

Lymph nodes metastasis of gastric cancer

Measurement with multidetector CT oblique multiplanar reformation—correlation with histopathologic results

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Abstract

The aim of this study was to retrospectively evaluate the ability of multidetector computed tomography (MDCT) oblique multiplanar reformation (MPR) for differentiating metastatic lymph nodes (LNs) in patients with gastric cancer.

Seventy-nine patients with gastric cancer underwent preoperative computed tomography (CT). One-to-one correlation of LN was made between CT oblique multiplanar reformation and histopathologic slides. Long diameters, short diameters, and short-to-long axis ratios of LNs were evaluated to differentiate metastasis.

Short diameters of nodes performed better for diagnosing metastasis than long diameters and short-to-long ratios. Sensitivity, specificity, accuracy, and area under the receiver operating characteristic curve of short diameter were 57.8%, 74.7%, 68.2%, and 0.713, respectively. With different thresholds of short diameters of nodes (No. 8 group >6mm and other groups >4mm), total sensitivity, specificity, and accuracy can reach 57.2%, 79.0%, and 70.3%, respectively.

MDCT oblique MPR images have certain reference value to distinguish metastasis of LNs in gastric cancer. The diagnostic power for LN metastasis of gastric cancer can be improved by using different threshold for No. 8 group LNs and other groups.

Abbreviations: AUC = area under the ROC curve, CT = computed tomography, LN = lymph node, MDCT = multidetector computed tomography, MPR = multiplanar reformation, ROC = receiver operating characteristic, ROI = region of interest.

Keywords: computed tomography, gastric cancer, lymph nodes metastasis, multiplanar reformation

1. Introduction

Despite declining incidence and mortality over several decades, gastric cancer is still one of the most common cancers and the

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fourth common cause of cancer death in the world.^[1] Lymph node (LN) status is the important prognostic factor regarding long-term survival in gastric cancer.^[2] Pretreatment knowledge of LN status may help in selecting patients who might benefit most from neoadjuvant chemotherapy.^[3] Also the LN metastasis may influence the surgery. If an accurate preoperative diagnosis of N2 staging for patients is made, then we could choose these patients to take an extended LN dissection. But it remains difficult to identify patients who have N2 disease.^[4]

At present, computed tomography (CT) has been used for preoperative staging widely. With the development of multidetector computed tomography (MDCT), 64 or more detectors and thinner scan collimation are used on abdominal scan. The 64-detector row CT has achieved less than 1-mm slice thickness. This may increase the possibility of the detection for LN less than 5 mm. The high quality multiplanar reformations (MPR) images of MDCT can perform the tomographic images in any direction. With the oblique MPR image, which is paralleled with the longest and shortest axis of LN on abdominal CT, the long and short diameters of LN will be measured more close to surgical specimen than those on the axial CT images. Thus, the purpose of our study was to retrospectively evaluate the efficacy of multidetector row CT oblique MPR images for measurement of LNs and to make a precise correlation with histopathologic results.

2. Methods

2.1. Patients

This retrospective study was approved by our institutional review board. Between January 2008 and September 2009, 182 patients with gastric cancer were administered contrast enhanced 64-channel CT examinations in 2 weeks preoperatively and received the radical

