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^{18}F-FDG-PET/CT therapy assessment of locally advanced pancreatic adenocarcinoma: impact on management and utilization of quantitative parameters for patient survival prediction

Sara Sheikhbahaei[a], Rick Wray[a], Brenda Young[a], Esther Mena[a], Mehdi Taghipour[a], Arman Rahmim[a] and Rathan M. Subramaniam[a,b,c,d]

Objectives **This study aims to evaluate the impact of therapy assessment PET/computed tomography (CT) scan on the management of locally advanced pancreatic adenocarcinoma (LAPC), and the value of qualitative versus quantitative PET/CT interpretation for patient outcome prediction.**

Materials and methods **Forty-two LAPC patients were retrospectively included. PET/CT was performed at a median of 4.6 weeks after completion of chemo ± radiotherapy to assess the primary treatment response. PET was interpreted visually using a qualitative five-point scale (Hopkins criteria for therapy assessment). Quantitative PET parameters including maximum and peak standardized uptake value (SUV_{max} and SUV_{peak}), total lesion glycolysis, and metabolic tumor volume (MTV) were also measured using the gradient segmentation method. Kaplan–Meier and Cox regression analyses were performed.**

Results **Thirty-five patients were followed up until death. Therapy assessment PET/CT led to a change in the overall management of 22 (52.4%) patients, prompting surgical resection (eight patients), adding radiation therapy (eight patients), or starting palliative chemotherapy (six patients). The median survival in patients with a negative or a positive PET scan, according to the Hopkins criteria, was 14.6 and 8.7 months, respectively ($P = 0.06$). The median quantitative thresholds of SUV_{peak} 2.64 [hazard ratio (HR) = 2.67, $P = 0.03$], total lesion glycolysis 44.0 g (HR = 2.64, $P = 0.005$), and MTV 24.7 ml (HR = 2.57, $P = 0.008$) were significant predictors of overall survival. Using combined quantitative scoring, patients with high SUV_{peak} and high MTV (> median cut point) had a 5.45-fold (95% confidence interval: 1.76–16.87) increased risk for death compared with those with both low SUV_{peak} and MTV (the reference group).**

Conclusion **PET-based volumetric parameters can predict survival outcomes of patients with LAPC. A combined quantitative PET/CT scoring system provides significantly improved prognostication.** *Nucl Med Commun* **37:231–238**

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Keywords: pancreatic adenocarcinoma, PET/CT, prognosis, therapy assessment

[a]Russell H Morgan Department of Radiology and Radiological Sciences, [b]Department of Oncology, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins School of Medicine, [c]Department of Health Policy and Management and Center for Health Services and Outcome Research, Johns Hopkins Bloomberg School of Public Health and [d]Armstrong Institute for Patient Safety and Quality, Johns Hopkins Medicine, Baltimore, Maryland, USA

Correspondence to Rathan M. Subramaniam, MD, PhD, MPH, Russell H Morgan Department of Radiology and Radiological Sciences, Johns Hopkins University, 601 N. Caroline Street, JHOC 3235, Baltimore, MD 21287, USA
Tel: +1 410 502 3956; fax: +1 443 287 2933; e-mail: rsubram4@jhmi.edu

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Introduction

As the fourth most prominent cause of cancer-related mortality in the USA, pancreatic cancer accounted for an estimated 39 590 deaths in 2014 [1]. Pancreatic adenocarcinoma is commonly presented as metastatic or locally advanced disease at diagnosis [2,3]. The overall 5-year survival rate for pancreatic cancer is 6.7%, varying widely according to disease stage, with 21.5% for localized disease, 8.6% for locally advanced disease, and 2.3% for metastatic disease [4]. Locally advanced pancreatic adenocarcinoma (LAPC) is initially treated with induction chemotherapy or concurrent chemoradiation therapy [2]. A response to initial therapy could prompt surgical exploration and subsequent resection of the tumor [5]. Thus, post-treatment follow-up could provide management and survival advantages and is recommended in these patients [5].

