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The association between statin prescription, recurrent venous thromboembolism and bleeding events: from the COMMAND VTE Registry

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On behalf of The COMMAND VTE Registry investigators

Background: Statin prevents occurrence and recurrence of atherosclerotic events. With regard to venous thromboembolism (VTE), a randomized controlled trial suggested that statin reduced occurrence of VTE, whereas its usefulness as secondary prevention of VTE remains to be elucidated.

Purpose: This study aimed to assess the association between statin prescription, recurrent VTE and bleeding events in patients with VTE.

Methods: The COMMAND VTE Registry is a multicentre registry enrolling consecutive 3027 patients with acute symptomatic VTE among 29 centres in Japan. We divided the cohort into the patients who were prescribed statin (N=437) and those not (N=2590), and compared the two groups. We assessed hazard ratios (HRs) of those with statin relative to those without for long-term clinical outcomes (recurrent symptomatic VTE and International Society of Thrombosis and Hemostasis [ISTH] major bleeding). Because the durations of anticoagulation therapy were widely different between the two groups, we constructed Cox's proportional hazard model incorporating status of anticoagulation during the follow-up period as a time-varying covariate. Also, because the incidences of death were strikingly different between the two groups due to the difference in the prevalence of active cancer, we used Fine-Gray's subdistribution hazard model in the presence of competing risks. We incorporated clinically relevant factors into these two models as covariates (10 factors for recurrent VTE and 11 for major bleeding).

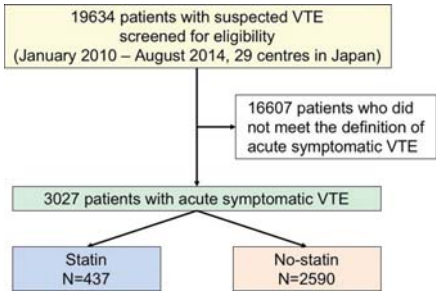
Results: The statin group was significantly older than the non-statin group (statin 71.2±11.8 vs. non-statin 66.5±15.8, $P<0.001$). The prevalence of active cancer in the statin group was less than one-half of that in the non-statin group (12% vs. 25%, $P<0.001$), and the cumulative 3-year incidence of death was significantly lower in the statin group than in the non-statin group (12.8% vs. 26.1%, log-rank $P<0.001$). The table shows the adjusted HRs of the statin group relative to the non-statin group. The HRs of the statin group relative to non-statin group for recurrent VTE were significantly low, but those for major bleeding were insignificant.

Conclusions: Prescription of satin was associated with significantly low risks for recurrent VTE, whereas that was not for major bleeding events. Statin could be a potential treatment option for secondary prevention of VTE.

Adjusted hazard ratios

Outcome measures	Model 1 Adjusted HR [95% CI]	P value	Model 2 Adjusted HR [95% CI]	P value
Recurrent VTE	0.59 [0.36–0.98]	0.042	0.53 [0.32–0.89]	0.02
Major bleeding	0.87 [0.60–1.24]	0.43	0.997 [0.69–1.43]	0.99

Model 1 derived from Cox's model with time-varying covariate of anticoagulation status. Model 2 derived from Fine-Gray's model.



Study flowchart