0.63-2.37) | 0.547 |
| <i>Risk factors for the index VTE</i> | | |
| Idiopathic | 1 (ref.) | |
| Transient risk factors | 0.47 (0.31-0.70) | <0.001 |
| Cancer | 0.77 (0.41-1.43) | 0.403 |
| <i>Initial therapy,</i> | | |
| LMWH | 2.73 (1.00-7.43) | 0.049 |

Comparison between patients with negative thrombophilia vs. other: *p <0.05 ; †p <0.01; ‡p <0.001.

FV Leiden - ¿más riesgo de recurrencia?

¿Necesidad de anticoagulación más larga?

PT 20210A - no presentan mayor riesgo de recurrencia

¿Seguimiento más largo antes de sacar conclusiones?



Gracias!