



Guidelines for the management of cancer and thrombosis – Special aspects in women

Rupert M. Bauersachs

Vascular Medicine, Medical Department IV, Klinikum Darmstadt GmbH, D-64283 Darmstadt, Germany

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ABSTRACT

Background: Occurrence of venous thromboembolism (VTE) in patients with cancer is associated with unfavorable prognosis, and VTE treatment is less effective and more complicated in cancer patients. Several women specific aspects related to the underlying cancer type and VTE management need to be considered.

Methods: Guidelines on VTE prevention and treatment in cancer patients issued from several international bodies are reviewed with respect to women specific recommendations, and general guideline recommendations are summarized.

Results: All guidelines recommend an initial parenteral treatment, preferably with low-molecular-weight heparin (LMWH), while fondaparinux or unfractionated heparin (UFH) can also be used. Long-term treatment, comprising 3 to 6 months after initial anticoagulation should preferably be performed with LMWH, or vitamin K antagonists (VKA), if LMWH is not available. For extended treatment beyond six months, there are no specific recommendations due to lack of evidence, and anticoagulation can be performed with LMWH or VKA. Novel or non-VKA oral anticoagulants (NOACs) have been studied in several trials in comparison to VKA in VTE patients, including 3–9% cancer patients. While NOACs showed comparable efficacy and safety to VKA in those cancer patients, results from trials comparing NOACs with LMWH are not available. Because of the paucity of data, there are no guideline recommendations for women specific cancer types or women specific issues in the prevention and treatment of VTE.

Conclusions: While there is agreement on general VTE management in cancer patients across different international guidelines, there is insufficient guidance on many women specific aspects commonly encountered during clinical practice. Future trials are required that specifically and prospectively address women specific issues in the management of VTE in cancer.

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Introduction and epidemiology

Malignancy and venous thromboembolism (VTE) constitute a double-sided clinical relationship [1,2] with a 6–7 fold increased risk of VTE compared to non-cancer patients [3,4], and VTE as the leading cause of death [5], while – on the other side – 20–25% of VTE patients have an underlying active cancer. Recurrence of VTE in a cancer patient is associated with a poor prognosis [6,7]. The reported incidence rates of VTE in different cancer types depend on the specific setting, and may be different in an outpatient environment [8] and in hospitalized patients [9,10]. When analyzing VTE incidence rates for different cancer types, women-specific malignancies such as breast cancer, uterine or ovary cancer appear to be associated with a relatively low VTE risk within the whole spectrum of malignancies (Fig. 1) [7].

Focusing on VTE incidence rates for specific cancer types may, however, be misleading with respect to the number of affected women and real-live burden. When considering the prevalence of different malignancies, with breast cancer representing the most common cancer in women, it becomes evident that – in spite of the low VTE incidence rate – breast cancer patients are frequently seen in VTE clinics, as documented in the RIETE-registry [11] (Fig. 2). Other leading women specific malignancies are ovarian and uterine cancer.

Treatment outcome in women receiving anticoagulant treatment for acute VTE is complicated, with a high rate of mortality, PE and DVT recurrence and increased risk of major bleeding during the first 30 days after presentation. In the RIETE registry, 2,474 women with cancer were analyzed from a population of 15,520 consecutive patients with VTE [11]. The thirty-day outcome of those patients is summarized in Fig. 3. Women presenting with initial symptomatic PE were more likely to recur with pulmonary embolism, and vice versa, patients with initial DVT more commonly had a DVT recurrence. In the overall cancer population, PE was the second most common cause of death within 30 days (4.1%) in patients with initial PE, followed by disseminated cancer as a cause of death.

* Correspondence to: Professor Rupert Bauersachs, MD, Vascular Medicine, Medical Department IV, Klinikum Darmstadt GmbH, Grafenstrasse 9, D-64283 Darmstadt, Germany. Tel.: +49 (0) 6151 107 4401; fax: +49 (0) 6151 107 4499.

E-mail address: bauersachs@em.uni-frankfurt.de (R.M. Bauersachs).

