Christian R. Habermann, MD
Florian Weiss, MD
Rasmus Riecken, MD
Human Honarpisheh, MD
Sabine Bohnacker, MD
Carsten Staedtler, MD
Christoph Dieckmann, MD
Volker Schoder, MD
Gerhard Adam, MD

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[1] From the Departments of Diagnostic and Interventional Radiology (C.R.H., F.W., R.R., C.D., G.A.), General Surgery (H.H.), Interdisciplinary Endoscopy (S.B.), and Pathology (C.S.) and Institute for Mathematics and Computer Science in Medicine (V.S.), University Hospital Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany. From the 2000 RSNA scientific assembly. Received July 22, 2002; revision requested September 26; final revision received May 22, 2003; accepted June 16. **Address correspondence to** C.R.H. (e-mail: *c.habermann@uke.uni-hamburg.de*).

Author contributions:
Guarantor of integrity of entire study, C.R.H.; study concepts, C.R.H., F.W., C.D.; study design, C.R.H., F.W., V.S.; literature research, C.R.H., R.R., H.H.; clinical studies, C.R.H., F.W., R.R.; data acquisition, C.R.H., R.R., S.B., C.S.; data analysis/interpretation, V.S., C.R.H., H.H.; statistical analysis, V.S., C.R.H., S.B.; manuscript preparation, C.R.H., R.R.; manuscript definition of intellectual content and editing, C.R.H., G.A.; manuscript revision/review, G.A., C.S., H.H.; manuscript final version approval, C.R.H., G.A.

Preoperative Staging of Gastric Adenocarcinoma: Comparison of Helical CT and Endoscopic US[1]

PURPOSE: To compare the performance of helical computed tomography (CT) and endoscopic ultrasonography (US) in the preoperative staging of gastric cancer.

MATERIALS AND METHODS: Fifty-one consecutive patients with a primary malignant gastric tumor (stage T2–T4) were preoperatively evaluated with both helical CT and endoscopic US within 3 days. Each tumor was staged according to the TNM classification system with both modalities. All patients subsequently underwent surgery. Results of CT and endoscopic US were compared with histologic staging of tumor invasion depth and regional lymph node metastasis. For comparison of CT and endoscopic US data, the marginal homogeneity test was used, and a *P* value of less than .05 was determined to indicate statistical significance.

RESULTS: In comparison with histologic results, CT achieved correct T staging in 39 patients (76%) and correct N staging in 35 patients (70%). The corresponding results for endoscopic US achieved correct T staging in 44 patients (86%) and correct N staging in 45 patients (90%). There was no significant difference between T staging ($P = .55$) and N staging ($P > .99$). Because of challenging detection of wall layers, correct T staging was difficult for CT and endoscopic US in the differentiation of T2 and T3 lesions.

CONCLUSION: Compared with endoscopic US, helical CT focused on the stomach provides valuable results regarding T and N staging in patients with gastric cancer.

Until 1988, adenocarcinoma of the stomach was the leading cause of death from cancer worldwide, and in the early 1980s an estimated 670,000 new cases developed annually. In the United States, the annual incidence of gastric cancer has decreased from a rate of 33 per 100,000 persons in 1935 to a rate of nine per 100,000 persons in the 1990s (1). In Japan, the incidence is highest (100 new cases per 100,000 persons per year), and stomach cancer is the leading cause of death from all malignant diseases (2).

Accurate evaluation of the local extent of gastric cancer is fundamental in the choice of an optimal therapeutic approach. Differentiation of intramural tumor extent and invasion beyond the gastric wall has considerable clinical importance, because the prognosis of the disease is directly related to the depth of invasion of the gastric wall and lymph node involvement (3–5).

The most fundamental aim of gastric cancer surgery is to excise the primary lesion adequately. To achieve this goal, the positions of the cancer and the tumor margin have to be known. There is agreement in current literature about the surgical approach regarding the primary lesion (6–10). Nevertheless, the overall cure rate for gastric cancer remains around 10% in most countries. In marked contrast, the results from Japan are much better, and overall cure rates of over 50% have been reported. These results are partly caused by the Japanese national screening program for gastric cancer. Still, comparison of 5-year survival data for similar stages of the disease reveal that results are up to 20% better in Japan than in the Western world (11). The reasons for these results are controversial. Japanese surgeons postulate radical gastric cancer surgery with its extensive lymph node dissections, even in early stages of the disease, is the main factor (12–15).

