Impact of Staging EUS – FNA on Treatment Choice in Patients with Pancreatic Lesions

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SUMMARY
Background: During the last years, endoscopic ultrasound (EUS) has become an important imaging procedure for diagnosis and management of pancreatic diseases. The clinical interest of EUS is now enhanced by interventional procedures. Fine-needle aspiration biopsy is one of the most important contributions of EUS, in particular for the investigation of patients with pancreatic cancer and cystic tumors. EUS-guided fine-needle aspiration appears to be a safe and reliable technique to obtain tissue from pancreatic masses with a low risk of complications. However, the impact of EUS – FNA confirmation of metastatic disease in patient with pancreatic tumors on treatment choice is the aim of this study. Objective: To determine the impact of pancreatic disease as determined by EUS staging on treatment choice in patients with pancreatic lesions. Design: Retrospective analysis of prospectively collected data. Setting: Tertiary university-based referral center. Patients: Patients with biopsy proven pancreatic adenocarcinoma who underwent staging EUS- FNA. The relationship of EUS nodal status and treatment was evaluated. Main Outcomes Measurements: Impact of EUS-FNA on therapy in patients with pancreatic cancer. Results: Of 22 patients with pancreatic tumor, EUS FNA confirmed metastatic disease in 72.7% of the patients. Patients who were node positive were more likely to receive chemotherapy and/or radiation therapy and were less likely to undergo surgery compared with patients who were node negative ( p< 0.0001). Limitations: Lack of surgical reference standard in all patients. Conclusions: Patients with node positive pancreatic cancer as detected by EUS FNA are more likely to receive neoadjuvant therapy and less likely to receive surgery. Preoperative EUS–FNA is a minimally invasive technique that provides important prognostic information in patient with pancreatic lesions.

Key words: endoscopic ultrasound, fine needle aspiration biopsy, pancreatic cancer, treatment

1. INTRODUCTIONS
Since its introduction, EUS has a significant impact on the diagnosis of pancreatic diseases. Indeed, diagnosis of obstructive jaundice and detection of small solid or cystic pancreatic lesions and endocrine pancreatic tumors have been improved by means of EUS. For the detection of small pancreatic tumors < 2 cm in diameter, EUS appaered to be the most sensitive method (1,2).

Besides its diagnostic performance, EUS is also accurate for the preoperative staging of pancreatic adenocarcinomas. Even if respectability is evaluated at the time of surgery, preoperative criteria of respectability, such as the presence of major peripancreatic and /or vascular involvement by the tumor, are currently used. Good preoperative staging could not only decrease the rate of laparatomies without resection, but also improve the quality of surgical resection, without evidence of residual disease that determines the rate of survival (4).

EUS appears to be a reliable technique to assist the medical and surgical management of pancreatic cancer patients. Comparison between different imaging technique for predicting respectability has been extensively evaluated, and both helical CT and EUS are effective. Recent studies included comparative evaluation multidetection CT scan, the resolution of with highly increases pancreatic visualization. Resectability of pancreatic carcinomas can be predicted in 71-90% and in 61-86% of the cases for CT scan and EUS, respectively.

Even if new generation high resolution CT scan can equally assess pancreatic cancer respectability, EUS may be useful for small tumors or for doubtful findings after CT scan. This is represented in figure 1 as a staging algorithm for patients clinically suspected of having pancreatic cancer, including first clinical and current ( CT scan) imaging procedures and secondly EUS evaluation. Previous studies led to propose this decisional algorithm, taking into account the high performance of helical CT (5,6).

2. OBJECTIVE
To determine the impact of pancreatic disease as determined by EUS staging on treatment choice in patients with pancreatic lesions.

3. PATIENTS AND METHODS
The department of gastroenterology and hepatology at the University of Sarajevo, Bosnia and Herzegovina prospectively maintains a database of all patients who undergo EUS and EUS- FNA. This database was the primary source for selecting the patients for our study. During the study period ( January 2005 to January 2008) 22 patients with a final diagnosis and biopsy proven pancreatic carcinoma were enrolled in this study. Data on subject characteristics, type of lesions examined, location of primary tumor and type of treatment were recorded in this database. Data were also available on other staging techniques, such as percutane ultrasonography, CT scan, CT angiography and MRI.

