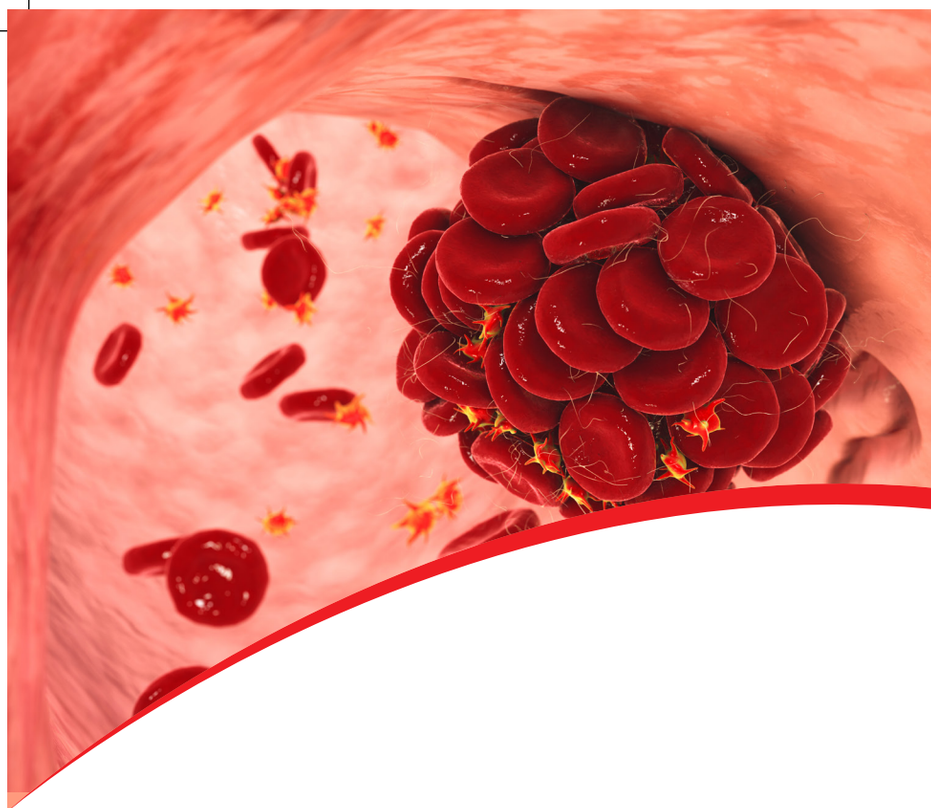

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# CASE STUDY

## Pulmonary Thromboembolism in a Patient after Gastric Cancer Surgery

## Introduction

Venous thromboembolism (VTE) is an important cause of morbidity and mortality among patients with cancer. It includes deep vein thrombosis (DVT) and pulmonary embolism (PE).[1] PE is an important cause of morbidity and death after major abdominal surgery.[2] Asymptomatic VTE is difficult to diagnose and is often diagnosed incidentally by imaging studies associated with other complications.[3] Cancer-associated VTE is a common and life-threatening condition in adult patients (≥18 years) with cancer. Patients with cancer are four to seven times more likely to develop VTE than patients without cancer. PE is one of the complications that can lead to intensive care unit admission for patients with cancer.[4]

The following case study is an example of pulmonary thromboembolism after surgery for primary adenocarcinoma of the stomach.

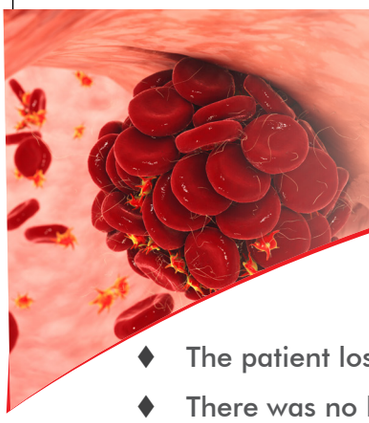
## Case Study

### Case presentation

A 62-year-old man presented to his physician with dyspepsia, which was not responsive to simple proton pump inhibitor treatment.

### History

- There was no known history of hypertension, diabetes, or other chronic illnesses.



- The patient lost appetite over the last few months and lost significant weight (>10 kg).
- There was no history of tobacco smoking and alcohol consumption.
- There was no family history of stomach cancer.
- There was no remarkable history or family history of VTE.

