Evaluation of diagnostics guidelines for hepatobiliary and pancreatic disease
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Abolition of diagnostic laparoscopy for patients with a periampullary carcinoma; implementation of a new diagnostic strategy

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Departments of Surgery¹ and Radiology² of the Academic Medical Center, Amsterdam

Submitted
Abstract

Background. Diagnostic laparoscopy has been generally accepted in staging of patients with a periampullary malignancy, despite controversy about its effectiveness to prevent unnecessary laparotomy. In our institution diagnostic laparoscopy was routinely used since 1992. However in 1998 it was eliminated from the protocol since in a prospective study a yield of only 6% was found with a histologically proven accuracy of 60% for distant metastases. The effect of implementation of the new protocol on the occurrence of unnecessary laparotomies and the outcome after bypass surgery was assessed.

Patients and Methods. Between January 1999 and December 2001, 186 consecutive patients with a potentially resectable periampullary carcinoma after radiological staging without diagnostic laparoscopy underwent explorative laparotomy with the intention to perform a curative pancreatoduodenectomy. Incidence of unresectability and outcome of palliative surgery were assessed.

Results. Resection could not be performed in 65 patients (34%) who underwent laparotomy because of metastatic disease (29 patients 16%) and loco regional tumor ingrowth (34 patients 18%). These patients underwent a bypass procedure with a median survival of 216 days.

Conclusion. At laparotomy distant metastases were detected in 16% of the patients. Considering the histologically proven accuracy for distant metastases of around 60% as found earlier by our group, the additional value of diagnostic laparoscopy could have been only 10%. This result together with the good results of palliation by bypass surgery, justify the use of staging laparoscopy only in selected patients.
Introduction

Adequate staging is the most important step in the management of patients with periampullary (pancreatic, ampullary, distal common bile duct (CBD) or duodenal) malignancies. Incurable patients, and in particular patients with metastatic disease should preferably be identified preoperatively, since palliation can nowadays be achieved by nonsurgical means.

Imaging modalities such as transabdominal ultrasonography, Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) can visualize the tumor but often failed to detect small metastases.

For that reason diagnostic laparoscopy was in the past decade generally accepted as a method to improve assessment of tumor stage and thereby to prevent unnecessary laparotomies. Diagnostic laparoscopy enables the detection and biopsy of small superficial metastases at the liver surface and peritoneum, whereas laparoscopic ultrasound was described to be sensitive for the detection of small intrahepatic metastases, enlarged lymph nodes and tumor ingrowth in vascular structures.

In our institution, from 1992 till 1998 diagnostic laparoscopy was performed in all patients with a periampullary malignancy as a routine staging procedure after noninvasive staging had shown the possibility of a curative resection. The initial results were promising but the yield decreased gradually over the years. Also a substantial number of patients who were treated by endoscopically placed endoprosthesis needed a late laparotomy due the gastrointestinal obstruction.

The accuracy and thus the indication of diagnostic laparoscopy in patients with periampullary carcinoma has been questioned in recent years. Selection of patients eligible for laparoscopy did increase, due to improved accuracy of radiological staging techniques like endoscopic ultrasonography and spiral CT and the benefit of diagnostic laparoscopy as a routine staging procedure is less strong. In a recent review, a reduction in the additional value of diagnostic laparoscopy in preventing unnecessary laparotomies from 4% -13% was described.

In a prospective study conducted in our institution it was shown that diagnostic laparoscopy had a limited overall additional value of 13% in preventing unnecessary laparotomy and that only 60% of the metastases were detected or could be proven by biopsy. In this study, patients with proven metastases were randomized for surgical or non-surgical palliation. Remarkably, the average hospital free survival of the patients with metastatic disease who underwent a bypass procedure was slightly better than of those who underwent endoscopy palliation. As a consequence diagnostic laparoscopy was left out of the diagnostic protocol since October 1998. Due to continued acceptance of diagnostic laparoscopy all over the world this change in strategy needed to be evaluated and justified.
Therefore, the aim of the present study was to analyze the new diagnostic protocol without diagnostic laparoscopy in the preoperative work-up of patients with a periampullary tumor. Detection of metastases, but also outcome, morbidity, mortality and survival after a bypass surgery were evaluated and compared with those in patients who underwent diagnostic laparoscopy in the previous study.

