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Prospective Multicenter Feasibility Study of Laparoscopic Sentinel Basin Dissection for Organ Preserving Surgery in Gastric Cancer

Quality Control Study for Surgical Standardization Prior to Phase III Trial

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Abstract: The clinical application of sentinel node biopsies in early gastric cancer is still controversial even though it appears promising. This study was conducted as a prerequisite quality control for surgical standardization of laparoscopic sentinel basin dissection (SBD) prior to the initiation of a phase III trial.

Laparoscopic SBD was performed in patients with preoperative stage T1-2N0 and tumor size <4 cm in diameter. Intraoperative endoscopic submucosal injection of a standardized dual tracer was administered. All retrieved sentinel basin nodes (SBN) were investigated with intraoperative frozen hematoxylin and eosin (H&E) staining. A strict checklist consisting of 7 essential steps was followed during laparoscopic SBD as the quality control study for a phase III trial. Completion of all essential steps in the checklist for 10 cases was used to define a qualified institution.

Seven institutions participated and 112 patients were enrolled in this study. However, 4 patients were excluded owing to screening failure. The mean number of cases required for institutional qualification was 15

cases (range, 13–20 cases). Sentinel basins (SB) were detected and dissected in 100 of the 108 patients (92.6%); the median number of SB and SBN was 2 and 7, respectively. Lymph node metastases were detected in 10 patients by postoperative permanent H&E staining and they were detected by SBD in all 10 patients. Frozen results of SBN were compatible with permanent staining reports.

Laparoscopic SBD is feasible and demonstrated improved sensitivity in detecting metastatic lymph nodes compared to the previous study. A future phase III randomized trial comparing laparoscopic SBD with organ-preserving gastrectomy and laparoscopic standard gastrectomy seems promising for qualified institutions.

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Abbreviations: AJCC = American Joint Committee on Cancer, BN = basin node, CT = computed tomography, EGC = early gastric cancer, EUS = endoscopic ultrasound, GN = green node, H & E = hematoxylin and eosin, HGN = hot and green node, HN = hot node, HSA = human serum albumin, ICG = indocyanine green, IHC = immunohistochemistry, IQR = interquartile range, SB = sentinel basin, SBD = sentinel basin dissection, SBN = sentinel basin node, SN = sentinel node.

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INTRODUCTION

Over the last decade, the proportion of early gastric cancer (EGC) among gastric cancer patients has markedly increased in Korea.¹ The nationwide screening program, which has been implemented since 1999 due to the high prevalence of gastric cancer, seems to have largely influenced the trend toward early detection and improved overall survival in gastric cancer patients in Korea.² As life expectancy became longer after curative surgery in EGC patients, the long-term quality of life of these patients became an important issue. There have been attempts to minimize surgical invasiveness, reduce the surgical extent of standard radical gastrectomy, and preserve remnant gastric function, unless these impair the survival of the patients.

One of these attempts is sentinel node (SN) navigation surgery. The SN concept was first introduced in penile cancer by Cabanas in 1977 and was then developed in melanoma by Morton et al in 1992.^{3,4} Since then, it has been well investigated and adopted in melanoma and breast cancer, allowing a reduction in the extent of surgical intervention with limited lymph node dissection.^{5,6} However, the clinical application of SN biopsy in EGC has long been debated due to the complicated

lymphatic flow around the stomach and the inconsistent results with somewhat unsatisfactory sensitivity reported by previously published studies.^{7,8} However, a recent multicenter trial from Japan showed quite promising results with a low false-negative rate of SN biopsy in early-staged gastric cancer patients.⁹ Based on these results, the Korean Surgical Society planned a multicenter phase III trial comparing conventional laparoscopic gastrectomy to laparoscopic SN biopsy with organ-preserving surgery in patients with clinical stage IA gastric cancer: the trial is currently underway (NCT01804998).¹⁰

In multicenter trials associated with surgical procedures, quality control of the participating institution is essential to achieve optimal outcomes. The present quality control study was conducted as a prerequisite for the phase III trial by all participating institutions (NCT01544413).¹¹ This study aimed to qualify the participating institutions for standardization of their surgical procedures before the phase III trial and also to evaluate the completion of the step-by-step procedure, learning curve, and feasibility of laparoscopic SN biopsy in gastric cancer patients.

