

Extensive screening for occult cancer in unprovoked venous thromboembolism: not so useful?

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Background

Approximately 10 % of patients with unprovoked venous thromboembolism (VTE) will be diagnosed with cancer within 1 year of their thrombotic event; some studies have suggested that a limited screening strategy for occult cancer in patient with unprovoked VTE—including history taking, physical examination, routine blood testing, and chest radiography—is adequate to detect most occult cancers, while others have suggested that a more extensive screening strategy [e.g., incorporating ultrasonography or computed tomography (CT) of the abdomen and pelvis, measurement of tumor markers, or a combination of these] can increase the rate of detection of occult cancer [1, 2].

Summary

Carrier et al. designed a randomized trial to assess the efficacy of adding computed tomography of the abdomen and pelvis (including a virtual colonoscopy and gastroscopy, biphasic enhanced CT of the liver, parenchymal pancreatography, and uniphasic enhanced CT of the distended bladder) to a limited screening strategy for occult cancer in cases of unprovoked thromboembolism [3]. Limited screening strategy consisted in basic blood testing, chest radiography and screening for breast, cervical and prostate cancer. The primary outcome was newly diagnosed cancer during 1-year follow-up period.

Among 3186 patients, 854 underwent randomization. Between randomization and 1-year follow-up, 3.2 % of the patients in the limited screening group and 4.5 % of the patients in the extensive screening group had a new diagnosis of cancer ($p = 0.28$). In the primary outcome analysis, only 4 patients (0.93 %) in the limited screening group and 5 (1.18 %) in the extensive screening group had a cancer detected after the completion of the initial screening ($p = 1.0$).

The authors conclude that routine screening with CT of the abdomen and pelvis would not provide a clinically significant benefit over a limited screening strategy: the CT screening strategy did not appear to detect significantly more occult cancer, shorten the time to cancer diagnosis or reduce cancer-related mortality.

Strengths of the study

It deals with a clinically relevant problem, as the decision on how deeply to investigate for occult cancer patients with first unprovoked venous thromboembolism is very difficult.

Weaknesses of the study

The rate of cancer detection in this study is significantly lower than expected by authors based on previous studies [1, 2]. Therefore, the study might be underpowered to detect a significant difference between groups.

Question marks

Only one quarter of the patients assessed for eligibility were randomized. One-third of the excluded patients had met the inclusion criteria. It would be interesting to know

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what further criteria not covered by the protocol led to the exclusion of such a significant number of patients, and we wonder if this might affect the study's external validity.

The mean age of the study population was 54 years, which is lower than what is usually observed in clinical practice. This might have contributed to the low incidence of cancer.

A proportion of patients in both groups were taking oral contraceptives or exogenous estrogens; having enrolled these patients in the study might be controversial, as their venous thromboembolic events might not be considered as idiopathic.

Patients were followed for 1 year to elicit information about a new cancer diagnosis, recurrent venous thromboembolism, or other adverse events. How deeply was cancer searched for during this period of time is unclear.

The screening for cancers in Canada is among the best in the world [4]; the study's findings could therefore not be applicable to populations where screening programs are not so well done, and where unprovoked venous thromboembolism most frequently may be the first manifestation of neoplasm.

Clinical bottom line

In a population of patients with a first unprovoked venous thromboembolism and a relatively low prevalence of occult cancer, adding a routine screening with CT of the abdomen

and the pelvis to a limited cancer screening strategy does not appear to provide a clinically significant benefit.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Statement of human and animal rights All procedures were in accordance with Helsinki Declaration.

Informed consent Informed consent was obtained from all participants.

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