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ORIGINAL ARTICLE

Endoscopic Estimation of Tumor Size in Early Gastric Cancer

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Abstract
Background Although the accurate estimation of tumor size is essential for proper patient selection for endoscopic resection in early gastric cancer (EGC), no study has been conducted to date on tumor size estimation. We aimed to evaluate the accuracy of endoscopic visual estimation of tumor size of EGC.
Methods In 508 EGC patients that underwent endoscopic resection, endoscopic visual estimations were performed retrospectively by independent two endoscopists using still images. Data were compared with pathologic measurements as gold standard. Inter-observer agreement was determined using the Bland–Altman method and intra-class correlation coefficients (ICC). Measurement discrepancies were presented as differences between measurements.
Results The ICC between the two endoscopists was 0.915 (95 % CI 0.900–0.928). Mean endoscopic estimates for both endoscopists were significantly lower than mean pathologic measurements (1.50 and 1.67 vs. 1.80 cm, $P < 0.001$). Absolute differences between average endoscopic estimates and pathologic measurements were found to be acceptable in most cases: an absolute difference of <0.4 cm was found for 80 % (404/508) of cases. Bland–Altman plot showed that 94 % of cases lay within the 95 % limits of agreement. Measurement discrepancy was proportional to tumor size and increased for an undifferentiated histology.
Conclusions Endoscopic visual estimations were found to show reliable agreement with pathologic measurement in EGC patients undergoing endoscopic resection, together with good inter-observer agreement. Further prospective study is needed to confirm the validity of this method.

Keywords Early gastric cancer · Endoscopy · Tumor size · Estimation · Measurement

Abbreviations

CI	Confidence interval
EGC	Early gastric cancer
ESD	Endoscopic submucosal dissection
EUS	Endoscopic ultrasonography
OR	Odds ratio
T1m	Mucosal early gastric cancer
T1sm	Submucosal early gastric cancer

Introduction

Early gastric cancer (EGC) is defined as gastric cancer confined to the mucosal or submucosal layers irrespective of lymph node metastasis [1]. Endoscopic resection for EGC is widely employed as a standard treatment in South Korea and Japan because it is minimally invasive and effective [2]. Recently, large data have been also reported from the Western world as endoscopic resection is gaining wide acceptance [3]. The established indications for endoscopic resection of EGC are a differentiated tumor of less than 2 cm in the absence of ulceration and lymphovascular invasion, because such tumors rarely metastasize to lymph nodes [4]. One study reported a significant

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correlation between a tumor size larger than 3 cm and an increased risk of lymph node metastasis [5]. Thus, gastric tumor size is fundamental for the selection of patients suitable for endoscopic resection.

Conversely, the size criteria for endoscopic resection are based largely on histopathologic findings of excised formalin-fixed specimens after surgery [4, 5]. In contrast, at the time of endoscopy, endoscopists estimate only approximate tumor size on the basis of endoscopic images, which might cause different measurements between endoscopic estimates and pathologic measurements. However, endoscopic tumor size estimation in EGC has not been previously examined, and, thus, the accuracy of endoscopic estimation has not been determined.

In the present study, we aimed to evaluate the agreement between endoscopic estimations of tumor size in patients with EGC that underwent endoscopic resection, and to identify the clinicopathologic features that affecting measurement discrepancies between endoscopic and pathologic measurements. In addition, we aimed to investigate the interobserver agreement between the two endoscopists' measurement.