PATIENTS AND METHODS

Patients

Patients with histologically confirmed adenocarcinoma in the stomach having clinical stage T1-2N0M0 according to the American Joint Committee on Cancer (AJCC) 7th edition were considered for inclusion in the present study.¹² The clinical stage was determined by preoperative endoscopy and abdominal computed tomography and/or endoscopic ultrasound (EUS); EUS was not routinely performed in all patients enrolled in the present study. Additional preoperative eligibility criteria for the present study included the following: a tumor of <4 cm in the longest diameter under endoscopic measurement; a tumor at least 2 cm from the pylorus or cardia; and age of 20 to 80 years. Patients with tumors satisfying absolute indications for endoscopic resection were excluded from the study. Pregnant patients and patients with a history of drug-related anaphylactic reaction, prior upper abdominal surgery except for laparoscopic cholecystectomy, or radiation therapy were also excluded.

Seven institutions participated in this multicenter prospective quality control study. All patients enrolled in this study were preoperatively registered in a central data center (eVelos System; Velos, Inc., Fremont, CA). All patients provided written informed consent before the surgery. This study was approved by the local institutional review boards of all participating institutions.

Procedures for SBD

A mixture of indocyanine green (IGC; Diagnogreen[®], Daiichi-Sankyo Co., Ltd., Tokyo, Japan; 2 mL, 5 mg) and radio-labeled human serum albumin (Tc^{99m}-HSA; 2 mL, 0.1 mCi/mL) was used as a tracer to detect the SNs. HSA was uniformly prepared at the study center; the quality of HSA was checked with limulus amoebocyte lysate assay and bacterial test. The particle size and radiolabeling efficiency was also verified. The tracer separately prepared at the study center was delivered to the participating institutions. HSA was radiolabeled and then mixed with ICG solution at the department of nuclear medicine at each institution on the day of surgery before the endoscopic procedure. A 4 mL volume of the dual tracer was injected into the submucosal layer in 4 quadrants of the primary tumor (1 mL at each quadrant) via an intraoperative endoscopic approach. After 15 min of the endoscopic tracer injection, stained lymphatics, and

lymph nodes were identified. At the same time, the hand held laparoscopic gamma probe was used to detect the radioactive SNs. The sentinel basins (SBs) containing sentinel nodes (green or hot) were carefully dissected and retrieved from the surgical field.^{13–15}

The harvested SBs were dissected to isolate lymph nodes at a back-table located in the operating room. Lymph nodes stained in green were defined as green nodes (GNs) and those with radioactivity of 10 times or more than background were defined as hot nodes (HNs). Lymph nodes retrieved from the SBs but neither green nor hot were defined as basin nodes (BNs). All the isolated lymph nodes from the SBs, defined as sentinel basin nodes (SBNs), were classified into HN, GN, both hot and green nodes (HGN), and BN, labeled with the respective lymph node station numbers, and sent to the pathologist for intraoperative frozen section.

After sentinel basin dissection (SBD), standard gastrectomy with lymphadenectomy of D1+ or more was carried out in all patients according to the Japanese gastric cancer treatment guidelines.¹⁶

Intraoperative Histologic Examination for SBNs and Permanent Pathologic Examination

The harvested nodes from the SBs were histologically examined intraoperatively by hematoxylin and eosin (H&E) staining using 1 representative cut plane of a frozen section.

After the conventional surgery was completed, the remaining lymph nodes were classified into each lymph node station according to the anatomical definition of the Japanese guidelines and sent for permanent pathologic examination by H&E staining.¹⁷

Checklist and Definition of Qualified Institutions

The protocol was provided under the format of a checklist consisting of 7 critical steps to assess the adequacy of the procedure to be performed by endoscopists, surgeons, and pathologists (Table 1). Success was defined as the accurate execution of all 7 steps.

