Clinical implication of positive oral contrast CT for the evaluation of postoperative leakage after gastrectomy for gastric cancer

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<ABSTRACT>

Clinical implication of positive oral contrast CT for the evaluation of postoperative leakage after gastrectomy for gastric cancer

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Purpose: The aim of this study was to evaluate the clinical usefulness of positive oral contrast CT for the detection of leakage and its relationship with the immediate postoperative outcome after a gastrectomy for gastric cancer.

Materials and Methods: A total of 210 patients with a clinical suspicion of leakage after a gastrectomy for gastric cancer underwent a positive oral contrast CT, and the results were retrospectively analyzed. Two radiologists reviewed the CT images, recorded the presence of extraluminal contrast leakage, and graded the amount of leaked contrast. The rate of postoperative intervention treatment, the length of postoperative hospital stay, and mortality rates were correlated with the presence and grades of leakage. Matching accuracy between CT and other diagnostic studies in detection of leakage was also evaluated.

Results: There were 162 patients without extraluminal contrast leakage (77.1%), 13 with grade 1 leakage (6.2%), 19 with grade 2 (9.0%), and 16 with grade 3 (7.6%). The postoperative intervention rate, the hospital stay, and the mortality were significantly higher in patients with visible leakage than in those without visible leakage (p<0.05). The postoperative hospital stays increased as the leakage grades increased (p=0.0008). The matching accuracy between the CT and other studies was 82.1% (n=32/39).

Conclusions: Positive oral contrast CT is a reliable tool for diagnosing

leakage after a gastrectomy in gastric cancer patients, and the immediate postoperative outcome may be related with the grade of leaked contrast on the CT.

Key words : oral contrast, CT, gastric cancer, postoperative leakage

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I. INTRODUCTION

Anastomotic leakage is one of the severe complications after a gastrectomy and is often associated with mortality (1-4). The incidence of leakage following gastric cancer surgery is approximately between 1.3% and 16.5% (2, 3, 5-8). Early detection and early intervention in patients can improve the ultimate outcome, especially with respect to mortality (9).

The imaging method of choice is computed tomography (CT) for the postoperative patient in whom overall surgical complications are suspected (10). However, the criteria for a definite diagnosis of anastomotic leakage on CT are not well defined in the literature. The expected findings in an anastomotic leak include pneumoperitoneum and a localized fluid collection or abscess (11). Unfortunately, pneumoperitoneum is a common, normal postoperative finding, and localized fluid collection or an abscess that is caused by an anastomotic leak may not be reliably differentiated from a transient postoperative serum collection with CT alone. A CT following oral administration of positive contrast may be an alternative technique, because a definitive diagnosis can be made by detecting the accumulation of extraluminal contrast.

The aim of this study was to evaluate the usefulness of CT with positive oral contrast for the detection of leakage and its relationship with the immediate

postoperative outcome in patients who have undergone a gastrectomy for gastric cancer.

II. MATERIALS AND METHODS

This retrospective study received institutional review board approval and was exempted from informed consent requirements

1. Patients

From December 2004 to December 2008, a total of 4241 patients underwent surgery for gastric cancer at our institution. Among these patients, consecutive symptomatic patients who had a clinical suspicion of an anastomotic leakage (fever, abdominal pain, tenderness, and leukocytosis) were referred by surgeons in our gastric cancer clinic to our radiologic department. A CT following an oral administration of positive contrast had been prospectively performed in these patients. A study coordinator retrospectively enrolled the 219 patients who underwent the positive oral contrast CT postoperatively. Among them, nine patients underwent a palliative bypass surgery without gastrectomy. Therefore, a total of 210 patients who underwent gastrectomy were finally included in this study. The demographics of the patients are presented in Table 1.