Methods

Patients and Treatment

From August 2005 to December 2009, patients with EGC scheduled for endoscopic resection at Seoul National University Hospital were initially considered for this retrospective study. Patients underwent pretreatment staging procedures, including endoscopic ultrasonography (EUS), abdominal multi-detector computed tomography (CT), and chest radiography. All patients initially underwent endoscopic resection as a curative treatment. Endoscopic resection was performed entirely by a single experienced endoscopist (S.G.K.) by endoscopic submucosal dissection (ESD), and it was indicated if the following criteria were met: a tumor diameter of <2 cm; well or moderately differentiated adenocarcinoma; no ulceration; and no evidence of lymph node or distant metastases on pretreatment staging [5]. However, patients beyond these criteria also underwent ESD for the following reasons: patient preference, an underlying comorbidity, or physician's opinion. Before ESD, tumor extent was demarcated by chromoendoscopy using indigo carmine solution. Next, a mixture of normal saline and indigo carmine solution containing diluted epinephrine (1: 100,000) was injected into the submucosal layer to separate it from the muscle layer. A circumferential mucosal incision was performed at 1 cm beyond the margin of the lesion, and submucosal dissection was performed using an insulated tip (IT)-knife. If massive submucosal invasion (sm2/sm3: penetration into the submucosal layer $\geq$500 μm from the muscularis mucosae), lymphovascular tumor invasion, or lateral resection margin positivity was found in the resected specimen, patients were urged to undergo additional gastrectomy with lymph node dissection. The study exclusion criteria were as follows: a fragmented resected tumor ($n = 3$); tumor removal by piecemeal resection ($n = 2$); recorded images did not permit the endoscopic estimation of tumor size ($n = 5$). In this study, 11 patients (2.2 %) who had multiple synchronous EGC lesions were excluded. A total of 508 consecutive patients were included in the study, which was approved by the Institutional Review Board of Seoul National University Hospital (IRB no. 1007-218-326).

Endoscopic Estimation of Tumor Size

GIF-H260 endoscopes (Olympus Optical, Tokyo) were used throughout the study. Endoscopic examinations were performed entirely by a single expert (S.G.K.) in a standardized manner during endoscopic resection. At least 30 still images per patient, including distant and close images of lesions, were taken and recorded electronically in a Picture Archiving Communication System (PACS). In addition, indigo carmine chromoendoscopy was used to precisely assess tumor margins. Endoscopic size estimation was performed retrospectively by two independent endoscopists by visual estimation using recorded still images. The experienced endoscopist (S.G.K.) had 14 years experience in endoscopy, whereas the less experienced (J.C.) had 5 years of experience. The less experienced endoscopist was trained by the experienced. Endoscopists estimated maximal tumor sizes using close images and chromoendoscopic images. Endoscopists were blinded to pathologic measurements during endoscopic estimations. The macroscopic tumor classification was as follows: type I (protruded); type IIa (superficial elevated); type IIb (flat); type IIc (superficial depressed); type III (excavated); and combination type (I + IIa, IIa + IIc, IIc + IIa, IIc + III) [6, 7]. Types I, IIa, I + IIa, and IIa + IIc were classified as the elevated type; types IIc, III, IIc + III, and IIc + IIa as the depressed type; and type IIb as the flat type. All cases were classified as elevated or flat/depressed types. Lesion locations were classified as the upper, middle, and lower thirds of the stomach. Lesions with active ulceration or accompanying fibrous scarring were regarded as ulceration.

Histopathologic Measurements

ESD specimens were stretched minimally to avoid overextension, since it can cause destruction of the specimen and were pinned on a styrofoam board and immediately

immersed in formalin fixative for 4 h. Each fixed specimen was placed between two sheets of an overhead projector transparency and the mucosal side was photocopied. This photocopy was utilized as an actual size map template to identify the precise locations of tissue blocks. Entire specimens were then serially sectioned into 2-mm slices parallel to the long axis, and each slice was embedded in paraffin. Mapping was performed using a single hematoxylin and eosin-stained section from each paraffin block [8]. Pathological tumor diameters were measured using the map template, which was considered the reference standard. Depth of invasion and lymphovascular invasion were also determined using map template. Degrees of differentiation were classified as differentiated (well- or moderately differentiated adenocarcinoma) or as undifferentiated (poorly differentiated adenocarcinoma or signet-ring cell carcinoma).

