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MSG Version 1.0

A multicenter, prospective, single arm clinical trial on the Feasibility of Middle Segmental Gastrectomy (MSG)

Version 1.3

Feature	Details
Study Title	A multicenter prospective single-arm clinical trial on the Feasibility of Middle Segmental Gastrectomy (MSG)
Version	1.3
IRB Number	NCC2025-0169
Funding Information	National Cancer Korea, Korea (NCC2542380-1)
Version Date	Aug. 06, 2025
Principal Investigator	Kim Young-woo, MD, PhD (Department of Gastric Cancer Surgery, National Cancer Center)
Study Phase	Phase 2 (Feasibility Study)
Design	Single Group, Interventional, Prospective, Multicenter
Total Study Duration	72 months from IRB approval

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Study Overview

Study title	A multicenter prospective single arm clinical trial on the Feasibility of Middle Segmental Gastrectomy (MSG)
Version	1.3
Study Objectives	This study aims to evaluate the short- and long-term outcomes of Middle Segmental Gastrectomy (MSG) in patients with gastric cancer, and to demonstrate its safety, feasibility, and clinical applicability.
Primary Endpoint	Incidence of Dumping Syndrome at 1 Year Postoperatively (Sigstad Score ≥7)
Secondary Endpoints	1. **Postoperative reflux symptoms**. 2. **Postoperative changes in weight, hemoglobin, glucose, serum iron, vitamin B12, albumin, and total protein levels**. 3. **Postoperative complications**. 4. **Mortality within 30 days of surgery**. 5. **Postoperative quality of life (EORTC QLQ-C30 and STO22)**. 6. **Three-year recurrence-free survival and overall survival**
Study design	1. Study Phase: Phase 2 (Feasibility Study) 2. Intervention Model: Single Group Assignment 3. Study Type: Interventional 4. Study Perspective: Prospective 5. Participating Centers: Multicenter
Study period	- Patient enrollment period: IRB approval date to 24 months after approval date - Intervention period: IRB approval date to 24 months after approval date - Participant study duration: IRB approval date to 60 months after approval date - Data collection period: IRB approval date to 60 months after approval date - Evaluation and analysis period: 12 months after completion of data collection - Total study duration: IRB approval date to 72 months after approval date

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<table>
<tr><td>Study Participants</td><td>1. Patients with gastric adenocarcinoma that is 4 cm or less in size, preoperative tumor location is in the mid or high body of the stomach, any histological diffeentiation, and preoperative stage is cT1N0/1M0 (reference)
2. Patients whose size is 4 cm or less, the tumor is located in the mid or high body of the stomach, the differentiation is well or moderate, the boundaries of the lesion are clear on endoscopy, and the stage cT2/3N0/1M0(reference)</td></tr>
<tr><td>Sample size</td><td>. 1) Set a hypothesis
The purpose of this study is to evaluate whether the incidence of Dumping Syndrome at 1 year postoperatively in the Middle Segmental Gastrectomy (MSG) group is statistically significantly different from the incidence of 15.8% (=p_0) in the Laparoscopic Distal Gastrectomy (LDG) group reported in the ~~original~~ KLASS 04 study.(reference) The statistical hypothesis for this study is as follows:
-Null hypothesis (H_0): p = 0.158
-Null hypothesis (H_1): p ≠ 0.158
The study will last a total of 5 years, including a 2-year patient recruitment period and a 3-year follow-up period from the last patient enrolled. The primary endpoint will be the incidence of dumping syndrome at 1 year post-operatively, and will examine whether the incidence in the MSG group is significantly lower than in the LDG group.

2) Calculate the number of audiences
As a preliminary study to calculate the number of subjects for this study, postoperative patients who visited the National Cancer Center outpatient department between March 20, 2025 and April 17, 2025 were assessed for the presence of dumping syndrome. The assessment utilized the Sigstad questionnaire, with a Sigstad score of 7 or higher defined as having dumping syndrome.
A total of 221 patients (Distal Gastrectomy (DG): 150, Proximal Gastrectomy (PG): 18 patients, Pylorus-Preserving Gastrectomy (PPG): 12, Total Gastrectomy (TG): 30 patients, Wedge Resection (WR): 11), the incidence of dumping syndrome by type of surgery was as follows:
<table><tr><th>Surgery type</th><th>Incidence of dumping</th></tr></table></td></tr>
</table>

	<table><tr><th></th><th>syndrome</th></tr><tr><td>DG</td><td>15% (23/150)</td></tr><tr><td>PG</td><td>22% (4/18)</td></tr><tr><td>PPG</td><td>0% (0/12)</td></tr><tr><td>TG</td><td>20% (6/30)</td></tr><tr><td>WR</td><td>0% (0/11)</td></tr></table> Among them, PPG is similar to the MSG surgery method that was performed in this study, so it can be used to estimate the likelihood of dumping syndrome in the MSG groupand the incidence of dumping syndrome in this group was 0% (0/12). However, the survey was conducted independent of the timing of the postoperative outpatient visit, and the time of survey response varied from 30.52 to 33.33 months postoperatively on average, depending on the type of surgery. This is different from the primary endpoint of this study, 1 year after surgery, and the small sample size of PPGs should be considered as a possible difference from the actual incidence. For this study, we conservatively assumed a dumping syndrome incidence rate of 5%($= p_a$) and calculated the number of subjects required using a one-sample proportion test with a power of 80% and a two-sided significance level of 0.05. 70 subjects were required, and a dropout rate of 10% was considered, resulting in 78 subjects. ■ **The result of the formula calculation** $$n = \frac{\left(z_{1-\frac{\alpha}{2}}\sqrt{p_0(1-p_0)} + z_{1-\beta}\sqrt{p_a(1-p_a)}\right)^2}{(p_0 - p_a)^2}$$ $$= \frac{\left(1.96\sqrt{0.158(1-0.158)} + 0.84\sqrt{0.05(1-0.05)}\right)^2}{(0.158 - 0.05)^2}$$ $$= 69.13$$ $$\cong 70$$ (i) Consider a 10% dropout rate: $n' = \frac{n}{(1-0.1)} = 77.78 \cong 78$
Study Methods	1. With the patient's consent, perform a Totally Laparoscopic Middle Segmental Gastrectomy (TLMSG). 2. surgical method and extent of lymph node dissection ① Perform laparoscopic Middle Segmental Gastrectomy (MSG) and

	lymph node dissection. (Resecting the middle segment of the stomach with a minimum 2-3 cm resection margin from the tumor, preserving the vascular branches (specifically, the right gastroepiploic artery and left gastroepiploic artery) along the lesser and greater curvature of the stomach. ② LN excision range is Nos. 1, 3, 4sb, 4d, 7, 8a, 9 (omitting Nos. 5 & 6) ③ Reconstruction: Modified delta shaped anastomosis using a straight automated anastomosis machine under laparoscopy. ④ Check for bleeding and anastomotic leaks ⑤ Suturing the abdominal wall after inserting a drain 3. Analyze incidence of postoperative dumping syndrome, survival, nutritional changes, postoperative symptoms and quality of life, gallstone incidence, postoperative endoscopic findings, etc.
Inclusion Criteria	① Diagnosed with gastric adenocarcinoma by tissue biopsy and capable of middle segmental gastrectomy by meeting the following oncologic characteristics on preoperative examination - The tumor is located in the mid body or high body - The tumor is 4 cm or less in size as described in endoscopy - cT1N0 or cT1N1, any differentiation - -cT2N0 or T2N1, well-differentiated or moderately-differentiated adenocarcinoma ~~②~~ Adult patients age 20 and older ③ ECOG performance is between 0 and 2 ④ ASA score class I – III ⑤ Signed written informed consent, approved by the institutional review board, to participate in this study freely and voluntarily, after being fully informed of the purpose, content, and risks of the study prior to participation.
Exclusion Criteria	① Borrmann type 4 stomach cancer ② Multiple gastric cancers or comorbid malignancies ③ Boundaries of the lesion are unclear

