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Meta-analysis and systematic review on laparoscopic-assisted distal gastrectomy (LADG) and totally laparoscopic distal gastrectomy (TLDG) for gastric cancer: Preliminary study for a multicenter prospective KLASS07 trial

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ABSTRACT

Background: The curative surgical treatment of gastric cancer in the current laparoscopic surgical era relies on the surgeon's preference, technical difficulties, and concerns regarding outcome have led to the availability of totally laparoscopic distal gastrectomy (TLDG) and laparoscopic-assisted distal gastrectomy (LADG). A consensus on which of the two procedures is preferable is necessary. Therefore, the aim of this study was to evaluate the differences between LADG and TLDG in terms of surgical outcomes, postoperative recovery, pain, and complications.

Methods: PubMed, Google Scholar, Medline, Embase, and Cochrane databases were explored up to 2017 to evaluate TLDG and LADG. Parameters including surgical outcomes, postoperative recovery, and postoperative complications were subjected to meta-analysis to calculate the odds ratio and weighted mean difference with 95% confidence intervals (c.i.).

Results: Twenty-five studies (24 non-RCT and 1 RCT) with a total of 4562 gastric cancer patients were included in the meta-analysis. Under reconstruction-matched analysis, overall complications and anastomotic complications were similar for TLDG and LADG. Nevertheless, short-term outcomes such as blood loss, time to first soft diet, hospital stay, analgesic use, and CRP level were favourable for TLDG, while all other surgical outcomes showed no difference.

Conclusions: TLDG and LADG did not show significant differences in surgical outcomes and postoperative complications, including anastomotic-related morbidity. Therefore, decisive factors in selecting surgical procedures, which previously consisted of surgical outcomes, have been superseded by extra-surgical values such as cosmesis, economics, and patient's quality of life. These factors will be explored in a future multicentre prospective study (KLASS07 trial).

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Introduction

Since the introduction of laparoscopic gastrectomy, gradual improvements in technical skills and instruments have eventually allowed surgeons to perform total laparoscopic procedures over laparoscopic-assisted surgeries. Although totally laparoscopic distal gastrectomy (TLDG) and laparoscopic-assisted distal gastrectomy (LADG) are both minimally invasive surgeries for gastric cancer with the same surgical treatment principles, in the former, all surgical processes are performed intracorporeally, while, in the latter, extracorporeal gastro-enteric anastomosis is achieved [1]. Whether the procedural differences between TLDG and LADG affect surgical outcomes is still under debate; hence, even in today's laparoscopic surgical era, the surgeon's preference, technical difficulty, and concerns about outcome have led to the co-existence of TLDG and LADG.

Despite numerous previous comparisons of TLDG and LADG, a firm consensus has yet to be reached. Some studies have suggested that TLDG is superior in postoperative recovery [2–4], while others regard LADG to be better [5,6]. Such discrepancies are observed not only in terms of postoperative recovery, but also in other aspects of surgical outcome. As previous studies have had different objectives and primary outcomes, the precise comparison of TLDG and LADG has not been feasible. Hence, it has become inevitable to systemically merge the available literatures to yield a firm consensus. This study is expected to lead researchers to a comparative TLDG vs LADG study, with suggestions regarding the objectives for further evaluation.

Thus, the aim of the present study was to compare TLDG and LADG procedures in terms of surgical outcomes, postoperative recovery, pain, and complications. Various outcomes have been explored using subgroup and sensitivity analysis to increase statistical power and minimize inconsistencies.

Methods

Literature search strategy

A systematic review was performed using the PubMed, Google Scholar, Medline, Embase, and Cochrane databases to identify articles published up to 2017 that compared TLDG and LADG. This meta-analysis was performed in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [7]. The search terms used were: [‘laparoscopic’(MeSH) and ‘distal gastrectomy’(MeSH)] and [‘laparoscopic assisted’(MeSH) or ‘totally laparoscopic’(MeSH) or ‘gastric cancer’(MeSH)]. Free-text and Mesh search terms were used as keywords. The “related articles” function and citations within identified articles' were also reviewed, to search for additional articles that may not have been indexed. A Korean paper with suitable data presented in English was also included.

Study selection criteria

Studies that met the following criteria were included: (1) studies comparing TLDG and LADG; (2) studies focusing on patients only with laparoscopic surgery; (3) studies presenting outcomes such as hospital stay, operation time, and postoperative complications. In cases where two studies were performed by the same author using identical cohorts, the study with the larger sample size was selected. Studies were excluded based on the following criteria: (1) studies that did not include outcomes of interest; (2) studies lacking the necessary statistical data such as variance; (3) studies with mixed groups of open and laparoscopic surgery; (4) studies that did not identify the surgical approach (totally laparoscopic or laparoscopic-assisted); and (5) posters, review papers, comments, and abstract-only publications.

Outcomes of interest

The primary outcomes were anastomotic-related and overall complications in LADG and TLDG procedures. Anastomotic complications included anastomotic leakage, bleeding, and stenosis, while overall complications included anastomotic complications, incision, pulmonary, pancreatic, intra-abdominal bleeding, intra-abdominal fluid collection or abscess, intestinal obstruction, gastric stasis, ileus, and duodenal stump leakage.

