Transabdominal ultrasonography in preoperative staging of gastric cancer

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AIM: To investigate the value of transabdominal ultrasonography (US) in the preoperative staging of gastric cancer.

METHODS: A total of 198 patients with gastric cancer underwent preoperatively transabdominal US, depth of tumor infiltration was assessed in 125 patients, and lymph node metastasis was assessed in 106 patients.

RESULTS: The staging accuracy of transabdominal US was 55.6%, 75.0%, 87.3% and 71.1% in T1, T2, T3 and T4 carcinomas, respectively. The overall accuracy was 77.6%. The detection rate for pancreatic invasion and liver invasion was 77.4%, 71.4%, respectively. The sensitivity, specificity, accuracy of transabdominal US in assessment of lymph node metastasis were 77.6%, 64.1%, 72.6%, respectively. Various shapes such as round, ovoid, spindle were encountered in benign and malignant lymph nodes. Majority of both benign and malignant lymph nodes were hyperechoic and had a distinct border. Benign lymph nodes were smaller than malignant lymph nodes in length and width (P = 0.000, 0.005). Irregular shape, fusional shape, infiltrative signs, inhomogenous echo were seen mainly in malignant lymph nodes (P = 0.045, 0.006, 0.027, 0.006).

CONCLUSION: Transabdominal US is useful for preoperative staging in gastric cancer, although it is difficult to differentiate benign from malignant lymph nodes.

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INTRODUCTION

Gastric cancer is one of the most prevalent malignant tumors[1,2]. An accurate preoperative staging is helpful for the prediction of prognosis and establishment of the individualized therapy. Although endoscopy and upper gastrointestinal series with double-contrast study have significantly improved the diagnostic accuracy in gastric cancer, they neither allow the assessment of the depth of tumor infiltration nor visualize perigastric lymph nodes[3,4]. Currently, endoscopic ultrasonography (EUS) has been considered as a useful modality for the preoperative staging of gastric cancer, and the accuracy of EUS in the assessment of the depth of tumor infiltration and lymph node metastasis is 67-92% and 63-78%[5-11], respectively. However, EUS procedure is relatively complex, and can not be performed successfully in some patients, due to marked obstruction of gastric lumen caused by tumor or noticeable discomfort during examination.

Transabdominal ultrasonography (US) is applied widely in clinical practice. When condition of patients is suitable, transabdominal US can detect lymph nodes with a diameter of 5 mm, and the normal wall of fluid-filled stomach after the patients drank water can be described as a 5-layer structure[12-14], which contributes to the assessment of the depth of tumor infiltration. Literature on the preoperative staging with transabdominal US is sparse[15,16]. The aim of our study was to further assess the accuracy and limitations of transabdominal US in preoperative staging of the depth of tumor infiltration and lymph node metastasis.

MATERIALS AND METHODS

Between January 2000 to July 2003, 198 patients with gastric cancer confirmed by endoscopic biopsy underwent transabdominal US preoperatively. Patients with preoperative transabdominal US findings and detailed operative and pathological findings were included in this study. The depth of tumor infiltration was assessed in 125 patients (78 males, 47 females, ranged 27-78 years). Lymph node metastasis was assessed in 106 patients (66 males, 40 females, ranged 31-78 years).

All patients were required to drink water to fill stomach for the assessment of the depth of tumor infiltration. Transabdominal US was performed 3-5 min after 500-700 mL boiled water was drunk. Patients were examined usually in the supine position. Sitting position, left or right lateral decubitus position might be taken for visualization of lesions according to different locations of tumors.

The wall of fluid-filled stomach is described as a 5-layer structure[12-14]. The innermost hyperechoic layer (the first layer) corresponds to the superficial mucosa, the second hyperechoic layer corresponds to the deep mucosa, the third hyperechoic layer corresponds to the submucosa plus the acoustic interface between the submucosa and muscularis propria, the fourth hyperechoic layer corresponds to the muscularis propria minus the acoustic interface between the submucosa and muscularis propria, the fifth hyperechoic layer corresponds to the subserosal fat and serosa.