	④ Clear mesenteric infiltration (T4) was determined at surgery. ⑤ Two or more lymph node infiltrates are visually connected at the time of surgery. ⑥ Patients with other malignancies that affect gastric function preservation metrics - A history of cancer in other organs - Cancer in other organs - ~~Patients with~~ A history of gastrectomy surgery ⑦ Vulnerable populations (incapacitated, pregnant, or planning to become pregnant) ⑧ Other patients deemed difficult to study
Efficacy endpoints	**Primary endpoint:** Incidence of Dumping Syndrome (Sigstad score ≥7) at 1 year postoperatively **Secondary** • Reflux symptoms after surgery • Post-operative changes in weight, hemoglobin, serum iron, vitamin B12, albumin, total protein level • Postoperative complications • **Mortality within 30 days of surgery** • Postoperative quality of life (QOL) assessment: EORTC QLQ-C30/STO22 • 3-year recurrence-free survival and overall survival
Safety assessment	Postoperative complication rates and mortality
Evaluation	3 weeks, 3, 6, 12, 18, 24, 30, 36 months post-op Dumping Syndrome Symptom Questionnaire and Blood Sugar Change Analysis Gastroscopy and computed tomograpy(ACT) Blood tests:
Statistical Analysis	**1. Primary Efficacy Endpoint** • **Incidence of Dumping Syndrome (Sigstad score $₩ge$ 7) at 1**

	year postoperatively:, • In the **ITT analysis of the KLASS 04 study**, the incidence of dumping syndrome at 1 year after surgery was reported to be **15.8% in the LDG group**., • This study performs a **one-sample proportion test** to evaluate whether the difference in frequency between the MSG group and the 15.8% reported for the LDG group in the KLASS 04 study is statistically significant., **2. Secondary Efficacy Endpoints** ** (1) Reflux Symptoms**, • ① **Subjective symptoms (Visick score)** are categorized by grade and presented as frequency and percentage (%). • ② **Endoscopy results for reflux esophagitis (endoscopic LA classification)** are presented as frequency and percentage (%)., ** (2) Nutritional Indicators**, • **Changes in postoperative weight, hemoglobin, glucose, serum iron, vitamin B12, albumin, and total protein levels.**, • To evaluate changes from preoperative baseline to 36 months postoperatively, a **linear mixed-effects model (linear mixed model)** is utilized for analysis. • The results will include **predicted means** and **95% confidence intervals** for each time point. ** (3) Complications and Mortality** • **Early and late postoperative complications** and **mortality within 30 days of surgery** are presented as frequencies and percentages (%)., ** (4) Quality of Life (QOL)**, • QOL is measured preoperatively and at **3, 12, 24, and 36 months postoperatively** using **EORTC QLQ-C30 and STO22**.,, • For each time point, the **mean $₩pm$ standard deviation** and the amount of change from the preoperative baseline are presented. • **EORTC QLQ-C30 analysis:** Includes 5 functional scales (physical, role, emotional, cognitive, and social functioning), 3 symptom scales

	(fatigue, pain, and nausea/vomiting), 1 global health status, and 6 single items., • **EORTC-STO22 analysis:** Includes 5 gastric cancer surgery-related scales (dysphagia, eating restriction, pain, reflux, and anxiety) and 4 single items (dry mouth, body image, taste, and hair loss)., ** (5) Survival Rates**, • **3 year Disease-free survival (DFS):**, o The **Kaplan-Meier Method** is used to estimate the median DFS and its 95% confidence interval., o DFS is defined as the time from the time of surgery (randomization) to postoperative recurrence or death; for censored patients, it is the time from the time of surgery to the last follow-up (censoring)., • **Overall survival (OS):**, o The **Kaplan-Meier Method** is used to estimate the median OS and its 95% confidence interval., o OS is defined as the time from surgery to death; for censored patients, it is the time from surgery to the last follow-up (censoring).,
Expected Outcomes and Academic Significance	**The optimization of gastric cancer surgery**, specifically through function-preserving techniques like **Middle Segmental Gastrectomy (MSG)**, can significantly **improve patient quality of life** by preserving digestive functions and minimizing common postoperative issues such as **dumping syndrome** and nutritional deficiencies. Furthermore, this research holds **high academic value** as it seeks to **establish a new standard of care** and clinical guidelines where none previously existed, potentially advancing the field of minimally invasive, function-sparing gastric surgery. This refinement aligns with the study's stated goals of evaluating the safety, utility, and clinical applicability of MSG to improve long-term outcomes for patients with mid- or high-body gastric cancer

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Research plan

1. study title

A multicenter prospective single arm clinical trial on the Feasibility of Middle Segmental Gastrectomy (MSG)

2. the name and address of the organization conducting the study

(Institution Name) National Cancer Center Gastric Cancer Center

(Address) 323, Ilsan-ro, Ilsandong-gu, Goyang-si, Gyeonggi-do, Republic of Korea

3. principal investigator and co-investigator names and titles

1) Principal Investigator

Youngwoo Kim, MD, Center for Gastric Cancer, Research Institute& Hospital, National Cancer Center, Goyang, Korea

2) Co-investigators

Keun-Won Ryu, MD Center for Gastric Cancer, Research Institute& Hospital, National Cancer Center, Goyang, Korea

Hong-Man Yoon, Center for Gastric Cancer, Research Institute& Hospital, National Cancer Center, Goyang, Korea

Bang Wool Eom, Center for Gastric Cancer, Research Institute& Hospital, National Cancer Center, Goyang, Korea

3) Collaborators

Clinical trial sites and investigators

Name	Institution	Position	Major

Dongjin Kim	Catholic University of Korea Eunpyeong St. Mary's Hospital	Associate Professor	Surgery
Shin Hye Park	Catholic University of Korea Eunpyeong St. Mary's Hospital	Assistant Professor	Surgery
Sung Gon Kim	Konyang University Hospital	Assistant Professor	Surgery
Jiyeon Park	Chilgok Gyeongbuk National University Hospital	Associate Professor	Surgery
Hyung Il Kim	Severance Hospital	Professor	Surgery
Sung-Yeop Ryu	Chosun University Hospital	Professor	Surgery
Sa-Hong Min	Asan Medical Center	Assistant professor	Surgery
Hyuk-Joon Lee	Seoul National University Hospital	Professor	Surgery
Yun-Suhk Suh	Seoul National University Hospital	Associate Professor	Surgery
Do Joong Park	Seoul National University Hospital	Professor	Surgery
Sang-hoon Ahn	Samsung Medical Center	Assistant Professor	Surgery
O Kyoung Kwon	Kungpook National University Hospital	Professor	Surgery
Sung Gon Kim	Konyang University Hospital	assistant professor	Surgery
Jong Won Kim	Chung-Ang University Gwangmyeong Hospital	associate professor	Surgery
Jong Han Kim	Korea University Ansan Hospital	Professor	Surgery
Joong-Min Park	Chung-Ang University Gwangmyeong Hospital	Professor	Surgery
Yong Hae Baik	Dongguk University Medical Center	Professor	Surgery
Sang Su Eom	University Ilsan Paik Hospital	Assistant professor	Surgery

4. Sponsor

Not applicable

5. study design and expected study duration

- Clinical trial phase: phase 2 (feasibility study)

- Intervention Model: single group

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- Interventional studies

- Research perspective: prospective

- Participating Institution: multicenter

- IRB approval date to 72 months after approval

6. Target disease for this research

1. Patients with gastric adenocarcinoma that is 4 cm or less in size, preoperative tumor location is in the mid or high body of the stomach~~upper trunk~~, and preoperative staging is cT1N0/1M0
2. Patients with a size of 4 cm or less, preoperative tumor location is in the mid or high body of the stomach, well to moderate differentiation, clear boundaries of the lesion on endoscopy, and staging cT2N0/1M0

7. Background and purpose of the study

(1) Research Background

1. Introduction

Gastric cancer (GC) is the fifth most commonly diagnosed cancer worldwide and the third leading cause of cancer deaths. In recent years, the proportion of early gastric cancer and gastric cancer without lymph node metastasis has been increasing in Korea, thanks to advances in screening and diagnostic techniques. In addition, surgical approaches are evolving with the introduction of minimally invasive surgery. Also globally, improving quality of life of the patients underwent gastric surgery is important issue.

2. conventional gastrectomy and function-sparing surgery

Distal gastrectomy (DG) and total gastrectomy (TG) are recognized as standard and safe procedures for the treatment of middle-body (MB) and high-body (HB) gastric cancer.

However, these surgeries are associated with Postgastrectomy Syndrome, which can decrease the patient's quality of life. Therefore, function-preserving surgeries with optimal lymph node dissection, such as Pylorus-Preserving Gastrectomy (PPG), Segmental Gastrectomy (SG), and Proximal Gastrectomy (PG), improve postoperative quality of life in selected patients has been developed(Reference) , and various surgical approaches ~~to~~ are being investigated.

3. What is a middle segmental gastrectomy (MSG) and its benefits

MSG resects the middle portion of the stomach while preserving the pylorus and upper portion of the stomach (cardia and fundus), which allows for preservation of digestive function and minimizes dumping syndrome and nutritional deficiencies. While conventional gastrectomy has contributed to improved survival rates, it is often associated with functional loss and poor postoperative quality of life. MSG has been recognized as an alternative to address these issues.

Middle Segmental Gastrectomy (MSG) is defined as a small circumferential gastrectomy that preserves the pylorus and segments, which does not include the PPG. Since the first variation of SG for GC, there has been very limited research on the safety and benefits of MSG.

For the oncological safety, adequate lymph node dissection is a key determinant of the extent of the surgery. We have explored large scale data and found the appropriate indication for the middle segmental gastrectomy, which is a inclusion criteria of this study.