PET/computed tomography (CT) has been shown to have diagnostic and prognostic advantages in the staging and therapy assessment of pancreatic adenocarcinoma [2, 5–7]. Fluorine-18 fluorodeoxyglucose (^{18}F-FDG)-avidity and PET-based quantitative parameters of baseline PET/CT have been shown to be useful in therapy planning [5,8] and in modification of the target volume and radiation field [2,5,9], and are considered as [10–13] prognostic indicators of survival in pancreatic adenocarcinoma [11–16]. Although several studies support the

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high performance of therapy assessment PET/CT in improving the management and predicting the outcome of patients with various solid tumors [17,18], little is known about the value of ^{18}F-FDG-PET/CT in therapy assessment of pancreatic adenocarcinoma, particularly of LAPC [10,19]. The objectives of this study were to establish the value of post-treatment PET/CT in the management of patients with unresectable LAPC treated with chemotherapy with or without radiotherapy and to investigate the prognostic significance of both qualitative (five-point visual scale, Hopkins criteria for therapy assessment [20]) and quantitative PET in therapy response assessment in patients with LAPC and propose a combined volumetric scoring system correlated with survival.

Materials and methods

Eligible patients

The present study was performed under a waiver of informed consent as approved by the Institutional Review Board. The guidelines of the Health Insurance Portability and Accountability Act (HIPAA) were followed. The medical records of patients with histologically confirmed pancreatic cancer who underwent ^{18}F-FDG-PET/CT at our institutions between June 2003 and June 2013, as part of their management, were retrospectively reviewed. Of them, patients with unresectable locally advanced pancreatic cancer who were referred for therapy assessment PET/CT scan after the completion of primary intended treatment were eligible for inclusion. Primary treatments were adjuant chemotherapy and chemotherapy alone or combined with radiation. None of the patients had metastatic disease, and all were initially considered to have unresectable tumors according to the clinicians' discretion either by staging imaging (CT, MR, or PET/CT) or by exploratory laparotomy. The post-treatment ^{18}F-FDG-PET/CT studies were ordered at the treating clinician's discretion to assess response to therapy. The change in management was assessed by comparing the pre-PET/CT management plans with post-PET/CT management plans for individual patients.

PET/CT image interpretation

Five-point qualitative post-therapy assessment scoring scale (Hopkins criteria)

The PET/CT images were scored using a structured qualitative five-point scale for therapy response assessment of pancreatic lesions based on ^{18}F-FDG-PET uptake. The activity in the mediastinal blood pool was taken as the background. The images were scored according to the five-point qualitative Hopkins criteria (Fig. 1) for therapy assessment. The five-point scale was dichotomized to negative (scores 1, 2, and 3) and positive (scores 4 and 5) results.

Reader qualifications: The PET/CT studies were retrieved from the institutional archiving system and were reviewed using MIM Vista viewing platform (version 6.3.2; MIM Software Inc., Cleveland, Ohio, USA). All images were interpreted independently by two board-certified nuclear medicine physicians (reader 1, R.W., and reader 2, E.M.) who were blinded to the outcome, according to the structured qualitative five-point scale (Hopkins criteria). Reader 1 is a current clinical PET/CT fellow with nuclear medicine board certification, and reader 2 is a current third-year nuclear medicine resident who is already board-certified in nuclear medicine outside the USA. Any discrepancies were adjudicated, independently, by a third reader who is an associate professor of Radiology, board-certified in Nuclear Medicine and Radiology.

Quantitative parameters

One reader (R.W.) also extracted the quantitative ^{18}F-FDG-PET/CT parameters of the pancreatic tumor, blinded to the outcome. Quantitative ^{18}F-FDG-PET/CT parameters including maximum standardized uptake value (SUV_{max}), peak standardized uptake value (SUV_{peak}), metabolic tumor volume (MTV), and total lesion glycolysis (TLG) were measured using the gradient segmentation method with MIM vista software analysis suite (version 6.3.2; MimVista Software Inc., Cleveland, Ohio, USA). Once the region of interest had been segmented, SUV_{max}, SUV_{peak}, MTV, and TLG were semiautomatically calculated by the software.

Receiver operating characteristic curve analysis for ^{18}F-FDG-PET/CT parameters: The median values for SUV_{max}, SUV_{peak}, and volumetric parameters of ^{18}F-FDG-PET/CT (MTV and TLG) were used as cutoff points for the estimation of death. In addition, using receiver operating characteristic curve analyses, the optimal cutoff values for each parameter were determined to differentiate those who survived after 12 months following post-therapy ^{18}F-FDG-PET/CT scan from those who died earlier.