Statistical Analysis

The continuous variables are presented as means ± standard deviations (SD) and 95 % confidence intervals (CI), and categorical variables are presented as proportions and percentages. The independent *t* test or one-way analysis of variance (ANOVA) were used to determine the significances of variables with a parametric distribution, and the Chi squared test, linear by linear association, or Fisher's exact test were used to compare proportions. The paired *t* test was used to determine the presence of a significant difference between paired measurements. Interobserver agreement between endoscopists' measurement was analyzed using the intraclass correlation coefficient method [9]. In the analysis of agreement between two quantitative measurements, neither Pearson correlation analysis or Cohen's kappa value is appropriate. Instead, the Bland–Altman method was used to assess the degree of agreement between endoscopic estimates and pathologic measurements [10]. Differences between endoscopic and pathologic measurements were plotted against the means of the two measurements, and 95 % limits of agreement were used to define discrepancies between the two methods, and were defined as mean difference ± 1.96SD of mean difference. Measurement discrepancies defined as pathologic size minus endoscopic size were calculated to evaluate overestimation or underestimation trends of endoscopic estimates. Relationships between absolute values of measurement discrepancies (ignoring the direction of differences) were also investigated with respect to clinicopathologic factors. All significance tests were two-tailed, and *P* values <0.05 were considered significant. The analysis was performed using the Statistical Package for the Social Sciences version 12.0 (SPSS, Chicago, IL, USA).

Results

Clinicopathologic Characteristics

A total of 508 patients (383 men; mean age 63.2 ± 9.6 years) were enrolled in this study. Endoscopic resection was initially performed in all patients. However, 51 patients underwent additional surgery for the following reasons: massive submucosal (sm2/sm3) invasion ($n = 23$); lymphatic invasion ($n = 3$); lymphatic and sm2/sm3 invasion ($n = 21$); or lateral resection margin positivity ($n = 4$). Finally, endoscopic resection was performed in 457 patients (90.0 %) and surgery in 51 (10.0 %) with curative intent. Most tumors had a flat/depressed morphology and no ulceration. In resected specimens, 409 cases (80.5 %) were confirmed to have a T1m tumor and 99 cases (19.5 %) to have a T1sm tumor. Most tumors were less than 3.0 cm in diameter (87 %, 444/508) had a well- or moderately differentiated histology (86 %, 438/508) (Table 1).

Interobserver Agreement

The Intraclass correlation coefficient of interobserver agreement between the two endoscopists was 0.915 (95 % CI 0.900–0.928). Absolute differences between the two endoscopists were acceptable in most cases: the rate of an absolute difference of ≤0.2 cm was 62 % (317/508); of ≤0.4 cm was 78 % (395/508); and of ≤0.6 cm was 90 % (455/508); and only 1 % of cases had an absolute difference of ≥1.0 cm.

Measurement Discrepancies Between Endoscopic and Pathologic Measurements

Mean pathologic tumor size was 1.80 ± 0.98 cm (95 % CI 1.72–1.89): 1.76 ± 0.99 cm for T1m; and 1.99 ± 0.95 cm for T1sm ($P = 0.03$). Mean endoscopic measurements were significantly smaller than mean pathologic measurements: 1.67 ± 0.86 cm (95 % CI 1.59–1.75) for the experienced endoscopist; and 1.50 ± 0.79 cm (95 % CI 1.43–1.57) for the less experienced endoscopist ($P < 0.001$ for each endoscopist).

The mean measurement discrepancy between each endoscopist's measurements and pathologic measurements were 0.13 cm (95 % CI 0.10–0.16) for the experienced and 0.30 cm (95 % CI 0.27–0.34) for the less experienced, respectively ($P < 0.001$). The mean measurement discrepancy between the average of the two endoscopists'measurements and pathologic measurements was 0.17 cm (95 % CI 0.14–0.20).

