



# Learning curve of laparoscopic and robotic total gastrectomy: A systematic review and meta-analysis

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## Abstract

**Purpose** Minimally-invasive total gastrectomy (MITG) is associated with lower morbidity in comparison to open total gastrectomy but requires a learning curve (LC). We aimed to perform a pooled analysis of the number of cases required to surmount the LC ( $N_{LC}$ ) in MITG.

**Methods** A systematic review of PubMed, Embase, Scopus and the Cochrane Library from inception until August 2022 was performed for studies reporting the LC in laparoscopic total gastrectomy (LTG) and/or robotic total gastrectomy (RTG). Poisson mean (95% confidence interval [CI]) was used to determine the  $N_{LC}$ . Negative binomial regression was performed as a comparative analysis.

**Results** There were 12 articles with 18 data sets: 12 data sets ( $n = 1202$  patients) on LTG and 6 data sets ( $n = 318$  patients) on RTG. The majority of studies were conducted in East Asia (94.4%). The majority of the data sets ( $n = 12/18$ , 66.7%) used non-arbitrary analyses. The  $N_{LC}$  was significantly smaller in RTG in comparison to LTG [RTG 20.5 (95% CI 17.0–24.5); LTG 43.9 (95% CI 40.2–47.8); incidence rate ratio 0.47,  $p < 0.001$ ]. The  $N_{LC}$  was comparable between totally-laparoscopic total gastrectomy (TLTG) and laparoscopic-assisted total gastrectomy (LATG) [LATG 39.0 (95% CI 30.8–48.7); TLTG 36.0 (95% CI 30.4–42.4)].

**Conclusions** The LC for RTG was significantly shorter for LTG. However existing studies are heterogeneous.

**Keywords** Gastrectomy · Gastric cancer · Learning curve · Minimally invasive surgical procedures · Laparoscopy

## Introduction

Globally, gastric cancer (GC) ranks fifth in terms of incidence and fourth in terms of mortality among the various cancers [1]. In 2020, there were over one million cases of newly diagnosed GC [1]. Gastrectomy remains the mainstay of curative treatment for non-metastatic GC.

Laparoscopic-assisted distal gastrectomy (LADG) was first introduced in 1994 by Kitano [2]. Subsequently, robot-assisted distal gastrectomy (RADG) was introduced by Hashizume et al. [3] in 2002. Since the advent of minimally

invasive gastrectomy (MIG), there has been an increasing trend of adoption in view of the potential benefits of MIG over conventional open gastrectomy [4]. A meta-analysis by Haverkamp et al. [5] on 8 studies with 619 patients showed significantly lower estimated blood loss, post-operative complications, and length of hospital stay, with similar in-hospital mortality and lymph node (LN) harvest when laparoscopic total gastrectomy (LTG) was compared to open total gastrectomy (OTG). Similarly, the comparison of robotic gastrectomy (RG) with open gastrectomy (OG) showed reduced estimated blood loss and length of hospital stay with a similar LN harvest [6].

As with any minimally invasive surgery (MIS), there is a long learning curve (LC), especially for oncological surgery, where there is a need for radical resection with LN dissection [7]. Surgeons will need to perform a number of cases to surmount the LC before reaping its benefits. Several studies have been conducted to determine this “magic number”. However, to our knowledge, no review has conducted qualitative and/or quantitative analyses of these studies.

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In addition, LTG and robotic total gastrectomy (RTG) are performed relatively less commonly in comparison to distal gastrectomy (DG), in view of the lower incidence of upper GC and associated technical difficulties with esophagojejunostomy (EJ) [8, 9]. Hence, this study aims to determine the number of cases required to surmount the LC in LTG and RTG.

## Materials and methods

### Study selection and search strategy

Studies selected for the meta-analysis and systematic review adhered to the quality and standards set by the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) [10]. The study protocol was registered on PROSPERO (Ref no: CRD42022349680). A literature search of published studies on MIG was performed using PubMed, Embase, Scopus, and the Cochrane Library for studies published from inception to 14 August 2022. The search was restricted to title, abstract, and keywords for all databases. The following search terms were identified and used in combination: (“minimally invasive” OR “laparoscop\*” OR “robotic” OR “robot-assisted”) AND (“gastrectomy” OR “gastric resection” OR “stomach resection”) AND (“learning curve” OR “residency” OR “proficiency” OR “education”). The detailed search strategy is appended in Supplementary Table S1. No filters were used to limit the search. Duplicates were removed before the study selection process.

The inclusion criteria were articles that reported the LC in LTG and/or RTG. Studies that reported on either intracorporeal (i.e., totally laparoscopic or robotic) and/or extracorporeal (laparoscopic-assisted or robot-assisted) reconstruction were included. Studies that included a mix of total gastrectomy (TG) and DG were included in the analysis if the incidence of TG was  $\geq 75\%$  of the entire cohort. The exclusion criteria were studies that were (1) not relevant to MITG, (2) only on OG, (3) feasibility studies of early experience and/or report only outcomes of MITG without a description of the LC, (4) novel methods or modifications to techniques of MITG without a description of the LC, (5) on outcomes of simulation training in MITG, (6) on the comparison of outcomes between consultant surgeons and surgical trainees, or the impact of institutional surgical volume on outcomes, (7) case reports, conference abstracts, editorials, letters to editor, expert opinions, review articles, or non-English texts.

