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Development of a Composite Risk Score and Real-world Outcomes in Advanced Pancreatic Adenocarcinoma: Prognostic Value of Baseline ^{18}F-FDG PET/CT Metabolic Parameters

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ABSTRACT

Aim: Reliable prognostic biomarkers are needed to improve risk stratification in patients with advanced pancreatic adenocarcinoma. We developed and validated a simple composite risk score that integrates clinical, laboratory, and ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) derived parameters to predict survival.

Methods: This retrospective single-center study included 50 patients with advanced pancreatic adenocarcinoma who underwent a baseline ^{18}F-FDG PET/CT before systemic treatment. Receiver operating characteristic (ROC) analysis was used to determine cut-off values for total lesion glycolysis (TLG), metabolic tumor volume (MTV), and serum carbohydrate antigen 19-9 (CA19-9). A composite risk score (0-4) was created by assigning one point each for liver metastasis, MTV above the cut-off, TLG above the cut-off, and CA19-9 >1000 U/mL. Overall survival (OS) and progression-free survival (PFS) were estimated using the Kaplan-Meier method and compared using the log-rank test.

Results: The median OS and PFS were 13.73 and 7.23 months, respectively. ROC analysis identified cut-off values of 15.55 cm^3 for MTV, 93.88 for TLG, and 1000 U/mL for CA19-9. Twenty-three patients (46.0%) were classified as low risk (score 0-1) and 27 (54.0%) as high-risk (score ≥2). High-risk patients had significantly shorter OS (10.35 vs. 14.62 months, p=0.018) and PFS (6.01 vs. 7.29 months, p=0.048) than low-risk patients. One-year OS rates were 41.7% and 81.0%, respectively.

Conclusions: The proposed composite risk score was associated with distinct survival outcomes in patients with advanced pancreatic adenocarcinoma. By integrating routinely available clinical, laboratory, and PET/CT-derived variables, this pragmatic model may assist baseline prognostic stratification. These findings require validation in larger prospective multicenter cohorts before clinical implementation.

Keywords: Pancreatic adenocarcinoma, metabolic tumor volume, total lesion glycolysis, CA19-9, composite risk score

Introduction

Pancreatic ductal adenocarcinoma (PDAC) is one of the most aggressive solid malignancies and is expected to become a leading cause of cancer-related mortality worldwide. Despite advances in systemic therapy, most patients are diagnosed with unresectable locally advanced or metastatic disease, and long-term survival remains poor [1,2]. Although multi-agent chemotherapy regimens, such as FOLFIRINOX and gemcitabine plus nab-paclitaxel, have improved outcomes in selected patients, median overall survival (OS) for metastatic PDAC remains below 12-15 months in real-world practice. Therefore,

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identifying reliable prognostic biomarkers that can improve risk stratification and facilitate individualized treatment decisions continues to be a major clinical challenge [3,4].

Current prognostic assessment in metastatic PDAC is primarily based on clinical performance status, metastatic burden, and serum carbohydrate antigen 19-9 (CA19-9) [5]. Among these, CA19-9 is the most widely used biomarker for disease monitoring; however, its prognostic performance is limited by substantial interpatient variability, Lewis antigen negativity, biliary obstruction, and inflammatory conditions. Consequently, additional imaging- and tumor biology-based biomarkers are needed to improve prognostic accuracy beyond conventional clinical parameters [6,7].

^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) provides quantitative information regarding tumor glucose metabolism and has emerged as a valuable imaging modality in pancreatic cancer. While the maximum standardized uptake value (SUV_{max}) has historically been the most frequently reported PET parameter, volumetric metabolic indices—including metabolic tumor volume (MTV) and total lesion glycolysis (TLG)—have gained increasing attention because they more comprehensively reflect whole-tumor metabolic burden [8,9]. Several studies have demonstrated that MTV and TLG may correlate more closely with tumor aggressiveness and patient survival than SUV_{max} alone; however, published results remain heterogeneous owing to differences in patient populations, treatment strategies, and PET acquisition protocols [10-12].