Endoscopic ultrasonography (US) is currently the most reliable nonsurgical method available for evaluating the primary tumor, with a diagnostic rate of 78%–93% for all T stages (16,17). A single study revealed a significantly higher degree of accuracy with use of US than with use of computed tomography (CT) for T staging (18). For N staging, endoscopic US was reported to provide only a slightly higher degree of accuracy when compared with CT (10,16,18,19).

The system for classifying the T stage of gastric lesions with helical CT is described in the literature (20–23). When using CT, there was a tendency to overstage T2 tumors as T3 tumors, because reticular strands surrounding the outer border of the tumor were defined as being representative of T3 tumors. In this study, we used a modification of the T staging system, in which the criteria of the CT staging system were adapted to the system used by endoscopists. The aim of our study was to compare helical CT and endoscopic US in the preoperative staging of gastric cancer.

MATERIALS AND METHODS

Patients

Between February 1998 and March 2000, 51 consecutive patients (34 men and 17 women; age range, 47–76 years; mean age, 62 years) with gastric cancer were examined with CT and endoscopic US prior to surgery. In this study, all CT examinations were performed according to the protocol for patients with gastric malignancies, as provided by the standard operation procedures of our department. Informed consent was obtained from every patient prior to the examination. The local institutional review board was consulted before the study began, and its approval was not required.

To confirm the diagnosis of gastric cancer in all patients, an endoscopic biopsy was performed prior to examination with CT and endoscopic US. Tumors were located in the fundus (n = 2), body (n = 14), antrum (n = 29), and pyloric region (n = 6). All patients underwent laparotomy and resection of the primary gastric tumor with at least D1-lymphadenectomy. According to the Japanese Research Society for Gastric Cancer, a D1-lymphadenectomy is defined as a limited lymphadenectomy, where all N1 nodes are removed en bloc with the stomach. Histologically, all tumors were diagnosed as adenocarcinomas of the gastric mucosa.

CT Imaging

CT was performed with a single–detector row CT scanner (Somatom Plus 4; Siemens, Erlangen, Germany). The patients had to fast for at least 6 hours prior to the examination. After receiving an intravenous infusion of 20 mg scopolamine butylbromide (Buscopan; Boehringer, Ingelheim, Germany), each patient drank 500–800 mL of tap water. Patients were placed in the prone position for imaging antral or pyloric tumors and in the supine position for imaging body or fundus tumors, according to the location of the tumor seen at endoscopy. Patients were instructed not to breathe during helical imaging to avoid motion artifacts.

First, an unenhanced scan was obtained to evaluate gastric distention. In case of insufficient filling of the stomach, at least 300 mL of tap water was given additionally. The scan parameters were 120 kV, 200–240 mAs, and 1 second rotation for all three passages. Unenhanced CT scans of the upper abdomen from the diaphragmatic domes to inferior pole of the kidneys were performed with 5-mm collimation, 8 mm/sec table speed, and 5-mm reconstruction interval. A 120-mL dose of the iodinated contrast material iopamidol (Solutrast 300; Byk Gulden, Konstanz, Germany) was administered into the antecubital vein at a flow rate of 2.5 mL/sec via a 20-gauge needle. The dual phasic helical scans were obtained at 30 seconds (arterial phase) and 70 seconds (portal-venous phase), whereas the extension of the arterial phase was determined by the gastric size and the portal-venous phase was determined according to unenhanced imaging. The imaging parameters for the early phase were 3-mm collimation, 5 mm/sec table speed, and 3-mm reconstruction interval. All patients underwent CT and endoscopic US examinations within 3 days.

Endoscopic US

Echoendoscopes with radial sector-scan transducers (frequency, 7.5 or 12.0 MHz) (GF-UM2, GF-UM3; Olympus, Tokyo, Japan) were used by an experienced endoscopist (S.B., 8 years). The maximal penetration of the ultrasound beam was 10 cm with the 7.5-MHz transducer and 3 cm with the 12.0-MHz transducer. The focus was 35 mm with the 7.5-MHz transducer and 25 mm with the 12.0-MHz transducer. Prior to the examination, 20 mg of scopolamine butylbromide was intravenously administered, and the echoendoscope was introduced. After evaluation of the primary lesion with endoscopic US, the stomach was filled with de-aerated water (approximately 300 mL) via the echoendoscope to enable observation of the gastric lesion through the water and evaluation of the depth of tumor invasion. Endoscopic US studies were independently analyzed by the endoscopist who performed the examination. If CT was performed prior to endoscopic US, the endoscopist had no knowledge of the CT results.