After the removal of duplicates, two authors (KSC, AMO) independently screened the studies for potential inclusion based on title and abstract in the first stage. The full texts of the included studies after the first screening stage were

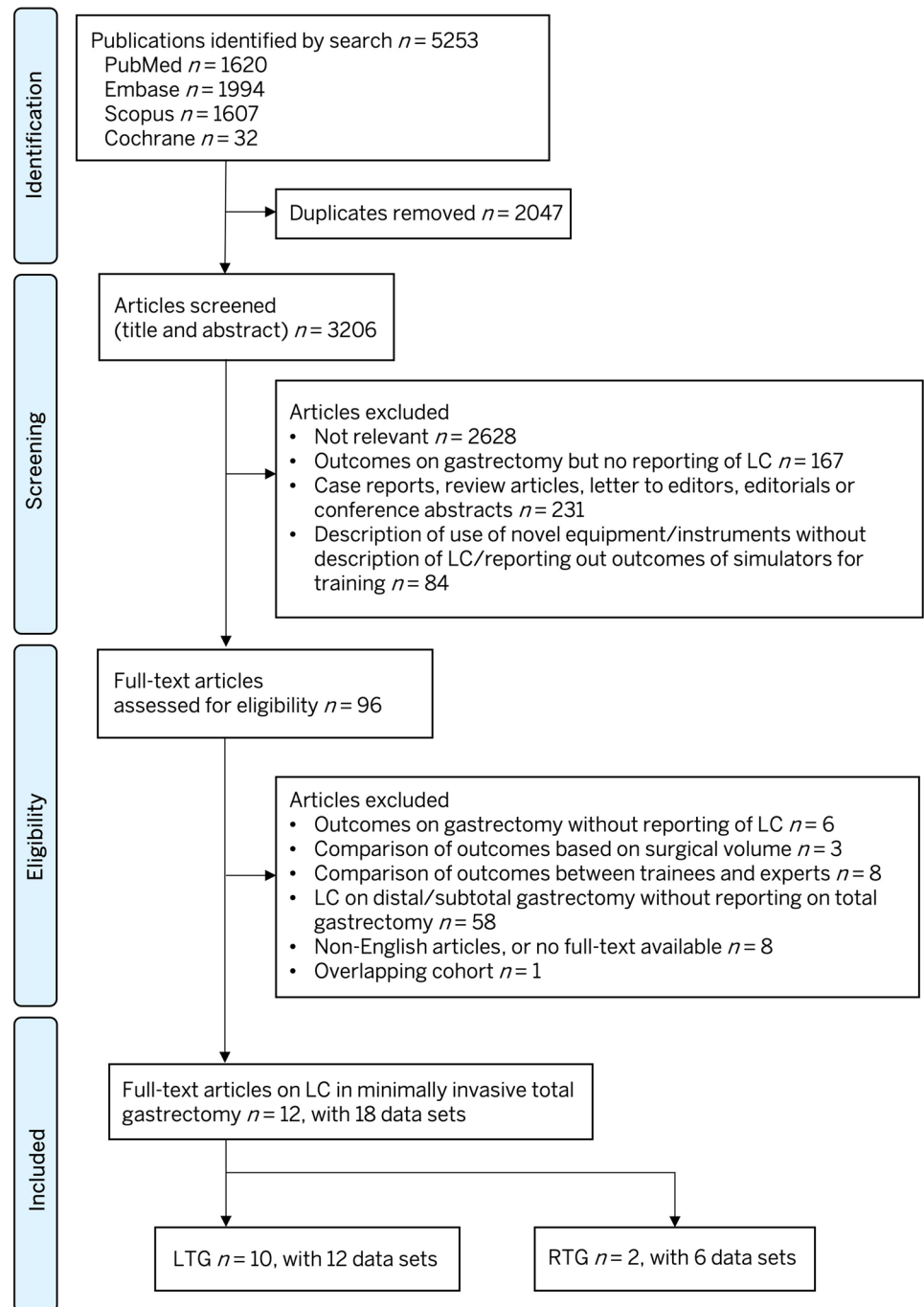
obtained and reviewed for eligibility based on the inclusion and exclusion criteria. Full-texts of studies that reported on DG were also read in entirety to ensure that there was no reporting of the LC in TG. All conference abstracts that reported the LC in MIG were also read in entirety to ensure adequacy of information. In view of the large number of peer-reviewed articles that reported on LC, we excluded conference abstracts as they have not undergone peer-review and would limit the interpretability of our study. Conflicts were resolved by consensus. This process is reflected in the PRISMA flow diagram (Fig. 1).

### Data extraction and definitions

Two independent authors (KSC, AMO) extracted the following information from each study separately: author, year of publication, study period, country of study, study design, patient demographics and tumor characteristics, surgical access (laparoscopic vs. robotic), type of anastomosis [extracorporeal (i.e., laparoscopic-assisted total gastrectomy; LATG, or robotic-assisted total gastrectomy; RATG) vs. intracorporeal (i.e., totally-laparoscopic total gastrectomy; TLTG, or totally-robotic total gastrectomy; TRTG)], type of lymphadenectomy, method of LC analysis, outcomes of LC analyzed, number of surgeons, prior surgical experience, type of LC (single-surgeon vs. institutional LC) and number required to surmount the LC for the studied outcomes(s). Both resection and lymphadenectomy in LATG and TLTG were performed laparoscopically, and both resection and lymphadenectomy in robot-assisted total gastrectomy (RATG) and totally-robotic total gastrectomy (TRTG) were performed via a robotic approach. The definitions of LATG, TLTG, RATG and TRTG were based on the type of anastomosis: LATG and RATG were defined as the use of a non-laparoscopic approach (e.g., extracorporeal anastomosis, hand-assisted laparoscopy) and the use of a non-robotic approach (e.g., laparoscopy for intracorporeal anastomosis, hand-assisted laparoscopy, or extracorporeal anastomosis), respectively, for either EJ and/or jejunojunctionostomy (JJ); TLTG and TRTG were defined as intracorporeal anastomosis via laparoscopy and robot, respectively, for both EJ and JJ.