Table 1. Demographics of gastric cancer patients who underwent the positive oral contrast CT with a clinical suspicion of postoperative leakage

Age at Time of Surgery		Mean 61.7 (35-84)
Sex	Male	153 (72.9%)
	Female	57 (27.1%)
Type of Gastrectomy	TG* with Roux-en-Y esophagojejunostomy	83 (39.5%)
	STG** with gastroduodenostomy (Billoroth I)	65 (31.0%)
	STG **with gastrojejunostomy (Billoroth II)	62 (29.5%)
Stage	I	110 (52.4%)
	II	35 (16.7%)
	III	50 (23.8%)
	IV	15 (7.1%)
Pathology	Adenocarcinoma	166 (79.0%)
	Signet ring cell carcinoma	42 (20.0%)
	Mixed glandular-endocrine cell carcinoma	2 (1.0%)

Note.-Data are numbers with ranges or percentages in parenthesis.

* TG= total gastrectomy

**STG= subtotal gastrectomy

2. CT technique

A CT following oral administration of positive contrast was performed as follows. All of the patients included in the study underwent 16 or 64-detector CT scanning (Somatom Sensation 16 or Somatom Sensation 64, Siemens Medical Solutions, Forchheim, Germany). To reduce the beam-hardening artifact caused by oral contrast, each patient drank 400 mL of diluted contrast agent (Iodinated contrast [Gastrografin; meglumine sodium diatrizoate, Schering, Germany], diluted 1:5 with 0.9% normal saline) 15-30 minutes before scanning. All of the patients received 150 mL of nonionic contrast material (Iopromide [Ultravist]; Schering, Berlin, diatrizoate meglumine [Hypaque] or iohexol [Omnipaque 300]; Nycomed Amersham, Princeton, NJ) intravenously using an automatic power injector at a rate of 3 mL/sec.

Scans were acquired in a craniocaudal direction with the following parameters: a detector collimation of 16x0.75 or 64x0.6 mm^2; 0.5-sec gentry rotation speed;

a 3-mm slice thickness and 3-mm increment reconstruction; a pitch of 1.0; and a tube current of 120 kVp and 160 mAs. An approximately 1-cm^2 region of interest (ROI) was placed at the abdominal aorta, and the attenuation value was measured. The CT scans were obtained at the pre-contrast phase and the portal venous phase (by adding 35 seconds after the attenuation value of the ROI when it reached 100 HU) in a supine position. The coronal images were reformatted with a section thickness of 3 mm with a 3 mm slice increment.

3. Image Analysis

Two gastrointestinal radiologists with ten and four years of experience, respectively, reviewed all of the CT images independently and retrospectively. The transverse and coronal images were retrieved on a picture archiving and communication system (PACS; GE Healthcare Integrated Imaging Solution, Milwaukee, USA). All except five of the patients underwent one oral contrast CT scan. In the remaining five cases, a CT that revealed a larger leakage was used in the review. The reviewers recorded the presence of oral contrast leakage and the location as anastomosis (gastroduodenostomy, gastrojejunostomy, esophagojejunostomy, or jejunojejunostomy), duodenal stump, or jejunal stump sites. Among the cases with visible extraluminal contrast on the CT, the reviewers graded the extraluminal contrast amount as follows: 1, a linear or small, loculated leak adjacent to the anastomosis site with a contrast leakage diameter < 3 cm; 2, a loculated leak adjacent to the anastomosis site with a contrast leakage diameter ≥ 3cm; 3, a disseminated leak in the peritoneal cavity. Any differences in assessment after independent review were resolved by consensus. In addition, any CT findings that indicated other postoperative complications, such as localized fluid collection, an abscess, pancreatitis, obstruction, hematoma, and/or infarction, were documented.

A. Postoperative outcome regarding the presence of extraluminal contrast and

the leakage grade on CT

Immediate postoperative outcomes including treatment options (re-operation, endoscopic clipping, percutaneous drainage, and conservative treatment), the length of the postoperative hospital stay, and the mortality rate were obtained by reviewing the electronic medical records. The rate of postoperative intervention treatments, the length of the hospital stays, and mortality were compared in patients with and without visible extraluminal contrast on the CT. Among the patients with visible extraluminal contrast, the rate of postoperative intervention treatments, the length of the hospital stay, and mortality were correlated with the leakage grades.

