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Systematic Review

Short-Term Outcomes Analysis Comparing Open, Lap-Assisted, Totally Laparoscopic, and Robotic Total Gastrectomy for Gastric Cancer: A Network Meta-Analysis

Michele Manara [1], Alberto Aiolfi [1,*], Gianluca Bonitta [1], Diana Schlanger [2], Calin Popa [2], Francesca Lombardo [1], Livia Manfredini [1], Antonio Biondi [3], Luigi Bonavina [4] and Davide Bona [1]

1 I.R.C.C.S. Ospedale Galeazzi–Sant'Ambrogio, Division of General Surgery, Department of Biomedical Science for Health, University of Milan, Via C. Belgioioso, 173, 20157 Milan, Italy; michele.mnra@gmail.com (M.M.); bbonit@icloud.com (G.B.); francesca.lombardo89@gmail.com (F.L.); manfredini.livia@gmail.com (L.M.); davide.bona@unimi.it (D.B.)
2 Surgery Clinic 3, Regional Institute of Gastroenterology and Hepatology "Prof. Dr. Octavian Fodor", "Iuliu Haţieganul" University of Medicine and Pharmacy, 400394 Cluj-Napoca, Romania; schlanger.diana@yahoo.com (D.S.); calinp2003@yahoo.com (C.P.)
3 G. Rodolico Hospital, Surgical Division, Department of General Surgery and Medical Surgical Specialties, University of Catania, 95131 Catania, Italy; abiondi@unict.it
4 IRCCS Policlinico San Donato, Division of General and Foregut Surgery, Department of Biomedical Sciences for Health, University of Milan, 20097 Milan, Italy; luigi.bonavina@unimi.it
* Correspondence: alberto.aiolfi86@gmail.com

Simple Summary: Minimally invasive approaches to total gastrectomy (TG) are gaining acceptance worldwide for the treatment of gastric cancer. Previous studies comparing short-term results were limited by pairwise comparisons and the inclusion of both total and distal gastrectomy. The present analysis aimed to compare the short-term outcomes of different techniques for TG comprehensively in the setting of GC. Lap-assisted TG (LATG), totally laparoscopic TG (TLTG), and robotic TG (RTG) seem to be associated with a lower overall complications rate and improved short-term functional outcomes compared to open TG (OTG). Severe postoperative complications and anastomotic leak seem comparable across techniques. Our findings support the adoption of minimally invasive TG techniques in the surgical management of gastric cancer.

Abstract: Background/Objectives: Total gastrectomy (TG) is the cornerstone treatment for gastric cancer (GC). While open TG (OTG) with D2 lymphadenectomy remains the gold standard, alternative techniques such as lap-assisted TG (LATG), totally laparoscopic TG (TLTG), and robotic TG (RTG) have been reported with promising outcomes. The present analysis aimed to compare the short-term outcomes of different techniques for TG comprehensively in the setting of GC. Methods: A systematic review and network meta-analysis were performed. The primary outcomes were overall complications (OC), severe postoperative complications (SPCs), and anastomotic leak (AL). Pooled effect-size measures included risk ratio (RR), weighted mean difference (WMD), and 95% credible intervals (CrIs). Results: Sixty-eight studies (44,689 patients) were included. Overall, 52.4% underwent OTG, 6.5% LATG, 39.2% TLTG, and 1.9% RTG. Both TLTG (RR 0.82; 95% CrI 0.73–0.92) and RTG (RR 0.75; 95% CrI 0.59–0.95) showed a reduced rate of postoperative OC compared to OTG. SPCs and AL RR were comparable across all techniques. Despite the longer operative time, LATG, TLTG, and RTG showed reduced intraoperative blood loss, time to first flatus, ambulation, liquid diet resumption, and hospital stay compared to OTG. Conclusions: Minimally invasive approaches seem to be associated with improved OC and functional outcomes compared to OTG.

Keywords: gastric cancer; total gastrectomy; short-term outcomes; postoperative complications; functional outcomes

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1. Introduction

Gastric cancer (GC) ranks fifth globally in incidence among malignancies and is the fifth leading cause of cancer-related mortality [1]. Surgery represents the cornerstone of curative-intent therapy for GC. Total gastrectomy (TG) is preferred over distal gastrectomy when tumor location precludes adequate proximal resection margins or when the invasion of an adjacent organ is reported [2]. Open total gastrectomy (OTG) with D2 lymphadenectomy is the gold standard treatment for locally advanced GC [3]. Since the description of the first laparoscopic and robotic TG, these minimally invasive approaches have gained increasing consensus worldwide, given improved functional outcomes and similar oncologic results [4–10].

Multiple studies and meta-analyses have previously been published to compare surgical techniques for TG. These articles were limited by the pairwise comparisons and by selection bias because of the inclusion of both TG and distal gastrectomy. Therefore, a comprehensive network analysis focusing on TG and simultaneously comparing all surgical approaches for TG is lacking [11,12].

The aim of the present network meta-analysis was to compare the short-term outcomes of different surgical approaches for TG in the setting of GC.

2. Materials and Methods

A systematic review was conducted following the preferred reporting items for systematic review and meta-analyses (PRISMA) guidelines [13]. The relevant literature was searched in scientific databases, including Scopus, PubMed, MEDLINE, Web of Science, Cochrane Central Library, Google Scholar, and ClinicalTrials.gov, accessed on 1 AUgust 2024 [14]. The search strategy employed both medical subheadings (MeSH) and truncated search words, with the Boolean operators AND/OR, employing the following terms: stomach cancer, total gastrectomy, laparoscopic total gastrectomy, laparoscopic assisted total gastrectomy, open total gastrectomy, robot assisted total gastrectomy, postoperative complication, severe postoperative complication, anastomosis leakage, short-term outcome, bleeding, anastomotic stenosis, duodenal stump leakage, pancreatic complications, pulmonary complications, surgical site infection, and thrombotic complication. The complete search strategy is reported in the Appendix A. Articles published up to 1 April 2024 were considered for inclusion, as well as the reference lists of the included studies. Ethical approval was not required for this study. This study was registered on PROSPERO (CRD42024558026).

2.1. Eligibility Criteria

Studies that provided data on short-term outcomes in patients who underwent TG for GC were examined for eligibility. We included all studies that compared OTG, lap-assisted TG (LATG), totally laparoscopic TG (TLTG), and RTG. Studies with potential overlapping populations were identified, and those with broader inclusion criteria were considered. Exclusion criteria comprised the following: (1) studies that did not report at least one of the predefined primary outcomes; (2) non-comparative analyses; (3) articles not written in English; (4) studies reporting mixed data, including other surgical procedures; and (5) articles with fewer than 5 patients per treatment arm.

2.2. Selection Process

The literature review was conducted independently by two authors (MM, DS) based on the predefined inclusion and exclusion criteria. Following the removal of duplicates, all articles underwent title screening. Those meeting the inclusion criteria underwent full-text review after abstract screening. Disagreements were resolved by two additional authors (AA, DB), blinded to the initial assessments.

2.3. Data Collection Process

Data collection was carried out by three independent authors (MM, AA, DS) who completed pro forma tables on Google Sheets containing predetermined variables. Collected variables include the following: author, publication year, country, study design, study period, patients demographics (number of patients, age, sex, body mass index (BMI), and American Society of Anesthesiologists physical status), tumor characteristics (location, histology, neoadjuvant and adjuvant therapy, and tumor size), surgical variables (surgical approach, anastomotic technique, lymphadenectomy extension, pathologic tumor staging, residual tumor classification, operative time, intraoperative blood loss, conversion, and number of lymph nodes retrieved), and postoperative short-term outcomes (anastomotic leak, overall complications, severe postoperative complications, in-hospital mortality, time to first flatus, time to first liquid intake, time to first ambulation, hospital length of stay, reintervention, transfusion requirement, bleeding, anastomotic stenosis, duodenal stump leak, pancreatic complications, pulmonary complications, thrombotic events, and surgical site infections). Following data collection, two other authors (DB, GB) compared all data at the conclusion of the review process to identify and resolve any discrepancies.

2.4. Outcomes of Interest and Definitions

Anastomotic leak (AL), overall postoperative complications (OC), and severe postoperative complications (SPCs) were the primary outcomes. AL was defined as radiographic evidence of contrast extravasation observed on a postoperative swallow study and/or computed tomography scans, endoscopic visualization of anastomotic dehiscence or fistula, or surgical drain output consistent with saliva. Postoperative complications were graded according to the Clavien–Dindo classification system, as follows: Grade 0, representing no complications; Grade 1, indicating any deviation from normal postoperative course without requiring medical intervention; Grade 2, involving complications necessitating pharmacological treatment; Grade 3, when complications required surgical, endoscopic, or radiological intervention (subcategorized as 3a for interventions not requiring general anesthesia and 3b for those requiring general anesthesia); Grade 4, in case of life-threatening complications necessitating intensive care unit management; and Grade 5, representing death [15]. SPCs were defined as those graded as Clavien–Dindo complications equal to or greater than 3. Secondary outcomes were operative time (OT, minutes), intraoperative blood loss (ml), number of retrieved lymph nodes, conversion to OTG, reintervention, postoperative bleeding requiring transfusion, anastomotic stenosis, duodenal stump leak, ileus, pancreatic complications, pulmonary complications, thrombotic events, surgical site infections, in-hospital mortality, time to first flatus (days), time to first liquid intake (days), time to ambulation (days), and hospital length of stay (LOS, days). TLTG was defined as a minimally invasive laparoscopic technique for gastric resection with intracorporeal anastomosis. LATG was outlined for laparoscopic gastric resection with extracorporeal anastomosis. RTG was characterized as robotic gastric resection, irrespective of the location of anastomosis formation.