According to the TNM (UICC) classification[17], the depth of tumor infiltration was divided into 4 categories. T1 = tumor confined to mucosa or submucosa. For mucosal carcinoma, tumor located in the first and second layers, the third layers (submucosa) was intact; for submucosal carcinoma, layers 1 to 3 were interrupted or thickened and the fourth and fifth layers were normal sonographically (Figure 1A). T2 = tumor invading muscularis propria (the fourth layer) which became thicken, and the fifth layer was intact sonographically (Figure 1B). T3 = tumor invading serosa (the fifth layer), with interruption...
or disappearance of all layers of wall sonographically (Figure 1C).

T4 = tumor invading adjacent organs which had an indistinct border and was indistinguishable from involved organs sonographically (Figure 1D).

Assessment of regional lymph node metastasis was performed in a fasting state before water was drunk for evaluation of tumor infiltration. Regional lymph nodes around the following organs or structures were examined: stomach, liver, pancreas, gallbladder, aorta, hilum of spleen, celiac hepatic aorta, superior mesenteric artery, celiac artery, and recorded number, size, shape, border, and echogenicity of lymph nodes.

Lymph nodes with a length of 5 mm or greater were considered metastatic. Regional lymph node staging was classified as N0 (no lymph node metastasis) and N+ (lymph node metastasis).

Lymph nodes detected with transabdominal US were divided into 3 groups according to their shapes: regular, irregular, fusional. Regular lymph nodes were classified into 3 categories of shape: spindle: width \( \leq \) half the length of the lymph node; ovoid: width \( \leq \) three quarters of the length of the lymph node; round: width \( > \) three quarters of the length of the lymph node\(^{18}\).

The followings were considered as “infiltrative signs” of lymph nodes: ill-defined border, indistinguishable from the adjacent structures or loss of movement.

Sonographic examinations were performed with commercially available real time image units (Toshiba 6000, Aloka 2000, DU-6), and transducer frequency varied between 3.5-6.0 MHz.

Data were analyzed with SPSS10.0 software. \( P < 0.05 \) was considered statistically significant.

**RESULTS**

*Assessment of depth of tumor infiltration*

Table 1 summarizes the findings of transabdominal US and operative or pathological findings in 125 patients with gastric cancer. The accuracy of transabdominal US in staging of T1 carcinomas was 55.6%, 75.0% in T2 carcinomas, 87.3% in T3 carcinomas, and 71.1% in T4 carcinomas. The overall accuracy was 77.6%.

Tumors were overstaged in 8 patients. T1 carcinoma was overstaged as a T2 carcinoma in 3 patients and as a T3 carcinoma in 1 patient (Figure 2), and T2 carcinoma was overstaged as a T3 carcinoma in 4 patients. Tumors were understaged in 20 patients. T3 carcinoma was understaged as a T2 carcinoma in 7 patients. T4 carcinoma was understaged as a T2 carcinoma in 2 patients and as a T3 carcinoma in 11 patients.

Invasion of adjacent organs confirmed by operative or pathologic findings was as follows (Table 2): pancreas (31 patients), liver (7 patients), spleen and hilum of spleen (3 patients), transverse colon (3 patients), diaphragm (2 patients), and duodenum (9 patients). The detection rate for pancreas and liver invasion with transabdominal US was 77.4% and 71.4%, respectively, whereas the detection rate for the invasion of other organs was low.

**Figure 1** Sonograms of T1-T4 carcinoma. A: Submucosal carcinoma (T1) in gastric antrum. Arrow indicates segmental thickening of layers 1-3 of the posterior wall, triangle indicates normal layers 4-5. B: T2 carcinoma. The posterior wall of Gastric body is thickening. Arrow indicates the third hyperechoic layer is obliterated and the fourth hypoechoic layer is thickening, triangle indicates normal layer 5. C: T3 carcinoma. Tumor located in the greater curvature of stomach (STO) is hypoechoic with disappearance of wall all layer (arrow). D: T4 carcinoma. Sonogram shows tumor located in antrum (AN) infiltrating duodenum. Arrow indicates the segmental wall thickening of duodenal bulb.

