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Prognostic value of CA 19-9 elimination rate for mortality in metastatic pancreatic cancer

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MAIN POINTS

- The CA 19-9 elimination rate is a strong prognostic biomarker in metastatic pancreatic cancer.
- Patients with a high elimination rate have significantly longer overall survival.
- CA 19-9 kinetics provide more informative risk stratification than baseline CA 19-9 levels alone.
- Dynamic biomarker monitoring can complement radiologic response in treatment evaluation.

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ABSTRACT

Aim: To evaluate the prognostic value of the CA 19-9 elimination rate on survival in patients with metastatic pancreatic cancer.

Materials and Methods: This single-center retrospective cohort study included 103 adult patients with metastatic pancreatic ductal adenocarcinoma who received systemic therapy. The CA 19-9 elimination rate was calculated using baseline and 3-month values. The optimal cut-off value was determined using maximally selected rank statistics. Overall survival was analyzed using the Kaplan–Meier method and compared using the log-rank test.

Results: The mean age of the patients was 64±10.1 years, and the overall mortality rate during follow-up was 87.4%. No significant differences were observed between mortality groups with respect to demographic, clinical, or pathological characteristics (all p>0.05). The optimal cut-off value for the elimination rate (ER) was 2.33 (ER $\geq$ 2.33: high elimination; < 2.33: low elimination). Median overall survival was 25 months (95% CI: 17–31) in the high-elimination group and 8 months (95% CI: 7–14) in the low-elimination group (p = 0.043). The 12-, 36-, and 60-month survival rates were 80.4%, 18.3%, and 11% in the high-elimination group, compared with 37.6%, 2.2%, and 0% in the low-elimination group.

Conclusion: The CA 19-9 elimination rate is a significant prognostic biomarker for survival in patients with metastatic pancreatic cancer. A higher elimination rate is associated with improved short- and long-term survival outcomes, suggesting its potential utility for risk stratification and for assessing treatment response in clinical practice.

Keywords: Pancreatic cancer, CA 19-9, Elimination rate, Metastatic disease, Prognostic biomarker

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INTRODUCTION

Pancreatic cancer remains one of the most lethal malignancies worldwide and continues to pose a major challenge for healthcare systems. According to recent global cancer statistics, more than 450,000 new cases are diagnosed each year, with incidence and mortality rates showing substantial geographic variation [1,2]. The highest rates are observed in Europe and North America, whereas much lower rates are reported in Southeast Asia. These differences are largely explained by variations in demographic structure, environmental exposures, lifestyle factors, and access to diagnostic facilities [3]. Because mortality closely follows incidence, pancreatic cancer ranks among the leading causes of cancer-related death globally [1,4].

Despite ongoing progress in medical oncology, long-term survival for pancreatic cancer remains poor. Five-year survival rates are below 10%, largely because most patients are diagnosed at an advanced stage when curative treatment is no longer possible. Clinical outcome is influenced not only by disease stage but also by tumor biology, molecular features, and patient-related factors such as functional status and comorbidities [5,6]. These elements together determine treatment tolerance, response to therapy, and overall prognosis.

Carbohydrate antigen 19-9 (CA 19-9) is the most widely used serum biomarker in pancreatic cancer. Elevated CA 19-9 is detected in approximately four out of five patients, making it a useful marker for monitoring disease activity during treatment and follow-up. However, CA 19-9 lacks tumor speci-

ficity and may be increased in benign biliary disease, liver dysfunction, and other gastrointestinal malignancies, which limits its value for screening or early diagnosis [7].

For this reason, increasing attention has been directed toward the dynamic behavior of CA 19-9 rather than its absolute value at a single time point. Changes in CA 19-9 during systemic therapy may better reflect treatment response and disease activity. Several clinical studies have suggested that the pattern and speed of CA 19-9 decline after therapy initiation are more closely associated with patient outcomes than baseline levels alone.

Based on this concept, we investigated whether the CA 19-9 elimination rate, calculated using baseline and three-month measurements, could serve as a prognostic indicator of mortality in patients with metastatic pancreatic ductal adenocarcinoma.

MATERIALS AND METHODS

Study design and patients

This single-center, retrospective cohort study used the medical oncology archive and digital patient record systems at a tertiary oncology center. Patients aged 18 years or older who were diagnosed with metastatic pancreatic ductal adenocarcinoma (PDAC) and who initiated systemic therapy between 2016 and 2025 were evaluated.

