

PEER-REVIEW REPORT

Reviewer's code: 03031179

COMMENTS TO AUTHORS

The authors investigated into the comparison of EJ after TG, especially in between TLTG and LATG. They employed linear stapler method in TLTG, circular stapler method in LATG. They have experienced numerous cases of TLTG and LATG; therefore this paper is worth to be published after some revisions.

1. The Authors used the terminology of "functional side-to-side anastomosis", however, is this terminology well-defined as surgical terminology? I think "functional end-to-end anastomosis" is the right words of your reconstruction procedure, because this procedure is not only functional but also actually side-to-side.

Answer) The reviewer is right - this terminology is not a well-defined surgical terminology. There are functional and overlapping methods for intracorporeal EJ anastomosis using linear stapler. The anastomotic method of this study was a functional type. This study was a comparison of intracorporeal with extracorporeal anastomosis; therefore, I will not use the terminology "functional side to side anastomosis" and use TLTG and LATG instead.

Title: Comparison of totally laparoscopic total gastrectomy using an endoscopic linear stapler with laparoscopic-assisted total gastrectomy using a circular stapler in patients with gastric cancer: a single-center experience.

Introduction: Since 2008, TLTG using endoscopic linear staplers has been performed in our institute on more than 400 patients by expert surgeons with much experience of laparoscopic surgery, and we have developed a secure and effective technique for reconstructing the EJ [15-17].

2. In Table 1, variables and results are not same line, modification of the table is required.

Answer) The reviewer is right. We fixed the table as follows.

Table 1. Clinical characteristics of patients who underwent LATG and TLTG

Variable	LATG (n=266)	TLTG(n=421)	p-value
Age (years, mean ± SD)	55.69 ± 11.96	57.78 ± 11.20	0.020

Gender (n, %)			0.583
Male	167 (62.8%)	273 (64.8%)	
Female	99 (37.2%)	148 (35.2%)	
ASA score (n, %)			0.064
I	181 (68.0%)	249 (59.1%)	
II	68 (25.6%)	145 (34.4%)	
III	17 (6.4%)	27 (6.4%)	
BMI (kg/m ²) (n, %)			0.883
< 23	198 (47.0%)	119 (44.7%)	
≥23, <25	103 (24.5%)	70 (26.3%)	
≥25, <30	110 (26.1%)	69 (25.9%)	
≥30	10 (2.4%)	8 (3.0%)	
History of Abdominal surgery(n, %)	33 (12.4%)	85 (20.2%)	0.008

Values are expressed as mean ± standard deviation or number (percentage)

n, number; LATG, laparoscopic assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy; ASA, American Society of Anesthesiologists physical status classification; BMI, body mass index

3. The authors recruited the patients with GC of upper stomach. In these cases, are there any cases undergoing splenectomy? If large type 3 or 4 tumor are located at the gigantic curvature of the upper stomach or lymph node metastasis of No. 4sa or 10, TG with D2 requires splenectomy. This population have included far advanced GC, so the authors have to mention about it.

Answer) Patients with gastric cancer were selected by preoperative diagnostic test under T3. Based on operative findings, patients with T4 advanced gastric cancer were converted to open surgery and were not included in this study. In case of advanced gastric cancer or with spleen hilar lymph node swelling, hilar lymph node was harvested

and intra-operative frozen biopsy was carried out. If the frozen biopsy result was positive, then splenectomy was also carried out. There was only one case of splenectomy because of splenic hilum metastasis. We added corresponding descriptions in the surgical technique and outcomes section as shown below.

MATERIAL AND METHOD:

Surgical technique: In case of advanced gastric cancer or with spleen hilar lymph node swelling, hilar lymph node was harvested and intra-operative frozen biopsy was carried out. If frozen biopsy result was positive, then splenectomy was also carried out.

RESULTS:

There were three splenectomy cases in the TLTG group. Splenectomy was carried out in two cases in order to control splenic bleeding, and one case because of the metastasis found in splenic hilar lymph node biopsy.

4. In surgical outcome, blood loss is essential measure. Please add in the document and the table.

Answer) There were no objective assessment variables to assess bleeding; therefore, we showed the change of Hct in Table 3 as follows.

