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ORIGINAL RESEARCH

Comparison of Totally Laparoscopic Total Gastrectomy and Laparoscopy-Assisted Total Gastrectomy on Short-Term Outcomes, Inflammatory Response Markers, and Glucose and Lipid Metabolism in Gastric Cancer Patients

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Objective: To investigate the therapeutic efficacy of totally laparoscopic total gastrectomy (TLTG) versus laparoscopy-assisted total gastrectomy (LATG) in gastric cancer (GC) treatment, as well as their effects on postoperative inflammation and glucose and lipid metabolic status.

Methods: Clinical data of 68 individuals with GC who underwent LATG (n=31) and TLTG (n=37) from January 2020 to December 2022 were procured. This included intraoperative blood loss, operative time, incision length, number of lymph nodes dissected, postoperative complication rates, and recovery indicators, such as inflammation, glucose metabolism, and lipid metabolism.

Results: The TLTG cohort demonstrated significant advantages in intraoperative blood loss, operative time, and incision length compared to the LATG cohort. Furthermore, TLTG was superior in reducing the incidence of complications. Nevertheless, no substantial variation was observed in the quantity of lymph nodes dissected. Additionally, TLTG showed benefits in postoperative recovery, including better control of the inflammatory response, reduction of complication risks, shorter hospital stay, and alleviation of postoperative pain. TLTG also exhibited a reduced impact on inflammation and demonstrated greater effectiveness in improving postoperative glucose and lipid levels.

Conclusion: TLTG surgery is associated with superior clinical outcomes in the treatment of GC compared to LATG, particularly in reducing surgical trauma and accelerating postoperative recovery. Furthermore, TLTG facilitates the resolution of postoperative inflammatory responses and the amelioration of metabolic disorders. The findings from this investigation advocate for the broader adoption of TLTG in the surgical treatment of GC.

Keywords: totally laparoscopic total gastrectomy, laparoscopy-assisted total gastrectomy, gastric cancer, inflammatory markers, glucose and lipid metabolism

Introduction

Gastric cancer (GC) ranks as the fourth most prevalent malignant neoplasm worldwide and is the second leading cause of cancer-associated deaths. The pathophysiological processes of GC and associated treatments can disrupt systemic glucose and lipid metabolism through the production of inflammatory cytokines during tumor growth.[1] These cytokines can impair pancreatic β-cell function and decrease insulin synthesis and secretion, leading to hyperglycemia. Additionally, tumor growth consumes a significant amount of energy, increasing lipid breakdown and elevating blood lipid levels. Both hyperglycemia and hyperlipidemia can promote tumor growth, thereby exacerbating the progression of GC.[2] Surgical intervention can mitigate these inflammatory responses and ameliorate metabolic disturbances.[3,4]

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In recent years, the development of laparoscopic technology popularized the use of laparoscopy-assisted total gastrectomy (LATG) and totally laparoscopic total gastrectomy (TLTG) as surgical interventions for managing GC.[5] LATG is a procedure that combines laparoscopic techniques with a semi-open approach wherein certain steps are conducted within the abdominal cavity, followed by the removal of the stomach and extracorporeal anastomosis.[6] In contrast, TLTG is performed entirely within the abdominal cavity through small incisions and, while challenging, this technique eliminates the need for open surgery.[7] Despite the extensive use of LATG and TLTG in treating GC, the therapeutic efficacy of either surgical method remains controversial.[8] This study provides evidence for the optimal surgical treatment of GC by comparing the efficacy of LATG and TLTG, as well as their effects on inflammatory markers and glucose and lipid metabolism.