Table 1 Clinicopathologic characteristics

Characteristics	*n*	%
Gender		
Male	383	75.4
Female	125	24.6
Mean age (SD), years	63.2 (9.6)	
Location		
Upper third	36	7.1
Middle third	75	14.8
Lower third	397	78.1
Gross morphology		
Type I	8	1.6
Type IIa	78	15.4
Type IIb	8	1.6
Type IIc	401	78.8
Type III	6	1.2
Mixed type	7	1.4
Gross morphology[a]		
Elevated	86	16.9
Flat/depressed	422	83.1
Ulcer findings		
Absent	472	92.9
Present	36	7.1
Treatment		
ESD	457	90.0
Surgery[b]	51	10.0
Tumor size, mean (SD), cm	1.8 (0.9)	
<1.0	118	23.2
1.0–2.0	236	46.5
2.0–3.0	90	17.7
3.0–4.0	48	9.5
4.0–5.0	16	3.1
Histology		
Well differentiated	245	48.2
Moderately differentiated	193	38.0
Poorly differentiated	39	7.7
Signet-ring cell	31	6.1
Histology (binary classification)[c]		
Differentiated	438	86.2
Undifferentiated	70	13.8
Depth of invasion		
T1m	409	80.5
T1sm	99	19.5
Submucosal invasion	($n = 99$)	
sm1	55	55.6
sm2/sm3	44	44.4
Total	508	100

ESD endoscopic submucosal dissection, *SD* standard deviation, *T1m* tumor limited to the mucosa, *T1sm* tumor invaded the submucosal layer, *sm1* tumor infiltration into the submucosal layer <500 μm from the muscularis mucosae, *sm2/sm3* tumor infiltration into the submucosal layer ≥500 μm

[a] Types I, IIa, I + IIa, and IIa + IIc were classified as the elevated type; Type IIb as flat type; Types IIc, III, IIc + III, and IIc + IIa as depressed

[b] Patients underwent additional surgery after endoscopic submucosal dissection

[c] Differentiated type includes well or moderately differentiated adenocarcinoma; undifferentiated type includes poorly differentiated adenocarcinoma or signet-ring cell carcinoma

The absolute measurement discrepancy between averaged endoscopists' and pathologic measurements was also acceptable in most cases: the rate of an absolute difference of ≤0.2 cm was 63 % (320/508); of ≤0.4 cm was 80 % (404/508); of ≤0.6 cm was 90 % (455/508); of ≤0.8 cm was 94 % (476/508); and only 2 % (11/508) of cases had an absolute difference of ≥1.0 cm.

Distribution of measurement discrepancies (pathologic measure—average endoscopists' measure) was found to proportional to pathologic tumor size: the mean measurement discrepancy was 0.04 cm for a tumor diameter of ≤1.0 cm; 0.14 cm for a tumor diameter of 1.0–2.0 cm; 0.31 cm for 2.0–3.0 cm; and 0.68 cm for 3.0–4.0 cm, respectively ($P < 0.001$ by linear-by-linear association). Absolute measurement discrepancy was also found to be proportional to tumor diameter. With regard to histologic differentiation, measurement discrepancy was greater for tumors with an undifferentiated than a differentiated histology (0.38 vs. 0.19 cm; $P < 0.001$). Particularly, tumors of signet-ring cell type had a larger measurement discrepancy than other tumor types (0.51 cm for the signet-ring cell type vs. 0.27 cm for the poorly differentiated type, and 0.21 cm for the moderately differentiated type) ($P < 0.001$ by Bonferroni adjustment for post hoc analysis of ANOVA). In contrast, no significant associations were found between measurement discrepancy and location, gross morphology, depth of invasion, presence of ulceration, or submucosal invasion (Table 2).

Agreement Between Endoscopic and Pathologic Measurement

The intraclass correlation coefficient of endoscopist and pathologic measurements was 0.943 (95 % CI 0.933–0.952) for the experienced endoscopist; 0.904 (95 % CI 0.887–0.919) for the less experienced endoscopist; and 0.941 (95 % CI 0.930–0.950) for averaged endoscopists' measurements. The Bland–Altman agreement plot of endoscopic and pathologic measurements showed: for the experienced endoscopist, a mean difference of 0.13 cm (lower and upper 95 % limits of agreement, −0.47–0.74 cm); for the less experienced endoscopist, a mean difference of 0.30 cm (−0.45–1.07 cm); and for averaged endoscopic measurements, a mean difference of 0.22 cm (−0.38–0.82 cm) (Fig. 1). In these plots, the experienced endoscopist showed a narrower scatter of measurement differences around the mean than the less experienced endoscopist. Furthermore, 95 % limits of agreement were also narrower for the experienced endoscopist. For averaged endoscopists' measurements, 94.2 % (479/508) of cases lay within the 95 % limits of agreement.

