IMPACT OF ENDOSCOPIC ULTRASOUND IN PREOPERATIVE EVALUATION OF GASTRIC CANCER

Muangu Yamba Willy, Chuanqing Wu and kaixiong Tao
Department of Gastrointestinal Surgery, Hepatobiliary Surgery, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei 430074, P.R China

Email: muangawilly@yahoo.fr
Telephone: 008615623035965

Second correspondence: Chuanqing Wu
Accepted 2016 February 3rd ID-SID 116

Abbreviations

EUS: Endoscopy Ultrasound

TNM: Tumour, regional nodes, distant metastases

T1: Tumor invades lamina propria or submucosa

T2: Invades muscularis or subserosa

T3: Penetrates serosa, no adjacent structure

Tis: Carcinoma in situ, no invasion of lamina

N: Nodes

HUST: Huazhong University of Sciences and Technology

CT: Computer tomography

GC: Gastric Cancer
Muangu et al. Impact of Endoscopic ultrasound in Preoperative evaluation of gastric cancer

Acknowledgements

First and foremost I would like to give thanks to my supervisor Professor Kaixiong Tao for giving me this opportunity to be his student, To Doctor Chuanqing Wu for helping me to undertake this project and research.

This work was supported by my tutor, Professor Kaixiong Tao, department of Gastrointestinal Surgery, Union hospital, Tongji Medical College, Huazhong University of Science and technology.

Author Contributions

Conceived and designed the experiments: Muangu Yamba Willy
Analyzed the data: Chuanqing Wu
Contributed reagents/materials/analysis tools: Muangu Yamba Willy

Abstract

Background: Gastric cancer remains one of the most common forms of cancer worldwide. The exact prevalence rate of gastric cancer in preoperative staging in any country is very difficult to predict with any degree of TNM accurate due to the invasive and subjective diagnostic procedures.
Nonetheless, the main unique situation in China is that more than half of the patients have T1 tumors that are early gastric cancer. This result is partly due to the mass screening system, which covers actually as little as 10% of the entire population over 40 years old [1].
However, non-invasive methods and technical for diagnosis gastric cancer in preoperative and postoperative management are currently under development, such as endoscopy ultrasound and CT scan; Definitive procedure of diagnosis of gastric cancer can only be achieved by surgical method via by laparoscopy. In fact, the
accuracy of laparoscopic staging has been documented, but its safety and impact on clinical decision making are less clear [2]. This study provides an update on EUS exam focusing on the specific management in gastric cancers.

The preoperative EUS was performed in 209 patients diagnosed with gastric cancer and performed laparoscopy like a minimal invasive technique. The purpose of this study consisted to assess the depth of invasion in the gastric wall by the infiltration by underlying organs and involvements of TNM.

**Aim and Objectives:** Firstly, the aim of this study is to evaluate the role of endoscopy ultrasound (EUS) as a method for predicting and evaluate the exact accuracy rate in preoperative staging in gastric cancer.

**Materials and Methods**

Two hundred nine cases of GC with lesions more than 2 cm in largest diameter were examined in this study by using EUS before surgery. All materials were collected at Union Hospital during 2011 to 2013; histological classification was made to evaluate the TNM. All specimens were fixed in 15% formalin after laparoscopy to examine the type of histological findings.

**Collection of data:** A retrospective clinical study was conducted from 2011 to 2013 in HUST (Union Hospital), a total of 209 patients were performed EUS, we consecutively identified gastric cancers among these patients in different staging of EUS.

**Results and discussion:** 209 patients were examined in this study. Among this findings, the accuracy rate of the depth of gastric cancer invasion about the sensitivity and specificity of EUS before surgery
in stage T staging was 52.15% and comparing with N stage (table 2) 54.07% and Kappa coefficient was 0.216 <0.40.

**Statistical analysis**

The data were collected; analyzed using Kappa coefficient test, chi square test was used to compare percentages and to assess the independence of two qualitative variables in all analyses, P<0.05 was considered to be significant. SAS R- 2.14.0 software windows X.P version 2007.

**Conclusion**

Based on the number of patients who were evaluated with EUS and underwent “gold-standard”, this study found that the overall rate of detection of and accuracy were 62.68% % respectively for stage T. The specificity and negative predictive value were not evaluated. Furthermore, accurate outcome can only be depended by laparoscopy, whereby some factors can be included such as the quality of equipment and the skills of the surgeon.