Materials and Methods

Patients and Methodologies

We retrospectively collected clinical data from 68 individuals who received either LATG (n=31) or TLTG (n=37) at the First Affiliated Hospital of Bengbu Medical University from January 2020 to December 2022. Inclusion and exclusion criteria were based on the "Laparoscopic Gastric Cancer Surgery Operation Guidelines (2007)"[9] Additional inclusion criteria were as follows: (1) individuals aged 18–80 years; (2) total gastrectomy was required; (3) Karnofsky Performance Scale (KPS) score >70;[10] and (4) no history of diabetes. Additional exclusion criteria were as follows: (1) history of upper abdominal open surgery; (2) history of upper abdominal radiotherapy; (3) emergency surgery was required; and (4) transfer laparotomy and palliative surgery was required. The research protocol received approval from the Ethics Committee of the First Affiliated Hospital of Bengbu Medical University.

All individuals were evaluated by gastroscopy, enhanced abdominal and pelvic CT, plain chest CT, and supraclavicular lymph node ultrasonography. All patients had histologically confirmed advanced gastric adenocarcinoma. Preoperative TNM staging was performed according to the 2012 National Comprehensive Cancer Network (NCCN) clinical practice guidelines for GC.[11]

Surgical Techniques

Both TLTG and LATG cohorts strictly adhered to the Japanese Gastric Cancer Classification, 3rd edition,[12] and the Japanese Gastric Cancer Treatment Guidelines 2014, 4th edition, performing standard D2 or D2+ lymph node dissections, including removal of lymph nodes at stations 1, 3, 4sb, 4d, 5, 6, 7, 8a, 9, 11p, and 12a.[13] All procedures were executed by an identical cohort of experienced surgeons.

In the TLTG cohort, digestive tract reconstruction was carried out intra-abdominally using a linear stapler post-lymphadenectomy, with a small vertical incision below the navel for specimen extraction.

In the LATG cohort, part or all of the reconstruction was executed externally via a midline laparotomy incision. In both cohorts, total gastrectomy reconstruction was performed using standard Roux-en-Y.

Data Collection

Patient characteristics were collected, including age, gender, BMI, hypertension, history of abdominal surgery, smoking history, drinking history, tumor location, and TNM stage. Intraoperative data included operation time, blood loss, number of lymph nodes cleared, anesthesia duration, and incision length. Postoperative recovery included average time to first flatus, time to start on a liquid diet, time to first mobilization, average hospital stay, and Visual Analog Scale (VAS) assessment of pain intensity on postoperative days one and three.[14] Postoperative complications were characterized as any unfavorable occurrences within 30 days post-operation and were classified according to the Clavien-Dindo system,[15] with grade 3 or above deemed a significant complication. Perioperative mortality was described as any fatality resulting from any cause within 30 days postoperatively.

White blood cell (WBC) count, and serum C-reactive protein (CRP) levels were assessed on the first and third postoperative days as indicators of the patient's immediate inflammatory responses. Fasting blood glucose and glycated hemoglobin (GHb) levels (mmol/L) were evaluated at one and three months postoperatively to assess glucose metabolism. Triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL), and high-density lipoprotein cholesterol (HDL) (mmol/L) were measured at one and three months postoperatively to evaluate lipid metabolism.

Statistical Analysis

The sample size was estimated using PASS software and the "two independent means" process, with blood loss serving as the main index for sample size calculation. The mean and standard deviation of the estimated blood loss of the two cohorts were obtained from the literature.[16] Utilizing a statistical power of 0.8 and a type I error of 0.05, the minimum sample size required for each cohort was 26 cases, totaling 52 cases. All statistical analyses were performed utilizing SPSS version 25.0. Quantitative data were denoted as mean ± standard deviation (±SD). For data exhibiting normal distribution and variance homogeneity, one-way analysis of variance (ANOVA) was employed, whereas the Mann–Whitney *U*-test was utilized for data not meeting these criteria. Categorical information was examined employing the chi-square test, with pairwise comparisons conducted via the SNK test. Correlation analysis was performed utilizing the Pearson approach. P values below 0.05 were deemed statistically significant.

Results

Patient Characteristics

A sum of 68 individuals participated in the investigation, 37 of whom underwent TLTG and 31 underwent LATG. Detailed clinical data for both cohorts are presented in Table 1.

