Risk factors of recurrence in patients with cancer-associated venous thromboembolism: from the COMMAND VTE Registry

Y. Nishimoto[1], Y. Yamashita[2], T. Morimoto[3], S. Saga[1], Y. Sato[1], T. Kimura[2]

[1]Hyogo Prefectural Amagasaki General Medical Center, Amagasaki, Japan; [2]Kyoto University Graduate School of Medicine, Department of Cardiovascular Medicine, Kyoto, Japan; [3]Hyogo College of Medicine, Department of Clinical Epidemiology, Nishinomiya, Japan

On behalf of the COMMAND VTE Registry Investigators

Funding Acknowledgement: Type of funding sources: Foundation. Main funding source(s): Research Institute for Production Development, Mitsubishi Tanabe Pharma Corporation

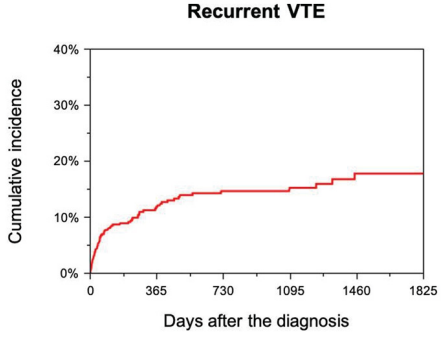
Background/Introduction: Cancer is a strong risk factor for the development of venous thromboembolism (VTE) including pulmonary embolism (PE) and deep vein thrombosis (DVT). Patients with VTE have a long-term risk of recurrence, which can be prevented by anticoagulation therapy. Prolonged anticoagulation therapy is recommended for patients with cancer-associated VTE, although the risk of recurrence might depend on the individual patient.

Purpose: We aimed to identify the risk factors of recurrence in patients with cancer-associated VTE.

Methods: The COMMAND VTE Registry is a multicenter retrospective registry enrolling 3027 consecutive patients with acute symptomatic VTE among 29 Japanese centers between January 2010 and August 2014. The present study population consisted of 695 cancer-associated VTE patients. The primary outcome measure in the present study was recurrent VTE, which was defined as PE and/or DVT with symptoms accompanied by confirmation of a new thrombus or exacerbation of the thrombus by objective imaging examinations or autopsy. Discontinuation of anticoagulation was defined as a withdrawal of anticoagulation therapy lasting >14 days for any reason. We selected clinically relevant variables and variables with P values <0.1 in a univariate analysis as potential risk factors, and constructed a multivariable Cox proportional hazard model for recurrent VTE incorporating the anticoagulation therapy status as a time-updated covariate.

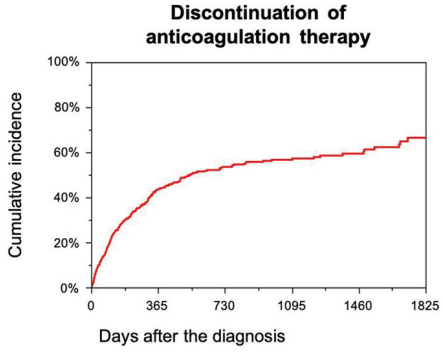
Results: Among the 695 study patients, recurrent VTE occurred in 78 patients, of whom 54 (69%) occurred within 6 months. The cumulative incidence of recurrent VTE was 7.7% at 3-months, 8.9% at 6-months, 11.8% at 1-year, and 17.7% at 5-years. The cumulative incidence of discontinuation of anticoagulation therapy was 18.0% at 3-months, 29.5% at 6-months, 43.4% at 1-year, and 66.5% at 5-years. The cumulative 5-year incidence of recurrent VTE was most frequent in patients with uterus/ovary cancer (26.0%), followed by those with lung cancer (24.7%). The multivariable Cox proportional hazard model revealed that chronic kidney disease (HR, 2.27; 95% CI, 1.36–3.77, P=0.002), a high D-dimer level at the time of VTE diagnosis (HR, 2.85; 95% CI, 1.71–4.74, P<0.001), advanced cancer (HR, 1.69; 95% CI, 1.05–2.72, P=0.03) and discontinuation of anticoagulation therapy (HR, 2.66; 95% CI, 1.53–4.63, P<0.001) were independently associated with an increased risk of recurrent VTE. No cancer site was independently associated with an increased risk for recurrent VTE when adjusting for the above mentioned risk factors in the multivariable Cox proportional hazard model, although the risk of recurrent VTE numerically differed according to the cancer site.

Conclusions: Among patients with cancer-associated VTE, chronic kidney disease, a high D-dimer level at the time of VTE diagnosis, advanced cancer, and discontinuation of anticoagulation therapy were independent risk factors of recurrence.



	0-day	90-day	180-day	1-year	2-year	3-year	5-year
N of patients with event		48	54	65	74	75	78
N of patients at risk	695	496	393	311	230	144	42
Cumulative incidence		7.7%	8.9%	11.8%	14.6%	15.2%	17.7%

Figure 1



	0-day	90-day	180-day	1-year	2-year	3-year	5-year
N of patients with discontinuation		103	159	215	248	256	266
N of patients at risk	614	429	316	213	136	77	17
Cumulative incidence		18.0%	29.5%	43.5%	53.5%	56.7%	66.5%

Figure 2