According to the previously published study from our institution, the learning period for SN mapping was estimated to be 26 cases to achieve a 95% success rate in cumulative sum analysis; the surgeons in the study succeeded in detecting sentinel lymph nodes in 84.6% of the cases during the learning

TABLE 1. Checklist for the Quality Control of the Participating Institution

Is the tracer injected at submucosal layer by intraoperative EGD?
Is the tracer injected at 4 sites by intraoperative EGD?
Is there any intraluminal or extraluminal leakage of tracer during the injection by intraoperative EGD?
Is the tracer injected within 3 min from 1st injection to 4th injection by intraoperative EGD?
Is there at least 1 SB identified during the laparoscopic surgery?
Is the SBN evaluated by intraoperative frozen biopsy?
Is the SBN (HN, GN, HGN, BN) identified at the back table and frozen section at least 5?

BN = basin node, EGD = esophagogastroduodenoscopy, GN = green node, HGN = hot and green node, HN = hot node, SB = sentinel basin, SBN = sentinel basin node.

period.¹⁸ Given that all participants, that is, the endoscopist, surgeon, and pathologist, are required to complete their own steps in the checklist to achieve “success” in the present study, the success rate of completing all 7 steps is estimated to be 31.0% applying a 84.6% success rate for each step. Therefore, success in a minimum of 10 cases at each institution was considered to be sufficient to surpass the initial learning curve and quality control of sentinel node navigation surgery for gastric cancer in the present study, qualifying the institution to participate in the upcoming phase III trial.¹⁰

Interim Analysis

The interim analysis was planned at the time point when 10 patients were enrolled at each institution to evaluate the safety of additional SBD in terms of postoperative complication occurrence compared to the standard surgery. The decision to continue the study was made at the investigators meeting based on the results of the interim safety analysis.

Study Assessment

The primary endpoint was to evaluate the performance of SBD, which was assessed by successful implementation of the checklist. The secondary endpoints were to calculate the detection rate of SBs and SBNs and the sensitivity and false-negative rate of the SBD in identifying metastatic lymph nodes.

Sensitivity and false-negative rate were defined as follows:

$$\text{Sensitivity} = \frac{\text{number of patients with a positive SBN}}{\text{number of patients with lymph node metastasis}} \times 100 (\%)$$

$$\text{False negative rate} = \frac{\text{number of patients with a neegative SBN}}{\text{number of patients with lymph node metastasis}} \times 100 (\%)$$

In addition, positive- and negative-predictive values were calculated to evaluate the predictability of non-SBN metastasis in SBN-positive patients.

$$\text{Positive predictive value} = \frac{\text{number of patients with non-SBN metastasis}}{\text{number of patients with a positive SBN}} \times 100 (\%)$$

$$\text{Negative predictive value} = \frac{\text{number of patients without non-SBN metastasis}}{\text{number of patients with a positive SBN}} \times 100 (\%)$$

RESULTS

The present quality control study was conducted in 7 participating institutions from April 2012 to September 2014; 112 patients were preoperatively enrolled. Interim analyses midway through the study revealed that the study protocol did not jeopardize the safety of the enrolled patients and the

study was continued thereafter. Four patients were excluded from the study because of screening failure (2 patients withdrew after enrolment, 1 double primary cancer, 1 poor bowel preparation for intraoperative endoscopic procedure), which left 108 patients eligible for the final analyses.

Laparoscopy-assisted distal gastrectomy was the most commonly performed surgical procedure after SBD (101/108, 93.5%) (Table 2). Eight patients (7.4%) experienced postoperative complications in the early postoperative period (<30 days), but none were directly related to the additional procedure of SBD.

TABLE 2. Clinicopathologic Characteristics of the Patients (n = 108)

	No. of Patients (%)
Sex	
Male	51 (47.2)
Female	57 (54.8)
Age (y, mean ± SD)	55.3 ± 11.1
BMI (kg/m ² , mean ± SD)	23.6 ± 3.0
Longitudinal locations of tumor	
Lower 1/3	60 (55.6)
Middle 1/3	46 (42.6)
Upper 1/3	1 (0.9)
Unknown	1 (0.9)
Circumferential location of tumor*	
Lesser curvature	31 (27.0)
Greater curvature	31 (27.0)
Anterior wall	28 (24.3)
Posterior wall	24 (20.9)
Unknown	1 (0.9)
Checklist and SBD result	
Success with SBN detection	72 (66.7)
Failure with SBN detection	28 (25.9)
Failure without SBN detection	8 (7.4)
Operation	
LADG	101 (93.5)
LATG	4 (3.7)
LAPPG	1 (0.9)
LPG	1 (0.9)
TLDG	1 (0.9)
Operating time (min, mean ± SD)	223.9 ± 68.6
Pathologic T stage [†]	
pT1a (m)	60 (55.6)
pT1b (sm)	37 (34.3)
pT2 (pm)	4 (3.7)
pT3 (ss)	6 (5.6)
pT4a (se)	1 (0.9)
Pathologic N stage [†]	
pN0	98 (90.7)
pN1	5 (4.6)
pN2	4 (3.7)
pN3	1 (0.9)
Pathologic stage [†]	
IA	90 (83.3)
IB	8 (7.4)
IIA	7 (6.5)
IIB	1 (0.9)
IIIA	1 (0.9)
IIIC	1 (0.9)