2.5. Quality Assessment

Methodological quality assessment was conducted by three authors (MM, AA, GB) utilizing the appropriate evaluation tools. Observational studies underwent assessment using the ROBINS-I tool, which evaluates domains such as confounding bias, selection bias, classification bias, intervention bias, missing data bias, outcomes measurement bias, and reporting bias [16]. Each domain was rated as “Low”, “Moderate”, “Serious”, or “Critical”, and overall judgment categories for each study included low, moderate, serious, or critical risk of bias. Randomized controlled trials were evaluated using the version 2 of the Cochrane risk-of-bias tool for randomized trials, focusing on bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, and bias in selection of the

reported result [17]. Trials were subsequently classified as having overall low risk (green circle), high risk (red circle), or unclear risk (yellow circle) of bias.

2.6. Statistical Analysis

We performed an arm-based random effect frequentist network meta-analysis [18]. For dichotomous variables, the risk ratio (RR) was chosen as the effect size. For continuous variables, the standardized mean difference (SMD) was chosen as the effect size. A generalized DerSimonian–Larid [19] estimator was used to estimate the between-study variance, assumed as common for each pairwise treatment comparison. A generalized I^2 was adopted to define heterogeneity as follows: low (<25%), moderate (25–75%), or high (>75%) [20]. To account for transitivity, the eligibility criteria of the included studies are framed in such a manner that the trials are primarily different in the tested interventions only. To assess transitivity, we generated descriptive statistics and compared the distributions of baseline characteristics across studies and treatment comparisons [21]. The node split was used as an assessment for the local inconsistency. The treatment ranking probability was estimated with the cumulative ranking curve (SUCRA). The network geometry was appraised, and the confidence of outcomes estimates was assessed with the Confidence in Network Meta-Analysis (CINeMA) instrument [22]. Two-sided *p*-values were considered statistically significant when less than 0.05, and the confidence intervals (CI) were computed at 95%. All analyses and graphs were carried out using R-CRAN statistical software (version 4.3.0) with the netmeta package [23].

3. Results

3.1. Systematic Review

The PRISMA flow diagram is depicted in Figure 1. The initial search strategy identified 2331 records. After duplicates removal, title and abstract screening, 293 articles were included for full-text evaluation. After full-text review, 68 articles were deemed eligible and included in the quantitative analysis. The study design was observational retrospective (60 studies, 25 of which employed propensity score matching), observational prospective (6 studies, 2 of which employed propensity score matching), and experimental (2 randomized controlled trials). The quality of the included studies is described in Table 1, Supplementary Figure S1, and Supplementary Table S1.

Baseline characteristics are shown in Table 1. Overall, data from 44,689 patients undergoing TG were analyzed. Surgical procedures were performed between 1995 and 2021. The surgical techniques were OTG (*n* = 23,414; 52.4%), LATG (*n* = 2918; 6.5%), TLTG (*n* = 17,499; 39.2%), and RTG (*n* = 858; 1.9%). The patient age ranged from 50.6 to 75 years, 73% were males, and preoperative BMI ranged between 19 and 32.1. Tumor location was specified in 39 studies and defined in the upper (68%), middle (29%), and distal (3%) portion of the stomach. Pathologic tumor staging was available in 51 studies, with pStage 0–I, II–III, and IV diagnosed in 27.8%, 71.9%, and 26% of cases, respectively. Neoadjuvant treatments were defined in 38 studies (9673 patients) and completed in 17.6% of subjects (1707 patients).

Table 1. Demographic and clinical characteristics of included patients.

Author, Year *Country*	Study Design	Period	Approach	No. pts	Age (yrs)	Sex (M)	BMI (kg/m^2)	Location (P-M-D)	pStage 0–I	pStage II	pStage III	pStage IV	Neoadj/ Periop tp	QoE
Eom, 2022 *Korea* [24]	Ret PSM	2012–2016	OTG TLTG	119 119	60.2 ± 11.6 62.3 ± 11.4	94 93	23.8 ± 3.3 23.3 ± 3.1	96-14-9 105-14-0	93 93	17 17	9 9	0 0	0 0	S
Illuminati, 2023 *Italy* [25]	Ret	2010–2021	OTG LATG	109 98	57.7 ± 8.5 59.4 ± 8.5	83 69	20.8 ± 2.8 21.1 ± 2.7	nr	0 0	8 7	92 101	0 0	36 40	S
Jia, 2023 *China* [26]	Ret PSM	2014–2021	RTG TLTG	147 371	62.9 ± 10 62.5 ± 9.4	118 294	25 ± 3.7 24.5 ± 3.4	90-57-0 239-132-0	44 121	41 92	62 158	0 0	0 0	M
Kinoshita, 2022 *Japan* [27]	Ret PSM	2008–2018	OTG TLTG	163 163	67 ± 3.5 69 ± 3	134 130	22.4 ± 1.1 22.2 ± 0.9	nr	56 91	54 33	53 39	0 0	17 16	M
Salvador-Roses, 2023 *Spain* [28]	Ret	2014–2021	OTG RTG	48 30	64 ± 13 68 ± 13	40 23	27 ± 4 26 ± 5	nr	nr	nr	nr	nr	26 13	S
Zheng, 2023 *China* [29]	Ret	2008–2018	OTG TLTG	57 89	63.3 ± 11.3 60.3 ± 10.1	48 69	nr	nr	6 16	15 35	36 38	0 0	57 89	M
Hu, 2022 *China* [30]	Ret PSM	2011–2018	OTG TLTG	69 69	53.9 ± 12.7 53.4 ± 13.4	52 53	22.8 ± 3.3 22.6 ± 3.1	22-37-10 28-34-7	0 0	22 27	44 38	3 4	69 69	S
Hikage, 2022 *Japan* [31]	Ret	2013–2020	RTG TLTG	36 58	72 ± 8 71 ± 9	26 46	23.1 ± 2 22.8 ± 3.2	nr	25 42	5 15	6 1	0 0	nr	S
Chen, 2022 *China* [32]	Pro PSM	2015–2020	RTG TLTG	48 96	61.3 ± 9.3 61.6 ± 7.6	38 79	22.3 ± 2.7 22.3 ± 3.2	31-17-0 66-30-0	13 22	16 29	19 45	0 0	nr	L
Cui, 2022 *China* [33]	Ret	2012–2019	OTG TLTG	75 61	56.8 ± 11.9 57.6 ± 10.4	59 47	23.7 ± 3.3 22.8 ± 2.7	46-29-0 40-21-0	24 9	16 22	34 29	1 1	75 61	S
Di Carlo, 2022 *Italy* [34]	Ret	2015–2021	OTG TLTG	53 39	71 ± 5.8 67 ± 6.5	33 25	24.5 ± 2.9 22.6 ± 2.2	nr	0 0	23 18	30 21	0 0	44 30	S
Li, 2022 *China* [35]	Pro	2018–2021	RTG TLTG	69 73	59.4 ± 9.9 58.9 ± 9.2	48 52	22.6 ± 2.8 22.9 ± 2.8	50-13-6 52-16-5	14 15	17 19	38 39	0 0	nr	L
Lin, 2023 *China* [36]	Ret PSM	2014–2018	LATG TLTG	208 104	nr	140 71	nr	68-106-34 32-57-15	59 29	64 30	85 45	0 0	208 104	S
Qiu, 2022 *China* [37]	Ret	2020	LATG TLTG	51 46	63.9 ± 8.2 63.3 ± 9.1	36 31	23.1 ± 4.2 23.7 ± 4	34-17-0 31-15-0	11 11	17 15	23 20	0 0	nr	M