Because pancreatic cancer progression is driven by both tumor biology and metastatic dissemination, prognostic evaluation based on a single biomarker is unlikely to capture the complexity of disease behavior. Composite prognostic models integrating clinical, laboratory, and imaging biomarkers have therefore attracted growing interest across multiple malignancies. Such multidimensional models may outperform individual biomarkers by combining complementary prognostic information and enabling more robust patient stratification [13]. Nevertheless, few studies have specifically evaluated integrated PET/CT-based composite risk scores in metastatic pancreatic adenocarcinoma, and most available reports have focused on either isolated PET parameters or conventional clinical variables rather than their combined prognostic utility [14-16].

Liver metastasis represents the most frequent site of distant spread in PDAC and is consistently associated with poorer survival. Likewise, elevated CA19-9 reflects increased tumor burden and biologically aggressive disease, whereas high MTV and TLG indicate extensive metabolically active tumor volume. These variables represent distinct but complementary aspects of tumor behavior, and therefore constitute rational candidates for incorporation into a clinically applicable prognostic model. A simple composite score derived from routinely available baseline PET/CT and laboratory findings could facilitate early identification of patients at particularly high-risk of adverse outcomes without increasing cost or requiring additional molecular testing.

Therefore, we developed and validated a novel composite risk score integrating the presence of baseline liver metastasis, MTV, TLG, and CA19-9 to predict survival in patients with advanced pancreatic adenocarcinoma who were treated in routine clinical practice. In addition, we investigated the prognostic value of baseline PET/CT metabolic parameters for progression-free survival (PFS) and OS, and assessed whether combining these variables into a simple composite score improves risk stratification compared with individual biomarkers.

Methods

Patient Data

We retrospectively enrolled 50 patients with histologically confirmed locally advanced or metastatic pancreatic adenocarcinoma who underwent baseline ^{18}F-FDG PET/CT before receiving first-line systemic chemotherapy at Pamukkale University. Approval was granted by the Pamukkale University Non-Interventional Clinical Research Ethics Committee (approval no: 12, date: 30.06.2026). All procedures adhered to the Declaration of Helsinki.

Eligible patients had an Eastern Cooperative Oncology Group performance status 0-2 and were considered suitable candidates for systemic chemotherapy. All patients had baseline ^{18}F-FDG PET/CT imaging, pretreatment laboratory data, including serum tumor markers, and complete clinical follow-up records. Patients with pancreatic neuroendocrine tumors, with non-adenocarcinoma histology, with unavailable baseline PET/CT imaging, or with insufficient baseline clinical data were excluded.

Outcome Measures

OS was measured from the date of diagnosis to death from any cause or, for survivors, to the last follow-up. PFS was measured from the start of first-line systemic chemotherapy to the first radiologically documented progression or death, whichever occurred first.

PET/CT Acquisition and Image Analysis

Baseline whole-body ^{18}F-FDG PET/CT was obtained in all patients before first-line systemic chemotherapy, according to the institutional protocol, with images reconstructed using the manufacturer's standard algorithm. All baseline ^{18}F-FDG PET/CT examinations were reviewed by two experienced nuclear medicine physicians according to the institutional imaging protocol. Quantitative metabolic parameters were obtained from pretreatment PET/CT images. The highest voxel-based SUV within the primary tumor was recorded as SUV_{max}. MTV was measured using a semi-automatic three-dimensional volume-of-interest segmentation method based on a 41% SUV_{max} isocontour threshold, in accordance with the institutional imaging protocol. TLG was calculated as the product of MTV and the corresponding mean SUV (SUV_{mean}), representing the total metabolically active tumor burden.

Composite Risk Score

A composite risk score ranging from 0 to 4 was developed using four baseline variables: liver metastasis, MTV above the ROC-derived cut-off, TLG above the ROC-derived cut-off, and serum CA19-9 >1000 U/mL. One point was assigned for each adverse factor present. Patients were subsequently classified into a low-risk group (score 0-1) and a high-risk group (score ≥2) for survival analyses. Each component was assigned one point to preserve transparency and ease of use. Coefficient-based weighting was not used because the modest sample size could have produced unstable, sample-dependent weights and increased the risk of overfitting. Equal weighting was therefore chosen as a pragmatic, exploratory approach and should not be interpreted as evidence that the four variables have identical biological effect sizes.

