

Pulmonary Embolism and Cancer: Challenging Data from a Feared Combination

Tromboembolismo pulmonar y cáncer, datos desafiantes de una combinación temida

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Venous thromboembolism (VTE), which includes deep venous thrombosis and pulmonary embolism (PE), is the main cause of morbidity and mortality among patients with cancer. The risk is 4 to 7 times higher when there is underlying malignancy. (1) VTE has been reported as the second cause of death in cancer patients, (2) with different risk variables depending on the age of the patient and the type of cancer; (3,4) it is more common in pancreas cancer, stomach cancer, central nervous system primary tumors, ovarian cancer, and lung cancer, followed by genitourinary tumors. (5-7)

The mortality rate due to acute PE is significantly higher in patients with cancer versus those with no cancer (19.6% vs 3.2%, $p < 0.001$). (2)

Patients with cancer who have developed VTE have a high risk of recurrence, which is even higher when the first event has been PE (OR 10.5, 95% CI 9.3-11.7). (3)

Malignant disease per se favors hypercoagulability via different mechanisms. The host shows an immune response promoting chronic inflammation, with metabolic and neuroendocrine changes leading to procoagulant reactions that alter vascular homeostasis. (8)

The pathogenesis of cancer-related coagulopathy is complex and multifactorial. Several clinical factors affect the increased risk of thrombosis in patients with cancer, making them high risk patients.

The most significant clinical factors are cancer-specific factors, the patient's characteristics, and cancer therapies.

Cancer-related factors depend on location (pancreas, stomach, central nervous system, lung, ovary), the stage of disease, the histologic grade, and the time to diagnosis. The risk is higher when closer to diagnosis and decreases with response to treatment.

Patient-related factors are age over 65, obesity, smoking, a family history of VTE, the performance status, and a reduced renal function.

Treatment-related factors play a role as well, with cisplatin, asparaginase, tamoxifen, bevacizumab (angiogenesis inhibitors), thalidomide and lenalidomide, immunotherapy, and erythropoiesis-stimulating agents involving a higher risk. (9)

Models have been developed to evaluate the risk of thrombosis in cancer patients, which makes it possible to identify patients with a high risk of developing thrombosis during chemotherapy. The Khorana model is based on 5 predictors: tumor location, platelet count, hemoglobin levels or the use of erythropoiesis-stimulating agents, leukocyte count, and body mass index. High risk is defined as a score ≥ 3 . (10,11)

By contrast, the Pulmonary Embolism Severity Index (PESI) (12) is a prognostic model used to estimate intrahospital and 30-day mortality when the patient has already developed PE and is very useful to identify high-risk patients (score ≥ 86). A simplified PESI (sPESI) score of > 1 has a similar use. (13) By definition, cancer patients are always part of the sPESI high-risk group, as a history of cancer adds one point to the score.

The paper by J. Bonorino et al., published in this issue of the Argentine Journal of Cardiology, (14) is very interesting, as there is limited information on whether cancer patients with PE and an intermediate or high PESI score (≥ 86 points) have a higher risk of unfavorable progression versus non-cancer patients. The group of patients in this paper is similar to global numbers, with gastrointestinal tumors being the most common.

From a cancer perspective, please note that the above-cited paper defines active cancer as solid or hematologic malignancy under chemotherapy and/or radiotherapy in the last year, or under no active treatment but with palliative care. We need to consider that this last group of patients have advanced disease with no chance of therapy, a poor general condition,

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and a longer time confined to bed, which increases the risk of developing PE.

In this study, cancer did not involve an adverse prognosis for patients with an intermediate to high PESI. While the reasons put forward by the authors may be considered (younger cancer patients with lower hypertension prevalence and right ventricular involvement), it is also important to consider the number of patients included, as power is low for finding a significant difference.

The study by Bonorino et al. should be continued to be able to figure out the close relationship among cancer, EP, and vital prognosis.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web/Additional material).

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