Check for updates

OPEN ACCESS

EDITED BY Beatrice Aramini, University of Bologna, Italy

REVIEWED BY

Maher Hendi, Sir Run Run Shaw Hospital, China Lorenzo Cinelli, San Raffaele Hospital (IRCCS), Italy

*CORRESPONDENCE Zonglin Li lizonglin85@163.com

SPECIALTY SECTION

This article was submitted to Surgical Oncology, a section of the journal Frontiers in Oncology

RECEIVED 19 July 2022 ACCEPTED 26 September 2022 PUBLISHED 18 October 2022

CITATION

Dong B, Zhang A, Zhang Y, Ye W, Liao L and Li Z (2022) Efficacy of indocyanine green fluorescence imaging-guided lymphadenectomy in radical gastrectomy for gastric cancer: A systematic review and meta-analysis. *Front. Oncol.* 12:998159. doi: 10.3389/fonc.2022.998159

COPYRIGHT

© 2022 Dong, Zhang, Zhang, Ye, Liao and Li. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or

reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms. Efficacy of indocyanine green fluorescence imaging-guided lymphadenectomy in radical gastrectomy for gastric cancer: A systematic review and meta-analysis

Bo Dong¹, Anyuan Zhang¹, Yuqiang Zhang¹, Wei Ye¹, Lan Liao¹ and Zonglin Li^{1,2*}

¹Department of General Surgery, The People's Hospital of Rongchang District, Chongqing, China, ²Department of Gastrointestinal Surgery, The Affiliated Hospital of Southwest Medical University, Luzhou, China

Background: Indocyanine green (ICG) imaging-guided lymphadenectomy has been introduced in gastric cancer (GC) surgery and its clinical value remains controversial. The aim of this study is to evaluate the efficacy of ICG fluorescence imaging-guided lymphadenectomy in radical gastrectomy for GC.

Methods: Studies comparing lymphadenectomy in radical gastrectomy between use and non-use of ICG fluorescence imaging up to July 2022 were systematically searched from PubMed, Web of Science, Embase and Cochrane Library. A pooled analysis was performed for the available data regarding the baseline features, the number of retrieved lymph nodes (LNs), the number of metastatic LNs and surgical outcomes as well as oncological outcomes. RevMan 5.3 software was used to perform the statistical analysis. Quality evaluation and publication bias were also conducted.

Results: 17 studies with a total of 2274 patients (1186 in the ICG group and 1088 in the control group) undergoing radical gastrectomy and lymphadenectomy were included. In the pooled analysis, the baseline features were basically comparable. However, the number of retrieved LNs in the ICG group was significantly more than that in the control group (MD = 7.41, 95% CI = 5.44 to 9.37, P < 0.00001). No significant difference was found between the ICG and control groups in terms of metastatic LNs (MD = -0.05, 95% CI = -0.25 to 0.16,

P = 0.65). In addition, the use of ICG could reduce intraoperative blood loss (MD = -17.96, 95% CI = -27.89 to -8.04, P = 0.0004) without increasing operative time (P = 0.14) and overall complications (P = 0.10). In terms of oncological outcomes, the use of ICG could reduce the overall recurrence rate (OR = 0.50; 95% CI 0.28-0.89; P = 0.02) but could not increase the 2-year overall survival rate (OR = 1.25; 95% CI 0.72-2.18; P = 0.43).

Conclusions: ICG imaging-guided lymphadenectomy is valuable for complete LNs dissection in radical gastrectomy for GC. However, more high-quality randomized controlled trials are needed to confirm this benefit.

KEYWORDS

gastric cancer, lymphadenectomy, indocyanine green, fluorescence imaging, minimally invasive surgery

Introduction

Gastric cancer (GC) is one of the most common cancers worldwide with more than one million new cases and 760,000 deaths in 2020 (1). At present, radical gastrectomy combined with D2 lymphadenectomy is still the most effective treatment for GC (2, 3). The status of lymph nodes (LNs) is a stronger prognostic factor for the survival of GC patients and sufficient lymphadenectomy can improve the prognosis of GC patients (4–6). Howerer, lymphadenectomy for GC is usually performed without the aid of visual instruments and complete lymphadenectomy is sometimes difficult, especially for inexperienced gastrointestinal surgeons, which always results in LNs residue and in turn leads to tumor recurrence as well as the death of these patient. Therefore, the application of intraoperative navigation technology to assist systematic and complete lymphadenectomy is essential for radical gastrectomy.

Indocyanine green (ICG), a lymphatic tracer with minimal adverse effects, can bind intensely with serum proteins *in vivo* and emits fluorescence on exposure to near-infrared rays of wavelength 760-780 nm (7, 8). In recent years, ICG fluorescence imaging for LNs tracing has attracted surgeons' attention and ICG imaging-guided lymphadenectomy has been introduced in GC surgery (9–11). Until now, several studies have reported that ICG imaging-guided lymphadenectomy was applied to GC surgery and showed promising results in increasing the number of retrieved LNs, without increasing operative time and overall complications (12–14). However, whether ICG imaging-guided lymphadenectomy is indeed beneficial for LNs dissection remains unclear. Therefore, further research is needed to validate the efficacy of ICG imaging-guided lymphadenectomy in radical gastrectomy for GC.

The aim of this meta-analysis is to evaluate the efficacy of ICG imaging-guided lymphadenectomy in radical gastrectomy for GC based on the current published studies.

Methods

This meta-analysis was carried out in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.

Search strategy

Studies comparing lymphadenectomy in radical gastrectomy between use and non-use of ICG fluorescence imaging up to July 2022 were systematically searched from PubMed, Web of Science, Embase and Cochrane Library. The keywords used for the search were "gastric cancer", "lymphadenectomy" and "ICG". Thus, the following search string was used across the above databases: ["gastric cancer" OR "gastric carcinoma" OR "gastric tumor" OR "stomach cancer" OR "stomach carcinoma" OR "stomach tumor"] AND ["lymphadenectomy" OR "lymph node excision" OR "IVmph node dissection"] AND ["indocyanine green" OR "ICG"]. Articles from previously published reviews were also checked for potential articles. The search was conducted independently by two authors (BD and AZ). The search was last performed on July 3, 2022.

Study selection and data extraction

The included studies met the following criteria: (1) GC patients with laparoscopic or robotic surgery; (2) lymphadenectomy performed in accordance with the guidelines for the treatment of GC; (3) comparative studies

about lymphadenectomy in radical gastrectomy between use and non-use of ICG fluorescence imaging; (4) studies with reported outcome including the number of retrieved LNs in the ICG and control groups; (5) original research published in English. The exclusion criteria were as follows: (1) studies published as reviews, comments, letters, case reports, animal studies and meeting abstracts; (2) studies without the outcome about the number of retrieved LNs; (3) unavailability of effective data for meta-analysis.

Two reviewers (BD and AZ) carried out the screening and extraction process independently. First, studies were screened by titles and abstract. Then, the potential studies were checked for full text. For the eligible articles, the following information from each article was recorded: first author, publication year, country, study interval, study design, study object, sample size, extent of lymphadenectomy, ICG dosage and imaging system. Furthermore, the following clinicopathological parameters were extracted from these studies: sex, age, body mass index (BMI), American Society of Anesthesiologists (ASA) score, tumor size, pathological stage, histologic type, method of gastrectomy, neoadjuvant chemoradiotherapy, the number of retrieved LNs, the number of metastatic LNs, operation time, intraoperative blood loss, overall complications, overall recurrence rate and 2-year overall survival (OS) rate. Results were checked by a third author (ZL).

Risk of bias assessment

Qualities of the selected studies were assessed according to the Cochrane Handbook. Biases including selection, performance, detection, attrition, reporting and others were evaluated and the outcomes were summarized in the form of a bias graph.

Statistical analysis

The odds ratio (OR) and mean difference (MD) with their 95% confidence interval (CI) were used as the effect size for dichotomous and continuous variables, respectively. For studies that only reported median and range, data were converted into mean and standard deviation (SD) following the method reported by Hozo SP et al. (15). Heterogeneity among studies was assessed by χ^2 and I² statistics. fixed-effects models and random-effects models were used in cases of nonsignificant (I² \leq 50%) and significant (I² > 50%) heterogeneity, respectively. For the assessment of publication bias, a funnel plot was conducted. A *P* value < 0.05 was considered significant. All of the statistical analyses were performed by RevMan 5.3 software (Cochrane, London, UK).

Results

Characteristics of studies

A total of 612 studies were identified, and 17 studies including 15 retrospective studies and 2 randomized controlled trials (RCTs) were ultimately included in this meta-analysis (13, 14, 16-30). The details of the selection procedures are shown to be in line with the PRISMA flowchart (Figure 1). General information from those included studies is summarized in Table 1. The total number of GC patients included was 2274 (1186 in the ICG group and 1088 in the control group). These studies were from five countries (i.e., China, Italy, Korea, Spain and Japan) and were published from 2017 to 2022. The sample size ranged from 20 to 514 patients. Laparoscopic or robotic radical total or distal gastrectomy combined with D1+ or D2 lymphectomy were performed in these studies. Nevertheless, the dosage of ICG and imaging systems considered differed in these studies. According to the Cochrane Handbook, the 17 studies were at slight or moderate risk of bias. The items evaluated for each study are shown in Figure 2.

Patient- and tumor-related baseline characteristics

For the patient- and tumor-related variables, sex (male and female), age (mean \pm SD), BMI (mean \pm SD), ASA score (ASA 1/2 and ASA 3/4), tumor size (mean \pm SD), pathological stage (stage 1/2 and stage 3/4), histologic type (differentiated and other types), method of gastrectomy (total gastrectomy and distal gastrectomy) and neoadjuvant chemoradiotherapy (with and without) were analyzed. Except for age (P = 0.0004) and the method of gastrectomy (P < 0.00001), other variables were all comparable between the ICG and control groups (P > 0.05) analysed by the fixed-effects models ($I^2 \leq 50\%$) and random-effects models ($I^2 > 50\%$). The baseline parameters between the two groups were basically statistically insignificant, as shown in Figure 3.

Efficacy of lymphadenectomy

The primary outcome of this study was to assess the efficacy of lymphadenectomy by using ICG fluorescence imaging. Ultimately, 17 studies (2274 patients) (13, 14, 16–30) reporting this outcome were included in our meta-analysis. The pooled analysis revealed that the number of retrieved LNs in the ICG group was significantly more than that in the control group (MD = 7.41, 95% CI = 5.44 to 9.37, P < 0.00001) (Figure 4A), but there is no significant difference in terms of metastatic LNs



between the ICG and control groups (MD = -0.05, 95% CI = -0.25 to 0.16, P = 0.65) (Figure 4B).

Surgical outcomes

14 studies (13, 14, 17–21, 23–29) reported the operation time and the pooled analysis showed no difference between the ICG and control groups (MD = -9.38, 95% CI = -21.70 to 2.93, P =0.14) (Figure 5A). However, 11 studies (13, 16–21, 23, 26–28) reported the intraoperative blood loss and showed that the use of ICG could reduce intraoperative blood loss (MD = -17.96, 95% CI = -27.89 to -8.04, P = 0.0004) (Figure 5B). 12 studies (13, 14, 16–21, 23, 26–28) reported the overall complications and there was a trend that the use of ICG was related to less overall complications with no statistic difference (OR = 0.78, 95% CI = 0.57 to 1.05, P = 0.10) (Figure 5C).

Oncological outcomes

In terms of oncological outcomes, four studies (19, 21, 22, 28) reported the overall recurrence rate and the pooled analysis

showed that the use of ICG could reduce the overall recurrence rate (OR = 0.50; 95% CI 0.28-0.89; P = 0.02) (Figure 6A). However, in terms of postoperative overall survival, two studies (19, 28) reported the 2-year overall survival rate but there was no difference between the ICG and control groups (OR = 1.25; 95% CI 0.72-2.18; P = 0.43) (Figure 6B).

Publication bias

The funnel plot was used to assess potential publication bias in the meta-analysis of the correlation between the use of ICG fluorescence imaging and the number of retrieved LNs. As shown in Figure 7, the funnel plot was symmetrical, which showed a low risk of publication bias in this study.