Statistical Analysis

Continuous data were reported as median and interquartile range and categorical data were reported as counts and percentages. ROC curve analysis, with 12-month mortality as the reference outcome, was used to determine optimal thresholds for SUV_{max}, MTV, TLG, and CA19-9; the cut-off was set at the maximum Youden index, and discriminative capacity was expressed as the area under the curve (AUC) with 95% confidence intervals (CIs). Continuous variables included in the composite score were dichotomized at these ROC-derived thresholds to enable a simple and clinically applicable point-based classification without requiring a regression formula. The ROC-derived thresholds were generated in the present cohort to explore the prediction of 12-month mortality. They are data-driven and cohort-specific, and should not be interpreted as universally applicable clinical cut-offs. OS and PFS were estimated by Kaplan-Meier analysis and compared with the log-rank test. Candidate predictors of survival were first screened by univariable Cox proportional hazards regression. All tests were two-sided, with $p<0.05$ taken as significant. Analyses were performed using IBM SPSS Statistics v.26.0 (IBM Corp., Armonk, NY, USA), and supplementary exploratory analyses and figures were produced using Python-based packages.

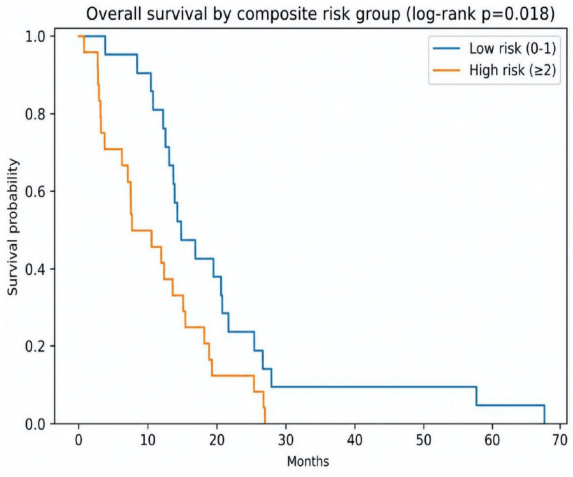

Figure 1. Kaplan-Meier overall survival curves according to the composite risk group

Results

Fifty patients with advanced pancreatic adenocarcinoma were analyzed. At the data cut-off, 49 of 50 patients (98.0%) had died, and the median follow-up from diagnosis was 13.73 months. The median age was 68.0 years (IQR, 59.2-74.0); 60.0% were men. The primary tumor arose in the pancreatic body in 38.0% of cases, in the head in 34.0%, and in the tail in 28.0; 76.0% of cases presented at stage IV. Liver metastases were present in 44.0% of patients, lung metastases in 14.0%, bone metastases in 6.0%, and lymph node involvement in 82.0%. Median baseline PET/CT values were SUV_{max} 5.21, MTV

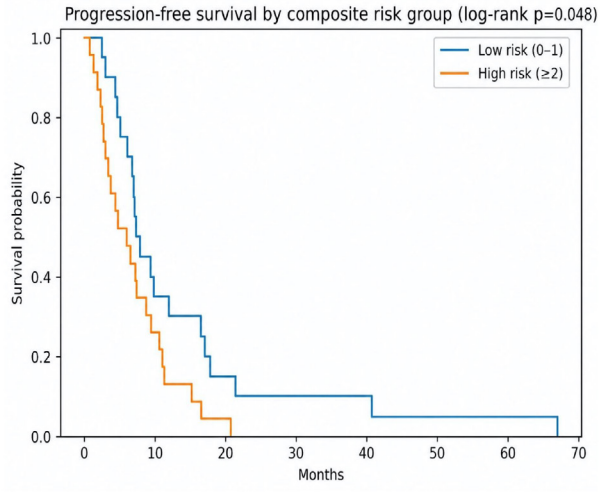

Figure 2. Kaplan-Meier progression-free survival curves according to the composite risk group

