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Clinical Science

Localized pancreatic cancer with positive peritoneal cytology as a sole manifestation of metastatic disease: a single-institution experience

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Abstract

BACKGROUND: Pancreatic cancer patients with positive peritoneal cytology (PPC) as a sole metastatic site are poorly characterized. Whether they behave similarly to other stage IV patients is unknown.

METHODS: Patients with stage IV disease at our institution between 2003 and 2013 were identified. Inclusion criteria for PPC cohort were PPC at laparoscopy and no laparoscopic and/or radiographic evidence of metastasis. Patients with gross metastasis had laparoscopic and/or radiographic evidence of metastasis.

RESULTS: Among 308 patients, 43 patients had PPC and 265 had gross metastasis. PPC cohort: 3 (7%) resectable, 8 (19%) borderline resectable, and 32 (74%) unresectable tumor. Disease progression occurred in 37 (86%). Sixteen of 43 (37%) also received local therapy (1 surgery and 15 chemoradiation). PPC vs gross metastasis cohort differed as follows: baseline Ca 19-9 (440 vs 1,904 IU/mL, $P < .0001$); Eastern Cooperative Oncology Group (ECOG) score ≤ 1 (98 vs 88%, $P = .04$); median overall survival (13.9 vs 9.4 months, $P = .0001$).

CONCLUSIONS: Patients with PPC failed to display long-term disease-free survival, although overall survival was superior compared with those with gross metastasis. Patients with PPC may need to be considered a specific subgroup for staging and survival analysis.

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Pancreatic adenocarcinoma is one of the leading causes of cancer-related mortality in the Western world.[1] Despite recent advances in oncologic therapy and surgery, overall and long-term survival remains poor, as most patients present with advanced disease. At the time of diagnosis,

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10% to 20% of patients present with a resectable tumor, 30% to 40% present with a locally advanced tumor, and 50% to 60% present with a metastatic disease.[2] A few centers (including our institution) advocate the use of peritoneal cytology in addition to standard imaging and laparoscopy as part of the staging work-up for pancreatic cancer. As malignant cells can be identified in 7% to 30% of peritoneal washing samples in pancreatic cancer,[3–5] patients who were initially thought to have localized disease can be upstaged as stage IV disease after positive peritoneal cytology (PPC) according to the American Joint Committee on Cancer staging system and National Comprehensive Cancer Network guidelines.[6,7] Therefore, patients who are discovered to have PPC as their only site of distant metastatic disease may be thought to behave similarly to other stage IV patients with respect to disease progression and survival. At our institution, peritoneal washing at the time of staging laparoscopy is routinely performed in patients with radiographically localized pancreatic cancer. Patients with PPC are subsequently classified as having stage IV disease regardless of the "tumor respectability" and hence excluded from upfront resection and undergo chemotherapy.

In this study, we share our experience of managing patients with locally advanced pancreatic cancer and isolated PPC without gross metastasis. Our objective was to evaluate the natural history of patients with PPC and the impact of consolidative chemoradiation in these patients and contrast their clinical characteristics and survival to those with gross metastasis.

Methods

Patient eligibility

From 2003 to 2013, 333 patients with stage IV pancreatic adenocarcinoma treated with oncologic therapy were identified using our pancreatic cancer patient database. Patients were included in PPC cohort if they had PPC at laparoscopy and no laparoscopic or radiographic evidence of metastasis. Patients in the gross metastasis cohort had laparoscopic and/or radiographic evidence of metastasis.

Definition of tumor resectability

Tumor resectability was determined after the review of initial computed tomography (CT) at a multidisciplinary meeting of surgeons, oncologists, and radiologists. All patients were evaluated using an early arterial and/or late portal venous phase multidetector CT with oral contrast with fine cuts (2 mm) through the pancreas. Outside imaging was reviewed by a staff radiologist and repeated if imaging quality was suboptimal. Tumors were considered localized and not currently resectable when CT showed involvement with an adjacent organ and/or abutment ($<$180 degrees of involvement), encasement ($\geq$180 degrees of involvement), or occlusion of a major blood vessel (portal vein, superior mesenteric vein, superior mesenteric artery, common hepatic artery, or celiac axis).

Laparoscopic evaluation

Peritoneal washing for cytology was obtained at diagnostic laparoscopy by injecting 300 to 500 cc of saline into the upper abdominal peritoneal cavity before inspection and biopsy of any visible lesions. Washing samples were sent for cytology. PPC was defined as peritoneal cytology containing malignant cells. Immunocytology and polymerase chain reaction studies were not performed.

Determination of response to oncologic therapy vs disease progression

All patients received chemotherapy after initial diagnosis. Patients received consolidative chemoradiation if there was no disease progression, after 6 to 12 months. Patients were considered as having responsive disease if Ca 19-9 and CT imaging indicated stable or improving disease. Local progression was defined as primary tumor growth prompting change or cessation of therapy. Systemic progression was defined as radiographic and/or pathologic evidence of new metastasis. Time to progression was measured from initial diagnosis to switch or cessation of therapy due to disease progression.

Data collection and statistical analysis

Patient demographics, clinical details, imaging results, and operative findings were collected via electronic medical records. Statistical analyses were performed using STATA (StataCorp LP, College Station, TX) and GraphPad Prism (GraphPad Software, In, La Jolla, CA). Categorical variables were compared using Fisher's exact test and continuous variables were compared using the Student's t test. Survival rates were calculated by the Kaplan–Meier method. Overall survival (OS) was defined as the period from initial diagnosis to death or last contact. A P value of $\leq$.05 was considered statistically significant.

The study was approved by our institution review board.

Results

Patient eligibility

A total of 572 patients underwent diagnostic laparoscopy at our institution between 2003 and 2013. Of those, complete information on follow-up and tumor resectability were available on 338 patients, as the remaining 234 patients were treated at another institution or lost to follow-up. Among the 339 patients with complete information, 3 of 38 patients (8%) with resectable tumor and 40 of 248 patients (16%) with borderline resectable or locally