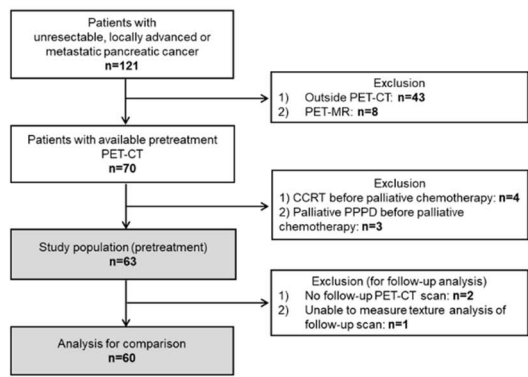
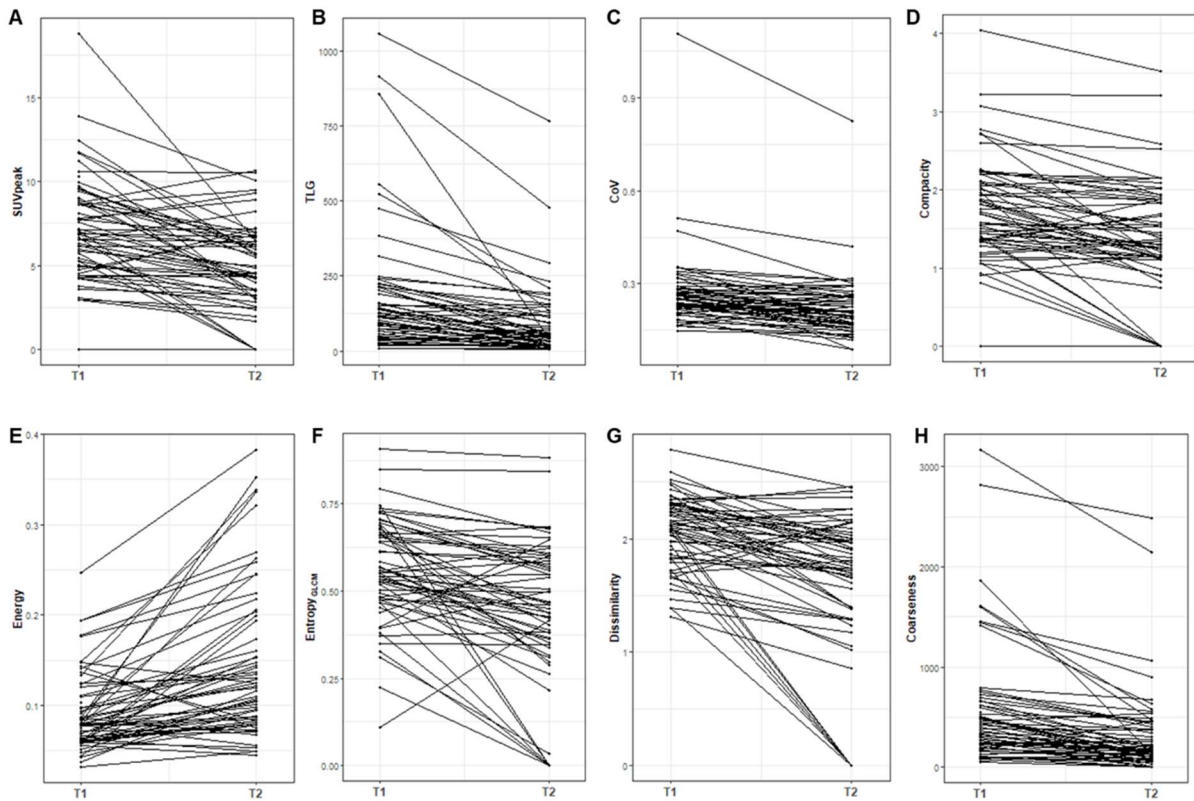