Table 2 Measurement discrepancy between endoscopic estimates and pathologic measurements and its absolute value with respect to clinicopathologic characteristics

Characteristics	Measurement discrepancy Mean (SD)	*P* value	Absolute value[a] Mean (SD)	*P* value
Location		0.23		0.31
Upper third	0.13 (0.26)		0.19 (0.22)	
Middle third	0.22 (0.28)		0.24 (0.27)	
Lower third	0.22 (0.31)		0.26 (0.28)	
Gross morphology		0.74		0.62
Type I	0.25 (0.50)		0.36 (0.42)	
Type IIa	0.21 (0.29)		0.25 (0.26)	
Type IIb	0.26 (0.35)		0.26 (0.35)	
Type IIc	0.22 (0.30)		0.25 (0.27)	
Type III	0.13 (0.18)		0.15 (0.17)	
Mixed type	0.38 (0.44)		0.38 (0.44)	
Gross morphology		0.91		0.88
Elevated	0.22 (0.31)		0.26 (0.28)	
Flat/depressed	0.22 (0.31)		0.25 (0.28)	
Ulcer findings		0.16		0.06
Absent	0.21 (0.30)		0.25 (0.27)	
Present	0.31 (0.40)		0.36 (0.35)	
Lymphovascular invasion		0.89		0.49
Absent	0.22 (0.30)		0.25 (0.27)	
Present	0.21 (0.36)		0.28 (0.30)	
Tumor size, mean (SD), cm		<0.001		<0.001
<1.0	0.04 (0.11)[b]		0.08 (0.09)[b]	
1.0–2.0	0.14 (0.20)[b]		0.18 (0.16)[b]	
2.0–3.0	0.31 (0.33)[b]		0.35 (0.29)[b]	
3.0–4.0	0.68 (0.27)[b]		0.68 (0.27)[b]	
4.0–5.0	0.80 (0.38)		0.82 (0.32)	
Histology		<0.001		<0.001
Well differentiated	0.17 (0.28)		0.21 (0.25)	
Moderately differentiated	0.21 (0.28)		0.25 (0.24)	
Poorly differentiated	0.27 (0.34)[b]		0.29 (0.33)[b]	
Signet-ring cell	0.51 (0.44)[b]		0.52 (0.43)[b]	
Histology (binary classification)		<0.001		<0.001
Differentiated	0.19 (0.28)		0.23 (0.25)	
Undifferentiated	0.38 (0.40)		0.39 (0.39)	
Depth of invasion		0.52		0.50
T1m	0.22 (0.30)		0.27 (0.25)	
T1sm	0.20 (0.31)		0.23 (0.29)	
Submucosal invasion	($n = 99$)	0.56		0.50
sm1	0.22 (0.30)		0.27 (0.25)	
sm2/sm3	0.18 (0.33)		0.23 (0.29)	
Total	508		508	

Measurement discrepancy was defined as the result of subtracting the average of two endoscopic measurements from the pathologic measurements

[a] Absolute value of measurement discrepancy

[b] Indicates $P < 0.05$ within groups with the use of Bonferroni adjustment for multiple comparisons

Agreement Between Endoscopic and Pathologic Measurements and Measurement Discrepancies with Respect to the Indications for Endoscopic Resection

