

Impact of EUS-guided FNA on management of gastric carcinoma CME

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Background: EUS is an integral part of the pretherapeutic evaluation program for patients with upper GI cancer.

Objective: To evaluate the impact of EUS-guided FNA on the clinical management of patients with gastric cancer.

Design: The study included patients with confirmed gastric carcinoma who were referred to the Department of Surgical Gastroenterology, Gentofte Hospital, Copenhagen University, Copenhagen, Denmark, during a 6-year period (2001-2007).

Setting: The patients underwent standard pretherapeutic evaluation. If no signs of incurability were detected, the patients were offered EUS and EUS-guided FNA. EUS-guided FNA was performed when lymph nodes or lesions were considered to be distant metastases. A board of surgeons was asked to evaluate the management of the patients after the results obtained by EUS-guided FNA were revealed.

Patients: This study involved 234 patients with gastric carcinoma.

Intervention: EUS-guided FNA.

Main Outcome Measurements: Number of patients with distant metastasis diagnosed by EUS-guided FNA, with the avoidance of unnecessary surgery.

Results: A total of 81 consecutive patients underwent EUS-guided FNA. Ninety-nine lesions were targeted, and 61 (62%) of these lesions were found to be malignant. In 38 of 81 patients (42%) distant metastases were confirmed by EUS-guided FNA. As judged by the board of surgeons, EUS-guided FNA changed the management plan in 34 of 234 patients (15%).

Limitation: The positive EUS-guided FNA diagnoses were not surgically verified.

Conclusion: EUS-guided FNA is a very important modality and should be integrated as a routine procedure in the preoperative staging algorithm of gastric cancer. (*Gastrointest Endosc* 2010;71:500-4.)

EUS has become an integral part of the pretherapeutic evaluation in patients with upper GI cancer.¹⁻¹¹ The role of EUS as an imaging modality in the assessment of locoregional involvement of cancer of the esophagus and stomach (tumor and nodal stages) is well established, whereas the role of EUS-guided FNA biopsy (EUS-FNA) in the management of these patients is less well-defined. There

Abbreviations: TNM, tumor, nodes, metastasis cancer staging method; UICC, International Union Against Cancer.

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are a number of publications evaluating EUS-FNA in the work-up of esophageal cancer, but no publications specifically have studied its role in patients with gastric cancer.

The prognosis and survival rate for gastric cancer is poor, closely related to the stage of disease.^{12,13} Surgery is the only curative treatment, but few patients are curable at

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the time of diagnosis because of tumor invasion of neighboring organs, peritoneal carcinomatosis, or metastatic spread to distant organs. Moreover, gastric cancer surgery has a high morbidity rate, and that is why accurate tumor staging is so important before curative surgery.

Although EUS has been integrated in the staging algorithm of gastric cancer evaluation for a long time, no data exist regarding the impact of EUS-FNA in the clinical management of these patients. The aim of this study is to evaluate the clinical impact of EUS-FNA in therapeutic decision making in patients with gastric carcinoma referred for an EUS staging evaluation.

PATIENTS AND METHODS

The study included patients with confirmed gastric carcinomas referred to the Department of Surgical Gastroenterology, Gentofte Hospital, Copenhagen University, Copenhagen, Denmark, during a 6-year period (2001-2007). A total of 234 patients with gastric carcinoma underwent standard pretherapeutic evaluation according to guidelines of the National Danish Board of Health.

The pretherapeutic work-up consisted of an outpatient interview with one of the surgeons in the department, at which time a case history was obtained and clinical assessment done. The patients were offered prescheduled appointments for EUS, CT of the thorax and abdomen, and US of the neck and staging laparoscopy including laparoscopic US scanning. At this interview, relevant information was given regarding different investigative procedures, including risks, complications, and informed consent.

A second evaluating interview was held before EUS and staging laparoscopy including laparoscopic US scanning to review the results of the other investigations. If no signs of incurability were detected at this point, the patients were offered EUS and, if relevant for patient management, EUS-FNA. Lymph nodes were considered to be metastatic by EUS imaging if 3 of the following 4 criteria were fulfilled: round shape, hypoechogenicity, well-defined borders, and diameter >1 cm. EUS-FNA was performed exclusively if confirmation of malignancy of a suspicious lesion outlined was considered to change the clinical management of the patient. Only when suspicious lymph nodes were considered to be distant metastases (tumor, nodes, metastasis [TNM] stage, according to the International Union Against Cancer [UICC] 2002 TNM Classification of Malignant Tumours, 6th edition) or in patients with suspicious lesions in distant organs did patients undergo EUS-FNA. In case of suspected involvement of more than one region, EUS-FNA was performed from all suspected regions.

Patients who were found incurable by either of the investigations were referred for palliative therapy including oncological treatment or palliative endoscopic procedures such as enteral stent placement.

Capsule Summary

What is already known on this topic

- EUS imaging may be inadequate in determining metastatic spread of gastric cancer.
- Because gastric cancer treatment decisions hinge on metastasis staging, a histological or cytological specimen is crucial.