B. Matching accuracy between CT and other studies in the detection of leakage

To evaluate the matching accuracy of positive oral contrast CT compared with the results of other diagnostic or therapeutic methods, cases in which other studies were performed in addition to the original CT were selected. Of the 210 patients, 44 underwent a diagnostic or therapeutic procedure that could reidentify the leakage during the hospital stay (endoscopy, contrast-swallowing fluoroscopy, 99mTc-diisopropyl IDA (DISIDA), and re-operation). Among them, five patients who underwent studies more than seven days after the CT were excluded because of the possibility of spontaneous healing or a newly developed leak. Therefore, the studies in 39 patients were reviewed for the evaluation of matching accuracy between CT and other studies for the detection of postoperative leakage.

4. Statistical analyses

Statistical analysis was performed using a statistics program, SAS version 9.1 (SAS Institute, Cary, NC, USA). Continuous data were compared with a Student’s t-test, and categorical data were compared with a Chi-squared or a

Fisher's exact test. The Cochran-Armitage trend test was used to test the trends over grade. A p value of <0.05 was regarded as statistically significant. To assess the interobserver agreement in the assessment of the presence of visible contrast leakage and its grade, the weighted kappa statistic was used. A kappa value of 0.00-0.20 indicated poor agreement; 0.21-0.40, fair agreement; 0.41-0.60, moderate agreement; 0.61-0.80, good agreement; and 0.81-1.00, excellent agreement (14).

III. RESULTS

The mean interval, in days, between the gastrectomy and the CT examination was 7.2 days (range: 0–31 days).

1. Postoperative outcome regarding the presence of extraluminal contrast

Of a total of 210 cases with a clinical suspicion of leakage, 48 (22.9%) showed visible extraluminal contrast on the CT. The kappa value for the interobserver agreement of leakage detection was excellent (κ value =0.97). Forty-one revealed leakage at the anastomosis site (Billroth I, n=19; Billroth II, n=10; TG, n=12), and seven revealed leakage at the duodenal stump (Billroth II, n=5; TG, n=2) (Figure 1).

Figure 1. Duodenal stump leakage

Transverse CT image of a portal venous phase shows a contrast leakage containing air bubbles with a duodenal stump defect (white arrow) after Billroth II surgery.

Postoperative intervention treatments including re-operation, endoscopic clipping, and percutaneous drainage were performed according to the patient's clinical necessity. The intervention rate with extraluminal contrast was significantly higher than that without extraluminal contrast (p<0.0001). In particular, a re-operation was done in the case of persisting leakage or clinical deterioration. In total, nine re-operations were required. Among them, eight revealed extraluminal contrast on the CT. In the sole case in which the extraluminal contrast was not visualized on the CT, the anastomotic leakage was confirmed in the operative field. Despite the fact that there was a missed case, the re-operation rates in patients with extraluminal contrast on CT were significantly higher than those without leakage (p=0.0003).

The mean postoperative hospital stays for all patients was 25 days (range: 6-203 days). A significant difference in the mean hospital stay was noted between the patients with (mean stay: 46 days) and without (mean stay: 18 days) extraluminal contrast (p<0.0001). Hospital mortality accounted for five patients. Four of the patients with extraluminal contrast died from sepsis that was secondary to anastomotic leakage, and one patient without extraluminal contrast died from postoperative respiratory failure. The mortality rate in patients with extraluminal contrast was significantly higher than in those without extraluminal contrast (p=0.0021). The comparison of postoperative

intervention, hospital stays, and mortality between patients with and without extraluminal contrast on oral contrast CT is presented in Table 2.

Table 2. Comparison of postoperative intervention, re-operation, hospital stay, and mortality between patients with and without extraluminal contrast on oral contrast CT

	Leakage (n=48)	No leakage (n=162)	*p* value
Intervention	41 (85.4%)	45 (27.8%)	<0.0001
Re-operation	8 (16.7%)	1 (0.6%)	0.0003
Mean postoperative hospital days	46	18	<0.0001
Mortality	4 (8.3%)	1 (0.6%)	0.0021

Note: Data are numbers or days with percentages in parenthesis.