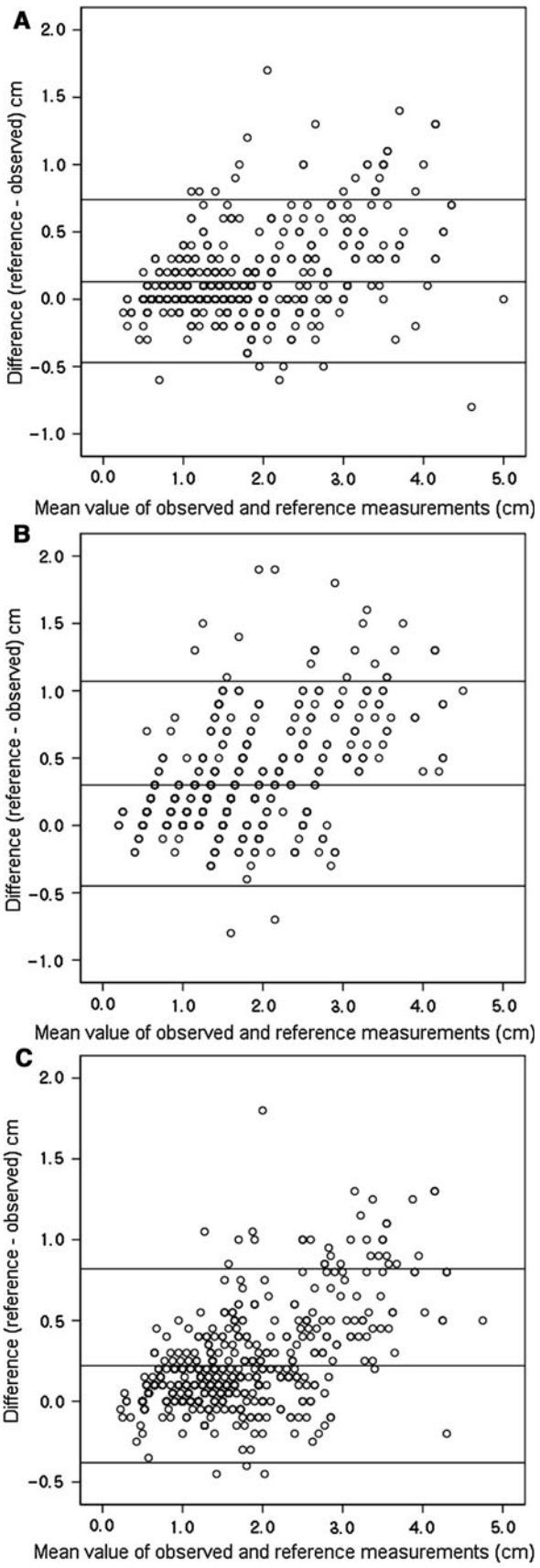
For tumors that fulfilled the conventional criteria for endoscopic resection [4], the absolute values of measurement discrepancies between endoscopists and pathology were 0.06–0.15 cm for the experienced endoscopist, and 0.12–0.19 cm for the less experienced endoscopist. The ranges of the 95 % limits of agreement were −0.13–0.51 cm for the experienced endoscopist, −0.13–0.70 cm for the less experienced.

For tumors that fulfilled the expanded criteria for endoscopic resection [11], the absolute values of measurement discrepancies between endoscopists and pathology were 0.13–0.18 cm for the experienced endoscopist, and 0.23–0.32 cm for the less experienced. The ranges of the 95 % limits of agreement were −0.29–0.65 cm for the experienced, and −0.32–0.94 cm for the less experienced. The averaged measurements of the two endoscopists showed reliable measurement discrepancy (0.17–0.22 cm) and an acceptable 95 % limit of agreement range (−0.27–0.69 cm) (Table 3).

Discussion

This study shows that endoscopic visual estimates of gastric tumor size agree well with pathologically determined tumor size, and that in 90 % of cases the absolute measurement discrepancy was <0.6 cm. Furthermore, 94 % of cases lay within the range of agreement as determined using Bland–Altman plots.

No previous study has addressed endoscopic size estimation in EGC. On the other hand, several studies on this issue for colonic polyps have found agreement between endoscopic estimates and actual polyp size measurements [12–14]. However, these studies also found that polyp sizes depended considerably on the estimation method, the reference standard used, and on observer's experience. One study compared the accuracies among various endoscopic estimation methods based on visual estimation, open biopsy forceps, and linear probe method [13]. In this previous study, it was found that the linear probe method correlated best with the reference standard, followed by visual estimation and open biopsy forceps was the least accurate. Although open biopsy forceps are commonly used for determining colonic polyp size in clinical practice, this method is probably prone to substantial measurement errors when used for gastric tumor size estimation. Generally, the open biopsy forceps method is performed by comparing tumor size to fully open jaws (maximal opening