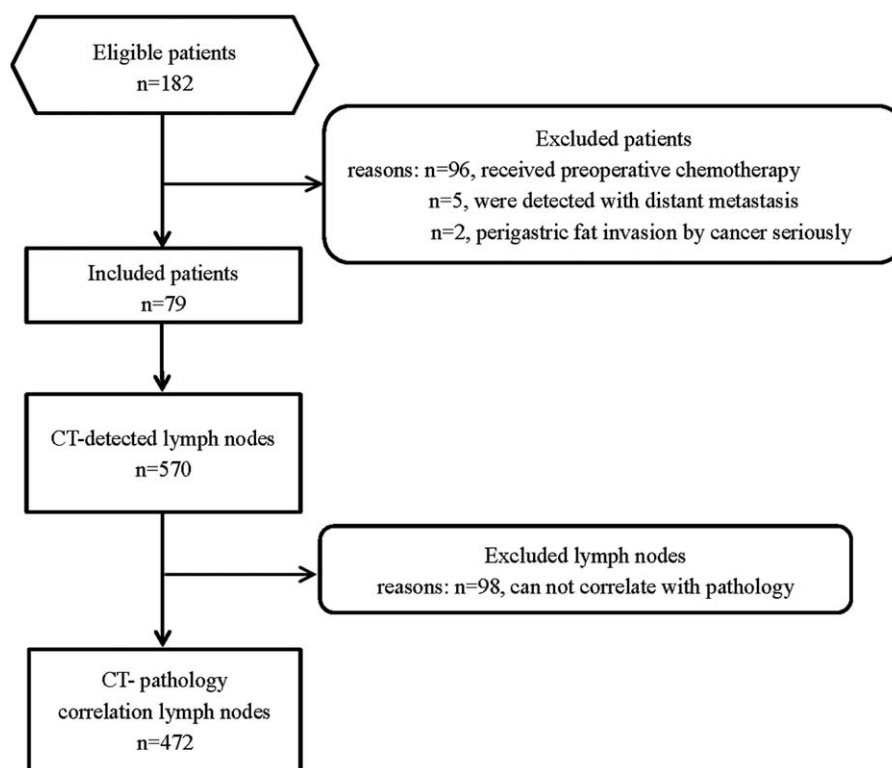


Figure 1. Flowchart of patient selection.

gastrectomy and D2 LNs dissection at our hospital. These patients were confirmed to have gastric cancer by the endoscopic biopsy and postoperative histopathology. Exclusion criteria were as follows: received preoperative neoadjuvant therapy, detected with distant metastasis in the preoperative examination or in the operation, and the fat around stomach was almost completely obliterated by the infiltration of the gastric cancer.

At last, 79 patients (59 male patients, 20 female patients; mean age, 58 years; range, 29–80 years) comprised our study population. A flowchart of the study profile is presented in Fig. 1.

2.2. Surgical and pathologic evaluation

D2 lymphadenectomy was performed for each of these 79 patients. The dissected LNs were classified according to the Japanese Classification of Gastric Carcinoma, second English edition (supplementary 1, <http://links.lww.com/MD/B306>).^[5] LNs were separated and grouped at surgery. All resected nodes were sent for histopathologic examination on a nodal group basis. Each LN was carefully extracted from the surgical specimen at the Department of Pathology. The pathologists would keep the LN's shape complete as much as possible. They removed the fat around the LN and the slice was taken through the central portion of any dissected LN. There was a detailed record about the group information for each LN on histologic slides.

2.3. CT protocol

MDCT was performed using a 64-detector row CT scanner (LightSpeed 64; GE Healthcare, Milwaukee, WI). Each patient had been fasting for more than 8 hours before the CT examination. To enable gastric distention and reduce gastric motility, the patients

received 8 g gas-producing crystals orally and an intramuscular injection of 10-mg anisodamine 10 to 15 minute before the examination. Upper abdominal unenhanced CT scans from the diaphragmatic domes to 2 cm below the lower margin of the air-distended gastric body were acquired with a collimation of 0.625 mm, 120 to 140 kVp, and 300 to 350 mAs. Subsequently, a total of 100 ml of nonionic contrast medium (Ultravist; Schering, Berlin, Germany) was administered intravenously through an 18-gauge angiographic catheter inserted into an antecubital vein at 3 mL/s by using an automatic injector. Contrast-enhanced CT scans were performed in the arterial phase (30 seconds) and in the portal venous phase (70 seconds). The portal venous phase was used to evaluate LN status. The portal venous phase axial CT images were reconstructed with a 5-mm section thickness and a 5-mm reconstruction interval for clinical interpretation and with a 0.625-mm section thickness for MPR reconstruction.

