Desayunos con Expertos

MEET THE EXPERT BREAKFAST SESSION

Problemas prácticos en el laboratorio de Trombofilia

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GRUPO CAHT

Why thrombophilia testing in patients with a history of VTE?

- To allow prediction of recurrent VTE in order to
  - guide future treatment
    - to prevent recurrence of VTE and treatment associated bleeding
    - Prevent death (from VTE or bleeding)
- To identify persons (relatives) at risk of primary manifestation of VTE in order to prevent VTE

Risk of recurrent VTE

Prospective follow up of patients from the Leiden Thrombophilia Study

	HR (95%CI)
Men vs women	2.7 (1.8-4.2)
Idiopathic vs. triggered	1.9 (1.2-2.9)
Inhibitor deficiency yes vs no	1.8 (0.9-3.8)
Factor V Leiden yes vs no	1.3 (0.3-2.0)

Christiansen et al, 2005, JAMA,293:1489

Recurrence in patients with natural inhibitor deficiency compared to patients without thrombophilia

Publication	Study design	Patient number	HR
Prandoni, 2007	Prospective cohort	37/undefined	Not increased
Christiansen, 2005	Prospective cohort	25/474	all:1.8
De Stefano, 2006	Prospective cohort	64/602	AT-def: 1.9 PC/PS-def 1.4

Does thrombophilia testing decrease the recurrence rate?

- 21% recurrence in tested and non-tested individuals

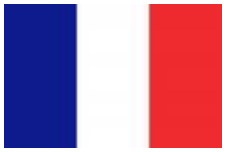
  Prandoni et al, Haematologica 2007, 92:199

- OR 1.2 for recurrence in tested versus non-tested individuals (patients from the MEGA study)

  Coppens et al, JTH 2008, 6:1747

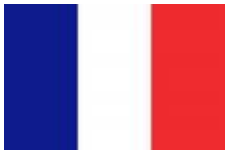
Guidelines for testing for heritable thrombophilia in patients with a history of VTE

No thrombophilia testing in unselected patients



Baglin et al, BJH 2010

- Testing suggested in selected patients with a strong family history (Grade C)

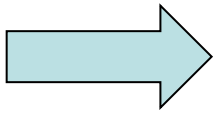


Pernod et al, JMV 2009 34:156

- In patients with a first unprovoked VTE before 60 years of age testing is recommended (Grade C), specific aim on inhibitor deficiency and homozygous forms

Summary/Conclusions

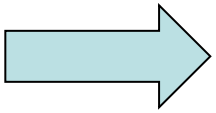
- Thrombophilia testing has not been shown to decrease rate of recurrence in prospective observational studies
- Heterozygous Factor V Leiden is a minor risk factor for recurrence (inferior to clinically defined risk factors)
- Probably patients with antithrombin deficiency and possibly those with protein C/S deficiency have a higher recurrence rate.



Presently there is no evidence to perform screening for hereditary thrombophilia in order to define duration of anticoagulation

Why I still think thrombophilia testing should be performed in selected cases

- There are certain hereditary defects with very strong predisposition for thrombosis, which would alter treatment strategies
  - e.g. individuals with homozygous inhibitor deficiency – very rare, replacement to be suggested
- Certain types of thrombophilia lead to a high risk of hormone- and pregnancy associated VTE (antithrombin deficiency, homozygous factor V Leiden)
- Families with a strong familiy history of thrombosis exist. Thrombophilia testing might alter individual counseling and recommendations for prophylaxis



In selected cases diagnosis of thrombophilia has an impact on the clinical management

Points to discuss

Which tests must be included in the thromphilia screening

- Patients selection
- Type of thrombosis
- Costs of laboratory studies
- Polimorphisms, SNPs?

Points to discuss

Methodological aspects

•Blood drawing, time and conditions of the patients to take into account

•Sample storage

•Laboratory tests to use, different aspects

•New test? Global Test?

