

The impact of multi-agent chemotherapy and stereotactic body radiation therapy on clinical outcomes in patients with unresectable pancreatic adenocarcinoma

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Abstract

Objectives: Historically, only 5-10% of patients with unresectable, locally advanced pancreatic cancer (LAPC) are surgical candidates. The purpose of this retrospective study was to determine if aggressive systemic and local therapy with multi-agent chemotherapy and stereotactic body radiation therapy (SBRT) improves the likelihood that LAPC patients undergo surgical resection and leads to improved long-term outcomes.

Methods: From July 2010 to April 2015, 135 patients with LAPC were treated with definitive SBRT to a median dose of 33 Gy (range, 25-33 Gy) at our institution. Eighteen patients were excluded from the analysis due to treatment with palliative intent or lack of follow-up. Kaplan-Meier survival estimates were calculated.

Results: Of the 117 analyzable patients, 51% were male, 84% were Caucasian, and 58% had head of pancreas lesions. Median duration of induction chemotherapy was 2.96 months (range, 0-22.3 months). Ninety-three percent of patients received induction chemotherapy prior to SBRT, 71% of whom received multi-agent chemotherapy. The most common multi-agent regimen consisted of FOLFIRINOX-based chemotherapy in 42% of patients. Median time of follow-up was 11.1 months (range, 1.1-53.1 months). Median OS from diagnosis and from the end of SBRT was 19.5 and 14.5 months, respectively. Patients who received induction chemotherapy survived significantly longer than those who did not (22.3 vs. 9.0 months; $p=0.01$). Multi-agent chemotherapy (versus single-agent chemotherapy; 23.5 vs. 15.7 months, $p=0.01$), FOLFIRINOX-based chemotherapy (versus multi-agent gemcitabine-based chemotherapy; 27.7 vs. 16.7 months, $p=0.004$), and chemotherapy =4 months (34.8 vs. 15.8 months, $p<0.0001$) were associated with superior OS. Median progression-free survival (PFS) was 14.5 months from diagnosis and 9.0 months from SBRT. Median local progression-free survival (LPFS) was 15.5 months from SBRT. Thirty-four (29%) patients were successfully resected, with margin- and node-negative resection rates of 91% and 82%, respectively. Six (5%) patients underwent irreversible electroporation (IRE) while the remaining 66% of patients did not make it to the operating room due to metastatic disease (39%), continued vessel involvement (15%), performance status (10%), or other complications (2%). Resected patients had significantly

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longer median OS (34.7 vs. 17.0 months, $p<0.0001$) and PFS (18.7 vs. 12.7 months, $p=0.01$). Patients who achieved a margin-negative resection survived significantly longer than patients with positive margins (34.8 vs. 15.7 months, $p<0.0001$). Interestingly, however, patients who underwent a node-negative resection had inferior survival (29.8 vs. 34.8 months, $p<0.0001$).

Conclusions: The combination of multi-agent chemotherapy, SBRT, and surgery results in favorable survival in patients with LAPC, with estimates approaching those of borderline resectable and resectable disease. Additional investigation is necessary to determine which subset of LAPC patients are likely to benefit from aggressive neoadjuvant therapy and surgery.