This study was approved by the Göztepe Prof. Dr. Süleyman Yalçın Training and Research Hospital Non-Interventional Clinical Research Ethics Committee (date: January 8, 2026; approval no: 2026/0009).

A total of 318 patient records were screened. Based on predefined eligibility criteria, 103 patients were included in the final analysis. Sample size estimation was performed assuming a type I error of 0.05, a power of 80%, and an effect size (d) of 0.5, resulting in a minimum required sample size of 102 patients.

Inclusion criteria

Patients meeting all of the following criteria were included:

- Age: ≥18 years at diagnosis
- Diagnosis: Histopathologically confirmed pancreatic ductal adenocarcinoma
- Stage: Radiologically confirmed metastatic disease (stage IV) at diagnosis or during follow-up
- Treatment and follow-up: Receipt of at least one line of systemic therapy with available clinical follow-up data
- CA 19-9 measurements:
  - Available baseline CA 19-9 level before treatment initiation
  - At least one follow-up CA 19-9 measurement after treatment initiation
  - Measurements performed using the same laboratory or a standardized method
- Elimination rate calculability: Availability of paired CA 19-9 time-value data to allow calculation of elimination rate
- Outcome data: Known vital status with date of death or last follow-up.

Exclusion criteria

Patients were excluded if any of the following applied:

Diagnosis-related

- No histopathological confirmation of pancreatic cancer
- Neuroendocrine tumors, acinar cell carcinoma, or other rare pancreatic tumor subtypes
- Non-metastatic disease(stages I–III)

CA 19-9–related

- Absence of baseline CA 19-9 measurement
- Absence of post-treatment CA 19-9 measurement
- Insufficient or irregular CA 19-9 measurements preventing elimination rate calculation
- Known Lewis antigen–negative status with inability to produce CA 19-9 (if data available)

Biochemical or clinical conditions

- Active cholestasis, obstructive jaundice, or acute cholangitis affecting CA 19-9 levels at the time of measurement
- Presence of another concurrent malignancy likely to significantly affect CA 19-9 levels

Treatment and follow-up

- No systemic therapy received
- Missing or insufficient treatment or follow-up data
- Unknown vital status

Other

- Age <18 years
- Missing essential clinical, pathological, or laboratory data

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Table 1. Comparison of demographic and clinical characteristics according to mortality status.

Variable		Exitus (n = 90, 87.4%)	Alive (n = 13, 12.6%)	p value
Age, median (IQR)		65.0 (59.0–69.0)	68.0 (64.0–71.0)	0.261
Sex	Female	44 (48.9)	8 (61.5)	0.578
	Male	46 (51.1)	5 (38.5)	
ECOG Performance Status	0	33 (36.7)	9 (69.2)	0.169
	1	40 (44.4)	3 (23.1)	
	2	16 (17.8)	1 (7.7)	
	3	1 (1.1)	0 (0.0)	
Timing of Metastasis	De novo	71 (78.9)	10 (76.9)	1.000
	Metachronous	19 (21.1)	3 (23.1)	
Smoking	Yes	46 (51.1)	6 (46.2)	0.970
	No	44 (48.9)	7 (53.8)	
Alcohol use	Yes	16 (17.8)	2 (15.4)	1.000
	No	74 (82.2)	11 (84.6)	
Tumor location	Head	50 (56.2)	9 (69.2)	0.556
	Body–tail	39 (43.8)	4 (30.8)	
T stage	T1	4 (4.5)	2 (15.4)	0.365
	T2	29 (33.0)	4 (30.8)	
	T3	26 (29.5)	2 (15.4)	
	T4	29 (33.0)	5 (38.5)	
N stage	N0	26 (29.9)	5 (38.5)	0.336
	N1	23 (26.4)	1 (7.7)	
	N2	38 (43.7)	7 (53.8)	
Lymphovascular invasion	Present	22 (91.7)	5 (83.3)	1.000
	Absent	2 (8.3)	1 (16.7)	
Perineural invasion	Present	22 (91.7)	6 (100.0)	1.000
	Absent	2 (8.3)	0 (0.0)	
Tumor grade	Grade 1–2	19 (48.7)	6 (85.7)	0.162
	Grade 3	20 (51.3)	1 (14.3)	
Liver metastasis	Present	68 (75.6)	6 (46.2)	0.061
	Absent	22 (24.4)	7 (53.8)	
Lymph node metastasis	Regional	33 (36.7)	1 (7.7)	0.116
	Distant	29 (32.2)	6 (46.2)	
	None	28 (31.1)	6 (46.2)	
Peritoneal metastasis	Present	24 (26.7)	7 (53.8)	0.094
	Absent	66 (73.3)	6 (46.2)	
Lung metastasis	Present	15 (16.7)	3 (23.1)	0.859
	Absent	75 (83.3)	10 (76.9)	
Bone metastasis	Present	7 (7.8)	2 (15.4)	0.702
	Absent	83 (92.2)	11 (84.6)	
Treatment regimen	Folfirinox	19 (21.1)	4 (30.8)	0.153
	Gemcitabine + Nab-paclitaxel	33 (36.7)	3 (23.1)	
	5-FU based	10 (11.1)	4 (30.8)	
	Gemcitabine based	28 (31.1)	2 (15.4)	
Baseline CA 19-9, median (IQR)		547.5 (38.9–5747.2)	491.0 (160.0–2442.0)	0.846
3-month CA 19-9, median (IQR)		233.0 (21.0–3655.0)	332.0 (89.2–1601.0)	0.996
Elimination rate, median (IQR)		1.1 (0.5–3.4)	1.7 (0.5–6.5)	0.872