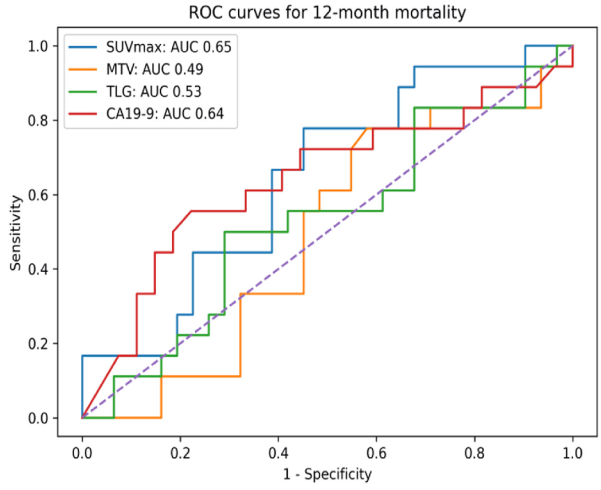

Figure 3. ROC curves of baseline PET/CT parameters and CA19-9 for 12-month mortality
ROC: Receiver operating characteristic, SUV_{max}: Maximum standardized uptake value, AUC: Area under the curve, MTV: Metabolic tumor volume, TLG: Total lesion glycolysis, CA19-9: Carbohydrate antigen 19-9, PET/CT: Positron emission tomography/computed tomography

Table 1. Baseline clinicopathological and imaging characteristics

Variable	Overall (n=50)
Age, years	68.0 (59.2-74.0)
Male sex	30 (60.0)
Primary tumor location: body	19 (38.0)
Primary tumor location: head	17 (34.0)
Primary tumor location: tail	14 (28.0)
Stage IV	38 (76.0)
Liver metastasis	22 (44.0)
Lung metastasis	7 (14.0)
Bone metastasis	3 (6.0)
Lymph node/LAP involvement	41 (82.0)
Other metastasis	5 (10.0)
SUV_{max}	5.21 (4.29-7.11)
MTV, cm^3	19.55 (12.55-37.98)
TLG	68.68 (38.37-110.77)
CA19-9, U/mL	273.60 (23.02-1541.75)
CEA, ng/mL	6.14 (4.01-19.03)

SUV_{max}: Maximum standardized uptake value, MTV: Metabolic tumor volume, TLG: Total lesion glycolysis, CA 19-9: Carbohydrate antigen 19-9, CEA: Carcinoembryonic antigen, LAP: Lymphadenopathy

19.55 cm^3, and TLG 68.68; median serum CA19-9 and CEA were 273.6 U/mL and 6.14 ng/mL, respectively (Table 1).

ROC analysis with respect to 12-month mortality showed that among PET-derived measures, SUV_{max} demonstrated the greatest discriminative ability (AUC=0.645), with CA19-9 close behind (AUC=0.642). Optimal thresholds were 4.96 for SUV_{max}, 15.55 cm^3 for MTV, 93.88 for TLG, and 1000 U/mL for CA19-9. MTV (AUC=0.492) and TLG (AUC=0.532) discriminated only weakly individually; however, their thresholds were retained in the composite score because of their biological relevance and potential complementary contribution (Table 2).

Metabolic activity was higher in patients with liver metastasis than in those without. SUV_{max} was higher in the liver metastasis group (6.21 vs. 4.55, p=0.003), as was TLG (96.22 vs. 48.24, p=0.025), whereas MTV showed no significant difference (p=0.249).

Patients with bone metastases likewise carried a heavier metabolic burden, with higher MTV (54.59 vs. 19.13 cm^3, p=0.027) and TLG (142.07 vs. 51.84, p=0.041); SUV_{max} was not significantly associated with bone involvement.

No significant links emerged between PET metabolic parameters and either lung metastases or lymph node involvement (all p>0.05), indicating that the volumetric indices were mainly associated with liver and bone dissemination (Table 3). The composite score distribution is shown in Table 4.