	No. of Patients (%)
Pathologic size of tumor (cm, mean ± SD) [‡]	2.5 ± 1.1
Postoperative complications	
Duodenal stump leakage	1 (0.9)
Intraluminal bleeding	1 (0.9)
Pancreatitis	2 (1.9)
Stasis	4 (3.7)

Data are presented as n (%) or mean ± standard deviation. BMI = body mass index, LADG = laparoscopy-assisted distal gastrectomy, LAPPG = laparoscopy-assisted pylorus preserving gastrectomy, LATG = laparoscopy-assisted total gastrectomy, LPG = laparoscopic proximal gastrectomy, SBD = sentinel basin dissection, SBN = sentinel sentinel basin node, SD = standard deviation, TLDG = totally laparoscopic distal gastrectomy.

*Multiple selections were allowed for the tumors lying across the boundaries of each location.

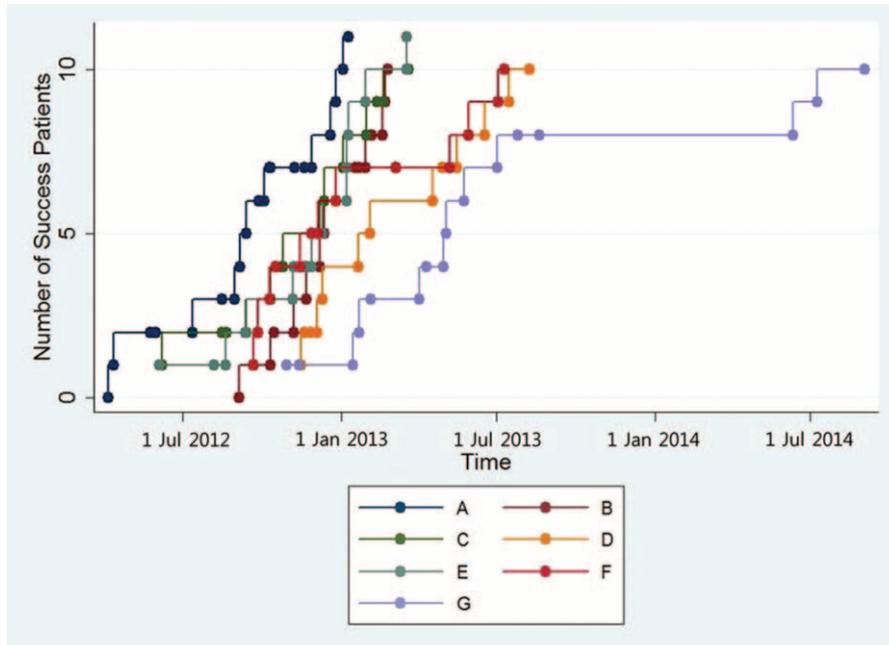
[†]Pathological stage according to 7th edition of American Joint Committee on Cancer staging manual.

[‡]Based on the longest diameter.

The mean number of cases required for institutional qualification was 15 cases (range, 13–20) and success was achieved in 72 out of 108 patients (66.7%) (Fig. 1). The process of patient enrolment and the time frame to complete the quality control study at each institution are schematized in Fig. 1.

SBs were detected and dissected in 100 of 108 patients (detection rate, 92.6%) whether they were designated as a success or not. These included 72 cases of success and additional 28 cases of failure with respect to the checklist completion. All the harvested SBs from these patients were subjected to further analyses to evaluate the characteristics of the SNs. The most frequently detected SB was station no. 3 (n = 64), followed by no. 4d (n = 43) (Table 3). Forty-one patients (41.0%) had 1 SB, 50 (50.0%) had 2, and 9 (9.0%) had 3 SBs. The median number of retrieved SBs was 2 (interquartile range [IQR], 1–2) overall.