Table 1. *Cont.*

Author, Year *Country*	Study Design	Period	Approach	No. pts	Age (yrs)	Sex (M)	BMI (kg/m^2)	Location (P-M-D)	pStage 0-I	pStage II	pStage III	pStage IV	Neoadj/ Periop tp	QoE
Shibasaki, 2022 *Japan* [38]	Ret PSM	2009–2021	RTG TLTG	100 100	69 ± 3.8 68 ± 3.5	69 67	23 ± 1.3 23.1 ± 1.1	nr	46 34	23 26	31 40	0 0	13 10	M
Wang, 2022 *China* [39]	Ret PSM	2016–2020	RTG TLTG	115 230	60.4 ± 9.4 60.3 ± 10.4	91 179	22.5 ± 3 22.4 ± 3	85-30-0 172-58-0	30 72	40 60	45 98	0 0	108 214	L
van der Wielen, 2021 *Europe* [40]	RCT	2015–2018	OTG TLTG	49 47	61.8 ± 10 59.4 ± 12.5	32 28	25.2 ± 4 26.5 ± 4.8	14-25-10 13-25-9	nr	nr	nr	nr	49 47	?
Challine, 2021 *France* [41]	Ret	2013–2018	OTG TLTG	5037 745	68 ± 4.5 64 ± 5	nr	nr	nr	nr	nr	nr	nr	nr	S
Fan, 2021 *China* [42]	Ret PSM	2011–2018	OTG LATG	131 131	nr	97 98	nr	90-41-0 93-38-0	23 24	40 41	68 66	0 0	12 14	M
Feng, 2021 *China* [43]	Ret PSM	2011–2015	OTG TLTG	225 225	61 ± 3.5 59 ± 4.3	164 154	22.2 ± 1 21.9 ± 1	nr	18 8	42 71	165 146	0 0	nr	M
Ko, 2021 *Korea* [44]	Ret PSM	2012–2018	OTG TLTG	61 61	58.7 ± 10.7 58.3 ± 11.3	41 40	24 ± 2.7 24 ± 3	nr	33 31	19 19	9 11	0 0	0 0	S
Kumamoto, 2022 *Japan* [45]	Ret	2017–2021	RTG TLTG	27 29	69 ± 3.5 70 ± 1.8	19 19	23.2 ± 0.7 22.4 ± 0.9	2-25-0 7-22-0	nr	nr	nr	nr	2 7	S
Roh, 2021 *Korea* [46]	Ret PSM	2009–2018	RTG TLTG	74 74	53.8 ± 11.6 54.6 ± 12.7	42 42	23.6 ± 2.9 23.8 ± 3.4	51-23-0 47-27-0	50 47	15 18	9 9	0 0	nr	M
Wang, 2021 *China* [47]	Ret PSM	2013–2018	OTG TLTG	46 23	59.7 ± 8.7 60.1 ± 9.7	36 18	23.3 ± 3.7 23.7 ± 3.8	46-0-0 23-0-0	15 4	17 11	13 8	0 0	46 23	M
Liu F, 2020 *China* [48]	RCT	2017–2018	OTG TLTG	109 105	59.4 ± 9.2 59.8 ± 9.4	80 75	23.7 ± 3.1 23.9 ± 3.1	nr	91 85	14 13	4 7	0 0	nr	+
Komatsu, 2020 *Japan* [49]	Ret PSM	200–2015	OTG TLTG	65 65	67 68	51 50	22 22	39-26-0 39-26-0	nr	nr	nr	nr	0 0	S
Yang, 2020 *China* [50]	Ret PSM	2010–2017	RTG LATG	126 126	60.3 ± 8.9 60.8 ± 9.1	105 100	22.1 ± 2.5 22.1 ± 2.8	58-68-0 61-65-0	3 3	30 27	93 86	0 0	0 0	M
Lee, 2020 *Korea* [51]	Ret PSM	2004–2014	OTG TLTG	51 51	63 ± 13.5 62.1 ± 12.3	36 37	nr	26-25-0 24-27-0	1 1	23 21	27 29	0 0	0 0	M

Table 1. *Cont.*

Author, Year *Country*	Study Design	Period	Approach	No. pts	Age (yrs)	Sex (M)	BMI (kg/m^2)	Location (P-M-D)	pStage 0-I	pStage II	pStage III	pStage IV	Neoadj/ Periop tp	QoE
Sakamamoto, 2020 *Japan* [52]	Ret PSM	2010–2017	OTG TLTG	12,229 12,229	nr	8998 9005	nr	nr	nr	nr	nr	nr	nr	S
Zhao, 2019 *China* [53]	Ret PSM	2012–2017	OTG TLTG	217 468	59 ± 10.6 60.4 ± 10.4	175 330	22.7 ± 2.6 22.5 ± 2.6	217-0-0 468-0-0	2 7	122 268	93 193	0 0	9 61	M
Ye, 2019 *China* [54]	Ret	2015–2018	RTG LATG	99 106	58.7 ± 6.7 59 ± 7.3	58 55	23.9 ± 1.9 23.9 ± 1.4	33-66-0 42-64-0	2 3	54 51	43 52	0 0	0 0	M
Aoyama, 2018 *Japan* [55]	Ret	2011–2016	OTG LATG	208 95	70 ± 9.2 69 ± 6.5	154 68	nr	nr	nr	nr	nr	nr	nr	S
Li, 2019 *China* [56]	Ret PSM	2008–2014	OTG LATG	296 296	nr	200 214	22.5 ± 2.9 22.8 ± 3.2	nr	47 47	119 119	130 130	0 0	0 0	L
Wang, 2019 *China* [57]	Ret	2009–2014	OTG LATG	43 32	61.9 ± 6 61.9 ± 8.7	23 21	nr	43-0-0 32-0-0	17 11	21 17	5 4	0 0	0 0	S
Etoh, 2018 *Japan* [58]	Pro PSM	2014–2015	OTG TLTG	512 512	nr	378 383	nr	nr	nr	nr	nr	nr	41 38	S
Chen K, 2017 *China* [59]	Ret	2007–2016	OTG TLTG	124 124	53.5 ± 14.6 52.7 ± 13.1	81 81	23 ± 3.7 23.9 ± 4.3	nr	59 60	28 29	37 35	0 0	nr	L
Chen XZ, 2017 *China* [60]	Ret PSM	2006–2015	OTG LATG	69 69	60.5 ± 9.3 57.1 ± 10.1	58 58	23 ± 3 21.1 ± 2.1	37-19-13 41-21-7	14 14	16 16	38 38	1 1	nr	M
Lin JX, 2017 *China* [61]	Ret PSM	nr	OTG LATG	346 346	61.3 ± 10.1 61.1 ± 10	274 274	22 ± 2.3 22 ± 2.9	188-136-22 191-136-19	51 46	62 53	233 247	0 0	nr	M
Kim EY, 2016 *Korea* [62]	Ret	2009–2014	LATG TLTG	29 27	59.3 ± 13.1 60.8 ± 9.1	20 22	23.3 ± 3.2 24 ± 2.9	17-12-0 21-6-0	12 25	6 1	10 1	1 0	nr	M
Kim HB, 2016 *Korea* [63]	Ret	2013–2015	TLTG LATG	30 24	51 ± 12.3 53 ± 11.3	16 14	22.2 ± 2.7 22.7 ± 11.8	19-11-0 12-12-0	nr	nr	nr	nr	nr	S
Wu H, 2016 *China* [64]	Ret PSM	2008–2013	OTG TLTG	74 74	60 ± 7.5 62 ± 9.5	50 53	21 ± 1.8 19 ± 1.5	nr	5 6	55 53	14 15	0 0	nr	M
Shu B, 2016 *China* [65]	Ret	2007–2014	OTG LATG	136 136	64 ± 5.2 65 ± 5	92 86	21 ± 1.8 20 ± 1.7	92-44-0 87-49-0	20 21	76 67	43 48	0 0	nr	M

Table 1. *Cont.*

Author, Year *Country*	Study Design	Period	Approach	No. pts	Age (yrs)	Sex (M)	BMI (kg/m^2)	Location (P-M-D)	pStage 0-I	pStage II	pStage III	pStage IV	Neoadj/ Periop tp	QoE
Lu Y, 2016 *China* [66]	Ret	2008–2015	OTG TLTG	61 61	57 ± 6.8 59 ± 7.8	37 39	22 ± 2 19 ± 1.3	nr	8 6	36 39	17 16	0 0	0 0	M
Huang, 2017 *China* [67]	Ret PSM	2007–2014	OTG LATG	171 171	61.4 ± 10 62.4 ± 8.9	152 152	21.9 ± 3 22.2 ± 2.9	171-0-0 171-0-0	29 27	42 47	100 97	0 0	0 0	M
Park, 2016 *China* [68]	Pro	2011–2012	TLTG RTG	30 42	57.1 ± 11.1 51.7 ± 12	18 26	nr	nr	26 28	4 14		0 0	nr	S
Shida, 2016 *Japan* [69]	Ret	2005–2013	OTG LATG	53 100	65.5 ± 12.3 63.8 ± 11.3	47 84	23.2 ± 3.6 23.6 ± 3.1	40-13-0 74-26-0	32 79	15 17	6 4	0 0	0 0	M
Zhang, 2017 *China* [70]	Ret	2009–2012	OTG LATG	85 69	72.9 ± 10.9 69.4 ± 10.5	50 38	22.3 ± 2.5 20.9 ± 2.1	73-12-0 57-12-0	nr	nr	nr	nr	nr	M
Ramagem CAG, 2015 *Brazil* [71]	Ret	2009–2013	OTG TLTG	64 47	60 ± 11.7 58 ± 10.5	43 34	32.1 ± 4.1 22.3 ± 4.4	6-27-31 4-24-19	21 14	16 13	27 20	0 0	0 0	M
Lee, 2015 *Korea* [72]	Ret	2003–2010	OTG LATG	502 251	57.6 ± 11.6 58.4 ± 12.7	319 160	23.1 ± 11.6 23.1 ± 3	371-131-0 200-51-0	nr	nr	nr	nr	0 0	S
Lu, 2015 *China* [73]	Ret PSM	2002–2012	OTG TLTG	252 252	nr	213 208	nr	183-69-0 177-75-0	56 52	45 56	151 144	0 0	0 0	M
Shen, 2016 *China* [74]	Ret	2011–2014	TLTG RTG	75 23	58.6 ± 11.6 57.3 ± 10.5	57 18	24.4 ± 3.7 24.6 ± 3.5	nr	23 10	21 4	31 9	0 0	nr	S
Song, 2015 *Korea* [75]	Ret	2009–2013	OTG TLTG	134 74	58.5 ± 12.3 55.9 ± 11.7	94 45	22.7 ± 3.7 22.9 ± 3	nr	nr	nr	nr	nr	nr	M
Lee, 2014 *Korea* [76]	Ret	2006–2009	OTG LATG	50 34	59 ± 4.1 61 ± 3.5	39 25	nr	30-20-0 15-19-0	25 22	13 7	12 5	0 0	35 23	S
Lee M, 2013 Korea [77]	Ret	2003–2010	OTG LATG	50 50	51 ± 22.6 50.6 ± 22.1	32 32	23 ± 3.4 23.2 ± 3.7	nr	24 24	13 13	9 9	4 4	nr	S
Bo T, 2013 *China* [78]	Ret PSM	2004–2010	OTG LATG	117 117	52.6 ± 13.6 54.5 ± 10.6	80 82	21.7 ± 3.8 21.1 ± 3	65-52-0 64-53-0	4 6	38 40	75 71	0 0	0 0	L
Guan G, 2013 *China* [79]	Ret	2007–2010	OTG LATG	56 41	57.8 ± 9.9 60.7 ± 9.1	40 33	nr	nr	25 18	25 20	6 3	0 0	nr	M
Kim HS, 2013 *Korea* [80]	Ret	2011	OTG TLTG	207 139	56 ± 8.8 58 ± 9	134 86	24.1 ± 3.1 23.6 ± 3.1	nr	nr	nr	nr	nr	nr	M