Supplemental Figure Legends

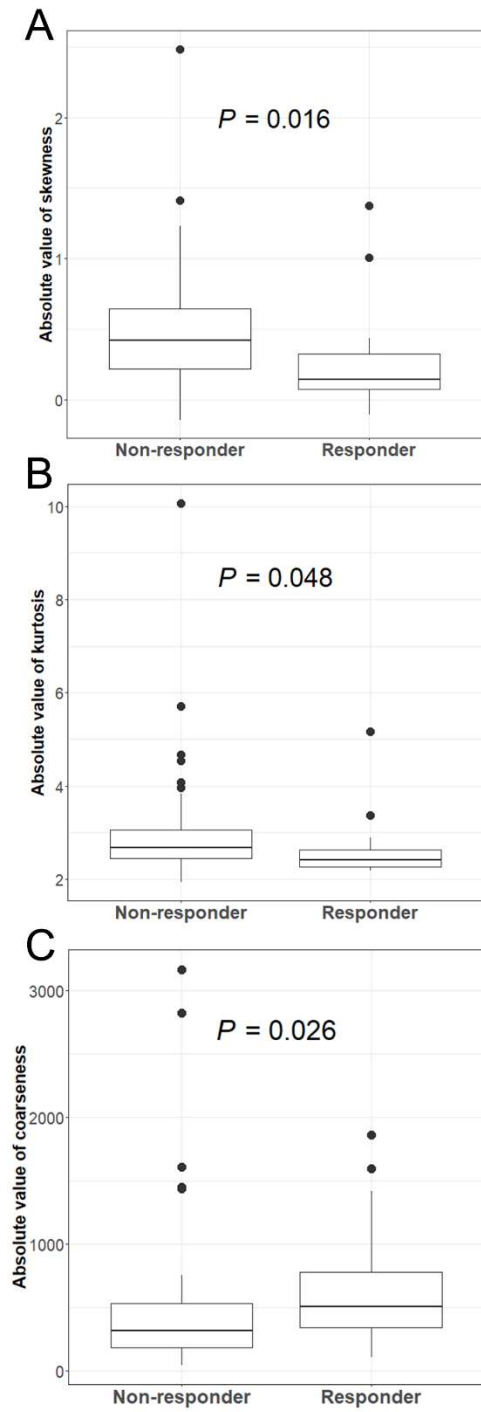


Supplemental Fig. 1 Flow chart of enrollment of study participants.



Supplemental Fig. 2 Changes in metabolic parameters between 2 time points (T1 and T2) showing individual linear plots for the following: SUVpeak (A), TLG (B), CoV (C), compacity (D), energy (E), entropy_{GLCM} (F), dissimilarity (G), and coarseness (H).

SUV= standardized uptake value; TLG = total lesion glycolysis; CoV = coefficient of variance; GLCM = gray-level co-occurrence matrix;



Supplemental Fig. 3 Baseline metabolic parameters in relation to best response: skewness (A), kurtosis (B), and coarseness (C).

Supplemental Table 1. Type of texture analysis parameters

Category	Parameter	Description
Histogram Indices	Skewness	measures the asymmetry of the grey-level distribution in the histogram
	Kurtosis	measures whether the grey-level distribution is peaked or flat relative to a normal distribution
	Entropy	measures the randomness of the distribution
	Energy	measures the uniformity of the distribution
Shape Indices	Sphericity	measures how spherical a volume of interest is
	Compactness	measures the degree to which the volume of interest is compact
GLCM	Correlation	linear dependency of grey-levels in GLCM
	Contrast	local variations in the GLCM
	Entropy	randomness of grey-level voxel pairs
NGLDM	Dissimilarity	variation of grey-level voxel pairs
	Coarseness	level of spatial rate of change in intensity
	Contrast	intensity difference between neighboring regions
	Busyness	spatial frequency of changes in intensity

GLCM = gray-level co-occurrence matrix; NGLDM = neighboring gray-level dependence matrix;

Supplemental Table 2. Baseline characteristics of study population (N=63)