4. Definition and Advantages of Middle Segmental Gastrectomy (MSG)

MSG does not require resection of LN station 6, which must be performed in PPG. In addition, MSG allows for preservation of a longer segment of the pyloric antrum, which may improve functional outcomes.

PPG is generally indicated for cancers in the lower and mid Body, while PG is appropriate for cancers in the Upper Third. However, if the cancer is located in the MB or HB, MSG may be considered, which may minimize the risk of GERD. In addition, MSG can achieve a larger residual volume compared to other function-preserving surgeries, which can contribute to better functional outcomes and improved quality of life.

5. Preliminary study and the purpose of this study

A previous cohort study of patients with gastric cancer who underwent surgery at the National Cancer Center from January 2000 to December 2015 confirmed that cT1N0M0 and cT1N1M0 gastric cancers with tumors 4 cm or smaller can undergo MSG without major lymph node (LN) dissection. However, surgeons may consider MSG in T1-staged gastric cancer if endoscopic submucosal dissection (ESD) is not an indication.

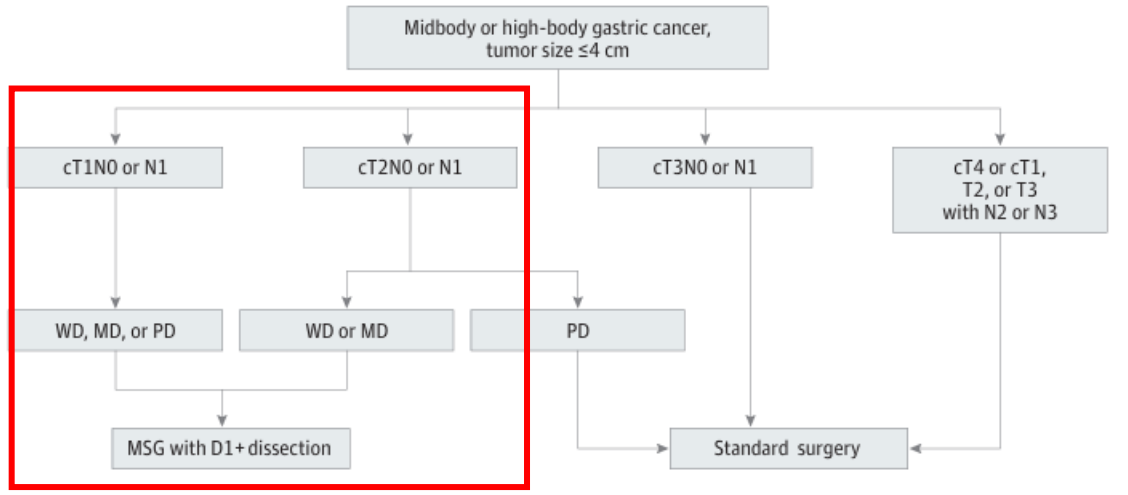
For cT2N0M0 and cT2N1M0 gastric cancer, we found that undifferentiated (PD) gastric cancer had an increased rate of metastasis to LN station 2, indicating the need for either standard resection or proximal segmentectomy (PG) with corresponding lymph node dissection. However, in well-differentiated (WD) and moderately differentiated (MD) cT2N0M0 and cT2N1M0 gastric cancers of 4 cm or less, the major lymph node zone metastasis rate was close to 0%, confirming that MSG can be safely performed.

The figure below presents an algorithm to analyze the applicability of MSG in middle-body (MB) and high-body (HB) gastric cancer, which we aim to validate in this clinical study.

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Figure. Algorithm of Middle Segmental Gastrectomy (MSG) for Middle-Body and High-Body Gastric Cancer



JAMA Network Open. 2021;4(3):e211840. doi:10.1001/jamanetworkopen.2021.1840

The primary objective of this study is to evaluate the incidence of dumping syndrome at 1 year postoperatively after MSG and to test whether the difference from the 15.8% frequency of dumping syndrome in LDG at 1 year postoperatively published in the ITT analysis of the KLASS 04 study (2) is significant. In addition, we aim to determine the short-term and long-term outcomes of Middle Segmental Gastrectomy in patients with gastric cancer and to demonstrate the safety, utility, and clinical applicability of Middle Segmental Gastrectomy.

(2) Research

The purpose of this study is to determine the short-term and long-term outcomes of Middle Segmental Gastrectomy in patients with gastric cancer and to demonstrate the safety, utility, and clinical applicability of Middle Segmental Gastrectomy.

1) Primary objective: Incidence of dumping syndrome (Sigstad score ≥7) at 1 year postoperatively

2) Secondary Goals

① **Postoperative reflux symptoms**.

② **Postoperative changes in weight, hemoglobin, glucose, serum iron, vitamin B12,**

albumin, and total protein levels.

③ **Postoperative complications**.

④ **Mortality within 30 days of surgery**.

⑤ **Postoperative quality of life (EORTC QLQ-C30 and STO22)**.

⑥ **Three-year recurrence-free survival and overall survival**

8. inclusion criteria, exclusion criteria, targeted number of subjects and rationale for calculations

(1) Selection Criteria

① Diagnosed with gastric adenocarcinoma by tissue biopsy and capable of middle segmental gastrectomy by meeting the following oncologic characteristics on preoperative examination

- If the tumor is located in the high body or mid body

- The tumor is 4 cm or less in size

- cT1N0 or cT1N1, any differentiation and cT2N0 or cT2N1 , well-differentiated or moderately-differentiated adenocarcinoma

Adult patients age 20 and older

ECOG performance is between 0 and 2

④ ASA score class I - III

Signed written informed consent, approved by the institutional review board, to participate in this study freely and voluntarily, after being fully informed of the purpose, content, and risks of the study prior to participation.

(2) Exclusion Criteria

① Borrmann type 4 stomach cancer

② Multiple gastric cancers or comorbid malignancies

③ boundaries of the lesion are unclear

④ Patients who have received chemotherapy or radiation for stomach cancer prior to surgery

⑤ Clear mesenteric infiltration was determined at the time of surgery.

⑥ Two or more lymph node infiltrates are visually connected at the time of surgery.

⑦ Patients with other malignancies that affect gastric function preservation metrics

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- You have a history of cancer in other organs
- You currently have cancer in other organs
- Patients with a history of gastrectomy surgery

⑧ Vulnerable populations (incapacitated, pregnant, or planning to become pregnant)

⑨ Other patients deemed difficult to study

(3) The number of people you've targeted and for the calculation

1) Set a hypothesis

The purpose of this study is to evaluate whether the incidence of Dumping Syndrome at 1 year postoperatively in the Middle Segmental Gastrectomy (MSG) group is statistically significantly different from the incidence of 15.8% ($=p_0$) in the Laparoscopic Distal Gastrectomy (LDG) group reported in the original KLASS 04 study. The statistical hypothesis for this study is as follows:

-Null hypothesis (H_0): $p = 0.158$

-Null hypothesis (H_1): $p \neq 0.158$

The study will last a total of 5 years, including a 2-year patient recruitment period and a 3-year follow-up period from the last patient enrolled. The primary endpoint will be the incidence of dumping syndrome at 1 year post-operatively, and will examine whether the incidence in the MSG group is significantly lower than in the LDG group.

2) Calculate the number of audiences

As a preliminary study to calculate the number of subjects for this study, postoperative patients who visited the National Cancer Center outpatient department between March 20, 2025 and April 17, 2025 were assessed for the presence of dumping syndrome. The assessment utilized the Sigstad questionnaire, and a Sigstad score of 7 or higher was defined as having dumping syndrome.

A total of 221 patients (Distal Gastrectomy (DG): 150, Proximal Gastrectomy (PG): 18 patients, Pylorus-Preserving Gastrectomy (PPG): 12, Total Gastrectomy (TG): 30 patients, Wedge Resection (WR): 11), the incidence of dumping syndrome by type of surgery was as follows:

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Surgery type	Incidence of dumping syndrome
DG	15% (23/150)
PG	22% (4/18)
PPG	0% (0/12)
TG	20% (6/30)
WR	0% (0/11)

Of these, PPG is similar to the MSG surgery performed in this study, so this allows us to estimate the likelihood of dumping syndrome in the MSG groupand the incidence of dumping syndrome in this group was 0% (0/12). However, the survey was conducted independent of the timing of the postoperative outpatient visit, and the time to respond to the survey varied from 30.52 to 33.33 months postoperatively on average, depending on the type of surgery. This is different from the primary endpoint of this study, which is 1 year after surgery, and the small sample size of PPGs should be considered as a possible difference from the actual incidence.

For this study, we conservatively assumed a dumping syndrome incidence rate of 5%($= p_a$) and calculated the number of subjects required using a one-sample proportion test with a power of 80% and a two-sided significance level of 0.05. 70 subjects were required, and a dropout rate of 10% was considered, resulting in 78 subjects.