Table 1. *Cont.*

Author, Year *Country*	Study Design	Period	Approach	No. pts	Age (yrs)	Sex (M)	BMI (kg/m^2)	Location (P-M-D)	pStage 0-I	pStage II	pStage III	pStage IV	Neoadj/ Periop tp	QoE
Kim KH, 2014 *Korea* [81]	Ret PSM	2002–2010	OTG LATG	60 60	56.7 ± 12.4 57.3 ± 13.2	36 35	22.8 ± 3.3 22.6 ± 3.1	nr	40 39	13 14	7 7	0 0	nr	M
Jeong O, 2013 *Korea* [82]	Ret PSM	2003–2011	OTG TLTG	122 122	62.6 ± 11.7 63.2 ± 11.2	93 89	23.5 ± 3.2 23.1 ± 3.4	87-35-0 94-28-0	99 105	16 13	7 4	0 0	0 0	S
Hong, 2013 *China* [83]	Ret	2008–2012	OTG TLTG	104 100	54.5 ± 10.4 53.2 ± 11.1	76 71	24.4 ± 1.2 24.1 ± 2.3	104-0-0 100-0-0	5 6	54 53	45 41	0 0	0 0	S
Eom BW, 2012 *Korea* [84]	Ret	2003–2008	OTG LATG	348 100	58.7 ± 11.5 54.9 ± 13.5	254 57	23.8 ± 2.9 22.7 ± 2.8	nr	nr	nr	nr	nr	0 0	S
Kim M, 2011 *Korea* [85]	Ret	2009–2010	OTG LATG	127 63	57.3 ± 11.1 55.9 ± 12.2	81 43	23.0 ± 2.9 22.7 ± 2.5	nr	nr	nr	nr	nr	nr	M
Yoon, 2012 *Korea* [86]	Ret	2009–2011	RTG LATG	36 65	53.9 ± 11.7 56.9 ± 12.3	18 31	23.2 ± 2.5 23.6 ± 3.4	nr	29 55	7 7	0 3	0 0	0 0	M
Sakuramoto S, 2009 *Japan* [87]	Ret	2003–2007	OTG LATG	44 30	67.2 ± 9.9 63.7 ± 9.2	10 12	22.5 ± 3.6 21.9 ± 2.7	28-16-0 18-12-0	15 25	17 2	12 3	0 0	nr	M
Kawamura, 2009 *Japan* [88]	Ret	2003–2008	OTG TLTG	35 46	65.2 ± 10.7 64 ± 10.4	25 36	22.9 ± 2.4 22.8 ± 3	35-0-0 46-0-0	35 46	nr nr	nr nr	nr nr	0 0	M
Mochiki, 2008 *Japan* [89]	Ret	1998–2007	OTG LATG	18 20	63 ± 2.2 66 ± 2.4	16 16	nr	15-3-0 18-2-0	nr	nr	nr	nr	nr	S
Topal B, 2008 *Belgium* [90]	Pro + Ret	2003–2006	OTG TLTG	22 38	69 ± 12 68 ± 12	17 23	nr	4-13-5 11-17-10	7 17	7 7	6 10	2 4	nr	S
Dulucq, 2005 *France* [91]	Pro	1995–2004	OTG TLTG	11 8	67 ± 14 75 ± 8	5 3	nr	nr	nr	nr	nr	nr	nr	S

Study design retrospective (Ret); prospective (Pro); propensity score matched (PSM); randomized controlled trial (RCT); surgical approach (Approach); open total gastrectomy (OTG); lap-assisted total gastrectomy (LATG); totally laparoscopic total gastrectomy (TLTG); robotic total gastrectomy (RTG); number of patients (No. pts); male (M); body mass index (BMI); tumor location (Location); proximal–middle–distal (P-M-D); pathologic tumor staging according to 7th–8th American Joint Committee on Cancer or 13th–14th–15th Japanese Classification of Gastric Carcinoma (pStage); neoadjuvant therapy (Neoadj tp); perioperative therapy (Periop tp); quality of the evidence (QoE); according to ROBINS-I tool, Low-Moderate–Serious risk of bias (L-M-S); Cochrane risk-of-bias tool 2, low–unclear risk of bias (Green–Yellow circle); *NR* not reported. Data are reported as numbers, mean ± standard deviation.

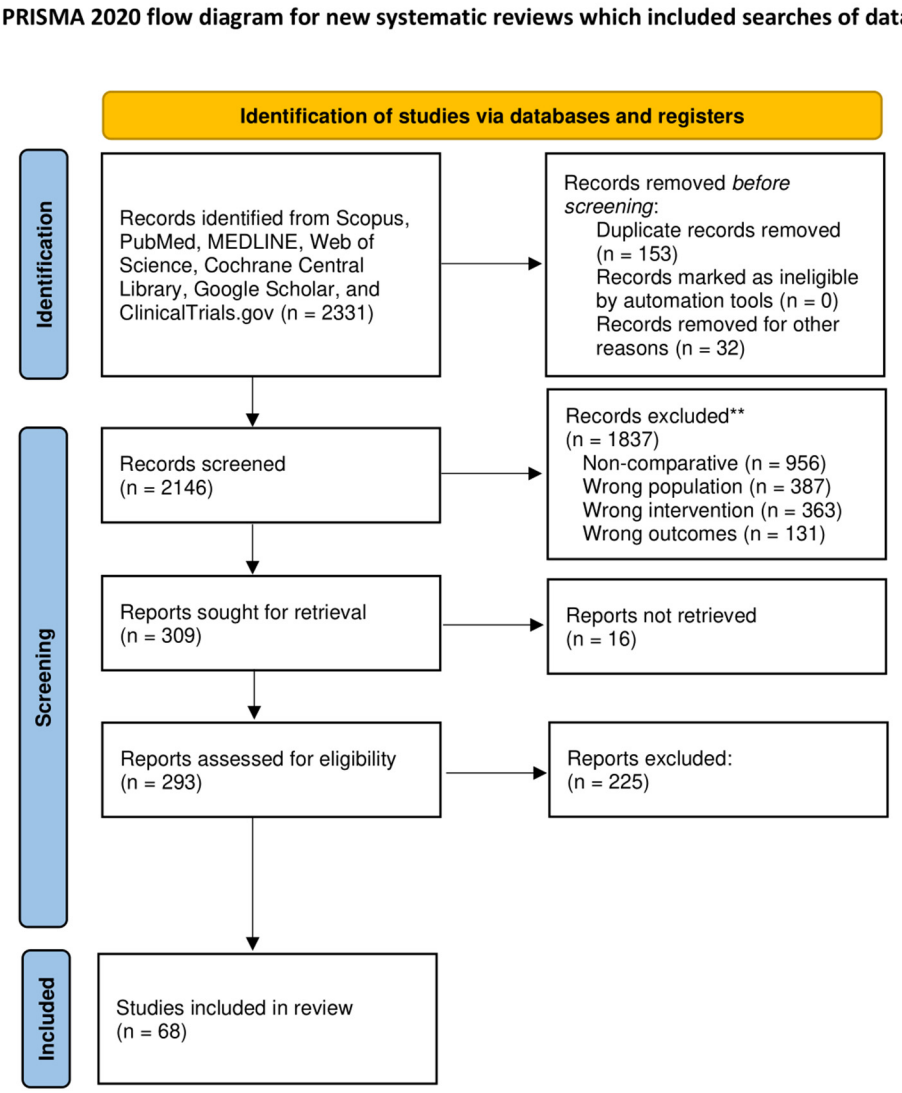

Figure 1. The preferred reporting items for systematic reviews checklist (PRISMA) diagram. **: If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

3.2. Meta-Analysis

3.2.1. Primary Outcomes

The postoperative OC rate (Figure 2) was defined in 65 studies (38,459 patients). TLTG (RR 0.82; 95% CrI 0.73–0.92) and RTG (RR 0.75; 95% CrI 0.59–0.95) were associated with reduced OC rates compared to OTG; no differences were observed for LATG vs. OTG (RR 0.92; 95% CrI 0.81–1.04) and TLTG vs. RTG (RR 1.09; 95% CrI 0.88–1.36). SPCs (Figure 3) were reported in 46 studies (10,306 patients). Compared to OTG, no differences were observed for LATG (RR 0.80; 95% CrI 0.59–1.07), TLTG (RR 0.96; 95% CrI 0.75–1.24), and RTG (RR 1.2; 95% CrI 0.75–1.91). AL (Figure 4) was conveyed in 61 studies (43,452 patients). No difference was observed for LATG vs. OTG (RR 1.15; 95% CrI 0.83–1.59), TLTG vs. OTG (RR 1.16; 95% CrI 0.95–1.43), and RTG vs. OTG (RR 1.27; 95% CrI 0.74–2.18). The treatment ranking evaluation showed that RTG had the lowest probability for SPCs (15%) and AL (31%).

