Prognosis Based on Early Loss of Muscle and Fat In Patients with Pancreatic Ductal Adenocarcinoma (PDAC) Treated with Chemotherapy +/- Radiotherapy

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Research Background

Prior CT-based body composition studies in PDAC have primarily focused on baseline sarcopenia as a prognostic factor1, with more recent work highlighting the importance of early longitudinal changes during systemic therapy2. Building on this evolving view, we evaluated early post-chemotherapy loss of skeletal muscle (SKM) and subcutaneous fat (SAF) within the context of subsequent treatment strategy in moderate-prognosis PDAC cohort. Early body composition loss delineated prognostic risk groups, but did not predict differential survival benefit from radiotherapy, underscoring its role as a marker of disease aggressiveness rather than treatment sensitivity. Within the 7-month landmark-selected, moderate-to-good prognosis cohort (N=107), the lack of detectable radiotherapy benefit across body composition-based risk groups may help refine risk stratification and help avoid unnecessary overtreatment in this aggressive cancer.

Purpose

Early body composition (BC) loss after chemotherapy associates with poor outcomes in PDAC, but its implications for treatment strategy remain unclear. Radiotherapy (RT) is sometimes considered after 6 months of chemotherapy for patients with unresectable disease. We focused on patients with intermediate to good prognosis to determine whether early changes in BC may aid in guiding therapy.

Methods and Materials

Using a 7-month landmark from chemotherapy initiation to mitigate immortal bias, we analyzed unresectable PDAC patients who survived beyond the landmark , representing a moderate-to-good-prognosis cohort. Using TotalSegmentator on L3-center axial CT at baseline and ~3months from chemotherapy, we calculated skeletal muscle (SKM), subcutaneous abdominal fat (SAF), visceral abdominal fat, and intermuscular fat and percentage loss from baseline were calculated. Inverse probability of treatment weighting (IPTW) anchored to the chemotherapy-alone group assessed survival with versus without RT. Weighted Kaplan-Meier and weighted-Cox regression characterized BC changes for risk stratification.

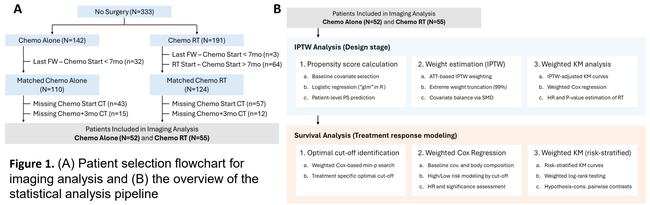
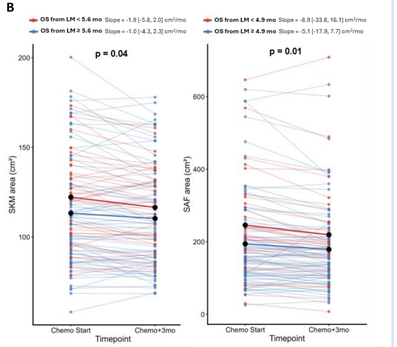


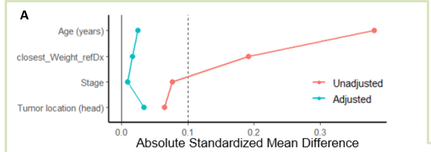
Figure 1. (A) Patient selection flowchart for imaging analysis and (B) the overview of the statistical analysis pipeline

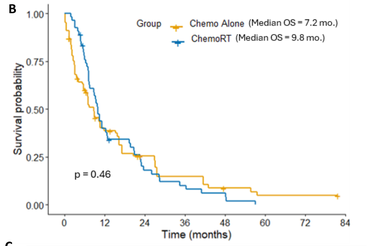
Figure 2. (A) Patient characteristics comparing chemotherapy alone and chemoradiation groups. (B) Early body composition trend from chemotherapy initiation and after 3 months for skeletal muscle area (SKM, left) and subcutaneous abdominal fat (SAF, right), compared by short- vs long-term survival status defined by cutoff survival from landmark (7 months from chemo start) using min-p methods; overall trend of each group is summarized by the corresponding slope between timepoints

A

Variable	Level	N (%) or Median [Min, Max] Chemo Alone (N = 52)	Chemo RT (N = 55)	P
Gender	Female	25 (48.08)	20 (36.36)	0.22
	Male	27 (51.92)	35 (63.64)	
Age at Diagnosis (yr)		67 [46, 89]	65 [38, 86]	0.056
Race	Asian	5 (9.62)	3 (5.45)	0.67
	Black	4 (7.69)	5 (9.09)	
	Hispanic	5 (9.62)	3 (5.45)	
	White	38 (73.08)	43 (78.18)	
	Unknown		1 (1.82)	
Stage	BR-PDAC	14 (26.92)	19 (34.55)	0.39
	LA-PDAC	38 (73.08)	36 (65.45)	
Topography	Head	27 (51.92)	25 (45.45)	0.53
	Body	4 (7.69)	5 (9.09)	
	Duct and Other	2 (3.85)	2 (3.64)	
	Overlap	17 (32.69)	17 (30.91)	
	Tail	2 (3.85)	2 (3.64)	
	Unknown		4 (7.27)	
CA 19-9 at Diagnosis	Normal	7 (13.46)	7 (12.73)	0.03
	Elevated	32 (61.54)	24 (43.64)	
	Uninterpretable	9 (17.31)	3 (5.45)	
	Unknown	4 (7.69)	21 (38.18)	
Type of Chemotherapy	FOLFIRINOX	27 (51.92)	30 (54.55)	0.78
	Gemcitabine and Abraxane	25 (48.08)	25 (45.45)	
Type of Radiotherapy	3D CRT		16 (29.09)	
	Conformal (IMRT or VMAT)		32 (58.18)	
	SBRT		7 (12.73)	
Total Dose (Gy)			50.4 [30.0, 98.0]	
Fractions			24.0 [4.0, 28.0]	