## Physical examination

- Weight: 60 kg
- Blood pressure: 140/80 mmHg
- Pulse: 90 beats per minute
- Temperature: 97.2 °F
- Per abdominal examination: Mild epigastric tenderness without a palpable mass; the liver did not seem enlarged

## Laboratory evaluation

- Results of complete blood count, plasma levels of electrolytes, and kidney and liver function tests were within normal limits.
- Upper gastrointestinal endoscopy (UGIE) showed Borrmann type 4 gastric carcinoma extending from the anterior wall of the mid-gastric curvature to the upper part of the gastric body. A biopsy sample was collected and sent for histopathological examination.
- Histopathological examination (HPE) of the gastric tissue specimen revealed adenocarcinoma.
- Upper gastrointestinal radiography revealed wall irregularity in the upper gastric bends.
- Contrast-enhanced computed tomography (CT) scan revealed wall thickening and sclerosis with contrast enhancement in the upper part of the gastric body and enlarged lymph nodes with a short diameter of 12 mm.
- Chest contrast-enhanced CT showed no obvious distant metastasis.

## Diagnosis

Based on the UGIE, HPE, and contrast-enhanced CT (chest), a preoperative diagnosis of gastric cancer, cT4aN1M0 c Stage III, was confirmed.

## Treatment for gastric adenocarcinoma

The multidisciplinary team decided to proceed with total gastrectomy with Roux-en-Y reconstruction, along with splenectomy and D2 lymphadenectomy. The duration of the surgery was about 6.1 hours.

An intermittent pneumatic compression pump was used during the perioperative period, and compression stockings were used until the patient was weaned from bed.

Postoperatively, the epidural catheter for pain control was removed on postoperative day 3, and a subcutaneous injection of enoxaparin 2,000 IU twice daily was started on postoperative day 4. The patient had a night-time intermittent fever of >100.3 °F since postoperative day 2, but the fever was still present on postoperative day 4, so investigations were performed on postoperative day 5.

## Follow-up investigations

- The white blood cell count was 8 × $10^3$ μL, C-reactive protein was 6 mg/dL, and the D-dimer was 16 μg/mL.
- Contrast-enhanced CT scan was performed, which showed a thrombus in the left upper lobe pulmonary artery A4/5 (Figure 1).
- Blood gas analysis showed partial pressure of oxygen ($pO_2$) of 95 mmHg and partial pressure of carbon dioxide ($pCO_2$) of 37 mmHg and alveolar-arterial oxygen gradient ($(A\text{-}aO_2)$ of 10.75.
- Anti-cardiolipin β2-glycoprotein antibody, lupus anticoagulant, protein C/S activity, and antigen levels were within normal limits.
- Ultrasonography of the lower extremities revealed a thrombus in the central branch of the right soleal vein.

**Figure 1: CT scan of the chest showing PE (arrow)**

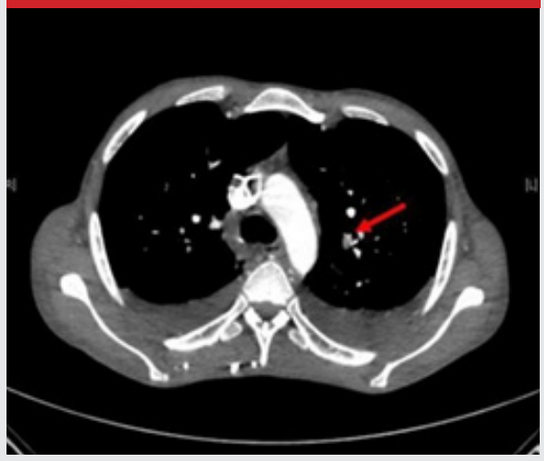


Image adapted from Issa *et al. Clinical and Experimental Gastroenterology*. 2011 Jan;4(1):1–7 and is meant for illustration and descriptive purpose only.

- Cardiac ultrasonography revealed no obvious thrombus and no evidence of pulmonary hypertension.
- There was no pneumonia or urinary tract infection at the beginning of the fever.

## Diagnosis

Pulmonary thromboembolism with DVT of the right leg is confirmed.