**Patients and Methods**

Between January 1999 and December 2001, 186 patients with periampullary cancer staged to be resectable after standard work-up underwent an explorative laparotomy in the Academic Medical Center (AMC), Amsterdam, The Netherlands. Standard preoperative staging included transabdominal ultrasonography with color Doppler and spiral CT (according to a dedicated protocol) of the pancreas and liver. When a tumor was suspected but could not be visualized by CT, endosonography or MRI was performed. Tumor location, tumor size, local ingrowth, lymph nodes and distant metastases were determined. All findings where analyzed by experienced radiologists and discussed with the team of gastro-enterologists and surgeons as previously reported. Limited encasement of the portal or superior mesenteric vein, artery or celiac trunc, or metastatic disease, that could not be proven with ultrasound or CT guided biopsy was not accepted as unresectable disease and consequently patients were planned for exploration. In all patients with obstructive jaundice, ERCP was performed with insertion of an endoprosthesis in the common bile duct as previously reported.

Exploration was planned in patients with the intention to perform a potentially curative (pylorus preserving) pancreaticoduodenectomy (PPD). In case of incurable disease found during exploration due to local ingrowth or distant metastases, a biliary bypass was made with or without a gastrojejunostomy (ongoing trial comparing biliary bypass alone with double bypass). Postoperative morbidity and mortality was evaluated prospectively in the patients with metastases who underwent a bypass procedure and compared with the results from the previously performed two-center trial in which diagnostic laparoscopy and laparoscopic ultrasound were performed in the work-up of 198 patients (inclusion in our center) with probably curable disease after radiological staging.
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Results

Patient characteristics and tumor localization of the 186 consecutive patients are shown in Table 1.

Table 1 Characteristics of and tumor localization in patients with a potentially resectable periampullary carcinoma

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n=186</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male / female</td>
<td>110/76</td>
</tr>
<tr>
<td>Median age (range)</td>
<td>64 (33-88)</td>
</tr>
<tr>
<td>Tumor localization</td>
<td></td>
</tr>
<tr>
<td>pancreatic head</td>
<td>119</td>
</tr>
<tr>
<td>papilla of Vater</td>
<td>46</td>
</tr>
<tr>
<td>distal CBD</td>
<td>17</td>
</tr>
<tr>
<td>duodenum near papilla</td>
<td>4</td>
</tr>
</tbody>
</table>

Resection was performed in 123 patients (66%) with microscopic radical margins in 88 patients (72%). No resection was performed in 63 patients (34%), in 29 patients (16%) because of distant metastases and in 34 patients (18%) because of loco regional ingrowth (Table 2).

Table 2 Causes of unresectable disease detected at laparotomy in patients with a resectable periampullary tumor after radiological staging

<table>
<thead>
<tr>
<th>Cause</th>
<th>n=186</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potentially resectable tumor</td>
<td></td>
</tr>
<tr>
<td>unresectable</td>
<td>n= 63 (34%)</td>
</tr>
<tr>
<td>Metastases</td>
<td></td>
</tr>
<tr>
<td>liver</td>
<td>20 (11%)</td>
</tr>
<tr>
<td>peritoneum</td>
<td>9 (5%)</td>
</tr>
<tr>
<td>Loco regional tumor ingrowth</td>
<td></td>
</tr>
<tr>
<td>vascular</td>
<td>16 (9%)</td>
</tr>
<tr>
<td>mesenteric</td>
<td>7 (4%)</td>
</tr>
<tr>
<td>lymph nodes</td>
<td>7 (4%)</td>
</tr>
<tr>
<td>other</td>
<td>4 (2%)</td>
</tr>
</tbody>
</table>
Metastatic disease was found more frequently at laparotomy in patients with a pancreatic head carcinoma (19%) than with a papillary carcinoma (6%) (p=0.04), in patients with a CBD or duodenum carcinoma metastases were seen in 18% and 0% respectively (Table 3). All 63 patients with unresectable disease underwent hepatico-jejunostomy; 46 patients (71%) had an additional gastrojejunostomy. Morbidity was seen in 12 of the patients who underwent a bypass (18%), mortality in 1 (2%); the mean survival was 216 days (6-863) and the median survival was 269 days.