Statistical analyses

Descriptive values were presented as mean ± SD or median [25th, 75th range] if the data were not normally distributed. Categorical variables were presented as frequency (percentage). The time to overall survival was measured from the date of the therapy assessment PET/CT scan until the date of death. Date of death was determined using a web-based mortality registry or available electronic medical records at our institution. The survival data for patients who were alive were censored at the last follow-up date at our institution. The Youden Index (J) was used to determine the optimum cutoff point for quantitative PET parameters in the receiver operating characteristic analysis: $J = \text{maximum}\ (\text{sensitivity} + \text{specificity} - 1)$. Patients were dichotomized on the basis of the qualitative Hopkins criteria (negative and positive groups) and quantitative PET

Fig. 1

Score	^{18}F-FDG	Response category	
1	Focal ^{18}F-FDG uptake less than mediastinal blood pool.	Complete metabolic response	Negative
2	Focal ^{18}F-FDG uptake greater than mediastinal blood pool but less than liver.	Likely complete metabolic response	
3	Diffuse ^{18}F-FDG uptake greater than mediastinal blood pool or liver.	Likely inflammation	
4	Focal ^{18}F-FDG uptake greater than liver.	Likely residual tumor	Positive
5	Focal and intense ^{18}F-FDG uptake greater than the liver (2–3 times)	Residual tumor	

Five-point qualitative scoring system (Hopkins criteria) for therapy response assessment. ^{18}F-FDG, fluorine-18 fluorodeoxyglucose.

parameters using optimum and median values for SUV_{max}, SUV_{peak}, TLG, and MTV (high and low groups). In each subgroup, survival probabilities were generated using Kaplan–Meier survival curves and compared using the Mantel–Cox log-rank test. Univariate and multivariate Cox regression analyses were performed considering death as the endpoints. The statistical significance level was set at P less than 0.05. Statistical analysis was performed using IBM SPSS Statistics 22.0 (IBM Corp., Armonk, New York, USA).

Results

Patients characteristics and follow-up

A total of 42 LAPC patients (31 men and 11 women) with a mean (SD) age of 66.4 (10) years were included in the study. Post-therapy ^{18}F-FDG-PET/CT scan was performed at a median of 4.6 weeks (range = 0.3–17.1 weeks) after completion of the primary intended treatment to monitor the disease response. Table 1 summarizes the demographics and clinical characteristics of the study population. Of a total of 42 patients, 35 (83.3%) died during the follow-up. The median follow-up duration from the date of therapy assessment PET/CT in all patients was 10.3 months (range: 1–39.4 months).

Post-treatment ^{18}F-FDG-PET/CT and change in treatment

^{18}F-FDG-PET/CT led to changes in the overall management of 22 of 42 (52.4%) patients. The management changes included prompt palliative chemotherapy or a new chemotherapeutic regimen (six patients, 14.3%), starting stereotactic body radiation therapy (SBRT) or adding radiation therapy to the previous protocol (eight patients, 19.1%), and, lastly, modifying the scope of the surgery (eight patients, 19.1%). In the last eight patients, post-treatment ^{18}F-FDG-PET/CT suggested locally resectable tumors without evidence of metastases, and as a result these patients underwent surgical tumor resection. Of these patients, one was found to have unresectable disease during surgery and was instead treated with chemotherapy.

Table 1 Demographics and clinical characteristics of the patients

Characteristics	Median (range) or *N* (%)
Age (years)	66 (43–88)
Sex	
Male	31 (73.8)
Female	11 (26.2)
Race	
White	37 (88.1)
African American	5 (11.9)
Site of primary tumor	
Head or uncinate process	32 (76.2)
Tail or body	8 (19)
Both	2 (4.8)
First treatment	
Chemotherapy	7 (16.7)
Chemoradiation	23 (54.7)
Chemo + stereotactic radiotherapy	12 (28.6)
Neoadjuant chemotherapy	
Yes	15 (35.7)
No	23 (54.8)
Unknown	4 (9.5)
Smoking	
Previous/current	23 (54.8)
No	17 (40.5)
Unknown	2 (4.7)
Diabetes mellitus at diagnosis	
Yes	16 (38.1)
No	26 (61.9)
CA19-9 level[a]	
At diagnosis	156.6 (61.1–624.3)
Near post-treatment scan	61.1 (22.7–212.35)
Interval between completion of treatment and PET scan (weeks)	4.6 (0.3–17.1)
Overall survival (months)	10.27 (1.1–39.4)

[a]CA19-9 level presented as median (interquartile range).