**Figure 2** Mucosal carcinoma (T1) was overstaged as a T3 carcinoma with transabdominal US. Sonogram of gastric body shows hypoechoic wall thickening with ulcer (arrow), loss of wall five-layer structure (triangle).
Table 1 Accuracy of transabdominal US in assessing the depth of tumor invasion in 125 patients

| Stage | n | Staged by operative and pathological findings |
|-------|---|-----------------------------------------------|
|       |   | T1 | T2 | T3 | T4 |
| T1    | 7 | 5  | 0  | 0  | 0  | 0  |
| T2    | 34 | 3  | 12 | 7  | 2  |
| T3    | 80 | 1  | 4  | 48 | 11 |
| T4    | 38 | 0  | 0  | 0  | 32 |

Accuracy (%) 55.6 (5/9) 75.0 (12/16) 87.3 (48/55) 71.1 (32/45)

Table 2 Detection rate of tumor invasion with transabdominal US

| Involved organs | Cases detected with transabdominal US | Detection rate (%) |
|-----------------|-------------------------------------|--------------------|
| Pancreas        | 31 24                               | 77.4               |
| Liver           | 7 5                                 | 71.4               |
| Spleen and hilum of spleen | 3 1 | 33.3 |
| Transverse colon | 3 1 | 33.3 |
| Diaphragm       | 2 0                                 | 0                  |
| Duodenum        | 9 4                                 | 44.4               |

Assessment of regional lymph node metastasis

Accuracy of assessment of regional lymph metastasis Swollen lymph nodes were found pathologically in 106 patients. Lymph node metastasis was confirmed in 67 of 106 patients. Swollen lymph nodes were detected in 66 of 106 patients with transabdominal US. All lymph nodes detected sonographically had a length of 5 mm or greater, and were considered as metastatic. Of the 66 patients, lymph node metastasis was confirmed by pathological examination in 52 patients, and swollen lymph nodes were benign in the remaining 14 patients. No swollen lymph nodes were detected sonographically in 40 of 106 patients, and lymph node metastasis was confirmed in 15 of these 40 patients. The sensitivity of transabdominal US in the assessment of lymph node metastasis was 77.6% (52 of 67 patients). The specificity was 64.1% (25 of 39 patients). The accuracy was 72.6% (77 of 106 patients) (Table 3).

Table 3 Accuracy of transabdominal US in assessing lymph node metastasis in 106 patients

| Diagnosis with transabdominal US | Pathological findings (n) |
|---------------------------------|---------------------------|
|                                 | N+ | N0 |
| N+                              | 52 | 14 |
| N0                              | 15 | 25 |

Sensitivity: 77.6% (52/67); Specificity: 64.1% (25/39); Accuracy: 72.6% (77/106).

Sonographic features of benign and malignant lymph nodes

All lymph nodes in 14 of 66 patients with swollen lymph nodes detected with transabdominal US were confirmed benign (lymph node without metastasis), and transabdominal US detected 46 lymph nodes in these patients. All lymph nodes in 11 of 52 patients with lymph node metastasis were confirmed malignant (metastatic), and transabdominal US detected 48 lymph nodes in these patients. Forty-six benign lymph nodes had a mean length of 1.26 cm and a mean width of 0.84 cm, 48 malignant lymph nodes had a mean length of 1.79 cm and a mean width of 1.25 cm. According to size, shape, echogenicity, and border, sonographic features of these benign and malignant lymph nodes were further analyzed (Table 4). The length and width of benign lymph nodes were significantly smaller than those of malignant lymph nodes (P = 0.000, 0.005). Sonographic features such as irregular or fusional shape, infiltrative signs, and inhomogenous echoes were found mainly in malignant lymph nodes (Figure 3). There was a significant difference between benign and malignant lymph nodes (P = 0.045, 0.006).