2.4. Image analysis

Two radiologists (ZLW, and TL, with 5 and 10 years of experience in abdominal CT, respectively) performed image analysis jointly to agreement. Axial CT images with 0.625-mm thickness and cine-mode display were used to detect the LN. Every LN detected with CT images was defined into the group with the same grouping system used at surgery. The abdominal major arteries were used as the landmarks for nodal grouping at CT.^[6]

With some very small LNs, it was hard to achieve the MPR reconstruction; therefore, we measured the long and short diameters for the LNs less than 5-mm-long diameter on the axial CT images. For the LNs larger than 5 mm, the oblique MPR images at the image workstation (AW 4.2; GE Healthcare) were used to make the measurement. When we detected a LN larger than 5 mm,

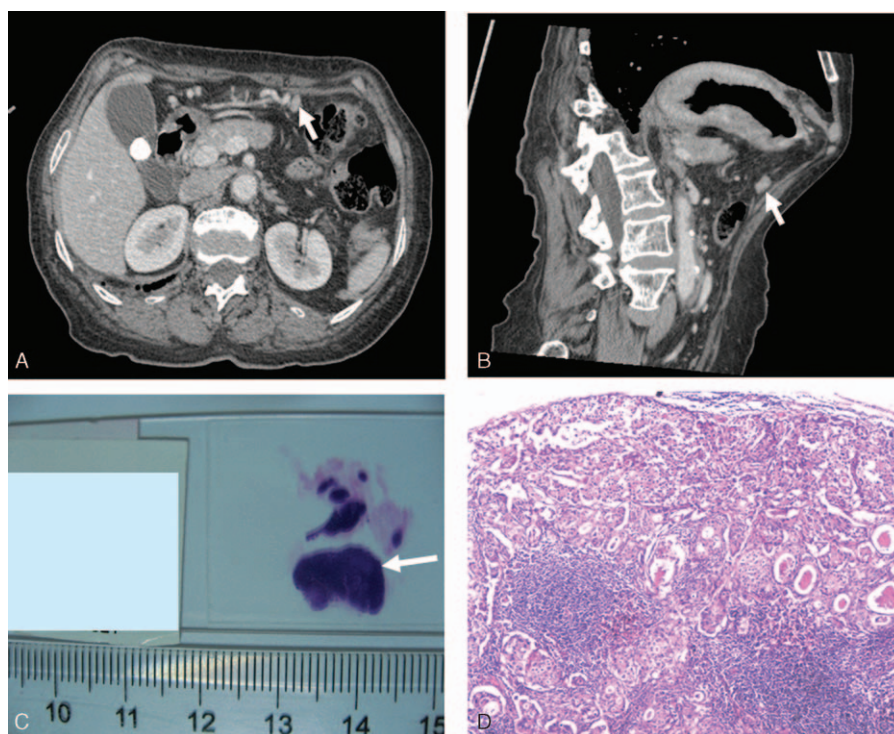


Figure 2. No. 4sb group lymph node in a 54-year-old woman with gastric cancer. (A) Axial computed tomography (CT) image shows a 10 × 8-mm lymph node (arrow) along the left gastroepiploic vessel. (B) Oblique MPR image shows that the size of this No. 4sb group lymph node is 12 × 9 mm (arrow). (C) The size of this No. 4sb group lymph node is also 12 × 9 mm at histologic slide (arrow). It can be correlated to the oblique multiplanar reformation (MPR) image. (D) Photomicrograph shows the signs of metastasis in this lymph node (hematoxylin–eosin stain; original magnification, ×40).

we would put the 3D-cursor on it. Then we took this LN as the center to make a rotation at the oblique MPR images. And the longest diameter of LN in the three-dimensional space could be found and measured. After the long axis of LN was confirmed, another rotation was made around the long axis to find the short axis of the LN. In this way, the long and short diameter of LN in three-dimensional space could be measured. It would be applied to make the correlation with the histologic results.

CT attenuation values of LNs were measured at the portal venous phase. We drew the oval region of interest (ROI) into the LNs and tried to avoid the partial volume effect with fat around. Short-to-long axis ratios were calculated for the LNs.

