ANALYSIS OF PROGNOSTIC FACTORS FOR SURVIVAL IN PATIENTS WITH METASTATIC PANCREATIC CANCER RECEIVING FIRST-LINE mFOLFIRINOX AT K HOSPITAL

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ABSTRACT

Objective: Evaluation of prognostic factors associated with survival outcomes in patients with metastatic pancreatic cancer receiving first-line mFOLFIRINOX.

Methods: A retrospective and prospective study on 36 patients diagnosed with metastatic pancreatic cancer at K Hospital were treated with the first-line mFOLFIRINOX regimen. The primary endpoints were overall survival (OS) and progression-free survival (PFS), with analyses of factors associated with OS and PFS. Secondary endpoints included response rate, treatment-related toxicity, and the rate of treatment interruption.

Results: The median follow-up was 15.6 months (95% CI, 3.8–27.3). The median progression-free survival was 6.7 months, and the median overall survival was 12.5 months. In univariate analysis, age <60 and ECOG performance status (PS) 0 were associated with prolonged progression-free survival (PFS) and overall survival (OS). ECOG PS 0 was identified as an independent prognostic factor for overall survival. The overall response rate (ORR) was 30.6 %, disease control rate (DCR) was 66.6%. Grade 3 or 4 toxicities were mainly hematologic, including neutropenia in 33.4% of patients and thrombocytopenia in 2.8%

Conclusion: The mFOLFIRINOX regimen demonstrated treatment efficacy. ECOG PS 0 was identified as favorable prognostic factors associated with prolonged survival in patients with metastatic pancreatic cancer.

Keyword: Pancreatic cancer, mFOLFIRINOX, chemotherapy, metastatic, prognostic factors.

1. INTRODUCTION

Pancreatic adenocarcinoma arises from the epithelial cells of the pancreatic tissue [1]. It ranks as the 12th most common cancer worldwide, with 495,773 new cases (2.6%) diagnosed annually. Pancreatic cancer is also the 7th leading cause of cancer-related mortality globally, accounting for 466,003 deaths (4.7%) [2].

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Surgical resection remains the only potentially curative treatment. However, most patients are diagnosed at an advanced stage, and only 15–20% are eligible for surgery. Systemic chemotherapy is the mainstay of treatment for patients with metastatic pancreatic cancer. The phase III PRODIGE 4/ACCORD 11 trial by Thierry Conroy et al. demonstrated that FOLFIRINOX significantly improved overall survival, progression-free survival, and quality of life compared with Gemcitabine, and has since become the standard first-line treatment for metastatic pancreatic cancer. However, high rates of neutropenia and febrile neutropenia were reported (45.7% and 5.4%, respectively) [3]a four-drug combination chemotherapy regimen was associated with objective responses in more than 30% of patients and increased survival by more than 4 months, as compared with standard gemcitabine. Pancreatic adenocarcinoma was the fourth leading cause of death from cancer in the United States in 2010,1 and it carries a grim prognosis: the 5-year survival rate is 6% in Europe and the United States.1,2 Gemcitabine became the reference regimen for advanced pancreatic cancer after a randomized trial showed significant improvement in the median overall survival as compared with fluorouracil administered as an intravenous bolus (5.6 vs. 4.4 months, P=0.002.

Dose reductions of Irinotecan and Fluorouracil bolus have been shown to reduce toxicity while maintaining efficacy, as demonstrated in a study by Masato Ozaka et al. (2018), evaluating modified FOLFIRINOX (mFOLFIRINOX) in patients with metastatic pancreatic cancer [4].

In Vietnam, the mFOLFIRINOX regimen has been increasingly adopted as a first-line treatment for metastatic pancreatic cancer due to its demonstrated efficacy. However, this is an intensive regimen associated with considerable toxicity, requiring patients to have good performance status and treatment tolerance. Therefore, appropriate patient selection—identifying those who can tolerate and truly benefit from this regimen—is of significant clinical importance. Based on this rationale, this study was conducted to evaluate factors associated with survival outcomes in patients with metastatic pancreatic cancer receiving first-line treatment with the mFOLFIRINOX regimen.

