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Patterns of Failure Following Neoadjuvant SBRT or Fractionated Chemoradiation in Resectable and Borderline Resectable Pancreatic Cancer

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Purpose/Objective(s): SBRT during neoadjuvant therapy in resectable and borderline resectable (BLR) pancreas cancer (PCa) involves smaller target volumes and condensed fractionation relative to chemoradiation (FxChemoRT). However, no randomized trials have compared SBRT to FxChemoRT to assess differences in downstaging, patterns of failure, or survival outcomes.

Materials/Methods: All patients with BLR or resectable PCa cancer undergoing neoadjuvant therapy from 10/2012-7/2017 were retrospectively reviewed. Twenty-two patients were treated with FxChemRT, which is the institutional standard. A subset of patients (n=18) were treated with SBRT on a prospective trial from 11/2014-7/2017. The FxChemoRT group received 50.4 Gy (28 fractions) to a customized CTV including the primary tumor, SMA, and celiac axis (5-10 mm PTV) using sensitizing gemcitabine or capecitabine. SBRT was delivered to the primary mass and abutting vessel with fiducials/abdominal compression to 33 Gy (5 fractions, 3 mm PTV). An optional elective CTV including the nodal space and mesenteric vessels was treated to 25 Gy. All patients were treated with 4 months of gemcitabine/abraxane or FOLFIRINOX prior to RT (table). Patients without disease progression at re-staging underwent resection. The cumulative incidence of local failure (LF), PFS, and OS were compared using a log rank test. The cumulative incidence of LF was defined as recurrence within conventional RT fields from the time of resection to LF or last CT without local disease.

Results: In the SBRT and FxChemoRT groups, there was no difference in resectable tumors (17% vs 32%, p=0.4), arterial abutment (83% vs 68%, p=0.5), or venous encasement (53% vs 36%, p=0.5). Resection was performed in 12 (57%) patients treated with FxChemoRT and 12 (67%) treated with SBRT (p=0.1). There was no difference in R0 rates in the SBRT or FxChemoRT groups [92% (11/12) vs 83% (10/12), p=0.1] or lymph node involvement [33% (4/12) vs 25% (3/12) p=0.6]. The PFS in patients treated with SBRT compared to FxChemoRT at 2 years was 7% vs 33% (p=0.04) for all patients and 11% vs 53% (p=0.01) in resected patients. At first progression, LF occurred in 0% (0/5) of FxChemoRT patients compared to 56% (5/9) of SBRT patients (table). LF rates at 1 year and 2 years from surgery in the SBRT vs FxChemoRT groups was (56% vs 20%) and (85% vs 20%) (p=0.01). The 2-year OS in the SBRT vs FxChemoRT groups was (46% vs 43%) (p=0.59) for all patients and (63% vs 58%) (p=0.83) in resected patients.

Conclusion: Patients treated with neoadjuvant SBRT had shorter PFS, more local only failures within conventional RT volumes, and less durable local control relative to FxChemoRT. Omission of elective vascular target volumes may result in unacceptable local recurrence patterns for patients undergoing curative resection.

Abstract SU_17_2164; Table 1

	SBRT		FxChemoRT		
	N=18	%	N=22	%	P-value
Gem/nab-paclitaxel	13	72%	14	64%	0.57
FOLFIRINOX	5	28%	8	36%	
Site of 1st Failure after Resection	N=9/12		N=5/12		
Distant	4	44%	5	100%	
Local only	4	44%	0	0%	
Local & distant	1	15%	0	0%	

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Proposition of Splenic Dose-Volume Constraints to Prevent Severe Lymphopenia after Chemoradiation for Pancreatic Cancer

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Purpose/Objective(s): Severe treatment-related lymphopenia (TRL) - i.e. $\leq 0.5\times10^9$/L - is a frequent complication of chemoradiation (CRT) for locally advanced pancreatic cancer (LAPC) and is associated with impaired survival. Recent investigations have shown a direct correlation between TRL and unplanned splenic irradiation. The aim of this study was to determine splenic dose-volume constraints for pancreatic radiotherapy (RT) treatment planning in order to decrease the incidence of TRL.

Materials/Methods: Forty-four patients treated with CRT for LAPC between 03/2009 and 10/2017 were retrospectively analyzed. Institutional Board Approval was obtained for this study. The dose prescribed to the PTV was 54 Gy in 30 fractions. Most of patients were treated with a VMAT technique (32 patients). A concomitant chemotherapy with capecitabine 800 mg/m^2 bid was systematically associated with RT. The exclusion criteria were as follows: (a) patients with a clinical condition impairing splenic metabolism (e.g. cirrhosis, portal vein thrombosis, and malignant hemopathy); (b) pre-treatment lymphopenia; (c) HIV or HBV infection; and (d) treatment with granulocyte colony-stimulating factor. The spleen was delineated on radiotherapy planning CT scan in accordance to RTOG Organ Contouring Consensus Guidelines by 2 radiation oncologists experimented in treatment of pancreatic cancer. Spleen dosimetric variables, including the mean spleen dose (MSD), V5Gy, V10Gy, and V20Gy, were extracted from treatment planning software. Complete blood cell counts were collected 0-3 days before the start of RT, then once a week until 12 weeks following completion of CRT. Student's t-test was used to assess the correlation between dosimetric variables and occurrence of TRL. Receiver operating characteristic (ROC) curve analysis was performed to select the most predictive cutoff value of spleen dosimetric variables for TRL.

Results: Thirty-one patients were included in the analysis. TRL occurred in 77% of cases (24 patients). MSD and V10Gy were significant factors correlated with TRL (p=0.015 and p=0.0013, respectively). V5Gy and V20Gy were not statistically associated with TRL (p=0.08). According to the ROC curve analysis, the predictive cutoff values of the MSD and V10Gy for TRL were 4.5Gy (Accuracy: 63.3%, AUC: 0.711) and 12% (Accuracy: 73.3%, AUC: 0.826), respectively.

Conclusion: MSD and V10Gy were the most predictive dosimetric parameters for severe lymphopenia. Hence, to decrease the incidence of TRL when treating pancreatic cancer by CRT, we recommend the following splenic dose-volume constraints: MSD<4.5Gy and V10Gy<12%. Further prospective investigations are warranted to determine whether avoidance of low-doses splenic irradiation could affect survival after CRT for pancreatic cancer.

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