2.5. CT–histopathology correlation

All LNs were detected with metastasis or not by the microscope. The long and short diameters in the histologic slide were measured as the size of each LN. In each LN in each group, one-to-one correlation was made between the size of the node at MDCT oblique MPR image and histologic slide. Firstly, for one LN detected on CT, we measured the long and short diameters on CT and confirmed the group of this node. Secondly, from the same group of LNs in surgical specimen, we tried to find one LN with same long and short diameters. If the long and short diameters are both same between CT and specimen, this LN could reach right one-to-one correlation. We ruled out some LNs which could not achieve CT–pathological correlation as follows: if there were more than two LNs that had the same size in one group at CT, they could not be correlated with the pathology and would be excluded; and if the same size of some LNs appeared in one group at pathology, we checked the metastatic status of these nodes. If some nodes were metastatic and some were not, they could not be correlated to the

LNs with the same size at CT. Because in this situation we could not confirm which LN on CT was metastatic.

2.6. Statistical analysis

After the CT–pathology one-to-one correlation, the LNs that achieved correlation successfully were categorized as metastasis-positive and metastasis-negative groups. We compared the CT findings including long and short diameter, CT attenuation values, and short-to-long axis ratios of LNs between the 2 groups. Data processing and analysis were performed by using SPSS/PC+ statistical software package version 17.0 (SPSS Inc., Chicago, IL). Independent sample *T*-test was used to evaluate the differences after the test of normality. The receiver operating characteristic (ROC) curves were drawn to evaluate the diagnostic performance of long diameter, short diameter, and short-to-long axis ratios of LNs for metastasis. The optimal threshold was chosen according to the maximum Youden Index, and the sensitivity and specificity were also calculated. The Medcalc software version 11.2 (Medcalc, Medcalc Software, Ghent, Belgium) was used to make the ROC curves and compare them. The *P*-value less than 0.05 was considered to indicate a significant difference statistically.

3. Results

3.1. CT–histopathology correlation results

A total of 2167 LNs were resected in 79 patients. There were 47 cases which had LN metastasis and 32 cases had not. According to the pathological results, 421 LNs were metastasis-positive and 1746 nodes were metastasis-negative. Five hundred seventy LNs were detected with the MDCT. Finally, 98 LNs were ruled out by the one-to-one correlation. Then, 472 of 570 nodes were correlated with histologic slides successfully. For example, Fig. 2

Table 1**Summary of long diameters of correlated lymph nodes between MDCT and histopathology.**

Long diameter, mm	MDCT-histopathology correlated lymph nodes			
	Number of nodes	No. of metastasis-positive nodes	No. of metastasis-negative nodes	Ratio of metastatic nodes
≤2	7	2	5	28.6% (2/7)
3–5	198	53	154	26.8% (53/198)
6–10	193	82	111	42.5% (82/193)
11–15	62	35	27	56.5% (35/62)
≥16	12	8	4	66.7% (8/12)

MDCT = multidetector computed tomography.

Table 2**Summary of short diameters of correlated lymph nodes between MDCT and histopathology.**

Short diameter, mm	MDCT-histopathology correlated lymph nodes			
	Number of nodes	No. of metastasis-positive nodes	No. of metastasis-negative nodes	Ratio of metastatic nodes
≤2	65	6	59	9.2% (6/65)
3–5	282	94	188	33.3% (94/282)
6–10	109	68	41	62.4% (68/109)
11–15	13	9	4	69.2% (9/13)
≥16	3	3	0	100% (3/3)

MDCT = multidetector computed tomography.

shows a LN of No. 4sb group correlated between MDCT oblique MPR image and the histologic slide. Of these nodes, 180 LNs were metastasis-positive and 292 nodes were metastasis-negative. The range of long and short diameters of LNs was demonstrated in Tables 1 and 2. Within the metastatic LNs, 6 to 10-mm long diameter nodes accounted for 45.6% (82/180), 3 to 5-mm short diameter nodes accounted for 52.2% (94/180). They constituted the largest proportion of all metastatic LNs. When all 2167 resected LNs were divided into different groups by the location, the mean values of long and short diameters of the metastatic LNs were listed in Fig. 3. The average long and short diameters of metastatic-positive LNs in No. 8 group (along the common hepatic artery) and No. 14 group (along the superior mesenteric artery) were both higher than those of other groups (Fig. 3).

