CHAPTER 12

The risk of cancer in patients with venous thromboembolism does not exceed that expected in the general population after the first 6 months


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Published in:
Venous thromboembolism (VTE) is a well-known marker of occult malignancy. Indeed, during the initial 6 months after thrombotic episode a new cancer is diagnosed in up to 10% of patients, especially in those with idiopathic VTE (1–5). While it would be of interest to know whether this increased risk for cancer persists over the long term, beyond this initial 6-month period, available information is controversial. In two population-based studies the risk for subsequent cancer in patients with newly diagnosed VTE significantly exceeded that observed in control subjects for up to 10 years after the thrombotic episode (2,3), whereas in two other similar studies this finding was not confirmed (4,5). Recently, we reported on the long-term follow-up of large cohort of consecutive patients with acute symptomatic VTE recruited at two Italian centers (6). In patients who were free from cancer at baseline, the risk for subsequent overt malignancy was substantial during the initial 3-6 months, and declined thereafter to 1.3% per year (6,7). To determine whether and to what extent this rate exceeds that expected in the general population, we assessed the risk of subsequent overt malignancy in 1495 patients who remained cancer free during the initial 6 months after the thrombotic episode, and in 1495 age- and sex-matched control subjects derived from the general population of three regions in northern Italy (8–10). For both study patients and controls the mean age was 60.0 ± 16.8 years, and 46% were males. In 825 (55%) patients with VTE, the episode was considered idiopathic. All patients and controls had follow-up for 30 months, which began at the 6-monthpoint after VTE. During the follow-up period, 115 patients (7.7%) and 70 controls (4.7%) died, while none was lost to follow-up. Neither in patients nor in controls was an extensive work-up done for occult malignancy. The analysis was conducted on an intention-to-treat basis. Kaplan–Meier estimates and associated 95% confidence intervals (CIs) were calculated. To compare the risk for new cancer in patients and matched controls, Cox proportional hazards modelling was used to calculate hazard ratios (HR), and 95% CIs, both in the entire cohort and in the subgroup of patients with idiopathic VTE. During the 30-month follow-up period, new objectively confirmed cancer developed in 48 patients with VTE and in 43 control subjects, resulting in a cumulative incidence of 3.2% (95% CI, 2.3–4.4) and 2.9% (95% CI, 2.0–4.0), respectively (Fig. 1). The HR for new cancer in patients with VTE as compared with controls was 1.09 (95% CI, 0.59–1.34). When the analysis was confined to the 825 patients with idiopathic VTE and their controls, the HR for cancer was 1.12 (95% CI, 0.61–1.36). The main limitation of this observation lies in the failure to obtain information on cancer stage. In spite of this limitation, we can reasonably conclude that in patients with a first VTE, including those with idiopathic thrombosis, the risk for subsequent cancer beyond the initial 6 months does not appear to exceed that expected in the general population. Accordingly, after the first uneventful months patients can be reassured that their subsequent risk for cancer appears no higher than that of the general population. Unless an extensive diagnostic work-up for occult malignancy has already been performed soon after the thrombotic episode, there is probably no further indication for it.
Cumulative incidence of cancer (%) vs. follow-up (months) for thrombotic patients and matched controls.

Cases at risk:
- Thrombotics: 1495, 1483, 1475, 1470, 1461, 1447
- Controls: 1495, 1489, 1479, 1468, 1465, 1452
References