The secondary outcomes were surgical outcomes (operative time, blood loss, retrieval of lymph nodes [LN]), postoperative recovery (flatus time, soft diet resume time, length of hospital stay), and postoperative pain-related factors (serum C-reactive protein (CRP) analgesic use). Both primary and secondary outcomes were assessed with matched-reconstruction analysis (subgroup analysis) to eliminate the potential bias due to differences in anastomosis between the groups.

Data extraction and quality assessment

Two independent reviewers (M.S. and H.E.) evaluated the original studies and extracted the data; including (1) characteristics of the study (authors, duration of study, year of publication, study design, location of the hospital, number of patients operated using each method); (2) background data of participating patients (age, sex, body mass index (BMI) location of tumour, size of tumour, tumour stage, LN dissection, anastomosis); (3) surgical outcomes (operation time, hospital stay, postoperative complications, number of retrieved LN, blood loss, time to first flatus, serum POD, CRP level). Overall, 24 non-randomised studies and one randomised controlled trial (RCT) (Table 1) [2–6,8–30] were qualitatively assessed on the basis of the Newcastle-Ottawa Scale (NOS) [31] (Supplementary Table 1). Studies were evaluated based on the following criteria: the selection of study groups, comparability of the groups, and ascertainment of outcomes. A score of 0–9 was allocated to each study and studies with a score of 6 or higher were considered eligible, while scores of 7 or higher were classified as high quality studies.

Subgroup analysis and sensitivity analysis

Since postoperative outcomes may potentially be affected by the type of reconstruction method, a subgroup analysis for anastomosis was performed for the time to first flatus, time to first soft diet, length of hospital stay, overall complications, and anastomotic complications. Sensitivity analysis, which excluded unmatched reconstruction groups and uncontrolled T stage studies, was further conducted to minimize heterogeneity and increase credibility.

Statistical analysis

Analysis was conducted using the statistical software Review Manager (RevMan Version 5.3; The Nordic Cochrane Centre, Copenhagen, Denmark). Dichotomous variables were analysed using odds ratio (OR) and continuous variables were analysed using weighted mean difference (WMD). ORs and WMDs were presented with 95% confidence intervals (c.i.). Statistical heterogeneity was estimated using Higgins I^2 statistics [32] and the Cochran Q test. I^2 values were graded as follows: <25% as low, 25–50% as moderate, and >50% as high heterogeneity [33]. If the heterogeneity was high ($I^2 > 50\%$ or $P < 0.100$), a random effects model was used for analysis. In case the heterogeneity level was low, a fixed effects model was selected. Where data were presented as median and range or

Table 1
Background and matched patients information of included studies.

Study name (year)	Study design	Study period	No. of patients		Age	Sex	BMI (kg/m^2)	Location of tumour	Size of tumour	Tumour stage	LN dissection	Anastomosis		Anastomosis composition between groups
			TLDG	LADG								TLDG	LADG	
KY Song et al. (2008)	OCS(P)	2005–2006	20	20	ns	ns	ns	–	ns	ns	ns	B1+RY	B1+B2	–
O Ikeda et al. (2009)	OCS(R)	2005–2007	56	24	ns	ns	ns	ns	ns	ns	ns	B1+RY	B1+RY	sig diff
Simon K.H.Wong et al. (2009)	OCS(R)	2001–2006	18	10	ns	ns	–	–	ns	Ns	–	B2+RY	B2+RY	–
T Kinoshita et al. (2011)	OCS(R)	2007–2009	42	41	ns	ns	–	–	–	Ns	ns	B1	B1	ns
BS Kim et al. (2011)	OCS(R)	2006–2009	180	268	ns	ns	ns	–	–	Ns	–	B1	B1	ns
J Lee et al. (2011)	OCS(R)	2004–2011	130	269	ns	ns	–	ns	ns	Ns	ns	B2	B2	ns
MG Kim et al. (2011)	OCS(R)	2009–2010	239	328	ns	ns	sig diff	–	ns	sig diff	–	B1	B1	ns
BS Choi et al. (2013)	OCS(R)	2007–2012	37	35	ns	ns	ns	–	ns	Ns	sig diff	B2+RY	B1+B2+RY	sig diff
DG Kim et al. (2013)	OCS(P)	2009–2012	60	106	ns	ns	ns	–	–	–	ns	B1	B1	ns
HG Kim et al. (2013)	OCS(R)	2005–2012	111	136	ns	ns	ns	–	ns	–	sig diff	B1+B2	B1+B2	sig diff
S Kanaji et al. (2014)	OCS(R)	2010–2012	40	74	ns	ns	ns	ns	–	–	–	B1+RY	B1+RY	ns
G Han et al. (2014)	OCS(R)	2005–2013	134	77	ns	ns	ns	sig diff	sig diff	sig diff	ns	B2+RY	B1+B2+RY	sig diff
B Zhang et al. (2015)	OCS(R)	2010–2014	24	45	ns	ns	–	–	–	–	–	B1	–	–
C Zhang et al. (2015)	OCS(R)	2012–2013	11	25	ns	ns	ns	–	–	Ns	ns	B2	B2	ns
J Woo et al. (2015)	RCT	2011–2013	55	55	ns	ns	ns	ns	ns	Ns	ns	B2	B2	ns
SH Lee et al. (2015)	OCS(R)	2008–2014	33	99	ns	ns	ns	ns	ns	Ns	ns	B1+B2	B1+B2	ns
SM Kim et al. (2015)	OCS(P)	2013–2014	102	100	ns	ns	sig diff	ns	ns	ns	–	B2	B1	sig diff
HH Lee et al. (2015)	OCS(R)	2004–2011	138	100	sig diff	sig diff	sig diff	ns	ns	ns	ns	B1	B1	ns
K Chen et al. (2015)	OCS(P)	2004–2014	198	115	ns	ns	ns	–	ns	ns	ns	B1+B2	B1+B2	ns
O Jeong et al. (2015)	OCS(P)	2013–2014	42	179	sig diff	ns	ns	ns	ns	ns	ns	B1	B1	ns
T Shinohara et al. (2016)	OCS(P)	2007–2013	57	43	ns	ns	sig diff	sig diff	sig diff	ns	–	B1+B2+RY	B1+RY	sig diff
KB Park et al. (2016)	OCS(R)	2013–2014	41	44	ns	ns	ns	ns	ns	ns	ns	B1	B1	ns
S Nishimura et al. (2016)	OCS(R)	2006–2014	126	69	ns	ns	–	ns	–	ns	ns	B1+B2+RY	B1+B2+RY	sig diff
M Lin et al. (2016)	caseCase-matched study	2011–2014	143	143	ns	ns	ns	–	ns	ns	–	B1	B1	ns
JH Kim et al. (2017)	matched Matched cohort study	2008–2013	60	60	ns	ns	ns	ns	ns	ns	–	B2	B2	ns