Thirteen of 42 patients (30.9%) continued on the previous chemotherapy or radiation therapy protocol after therapy response ^{18}F-FDG-PET/CT evaluation. In five other patients (11.9%), the treatment was stopped because of patient preference (two patients), poor

tolerance to systemic therapy (two patients), or switching to hospice care (one patient). The treatment impact was unknown in two patients.

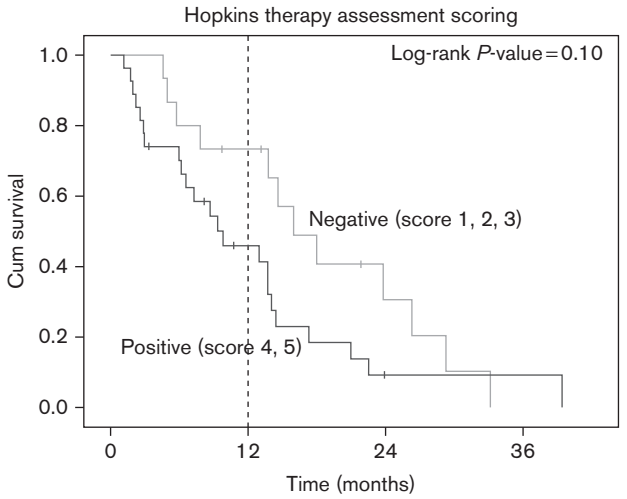
Qualitative post-therapy assessment scoring (Hopkins criteria) and survival outcome

On the basis of the scores, 27 (64.3%) of 42 patients were categorized as positive (score 4 and 5). The median survival of patients with positive scans was 8.7 months (range: 1.1–39.4 months; 23 deaths). In contrast, the median survival of the 15 patients with negative scans was 14.6 months (range: 4.6–33.1 months; 12 deaths) ($P=0.057$). The Kaplan–Meier survival analysis did not show a significant difference in the overall survival of patients who were classified as positive (Hopkins score 4, 5) and those who were classified as negative (Hopkins score 1, 2, 3) ($P=0.105$). Hopkins therapy assessment criteria were also not significant predictors of 1-year survival in LAPC patients ($P=0.08$) (Fig. 2).

Quantitative post-therapy ^{18}F-FDG-PET/CT parameters and survival outcome

The median (range) values for the SUV_{max}, SUV_{peak}, TLG, and MTV in the study population were 3.54 (2.73, 4.33), 2.64 (2.18, 3.23), 44.0 (20.7, 121.3), and 24.7 (12.0, 52.2), respectively. The Kaplan–Meier survival plots of the patients classified according to the median values of ^{18}F-FDG-PET/CT parameters yielded a significant result for SUV_{peak} ($P=0.035$), TLG ($P=0.005$), and MTV ($P=0.008$), but not for SUV_{max} ($P=0.20$) (Fig. 3).

Fig. 2



Kaplan–Meier survival plot by qualitative PET/CT result: survival (months) between patients who were categorized as positive and negative by the five-point post-therapy Hopkins interpretation criteria did not differ significantly at 1 year [log-rank, $P=0.08$; HR (95% CI) = 2.45 (0.90–6.66)] or during the follow-up period [log-rank, $P=0.1$; HR (95% CI) = 1.79(0.87–3.67)]. CI, confidence interval; CT, computed tomography; HR, hazard ratio.

Cox regression models were performed including the following variables: age, sex, race, serum level of post-treatment CA19-9, median SUV_{max}, median SUV_{peak}, median TLG, and median MTV. In univariate analysis, the median SUV_{peak} 2.64 [hazard ratio (HR) = 2.67, $P=0.043$], TLG 44.0 g (HR = 2.64, $P=0.007$), and MTV 24.7 ml (HR = 2.57, $P=0.01$) significantly predicted death during the follow-up period. In multivariate Cox regression analysis, the median SUV_{peak} (HR = 6.15, $P=0.006$), TLG (HR = 2.97, $P=0.01$), and MTV (HR = 2.69, $P=0.03$) remained significant predictors of overall survival even after adjustment for age, sex, race, and serum level of post-treatment CA19-9 (Table 2).