Intraoperative Comparison

The TLTG cohort demonstrated markedly reduced surgical duration (244.76±6.74 minutes) than the LATG cohort (289.94±5.94 minutes; P<0.001). The intraoperative blood loss was markedly less in the TLTG cohort compared to the LATG cohort (92.41±3.52 vs 97.84±4.66 mL; P<0.001). The quantity of lymph nodes dissected did not differ markedly between the TLTG and LATG cohorts (31.70±1.56 vs 32.26±1.75; P=0.171). The incision length in the TLTG cohort (2.78±0.79 cm) was markedly shorter than the LATG cohort (7.29±1.62 cm; P<0.001). There were no operative mortalities (Table 2).

Table 1 General Baseline Data for TLTG and LATG Groups $(\overline{X} \pm SD, n\%)$

Category		TLTG	LATG	P
n		37	31	
Age (years)		61.08±11.36 (37–81)	65.74±10.72 (28–78)	0.089
Gender	Male	25	19	0.590
	Female	12	12	
BMI (kg/m^2)		21.25±1.71	22.64±1.88	0.002
Tumor Location	Cardia	7	5	0.653
	Fundus	3	1	
	Body	14	10	
	Antrum	13	15	
TNM Stage	I	4	4	0.969
	II	14	12	
	III	17	14	
	IV	2	1	

(*Continued*)

Table 1 (Continued).

Category	TLTG	LATG	P
KPS Score	94.54±3.07	95.87±3.84	0.117
Smoking History (Yes)	25	21	0.988
Alcohol History (Yes)	19	17	0.774
History of Lower Abdominal Surgery (Yes)	4	3	0.878
Hypertension (Yes)	18	16	0.808
Preoperative Blood Glucose (mmol/L)	5.77±0.44	5.80±0.73	0.802
GHb (mmol/L)	5.89±1.93	5.91±1.61	0.958
TG (mmol/L)	2.66±0.51	2.70±1.02	0.845
TC (mmol/L)	8.10±0.70	7.89±0.81	0.282
LDL (mmol/L)	3.31±0.50	3.20±0.51	0.367
HDL (mmol/L)	2.03±0.5	1.99±0.6	0.776

Abbreviations: BMI, body mass index; TLTG, totally laparoscopic total gastrectomy; LATG, laparoscopy-assisted total gastrectomy; KPS, Karnofsky performance scale; TNM, tumor node metastasis; GHb, glycated hemoglobin; TG, triglycerides; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

Table 2 Intraoperative Comparison Between TLTG and LATG Groups $(\bar{X} \pm SD)$

Category	TLTG	LATG	P
Operative Time (min)	244.76±6.74	289.94±5.94	<0.001
Intraoperative Blood Loss (mL)	92.41±3.52	97.84±4.66	<0.001
Number of Lymph Nodes Dissected	31.70±1.56	32.26±1.75	0.171
Incision Length (cm)	2.78±0.79	7.29±1.62	<0.001

Abbreviations: TLTG, totally laparoscopic total gastrectomy; LATG, laparoscopy-assisted total gastrectomy.

Postoperative Recovery Comparison

The time to first flatus for the TLTG cohort (2.97±0.80 days) was markedly less than the LATG cohort (3.94±0.98 days; P<0.001). Individuals in the TLTG cohort started a liquid diet sooner compared to the LATG cohort (4.46 ±1.04 days vs 0.81±1.11 days; P<0.001). The TLTG cohort also had a markedly shorter time to mobilization (2.03 ±0.90 days) compared to the LATG cohort (4.42±1.18 days; P<0.001). The duration of hospital stay was markedly shorter for the TLTG cohort (8.92±0.95 days) than that for the LATG cohort (12.48±1.18 days; P<0.001). Two patients (5.4%) experienced postoperative complications in the TLTG cohort, including one patient with Anastomosis leakage and one patient with Delayed emptying. This is markedly fewer relative to the seven patients (22.5%) in the LATG cohort (P<0.05), of which 2 had Anastomosis leakage, 3 had Delayed emptying, 1 had Anastomosis stenosis and 1 had Wound infection (P<0.05) (Table 3 and Supplementary Table 1).