The methods of LC analyses were defined as either arbitrary or non-arbitrary. An arbitrary analysis was defined as an analysis using arbitrary cut-off values (e.g., number of cases or time period). Non-arbitrary analyses included (1) a cumulative sum control chart (CUSUM) analysis or (2) other non-arbitrary statistical analyses, such as moving weighted average or local regression. Short-term outcomes included operating time, estimated blood loss, open conversion, any morbidity, major morbidity (defined as Clavien-Dindo Grade IIIA or higher), textbook outcomes (TBO), anastomotic complications (leakage, stenosis, bleeding), pancreatic leak

**Fig. 1** Preferred reporting items for systematic reviews and meta-analyses (PRISMA) figure showing the study selection process. LC, learning curve; LTG, laparoscopic total gastrectomy; RTG, robotic total gastrectomy



or fistula, pneumonia, surgical site infection, length of hospital stay, time to flatus, liquid diet and oral diet, mortality (30-day or in-hospital) and need for re-intervention. Oncological outcomes included lymph node (LN) harvest, splenic hilar LN harvest, and R0 resection. For studies on RTG reporting on operating time, the overall operating time was defined as the time from skin incision to skin closure (i.e., inclusive of docking time).

Studies that did not report whether the LC was the single-surgeon LC vs. the institutional LC, they were

analyzed as institutional LC. For studies that defined LC based on a single surgical team, this was assumed to be a single-surgeon study as a surgical team usually consist of one main surgeon with surgical assistants. All included studies were also stratified based on the IDEAL (innovation, development, exploration, assessment, long term) paradigm as described by Barkun et al. [11]. We arbitrarily defined IDEAL 3 based on inclusion of cases for LC analysis after 2010 and 2015 for LTG and RTG respectively. Studies with inclusion period straddling the cut-off

year defined were classified under IDEAL 3 if majority of cases included were after the cut-off year.

Our study outcome was the number of cases required to surmount the LC ( $N_{LC}$ ), defined as the number of cases required to reach stability or technical competence (for non-arbitrary analysis) or as described in the results of the studies (arbitrarily grouped based on case log or time span).

### Assessment of study quality

Quality assessment of the finalized studies was performed by two independent authors (KSC, AMO). Observational studies were assessed using the modified Newcastle Ottawa scale (Supplementary Table S2). Disagreements between authors were resolved by consensus.

### Statistical analysis

Study variables were extracted and tabulated in Microsoft® Excel 365 (Microsoft®, Washington, United States). Categorical variables were described as  $n$  (%) and continuous variables were described as median (interquartile range (IQR)) or mean  $\pm$  standard deviation as described in the original studies. For studies that reported only the mean and standard deviation of individual groups, the overall mean and standard deviation were estimated from the individual groups using the method described by Altman et al. [12] This study aimed to systematically review the current relevant literature on the LC in MIG. Quantitative analyses were conducted using Poisson mean and 95% confidence intervals (CIs) to provide further insights to readers on the number of cases required to surmount the LC ( $N_{LC}$ ). The “average” number of participants across studies required to surmount the LC was modelled using Poisson mean, which can be interpreted as a type of central tendency for count data (analogous to the arithmetic mean for continuous normally distributed data). For studies that reported multiple  $N_{LC}$ , the  $N_{LC}$  reported in the conclusion was used; if the  $N_{LC}$  was not described in the conclusion, the  $N_{LC}$  required for the first change in the curve or to reach a plateau (for CUSUM analyses) was used. For studies that performed multiple CUSUM analyses for various outcome variables, the highest  $N_{LC}$  was used. For studies that used an arbitrary analysis with  $> 2$  groups and that showed statistical significance between groups, the higher  $N_{LC}$  of the latter group was used (e.g., if comparing cases 1–20, 21–40 and 41–60, with statistically significant differences, a  $N_{LC}$  of 40 was used). While this study is not a traditional meta-analysis where effect size is expressed as odds ratio, risk ratio or hazards ratio, comparative analyses (e.g., comparing the  $N_{LC}$  between LTG and RTG) were performed using negative binomial regression which allows better handling of overdispersion and were expressed using the incidence rate ratio (IRR). Basic study

characteristics and clinical demographics were summarized as  $n$  (%) for categorical variables and mean  $\pm$  standard deviation for continuous variables. All statistical analyses were performed in Stata (version 17.0, StataCorp, United States). Statistical significance was defined as  $p < 0.05$ .

### Results

Our initial search identified 5253 articles. No cross-references were made as there were no existing systematic reviews on LTG and/or RTG. After screening of duplicates, titles, and abstracts, we obtained 101 full-text articles. There were 72 full-text articles that reported on the LC in LG and/or RG. There were 13 articles that reported on LTG and/or RTG. Of the final full-text articles, there were 2 articles with overlapping cohorts (Wang et al. [13] and Chen et al. [14]); the study by Wang et al. [13] was included in view of the longer study period. There are 3 articles with that analyzed multiple data sets: Jeong et al. [8] and Jung et al. [15] with 2 data sets each, and Zheng-Yan et al. [16] with 5 data sets. Hence, a total of 12 full-text articles with 18 data sets were included in the final analyses. There were 10 articles with 12 data sets that reported on LTG [8, 15, 17–24], and 2 articles with 6 data sets that reported on RTG [13, 16]. All included studies were on patients with TG only.