What this study adds to our knowledge

- Distant spread to lymph nodes in the mediastinum was confirmed by EUS-guided FNA in 27 of 81 patients with gastric cancer, and treatment was changed in 15%.

The following information was gathered for each patient: age, sex, location of the gastric cancer, histology reports, findings of EUS, EUS-FNA cytology, CT of thorax and abdomen, and US of the neck. Records of other radiological procedures, type of therapy (radical or palliative), follow-up and final pathology diagnosis were also recorded.

In order to evaluate the clinical impact of EUS-FNA in the management of gastric cancer patients, a board of surgeons from the department was blinded to the cytology results obtained by EUS-FNA and was asked to evaluate the further management of the patient based on available data. After the cytological diagnosis obtained by EUS-FNA was revealed, the board of surgeons was asked to reconsider the treatment strategy again according to the additional information obtained by EUS-FNA. Both treatment decisions were entered into a database and compared. Approval from the committee on human subjects was obtained.

EUS-FNA procedure

EUS was performed by using an echo endoscope with a curved array transducer (Pentax EG38 U and FG34 UA; Pentax, Tokyo, Japan). All EUS-FNAs were performed with 22 gauge, Sono-Tip II needles (Medi-Globe GmbH; Medi-Globe, Achenmühle, Germany). After the positioning of the transducer was corrected, the lesion was punctured under EUS guidance. Penetration of the needle through obvious neoplastic tissue in the gut wall was avoided. Aspiration was performed with a 10-mL syringe, with movement of the needle back and forth inside the lesion. In general, 1 to 3 passes were necessary to obtain sufficient material for cytology. In most cases, EUS-FNA was performed on an outpatient basis. Limitations and contraindications included lesions smaller than 5 mm, distance to the probe more than 6 to 7 cm, interposed vessels, and clotting abnormalities such as international normalized ratio of >1.2 and platelet count of <80,000/mm³.

TABLE 1. Location of lesions targeted by EUS-guided FNA as well as number of lesions found positive for malignancy in 81 patients with gastric cancer

Site of lesion	Total no. FNAs	No. positive FNAs
Mediastinal lymph node	78	42
Liver	7	6
Celiac	1	1
Paraortic region	3	3
Omentum	1	1
Adrenal gland	1	1
Ascites	5	4
Portal lymph node	3	3
Total	99	61

TABLE 2. The number of patients (38 of 81) with distant metastases confirmed by EUS-guided FNA according to the primary lesion in the stomach

	Cardia	Body	Antrum	Linitis plastica
Liver	3	3		
Ascites	1	3		
Omentum		1		
Subclavian LN	5	1		
Aortopulmonary LN	10	4	1	
Subcarinal LN	3	1		
Lower mediastinum LN	1			1
Total	23	13	1	1

LN, lymph node.

RESULTS

Eighty-one of 234 consecutive patients referred with confirmed gastric cancer underwent EUS-FNA because of suspected distant metastasis (35%). Median patient age was 65 years, range 34 to 90 years. Fifty-nine patients were male, and 22 were female. The location of cancer was the cardia in 48 patients, body in 30 patients, linitis plastica in 2 patients, and pylorus in 1 patient.

Ninety-nine lesions were targeted in 81 patients, and 61 (62%) of these lesions were found to be malignant by EUS-FNA. Table 1 shows the total number of targeted lesions and the total number of positive FNAs, according to the site of the lesion. Seventy-eight of 99 lesions were suspicious lymph nodes in the mediastinum—6 along the right jugular vein, 9 at the left subclavian artery, 5 right pulmonary hilum, 28 aortopulmonary window, 28 subcarinal region, and 2 in the lower mediastinum. Other sites of gastric cancer metastases detected by EUS-FNA were the liver, paraortic lymph nodes, portal lymph nodes, omentum, celiac lymph nodes, and adrenal gland. In 38 of 81 patients (42%) distant metastases were confirmed by EUS-FNA. In 27 of these patients, the distant metastasis was located in the mediastinum. Table 2 shows the total number of patients with distant metastasis according to the site of the primary tumor and the correlation with the site of FNA. Ascites containing malignant cells was found by EUS in 4 patients, after needle aspiration of ascitic fluid. In 4 of 6 patients, in whom EUS confirmed distant metastasis in the liver, CT demonstrated lesions suspected of being liver metastases, but these were not verified by CT-guided FNA. Neither CT of the thorax or abdomen nor any other radiological modalities showed any suspicion of distant metastases in the remaining 34 of 38 patients. Table 3

TABLE 3. No. of malignant EUS-FNA diagnoses according to the site of primary tumor in the stomach

	Cardia	Body	Antrum	Linitis plastica
Liver	3	3		
Paraortic LN	3			
Adrenal gland		1		
Ascites	1	3		
Portal LN	2	1		
Omentum		1		
Celiac LN	1			
Subclavian LN	5	3		
Aortopulmonary LN	13	6	1	
Subcarinal LN	7	5		1
Lower mediastinum LN				1
Total	35	23	1	2

LN, lymph node.

shows the number of malignant EUS-FNA diagnoses according to the location of the primary tumor.