Table 2. ROC analysis for 12-month mortality

Variable	AUC	95% CI	Cut-off	Sensitivity, %	Specificity, %
SUV_{max}	0.645	0.474-0.800	4.96	77.8	54.8
MTV	0.492	0.337-0.660	15.55	77.8	41.9
TLG	0.532	0.355-0.713	93.88	50.0	71.0
CA19-9	0.642	0.460-0.826	1000.00	55.6	77.8

AUC confidence intervals were obtained by bootstrap resampling. Cut-offs were selected using the maximum Youden index
SUV_{max}: Maximum standardized uptake value, MTV: Metabolic tumor volume, TLG: Total lesion glycolysis, CA 19-9: Carbohydrate antigen 19-9, AUC: Area under the curve

Table 3. PET parameters according to metastatic site

Metastatic site	PET parameter	Absent	Present	p
Liver metastasis	SUV_{max}	4.55 (4.09-5.43)	6.21 (5.02-8.77)	0.003
Liver metastasis	MTV	15.80 (12.06-30.57)	21.54 (14.36-38.59)	0.249
Liver metastasis	TLG	48.24 (36.72-92.07)	96.22 (44.20-152.63)	0.025
Lung metastasis	SUV_{max}	5.17 (4.17-7.10)	5.56 (4.86-7.04)	0.442
Lung metastasis	MTV	21.31 (12.98-38.75)	13.95 (12.06-19.36)	0.166
Lung metastasis	TLG	75.31 (39.03-122.25)	42.13 (38.34-80.31)	0.410
Bone metastasis	SUV_{max}	5.26 (4.31-7.10)	4.23 (4.05-6.12)	0.567
Bone metastasis	MTV	19.13 (12.38-34.52)	54.59 (47.14-58.78)	0.027
Bone metastasis	TLG	51.84 (37.51-106.82)	142.07 (125.69-191.47)	0.041
Lymph node/LAP involvement	SUV_{max}	4.96 (3.85-5.89)	5.39 (4.45-7.80)	0.174
Lymph node/LAP involvement	MTV	19.13 (12.79-34.52)	19.77 (12.57-38.39)	0.936
Lymph node/LAP involvement	TLG	82.17 (28.48-93.70)	51.84 (39.86-132.94)	0.484

SUV_{max}: Maximum standardized uptake value, MTV: Metabolic tumor volume, TLG: Total lesion glycolysis, LAP: Lymphadenopathy, PET: Positron emission tomography

During follow-up, median OS for the whole cohort was 13.73 months, with OS of 83.7%, 63.3%, and 22.4% at 6, 12, and 24 months, respectively. Median PFS was 7.23 months; PFS at the same time points were 66.0%, 23.4%, and 6.4%.

Survival was better in the low-risk group (score 0-1) than in the high-risk group (score ≥2). Median OS was 14.62 months versus 10.35 months (log-rank p=0.018); median PFS was 7.29 months versus 6.01 months (log-rank p=0.048). One-year OS was 81.0% in the low-risk group and 41.7% in the high-risk group; the corresponding one-year PFS rates were 30.0% and 13.0%, demonstrating clear separation by composite risk (Table 5).

In univariable Cox proportional hazards regression analysis, a baseline CA19-9 >1000 U/mL was significantly associated with worse OS (HR=2.41, 95% CI: 1.23-4.69; p=0.010). Likewise, patients in the high composite risk group (score ≥2) had significantly higher mortality than those in the low-risk group (HR=1.91, 95% CI: 1.04-3.51; p=0.036). No significant associations were observed for age, sex, tumor location, stage, metastatic sites, SUV_{max}, MTV, TLG, or CEA (Table 6).

