Davis CH, et al., Archiv Surg S Educ 2021, 3: 019
DOI: 10.24966/ASSE-3126/100019

HSOA Archives of Surgery and Surgical Education

Short Communication

Neoadjuvant Therapy for Pancreatic Malignancy: Paradigm Shifts in Multidisciplinary Car

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Pancreatic Ductal Adenocarcinoma (PDAC) accounts for the third leading cause of cancer death in the United States and portends a poor prognosis, with over five-year survival rates of about ten percent [1]. The disease has been widely studied in recent years and several portenders of poorer survival outcomes have been identified, including surgical margin status [2]. PDAC is a challenging disease to manage surgically and positive margin rates may be as high as 25% in surgically resectable patients. These rates are even higher in patients deemed borderline resectable based on preoperative imaging [3,4]. Given the high positive margin rate and associated poorer overall survival outcomes of patients with borderline resectable PDAC, Neoadjuvant Therapy (NAT), consisting of preoperative chemotherapy with or without radiation, is now the standard of care [5,6]. Despite high positive margin rates in resectable PDAC patients, however, there are no current recommendations for the use of NAT and practice is widely variable.

To address this clinical problem, authors Greco, Langan, et al performed a study comparing margin positivity rates in PDAC patients who did and did not receive NAT, published Surgery Open Science in December 2020 [7]. The National Cancer Database (NCDB), extracting data from 2004-2014, was chosen due to its ability to study surgical margins as well as long term survival outcomes. Clinical T1 and T2 tumors (T1: <2cm, limited to the pancreas; T2: >2cm, limited to the pancreas) of the head of the pancreas were selected as inclusion criteria as a surrogate for patients with favorable/resectable tumors. The primary outcome included surgical margin status (negative versus positive margin), and secondary outcomes included Overall Survival (OS) and 30- and 90-day mortality. Of 8,472 patients with available data, 758 (9%) received NAT. Regarding adjuvant therapy, 32% of patients received chemotherapy alone, 28% received chemotherapy and radiation, 31% received no adjuvant therapy, and 0.7% received radiation alone. In this retrospective cohort analysis, the group receiving NAT was younger, male-predominant, had less comorbidities, was more likely to be treated at an Academic center and have private insurance. Additionally, the NAT group was more likely to have clinically node positive disease.

The overall margin positivity rate of all patients was 21.3%, however this rate was significantly lower in patients who received NAT compared to those who did not (15.5% vs. 21.8%, $p<0.001$). Further, patients who received both neoadjuvant chemotherapy and radiation had significantly lower margin positivity rates as compared to those who received neoadjuvant chemotherapy alone (13.4% vs. 18.6%, $p<0.001$). On multivariable analysis, NAT was found to be an independent predictor of positive margin status, in addition to lower Charlson-Deyo comorbidity score (0-1), treatment at an academic facility, clinical node negative status, and smaller tumor size. NAT was also associated with lower rates of pathologically positive lymph nodes (6% vs. 13.6%, $p<0.0001$). Further, patients who received NAT had fewer mean positive lymph nodes than patients who did not receive NAT (1.44 vs. 2.30, $p<0.0001$).

The study identified a significant association between surgical margin status and median OS: median OS was 14.9 months in patients with positive margins vs. 23.9 months in those with negative margins (HR 1.702, $p<0.0001$). Additionally, there was a survival advantage found for those patients who received either NAT or adjuvant therapy compared to patients who received surgery alone (NAT=24.7 months, HR 0.712; adjuvant therapy=23.8 months, HR 0.706; surgery alone 15.2 months, $p<0.0001$). However, there was no difference identified in OS between patients who received NAT as compared to adjuvant therapy. Multivariable analysis identified negative surgical margin status, NAT, younger age, Caucasian race, lower Charlson-Deyo comorbidity score (0-1), treatment at an academic facility, treatment in the Northeastern United States, clinical and pathologic node negative status, and smaller tumor size and grade as independent predictors of improved OS. Despite a difference in OS, this difference was not seen on analysis of early mortality (30-day: 8.5% vs. 8.1%, $p=0.07$; 90-day: 8.4% vs. 10.8%, $p=0.8$).

Given these compelling data, the authors suggest that NAT should be considered not only for borderline resectable PDAC but also for "select high-risk" patients with resectable PDAC of the pancreatic head. These patients include those with larger tumor size, higher CA 19-9 levels, or those with large regional lymph nodes. A recent

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Citation: Davis CH, Langan RC (2021) Neoadjuvant Therapy for Pancreatic Malignancy: Paradigm Shifts in Multidisciplinary Care. Archiv Surg S Educ 3: 019.