- **The result of the formula calculation**

$$
\begin{aligned}
n &= \frac{\left(z_{1-\frac{\alpha}{2}}\sqrt{p_0(1-p_0)} + z_{1-\beta}\sqrt{p_a(1-p_a)}\right)^2}{(p_0 - p_a)^2} \\
&= \frac{\left(1.96\sqrt{0.158(1-0.158)} + 0.84\sqrt{0.05(1-0.05)}\right)^2}{(0.158 - 0.05)^2} \\
&= 69.13 \\
&\cong 70
\end{aligned}
$$

(ii) Consider a 10% dropout rate: $n' = \frac{n}{(1-0.1)} = 77.78 \cong 78$

- **PASS calculation results**

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PASS 2024, v24.0.2 2025-04-22 오후 1:13:34 1

Tests for One Proportion

Numeric Results

Solve For: Sample Size
Test Type: Exact Test
Alternative Hypothesis: Two-Sided (H0: P = P0 vs. H1: P ≠ P0)

		Proportion				
Power*	Sample Size n	Null P0	Alternative P1	Alternative Difference P1 - P0	Alpha	Reject H0 If R ≤ | R ≥
0.80672	70	0.158	0.05	-0.108	0.05	4 | 18
0.90122	85	0.158	0.05	-0.108	0.05	6 | 21

* Power was computed using the normal approximation method.

Power	The probability of rejecting a false null hypothesis when the alternative hypothesis is true.
n	The size of the sample drawn from the population.
P0	The value of the population proportion under the null hypothesis.
P1	The value of the population proportion under the alternative hypothesis.
P1 - P0	The difference to be detected by the study.
Alpha	The probability of rejecting a true null hypothesis.
Reject H0 If...	Gives the critical value(s) for the test.

Summary Statements

A single-group design will be used to test whether the proportion is different from 0.158 (H0: P = 0.158 versus H1: P ≠ 0.158). The comparison will be made using a two-sided, one-sample exact test, with a Type I error rate (α) of 0.05. To detect a difference (P1 - P0) of -0.108 with 80% power, 70 subjects will be needed. The sample size was computed using PASS 2024, version 24.0.2.

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Lachin, John M. 2000. Biostatistical Methods. John Wiley & Sons. New York.

Machin, D., Campbell, M., Fayers, P., and Pinol, A. 1997. Sample Size Tables for Clinical Studies, 2nd Edition. Blackwell Science. Malden, Mass.

Ryan, Thomas P. 2013. Sample Size Determination and Power. John Wiley & Sons. Hoboken, New Jersey.

Zar, Jerrold H. 2010. Biostatistical Analysis (Fifth Edition). Prentice-Hall. Englewood Cliffs, New Jersey.

(4) Data analysis and statistical analysis

A. Analysis Set

1) Intention to treatment (ITT) group

All patients who have undergone gastrectomy since entering the study are included.

2) Per-protocol (PP) families

Patients who have undergone laparoscopic Middle Segmental Gastrectomy (MSG)

3) Safety Analysis Set

Defined as all patients who participated in this study and underwent surgery.

B. Statistical analysis methods

제공해주신 한글 연구계획서 내용을 바탕으로, 소스 자료에 사용된 전문 용어와 통계적 기법을 반영하여 완성한 **영문 번역본**입니다.

Efficacy Endpoints

1. Primary Efficacy Endpoint

- **Incidence of Dumping Syndrome (Sigstad score $₩ge$ 7) at 1 year postoperatively:**
    - Dumping syndrome is defined as a **Sigstad score of 7 or higher**, while a score below 7 is defined as non-dumping.
    - This study aims to test whether the incidence of dumping syndrome in the MSG group at 1 year postoperatively is significantly different from the **15.8% incidence reported for the LDG group** in the ITT analysis of the original KLASS 04 study.
    - A **one-sample proportion test** will be performed with a **two-sided significance level ($₩alpha$) of 0.05**, and the 95% confidence interval (CI) for the incidence will be presented.

2. Secondary Efficacy Endpoints

- **Postoperative Reflux Symptoms:**
    - **Subjective symptoms (Visick score)** will be categorized by Grade and presented as frequencies and percentages (%).
    - **Endoscopic findings for reflux esophagitis (endoscopic LA classification)** will be

presented as frequencies and percentages (%).

- **Nutritional Indicators:**
    - Changes in postoperative **body weight, hemoglobin, serum iron, vitamin B12, albumin, and total protein levels**.
    - To evaluate changes from preoperative baseline to 36 months postoperatively, a **linear mixed-effects model (linear mixed model)** with repeated measures will be used for analysis.
    - The results will include **predicted means** and **95% confidence intervals** for each time point.
- **Postoperative Complications:**
    - The incidence of **early and late postoperative complications** will be presented as frequencies and percentages (%).
- **Mortality within 30 days of surgery:**
    - The occurrence of death within 30 days postoperatively will be presented as frequency and percentage (%).
- **Postoperative Quality of Life (QOL):**
    - QOL is assessed using **EORTC QLQ-C30 and STO22** preoperatively and at **3, 12, 24, and 36 months** postoperatively. (Note: KOQUSS40 is also utilized at specific time points).
    - For each time point, the **mean $₩pm$ standard deviation** and the change from the preoperative baseline will be presented.
    - **EORTC QLQ-C30 analysis:** Includes 5 functional scales (physical, role, emotional, cognitive, and social functioning), 3 symptom scales (fatigue, pain, and nausea/vomiting), 1 global health status, and 6 single items.
    - **EORTC STO22 analysis:** Includes 5 gastric cancer surgery-related scales (dysphagia, eating restriction, pain, reflux, and anxiety) and 4 single items (dry mouth, body image, taste, and hair loss).

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- **3-Year Recurrence-Free Survival and Overall Survival:**
    - **Disease-Free Survival (DFS):**
        - The **Kaplan-Meier Method** will be used to estimate the median DFS and its 95% confidence interval.
        - DFS is defined as the time from the date of surgery (randomization) to postoperative recurrence or death; for censored patients, it is the time from the date of surgery to the last follow-up (censoring).
    - **Overall Survival (OS):**
        - The **Kaplan-Meier Method** will be used to estimate the median OS and its 95% confidence interval.
        - OS is defined as the time from the date of surgery to death; for censored patients, it is the time from the date of surgery to the last follow-up (censoring).

Details regarding the statistical analysis are further elaborated in the separately documented **Statistical Analysis Plan (SAP)**.

(5) Recruitment plan for study subjects

The study will not be recruited by posting a recruitment notice, but by explaining the study to all eligible patients who visit the outpatient clinic and who meet all inclusion criteria and do not include any exclusion criteria, and obtaining signed informed consent from patients who are willing to participate. Patients will be recruited competitively.

The principal investigator and co-investigators of this study will not exclude potential patients from participation in this based solely on race or socioeconomic status. Every effort will be made to include patients in this study who are eligible if they meet the inclusion criteria for this study

Vulnerable research subjects (pregnant women/ adults with impaired consent capacity/ students, employees/ prisoners) will be excluded from the study to ensure that no inherently vulnerable research subjects are included in this clinical study.

9. research methods

(1) Specific research methods

① Standardization and quality control of surgery

- Surgeons participating in this study will be those who perform at least 80 gastrectomies per year at each institution, and each individual will have experience with at least 50 open gastrectomies and 50 laparoscopic gastrectomies.
- Collaborators One unedited surgical video will be reviewed by the Steering Committee and selected as the final collaborator.
- Conduct regular and ad hoc investigator meetings to review study protocols, standardize surgical techniques, and respond to unexpected adverse events and outcomes in a timely manner.

② Progress and patient enrollment at participating sites

- Once this study is approved by the institutional review board, you will begin enrolling patients who meet the inclusion criteria by obtaining their consent to participate in the study.
- How to enroll patients

  Confirm that the patient to be enrolled meets all the inclusion criteria and does not include any of the exclusion criteria, explain to the patient about participation in the study, obtain a signed informed consent form, enroll the patient, and perform the surgery. Enrollment is based on the principle that each institution enrolls competitively.
- Complete the case record form (CRF) and transfer the CRF to the data center.
- Laparoscopic middle segmental gastrectomy (TLMSG) is performed for patients with gastric adenocarcinoma of cT1N0/1M0 preoperative staging, size 4 cm or less, tumor

location is in the body of the stomach, as diagnosed by preoperative endoscopy, abdominal computed tomography, or histology; size 4 cm or less, tumor location is in the body of the stomach, well to moderately differentiated, endoscopically clear boundaries of the lesion, and preoperative staging is cT2N0/1M0.