The median number of SBNs examined at the back-table was 9 (IQR, 6–12). However, there was some difference in the actual number of identified SBNs by the permanent pathologic examination and the number tended to be smaller (median, IQR; 7, 5–7) (Table 3). More than half were BNs (54.1%), while HNs



Institutions	Total	Success	Failure
A	20	11	9
B	16	10	6
C	14	10	4
D	13	10	3
E	15	11	4
F	13	10	3
G	17	10	7
Total	108	72	36

FIGURE 1. The time frame and the number of cases required to complete the quality control study at each institution.

TABLE 3. Frequency of the Harvested Sentinel Basins at Each Nodal Station and the Mean Number of Identified Sentinel Basin Nodes Among the Patients Whose Sentinel Basins Were Detected (n = 100)

	No. of Patients
Frequency of the SBs*	
Station No. 1	3
Station No. 3	64
Station No. 4sa or 4sb	16
Station No. 4d	43
Station No. 5	11
Station No. 6	19
Station No. 7	8
Station No. 8a	2
Station No. 9	1
Station No. 11d	1
Median number of harvested SBs (median, IQR)	2 (1–2)
Median number of SBNs† (median, IQR)	7 (5–10)
HNs	2 (1–4)
GNs	0 (0–1)
HGNs	0 (0–2)
BNs‡	5 (3–7)

BN = basin node, GN = green node, HGN = hot and green node, HN = hot node, IQR = interquartile range, SB = sentinel basin, SBN = sentinel basin node.

* According to the anatomical definition of the lymph node stations suggested in the Japanese guidelines.

† Based on the postoperative permanent pathologic results by hematoxylin and eosin stain.

‡ Nodes contained in sentinel basin, but not hot nor green.

(28.7%) were the most prevalent among the true SNs based on the permanent pathology test.

Ten patients (9.3%) had lymph node metastasis at permanent pathologic examination by H&E staining. There were no patients with metastasis in non-SBNs alone without metastatic SBs nodes according to the final pathologic results, which indicated 100% and 0% sensitivity and false-negative rate of SBD, respectively (Table 4). In 3 patients, the metastatic lymph nodes were neither hot nor green but confined to the SBs. The positive predictive value of SBD was 40.0% for the metastasis in non-SBNs in patients with positive SBNs.

Lymph node metastasis was detected by intraoperative frozen section in 10 patients (Table 5). No patients were proven to have metastatic node on permanent H&E examination after negative findings on frozen sections and vice versa. Based on these results, the method of intraoperative pathologic examination used in the present study had an accuracy rate of 100.0% in terms of detecting metastatic lymph node when compared to the permanent pathologic results by H&E staining.

DISCUSSION

The present study demonstrated that the quality control for surgical standardization of laparoscopic SBD could be achieved after experience with an average of 15 cases. Based on the detection rate and the sensitivity of this quality control study, laparoscopic SN navigation surgery using SBD is technically

TABLE 4. Evaluation of the Sentinel Basins and Nonsentinel Basins by Postoperative Pathologic Examination With Hematoxylin and Eosin Stain (n = 100)

No. of Patients	Non-SBN (+)	Non-SBN (–)
SBN (+)	4	6
SBN (–)	0	90
Sensitivity		100%
False-negative rate		0%
Positive predictive value*		40%
Negative predictive value*		100%

SBN = sentinel basin node.

* In predicting nonsentinel basin node metastasis in sentinel basin node-positive patients.

feasible and can be safely applied in the upcoming phase III clinical trial.¹⁰

The checklist used in the present study consisted of 7 items describing mandatory requirements for performing the SBD. The details of the checklist were established via comprehensive discussion among participating investigators. The checklist not only involves surgeons but also demands that endoscopists and pathologists follow specific steps during the procedure; 4 items are directly related to the endoscopic procedures; 2, to surgeons; and 2, to pathologists. This indicates that close cooperation among these participants is essential to complete the checklist, which will be required in the subsequent phase III clinical trial to achieve optimal outcomes from SBD in gastric cancer.