Image Evaluation

The mural invasion of cancer depicted with CT was graded according to the classification of the American Joint Committee on Cancer (24). The image criteria used in the literature were applied (20,25). On CT scans, a tumor was defined as an abrupt thickening of the thin, three-layered gastric wall. Modifications of the mentioned image criteria were made regarding the differentiation between T2 and T3 tumors. T1 tumors were defined as those with focal thickening of the inner layer with a visible outer layer of the gastric wall and a clear fat plane around the tumor. T2 tumors were defined as those with focal or diffuse thickening of the gastric wall with transmural involvement and a smooth outer border of the wall or only a few small linear strands of soft tissue extending into the fat plane involving less than one-third of the tumor extent. T3 tumors were defined as transmural tumors with obvious blurring of at least one-third of the tumor extent or wide reticular strands surrounding the outer border of the tumor. T4 tumors were defined as those with obliteration of the fat plane between the gastric tumor and an adjacent organ or invasion of an adjacent organ.

It is common for endoscopic US to show five different layers of the gastric wall. A T1 tumor is seen as a hypoechoic disruption of the first three layers. A T2 tumor invades the fourth layer and/or shows hyperechoic appearance of the surrounding fat measuring less than one-third of the tumor extent. A T3 tumor penetrates the fifth layer or invades the surrounding fat, involving at least one-third of the tumor extent. A T4 tumor invades adjacent organs and structures (17,18).

Regional lymph nodes were considered to be involved by metastases if they were larger than 8 mm in short-axis diameter. In relation to the lymph node dissection, the nomenclature established by the Japanese Research Society for Gastric Cancer was used (5). Enlarged perigastric nodes

TABLE 1
Comparison of T Staging with CT versus T Staging with Histologic Evaluation

Histologic Findings	CT Findings			Total (n = 51)
	T2	T3	T4	
T2	24 (83)	5 (17)	0	29
T3	5 (26)	12 (63)	2 (10)	19
T4	0	0	3 (100)	3

Note.—Numbers in parentheses are percentages.

TABLE 2
Comparison of T Staging with Endoscopic US versus T Staging with Histologic Evaluation

Histologic Findings	Endoscopic US Findings			Total (n = 51)
	T2	T3	T4	
T2	26 (90)	3 (10)	0	29
T3	4 (21)	15 (79)	0	19
T4	0	0	3 (100)	3

Note.—Numbers in parentheses are percentages.

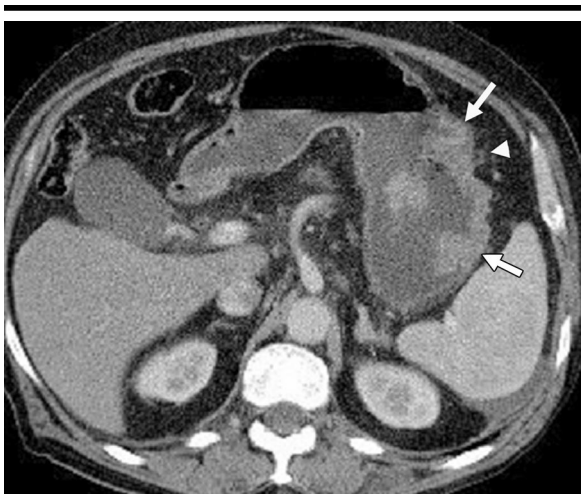


Figure 1. Transverse CT image of a 75-year-old man with tumor in the body of the stomach (arrows) and transmural involvement with linear stranding in the perigastric fat (arrowhead). This tumor was correctly staged as T2.

closer than 3 cm to the primary lesion were graded as N1, and enlarged distant (>3 cm) paragastric nodes and the nodes along the main arteries supplying the stomach were assessed as representative of N2.