Variables	N	%
Age (yr), median (range)	60	40-84
≥60	34	54.0
<60	29	46.0
Gender		
Male	39	61.9
Female	24	38.1
Initial disease status		
Locally advanced, unresectable	14	22.2
Metastatic	49	77.8
T stage		
T2	5	7.9
T3	18	38.6
T4	40	63.5
N stage		
N0	1	1.6
N1	20	31.7
N2	42	66.7
Comorbidity		
Hypertension	16	25.4
DM	22	34.9
ECOG performance status		
0	22	34.9
1-2	41	65.1
BMI (kg/m²), median (range)	22.2	16.1-29.7
≥25	16	25.4
20-24.9	38	60.3
<20	9	14.3
CEA (ng/mL), median (range)	4.2	0.5-12990
CA 19-9 (U/mL), median (range)	755	2-107400
WBC (x10³/uL), median (range)	6.3	2.6-13.8

Total bilirubin (mg/dL), median (range)	0.6	0.3-2.7
Albumin (mg/dL), median (range)	4	2.8-4.9
First-line chemotherapy		
Regimen		
FOLFIRINOX	44	69.8
Gemcitabine/nab-Paclitaxel	8	12.7
Gemcitabine/Cisplatin	6	9.5
Gemcitabine/Erlotinib	2	3.2
Gemcitabine alone	3	4.8
Duration of first-line chemotherapy (mo), median (range)	5.2	0.8-29.4
Number of first-line chemotherapy cycles, median (range)	8	2-39
Dose reduction rate (%), median (range)	20	0-40
Best Response		
Partial response	16	25.4
Stable disease	39	61.9
Progressive disease	7	11.1
Not evaluable	1	1.6
Time to best response (mo), median (range)	1.7	1-7.5
Cycles till best response, median (range)	3	2-12
Progression-free survival (mo), median (95% CI)	7.1	5.1-9.7
Overall survival (mo), median (95% CI)	10.1	8.6-12.7
Follow-up duration (mo), median (range)	11.2	1.3-31.6

yr = year; ECOG = Eastern Cooperative Oncology Group; BMI = body-mass index; CEA = Carcinoembryonic antigen; CA 19-9 = carbohydrate antigen 19-9; WBC = white blood cell; FOLFIRINOX = folfirinic acid/fluorouracil/irinotecan/oxaliplatin; mo = month; CI = confidence interval;

Supplemental Table 3. Metabolic parameters at baseline (T1) and the first assessment (T2), and percent changes

Parameter	T1 (baseline) (N=63)				T2 (first assessment) (N=60)				Percent change* (N=60)				P
	Mean	Sd	Median	Range	Mean	Sd	Median	Range	Mean	Sd	Median	Range	
Conventional Indices													
SUV _{max}	8.62	3.36	8.21	3.39—20.63	6.35	2.71	6.1	2.04—12.70	-22.03	29.06	-27.71	-71.74—67.47	<0.001
SUV _{peak}	7.13	3.14	6.86	0—18.78	4.89	2.66	4.73	0—10.66	-27.69	33.24	-28.96	-100—60.50	<0.001
TLG	177.26	209.25	116.84	7.14—1058.73	88.57	121.89	49.72	4.58—765.95	-40.22	48.9	-47.16	-96.42—158.51	<0.001
CoV	0.27	0.13	0.25	0.15—1.11	0.22	0.10	0.21	0.09—0.82	-15.99	21.86	-16.54	-72.19—55.54	<0.001
MTV	40	50.88	25.65	1.71—332.75	26.12	44.71	11.64	1.16—298.89	-29.43	48.12	-35.19	-96.93—123.51	<0.001
Histogram Indices													
Skewness	0.43	0.43	0.35	-0.14—2.48	0.40	0.36	0.37	-0.24—1.77	33.93	227.62	-17.53	-370.11—1069.95	0.757
Kurtosis	2.93	1.17	2.6	1.94—10.06	2.92	0.76	2.76	1.93—6.53	3.76	21.69	3.18	-47.73—67.91	0.242
Entropy (log ₂)	3.79	0.61	3.83	2.31—5.17	3.19	0.78	3.27	1.57—4.62	-15.38	17.41	-16.29	-51.53—32.32	<0.001
Energy	0.09	0.04	0.08	0.03—0.25	0.15	0.08	0.12	0.05—0.38	69.3	87.55	45.99	-47.48—341.29	<0.001
Shape Indices													
Sphericity	0.98	0.19	1.0	0—1.11	0.9	0.33	1.02	0—1.12	-9.14	31.19	-0.08	-100—18.16	0.055
Compacity	1.74	0.67	1.7	0—4.04	1.38	0.73	1.32	0—3.52	-22.53	33	-15.35	-100—38.92	<0.001
GLCM													
Contrast	0.41	0.09	0.4	0.24—0.63	0.42	0.18	0.42	0—0.72	5.25	41.01	11.9	-100—90.09	0.601
Correlation	0.015	0.013	0.01	0.002—0.074	0.027	0.033	0.015	0—0.17	128.78	232.49	79.41	-100—1157.532	<0.001
Entropy (log ₂)	0.57	0.15	0.56	0.11—0.91	0.43	0.22	0.46	0—0.88	-18.96	52.77	-17.09	-100—281.39	<0.001
Dissimilarity	2.06	0.32	2.11	1.31—2.78	1.59	0.68	1.77	0—2.46	-22.07	30.49	-16.38	-100—29.33	<0.001
NGLDM													
Coarseness	569.06	610.23	399.42	49.18—3167.41	312.78	438.46	169.33	0—2486.26	-39.46	49.51	-44.51	-100—158.43	<0.001
Contrast	0.89	0.05	0.9	0.73—0.96	0.77	0.29	0.87	0—0.96	-12.36	30.29	-2.06	-100—6.90	<0.001
Busyness	0.022	0.015	0.018	0.004—0.071	0.03	0.02	0.02	0—0.09	69.48	154.68	30.37	-100—825.26	0.02