Discussion

GC is one of the most common malignant tumors of digestive tract and radical surgery is the mainstay of treatment, which involves performing gastric resection with negative margins and adequate systemic LNs dissection. The status of

Reference	Country	Study interval	Study object	Study design	Sample size (ICG: Control)	Method of gastrectomy	Extent of lymphadenectomy	ICG dosage	ICG injection method	ICG injection time	ICG imaging system	Outcomes
Chen QY (13)	China	2018-2019	pT1-4aN0-3M0	S;RCT	129: 129	laparoscopic TG and DG	D2	2.5 mg	endoscopic submucosal injection	1 day before surgery	Stryker	1, 2, 3, 4, 5
Cianchi F (14)	Italy	2014-2018	pT1-3N0-3M0	S;R	37: 37	laparoscopic TG and DG	D2	2.5 mg	endoscopic submucosal injection	1 day before surgery	Firefly	1, 2, 3, 5
Huang ZN (16)	China	2010-2020	cT1-4N0-3M0	M;R;PSM	94: 94	laparoscopic TG and DG	D2	4.5 mg	subserosal injection	intraoperative	Stryker	1, 4, 5
Kwon IG (17)	Korea	2012-2014	pT1-2N0-1M0	S;R;PSM	40: 40	robotic TG and DG	D1+ or D2	3 mg	endoscopic submucosal injection	1 day before surgery	NA	1, 3, 4, 5
Lan YT (18)	China	2011-2016	pT1-4N0-3M0	S;R	14: 65	robotic TG and DG	D1+ or D2	6 mg	subserosal injection	intraoperative	NA	1, 3, 4, 5
Lee S (19)	Korea	2013-2018	pT1-4aN0-3M0	S;R	74: 94	laparoscopic or robotic TG	D2 + No. 10	1.5-3.0 mg	endoscopic submucosal injection	1 day before surgery	Firefly and Pinpoint	1, 3, 4, 5, 6, 7
Liu M (20)	China	2017-2019	pT1-4N0-3M0	S;R	61: 75	laparoscopic DG	D2	1.25 mg	endoscopic submucosal injection	20 to 30 hours before surgery	Stryker	1, 2, 3, 4, 5
Lu X (21)	China	2015-2019	pT1-4N0-3M0	S;R;PSM	28: 28	laparoscopic TG, DG and PG	D2	2.5 mg	endoscopic submucosal injection	intraoperative	Pinpoint	1, 3, 4, 5, 6
Maruri I (22)	Spain	2018-2019	cT1-4N0-3M0	S;R	17: 17	laparoscopic TG and DG	D1+ or D2	3 mg	endoscopic submucosal injection	18 to 24 hours before surgery	NA	1, 2, 6
Park SH (23)	Korea	2017-2018	pT1-4N0-3M0	S;R;PSM	20: 60	laparoscopic DG	D1+ or D2	0.5 mg	endoscopic submucosal injection	intraoperative	Pinpoint	1, 3, 4, 5
Puccetti F (24)	Italy	2015-2021	pT1-3N0-3M0	S;R	38: 64	laparoscopic TG	D2	0.25 mg	endoscopic submucosal injection	12 to 24 hours before surgery	NA	1, 2, 3
Romanzi A (25)	Italy	2018-2019	pT1-4bN0-3M0	S;R	10: 10	robotic DG	D2	3 mg	endoscopic submucosal injection	18 hours before surgery	Firefly	1, 3
Tian Y (26)	China	2019-2020	NA	S;R	27: 32	robotic DG	D2	5 mg	endoscopic submucosal injection	1 day before surgery	NA	1, 3, 4, 5
Ushimaru Y (27)	Japan	2015-2017	pT1-4N0-3M0	S;R;PSM	84: 84	laparoscopic TG and DG	D1+ or D2	0.1 mg	endoscopic submucosal injection	1 day before surgery	STORZ	1, 3, 4, 5
Wei M (28)	China	2018-2019	pT1-4aN0-3M0	S;R	107: 88	laparoscopic TG and DG	D2	2.5 mg	endoscopic submucosal injection	12 to 24 hours before surgery	Stryker	1, 2, 3, 4, 5, 6, 7
Yoon BW (29)	Korea	2010-2020	pT1-4aN0-3M0	S;R;PSM	21: 42	laparoscopic DG	D2	0.4 mg	endoscopic submucosal injection	1 day before surgery	NA	1, 2, 3
Zhong Q (30)	China	2018-2020	pT1-4aN0-3M0	M;RCT	385: 129	laparoscopic TG and DG	D2	4.5 mg	subserosal injection	intraoperative	Stryker	1, 2

ICG, indocyanine green; S single centre; M, multicentre; R, retrospective study; PSM, propensity score matching; RCT, randomized controlled trial; NA, not available, 1= number of retrieved lymph nodes, 2= number of metastatic lymph nodes, 3=operative time, 4=intraoperative blood loss, 5=overall complications, 6=overall recurrence rate, 7 = 2-year overall survival.



FIGURE 2

Risk of bias summary for the included studies.

Δ		100	Control		Odda Batia	Odda Patio
~	Study or Subgroup	Events Total	Events Tota	Weight I	I-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
	Chen QY 2020	86 129	87 129	11.8%	0.97 [0.57, 1.62]	
	Huang ZN 2020	22 37 69 94	21 37 74 94	3.5% 8.0%	1.12 [0.44, 2.82] 0.75 [0.38, 1.46]	
	Kwon IG 2019	21 40	19 40	3.7%	1.22 [0.51, 2.94]	
	Lan YT 2017	7 14	38 65	2.7%	0.71 [0.22, 2.26]	
	Liu M 2020	33 61	47 75	7.9%	0.70 [0.35, 1.40]	
	Lu X 2021 Maruri I 2022	19 28 7 17	20 28	2.6%	0.84 [0.27, 2.64]	
	Park SH 2020	15 20	45 60	2.3%	1.00 [0.31, 3.22]	
	Puccetti F 2022 Romanzi A 2021	22 38 5 10	40 64	5.1%	0.82 [0.36, 1.87]	
	Tian Y 2022	14 27	14 32	2.5%	1.38 [0.50, 3.87]	_
	Ushimaru Y 2019 Wei M 2022	47 84 57 107	46 84 48 88	8.2% 10.0%	1.05 [0.57, 1.93] 0.95 [0.54, 1.67]	
	Yoon BW 2022	15 21	29 42	2.2%	1.12 [0.35, 3.54]	<u> </u>
	Zhong Q 2021	259 385	87 129	17.3%	0.99 [0.65, 1.52]	
	Total (95% CI)	1186	1088	100.0%	0.93 [0.78, 1.11]	•
	Heterogeneity: Chi ² = §	0.67, df = 16 (P =	0.88); l ² = 0%		L	
	Test for overall effect:	Z = 0.80 (P = 0.42	?)		0.01	Favours [ICG] Favours [control]
в						
_	Study or Subgroup M	ean SD Tota	Mean SD	Total Weigh	Mean Difference	IV. Fixed. 95% Cl
	Chen QY 2020 Cianchi F 2020	57.8 10.7 129 72.2 9.8 37	60.1 9.1 72.4 8.9	129 1.8% 37 0.6%	-2.30 [-4.72, 0.12] -0.20 [-4.47, 4.07]	4
	Huang ZN 2021 6 Kwon IG 2019	0.04 10.51 94	60.47 9.92 52.1 11.3	94 1.3% 40 0.4%	-0.43 [-3.35, 2.49]	
	Lan YT 2017	66 12.4 14	67.8 15.6	65 0.2%	-1.80 [-9.32, 5.72]	
	Lee S 2022 Liu M 2020 5	5.11 13 74 5.11 10.76 61	56.3 13.5 58.4 10.71	94 0.7% 75 0.8%	-0.20 [-4.23, 3.83] -3.29 [-6.92, 0.34]	
	Lu X 2021 5 Maruri I 2022	7.96 12.66 28 63.6 9.775 17	59.17 9.17 66.4 8.7	28 0.3%	-1.21 [-7.00, 4.58]	
	Park SH 2020	60.1 11.09 20	61.67 11.47	60 0.3%	-1.57 [-7.23, 4.09]	+
	Puccetti F 2022 Romanzi A 2021	₆₉ 3.5 38 64.1 7.5 10	70 2.25 75.2 13.75	64 7.0% 10 0.1%	5 -1.00 [-2.24, 0.24] 5 -11.10 [-20.81, -1.39]]
	Tian Y 2022 5 Ushimaru Y 2019	7.67 10.48 27 66.2 1.2 ⁸⁴	58.59 12.14 66.6 1.2	32 0.3% 84 81.5%	-0.92 [-6.69, 4.85] -0.40 [-0.76, -0.04]	
	Wei M 2022 5	9.27 8.99 107	61.53 10.3	88 1.4%	-2.26 [-5.00, 0.48]	Ę
	∠nong Q 2021	00.0 10.7 385	9.1 9.1	129 3.0%	-1.60 [-3.50, 0.30]	1
	Total (95% Cl) Heterogeneity: Chi ² = 13.	1165 43. df = 15 (P = 0.5	7); l² = 0%	1046 100.0%	。 -0.59 [-0.92, -0.26] ⊢	<u> </u>
	Test for overall effect: Z =	3.52 (P = 0.0004)			-50	-25 0 25 50 Favours [ICG] Favours [control]
c						
Ŭ	Study or Subgroup	ICG fean SD Tota	Control Mean SD	Total Weig	Mean Difference ht IV. Fixed. 95% Cl	Mean Difference IV. Fixed. 95% Cl
	Chen QY 2020 Cianchi E 2020	23.2 3.2 12 23.3 3.07 3	9 22.8 3.1 7 23.2 3.04	129 1.7	% 0.40 [-0.37, 1.17] % 0.10 [-1.29, 1.49]	ļ.
	Kwon IG 2019	23.3 2.6 4	23.3 3.4	40 0.6	% 0.00 [-1.33, 1.33]	±
	Lan YT 2017 Lee S 2022	24 4.1 1 23.5 4.2 7	1 24.4 3.1 1 22.9 2.8	65 0.2 94 0.8	% -0.40 [-2.68, 1.88] % 0.60 [-0.51, 1.71]	+
	Liu M 2020 2	3.75 3.49 6	1 23.51 2.51 3 22.86 2.73	75 0.9 28 0.6	% 0.24 [-0.80, 1.28] % -0.61 [-1.94, 0.72]	1
	Maruri I 2022	25 4.125 1	7 26 3.125	17 0.2	% -1.00 [-3.46, 1.46]	1
	Park SH 2020 2 Puccetti F 2022	4.89 3.22 2 25 7 3) 24.09 2.8 3 22 9	60 0.4 64 0.1	% 0.80 [-0.78, 2.38] % 3.00 [-0.13, 6.13]	-
	Tian Y 2022 2	3.76 2.91 2	7 23.52 2.85	32 0.5 84 89 6	% 0.24 [-1.24, 1.72]	+
	Wei M 2022	24.6 3.41 10	7 24.95 2.65	88 1.4	% -0.35 [-1.20, 0.50]	Ŧ
	∠hong Q 2021	22.7 3.2 38	22.8 3.1	129 2.6	·% -0.10 [-0.72, 0.52]	
	Total (95% CI) Heterogeneity: Chi ² = 9.0	106 5, df = 13 (P = 0.7	 7); ² = 0%	942 100.0	% 0.09 [-0.01, 0.19]	
	Test for overall effect: Z	= 1.74 (P = 0.08)			-50	-25 0 25 50 Favours [ICG] Favours [control]
D						
	Study or Subgroup	ICG Events Total	Control Events Total	Weight /	Odds Ratio I-H. Fixed, 95% Cl	Odds Ratio M-H. Fixed, 95% Cl
	Cianchi F 2020	25 37	25 37	20.3%	1.00 [0.38, 2.65]	
	Lee S 2022	59 74 61 61	75 94	33.5%	1.00 [0.47, 2.13] Not estimable	
	Lu X 2021	13 28	13 28	17.4%	1.00 [0.35, 2.86]	
	Maruri I 2022 Romanzi A 2021	9 17 8 10	8 17	9.4% 3.5%	1.27 [0.33, 4.87] 1.71 [0.22, 13 41]	
	Ushimaru Y 2019	84 84	84 84	0.070	Not estimable	
	Wei M 2022	99 107	78 88	16.0%	1.59 [0.60, 4.21]	
	Total (95% CI)	418	433	100.0%	1.14 [0.75, 1.75]	+
	i otal events Heterogeneity: Chi ² = 0	358 1.87, df = 5 (P = 0	305 .97); l² = 0%		L	
	Test for overall effect:	Z = 0.62 (P = 0.54)		0.01	Favours [ICG] Favours [control]
F						
E	Study or Subgroup	ICG lean SD Tota	Control Mean SD	Total Weigh	Mean Difference	Mean Difference
	Cianchi F 2020	3.8 1.9 37	3.9 2.19	37 5.89	6 -0.10 [-1.03, 0.83]	
	Huang ZN 2021 Kwon IG 2019	4.36 1.84 94 2.54 1.77 40	4.63 2.28 2.18 1.33	94 8.49 40 7.69	6 -0.27 [-0.86, 0.32] 6 0.36 [-0.33, 1.05]	
	Lan YT 2017	3.7 1.7 14	3.4 1.6	65 5.69	6 0.30 [-0.67, 1.27]	+
	Liu M 2020	2.6 1.29 61	4 1.025 2.68 1.21	54 11.09 75 9.89	-0.00 [-0.80, -0.34] -0.08 [-0.50, 0.34]	· · · · · · · · · · · · · · · · · · ·
	Park SH 2020 Tian Y 2022	3.03 1.25 20 2.93 0.88 27	2.82 1.6 2.84 1.28	60 7.7° 32 8.7°	6 0.21 [-0.47, 0.89] 6 0.09 [-0.46, 0.64]	—
	Ushimaru Y 2019 Wei M 2022	4.26 0.23 84	3.87 0.23	84 11.8	6 0.39 [0.32, 0.46]	·
	Yoon BW 2022	2.58 1.58 21	2.56 1.56	42 6.6	6 0.02 [-0.80, 0.84]	
	Zhong Q 2021	3.9 2.4 385	4.4 2.2	129 9.69	6 -0.50 [-0.95, -0.05]]
					0.047.0.00	▲
	Total (95% CI) Heterogeneity: Tau ² = 0.2	964 2; Chi² = 74.44. df	= 11 (P < 0.000	840 100.05 1); l ² = 85%	% -0.04 [-0.36, 0.28] ⊢	<u> </u>
	Total (95% CI) Heterogeneity: Tau ² = 0.2 Test for overall effect: Z =	964 2; Chi² = 74.44, df 0.24 (P = 0.81)	= 11 (P < 0.000	840 100.05 11); I ² = 85%	% -0.04 [-0.36, 0.28] ⊢ -4	-2 0 2 4 Favours [ICG] Favours [control]
	Total (95% CI) Heterogeneity: Tau ² = 0.2 Test for overall effect: Z =	964 2; Chi² = 74.44, df 0.24 (P = 0.81)	= 11 (P < 0.000	840 100.05 11); I ² = 85%	‰ -0.04 [-0.36, 0.28] ⊢ -4	-2 0 2 4 Favours [ICG] Favours [control]