Changes in Inflammatory Response and Metabolism

Inflammatory levels were measured on the first and third days post-operation. On the first day, the WBC count for the TLTG cohort ($10.42\pm1.20\times10^9$/L) was markedly lower than that of the LATG cohort (P<0.001), indicating a milder inflammatory response. However, by the third postoperative day, no significant differences in WBC counts were observed between the two cohorts (P=0.564). The levels of CRP, a more sensitive indicator of inflammation, showed significant differences on both the first and third postoperative days, with markedly lower levels in the TLTG cohort (P<0.001). In terms of glucose metabolism, fasting blood glucose and GHb levels one and three months postoperatively were slightly higher in the TLTG cohort compared to the LATG cohort (P <0.05), suggesting a potential advantage of TLTG surgery in modulating blood sugar. Regarding lipid metabolism, TG levels at one and three months postoperatively showed no significant difference between the TLTG and LATG cohorts (P>0.05).

Table 3 Postoperative Recovery Indicators Comparison Between TLTG and LATG Groups $(\bar{X} \pm SD,\ n\%)$

Category		TLTG	LATG	P
Average Time to First Flatus (days)		2.97±0.80	3.94±0.98	<0.001
Average Time to Liquid Diet (days)		4.46±1.04	5.81±1.11	<0.001
Time to Ambulation (days)		2.03±0.90	4.42±1.18	<0.001
Average Hospital Stay (days)		8.92±0.95	12.48±1.18	<0.001
Pain Intensity	1 Day Postoperative	3.54±1.79	8.03±1.25	<0.001
	3 Day Postoperative	2.24±1.14	5.16±1.04	<0.001
Total Number of Complications		2	7	0.037
Clavien-Dindo Classification	I	1	3	
	II	1	3	
	III	0	1	
	IV	0	0	
	V	0	0	

Abbreviations: TLTG, totally laparoscopic total gastrectomy; LATG, laparoscopy-assisted total gastrectomy.

However, TC, LDL, and HDL levels at three months post-operation were lower in the TLTG cohort compared to the LATG cohort (P <0.001), indicating a potential advantage of TLTG surgery in improving postoperative lipid metabolism (Table 4).

Table 4 Changes in Inflammation Levels and Glucose-Lipid Metabolism in Patients After Two Types of Surgery$(\bar{X} \pm SD,\ n\%)$

Category	Postoperative time	TLTG	LATG	P
Inflammatory Levels				
WBC (10^9/L)	1 day	10.42±1.20	11.72±1.07	<0.001
	3 day	8.36±0.72	8.46±0.69	0.564
CRP (mg/L)	1 day	21.87±6.49	31.74±6.89	<0.001
	3 day	83.22±4.69	115.63±10.82	<0.001
Glucose Metabolism Levels				
Fasting Blood Glucose (mmol/L)	1 Month	3.89±0.31	3.32±0.52	<0.001
	3 Month	5.00±0.54	4.71±0.52	0.026
GHb	1 Month	4.12±0.23	3.49±0.61	0.002
	3 Month	5.21±0.41	4.82±1.02	0.003
Lipid Metabolism Levels				
TG (mmol/L)	1 Month	1.78±0.32	1.85±0.46	0.438
	3 Month	1.92±0.30	2.00±0.27	0.377
TC (mmol/L)	1 Month	6.47±0.72	6.70±0.59	0.143
	3 Month	4.52±0.65	5.50±0.78	<0.001
LDL (mmol/L)	1 Month	2.47±0.22	2.80±0.81	0.012
	3 Month	1.46±0.90	2.10±0.37	<0.001
HDL (mmol/L)	1 Month	1.49±0.51	1.80±0.23	0.014
	3 Month	1.32±0.49	1.39±0.17	0.431