### Characteristics of LC studies

A total of 1520 patients [LTG  $n = 1202$  (79.1%), RTG  $n = 318$  (20.9%)] were included in the LC analysis. No RCTs were included. The majority of the data sets were retrospective ( $n = 17/18$ , 94.4%) and the majority of the studies were conducted in East Asia ( $n = 17/18$ , 94.4%). The mean study period was  $7.4 \pm 3.0$  years. Table 1 summarizes the overall patient demographics in the included data sets. Detailed patient demographic data for the individual studies are shown in Supplementary Tables S3 and S4. The mean age of the patients in the included studies ranged from 55.9 to 68.4 in LTG, and 55.3 to 62.0 in RTG. The study population showed a male predominance [male: 73.8% ( $n = 599/812$ )]. Three data sets were exclusively on early GC [8, 18, 25], and 2 were exclusively on advanced GC [13, 20]. The majority of patients had an ASA score of I or II ( $n = 534/630$ , 84.8%). There were 12.8% ( $n = 25/196$ ) patients who received prior endoscopic mucosal resection or endoscopic submucosal dissection. There were 6 data sets that reported MITG alone without splenectomy only [13, 15, 19, 20, 22, 24], and 1 data set that reported MITG with splenectomy only (Supplementary Table S3 and S4) [15]. There were 5 data sets that reported Roux-en-Y EJ [8, 17, 18, 24], 5 data sets that reported EJ (without mentioning whether it was Roux-en-Y EJ) [15, 21, 22, 25], 1 data set that reported mixed methods

**Table 1** Summary of patient demographics and study characteristics in all included studies (n = 12, with 18 data sets)

	LTG (n = 12 data sets)	RTG (n = 6 data sets)
Patients, total <sup>a</sup>	1202	318
Study period, years (mean ± SD)	6.68 ± 3.27	8.92 ± 1.76
Type of study, no. of studies (%)		
Prospective	1 (8.3)	0
Retrospective	11 (91.7)	6 (100)
Male, no. of patients (%)	347/494 (70.2)	252/318 (79.2)
ASA, no. of patients (%)		
I	77/312 (24.7)	I, II: 267/318 (84.0)
II	190/312 (60.9)	
III	39/312 (12.5)	51/318 (16.0)
IV	6/312 (1.9)	
Previous abdominal surgery, no. of patients (%)	56/317 (17.7)	NR
Previous EMR or ESD, no. of patients (%)	25/196 (12.8)	NR
Clinical stage, no. of patients (%)		
Early	438/616 (71.1)	0/35 (0)
Advanced	178/616 (28.9)	35/35 (100)
Histology, no. of patients (%)		
Differentiated	63/113 (55.8)	NR
Undifferentiated	50/113 (44.2)	NR
Type of reconstruction, no. of studies (%)		
Extracorporeal (assisted)	2 (16.7)	NR
Intracorporeal (total)	4 (33.3)	NR
Mixed	5 (41.7)	NR
Not reported	1 (8.3)	NR

All categorical variables are expressed as n (%), and all continuous variables are expressed as the mean ± SD unless otherwise specified

ASA, American Society of Anesthesiologists; EMR, Endoscopic mucosal resection; ESD, endoscopic submucosal dissection; LTG, laparoscopic total gastrectomy; NR, not reported; RTG, robotic total gastrectomy; SD, standard deviation

<sup>a</sup>For studies that included overall demographics but did not report demographics specific to patients who were included in the learning curve analysis, the results were not included in this pooled table, but were included in the table on patient demographics for the respective individual studies

of reconstruction (majority with Roux-en-Y EJ; we only included data on TG in our study; however, their study did not specify the specific method of reconstruction for TG) [19], and 7 data sets that did not report the method of reconstruction [13, 16, 20]. Only 2 data sets included patients with D2 lymphadenectomy only [19, 20]. The majority of data sets reported the single-surgeon LC (n = 14/18, 77.8%).

### Types of LC analyses

The majority of data sets used non-arbitrary analyses (n = 12/18, 66.7%). The risk-adjusted CUSUM was used in 1 study with 5 data sets (27.8%) to address confounding factors [16], all of which were on RTG only. The LC analyses were stratified based on the overall LC, analysis method, type of LC, and study period (Table 2). Supplementary Table S5 summarizes the  $N_{LC}$  reported for each outcome parameter studied. Details regarding the LC analyzed in

individual studies are summarized in Tables 3 and 4. The surgeons' prior experiences are reported in Tables 3 and 4.

The overall  $N_{LC}$  for LTG and RTG was 43.9 (95% CI 40.2–47.8) and 20.5 (95% CI 17.0–24.5) respectively. The  $N_{LC}$  was significantly smaller in RTG in comparison to LTG (IRR 0.47, 95% CI 0.34–0.65,  $p < 0.001$ ). We also performed an analysis of the  $N_{LC}$  for specific outcome variables (Supplementary Table S5); the  $N_{LC}$  was significantly lower in RTG in comparison to LTG for operating time (IRR: 0.50, 95% CI 0.34–0.74,  $p = 0.001$ ) and LN harvest (IRR: 0.42, 95% CI 0.27–0.67,  $p < 0.001$ ). A subgroup analysis of 4 data sets that included only early GC patients who underwent LTG showed a  $N_{LC}$  of 32.0 (95% CI 26.7–38.0) [8, 18, 25]. A subgroup analysis of 5 data sets that included patients who underwent LTG with splenic preservation only showed a  $N_{LC}$  of 42.2 (95% CI 36.7–48.3) [15, 19, 20, 22, 24].

There were 7 data sets (58.3%) that used non-arbitrary analysis methods in LTG [8, 19–22, 24, 25], and 5 data sets

**Table 2** Summary of the number of cases to surmount learning curves stratified based on the analysis method, and the IDEAL period in laparoscopic total gastrectomy (LTG) and robotic total gastrectomy (RTG)