SUV = standardized uptake values; TLG = total lesion glycolysis; CoV = coefficient of variation; MTV = metabolic tumor volume; GLCM = gray-level co-occurrence matrix; NGLDM = neighboring gray-level dependence matrix;

*The percent change was calculated by $100 \times [\text{value at the first assessment (T2)} - \text{value at the baseline (T1)}] / \text{value at the baseline (T1)}$

Supplemental Table 4. ROC curve of Parameters

	PFS		OS	
	Cut-off value	AUC-ROC	Cut-off value	AUC-ROC
T1 (baseline)				
Conventional Indices				
SUV _{max}	5.078	0.590	7.603	0.600
SUV _{peak}	4.418	0.604	4.418	0.607
TLG	81.351	0.669	81.351	0.643
CoV	0.185	0.551	0.229	0.625
MTV	17.786	0.635	17.786	0.627
Histogram Indices				
Skewness	0.151	0.621	0.119	0.579
Kurtosis	2.614	0.627	2.562	0.620
Entropy (log2)	3.885	0.573	3.942	0.609
Energy	0.043	0.449	0.048	0.402
Shape Indices				
Sphericity	0.971	0.632	0.956	0.552
Compacity	1.403	0.649	1.403	0.652
GLCM				
Contrast	0.332	0.43	0.246	0.44
Correlation	0.0037	0.452	0.0043	0.402
Entropy (log2)	0.494	0.489	0.644	0.556
Dissimilarity	1.791	0.576	1.816	0.611
NGLDM				
Coarseness	297.301	0.588	297.301	0.611
Contrast	0.881	0.585	0.884	0.568
Busyness	0.047	0.397	-Inf	0.394
T2 (first assessment)				
Conventional Indices				
SUV _{max}	7.037	0.731	7.738	0.614
SUV _{peak}	5.733	0.755	4.529	0.59
TLG	48.946	0.802	69.265	0.663
CoV	0.215	0.787	0.178	0.65
MTV	8.717	0.796	25.099	0.669
Histogram Indices				
Skewness	0.552	0.579	0.348	0.521
Kurtosis	2.943	0.648	2.448	0.562
Entropy (log2)	3.536	0.768	2.474	0.622
Energy	0.045	0.261	0.072	0.381