Table 3. Early surgical outcomes in patients undergoing LATG and TLTG

Variables	LATG (n=266)	TLTG(n=421)	p-value
Operation time (min)	170 (65~453)	149 (75~342)	<0.001
Hematocrit change(%)	4.04	3.49	0.002
Intra-operative transfusion (n)	(-3.8~15.2)	(-4.9~18.6)	1.000
Post operative transfusion (n)	1 (0.4%)	1 (0.2%)	0.320
Intra-operative event (n)	28 (10.5%)	55 (13.1%)	< 0.001
Intra-operative anastomosis event (n)	27 (10.2%)	13 (3.1%)	0.003
Combined operation (n)	19 (7.1%)	10 (2.4%)	1.000
Time to first flatus (days, range)	17 (6.4%)	27 (6.4%)	< 0.001
Time to soft diet (days, range)	3.60 (1~7)	3.30 (1~7)	< 0.001
Pick of pain score (score, range)	4.61 (2~68)	4.30 (3~36)	0.912

8AM Pain score of POD #1 (score, range)	7.11 (2~10)	6.96 (3~10)	0.841
8AM Pain score of POD #3 (score, range)	3.45 (0~10)	3.49 (0~10)	0.529
8AM Pain score of POD #5 (score, range)	2.44 (0~9)	2.54 (0~7)	0.055
Number of administration of analgesics (n, range)	1.75 (0~10)	1.51 (0~8)	0.131
	2.49 (0~69)	2.86 (0~67)	0.005
Post-operative hospital stay (days, range)	7.02 (5~1117)	6.75 (4~82)	

5. In this study, are pain scale comparisons necessary? LATG usually requires small incision to pick out the specimen and perform EJ, therefore, pain scale of LATG may be worse than TLTG. From this reason, TLTG is less-invasive than LATG, in general. But, there are no significant differences in postoperative pain between two groups in this study. The authors have to mention about relationships this curious results and earlier recovery of abdominal function in TLTG patients.

Answer) We agree with the reviewer's comment. In a study that compared between laparoscopic and open gastrectomy, pain scale of laparoscopic gastrectomy was lower than that of open gastrectomy. However, in this study, there was no significant difference. It may be due to the active pain control using patient-controlled analgesia. This point was added to the Discussion section.

DISCUSSION: Although TLTG is less invasive than LATG, there was no significant difference in pain score, which was probably due to the use of active pain control such as patient-controlled analgesia.

Reviewer's code: 00579619

COMMENTS TO AUTHORS

Authors showed the short-term advantages of totally laparoscopic total gastrectomy (TLTG) with esophagojejunostomy using a linear stapler in gastric cancer patients as compared with laparoscopic-assisted total gastrectomy (LATG) using a circular stapler. However, this manuscript has several critical problems to be addressed. Major revision 1. How did you choose TLTG or LATG? Did you change LATG to TLTG between 2008 and 2014? If so, you should explain when or why you change the procedure of total gastrectomy in the Method section. The different numbers of harvested lymph nodes



**Baishideng
Publishing
Group**

7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

might be caused by the different period of two procedures.

Answer) Our gastric cancer surgery team has been practicing the laparoscopic surgery from 2004. Before 2008, the number of gastrectomy cases carried out by our team had reached almost one thousand. As the reviewer has pointed out, the numbers of harvested lymph nodes carried in this study. However, the number of retrieved lymph nodes were more than 34, which is enough for oncological resection. As the reviewer asked, LATG and TLTG operations were performed at different periods of time, it is one of the limitations of this study. We described this issue in the Discussion section.

DISCUSSION

This study has certain limitations. It is a retrospective study from a single institution and the baseline clinical characteristic of the two groups were different. Although the pathologic results for the patients in the LATG and TLTG groups were similar, the LATG and TLTG operations were performed at different periods of time. In addition, cancer recurrence and long-term survival rates were not analyzed because approximately half the patients underwent surgery, and five years had not yet passed. Therefore, long-term outcomes are still needed in order to compare the oncological adequacy of these two methods.

2. Please show the postoperative schedule in TG. Was it same between two groups? Did you start soft diet after flatus was confirmed? How did you decide the discharge day from hospital? If ERAS or fast track surgery is performed, do you think the advantage of early oral intake or early discharge would be lost?

Answer) From 2008 to 2014, we used our standardized clinical pathway (CP), which was developed in 2001. I added this table as reference and supplementary table.