③ Preoperative examination

- The following preoperative tests were performed in the outpatient setting

A. Blood tests: WBC, Hemoglobin, Platelet, ANC, Albumin, total protein, vitamin B12, iron, tumor markers (AFP, CEA, CA 19-9)

B. Imaging studies: upper GI endoscopy, computed tomography of the abdomen

④ Surgical Methods

Patient consents to undergo Totally Laparoscopic Middle Segmental Gastrectomy (TLMSG). 1.

2. surgical method and extent of lymph node dissection

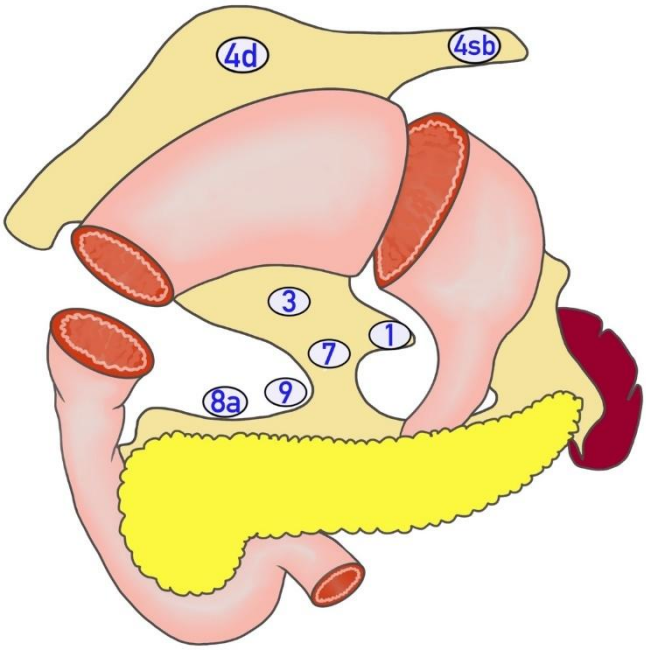
① Perform laparoscopic Middle Segmental Gastrectomy (MSG) and lymph node dissection. (Resecting the middle segment of the stomach with a minimum 2-3 cm resection margin from the tumor, preserving the vascular branches (specifically, the right gastroepiploic artery and left gastroepiploic artery) along the lesser and greater curvature of the stomach.

⑥ LN excision range is Nos. 1, 3, 4sb, 4d, 7, 8a, 9 (omitting Nos. 5 & 6)

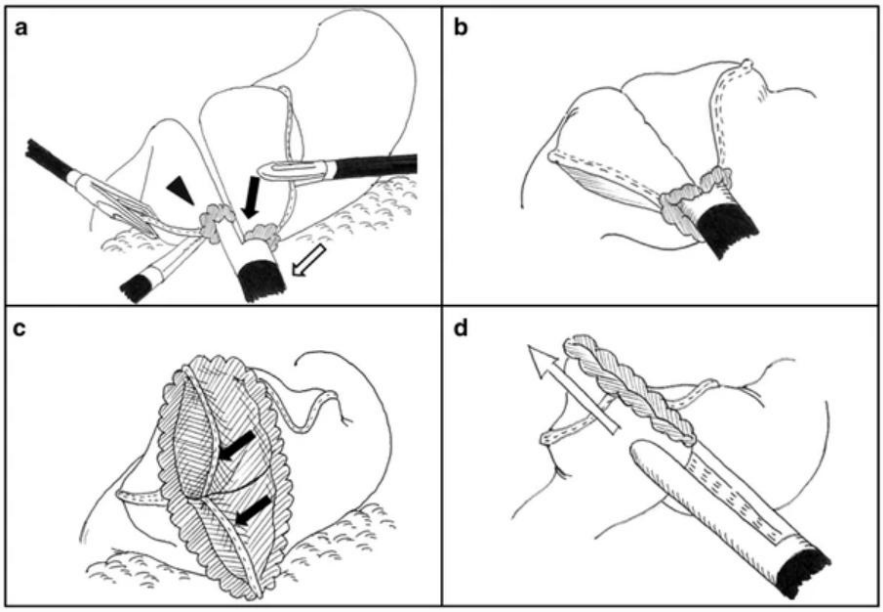
⑦ Reconstruction: Modified delta shaped anastomosis using a straight automated anastomosis machine under laparoscopy.

⑧ Check for bleeding and anastomotic leaks

⑨ Suturing the abdominal wall after inserting a drain



Modified delta shaped anastomosis



④ Postoperative care

- Patients participating in the study are managed according to patient management guidelines, following a predetermined critical pathway, but ensuring that all post-operative assessments are completed.
- Use perioperative mechanical lower extremity compression devices, elastic stockings, or anticoagulation as per investigator's judgment for postoperative thromboprophylaxis.
- Continue prophylactic antibiotics used preoperatively for an appropriate period of time postoperatively.
- Post-operative testing to check for esophagogastric anastomotic leaks may be performed at the discretion of the individual investigator.
- The postoperative dietary progression is as follows: fasting, followed by water, followed by food, followed by porridge, and the dietary progression may be adjusted at the discretion of the individual investigator.

- Post-operative pain control will be administered with appropriate pain control, such as a self-controlled analgesic device (PCA), and additional medications may be administered if requested by the patient.
- Chemotherapy is recommended within 4-6 weeks after if the postoperative pathology is Stage II or higher. (The type and number of cycles of chemotherapy should be documented in the case report after the completion of adjuvant anti-cancer therapy so that it can be included in the analysis.
- Postoperative patient progress notes

Record the following complications that occur during the postoperative hospitalization.

Complications are classified according to the Clavien-Dindo Classification (Definition and grading of complication) and scored by The comprehensive complication index (http://assessurgery.com).

Early Complications	The following events occurring within 30 days after surgery
1. Abdominal wound complications (wound site complications): Occurrence of seroma, hematoma, wound infection, wound dehiscence, wound evisceration, etc. at the site of a surgical wound that requires additional hospitalization.	
2. Fluid collection/intra-abdominal abscess (intra-abdominal infection): Abdominal ultrasound or tomography confirms intra-abdominal abscess, elevated white blood cells, fever, and antibiotics have been used.	
3. Intra-abdominal bleeding (Intra-abdominal bleeding)	
4. Intra-luminal bleeding (intestinal bleeding)	
5. Intestinal obstruction: No gas passage and abdominal plain film findings suggestive of mechanical intestinal obstruction or other symptoms suggestive of intestinal obstruction.	
6. Anastomotic stenosis (stricture): Stenosis of the anastomosis seen on gastroscopy or upper gastrointestinal endoscopy.	
7. Anastomotic leakage (leak): When intestinal contents drain into the drainage tube, or when there is leakage on endoscopy or upper GI examination.	

8. Pancreatic leakage: Drain amylase is greater than or equal to 3 times the upper limit of normal serum amylase and is clinically significant.
9. Pancreatitis: A meaningfully elevated serum amylase level (>150) with symptoms suggestive of pancreatitis.
10. Atelectasis: Imaging diagnosis and symptoms such as fever, shortness of breath, etc.
11. Pneumonia: Imaging diagnosis and presence of fever, elevated white blood cells, etc.
12. Urinary tract infection (urinary tract infection): Symptoms such as oliguria, nocturia, dysuria, or a significant increase in WBC on urinalysis.
13. Renal Dysfunction: Acute kidney failure requiring dialysis.
14. Hepatic Dysfunction (liver dysfunction): When accompanied by elevated bilirubin and decreased albumin, decreased blood clotting factors, etc. (not simply elevated liver enzyme levels)
15. Cardiac Disease (heart dysfunction): If you developed symptoms of heart failure, myocardial ischemia, and infarction after surgery and required treatment.
16. Delayed gastric emptying (food stasis): When food has difficulty passing through the anastomosis even though there is no evidence of intestinal obstruction, stricture, leakage, or peritonitis.

