

# Incidence of Venous Thromboembolic Events in Patients with Metastatic Pancreatic Adenocarcinoma Receiving Palliative Chemotherapy: A Retrospective Cohort Study

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## Abstract

**Introduction:** Pancreatic cancer is strongly associated with venous thromboembolism (VTE), contributing to significant morbidity and mortality. The aim of this study was to determine the incidence of venous thromboembolism (VTE) among patients with metastatic pancreatic adenocarcinoma receiving palliative chemotherapy at the Medical Oncology Department, Hassan II University Hospital, Fez. **Methods:** Retrospective cohort including 67 patients treated with FOLFIRINOX or gemcitabine from January 2021 to December 2023. Patients with prior VTE or on anticoagulation were excluded. Cumulative incidence of VTE was estimated considering death as a competing risk. **Results:** Mean age 63.5 years; male-to-female ratio 4:1. Tumors were mainly in the pancreatic head (65%). At follow-up, 46 patients had died, 6 were lost to follow-up, and 15 were alive. VTE occurred in 28 patients (41.8%): isolated DVT 42.9%, isolated PE 35.7%, combined PE + DVT 21.4%. Cumulative incidence was 26.9% at 12 months and 38.8% at 36 months, with most events occurring during the first year. **Conclusion:** VTE is common and occurs early in patients with metastatic pancreatic adenocarcinoma under palliative chemotherapy, highlighting the need for appropriate prophylactic strategies.

## Keywords

Metastatic Pancreatic Adenocarcinoma, Venous Thromboembolism, Palliative Chemotherapy, Incidence

## 1. Introduction

Pancreatic cancer is highly lethal and represents a major cause of cancer-related mortality [1]. The occurrence of a first venous thromboembolic (VTE) event is associated with cancer in approximately 20% of cases [2]. VTE in cancer patients is defined as the occurrence of deep vein thrombosis (DVT) or pulmonary embolism (PE), confirmed by standardized imaging techniques [3]. As early as 1938, autopsy data first highlighted a significant association between VTE and pancreatic cancer, reporting PE in 57% of patients with pancreatic cancer, compared to 15% - 25% in patients with other malignancies [4]. In another study, autopsy of 441 patients with pancreatic cancer revealed fatal PE in 14% of cases. Additionally, fatal or non-fatal PE was observed in 42% of patients with metastatic disease [5]. Moreover, chemotherapy further increases the risk of VTE [6].

## 2. Materials and Methods

This was a retrospective, descriptive, observational cohort study including 67 patients aged 18 years or older with histologically confirmed metastatic pancreatic adenocarcinoma, who received palliative chemotherapy at the Medical Oncology Department, Hassan II University Hospital, Fez, between January 1, 2021, and December 31, 2023. All patients received first-line chemotherapy tailored to their general condition (FOLFIRINOX or gemcitabine). Patients with a prior venous thromboembolic (VTE) event before the diagnosis of metastatic disease or receiving anticoagulant therapy before that date were excluded. No patient received primary prophylaxis during the follow-up period. Each patient was followed from the date of metastatic diagnosis until the first incident VTE event, death, loss to follow-up, or December 31, 2023, whichever occurred first. The primary outcome was the occurrence of an incident VTE confirmed using standardized imaging techniques, including venous Doppler ultrasonography for deep vein thrombosis (DVT) and CT pulmonary angiography for pulmonary embolism (PE). Death without VTE was considered a competing risk, as it precludes the occurrence of the event of interest. Cumulative incidence of VTE was estimated using the cumulative incidence function (CIF) to account for this competing risk. Ninety-five percent confidence intervals were calculated, and all statistical analyses were performed using the SPSS software. This retrospective study was conducted in accordance with applicable local and international ethical standards. Patient data were anonymized to ensure confidentiality, and no direct contact with patients was required.