REFERENCE

21 **Kim HS**, Kim SO, Kim BS. Use of a clinical pathway in laparoscopic gastrectomy for gastric cancer. *World J Gastroenterol* 2015;21:13507-17 [PMID: 26730162 DOI: 10.3748/wjg.v21.i48.13507]

Structure of the CP for lap-gastrectomy is below

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4690180/table/T1/>

Table 1
Structure of the clinical pathway for laparoscopic gastrectomy

Activities date	1 d before OP (Admission)	Pre-OP (the day of OP)	Operation(the day of OP)	Post-OP(the day of OP)	POD 1	POD 2	POD 3	POD 4	POD 5 and 6 (D/C)
Nursing care	Admission to room: (1-3 per)Fluid balance/Surveillance V/S/Weight measurement	Room nurse:Fluid balance,Check V/S	Surgical nurse:OP preparation	Room nurse:Fluid balance,Check V/S,drainage	Room nurse:Fluid balance,Check V/S,drainage	Room nurse:Fluid balance,Check V/S,drainage	Room nurse: Fluid balance, Check V/S, Drainage	Room nurse:Check V/S	Room nurse:Check V/S
Activity	Usual	Bed rest	Bed rest	Bed rest	Ambulation	Ambulation	Ambulation	Ambulation	Ambulation
Treatment procedure	Skin preparation:No Lev in tube Breathing exercises: use of IS Bowel preparation: Magcorol solution, 250 mL... Doloax supplement, 2 sup		Surgical nurse:Foley catheter/insertion	Breathing exercises: use of IS	Breathing exercises: use of IS	Breathing exercises: use of IS	Breathing exercises: use of IS	Breathing exercises: use of IS	Breathing exercises: use of IS
Medication		Prophylaxis: TE	Prophylaxis: ATB	Anesthesiologist:PCA (Fentanyl 3000 mg) agent	Prophylaxis: TE				
Medication on demand			Anesthesiologist: PCA	Anesthesiologist: PCA	PCA	PCA	PCA		
Laboratory test			Pain killer: (IV) Demerol NSAIDs Antiemetics	Pain killer: (IV) Demerol NSAIDs Antiemetics	Pain killer: (IV) Demerol NSAIDs Antiemetics	Pain killer: (IV) Demerol NSAIDs Antiemetics	Pain killer: (IV) Demerol NSAIDs Antiemetics	Pain killer: (Oral) NSAIDs	Pain killer: (Oral) NSAIDs
Diet	Usual diet at breakfast/NPO after breakfast	NPO	NPO	NPO	SOW: post 24 h OP		LD at breakfast/SD after G O	SD	SD
Education and information	Information on CP/Permission		Information on leaving OP room				Education: diet for patient and/or relative	Education: diet for patient and/or relative	Information on D/C

OP: Operation; V/S: Vital signs; IS: Incentive spirometry; NPO: Nil per os; CP: Clinical pathway; TE: Thromboembolic; ATB: Antibiotic; PCA: Patients controlled analgesia; IV: Intravenous; NSAIDs: Nonsteroidal anti-inflammatory drugs; POD: Postoperative day; SOW: Sips of water; JP: Jackson-Pratt; LD: Liquid diet; SD: Soft diet; D/C: Discharge; S O: Stata out; G O: Gas out.

3. What was the intraoperative event or intraoperative anastomotic event? Did they mean intraoperative bleeding or injury? Please show the definition of them in the Method section.

Answer) As per reviewer's comment, we described this issue in the Material and method section.

MATERIAL AND METHODS

Intra-operative events include jejunojejunostomy site kicking or narrowing, emphysema, and injury to organs such as pancreas, spleen, colon, small bowel, liver and major vessels. Intra-operative anastomosis events-related EJ refers to all unexpected event related EJ anastomosis such as leakage after anastomosis, small bowel or esophagus injury caused by small diameter, pseudo-lumen stapling, sticking crus muscle together, etc.

4. The short-term advantages, such as short operating time and early recovery, seemed to be obtained by the totally laparoscopic procedure, but not the anastomotic procedure using a linear stapler, because anastomotic complications were similar between two groups. Please discuss the advantage of total laparoscopic approach, or that of anastomosis using linear staplers, separately.

Answer) We agree. The advantages of total laparoscopic approach and those of anastomosis using linear stapler are different. So, we carefully revised the Discussion section as follows.

DISCUSSION : The procedure of LATG and TLTG differ in many ways. First, TLTG is less invasive, and requires a smaller incision than does LATG. Second, the wider working space in TLTG ensures safe reconstruction of the EJ. Therefore, laparoscopic surgeons are more comfortable with intracorporeal than the extracorporeal one. Furthermore, using a linear stapler in TLTG has another advantage in that whereas circular staplers have only two staggered rows, endoscopic linear staplers have three staggered rows and provide better staple line security.

5. Anastomotic stricture was much in TLTG using linear staplers than in LATG using a circular staple. However, it is contradictory to the figures of anastomosis that you show. Please explain why anastomotic stricture was more frequent in TLTG.

Answer) The reviewer is right, and the results do not seem to match. Therefore, we revised the case. After revision, the five anastomosis stricture cases of TLTG did not occur at the anastomosis site. In the TLTG cases, we performed more hiatus dissection for using linear stapler and EJ anastomosis went up to the diaphragm. Therefore, five strictures occurred at below the EJ anastomosis (proximal E-loop), and not EJ anastomosis. We corrected the table accordingly.