Blank with (–) indicates no information presented by study. 'ns' indicates no significant differences between the two groups($P > 0.05$). 'sig diff' indicates significant differences between two groups(TLDG vs LADG, $P > 0.05$). OCS, observational clinical study; (R), retrospectively collected data; (P), prospectively collected data; RCT, randomised controlled trial; B1, Billroth I; B2, Billroth II; RY, roux-en Y; T LDG, totally laparoscopic distal gastrectomy; LADG, laparoscopic-assisted distal gastrectomyLegends to figures.

interquartile range, it was converted to mean and standard deviation according to the Cochrane handbook [34] and other reference formulas [35,36].

Results

Selected studies

A total of 1013 studies were identified from PubMed, Google Scholar, Medline, Embase, and Cochrane databases and 879 articles remained after screening duplicates (Supplementary Fig. 1). Next, 571 non-relevant articles and 40 abstracts only studies were further removed. Papers from the same first authors or from identical hospitals were reviewed and 10 papers from identical patient pools were excluded. The remaining 132 papers were cautiously reviewed in full text and studies lacking essential statistical data for meta-analysis such as variance, and those in which the operation type (LADG/TLDG) could not be identified were excluded. Finally, 25 studies were included for the meta-analysis (Table 1) [2–6,8–30].

Surgical Outcomes: *Operative Outcome, Blood Loss, Number of Lymph Nodes Retrieved.*

Twenty-five studies provided data on operative time, 21 on blood loss, and 21 on the number of LNs retrieved. The meta-analysis showed no statistically significant differences between the TLDG and LADG in terms of operative time (Fig. 1A, WMD −4.51; 95% c.i. −13.93 to 4.92, $I^2 = 95\%$, $P = 0.35$). In contrast, there was significantly lower blood loss (Fig. 1B WMD −35.67; 95% c.i. −61.09 to −10.25, $I^2 = 97\%$, $P = 0.006$) and a higher number of LNs retrieved (Fig. 1C, WMD 2.10; 95% c.i. 0.78 to 3.41, $I^2 = 69\%$, $P = 0.002$) in the TLDG than in LADG procedures.

Nevertheless, when the extent of LN dissections was matched, there was no statistically significant difference in terms of the number of LNs retrieved (Fig. 1D, WMD 0.41; 95% c.i. −0.44 to 1.26, $I^2 = 0\%$, $P = 0.34$).

Postoperative Recovery: *Time to First Flatus, Time to First Soft Diet, and Length of Hospital Stay.*

Seventeen studies that reported data regarding time to first flatus, 15 reported time to first soft diet, and 23 reported length of postoperative hospital stay. While meta-analysis revealed no statistically significant differences between TLDG and LADG in the time to first flatus (Fig. 2A, WMD −0.17; 95% c.i. −0.41 to 0.06, $I^2 = 94\%$, $P = 0.14$), TLDG allowed a faster return to soft diets (Fig. 2B, WMD −0.29; 95% c.i. −0.52 to −0.06, $I^2 = 80\%$, $P = 0.02$) and a shorter period of hospital stay (Fig. 2C, WMD −0.76; 95% c.i. −1.16 to −0.36, $I^2 = 78\%$, $P = 0.0002$) than the LADG procedure.

Additional subgroup analyses were performed to determine whether the difference in time to first soft diet and length of hospital stay between the TLDG and LADG was due to the reconstruction approach (TLDG: intracorporeal vs LADG: extracorporeal) or the type of anastomosis (Billroth I (B1), Billroth II (B2), Roux-en-Y (RY)). These subgroup analyses (Fig. 2B and C) revealed that, in terms of time to first soft diet, there was a significant difference in Billroth I (TLDG_B1 vs LADG_B1), but not in Billroth II (TLDG_B2 vs LADG_B2), while with regard to the length of hospital stay, there was a significant difference in Billroth II but not in Billroth I. Therefore, the presence of a statistically significant difference was contradicted by the reconstruction subgroups.