Table 4 Sonographic features of 46 benign and 48 malignant lymph nodes

| Sonographic feature | Pathologic findings |
|---------------------|---------------------|
|                     | Benign lymph nodes (%) | Malignant lymph nodes (%) |
| Length (cm)         |                      |
| <0.5                | 0                    | 0                        | 0.000 |
| 0.5-1.0             | 26 (56.5)            | 9 (18.8)                 |       |
| 1.1-1.5             | 9 (19.6)             | 16 (33.3)                |       |
| 1.6-2.0             | 9 (19.6)             | 8 (16.7)                 |       |
| ≥2.1                | 2 (4.3)              | 15 (31.2)                |       |
| Length (cm)         |                      |
| <0.5                | 0                    | 0                        | 0.005 |
| 0.5-1.0             | 26 (56.5)            | 9 (18.8)                 |       |
| 1.1-1.5             | 9 (19.6)             | 16 (33.3)                |       |
| 1.6-2.0             | 9 (19.6)             | 8 (16.7)                 |       |
| ≥2.1                | 2 (4.3)              | 15 (31.2)                |       |
| Width (cm)          |                      |
| <0.5                | 5 (10.9)             | 2 (4.2)                  | 0.005 |
| 0.5-1.0             | 34 (73.9)            | 22 (45.8)                |       |
| 1.1-1.5             | 4 (8.7)              | 10 (20.8)                |       |
| 1.6-2.0             | 3 (6.5)              | 11 (22.9)                | 0.045 |
| ≥2.1                | 0 (0)                | 3 (6.3)                  | 0.006 |
| Shape               |                      |
| Spindle             | 9 (19.6)             | 5 (10.4)                 |       |
| Ovoid               | 15 (32.6)            | 10 (20.8)                |       |
| Round               | 20 (43.5)            | 17 (35.4)                |       |
| Irregular           | 2 (4.3)              | 8 (16.7)                 | 0.004 |
| Fusional            | 0 (0)                | 8 (16.7)                 | 0.006 |
| Border              |                      |
| Distinct            | 34 (73.9)            | 29 (60.4)                |       |
| Indistinct          | 12 (26.1)            | 13 (27.1)                |       |
| Infiltrative signs  | 0 (0)                | 6 (12.5)                 | 0.027 |
| Echogenicity         |                      |
| Hypoechoic          | 40 (87.0)            | 38 (79.1)                |       |
| Slightly hypoechoic | 6 (13.0)             | 2 (4.2)                  |       |
| Inhomogenous        | 0                    | 8 (16.6)                 | 0.006 |

Figure 3 Metastatic lymph node. A: Sonogram shows a irregular lymph node (arrow) adjacent to the portal vein (PV) with a distinct border and 2.1×1.7 cm in size. B: Sonogram shows fusional-shaped lymph node (arrow) (4×3 cm) adjacent to the stomach (STO), invading adjacent tissues and having an indistinct border.
Pancreas was the most common organ invaded by tumor, the detection rate in this study was 77.4%. In 3 of 7 patients undetected by transabdominal US, pancreas was invaded slightly, and the boundary between pancreas and tumor seemed to exist on sonogram, thus leading to understaging. In the remaining 4 patients, the tail of pancreas was invaded, which was not detected by transabdominal US due to interference of bowel gas and ribs.

The detection rate for liver invasion was higher (71.4%). Tumors invading liver located in anterior wall of stomach or lesser curvature and were close to the liver. The relationship between tumor and liver could be visualized clearly by using ultrasonographic beam through liver without interference of bowel gases.

Transverse colon was invaded in three patients, of them, correct diagnosis was made in 1 patient because complete circumference of transverse colon was invaded and marked tumor was detected. In two others undetected by transabdominal US, transverse colon was slightly invaded and bowel gases interfered severely. Correct diagnosis was made preoperatively in 1 of 3 patients with spleen and its hilum invasion. None was diagnosed preoperatively for diaphragm invasion. Spleen and its hilum, and diaphragm could not be observed completely with transabdominal US, leading to the low detection rate.

Correct diagnosis was made preoperatively in 4 of 9 patients with duodenal invasion. It was necessary to fill duodenum by drinking water for the assessment of duodenum. Because tumor caused gastric lumen obstruction, duodenum was not filled adequately and visualized clearly, leading to misdiagnosis of duodenal invasion.

Assessment of lymph node metastasis and differentiation between benign and malignant lymph nodes

The sensitivity of transabdominal US for lymph node metastasis was 77.6%, and the false positive rate was 13.2% (14 of 106 patients). The results showed transabdominal US did not permit the differentiation between benign and (metastatic) malignant lymph nodes in gastric cancer (Figures 4, 5).