In addition to the diagnosis of leakage, the CT showed variable postoperative complications in 74 patients (35.2%). The CT detected localized fluid collection or abscesses in 27 cases, pancreatitis in 22, splenic infarction in 17, hematoma in 7, partial small bowel obstruction in 7, and liver segmental infarction in 1. Seven patients had two or more postoperative complications.

2. Postoperative outcome regarding the grade of leakage on the CT

Among the 48 cases that revealed extraluminal contrast on the CT, the contrast amount leaked was graded: 13 patients had grade 1 leakage (Figure 2); 19 had grade 2 leakage (Figure 3); and 16 had grade 3 leakage (Figure 4). The kappa value for the interobserver agreement of the leakage grade was excellent (κ value = 0.86).

Figure 2. Grade 1 leakage

Transverse CT image of a portal venous phase shows linear contrast leakage (arrow) anterior to the gastroduodenostomy site after Billroth I surgery

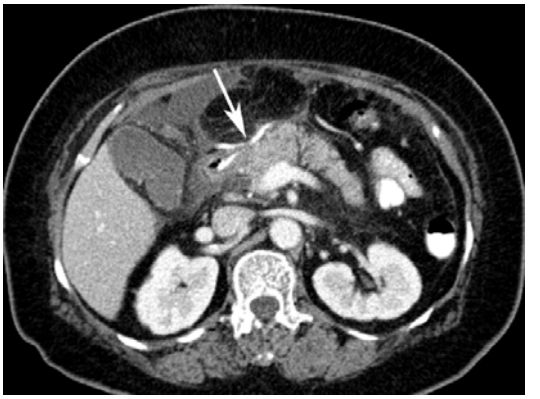
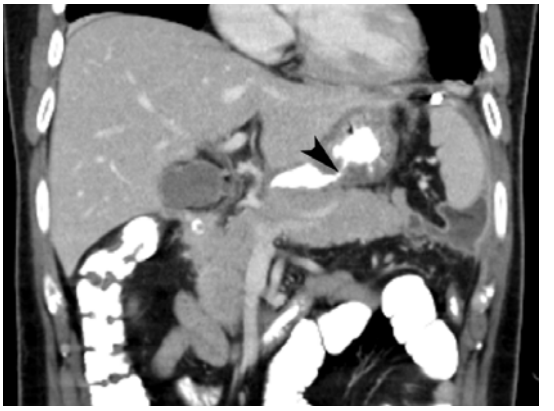


Figure 3. Grade 2 leakage

A. Transverse CT image of a portal venous phase shows loculated contrast leakage larger than 3cm in diameter (white arrow) adjacent to the gastrojejunostomy site after Billroth II surgery.

B. Coronal image shows an anastomotic defect filled with oral contrast (black arrow head).

A.

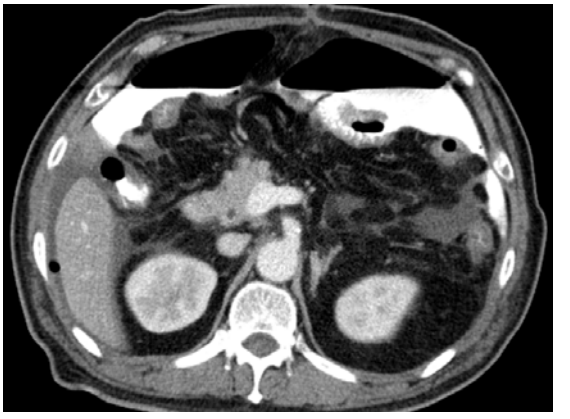


B.

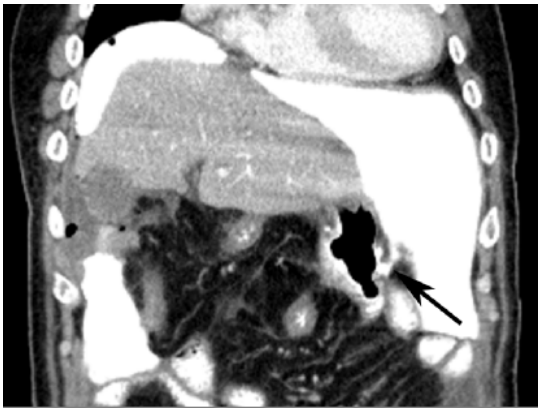
Figure 4. Grade 3 leakage

A. Transverse CT image of a portal venous phase shows disseminated leak in the peritoneal cavity after Billroth II surgery.