Postoperative Pain Related Factors: *Analgesic Use, Serum CRP.*

The TLDG procedure required less analgesic use (Fig. 3A, WMD −0.79; 95% c.i. −1.52 to −0.05, $I^2 = 83\%$, $P = 0.04$) postoperatively and resulted in lower serum CRP levels (Fig. 3B, WMD −0.75; 95% c.i. −1.25 to −0.25, $I^2 = 0\%$, $P = 0.003$) than the LADG procedure.

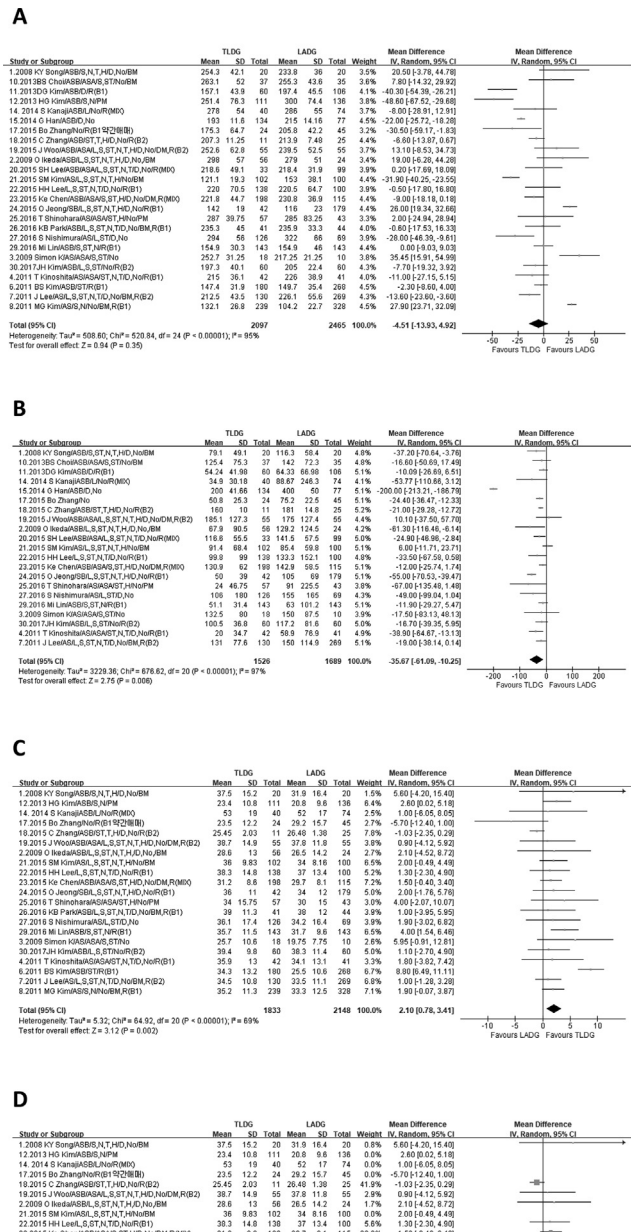


Fig. 1. Forest plot comparing surgical outcomes **A**: Operative time, **B**: Blood loss, **C**: Number of lymph nodes retrieved, **D**: Number of lymph nodes retrieved with matched lymph node dissection.

Postoperative complications

Overall complications

There was no statistically significant difference between the TLDG and LADG procedures with regard to overall complications (Fig. 4A, OR = 0.97; 95% c.i. 0.79 to 1.19, $I^2 = 14\%$, $P = 0.78$). To exclude the effects from types of reconstructions and tumour stages, subgroup and sensitivity analyses were performed.

For the reconstruction-matched patients (Fig. 4A), subgroups were categorised according to anastomosis (B1, B2, RY) site. The