**Keywords**: endoscopic ultrasonography, EUS, gastric cancer, locoregional staging, TNM.
INTRODUCTION

Gastric cancer is one of the most common cancers worldwide. Despite the decreasing incidence and mortality, gastric cancer remains the second leading cause of cancer-related deaths in the world [3]. In China, gastric cancer has been the most common cause of death due to the cancer; the prognosis of this malignancy disease is strongly related to the depth invasion. The prognosis of patients with gastric cancer is determined by the tumor extent and includes both nodal involvement and direct tumor extension beyond the gastric wall [4-5]. However, accurate staging of gastric cancers is indispensable for well-informed decisions on patient management. This significant problem: which patients qualify for curative therapy and is becoming increasingly essential with improvements in non-surgical treatment regimens, Surgery is the major stay of therapeutic for gastric cancers. While patients with early localized disease clearly benefit from complete surgical resection, Accurate local cancer staging provides the information necessary for such important decisions to be made while not denying patients potentially curative surgical resection, with or without neoadjuvant therapy the development of other non-surgical techniques at. Both ends of the disease spectrum have also reinforced the need for accurate cancer staging.

The postoperative 5 year survival rate of patients with gastric cancer depends on the depth of tumor infiltration and the extent of lymph node metastasis [6-7].

Gastrointestinal cancer using laparoscopy treatment has recently been undertaken like a good way to treat gastric tumor. Accordingly to our clinical skills, it is very important to assess preoperative in management of gastric cancer by using EUS [8-9].
The depth of tumour infiltration and the extent of lymph node lack of adequate imaging techniques, however accurate assessment is often difficult. Endoscopic ultrasound has recently been developed to improve diagnostic accuracy by directly imaging the target lesion via the gastrointestinal lumen. However, this new technique is predictable to provide an accurate assessment of the extent of tumor invasion of the upper gastrointestinal tract because of the clear visualization of tumor infiltration and the involvement of adjacent lymph nodes. In this study we assess the practical purpose of endoscopic ultrasound in diagnosing the depth of cancerous invasion into the gastric wall, involvement of the perigastric lymph nodes, and direct infiltration into the adjacent organs by comparing its results with the histological findings [10].

PATIENTS AND METHODS

Methods: This study was designed to evaluate the impact of EUS in preoperative and postoperative by using laparoscopy like a minimal management and retrospectively compared the diagnostic accuracy of EUS for gastric cancer among these patients. However, patient permission was obtained for examination in this study. All EUS were performed before the laparoscopy exploration, in fact that ensures that the operator is blind to the endoscopic diagnosis. The instruments used were 3 D-EUS, EUIP2 viewer 12, 20 MHz (Olympus Medical Systems, Tokyo, Japan). EUS was carried out using a water filling technique. An image was chosen from the 3-D images, and diagnostic accuracy of EUS was investigated. The diagnosis of tumor depth in cases with ulcer scar was based on the classification by Kida et al. [11-12].
We compared the results from EUS to histology and focused on the difference in the echo level between the area of scar invasion and that of fibrosis, we set several areas of interest in the image of the third or deeper layers.

**Patients**
Between 2011 and 2013, we performed preoperative endoscopic ultrasound in 209 patients with diagnosis findings of gastric cancer that had been confirmed by endoscopic biopsy specimen. They underwent laparoscopy after preoperative examinations. nevertheless, all the resected specimens, including lymph nodes, were examined histopathologically. However, results of the preoperative endoscopic ultrasound scanning were compared with both the intraoperative macroscopic findings and the pathology of the resected specimens.

Echoendoscopes with radial sector scan transducers.

**Sample processing**
Resected tumors were fixed with neutral formalin and sent for pathological examination; the samples were immunohistochemically stained for CD34, DC117, Dog-1, S-100, and SMA.

**RESULTS**

**Histopathologic findings**
Clinicopathological factors for considerations of less invasive surgery included cancer depth (T), nodal involvement (N) and histological location.

Gastric cancer (T1 cancer) was further divided into mucosal (T1-M) and Submucosal (T1). Nodal involvement followed the updated definitions of the Japanese association [13]
Muangu Willy et al. Impact of Endoscopic ultrasound in Preoperative evaluation of gastric cancer

All specimens were classified as T1-T4 and NO-N2 according to the TNM system established in worldwide.

2.1 Findings in patients with EUS T staging of gastric cancer compared with postoperative T stage results

① will prevail T2-3 similar to low

Table 1 EUS T staging of gastric surgery and postoperative T stage result of the comparison

<table>
<thead>
<tr>
<th>EUS Staging</th>
<th>Pathological staging</th>
<th>Kappa Index</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>T1: 7, T2: 3, T3: 6, T4: 0, Tis: 0</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>T1: 12, T2: 15, T3: 39, T4: 8, Tis: 1</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>T1: 12, T2: 4, T3: 84, T4: 10, Tis: 1</td>
<td>111</td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td>T1: 0, T2: 0, T3: 4, T4: 2, Tis: 0</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Tis</td>
<td>T1: 0, T2: 0, T3: 0, T4: 0, Tis: 1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>T1: 31, T2: 22, T3: 133, T4: 20, Tis: 3</td>
<td>209</td>
<td></td>
</tr>
</tbody>
</table>

