CASE – CONTROLLED ANALYSIS OF PATHOLOGIC RESPONSE TO NEOADJUVANT ABLATIVE RADIOTHERAPY FOR PANCREATIC CANCER

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Introduction

Ablative neoadjuvant radiotherapy delivered with a magnetic resonance imaging-guided linear accelerator (MR-LINAC) is emerging as an option for treating patients with borderline resectable pancreatic ductal adenocarcinoma (PDAC) compared to standard low dose neoadjuvant radiation therapy (RT). This study evaluated the pathological response to ablative RT and chemotherapy before surgery compared to neoadjuvant chemotherapy alone.

Methods

We conducted a single institution retrospective analysis of patients who received neoadjuvant chemotherapy and ablative RT followed by pancreatic resection from December 2019 to February 2024. These patients were matched in a 1:2 fashion with patients who underwent neoadjuvant chemotherapy alone according to age, gender, Charlson Comorbidity Index and tumor size. The pathologic response to treatment was evaluated using the CAP score in resected surgical specimens.

Results

We evaluated a total of 57 patients, 19 who had neoadjuvant chemotherapy followed by ablative RT and 38 patients who underwent neoadjuvant chemotherapy alone. No statistically significant difference was observed in the number of neoadjuvant chemotherapy cycles between the groups (10.4 vs 7.7, p = 0.49). The patients who received neoadjuvant RT had more advanced disease by radiographic resectability criteria (100% borderline resectable versus 44.7% borderline resectable (p < 0.005) and were more likely to undergo pancreatoduodenectomy (84.2% vs 47.3, p = 0.02) instead of distal pancreatectomy (15.8% vs 52.7%, p = 0.02). There were no differences in type of chemotherapy given (p = 0.28), number of cycles given (p = 0.49), CA 19-9 levels before surgery, or other demographic information. There were also no differences in T stage of the tumors. All patients received 5 fractions of RT with overall dose of 40 Gray in 8 patients and 50 Gray in 11 patients, with no difference in tumor response between the groups (p = 0.11). Those who received ablative RT had significantly better pathologic response to therapy than those who had neoadjuvant chemotherapy alone (CAP grade 0: 5.2 % vs 0%; grade 1: 26.3% vs 13.1%; grade 2: 68.4% vs 52.6%; grade 3: 0% vs 34.2%) p = 0.016. The mean number of lymph nodes involved by tumor was 0.5 in the ablative radiation cohort compared to 1.3 (p = 0.04).

Characteristics	Cases (n=19)	Controls (n=38)	P value
Age, y	64.8 (10.4)	66.9 (9.5)	.48
Men	13 (68.4)	19 (50.0)	.18
BMI, kg/m²	29.5 (7.4)	27.5 (6.0)	.24
CMI	4.5 (1.4)	5.2 (1.6)	.13
CA 19-9	853 (1614)	567 (1144)	.51
Albumin	3.9 (0.4)	2.8 (1.4)	>.99
Resectable	0 (0)	21 (55.3)	
Borderline Resectable	19 (100.0)	17 (44.7)	<.005
Neoadjuvant therapy			
Folfirinox	16 (84.2)	27 (71.1)	
Other	3 (15.8)	11 (28.9)	.28
Number of Chemotherapy Cycles	10.4 (3.4)	7.7 (3.3)	.49
Time interval, Days (Chemotherapy to Surgery)	99.4 (39.1)	38.0 (19.9)	>.99
Radiotherapy dose 40 Gy	8 (42.1)	0 (0)	
Radiotherapy dose 50 Gy	11 (57.9)	0 (0)	.11
Time interval RT to Surgery, days (40 vs 50 Gy)	38.0 (14.3)	67.7 (20.9)	.002
Perioperative details			
Whipple Procedure	16 (84.2)	19 (47.3)	
Distal Pancreatectomy	3 (15.8)	20 (52.7)	.02
LOS, d	7.5 (3.8)	8.2 (7.0)	.37
Size of the Tumor (mm)	20.7 (22.7)	20.6 (14.8)	.49
Tumor response to Treatment			
Grade 0	1 (5.2)	0 (0)	
Grade 1	5 (26.4)	5 (13.1)	
Grade 2	13 (68.4)	20 (52.7)	
Grade 3	0 (0)	13 (34.2)	.016
Lymph nodes Harvested, n	19.4 (6.4)	22.7 (10.3)	>.99
Positive Lymph Nodes	0.5 (1.2)	1.3 (2.7)	.04
p T-Stage I	12 (63.2)	19 (50.0)	
p T-Stage II	6 (31.6)	14 (36.9)	
p T-Stage III	1 (5.2)	5 (13.1)	.53
Lymphovascular Invasion	2 (10.5)	5 (13.1)	.37
Perineural Invasion	4 (21.1)	15 (39.5)	.18
R0 Resection	17 (94.4)	35 (92.1)	.39

Abbreviations: BMI, body mass index; LOS, length of stay; CMI, Charlson Comorbidity Index; Gy, Gray. a Values are mean (SD) or No. of patients (%).

Conclusion

Neoadjuvant chemotherapy and ablative 5-fraction RT resulted in more favorable pathologic outcomes compared to neoadjuvant chemotherapy alone. Future studies should evaluate whether these differences in pathologic outcomes translate into meaningful differences in local recurrence rates and overall survival. Additionally, patients receiving neoadjuvant chemotherapy followed by ablative radiation showed a significantly lower rate of positive lymph nodes. Larger patient samples in future studies are necessary to reach more definitive conclusions

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