Table 4. Distribution of the composite risk score

Composite risk score	Number of patients	Percentage
0	14	28.0%
1	9	18.0%
2	10	20.0%
3	16	32.0%
4	1	2.0%

The composite score assigned one point each for liver metastasis, MTV >15.55, TLG >93.88, and CA19-9 >1000
MTV: Metabolic tumor volume, TLG: Total lesion glycolysis, CA19-9: Carbohydrate antigen 19-9

Table 5. Kaplan-Meier survival estimates

Endpoint	Group	Median, months	6 month, %	12 month, %	24 month, %	Log-rank p
Overall survival	All valid cases	13.73	83.7	63.3	22.4	-
Overall survival	Low-risk (0-1)	14.62	95.2	81.0	-	0.018
Overall survival	High-risk (≥2)	10.35	70.8	41.7	-	0.018
Progression-free survival	All valid cases	7.23	66.0	23.4	6.4	-
Progression-free survival	Low-risk (0-1)	7.29	75.0	30.0	-	0.048
Progression-free survival	High-risk (≥2)	6.01	52.2	13.0	-	0.048

Low-risk group (composite risk score 0-1); high-risk group (composite risk score ≥2)

Table 6. Univariable Cox regression analysis for overall survival

Variable	Comparison	HR (95% CI)	p value
Age	Per 1-year increase	1.015 (0.989-1.041)	0.261
Sex	Male vs. female	1.711 (0.927-3.156)	0.086
Primary tumor location	Body vs. head	1.241 (0.620-2.485)	0.542
Primary tumor location	Tail vs. head	1.876 (0.876-4.017)	0.105
Stage	IV vs. III	1.252 (0.696-2.252)	0.452
Liver metastasis	Present vs. absent	1.352 (0.757-2.413)	0.308
Lung metastasis	Present vs. absent	1.246 (0.553-2.807)	0.596
Bone metastasis	Present vs. absent	0.529 (0.127-2.201)	0.381
Lymph node involvement	Present vs. absent	0.624 (0.298-1.307)	0.211
SUV_{max}	>4.96 vs. ≤4.96	1.313 (0.736-2.343)	0.356
MTV	>15.55 vs. ≤15.55 cm^3	1.452 (0.802-2.629)	0.218
TLG	>93.88 vs. ≤93.88	1.230 (0.664-2.280)	0.510
CA19-9	>1000 vs. ≤1000 U/mL	2.407 (1.234-4.693)	0.010
CEA	>6.14 vs. ≤6.14 ng/mL	1.125 (0.598-2.118)	0.715
Composite risk group	High (≥2) vs. low (0-1)	1.914 (1.043-3.512)	0.036

SUV_{max}: Maximum standardized uptake value, MTV: Metabolic tumor volume, TLG: Total lesion glycolysis, CA 19-9: Carbohydrate antigen 19-9, CEA: Carcinoembryonic antigen, HR: Hazard ratio, CI: Confidence interval

Discussion

This real-world study evaluated the prognostic significance of baseline ^{18}F-FDG PET/CT-derived metabolic parameters and explored a simple composite risk score integrating liver metastasis, MTV, TLG, and CA19-9 in patients with advanced pancreatic adenocarcinoma. The principal findings of this study can be summarized as follows. First, patients classified as high risk according to the composite score experienced significantly shorter OS and PFS than those classified as low risk. Second, baseline CA19-9 concentrations above 1000 U/mL were associated with inferior OS in a univariable Cox regression analysis. Third, although MTV and TLG demonstrated relatively modest discriminatory performance when evaluated individually by ROC analysis, their incorporation into a composite model that included liver metastasis and CA19-9 appeared to improve prognostic stratification. Taken together, these findings suggest that integrating routinely available clinical, laboratory, and metabolic imaging variables may provide complementary prognostic information beyond that obtained from individual biomarkers.

Among PET-derived metabolic parameters, SUV_{max} has historically been the most widely reported index because of its simplicity and reproducibility. However, SUV_{max} represents the single voxel with the highest glucose uptake and, therefore, reflects only a limited portion of the tumor. It does not account for tumor volume, spatial heterogeneity, or total metabolically active disease burden [17]. In contrast, MTV quantifies the volume of metabolically active tumor tissue, whereas TLG combines MTV with average glucose uptake, thereby providing a more comprehensive estimate of whole-tumor metabolic burden [18].