	Study or Subgroup Study or Subgroup Chen QY 2020 Cianchi F 2020 Huang ZN 2021 Lan YT 2017 Lee S 2022 Liu M 2020 Lu X 2021 Puccetti F 2022 Romanzi A 2021 Tian Y 2022 Ushimaru Y 2019 Yoon BW 2022	83 21 70 10 49 55 25 26	129 37 94 14 74 61	74 74 17 65 58 70	10tal 129 37 94 65	17.6% 4.9% 11.1%	1.34 [0.81, 2.21] 1.54 [0.62, 3.86] 1.30 [0.69, 2.46]	1	
	Cianchi F 2020 Huang ZN 2021 Lan YT 2017 Lee S 2022 Liu X 2021 Puccetti F 2022 Romanzi A 2021 Tian Y 2022 Ushimaru Y 2019 Yoon BW 2029	83 21 70 10 49 55 25 25 26	37 94 14 74 61	74 17 65 58 70	129 37 94 65	4.9% 11.1%	1.54 [0.62, 3.86] 1.30 [0.69, 2.46]		
	Utanichi F 2020 Huang ZN 2021 Lan YT 2017 Lee S 2022 Liu X 2020 Lu X 2021 Puccetti F 2022 Romanzi A 2021 Tian Y 2022 Ushimaru Y 2019 Yoon BW 2022	21 70 10 49 55 25 26	37 94 14 74 61	65 58	37 94 65	4.9% 11.1%	1.30 [0.69, 2.46]		
	Lan YT 2017 Len YT 2017 Lee S 2022 Liu M 2020 Lu X 2021 Puccetti F 2022 Romanzi A 2021 Tian Y 2022 Ushimaru Y 2019 Yoon BW 2022	10 49 55 25 26	94 14 74 61	58 70	94 65	11.1%	L.JU IU.69. Z.46		
	Lan 11 2017 Lee S 2022 Liu M 2020 Lu X 2020 Puccetti F 2022 Romanzi A 2021 Tian Y 2022 Ushimaru Y 2019 Yoon BW 2022	10 49 55 25 26	14 74 61	58 70	nn.	2 00'	0.00 [0.07, 4.00]		
	Lee S 2022 Liu M 2020 Lu X 2021 Puccetti F 2022 Romanzi A 2021 Tian Y 2022 Ushimaru Y 2019 Yoon BW 2022	49 55 25 26	74 61	(1)	00	3.9%	0.30 [0.07, 1.22]		
	Liu M 2020 Lu X 2021 Puccetti F 2022 Romanzi A 2021 Tian Y 2022 Ushimaru Y 2019 Yoon BW 2022	55 25 26	61	70	94	13.9%	0.67 [0.34, 1.31]		
	Lu X 2021 Puccetti F 2022 Romanzi A 2021 Tian Y 2022 Ushimaru Y 2019 Yoon BW 2022	25 26	00	64	75	3.8%	1.58 [0.55, 4.54]		
	Romanzi A 2022 Tian Y 2022 Ushimaru Y 2019 Yoon BW 2022	26	28	22	28	1.6%	2.27 [0.51, 10.18]		
	Romanzi A 2021 Tian Y 2022 Ushimaru Y 2019 Yoon BW 2022		38	49	64	7.7%	0.66 [0.27, 1.62]	_	
	Tian Y 2022 Ushimaru Y 2019 Yoon BW 2022	8	10	9	10	1.2%	0.44 [0.03, 5.88]		
	Ushimaru Y 2019 Yoon BW 2022	20	27	24	32	3.8%	0.95 [0.29, 3.08]		
	Yoon BW 2022	77	84	72	84	4.0%	1.83 [0.68, 4.91]		
		21	21	42	42		Not estimable		_
<text></text>	Zhong Q 2021	247	385	74	129	26.5%	1.33 [0.89, 2.00]		† - -
Table SPS (D) 102 80 100 M 118 (0.5 1.40) Hettorogenety, CH = 114,2, df = 11 (P = 0.41); f = 43. 10 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0									
	Total (95% CI)		1002		883	100.0%	1.18 [0.95, 1.46]		₹
	Total events	712		640					
	Heterogeneity: Chi ² = 1	1.42, df =	= 11 (P =	0.41); l ²	² = 4%				
	Test for overall effect: Z	z = 1.46 (F	P = 0.15)					0.01	0.1 I IO IOO
<text></text>			,						Favours [ICG] Favours [control]
G <u>The variable from the form the variable from the variable form the variable for</u>									
Image: Name of the state o									
Budy of Subgroup Fund Total Fund Total Fund F		ICG		Contro	ol		Odds Ratio		Odds Ratio
$H = \frac{1}{10000} \frac{1}{10000000000000000000000000000000000$	Study or Subgroup	Evente	Total F	Evente	Total	Weight	M-H Eived 95% Cl		M-H Eived 95% CI
Cherch (Y 2020) 75 129 90 129 33, 056 0.80 [0.81, 10] Hung ZN 2021 51 94 65 94 22 23, 06 41 [0.07, 150] Have M 2022 30 107 38 88 24.9% 0.56 [0.31, 1.02] Total events 213 252 Total events 253 Total events 254 25 Total events 254 257 Total eve	Study of Subgroup	Evenus	TOTAL	vents	Total	weight	IM-H. FIXED. 95% C		MI-H. FIXEd. 35% CI
$H_{\text{Hung}} 2 2021 \\ \text{Hung}} 3 0 \frac{37}{202} \frac{28}{7} \frac{37}{2} \frac{28}{2} \frac{37}{2} \frac{4}{2} \frac{37}{2} \frac{11}{2} \frac{18}{2} \frac{18}{2} \frac{16}{1} \frac{58}{2} \frac{16}{2} \frac{10}{2} \frac{10}{2} \frac{10}{2} \frac{10}{2} \frac{11}{2} \frac{28}{2} \frac{11}{2} \frac{28}{2} \frac{18}{2} \frac{11}{2} \frac{28}{2} \frac{18}{2} \frac{11}{2} \frac{28}{2} \frac{18}{2} \frac{10}{2} $	Chen QY 2020	75	129	90	129	33.0%	0.60 [0.36, 1.01]		
Hung 2N 2021 51 94 55 94 22 20% 0.84 [0.71, 150] 147 150 [0.32, 2.42] 148 150 [0.35, 0.32, 2.42] 148 150 [0.35, 0.32, 2.42] 148 150 [0.35, 0.32, 2.42] 148 150 [0.35, 0.32, 2.42] 148 150 [0.35, 0.32, 2.42] 148 150 [0.35, 0.32, 2.42] 148 150 [0.35, 0.32, 2.42] 148 150 [0.35, 0.35, 0.35] 150 [0.35, 0.32, 0.32] 150 [0.35, 0.35] 150 [0.35	Cianchi F 2020	30	37	26	37	4.3%	1.81 [0.61, 5.36]		
H = X = X = X = X = X = X = X = X = X =	Huang ZN 2021	51	94	55	94	22.0%	0.84 [0.47, 1.50]		
Park SH 2020 9 20 25 60 70% 0.87 [0.32, 2.42] We M 2022 3 0 107 36 88 24.9% 0.56 [0.31, 1.02] Total (9%) (c) 442 48 100.0% 0.78 [0.59, 1.02] Heterogeneity: Ch ² = 6.59, df = 6 (P = 0.36); F = 9% Heterogeneity: Ch ² = 6.59, df = 6 (P = 0.36); F = 9% Heterogeneity: Ch ² = 1.82 (P = 0.36); T = 9% Study or Subgroup Events Total Events Total Weight MH. Fixed 85% Cl Chen Ch ² 2020 58 129 86 129 24.9% 0.41 [0.25, 0.68] Chen Ch ² 2020 58 129 86 129 24.9% 0.41 [0.25, 0.68] Chen Ch ² 2020 58 129 86 129 24.9% 0.41 [0.25, 0.68] Chen Ch ² 2020 58 129 86 129 24.9% 0.41 [0.25, 0.68] Chen Ch ² 2020 179 94 62 94 6.9% 0.71 [0.24, 1.76] Koon [C2019 16 40 84 0.97 K 0.71 [0.34, 1.76] Koon [C2019 16 40 84 10 75 No testimable Lu X 2021 10 17 12 17 2.6% 0.60 [0.14, 2.47] Proceedit F 2022 10 17 17 12 17 2.6% 0.60 [0.14, 2.47] Proceedit F 2022 10 17 17 12 17 2.6% 0.60 [0.14, 2.47] Proceedit F 2022 10 17 17 12 17 2.6% 0.60 [0.14, 2.47] Proceedit F 2022 10 27 0 32 No testimable Lu X 2021 10 16 102 No testimable Total (9%, C) 11166 1022 100.0% 0.56 [0.45, 0.71] Total (9%, C) 11166 1023 100.0% 0.56 [0.45, 0.71] Total (9%, C) 11166 1023 100.0% 0.56 [0.45, 0.71] Total (9%, C) 11166 1023 100.0% 0.56 [0.45, 0.71] Total (9%, C) 1196 102 30.00% 0.56 [0.45, 0.71] Total (9%, C) 199 0 84 4 48 4 2.4% 0.41 [0.01, 2.00] We M 2022 0 211 0 17 2.0% 10.00 No testimable No testimable Not testimable No	Lu X 2021	11	28	11	28	5.8%	1.00 [0.34, 2.92]		
Tim Y 2022 30 107 36 82 24 9% 0.56 [0.31, 1.02] Total events 213 252 Hereins 213 253 25 Hereins 215 25 Hereins 255 25 Hereins 25	Park SH 2020	9	20	29	60	7.0%	0.87 [0.32, 2.42]		
We M 2022 30 107 36 88 249% 0.56 [0.31, 1.02] Total (95% (C)) 442 46 100.0% 0.78 [0.59, 1.02] total (95% (C)) 442 46 100.0% 0.78 [0.59, 1.02] total (95% (C)) 442 46 100.0% 0.78 [0.59, 1.02] total (95% (C)) 442 46 100.0% 0.78 [0.59, 1.02] total (95% (C)) 442 46 100.0% 0.78 [0.59, 1.02] total (95% (C)) 442 46 100.0% 0.78 [0.59, 1.02] total (95% (C)) 442 46 100.0% 0.78 [0.59, 1.02] total (95% (C)) 442 46 100.0% 0.78 [0.59, 1.02] total (95% (C)) 442 46 100.0% 0.78 [0.59, 1.02] total (95% (C)) 442 46 100.0% 0.78 [0.59, 1.02] total (95% (C)) 442 46 100.0% 0.71 [0.31, 1.02] total (95% (C)) 442 46 100.0% 0.71 [0.31, 1.02] total (95% (C)) 442 46 100.0% 0.71 [0.31, 1.02] total (95% (C)) 440 8 40 36% 0.71 [0.22, 2.26] total (95% (C)) 440 8 40 36% 0.71 [0.22, 2.26] total (95% (C)) 17 9 44 84 2.4% 0.60 [0.14, 2.47] Heirogeneity: Chi = 16 82.02 1 17 12 17 2.6% 0.60 [0.14, 2.47] We M 2022 10 17 12 17 2.78 0.60 [0.14, 2.47] We M 2022 10 17 12 17 2.78 0.60 [0.14, 2.47] We M 2022 10 17 116 10 0 10 Not estimable N	Tian Y 2022	7	27	5	32	3.0%	1.89 [0.52, 6.83]		
$\frac{1}{10 \text{ dial} (85\%, 0)} + \frac{42}{23} + \frac{48}{23} + 100.0\%} + \frac{0.78}{26} (0.59, 1.02) + \frac{1}{9} + \frac{1}$	Wei M 2022	30	107	36	88	24.9%	0.56 [0.31, 1.02]		
Total (95% C1) 442 468 100.0% 0.78 [0.59, 1.02] Heterogeneity: Ch ^H = 6.56, df = 6 (P = 0.36); P = 90; Test for overall effect: Z = 1.79 (P = 0.37); P = 90; Test for overall effect: Z = 1.79 (P = 0.37); P = 90; Test for overall effect: Z = 1.79 (P = 0.37); P = 90; Test for overall effect: Z = 1.79 (P = 0.37); P = 90; Test for overall effect: Z = 1.79 (P = 0.37); P = 90; Test for overall effect: Z = 1.79 (P = 0.37); P = 90; Test for overall effect: Z = 1.79 (P = 0.37); P = 90; Test for overall effect: Z = 1.79 (P = 0.37); P = 90; Test for overall effect: Z = 1.79 (P = 0.37); P = 90; Test for overall effect: Z = 1.79 (P = 0.05); P = 0.05; P = 0.05); P = 0.05; P = 0.0									