3.2.2. Secondary Outcomes

Conversion rate (23 studies, 2390 patients) was significantly lower for LATG vs. TLTG (RR 0.32; 95% CrI 0.11–0.92) and LATG vs. RTG (RR 0.40; 95% CrI 0.21–0.74). OT (65 studies,

14,365 patients) was significantly shorter for OTG compared to LATG (SMD −0.95; 95% CrI −1.41; −0.48), TLTG (SMD −1.14; 95% CrI −1.57; −0.71), and RTG (SMD −2.02; 95% CrI −2.74; −1.30); RTG showed longer OT vs. LATG (SMD 1.07; 95% CrI 0.31; 1.84) and TLTG (SMD 0.88; 95% CrI 0.23; 1.53). Intraoperative blood loss (56 studies, 11,983 patients) was significantly higher in OTG compared to LATG (SMD 1.15; 95% CrI 0.76; 1.54), TLTG (SMD 1.43; 95% CrI 1.08; 1.78), and RTG (SMD 1.68; 95% CrI 1.08; 2.28). LATG showed fewer lymph nodes retrieved compared to OTG (SMD −0.22; 95% CrI −0.39; −0.04), TLTG (SMD −0.28; 95% CrI −0.49; −0.06), and RTG (SMD −0.44; 95% CrI −0.74; −0.15). Postoperative bleeding requiring transfusion (48 studies, 16,598 patients) was significantly higher for TLTG vs. OTG (RR 1.28; 95% CrI 1.05–1.57). No differences were observed for anastomotic stenosis, duodenal stump leak, pancreatic complications, pulmonary complications, surgical site infections, postoperative thrombotic events, postoperative transfusion, postoperative ileus, reintervention, and in-hospital mortality among treatments.

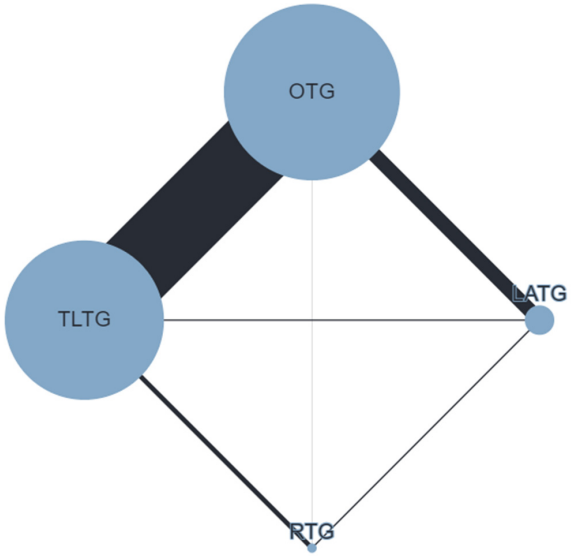

Figure 2. Network geometry for postoperative overall complications (OC). Node sizes reflect the sample size, while edge widths reflect the number of studies for a specific pairwise comparison.

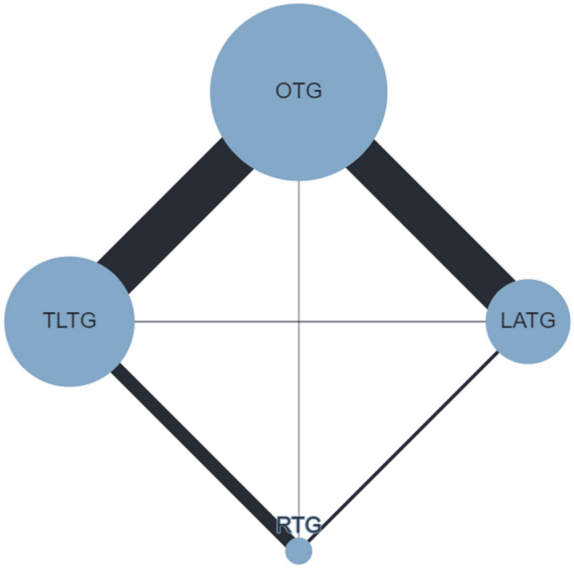

Figure 3. Network geometry for postoperative severe complications (SPCs). Node sizes reflect the sample size, while edge widths reflect the number of studies for a specific pairwise comparison.

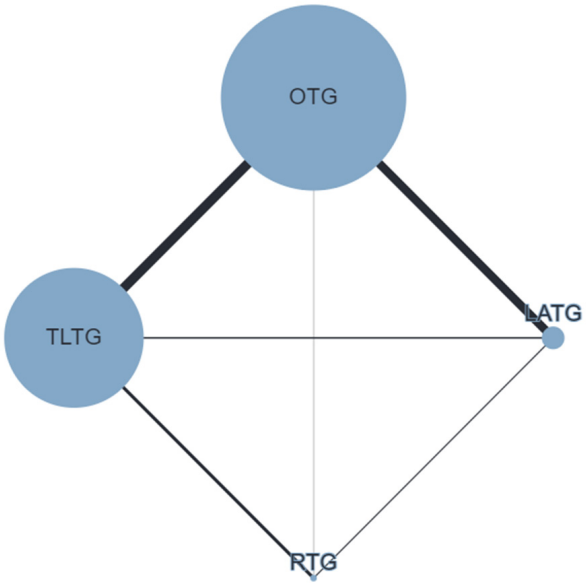

Figure 4. Network geometry for postoperative anastomotic leak (AL). Node sizes reflect the sample size, while edge widths reflect the number of studies for a specific pairwise comparison.

3.2.3. Functional Results

LOS (64 studies, 44,076 patients) and time to first flatus (36 studies, 8084 patients) were comparable between LATG, TLTG, and RTG; OTG showed longer HLOS and time to first flatus when compared to LATG (SMD 0.46; 95% CrI 0.21; 0.71; and SMD 0.97; 95% CrI 0.61; 1.33 respectively), TLTG (SMD 0.55; 95% CrI 0.33; 0.77; and SMD 0.71; 95% CrI 0.38; 1.04 respectively), and RTG (SMD 0.84; 95% CrI 0.45; 1.22; and SMD 1.22; 95% CrI 0.59; 1.85 respectively). Time to first liquid intake (28 studies, 31,465 patients) and time to first ambulation (14 studies, 3530 patients) were shorter for TLTG compared to OTG (SMD −0.87; 95% CrI −1.52; −0.21; and SMD −0.81; 95% CrI −1.52; −0.09, respectively). Descriptive statistics and the league table are depicted in Tables 2 and 3, respectively. The node split analysis did not show evidence of inconsistence. The leverage plots did not show evidence of study outliers into this network meta-analysis. For all outcomes, there was no evidence of non-MCMC convergence using the diagnostic tools described in the statistical analysis section. The assessments of confidence in the estimates using CINeMA show moderate-to-very-low confidence, essentially due to study limitation, imprecision, and inconsistence.

Table 2. Descriptive statistics stratified according to different treatments.

	OTG	LATG	TLTG	RTG
OC	18 (5–46)	18 (5–41)	17 (0–39)	16 (3–25)
SPCs	7 (0–23)	6 (0–14)	6 (0–27)	6 (0–58)
AL	8 (0–27)	3 (0–10)	4 (0–28)	2 (0–25)
Anastomotic stenosis	2 (0–9)	3 (0–9)	1 (0–10)	4 (3–17)
Duodenal stump leak	1 (0–4)	1 (0–3)	1 (0–7)	2 (0–8)
Pancreatic complications	2 (0–6)	1 (0–6)	1 (0–5)	1 (0–3)
Pulmonary complications	8 (0–79)	5 (0–15)	5 (0–25)	7 (0–17)
SSI	4 (0–18)	3 (0–29)	2 (0–10)	2 (1–17)

Table 2. *Cont.*

	OTG	LATG	TLTG	RTG
Thrombotic events	2 (0–6)	0 (0–1)	1 (0–4)	2 (1–11)
Bleeding	5 (0–8)	2 (0–6)	4 (0–10)	2 (0–17)
Transfusion requirement	17 (6–27)	4 (0–7)	10 (0–19)	10 (4–16)
Ileus	2 (0–7)	1 (0–7)	2 (0–8)	2 (0–8)
Reintervention	15 (0–18)	1 (0–5)	9 (0–16)	2 (0–11)
In-hospital mortality	1 (0–9)	0 (0–2)	1 (0–3)	0 (0–8)
OT	208.9 (109.4–323)	240.5 (150.8–338.7)	248.3 (144–466)	297.5 (203.9–550)
Intraoperative blood loss	247.9 (99.2–758)	133.8 (50–299)	107.2 (10–275.3)	89 (32.5–207.1)
No LN retrieved	36 (15–54.3)	35 (18–48.4)	36.3 (18–54)	39.1 (22–48)
Time to first flatus	3.9 (3–5.4)	4.8 (2.4–23.4)	3.3 (1.9–5.7)	6.9 (2.2–23.1)
Time to first liquid intake	4.9 (2–10.7)	4.9 (3.5–9.1)	3.9 (1.5–9.1)	3.8 (3.5–3.9)
Time to first ambulation	3.7 (0.7–10.4)	3.6 (0.6–9.1)	2.2 (1.7–3.1)	2.3 (1.8–2.8)
LOS	14.2 (6–29)	10.8 (7–19)	13.1 (5–18)	9.8 (7–13)

Open total gastrectomy (OTG); lap-assisted total gastrectomy (LATG); totally laparoscopic total gastrectomy (TLTG); robotic total gastrectomy (RTG); overall complications (OC); severe postoperative complications (SPCs); anastomotic leak (AL); surgical site infections (SSI); operating time (OT); hospital length of stay (LOS). Values are presented as percentages for categorical variables and as mean (range) for continuous variables.