Table 4. Early and late post-operative complications

	Early complications			Late complications		
	LATG (n=266)	TLTG (n=421)	p-value	LATG (n=266)	TLTG (n=421)	p-value
CDC			0.447			0.715
0	213 (80.1%)	334 (79.3%)		245 (92.1%)	384 (91.2%)	
1	24 (9.0%)	26 (6.2%)		10 (3.8%)	15 (3.6%)	
2	13 (4.9%)	26 (6.2%)		0 (0%)	4 (1.0%)	
3	12 (4.5%)	33 (7.8%)		11 (4.1%)	18 (4.3%)	
4	4 (1.5%)	2 (0.5%)		0 (0%)	0 (0%)	
Cx of EJ			0.211			0.439
None	252 (94.7%)	407 (96.7%)		262 (98.5%)	418 (99.3%)	
Leakage	14 (5.3%)	14 (3.3%)		1 (0.4%)	1 (0.2%)	
	0 (0.0%)	0 (0.0%)		3 (1.1%)	2 (0.5%)	
Stricture						

Values are expressed as number(percentage)

n, number; LATG, laparoscopic assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy; CDC, Clavien-Deindo Classification; EJ, Esophagojejunostomy; Cx, complications

6. BMI was significant high in the TLTG group. However, BMI was 23.7 and 23.1 in the TLTG group and the LATG group, respectively. It is similar. It is not clear whether obese patients were much in the TLTG group. You should compare the number of obese patients (BMI > 25 or BMI > 30) between two groups.

Answer) The reviewer is right, and we divided the patient groups according to BMI and fixed Table 1. In this study, there was no significant difference in BMI between TLTG group and LATG group. Therefore, we revised the all discussions regarding BMI.

Table 1. Clinical characteristics of patients who underwent LATG and TLTG

Variable	LATG (n=266)	TLTG(n=421)	p-value
Age (years, mean ± SD)	55.69 ± 11.96	57.78 ± 11.20	0.020
Gender (n, %)			0.583
Male	167 (62.8%)	273 (64.8%)	
Female	99 (37.2%)	148 (35.2%)	
ASA score (n, %)			0.064
I	181 (68.0%)	249 (59.1%)	
II	68 (25.6%)	145 (34.4%)	
III	17 (6.4%)	27 (6.4%)	
BMI (kg/m²) (n, %)			0.883
< 23	198 (47.0%)	119 (44.7%)	
≥23, <25	103 (24.5%)	70 (26.3%)	
≥25, <30	110 (26.1%)	69 (25.9%)	
≥30	10 (2.4%)	8 (3.0%)	
History of Abdominal surgery(n, %)	33 (12.4%)	85 (20.2%)	0.008

Values are expressed as mean ± standard deviation or number (percentage)

n, number; LATG, laparoscopic assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy; ASA, American Society of Anesthesiologists physical status classification; BMI, body mass index

Minor revision

1. Please show the percentage and the statistical significance of individual postoperative complications in Table 5.

Answer)

Table 5. Post-operative complications in patients who underwent LATG and TLTG

	LATG(n=266)	TLTG(n=421)
Bleeding	4 (1.50%)	8 (1.90%)
EJ leakage	15 (5.64%)	15 (3.56%)
EJ stricture	3 (1.13%)	2 (0.48%)
Intra-abdominal fluid collection	8 (3.01%)	26 (6.18%)
Internal hernia	5 (1.88%)	12 (2.85%)
Mechanical ileus	10 (3.76%)	28 (6.65%)
Paralytic ileus	3 (1.13%)	7 (1.66%)
Wound infection	18 (6.77%)	9 (2.14%)
Other surgical complications	4 (1.50%)	8 (1.90%)
Medical complications	4 (1.50%)	2 (0.48%)

2. The median value of postoperative hospital stay was same despite of the significant difference between two groups. Was the Mann-Whitney test used in this analysis? I wonder the result.

Answer) As described in the foot notes, the values are the median values and not average. We used the Mann-Whitney test and there were some mistakes in displaying the decimal point, which we have fixed in this revision.