## Treatment for pulmonary thromboembolism

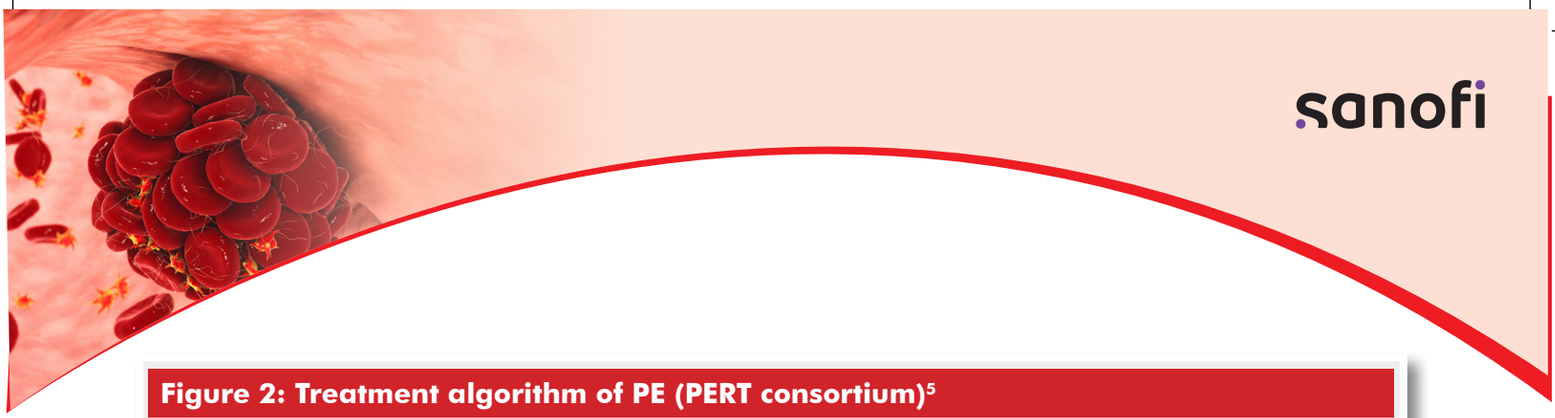
After diagnosis, anticoagulation with enoxaparin 1 mg/kg subcutaneously every 12 hours was started. Blood pressure was monitored at regular intervals and was within the normal range. The electrocardiogram and cardiac enzymes were normal. In addition, laboratory monitoring showed that both prothrombin time and thrombin time were normal during the treatment. The patient recovered well after 10 days of the treatment.

D-dimer had decreased to 10.0 μg/mL 3 days later, 7.0 μg/mL 7 days later, and 3.1 μg/mL 14 days later. Contrast-enhanced CT scan was performed again on day 17 after the start of medication, and the thrombus in the left upper lobe pulmonary artery A4/5 had disappeared. The patient was discharged from the hospital on postoperative day 20 as he made good progress.

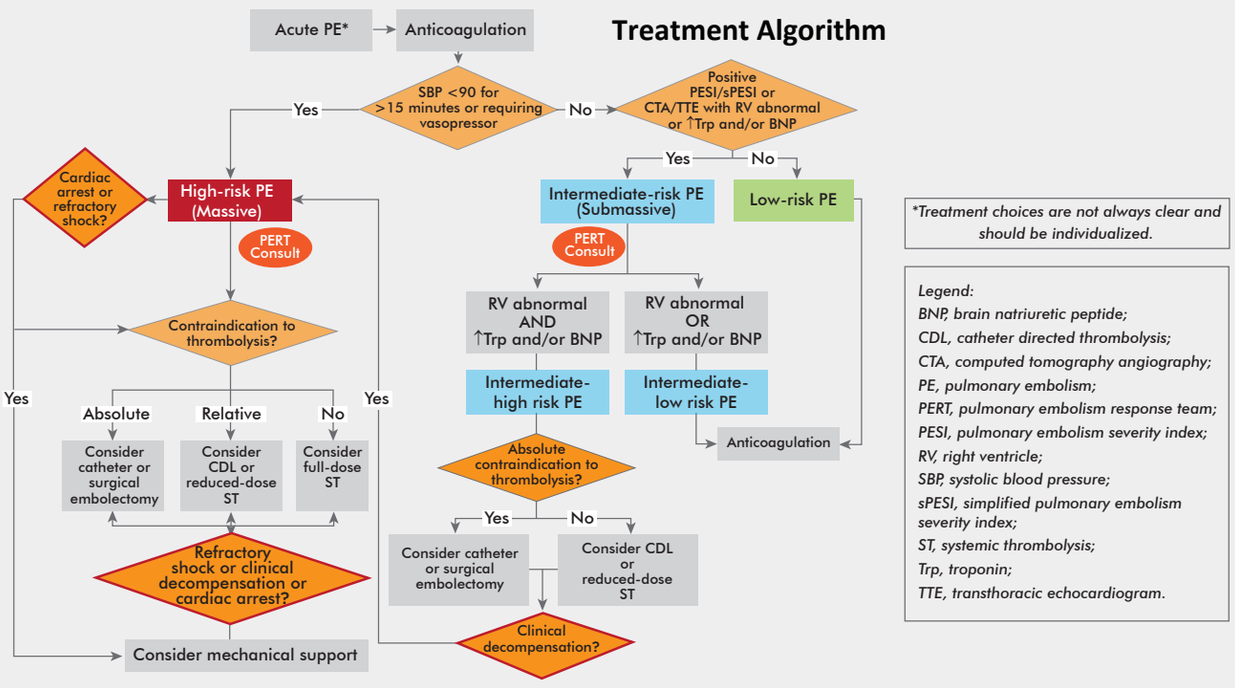
A lower extremity venous ultrasonography performed on day 7 after discharge showed a reduction of the thrombus in the right soleal vein (Figure 2).[5]

