Combined endoscopic and laparoscopic ultrasound as preoperative assessment of patients with pancreatic cancer

C. W. FRISTRUP, M. B. MORTENSEN, T. PLESS, J. DURUP, A. AINSWORTH, C. HOVENDAL & H. O. NIELSEN

Department of Surgical Gastroenterology, Odense University Hospital, Odense, Denmark

Abstract

Background. An accurate pre-therapeutic assessment of the resectability in pancreatic cancer patients is essential to reduce the number of futile surgical explorations. The aim of this study was to assess the combination of endoscopic ultrasound (EUS) and laparoscopic ultrasound (LUS) regarding the detection of patients with non-resectable tumours.

Patients and methods. From 2002 to 2004, 179 consecutive patients with pancreatic cancer referred for surgical treatment were eligible. Thirty-one (17%) patients were excluded due to co-morbidity and poor performance status. Two patients (1%) were excluded due to metastasis seen on CT scans prior to referral. Thus, 146 patients entered the study. Patients were first examined with EUS followed by LUS, if EUS found no signs of non-resectability. Only patients with tumours found to be resectable or possibly resectable at EUS and LUS were offered surgical treatment. Resectability criteria were defined prior to the study.

Results. In all, 108 (74%) patients had non-resectable tumours by the pre-defined criteria. EUS identified 68 (63%) patients and LUS identified an additional 26 (24%) patients. Thus, a total of 94 (87%) patients were non-resectable at either EUS or LUS. Fifty-two (36%) patients underwent surgery. Six patients had surgical exploration and three patients had palliative surgery. Forty-three patients (29%) were resected with curative intention, of whom 38 (88%) had an R0 resection and 5 (12%) had a palliative resection.

Discussion. The combination of EUS and LUS is accurate in identifying the non-resectable patients and has a high predictive value for complete resection.

Key Words: Pancreatic cancer, endoscopic ultrasound, laparoscopic ultrasound, staging, resectability

Introduction

Pancreatic cancer is often diagnosed in an advanced stage. Radical surgery is the only curative treatment, but even after complete resection the overall prognosis is poor [1–3]. Surgery carries a significant morbidity and mortality[4–6], and as extended surgery may not improve outcome, careful selection of patients for surgery is necessary to avoid futile explorations [7,8]. Several imaging modalities have been shown to be of value in staging of pancreatic cancer [9–14], but no single modality has a high predictive value for complete resection. The combination of endoscopic and laparoscopic ultrasound (EUS and LUS) has been shown to be a cost-effective strategy for patients with non-resectable upper gastrointestinal tumours [15].

The aim of this study was to evaluate the combination of EUS and LUS in the preoperative assessment of patients with pancreatic cancer. The major end points of the evaluation were the predictive value for complete resection (R0 resection) and the number of futile explorative laparotomies.

Materials and methods

All patients with histologically verified carcinoma of the pancreas referred to the Department of Surgical Gastroenterology, Odense University Hospital, in the period from 1 January 2002 to 29 February 2004 were included. All patients had either CT or abdominal ultrasound as initial examination before referral. Patients with known metastasis or non-resectability from prior CT or ultrasound were excluded. Patients with poor performance status and re-evaluation after down-staging with chemo-radiotherapy were also excluded.

The evaluation strategy is shown in Figure 1. Patients with local tumour infiltration of the portal vein, superior mesenteric vessels, coeliac trunk and transverse mesocolon were considered non-resectable. Patients with carcinoma, non-regional lymph nodes and liver metastasis were considered incurable. Regional metastatic lymph nodes were not considered as non-resectability. All metastatic lesions were histologically verified by fine needle aspiration. Using these criteria, EUS and LUS designated each patient into...
Patients were divided into one of three groups: (1) resectable, (2) possibly resectable, and (3) non-resectable. Patients in groups 1 and 2 would proceed to laparoscopic ultrasound (LUS) and possibly surgery, whereas patients in group 3 would be discussed with the oncologists. Patients in group 1 would be scheduled for both LUS and resection on the same day. Patients designated to group 2 by endoscopic ultrasound (EUS) had LUS performed as a separate procedure, as it was expected that only a small proportion of these patients were actually resectable.

Surgical bypass was only offered to patients, where endoscopic (or radiological) palliation failed.

All examinations were prospectively registered. EUS was performed by surgeons with wide experience in endosonography (>300 staging procedures performed prior to the study). Likewise, LUS was performed by experienced surgeons (>100 staging procedures).

Statistics

For categorical data Fisher’s exact test was used. p values <0.05 were considered significant. Confidence intervals (CI) are reported as 95%.