2. METHODS

2.1. Subjects

Patients with metastatic pancreatic cancer who received first-line treatment with the modified FOLFIRINOX (mFOLFIRINOX) regimen at K Hospital between January 2019 and June 2025.

Inclusion criteria: Patients were eligible if they met the following criteria: histologically confirmed metastatic pancreatic adenocarcinoma; age ≥18 years; ECOG 0–1; adequate hepatic, renal, and hematologic function; at least one measurable lesion according to RECIST 1.1; and receipt of at least four cycles of mFOLFIRINOX.

Exclusion criteria: Patients were excluded if they had received prior chemotherapy or radiotherapy; had grade ≥2 peripheral neuropathy; had a history of other malignancies; or had severe medical or surgical comorbidities associated with a high risk of early mortality.

2.2. Methods

Study design: This was a retrospective–prospective descriptive study. Patients treated between January 2019 – March 2025 were identified retrospectively, while those treated between April 2025 -June 2025 were enrolled prospectively. The final follow-up and study cut-off date was November 1,2025.

Sample size and sampling method: Consecutive sampling was applied, including all eligible patients (convenience sampling).

Treatment protocol: Patients received the mFOLFIRINOX regimen every 2 weeks, consisting of Oxaliplatin 85 mg/m² administered as a 120-minute intravenous infusion on day 1; Leucovorin 400 mg/m² administered intravenously over 120 minutes on day 1; Irinotecan 150 mg/m² administered intravenously over 90 minutes; and Fluorouracil administered as a continuous

intravenous infusion over 46 hours on days 1–2. Prophylactic granulocyte colony-stimulating factor (G-CSF) (PegGrafeel) was administered following chemotherapy to prevent neutropenia.

Treatment could be delayed by at least 7 days beyond the scheduled cycle under the following conditions: (1) any adverse event of grade ≥3; (2) persistent grade 2 toxicity over two consecutive assessments despite supportive care; or (3) first occurrence of grade 2 toxicity in patients aged ≥70 years.

Assessment of treatment efficacy and toxicity: Tumor response was evaluated every four cycles according to RECIST 1.1[5]. Overall survival (OS) was defined as the time from initiation of chemotherapy to death from any cause. Progression-free survival (PFS) was defined as the time from initiation of chemotherapy to disease progression or death. Adverse events were recorded and graded according to CTCAE v5.0. Treatment interruption was defined as discontinuation of therapy for at least one full chemotherapy cycle (≥14 days) between two treatment courses.

Data analysis: Data was collected and analyzed using SPSS version 26.0. Survival outcomes (OS and PFS) were estimated using the Kaplan–Meier method and compared between groups using the log-rank test. Factors associated with survival were evaluated using Cox proportional hazards regression models. Clinical and paraclinical variables were first assessed in univariate analysis; variables with statistical significance ($p < 0.05$) or clinical relevance were included in multivariate analysis to identify independent prognostic factors. Results were reported as hazard ratios (HRs) with 95% confidence intervals (CIs).

3. RESULTS

3.1. Patient characteristics

Between January 2019 and June 2025, a total of 36 patients were included in this ambispective cohort, comprising 31 retrospective and 5 prospective cases. The median follow-up time was 15.6 months (95% CI, 3.8–27.3). A total of 25 patients (69.4%) had an ECOG performance status of 0. The primary tumor was most commonly located in the head of the pancreas (58.3%). 8 patients presented with biliary obstruction prior to treatment. The most common metastatic site was the liver (66.7%), followed by the peritoneum and lymph nodes (each 22.2%), while lung and other sites were less frequent. Elevated carbohydrate antigen 19-9 (CA19-9) levels >1000 U/mL were observed in 33.3% of patients. Detailed patient characteristics are summarized in Table 1.

