Patients with venous thromboembolism caused by no apparent risk factor have a greater risk of developing cancer. How extensive should the screening be?

Cancer screening after idiopathic venous thromboembolism?

Venous thromboembolism, a collective term for deep venous thrombosis and pulmonary embolism, affects between 7 000 and 10 000 Norwegians every year. No apparent risk factor is found in 30–50 % of the cases, and the condition is called idiopathic. Cancer is a well-established risk factor for venous thromboembolism. Studies have also shown that in approximately 10 % of cases idiopathic venous thromboembolism is accompanied by newly-diagnosed cancer the following year (1). The venous thromboembolism is therefore considered a sign of underlying occult cancer. Systematic malignancy screening of these patients seems to be a rational strategy since it may result in the detection of cancer at an early stage and may make curative treatment possible, thus improving the prognosis. It has been debated for many years whether patients with idiopathic venous thromboembolism should undergo systematic malignancy screening.

International guidelines recommend that patients with idiopathic venous thromboembolism should undergo limited screening for malignancy, while more extensive screening is reserved for patients with abnormal findings in the limited screening (2–4). In this edition of the Journal of the Norwegian Medical Association, Semb and Tveit have published a retrospective study from Bærum hospital on cancer detection following limited malignancy screening of patients with idiopathic venous thromboembolism (5). The limited screening consisted of patient-reported history focusing on possible malignancy symptoms, and targeted clinical, laboratory and imaging diagnostic tests. Limited screening of 499 patients with idiopathic venous thromboembolism resulted in 98 (20 %) positive findings without cancer being detected, and cancer was detected in 44 (9 %) patients in the course of one year after the thromboembolism. Three patients with negative findings from the initial limited screening were subsequently diagnosed with cancer.

The biggest challenge, however, is whether patients with idiopathic venous thromboembolism should undergo limited or extensive systematic malignancy screening. Extensive screening also includes a CT thorax and abdomen, a mammogram and possibly an endoscopy. In principle, one would expect an approach of this type to diagnose cancer at an earlier stage and thus improve patients' prognoses. Even though a number of studies have revealed that in some patients who have been diagnosed with occult cancer the disease is still at an early stage (6), it is not clear whether early detection resulting from extensive screening is significant for the prognosis of the patients (1, 7, 8).

Only one randomised study has compared limited and extensive malignancy screening of patients with idiopathic thromboembolism. Those who underwent extensive screening had cancer diagnosed earlier, but after two years' follow-up the prognosis was the same (7). However, it is difficult to interpret the findings since the study was discontinued after only 201 of a total of 1 000 planned patients had been included (because those who were randomised to undergo limited screening were in practice given more extensive screening than was indicated by the protocol). A prospective controlled multi-centre study that included 630 patients from ten university clinics in the Netherlands revealed just as many cancer cases and cancer-related deaths among those who had undergone limited screening as among those who had undergone extensive screening (8). New strategies for malignancy screening with FDG-PET/CT are currently being tested, but the first study that has used this strategy has not demonstrated an improved ability to detect cancer or to reduce costs (9).

Credit goes to the medical community at Bærum hospital: they had established limited malignancy screening for patients with idiopathic venous thromboembolism even earlier than 2003. Their data also shed light on one particular challenge of systematic screening – namely the identification of false positive findings with accompanying mental burden (fear of serious illness) and physical burden (diagnostic procedures with health risks in the form of radiation in connection with radiological procedures and puncture/biopsy). In the Bærum study there were twice as many patients with false positive findings (n = 98) as with true positive.

Thus there is no documentation to show that systematic malignancy screening is better than a Calvinistic approach with patient-reported history and physical examination focusing on signs and symptoms of possible malignancy and standard blood tests. Supplementary examinations are only indicated in the event of positive findings or clinical suspicion of occult malignancy. An extremely simple screening strategy also saves resources for both the health service and the individual patient. Most patients with venous thromboembolism are diagnosed and start treatment at outpatient consultations. If this very simple screening raises any suspicion of occult malignancy, consultation with the primary doctor must therefore determine whether the patient should be hospitalised for further evaluation or monitored as an outpatient or in the primary health service.

John-Bjarne Hansen
john-bjarne.hansen@uit.no

John-Bjarne Hansen (born 1961) is Professor of Haemotology at the University of Tromsø, and senior consultant at the University Hospital of North Norway. He heads the newly-established K.G. Jebsen Thromboembolism Research and Expertise Centre (TREC).

References

1. Carrier M, Le Gal G, Wells PS et al. Systematic review: the Trousseau syndrome revisited: should we screen extensively for cancer in patients with venous thromboembolism? Ann Intern Med 2008; 149: 323–33.
2. Torbicki A, Perrier A, Konstantinides S et al. Guidelines on the diagnosis and management of acute pulmonary embolism: the Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). Eur Heart J 2008; 29: 2276–315.
3. Chong LY, Fenu E, Stansby G et al. Management of venous thromboembolic diseases and the role of thrombophilia testing: summary of NICE guidance. BMJ 2012; 344: e3979.
4. Rosovsky R, Lee AYY. Evidence-based mini-review: Should all patients with idiopathic venous thromboembolic events be screened extensively for occult malignancy? ASH Education Book 2010; 2010: 150–2. http://asheducationbook.hematologylibrary.org/content/2010/1/150.full (3.2.2014).
5. Semb VB, Tveit A. Begrenset malignitetsutredning ved idiopatisk venøs trombose. Tidsskr Nor Legeforen 2014; 134: 407–11.
6. Monreal M, Lensing AWA, Prins MH et al. Screening for occult cancer in patients with acute deep vein thromboembolism or pulmonary embolism. J Thromb Haemost 2004; 2: 876–81.
7. Piccioli A, Lensing AWA, Prins MH et al. Extensive screening for occult malignant disease in idiopathic venous thromboembolism: a prospective randomized clinical trial. J Thromb Haemost 2004; 2: 884–9.
8. Van Doormaal FF, Terpstra W, Van der Griend R et al. Is extensive screening for cancer in idiopathic venous thromboembolism warranted? J Thromb Haemost 2011; 9: 79–84.
9. Rondina MT, Wanner N, Pendleton RC et al. A pilot study utilizing whole body 18 F-FDG-PET/CT as a comprehensive screening strategy for occult malignancy in patients with unprovoked venous thromboembolism. Thromb Res 2012; 129: 22–7.