Shape Indices				
Sphericity	0.961	0.604	0.936	0.447
Compacity	1.14	0.817	1.171	0.659
GLCM				
Contrast	0.368	0.566	0.319	0.535
Correlation	0	0.473	0.009	0.503
Entropy (log2)	0.365	0.842	0.498	0.673
Dissimilarity	1.768	0.782	1.289	0.609
NGLDM				
Coarseness	141.094	0.803	104.343	0.67
Contrast	0.797	0.652	0.856	0.556
Busyness	0	0.426	0	0.429
Percent change				
Conventional Indices				
SUV _{max}	-1.427	0.559	-22.688	0.475
SUV _{peak}	-15.454	0.625	9.566	0.468
TLG	-86.113	0.64	-86.113	0.493
CoV	-26.869	0.778	-26.869	0.558
MTV	-69.988	0.648	-78.286	0.51
Histogram Indices				
Skewness	-370.108	0.386	-348.952	0.507
Kurtosis	-25.780	0.487	14.883	0.423
Entropy (log2)	-17.802	0.76	-13.379	0.556
Energy	234.991	0.317	4.415	0.472
Shape Indices				
Sphericity	-11.001	0.477	-6.102	0.417
Compacity	-37.465	0.705	-13.403	0.554
GLCM				
Contrast	-100	0.54	-3.631	0.538
Correlation	-100	0.449	-18.871	0.539
Entropy (log2)	-26.118	0.861	-26.118	0.593
Dissimilarity	-21.951	0.742	-21.545	0.535
NGLDM				
Coarseness	-73.38	0.669	-43.184	0.54
Contrast	-15.94	0.559	-15.940	0.478
Busyness	-9.242	0.48	-25.591	0.492

ROC = receiver operating characteristics; AUC-ROC = area under the ROC curve; PFS = progression-free survival; OS = overall survival; SUV = standardized uptake values; Sd = standard deviation; TLG = total lesion glycolysis; CoV = coefficient of variation; MTV = metabolic tumor volume; GLCM = gray-level co-occurrence matrix; NGLDM = neighboring gray-level dependence matrix;

Supplemental Table 5. Univariate Cox regression analysis for PFS and OS

	PFS			OS		
	HR	95% CI	P	HR	95% CI	P
Clinical variables						
Age (≥ 60 vs. < 60 (ref))	1.1	0.65-1.89	0.716	1.31	0.76-2.25	0.336
Gender (male vs. female (ref))	1.31	0.75-2.31	0.344	1.05	0.60-1.82	0.868
Initial disease status (metastatic vs. locally advanced (ref))	1.48	0.76-2.89	0.246	1.56	0.78-3.10	0.208
First-line chemotherapy regimen (FOLFIRINOX vs. gemcitabine-based (ref))	0.66	0.37-1.18	0.165	0.66	0.37-1.19	0.170
BMI (≥ 25 vs. 20-24.9 (ref))	1.08	0.57-2.03	0.807	0.78	0.34-1.76	0.546
BMI (< 20 vs. 20-24.9 (ref))	0.44	0.18-1.05	0.062	1.46	0.72-2.55	0.342
DM (yes vs. no (ref))	0.84	0.46-1.55	0.578	1.1	0.62-1.96	0.749
Hypertension (yes vs. no (ref))	0.97	0.54-1.72	0.907	0.84	0.46-1.53	0.564
ECOG performance status (1-2 vs. 0 (ref))	0.98	0.56-1.72	0.942	1.16	0.66-2.03	0.606
CEA (≥ 10 vs. < 10 (ref))	1.31	0.74-2.32	0.354	1.62	0.92-2.88	0.096
CA 19-9 (≥ 755 vs. < 755 (ref))	1.86	1.08-3.19	0.024	1.81	1.05-3.11	0.031
Total bilirubin (≥ 1.3 vs. < 1.3 (ref))	1.05	0.42-2.65	0.919	0.9	0.32-2.51	0.843
Albumin (< 3.3 vs. ≥ 3.3 (ref))	1.81	0.77-4.26	0.176	2.15	0.90-5.13	0.084
Best response (non-responder vs. responder (ref))	1.91	1.03-3.54	0.039	1.42	0.77-2.59	0.258
T1 (baseline)						
Conventional Indices						
SUV _{max}		<i>Not included*</i>		1.53	0.87-2.67	0.138
SUV _{peak}	1.68	0.84-3.36	0.144	3.02	1.36-6.74	0.007
TLG	1.31	0.72-2.38	0.378	1.60	0.87-2.95	0.129
CoV		<i>Not included</i>		1.64	0.91-2.93	0.098
MTV	1.51	0.85-2.69	0.158	1.42	0.80-2.54	0.228
Histogram Indices						
Skewness	2.07	1.14-3.77	0.017		<i>Not included</i>	
Kurtosis	1.69	0.99-2.90	0.056	1.41	0.82-2.43	0.209
Entropy (log ₂)		<i>Not included</i>		1.43	0.83-2.45	0.196
Shape Indices						
Sphericity	1.74	0.87-3.47	0.118		<i>Not included</i>	
Compacity	1.85	1.01-3.36	0.045	1.89	1.92-3.49	0.042
GLCM						
Dissimilarity		<i>Not included</i>		2.16	1.05-4.47	0.037
NGLDM						
Coarseness		<i>Not included</i>		1.68	0.93-3.04	0.087
T2 (first assessment)						