Abbreviations: WBC, white blood cell count; CRP, C-reactive protein; TLTG, totally laparoscopic total gastrectomy; LATG, laparoscopy-assisted total gastrectomy; GHb, glycated hemoglobin; TG, triglycerides; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

Discussion

GC represents a significant global health burden, and treatment strategies are continuously evolving. Surgical intervention plays a crucial role in the management of GC, particularly through two primary approaches: LATG and TLTG.[17,18] LATG is widely used due to its mixed operation, which integrates the advantages of both laparoscopy and open surgery.[19] In contrast, TLTG is a fully laparoscopic procedure that represents a more technologically advanced surgical approach and concept.[20] However, the distinct clinical advantages and disadvantages of each technique have been the subject of significant attention and debate.[21] In this study, we analyzed the efficacy of LATG and TLTG. Our results suggest that TLTG demonstrates significant improvements in intraoperative performance, postoperative recovery, and associated complications compared to LATG.

Our findings indicate that TLTG markedly outperformed LATG in reducing surgical duration and minimizing intraoperative bleeding, both critical factors that influence postoperative recovery and complication rates.[16,22] These results demonstrate the intraoperative advantages of TLTG. However, there was no significant difference between the number of lymph nodes harvested, indicating that both surgical methods were equally effective. Additionally, TLTG resulted in faster postoperative gas passage and ambulation times. Early recovery of intestinal function and mobility can effectively prevent postoperative complications and facilitate patient recovery.[23] Patients undergoing TLTG demonstrated a markedly shorter time to initiate liquid intake compared to LATG. However, this observation may be unrelated to surgical intervention, as other factors influencing postoperative recovery, such as pain control and subjective recovery experiences, may affect the patient's ability to intake fluids. The average length of time spent in the hospital in the TLTG cohort was markedly shorter than that in the LATG cohort. This result is likely attributable to the ability of TLTG surgery to improve postoperative exhaustion and activity time. Patients in the TLTG cohort exhibited reduced postoperative pain scores and WBC counts, demonstrating the advantages of TLTG in mitigating pain and eliciting a milder inflammatory response. Reducing these factors may directly influence the incidence of complications, an important metric for assessing surgical outcomes.[12,24] The results of this study indicate that the complications associated with surgery, such as pulmonary, incisional, cardiac, and gastrointestinal complications, were markedly lower in the TLTG cohort compared to the LATG cohort. This may be related to the minimally invasive nature of TLTG, smaller incision length, shorter operation time, reduced intraoperative blood loss, and other factors associated with TLTG. Additionally, the reduced incidence of postoperative complications not only facilitates patient recovery but also has the potential to shorten hospital stays and lower treatment costs.

The progression of GC is often accompanied by an enhanced systemic inflammatory response, including increased WBC and elevated CRP levels. The levels of these inflammatory markers are closely associated with patient prognosis.[25] In the present study, it was observed that, immediately after surgery, the WBC and CRP levels in the TLTG cohort were markedly lower than those in the LATG cohort. This difference may be attributed to the minimally invasive nature of TLTG. Minimally invasive surgery has been shown to reduce tissue damage, subsequently ameliorating systemic inflammation immediately after surgery. However, three days post-operation, WBC counts were no different between the cohorts, whereas CRP levels were lower in the TLTG cohort. This observation may be attributed to the fact that CRP is a more sensitive inflammatory marker that more accurately reflects the systemic inflammatory response induced by surgery.[26]

In addition to increased inflammatory responses, recent studies have shown that patients with GC may exhibit abnormalities in glucose metabolism. Glucose metabolic disorders are prevalent issues among GC patients, primarily characterized by hyperglycemia.[27] These disturbances can markedly impact patient outcomes. Hyperglycemia has been shown to damage the vascular endothelium, reduce vascular elasticity, and increase the risk of arteriosclerosis, leading to insufficient tumor blood supply, disruption of the tumor microenvironment, and further malignant progression. In the present study, postoperative fasting glucose and GHb levels were slightly higher in the TLTG cohort compared to the LATG cohort. This may be due to the amelioration of systemic inflammation after TLTG surgery, which subsequently improved perioperative risk factors, enhanced pancreatic β-cell function, and increased insulin synthesis and secretion, thereby positively influencing the metabolic health of GC patients.