To predict the risk for death within 12 months after the therapy assessment ^{18}F-FDG-PET/CT scan, the optimum cutoff points of ^{18}F-FDG-PET parameters were determined. Table 3 summarizes the optimum cutoff points, their corresponding sensitivity and specificity, and the 1-year survival probabilities in LAPC patients. An optimum threshold of 3.62 for SUV_{max} had 73% sensitivity and 80% specificity in predicting those who survived after 12 months. The Cox regression analyses showed that the optimum SUV_{max} (HR = 5, $P=0.001$), SUV_{peak} (HR = 4.18, $P=0.002$), TLG (HR = 2.82, $P=0.01$), and MTV (HR = 3.6, $P=0.003$) could significantly predict death within 1 year following the therapy assessment ^{18}F-FDG-PET/CT scan (Table 3).

Overall effect of ^{18}F-FDG-avidity and total tumor burden on survival

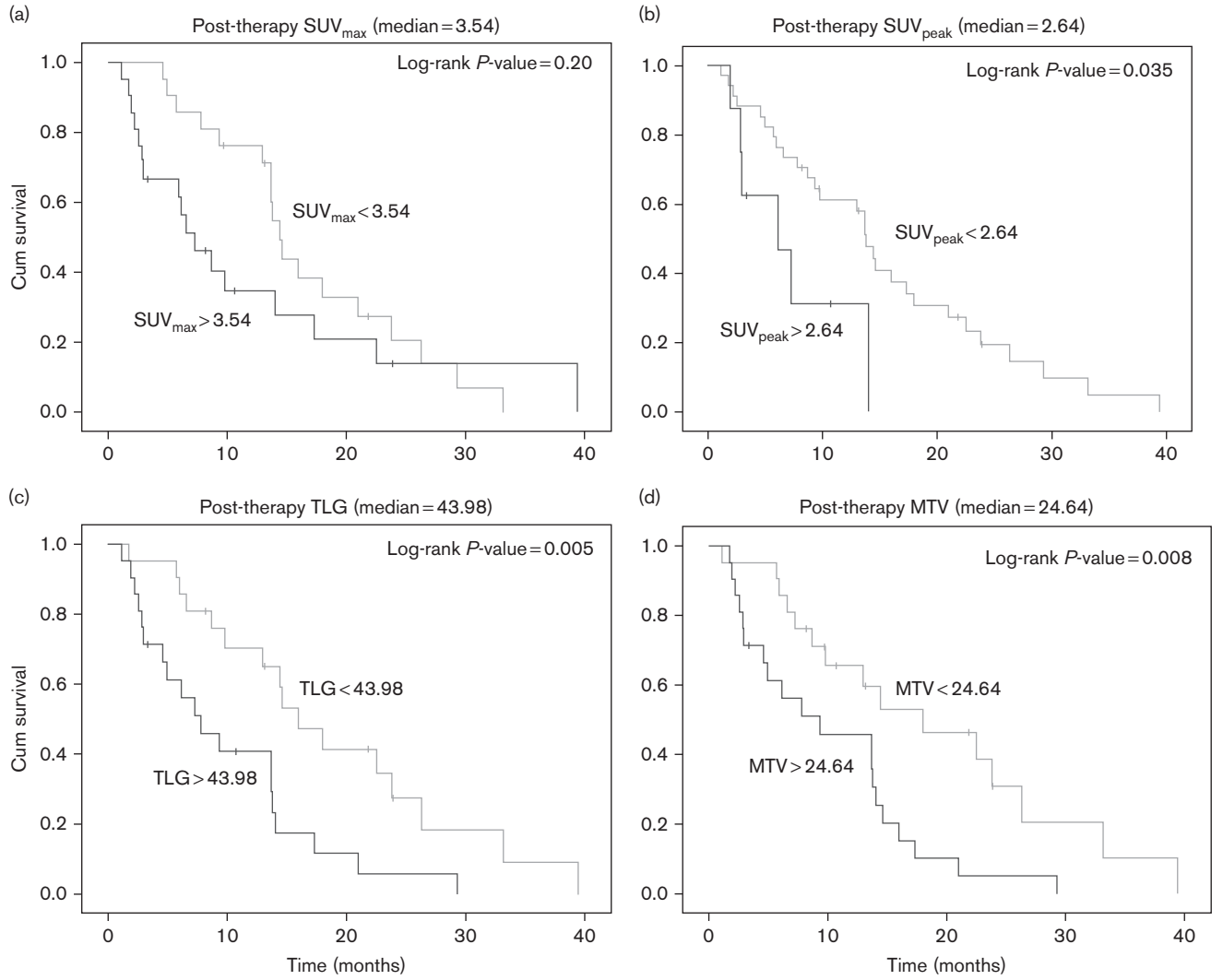
The combined predictive effect of ^{18}F-FDG-avidity and total tumor volume on survival was investigated by risk-grouping patients according to the median cutoff points of SUV_{peak} and MTV values. Group I included patients with both SUV_{peak} and MTV lower than the cutoff points (19 patients); group II included patients who had either SUV_{peak} or MTV above the cutoff points (17 patients); and group III included patients who had both SUV_{peak} and MTV above the cutoff points (six patients). The Kaplan–Meier survival curves were significantly different between these three subgroups (Fig. 4). Considering group I as reference (HR = 1), group II and group III were associated with a 2.32-fold [95% confidence interval (CI): 1.07–4.99] and 5.45-fold (95% CI: 1.76–16.87) increased risk for death, respectively (Table 2).

