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Neoadjuvant Chemotherapy is Associated with Improved Outcomes in Patients with Stage 1A and 1B Pancreatic Cancer Undergoing Surgery: An NCDB Study

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Background:

The use of neoadjuvant chemotherapy (NAC) for pancreatic ductal adenocarcinoma (PDAC) has shown clear advantages in locally advanced and borderline resectable disease. The benefit in upfront resectable PDAC is debated. Moreover, in early clinical stages IA/IB, potential benefits including improved R0 resection rate, decreased tumor upstaging, and survival, are not clear. We hypothesize that NAC will be associated with improved outcomes and survival compared to adjuvant therapy in patients with clinical stage IA/IB PDAC.

Methods:

The National Cancer Database (NCDB) PUFs (2004-2017) were used to perform a retrospective review of patients with clinical stage IA or IB PDAC undergoing surgery. Treatment groups were selected based on timing of chemotherapy. Patients receiving chemotherapy or surgery alone were excluded.

Results:

We identified 6,613 patients with clinical stage IA or IB PDAC who underwent surgery. The neoadjuvant therapy group (NAT) included 1,533 patients who received neoadjuvant or perioperative chemotherapy, and the adjuvant therapy group (AT) contained 5080 patients who received chemotherapy after surgery. Patients in the NAT had higher rates of T1 and T2 disease and lower rates of T3 pathology compared to the AT (pT1: 18.7% vs 7.8%; pT2: 20.1 vs 18.6%; pT3: 59.3% vs 72.1%, $p<0.0001$). Additionally, the NAT had significantly higher rates of N0 disease and less N1 pathology (pN0: 54.6% vs 37.5%; pN1: 45.4% vs 62.5%, $p<0.0001$). The R0 resection rate was higher in the NAT (83.2% vs 62.3%, $p=0.0197$) and there was less lymphovascular invasion (LVI) compared to the AT (34.8% vs 48.1%, $p<0.0001$). Using Kaplan Meier estimates, the NAT was associated with improved overall survival (OS) compared to the AT (median OS: 33.4 vs 27.5 months, $p<0.0001$). On multivariable analysis, R0 resection (HR=0.715, CI: 0.619-0.825, $p<0.0001$), LVI (HR=1.126, 95% CI: 1.038-1.222, $p=0.0043$) but not receipt of NAC (HR=0.94, 95% CI: 0.852-1.038, $p=0.2229$) were independent risk factors for OS.

Conclusions:

NAC is beneficial in patients with stage IA/IB PDAC undergoing surgical resection as it is associated with improved oncologic outcomes including increased R0 resection rate, decreased tumor upstaging, lymph node metastasis, and LVI. Furthermore, patients receiving NAC were found to have improved survival over those getting adjuvant therapy. Based on these results, we recommend all patients diagnosed with PDAC be considered for NAC prior to surgery.

Patient characteristics	AT (5080) n (%)	NAT (1533) n (%)	p-value
Pathologic T stage			<0.0001
pT1	369 (7.8)	248 (18.7)	
pT2	876 (18.6)	267 (20.1)	
pT3	3401 (72.1)	787 (59.3)	
Pathologic N stage			<0.0001
pN0	1751 (37.5)	749 (54.6)	
pN1	2922 (62.5)	622 (45.4)	
R0 Resection	4000 (62.3)	1216 (83.2)	0.0197

LVI	1749 (48.1)	354 (34.8)	<0.0001
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LVI = lymphovascular invasion; AT = adjuvant therapy group; NAT = neoadjuvant Therapy group.