	LTG (n = 12 data sets)	RTG (n = 6 data sets)
Method of analysis, no. of data sets (%)		
CUSUM only	2 (16.7)	5 (83.3)
Other statistical methods only	4 (33.3)	0
Arbitrary only	4 (33.3)	1 (16.7)
CUSUM + other statistical methods	1 (8.3)	0
Arbitrary + non-arbitrary methods	1 (8.3)	0
Overall $N_{LC}$ (No. of data sets, Poisson mean (95% CI))	43.9 (40.2–47.8)	20.5 (17.0–24.5)
$N_{LC}$ based on method of LC analysis (No. of data sets, Poisson mean (95% CI))		
CUSUM	n = 3, 42.3 (35.3–50.4)	n = 5, 20.6 (16.8–25.0)
Non-CUSUM and non-arbitrary	n = 4, 48.5 (41.9–55.8)	NA
Non-arbitrary	n = 7, 45.9 (41.0–51.2)	n = 5, 20.6 (16.8–25.0)
Arbitrary	n = 5, 41.2 (35.8–47.2)	n = 1, 20.0 (12.2–30.9)
$N_{LC}$ based on type of LC (No. of data sets, Poisson mean (95% CI))		
Single-surgeon	n = 9, 39.1 (35.1–43.4)	n = 5, 20.6 (16.8–25.0)
Institutional	n = 3, 58.3 (50.0–67.6)	n = 1, 20.0 (12.2–30.9)
$N_{LC}$ based on IDEAL period (No. of data sets, Poisson mean (95% CI))		
IDEAL 1-2B	n = 5, 40.8 (35.4–46.8)	n = 6, 20.5 (17.0–24.5)
IDEAL 3 <sup>a</sup>	n = 7, 46.1 (41.2–51.5)	NA

All categorical variables are expressed as n (%) unless otherwise specified

CI, confidence interval; CUSUM, cumulative sum control chart; IDEAL, innovation, development, exploration, assessment, long term; LTG, laparoscopic total gastrectomy; NA, not applicable;  $N_{LC}$ , number of cases required to surmount the learning curve; RTG, robotic total gastrectomy

<sup>a</sup>Cut-off of 2010 and beyond was used to determine IDEAL 3 for LTG, and 2015 and beyond was used to determine IDEAL 3 for RTG

(83.3%) that used non-arbitrary analysis methods in RTG [16]. The subgroup analysis of the non-arbitrary based  $N_{LC}$  similarly showed a smaller  $N_{LC}$  in RTG in comparison to LTG (RTG: 20.6, 95% CI 16.8–25.0; LTG: 45.9, 95% CI 41.0–51.2; IRR: 0.45, 95% CI 0.32–0.63,  $p < 0.001$ ).

Seventy-five percent ( $n = 9/12$ ) of the data sets in LTG evaluated the single-surgeon LC [8, 15, 20–22, 24, 25], and 83.3% ( $n = 5/6$ ) data sets in RTG evaluated the single-surgeon LC [16]. The single-surgeon  $N_{LC}$  was smaller in comparison to the institutional  $N_{LC}$  in LTG (Table 2) (IRR: 0.67, 95% CI 0.47–0.96,  $p = 0.028$ ). However, this was comparable in RTG (Table 2) (IRR 1.03, 95% CI 0.61–1.74,  $p = 0.912$ ). We also performed an analysis based on the IDEAL period for LTG:  $N_{LC}$  in IDEAL 3 was comparable to IDEAL 1-2B period (IRR 1.13, 95% CI 0.78–1.65,  $p = 0.522$ ) (Table 2). A comparison based on the IDEAL period was not possible for RTG as there were no IDEAL 3 studies.

The  $N_{LC}$  was similar between TLTG and LATG (LATG: 2 data sets,  $N_{LC}$ : 39.0 (95% CI 30.8–48.7); TLTG: 4 data sets,  $N_{LC}$ : 36.0 (95% CI 30.4–42.4); IRR: 0.92, 95% CI 0.59–1.44,  $p = 0.723$ ). Of all the studies on RTG, there was no specification on whether reconstruction was performed intracorporeally or extracorporeally. Hence, the

comparison of the  $N_{LC}$  in RTG according to the method of reconstruction was not possible.

## Discussion

The advantages of MIG over OG has led to its increasing adoption worldwide [26]. Several retrospective studies have been conducted to evaluate the LC in LTG and RTG. However, to the best of our knowledge, this is the first systematic review to summarize the literature on the LC in LTG and RTG.

We demonstrated that approximately 44 cases were required to surmount the LC in LTG, and 21 cases were required to surmount the LC in RTG. The  $N_{LC}$  was also significantly smaller for RTG in comparison to LTG. This finding is not novel and has been demonstrated in other gastrointestinal surgeries. A systematic review by Chan et al. [27] similarly showed smaller  $N_{LC}$  in robotic pancreaticoduodenectomy in comparison to laparoscopic pancreaticoduodenectomy. Firstly, the fundamentals of surgical training begin with open surgery. Open surgery allows for better exposure of the organs and appreciation of the surgical anatomy, allowing for trainees to master

**Table 3** Studies evaluating laparoscopic total gastrectomy (n = 10 studies, with 12 data sets)

No	Author, year	Country	Institution	Study period	Type of study	n	Surgical access	Method of LC analysis	Outcome parameters studied in CUSUM/non-arbitrary analysis	Outcome parameters studied in overall LC	Single-surgeon vs institutional LC	No. of surgeons analyzed	Surgeons' experience	N <sub>LC</sub> in discussion/conclusion <sup>a</sup>
1	Nagai E, 2013	Japan	Kyushu University Hospital	Aug 2002–Dec 2010	Retrospective	94	TLTG	Arbitrary based on time period (first 37 vs next 57)	NA	OT, EBL, anastomotic leakage, anastomotic stenosis, anastomotic bleeding, pancreatic leak, duodenal stump leak, pneumonia, mortality, time to liquid, time to oral, LOS, LN, metastatic LN	Institutional	NR	NR	37
2	Yasukawa D, 2017	Japan	Tenriyoroduso-danjo Hospital	Apr 2007–Mar 2016	Retrospective	83	TLTG: 24.1% (n=20/83) LATG: 75.9% (n=63/83)	Arbitrary based on time period (14 vs 51 vs 18)	NA	OT, EBL, open conversion, morbidity, anastomotic leak, anastomotic stenosis, pancreatic leak, intra-abdominal bleeding, LOS, in-hospital mortality, LN	Institutional	12	NR	65

Table 3 (continued)