Table 1: Patient Characteristics

Table 1 Demographic and baseline characteristics of patients		
Characteristics	N = 36	
	No. of patients	%
Median age at diagnosis in years (range)	57 (27-74)	
Sex		
Male	22	61.1
Female	14	38.9
ECOG performance status		
0	25	69.4
1	11	30.6
Pancreatic tumor location		
Head	21	58.3
Body	6	16.7
Tail	9	25
Intervention for biliary obstruction		
Biliary stent	3	8.3
Percutaneous transhepatic biliary drainage	3	8.3
Operative biliary-enteric bypass	2	5.6
No	28	77.8
No. of metastatic sites involved		
1	29	80.6
2	5	13.9
3	2	5.6

Table 1 Demographic and baseline characteristics of patients		
Prior surgery		
No	29	80.6
Yes	7	19.4
CA19-9 (U/ml)		
Median (range)	258.25 (0.8-47430)	
<37 U/ml	13	36.1
37≤1000 U/ml	11	30.6
≥1000 U/ml	12	33.3
*ECOG, Eastern Cooperative Oncology Group; CA19-9, Carbohydrate antigen 19-9		

3.2. Treatment adherence

The median number of treatment cycles was 9 (range, 4–34), with 20 patients (55.6%) receiving more than 8 cycles. Dose reductions were required in 5 patients during treatment. Treatment interruption occurred in 14 patients (38.9%), of whom 7 were switched to a 3-week cycle after experiencing grade 2 toxicity for three consecutive cycles.

Neutropenia was the most common cause of treatment interruption. 2 patients discontinued treatment due to toxicity. Among the 29 patients who experienced disease progression on first-line therapy, 25 (86.2%) received second-line treatment, with gemcitabine-based regimens being the most commonly used (Total 27 patients).

3.3. Treatment outcomes

Table 2: Treatment response according to RECIST 1.1

Treatment response	N=36	
	n	%
Complete response (CR)	0	0
Partial response (PR)	11	30.6
Stable disease (SD)	13	36.1
Progressive disease (PD)	12	33.3
Overall response rate (ORR)	11	30.6
Disease control rate (DCR)	24	66.7
*ORR = CR + PR, DCR = CR + PR +SD		

Comment: The rates of partial response, stable disease, and progressive disease were 30.6%, 36.1%, and 33.3%, respectively. The overall response rate (ORR) was 30.6%, and the disease control rate (DCR) was 66.7%.

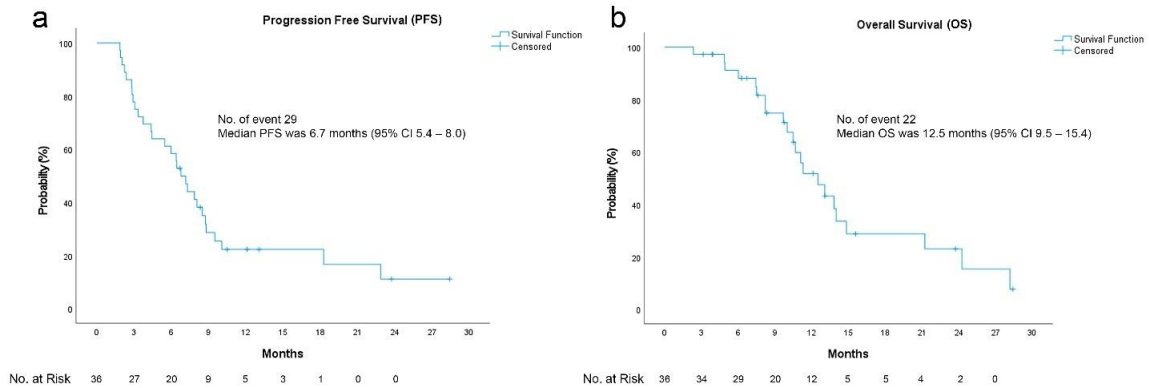

Figure 1. Kaplan-Meier curves for progression-free survival (PFS) (a) and overall survival (OS) (b).