Growing evidence suggests that volumetric PET parameters may be more closely associated with patient outcomes than SUV_{max} alone. In a systematic review and meta-analysis including multiple studies of pancreatic carcinoma, Zhu et al. [19] demonstrated that elevated MTV and TLG were consistently associated with poorer survival, although substantial heterogeneity existed regarding patient selection, disease stage, treatment modality, PET acquisition protocols, and segmentation methods. Similarly, Lee et al. [20] reported that both MTV and TLG were significant prognostic markers in patients undergoing surgery for pancreatic cancer and suggested that volumetric PET parameters better reflected tumor biology than conventional SUV measurements [20]. Mohamed and colleagues subsequently observed that increased TLG was associated with inferior OS in patients with pancreatic adenocarcinoma and remained prognostically relevant after adjustment for selected clinical variables [21].

Our findings are generally consistent with previous observations, while also emphasizing several important practical considerations. In the present study, MTV and TLG individually demonstrated only modest discriminatory ability for predicting 12-month mortality. Their ROC-derived AUC values were relatively low and numerically inferior to those observed for CA19-9 and SUV_{max}. Rather than indicating that volumetric PET parameters lack prognostic value, these findings likely reflect the considerable biological and clinical heterogeneity encountered in routine oncology practice.

Methodological variability may also contribute to the heterogeneous performance of volumetric PET biomarkers reported in the literature. MTV and TLG measurements are influenced by scanner characteristics, reconstruction algorithms, uptake time, blood glucose levels, lesion delineation techniques, and segmentation thresholds [17,18]. Consequently, absolute cut-off values reported across studies vary considerably. Previous investigators have employed fixed SUV thresholds, percentage-based thresholds, adaptive segmentation techniques, and liver-background methods, making direct comparison challenging [18-21]. In the present study, MTV was measured using a standardized semi-automatic 41% SUVmax isocontour threshold according to institutional imaging protocols. Although this approach ensured methodological consistency within our cohort, the proposed cut-off values should not be considered universally applicable and require validation across different PET/CT platforms and imaging protocols.

Another noteworthy observation was the relationship between metabolic parameters and metastatic distribution. Patients with liver metastases exhibited significantly higher SUV_{max} and TLG, whereas patients with bone metastases exhibited significantly higher MTV and TLG. Although the number of patients with bone metastases was limited, these findings are biologically plausible because increasing metastatic dissemination would be expected to increase the total metabolically active tumor burden. By contrast, no significant associations were observed between PET-derived metabolic parameters and lung metastases or lymph node involvement. These observations suggest that different metastatic sites may reflect distinct biological patterns of disease spread, rather than uniformly increasing the metabolic tumor burden.

Collectively, these findings support the concept that PET-derived volumetric parameters provide clinically relevant information regarding tumor burden; however, they also indicate that their prognostic utility may be limited when interpreted in isolation. The modest discriminatory performance observed for MTV and TLG individually suggests that metabolic tumor burden represents only one dimension of disease biology. Consequently, integrating PET-derived metabolic information with complementary clinical and laboratory variables may provide a more comprehensive assessment of prognosis than reliance on a single biomarker. This concept formed the rationale for developing the exploratory composite risk score evaluated in the present study.

Although neither MTV nor TLG demonstrated strong discriminatory performance in ROC analyses, patients classified as high-risk according to the composite score experienced significantly shorter OS and PFS than those classified as low risk. MTV and TLG were nevertheless retained because they reflect whole-body metabolic tumor burden, a biologically relevant dimension intended to provide complementary rather than stand-alone prognostic information. These

observations suggest that integrating multiple baseline variables reflecting different biological aspects of advanced pancreatic adenocarcinoma may provide complementary prognostic information. However, because the score was developed and evaluated within the same cohort, its apparent performance should be interpreted cautiously until confirmed in independent populations.