No	Author, year	Country	Institution	Study period	Type of study	<i>n</i>	Surgical access	Method of LC analysis	Outcome parameters studied in CUSUM/ non-arbitrary analysis	Single-surgeon vs institutional LC	No. of surgeons analyzed	Surgeons' experience	<i>N<sub>LC</sub></i> in discussion/conclusion <sup>a</sup>
3	Jung DH, 2014	Korea	Seoul National University College of Medicine	Jan 2003–Dec 2012	Retrospective	132 <sup>b</sup> (for pure LTG without spleen resection) 53 <sup>b</sup> (for LTG with spleen resection only)	Both TLTG and LATG (majority were TLTG, but numbers not specified)	Arbitrary based on number (3 phases—33 vs 21 vs 78)	NA	Single-surgeon	1	Introduced and standardized laparoscopic gastrectomy at our institution	54
4							Arbitrary based on number (2 phases—26 vs 27)	NA	OT, EBL, any morbidity, LOS, LN	Single-surgeon			26
5	Brenkman HJF, 2022	The Netherlands	Multicenter (5 centers)	2011–2018	Prospective	288 <sup>b</sup>	NR	Generalized additive model and two-piece model with break point (transition point from learning phase to plateau phase)	Open conversion, any morbidity, anastomotic leak, TBO, 30-d readmission, reoperation, LN, R0 resection	Institutional	Multiple	Surgeons' experience with performing open gastrectomy and laparoscopic gastrotomy	73
6	Huang ZN, 2016	China	Union Hospital, Fujian Medicine University	Apr 2012–Mar 2013	Retrospective	130	TLTG (using Huang's 3-step maneuver)	CUSUM Moving average—for this study, CUSUM results were used	CUSUM: DT, EBL Moving average: DT, EBL	Single-surgeon	1	> 100 cases of laparoscopic splenopreserving splenic hilar lymphadenectomy	40
7	Jeong O	Korea	Chonnam National University Hwasun Hospital	Apr 2004–May 2013	Retrospective	66 <sup>b</sup> (Surgeon A) 96 <sup>b</sup> (Surgeon B)	Both TLTG and LATG	CUSUM	any morbidity	Single-surgeon	1	NR	43
8							CUSUM	any morbidity	any morbidity	Single-surgeon	1	NR	44



**Table 3** (continued)

No	Author, year	Country	Institution	Study period	Type of study	<i>n</i>	Surgical access	Method of LC analysis	Outcome parameters studied in CUSUM/non-arbitrary analysis	Outcome parameters studied in overall LC	Single-surgeon vs institutional LC	No. of surgeons analyzed	Surgeons' experience	$N_{LC}$ in discussion/conclusion <sup>a</sup>
9	Kwon Y, 2014	Korea	Korea University Anam Hospital	Mar 2009–Dec 2011	Retrospective	36	LATG	Spearman's correlation coefficients, arbitrary (3 groups of 12)—for this study, arbitrary analysis was used	OT	OT, any morbidity, EI-related morbidity	Single-surgeon	1	NR	24
10	Song JH, 2015	Korea	Severance Hospital	Apr 2009–Dec 2013	Retrospective	74	LATG	Moving average and non-linear regression model	OT	OT	Single-surgeon	1	> 100 cases of OTG and 15 cases of LDG	54
11	Kunisaki C, 2016	Japan	Yokohama City University	Aug 2010–Jul 2015	Retrospective	77	TLTG (only reduced port TLTG)	Post-hoc analysis (not specified)	OT during LN dissection, OT during reconstruction, EBL during LN dissection, EBL during reconstruction	OT during LN dissection, OT during reconstruction, EBL during LN dissection, EBL during reconstruction	Single-surgeon	1	> 400 laparoscopic gastrectomy (including 173 LADG, 93 LATG, 29 LAPG)	40
12	Park SY, 2019	Korea	Asan Medical Center	Jan 2015–Aug 2017	Retrospective	73 <sup>b</sup>	TLTG (only for early gastric cancer)	Exponentially weighted moving average	OT	OT	Single-surgeon	1	NR	27

CUSUM, cumulative sum control chart; DT, dissection time; EBL, Estimated blood loss; LADG, laparoscopic-assisted distal gastrectomy; LAPG, laparoscopic-assisted proximal gastrectomy; LATG, laparoscopic-assisted total gastrectomy; LC, learning curve; LN, lymph node; LOS, length of stay;  $N_{LC}$ , number of cases required to surmount the learning curve; NA, not applicable; NR, not reported; OT, operating time; TBO, textbook outcome; TLTG, totally-laparoscopic total gastrectomy

<sup>a</sup>Refers to the  $N_{LC}$  reported in the conclusion, or if not reported, refers to the highest number of cases required to surmount the learning curve across all outcome parameters

<sup>b</sup>Patient demographics were provided only for the overall cohort, and were not specific to those patients who were included in the learning curve analysis

**Table 4** Studies evaluating robotic total gastrectomy (n = 2 studies, with 6 data sets)

No	Author, year	Country	Institution	Study period	Type of study	n	Surgical access (totally robotic vs robot assisted)	Method of LC analysis	Outcome parameters studied in CUSUM/ non-arbitrary analysis	Outcome parameters studied in overall	Single surgeon vs institutional LC	No. of surgeons analyzed	Surgeons' experience	N <sub>LC</sub> in discussion/ conclusion <sup>a</sup>
1	Zheng-Yan, 2021	Korea	Southwest Hospital of Third Military Medical University, Xijing Hospital of Fourth Military Medical University	Mar 2010–Sep 2019	Retrospective	80	NR	CUSUM—RA—CUSUM—adjusted for age, sex, BMI, ASA, TNM stage, extent of LN dissection, tumor size, histology	CUSUM: OT RA—CUSUM: any morbidity	OT, EBL, any morbidity, major morbidity, LOS, LN (variables are split based on the number obtained from RA—CUSUM, except for OT)	Single	1	321 LDG, 118 LTG, 10 RDG	25
2						46	NR				Single	1	168 LDG, 82 LTG, 26 RDG	16
3						76	NR				Single	1	127 LDG, 77 LTG, 24 RDG	15
4						42	NR				Single	1	149 LDG, 59 LTG, 7 RTG	29
5						39	NR				Single	1	112 LDG, 62 LTG, 19 RDG	18
6	Wang J, 2019	China	Fujian Medical University Union Hospital	Apr 2012–Jul 2017	Retrospective	35	NR (all had spleen-preserving splenic hilar lymphadenectomy, only advanced gastric cancer)	arbitrary (first 20 vs next 15)	NA	OT, DT, EBL, any morbidity, 30-day mortality, in-hospital mortality, LOS, LN, R0 resection	Single	Multiple	NR	20