Table 3. League table. Each row represents a specific outcome.

Outcomes					I^2 (95% CrI)
OC	**OTG**	0.92 (0.81–1.04)	0.82 (0.73–0.92)	0.75 (0.59–0.95)	22.5 (0–43.9)
	1.08 (0.96–1.23)	**LATG**	0.89 (0.76–1.04)	0.81 (0.63–1.05)	
	1.22 (1.09–1.36)	1.13 (0.96–1.32)	**TLTG**	0.92 (0.74–1.14)	
	1.33 (1.05–1.68)	1.23 (0.95–1.58)	1.09 (0.88–1.36)	**RTG**	
SPCs	**OTG**	0.80 (0.59–1.07)	0.96 (0.75–1.24)	1.20 (0.75–1.91)	27.5 (0–50.3)
	1.25 (0.93–1.69)	**LATG**	1.21 (0.84–1.75)	1.50 (0.91–2.49)	
	1.04 (0.81–1.34)	0.83 (0.57–1.20)	**TLTG**	1.24 (0.80–1.94)	
	0.84 (0.52–1.33)	0.67 (0.40–1.10)	0.80 (0.51–1.26)	**RTG**	
AL	**OTG**	1.15 (0.83–1.59)	1.16 (0.95–1.43)	1.27 (0.74–2.18)	17.6 (0–40.9)
	0.87 (0.63–1.20)	**LATG**	1.01 (0.70–1.47)	1.11 (0.61–2.01)	
	0.86 (0.70–1.05)	0.99 (0.68–1.43)	**TLTG**	1.09 (0.65–1.85)	
	0.79 (0.46–1.35)	0.90 (0.50–1.64)	0.92 (0.54–1.55)	**RTG**	
Anastomotic stenosis	**OTG**	1.46 (0.95–2.24)	1.25 (0.66–2.38)	2.95 (0.81–10.81)	0 (0–42.5)
	0.69 (0.45–1.05)	**LATG**	0.86 (0.42–1.77)	2.02 (0.57–7.21)	
	0.80 (0.42–1.51)	1.16 (0.57–2.39)	**TLTG**	2.35 (0.63–8.78)	
	0.34 (0.09–1.24)	0.49 (0.14–1.77)	0.43 (0.11–1.59)	**RTG**	
Duodenal stump leak	**OTG**	0.79 (0.40–1.57)	1.96 (0.64–5.98)	1.40 (0.42–4.66)	0 (0–52.3)
	1.26 (0.64–2.49)	**LATG**	2.47 (0.71–8.61)	1.77 (0.54–5.78)	
	0.51 (0.17–1.56)	0.40 (0.12–1.41)	**TLTG**	0.72 (0.16–3.18)	
	0.71 (0.21–2.37)	0.57 (0.17–1.85)	1.40 (0.31–6.22)	**RTG**	

Table 3. *Cont.*

Outcomes					I^2 (95% CrI)
Pancreatic complications	**OTG**	0.79 (0.40–1.57)	1.96 (0.64–5.98)	1.40 (0.42–4.66)	0 (0–40.2)
	1.26 (0.64–2.49)	**LATG**	2.47 (0.71–8.61)	1.77 (0.54–5.78)	
	0.51 (0.17–1.56)	0.40 (0.12–1.41)	**TLTG**	0.72 (0.16–3.18)	
	0.71 (0.21–2.37)	0.57 (0.17–1.85)	1.40 (0.21–6.22)	**RTG**	
Pulmonary complications	**OTG**	0.96 (0.74–1.24)	0.99 (0.91–1.08)	0.84 (0.56–1.26)	0 (0–33.8)
	1.04 (0.80–1.35)	**LATG**	1.03 (0.79–1.35)	0.88 (0.55–1.40)	
	1.01 (0.93–1.10)	0.97 (0.74–1.27)	**TLTG**	0.85 (0.57–1.26)	
	1.19 (0.79–1.78)	1.14 (0.71–1.83)	1.18 (0.79–1.75)	**RTG**	
SSI	**OTG**	0.58 (0.42–0.81)	0.90 (0.80–1.00)	1.13 (0.58–2.21)	0 (0–33.8)
	1.72 (1.24–2.40)	**LATG**	1.54 (1.09–2.18)	1.94 (0.98–3.85)	
	1.12 (1.00–1.25)	0.65 (0.46–0.92)	**TLTG**	1.26 (0.65–2.46)	
	0.89 (0.45–1.73)	0.51 (0.26–1.02)	0.79 (0.41–1.55)	**RTG**	
Thrombotic events	**OTG**	1.11 (0.25–4.99)	0.93 (0.70–1.24)	1.96 (0.59–6.56)	0 (0–42.5)
	0.90 (0.20–4.02)	**LATG**	0.83 (0.18–3.76)	1.76 (0.31–10.12)	
	1.08 (0.81–1.44)	1.2 (0.27–5.41)	**TLTG**	2.11 (0.65–6.86)	
	0.51 (0.15–1.70)	0.57 (0.10–3.26)	0.47 (0.15–1.54)	**RTG**	
Bleeding	**OTG**	1.05 (0.68–1.62)	1.28 (1.05–1.57)	1.72 (0.84–3.51)	0 (0–34.2)
	0.95 (0.62–1.47)	**LATG**	1.22 (0.77–1.95)	1.64 (0.75–3.57)	
	0.78 (0.64–0.95)	0.82 (0.51–1.30)	**TLTG**	1.34 (0.67–2.69)	
	0.58 (0.28–1.19)	0.61 (0.28–1.33)	0.75 (0.37–1.50)	**RTG**	
Transfusion requirement	**OTG**	0.40 (0.18–0.88)	0.75 (0.50–1.11)	0.78 (0.36–1.68)	57 (13–78.8)
	2.50 (1.13–5.51)	**LATG**	1.86 (0.77–4.52)	1.94 (0.64–5.86)	
	1.34 (0.90–1.99)	0.54 (0.22–1.30)	**TLTG**	1.04 (0.54–2.02)	
	1.29 (0.59–2.78)	0.52 (0.17–1.56)	0.96 (0.50–1.86)	**RTG**	
Ileus	**OTG**	0.88 (0.59–1.31)	0.97 (0.83–1.13)	1.03 (0.53–1.97)	0 (0–33.8)
	1.14 (0.76–1.69)	**LATG**	1.10 (0.73–1.67)	1.17 (0.56–2.41)	
	1.03 (0.89–1.20)	0.91 (0.60–1.37)	**TLTG**	1.06 (0.56–2.01)	
	0.98 (0.51–1.88)	0.86 (0.42–1.77)	0.95 (0.50–1.80)	**RTG**	
Conversion	**LATG**	3.10 (1.09–8.84)	2.52 (1.35–4.70)		0 (0–64.8)
	0.32 (0.11–0.92)	**TLTG**	0.81 (0.33–1.97)		
	0.40 (0.21–0.74)	1.23 (0.51–2.99)	**RTG**		
Reintervention	**OTG**	1.06 (0.27–4.16)	1.09 (0.67–1.77)	1.03 (0.38–2.77)	74.7 (61.7–83.3)
	0.94 (0.24–3.69)	**LATG**	1.02 (0.24–4.28)	0.97 (0.19–4.91)	
	0.92 (0.57–1.50)	0.98 (0.23–4.10)	**TLTG**	0.95 (0.40–2.27)	
	0.97 (0.36–2.60)	1.03 (0.20–5.19)	1.05 (0.44–2.51)	**RTG**	
In-hospital mortality	**OTG**	0.89 (0.46–1.74)	1.04 (0.80–1.36)	1.88 (0.70–5.11)	74.7 (61.7–83.3)
	1.12 (0.58–2.17)	**LATG**	1.17 (0.58–2.35)	2.11 (0.71–6.28)	
	0.96 (0.74–1.25)	0.86 (0.43–1.72)	**TLTG**	1.80 (0.67–4.89)	
	0.53 (0.20–1.44)	0.47 (0.16–1.42)	0.55 (0.20–1.50)	**RTG**	
OT	**OTG**	0.95 (0.48; 1.41)	1.14 (0.71; 1.57)	2.02 (1.30; 2.74)	98.3 (98.1–98.5)
	−0.95 (−1.41; −0.48)	**LATG**	0.19 (−0.37; 0.76)	1.07 (0.31; 1.84)	
	−1.14 (−1.57; −0.71)	−0.19 (−0.76; 0.37)	**TLTG**	0.88 (0.23; 1.53)	
	−2.02 (−2.74; −1.3)	−1.07 (−1.84; −0.31)	−0.88 (−1.53; −0.23)	**RTG**	
Intraoperative blood loss	**OTG**	−1.15 (−1.54; −0.76)	−1.43 (−1.78; −1.08)	−1.68 (−2.28; −1.08)	98.45 (87.3–99.2)
	1.15 (0.76; 1.54)	**LATG**	−0.27 (−0.73; 0.19)	−0.53 (−1.17; 0.12)	
	1.43 (1.08; 1.78)	0.27 (−0.19; 0.73)	**TLTG**	−0.25 (−0.78; 0.27)	
	1.68 (1.08; 2.28)	0.53 (−0.12; 1.17)	0.25 (−0.27; 0.78)	**RTG**	
No LN retrieved	**OTG**	−0.22 (−0.39; −0.04)	0.06 (−0.11; 0.22)	0.23 (−0.05; 0.51)	98.3 (77.3–98.4)
	0.22 (0.04–0.39)	**LATG**	0.28 (0.06; 0.49)	0.44 (0.15; 0.74)	
	−0.06 (−0.22; 0.11)	−0.28 (−0.49; −0.06)	**TLTG**	0.17 (−0.08; 0.42)	
	−0.23 (−0.51; 0.05)	−0.44 (−0.74; −0.15)	−0.17 (−0.42; 0.08)	**RTG**	