## Follow-up

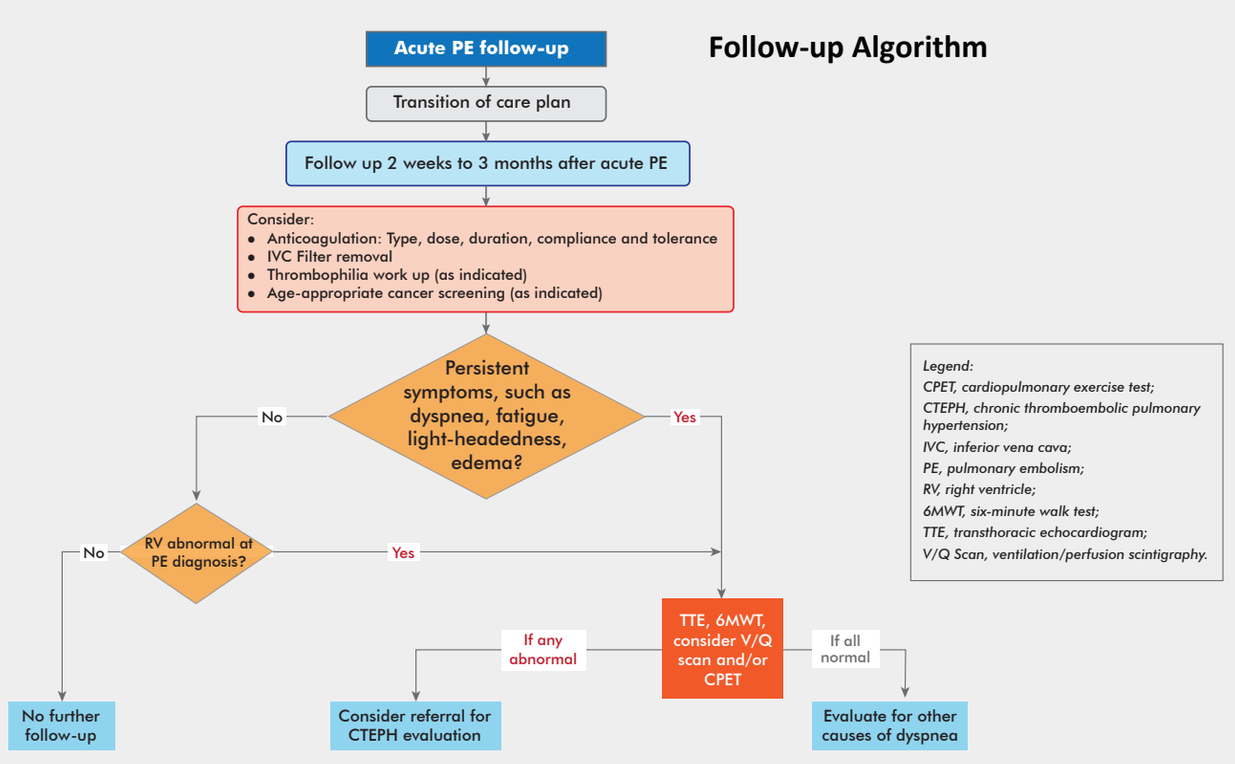
The patient was free of symptoms and signs of recurrent DVT during a 3-month follow-up visit (Figure 3).[5]