Discussion

Treatment response is an important factor for management planning and prognosis in pancreatic adenocarcinoma, particularly for those with LAPC and borderline resectable disease [5,7]. PET/CT-based metabolic response assessment following chemoradiation therapy is known to be superior to contrast-enhanced multidetector computed tomography in various tumors as it can effectively distinguish between treatment-induced fibrosis/necrosis and tumor progression [5,17,21].

According to the current guidelines in pancreatic adenocarcinoma, contrast-enhanced multidetector computed

Fig. 3



Kaplan–Meier survival plot by median threshold of PET/CT quantitative parameters: (a) post-treatment SUV_{max} [log-rank, $P = 0.20$; HR (95% CI) = 1.55 (0.79–3.07)], (b) post-treatment SUV_{peak} [log-rank, $P = 0.03$; HR (95% CI) = 2.67 (1.03–6.93)], (c) post-treatment TLG [log-rank, $P = 0.005$; HR (95% CI) = 2.64 (1.30–5.36)], (d) post-treatment MTV [log-rank, $P = 0.008$; HR (95% CI) = 2.57 (1.25–5.26)]. CI, confidence interval; CT, computed tomography; HR, hazard ratio; MTV, metabolic tumor volume; SUV_{max}, maximum standardized uptake value; SUV_{peak}, peak standardized uptake value; TLG, total lesion glycolysis.

tomography is considered the diagnostic imaging modality of choice for routine staging and has been shown to have higher sensitivity in nodal staging compared with PET/CT scans [22–24]. However, PET/CT is recommended for initial staging of high-risk patients and for those with indeterminate conventional imaging results [7], and has been suggested to aid in determining the biological target volume for nonuniform radiotherapy dose prescription [5,9,22,23].

Moreover, as with other neoplasms, PET/CT is found to be useful in monitoring the response to therapy and in evaluating treatment efficacy and may affect patient management [6,7,25]. In LAPC, adequate assessment of resectability after chemotherapy or radiation treatment could validate surgical resection in those with regional control or metabolic responses, whereas rapid development of distant metastasis early after treatment could prompt palliative treatment [25]. In concordance with the limited literature published [7,26], this study showed that therapy assessment PET/CT can be beneficially used in LAPC to tailor future therapeutic approaches, in deciding whether to continue or withdraw current treatment.

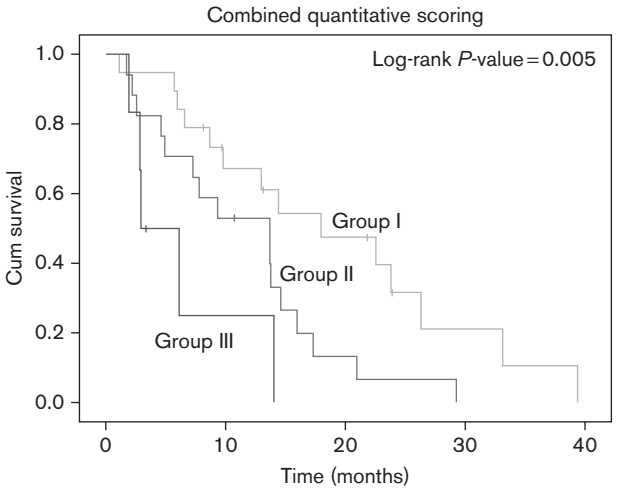
Further, baseline and post-therapy PET parameters have been shown to correlate with prognosis in pancreatic adenocarcinoma [5]. A previous meta-analysis including 198 patients with pancreatic adenocarcinoma (six studies)