Definition and grading of complication (Clavien-Dindo Classification)

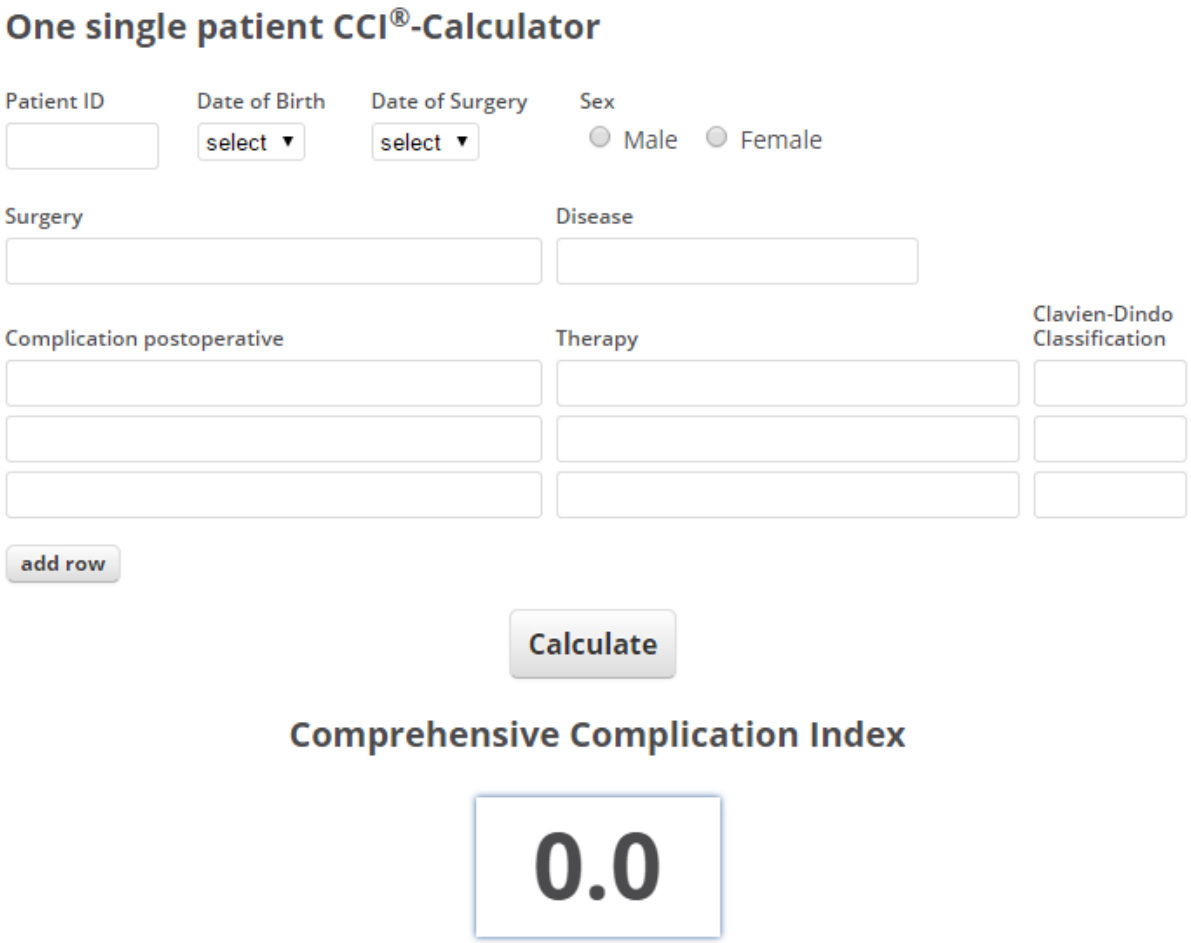
Grade	Definition
Grade I	Circumstances that do not require any medication, endoscopy, surgery, or imaging after surgery, but are different from the normal recovery process These include the need for treatment with antimetabolites, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy, as well as wound problems that can be treated in bed without local anesthesia.
Grade II	Situations requiring a different level of medication administration than Grade I This includes prolonged fasting, including blood transfusions and intravenous nutrition.
Grade III Grade IIIa	Situations requiring surgical, endoscopic, and imaging interventions Treatments that don't require general anesthesia

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Grade IIIb	Treatments requiring general anesthesia
Grade IV Grade IVa Grade IVb	Life-threatening complications requiring intensive care unit care (including central nervous system complications) Single organ failure (including dialysis) Multi-organ failure
Grade V	Patient death
Suffix "d"	If the patient still has complications at discharge, add a suffix "d" after the grade These patients required follow-up after discharge from the hospital.

◆ **http://assessurgery.com**



- **Dumping Symptom Assessment Index (Sigstad Score)**

Incidence of Dumping syndrome, assessed by Sigstad score (≥7) at 1 years

postoperatively

Sigstad score questionnaire defines a score **of** 7 or higher as dumping and a score of 7 or lower as non-dumping **(Table)**

Table. Questionnaire of Sigstad Score(3)

Symptom	Symptoms	Score
Pre-shock, shock	Shock (low blood pressure severe enough to take to the hospital)	+5
"Almost fainting", syncope, unconsciousness	Fainting, confusion	+4
Desire to lie or sit down	Want to lie down or sit up	+4
Breathlessness, dyspnea	Dyspnea	+3
Weakness, exhaustion	Generalized weakness, helplessness	+3
Sleepiness, drowsiness, yawning, apathy, falling asleep	Sleepiness, yawning	+3
Palpitation	Heart palpitations	+3
Restlessness	Restlessness	+2
Dizziness	Dizziness	+2
Headache	Headaches	+1
Feeling of warmth, sweating, pallor, clammy skin	Pale face, night sweats	+1
Nausea	Nausea	+1
Fullness in the abdomen, meteorismus	Abdominal bloating	+1
Borborygmia	Belly rumbling	+1
Eructation	Trim	-1
Vomiting	Vomiting	-4

⑤ Outpatient visits after discharge

A. outpatient visits will be performed at 3 weeks (± 2 weeks) postoperatively for the first visit and then at 3, 6, 12, 18, 24, 30, and 36 months with weight, , WBC, Hgb, Platelet,

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ANC, Glucose, , Albumin, Total Protein, serum iron, vitamin B12, and tumor markers (CEA, AFP, CA 19-9) measured at each visit

B. Check for reflux symptoms at each outpatient visit.

* Visick score (patient's subjective symptoms)

Table I. Visick score.

I	No symptoms, resolved
II	Mild occasional symptoms easily controlled, improved
III	Mild symptoms not controlled, unchanged
IV	Not improved, worsened

C. Check for dumping symptoms at each outpatient visi

Symptom	Symptoms	Score
Pre-shock, shock	Shock (low blood pressure severe enough to take to the hospital)	+5
"Almost fainting", syncope, unconsciousness	Fainting, confusion	+4
Desire to lie or sit down	Want to lie down or sit up	+4
Breathlessness, dyspnea	Dyspnea	+3
Weakness, exhaustion	Generalized weakness, helplessness	+3
Sleepiness, drowsiness, yawning, apathy, falling asleep	Sleepiness, yawning	+3
Palpitation	Heart palpitations	+3
Restlessness	Restlessness	+2
Dizziness	Dizziness	+2
Headache	Headaches	+1
Feeling of warmth, sweating, pallor, clammy skin	Pale face, night sweats	+1
Nausea	Nausea	+1

Fullness in the abdomen, meteorismus	Abdominal bloating	+1
Borborygmia	Belly rumbling	+1
Eructation	Trim	-1
Vomiting	Vomiting	-4

D. Gastroscopy will be performed preoperatively and at 3, 12, 24, and 36 months postoperatively

* Endoscopic valuation of reflux esophagitis (Los Angeles classification)

* Endoscopy will be performed preoperatively and at 3, 12, 24, and 36 months postoperatively to assess the visual and histologic appearance of the mucosa affected by GERD and response to therapy. (LA -A, B, C, D)

E. Computed tomography of the abdomen will be performed at 12, 24, and 36 months postoperatively.

F. Measure changes in patient quality of life using the KOQUSS40, EORTC-C30, STO 22 questionnaire preoperatively (EORTC-C30, STO 22) and at 3, 12, 24, and 36 months postoperatively .

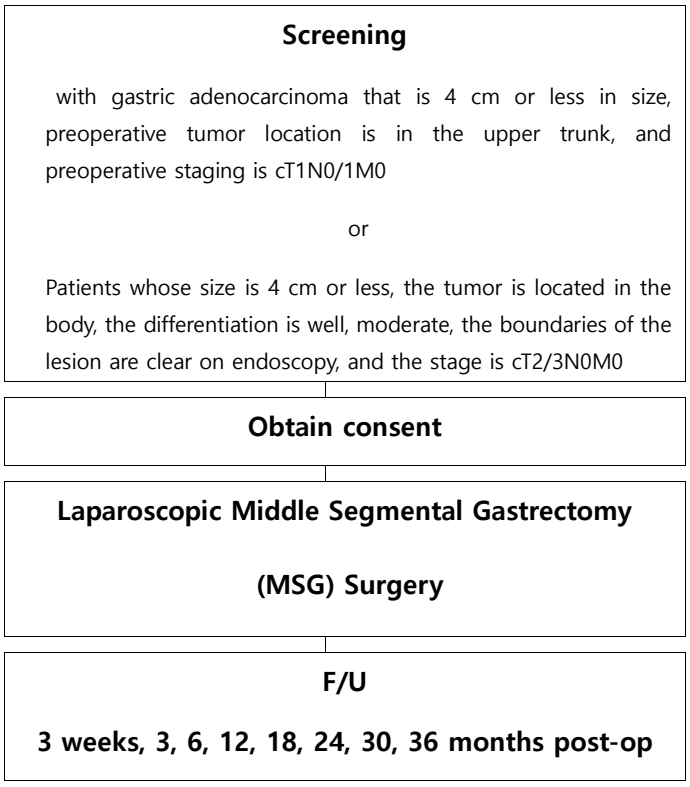
G. At each visit, the following complications that occur during the 30 days after surgery will be recorded. Complications will be classified according to the Clavien-Dindo Classification (Definition and grading of complication) and scored by The comprehensive complication index (http://assessurgery.com).