As judged by the board of surgeons, EUS-FNA changed the management plan in 34 of 234 patients (15%) undergoing EUS for staging, avoiding unnecessary surgery, and all of these patients underwent palliative treatment. The 4 patients in whom a positive EUS-FNA did not change patient management were the patients with liver metastases suspected by CT and in whom the treatment decision

was unchanged by EUS findings. All 38 patients with verified distant metastases were treated by palliative chemotherapy with or without endoscopic palliative procedures. Of these patients, 12 underwent enteral stenting, and 1 patient additionally received radiotherapy.

DISCUSSION

A correct staging of gastric carcinoma is necessary before a treatment decision is made. According to the UICC classification, involvement of other organs by lymphatic or hematogenous spread as well as predefined lymph node stations in distant regions is considered to be distant metastases, and surgery is not recommended. According to the UICC classification, the regional lymph nodes of the stomach are the perigastric nodes along the lesser and greater curvatures; the nodes along the left gastric, common hepatic, splenic, and celiac arteries; and the hepatoduodenal nodes. The regional lymph nodes of the gastroesophageal junction are the paracardial, left gastric, celiac, diaphragmatic, and the lower mediastinal paraesophageal. Involvement of other intraabdominal lymph nodes such as retropancreatic, mesenteric, and paraaortic are classified as distant metastases. Involvement of lymph nodes in the mediastinum, away from the tumor such as lymph nodes in the aortopulmonary window, above the aortic arch, and nodes in the vicinity of the subclavian vessels are regarded as distant metastasis. These lymph nodes are not resected during surgical treatment for gastric carcinoma.

Many publications on EUS assessment of the TN stage of gastric cancer are available,¹⁴⁻¹⁷ but data regarding the clinical impact of EUS-FNA on preoperative staging and its further impact on final management of gastric cancer patients are lacking. Recently, EUS-FNA of peri-intestinal lymph nodes has proved to be a safe and accurate technique.¹⁸ The reported accuracy for evaluating peri-intestinal lymph nodes by EUS-FNA has ranged from 86% to 95%. The accuracy of EUS imaging in determining metastatic spread to lymph nodes or organs such as the liver, adrenal glands, lungs, and omentum is poor, and because treatment decisions depend on lymph node as well as distant metastasis staging, a histological or cytological characterization of the suspected metastatic lesion is of great importance. In our study, 3 patients had T4 stage tumors by EUS, which alone is a sign of inoperability, and in addition to this, EUS-FNA was able to confirm signs of distant metastasis by FNA cytology, confirming inoperability in these patients. Recently published series concerning EUS-FNA have shown that this modality has a specificity of 95% in discriminating between malignant and inflammatory lymph nodes.¹⁹⁻²⁹ Binmoeller et al³⁰ reported their experience in 35 patients with esophageal or cardia malignancies in whom EUS-FNA of lymph nodes was performed. The authors concluded that none of the morphologic features of lymph nodes on EUS were pre-

dictive of malignancy, and comparison of EUS-FNA findings with surgical pathology results in 24 patients (36 nodes) revealed a sensitivity of 97% and a specificity of 100%. Based on the findings from EUS and EUS-FNA, surgery was not carried out in 20% of 130 patients with esophagogastric cancer.³⁰

In the present study, it should be noted that most of FNAs (79%) were performed on suspected mediastinal lymph nodes. Distant spread to lymph nodes in the mediastinum was confirmed by EUS-FNA in 27 of 81 patients with gastric carcinoma, which is a significant observation. It is also important to mention that 48 of 81 gastric cancer patients who underwent EUS-FNA had cancer of the cardia, which may explain the high percentage of mediastinal lymph node metastases in these patients, when no other radiological modality was able to confirm the presence of distant metastases. Ninety-nine lesions in 81 patients were targeted, and 61 of these were malignant. This means that many of the 81 patients had more than 1 lesion targeted. Each of these lesions suspected to be distant metastases was carefully selected by the endoscopist, based on clinical experience with surgical management of gastric cancer. The present study demonstrates that by using EUS-FNA in the evaluation of gastric cancer patients, the treatment plan was changed in 15% of cases, which significantly demonstrates its usefulness in pretherapeutic evaluation and management of the patients, mainly by the avoidance of futile surgery.

A limitation of the study is that the positive EUS-FNA diagnoses were not surgically verified, although the scope of this problem should be negligible because biopsy through the primary lesion was avoided to reduce the potential risk of false positive diagnoses.

CONCLUSION

The present study demonstrates that EUS-FNA is valuable in the confirmation of distant metastases in patients with gastric carcinoma. Most distant metastases were located in the mediastinum. EUS-FNA significantly changed patient management in 15% of patients fit for surgery. The study proves that EUS-FNA is a very important modality and should be integrated as a routine procedure in the preoperative staging algorithm of gastric cancer.

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