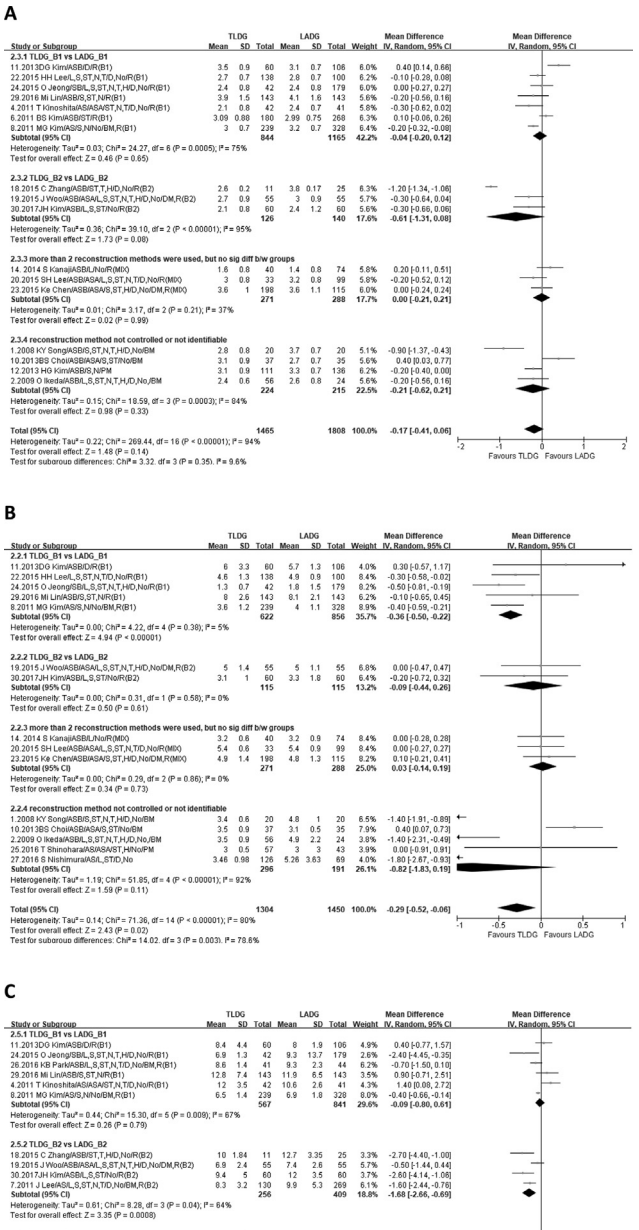


Fig. 2. Subgroup analysis of postoperative recovery with matched reconstruction **A**: Time to first flatus, **B**: Time to first soft diet, **C**: Length of hospital stay.

TLDG_B1 vs LADG_B1 subgroups included studies that only used Billroth I and compared intracorporeal (TLDG) and extracorporeal (LADG) reconstructions, which on analysis revealed no significant differences (Fig. 4A, TLDG_B1 vs LADG_B1, OR = 1.08; 95% c.i. 0.78 to 1.48, $I^2 = 7\%$, $P = 0.64$). The TLDG_B2 vs LADG_B2 subgroup included studies that only used Billroth II and compared intracorporeal (TLDG) and extracorporeal (LADG); again no significant differences were identified (Fig. 4A, TLDG_B2 vs LADG_B2, OR = 0.60; 95% c.i. 0.26 to 1.36, $I^2 = 0\%$, $P = 0.22$). The third subgroup analysis evaluated studies that provided data on similar ratio (differences in ratio $P > 0.05$) of two or more reconstruction methods (B1, B2, RY). The analysis also resulted in no significant differences (Fig. 4A OR = 0.69; 95% c.i. 0.38 to 1.25, $I^2 = 0\%$, $P = 0.22$). The final subgroup analysis included studies with uncontrolled or unidentifiable reconstruction methods (differences in ratio $P < 0.05$), and this analysis also revealed no significant differences (Fig. 4A OR = 1.05; 95% c.i. 0.75 to 1.45, $I^2 = 39\%$, $P = 0.79$).

In the sensitivity analysis (Fig. 4B, OR = 0.89; 95% c.i. 0.67 to 1.17, $I^2 = 0\%$, $P = 0.41$), the final subgroup (uncontrolled or unidentifiable reconstruction methods) was excluded in order to exclusively include matched reconstruction studies, while studies with uncontrolled T stage were also excluded as tumour stage may have effects on postoperative complications. The results were no different from those before the exclusion, demonstrating the robustness of the results.

Anastomotic complications

Likewise, the reconstruction-matched subgroup analysis of anastomotic complications (Fig. 5A, OR = 1.16; 95% c.i. 0.72 to 1.88, $I^2 = 0\%$, $P = 0.55$), which included anastomotic leakage, bleeding, and stenosis (Fig. 5B–D), revealed no significant differences.

Other complications

Other complications included non-anastomotic complications (Supplementary Fig. 2) such as incision, pulmonary, pancreatic or intra-abdominal bleeding, intra-abdominal fluid collection and abscess, duodenal gastric emptying, intestinal obstruction, gastric stasis, ileus, and duodenal stump leakage, all of which showed no statistically significant differences between the TLDG and LADG procedures.

Risk of bias

Studies were evaluated to create risk of bias graph and summary (Supplementary Fig. 3A) using RevMan software (The Nordic Cochrane Centre). It was impossible to blind the type of procedure (TLDG or LADG) to the operators (surgeons) since the procedures are undeniably different. However, the absence of blinding did not necessarily affect the surgical outcomes; thereafter, performance bias was evaluated as low risk. The detection and reporting biases were not clearly mentioned in most of the studies; hence, these were classified as unclear. Publication bias, assessed with the funnel plot in RevMan, showed no potential risks (Supplementary Fig. 3B).

Discussion

Intracorporeal versus extracorporeal approach is a general issue across diverse surgical disciplines including gastrectomy and hemicolectomy; yet, their applicability and effectiveness are still being debated. Comparing gastrectomy and right colectomy results may provide meaningful implications and extrapolations and help draw an agreeable conclusion. A meta-analysis that investigated intracorporeal versus extracorporeal anastomosis on right hemicolectomy suggested that intracorporeal anastomosis is better in outcomes with respect to the length of hospital stay and time to soft diet [37], and these are consistent with our results although we observed different results on reconstruction methods. While their findings supported the superiority of intracorporeal anastomosis in short-term morbidity [37], we found no differences in terms of overall as well as anastomotic-related complications. This difference may be attributable to our reconstruction-matched analysis, which we introduced to focus on purely the difference between