Comment: The median follow-up was 15.6 months (95% CI, 3.8–27.3). Disease progression was observed in 29 patients, and 22 patients had died at the time of analysis. The median progres-

sion-free survival (PFS) was 6.7 months (95% CI, 5.4–8.0), and the median overall survival (OS) was 12.5 months.

3.4. Treatment-related toxicity

Table 3: Treatment-related adverse events according to CTCAE v5.0

N=36		Grade 1/2		Grade 3/4	
		n	%	n	%
Hematologic	Anemia	19	52.7	2	5.6
	Febrile neutropenia			0	0.0
	Neutropenia	11	30.6	12	33.4
	Thrombocytopenia	17	42.2	1	2.8
Non-hematologic	Increased liver enzymes	21	58.3	2	5.6
	Bilirubin	0	0.0	3	8.4
	Diarrhea	10	27.8	2	5.6
	Fatigue	17	47.3	1	2.8
	Vomiting	24	66.6	3	8.4
	Peripheral neuropathy	13	36.1	2	5.6

Comment: Most adverse events were grade 1–2. Grade 3–4 toxicities were predominantly hematologic, including neutropenia (33.4%), thrombocytopenia (2.8%), and anemia (5.6%), with no cases of febrile neutropenia observed during treatment. Non-hematologic grade 3–4 toxicities included elevated liver enzymes (5.6%), hyperbilirubinemia (8.3%), diarrhea (5.6%), fatigue (2.8%), and peripheral neuropathy (5.6%).

3.5. Prognostic factor analysis for survival

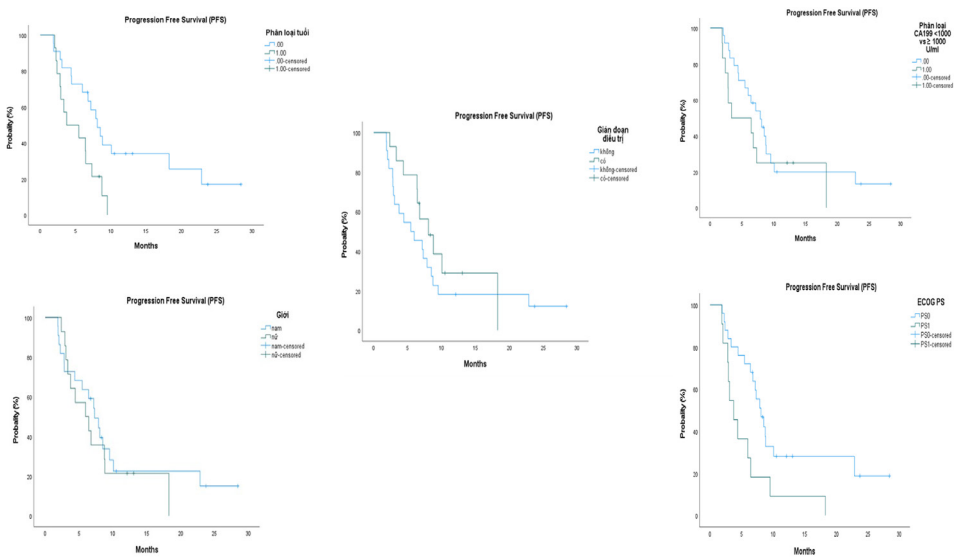

Figure 2. Kaplan–Meier estimates of progression-free survival (PFS) according to prognostic factors