$\frac{1}{10 \text{ dot} \text{ series}}_{\text{Test for overall effect; Z = 1.79}} \frac{2.32}{10 \text{ dot} 0.30; P = 9\%}_{\text{Test for overall effect; Z = 1.79}} \frac{1}{(P = 0.36); P = 9\%}_{\text{Test for overall effect; Z = 1.79}} \frac{1}{(P = 0.36); P = 9\%}_{\text{Test for overall effect; Z = 1.79}} \frac{1}{(P = 0.36); P = 9\%}_{\text{Test for overall effect; Z = 1.79}} \frac{1}{(P = 0.36); P = 0.36}, P = 9\%}_{\text{Test for overall effect; Z = 1.79}} \frac{1}{(P = 0.36); P = 0.36}, P = 9\%}_{\text{Test for overall effect; Z = 1.79}} \frac{1}{(P = 0.36); P = 0.36}, P = 9\%}_{\text{Test for overall effect; Z = 1.79}} \frac{1}{(P = 0.36); P = 0.36}, P = 9\%}_{\text{Test for overall effect; Z = 1.79}} \frac{1}{(P = 0.36); P = 0.36}, P = 9\%}_{\text{Test for overall effect; Z = 0.7}} \frac{1}{(P = 0.36); P = 0.36}, P = 9\%}_{\text{Test for overall effect; Z = 0.27}} \frac{1}{(P = 0.36); P = 0.36}, P = 9\%}_{\text{Test for overall effect; Z = 0.27}} \frac{1}{(P = 0.36); P = 0.36}, P = 9\%}_{\text{Test for overall effect; Z = 0.27}} \frac{1}{(P = 0.36); P = 0.36}, P = 9\%}_{\text{Test for overall effect; Z = 0.27}} \frac{1}{(P = 0.36); P = 0.36}, P = 0.36; P$	Total (95% CI)		442		468	100.0%	0.78 [0.59, 1.02]		•
$\frac{1}{12} \frac{1}{12} \frac$	Total events	213		252					-
$1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \\$	Heteresensity Chi2 - C	213	e (n = 0.2	202	09/			<u> </u>	
Factor Vertail effect: Z = 1.91(P = 0.07) Favours [CG] Favours [control] Favours [CG] Favo	Test for event " offer the 7	.59, di = 6	D = 0.07	50); 1- =	9%			0.01	0.1 1 10 100
H 1	Test for overall effect: 2	. = 1.79 (P	P = 0.07						Favours [ICG] Favours [control]
H KG Control Odds Ratio Odds Ratio Chen QY 2020 58 129 74 9% 0.41 [0.25, 0.68] H.H. Fixed, 95% Cl Glanchi 12020 79 94 82 94 6.9% 0.71 [0.24, 1.76] Lun Y 2017 3 14 6 65 0.9% 2.68 [0.58, 1.23] 0 0 Lun YT 2017 3 14 6 65 0.9% 2.68 [0.58, 1.23] 0 <td< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></td<>									
IddIddControlOdds RatioOdds RatioStudy or SubgroupFventsTotalWeightM-H. Fixed. 95% CIM-H. Fixed. 95% CIClamch F 202073712375.1%0.49 [0.27, 142]Huang ZV 202173742946.9%0.77 [0.24, 1.75]Kwon IG 20196408403.6%0.77 [0.22, 2.26]Lan YT 20173146650.9%2.88 [0.58, 12.36]Lan YT 20173146650.9%2.88 [0.58, 12.36]Law Y202115289282.2%2.44 [0.82, 7.22]Maruni 12022101712172.6%0.60 [0.14, 2.47]Puccett IF 202238386464Not estimableRomanzi A 2021010010Not estimableWei M 2022021077886Van BW 20220210.747886Yoon BW 20220210.0%0.56 [0.45, 0.71]Total (95% CI)11661023100.0%0.56 [0.45, 0.71]Huang ZN 20219949494 <td< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></td<>									
$\frac{\text{Study or Subgroup}}{\text{Chen CY 2020}} \frac{\text{Events}}{129} \frac{\text{Total}}{129} \frac{\text{Fvents}}{129} \frac{\text{Total}}{129} \frac{\text{Vents}}{129} \frac{\text{Total}}{129} \frac{\text{Vents}}{129} \frac{\text{Vents}}{119} \text{$		ICG		Contr	ol		Odds Ratio		Odds Ratio
$\frac{1}{100} \frac{1}{100} \frac{1}$	Study or Subgroup	Evente	Total F	Evente	Total	Weight	M-H Eixed 95% C		M-H Eixed 95% Cl
Chen UY 2020 58 129 86 129 24 97 0.41 [0.25, 0.68] Huang ZN 2021 79 94 82 94 6.9% 0.77 [0.34, 1.75] Kwon IG 2019 6 40 8 40 6.8 40 3.6% 0.77 [0.34, 1.76] Lee S 2022 74 74 94 94 94 Not estimable Liu M 2020 0 6 61 0 75 Not estimable Lu X 2021 15 28 9 28 2.2% 2.44 [0.82, 7.22] Maruti 2022 10 17 12 17 2.6% 0.66 [0.45, 2.72] Maruti 2022 0 27 0 32 Not estimable Total (95% CI) 1166 1028 100.9% 0.56 [0.45, 0.71] Vei M 2022 0 21 0 44 2 Not estimable Total (95% CI) 1166 1028 100.9% 0.56 [0.45, 0.71] Not estimable Total (95% CI) 1166 1028 100.9% 0.56 [0.45, 0.71] Not estimable Maruti 2022 1 2 3 37 2 37 22.7% 1.00 [0.13, 7.50] Heterogeneity: Chi ² = 1.82, df = 0[P < 0.05]; P = 46% Total (95% CI) 116 100 Not P = 46% Total (95% CI) 116 1028 100.9% 0.56 [0.45, 0.71] Not estimable Maruti 2022 2 3 37 2 37 2.2.7% 1.00 [0.13, 7.50] Heterogeneity: Chi ² = 1.82, df = 0[P < 0.05]; P = 46% Total (95% CI) 116 1005 1028 100.9% 0.56 [0.45, 0.71] Heterogeneity: Chi ² = 4.81 (P < 0.00001) Not estimable Maruti 2022 2 2 3 37 2 37 2.2.7% 1.00 [0.13, 7.50] Heterogeneity: Chi ² = 4.81 (P < 0.00001) Heterogeneity: Chi ² = 4.83 (df = 3 (P = 0.02); P = 69% Total events 122 130 Hold 34.7% 2.45 [1.08, 5.88] Romanzi A 2021 1 10 1 10 15.5% 1.00 [0.51, 8.57] Heterogeneity: Tau ² = 1.48; Chi ² = 9.83, df = 3 (P = 0.02); P = 69% Total events 122 130 Hold events 122 130 Hold 34.7% 2.45 [1.08, 5.88] Romanzi A 2021 1 10 1 10 15.5% 1.00 [0.51, 8.57] Total events 122 130 Hold 22 130 Hold 34.7% 2.45 [1.08, 5.88] Romanzi A 2021 1 10 1 10 15.5% 1.00 [0.51, 8.57] Total events 122 130 Hold events 122 130 Hold events 122 130 Hold 34.7% 2.45 [1.08, 5.85] Romanzi A 2021 1 100 11	Study of Subgroup	Evenus	TOTAL	vents	Total	weight	MI-H. FIXED STA		MI-H, FIXEd, 55% CI
$\begin{aligned} & Lianch F 2020 & 7 & 33 & 12 & 33 & 5.1\% & 0.49 [0.17, 1.42] \\ & Huang 2V 2021 & 79 & 94 & 82 & 94 & 82 & 94 & 6.9\% & 0.77 [0.34, 1.75] \\ & Lan YT 2017 & 3 & 14 & 6 & 65 & 0.9\% & 2.68 [0.58, 12.36] \\ & Lan YT 2017 & 3 & 14 & 6 & 65 & 0.9\% & 2.68 [0.58, 12.36] \\ & Lie S 2022 & 74 & 74 & 94 & 94 & Not estimable \\ & Liu W 2020 & 0 & 61 & 0 & 75 & Not estimable \\ & Liu W 2020 & 15 & 28 & 9 & 28 & 2.2\% & 2.44 [0.82, 7.22] \\ & Maruri 2022 & 10 & 17 & 12 & 17 & 2.6\% & 0.60 [0.14, 2.47] \\ & Pucceti F 2022 & 38 & 38 & 64 & 64 & Not estimable \\ & Romanzi A 2021 & 0 & 10 & 0 & 10 & Not estimable \\ & Romanzi A 2021 & 0 & 10 & 0 & 10 & Not estimable \\ & Ushimaru Y 2019 & 0 & 84 & 4 & 84 & 2.4\% & 0.11 [0.01, 2.00] \\ & Wei M 2022 & 48 & 107 & 47 & 88 & 150\% & 0.71 [0.40, 1.26] \\ & Yoon BW 2022 & 0 & 2.1 & 0 & 42 & Not estimable \\ & Zhong Q 2021 & 178 & 385 & 86 & 129 & 36.5\% & 0.43 [0.28, 0.65] \\ & Total (95\% CI) & 1166 & 1028 & 10.0\% & 0.56 [0.45, 0.71] \\ & Heterogeneity Ch^{\mu} = 16.82, df = 9 (P = 0.05); P = 46\% \\ & Heterogeneity Ch^{\mu} = 16.82, df = 9 (P = 0.05); P = 46\% \\ & Huang 2V 2021 & 94 & 94 & 94 & 94 \\ & Not estimable \\ & Maruri 12022 & 3 & 17 & 0 & 17 & 72 & 77 & 10.00 (1.3, 7.6] \\ & Huang 2V 2021 & 94 & 94 & 94 & 94 \\ & Not 0.516 [0.03, 0.73] \\ & Pucceti F 2022 & 2 & 38 & 23 & 64 & 34.7\% & 2.45 [10.8, 5.88] \\ & Romanzi A 2021 & 1 & 10 & 1 & 10 & 15.5\% & 1.00 [0.05, 18.57] \\ & Total (95\% CI) & 196 & 222 & 100.0\% & 0.82 [0.18, 5.6] \\ & Total (95\% Ci) & 196 & 222 & 100.0\% & 0.82 [0.18, 5.8] \\ & Romanzi A 2021 & 1 & 10 & 1 & 10 & 15.5\% & 1.00 [0.05, 18.57] \\ & Total (95\% Ci) & 196 & 222 & 100.0\% & 0.82 [0.18, 5.8] \\ & Romanzi A 2021 & 1 & 10 & 1 & 10 & 15.5\% & 1.00 [0.05, 18.57] \\ & Total (95\% Ci) & 196 & 222 & 100.0\% & 0.82 [0.18, 5.8] \\ & Total (95\% Ci) & 196 & 222 & 100.0\% & 0.82 [0.18, 5.8] \\ & Romanzi A (201 & 1 & 10 & 15.5\% & 1.00 [0.05, 18.57] \\ & Total (95\% Ci) & 196 & 222 & 100.0\% & 0.82 [0.18, 5.8] \\$	Chen QY 2020	58	129	86	129	24.9%	0.41 [0.25, 0.68]		
