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Rosuvastatin reduces the occurrence of symptomatic venous thromboembolism

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This was a substudy of the JUPITER trial.

It was a randomized, double-blind, placebo controlled, multicenter trial.

Between March 2003 and December 2006, 17802 apparently healthy men and women with both low-density lipoprotein (LDL) cholesterol levels of less than 130 mg per deciliter and high-sensitivity C-reactive protein levels of 2,0 mg per liter or higher were randomly assigned to receive rosuvastatin 20 mg daily or placebo. The endpoint was the first occurrence of venous thromboembolism (a secondary endpoint in JUPITER trial).

Cases of venous thromboembolism included all cases of diagnosed pulmonary embolism or deep-vein thrombosis. Confirmation of the event was done by a venous ultrasonogram or venogram for confirmation of deep-vein thrombosis and an angiogram, computed tomographic scan, or ventilation–perfusion scan for confirmation of pulmonary embolism.

Deep-vein thrombosis or pulmonary embolism was classified as unprovoked if it occurred in the absence of any recent trauma, hospitalization, or surgery (i.e. occurring within 3 months before the event) and in the absence of a malignant condition that was diagnosed before or up to 3 months after the event. The thrombotic disorder was classified as provoked if it occurred in a patient with cancer or if it occurred during or shortly after trauma, hospitalization, or surgery.

The median follow-up period was 1.9 years with a maximum of 5 years.

Symptomatic venous thromboembolism occurred in 94 participants: 34 in the rosuvastatin group and 60 in the placebo group. The rates of venous thromboembolism were 0.18 and 0.32 event per 100 person-years of follow-up in the rosuvastatin and placebo groups, respectively (hazard ratio with rosuvastatin, 0.57; 95% confidence interval [CI], 0.37 to 0.86; P = 0.007); the corresponding rates for unprovoked venous were 0.10 and 0.17 (hazard ratio, 0.61; 95% CI, 0.35 to 1.09; P = 0.09) and for provoked venous thromboembolism, 0.08 and 0.16 (hazard ratio, 0.52; 95% CI, 0.28 to 0.96; P = 0.03).

The rates of pulmonary embolism were 0.09 in the rosuvastatin group and 0.12 in the placebo group (hazard ratio, 0.77; 95% CI, 0.41 to 1.45; P = 0.42).

The rates of deep-vein thrombosis only were 0.09 and 0.20, respectively (hazard ratio, 0.45; 95% CI, 0.25 to 0.79; P = 0.004).

Consistent effects were observed in all the subgroups (sex, age, ethnic group, body-mass index, waist circumference, metabolic syndrome, smoking, LDL, HDL cholesterol levels, triglycerides, high-sensitivity CRP) examined.

No significant differences were seen between treatment groups in the rates of bleeding episodes.

The authors discuss that the observed treatment effect was similar to, and independent of, the previously observed effect for arterial events. The apparent benefit was also similar whether venous thromboembolism was provoked or unprovoked. The benefit was larger for the end point of deep-vein thrombosis only than for the end point of pulmonary embolism. Consistent effects were seen across subgroups, with a larger benefit observed in the subgroups of older participants and those with elevated waist circumference. The authors also discuss that the limitations of this study include its restriction to initially healthy participants and the limited long-term follow-up. Also the authors didn't elaborate the potential mechanism of action of statins with respect to the prevention of venous thromboembolism. The study does not allow for an evaluation of the relationship between the dose of the statin and the risk of venous thromboembolism.

The authors' conclusion is that this randomized trial of apparently healthy men and women, rosuvastatin was associated with a significant reduction in the risk of venous thromboembolism. The risk reduction appears to be an independent benefit of statin use, beyond the reduction in the risk of arterial thrombosis. ❑

Comment on a paper:
Robert JG, ScD, Eleanor Danielson et al – A Randomized Trial of Rosuvastatin in the Prevention of Venous Thromboembolism. *N Engl J Med* 2009; 360:1851-1861