Table 2 Post-treatment ^{18}F-FDG-PET/CT parameters in the prediction of overall survival during follow-up

	Cut-point (median)	Unadjusted model HR (95% CI)	Adjusted model[a] HR (95% CI)
Post-treatment PET parameter			
SUV_{max}	3.54	1.55 (0.79–3.07)	1.48 (0.65–1.07)
SUV_{peak}	2.64	2.67 (1.03–6.93)	6.15 (1.68–22.42)
TLG	44.0	2.64 (1.30–5.36)	2.97 (1.28–6.88)
MTV	24.7	2.57 (1.25–5.26)	2.69 (1.09–6.66)
Combined quantitative PET scoring			
Group I		1	1
Group II		2.32 (1.07–4.99)	2.58 (1.00–6.65)
Group III		5.45 (1.76–16.87)	7.68 (1.75–33.69)

Group I defined as SUV_{peak} AND MTV lower than median points; group II defined as SUV_{peak} OR MTV higher than median points; group III defined as SUV_{peak} AND MTV above the median points.
CI, confidence interval; CT, computed tomography; ^{18}F-FDG, fluorine-18 fluorodeoxyglucose; HR, hazard ratio; MTV, metabolic tumor volume; SUV_{max}, maximum standardized uptake value; SUV_{peak}, peak standardized uptake value; TLG, total lesion glycolysis.
[a]HR adjusted for age, sex, race, serum levels of CA19-9 after treatment.

Fig. 4



Kaplan–Meier survival plot by combined quantitative PET scoring result: overall survival (months) between patients who were scored as 0 (group I), those scored as 1 (group II), and those scored as 2 (group III) differed significantly (log-rank, $P = 0.005$). Group I (score 0) was defined as SUV_{peak} AND MTV lower than median points; group II (score 1) was defined as SUV_{peak} OR MTV higher than median points; and group III (score 2) was defined as SUV_{peak} AND MTV above the median points. MTV, metabolic tumor volume; SUV_{peak}, peak standardized uptake value.

reported that high baseline SUV_{max} is a significant predictor of death (HR = 2.39, 95% CI: 1.57–3.63) [27]. Baseline SUV_{max}, MTV, and TLG have consistently been reported as potential predictive factors for survival in LAPC [11–16,28].

In contrast to initial PET/CT, there are not as many studies determining the role of therapy response PET/CT in the prediction of outcome for LAPC patients after primary chemoradiation treatment [7]. A summary is presented in Table 4 [19,25,29–31]. Previous studies showed that patients with low ^{18}F-FDG uptake or reduction in ^{18}F-FDG-avidity (%change in SUV_{max}) in post-therapy PET/CT had higher survival [10,19,30]. In keeping with the current literature, this study showed that the quantitative parameters of post-therapy PET/CT, including SUV_{peak}, MTV, and TLG, are significant prognostic markers of survival in LAPC, even after adjustment for CA19-9 level at the time of the scan.

Our previous study had shown that the five-point qualitative interpretation (Hopkins criteria) can predict treatment response and outcome in head and neck squamous cell carcinoma [20]. In this study we investigated the predictive value of Hopkins criteria for survival outcomes in the therapy response assessment of patients with LAPC. Our results indicated that positive qualitative interpretation (Hopkins criteria) could not predict the overall survival of the patients. The lack of statistical significance is likely due to the small number of patients in our study, particularly in the negative group (scores 1, 2, and 3), as the Kaplan–Meier curves did not cross.

