Am J Transl Res 2021;13(10):11764-11770
www.ajtr.org /ISSN:1943-8141/AJTR0134337

Original Article

Ultrasound intervention combined with multi-slice spiral CT has excellent diagnostic value in lymph node metastasis of gastric cancer

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Received April 16, 2021; Accepted July 28, 2021; Epub October 15, 2021; Published October 30, 2021

Abstract: Objective: To investigate the diagnostic value of contrast-enhanced ultrasound (CEUS) combined with multi-slice helical CT (MSCT) for gastric carcinoma and its lymph node metastasis (LNM). Methods: 150 patients with gastric carcinoma diagnosed in our hospital from July 2017 to July 2020 were enrolled for this retrospective study. The patients were all confirmed with gastric carcinoma by biopsy pathology. CEUS and MSCT were performed within one week before surgery. Logistic regression analysis was conducted to analyze the risk factors for LNM of gastric carcinoma. The diagnostic efficiency of CEUS and MSCT in gastric carcinoma and the screening efficiency of LNM were compared, and the sensitivity and specificity were calculated with the postoperative pathologic finding as the gold standard. The scores of lymph node reinforcement were compared. Results: There were 115 cases diagnosed with LNM while 35 were diagnosed without it by CEUS. MSCT results confirmed that there were 112 cases with LNM while 38 without. CEUS combined with MSCT confirmed that there were 116 cases with LNM while 34 cases were without. The sensitivity, specificity, and diagnostic coincidence rate of CEUS for LNM of gastric carcinoma were 89.07%, 70.96% and 85.33%, respectively. Those of MSCT were 84.87%, 64.51% and 80.66%, respectively. Those of CEUS combined with MSCT were 94.11%, 87.10%, and 92.67%, respectively. The reinforcement of CEUS combined with MSCT was better than either alone. Conclusion: CEUS combined with MSCT is more effective in the diagnosis of LNM in gastric carcinoma patients. Hence, the combination of the two is helpful to enhance the accuracy of LNM diagnosis before operation.

Keywords: Gastric carcinoma, lymph node metastasis, contrast-enhanced ultrasound, multi-slice helical CT, diagnosis

Introduction

Gastric carcinoma is a common malignancy of digestive tract in clinical practice, and its incidence is increasing year by year [1, 2]. At present, surgical intervention is commonly used for tumor removal; however, radical surgery can not completely remove metastatic lymph nodes, thus affecting the prognosis of patients [3]. In addition, blind lymphadenectomy may lead to over treatment of non-metastatic lymph nodes, thus destroying the barrier of lymph node system, leading to a decrease of patients' immunity to tumor, affecting the curative effect of operation, and even increasing the mortality and complications related to operation [4, 5]. Therefore, it is of great significance to judge lymph node metastasis (LNM) and distribution accurately before operation.

There are many approaches for the diagnosis of gastric carcinoma before operation [6], including multi-slice helical CT (MSCT) for tumor staging, preoperative diagnosis, and curative effect evaluation [7]. With the continuous development of medical imaging, the resolution of MSCT is also constantly improving. Multi-phase scanning of target organs of patients is carried out to establish multi-level scanning data, thus providing a relatively comprehensive imaging basis for diagnosing gastric carcinoma [8, 9]. Some studies have shown that MSCT has a high rate of missed diagnosis and misdiagnosis, and it is less sensitive for smaller lesions or meta-

static lesions less than 5 mm. It is also easy to misdiagnose inflammatory swelling of lymph nodes as LNM, thus leading to a deviation between the results and pathologic diagnosis [10, 11]. The progression of contrast medium for the diagnosis of functional gastrointestinal diseases has been the focus of clinical research; it has shown that contrast medium shows promise in the examination of functional gastrointestinal diseases, and will not affect the detection of gastric emptying [12]. Researchers have shown that [13] contrast-enhanced ultrasound (CEUS) is a special contrast agent, namely microbubbles, which is mainly composed of an air core and a stable biological shell. These compounds can visualize small vascular beds to improve the anatomical structure and pathological characteristics; and they are relatively safe, mainly excreted through the lungs. As indicated by Wang [14], CEUS is a simple, non-invasive and high-precision tool, that can be used as the main imaging technique for T staging of advanced gastric carcinoma.

However, the clinical exploration of the diagnosis of LNM of gastric carcinoma through CEUS is uncertain. This study applied CEUS combined with MSCT to diagnose LNM of gastric carcinoma, aiming at providing better imaging examination for evaluation and prognosis.

