Abstract:

Neoadjuvant Stereotactic Body Radiation Therapy followed by Pancreatic Cancer Resection with Intra-Operative Electron Radiation Therapy (IOeRT) boost: Initial Experience and Clinical Outcomes

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Purpose:
Pancreatic cancer is an aggressive disease with limited treatment options and poor prognosis, making it one of the deadliest forms of cancer. Surgical resection is the primary treatment, but local recurrence remains a significant challenge. Innovative approaches to improve locoregional control, such as neoadjuvant Stereotactic Body Radiation Therapy (SBRT) with intraoperative electron radiation therapy (IOeRT) boost, are being used at our institution in an attempt to improve oncologic outcomes.

Methods and Materials:
We conducted a single-institution retrospective review of consecutive patients treated from February 2021 to October 2023, who underwent neoadjuvant SBRT followed by pancreatic resection with IOeRT. SBRT was delivered at 35-40 Gy to the gross disease and 25 Gy to region deemed at risk for harboring microscopic disease in 5 fractions. At the time of surgical intervention an intraoperative radiation applicator measuring 40-60mm was placed flush against the post-operative bed deemed at high risk by the surgeon and a 10-12 Gy boost was delivered using a mobile, self-shielded electron-beam linear accelerator. Toxicity was assessed using CTCAE v5 and Clavien-Dindo Classification. Kaplan−Meier overall survival and progression-free survival estimates were calculated.

Results:
Fourteen patients (10 male, 4 female; median age 66.7) were included. Median follow-up was 16 months (range 7-32 months). Nine patients (64%) were borderline resectable and received neoadjuvant chemotherapy prior to SBRT, while five were resectable at diagnosis and received upfront SBRT. Eight patients underwent distal pancreatectomy for tumors in the body/tail, and six underwent Whipple pancreatectomy for tumors in the head of the pancreas. Twelve patients (85.7%) underwent R0 resection, and two patients with BRCA2 had a complete pathological response.

Acute toxicities from SBRT included grade 1 and 2 fatigue and nausea (42.8%) and grade 1 and 2 abdominal pain (35.7%) using CTCAE v5 criteria. Based on Clavien-Dindo Classification, four patients experienced grade 1 toxicity (ileus and surgical site infection), four patients with grade 2 toxicity (infection, DVT), one patient with grade 3 toxicity (repeat surgical intervention), and one patient experienced grade 5 toxicity, dying from early post-operative complications. Another patient died from long-term complications (hepatic artery occlusion, biloma and biliary sepsis), possibly related to radiotherapy.

Median overall survival and progression-free survival was 10 months (range 7-22 months) and 12 months (range 8-20 months), respectively. Survival analysis showed that seven patients (50%) were alive at the time of assessment.

In total, 43.9% (6/14) patients experienced progression at any point during follow-up, one patient (7.1%) exhibited local recurrence while five patients (35.7%) developed metastatic disease. A total of seven patients (50.0%) died due to various causes, including distant metastases (5), sepsis (1), and post-operative complications (1).

Conclusions:
Local control and margin-negative resection rates were high with preoperative SBRT and IOeRT in surgically resected pancreatic cancer patients. Distant recurrence was the predominant site of failure, with only one case of isolated locoregional recurrence. Optimal patient selection is critical to maximize the benefits of this treatment strategy.