When our 209 cases were evaluated, the predictive and specificity value of EUS was 52.12% of the accuracy. Where in T1 22.58%, T2 68.18%, T3 63.16%, T4 9.68%, Tis 33.33%. T2, T3 higher accuracy, more than 60%. Kappa coefficient was 0.216 <0.40, poor consistency.
② will T2-3 similar to a high value, whichever

Table 2 EUS T staging of gastric surgery and postoperative T stage result of the comparison

<table>
<thead>
<tr>
<th>EUS Staging</th>
<th>Pathological staging</th>
<th>Kappa Index</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T1</td>
<td>T2</td>
<td>T3</td>
</tr>
<tr>
<td>T1</td>
<td>6</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>T2</td>
<td>9</td>
<td>13</td>
<td>33</td>
</tr>
<tr>
<td>T3</td>
<td>16</td>
<td>6</td>
<td>90</td>
</tr>
<tr>
<td>T4</td>
<td>0</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Tis</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>31</td>
<td>22</td>
<td>133</td>
</tr>
</tbody>
</table>

T gastric cancer before EUS accuracy was 54.07% of the total. Wherein T1 19.35%, T2 59.09%, T3 67.67%, T4 15.00%, Tis 33.33%. Kappa coefficient was 0.202 <0.40, poor consistency.

(Above two methods, the second overall accuracy rate higher, may be the second category)

2.2 EUS staging of lymph node metastasis in gastric surgery compared with pathological staging results (due to lack of Radiographic detection N3 result, it will be merged, divided into N+, N-)
**Table 3 EUS staging of lymph node metastasis in gastric surgery compared with pathological staging results**

<table>
<thead>
<tr>
<th>EUS Staging</th>
<th>Pathological staging</th>
<th>Total</th>
<th>$\chi^2$</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N+</td>
<td>N-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N+</td>
<td>85</td>
<td>10</td>
<td>95</td>
<td></td>
</tr>
<tr>
<td>N-</td>
<td>68</td>
<td>46</td>
<td>114</td>
<td>33.77</td>
</tr>
<tr>
<td></td>
<td>153</td>
<td>56</td>
<td>209</td>
<td></td>
</tr>
</tbody>
</table>

EUS for preoperative N staging of gastric overall accuracy rate of 62.68% for lymph node metastasis N +, N- correct rate of 55.56%, 82.14% respectively, there was significant difference with the pathological staging.

2.3 Relationship between the Depth of lesion T and N staging findings:

There was significant difference in this table according the results we found

Comparison of different lesions and T, N staging of judgment between right
the lesion is divided into cardia, fundus, gastric body, antrum, and pylorus, compare different parts of EUS to determine whether there is a difference between the correct rates of staging. The results showed that the detection accuracy in different parts of no significant difference between both groups.
### Table 4 Pathological diagnosis in different lesions of gastric cancer

<table>
<thead>
<tr>
<th>EUS Staging</th>
<th>Lesions</th>
<th></th>
<th></th>
<th></th>
<th>Total</th>
<th>$\chi^2$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cardia</td>
<td>Fundus</td>
<td>Gastric</td>
<td>Antral</td>
<td>Pylorus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T +</td>
<td>11</td>
<td>11</td>
<td>45</td>
<td>43</td>
<td>3</td>
<td>113</td>
<td></td>
</tr>
<tr>
<td></td>
<td>14</td>
<td>13</td>
<td>39</td>
<td>27</td>
<td>3</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td>T -</td>
<td>16</td>
<td>16</td>
<td>52</td>
<td>42</td>
<td>5</td>
<td>131</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>8</td>
<td>32</td>
<td>28</td>
<td>1</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>24</td>
<td>84</td>
<td>70</td>
<td>6</td>
<td>209</td>
<td></td>
</tr>
</tbody>
</table>

**Comparison of different times the correct rate of EUS**
Understanding the correct rate in different years EUS detected by chi-square test showed different years of testing the accuracy of the difference was not statistically significant.
US staging of lymph node metastasis in gastric surgery

Table 5 different years compare EUS accuracy rate (%/o)
DISCUSSION

We conducted a retrospective study to evaluate the impact of EUS in the management of gastric cancer.