Two experienced radiologists (C.R.H. and F.W., each with 7 years) reviewed the CT images together in consensus. They had no knowledge of the endoscopic US results. All images were evaluated at a monochrome 1,024 pixel picture archiving and communication system monitor (Simomed; Siemens). The window settings were fixed at a window width of 360 HU and a window center of 60 HU. To depict a feasible fat stranding, the window width was extended to 450 HU. The interpretation of the endoscopic US images for T staging was performed according to the criteria used for CT. Well-defined round or elliptical structures adjacent to the gastric wall that had a more hypoechoic pattern than the surrounding tissue were considered to represent metastatic lymph nodes.

Surgery

All 51 patients underwent partial or complete gastrectomy, without pretherapeutic laparoscopic staging. Lymphadenectomy was performed on the basis of the preoperative staging at CT and endoscopic US and findings of the frozen section obtained during every surgical procedure. Of the 51 patients, 32 were treated with a D1-lymphadenectomy, and the remaining 19 were treated with a D2-lymphadenectomy. A D2-lymphadenectomy was defined according the Japanese Research Society for Gastric Cancer as a resection of all N1 and N2 nodes with en bloc resection of the stomach. If any of the second-tier stations were not resected, then this was downgraded to represent a D1-lymphadenectomy. A node-by-node analysis was not performed between the nodes identified at CT and endoscopic US and those evaluated at histopathologic examination.

Statistical Analysis

Data are presented as percentages. In all cases, 95% CIs for sensitivity and specificity are given to allow the reader to consider variability in the results. For comparison of CT and endoscopic US data, the marginal homogeneity test was used, which is a generalization of the McNemar test for more than two categories. A P value of less than .05 indicated a significant difference. For data analysis, statistical software (SPSS version 11.0, SPSS, Chicago, Ill; StatXact 5, Cytel Software, Cambridge, Mass) was used.

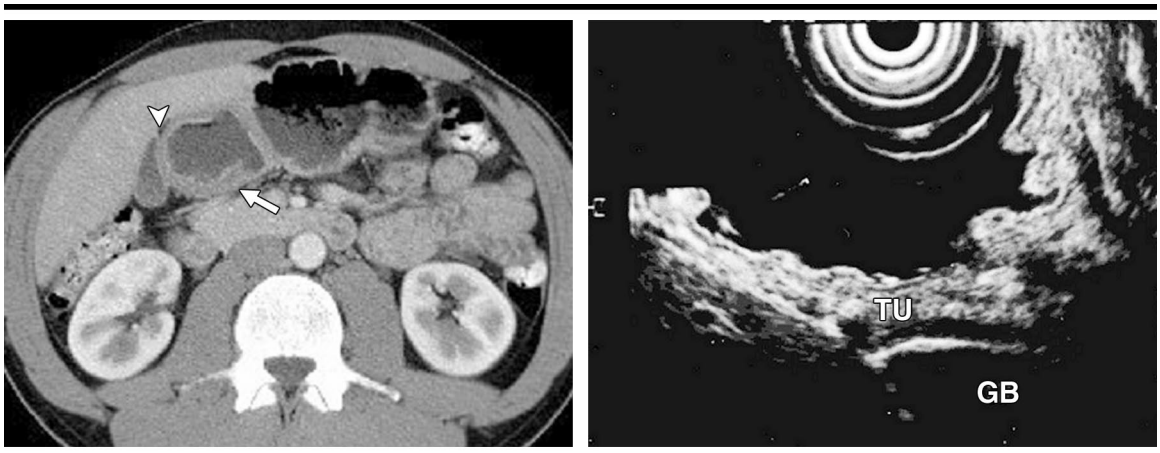
RESULTS

Detection of Primary Tumor

In all 51 patients, both CT and endoscopic US depicted the primary lesions, and TNM staging was performed. Twenty-nine T2 tumors (Fig 1), 19 T3 tumors, and three T4 tumors were diagnosed with histologic analysis. None of the patients included in this study had a T1 tumor or a second gastric mass. In all patients, helical CT showed destruction of the multilayered pattern with a thickening of the gastric wall at the tumor location.

Depth of Invasion of Gastric Wall

Regarding T staging, 39 (76%) of 51 lesions were staged correctly with CT (Table 1), whereas 44 (86%) of 51 tumors were staged correctly with endoscopic US (Table 2). Five of the T2 tumors were overstaged as T3 tumors with CT and three were overstaged with endoscopic US. The sensitivity for discrimination of T2 lesions from T3 and T4 tumors was 83% (24 of 29) for CT and 90% (26 of 29)



a. b.