## Figure 2: Treatment algorithm of PE (PERT consortium)[5]




## Figure 3: PE follow-up algorithm[5]



## Discussion

Thrombosis is the second leading cause of death in patients with cancer and causes a substantial burden on the healthcare system.[6]

In patients with no preoperative DVT, it appears that both venous congestion and stasis start during the operation, and thereafter thrombi form in the deep veins. When PE occurs either during or just after surgery in such patients, the causes include the posture adopted during the operation, a long operation duration, the type of anesthesia used, and special dehydrate infusion control. When PE occurs in the late phase after surgery when the patient starts walking, the causes include the release of thrombus that formed in the early phase, the dehydrate infusion used postoperatively, the prolonged adoption of a supine position, and the postoperative hypercoagulative state. Therefore, the onset of PE can be divided into these two phases, and, in general, the development of PE can be attributed to two factors, namely venous stasis and hypercoagulability.[7]

A low-grade fever is not uncommon in PE, and a high fever, although rare, may occur. Fever need not be accompanied by pulmonary hemorrhage or infarction.[8]

Patients with cancer are generally considered at high risk of thromboembolism due to the hypercoagulability state. When such patients are posted for surgery, it becomes essential to evaluate their VTE risk based upon the Caprini risk assessment model (RAM) since the Caprini RAM is the preferred model for VTE risk assessment in surgical patients.[6,9] Anticoagulant prophylaxis in patients undergoing cancer surgery has reduced the incidence of VTE events by approximately one-half in placebo-controlled trials.[10]

Comprehensive management of VTE in patients with cancer includes both the identification of patients who are most likely to benefit from pharmacological prophylaxis and the effective treatment to reduce the risk of VTE recurrence and mortality.[1]

In the above case, as per the Caprini score, the patient had the highest risk for VTE (Table 1).[11] The major risk factors for VTE were higher age, malignancy, and prolonged major surgery [In this case, a total score of 9]. The incidence of DVT in such patients is about 40%–60%, and hence, thromboprophylaxis is recommended. VTE prophylaxis is given to most patients with cancer during their hospitalization but is discontinued after discharge from the hospital.[12]

According to the International Initiative on Thrombosis and Cancer (ITAC) 2022 guidelines, low molecular weight heparin (LMWH) is recommended for the initial treatment of established VTE in patients with cancer when creatinine clearance is ≥30 mL/min (grade 1A). The use of LMWH once daily (when creatinine clearance is ≥30 mL/min) or low-dose unfractionated heparin thrice daily is recommended to prevent postoperative VTE in patients with cancer. Pharmacological prophylaxis should be started 2–12 h preoperatively and continued for at least 7–10 days.[6]

The possible hurdles to providing extended VTE prophylaxis include perceived cost, outpatient medication administration, and lack of awareness of evidence-based guidelines.[4] The implementation of pharmacological thromboprophylaxis is poor in clinical practice due to various physician-related factors, such as lack of awareness about the extent of risk of VTE, lack of confidence and motivation to alter the existing practice patterns, increased risk of bleeding, and multiple guidelines with varied protocols.[8]

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**Table 1: Caprini risk factors and score risk category association[11]**