Late Complications	The following events occurring after 30 days after surgery
1. Intestinal Obstruction (Ileus): Requires hospitalization.	
2. Anastomotic Stenosis: If patient is symptomatic and requires an endoscopic procedure	
3. other	

H. If anemia develops during follow-up and the hemoglobin level is less than 10 g/dL, oral iron ferrous sulfate 256 mg (80 mg iron) twice daily for 12 weeks or until the hemoglobin level is normalized. Injectable iron (ferinject, venoferrum) may also be used. If you use iron, be sure to keep accurate records of the frequency and amount.

I. During follow-up, administer vitamin B12 injectable (Actinamide 1mg/2ml (Cobamamide)) or oral (cyanocobalamin (total 1500 μg)) if the vitamin B12 screening level is less than 200 pg/ml, ensuring that the frequency and amount is accurately documented.

■ **Study flow sheet**



- Patient enrollment period: IRB approval date to 24 months after approval date
- Intervention period: IRB approval date to 24 months after approval date
- Participant study duration: IRB approval date to 60 months after approval date
- Data collection period: IRB approval date to 60 months after approval date

- Evaluation and analysis period: 12 months after completion of data collection
- Total study duration: IRB approval date to 72 months after approval date

Enforcement	**Screening/Preoperative** [A]	**Surgery**	**1 day to discharge date**	**After surgery 3 weeks**	**After surgery 3 months to 36 months**	**End of study**
Allowed visitation days				± 14 days	± 30 days	
Obtaining consent [b]	V					
Check your exclusion criteria	V					
Medical History, ASA, ECOG	V					
Weight	V			V	V	
Visick score	V			V	V	
General blood tests	V			V	V	
Blood chemistry tests	V			V	V	
Tumor marker tests	V			V	V	
Computed tomography of the abdomen	V				V	
Gastroscopy	V				V	
Identify early			V	V		

complications						
Identify late complications					V	
View pathology results				V		
Adverse events		V	V	V	V	
EORTC-C30, STO22 Questionnaire [f]	V				V	
KOQUSS40 Questionnaire					V	
Dumping Symptom Survey (Sigstad)	V				V	
Check for recurrence and survival					V	
Case conclusion						V

1. **Pre-operative testing** for **screening** is allowed **up to 3 months** before surgery,.
2. If the surgery is performed **more than 30 days after the consent** is obtained, a **re-consent process** will be performed,.
3. **Tumor markers** (CEA, CA19-9, AFP) are performed **preoperatively** and at **3, 6, 12, 18, 24, 30, and 36 months** postoperatively,,,.
4. **Computed tomography (CT) of the abdomen** will be performed at the **12-month postoperative visit** and every **12 months thereafter**,,,. (Note: If performed at an **outside hospital**, the date must be recorded as the **actual date performed** at that institution; bringing medical records is mandatory),.
5. **Endoscopy** is performed at the **3-month postoperative visit** and every **12 months thereafter** (at 12, 24, and 36 months post-op),,,.
6. **Preparation before the endoscopy**: Eat **only soft, bland foods** (such as thin rice gruel) until **breakfast the day before** the test, and **do not eat after lunch** the day before the test,. (However, you should drink **plenty of sugar water** throughout the day before the test and before bedtime; you may drink water or sugar water **up to 4 hours before the test**, but must **fast starting 4 hours before** the test),.
7. **Final pathology results** are checked to **evaluate whether to proceed** with the clinical trial,.
8. **Adverse event assessments** will be performed **up to 36 months** postoperatively (POD),.
9. **Quality of Life** (EORTC-C30, EORTC QLQ-STO22) is measured **preoperatively** and at the **3, 12, 24, and 36-month**

postoperative visits,.

10. The **Dumping Symptoms Questionnaire** will be administered **preoperatively** and at **each visit** postoperatively,.

10. Efficacy Endpoints

1) Primary endpoint

Incidence of Dumping syndrome, assessed by Sigstad score (≥7) at 1 years postoperatively

- Sigstad score questionnaire defines a score of 7 or higher as dumping and a score of 7 or lower as non-dumping **(Table)(**3)

Table 6. Questionnaire of Sigstad Score

Symptom	Symptoms	Score
Pre-shock, shock	Shock (low blood pressure severe enough to take to the hospital)	+5
"Almost fainting", syncope, unconsciousness	Fainting, confusion	+4
Desire to lie or sit down	Want to lie down or sit up	+4
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Restlessness	Restlessness	+2
Dizziness	Dizziness	+2
Headache	Headaches	+1
Feeling of warmth, sweating, pallor, clammy skin	Pale face, night sweats	+1
Nausea	Nausea	+1
Fullness in the abdomen, meteorismus	Abdominal bloating	+1
Borborygmia	Belly rumbling	+1
Eructation	Trim	-1

2) Secondary endpoints

① **Postoperative reflux symptoms**.

② **Post-operative changes in weight, hemoglobin, serum iron, vitamin B12, albumin, and total protein levels**.

③ **Postoperative complications**.

④ **Mortality within 30 days of surgery**.

⑤ **Postoperative quality of life (QOL) assessment: EORTC QLQ-C30/STO22**.

⑥ **Three-year recurrence-free survival and overall survival**.

11. Benefits and Risks to Research Subjects

Benefits

- Additional explanations and counseling with your healthcare team, including your study coordinator and research nurse.
- May contribute to medical advances in terms of guidelines for gastric cancer treatment

Risk

- Common complications after gastrectomy may be seen with either method of gastrectomy for gastric cancer, and the unpredictable risk of the study method is likely due to the risk of gastrectomy for gastric cancer rather than the risk of the study method of surgery itself.
- That you will take appropriate medical action in response to any medical situation that arises.
- However, quality control of co-investigators who are not technically familiar with laparoscopic mid-segmental gastrectomy (MSG) will be necessary and will review one unedited surgical video prior to study participation.

11. Withdraw Criteria

① All surgeries will be performed laparoscopically. Patients will be excluded from the study if they are open.

② Exclusions based on surgical findings

- Visually connected infiltration of two or more lymph nodes on laparoscopic surgical findings.

- Remove patients from the study if they have clear serosal infiltration.
- Patients who, in the judgment of the investigator, gastrectomy and lymphadenectomy are futile or impossible will not undergo further surgery and will be removed from the study.

③ If the subject wishes to withdraw consent, they can do using the

13. Study timeline

What we're working on	Study timeline (months)														
	4	8	12	16	20	24	28	32	36	40	44	48	52	56	60
IRB approval															
Patient registration															
Follow-up															
Analyze your data															
Build reports															

14. Ethical consideration Ethical consideration

1) Ethical Conduct of the Study

The trial will be conducted in accordance with the World Medical Association's (WMA) Declaration of Helsinki (as amended by the 59thWMA General Assembly, Seoul, October 2008) and the ICH Guidelines for GCPs. The Lead Sponsor will use its best efforts to ensure that the trial complies with local and national regulatory requirements. If full compliance with the above declarations, guidelines, and regulations is not planned, an explanation of the exception is required for the acceptability of the study data.

Investigators must ensure the anonymity of all subjects. Each subject is assigned a unique number and this number should be used in documentation about the subject.

All anonymity information is the property of the host organization.

. 2) Privacy measures

- Personally identifiable information, such as case number, name, and contact information, is collected for patient scheduling purposes.
- Types of personal information to be collected: case number, name, contact information, age, gender, weight, height, past medical history, time period between endoscopic submucosal dissection and surgery, preoperative examination (endoscopy, CT, staging after endoscopic resection), date of surgery, name of surgery, extent of lymph node dissection, surgical findings (tumor location, size staging, etc.), postoperative pathological findings (tumor location, size staging, etc.), operation time, amount of bleeding, financial resources, postoperative complications
- Purpose of Retention: To analyze the clinicopathologic features and surgery-related

complications of enrolled patients.

- The clinical information collected will be used only for the analysis of this study.
- Retention period: IRB approval to 3 years after study closure
- Disposition: The document will be disposed of by the principal investigator by deleting files and shredding.

3) How we use personal information, including personally identifiable information

- Personally identifiable information is only collected for case number, full name, and contact information.
- At the end of data collection, we remove case numbers, names, and contact information and analyze the data into a file consisting only of study serial numbers and simple clinical information.
- Data containing case numbers is kept separately in a password-protected file.
- Data containing case numbers and all personal data will be kept for 3 years from the end of the study and then destroyed by the principal investigator by file deletion and shredding.
- Personally identifiable information will not be disclosed to any researchers/institutions other than those at this institution.