Conventional Indices						
SUV _{max}	2.16	1.18-3.97	0.013	2	1.10-3.65	0.024
SUV _{peak}	1.84	1.01-3.34	0.046		<i>Not included</i>	
TLG	1.5	0.86-2.61	0.149	2.18	1.21-3.92	0.01
CoV	2.57	1.38-4.78	0.003	2.52	1.32-4.79	0.005
MTV	1.75	0.99-3.10	0.053	1.61	0.90-2.86	0.108
Histogram Indices						
Kurtosis	1.8	0.98-3.31	0.059		<i>Not included</i>	
Entropy (log ₂)	1.83	1.02-3.28	0.041	2.42	1.13-5.21	0.024
Shape Indices						
Sphericity	1.96	0.94-4.08	0.071		<i>Not included</i>	
Compacity	1.72	0.94-3.14	0.077	1.8	1.00-3.24	0.049
GLCM						
Entropy (log ₂)	1.89	1.03-3.49	0.041	2.23	1.23-4.03	0.008
Dissimilarity	2.15	1.19-3.90	0.011	2.59	1.15-5.84	0.021
NGLDM						
Coarseness	1.54	0.87-2.73	0.141	2.43	1.24-4.79	0.01
Contrast	1.95	0.98-3.87	0.057		<i>Not included</i>	
Percentage changes						
Conventional Indices						
SUV _{peak}	2.04	1.13-3.68	0.018		<i>Not included</i>	
TLG	2.51	1.10-5.75	0.029		<i>Not included</i>	
CoV	3.79	1.81-7.92	<0.001		<i>Not included</i>	
MTV	1.64	0.86-3.11	0.131		<i>Not included</i>	
Histogram Indices						
Entropy (log ₂)	2.2	1.19-4.06	0.011		<i>Not included</i>	
Shape Indices						
Compacity	1.64	0.86-3.12	0.132		<i>Not included</i>	
GLCM						
Entropy (log ₂)	3.62	1.75-7.46	<0.001		<i>Not included</i>	
Dissimilarity	2.68	1.35-5.34	0.005		<i>Not included</i>	
NGLDM						
Coarseness	1.62	0.88-2.99	0.124		<i>Not included</i>	

PFS = progression-free survival; OS = overall survival; HR = hazard ratio; CI = confidence interval; FOLFIRINOX = folfirinic acid/fluorouracil/irinotecan/oxaliplatin; BMI = body-mass index; DM = diabetes mellitus; ECOG = Eastern Cooperative Oncology Group; CEA = Carcinoembryonic antigen; CA 19-9 = carbohydrate antigen 19-9; SUV = standardized uptake values; TLG = total lesion glycolysis; CoV = coefficient of variation; MTV = metabolic tumor volume; GLCM = gray-level co-occurrence matrix; NGLDM = neighboring gray-level dependence matrix;

*Variables with the area under the time-dependent receiver operating characteristics curve <0.6 were not included in the univariate analysis.