B. Coronal image shows an anastomotic defect filled with oral contrast at gastrojejunostomy site (black arrow).



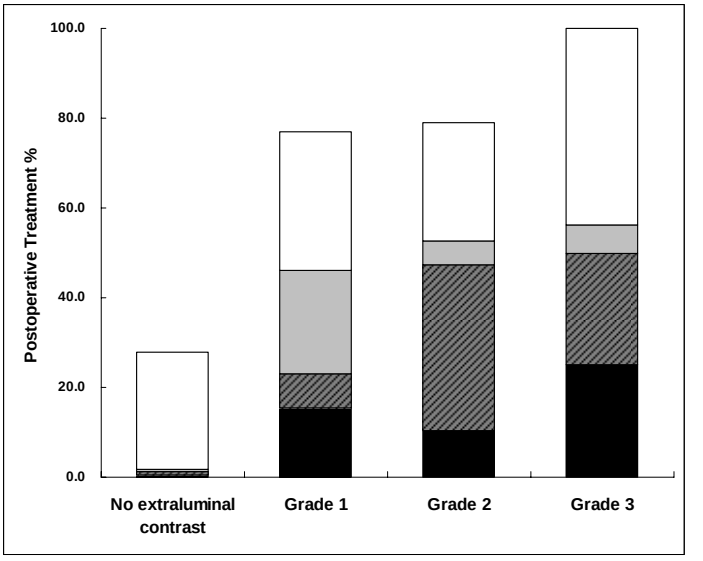
A.



B.

The rates of postoperative intervention treatment according to the CT-grade of leakage tended to increase along with the grades, although there was no statistical significance (p=0.0696): grade 1 was 76.9% (10/13); grade 2 was 78.9% (15/19), and grade 3 was 100% (16/16) (Figure 5).

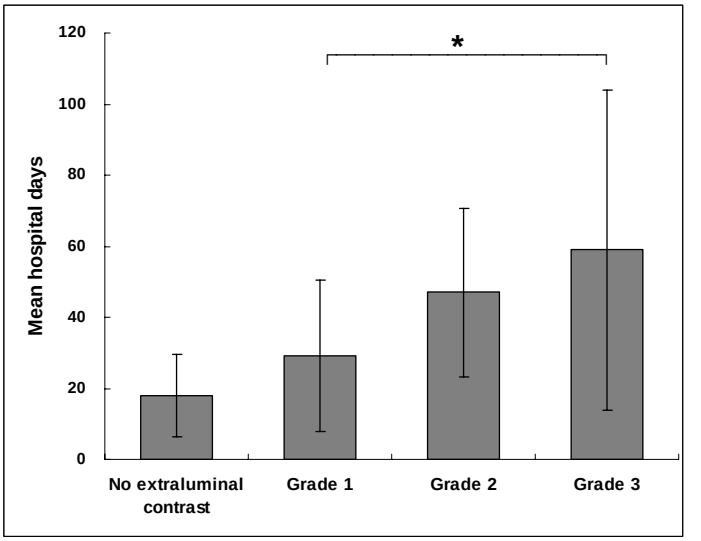
Figure 5. Postoperative intervention treatment according to the grade of leakage on the CT.



White = percutaneous drainage, light gray = endoscopic clipping, gray with oblique lines = endoscopic clipping combined with percutaneous drainage, black = re-operation.

The mean postoperative hospital stay for grade 1 was 29 days; it was 47 days for grade 2 and 59 days for grade 3 (Figure 6). A significant increasing trend in the mean hospital stay was noted with an increase of the leakage grades by the Cochran-Armitage trend test (p=0.0008).

Figure 6. Mean postoperative hospital days according the CT leakage grade



Note - Error bars indicate standard deviation, asterisk indicates significant (p<0.05) increasing trend with the grade on a Cochran-Armitage trend test.