Table 3. *Cont.*

Outcomes					I^2 (95% CrI)
Time to first flatus	**OTG**	−0.97 (−1.33; −0.61)	−0.71 (−1.04; −0.38)	−1.22 (−1.85; −0.59)	90.4 (67.3–99.4)
	0.97 (0.61; 1.33)	**LATG**	0.26 (−0.16; 0.69)	−0.25 (−0.89; 0.38)	
	0.71 (0.38; 1.04)	−0.26 (−0.69; 0.16)	**TLTG**	−0.51 (−1.10; 0.07)	
	1.22 (0.59; 1.85)	0.25 (−0.38; 0.89)	0.51 (−0.07; 1.10)	**RTG**	
Time to first liquid intake	**OTG**	−0.46 (−1.35; 0.44)	−0.87 (−1.52; −0.21)	−1.20 (−2.54; 0.14)	99.3 (99.2–99.4)
	0.46 (−0.44; 1.35)	**LATG**	−0.41 (−1.39; 0.56)	−0.74 (−2.27; 0.78)	
	0.87 (0.21; 1.52)	0.41 (−0.56; 1.39)	**TLTG**	−0.33 (−1.5; 0.84)	
	1.20 (−0.14; 2.54)	0.74 (−0.78; 2.27)	0.33 (−0.84; 1.50)	**RTG**	
Time to first ambulation	**OTG**	−0.80 (−1.63; 0.03)	−0.81 (−1.52; −0.09)	−1.02 (−2.29; 0.26)	97.7 (97–98.3)
	0.80 (−0.03; 1.63)	**LATG**	−0.01 (−1.01; 0.99)	−0.22 (−1.67; 1.23)	
	0.81 (0.09; 1.01)	0.01 (−0.99; 1.01)	**TLTG**	−0.21 (−1.27; 0.85)	
	1.02 (−0.26; 2.29)	0.22 (−1.23; 1.67)	0.21 (−0.85; 1.27)	**RTG**	
LOS	**OTG**	−0.46 (−0.71; −0.21)	−0.55 (−0.77; −0.33)	−0.84 (−1.22; −0.45)	96.8 (96.4–97.2)
	0.46 (0.21; 0.71)	**LATG**	−0.09 (−0.39; 0.21)	−0.38 (−0.79; 0.03)	
	0.55 (0.33–0.77)	0.09 (−0.21; 0.39)	**TLTG**	−0.29 (−0.64; 0.06)	
	0.84 (0.45; 1.22)	0.38 (−0.03; 0.79)	0.29 (−0.06; 0.64)	**RTG**	

Values in each column represent the relative effect of the referral treatment (bold) with the comparator. Open total gastrectomy (**OTG**); lap-assisted total gastrectomy (**LATG**): totally laparoscopic total gastrectomy (**TLTG**); and robotic total gastrectomy (**RTG**); overall complications (**OC**); severe postoperative complications (**SPCs**); anastomotic leak (**AL**); surgical site infections (**SSI**); operating time (**OT**); hospital length of stay (**LOS**). Values are expressed as risk ratio (RR) and 95% credible intervals (95% CrIs). I^2: heterogeneity.

4. Discussion

The present study shows comparable SPCs and AL RR for OTG, LATG, TLTG, and RTG. Despite longer OT, LATG, TLTG, and RTG showed reduced OC, intraoperative blood loss, time to first flatus, time to ambulation, time to liquid diet resumption, and HLOS compared to OTG.

GC incidence is progressively increasing in both low- and high-risk countries, with risk factors ranging from genetic susceptibility and Helicobacter pylori infection to lifestyle factors such as alcohol consumption and smoking [92]. In Western countries, GC is often diagnosed at an advanced stage due to inadequate screening protocols [93]. For individuals with resectable GC, a multimodal approach involving surgery alongside systemic therapy appears to confer survival benefits [94]. The backbone of curative treatment for GC is surgical resection [95]. The optimal surgical approach is still a matter of debate, with international guidelines stating that open total or distal gastrectomy are the current gold standard for clinically node-positive or T2–T4a tumors [2,3]. OTG has been flanked by minimally invasive approaches with promising results [24,96–98]. The technical advantages of these techniques with minimized surgical trauma have driven their wider worldwide adoption [10,29,99,100]. This shift from open surgery to minimally invasive approaches has been recently documented in a Korean nationwide survey; specifically, the frequency of the open approach decreased from 49.8% to 27.6% between 2014 and 2019. On the contrary, laparoscopic TG frequency increased by 18.2% in 2014 to 44.3% in 2019 (26.1%) [101,102].

Our network analysis showed OC rates of 18/% for OTG and LATG, 17% for TLTG, and 16% for RTG. These results are similar to the CLASS-02 trial, which reported OC rates of 19.1% and 20.2% for laparoscopic and open gastrectomy, respectively [48]. Interestingly, the quantitative analysis showed higher OC RR for OTG compared to TLTG and RTG with a low related heterogeneity (I^2 = 22.5%). Our data are similar to a recent Korean analysis that observed a lower overall morbidity rate for minimally invasive vs. open gastrectomy (17.5% vs. 21.9%, p = 0.001) [103]. Similarly, Lei et al., in recently published RCTs meta-analysis, showed a lower OC rate for laparoscopic compared to open gastrectomy (OR 0.65, $p < 0.001$) [4]. These results may be theoretically explained by the reduced surgical trauma for minimally invasive gastrectomy with smaller surgical incisions, less surgical stress, and finest surgical dissection determining a lower risk of postoperative SSI and bleeding [104].

Interestingly, the postoperative SPCs RR were comparable across treatments. Our results are similar to those presented in the recent JLSSG0901 RCT, which reported no differences in SPCs between open (4.7%) and laparoscopic-assisted distal gastrectomy (4.7% vs. 3.5%; $p = 0.641$) [105]. Conversely, Wang et al. reported a lower SPCs rate for laparoscopic compared to robot-assisted gastrectomy (8.9% vs. 17.5%, $p = 0.002$) [106]. The incidence of AL after total gastrectomy for GC has been previously reported to be up to 6.6% [107]. The present analysis showed that OTG, LATG, TLTG, and RTG were associated with 8%, 6%, 4%, and 2% AL rates, respectively. Again, the quantitative analysis showed no significant RR differences among treatments. Our results are consistent with Yang et al., who reported comparable AL for laparoscopic TG vs. OTG (OR 0.94; 95% CI 0.61–1.47) [108]. Despite the related heterogeneity being low–moderate for these primary outcomes, selection bias, temporal bias, and reporting bias should be pondered while interpreting these outcomes. The surgical technique use to perform TG seems to have no influence on AL. Contrarily, AL may depend on other factors such as anastomotic tension, malnutrition, inadequate blood supply, and comorbidities [109].

In our meta-analysis, OTG exhibited the shortest OT. This is in contrast to what was reported by Garbarino et al. and Trastulli et al., which conveyed longer OT for open gastrectomy compared to laparoscopic (WMD 47.4 min; $p < 0.001$) and robotic gastrectomy (WMD 56.9 min; $p < 0.001$) [110,111]. These results mandate thoughtful insights as it is well known that in case of minimally invasive approaches, OT encompass both "effective" surgical time (dissection and reconstruction phases) and "junk time", which involves setting, docking, and surgical instruments adjusting. Liu et al. previously reported comparable effective operative for robotic and laparoscopic distal gastrectomy (145.9 vs. 130.6; $p = 0.09$) [112]. Similarly, Omori et al. reported shorter OT for robotic compared to laparoscopic gastrectomy in a propensity-matched cohort of 1189 patients [113]. It has been shown that longer OT seems to be associated with an increased risk of postoperative complication [114]. Specifically, Park et al. identified 240 min as the cut-off associated with an increased risk of postoperative complications [115]. Interestingly our analysis reported 208, 248, 240, and 297 min estimated OT for OTG, LATG, TLTG, and RTG, respectively. These data suggest that even if a statistically significant difference is perceived, its clinical relevance may be limited. Further, OTG was associated with longer HLOS compared to minimally invasive approaches. These results are similar to Straatman et al., who reported shorter time to first flatus (WMD −1.05 days, $p < 0.00001$) and shorter HLOS (WMD: −2.43 days, $p = 0.0002$) for minimally invasive compared to open gastrectomy [116]. No significant differences were found in terms of harvested lymph nodes among techniques. These results reflect what was reported by Yang et al., which conveyed no significant difference between laparoscopic and open TG [108]. Conversely, Trastulli et al. stated a statistically significant higher number of lymph nodes harvested in robotic vs. open gastrectomy (30 vs. 25.5, $p = 0.014$) [111]. Additionally, a recent meta-analysis showed a higher number of lymph nodes retrieved in the robotic compared to laparoscopic gastrectomy (OR: 1.75; $p < 0.0001$) [117]. Minimally invasive approaches were associated with a trend toward improved time to first flatus, time to first liquid intake, and time to ambulation. These results may reflect the minimized abdominal wall and bowel surgical trauma determining reduced perceived pain with earlier mobilization, ambulation, and time to fist flatus. Notably, the global heterogeneity for secondary outcomes was moderate–high. Factors that could have influenced this issue include patients' comorbid conditions, body mass index, ASA grade, smoking status, postoperative antibiotic therapy, outcome reporting, tumor types and size, technique for intestinal reconstruction, lymphadenectomy (D1 vs. D1+ vs. D2), omentectomy (total versus partial versus non-performed), hospitals protocols, implementation of enhanced recovery after surgery protocols, surgeons' experience, and hospital volumes.