The number of cases required for quality control in the present study was on average 15 due to the reduced failure rate, which was below the estimated number based on the 26 cases of the learning curve in the previous report.¹⁸ Plausible reasons could include: prior experience with SN biopsy in gastric cancer at most of the participating institutions,^{13,19–21} repeated review of the instructional video, in-depth discussion of the lessons learned through trial and error in prior experience, and expertise in laparoscopic surgery of all the participating surgeons. Nonetheless, the accuracy and the sensitivity of SBD appeared to be

TABLE 5. Number of Patients With Metastatic Sentinel Basin Nodes

	Frozen Section	H&E Stain
HNs	4 (7)	4 (7)
GNs	3 (4)	3 (4)
HGNs	5 (5)	5 (5)
BNs*	6 (7)	7 (8)†
Total	10 (23)	10 (24)

The figures are presented as the number of patients (the number of tumor positive nodes). H&E = hematoxylin and eosin, HN = hot node, GN = green node, HGN = hot and green node, BN = basin node.

* Nodes contained in sentinel basin, but not hot nor green.

† In 1 patient, the number of HNs, GNs, and BNs were 6, 5, and 17, respectively. Since the GNs and the HNs were proven tumor-positive earlier during the intraoperative pathologic examination and the number of total sentinel basin nodes was too many, the BNs were not sent further for the frozen section.

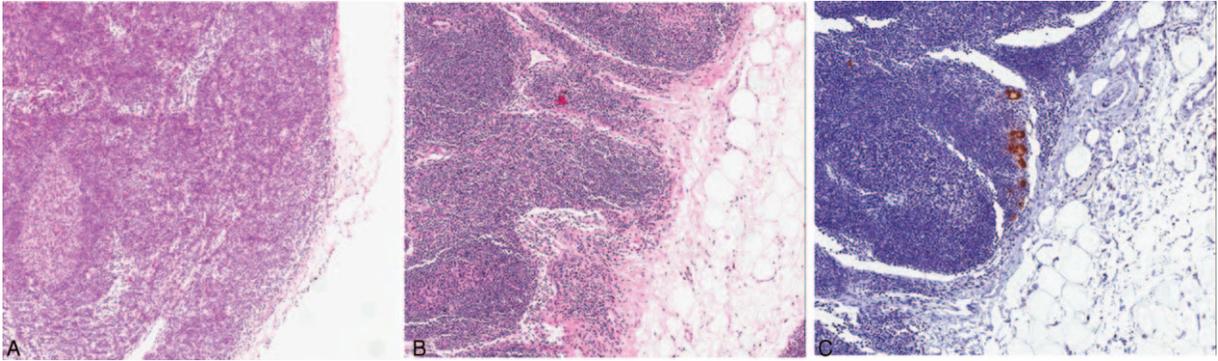


FIGURE 2. Microscopic view of the micrometastatic lymph node detected by additional immunohistochemistry (IHC) with cytokeratin. (A) Frozen section with hematoxylin and eosin (H&E) staining, (B) permanent pathology by H&E stain, and (C) IHC with cytokeratin.

acceptable in the present study indicating that the SBD is feasible as long as the participants adequately comply with the details of each step in the checklist.

Several factors appeared to influence the surgical performance of SBD in the present study. The primary tumors located at the lesser curvature were usually more difficult to deal with than those at the greater curvature. It might be attributable to more complicated lymphatic drainage and vascular structures; the tracers sometimes spread diffusely and quickly to the second tier nodal stations causing difficulties in determining the exact range of SBs. SBs in lesser curvature were also subjected to frequent bleeding during surgery due to abundant blood supply. Tumors near the pyloric ring or esophagogastric junction were tricky to handle because it is easy to damage major nerve branches during SBD.

