

To screen or not to screen patients with an idiopathic venous thrombosis for an occult cancer: Netherlands versus the World: I-O?

M.R. Nijziel

Department of Internal Medicine, Maxima Medisch Centrum, Veldhoven, the Netherlands,
e-mail: m.nijziel@mmc.nl

Ever since Armand Trousseau reported the association between venous thromboembolism and cancer, we have been speculating whether screening patients with an idiopathic venous thrombosis for an occult cancer is useful. It is only worthwhile to do that when the cancer that we want to discover is limited and can be treated with curative intent. In the Netherlands, our Calvinistic approach has always been to do a thorough medical history and physical examination. When no alarming symptoms or abnormalities are found, we have always been taught that screening for a hidden cancer is not justified. In many other countries the same patient would have been screened thoroughly with total body CT scans, endoscopy, urological and gynaecological examinations, mammography and extensive laboratory tests including all tumour markers that are currently known. It has never been established which approach is the best.^{1,2}

Until recently, only one randomised trial had been done to try to answer this question: to screen or not to screen patients with an idiopathic venous thrombosis for an occult cancer. Unfortunately this study failed and was stopped prematurely. The main reason for stopping the trial was that in the group with limited screening, patients and doctors requested more screening tests than previously agreed in the protocol. Therefore, the patient group with limited screening was in fact not very different from the group with extensive screening. Moreover, patient accrual was difficult because patients wanted to be screened in the extensive and not the limited way. No differences were found.³

It has been the merit of the Dutch Trousseau investigators that they have again tried to answer this question. Of course, the Netherlands was the ideal country to investigate the limited approach with only medical history, physical examination, chest X-ray and routine laboratory tests. This approach was compared with an extensive (or as the rest of the world would call it: less limited) approach, including

an additional CT scan of the thorax and abdomen and mammography in women. Extensive screening detected slightly more cancers than the limited approach of which half were not curable. There was no difference in overall survival. It was definitely concluded that routine screening with CT scans and mammography in patients with an idiopathic venous thrombosis is not justified.⁴

In this Journal the same group (Kleinjan *et al.*) reports that the extensive screening with CT scans and mammography in the Trousseau study leads to additional costs due to a high percentage of false-positive findings.⁵ In an era in which the costs in healthcare are extensively debated all over the world it is important to investigate whether a screening approach is cost-effective. Moreover, screening strategies resulting in false-positive findings leading to costly and invasive procedures potentially harming patients should be avoided. New approaches with FDG-PET/CT as screening strategy are currently under investigation, but the first reports do not show improvement in the cancer detection rate and costs.⁶

Hence, screening patients with an idiopathic venous thrombosis for an occult cancer with (PET) CT scans should **not** be implemented. It leads to extra costs, does not lead to the detection of curable cancers and does not lead to a better overall survival. The Trousseau study even raises the question whether the limited approach with medical history, physical examination, chest X-ray and routine laboratory testing is too extensive. There is no evidence that this approach is any better than a very limited approach with a precise medical history, a complete physical examination and only additional tests when abnormalities are found. Therefore, in patients with an idiopathic venous thrombosis screening for an occult cancer should be limited. The old Calvinistic Dutch approach does not seem to be that bad at all and this (very) limited approach should be adopted by the rest of the world.

REFERENCES

1. Piccioli A, Prandoni P. Screening for occult cancer in patients with idiopathic venous thromboembolism: yes. *J Thromb Haemost.* 2003;1:2271-2.
2. Lee AY. Screening for occult cancer in patients with idiopathic venous thromboembolism: no. *J Thromb Haemost.* 2003;1:2273-4.
3. Piccioli A, Lensing AW, 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.
4. 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.
5. Kleinjan A, van Doormaal FF, Prins MH, Buller HR, Otten JJMB. Limitations of screening for occult cancer in patients with idiopathic venous thromboembolism. *Neth J Med.* 2012;70:311-7.
6. 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.