◀ **Fig. 1** Bland-Altman plots of agreement between pathologic reference and endoscopic measurement for each observer: **a** the experienced endoscopist; **b** the less experienced endoscopist; and **c** averaged endoscopists' measurements. The *middle horizontal line* represents mean difference between reference and observer measurement. The *upper* and *lower horizontal lines* represent the 95 % limits of agreement between reference and observer measurement

7 mm) pushed against the tumor [15]. Accordingly, if the diameter of the gastric tumor exceeds that of the forceps, measurements are likely to be inaccurate. Instead, we adapted the visual estimation method using recorded still images. Our study shows that even visual estimation alone can successfully determine tumor size.

Previous reports have found that visual estimations of tumor sizes may be subject to considerable error, because estimated sizes can be markedly affected by endoscopic distance from lesions [16], and, thus, when the observer retrospectively assesses tumor size using still images, measurement errors would be expected to increase. In the present study, although estimations were performed retrospectively using still images, a single experienced endoscopist photographed images in a consistent, standardized manner, and two trained endoscopists independently assessed tumor sizes using the close images and chromoendoscopic images. Consequently, endoscopic visual estimation was found to be accurate and agreed by both endoscopists.

Colonic polyps generally protrude and are well demarcated from surrounding normal mucosa, and, thus, actual polyp size can be measured using a millimeter ruler immediately after resection or after formalin fixation [13, 14]. In contrast, it is sometimes difficult to recognize the margin of a gastric tumor, especially one with a superficial/flat morphology or if surrounded by intestinal metaplasia. Accordingly, ruler-based measurements of resected specimens may be prone to error. In the present study, we used histologically mapped specimens in the measurement of tumor size instead of ruler measurement, which allowed the pathologist to measure the exact tumor size.

With regard to endoscopy, we used a high-resolution endoscope (GIF-H260) and indigo carmine dye to delineate tumor margins, which allowed the endoscopist to more precisely assess the tumor size. Currently, magnifying endoscopy with narrow-band imaging appears to depict gastric tumors well [17].

Improvements in endoscopic techniques and instruments have led to endoscopic resection being the standard treatment for early gastric cancer. Indications for therapeutic ESD have recently been expanded from a large-scale study [5]. If a tumor is a differentiated mucosal cancer without ulceration, ESD can theoretically be performed on a tumor of any size, because the risk of lymph node metastasis is negligible for tumors fulfilling these criteria. However, a

Table 3 Absolute difference and 95 % limits of agreement between endoscopist and pathologic reference in relation to expanded and conventional criteria for endoscopic resection

Criteria	Experienced		Less experienced		Average of two endoscopists	
	Absolute difference	95 % limits of agreement	Absolute difference	95 % limits of agreement	Absolute difference	95 % limits of agreement
Expanded criteria						
Intramucosal cancer						
Differentiated type, ≤3 cm, irrespective of ulceration	0.13 (0.17)	−0.20–0.46	0.26 (0.26)	−0.24–0.76	0.17 (0.17)	−0.16–0.50
Differentiated type, without ulceration, any size	0.17 (0.23)	−0.28–0.62	0.32 (0.32)	−0.30–0.94	0.22 (0.24)	−0.25–0.69
Undifferentiated type, ≤2 cm, without ulceration	0.18 (0.24)	−0.29–0.65	0.23 (0.28)	−0.32–0.79	0.18 (0.23)	−0.27–0.64
Submucosal cancer (sm1)						
Differentiated type, ≤3 cm	0.14 (0.20)	−0.25–0.53	0.30 (0.27)	−0.23–0.84	0.22 (0.20)	−0.17–0.61
Conventional criteria						
Intramucosal cancer						
Differentiated type, ≤2 cm, elevated morphology	0.15 (0.18)	−0.20–0.51	0.19 (0.26)	−0.32–0.70	0.14 (0.17)	−0.19–0.47
Differentiated type, ≤1 cm, flat/depressed morphology	0.06 (0.10)	−0.13–0.25	0.12 (0.13)	−0.13–0.37	0.08 (0.09)	−0.10–0.27

All measurements are presented in centimeters. Numbers in parentheses denote standard deviations

recent Korean study demonstrated that the risk of nodal metastasis is not negligible even for tumors that fulfill these criteria [18]. Furthermore, in clinical practice, endoscopists must consider the technical feasibility and potential complications of ESD, as large tumors have a considerable impact on ESD-related perforation and noncurative resection [19, 20]. Consequently, tumor size estimation is important for the proper selection of candidates for endoscopic resection.