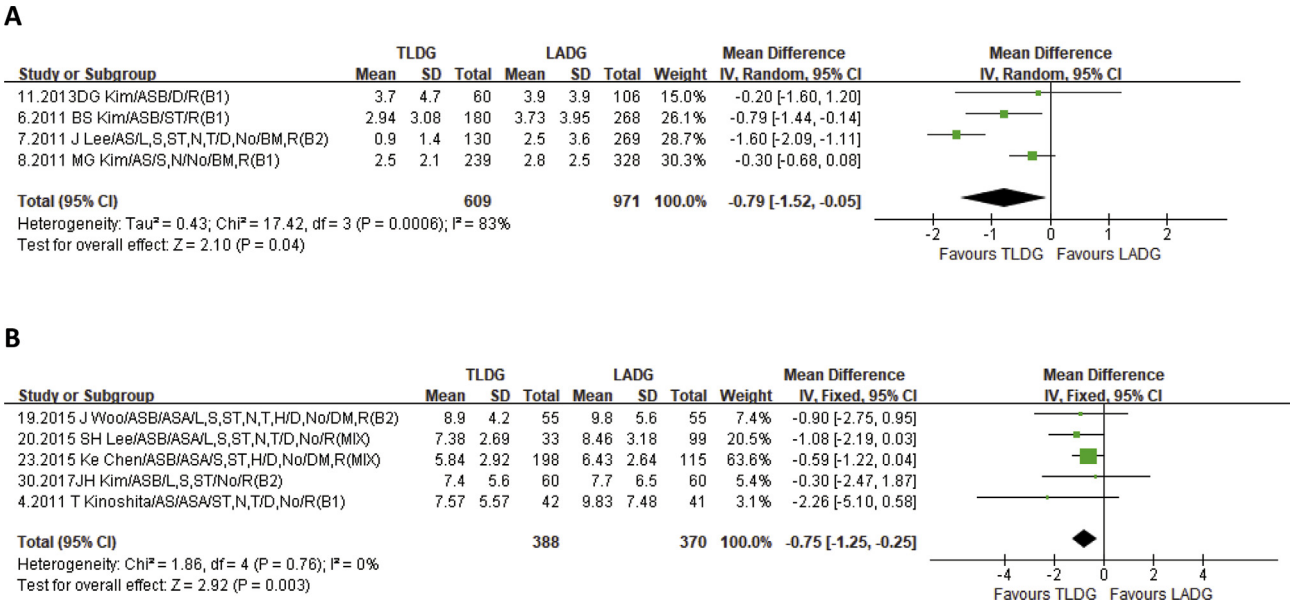


Fig. 3. Forest plot comparing postoperative pain **A**: Analgesic Use, **B**: Serum CRP.

intracorporeal and extracorporeal approach.

Regardless of the improvements in the TLDG procedures, apprehension towards operative complications still exists; therefore, the preference over the two laparoscopic distal gastrectomy procedures with regard to postoperative complications still remains controversial. There is a lack of consensus among previous studies on this issue as some suggest TLDG to be better [4], while others suggest the opposite [6]. Such contradicting results may possibly be explained by examining the impact of anastomosis. Consequently, unlike the most recent meta-analysis [30], the subgroup and sensitivity analysis considering anastomosis was conducted to elucidate the true effect of the intracorporeal and extracorporeal techniques in surgical outcomes. As a result, this study provides comprehensive analysis of differences between the TLDG and LADG procedures using meta-analysis to objectively evaluate the effective therapeutic value of both TLDG and LADG.

The present study showed that even with matched anastomosis, there was no significant difference in the rate of overall postoperative complications. As for morbidities, anastomotic-related complications have been the focus of interest, as these are technically demanding in TLDG; nevertheless, it has not been explicitly explored in previous studies. Based on the results of this study, and contrary to the surgeons' fears, the TLDG was not inferior to the LADG procedure in terms of anastomotic-related complications.

While there were no differences between TLDG and LADG in terms of complications, a statistically significant difference was observed in short-term outcomes: blood loss, time to first soft diet, length of hospital stay, serum CRP and analgesic use, in which the TLDG procedure was superior to LADG, with the remaining factors showing no significant difference. Although previous studies [4,15,26] have already suggested time to first soft diet and hospital stay were significantly shorter in TLDG, this hypothesis was exclusively re-evaluated in this study controlling for reconstruction type. However, subgroup and sensitivity analysis of anastomosis presented conflicting results (Fig, 3B–3C), in which a significant difference in Billroth I was present but not with Billroth II or vice versa, indicating that the type of anastomosis may be the reason for the differences between the TLDG and LADG procedures. Therefore, it is difficult to definitively conclude that the statistically significant difference in recovery parameters (time to first soft diet and hospital stay) is attributable exclusively to the type of procedure (TLDG vs LADG) and not to the type of anastomosis (BI, BII, RY).

Further, oncological outcomes are highly relevant in this context and must therefore be considered and analysed when comparing TLDG and LADG. Among all the enrolled studies, only one study by Lee et al. [21] has mentioned the oncological outcome in terms of 5-year-disease free and overall survival rates. According to the study, there were no statistically significant differences in the 5-year-disease-free and overall survival rates between TLDG and LADG.

Furthermore, the technical difficulty has been another big issue for surgeons. TLDG is known to be technically more demanding due to limitations in performing anastomosis in terms of field of vision and space constraints [8]. However, according to the results of this study, there was no statistically significant difference between the TLDG and LADG procedures in terms of surgical outcomes, suggesting that the technical difficulty did not have a substantial impact on the surgical outcome; therefore, the technical challenge should no longer be the determining factor for selection of procedures.