•Quality controls of the laboratory tests to minimize inter assay and

interlaboratory variations

Points to discuss

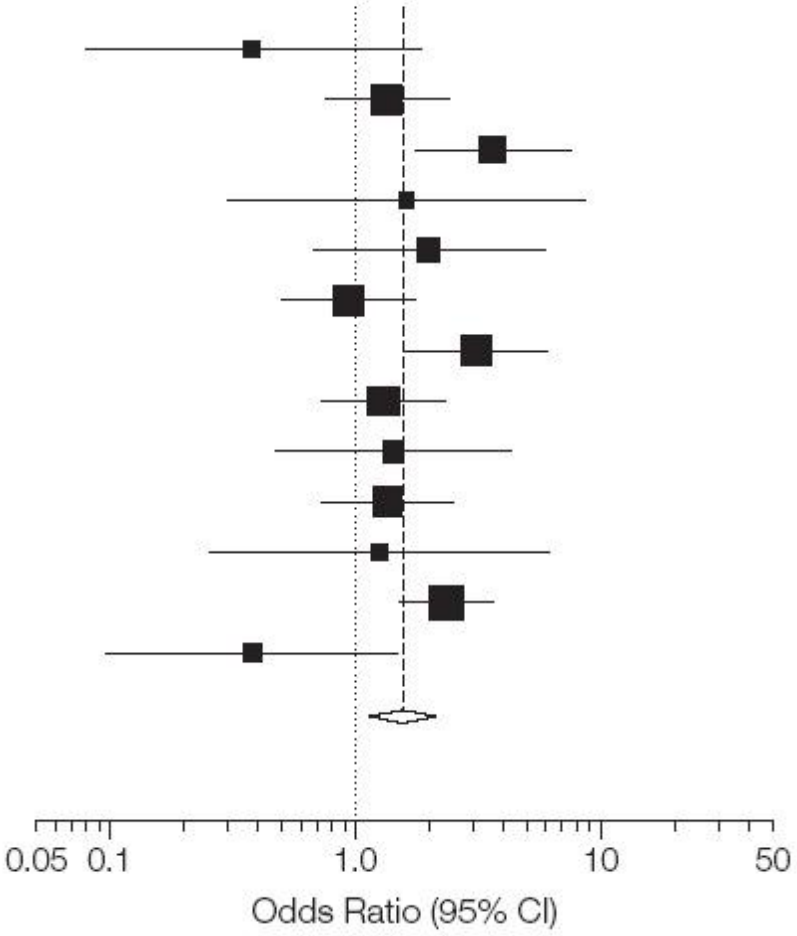
- Interpretation of results
- Clinical impact: usefulness as recurrence predictors
- Psychological consequences of a positive results
- Family studies?

Predictive value of heterozygous factor V Leiden for recurrent VTE

A Probands heterozygous for factor V Leiden mutation

Source	Odds Ratio (95% CI)
Kearon et al,[23] 1999	0.38 (0.08-1.87)
Lindmarker et al,[14] 1999	1.35 (0.75-2.43)
Simioni et al,[15] 2000	3.62 (1.74-7.53)
Høibraaten et al,[20] 2001	1.61 (0.30-8.62)
Miles et al,[25] 2001	1.99 (0.67-5.90)
Eichinger et al,[18] 2002	0.94 (0.50-1.76)
Palareti et al,[17] 2003	3.12 (1.61-6.04)
Christiansen et al,[13] 2005	1.30 (0.73-2.31)
González-Porras et al,[19] 2006	1.43 (0.48-4.29)
Wåhlander et al,[22] 2006[a]	1.36 (0.73-2.51)
Wåhlander et al,[22] 2006[b]	1.26 (0.26-6.14)
Prandoni et al,[21] 2007	2.33 (1.51-3.61)
Kearon et al,[24] 2008	0.38 (0.10-1.50)
Overall	1.56 (1.14-2.12)

Test for heterogeneity: $I^2 = 48\%$; $P = .03$
Test for overall effect: $P = .005$