Huang ZM 2021 79 94 82 94 6.9% 0.77 [0.34, 1.75] Lan YT 2017 3 14 6 65 0.9% 2.68 [0.58, 12.36] Lee S 2022 74 74 74 94 94 94 Not estimable Liu W 2020 0 661 0 75 Not estimable Lu X 2021 15 28 9 28 2.2% 2.44 [0.82, 7.22] Maruil 2022 10 17 12 17 2.6% 0.000 [0.14, 247] Puccetli F 2022 38 38 64 64 Not estimable Romanzi A 2021 0 10 0 10 Not estimable Tian Y 2022 0 27 0 32 Not estimable Ushimary 2019 0 84 4 84 2.4% 0.11 [0.01, 20] Yoon BW 2022 0 21 0 42 Not estimable Zhong Q 2021 178 385 86 129 36.5% 0.36 [0.45, 0.71] Total (95% CI) 1166 1028 100.9% 0.56 [0.45, 0.71] Total (95% CI) 1166 1028 100.9% 0.56 [0.45, 0.71] Heterogeneity: Ch ² = FazQurs [CoTc] Study or Subgroup Events Total Weight M-H. Random .95% CI Huang ZN 2021 94 94 94 94 94 Not estimable Maruil 2022 2 2 3 17 0 17 2.7% 1.00 [0.13, 7.50] Huang ZN 2021 94 94 94 94 94 Not estimable Maruil 2022 2 3 17 10 17 2.70% 0.15 [0.03, 0.73] Puccetli F 2020 2 3 3 7 2 37 22.7% 1.00 [0.13, 7.50] Huang ZN 2021 94 94 94 94 94 Not estimable Maruil 2022 2 1 10 1 10 15.5% 1.00 [0.13, 7.50] Huang ZN 2021 94 94 94 94 94 Not estimable Maruil 2022 2 1 30 6 34.37% 2.24 [0.168, 5.58] Romanzi A 2021 1 10 1 1 0 15.5% 1.00 [0.05, 18.57] Total (95% CI) 196 222 100.0% 0.82 [0.18, 5.58] Romanzi A 2021 1 10 1 10 15.5% 1.00 [0.05, 18.57] Total (95% CI) 196 222 100.0% 0.82 [0.18, 5.61] Total (95% CI) 196 222 100.0% 0.82 [0.18, 5.61] Tot	Cianchi F 2020	7	37	12	37	5.1%	0.49 [0.17, 1.42]		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Huang ZN 2021	79	94	82	94	6.9%	0.77 [0.34, 1.75]		
Lan YT 2017 3 14 6 6 60 0.9% 2.68 [0.58, 12.36] Lee S 2022 74 74 74 94 94 94 Not estimable Lu X 2020 0 6 61 0 75 Not estimable Lu X 2021 15 28 9 28 2.2% 2.44 [0.82, 7.22] Maruri 2022 30 37 17 12 17 2.6% 0.60 [0.14, 247] Puccetti F 2022 38 38 64 64 Not estimable Romaniz A 2021 0 10 0 1 10 Not estimable Ushimarv Y 2019 0 84 4 84 4 2.4% 0.11 [0.01, 2.0] Yeon BW 2022 0 27 0 32 Not estimable Zhong Q 2021 178 385 86 129 36.5% 0.43 [0.28, 0.65] Total (95% Cl) 1166 1028 100.0% 0.56 [0.45, 0.71] Total events 516 510 Heterogeneity: Chi ² = 6.82, df = 9[r = 46% Test for overall effect: Z = 4.81 (P < 0.00001) Study or Subgroup Events Total Weight M-H. Random .95% Cl Huang ZN 2021 9 4 94 94 94 Not estimable Maruri 12022 2 3 17 2 37 22.7% 1.00 [0.15, 10.3, 0.73] Puccetti F 2020 2 3 3 64 34.7% 2.45 [10.8, 5.88] Romaniz A 2021 1 10 15 5% 1.00 [0.05, 18.57] Total (95% Cl) 196 222 100.0% 0.82 [0.18, 5.8] Romaniz A 2021 1 10 15 5% 1.00 [0.05, 18.57] Total (95% Cl) 196 222 100.0% 0.82 [0.18, 5.8] Romaniz A 2021 1 10 196 222 100.0% 0.82 [0.18, 5.8] Romaniz A 2021 1 10 10 15 5% 1.00 [0.05, 18.57] Total (95% Cl) 196 222 120.00% 0.82 [0.18, 5.8] Romaniz A 2021 1 10 1 10 15 5% 1.00 [0.05, 18.57] Total (95% Cl) 196 222 100.0% 0.82 [0.18, 5.8] Romaniz A 2021 1 10 1 10 15 5% 1.00 [0.05, 18.57] Total events 122 130 Heterogeneity: Tau ^a = 1.48; Ch ^a = (P = 0.02); P = 69% Total events 122 10.0% 0.82 [0.18, 5.8] Romaniz M 2021 (P = 0.79)	Kwon IG 2019	6	40	8	40	3.6%	0.71 [0.22, 2.26]		
Luk 2020 Luk 2020 Luk 2020 Haruri 2022 Maruri 2022	Lan YT 2017	3	14	6	65	0.9%	2.68 [0.58, 12.36]		
Lu M 2020 Lu X 2021 15 28 9 28 27% 24 (0 82, 722) Maruri 2022 10 17 12 17 2.6% 0.60 [0.1, 2.47] Pucceti F 2022 38 38 64 64 Not estimable Romari X 2021 10 10 0 10 0 tot stimable Tian Y 2022 0 27 0 32 Not estimable Tian Y 2022 0 27 0 32 Not estimable Tian Y 2022 0 27 0 32 Not estimable Total (95% Cl) 1166 1028 100.0% 0.56 [0.45, 0.71] Total events 516 510 Heterogeneity: Ch ² = 5.82, df = 9 ($r = 0.05$); $l^{2} = 46\%$ Test for overall effect: Z = 4.81 ($P < 0.0001$) Study or Subgroup Events Total Weight. M-H. Random 95% Cl Huang ZN 2021 9 4 94 94 94 Not estimable Maruri 12022 2 3 17 0 17 27.0% 0.15 [0.03, 7.3] Pucceti F 2020 2 3 3 23 64 34.7% 2.45 [1.08, 5.58] Romanzi A 2021 1 10 196 222 100.0% 0.82 [0.18, 5.58] Romanzi A 2021 1 10 196 222 100.0% 0.82 [0.18, 5.58] Romanzi A 2021 1 10 196 222 100.0% 0.82 [0.18, 5.58] Romanzi A 2021 1 10 196 222 100.0% 0.82 [0.18, 5.68] Romanzi A 2021 1 10 1 10 15.5% 1.00 [0.58, 18.57] Total (95% Cl) 196 222 120 0.0% 0.82 [0.18, 5.68] Romanzi A 2021 1 10 1 10 15.5% 1.00 [0.58, 18.57] Total (95% Cl) 196 222 120 0.0% 0.82 [0.18, 5.68] Romanzi A 2021 1 10 1 10 15.5% 1.00 [0.58, 18.57] Total (95% Cl) 196 222 120 0.0% 0.82 [0.18, 5.68] Romanzi A 2021 1 10 1 10 15.5% 1.00 [0.58, 18.57] Total (95% Cl) 196 222 120 0.0% 0.82 [0.18, 5.68] Romanzi A 2021 1 10 1 10 15.5% 1.00 [0.58, 18.57] Total (95% Cl) 196 222 120 0.0% 0.82 [0.18, 5.68] Romanzi A 2021 1 10 1 10 15.5% 1.00 [0.58, 18.57] Total (95% Cl) 196 222 120 0.0% 0.82 [0.18, 5.68] Romanzi A 2021 1 10 1 10 15.5% 1.00 [0.58, 18.57] Total (95% Cl) 196 222 120 0.0% 0.82 [0.18, 5.68] Romanzi A 2021 1 1 0 1 10 15.5% 1.00 [0.58, 18.57] Total (95% Cl) 196 222 120 0.0% 0.82 [0.18, 5.68] Romanzi A 2021 1 1 0 1 10 15.5% 1.00 [0.58, 18.57] Total (95% Cl) 196 222 (0.00% 0.82 [0.18, 5.68] Romanzi A 2021 1 1 0 1 10 15.5% 1.00 [0.58, 18.57] Total (95% Cl) 196 222 (0.00% 0.82 [0.18, 5.68] Romanzi A 2021 1 1 00 1 100 [0.56, 18.57] Total (95% Cl) 196 222 (0.00% 0.82 [0.18, 3.62] Total events 122 130 Hetero	Lee S 2022	74	74	94	94		Not estimable		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Liu M 2020	0	61	0	75		Not estimable		
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Lu X 2021	15	28	9	28	2.2%	2.44 [0.82, 7.22]		<u>+</u>
Puccetii F 2022 Romanzi A 2021 1 0 10 0 0 10 Not estimable Tian Y 2022 0 27 0 32 Not estimable Ushimaru Y 2019 Wei M 2022 1 0 84 4 84 2.4% 0 11 [0.01, 2.00] Wei M 2022 0 21 0 42 Yoon BW 2022 0 21 0 42 Yoon BW 2022 0 21 178 385 86 129 36.5% 0 .43 [0.28, 0.65] T otal (95% Cl) T otal (95% Cl) T otal events T est for overall effect. Z = 4.81 (P < 0.0001) Hearogeneity: Chi ^P = 16.82, df = 9 (P = 0.05); P = 46% T est for overall effect. Z = 4.81 (P < 0.00001) T otal (P < 0.000001) T otal (P < 0.00001) T otal (P < 0.000001) T otal (P < 0.000001) T otal (P < 0.000001) T otal (P < 0.0000000000000000000000000000000000	Maruri 2022	10	17	12	17	2.6%	0.60 [0.14, 2.47]		
Romanzi A 2021 0 10 0 10 Not estimable Tian Y 2022 0 27 0 32 Not estimable Ushimative Void stimable Void stimable Void stimable Wei M 2022 0 27 0 32 Not estimable Yoon BW 2022 0 21 0 0.56 0.71 0.40 1.25 Yoon BW 2022 0 21 1166 1028 100.0% 0.56 0.43 0.28, 0.65	Puccetti F 2022	38	38	64	64		Not estimable		
Tian Y 2022. 0 27 0 32 Not estimable Ushimaru Y 2019 0 84 4 84 2.4% 0.11 [0.01, 2.00] Wei M 2022 48 107 47 68 15.9% 0.71 [0.40, 1.20] Yoon BW 2022 0 21 0 42 Not estimable Zhong Q 2021 178 355 86 129 36.5% 0.43 [0.28, 0.65] Total (95% Cl) 1166 1028 100.0% 0.56 [0.45, 0.71] Heterogeneity: Chi ² = 16.82, df = 9 (P = 0.05); P = 46% Test for overall effect: Z = 4.81 (Ve 0.00001) I CG Control Odds Ratio Study or Subgroup Events Total Events Total Weight MH: Random. 95% Cl Glianch iF 2020 2 3 17 0 177 2.7% 100 [0.13, 7.6] Huang ZN 2021 3 4 94 94 94 94 Puccetti F 2022 22 38 23 64 34.7% 2.45 [10.8, 5.88] Romanzi A 2021 1 10 196 222 100.0% 0.82 [0.18, 5.6] Total (95% Cl) 196 222 100.0% 0	Romanzi A 2021	0	10	0	10		Not estimable		
Using any 2019 0 8 4 8 4 24% 0.11001.200 Wei M 2022 48 107 47 88 150% 0.71 [0.01, 2.05] Yoon BW 2022 0 21 0 42 Not estimable Total (95% CI) 1166 1028 100.0% 0.56 [0.45, 0.71] Total events 516 510 Heterogeneity: Chi ² = 16.82, df = 9 ($P = 0.05$); $P = 46\%$ Test for overall effect: Z = 4.81 ($P < 0.00001$) Clanch F 2020 2 37 2 37 22.7% 1.00 [0.13, 7.50] Huang ZN 2021 94 94 94 94 94 94 Marvai 2022 2 3 16 4 34.7% 2.45 [10.8, 5.58] Romanzi A 2021 1 0 1 10 155% 1.00 [0.05, 18.57] Total (95% CI) 196 222 100.0% 0.82 [0.18, 5.58] Romanzi A 2021 91 96 222 100.0% 0.82 [0.18, 5.58] Romanzi A 2021 1 10 1 10 155% 1.00 [0.05, 18.57] Total (95% CI) 196 222 100.0% 0.82 [0.18, 5.58] Romanzi A 2021 1 10 1 10 155% 1.00 [0.05, 18.57] Total (95% CI) 196 222 100.0% 0.82 [0.18, 5.68] Romanzi A 2021 1 10 1 10 155% 1.00 [0.05, 18.57] Total (95% CI) 196 222 100.0% 0.82 [0.18, 5.68] Romanzi A 2021 1 10 1 10 155% 1.00 [0.05, 18.57] Total (95% CI) 196 222 100.0% 0.82 [0.18, 5.68] Romanzi A 2021 1 10 1 10 155% 1.00 [0.05, 18.57] Total (95% CI) 196 222 100.0% 0.82 [0.18, 5.68] Romanzi A 2021 1 10 1 10 155% 1.00 [0.05, 18.57] Total (95% CI) 196 222 100.0% 0.82 [0.18, 5.68] Romanzi A 2021 1 10 1 10 155% 1.00 [0.05, 18.57] Total (95% CI) 196 222 100.0% 0.82 [0.18, 5.68] Romanzi A 2021 1 10 1 10 155% 1.00 [0.05, 18.57] Total (95% CI) 196 222 100.0% 0.82 [0.18, 5.68] Romanzi A 2021 1 10 1 10 155% 1.00 [0.05, 18.57] Total events 122 130 Heterogeneity: Tau ² = 1.48; Chi ² = 9.63, df = 3 (P = 0.02; P = 69% Test for overall effect: Z = 0.27 (P = 0.79)	Tian V 2022	0	27	0	32		Not estimable		