Abbreviations: ECOG, Eastern Cooperative Oncology Group; FU, fluorouracil; FOLFIRINOX, 5-fluorouracil + leucovorin + irinotecan + oxaliplatin; IQR, interquartile range; LVI, lymphovascular invasion; PNI, perineural invasion.

Data collection

Demographic, clinical, and pathological data; disease stage at diagnosis; metastatic sites; treatment regimens; and survival outcomes were obtained from electronic medical records and archival files. Baseline and follow-up CA 19-9 levels were recorded; efforts were made to ensure consistency in laboratory methodology. Overall survival was calculated from the date of diagnosis to the date of death or last follow-up.

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Table 2. Kaplan–Meier survival analysis.

CA 19-9 Elimination Rate	Number of Patients	Events	Mean Survival (months)	SE	Median Survival (months)	95% CI for Median (Lower–Upper)	p value
High	31.0	26	27.7	4.01	25.00	17.00-31.0	**0.043**
Low	62.0	55	12.1	1.18	8.00	7.00-14.0	

Table 3. Survival rates at 1, 3, and 5 years according to CA 19-9 elimination rate.

Elimination Rate	Time (months)	Patients at Risk	Deaths (n)	Survival (%)	Lower Limit (%)	Upper Limit (%)
High	12	23	6	80.4	67.5	95.8
High	36	5	17	18.3	8.3	40.3
High	60	2	2	11.0	3.8	31.8
Low	12	23	37	37.6	27.0	52.4
Low	36	2	17	2.2	0.3	14.9
Low	60	0	1	0.0	NaN	NaN

Calculation of CA 19-9 elimination rate

The CA 19-9 elimination rate was calculated using baseline and 3-month CA 19-9 values.

Elimination Ratio= $\frac{Baseline\ CA19-9 level - 3rd\ month\ CA19-9\ level}{Baseline\ CA19-9\ level}$

Statistical analysis

All statistical analyses were performed using JAMOVI version 2.6.17. The distributions of continuous variables were assessed using the Shapiro–Wilk test. Normally distributed variables were expressed as mean ± standard deviation, and non-normally distributed variables as median (interquartile range). Categorical variables were presented as numbers and percentages.

Comparisons between groups were performed using the Mann–Whitney U test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables, as appropriate. Survival analyses were conducted using the Kaplan–Meier method, and group differences were evaluated using the log-rank test. The optimal cut-off value for the CA 19-9 elimination rate was determined using maximally selected rank statistics. A p-value < 0.05 was considered statistically significant.

RESULTS

Patient characteristics

The mean age of the study population was 64 ± 10.1 years (range: 24–84 years). During the follow-up period, 87.4% of the patients died. Of 103 patients, survival analysis based on elimination rate was performed in 93 patients due to availability of complete paired CA 19-9 measurements for cut-off classification. Baseline demographic, clinical, and pathological characteristics were compared by mortality status.