It has been postulated that the operating surgeon's learning curve and expertise have a significant influence on short-term outcomes and could be a notable source of background bias. Specifically, operating-surgeon-related factors are critical in determining operative time, intraoperative blood loss, total number of harvested lymph nodes, and overall

complications [118]. Chan et al. reported that the learning curve for minimally invasive approaches to TG is approximately 44 cases for TLTG and 21 cases for RTG. Similarly, Seika and colleagues conveyed that 44 cases are required for experienced laparoscopic surgeons to achieve LATG technical competency [119–121]. In the present meta-analysis, only a few studies specifically reported the operating surgeon's proficiency; therefore, our conclusions should be cautiously interpreted.

To the best of our knowledge, this is the first network meta-analysis reporting outcomes exclusively for TG and performing a comprehensive analysis on all the principal techniques for TG. The previous literature on gastrectomy in GC is based mainly on pairwise analyses and studies evaluating results from both total and distal gastrectomy. On the plea for a granular analysis of short-term outcomes focused on TG, we performed an analysis of a homogeneous population of patients undergoing TG for GC. In the present analysis, network meta-analytic methods allowed us to combine data from a large number of studies with the assessment of both direct/indirect comparisons and treatment ranking. Some limitations should be assessed in interpreting our results. First, surgical data are derived from a long time span, from 1995 to 2021 (temporal bias), thus leading to possible differences in both the surgical environment and perioperative systemic therapy protocols with related nonhomogeneous postoperative complication risks. Second, non-uniform measuring methods for postoperative outcomes were seen among different studies, thus leading to possible detection bias. Third, the inclusion of both early and locally advanced GC can lead to potential selection bias. Because data were reported as aggregated, a robust stratified analysis was not feasible. Fourth, all procedures were performed by experienced surgeons in high-volume referral centers, representing the best predictable outcomes; applicability of these results should be considered in light of the surgeon's proficiency and learning curve. Only a few studies specifically analyzed RTG outcomes; therefore, the available evidence remains preliminary and limited. Hence, no definitive and robust conclusions can currently be drawn regarding the safety and efficacy of this approach. Lastly, there was significant heterogeneity among the included studies in terms of postoperative management, rehabilitation protocols, and the application of enhanced recovery after surgery pathways.

5. Conclusions

LATG, TLTG, and RTG seem to be associated with improved OC, time to first flatus, time to first liquid intake, and time to ambulation compared to OTG in the setting of GC. Our network meta-analysis supports the implementation of minimally invasive TG techniques in the surgical treatment of GC.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/cancers16193404/s1: Figure S1. Risk of bias for randomized controlled trials (RCT) assessed with use of the Cochrane risk-of-bias tool 2. Green circle: low risk of bias; red circle: high risk of bias; yellow circle: unclear risk of bias. Bias arising from the randomization process (R); bias due to deviations from intended interventions (D); bias due to missing outcome data (Mi); bias in measurement of the outcome (Me); bias in selection of the reported result (S); overall risk of bias (O). Table S1. Quality assessment of the included studies (ROBINS-I tool). Each domain is evaluated with one of the following: low, moderate, serious, critical, NI (no information). The categories of judgement for each study are low, moderate, serious, and critical risk of bias. File S1. PRISMA 2020 Checklist.

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Appendix A

Complete search strategy: ('stomach cancer'/exp OR 'cancer of the cardia' OR 'cancer of the gastric antrum' OR 'cancer of the gastric body' OR 'cancer of the gastric cardia' OR 'cancer of the gastric fundus' OR 'cancer, stomach' OR 'cardia cancer' OR 'gastric antral cancer' OR 'gastric antrum cancer' OR 'gastric body cancer' OR 'gastric cancer' OR 'gastric cardia cancer' OR 'gastric cardiac cancer' OR 'gastric malignancies' OR 'gastric malignancy' OR 'malignancies of the stomach' OR 'malignancy of the stomach' OR 'malignant gastric neoplasm' OR 'malignant gastric tumor' OR 'malignant neoplasm of the stomach' OR 'malignant neoplasms of the stomach' OR 'malignant tumor of the stomach' OR 'malignant tumors of the stomach' OR 'malignant tumour of the stomach' OR 'malignant tumours of the stomach' OR 'pyloric cancer' OR 'stomach cancer' OR 'stomach malignancies' OR 'stomach malignancy') AND (('total gastrectomy'/exp OR 'complete gastric resection' OR 'stomach total resection' OR 'total gastrectomy' OR 'total gastric resection' OR 'total stomach resection') AND ('open surgery'/exp OR 'open surgery' OR 'open surgical repair')) AND (('laparoscopic total gastrectomy'/exp OR 'laparoscopic assisted total gastrectomy' OR 'laparoscopic total gastrectomy' OR 'laparoscopyassisted total gastrectomy' OR 'total laparoscopic gastrectomy' OR 'total laparoscopic-assisted gastrectomy') OR ('robot assisted surgery'/exp OR 'robot aided surgery' OR 'robot assisted surgery' OR 'robot surgery' OR 'robotic aided surgery' OR 'robotic surgery' OR 'robotic surgical procedure' OR 'robotic surgical procedures' OR 'robotically assisted surgery')) AND (('postoperative complication'/exp OR 'complication after operation' OR 'complication after surgery' OR 'complication, postoperative' OR 'complication, surgical' OR 'post-operation complication' OR 'post-operative complication' OR 'post-operative complications' OR 'post-surgery complication' OR 'post-surgical complication' OR 'postoperation complication' OR 'postoperative complication' OR 'postoperative complications' OR 'postsurgery complication' OR 'postsurgical complication' OR 'surgery complication' OR 'surgery complications' OR 'surgery-associated complication' OR 'surgery-derived complication' OR 'surgery-induced complication' OR 'surgery-related complication' OR 'surgical complication') OR ('anastomosis complication'/exp OR 'anastomosis complication' OR 'anastomotic complication') OR 'short term outcome'/exp OR (bleeding/exp OR 'abnormal bleeding' OR 'bleeding' OR 'bleeding complication' OR 'blood effusion' OR 'blood loss' OR 'capillary bleeding' OR 'haemorrhage' OR 'haemorrhage model' OR 'haemorrhagic activity' OR 'haemorrhaging' OR 'hemorrhage' OR 'hemorrhage model' OR 'hemorrhagia' OR 'hemorrhagic activity' OR 'hemorrhaging' OR 'spontaneous haemorrhage' OR 'spontaneous hemorrhage') OR 'duodenal stump leakage'/exp OR 'duodenal stump leak'/exp OR 'duodenal stump fistula'/exp OR ('acute pancreatitis'/exp OR 'acute pancreatitis' OR 'pancreatitis acuta') OR 'pancreatic leak'/exp OR ('pancreas fistula'/exp OR 'pancreas fistula' OR 'pancreatic fistula') OR 'pancreatic leakage'/exp OR ('lung complication'/exp OR 'complication, lung' OR 'lung complication' OR 'pulmonary complication') OR ('surgical infection'/exp OR 'SSI (surgical site infection)' OR 'infected surgical site' OR 'infected surgical wound' OR 'infection at the operative site' OR 'infection at the surgery site' OR 'infection at the surgical site' OR 'infection of the operative site' OR 'infection of the surgery site' OR 'infection of the surgical site' OR 'infection of the surgical wound' OR 'infection, surgical' OR 'operative site infection' OR 'post-operative wound infection' OR 'postoperative wound infections' OR 'postoperative wound infection' OR 'postoperative wound infections' OR 'surgery site infection' OR 'surgical infection' OR 'surgical infections' OR 'surgical site infection' OR 'surgical wound infection' OR 'surgical wound infections') OR (thrombosis/exp OR

'acute thrombosis' OR 'arm thrombosis' OR 'atherothrombosis' OR 'rethrombosis' OR 'sclerothrombosis' OR 'thrombo-obliterative disease' OR 'thrombo-occlusive disease' OR 'thromboocclusive disorder' OR 'thromboobliterative disease' OR 'thromboocclusive disease' OR 'thromboocclusive disorder' OR 'thrombosis' OR 'thrombosis induction' OR 'thrombotic disease' OR 'thrombotic disorder' OR 'thrombotic occlusion')).

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