Figure 2. Images of a 73-year-old-man. **(a)** Transverse CT image of an antral transmural tumor close to the gallbladder (arrow) with no infiltration of the gallbladder and no visible blurring (arrowhead). This tumor was staged as T2. **(b)** Endoscopic US image of the tumor (*TU*) in a corresponding plane with a transmural lesion and no wall thickening of the gallbladder (*GB*). This tumor was staged correctly as T2.

for endoscopic US (Fig 2). Proportion of T3 and T4 tumors that were incorrectly classified as T2 tumors was five of 22 with CT and four of 22 with endoscopic US. Referring to the 19 tumors that were assessed as T3 with histologic analysis, two were staged as T4 and five were staged as T2 with CT, whereas four tumors were staged as T2 and none were staged as T4 with endoscopic US (Fig 3). With both modalities, the three T4 tumors were staged correctly (Fig 4). The proportion of T2 and T3 tumors that were incorrectly classified as T4 tumors was two of 48 with CT and none of 48 with endoscopic US.

The 95% CI for CT was calculated to be 0.69 to 0.96 for T2 staging and 0.415 to 0.847 for T3 staging. The 95% CI for endoscopic US was 0.786 to 1.000 for T2 staging and 0.606 to 0.972 for T3 staging. When comparing CT and endoscopic US regarding T staging, there was no significant difference between the two methods ($P = .55$, test of marginal homogeneity).

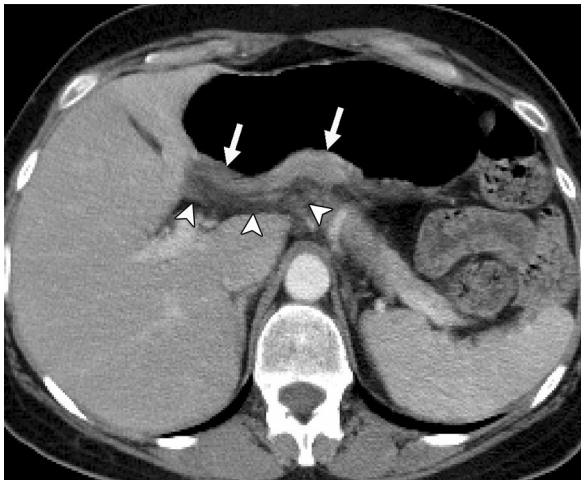


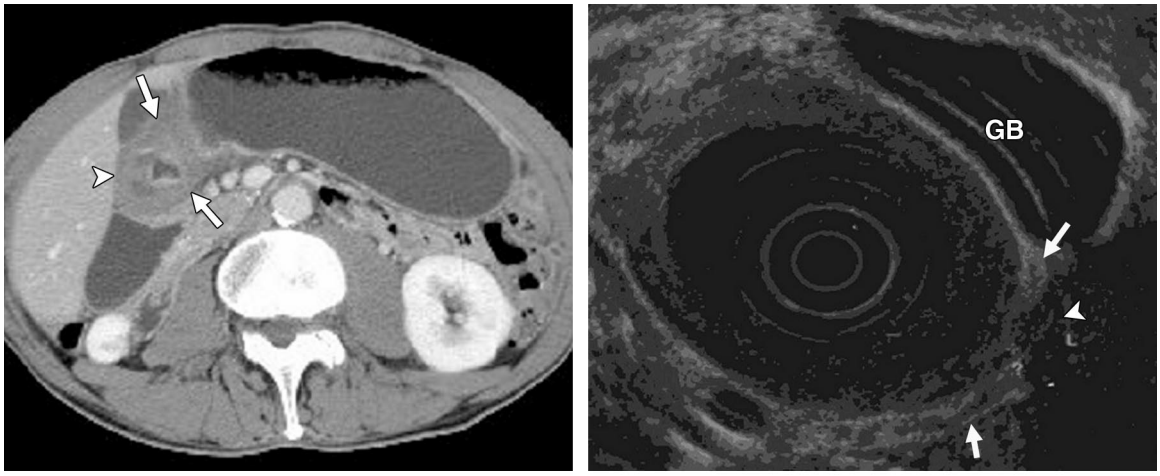
Figure 3. Transverse CT scan of a 47-year-old woman shows an antral tumor (arrows) with blurring of more than one-third of the tumor extent (arrowheads). The lesion was correctly staged as T3.