$ \begin{array}{c} \text{Weik M 2022} & 48 & 107 & 47 & 88 \\ \text{Yoon BW 2022} & 0 & 21 & 0 & 42 \\ \text{Yoon BW 2022} & 0 & 21 & 0 & 42 \\ \text{Yoon BW 2022} & 0 & 21 & 0 & 42 \\ \text{Not estimable} \\ \text{Zhong Q 2021} & 178 & 385 & 86 & 129 & 365\% & 0.43 [0.28, 0.65] \\ \text{Total (95\% CI)} & 1166 & 1028 & 100.0\% & 0.56 [0.45, 0.71] \\ \text{Heterogeneity: Chi2 = 16.82, df = 9 (P = 0.05); P = 46\% \\ \text{Test for overall effect: Z = 4.81 (P < 0.00001)} \\ \text{Study or Subgroup} \\ \text{Events} \\ \text{Total (95\% CI)} & 100 (100, 75.0] \\ \text{Huang ZN 2021} & 94 & 94 & 94 \\ \text{Marvin 12022} & 3 & 17 & 2 & 37 & 22.7\% & 10.00 (1.3, 7.6) \\ \text{Haang ZN 2021} & 94 & 94 & 94 & 94 \\ \text{Marvin 12022} & 3 & 17 & 10 & 17 & 72.0\% & 0.15 [10.03, 0.73] \\ \text{Marvin 12022} & 23 & 37 & 22.7\% & 1.00 (1.05, 18.58] \\ \text{Romanzi A 2021} & 1 & 10 & 10 & 15.5\% & 1.00 [0.05, 18.57] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 5.68] \\ \text{Romanzi A 2021} & 148; Ch2 = 9.63, df = 3 (P = 0.02); P = 69\% \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 5.62] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 3.62] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 5.62] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 5.62] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 5.62] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 5.62] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 5.62] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 5.62] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 5.62] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 5.62] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 5.62] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 5.62] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 5.62] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 5.62] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 5.62] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 5.62] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 5.62] \\ \text{Total (95\% CI)} & 196 & 222 & 100.0\% & 0.82 [0.18, 3.62] \\ Tot$	Ushimaru Y 2010	0	21	4	94	2 10/	0 11 [0 01 2 00]	←	
$\begin{tabular}{ c c c c c c c c c c c c c c c c c c c$	Wei M 2022	40	107	4	04	2.4%	0.11[0.01, 2.00]		_ _
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Wei M 2022	48	107	4/	88	15.0%	0.71 [0.40, 1.25]		
Zhong Q 2021 178 385 86 129 36.5% 0.43 [0.28, 0.65] Total (95% Cl) 1166 1028 100.0% 0.56 [0.45, 0.71] Total events 516 510 0.01 0.1 10 100 Favours [ICG] Favours [ICG] Favours [ICG] Favours [ICG] Godds Ratio Odds Ratio Favours [ICG] Odds Ratio Clanch F 2020 2 37 2 37 2.7% 100 [0.13, 7.60] HL Random. 95% Cl HL Random. 95% Cl HL Random 404 Si cl Si	YOON BW 2022	0	21	0	42		Not estimable		_
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	∠hong Q 2021	178	385	86	129	36.5%	0.43 [0.28, 0.65]		-
Total (95% CI) 1166 1028 100.0% 0.56 [0.45, 0.71] Total events 516 510 Heterogeneity: Chi ² = 16.82, df = 9 (P = 0.05); l ² = 46% Test for overall effect: Z = 4.81 (P < 0.00001) Total (95% CI) 196 222 100.0% 0.15 [0.03, 0.73] Puccetti F 2022 2 3 37 2 37 2.7% 1.00 [0.13, 7.60] Huang ZN 2021 94 94 94 94 94 Marcui 2022 3 17 10 17 27.0% 0.15 [0.03, 0.73] Puccetti F 2022 22 38 23 64 34.7% 2.45 [1.08, 5.88] Romanzi A 2021 1 10 1 10 15.5% 1.00 [0.05, 18.57] Total (95% CI) 196 222 100.0% 0.82 [0.18, 3.62] Total (95% CI) 196 222 100.0% 0.82 [0.18, 3.62] Heterogeneity: Tau ² = 1.48; Ch ² = 9.63, df = 3 (P = 0.02); l ² = 69% Test for overall effect: Z = 0.27 (P = 0.79)									
Total events 516 510 Heterogeneity: Ch ² = 682, df = 9(P < 0.0001) Total events 616 22 = 4(P < 0.00001) Test for overall effect: Z = 4.81 (P < 0.00001) Test for overall effect: Z = 4.81 (P < 0.00001) Total events 122 130 Heterogeneity: Tau ² = 1.48; Ch ² = 9.63, df = 3 (P = 0.02); P = 69% Test for overall effect: Z = 0.27 (P = 0.79) Total events 122 130 Heterogeneity: Tau ² = 1.48; Ch ² = 9.63, df = 3 (P = 0.02); P = 69% Test for overall effect: Z = 0.27 (P = 0.79) Total events 122 130 Heterogeneity: Tau ² = 1.48; Ch ² = 9.63, df = 3 (P = 0.02); P = 69% Test for overall effect: Z = 0.27 (P = 0.79) Total events 122 130 Heterogeneity: Tau ² = 1.48; Ch ² = 9.63, df = 3 (P = 0.02); P = 69% Test for overall effect: Z = 0.27 (P = 0.79)	Total (95% CI)		1166		1028	100.0%	0.56 [0.45, 0.71]		▼
Heterogeneity: Ch ^{III} = 16.82, df = 9 ($P = 0.05$); $P = 46\%$ Test for overall effect: Z = 4.81 ($P < 0.00001$) I I I I I I I I I I I I I	Total events	516		510					
Test for overall effect: Z = 4.81 (P < 0.0001)	Heterogeneity: Chi ² = 1	6.82, df =	9 (P = 0	.05); l ² =	= 46%			0.01	
Image: constraint of the second s	Test for overall effect: Z	z = 4.81 (F	P < 0.000	001)				0.01	U.I I IU 100
ICG Control Odds Ratio Odds Ratio Study or Subgroup Events Total Veight M-H. Random 95% CI M-H. Random 95% CI Glanch F 2020 2 37 2 37 22.7% 1.00 [0.13, 7.50] Huang ZN 2021 94 94 94 Not estimable M-H. Random 95% CI Marrii 12022 3 1 10 15 [0.03, 0.73] Image: Static s		(,					Favours [ICG] Favours [control]
ICG Control Odds Ratio Study or Subgroup Events Total F000 100 101.13, 7.60 M-H. Random. 95% CI M-H. Random. 95% CI M-H. Random. 95% CI Marcui 100 101.13, 7.60 Notestimable F000 F000<									
ICG Control Odds Ratio Odds Ratio Study or Subgroup Fvents Total Events Total Vents Total (95% Cl) H-H. Random 95% Cl H-H. Random 95% Cl Cianchi F 2020 2 37 2 37 22.7% 1.00 [0.13, 7.50] Huang ZN 2021 94 94 94 Not estimable Not estimable Maruni 2022 2 38 23 64 34.7% 2.45 [1.08, 5.58] Puccetti F 2020 2 38 23 64 34.7% 2.45 [1.08, 5.58] Romaniz A 2021 1 1 1 15.5% 1.00 [0.05, 18.57] Total (95% Cl) 196 222 100.0% 0.82 [0.18, 3.62] Total events 122 130 0.02]; I* e 69% 1.00 [0.01 0.1 1 10 1000 Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P									
Study or Subgroup Events Total Events Total Weight M-H. Random. 95% Cl M-H. Random. 95% Cl Clanchi F 2020 2 37 2 37 22.7% 1.00 [0.13, 7.50] M-H. Random. 95% Cl M-H. Random. 95% Cl Huang ZV 2021 94 94 94 94 Not estimable Maruri I 2022 3 17 10 17 27.0% 0.15 [0.03, 0.73] Puccetti F 2022 22 38 23 64 34.7% 2.45 [10.85, 58] Romanzi A 2021 1 10 15.5% 1.00 [0.05, 18.57] 1.00 [0.05, 18.57] Total (95% Cl) 196 222 100.0% 0.82 [0.18, 3.62] 1.00 [0.01 1.00 [0.05, 18.57] Total (95% Cl) 196 222 100.0% 0.82 [0.18, 3.62] 1.00 [0.01 1.00 [0.01 1.00 [0.01 1.00 [0.01 1.00 [0.01 1.00 [0.01 1.00 [0.01 1.00 [0.01 1.00 [0.01 1.00 [0.01 1.00 [0.01 1.00 [0.01 1.00 [0.01 1.00 [0.01 1.00 [0.01 1.00 [0.01 <		ICG		Contro	d l		Odds Ratio		Odds Ratio
Clanchi F 2020 2 37 2 37 22.7% 1.00 [0.13, 7.50] Huang ZN 2021 94 94 94 94 Not estimable Marui 12022 3 17 10 17 27.0% 0.15 [0.03, 0.73] Puccetli F 2022 22 38 23 64 34.7% 2.45 [10.8, 5.58] Romanzi A 2021 1 1 0 1.55% 1.00 [0.5, 18.57] Total (95% Cl) 196 222 130 Heterogeneity: Tau² = 1.48; Chi² = 9.63, df = 3 (P = 0.02); P = 69% 0.82 [0.18, 3.62] Test for overall effect: Z = 0.27 (P = 0.79) Fesours [ICG] Favours [ICG] Favours [COI Favou	Study or Subaroup	Events	Total E	vents	Total N	Weight	M-H. Random. 95% (M-H. Random. 95% CI