In the four patients with leaks who died during their hospital stays, three had grade 2 leaks, and one had a grade 3 leak on the CT contrast scan. The mortality rates were not significantly increased with grades (p=0.6132).

3. Matching accuracy between the CT and other studies in the detection of leakage

In a total of 39 patients, endoscopy (n=24), re-operation (n=9), contrast swallow fluoroscopy (n=4), DISIDA (n=1), and DISIDA combined with endoscopy (n=1) were performed within seven days of a CT for leakage

diagnosis, follow-up, or treatment. The matching accuracy between the oral contrast CT and the other studies was 82.1% (n=32/39) (Table 3). Among the mismatched cases, the CT identified the extraluminal contrast in four cases in which there was no evidence of leakage by the other studies, which included endoscopy (n=2), fluoroscopy (n=1), and DISIDA (n=1). These leaks were located in the anastomosis site for two (Billroth I, TG) and in the duodenal stump for two (all Billroth II). However, there was no visible extraluminal contrast in three cases for whom a mural defect at the anastomosis or stump site was found on re-operation (n=1), endoscopy (n=1), and both DISIDA and endoscopy (n=1) (Figure 7). These leaks were located in the anastomosis site for two (both Billroth I) and in the duodenal stump for one (Billroth II).

Table 3. Matching and mismatching of CT and other studies for the detection of postoperative leakage

		Number of Cases
Matching	CT (+), Other study (+)	31
	CT (-), Other study (-)	1
Mismatching	CT (+), Other study (-)	4
	CT (-), Other study (+)	3

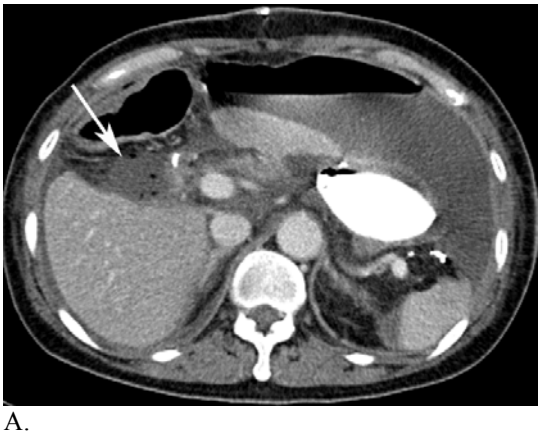
*Other study including re-operation, endoscopy, contrast swallow fluoroscopy, or 99mTc-diisopropyl IDA (DISIDA).

Figure 7. Duodenal stump leakage missed on an oral contrast CT.

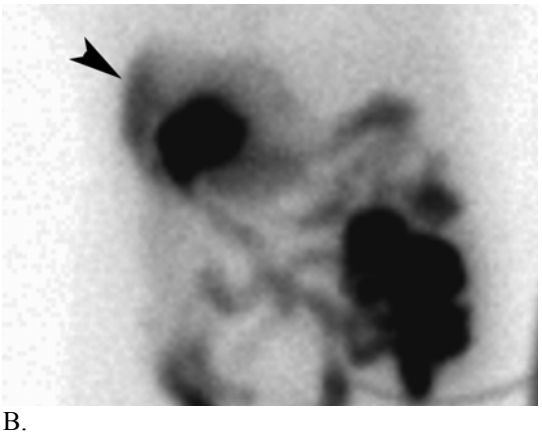
A. Transverse CT image of a portal venous phase shows loculated fluid containing air bubbles (white arrow) adjacent to the duodenal stump without contrast leakage after Billroth II surgery. Oral contrast failed to fill the duodenal stump.

B. ^{99m}Tc-diisopropyl IDA (DISIDA) image at eight hours shows perihepatic accumulation (black arrow head) indicating leakage.