Nodal Involvement

In 19 of 51 patients, the histologic work-up showed no involvement of peri- (N1) or paragastric (N2) lymph nodes. In 31 patients an involvement could be proved, whereas in a single patient the nodal involvement was staged as NX due to insufficient tissue samples. Twelve patients showed an involvement of N1 nodes. In 19 patients, an involvement of N2 nodes had to be confirmed. In total, nodal involvement was correctly assessed with CT in 35 (70%) of 50 patients (Table 3) and with endoscopic US in 45 (90%) of 50 patients (Table 4). Endoscopic US was used to make a correct diagnosis in all 19 patients with nodes that were negative for carcinoma. The CT scans showed suspicious enlargement of the paragastric nodes in three patients, which led to the diagnosis of N2 node involvement. Nodes in the remaining 16 patients were graded correctly as negative.

In patients with lesions that were staged as N1 at histologic analysis, five lesions were staged correctly with CT, whereas three nodes were graded as negative, and four lesions were graded as N2. At US, lesions in 10 of these patients were staged accurately as N1, and lesions in two patients were overstaged as N2. Fourteen of 19 histologically proved N2 nodes were staged accurately with CT, and sixteen were staged accurately with endoscopic US.

The sensitivity for detecting pathologic lymph nodes was 74% (23 of 31) for CT and 97% (30 of 31) for endoscopic US, achieving a specificity of 84% (16 of 19) and 100% (19 of 19), respectively. For discrimination between N1 and N2 nodes, the sensitivity and specificity were slightly lower with both modalities. For CT, sensitivity was 74% (14 of 19) and specificity was 77% (24 of 31). For endoscopic US, sensitivity was 84% (16 of 19) and specificity was 94% (29 of 31). The 95% CI for CT was 0.667 (0.436, 0.898)



a. **b.**

Figure 4. Images of a 52-year-old woman. **(a)** Transverse CT image of a transmural tumor of the antrum (arrows) with blurring and obliteration of the fat plane between the gastric wall and the liver and additional invasion of the liver (arrowhead). This tumor was correctly staged as T4. **(b)** Endoscopic US image that corresponds to **a** shows a tumor (arrows) involving the gastric wall and the adjacent liver (arrowhead). (*GB* = gallbladder).

TABLE 3
Comparison of N Staging with CT versus N Staging with Histologic Evaluation

Histologic Findings	CT Findings			Total (n = 50)
	N0	N1	N2	
N0	16 (84)	0	3 (16)	19
N1	3 (25)	5 (42)	4 (33)	12
N2	5 (26)	0	14 (74)	19

Note.—Numbers in parentheses are percentages.

TABLE 4
Comparison of N Staging with Endoscopic US versus N Staging with Histologic Evaluation

Histologic Findings	Endoscopic US Findings			Total (n = 50)
	N0	N1	N2	
N0	19 (100)	0	0	19
N1	0	10 (83)	2 (17)	12
N2	1 (5)	2 (10)	16 (84)	19

Note.—Numbers in parentheses are percentages.

concerning N1 staging and 0.737 (0.539, 0.935) concerning N2 staging. For endoscopic US, the 95% CI was calculated to be 0.83 (0.619, 1) regarding N1 staging and 0.842 (0.583, 1) regarding N2 staging. When evaluating the consistency of both modalities, there was no statistically significant difference ($P > .99$, test of marginal homogeneity).

DISCUSSION

In a routine clinical setting, patients with gastric cancer most commonly undergo staging with CT and endoscopic US. CT is used for evaluation of distant metastases, and endoscopic US is used for assessment of local tumor extent and lymph node involvement. Controversy about the role of CT in preoperative staging is discussed in current literature (21–23,25–37). In these studies, the CT equipment and techniques varied greatly. Some of the unsatisfactory results of CT concerning T and N staging are most likely due to the use of incremental imaging techniques (20,30,31,36–38). Nevertheless, investigations with helical CT and negative oral contrast material also can refer to results of inadequate tumor staging (21,25,32).

The problem is the differentiation between T2 and T3 tumors. In these studies, a sharp tumor contour and a clear stomach fat plane or only a few small linear strands of soft tissue extending into the fat plane were defined as representative of T2 cancer. Blurring and wide reticular strands surrounding the outer border of the tumor were the criteria used to diagnose a T3 cancer. We were aware of these difficulties, and according to the endoscopic US criteria used in our institution, a fat stranding involving more than one-third of the tumor borders was defined as representative of an involvement or penetration of the adventitial layer (T3 cancer). This classification did not lead to an increase of overstaged T2 tumors.