Huang ZN 2021 94 94 94 94 94 05 Not estimable Maruri I 2022 3 17 10 17 27.0% 0.15 [0.03, 0.73] Puccetif Z022 22 38 23 64 34.7% 2.45 [1.08, 5.58] Romanzi A 2021 1 10 1 10 15.5% 1.00 [0.05, 18.57] Total (95% Cl) 196 222 100.0% 0.82 [0.18, 3.62] Total events 122 130 Heterogeneity: Tau' = 1.48; Chi' = 9.63, df = 3 (P = 0.02); P = 69% Test for overall effect: Z = 0.27 (P = 0.79)	Cianchi F 2020	2	37	2	37	22.7%	1.00 [0 13 7 50	1	_
Maruil 12022 3 17 10 17 27.0% 0.15 [0.03, 0.73] Puccetli F 2022 22 38 23 64 34.7% 2.45 [1.08, 5.58] Romanzi A 2021 1 10 15.5% 1.00 [0.05, 18.7] Total (95% Cl) 196 222 100.0% 0.82 [0.18, 3.62] Total events 122 130 13 (P = 0.02); P = 69% Heterogeneity: Tau ² = 1.48; Chi ² = 9.63, df = 3 (P = 0.02); P = 69% 0.01 0.11 10 Test for overall effect: Z = 0.27 (P = 0.79) Favours [ICG] Favours [CG] Favours [COI]	Huang 7N 2021	94	94	94	94		Not estimable		
Total (95% Cl) 122 130 130 142 15% 1.00 [0.05, 18.57] Total (95% Cl) 196 222 100.0% 0.82 [0.18, 3.62] Total (95% Cl) 196 222 130 0.82 [0.18, 3.62] Heterogeneity: Tau ² = 1.48; Ch ² = 9.63; df = 3 (f = 0.02); P = 69% 0.001 0.1 10 1000 Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest for overall effect: Z = 0.27 (P = 0.79) Fest fo	Maruri I 2021	34	17	10	17	27 0%	0.15 0.02 0.72	1	_ _
Romaniz A 2021 1 1 1 1 15.5% 1.00 [0.05, 18.7] Total (95% Cl) 196 222 100.0% 0.82 [0.18, 3.62] Total events 122 130 0.021; P = 69% 0.021; P = 69% Heterogenelty: Tau ² = 1.48; Chi ² = 9.63, df = 3 (P = 0.02); P = 69% 0.01 0.1 1 10 Test for overall effect: Z = 0.27 (P = 0.79) Favours [ICG] Favours [ICG] Favours [CO] Favours [ICG] Favours [CO]	Puccetti E 2022	22	32	22	64	34 7%	2 45 14 09 5 50	1	- - -
Total (95% Cl) 122 130 1.00 [0.05, 18.57] Total (95% Cl) 122 130 0.82 [0.18, 3.62] Total events 122 130 0.001 0.1 10 1000 Heterogeneily: Tau ² = 1.48; Chi ² = 9.63, df = 3 (P = 0.02); l ² = 69% 0.001 0.1 10 1000 Test for overall effect: Z = 0.27 (P = 0.79) Favours [ICG] Favours [ICG] Favours [control]	Pomonzi A 2024	22	30	23	10	J-4.770	2.45 [1.00, 5.58	1	_
Total (95% Cl) 196 222 100.0% 0.82 [0.18, 3.62] Total events 122 130 Heterogeneity: Tau ² = 1.48; Chi ² = 9.63, df = 3 (P = 0.02); P = 69% 0.001 0.1 1 10 1000 Test for overall effect: Z = 0.27 (P = 0.79) Favours [ICG] Favours [ICG] Favours [Control]	Romanzi A 2021	1	10	1	10	15.5%	1.00 [0.05, 18.57	1	Ţ
Total (95% v1) 190 222 100.07% 0.62 [0.16, 3.62] Total events 122 130 Heterogeneity: Tau ² = 1.48; Chi ² = 9.63, df = 3 (P = 0.02); I ² = 69% 0.001 0.1 1 10 1000 Test for overall effect: Z = 0.27 (P = 0.79) Favours [ICG] Favours [ICG] Favours [control]	Total (05% CI)		100		222	100.0%	0.0270.40.0.00		—
Total events 122 130 Heterogeneity: Tav = 148: ChiP = 6.63, df = 3 (P = 0.02); P = 69% 0.001 0.1 1 1000 Test for overall effect: Z = 0.27 (P = 0.79) Favours [ICG] Favours [ICG] Favours [ICG] Favours [ICG]	I otal (95% CI)		196		222	100.0%	0.82 [0.18, 3.62]	1	
Heterogeneity: Tau ² = 1.48; Chi ² = 9.63, df = 3 (P = 0.02); P = 69% Test for overall effect: Z = 0.27 (P = 0.79) Favours [ICG] Favours [control]	Total events	122		130				L	
Test for overall effect: Z = 0.27 (P = 0.79) Favours [ICG] Favours [ICG] Favours [Control]	Heterogeneity: Tau ² = 1	.48; Chi ² =	= 9.63, df	= 3 (P =	= 0.02);	l ² = 69%		0.001	0.1 1 10 1000
Latona [loc] Latona [louito]	Test for overall effect: Z	= 0.27 (P	9 = 0.79)					0.001	Favours [ICG] Favours [control]
									r avours [roo] - r avours [control]
		Study or Subgroup Chen QY 2020 Chen QY 2020 Lu X 2021 Lu X 2021 Park SH 2020 Wei M 2022 Woi M 2022 Total (95% CI) Total events Heterogeneity: Chi ² = 6 Test for overall effect: 2 Study or Subgroup Chen QY 2020 Chen QY 2020 Lu X 2021 Huang ZN 2021 Kwon IG 2019 Lan YT 2017 Lu X 2021 Maruri 1 2022 Puccetti F 2022 Romanzi A 2021 Total (95% CI) Total (95% CI)	IGG Study or Subgroup Events Chen QY 2020 75 Canchi F 2020 30 Huang ZN 2021 51 Lu X 2021 11 Park SH 2020 9 Tian Y 2022 30 Total versits 213 Heterogeneity: Chi ² = 6.59, df = 75 Heterogeneity: Chi ² = 6.59, df = 74 Kudy or Subgroup Events Chen QY 2020 78 Cianchi F 2020 74 Lun X 2021 10 Waruni (2021 74 Lun X 2021 10 Ruang ZN 2021 74 Lun X 2021 10 Ruang ZN 2021 10 Maruni (2022 00 Ushimaru Y 2019 0 Zoon BW 2022 0 Nong Q 2021 1	ICG Study or Subgroup Events Total I Chen QY 2020 75 129 Clanch IF 2020 30 37 Huang ZN 2021 51 94 Lu X 2021 11 28 Park SH 2020 9 20 Tian Y 2022 30 107 Total (95% CI) 442 Total (95% CI) 442 Total (95% CI) 442 Total (95% CI) 442 Clanch F 2020 58 129 Chen CY 2020 58 129 Chen CY 2020 58 129 Kwon IG 2019 6 40 Law X021 10 17 Huang ZN 2021 74 74 Lu M 2020 0 61 Lu X 2021 10 17 Rarrui 12022 10 17 Rarui 12022 0 27 Yoon BW 2022 0 27 Total 95% CI) 1166	ICG Contr Study or Subgroup Events Total Events Chen OY 2020 75 129 90 Canchi F 2020 30 37 26 Huang ZN 2021 51 94 55 Lux X201 11 28 11 Park SH 2020 9 20 29 Tan Y 2022 30 107 36 Total (95% CI) 442 252 Heterogeneity: Chi" = 6.59, df = 6 (P = 0.36); F = Test for overall effect: Z = 1.79 (P = 0.07) Iterogeneity: Chi" = 6.59, df = 6 (P = 0.36); F = Test for overall effect: Z = 1.79 (P = 0.07) Kwon IG 2010 58 129 86 Cianch F 2020 58 129 86 Cianch F 2020 74 74 94 LuM 2020 0 61 0 Lee S 2022 74 74 94 Lu M 2020 0 61 0 Ua M2021 10 17 12 Puccetti F 2022 38	ICG Control Study or Subgroup Events Total Events Total Chen QY 2020 75 129 90 129 Glanch F 2020 30 37 26 37 Huang ZN 2021 51 94 55 94 LX 2021 11 28 11 28 Park SH 2020 9 20 29 60 Tan Y 2022 30 107 36 88 Total (95% CI) 442 468 704 90.7 Test for overall effect: Z = 1.79 (P = 0.07) Test for overall effect: Z = 1.79 (P = 0.07) Test for overall effect: Z = 1.79 (P = 0.07) ICG Control Study or Subgroup Events Total Events Total Chen QY 2020 58 129 86 129 Chanch F 2020 7 37 12 37 Huang ZN 2021 79 94 82 94 Kwon IG 2019 6 40 84 40 In Vacotti F 20	ICG Control Study or Subgroup Events Total Events Total Weight Chen QY 2020 75 129 90 129 33.0% Glanch F 2020 30 37 26 37 4.39 Huang ZN 2021 51 94 55 94 22.0% LuX 2021 11 28 11 28 51.9% Park SH 2020 9 20 29 60 7.0% Tian Y 2022 30 107 36 88 24.9% Total (95% CI) 442 468 100.0% Total (95% CI) 442 468 100.0% Total (95% CI) 442 468 100.0% Total (95% CI) 144 66 6.9% Kwon IG 2019 6 40 8 40 3.6% Lee S 2022 74 74 94 94 114 65 10% Lu M 2020 0 61 0 10 10 <td>ICG Control Odds Ratio Study or Subgroup Events Total Events Total Weight M-H. Fixed. 95% C Chen OY 2020 75 129 90 129 33.0% 0.60 [0.36, 1.01] Granch F 2020 30 74 3.4% 1.81 [0.61, 5.36] Huang ZN 2021 51 94 55 94 22.0% 0.84 [0.47, 1.50] Lx X 2021 11 28 1.88 [0.62, 6.83] Nei N. 2022 30 107 36 88 24.9% 0.56 [0.31, 1.02] Total events 213 252 Heterogeneity: Cht" = 6.59, df = 6 (P = 0.36); l" = 9% Test for overall effect: Z = 1.79 (P = 0.07) Test for overall effect: Z = 1.79 (P = 0.07) Total events 213 51 4.49 (0.17, 1.42) Huang ZN 2021 79 94 82 94 6.9% 0.77 [0.34, 1.75] Huang ZN 2021 79 94 82 94 6.9% 0.77 [0.34, 1.76] Huang ZN 2021 74 74 94 94 Not estimable</td> <td>$\begin{array}{c c c c c c c c c c c c c c c c c c c$</td>	ICG Control Odds Ratio Study or Subgroup Events Total Events Total Weight M-H. Fixed. 95% C Chen OY 2020 75 129 90 129 33.0% 0.60 [0.36, 1.01] Granch F 2020 30 74 3.4% 1.81 [0.61, 5.36] Huang ZN 2021 51 94 55 94 22.0% 0.84 [0.47, 1.50] Lx X 2021 11 28 1.88 [0.62, 6.83] Nei N. 2022 30 107 36 88 24.9% 0.56 [0.31, 1.02] Total events 213 252 Heterogeneity: Cht" = 6.59, df = 6 (P = 0.36); l" = 9% Test for overall effect: Z = 1.79 (P = 0.07) Test for overall effect: Z = 1.79 (P = 0.07) Total events 213 51 4.49 (0.17, 1.42) Huang ZN 2021 79 94 82 94 6.9% 0.77 [0.34, 1.75] Huang ZN 2021 79 94 82 94 6.9% 0.77 [0.34, 1.76] Huang ZN 2021 74 74 94 94 Not estimable	$ \begin{array}{c c c c c c c c c c c c c c c c c c c $