Kaminishi et al. (2011, suggested that EUS is accepted today as the best approach management to evaluate the patients in preoperative about gastric cancer in pre staging involvement because it conserves the accuracy and then it allows to assess the staging for the tumors. Another author discusses in the same direction as the previous confirms the importance of EUS as the leading exams for detecting tumors stage [14]. Nonetheless, knowledge and skills in EUS by using laparoscopy has been now indicated and reported in many others countries especially in China. As indicated in previous study EUS becomes reasonably recurrent procedure in China. Based on all the above, in 2014, a large multicenter of research published at January to June 2014 studied 1000 gastric cancers in 975 patients divided in two principal groups (502 men and 498 women, the mean age for patients was 62.4 years range 43-82 years) the author observed the role of EUS like a major source to evaluate the accuracy in preoperative surgery about gastric cancer, it appears that the accuracy rate for this study was 82%, correspondingly to the first experience [15-16].

<table>
<thead>
<tr>
<th>Years</th>
<th>T Correct rate</th>
<th>N Correct rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>60.0</td>
<td>55.0</td>
</tr>
<tr>
<td>2012</td>
<td>47.9</td>
<td>62.5</td>
</tr>
<tr>
<td>2013</td>
<td>59.1</td>
<td>64.5</td>
</tr>
<tr>
<td>$\chi^2$</td>
<td>2.709</td>
<td>0.640</td>
</tr>
<tr>
<td>$P$</td>
<td>0.258</td>
<td>0.726</td>
</tr>
</tbody>
</table>
A previous authors reported that the rate of accurate decide the depth of tumor invasion. Some studies have been focused to evaluate the accuracy of EUS and these conclusions shows the results around of 85% of accuracy.

In comparison, 2 previous studies reported that, the rate of accurate determination of the depth of tumor invasion in 204 gastric cancer Cases were 85.3%. For the 109 T2 cases, the accuracy was 85.3% for those rated as M and 67%.4% for those rated as N.Chonan et al., reported accuracy for 100 cases of type II early gastric cancer (SM!)96, 6% with EUS and 94, 2% with endoscopy. For 5 PSM2 cases, the accuracy was 62.5 % with EUS and 75 % with endoscopy. The accuracy will rise to 80 %, approximately, when EUS images are Analyzed in comparison to the pathology, including review of cases with overdiagnosis resulting from micro invasion and ulceration [17-18].

This reinforces our study to confirm that EUS is now recognizing in the world especially in China as a best preoperative procedure to evaluate the stage of gastric cancer it provides an elevated curative by adding laparoscopy. This exam allows a very significant lecture for all patients who are supposed to perform laparoscopy in GC.

Although laparoscopy is performed primarily treat many gastric cancer patients, it is inversely the final chance for survival of cancer cells. Therefore, the preoperative prevention of early diagnosis is important when curative surgery is performed.

EUS is widely accepted as a good accurate in surgery procedure for obtaining diagnostic assessment about gastric cancer [19-20]. In our study we show that EUS is the most reliable technique and
procedures for preoperative evaluation of the gastric cancer because it allows finding correctly the depth of tumor infiltration (T stage). This study shows the exact accuracy rate 52.15 % (table 1). The kappa coefficient was 0.216<0.40 significantly poor with the T2-3 similar to a high value (Table 2).

The prognosis of gastric cancer depends mainly on the tumor stage; however 5 year survival rate after surgery was was 52.15% of the total walls at stage I (T1, NO), 68.18% to stage T2, 63.16% T#, 9.68% to T4. T2 and T3 is the highest accuracy. The selection management for gastric cancer depends on preoperative tumor staging because survival rates and morbidity differ significantly and depends on resection of laparoscopy. In addition, the accurate of preoperative and intraoperative assessment about TNM stage is a principal criterion to evaluate inappropriate management.

**CONCLUSION**

- EUS is an acceptable method for analysis, loco regional staging and presence of infiltrated paragastric lymph nodes in gastric cancer [18].
- The accuracy of EUS-guided T-staging ranges in several studies between 60% and 90%; N-staging accuracies are rather lower.
- The impact of EUS on patient management remains controversial; it seems to have a greater impact on management of early stages rather than in advanced gastric cancer.
- In this Present study, we support that EUS could be included as a regular procedure in the preoperative staging algorithm of gastric cancer.
- TNM-restaging with EUS shows a low accuracy; it seems that in this scenario, 3D EUS-reconstructions of tumor volume changes could possibly be better suited.
• In early gastric cancer, EUS for differentiation of mucosal from submucosal infiltration prior to endoscopic resection is not mandatory, provided the endoscopist has enough incidences with the macroscopic assessment of early lesions. EUS could possibly recognize lymph nodes in early gastric cancer; the role of EUS in these locations needs to be further clarified [21].

• Laparoscopic staging is suggested in gastric cancer, because it causes significant changes to the management plan in one-third of patients, and the risks of port site metastasis decreasing.

References


8. Rösch T. The radial echoendoscope: here to wait or gone tomorrow? *Gastrointest Endosc* 2014;69(Suppl).