The present study is the first investigation, to our knowledge, to examine the value of the volumetric parameters of post-treatment PET/CT and to propose a combined quantitative scoring system based on the PET/CT parameters for LAPC patient outcome prediction. In a similar study by Schellenberg *et al.* [29], PET/CT was performed after one cycle of chemotherapy and before radiotherapy in 55 patients with LAPC. They indicated that high MTV is associated with lower survival time among LAPC patients. They also showed that the median survival in low-risk patients (low SUV_{max} and low MTV) is significantly longer than that in the high-risk group (high SUV_{max} and high MTV). Our result demonstrated that the scoring system combining

Table 3 Post-treatment ^{18}F-FDG-PET/CT parameters, survival probabilities, and prediction within 12 months following the scan

	ROC analysis			Survival rates at 1 year			
	Optimum cutoff point	SN (%)	SP (%)	< Cutoff point (%)	≥ Cutoff point (%)	*P*	HR (95% CI)
SUV_{max}	3.62	73	80	72.7	20	0.001	5.00 (1.94–12.89)
SUV_{peak}	2.69	68	80	69.6	21.1	0.002	4.18 (1.69–10.37)
TLG	57.92	55	75	60.7	21.4	0.018	2.82 (1.21–6.60)
MTV	37.41	50	85	60	29.4	0.050	3.60 (1.54–8.46)

CI, confidence interval; CT, computed tomography; ^{18}F-FDG, fluorine-18 fluorodeoxyglucose; HR, hazard ratio; MTV, metabolic tumor volume; ROC, receiver operating characteristic; SN, sensitivity; SP, specificity; SUV_{max}, maximum standardized uptake value; SUV_{peak}, peak standardized uptake value; TLG, total lesion glycolysis.

Table 4 Summary of studies evaluating the role of therapy assessment PET/CT in survival from pancreatic adenocarcinoma

References	Type	Number of patients	Disease	Time of scan	PET parameter	Cutoff point	Overall survival (median, months)			Follow-up (months)
							< Cutoff	≥ Cutoff	*P*	
Schellenberg *et al.* [29]	R	55	LAPC, M0	After 1 cycle of CTx	SUV_{max}	6.2	15.3	9.8	< 0.01	13 (2.8–37.7)
					MTV	57.45	18	10.1	0.01	
Choi *et al.* [30]	R	20	LAPC, NR	After 1 cycle of CTx	%Change in SUV_{max}	50	8.4	26.1	< 0.05	NR
Topkan *et al.* [10]	P	32	LAPC, M0	12 Weeks after CCRTx	%Change in SUV_{max}	63.7	9.8	17	0.009	16.1 (4.2–34.1)
Chang *et al.* [19]	R	260	LAPC, M0	1.9 Months after CCRTx	%Change in SUV_{max}	60	41.9	16.0	< 0.001	32.3 (10–99.1)
Maisey *et al.* [31]	R	11	LAPC, M1	1 Month after CTx	^{18}F-FDG uptake	+/−	7.5	8.2	0.034	8 (2.8–48.6)

CCRTx, concurrent chemoradiation therapy; CT, computed tomography; CTx, chemotherapy; ^{18}F-FDG, fluorine-18 fluorodeoxyglucose; LAPC, locally advanced pancreatic cancer; M, metastasis; MTV, metabolic tumor volume; NR, not reported; P, prospective; R, retrospective; SUV_{max}, maximum standardized uptake value.

^{18}F-FDG-avidity and total tumor burden is helpful in risk-grouping patients after treatment completion, as patients with both high SUV_{peak} and MTV showed a more than five-fold increased risk for death compared with those with a low SUV_{peak} and MTV. Although TLG is a product of mean SUV and MTV, this study suggested that using a combined quantitative PET/CT scoring system (SUV_{peak}, and MTV) provides better prognostication than SUV, MTV, or TLG alone, and could serve as a surrogate marker for prediction of outcome in LAPC patients.

There were some limitations to our study. First, enrollment of patients over 10 years in a retrospective manner can be associated with inherent unavoidable biases. Although we did include patients with fairly similar clinical conditions, nonresectable LAPC, the nonuniform and heterogenous treatment regimens (various cycles of chemotherapy with or without radiation, and different maximum radiation doses) may have affected the survival of the patients and introduced biases. Besides, the wide range in time interval between the completion of primary treatment and the post-therapy PET/CT could represent a bias in comparing the results particularly in those treated with radiation therapy. The presence of a draining biliary stent in some patients could be another potential confounder, as these stents often demonstrate inflammatory uptake that might be confused if the tumor was in close proximity to the stent. Further, the quantitative segmentation was performed by one reader using a single vendor's commercial segmentation algorithm.

Conclusion

PET-based volumetric parameters can predict survival outcomes in patients with LAPC. A combined quantitative PET/CT scoring system based on SUVpeak and MTV could provide better prognostication.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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