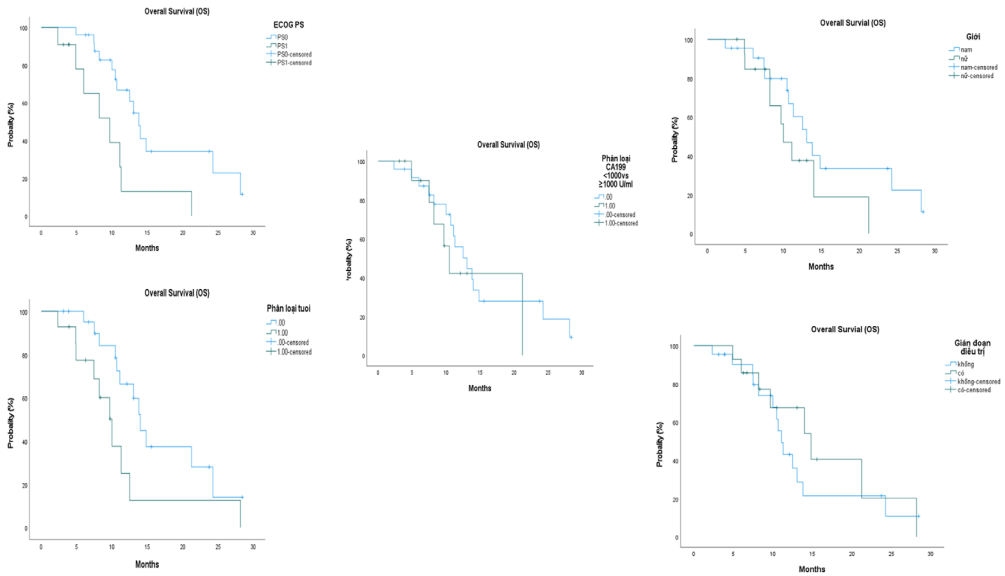

Figure 3. Kaplan–Meier curves of overall survival (OS) stratified by prognostic factors

Table 4. Univariate and multivariate analyses of factors associated with progression-free survival (PFS)

Variables	HR (95%CI), Univariable Cox	p	HR (95%CI) Multivariable Cox	p
Age < 60 vs ≥60	0.37 (0.17-0.83)	0.015	0.45 (0.19-1.03)	0.058
Male vs Female	0.81 (0.38-1.71)	0.577	-	-
ECOG PS 0 vs 1	0.3 (0.18-0.84)	0.017	0.51(0.23-1.18)	0.116
CA19-9 <1000 U/ml	0.67 (0.31-1.47)	0.325	0.75 (0.34-1.67)	0.48
TI Yes or No	0.68 (0.31-1.48)	0.335	-	-
Multivariable Cox regression model				0.016
* ECOG PS, Eastern Cooperative Oncology Group Performance Status; TI, Treatment interruption; HR, Hazard ratio; CI, Confidence interval				

Comment: Univariate analysis using the Cox regression demonstrated that age <60 years and ECOG performance status (PS) 0 were associated with prolonged progression-free survival (PFS) ($p < 0.05$). The multivariable Cox regression model was statistically significant, indicating the prognostic value of the combined variables. However, in the multivariable analysis, no individual variable reached statistical significance. Age <60 years showed a trend toward longer PFS ($p = 0.058$).

Table 5. Univariate and multivariable analyses of factors associated with overall survival (OS)

Variables	HR (95%CI), Univariable Cox	p	HR (95%CI) Multivariable Cox	p
Age < 60 vs ≥60	0.39 (0.16-0.94)	0.036	0.43 (0.17-1.08)	0.073
Male vs Female	0.54 (0.22-1.33)	0.186	-	-

ECOG PS 0 vs 1	0.31 (0.12-0.78)	0.012	0.36 (0.13-0.98)	0.047
CA19-9 <1000 U/ml	0.71 (0.28 -1.88)	0.49	0.85 (0.29-2.46)	0.773
TI Yes or No	0.72 (0.30-1.74)	0.469	-	-
Multivariable Cox regression model				0.015
* ECOG PS, Eastern Cooperative Oncology Group Performance Status; TI, Treatment interruption; HR, Hazard ratio; CI, Confidence interval				

Comment: In the univariate Cox regression, the patient group with age <60 years and ECOG performance status (PS) 0 were associated with prolonged overall survival (OS. In the multivariable Cox regression analysis, only ECOG PS 0 remained an independent prognostic factor for OS (HR 0.36; 95% CI, 0.13–0.98; p = 0.047).