ASA, American Society of Anesthesiologists; BMI, body mass index; CUSUM, cumulative sum control chart; DT, dissection time; EBL, estimated blood loss; LC, learning curve; LDG, laparoscopic distal gastrectomy; LN, lymph node; LOS, length of stay; LTG, laparoscopic total gastrectomy; N<sub>LC</sub>, number of cases required to surmount the learning curve; NA, not applicable; NR, not reported; OT, operating time; RA-CUSUM, risk-adjusted cumulative sum control chart; RDG, robotic distal gastrectomy; RTG, robotic total gastrectomy; TNM, tumor, nodes, metastasis

<sup>a</sup>Refers to the N<sub>LC</sub> reported in conclusion, or if not reported, refers to the highest number of cases required to surmount the learning curve across all outcome parameters

their surgical techniques [28]. Training for open surgery is also less demanding and less time-consuming in comparison to MIS [29]. Trainees are first exposed to open surgery, then laparoscopic surgery, and finally robotic surgery. The study by Zheng-Yan et al. [16] who evaluated the LC in RTG, included surgeons had performed at least 100 cases of LDG, 50 cases of LTG, and 7–26 cases of RDG. Studies that evaluated LC in LTG described prior surgical experience to be “more than 100 cases of OTG”, to “more than 400 cases of laparoscopic gastrectomy” and “experience with performing open gastrectomy and laparoscopic gastrointestinal surgery” [19, 21, 22]. Most surgeons who practice robotic surgery usually have prior experience in laparoscopic surgery; having more experience would naturally translate to a smaller  $N_{LC}$ . Secondly, RTG is guided by the same principles as LTG. Thirdly, RTG confers additional advantages over LTG: the presence of a 3-dimensional view for depth perception, the elimination of physiological challenges such as hand tremors, and free manipulation of the robotic arms with a wider degree of movement [30].

The type of LC evaluated (i.e., single-surgeon LC vs. institutional LC) will also affect the  $N_{LC}$  that is obtained. We showed that the institutional  $N_{LC}$  was higher than the single-surgeon  $N_{LC}$ . This finding is expected as studies evaluating the institutional LC compile consecutive cases that are performed as an institution. Individual surgeons may not have sufficient experience and therefore will not reflect as an inflection point (for a CUSUM analysis) or improvement in outcomes (for an arbitrary analysis) on the institutional LC. This was similarly shown in systematic reviews comparing between laparoscopic and robotic access in pancreaticoduodenectomy, distal pancreatectomy and esophagectomy [27, 31]. However, for RTG, there was no difference between the single-surgeon  $N_{LC}$  and the institutional  $N_{LC}$ . Only one study, which used an arbitrary analysis, has reported the institutional  $N_{LC}$  in RTG [13]; arbitrary analyses have been shown to yield a smaller  $N_{LC}$  in comparison to non-arbitrary analyses due to the non-specific categorization of patients into groups [27]. However, our study did not show any difference between non-arbitrary and arbitrary analyses. The lack of significance may be due to the “correct” categorization of patients into each phase of the LC. This needs to be validated in further studies.

Our study also demonstrated a similar  $N_{LC}$  between LATG and TLTG. While we had 12 data sets that reported the  $N_{LC}$  in LTG, only 6 were included in this comparison. The remaining studies either included both LATG and TLTG, or did not report on the method of reconstruction (intracorporeal vs. extracorporeal). We were unable to compare between methods of reconstruction in RTG as the data were not reported. The benefits of intracorporeal anastomosis include reduced tissue trauma, a smaller

wound size, better visualization and more rapid post-operative recovery [32–34]. However, intracorporeal anastomosis is more technically challenging in comparison to extracorporeal anastomosis; there is also added difficulty in performing EJ in comparison to gastrojejunostomy in LDG. While we showed a similar  $N_{LC}$  in LATG and TLTG in the present study, the number of studies was small. This also highlights the lack of reporting on reconstruction methods; further studies should specify whether LATG or TLTG was performed, as TLTG is more technically difficult in comparison to LATG and may influence outcomes.

The 8th edition of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual states that a minimum of 16 LNs is required for LN dissection for better staging, but  $\geq 30$  LNs is preferred for accurate staging and prognostic determination [35]. Similarly, a large international study on 25,290 patients showed improved survival with  $\geq 29$  LNs across stage IA to IIIC gastric cancer [36]. The evidence on the survival benefits of the retrieval of  $\geq 30$  LNs is however equivocal [37, 38]. Our review showed that approximately 49 cases and 21 cases were required to surmount the LC for the overall LN harvest in LTG and RTG, respectively (Supplementary Table S5). Among the five individual surgeons who performed RTG, the mean LN was 20.5–30.8 before the LC, and 30.0–44.9 after the LC [16]. For LTG, Yasukawa et al. [18] showed that the mean LN harvest was 29.4 in the first period ( $n = 14$ ), 40.8 in the second period ( $n = 51$ ), and 51.1 in the third period ( $n = 18$ ). Jung et al. [15] reported that the mean LN was 41.9 in the first phase ( $n = 33$ ), 53.1 in the second phase ( $n = 21$ ) and 61.9 in the third phase ( $n = 78$ ). For all the studies that reported on the LN harvest in LTG or RTG, the mean LN harvest, even prior to completion of the LN, was more than the minimum of 16 LNs that would allow for adequate staging, as stated in the 8th edition AJCC Cancer Staging Manual [35]. However, they fall short of the minimum of 30 LNs, which may have survival benefits [37, 38]. This adds on to the importance of future studies reporting the long-term survival outcomes and the correlation between the LN harvest before and after surmounting the LC, as well as long-term survival before and after surmounting the LC.