Table 3. Early surgical outcomes in patients undergoing LATG and TLTG

Variables	LATG (n=266)	TLTG(n=421)	p-value
Operation time (min)	170 (65~453)	149 (75~342)	<0.001
Hematocrit change(%)	4.04 (-3.8~15.2)	3.49 (-4.9~18.6)	0.002
Intra-operative transfusion (n)	1 (0.4%)	1 (0.2%)	1.000
Post operative transfusion (n)	28 (10.5%)	55 (13.1%)	0.320

Intra-operative event (n)	27 (10.2%)	13 (3.1%)	< 0.001
Intra-operative anastomosis event (n)	19 (7.1%)	10 (2.4%)	0.003
Combined operation (n)	17 (6.4%)	27 (6.4%)	1.000
Time to first flatus (days, range)	3.60 (1~7)	3.30 (1~7)	< 0.001
Time to soft diet (days, range)	4.61 (2~68)	4.30 (3~36)	< 0.001
Pick of pain score (score, range)	7.11 (2~10)	6.96 (3~10)	0.912
8AM Pain score of POD #1 (score, range)	3.45 (0~10)	3.49 (0~10)	0.841
8AM Pain score of POD #3 (score, range)	2.44 (0~9)	2.54 (0~7)	0.529
8AM Pain score of POD #5 (score, range)	1.75 (0~10)	1.51 (0~8)	0.055
Number of administration of analgesics (n, range)	2.49 (0~69)	2.86 (0~67)	0.131
Post-operative hospital stay (days, range)	7.02 (5~1117)	6.75 (4~82)	0.005

Values are expressed as median (range) or number(percentage)

Hematocrit change means the difference between preoperative hematocrit and post-operative hematocrit.

n, number; LATG, laparoscopic assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy; n, number; POD, post operative days

Reviewer's code: 00505467

COMMENTS TO AUTHORS

You should perform a prospective study. The lack of pathological comparable results concerning cancer recurrence, leaves queries about the safety of each method, and you are describing an oncological surgery. The results concerning the difference concerning the harvested lymph nodes should be analyzed.

Answer) Thank you for your opinion. We plan to tackle that issue in a future study. In this study, we observed statistically significant difference in retrieved lymph node numbers. But in the LATG group, the retrieved LN number was 34.91 ± 13.92 . This number was enough to be oncologically safe.

DISCUSSION



**Baishideng
Publishing
Group**

7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

This study has certain limitations. It is a retrospective study from a single institution and the baseline clinical characteristic of the two groups were different. Although the pathologic results for the patients in the LATG and TLTG groups were similar, the LATG and TLTG operations were performed at different periods of time. In addition, cancer recurrence and long-term survival rates were not analyzed because approximately half the patients underwent surgery, and five years had not yet passed. Therefore, long-term outcomes are still needed in order to compare the oncological adequacy of these two methods.

Reviewer's code: 03253691

COMMENTS TO AUTHORS

Authors presented large series underwent laparoscopic total gastrectomy and concluded that using linear stapler S-to-S anastomosis is safer and more appropriate. Although TLTG seems safer in terms of complications, op time, hospital stay, i believe it is difficult to have exact conclusion as regard to define it safer. because of retrospective nature, non-randomized nature, and more importantly difference in time period may avoid to have exact conclusion. The authors started using TLTG technique after high experience in LTG (with other method). this time difference and difference on experience may have a serious bias. as a reder, i want to see more regarding intraoperative events. what are they? can you please describe them more?

Answer) The reviewer is right. It is difficult to draw a firm conclusion and to define it as a safer method. There is no evidence clearly presented to defend this. We revised the Discussion and Conclusion. Furthermore, we added the intraoperative events.

MATERIAL AND METHODS

Clinical analysis of surgical outcomes: Intra-operative events include jejunojejunostomy site kicking or narrowing, emphysema, and injury to organs such as pancreas, spleen, colon, small bowel, liver and major vessels. Intra-operative anastomosis events-related EJ refers to all unexpected event related EJ anastomosis such as leakage after anastomosis, small bowel or esophagus injury caused by small diameter, pseudo-lumen stapling, sticking crus muscle together, etc.

Intraoperative event also described at our another study.

REFERENCE 21. **Kim HS**, Kim SO, Kim BS. Use of a clinical pathway in laparoscopic gastrectomy for gastric cancer. *World J Gastroenterol* 2015;21:13507–17 [PMID: 26730162 DOI: 10.3748/wjg.v21.i48.13507]

Table 3 Events during operation

	Intra N= 25 (%)	Extra N=52 (%)
Anastomosis failure (N=31)	8	23
Esophagojejunostomy failure	7	9
Gastroduodenostomy failure	1	14
Organ injury (N=30)	10	20
Spleen injury	6	10
Duodenum	0	5
Small bowel injury	1	1
Colon injury	1	2



**Baishideng
Publishing
Group**

7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

Pancreas injury	1	1
Liver injury	1	1
Vessel injury (N=12)	4	8
Splenic artery injury	2	6
Splenic vein injury	0	1
Common hepatic artery injury	1	1
Proper hepatic artery injury	1	0
Emphysema (N=4)	3	1

Intra Intracorporeal anastomosis; *Extra* Extracorporeal anastomosis; *N* Number of patient.