The dual tracer of dye and radioisotope is known to provide high detection rate of SNs and better sensitivity than the dye-guided method.^{22,23} The dye washes out and flows into the second tier nodes quickly because it is small in size and water soluble; this, however, makes it difficult to identify GNs at the back-table. The present study also showed that a very small number of true GNs remained after back-table dissection. It is particularly difficult to directly visualize stained nodes in a deep-seated area, particularly in patients with visceral obesity. The radioisotope serves as a supplementary measure to compensate for the low retention rate and poor visibility of the dye method. Although radiolabeled tin colloid has been used in most studies regarding SN biopsy in gastric cancer, the relatively large particle size resulted in slow migration and a redundant endoscopic procedure was required before surgery.⁹ The small particle-sized HSA (2–3 nm) used in the present study served as an ideal tracer to be applied during the surgery simultaneously with ICG. HSA is very stable, readily available, and biodegradable and with reduced potential for allergic reactions.^{14,24,25} The use of the dual tracer resulted in a 92.6% detection rate of SBs in the present study, which is within the range of reported rates of 91.2% to 97.5% in previous studies using dual tracer methods.^{9,13,22} Since the present study included cases during the learning period, the SB detection is expected to further improve in future studies.

Miyashiro et al reported a high false-negative rate in the Japanese multicenter trial (JCOG0302 trial) that was a result of the unreliability of the frozen section examinations using only a single plane.²⁶ Nonetheless, the present study demonstrated a 100% accuracy rate of intraoperative H&E staining using bivalve frozen sections. All patients with lymph node metastasis

by permanent H&E stain were identified by intraoperative pathologic diagnosis using H&E stain on bivalve frozen sections. However, 1 participating institution routinely performed immunohistochemistry (IHC) with cytokeratin for gastric cancer patients in parallel with the appointed protocol in the present study. The additional IHC revealed that 1 patient with submucosal cancer had micrometastasis in 1 of the HNs that was not detected by H&E staining (Fig. 2) and there were no additional lymph nodes with evidence of metastasis. Thus, is it truly necessary to adopt more precise intraoperative diagnostic methods, such as step section analysis, rapid IHC, or real-time reverse transcriptase polymerase chain reaction, for SN navigation surgery for gastric cancer? In the ordinary clinical setting, these appear to be neither clinically practical nor universally feasible, and furthermore, costly and time consuming. Some investigators suggested the application of SBD instead of pick-up biopsy of individual SNs.^{13,15} Kitagawa et al revealed that all patients with a false-negative intraoperative pathologic diagnosis proved to have metastatic spread confined to the SNs per se or within the SBs.⁹ The present study also showed consistent results demonstrating that all patients with node metastasis were successfully identified by adopting the SBD method because positive nodes were present within the SBs even in those without HN or GN involvement. Although the number of relevant cases in the present study was very small due to the low incidence of lymph node metastasis in EGC, this indicates that SBD instead of pick-up biopsy can compensate for an incomplete intraoperative pathologic examination. Even if a true metastatic node were falsely diagnosed as negative intraoperatively, the node would have been already cleared during SBD and, consequently, would not have any critical influence on the disease-free survival of the patient. However, long-term results with disease-free survival need to be investigated in well-designed studies in the future.

The risk of skip metastasis seems to be very low in EGC given the results of the present study demonstrating 0% detection of metastasis in non-SBs node alone with no metastatic SBs nodes. In previously published literature, tumor size was reported to be closely related to the presence of skip metastasis in EGC patients.^{27,28} Tumor size is also important in the control of primary tumor during SN navigation surgery to secure safe margins, as the accuracy in measurement of tumor size generally decreases in larger tumors.²⁹ Therefore, the indications for SN navigation surgery should be limited to small-sized tumors and it should be strictly respected in the upcoming phase III clinical trial to minimize the false-negative rate and insufficient

treatment. Nonetheless, the relatively high positive predictive value in the present study suggests that cancer-positive SBNs are strongly suggestive of the probability of non-SB involvement even in EGC patients. When the intraoperative pathologic examination reveals the presence of metastasis in SBNs, standard radical lymph node dissection is imperative in order to prevent the risk of not eliminating metastatic lymph nodes.

The present quality control study has shown that laparoscopic SBD is feasible and applicable in EGC patients with improved sensitivity compared with previous studies. This study has provided a basis for the planned phase III randomized trial comparing laparoscopic SBD with organ-preserving gastrectomy to conventional laparoscopic distal or total gastrectomy for qualified institutions. The future phase III trial is expected to corroborate the oncologic safety as well as the clinical benefit of organ-preserving gastrectomy with SBD in terms of quality of life in EGC patients.

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