Hyperlipidemia is a lipid metabolic disorder prevalent in GC patients and also represents a significant factor that influences cancer progression. Lipid peroxidation products may directly cause DNA damage, contributing to the onset of cancer. Additionally, hyperlipidemia can induce a chronic low-grade inflammatory state that stimulates tumor development, modulates the tumor microenvironment, and hampers treatment outcomes.[28] In this study, the TLTG cohort showed superior postoperative lipid metabolism levels, with markedly lower TC, LDL, and HDL three months post-surgery compared to the LATG cohort. Similar to the observed alterations in glucose metabolism, this may be due to the ability of TLTG surgery to improve systemic inflammatory responses, which in turn regulates lipid metabolism.[4] No significant difference was found in TG levels between the TLTG and LATG cohorts one and three months post-surgery. However, a comprehensive assessment of lipid metabolism should consider TG, TC, LDL, and HDL levels in combination to provide a more accurate understanding of a patient's metabolic health.

Overall, this study found that TLTG has certain advantages over LATG in regulating postoperative inflammatory responses and improving glucose and lipid metabolism. These findings provide new insights into the treatment of GC and a basis for further optimizing treatment strategies. However, clinical practice cannot rely solely on evident data, and additional factors and potential future prospects should be considered. While current research has demonstrated the advantages of TLTG in several aspects,[29] its surgical complexity and technical demands have also increased.[30] Moreover, with advancements in laparoscopic technology, future applications of LATG may also improve in terms of surgery duration and blood loss, minimizing the differences between LATG and TLTG. The optimal choice should be made based on specific circumstances and technical conditions.[27,30] In clinical practice, we recommend that physicians first evaluate the patient's specific circumstances, such as lesion status and physical condition, before choosing the surgical approach based on the medical team's expertise and equipment availability. Additionally, to improve surgical efficiency and safety, healthcare providers should actively adopt new technologies and concepts to determine the most suitable option between TLTG and LATG. Furthermore, it is crucial to fully consider the patient's postoperative recovery and quality of life, opting for the least invasive surgical method whenever possible.

This study has several limitations. Firstly, this study did not explore the differences in disease prognosis and quality of life between TLTG and LATG patients, which is undoubtedly an important research direction. Secondly, there are challenges in quantifying and incorporating postoperative recovery into the clinician decision-making process which requires further exploration. Additionally, the cost-effectiveness ratio of TLTG and LATG was not considered, which is especially important in resource-limited healthcare settings. Further studies should focus on enhancing surgical efficiency and safety, thereby benefiting more patients, particularly those in resource-limited environments, while maintaining quality.

Conclusions

In conclusion, we demonstrated that TLTG surgery is superior in terms of short-term clinical outcomes compared to LATG for the treatment of GC. Specifically, TLTG exhibited markedly reduced surgical trauma, accelerated post-operative recovery, milder postoperative inflammatory responses, and the alleviation of metabolic disorders. The results of this study support the broader adoption of TLTG in the surgical treatment of GC. Nevertheless, further studies are required to elucidate the long-term effects.

Data Sharing Statement

All data generated or analysed during this study are included in this manuscript.

Ethics Approval

This study complied with the Declaration of Helsinki. Because of the retrospective nature of the study, patient consent for inclusion was waived.

Consent for Publication

Written informed consent for publication was obtained from all participants.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no conflict of interest.

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