3.2. CT findings of metastatic nodes

The long and short diameters of metastasis-positive LNs were 8.4 ± 4.5 mm (mean \pm standard deviation) and 5.7 ± 3.1 mm,

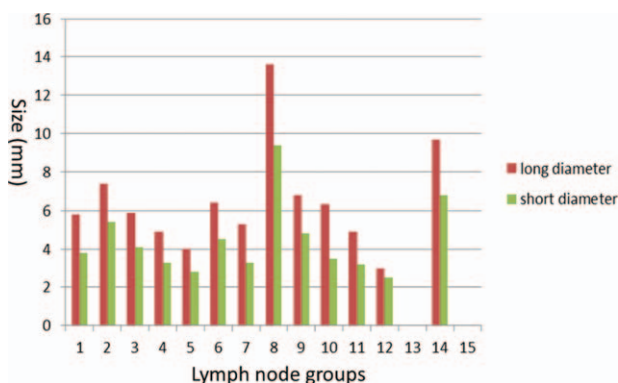


Figure 3. The mean values of long and short diameters of the all resected metastasis-positive lymph nodes with different groups.

respectively. The long and short diameters of negative nodes were 6.3 ± 3.1 mm and 3.9 ± 2.0 mm, respectively. The differences between positive and negative LNs in long and short diameters were both significant ($P < 0.001$) (Table 3).

The attenuation values of LNs on MDCT were 73.1 ± 22.0 HU for metastatic nodes and 67.0 ± 19.9 HU for negative nodes. This difference was not statistically significant ($P = 0.129$) (Table 3). The short-to-long axis ratios were 0.66 ± 0.14 for positive nodes and 0.58 ± 0.14 for negative nodes. The difference was statistically significant ($P < 0.001$) (Table 3).

When 7-mm long diameter of LN was applied as the threshold, the sensitivity, specificity, and accuracy for assessing metastasis were 54.4% (98/180), 75.3% (220/292), and 67.4% (318/472). The area under the ROC curve (AUC) was 0.661. When 4 mm was selected as threshold for the short diameter of LN, the sensitivity, specificity, and accuracy for assessing metastasis were 57.8% (104/180), 74.7% (218/292), and 68.2% (322/472). The AUC was 0.713. When the short-long diameter ratio of LN > 0.6 was selected as threshold for assessing metastasis, the sensitivity, specificity, and accuracy were 67.2% (140/180), 48.0% (112/292), and 53.4% (252/472), respectively. The AUC was 0.598 (Table 4, Fig. 4). The comparison between the AUC of short diameter curves with AUCs of long diameter and short-long ratio curve were statistically significant ($P < 0.001$).

The results above of all resected LNs showed that the long and short diameter of No. 8 and No. 14 groups LNs were higher than those of other groups obviously. We calculated the diagnostic performance index of long and short diameters of No. 8 group LNs for diagnosing metastasis (Table 5). When 6-mm short diameter of LN was used to diagnose metastasis, the sensitivity (88.9%, 8/9) and accuracy (68.3%, 28/41) achieved to best performance. And the AUC could reach 0.797. Because there were only 4 LNs of No. 14 group in the total 472 LNs, we analyzed these nodes of No. 14 group with other groups together. Then, using different diagnostic threshold for No. 8 group LNs and other group LNs, short diameters of LNs performed slightly better than long diameter for judging metastatic nodes. The

Table 3**Comparison of CT features between metastasis-positive and metastasis-negative lymph nodes.**

CT features of lymph nodes	Lymph node metastasis (mean \pm SD)			T	P
	Positive	Negative			
Long diameter, mm	8.4 \pm 4.5	6.3 \pm 3.1		5.579	<0.001
Short diameter, mm	5.7 \pm 3.1	3.9 \pm 2.0		6.872	<0.001
CT attenuation, HU	73.1 \pm 22.0	67.0 \pm 19.9		1.527	0.129
Short-long axis ratio	0.66 \pm 0.14	0.58 \pm 0.14		3.630	<0.001

CT=computed tomography, HU=Hounsfield unit, SD=standard deviation.