In the present study, we found that the accuracy of the endoscopic measurements depended on endoscopist experience. Both endoscopists were found to underestimate tumor diameters, by approximately 0.1–0.3 cm, which is in agreement with the findings of previous studies [21, 22]. On the other hand, another study reported that colonoscopy tended to overestimate tumor size [13]. Further research is required to solve this uncertainty regarding endoscopic estimations of tumor size. However, in the present study, the intraclass correlation coefficient of inter-rater agreement for two endoscopists was 0.915 (95 % CI 0.900–0.928), and the absolute measurement discrepancy between the two endoscopists was acceptable in most cases: 90 % (455/508) of cases had an absolute difference of less than 0.6 cm. In view of different endoscopic experiences in clinical practice, averaged endoscopic measurements should be used. In the present study, averaged measurement discrepancies between endoscopic and pathologic measures are acceptable in most cases [≤0.6 cm was 90 % (455/508) and only 2 % (11/508) of cases had an absolute difference of ≥1.0 cm]. These findings indicate that endoscopic visual estimation could provide a reliable means of determining tumor sizes. When performing ESD as a treatment of EGC, trained endoscopists can predict reliable tumor size by visual estimation, and thus they can make proper selection of patients suitable for ESD.

Although overall measurement accuracy was found to be acceptable, measurement discrepancies were greater for larger tumors and for tumors with an undifferentiated histology. For these tumors, most endoscopic estimations resulted in underestimation. Thus, for larger tumors with an undifferentiated histology, endoscopists should interpret estimated sizes with caution. In particular, endoscopists should note that these tumors are likely to extend more than expected, and, therefore, care should be taken to ensure an adequate tumor-negative lateral margin at the time of endoscopic resection. Essentially, our cohort was drawn from patients scheduled for endoscopic resection, and, thus, larger tumors with an undifferentiated histology only accounted for 14 % (71/511) of cases. Further studies are required to determine the accuracy of tumor size estimations in these tumors.

Several limitations of the present study require further discussion. First, endoscopic visual estimation was performed by trained endoscopists with experience of assessing tumor size, whereas in practice this is likely to be performed by a less experienced endoscopist. Accordingly, additional studies are required to determine the reliability of this method in a practical setting. Second, endoscopic

estimations were carried out retrospectively using still images. Third, one of the endoscopists (S.G.K.) who made endoscopic assessments was the same endoscopist who performed all endoscopic examinations and ESDs. However, he was blinded to the result of the pathological measurements during the review of the endoscopic still images. Moreover, there may be selection bias, because our study included the patients with EGC treated by only ESD or ESD followed by surgical resection, which would be not more than 2 cm in size. If the patients treated initially by surgical resection were enrolled, the endoscopic size estimation might be extended to the larger size of more than 2 cm. Endoscopists underestimated the endoscopic tumor size compared to pathologic measurement. Most cases in the study fulfilled ESD resectability criteria, and thus the endoscopist might be prone to estimate tumor size closer to the 2 cm resectability cutoff. Despite these limitations, this is the first study to be conducted on the endoscopic estimation of gastric tumor size in a large number of EGC patients. We suggest that a further prospective study using video imaging should be performed to confirm the validity of this method.

Summarizing, endoscopic visual estimations of tumor size in EGC patients undergoing endoscopic resection were found to agree well with pathologic measurements and to have acceptable measurement discrepancies. The present study shows that endoscopic estimations provide a feasible means of determining gastric tumor size. Nevertheless, further prospective studies are required to confirm the efficacy of this method.

Conflict of interest There are no financial or other conflicts of interest to disclose.

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