4) Security measures, such as encrypting files

- The information collected is kept in a password-protected file in a locked lab.
- The computers used for data analysis are located in a locked room and are encrypted.

- Access to the file is limited to the principal investigator and the coordinators of the study (Youngsook Kim, Susie Kim, and Jinhee Choi, Yuri Jeong Department of Gastric Cancer Research).

- The data will be kept until the end of the study and kept in a password-protected file under the supervision of the researcher, Youngwoo Kim.

- Files will be kept for 3 years from the end of the study and then deleted by the principal investigator.

3) Institutional Review Board or Ethics Committee Institutional Review Board or EC/IEC

Investigators must submit protocols and amendments to protocols, informed consent forms, and any other documents required by the IRB/EC/IEC to the IRB/EC/IEC for review and approval. Investigators must also allow the IRB/EC/IEC to periodically inspect the progress of the trial and renew the trial authorization annually, if necessary.

15. Measures to manage related documents such as consent forms, case notes, questionnaires, etc.

(1) Obtain consent

To comply with the Declaration of Helsinki, federal regulations, and ICH guidelines, an informed consent form (ICF) will be used, which must be approved by the IRB/EC/IEC prior to use. The investigator or authorized personnel must be able to explain the purpose of the trial and the treatment, and in doing so, demonstrate that they are aware of the benefits and risks of the trial. Subjects must also be aware that participation in the study is voluntary and that they may withdraw from the study at any time without consequence. Ensure that subjects have adequate time to think about and discuss their decision to participate with their families before signing the ICF, and

that procedures are in place to provide new information about the study as it available and to confirm continued consent to participate.

Inform patients in the consent form what personal information you are collecting, the purpose of the collection, how long you will retain and use the personal information, and that they have the right to refuse consent.

(2) Document management measures

- Collected documents stored in a locked cabinet in a locked lab.
- Access to the documents was limited to the principal investigator and the coordinators of the study (Kim Young-sook, Kim Soo-ji, Choi Jin-hee, and Choi Jung-ri).
- Will be kept for 3 years from the end of the study and then destroyed by shredding by the principal investigator.

16. the criteria for safety, including adverse events, how they are evaluated and how they are reported

1) Adverse Events

An adverse event (AE) is an untoward medical occurrence in a subject in a clinical trial that is not necessarily causally related to the treatment. Therefore, an AE is any undesirable and unintended sign (e.g., abnormal laboratory test result), symptom, or disease that occurs temporarily and is not causally related to surgery. The severity of the adverse event is graded based on the NCI-CTCAE, Version 4.03, and detailed information should be documented in the case record. For adverse events that do not fall within the NCI-CTCAE grading system, they are categorized into five levels as follows

1st degree: Mild AE

2nd degree: Moderate AE

Grade 3: Severe AE

4th degree: Life-threatening or disabling AE

5th Degree: AE-related death

Assessment of causality between the adverse event and treatment is required. Detailed terminology and causality scales are provided in Exhibit 7.

2) serious adverse events

An adverse event is defined as a serious adverse event if it is

A. Any death within 30 days of surgery: Reported as a serious adverse event regardless of causal relationship to surgery.
B. Report if you believe the following items are causally related to the study within 30 days of surgery. (Causality is reported as definite, probable, or possible).
   ① Hospitalization for serious complications after surgery or an extended hospital stay
   ② If you require a second surgery (re-surgery: surgery that requires general anesthesia in the operating room)
   ③ Permanent or significant disability that is undeniably related to the surgery: sequelae disability, including brain lesions that leave permanent residual effects related to the surgery.
   ④ Other adverse events that, in the investigator's judgment, are related to the surgery

3) Adverse event notification and recording

All adverse events should be documented in the patient chart and reported in the CRF.

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4) Notify and record serious adverse events

If a serious or medically significant clinical adverse event or laboratory test value occurs during the study or during the post-treatment period, regardless of the treatment received by the subject, the investigator or study personnel must document it in the CRF, report it to the sponsor, and report it to the site's Institutional Review Board (IRB).

5) Reporting of a Suspected Unexpected Serious Adverse Reaction ((SUSAR))

Both the Institution and other institutions are required to report any unexpected adverse events that are related to the research design or procedure, or are suspected to be related to the procedure (Suspected Unexpected Serious Adverse Reaction (SUSAR): Unexpected serious adverse events related to the procedure), the Institutional Research Director or his/her representative shall complete a SUSAR Report within 24 hours of learning of the serious adverse event and report it to the Principal Investigator (fax.031-920-2898), and the Principal Investigator shall report it to the Steering Committee, and the Steering Committee shall deliberate on it

17. Compensation for clinical trials

Provide best medical care for any medical condition that arises directly related to the study procedures under the protocol.

18. Support for subjects

- The study method, middle segmental gastrectomy, has no additional costs associated with participation in the study, so there is no financial support.

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19. Access to Trial Data/Documents Access to Trial Data/Documents

1) Data Quality Assurance

The Clinical Research Coordinator (CRC) at the National Cancer Center, the study's principal investigator, will serve as the Clinical Research Associate (CRA).

Steps to ensure the reliability and accuracy of the data include the selection of qualified medical staff and appropriate study sites, review of protocol procedures by medical staff and relevant personnel prior to conducting the study, and periodic visits by a Clinical Research Associate (CRA) from the study's lead organization. The CRA will review the CRF for accuracy and completeness following the site visit and release of the clinical research database, and the central data monitor will identify any discrepancies with the assistance of the medical staff and nominated experts.

Representatives from the Clinical Quality Assurance department of the Lead Sponsor or a separate Clinical Quality Assurance group may visit the site to audit compliance with regulatory guidelines and policies. For the audit, CRAs are allowed access to all study records, including source documents, and use them for comparison with the CRF. However, patient privacy must also be respected. Provide sufficient notice prior to the audit so that the medical staff can adequately prepare for the audit.

Case Report Forms and Source Documentation

Healthcare providers are responsible for completing the CRF accurately and in a timely manner. One CRF must be completed for each subject participating in the study. Any modifications to the CRF can only be made by the investigator or an authorized person.

Study data must be recorded in the CRF. The AE page of the CRF must also be signed and dated by the investigator.

The CRF should be completed within a maximum of 5 days of the subject's visit, including visits that occurred outside of the investigator's work location, to ensure

that the CRF always records the most recent observations of the subject.

The completed CRF will be checked by the monitor for proper recording. If necessary, questions may be raised, which will be forwarded to the study hospital for resolution.

2) Access to Source Data

The CRA of the lead organization shall visit each site to ensure that the study is being conducted in accordance with the protocol. The date of the visit should be recorded in the hospital visit record by the monitor. The first visit should occur as soon as possible after the first patient is enrolled after the start of the study. During the visit, the monitor will compare the data recorded in the CRF with the hospital clinical record (source document). The source document should be able to provide information on the correct informed consent process, adherence to the protocol process, accurate reporting and follow-up of AEs, and whether other medications were administered during the same period. The source document should be reviewed by the investigator prior to the start of the study if there are any specific items that must be included in the source document. Discuss findings from the CRF and source document review with the investigator.

At the time of the CRA's visit, the investigator (and study coordinator, if necessary) and source documentation should always be available, and an appropriate environment should be provided for the review of study-related documents.

20. Monitoring plan

① After approval of the study by each institution, a study initiation meeting is held.

② The CRA of the National Cancer Center conducts monitoring in the order of the institutions that enrolled the first subject, and conducts monitoring after the first subject enrollment to check the progress of the study, and then conducts visits in the order of the institutions that enrolled the first five subjects, and if there are no more than five subjects, the CRA visits the study

site after the end of the clinical study to check the completeness of the subject records, the accuracy of the case records, and to review whether the study process was conducted in accordance with the regulations.

③ Visit check criteria will include the presence of informed consent, adherence to inclusion/exclusion criteria, recording of serious adverse events, and standardized verification of data records for all efficacy outcome variables and safety outcome variables. Not revealing any information about the identity of subjects in the supporting documentation.

④ Clinical research staff at each site manage the data, which includes demographic and medical information, as well as results from other tests and assessments

21. Publication Policy Publication Policy

The Lead Sponsor will create a publication committee to propose and write manuscripts or abstracts for submission to journals based on the trial data. Investigators may not personally use any or all of the trial results to make presentations or publish papers. Manuscripts or abstracts written by investigators must be approved in writing by the Lead Sponsor before submission. Published papers will include the names of all investigators who participated in the trial.

The authorship of the publication committee for this examination will be organized according to the requirements of the International Committee of Medical Journal Editors. This means that the authors have met all three of the following conditions

- Made substantial contributions to the conception, design, analysis, interpretation, or collection of data
- Written a paper or made significant intellectual revisions
- Approved the final version for publication

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22. References

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