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Group**

7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

Reviewer's code: 00058696

COMMENTS TO AUTHORS

I have examined this manuscript. My major questions are summarized below:

1) The English grammar is flawed in several areas providing indefinite statements. The authors need to consider obtaining an English consultant.

Answer) As per reviewer's suggestion, we received English editing from a professional consultant at our hospital.

2) Title: consider "with" between linear stapler and laparoscopic-assisted total gastrectomy.

Answer) We changed the title accordingly.

Title : Comparison of totally laparoscopic total gastrectomy using an endoscopic linear stapler with laparoscopic-assisted total gastrectomy using a circular stapler in patients with gastric cancer: a single-center experience.

3) Abstract and Core Tips: "Safer": no evidence clearly presented to defend this claim; "more obese": not under WHO guidelines; the best that can be said is that there is minimally higher body mass index; "superior to": no evidence clearly presented to defend this claim.

Answer) The reviewer is correct to point these out. We fixed the Conclusion and the core tips as follows.

CONCLUSION: The intracorporeal method for reconstruction of EJ using a linear stapler may be considered a feasible procedure comparing with extracorporeal anastomosis using circular stapler because TLTG is simpler and more straightforward than LATG. Therefore, TLTG can be recommended as an appropriate procedure for gastric cancer.

Core tip : There are many studies that compared totally laparoscopic total gastrectomy (TLTG) with laparoscopic assisted total gastrectomy (LATG). Moreover, various modified methods of intracorporeal esophagojejunostomy (EJ) have been presented, but standardized methods have not been established. Our results show that TLTG by EJ intracorporeal anastomosis using linear stapler is an easier and more straightforward procedure compared with LATG by extracorporeal anastomosis using circular stapler.

4) Introduction; bottom of Paragraph 2: need references after "secure and effective technique for reconstructing the EJ".

Answer) We added the reference as follows.

INTRODUCTION: Since 2008, TLTG using endoscopic linear staplers has been performed in our institute on more than 400 patients by expert surgeons with much experience of laparoscopic surgery, and we have developed a secure and effective technique for reconstructing the EJ [15-17].

5) Methods, Patients: “upper and middle stomach”; are you referring to the gastric fundus and corpus? Surgical techniques: need references after “in LATC” and after (Fig 1).

Answer) The terms “upper and middle stomach” come from the JGCA guideline. Japanese Gastric Cancer Association Japanese classification of gastric carcinoma: 3rd English edition. Gastric Cancer. 2011;14:101-112. doi: 10.1007/s10120-011-0041-5

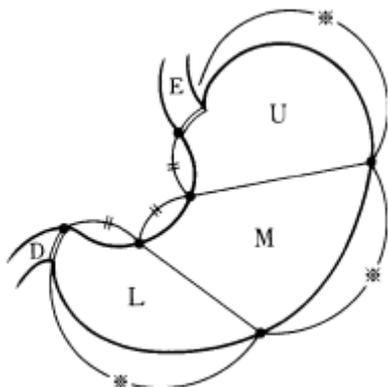


Fig. 1 The three portions of the stomach. *U* upper third, *M* middle third, *L* lower third, *E* esophagus, *D* duodenum

Details of TLTG technique have been described previously [16,17]

6) Results: Higher BMI likely not clinically significant since for a 170 cm tall person we are talking about the difference in weight between 69.1 kg and 70.7 kg. What were the authors' criteria for conversion to an open procedure. There is a range of up to 453 minute operation time. Was this the patient who was the outlier for hospital stay of 1117 days? Why not present the Mean +/- SD for hospital stays? If there were criteria for conversion to open procedure, perhaps there would be no statistical difference between hospital stay and operation time. Heading “Post-operative complications” states no differences in early and late post-operative complications: but then in the discussion, paragraph 5 which starts with “Postoperative morbidity”, the authors claim “results show that the TLTG method is advantageous”? Please explain.

Answer) BMI results were divided into 3 groups, and there were no statistically difference between TLTG and LATG group. Therefore, we fixed the Conclusion and Discussion accordingly.

RESULTS

Clinical features and pathological characteristics : There were no significant differences in gender (p=0.583), ASA score (p=0.064) and BMI (p=0.883) between the two groups. Frequencies of abdominal surgery were 12.4% and 20.2% (p=0.008) in LATG and TLTG groups, respectively. In summary, the TLTG group was slightly older and had more histories of abdominal surgery than LATG group.