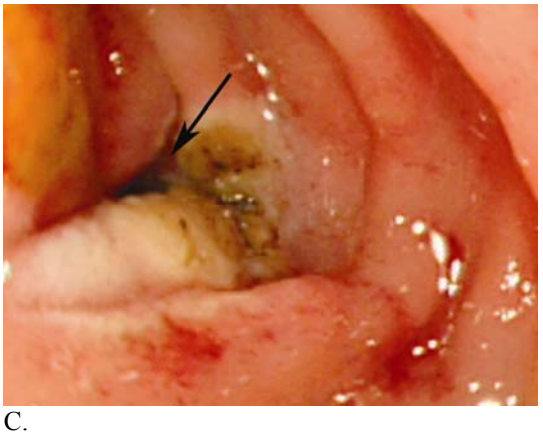
C. The patient underwent endoscopy after DISIDA, and the duodenal stump defect (black arrow) was revealed.



A.



B.



C.

IV. DISCUSSION

Postoperative leakages after gastric cancer surgery are the most serious and life-threatening complication for this surgery. Although clinical signs including fever, leukocytosis, abdominal pain, and tenderness during the postoperative period can be associated with leakage, these findings are often nonspecific. Fluoroscopy with oral contrast (water soluble contrast alone or followed by barium sulphate) has been widely used for postoperative evaluation of anastomotic leakage after gastrectomy (3). Although highly specific, this technique is limited by its low sensitivity (7, 12). Furthermore, the fluoroscopy is often ill-tolerated by postoperative patients owing to general morbidity and difficulty with mobilization (13). Endoscopy is useful to identify an anastomotic defect that would not be seen on contrast swallow or CT and to close any defects using a clip (14). However, it has been regarded as a hazardous investigation due to a potential disruption of the anastomotic site.

CT using positive oral contrast has the benefits of being easier to perform in very ill patients and allowing for the determination of leakage through the detection of accumulated extraluminal contrast (15). Although there have been a few reports (13, 15) assessing CT using oral contrast in patients after gastric surgery, the number of patients in these reports has been small. Our study was based on a relatively large number of patients (n=210) who underwent oral contrast CT.

In the diagnostic accuracy evaluation for anastomotic leakage, the establishment of a complete standard of reference would actually be impossible in clinical practice, because postoperative CT is not a routine screening method in asymptomatic patients after gastrectomy and is usually performed in the clinical setting only in the case of a suspicious complication. In addition, the detection of extraluminal contrast itself confirms the diagnosis of leakage. Further studies would not be required in such cases. Therefore, we compared the immediate postoperative outcome in patients with or without extraluminal

contrast in order to evaluate the clinical implication of a positive oral contrast CT. In our study, oral contrast CT was performed only in patients who had a clinical suspicion of leakage or other complications. There may actually be leakage cases in patients without visible extraluminal contrast on CT, as reported in our study. However, those patients without extraluminal contrast show a favorable outcome including a lower intervention rate, shorter postoperative hospital stay, and a lower mortality rate than those with extraluminal contrast ($p<0.05$), Therefore, positive oral contrast CT can be reliable at least for diagnosing clinically significant leakage.

Previous studies have proposed systems for classifying upper gastrointestinal leaks with contrast swallow fluoroscopy (3, 6, 16, 17). However, no study has classified leakages found on a CT using oral contrast. We graded these leakages as grade 1, 2, or 3, according to the amount of extraluminal contrast on the CT. Postoperative hospital stays showed a significantly increased trend according to the CT grades ($p=0.0008$). Although there was no statistical significance, postoperative intervention rates were increased with the leakage grades ($p=0.0696$). The reason may be related with the possibility that our grading system may be correlated with the mural defect size. In addition, the disseminated form of leakage (grade 3) may result in a more aggressive form of peritoneal abscess or panperitonitis in comparison with linear or small loculated forms of contrast leakage.