## 3. Results

The cohort included 67 adult patients with metastatic pancreatic adenocarcinoma who received palliative chemotherapy between January 1, 2021, and December 31, 2023. The mean age was 63.5 years ( $\pm 7.2$ ), and the population was predominantly male, with a male-to-female ratio of 4:1 (54 men, 13 women). The majority of patients (59.7 %) had few or no comorbidities, and 8% had a family history of

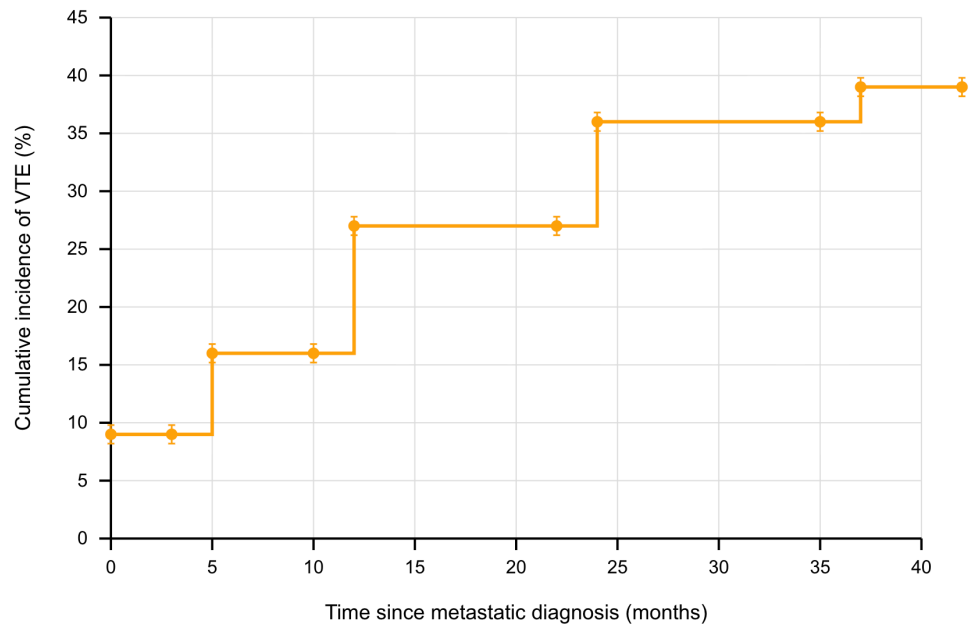
cancer. Tumors were mainly located in the pancreatic head (65.7%), followed by the body (25.4%) and tail (9%). Most patients presented with hepatic metastases (59.7%) and/or pulmonary metastases (22.4%) at the time of diagnosis, while 17.9% had concurrent hepatic and pulmonary metastases. The main presenting symptoms were abdominal pain (65%), weight loss (45%), and jaundice (30%), with some patients presenting multiple symptoms simultaneously. All patients received first-line chemotherapy tailored to their performance status, either FOLFIRINOX or gemcitabine (**Table 1**).

**Table 1.** Baseline characteristics of patients.

Characteristic	Number of patients (n = 67)	Pourcentage (%)
<b>Sex</b>		
Male	54	80.6
Female	13	19.4
<b>Tumor location</b>		
Head	44	65.7
Body	17	25.4
Tail	6	9.0
<b>Comorbidities</b>		
None or Midl	40	59.7
Moderate/Severe	27	40.3
<b>First-line chemotherapy</b>		
Folfirinox	30	44.8
Gemcitabine	37	55.2
<b>Metastatic site</b>		
Liver	40	59.7
Lung	15	22.4
Liver + Lung	12	17.9

At follow-up, 46 patients (68.7%) had died, 6 (9%) were lost to follow-up, and 15 (22.3%) were alive at the end of the study (December 31, 2023). The cumulative incidence of VTE, estimated using the cumulative incidence function (CIF) to account for death as a competing risk, was 9% at 3 months, 16.4% at 6 months, 26.9% at 12 months, 35.8% at 24 months, and 38.8% at 36 months (**Figure 1**).

Most events occurred within the first year following diagnosis, after which the incidence plateaued. Among the 28 patients (41.8%) who developed VTE during follow-up, 12 (42.9%) had isolated Deep Vein Thrombosis (DVT), 10 (35.7%) had isolated Pulmonary Embolism (PE), and 6 (21.4%) had combined PE + DVT (**Table 2**).