Table 1. Clinical characteristics of patients who underwent LATG and TLTG

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Age (years, mean ± SD)	55.69 ± 11.96	57.78 ± 11.20	0.020
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III	17 (6.4%)	27 (6.4%)	
BMI (kg/m ²) (n, %)			0.883
< 23	198 (47.0%)	119 (44.7%)	
≥23, <25	103 (24.5%)	70 (26.3%)	
≥25, <30	110 (26.1%)	69 (25.9%)	
≥30	10 (2.4%)	8 (3.0%)	

History of Abdominal surgery(n, %)	33 (12.4%)	85 (20.2%)	0.008
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Values are expressed as mean ± standard deviation or number (percentage)

n, number; LATG, laparoscopic assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy; ASA, American Society of Anesthesiologists physical status classification; BMI, body mass index

At “MATERIALS AND METHODS, Patients”, we described that based on operative findings, patients with serosa-exposed advanced gastric cancer were converted to open surgery and were not included in this study.

When the intra-operative event or intra-operative anastomosis event occurred, we considered conversion to open surgery. But after 2005, laparoscopic total gastrectomies were carried out by done by expert surgeons, and we were able to overcome the intra-operative problems. Therefore, we have no case of conversion into open surgery except for grossly serosa exposure. The case with operation time 453 min was very obese individual who had deep position of GEJ. So after EJ stapling, there was anastomosis tearing and we needed another manual suture and methylene blue leakage test. Hospital stay 1117 days patient was another person. The patient received LATG and re-operation due to EJ anastomosis leakage with sepsis. However, after surgery, aspiration pneumonia and multi-organ failure occurred, and a prolonged ICU care was needed. Hospital stay does not have a normal distribution; therefore, we used median and range values rather than mean and SD.

The reviewer is also correct to point out that. There were no significant differences in terms of complications. We revised the discussion accordingly.

DISCUSSION : Postoperative morbidity after LATG has been reported to range from 17% to 27% [33–38]. In our study, early complication occurring within 30 days following LATG and TLTG classified as CDC grade ≥III were observed in 16 (6.0%) and 35 (8.3%) patients; late complications developing after 30 days following LATG and TLTG were observed in 11 (4.1%) and 18 (4.3%) patients. These results show that there were no significant differences between LATG and TLTG in terms of postoperative complications.

7) Discussion: how is this manuscript different than results in previously published reference 28? The authors mention several time that the TLTG group has “more obese patients”; what percentage of patients in each of the two groups were actually obese under WHO guidelines?

Answer) Reference 28 had relatively small number of cases (113 patients) that were only EGC cases. Furthermore, LATG group was only 23 cases. In this study, under WHO guidelines, there was no BMI difference between LATG and TLTG groups. We fixed this point in the revised manuscript.

RESULT : There were no significant differences in gender ($p=0.583$), ASA score ($p=0.064$) and BMI ($p=0.883$) between the two groups. Frequencies of abdominal surgery were 12.4% and 20.2% ($p=0.008$) in LATG and TLTG groups, respectively. In summary, the TLTG group was slightly older and had more histories of abdominal surgery than LATG group.

DISCUSSION : In the present retrospective study, the TLTG patients had similar BMIs and tended to be slightly older, with more histories of abdominal surgery compared with LATG patients

DISCUSSION : In the current study, the TLTG group was older and had more histories of abdominal surgery.

8) Table 1: the authors state that 430 patients are “ASA Score I”; these are patients with known gastric cancer and so by definition none are ASA Score I. For each of the two groups, how many patients had BMI < 18.5 kg/m²: e.g. how many patients had evidence in support of malnutrition and did malnutrition explain clinical differences between the two groups? Table 2: TLTG has a higher percentage of IIIB patients; did this effect the results of operative times and days in hospital? Table 3: Post-operative hospital stay: are these mean values (the two 7s listed); if they are mean values, one assumes that the p value is generated by using non-parametric statistics? Is that correct? Table 5: How do the authors distinguish “intra-abdominal fluid collection” (many with TLTG) from the “wound infection” (more in LATG)? Were all sampled for culture, etc? Fig 1: Boxes G and H are not properly labelled in the Figure Legend. Fig 2: is not needed as it provides no data that was analyzed in this present study.

Answer) ASA score classification ignores those with malignancy. We checked the ASA scores in the preoperative anesthesiologist’s report.

Our patients were clinically T3 lesion patients. Therefore, we ignored the malnutrition. 11 (4.14%) LATG patients and 17 (4.04%) TLTG patients had BMI <18.5. There was no significant difference.