Materials and methods

General data

Altogether 150 patients with gastric carcinoma from July 2017 to July 2020 were enrolled in this study. All the patients were confirmed with gastric carcinoma by biopsy pathology [15]. CEUS and MSCT were applied for patients in Handan Central Hospital within one week before surgery.

Inclusion criteria: Patients had complete clinical data; patients had not received the intervention of radiotherapy and chemotherapy before treatment; patients with high cooperation and compliance; patients whose image quality met the diagnostic requirements.

Exclusion criteria: Patients allergic to iodine contrast medium; patients with contraindications for hypotensive drugs such as drugs for glaucoma and prostatic hypertrophy; patients with allergic constitution; patients with distant metastasis of gastric carcinoma or complicated with failure of important organs before operation; patients with incomplete clinical data; those who were unable to be judged of the diagnosis result normally; patients with mental abnormalities; patients who quitted the experiment halfway, or were lost to follow-up.

This study conformed to the Ethics Committee (SQ-700-258), and both the subjects and the families signed the informed consent forms.

Detection methods

CEUS: Siemens Sequoia 512 CEUS diagnostic instrument, convex array probe of 3-7 MHz, and linear array probe of 8-14 MHz were applied. Before the examination, the patients were fasted for 8-12 h, and the stomach was scanned routinely in the supine position on an empty state. Then, the patient was instructed to drink about 500 ml of CEUS agent and then the stomach was scanned. During the scanning, the patient was taken to the right lateral position and scanned continuously from cardia to pylorus along the long axis and short axis of the stomach. The lesions were clearly displayed, and the infiltration depth of the mass, and involvement of lymph nodes around the stomach (including lymph nodes around the stomach wall and abdominal lymph nodes) and surrounding organs were observed. The shallow part of the anterior wall of stomach was examined with high-frequency CEUS probe with increased image magnification and focused scanning.

MSCT: Patients were fasted 8 h before examination, given 600-1000 ml of drinking water 20 min before examination, and then given 20 mg of anisodamine by intramuscular injection (Harbin Pharm. Group Sanjing Pharmaceutical Shareholding Co., Ltd, Harbin, China, H23023-5631). According to the focus of patients, supine, prone or lateral position was selected. First, CT plain scan was performed, and then dynamic enhanced scan was performed. The scanning scale was from the right diaphragmatic top to the horizontal segment of duodenum. The parameters were set as follows: voltage: 120 kV, rated current: 250-300 mA, layer thick-

Table 1. General data of gastric carcinoma patients [n (%)]

Group	Number of cases
Gender	
Male	84 (56.00)
Female	66 (44.00)
Age	
<55	61 (40.67)
≥0.	89 (59.33)
Drinking history	
Yes	81 (54.00)
No	69 (56.00)
Smoking history	
Yes	94 (62.67)
No	56 (37.33)
Obesity	
Yes	91 (60.67)
No	59 (39.33)
Lesion distribution	
Fundus of stomach	39 (26.00)
Body of stomach	42 (28.00)
Antrum of stomach	31 (20.67)
Whole stomach	38 (25.33)

ness: 5 mm, pitch: 1.25 mm, and reconstruction layer thickness: 0.625 mm. During the enhanced scanning period, a contrast agent, iopromide injection (Bayer Healthcare Co., Ltd., Guangzhou, China, H10970164), was injected into the elbow vein with a high-pressure syringe at 3.5 mL/s. Contrast agent was injected for 30 s, and enhanced arterial scan was performed in the esophagus, abdomen and whole stomach. After injection of contrast medium for 60 s, venous phase scanning was performed to observe the adjacent tissue damage, liver, and distant metastasis.

LNM diagnosis

Images showed that short diameter was more than 6 mm, short diameter/long diameter ratio was more than 0.6, portal vein was more than 70 Hu, and plain CT value was more than or equal to 25 HU or enhanced venous phase was more than or equal to 75 HU (mild or moderate enhancement). If the above conditions were not met, there were many instances of lymph nodes fused into solid masses, which were also confirmed as LNM.

Outcome measures

The detection rates and diagnostic efficiency of three different diagnostic methods for LNM of gastric carcinoma were compared.

Statistical methods

SPSS22.0 (Beijing Easybio Technology Co., Ltd., China) was used for statistical analysis. The counted data ware represented as the number/percentage [n (%)], and the measured data are represented by mean ± SD and compared by independent sample t test. The risk factors affecting LNM of gastric carcinoma patients were tested by logistic multivariate regression. $P<0.05$ indicated a significant difference.

