



Interferon-based adjuvant chemoradiation therapy after pancreaticoduodenectomy for pancreatic adenocarcinoma

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Background

Historically, 5-year survival rates in patients with locally advanced pancreatic cancer have been dismal (<10%), even following a Whipple resection. Disease recurrence is typically both local and distant. Further advances in the management of pancreatic cancer led to the incorporation of chemotherapy and radiotherapy following surgery, with a subsequent improvement in 2-year survival from 18% to 43% according to the GITSG studies. In 2000, Nukui et al reported the results of a phase II study using more aggressive chemoradiation in addition to interferon for the treatment of locally advanced pancreatic cancer. The study employed continuous infusion 5-FU, weekly cisplatin, and subcutaneous interferon concurrent with radiation in the post-operative setting. The rationale for interferon was possible enhancement of tumoricidal effects of certain chemotherapeutic agents. The authors reported a 2-year survival rate of 84% with this aggressive treatment approach. This current article by Picozzi et al serves as an update to the results reported by Nukui et al in 2000.

Materials and Methods

- A cohort of 43 patients were evaluated, all with ductal adenocarcinoma of the pancreatic head and of pancreatic origin
- Primary tumors of the distal common bile duct, ampulla, and duodenum were excluded
- All patients underwent pancreaticoduodenal resection (Whipple)
- Approximately 6-8 weeks following resection, patients were begun on concurrent chemo-radiation as well as interferon therapy
- Radiation therapy was external beam, 45 Gray (Gy) – 54 Gy, given over 5 weeks in 25 daily fractions, delivered to the pancreatic bed
- Chemotherapy consisted of continuous infusion 5-FU (200mg/m²) on days 1-35 and weekly cisplatin (30mg/m²) on days 1, 8, 15, 22, and 29
- Interferon was given as a subcutaneous injection, 3 million units QOD for 5 weeks
- All patients received adjuvant chemotherapy in the form of 5-FU (200mg/m²) on days 64-105, then again on days 120-161
- Several factors were analyzed, including resection type, blood loss, nodal status, treatment toxicity, and survival
- Follow-up was obtained by telephone contact, and evidence of relapse was determined by physical examination, CXR, and CT scans
- Statistical evaluation was done using Kaplan-Meier analysis

Results

- Between 1995-2002, 43 patients were accrued, with a median patient age of 62 years
- Median patient follow-up was 21.8 months (range of 4-86 months)
- All but 7% of patients had pylorus-preserving surgery, and 2 had total pancreatectomies
- Two percent of patients had stage I disease, 12% had stage II, 72% had stage III, and 14% had stage IVa disease
- Eighty-four percent of patients had positive lymph nodes with an average of 2.2 nodes per patient
- With regard to histology, 26% were poorly differentiated, and there was perineural invasion in 68% of samples
- A total of 19% patients had gross or microscopic positive margins
- Ninety-five percent of patients completed their radiation course
- Ninety-three percent of patients received greater than 85% of the intended 5-FU dose, while the last dose of cisplatin was held in 28% of patients
- With regard to adjuvant chemotherapy, 56% of patients got 100% of the intended 5-FU dose, and 70% received >85% of the intended dose
- Treatment-related toxicity was mostly gastrointestinal, with grade 3 toxicity in 70% of the patients; 70% had some form of delay in their chemoradiotherapy, while 43% of patients were hospitalized for treatment-related toxicity
- Actuarial overall survival at 1, 2, and 5 years was 95%, 64%, and 55% respectively; disease-free survival was 67%, 52%, and 52% at 1, 2, and, 5 years respectively

Discussion

- When compared to other studies using adjuvant chemotherapy, the results of this study demonstrate the highest survival rates to date, and thus are very encouraging
- However, this improvement in survival comes at the cost of significantly increased treatment-related toxicity requiring hospitalization in 42% of patients
- Though toxicity was high, there was no treatment-related mortality
- There was no mention of the performance status of enrolled patients, but one should assume that patients were carefully selected for this aggressive treatment regimen
- All surgeries were performed at a single institution with one surgeon performing 91% of the resections; it will be interesting to see if the same results will hold when surgery is performed at other centers.

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