Risk of recurrence after venous thromboembolism in men and women: patient level meta-analysis

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STUDY QUESTION

In patients with a first episode of venous thromboembolism, are men at higher risk than women of developing recurrence of disease?

SUMMARY ANSWER

Men have a 2.2-fold higher risk of recurrent disease than women after unprovoked venous thromboembolism, but the risk of recurrence after provoked venous thromboembolism is similar in men and women.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Whether men have a higher risk of recurrent venous thromboembolism than do women is uncertain, partly because previous studies did not control for potential sources of bias. The finding of a higher risk in men in a patient level meta-analysis suggests that indefinite anticoagulation should be given greater consideration in men than in women after a first venous thromboembolism.

Selection criteria for studies

Included studies were randomised trials or prospective cohort studies of patients with a first venous thromboembolism with symptoms, who received standardised anticoagulation (five to 10 days of heparin and at least three months of a vitamin K antagonist), were followed up for recurrent venous thromboembolism after anticoagulation was stopped, and had D-dimer measured after anticoagulation was stopped. (The last characteristic was not needed for the analysis reported here but was used for companion studies).

Primary outcome

The primary outcome was risk of recurrent venous thromboembolism in men and women.

Main results and role of chance

We studied 2554 patients with a first venous thromboembolism who had clinical follow-up for a mean of 27.1 (SD 19.6) months. The one year incidence of recurrent venous thromboembolism was 5.3% (95% confidence interval 4.1% to 6.7%) in women and 9.5% (7.9% to 11.4%) in men; the three year incidence of recurrence was 9.1% (7.3% to 11.3%) in women and 19.7% (16.5% to 23.4%) in men. In patients with unprovoked venous thromboembolism, men had a higher risk of recurrence than did women (hazard ratio 2.2, 95% confidence interval 1.7 to 2.8). After adjustment for women with hormone associated initial venous thromboembolism, the risk of recurrence remained higher in men (hazard ratio 1.8, 1.4 to 2.5). In patients with provoked venous thromboembolism, occurring after exposure to a major risk factor, we found no difference in recurrence of disease in men and women (hazard ratio 1.2, 0.6 to 2.4).

PREDICTORS OF RECURRENT VENOUSTHROMBOEMBOLISM (VTE) IN MULTIVARIABLE COX REGRESSION ANALYSIS

Groups of patients for comparison	Risk of recurrent VTE—hazard ratio (95% CI)*
Initial VTE unprovoked (occurring in absence of major antecedent risk):	
Men *v* all women†	2.2 (1.7 to 2.8)
Men *v* women (excluding women with previous hormone associated VTE)§	1.8 (1.4 to 2.5)
Women with previous hormone associated VTE *v* women without previous hormone associated VTE and no other antecedent risk factors	0.5 (0.3 to 0.8)
Initial VTE provoked (occurring in presence of antecedent transient major risk):	
Men *v* all women†	1.2 (0.6 to 2.4)
Men *v* women (excluding women with previous hormone associated VTE)‡	1.2 (0.6 to 2.3)

*All estimates came from study stratified Cox regression model with fixed effect.
†Model including age, unprovoked/provoked VTE, interaction between unprovoked/provoked VTE and sex, and proximal/distal VTE as covariates.
‡Model including use/non-use of hormonal therapy, age, unprovoked/provoked VTE, interaction between unprovoked/provoked VTE and sex, and proximal/distal VTE as covariates.

Bias, confounding, and other reasons for caution

Potential unmeasured variables could have affected the risk of recurrent venous thromboembolism, and the study population was predominantly white.

Study funding/potential competing interests

We received no funding for this study.

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