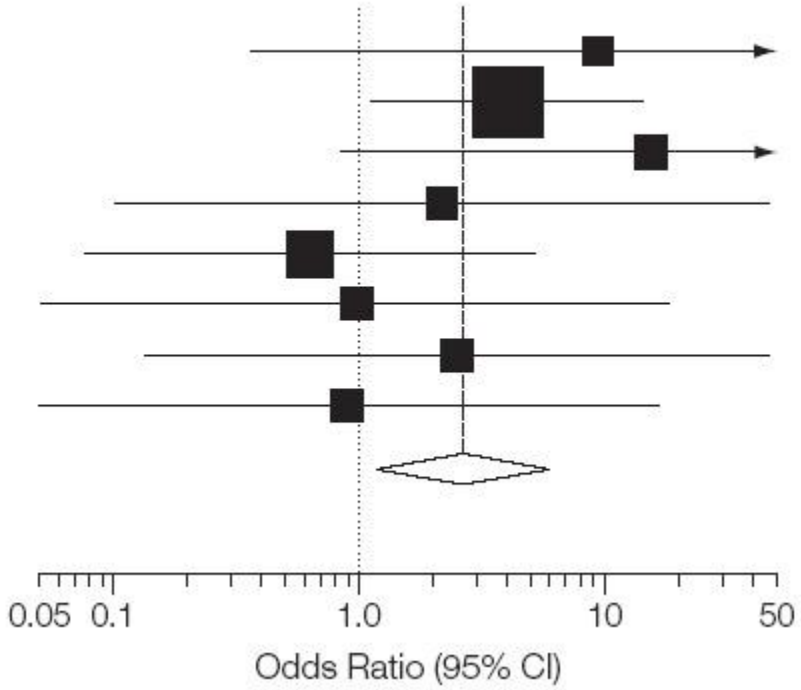
Segal at al, JAMA 2009, 301:2472

Predictive value of homozygous factor V Leiden for recurrent VTE

B Probands homozygous for factor V Leiden mutation

Source	Odds Ratio (95% CI)
Kearon et al,[23] 1999	9.44 (0.36-245.69)
Lindmarker et al,[14] 1999	4.03 (1.13-14.34)
Høibraaten et al,[20] 2001	15.33 (0.85-276.51)
Palareti et al,[17] 2003	2.18 (0.10-46.20)
Christiansen et al,[13] 2005	0.64 (0.08-5.26)
Wåhlander et al,[22] 2006[a]	0.98 (0.05-18.50)
Wåhlander et al,[22] 2006[b]	2.50 (0.13-46.47)
Kearon et al,[24] 2008	0.89 (0.05-16.72)
Overall	2.65 (1.18-5.97)

Test for heterogeneity: $I^2 = 0\%$; $P = .62$
Test for overall effect: $P = .08$



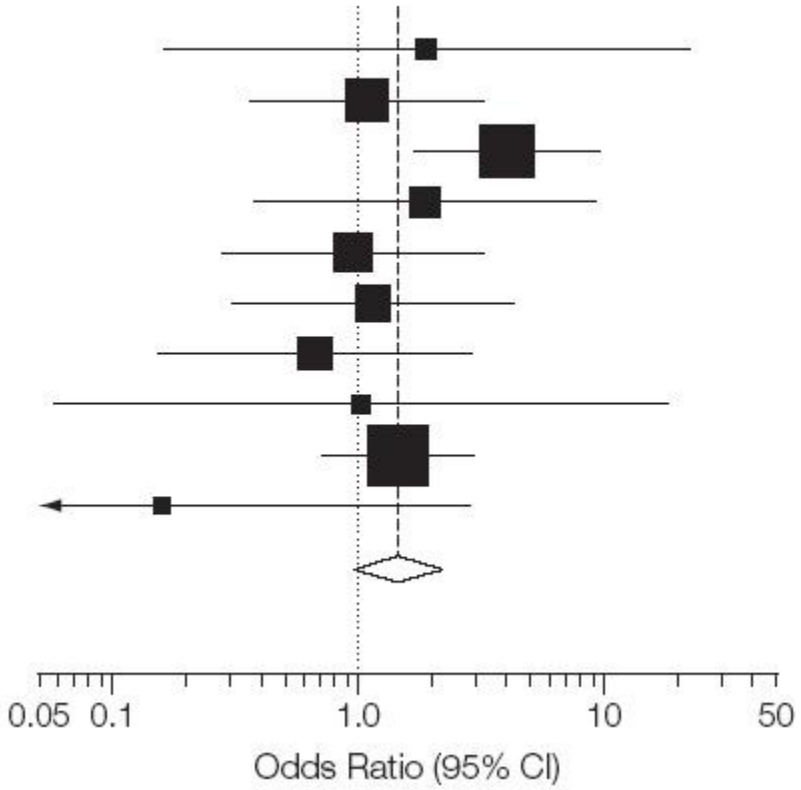
Segal at al, JAMA 2009, 301:2472

Predictive value of prothrombin variation for recurrent VTE

C Probands heterozygous for prothrombin G20210A mutation

Source	Odds Ratio (95% CI)
Kearon et al,[23] 1999	1.90 (0.16-22.39)
Lindmarker et al,[14] 1999	1.08 (0.36-3.24)
Simioni et al,[15] 2000	4.03 (1.67-9.68)
Miles et al,[25] 2001	1.86 (0.37-9.25)
Palareti et al,[17] 2003	0.95 (0.28-3.21)
González-Porras et al,[19] 2006	1.15 (0.30-4.33)
Wåhlander et al,[22] 2006[a]	0.66 (0.15-2.88)
Wåhlander et al,[22] 2006[b]	1.02 (0.06-18.03)
Prandoni et al,[21] 2007	1.45 (0.72-2.94)
Kearon et al,[24] 2008	0.16 (0.01-2.85)
Overall	1.45 (0.96-2.21)

Test for heterogeneity: $I^2 = 7.91\%$; $P = .37$
Test for overall effect: $P = .08$



Segal at al, JAMA 2009, 301:2472