In addition, the cost of healthcare may be an important decisive factor for patients. A study by Shinohara et al. [26] comparing the costs of TLDG and LADG suggested that TLDG has a higher operation cost (¥982,000 for TLDG vs ¥879,830 for LADG) due to use of specialised instruments such as staplers [5]. Nevertheless, in terms of the overall hospital costs, given the shorter hospital stay following TLDG as suggested in this study, the higher operation-related costs for TLDG procedures may be offset by a reduction in costs resulting from shorter hospital stays. Thus, a further comparison of the overall hospital costs and consideration of hospital stays required for TLDG and LADG, is not only essential but inevitable to accurately determine whether the cost of TLDG is comparable with that of LADG in future studies.

As previously mentioned, while the TLDG can provide better quality of life in the short term due to faster recovery and less postoperative pain, there is no substantial difference in surgical outcomes and postoperative complications between TLDG and LADG. With technical difficulty and costs no longer being major decisive factors when choosing between TLDG and LADG, additional extra-surgical factors such as cosmesis and quality of life assessment must be taken into consideration when determining

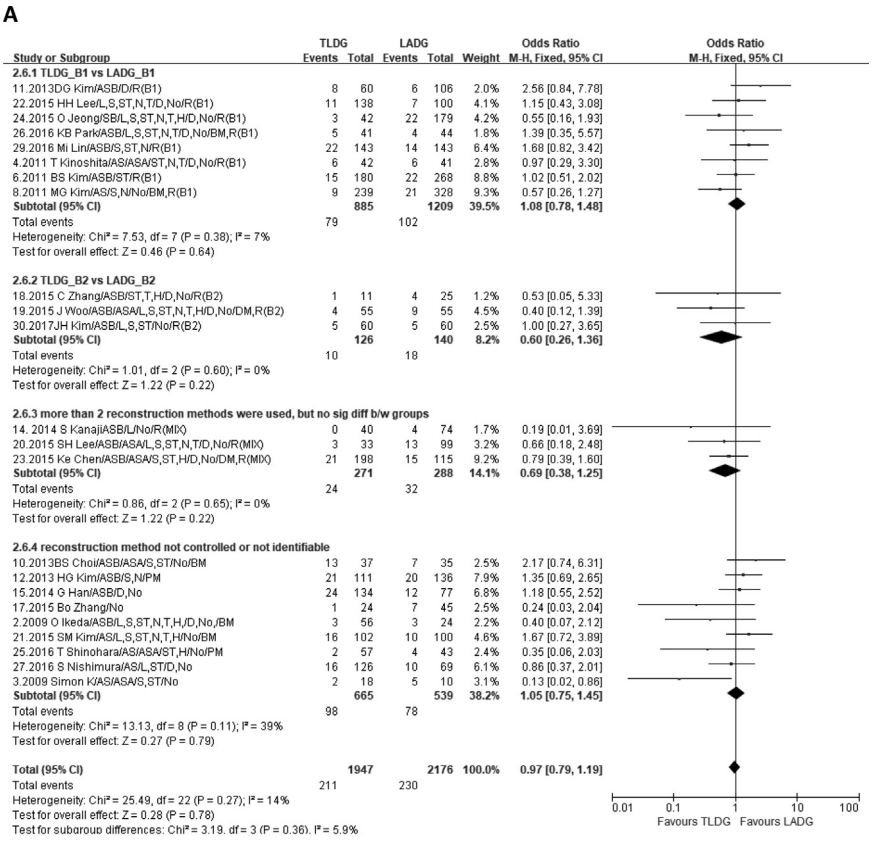
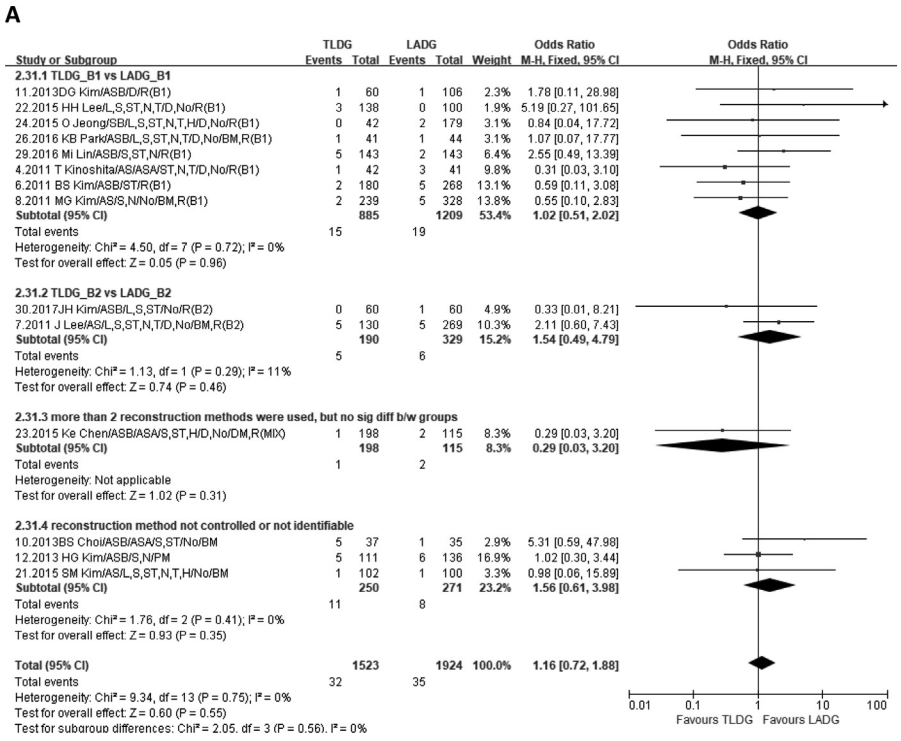
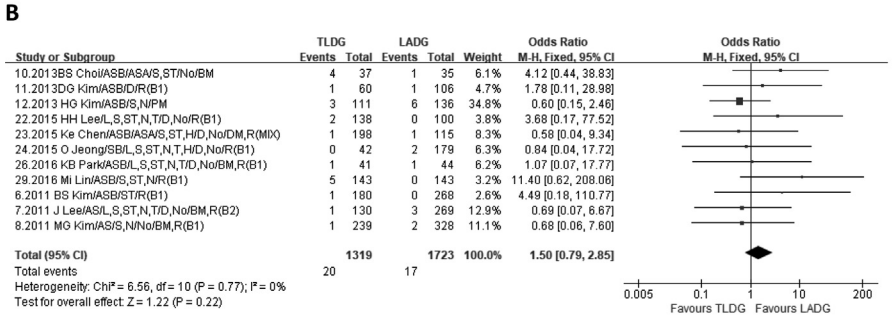
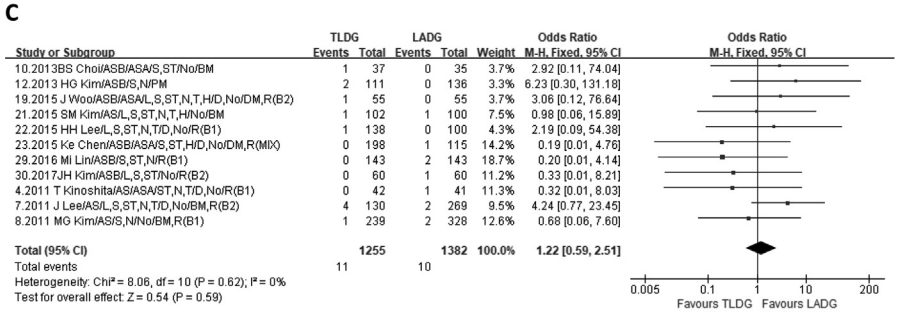