Regardless of whether the permanent biopsy result was IIIB or IIIC, intra-operative grossly findings were T3 lesion. There was no significant difference in terms of operative procedure (OP time) and post-operative hospital stay.

Table 3, hospital stay; As described in the foot notes, the values are median and not average. We used the Mann-Whitney test and there were some mistakes in displaying the decimal point, which have been fixed in the revised manuscript.

Table 5, After POD #4, if the patients had high fever or WBC count abnormally increased, then we checked the abdominal CT. By CT scan, we can find the intra-abdominal fluid collection or wound infection. As you know, we can also find the wound infection by physical examination. If pus drainage was possible, all pus was cultured.

Fig 1, There are some typos, and we fixed them in the revised manuscript.

Fig 2, The reviewer is correct in that there is no exact data. We deleted Fig 2.

Table 3. Early surgical outcomes in patients undergoing LATG and TLTG

Variables	LATG (n=266)	TLTG(n=421)	p-value
Operation time (min)	170 (65~453)	149 (75~342)	<0.001
Hematocrit change(%)	4.04 (-3.8~15.2)	3.49 (-4.9~18.6)	0.002
Intra-operative transfusion (n)	1 (0.4%)	1 (0.2%)	1.000
Post operative transfusion (n)	28 (10.5%)	55 (13.1%)	0.320
Intra-operative event (n)	27 (10.2%)	13 (3.1%)	< 0.001
Intra-operative anastomosis event (n)	19 (7.1%)	10 (2.4%)	0.003
Combined operation (n)	17 (6.4%)	27 (6.4%)	1.000
Time to first flatus (days, range)	3.60 (1~7)	3.30 (1~7)	< 0.001
Time to soft diet (days, range)	4.61 (2~68)	4.30 (3~36)	< 0.001
Pick of pain score (score, range)	7.11 (2~10)	6.96 (3~10)	0.912
8AM Pain score of POD #1 (score, range)	3.45 (0~10)	3.49 (0~10)	0.841
8AM Pain score of POD #3 (score, range)	2.44 (0~9)	2.54 (0~7)	0.529
8AM Pain score of POD #5 (score, range)	1.75 (0~10)	1.51 (0~8)	0.055
Number of administration of analgesics (n, range)	2.49 (0~69)	2.86 (0~67)	0.131
Post-operative hospital stay (days, range)	7.02 (5~1117)	6.75 (4~82)	0.005

Values are expressed as median (range) or number(percentage)

Hematocrit change means the difference between preoperative hematocrit and post-operative hematocrit.

n, number; LATG, laparoscopic assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy; n,

number; POD, post operative days

Table 5. Post-operative complications in patients who underwent LATG and TLTG

	LATG(n=266)	TLTG(n=421)
Bleeding	4 (1.50%)	8 (1.90%)
EJ leakage	15 (5.64%)	15 (3.56%)
EJ stricture	3 (1.13%)	2 (0.48%)
Intra-abdominal fluid collection	8 (3.01%)	26 (6.18%)
Internal hernia	5 (1.88%)	12 (2.85%)
Mechanical ileus	10 (3.76%)	28 (6.65%)
Paralytic ileus	3 (1.13%)	7 (1.66%)
Wound infection	18 (6.77%)	9 (2.14%)
Other surgical complications	4 (1.50%)	8 (1.90%)
Medical complications	4 (1.50%)	2 (0.48%)

Values are expressed as number

n, number; LATG, laparoscopic assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy; EJ, Esophagojejunostomy

Fig.1. Forming an esophagojejunostomy.

(A) Nearly two-thirds of the esophagus diameter is transected 2 cm above the gastroesophageal junction using an endoscopic linear stapler. (B) The first intracorporeal suture is made at the end of the staple line of the esophageal stump. (C) The unstapled esophagus is transected with laparoscopic scissors after the remnant stomach has been clipped with manual titanium clips to avoid spillage of cancer cells. (D) The second and third intracorporeal sutures are made at the esophagostomy site of the esophageal stump (E) To create an esophagojejunostomy, an endoscopic linear stapler is inserted by the operator between the esophagostomy and enterostomy of the jejunum. At this time the first assistant retracts the first thread towards the operator's direction inside the abdominal cavity, and the second assistant retracts the second thread through the right lower trocar from the outside of the abdomen. (F) After an esophagojejunostomy has been constructed, the entry hole is held with tress suturing to approximate the tissue. (G) The remnant entry hole is closed by the operator with an endoscopic linear stapler. (H) An esophagojejunal anastomosis after completion of the reconstruction.



Baishideng Publishing Group

7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
<https://www.wjgnet.com>