Table 4**The diagnostic power of CT features for judging metastatic lymph node.**

CT features of lymph nodes	Sensitivity	Specificity	Accuracy	AUC
Long diameter (>7 mm)	54.4%	75.3%	67.4%	0.661
Short diameter (>4 mm)	57.8%	74.7%	68.2%	0.713
Short-long ratio (>0.6)	67.2%	48.0%	53.4%	0.598

AUC=area under the receiver operating characteristic (ROC) curve, CT=computed tomography.

sensitivity, specificity, and accuracy of short diameters were 57.2%, 79.0%, and 70.3% (Table 6).

4. Discussion

In 1995, Fukuya et al indicated that helical CT was effective method for detection of metastatic lymphadenopathy from gastric cancer.^[6] And in this study, they used the axial CT images of LNs to make the one-to-one correlation with histopathologic specimens. They showed a detailed description of method about the correlation based on the LN group. However, the long axis of the LN in abdomen and in the pathologic specimen could be at various directions. The largest diameter of LN on transverse CT images may not be the real largest diameter in abdomen. So the correlation was not accurate enough. And the CT findings about the relationship between the sizes, CT attenuation of the LN with metastasis might be not reliable based on the correlation. But this situation was limited by the CT technique at that time.

Recently, the MDCT scanner allows less than 1-mm thickness and faster scanning. It can achieve excellent imaging resolution and generate three-dimensional image reconstruction easily. The three-dimensional reconstruction of MDCT has been used at the gastric cancer TNM staging preoperatively. Many studies indicate that the three-dimensional MDCT of the stomach may enhance the performance of CT in the preoperative evaluation of patients who have gastric cancer.^[7-12] For the N staging, Chen et al reported that overall accuracy for LN (N) staging was 78% (43 of 55) with MPR images and 71% (39 of 55) with transverse images. But this difference was not significant.^[11] Hur et al also indicated that using MPR images did not enable more accurate N staging of gastric cancer in either TNM or Japanese classification system.^[13] These 2 studies used transverse, coronal, and sagittal images to evaluate LNs simultaneously. Using MPR method seems to make a step forward to the axial CT image. But the LN on the triple cross-section images was somewhat different with the real position in abdomen. In our study, the MDCT oblique MPR image along the largest axis of LN by the multiple direction rotation is used for measurement. In this way, we can obtain the real long and short diameters of nodes to make a correlation with histopathology. We consider that the analysis about CT features of LNs is more meaningful based on the precise correlation.

Since this was a retrospective study, we used the histologic slides of LNs to make the measurement instead of specimens. There was a similar study using histologic slides to measure the diameters of LNs in gastric carcinoma.^[14] The histologic specimen and slide had some difference. Because the specimen often contained some fat around it, the measurement of specimen may be slightly larger than the real diameters of LNs. While the margin of LN was clear with the hematoxylin-eosin stain. It was easy to take the accurate measurement for nodes. The shape of LN may be incomplete after the slicing process. These obviously incomplete LNs were excluded because it would affect the accuracy of the measurement. We also made a comparison between the specimen and slide in another prospective case. The diameters of LN were very close (Fig. 4). It can ensure us that the measurement with LN histologic slide was acceptable.

Some researchers reported that LN size was not a reliable indicator for LN metastasis in gastric cancer. The reason was that there were some small metastatic LNs.^[15,16] In our study, the criterion of metastasis with 7 mm (long diameter) or 4 mm (short