This concept is consistent with the current understanding that prognosis in advanced pancreatic adenocarcinoma is determined by multiple interacting biological processes. Patients with apparently similar tumor, node, metastasis stage frequently demonstrate markedly different clinical outcomes, suggesting that anatomical staging alone is insufficient for accurate prognostic assessment [13]. Increasing attention has therefore been directed toward multidimensional prognostic models incorporating clinical, laboratory, and imaging biomarkers rather than relying on isolated parameters [22,23].

The present findings also support the biological relevance of liver metastasis as an important component of the composite score. Liver involvement is the most common pattern of distant dissemination in pancreatic adenocarcinoma and has consistently been associated with unfavorable survival outcomes [24]. Beyond simply representing metastatic spread, liver metastasis is frequently considered a surrogate marker of aggressive tumor biology, increased systemic tumor burden, and impaired hepatic reserve. Consistent with these observations, patients with liver metastases in the present study demonstrated significantly higher SUV_{max} and TLG values, suggesting that hepatic dissemination was accompanied by increased metabolic tumor activity.

Similarly, CA19-9 remains the most extensively investigated serum biomarker in pancreatic adenocarcinoma despite its well-recognized limitations. Elevated baseline CA19-9 concentrations have repeatedly been associated with increased tumor burden and inferior survival across different treatment settings [5]. In a meta-analysis including more than 6,000 patients, elevated pretreatment CA19-9 was consistently associated with shorter OS irrespective of disease stage [25]. Furthermore, Pelzer et al. [26] demonstrated that patients with baseline CA19-9 concentrations above 1000 U/mL experienced substantially shorter survival than those with lower values. The optimal ROC-derived threshold identified in the present study was identical to the previously reported value, providing indirect support for the biological plausibility of the selected cut-off.

The relatively stronger association between the composite score and OS, compared with that for PFS, also deserves consideration. Although the score significantly separated Kaplan-Meier curves for both endpoints, the association appeared more robust for OS. Progression represents only one event during the disease course, whereas OS reflects the cumulative influence of baseline disease burden, treatment sensitivity, subsequent therapies, supportive care, and patient-related factors. Consequently, a prognostic model based on baseline tumor burden would be expected to demonstrate a more stable relationship with OS than with the timing of first radiological progression.

Study Limitations

Several limitations of this study should be considered. The retrospective single-center design and relatively small sample size may have reduced the statistical robustness and limited the generalizability of the results. In addition, post-progression treatment regimens were heterogeneous, which may have influenced OS. Although 49 of the 50 patients experienced the study endpoint, multivariable Cox regression was not performed because the cohort was limited and the analysis was exploratory, which could have resulted in unstable estimates and overfitting. For the same reasons, internal validation was considered unreliable, and external validation could not be performed because an independent cohort was unavailable.

Conclusion

In conclusion, this real-world study suggests that a simple composite risk score integrating liver metastasis, MTV, TLG, and serum CA19-9 may improve baseline prognostic stratification in patients with advanced PDAC. While individual PET-derived volumetric parameters showed limited discriminatory performance, their integration with clinical and laboratory variables may provide complementary prognostic information. Given the exploratory nature of this study, external validation of the proposed risk score in larger prospective multicenter cohorts is essential to confirm its reproducibility and clinical utility before routine clinical implementation.

Ethics

Ethics Committee Approval: Approval was granted by the Pamukkale University Non-Interventional Clinical Research Ethics Committee (approval no: 12, date: 30.06.2026).

Informed Consent: Because the study was designed retrospectively no written informed consent form was obtained from the patients.

Footnotes

Authorship Contributions

Surgical and Medical Practices: T.G.K., A.A.K., A.Y., Concept: T.G.K., A.A.K., B.Y.T., A.G.D., T.Ş., G.G.D., Design: T.G.K., T.D., S.T., B.Y.T., A.G.D., A.Y., T.Ş., G.G.D., Data Collection or Processing: T.G.K., T.D., S.T., Analysis or Interpretation: T.G.K., T.D., S.T., A.Y., T.Ş., G.G.D., Literature Search: T.G.K., B.Y.T., A.G.D., Writing: T.G.K., A.A.K.

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