Received: April 07, 2021; **Accepted:** April 13, 2021; **Published:** April 22, 2021

randomized controlled trial, PREOPANC, examined NAT consisting of gemcitabine-based chemoradiotherapy [8]. This study demonstrated that NAT patients had significantly lower positive margin status (29% vs. 60%, p<0.001) and improved disease-free survival (HR 0.73, p=0.032). Though there were no differences in median OS between groups, patients who received both NAT and adjuvant therapy did experience an OS benefit (35.2 vs 19.8 months, p=0.029). Further, the data suggested improved compliance with preoperative therapy: 89% of patients who completed their NAT regimen compared to 58% of patients completing adjuvant therapy.

Despite the reported benefits of NAT, several potential disadvantages of NAT must also be addressed. First, NAT delays time from diagnosis to surgery. This delay may be exacerbated if treatment complications are encountered. NAT also often necessitates procedures which are not needed by patients who undergo upfront surgery, including tumor biopsy and biliary stenting. Further, upwards of 30% of patients who initiate NAT may not undergo planned surgical resections due to complications or progression of disease [9,10]. Additionally, NAT regimens are not currently standardized. Given, however, that FOLFIRINOX is currently being utilized more frequently than gemcitabine-based regimens, an ongoing randomized controlled trial, PREOPANC-2, is currently investigating the role of FOLFIRINOX-based NAT in PDAC.

In summary, this retrospective cohort study utilizing data from the NCDB demonstrates that NAT is associated with lower positive surgical margin rates, fewer pathologically positive lymph nodes, and improved median OS for patients with clinical T1 or T2 PDAC of the pancreatic head. There are numerous other retrospective studies with concordant results and there are currently ongoing clinical trials randomizing patients to either upfront surgery followed by systemic therapy or neoadjuvant therapy followed by surgery and adjuvant therapy.

References

1. NIH (2021) Cancer Stat Facts: Pancreatic Cancer. National Cancer Institute, USA.
2. Ethun CG, Kooby DA (2016) The importance of surgical margins in pancreatic cancer. J Surg Oncol 113: 283-288.
3. Mokdad AA, Minter RM, Zhu H, Augustine MM, Porembka MR, et al. (2016) Neoadjuvant therapy followed by resection versus upfront resection for resectable pancreatic cancer: A propensity score matched analysis. J Clin Oncol 35: 515-522.
4. Mirkin KA, Hollenbeak CS, Gusani NJ, Wong J (2017) Trends in utilization of neoadjuvant therapy and short-term outcomes in resected pancreatic cancer. Am J Surg 214: 80-88.
5. Murphy JE, Wo JY, Ryan DP, Jiang W, Yeap BY, et al. (2018) Total Neoadjuvant therapy with FOLFIRINOX followed by individualized chemoradiotherapy for borderline resectable pancreatic adenocarcinoma: A phase 2 clinical trial. JAMA Oncol 4: 963-969.
6. Katz MH, Ou FS, Herman JM, Ahmad SA, Wolpin B, et al. (2017) Alliance for clinical trials in oncology (ALLIANCE) trial A021501: Preoperative extended chemotherapy vs. chemotherapy plus hypofractionated radiation therapy for borderline resectable adenocarcinoma of the head of the pancreas. BMC Cancer 17: 505.
7. Greco SH, August DA, Shah MM, Chen C, Moore DF, et al. (2020) Neoadjuvant therapy is associated with lower margin positivity rates after pancreaticoduodenectomy in T1 and T2 pancreatic head cancers: An analysis of the national cancer database. Surg Open Sci 3: 22-28.
8. Versteijne E, Suker M, Groothuis K, Akkermans-Vogelaar JM, Besselink MG, et al. (2020) Dutch pancreatic cancer group. Preoperative chemoradiotherapy versus immediate surgery for resectable and borderline resectable pancreatic cancer: Results of the Dutch randomized phase III PREOPANC trial. J Clin Oncol 38: 1763-1773.
9. Palmer DH, Stocken DD, Hewitt H, Markham CE, Hassan AB, et al. (2007) A randomized phase 2 trial of neoadjuvant chemotherapy in resectable pancreatic cancer: Gemcitabine alone versus gemcitabine combined with cisplatin. Ann Surg Oncol 14: 2088-2096.
10. Shubert CR, Bergquist JR, Groeschl RT, Habermann EB, Wilson PM, et al. (2016) Overall survival is increased among stage III pancreatic adenocarcinoma patients receiving neoadjuvant chemotherapy compared to surgery first and adjuvant chemotherapy: An intention to treat analysis of the national cancer database. Surgery 160: 1080-1096.

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