Benign swollen lymph nodes due to immune reaction in patients with tumor are misdiagnosed easily as malignant lymph nodes. According to the analysis of sonographic features of lymph nodes (Table 4), benign lymph nodes were smaller than malignant lymph nodes in length and width ($P = 0.000, 0.005$). From Table 5, if the length $\geq 1.1$ cm or 1.6 cm was defined as diagnostic criteria of malignant lymph nodes, the sensitivity was 81.3% and 47.9%, respectively, and the specificity was 56.5% and 76.1%, respectively. Hence the criteria could not differentiate benign from malignant lymph nodes. If the length $\geq 2.1$ cm or the width $\geq 1.6$ cm was defined as diagnostic criteria of malignant lymph nodes, the sensitivity was 33.3% and 29.2%, respectively, and the specificity was 95.7% and 93.5%, respectively. This result showed that lymph node with a length $\geq 2.1$ cm or width $\geq 1.6$ cm increased significantly the probability of metastasis. From the literature and our study, although benign lymph nodes were smaller than malignant lymph nodes, it is clear that there was a considerable overlap in size between benign and malignant lymph nodes; therefore, the value of lymph node size is limited for discriminating benign lymph nodes from malignant lymph nodes ($P = 0.045, 0.006$). It was reported that
abdominal malignant lymph nodes were round or ovoid in shape, conversely, benign lymph nodes in people who were healthy or affected by benign disease were spindle or flat in shape [9,18,24,26-30]. However in our study, both benign and malignant lymph nodes were mostly round in shape, and round shape did not allow the correct differentiation between benign and malignant lymph nodes. Immune reaction caused by tumor was different from that caused by benign diseases such as hepatitis or entities, which may be a cause for difficulties in differentiation between benign and malignant lymph nodes.

In our study the majority of benign and malignant lymph nodes had a distinct border (Figure 5), without statistical difference between them (Table 4). “Infiltrative signs” of lymph nodes were seen only in malignant lymph nodes (P = 0.027), which were typical and helpful for diagnosing malignant lymph nodes. Heintz et al. [31] reported that both benign and malignant lymph nodes had an indistinct or distinct border by studying surgical resection specimens of patients with esophageal and gastric carcinomas. The study reported by Akahoshi et al. [29,32] showed that malignant lymph nodes had a distinct border.

Table 4 shows that both benign and malignant lymph nodes were hypoechoic mostly (Figures 3-5), and the small number of lymph nodes was hyperechoic. Inhomogenous echogenicity was seen only in malignant lymph nodes, there was a significant difference between benign and malignant lymph nodes (P = 0.006) and majority of inhomogenous lymph nodes were 2 cm greater in length. Contradictory data were published for echogenicity of lymph nodes. Heintz et al. [31] stressed that echogenicity did not allow the correct differentiation between benign and malignant lymph nodes. Other authors [24,33] reported that most malignant lymph nodes were hypoechoic, and most benign lymph nodes were isoechoic or slightly hyperechoic. The different results might result from different patients studied.

In our study, the following 4 sonographic features were taken as the diagnostic criteria of malignant lymph nodes (Table 5): irregular shape, fusional shape, infiltrative signs, and inhomogenous echo. The sensitivity of the criteria was lower than 20 percent, and the specificity was higher than 90 percent. One of these 4 features was helpful to suggest malignant, however the similar sonographic features were observed in abdominal tuberculosis. Differential diagnosis was made on the basis of medical history.

Table 5 Diagnostic results of 46 benign and 48 malignant lymph nodes

| Criterion       | Sensitivity (%) | Specificity (%) |
|-----------------|-----------------|-----------------|
| Length ≥1.1cm   | 81.3 (39/48)    | 56.5 (26/46)    |
| ≥1.6 cm         | 47.9 (23/48)    | 76.1 (35/46)    |
| ≥2.1 cm         | 33.3 (15/48)    | 95.7 (44/46)    |
| Width ≥1.1 cm   | 50.0 (24/48)    | 84.8 (39/46)    |
| ≥1.6 cm         | 29.2 (14/48)    | 93.5 (43/46)    |
| Irregular       | 16.7 (8/48)     | 95.7 (44/46)    |
| Fusional        | 16.7 (8/48)     | 100 (46/46)     |
| Infiltrative signs | 12.5 (6/48)     | 100 (46/46)     |
| Inhomogenous    | 16.7 (8/48)     | 100 (46/46)     |
Swollen lymph nodes were found pathologically in 106 patients. But no swollen lymph nodes were detected with transabdominal US in 40 of 106 patients, and lymph nodes metastases were confirmed pathologically in 15 of these 40 patients. Missing lymph nodes were associated with the size of lymph nodes mainly. Lymph nodes less than 5 mm in size were usually undetectable with transabdominal US. In addition, obesity and bowel gas were unfavorable for detection of lymph nodes.

In conclusion, transabdominal US is useful for preoperative staging of gastric cancer, especially for assessment of advanced gastric cancer invasion. Although it is difficult to differentiate benign from malignant lymph nodes, typical sonographic features might contribute to diagnosis.

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