3.1. EUS guided FNA technique
EUS was performed under minimum or moderate sedation. Patient underwent...
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EUS examination with the curveliner echoendoscope (Olympus).

All EUS-FNA were performed by using 22 gauge adjustable – length Echotip needles. FNA is now considered a safe and reliable procedure for the histological diagnosis of pancreatic neoplasms. Immediate complications were assessed by endosonographer. All patients provided informed consent before all the procedures.

3.2. Statistical analyses

The relationship between EUS nodal status and patient and tumor factors were evaluated by X² analysis. The relationship between the EUS nodal status and patient treatment choice was evaluated. For all analysis, P< 0.05 was deemed statistically significant.

4. RESULTS

During the study period 22 patients with biopsy proven adenocarcinoma were enrolled and underwent staging EUS. The mean age (±SD) of the patients was 60.95 ± 9.5 years; 59% were women, 41% men. The most common location of the primary tumor was the caput pancreatis (n=16), corpus (n=4), and cauda (n=2).

Before EUS all patients underwent radiological diagnostic procedure (percutaneous ultrasonography, CT, CT-angiography, MRI). The baseline characteristics of patients with or without lymph nodes or metastases detected by EUS are shown in Table 1.

Patients with node positive disease (N2 or N3 disease) were more likely to receive chemotherapy and/or radiotherapy and less likely to undergo surgery compared with patients who were node negative (p< 0.0001) (Table 4,5,6).

5. DISCUSSION

For the diagnosis of pancreatic adenocarcinomas the sensitivity of EUS guided FNA is from 76 to 90 %. The presence of trained cytopathologist at the time of procedure max increase total yield and decrease the rate of unsatisfactory samples for evaluation (7,8).

The feasibility varies from 90 to 98% , and efficiency in terms of collecting analyzable biopsy specimens varies from 80 to 95%. It has been demonstrated that EUS guided tissue sampling of pancreatic masses is an accurate as CT/US guided sampling and surgical biopsies (9) EUS allows also a Doppler analysis to visualize and characterize the collateral venous system in case of splenic mesenteroportal vein thrombosis and then to perform FNA with a low risk, when the percutaneous route is not indicated (1). EUS guided FNA is the only preoperative procedure which can demonstrate invasion of lymph nodes ( celiac, lumboaortic, retroduode-
n pancreas, superior mesenteric region) (10).

Finally EUS guided FNA can take a special place when nonresectability of pancreatic carcinoma has been proven by abdominal US and CT scan: EUS may play role in the conformation of the histological diagnosis. Neoadjuvant radio and/or chemotherapy allows under certain conditions an increasing rate or tumor respectability and patient survival. Malignant pancreatic tumors comprise in 5-10% of the cases lymphomas, endocrine carcinomas, or metastases. All these lesions can be confirmed by EUS guided FNA (11, 12).

6. CONCLUSION

The presence of the solid mass within the pancreas does not necessarily imply the diagnosis of pancreatic cancer. It is sometimes difficult to differentiate pseudotumor chronic pancreatitis from a pancreatic cancer, even by means of all available imaging procedures, including standard EUS. FNA can be key examination to solve such a paradigm.

### Table 3. Staging of pancreatic tumors

<table>
<thead>
<tr>
<th>Stage</th>
<th>EUS Negative lymph nodes n=6</th>
<th>EUS Positive lymph nodes n=16</th>
<th>Total</th>
<th>p &lt; 0.0001</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3 (13,6%) 0.0 (0.0%) 3 (13,6%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2 (9,0%) 0.0 (0.0%) 2 (9,0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1 (4,5%) 7 (31,8%) 8 (36,3%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>0.0 (0.0%) 9 (40,8%) 9 (40,8%)</td>
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</table>

### Table 7. Location of pancreatic tumor

<table>
<thead>
<tr>
<th>EUS Negative lymph nodes n=6</th>
<th>EUS Positive lymph nodes n=16</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caput pancreatis 4 (18.1%) 12 (54.5%) 16 (72.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corpus pancreatis 1 (4.5%) 3 (13.6%) 4 (18.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cauda pancreatis 1 (4.5%) 1 (4.5%) 2 (9.0%)</td>
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Further developments are expected by improvement of needle devices such as pancreatic pseudocyst drainage kits. In the future, EUS might be also a support for local application of new treatments of pancreatic tumors, such as gene or cellular therapy products.

### REFERENCES

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