Results

General data

There was no evident difference in gender, age, drinking, smoking, obesity and lesion distribution of gastric cancer patients ($P>0.05$) (**Table 1**).

Risk factors for LNM

Univariate analysis revealed that tumor diameter, number of lymph nodes sent for examination, depth of tumor invasion, Borrmann classification, and number of lymph nodes sent for examination were related to lymph node metastasis in gastric carcinoma patients ($P<0.05$). The tumor diameter, depth of tumor invasion, and Borrmann classification were included in the multivariate logistic regression analysis. Results showed that tumor diameter, number of lymph nodes, and depth of tumor invasion were risk factors for lymph node metastasis in gastric cancer patients (**Tables 2**, **3**).

Postoperative pathologic examination results

Pathologic examination of 150 patients showed that there were 119 cases with LNM while 31 cases were without LNM.

Diagnosis of LNM of gastric carcinoma by CEUS

With the results of pathologic examination as the gold standard, 150 patients were detected

Table 2. Univariate analysis of LNM in patients with gastric carcinoma [n (%)]

Clinical factor	n	LNM (case)	χ^2	P
Gender			0.250	0.617
Male	84	54 (64.29)		
Female	66	45 (68.18)		
Age			0.304	0.580
<55	61	35 (57.38)		
≥7	89	47 (52.81)		
Tumor diameter (cm)			32.721	<0.001
>4	60	21 (35.00)		
≤5	90	73 (81.11)		
Number of lymph nodes sent for examination (pieces)			11.261	0.001
<16	84	31 (36.90)		
≥6	66	42 (63.62)		
Depth of tumor invasion			8.633	0.034
pT1	20	1 (5.00)		
pT2	35	6 (17.14)		
pT3	26	9 (34.62)		
pT4	69	43 (62.32)		
Lauren type			1.519	0.468
Intestinal type	72	12 (16.67)		
Diffuse type	19	4 (21.05)		
Mixed type	59	15 (25.42)		
Borrmann type			9.730	0.021
I type	27	11 (40.74)		
II type	41	16 (39.02)		
III type	63	42 (66.67)		
IV type	19	9 (47.37)		

Table 3. Multivariate logistic regression analysis of LNM in patients with gastric carcinoma

Variable	B	S.E	Wals	P	OR	95% CI
Tumor diameter	1.003	0.213	22.463	0.043	2.716	1.358-5.432
Number of lymph node dissection	-0.674	0.183	13.647	0.021	1.972	0.086-3.944
Number of lymph nodes sent for examination	-1.543	0.353	10.473	0.019	0.268	0.057-0.314
Depth of tumor invasion	-2.734	0.758	9.799	0.011	0.095	0.047-0.190

Table 4. Diagnostic results of CEUS in LNM of gastric carcinoma [n (%)]

Pathology	CEUS (n=150)	
	Metastasis	Without metastasis
Metastasis (n=119)	106	13
Without metastasis (n=31)	9	22
Total	115	35

by ultrasound. The results showed that there were 115 cases with LNM while 35 were without (**Table 4**).

Diagnosis of LNM of gastric carcinoma by MSCT

With pathologic results as the gold standard control, 150 patients were subjected to multi-slice spiral CT. The results manifested that there were 112 cases with LNM while 38 were without LNM (**Table 5**).

Diagnosis of LNM in gastric carcinoma by CEUS combined with MSCT

With pathologic results as the gold standard control, 150 patients were subjected to ultra-

Table 5. Diagnostic results of MSCT in LNM of gastric carcinoma [n (%)]

Pathology	MSCT (n=150)	
	Metastasis	Without metastasis
Metastasis (n=119)	101	18
Without metastasis (n=31)	11	20
Total	112	38

Table 6. Diagnostic results of CEUS combined with MSCT in LNM of gastric carcinoma [n (%)]

Pathology	CEUS combined with MSCT (n=150)	
	Metastasis	Without metastasis
Metastasis (n=119)	112	7
Without metastasis (n=31)	4	27
Total	116	34

sound combined with multi-slice spiral CT. It was found that there were 116 cases with LNM while 34 were without LNM (**Table 6**).