| Each risk factor = 1 point | Each risk factor = 2 points | Each risk factor = 3 points |
|---|---|---|
| • Age 40–59 years<br>• Minor surgery planned<br>• BMI ≥30 kg/m$^2$<br>• History of prior major surgery (<1 month)<br>• Swollen legs (current)<br>• Varicose veins<br>• Sepsis (<1 month)<br>• Abnormal pulmonary function (COPD)<br>• Acute myocardial infarction<br>• Congestive heart failure (<1 month)<br>• History of IBD<br>• Medical patients currently at bed rest | • Age 60–74 years<br>• Arthroscopic surgery<br>• Major open surgery (>45 minutes)<br>• Laparoscopic surgery (>45 minutes)<br>• Prior cancer (except non-melanoma skin cancer)<br>• Present cancer (except breast and thyroid)<br>• Confined to bed (>72 hours)<br>• Immobilizing plaster cast<br>• Central venous access | • Age ≥75 years<br>• History of VTE<br>• Family history of VTE<br>• Present chemotherapy<br>• Positive Factor V Leiden<br>• Positive prothrombin 20210A<br>• Positive lupus anticoagulant<br>• Elevated anticardiolipin antibodies<br>• Elevated serum homocysteine<br>• Heparin-induced thrombocytopenia<br>• Other congenital or acquired thrombophilias |
| **For women only (1 point each)** | **Caprini risk category based on total risk score** | **Each risk factor = 5 points** |
| • Pregnant of post-partum<br>• History of unexplained or recurrent spontaneous abortion<br>• Oral contraceptives or hormone replacement therapy | | • Major surgery lasting >6 hours<br>• Stroke (<1 month)<br>• Elective major lower extremity arthroplasty<br>• Hip, pelvis, leg fracture (<1 month)<br>• Acute spinal cord fracture or paralysis (<1 month)<br>• Multiple traumas (<1 month) |

| Total score | Category |
|---|---|
| 0–4 | Low |
| 5–8 | Moderate |
| ≥9 | High |

**Total score = 9**

BMI, body mass index; COPD, chronic obstructive pulmonary disease; IBD, irritable bowel disease; VTE, venous thromboembolism.

## Need for extended thromboprophylaxis in patients with cancer undergoing surgery

In Italy, a prospective study (@RISTOS study) of the incidence of VTE in 2,373 patients undergoing cancer surgery found that age (>60 years), previous VTE, anesthesia time (>2 hours), cancer stage, and length of bed rest (>4 days) were risk factors for VTE. The odds ratio of developing VTE in the presence of these risk factors was 2.6 to 6.0. The study highlighted the persistence of VTE risk after the perioperative period and showed that 40% of VTE events occurred more than 21 days after surgery. Additionally, antithrombotic prophylaxis was extended beyond 3 weeks after surgery in only 23% of patients, and almost half of the VTE events occurring later than 21 days took place after withdrawal of prophylaxis.[13]

Prospective studies have revealed that VTE is the leading cause of mortality at 30 days postoperatively in patients undergoing cancer surgery.[14]

Guidelines recommend that extended VTE prophylaxis be prescribed for patients undergoing abdominopelvic surgery for cancer (Table 2).[12]

**Table 2: Guideline recommendations for patients undergoing abdominopelvic surgery for cancer**

| ITAC (2022)[6] | ASCO (2019)[1] | NCCN (2015)[14] | ACCP (2012)[15] |
|---|---|---|---|
| Extended prophylaxis (4 weeks) with LMWH after major abdominal or pelvic surgery (laparotomy) is recommended in patients with cancer who have a high risk of VTE and low risk of bleeding.<br><br>The same recommendation can be applied for laparoscopic surgery. | Extended prophylaxis for up to 4 weeks after major open or laparoscopic abdominal or pelvic surgery for cancer is recommended in patients with high-risk features, such as restricted mobility, obesity, history of VTE, or additional risk factors. | Prophylaxis is recommended for up to 4 weeks postoperatively, particularly for high-risk abdominal or pelvic cancer surgery, such as:<br>♦ Prolonged anesthesia<br>♦ Previous VTE<br>♦ Advance cancer stage<br>♦ Immobility >4 days | For patients with high VTE risk undergoing abdominal or pelvic surgery who are not otherwise at high risk for bleeding, extended duration prophylaxis (4 weeks) with LMWH is recommended. |

ACCP, American College of Clinical Pharmacy; ASCO, American Society of Clinical Oncology; ITAC, International Initiative on Thrombosis and Cancer; LMWH, low molecular weight heparin; NCCN, National Comprehensive Cancer Network; VTE, venous thromboembolism.

Thus, it is emphasized that VTE is found in patients with a persistent fever after gastric cancer surgery. In this case, the chief complaint was fever, and the fever disappeared with an anticoagulant.

## Key Takeaways

- Patients with cancer are four to seven times more likely to develop VTE than patients without cancer.
- A low-grade fever is not uncommon in PE, and a high fever, although rare, may occur.
- Caprini is the preferred VTE risk assessment model for surgical patients.
- Patients with cancer, especially those undergoing surgery for cancer, are at extremely high risk for developing VTE.

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