Median age did not differ significantly between patients who died during follow-up and those who remained alive (p = 0.261). Similarly, no significant differences were observed between mortality groups in sex distribution (p = 0.578), ECOG performance status, timing of metastasis (de novo vs. metachronous), smoking or alcohol use, or primary tumor location (all p>0.05). Surgical resection status was not associated with mortality (p = 0.190).

Tumor stage–related parameters, including T stage, N stage, and stage grouping, did not differ significantly between mortality groups (p = 0.365, p = 0.336, and p = 1.000, respectively). The presence of lymphovascular invasion (LVI) and perineural invasion (PNI) were also not associated with mortality (both p = 1.000). Tumor grade did not differ significantly between groups (p = 0.162).

Regarding metastatic patterns, the presence of liver, lymph node, and peritoneal metastases was not significantly associated with mortality; however, a borderline association was observed for liver metastases (p = 0.061). Lung and bone metastases were not associated with mortality (p = 0.859 and p = 0.702, respectively).

Treatment-related variables, including receipt of adjuvant chemotherapy and the type of chemotherapy regimen administered, were not significantly associated with mortality (all p>0.05). Baseline and 3-month CA 19-9 levels, the absolute change in CA 19-9, and the CA 19-9 elimination rate also did not differ significantly between mortality groups (all p>0.05) (Table 1).

Determination of the optimal cut-off for CA 19-9 elimination rate

Figure 1 shows the distribution of CA 19-9 elimination rate values and the results of maximally selected rank statistics. Lower elimination-rate values occurred more frequently, whereas higher values spanned a wider range.

Using maximally selected rank statistics, the optimal cut-off value for the CA 19-9 elimination rate was determined to be 2.33; at this value, the standardized log-rank statistic reached its maximum, indicating the greatest separation in survival between groups. Patients with an elimination rate ≤2.33 were classified as having a low elimination rate, whereas those with values >2.33 were classified as having a high elimination rate.

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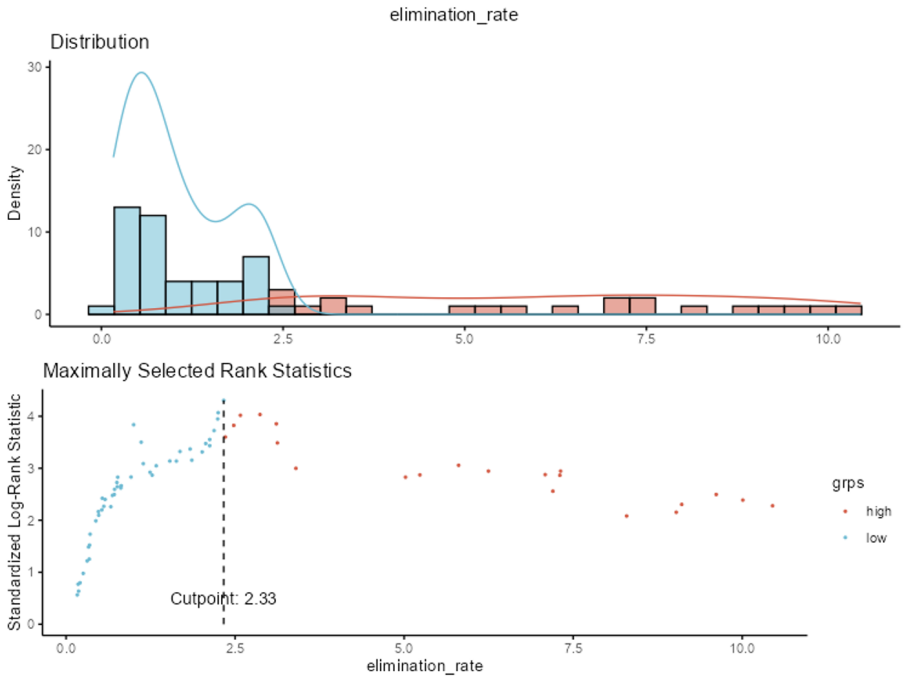

Figure 1. Elimination rate (according to cut-off group).