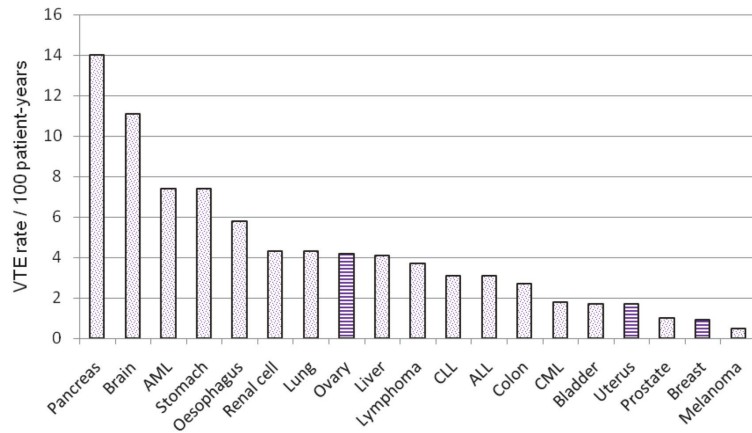


Fig. 1. Venous thromboembolism (VTE) associated with specific types of cancer. VTE rate per 100 patient years. Women specific types of malignancies are depicted as hashed bars. Modified from [7].

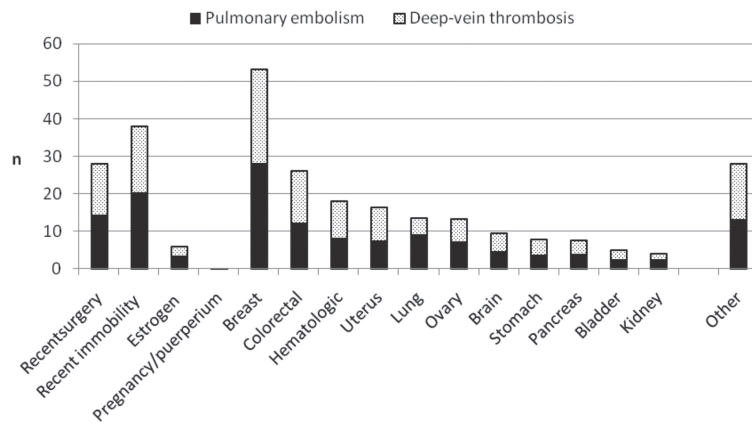


Fig. 2. Clinical characteristics of 3978 women with cancer and acute VTE, according to initial presentation. Pulmonary embolism – black bars; deep vein thrombosis – dotted bars. Data from the RIETE registry [11].

In patients with DVT, fatal PE occurred within 30 days in 0.3%, compared to 4.1% in patients who initially presented with PE. Overall death was also lower in DVT patients (8.2%) compared to patients presenting with initial PE (14%), respectively [11] (Fig. 3).

Material and methods

This review will focus on guideline recommendations on these three women specific malignancies and summarizes general guide-

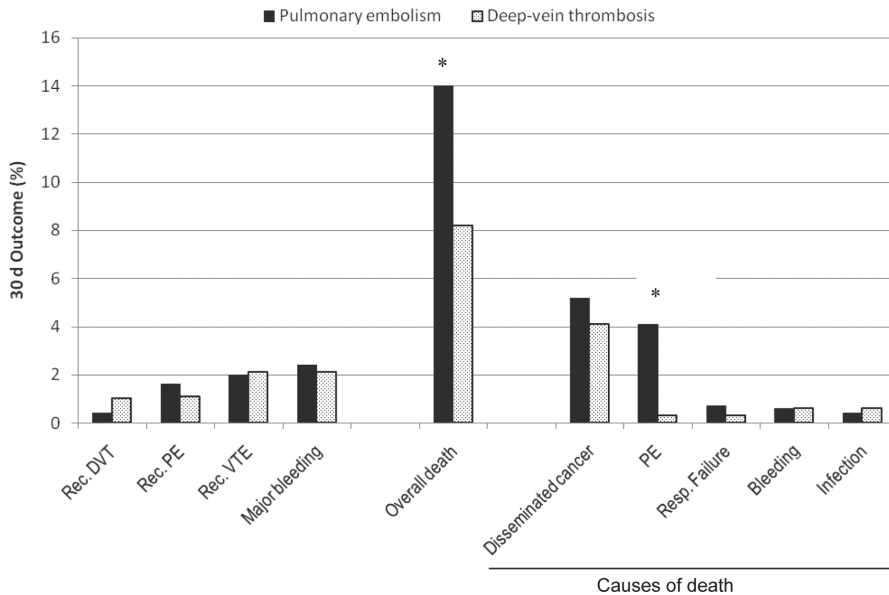


Fig. 3. Thirty-day outcome in women with cancer treated for acute VTE, according to initial presentation. Pulmonary embolism – black bars; deep vein thrombosis – dotted bars. Modified from [11]. *p < 0.05.

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