**Table 3** Metastases detected at laparotomy in patients with a resectable periampullary tumor after radiological staging; divided according to tumor localization

<table>
<thead>
<tr>
<th>Potentially resectable tumor</th>
<th>n=186</th>
<th>Metastases found at laparotomy</th>
<th>29 (16%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatic head</td>
<td>23/119 (19%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal CBD</td>
<td>3/17 (18%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Papilla</td>
<td>3/47 (6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duodenum</td>
<td>0/4 (0%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

As compared with patients that underwent a bypass procedure between 1996-1998 after diagnostic laparoscopy no differences were seen in patient characteristics, resectability rate, complication- or mortality rate. Survival was longer but not statistically significant (Table 4). During the same period, the guideline not to perform a diagnostic laparoscopy was not followed in nine other patients (seven pancreatic head, one ampullary and one distal CBD tumor, 5%) because it was thought that these patients had advanced disease and unresectability could be proven during laparoscopy. Diagnostic laparoscopy, however, could not histologically confirm unresectability in these patients whereas at laparotomy they all had incurable disease.
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Table 4 Complications, mortality and survival in patients with a periampullary carcinoma, having peroperative metastatic disease. Comparison between cohort 1996-1998 (with diagnostic laparoscopy) and 1999-2001 (without diagnostic laparoscopy)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>n=173</td>
<td>n=186</td>
<td></td>
</tr>
<tr>
<td>Bypass</td>
<td>55 (32%)</td>
<td>63 (19%)</td>
</tr>
<tr>
<td>Complications</td>
<td>10 (18%)</td>
<td>12 (18%)</td>
</tr>
<tr>
<td>Mortality</td>
<td>0</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Survival (mean;days)</td>
<td>192</td>
<td>269</td>
</tr>
</tbody>
</table>

Discussion

In an earlier study in patients with a periampullary carcinoma, diagnostic laparoscopy had an additional value over radiological imaging alone of 13% in preventing an unnecessary laparotomy. But a further 11% of patients were shown to have incurable disease at laparotomy due to metastases so the sensitivity for detection of metastases was 60%.\textsuperscript{18} On the basis of this modest benefit, diagnostic laparoscopy was abolished from routine work-up in patients with periampullary tumors since October 1998. The present study was performed to evaluate the results 3 years after this new diagnostic strategy had been introduced.

The guideline (not to perform a diagnostic laparoscopy) was implemented in 95% of the patients. This change in diagnostic work-up did not affect the rate of resectability (and thus the percentage of bypass surgery) i.e.32% from 1996-1998 (with diagnostic laparoscopy) and 35% from 1999-2001 (without diagnostic laparoscopy). These overall resectability rates are in concordance with the literature.\textsuperscript{3,6,13,24,25}

In the recent study, the strategy without diagnostic laparoscopy yielded distant metastases at laparotomy in 29 of the 186 (16%) patients as cause of unresectability. Thus, diagnostic laparoscopy could have had a maximal value of 16%. As found by others, unfortunately not all metastases will be detected.\textsuperscript{14,26,27,12} When the false-negative results regarding the detection rate of the previous study (only about 60% of the metastases detected at diagnostic laparoscopy), would be taken into account, the additional value would decrease from 16% to around 10%.

Reasons for the limited additional value of diagnostic laparoscopy can be found in the ever improving radiological staging, especially by the use of spiral CT scans,
obtained according to a dedicated pancreatic protocol and assessed by radiologists specialized in hepatic, pancreatic or biliary disease. Furthermore, as described by Pisters et al. performing diagnostic laparoscopy early in the diagnostic work-up (before a dedicated spiral CT is performed) or in patients with locally advanced disease might introduce bias and overestimate its use.

In about half of the patients with a pancreatic head carcinoma unresectable disease was found at laparotomy, in 19% due to metastases, compared to 18% of the patients with a distal CBD and 6% of those with an ampullary carcinoma. Even if the indication for diagnostic laparoscopy would be restricted to pancreatic head tumors, the maximal benefit would still be limited to around 11%, considering metastases the not detected at laparoscopy. Comparable results have been shown by Schirmer et al. who pointed out the need to use resources wisely and select patients to benefit from a diagnostic laparoscopy more carefully.

The average survival in the patients with metastatic disease (detected at exploration) who underwent a bypass procedure was relatively good, probably partly due to selection criteria (locally confined tumors and patients fit to undergo major surgery). The less favorable outcome in previous studies in patients with an periampullary tumor palliated by a bypass procedure has led others to recommend endoscopic palliation. As no survival difference can be found in comparison to endoscopic palliation preference, for this procedure on these grounds is not present.

In conclusion, this study has shown that the new guideline in our institution, i.e. not to perform diagnostic laparoscopy routinely in patients with a periampullary malignancy, was adopted and could be implemented in almost all patients. The limited number of metastases detected at laparotomy together with an acceptable morbidity and mortality rate after the bypass procedure and the suggestion of even higher survival again leads to the conclusion that the possible benefit of staging laparoscopy is too limited to justify its use as a routine staging procedure.

References

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