Diagnostic efficiency of different detection methods

The sensitivity, specificity, and diagnostic concordance of CEUS for LNM of gastric carcinoma were 89.07% (106/119), 70.96% (22/31), and 85.33% (128/150), respectively. Those in MSCT were 84.87% (101/119), 64.51% (20/31), and 80.66% (131/150), respectively. Those in CEUS combined with MSCT were 94.11% (112/119), 87.10% (27/31) and 92.67% (116/150). There was no significant difference in diagnosis CEUS and MSCT ($P>0.05$). However, the diagnostic results of CEUS combined with MSCT were better than those of a single detection method ($P<0.05$) (**Table 7**).

Discussion

Gastric carcinoma is a serious malignancy of digestive tract, with high incidence [16]. Under tolerable conditions, radical operation is an important choice [17]; it is also the best choice for curing gastric carcinoma [18]. Researchers have shown that the prognosis of patients with gastric carcinoma is directly related to the occurrence of LNM and the depth of invasion [19]. LNM is a vital independent risk factor, that is correlated with prognosis [20]. Thus, preoperative diagnosis of LNM is of great significance to the choice of surgical methods, postoperative efficacy, and prognosis.

LNM is correlated to the prognosis of patients with gastric carcinoma, and the risk factors have been tested [21, 22]. The results revealed that tumor diameter, the number of lymph nodes sent for examination, and the depth of tumor invasion were risk factors. When tumor diameter exceeds 4 cm and when the depth of invasion exceeds T2 stage, LNM may exist. This has guiding significance for preoperative observation of LNM. Others have indicated that there is a positive correlation between the number of lymph nodes and the positive rate [23]. The results of this study revealed that a number of lymph nodes more than or equal to 16 was a risk factor for LNM. However, there is still no gold standard for preoperative diagnosis of LNM, so the diagnostic value of CEUS combined with MSCT in LNM of gastric carcinoma patients was investigated. Pathologic examination showed that there were 119 cases with LNM and 31 without. With the pathologic diagnosisas the gold standard, 115 cases were diagnosed with LNM and 35 were without by CEUS; 112 cases with LNM while 38 were without by MSCT; and 116 cases had LNM while 34 were without by combined detection. Clinically, oral administration of CEUS imaging agent can improve the display rate of perigastric lesions and the rate of correct diagnosis. Lymph node size and the ratio of short to long diameter are often used for diagnosing LNM, but there is still no uniform standard at present [24]. The resolution of MSCT in soft tissue is slightly poor, and the accuracy for lymph nodes with diameter less than 0.3 cm is low, so it may easily miss them and it is not conducive to detecting lymph node metastasis. In this study, a combined detection method was applied, and the effect was higher than that of single detection. Single application of CEUS or MSCT can diagnose LNM of gastric carcinoma, but the diagnostic rate is lower than that of the combined method, suggesting that the combined advantages of the two improved the diagnostic accuracy. In the study of Zhou [25], ovarian carcinoma patients were diagnosed using CEUS combined with CT. It showed that the sensitivity, specificity and accuracy of combined diagnosis we-

Table 7. Diagnostic efficiency of different detection methods

Group	Sensitivity	Specificity	Diagnostic coincidence rate
Contrast-enhanced ultrasound	89.07%	70.96%	85.33%
MSCT	84.87%	64.51%	80.66%
Combined detection	94.11%	87.10%	92.67%

re 96.49%, 90.91% and 93.75%, respectively, and the combined application had higher diagnostic accuracy, similar to the results of this study. Our results showed that the sensitivity, specificity, and diagnostic coincidence rate of CEUS for LNM of gastric carcinoma were 89.07%, 70.96%, and 85.33%, respectively. Those of MSCT were 84.87%, 64.51%, and 80.66%, respectively. Those of CEUS combined with MSCT were 72.66%, 87.10%, and 90.67%, respectively. The reinforcement from CEUS combined with MSCT was higher than that of the single approach. This suggests that CEUS can better reveal the structure of mucosa and muscularis and has better diagnostic value for lymph nodes combined with muscularis and mucosa. MSCT is suitable for the diagnosis of LNM, but it can easily miss diagnosis or cause misdiagnosis, and the combined detection of the two can complement each other to improve the diagnostic efficiency.

In this study, the diagnostic efficacy of CEUS combined with MSCT in lymph nodes of patients with gastric carcinoma was analyzed. However, there are still some shortcomings in the research design, such as the lack of diagnosis of TNM staging and Borrmann type accuracy. Hence, we will continue to explore and improve our study later.

CEUS combined with MSCT is more effective in the diagnosis of LNM in gastric carcinoma patients, and the combination of the two is helpful to improve the accuracy of lymph node diagnosis before operation.

Disclosure of conflict of interest

None.

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