Our study showed a high matching accuracy between the CT and other studies (82.1%) in the detection of postoperative leakage. Among the mismatched cases, a positive CT and a negative result for the other study may be accounted for by false negative findings of the other studies or by spontaneous healing, even though the interval between the studies was less than seven days. A negative CT and a positive result for the other study may be accounted for by positional effect. CT has a limitation such that the examination can only be performed in the supine position, in contrast to fluoroscopic examination, which can be

performed in multiple positions. In addition, any leakage located in a nondependent portion could have been missed on the CT scan. Additional CT scanning after a position change could aid in the detection of leaks in a nondependent position. Similar to fluoroscopic examination, a duodenal stump leakage after Billroth II or a total gastrectomy may be another challenge for the use of positive oral contrast CT for the diagnosis of leakage in those cases in which the ingested contrast does not reach the stump level (Figure 7A). One duodenal stump leakage case was missed even on endoscopy because of a technical failure in reaching the duodenal stump. DISIDA permits a direct visualization of the afferent loop (18, 19) and is expected to help with the detection of duodenal stump leakage.

CT could identify other postoperative complications, such as localized fluid collection, pancreatitis, hematoma, obstruction and hepatic or splenic infarction (10, 20, 21). The initial clinical presentation of these complications may mimic postoperative leakage. We used positive oral contrast CT with intravenous contrast enhancement to identify postoperative complications, and 74 patients (35.2%) showed variable complications (except leakage) in our study.

Our study has some limitations. First, the CT leakage grade could be altered with changes in the amount of contrast swallowed, scanning position, or time passed. To decrease these effects, we tried to keep relatively constant conditions. Second, the amount of extraluminal contrast in CT may induce the surgeon to perform an intervention treatment, which, therefore, would increase the rate of intervention treatment with increased leakage grades. However, postoperative intervention, including re-operation, is usually performed according to the patient's clinical status. Third, we acknowledge that the other postoperative complications, except leakage, may function as a bias in the evaluation of postoperative outcome according to the presence of extraluminal contrast or the leakage grading.

V. CONCLUSION

In conclusion, positive oral contrast CT is a reliable tool for diagnosing leakage after a gastrectomy in gastric cancer patients in addition to diagnosing other postoperative complications, and the immediate postoperative outcome may be related with the grade of leaked contrast on the CT.

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<ABSTRACT (IN KOREAN)>

위절제술을 시행받은 위암 환자에서 발생한 문합부 누출을 진단을 위한 경구 조영제를 이용한 CT의 임상적 유용성

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목적: 경구 조영제를 이용한 CT가 위암의 절제술 후 발생한 문합부 누출의 진단과 수술 직후 경과 예측에 임상적으로 유용한지 알아보고자 한다.

재료 및 방법: 위암으로 위절제술을 받은 후 임상적으로 문합부 유출이 의심되는 환자 중 경구 조영제를 이용한 CT를 촬영한 210명의 환자를 대상으로 하였다. 두 명의 영상의학 전문의가 CT 영상에서 조영제의 누출여부와 누출된 조영제의 양에 따른 등급(gade 1, 선형 또는 3cm미만의 소방형 조영제 누출; grade 2, 3cm 이상의 소방형 조영제 누출; grade 3, 복막내 산재된 조영제 누출)을 평가하였다. 수술후 치료(재수술, 내시경 clipping, 체외 배액, 보존적 치료), 수술후 재원 기간, 사망률을 조영제 누출여부와 누출 등급(grade)과 비교하였다. CT와 다른 진단적 검사의 문합부 누출 진단의 정확도도 평가하였다.

결과: 210명의 CT영상에서 162명(77.1%)은 조영제 누출이 관찰되지 않았으며 13명(6.2%)이 grade 1, 19명(9.0%)이 grade 2, 16명(7.6%)이 grade 3의 조영제 문합부 누출을 보였다. 조영제 누출이 관찰되는 환자는 그렇지 않은 환자에 비해 수술후 중재적 치료, 수술후 재원기간, 사망률이 높았다(p<0.05). 조영제 누출 등급(grade)이 높아짐에 따라 수술후 재원 기간이 높아지는

양상을 보였다(p=0.0008). CT와 다른 검사간의 정확도는 82.1% (n=32/39) 였다.

결론: 경구 조영제를 이용한 CT는 위암의 수술후 문합부 누출을 발견하는데 유용하며 누출된 조영제의 양은 수술후 임상경과와 유의한 상관관계를 보인다.

핵심되는 말 : 경구 조영제, CT, 위암, 문합부 누출