4. DISCUSSION

In this study, the mFOLFIRINOX regimen demonstrated treatment efficacy in patients with metastatic pancreatic cancer in Vietnam, with median progression-free survival (PFS) and overall survival (OS) of 6.7 months (95% CI, 5.4–8.0) and 12.5 months (95% CI, 9.5–15.4), respectively. The median PFS was comparable to that reported in the phase III PRODIGE 4/ ACCORD 11 trial (6.7 vs 6.4 months; 95% CI, 5.5–7.2), while the median OS in our study showed a trend toward improvement (12.5 vs 11.1 months; 95% CI, 9.0–13.1)[6].

Compared with the study by Masato Ozaka et al. conducted in an Asian population, both PFS and OS in our study were slightly longer (6.7 vs 5.5 months [95% CI, 4.1–6.7] and 12.5 vs 11.2 months, respectively) [4]. Although these differences are modest, they may still be clinically meaningful in the context of the poor prognosis associated with pancreatic cancer.

Variations in survival outcomes across studies may be related to differences in treatment strategies and supportive care. In our study, all patients received prophylactic peg filgrastim from the initiation of treatment. In addition, a flexible treatment strategy was applied, including treatment delays or interruptions in response to toxicity, with patients allowed an additional 7-day delay beyond the standard cycle when necessary. These measures may have contributed to improved treatment tolerance and prolonged exposure to triplet chemotherapy.

In subgroup analysis, median OS tended to be longer in patients with treatment interruption compared with those without (14.1 months [95% CI, 8.5–21.1] vs 11.1 months [95% CI, 9.9–12.3]).

Univariate analyses identified age <60 years and ECOG performance status (PS) 0 as factors associated with prolonged survival, with consistent findings across log-rank testing and univariate Cox regression. This consistency strengthens the reliability of these results and supports their prognostic significance. In multivariable analysis, ECOG PS 0 was identified as an independent prognostic factor for overall survival, consistent with previous studies demonstrating the prognostic importance of performance status in pancreatic cancer [7-9].

Although other individual variables did not reach statistical significance, the overall multivariable Cox model remained significant ($p < 0.05$), suggesting that clinical factors—including age, ECOG PS, and biological markers—may have a cumulative effect on prognosis rather than acting independently. In clinical practice, younger age (<60 years) and good performance status (ECOG 0) reflect better overall patient condition and fewer comorbidities, which may enhance tolerance to intensive chemotherapy

regimens. Combined with a flexible treatment strategy, these factors may contribute to improved survival outcomes.

The toxicity profile of mFOLFIRINOX in this study was generally consistent with previous reports, with an acceptable rate of grade 3–4 neutropenia and no cases of febrile neutropenia observed. Compared with the PRODIGE 4/ ACCORD 11 trial and other Asian studies[4, 6], the incidence of hematologic toxicity appeared lower, possibly due to routine use of G-CSF prophylaxis and adaptive treatment modifications. However, the overall toxicity burden remains considerable, underscoring the importance of appropriate patient selection in clinical practice.

This study has several limitations. The single-center ambispective design may introduce selection bias and limit the generalizability of the findings. The relatively small sample size reduces the statistical power of multivariable analyses. Additionally, some potentially relevant factors, such as comorbidities and quality of life, were not fully assessed. Differences in patient accrual periods may also introduce temporal bias in treatment practices.

5. CONCLUSION

The mFOLFIRINOX regimen demonstrated clinical efficacy in patients with metastatic pancreatic cancer. Good performance status (ECOG PS 0) was identified as favorable prognostic factors associated with improved survival outcomes.

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