Fig. 4. Forest plot comparing postoperative complications **A**: Subgroup analysis of overall complications with matched reconstruction procedures, **B**: Sensitivity analysis of overall complications with matched reconstruction procedures and matched T stage.







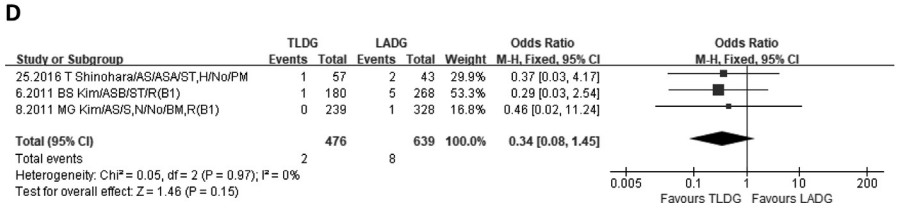


Fig. 5. Forest plot comparing anastomotic complications **A**: Subgroup analysis of anastomotic complications with matched reconstruction, **B**: Anastomotic leakage, **C**: Anastomotic bleeding, **D**: Anastomotic stenosis.

which of the two laparoscopic gastrectomy procedures is preferable.

With respect to cosmesis, this may be the most notable difference between TLDG and LADG for patients whose long-term survival is expected. There is no study or evidence currently available concerning patients' satisfaction on operation scars. Nevertheless, cosmesis is a crucial factor that may directly have an impact on the patients' postoperative quality of life. Thus, it must be underlined that long-term quality of life must be taken into account during the decision-making process. In essence, it is necessary to compare the degree of satisfaction and postoperative quality of life of patients undergoing TLDG and LADG. This is a major endpoint of the future prospective randomised trial, KLASS07, to be assessed using validated questionnaires.

There are several limitations to this study. First, even with reconstruction-matched analysis, there are certain aspects that were impossible to control such as the type of staplers used. Second, among the 25 studies subjected to meta-analysis, there is only one RCT. Finally, the racial dominance of East Asians limits the generalisability of the study results on worldwide population.

In conclusion, the TLDG was found to be preferable with respect to postoperative pain and recovery, but there was no significant difference between TLDG and LADG in terms of surgical outcomes and postoperative complications even with controlled anastomosis. In addition, technical difficulty no longer appears to have substantial impact on surgical outcomes, and the cost of TLDG may be comparable with LADG when considering the shorter hospital stay required by TLDG procedures. Consequently, what have previously been considered as key decisive factors, such as surgical outcomes, postoperative complications, technical difficulty, and costs, may no longer be considered significant when choosing between the two procedures. Instead, the focus has shifted to patient-oriented elements such as cosmesis and quality of life.

Further evaluation of such factors including costs, cosmesis, and quality of life should and will be conducted in the on-going RCT KLASS 07(CKLASS 01), which is registered at www.clinicaltrials.gov as NCT03393182.

Disclosures

The authors declare they have no conflicts of interest or financial ties to disclose.

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All authors confirm that we had complete access to the study data that support the publication.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2019.06.030.

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