**Figure 1.** Cumulative incidence function (CIF) of venous thromboembolism (VTE) considering death as a competing risk.

**Table 2.** Distribution of thromboembolic events during follow-up (n = 28).

Type of Thromboembolic Event	Number of Patients (n = 28)	Percentage (%)
Isolated Deep Vein Thrombosis (DVT)	12	42.9
Isolated Pulmonary Embolism (PE)	10	35.7
Combined PE + DVT	6	21.4

All diagnosed VTE events were initially treated with low-molecular-weight heparin (LMWH). A switch to a direct oral anticoagulant (DOAC) was introduced in some patients when clinically appropriate. Overall, the study population was predominantly male, with a mean age of 63.5 years and tumors mainly located in the pancreatic head. VTE events occurred primarily within the first year after diagnosis, highlighting the need for early and targeted surveillance in high-risk patients.

#### 4. Discussion

In our cohort, the cumulative incidence of VTE was 9% at 3 months, 16.4% at 6 months, 26.9% at 12 months, 35.8% at 24 months, and 38.8% at 36 months. These findings confirm the particularly high thrombotic risk in this population, not only during the early months of treatment but also over the long term. Our data are consistent with previously published studies. A French study reported a cumulative incidence of 8% at 3 months and 19% at 12 months, which is close to our short-term results [7]. A Korean study found 4.7% at 3 months, 9.9% at 6 months, and 16.9% at 12 months, slightly lower than our cohort, possibly due to differences in population characteristics or treatment regimens [8].

Some differences with the existing literature may also be influenced by the type of chemotherapy used, the imaging protocols applied, and the absence of primary prophylaxis. Due to the limited number of events, it was not possible to explore these factors in greater detail, which represents a limitation of our study.

These findings reinforce the notion that VTE occurrence in this context is frequent and clinically significant. Our results highlight the need for intensified surveillance from the start of treatment, particularly during the first 6 - 12 months when the risk is highest.

International guidelines, such as those from the American Society of Clinical Oncology (ASCO) and the International Initiative on Cancer and Thrombosis (ITAC), emphasize the importance of primary prophylaxis in this high-risk population. According to the updated ASCO guidelines, VTE prophylaxis is recommended in ambulatory patients with advanced or metastatic pancreatic cancer receiving chemotherapy, in the absence of contraindications to bleeding. Options include low molecular weight heparin (LMWH) or direct oral anticoagulants (DOACs) such as apixaban or rivaroxaban. These recommendations are based on high-quality evidence and strong recommendations [3].

Similarly, ITAC guidelines recommend the use of LMWH or DOACs (apixaban or rivaroxaban) for primary prophylaxis in ambulatory patients with advanced or metastatic pancreatic cancer receiving anticancer therapy, provided bleeding risk is low. These recommendations are also supported by high-quality evidence [9].

Finally, despite the strength of our prolonged follow-up, our study has certain limitations: it is single-center, includes a relatively small sample size, and does not stratify patients according to chemotherapy regimens. This is a descriptive observational study, and the primary objective was to report the incidence of VTE. Future studies could explore the impact of different therapeutic protocols on VTE risk, as well as optimize prophylaxis based on validated risk scores. Due to the limited number of events (28 VTE), it was not possible to perform a robust multivariate analysis to identify independent factors associated with VTE occurrence. In addition, the retrospective design of the study carries a risk of under-detecting VTE, particularly asymptomatic pulmonary embolisms. The single-center nature of the study also limits the generalizability of the findings. Larger prospective studies would be necessary to confirm these observations.

## 5. Conclusion

Our study highlights a substantial incidence of venous thromboembolic events (VTE) in patients with metastatic pancreatic adenocarcinoma receiving palliative chemotherapy, with most events occurring within the first year after diagnosis. These findings emphasize the persistently high thrombotic risk in this population and support the need for early and prolonged surveillance, as well as targeted prophylactic strategies, including anticoagulation, to reduce morbidity, prevent complications, and maintain continuity of anticancer therapy. Despite the single-center design and limited sample size, these results provide valuable data to guide

VTE management in patients with metastatic pancreatic cancer.

### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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