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High serum CA 19-9 but not tumor size should select patients for staging laparoscopy in radiological resectable pancreas head and peri-ampullary cancer☆

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Abstract

Background: The objective of this study was to validate current recommendations for the selective use of staging laparoscopy in patients with radiological resectable pancreas head and peri-ampullary tumors.
Methods: Data from a prospectively collected database (2007–2013) of 136 patients with peri-pancreatic head cancer were analyzed.
Results: Over a 6 year time period, 136 patients were evaluated, 126 patients were deemed radiological resectable and underwent laparotomy and 10 patients were characterized radiological unresectable. There were 111 patients with pancreas head resection and 15 without resection (8 due to extensive vascular involvement and 3 due to peritoneal/liver metastases). The sensitivity, specificity, PPV and NPV of pre-operative radiological imaging in determining unresectability due to liver/peritoneal metastases were 42%, 100%, 100% and 94.7% respectively. There was a significant difference in CA 19-9 values between metastatic and non-metastatic disease ($p = 0.020$). ROC curve analysis calculated the optimal CA 19-9 cutoff point for predicting metastasis at 215.37 U/ml with a sensitivity of 72.7%, a specificity of 58.3%, PPV of 15.1% and NPV of 95.5%. Tumor diameter was not a significant factor in predicting resectability. Laparoscopy would have been useful in only 5.3% of patients in the present series.
Conclusion: High CA 19-9 values (>215 U/ml) and not tumor size should select patients with radiological resectable peri-pancreatic cancer for staging laparoscopy.

Keywords: Pancreas cancer; Peri-ampullary cancer staging laparoscopy; CA 19-9

Introduction

Most of the patients with pancreas cancer present with metastatic disease (~60%) and only 10% have local disease and about 30% have regional disease.[1,2] Detection of metastatic disease is critical because it prevents the patient from undergoing unnecessary surgery as even exploratory laparotomy has high morbidity (up to 30%)[3] and also allows for endoscopic/minimally invasive palliation.

The role of laparoscopic assessment (laparoscopy with or without intra-operative ultrasound) in the pre-operative staging in suspected peri-pancreatic head malignancy is controversial. With improvements in multi-detector computed tomography and Magnetic Resonance Imaging, the number of patients benefiting from pre-operative laparoscopy is reduced to 6–16% in the last 10 years.[4–6] Current recommendations are for a selective use in patients with pancreas head tumors > 3 cm and with CA 19-9 values >100 U/ml.[7]

The aim of this study was to validate the above recommendations in a contemporary cohort of patients with pancreas head/peri-ampullary cancer who were considered

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radiological resectable, using the indirect assessment method.

Patients and methods

The present study is based on the STARD (Standards for Reporting of Diagnostic accuracy) recommendations.

From 2007 to 2013, consecutive patients who met radiological criteria for potentially resectable peri-pancreatic head tumors were identified from the prospective departmental HPB cancer database. Each tumor was characterized as resectable, marginally resectable or unresectable on the basis of CT/MRI findings. The majority of patients had internal multi-detector CT scanning. Patients with external imaging judged to be of high quality, did not had repeat imaging.

The tumor was considered local and resectable if there were: a) no distant metastases, b) no radiographic evidence of SMV and portal vein abutment, distortion, tumor thrombus, or venous encasement, c) normal fat planes around the celiac axis, hepatic artery, and SMA.[7,8] Criteria for unresectability were peritoneal metastases, liver metastases, or ascites; encasement of the celiac, superior mesenteric or hepatic artery and extensive involvement of major venous structures by tumor was a contraindication to surgical resection. The presence of enlarged lymph nodes per se, in the absence of any other evidence of unresectability, was not considered a contraindication to attempted resection.[9] A vessel was considered to be involved if it showed a focal reduction in caliber, circumferential (>180°) encasement by tumor, or frank thrombosis.[8] The American Hepato-Pancreato-Biliary Association criteria for marginally resectable peri-pancreatic head tumors were used.[7]

Demographics, laboratory data, radiologic findings, histology, and final outcome were documented. Patients with gastric outlet obstruction necessitating surgical bypass (even if the tumor was unresectable) were excluded from the present analysis. During operation, local tumor invasion, local vessel involvement and the presence or absence of liver or other metastases, were noted. Patients deemed to have resectable disease underwent a standard or pylorus preserving Kausch-Whipple pancreatoduodenectomy or a total pancreatectomy – if needed. Only patients with a final histology of cancer were analyzed.

Statistics

Quantitative values are expressed as median (with interquartile range – IQR). Qualitative variables are expressed as absolute and relative frequencies. Diagnostic accuracy is expressed as sensitivity, specificity, PPV and NPV. The Mann–Whitney *U* test was used to compare median values. ROC analysis was used to determine the optimal sensitivity and specificity of cutoff values of tumor diameter and CA 19-9 for the prediction of tumor resectability. Data analysis was performed with SPSS v. 22 (IBM, USA).

Results

A flow chart of the study is shown in Fig. 1. Over a 6 year time period, 136 patients with pancreas head and/or peri-ampullary tumors were referred and evaluated.

Pre-operative imaging studies reveal radiographically resectable tumors in 126 patients (92.6%) who underwent laparotomy with curative intent. These included 10 (7.9%) patients with equivocal radiological findings for resectability. There were 10 patients (8%) who were deemed radiological unresectable (5 due to vascular involvement and 5 due to peritoneal/liver metastases). Of the 126 patients that proceeded to laparotomy, 111 underwent resection (107 underwent Kausch-Whipple operation and 4 underwent total pancreatectomy). Of the remaining 15 patients who were unresectable, this was due to extensive vascular involvement in 8 and metastatic disease (liver/peritoneum) in 7.

Characteristics of 126 patients that underwent exploratory laparotomy are shown in Table 1. Table 2 presents the frequency of tumor type, serum CA 19-9 levels and tumor diameter in patients with disease considered radiological resectable.

For patients with histologically confirmed pancreas head/peri-ampullary cancer the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of pre-operative radiological imaging in determining unresectability due to liver and/or peritoneal metastases were 41.6%, 100%, 100% and 94.7% and 94.8% respectively. There were no patients with false positive results.

Median CA 19-9 values were 340.15 U/ml for all unresected patients (range: <2 U/ml–49,044.2 U/ml) and

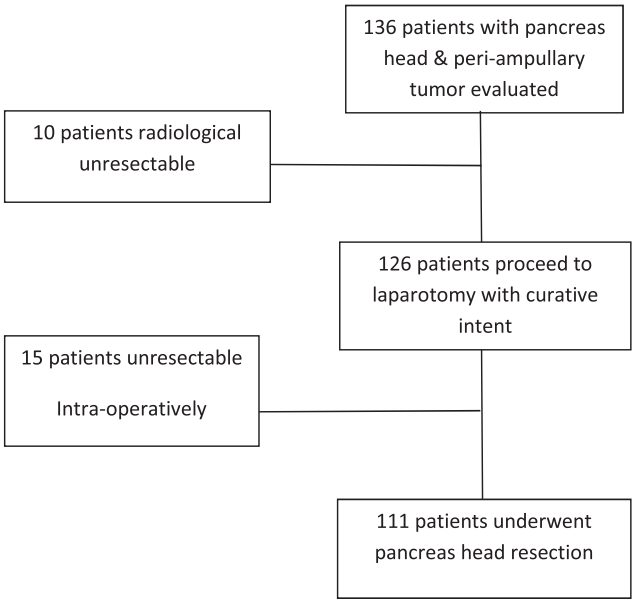

Figure 1. Flow chart of the study.