Results

A total of 179 patients were referred in the study period. Of these, 82 (46%) were women and 97 (54%) males, with a median age of 66 years (range 22–89). Of the 179 patients, 31 (17%) were not fit for surgery due to poor performance status and were excluded. In two (1%) patients initial CT scans revealed liver metastases, the patients were referred for biopsy only, and both were excluded from the study. Thus, 146 patients entered the study. The results of EUS, LUS and surgery are shown in Figure 2, and the reason(s) for non-resectability are shown in Table I. There were no complications after EUS or LUS.

A total of 108 non-resectable patients were found, 68 by EUS, 26 by LUS and 14 at surgery. The combined preoperative assessment identified 94 (87%, CI 79–93%) of the non-resectable patients. Of the 108 non-resectable patients 3 patients underwent R0 resection after down-staging with chemo-radiotherapy.

EUS found 51 patients to be resectable (group 1), of these 32 (63%) underwent an R0 resection. In comparison EUS found 24 to be possibly resectable (group 2) and of these only 4 (17%) underwent an R0 resection (p <0.01). In three (2%) patients EUS was not possible.

Following laparoscopy and LUS an additional 26 non-resectable tumours were found. Thus, 52 patients were scheduled for resection. Of these 38 (73% CI 59–84%) patients had an R0 resection, five (10%) patients had an R1 or R2 resection, three (6%) patients had a surgical bypass and six (12%) patients had a futile explorative laparotomy.

Discussion

With EUS as first examination 47% of the patients could be classified as non-resectable and avoid further examination(s). Laparoscopic staging found non-resectable tumours in 33% of the remaining patients. This is comparable to other studies [9–11,16], although one study reported a very low effect of laparoscopic staging [17]. However, this study may be biased as biopsy to prove non-resectability during LUS was required, whereas the normal staging with CT did not include biopsy to prove non-resectability. Vascular invasion is difficult to prove with biopsy with any imaging modality, and even at surgery it can be difficult to assess whether there is tumour infiltration or just tumour adhesion or inflammation [7].

One limitation of the present study with regard to local non-resectability is the lack of histopathological proof of non-resectability. From resections of the portal and superior mesenteric vein it has been shown that only in 57% of patients with suspected infiltration is there histopathological evidence of tumour infiltration [7]. However, the criteria used for non-resectability have proved to be accurate, and other studies have shown only very few over-staged patients using this approach [10,11,13,18,19].
The predictive value for R0 resection was 73%, but with a wide confidence interval due to the small number of resections. A recent study using solely CT as preoperative staging showed a predictive value of 44% (CI 39–49%) [2], and a large study of CT and LUS as staging strategy showed a predictive value for R0 resection of 62% (CI 56–69%) [17].

One of the main differences between studies is the number of patients treated with surgical bypass. In our study only three patients could not be managed with endoscopic palliation alone. However, if surgical bypass is widely used, the impact of any preoperative assessment will be low, as a high proportion of patients will require laparotomy regardless of the assessment. The choice between surgical and endoscopic palliation has long been debated [20–26]. Endoscopic palliation has a higher rate of re-intervention, but shorter hospital stay and lower morbidity. As patients with non-resectable pancreatic cancer have a very short life expectancy, we find the endoscopic palliation to be more attractive, even if it requires more re-interventions. Thus, the impact of EUS and LUS is high with regard to avoiding unnecessary surgical explorations. We found only 12% futile laparotomies when using EUS and LUS in a combined strategy.

In conclusion the combination of EUS and LUS as preoperative assessment for patients with pancreatic cancer is efficient in identifying the non-resectable patients and has a high predictive value for complete resection.

Table I. Number of patients with non-resectable tumours and reason(s) for non-resectability.

<table>
<thead>
<tr>
<th>Reason</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver metastasis</td>
<td>12</td>
</tr>
<tr>
<td>Tumour infiltration and metastasis</td>
<td>13</td>
</tr>
<tr>
<td>Local tumour infiltration</td>
<td>43</td>
</tr>
<tr>
<td>Carcinosis</td>
<td>3</td>
</tr>
<tr>
<td>Liver metastasis</td>
<td>5</td>
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<tr>
<td>LUS (n = 17)</td>
<td></td>
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<tr>
<td>Liver metastasis</td>
<td>4</td>
</tr>
<tr>
<td>Local tumour infiltration</td>
<td>13</td>
</tr>
</tbody>
</table>

Figure 2. Evaluation results. *1, two patients with known metastasis referred for biopsy; *2, in three patients EUS could not be completed; *3, in five patients LUS was not possible due to adhesions.

References