Our study excluded the LC on subtotal or distal gastrectomy in view of the varying technical difficulties. MITG is more technically challenging in comparison to MIDG due to the need for EJ, as well as LN dissection at the splenic hilum or along the distal splenic LNs for certain cases. While older guidelines suggest the need for routine splenic hilar lymphadenectomy (station 10) [39], the latest 6th edition Japanese Gastric Cancer Treatment Guideline (JGCTG) in 2021 recommends that station 10 lymphadenectomy should not be routinely performed, unless for advanced GC invading the greater curvature of the stomach, due to the lack of a

survival benefit [40, 41]. Splenic hilar lymphadenectomy has been considered to be the most challenging part in total gastrectomy [42–44].

However, there is considerable heterogeneity in our included data sets. The methods of anastomosis varied across studies: studies reported the use of transoral anvil with OrVil™ (Covidien, Dublin, Ireland) circular stapler, linear stapler, and/or hand-sewn purse-string suture without standardization of the EJ anastomosis technique. A recent meta-analysis by Milrone et al. [45] in 2022 on 8 studies with 1854 patients showed that linear stapler was associated with reduced overall anastomotic complications (risk difference 0.06, 95% CI 0.02–0.11,  $p=0.01$ ), with comparable anastomotic stenosis, bleeding, operating time, and post-operative complications. However, circular staplers have been described to be more technically challenging when used in minimally invasive surgery, due to the limited view, difficulty in making purse-string sutures, indwelling the anvil into the esophagus, and manipulating the circular stapler [46]. Additionally, some of the data sets evaluated only the  $N_{LC}$  in specific subgroups: four included only early GC [8, 18, 25], two included only advanced GC with splenic hilar lymphadenectomy [13, 20], one included only reduced port LTG [22], and one which included only LTG with spleen resection [15]. While reduced-port LG has better cosmesis in comparison to conventional 5-port gastrectomy with comparable post-operative morbidity, reduced-port LG requires a significantly longer operating time and is associated with higher estimated blood loss [47]. Splenic hilar lymphadenectomy is also considered the most challenging part in total gastrectomy [42–44]. Hence, the inclusion of these specific subgroups in our pooled analysis may have led to the overestimation of the  $N_{LC}$ .

Our study has some strengths. Firstly, to the best of our knowledge, this is the first study to evaluate the  $N_{LC}$  in LTG and RTG. This is especially timely with the increasing trend in MITG over open total gastrectomy due its benefits [4]. Our study also had strict inclusion criteria, where only studies on total gastrectomy were included. Distal or subtotal gastrectomy were excluded as MITG is more technically challenging in comparison to MIDG due to the need for EJ, as well as LN dissection at the splenic hilum or along the distal splenic LNs for certain cases (JGCTG 2021 guidelines) [40]. We also included the prior surgical experience of the surgeons who were analyzed in the included data sets, and the majority of the included studies were on single-surgeon LC. We also provided quantitative analyses to provide readers with insight on the approximate  $N_{LC}$  required to surmount the LC, although caution is required in its interpretation as described in our discussion above. There are, however, several limitations to be addressed. Firstly, the majority of the included data

sets were retrospective with an inherent selection bias. The majority of the included data sets (94.4%) were also conducted in East Asian cohorts and may not be applicable to Western cohorts. In Western cohorts, GC more frequently presents with a proximal and diffuse histological subtype, which has a worse prognosis [48]. D2 lymphadenectomy is also less commonly performed in Western countries due to lower annual caseloads [48]. Secondly, data sets were heterogeneous (e.g., included a mix of intracorporeal and extracorporeal anastomosis, a mix of D1+ and D2 lymphadenectomy, a mix of cases with splenectomy vs. spleen-preserving procedures) and some of the analyzed data sets included specific subgroups of LTG and/or RTG, as described above, which may lead to the overestimation of the  $N_{LC}$ . Caution is required in the direct interpretation of the estimated  $N_{LC}$ . While we included prior surgical experience, some were qualitative descriptions, which also limits the interpretation. Furthermore, only a few studies ( $n=3/18$  data sets, 16.7%) reported the clinical stage prior to gastrectomy. The outcomes analyzed in the LC were also limited to short-term outcomes without an analysis of survival outcomes and patient-reported outcome measures. Only one study reported on TBO, but this should be more widely reported in future studies as TBO serves as a better measure of proficiency [49].

## Conclusion

This review provided a detailed summary of evidence on LC in LTG and RTG. The overall  $N_{LC}$  for LTG and RTG were approximately 44 cases and 21 cases, respectively. The LC for RTG was significantly shorter in comparison to LTG, which may be due to prior surgical experience and overcoming the LC for LTG before attempting RTG. A comparison of  $N_{LC}$  in TLTG and RLTG versus LATG and RATG is limited due to the small number of studies that reported the method of reconstruction. Further studies using non-arbitrary analyses with standardized outcome parameters should be conducted. Studies should also be conducted to evaluate patient-related outcome measures and oncological outcomes.

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**Data availability** All extracted data were from articles published in international peer-reviewed journals which are publicly available. Requests may be made to the corresponding author for extracted data upon reasonable request.

## Declarations

**Conflict of interest** The authors declare no conflicts of interest in association with the present study.

**Ethical standards** This study does not require approval from an ethics committee or institutional review board as this is a systematic review of existing published literature without any patient contact or attempts made to retrieve individual patients' records.

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