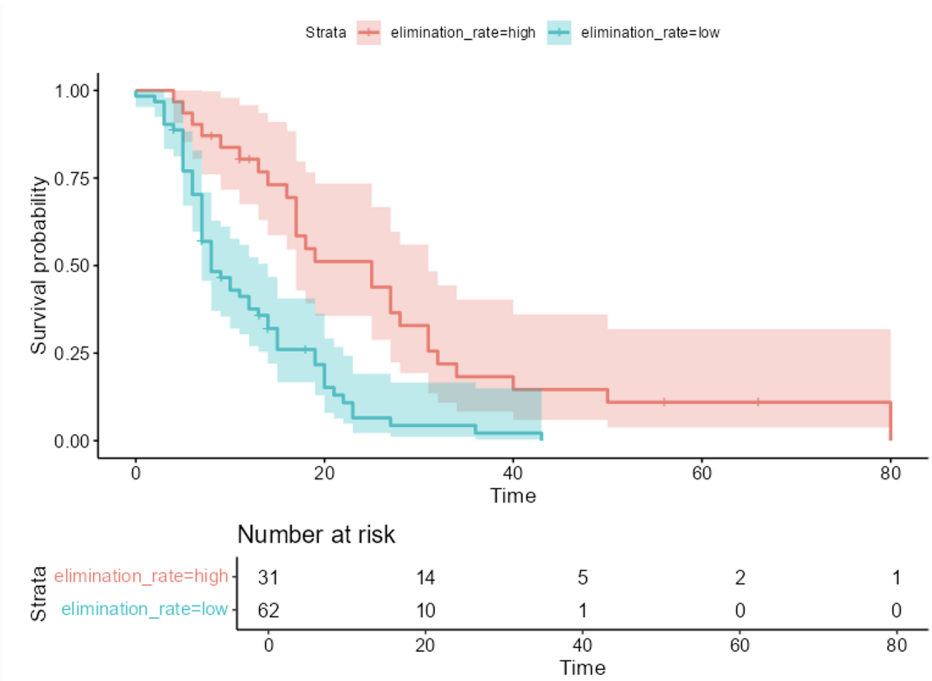

Figure 2. Survival according to elimination rate.

Survival according to CA 19-9 elimination rate

Median overall survival in the high-elimination group was 25 months (95% CI: 17–31), compared with 8 months (95% CI: 7–14) in the low-elimination group (p = 0.043) (Table 2, Figure 2).

Patients with a high CA 19-9 elimination rate had a substantially lower risk of death during follow-up compared with those with a low elimination rate.

Long-term survival outcomes

In the high-elimination group, the 12-, 36-, and 60-month survival rates were 80.4%, 18.3%, and 11.0%, respectively. In contrast, in the low-elimination group, the corresponding survival rates were 37.6%, 2.2%, and 0%, respectively (Table 3).

These findings demonstrate a marked and persistent survival advantage in patients with a high CA 19-9 elimination rate across short-, intermediate-, and long-term follow-up periods.

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DISCUSSION

CA 19-9 is the most widely used biomarker in pancreatic cancer and plays an important role in routine clinical monitoring. Numerous studies have established its diagnostic and prognostic relevance, as well as its usefulness for evaluating response to treatment [8].In addition to reflecting tumor burden, CA 19-9 has also been shown to correlate with surgical resectability, pathological stage, and likelihood of achieving complete tumor removal [9].

In this study, we demonstrated that the rate of decline in CA 19-9 after initiation of systemic therapy has a strong association with survival in patients with metastatic pancreatic ductal adenocarcinoma. Patients with a high CA 19-9 elimination rate experienced significantly longer overall survival and markedly better long-term survival rates compared with those with low CA 19-9 elimination rate. These findings indicate that CA 19-9 kinetics provide clinically meaningful prognostic information beyond baseline measurements.

Previous investigations have highlighted the importance of CA 19-9 dynamics. In a prospective study of locally advanced pancreatic cancer, Vainshtein and colleagues showed that both baseline CA 19-9 level and increases during chemoradiotherapy were independent predictors of progression-free and overall survival [10]. Notably, changes in CA 19-9 were more closely associated with outcome than radiologic progression, suggesting that biochemical markers may capture biologic tumor activity that is not fully reflected by imaging.

Similarly, Yoo et al. demonstrated that combining contrast-enhanced computed tomography (CT), ^{18}F-FDG Positron emission tomography (PET)/MRI, and CA 19-9 improved the prediction of treatment response and resectability in patients receiving neoadjuvant therapy [11].These data support the concept that serum biomarkers and advanced imaging modalities provide complementary information, particularly in pancreatic cancer, where fibrosis and desmoplastic reaction can obscure viable tumor tissue on conventional CT.