In our study, only five (17%) of the T2 tumors were overstaged as T3 tumors with CT, while endoscopic US was used to grade three (10%) of the T2 tumors as T3 tumors; however, this classification led to an underestimation of five (26%) of the T3 tumors. In comparison, four (21%) of the T3 lesions were underestimated with endoscopic US. Thus, CT led to more sufficient results in differentiating T2 and T3 tumors with comparable and no significant results when compared with endoscopic US. This was probably due to the extensive distention of the stomach, which was verified at unenhanced imaging, and the slightly different criteria. Another explanation might be the 3-mm collimation in our study. Most other studies used 5-mm collima-

tion, which influences not only T staging but also N staging (21,25,32).

With CT, two (11%) T3 tumors were overstaged as T4 tumors. The fat plane between the gastric tumor and the adjacent liver was obliterated. These two lesions were staged correctly with endoscopic US, which provides online information of gastric motion with continuous breathing during the examination. This drawback of CT could be avoided by obtaining an additional scan with the patient in a different position.

One of the most important factors that affects the prognosis in patients with gastric cancer is lymph node involvement and lymphadenectomy (3–5). According to Fukuya et al (25), a short-axis diameter of more than 0.8 cm was defined to represent metastatic involvement. The different attenuation in unenhanced and contrast-enhanced imaging was not considered. Nevertheless, the nodal involvement was assessed correctly with CT in 35 (70%) of 50 patients. Endoscopic US was used to grade the metastatic involvement correctly in 45 (90%) patients. No significant difference was observed between the modalities. The results we achieved with CT are comparable with the results of most studies (10,25,38), whereas other studies present sensitivities of 51% (32) and 97% (29). A review article with a meta-analysis of 27 publications showed correct staging in 79% of patients (17).

Preoperative CT is still indispensable in the evaluation of the presence of distant metastases; therefore, a CT examination focused on the stomach and the upper abdomen, as presented in our study, could probably replace endoscopic US. Our results suggest that both modalities have similar accuracy for T staging. Even with reference to N staging, there is no significant difference.

Referring to the previously mentioned Japanese treatment of gastric cancer with surgery with at least a D2-lymphadenectomy, or better, a D3-lymphadenectomy, devalues preoperative N staging in all patients. Unfortunately, even with the highest effort, the Japanese results are still not applicable to the Western world (39).

According to the results of our study, even if surgery is performed with lymphadenectomy in accordance with preoperative staging and histologic analysis as it is performed in the West, CT with an optimized scan protocol focused on the stomach is in position to replace preoperative endoscopic US.

The limitation of our study was that none of the patients had a T1 tumor, so comparison between CT and endoscopic US in regard to this early stage could not be performed. This study was not designed to determine the sensitivity and specificity of CT in the detection of gastric cancer or in the discrimination of gastric cancer from other differential diagnoses such as gastric ulcer; therefore, patients with no gastric malignancy were excluded. To the knowledge of both reviewing radiologists, gastric cancer was already histologically proved with biopsy in all patients.

An additional limitation might be that the removed lymph nodes were not mapped in a one-to-one correspondence by site to correlate with the findings at imaging; however, both imaging modalities used the same criteria for lymph node staging. Surgery was performed unblinded to the preoperative staging with CT and endoscopic US. Nevertheless, we were aware of the limitations of preoperative staging, and thorough intraoperative staging was performed. Thus, N1 or N2 nodes were found in patients whose nodes were preoperatively staged as N0 or N1, respectively.

A bias introduced by this unblinded study design, in that N1 or N2 nodes are missed in patients who were preoperatively staged as N0 or N1, respectively, seems unlikely but cannot be excluded. Since no preliminary sample size estimation was performed, it is possible that some clinically relevant differences between CT and endoscopic US could not be detected due to a lack of power. Nevertheless, it is our opinion that the present study offers valuable findings for everyday, clinical, routine, and future research. In conclusion, because of the increased value of helical CT focused on the stomach with negative oral contrast medium, helical CT may be able to replace preoperative endoscopic US, even when surgery is performed as it currently is in the Western world.

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