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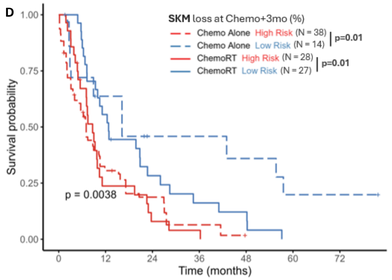
Covariate	HR (95% CI)	P
Age at diagnosis (yr)	0.983 (0.964 - 1.001)	0.067
Gender; Male* vs Female	0.791 (0.517 - 1.210)	0.28
Stage; LA-PDAC* vs BR-PDAC	0.850 (0.522 - 1.386)	0.516
Tumor location; Non-head* vs Head	0.724 (0.475 - 1.103)	0.133
SKM at chemo start†	0.472 (0.282 - 0.790)	**0.004**
SKM loss from chemo start†	2.147 (1.387 - 3.322)	**0.001**
SAF at chemo start†	1.151 (0.749 - 1.768)	0.522
SAF loss from chemo start†	1.769 (1.168 - 2.679)	**0.007**
VAF at chemo start†	0.683 (0.451 - 1.033)	0.071
VAF loss from chemo start†	1.483 (0.957 - 2.300)	0.078
IMF at chemo start†	0.434 (0.277 - 0.679)	**<0.001**
IMF loss from chemo start†	1.396 (0.873 - 2.230)	0.163

* Reference, † Low risk (ref) vs High risk



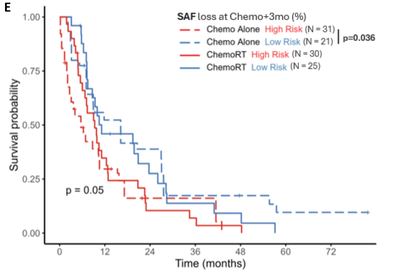


Figure 3. (A) Absolute standardized mean differences before and after IPTW, demonstrating improved covariate balance (maximum absolute SMD: from 0.39 to 0.08). (B) IPTW-weighted Kaplan-Meier curves for overall survival from the landmark timepoint (7 months from chemotherapy initiation) by treatment groups, with treatment effects estimated using IPTW-weighted Cox regression. (C) Weighted univariable/multivariable Cox regression results for baseline covariates and body composition metrics, including baseline values and loss percentage at 3 months from chemotherapy initiation. (D, E) Weighted Kaplan-Meier curves stratified by risk groups (high risk = greater loss) defined by cutoffs derived from weighted Cox models for 3-mongth SKM and SAF percentage loss, shown within each treatment group, with log-rank p-values.

Abbreviations: Chemo, chemotherapy; RT, radiotherapy; BR-PDAC, borderline resectable pancreatic ductal adenocarcinoma; LA-PDAC, locally advanced pancreatic ductal adenocarcinoma; CA 19-9, carbohydrate antigen 19-9; CRT, conformal radiotherapy; IMRT, intensity modulated radiotherapy; VMAT, volumetric modulated arc therapy; SBRT, stereotactic body radiation therapy; OS, overall survival; LM, landmark; SKM, skeletal muscle area; SAF; subcutaneous abdominal fat. SMD, standardized mean distance.

Results

Among total 107 patients (chemoradiotherapy n=55), early loss of SKM and SAF after 3-months from chemotherapy occurred in 62.6% and 74.8% of patients and was more pronounced among short-term survivors, with greater declines (SKM:-1.9vs-1.0 cm2/mo., p=0.04; SAF: -8.9vs-5.1, p=0.01; Wilcoxon rank-sum test). IPTW improved baseline balance (maximum absolute SMD: from 0.39 to 0.08). Use of RT was not associated with improved survival (median OS: 7.2 vs 9.8 months for chemotherapy alone vs RT; P=0.46), with no differential benefit across body composition risk groups. In weighted Cox regression, greater early SKM and SAF loss was associated with worse survival (univariable: SKM HR=2.15, p<0.001; SAF HR=1.77, p<0.01; multivariable: SKM HR=2.07, p<0.01; SAF HR=1.54, p=0.057)

Discussion

- Early loss of SKM and SAF within 3 months of chemotherapy was common and more pronounced in short term survivors in the selected moderate-to-good prognosis PDAC cohort. (Figure 2B)
- Greater early loss of SKM and SAF was strongly associated with worse overall survival in IPTW-weighted analyses. (Figure 3C–E)
- Addition of radiotherapy was not associated with improved survival, either overall or across body composition–defined prognostic risk groups. (Figure 3B–D)
- These findings indicate that early body composition loss is a prognostic marker of disease aggressiveness rather than a predictor of radiotherapy benefit.

Conclusions

Early post-chemotherapy SKM and SAF loss was common and associated with poorer survival in this moderate-to-good-prognosis PDAC cohort.

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References

1. Ninomiya, Go, et al. "Clinical impact of sarcopenia on prognosis in pancreatic ductal adenocarcinoma: A retrospective cohort study." International Journal of Surgery 39 (2017): 45-51.
2. Basile, Debora, et al. "The IMPACT study: early loss of skeletal muscle mass in advanced pancreatic cancer patients." Journal of cachexia, sarcopenia and muscle 10.2 (2019): 368-377.

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