Our results are consistent with these observations, but extend them to metastatic disease by applying a quantitative kinetic parameter, rather than static CA 19-9 values. Instead of categorizing patients simply as responders or non-responders, clinicians can use the elimination rate to continuously stratify tumor behavior and prognosis.

The clinical importance of integrating CA 19-9 with radiologic findings was clearly demonstrated by Kim et al. In patients treated with first-line FOLFIRINOX, radiologic response based on RECIST criteria alone was insufficient to distinguish survival between patients with partial response and stable disease [12]. When CA 19-9 response was added, survival differences became evident, with the best outcomes observed in patients who achieved both disease control on imaging and biochemical normalization. This finding highlights a key limitation of morphology-based imaging and emphasizes the value of biochemical monitoring.

Our data further refine this approach by showing that the rate of CA 19-9 decline has important prognostic significance. Patients with rapid biomarker elimination had substantially longer survival, suggesting that CA 19-9 kinetics may reflect underlying tumor sensitivity to chemotherapy and biological aggressiveness more accurately than absolute values.

Accurate assessment of disease extent remains challenging in pancreatic cancer, as micrometastatic spread and true tumor burden are often underestimated by imaging alone [12]. In this setting, biomarkers that capture systemic tumor activity become particularly valuable. In resectable pancreatic cancer, Jeong et al. reported that a preoperative risk model incorporating CA 19-9, CT, and ^{18}F-FDG PET/CT predicted recurrence-free survival with accuracy comparable to pathological staging [13]. Likewise, Zhong et al. developed nomograms combining CT features and CA 19-9 to estimate progression-free survival in locally advanced disease [14]. However, these models relied on static CA 19-9 measurements, whereas our findings indicate that dynamic CA 19-9 elimination provides additional prognostic information in metastatic disease.

Early combined assessment of CA 19-9 and imaging has also been shown to improve prediction of outcomes. Kim et al. demonstrated that CT together with CA 19-9 response at eight weeks was superior to RECIST criteria alone for predicting survival in non-metastatic pancreatic cancer [15] Our study builds on this concept by demonstrating that continuous biomarker kinetics remain prognostically informative even in advanced-stage disease.

Current NCCN guidelines recommend interpretation of CA 19-9 in conjunction with imaging when assessing treatment response in pancreatic cancer [16]. Our results support this recommendation and suggest that incorporating the CA 19-9 elimination rate into routine follow-up may improve early risk stratification and help guide treatment decisions for patients with metastatic pancreatic cancer.

Limitations

This study has several limitations. First, its single-center design and the cohort's high mortality rate may introduce selection bias. Second, the retrospective nature of the study and reliance on medical records may result in information bias due to missing or incomplete data. In addition, variations in the timing of CA 19-9 measurements and in treatment regimens may have influenced biomarker dynamics. Another limitation of this study is the absence of multivariable Cox regression analysis. Due to the retrospective design and the limited sample size, adjustment for potential confounders was not performed. Therefore, the findings should be interpreted as demonstrating an association rather than independence.

However, a major strength of this study is the evaluation of CA 19-9 using a dynamic kinetic parameter, the elimination rate, rather than relying solely on static absolute values. This

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approach provides a more nuanced assessment of treatment response and tumor behavior and constitutes a novel contribution compared with most previous studies.

CONCLUSION

In conclusion, dynamic changes in CA 19-9 after initiation of systemic therapy are a significant prognostic factor for mortality in patients with metastatic pancreatic cancer. A higher CA 19-9 elimination rate is associated with superior short-, intermediate-, and long-term survival outcomes. These findings suggest that the CA 19-9 elimination rate may serve as a useful complementary tool for risk stratification and treatment response monitoring in clinical practice. Prospective studies integrating CA 19-9 kinetics with imaging-based parameters are warranted to further refine individualized treatment strategies in pancreatic cancer.

Ethics Committee Approval: This study was approved by the Göztepe Prof. Dr. Süleyman Yalçın Training and Research Hospital Non-Interventional Clinical Research Ethics Committee (date: January 8, 2026; approval no: 2026/0009).

Informed Consent: Written informed consent was waived due to the retrospective design of the study and the use of anonymized data.

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Conflict of Interest: The authors declare that they have no conflict of interest.

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