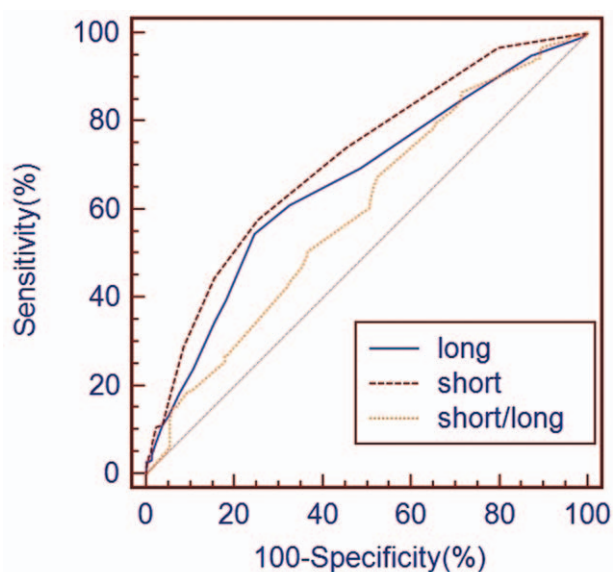


Figure 4. The area under the receiver operating characteristic (ROC) curve (AUC) of long diameter, short diameter, and short-to-long ratio in diagnosing metastasis were 0.661, 0.713, and 0.598, respectively.

Table 5**The diagnostic power of CT features for judging metastatic lymph node of No. 8 group (along the common hepatic artery).**

CT features of lymph nodes	Sensitivity	Specificity	Accuracy	AUC
Long diameter (>12 mm)	66.7%	68.8%	68.3%	0.701
Short diameter (>6 mm)	88.9%	62.5%	68.3%	0.797
Short-long ratio (>0.56)	100%	53.1%	63.4%	0.677

AUC=area under the receiver operating characteristic (ROC) curve, CT=computed tomography.

Table 6**Using different diagnostic threshold for No. 8 group lymph node (along the common hepatic artery) and other group lymph node, the total diagnostic power of CT features for judging metastasis of lymph nodes.**

CT features of lymph nodes	Sensitivity	Specificity	Accuracy
Long diameter (No. 8 group >12 mm and other group >7 mm)	52.8%	80.8%	70.1%
Short diameter (No. 8 group >6 mm and other group >4 mm)	57.2%	79.0%	70.3%
Short-long ratio (No. 8 group >0.56 and other group >0.6)	68.9%	47.3%	55.5%

diameter) of LN had moderate diagnostic ability (AUC=0.663 or 0.713). The criterion of LN size was less than some other previous studies. It may be due to detection of more small LNs in our study. The result of CT attenuation was different from other studies.^[6] The reason might be that CT attenuation value was influenced by the speed of blood circulation. The short-to-long axis ratios of metastatic LN were larger than negative nodes. This result was same as that of other studies.^[6,14]

The groups of LNs for gastric cancer were classified according to the Japanese Classification of Gastric Carcinoma (supplementary 1, <http://links.lww.com/MD/B306>). To our knowledge, prior published reports did not provide analysis on CT images by LN groups. And no research used different diameter threshold for diagnosing LN metastasis in gastric cancer. The results from our study indicated that the average diameters of No. 8 group metastatic LNs were significantly larger than those of other group. The lymphatic flows to LNs along the common hepatic artery were not only from the stomach but also from the liver, gall bladder, or pancreas.^[17-19] We speculated that No. 8 group LNs (along the common hepatic artery) had more incidence rates than other perigastric groups to be enlarged caused by the inflammatory diseases of liver, gall bladder, or pancreas. When we used larger diameter threshold for No. 8 group LNs, the diagnostic results were improved. For all LNs, using different diagnostic threshold for different groups showed mildly better results than using same threshold.

Our study had some limitations. First, although the 0.625-mm thickness images might increase the detection of small lymph, the noise of CT images also increased. This might influenced the measurement for small LNs. Second, in a few patients with less abdominal fat, the LN group ascertained with CT might not correspond to the surgical group. This situation may cause some correlation error.

In conclusion, the MDCT oblique MPR images of LNs in gastric cancer can be used to make precise correlation with histopathology. LN size has moderate diagnostic ability for diagnosing metastasis. The short diameter is better than long and short-long diameter ratio. The average diameter of No. 8 group LNs was larger than those of other groups. The diagnostic power for judging metastatic nodes can be improved by using different diagnostic threshold for No. 8 group LNs and other groups.

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