FIGURE 3 Forest plots

score, (E) tu

LNs is a stronger prognostic factor for the survival of GC patients and radical lymphadenectomy can significantly improve the long-term survival (31, 32). In addition, whether or not the resected LNs have metastasis, complete perigastric lymphadenectomy is important for the accurate staging of tumors and the decision of subsequent treatment (33-35). So the retrieval of more LNs in radical gastrectomy has become the special requirement for gastrointestinal surgeons.

Currently, minimally invasive surgery, including laparoscopic and robotic methods, has been widely used in the

treatment of GC, especially for early GC (36, 37). However, the oncological efficacy of minimally invasive techniques for the treatment of advanced GC is still controversial because of the concern about not being able to perform an accurate D2 lymphadenectomy and the oncological safety (38, 39). At present, lymphadenectomy in radical gastrectomy is often performed depending on the surgeon's experience and without the aid of visual instruments. However, due to the complex lymphatic drainage and abundant LNs around the stomach, it is often difficult for surgeons, especially for those younger and

		ICG		0	Control			Mean Difference	Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% CI	IV. Random, 95% CI	-
Chen QY 2020	50.5	15.9	129	42	10.3	129	7.0%	8.50 [5.23, 11.77]	-	
Cianchi F 2020	50.8	17.1	37	40.1	23	37	3.0%	10.70 [1.47, 19.93]		
Huang ZN 2021	40.8	13.7	94	31.8	13.5	94	6.4%	9.00 [5.11, 12.89]		
Kwon IG 2019	48.9	14.6	40	35.2	11.2	40	5.0%	13.70 [8.00, 19.40]		
Lan YT 2017	35.8	11.4	14	30	11.8	65	4.4%	5.80 [-0.82, 12.42]	<u>+</u>	
Lee S 2022	69	9.25	74	56	6	94	7.6%	13.00 [10.57, 15.43]	-	
Liu M 2020	33.72	9.06	61	29.36	8.76	75	7.2%	4.36 [1.34, 7.38]	-	
Lu X 2021	27.5	10.6	28	21.79	6.73	28	5.8%	5.71 [1.06, 10.36]		
Maruri I 2022	42	22.5	17	28	13	17	2.0%	14.00 [1.65, 26,35]		
Park SH 2020	30,15	9.27	20	30.15	9.27	60	5.8%	0.00 [-4.69, 4.69]	-+-	
Puccetti E 2022	43.5	6	38	32	4.25	64	7.8%	11.50 [9.33, 13.67]	-	
Romanzi A 2021	40	11 25	10	24	6 25	10	3.6%	16 00 [8 02 23 98]		
Tian Y 2022	39 19	8 97	27	35 28	9	32	5.9%	3 91 [-0 69 8 51]	+	
Lishimaru V 2019	47.5	1 7	84	42.6	17	84	8.6%	4 90 [4 39 5 41]		
Wei M 2022	49.55	12 72	107	42.0	10 208	88	7.0%	5 11 [1 80 8 33]		
Veen M 2022	49.00	0 42	21	21 22	11.200	42	7.0% E E9/	0.10[5.20,4.01]		
70011 BW 2022	40.0	44.0	205	31.33	10.0	42	7 70/	-0.19[-0.29, 4.91]	-	
Heterogeneity: Tau ² = Test for overall effect:	11.70; C Z = 7.38	hi² = 10 (P < 0.0	9.42, d 00001)	f = 16 (l	⊃ < 0.00	000); I ²	= 85%	1.41 [0.44, 0.01]	-50 -25 0 25 50 Favours [ICG] Favours [control]	
В		ICG			Control			Mean Difference	Mean Difference	
Study or Subaroup	Mean	<u>SD</u>	Tota	I Mear	SD SD	lotai	Weight	IV. Fixed, 95% CI	IV. Fixed, 95% CI	_
Study or Subgroup Chen QY 2020	Mean 5.6	<u>SD</u> 11,2	Tota 129	<u> Mear</u>	<u>SD</u> 8,9	10tal 129	Weight 0.7%	IV. Fixed, 95% CI -0.10 [-2.57, 2.37]	IV. Fixed, 95% Cl	-
Study or Subgroup Chen QY 2020 Cianchi F 2020	<u>Mean</u> 5.6 4	<u>SD</u> 11.2 5.4	Tota 129 37	<u> Mear</u>) 5.7	SD 8.9	10tal 129 37	0.7%	IV. Fixed. 95% CI -0.10 [-2.57, 2.37] -0.40 [-3.20, 2.40]	IV. Fixed, 95% Cl	-
<u>Study or Subgroup</u> Chen QY 2020 Cianchi F 2020 Liu M 2020	Mean 5.6 4	5.4 3.21	Tota 129 37 61	Mear 5.7 4.4	SD 8.9 6.8	10tal 129 37 75	Weight 0.7% 0.5% 3.6%	IV. Fixed. 95% Cl -0.10 [-2.57, 2.37] -0.40 [-3.20, 2.40] 0.00 [-1.08, 1.08]	IV. Fixed. 95% Cl	-
<u>Study or Subgroup</u> Chen QY 2020 Cianchi F 2020 Liu M 2020 Maruri I 2022	Mean 5.6 4 1.56	5.4 3.21	Tota 129 37 61	<u>Mear</u> 5.7 4.4 1.56	SD 8.9 6.8 3.21 9 4 75	10tal 129 37 75 17	Weight 0.7% 0.5% 3.6% 0.5%	IV. Fixed, 95% Cl -0.10 [-2.57, 2.37] -0.40 [-3.20, 2.40] 0.00 [-1.08, 1.08] -2.00 [-4.80, 0.80]	IV. Fixed. 95% Cl	-
Study or Subgroup Chen QY 2020 Cianchi F 2020 Liu M 2020 Maruri I 2022 Purcetti F 2022	Mean 5.6 4 1.56 0	SD 11.2 5.4 3.21 3.5 12	Tota 129 37 61 17	Mear 5.7 4.4 1.56	SD 8.9 6.8 3.21 2 4.75 8 10	129 37 75 17 64	Weight 0.7% 0.5% 3.6% 0.5% 0.2%	IV. Fixed. 95% Cl -0.10 [-2.57, 2.37] -0.40 [-3.20, 2.40] 0.00 [-1.08, 1.08] -2.00 [-4.80, 0.80] 4.00 [-0.80, 8, 80]	IV. Fixed, 95% Cl	-
Study or Subgroup Chen QY 2020 Cianchi F 2020 Liu M 2020 Maruri I 2022 Puccetti F 2022 Wei M 2022	Mean 5.6 4 1.56 0 12	SD 11.2 5.4 3.21 3.5 13	Tota 129 37 61 17 38	Mear 5.7 4.4 1.56	SD 7 8.9 4 6.8 5 3.21 2 4.75 3 10 2 6.45	129 37 75 17 64	Weight 0.7% 0.5% 3.6% 0.5% 0.2%	IV, Fixed, 95% Cl -0.10 [-2.57, 2.37] -0.40 [-3.20, 2.40] 0.00 [-1.08, 1.08] -2.00 [-4.80, 0.80] 4.00 [-0.80, 0.80] 2.12 [0.64, 5.62]	IV. Fixed. 95% Cl	-
Study or Subgroup Chen QY 2020 Cianchi F 2020 Liu M 2020 Maruri I 2022 Puccetti F 2022 Wei M 2022	Mean 5.6 4 1.56 0 12 6.45	<u>SD</u> 11.2 5.4 3.21 3.5 13 10.96	Tota 129 37 61 17 38 107	<u> Mear</u> 9 5.7 4.4 1.56 3 8 8 8 3.33	SD 7 8.9 4 6.8 5 3.21 2 4.75 3 10 3 6.45	129 37 75 17 64 88	Weight 0.7% 0.5% 3.6% 0.5% 0.2% 0.7%	IV. Fixed. 95% Cl -0.10 [-2.57, 2.37] -0.40 [-3.20, 2.40] 0.00 [-1.08, 1.08] -2.00 [-4.80, 0.80] 4.00 [-0.80, 8.80] 3.12 [0.64, 5.60]	IV. Fixed. 95% Cl	-
Study or Subaroup Chen QY 2020 Cianchi F 2020 Liu M 2020 Maruri I 2022 Puccetti F 2022 Wei M 2022 Yoon BW 2022	Mean 5.6 4 1.56 0 12 6.45 0.14	SD 11.2 5.4 3.21 3.5 13 10.96 0.36	Tota 129 37 61 17 38 107 21	Mear 5.7 4.4 1.56 3.33 0.19	SD 8.9 6.8 3.21 4.75 3.0 3.6.45 9.0.49	129 37 75 17 64 88 42	Weight 0.7% 0.5% 3.6% 0.5% 0.2% 0.7% 92.4%	IV. Fixed. 95% Cl -0.10 [-2.57, 2.37] -0.40 [-3.20, 2.40] 0.00 [-1.08, 1.08] -2.00 [-4.80, 0.80] 3.12 [0.64, 5.60] -0.05 [-0.26, 0.16]	IV. Fixed. 95% Cl	-
Study or Subgroup Chen QY 2020 Cianchi F 2020 Liu M 2020 Maruri I 2022 Puccetti F 2022 Wei M 2022 Yoon BW 2022 Zhong Q 2021	Mean 5.6 4 1.56 0 12 6.45 0.14 4.5	SD 11.2 5.4 3.21 3.5 13 10.96 0.36 8.6	Tota 129 37 61 17 38 107 21 385	Mean 9 5.7 4.4 1.56 1 1.56 3 8 3 8 3 8 3 8 3 3.33 0.19 5.7	SD 7 8.9 4 6.8 5 3.21 2 4.75 3 10 3 6.45 9 0.49 7 8.9	129 37 75 17 64 88 42 129	Weight 0.7% 0.5% 3.6% 0.5% 0.2% 0.7% 92.4% 1.4%	IV. Fixed. 95% CI -0.10 [-2.57, 2.37] -0.40 [-3.20, 2.40] 0.00 [-1.08, 1.08] -2.00 [-4.80, 0.80] 4.00 [-0.80, 8.80] 3.12 [0.64, 5.60] -0.05 [-0.26, 0.16] -1.20 [-2.96, 0.56]	IV. Fixed. 95% Cl	-

inexperienced surgeons, to perform an accurate and effective D2 lymphadenectomy without increasing surgical complications.

In recent years, ICG fluorescence imaging for LNs tracing has attracted surgeons' attention and ICG imaging-guided lymphadenectomy has been introduced in GC surgery. Chen QY et al. (13) performed a RCT and indicated that ICG can noticeably improve the number of retrieved LNs without increased complications in GC patients undergoing D2 lymphadenectomy and they recommend ICG fluorescence imaging should be performed for routine lymphatic mapping during laparoscopic gastrectomy, especially total gastrectomy. Kwon et al. (17) also reported that ICG-guided lymphadenectomy is effective in retrieving more LNs than conventional surgery and had a similar incidence of postoperative complications to conventional surgery. Lee S et al. (19) point out ICG fluorescence imaging-guided lymphadenectomy is an effective tool for complete LNs dissection at the splenic hilum and it may help select patients who do not need splenic hilar LNs dissection during a total gastrectomy. However, Lan et al. (18) reported that the number of retrieved LNs in the ICG group was not improved compared with the non-ICG group. According to the pooled analysis in our study, the number of retrieved LNs in the ICG group was significantly more than that in the control group (P < 0.00001) and the use of ICG could reduce intraoperative blood loss (P =

0.0004) without increasing operative time (P = 0.14) and overall complications (P = 0.10). Theoretically, total gastrectomy could obtain more LNs than distal gastrectomy. In our combined analysis, the proportion of total gastrectomy in the ICG group is lower than that in the control group (44.3% vs. 49.6%), but more LNs were obtained, which further indicated that ICG fluorescence imaging-guided lymphadenectomy could increased the number of retrieved LNs. Also, Yoon BW et al. (29) reported that the use of ICG could secure the oncologically safe of proximal resection margin in totally laparoscopic distal gastrectomy, with the advantage of reducing the operation time and has the benefit of locating the tumor. These results suggest that the ICG fluorescence imaging-guided lymphadenectomy is valuable in terms of LNs dissection and short-term outcomes. Nevertheless, the present meta-analysis demonstrated that there was no significant difference in metastatic LNs between the ICG and control groups. The reasons for this outcome may be explained as follows: (1) The metastatic LNs can be removed completely by standard D2 lymphectomy without the use of ICG imaging-guided lymphadenectomy, and (2) Some researchers removed all the fluorescent LNs, even these LNs were outside the extent of D2 lymphectomy (13).

Reducing postoperative tumor recurrence and prolonging patients' survival time are the ultimate goals of standardized and systematic lymphectomy (40–42). Lees et al. (19) reported that

	Study or Subgroup	ICG Control <u>Mean SD Total Mean SD Total</u>	Mean Difference Weight IV, Random, 95% C	Mean Difference I IV. Random, 95% Cl
	Chen QY 2020	196.1 47.8 129 190.4 47.6 129	8.4% 5.70 [-5.94, 17.34]	l +=-
	Cianchi F 2020	293.1 61 37 321.2 77.8 37	5.7% -28.10 [-59.96, 3.76]	
	Kwon IG 2019	191 39.5 40 209 55.3 40	7.2% -18.00 [-39.06, 3.06]	
	Lan YI 2017	327 79.7 14 349.8 120.9 65	3.6% -22.80 [-73.86, 28.26] 7.3% 19.20 [-1.14, 39.54]	
	Liu M 2020	207.21 33.63 61 239.25 44.19 75	8.3% -32.04 [-45.13, -18.95]	
	Lu X 2021	260.18 46.7 28 277.86 69.15 28	5.8% -17.68 [-48.59, 13.23]	
	Park SH 2020	228.85 33.17 20 213.87 38.48 60	7.7% 14.98 [-2.52, 32.48]	
	Puccetti F 2022	212 44 38 212 48 64	7.6% 0.00 [-18.28, 18.28]	
	Tian V 2022	311 42.5 10 294 41.25 10 230 52 20 71 27 238 78 34 44 32	5.0% 17.00 [-19.71, 53.71] 8.1%8.26 [-22.52.6.00]	
	Ushimaru Y 2019	206.1 5 84 237 5 84	9.1% -30.90 [-32.41, -29.39]	•
	Wei M 2022	198.22 13.14 107 198.22 13.14 88	9.0% 0.00 [-3.71, 3.71]	i t
	Yoon BW 2022	239.3 42.3 21 273 36.6 42	7.2% -33.70 [-54.91, -12.49]	
	Total (95% CI)	690 848	100.0% -9.38 [-21.70, 2.93]	•
	Heterogeneity: Tau ² = 4	32.97; Chi ² = 317.99, df = 13 (P < 0.00001); l ²	² = 96%	
	Test for overall effect: 2	.= 1.49 (P = 0.14)		Favours [ICG] Favours [control]
B	i i		Maan Difference	Maan Difference
	Study or Subgroup	Mean SD Total Mean SD Total	Mean Difference	Mean Difference
	Chen QY 2020	51.5 133.6 129 54.3 125 129	5.8% -2.80 [-34.37, 28.77]	•
	Huang ZN 2021	45.6 19.1 94 89.6 89.3 94	9.3% -44.00 [-62.46, -25.54]	
	Kwon IG 2019	46.8 35.3 40 47.9 42.1 40	9.8% -1.10 [-18.13, 15.93]	
	Lan YT 2017	75.7 96.7 14 78.3 79.8 65	2.7% -2.60 [-56.84, 51.64]	
	Lee S 2022	64.5 18.75 74 100 37.5 94	12.5% -35.50 [-44.20, -26.80]	· -
	Lu X 2021	144.64 83.15 28 167.5 141.23 28	2.2% -22.86 [-83.56, 37.84]	· · · · ·
	Park SH 2020	82.65 57.88 20 124.02 82.15 60	5.5% -41.37 [-74.17, -8.57]	· · · · · · · · · · · · · · · · · · ·
	Tian Y 2022	40.19 18.21 27 44.69 13.73 32	12.6% -4.50 [-12.86, 3.86]	
	Ushimaru Y 2019	10.1 6.6 84 36.9 6.6 84	13.7% -26.80 [-28.80, -24.80]	•
	Well M 2022	21.51 12.65 107 52.02 17.99 66	-4.31 [-0.99, -0.03]	
	Total (95% CI)	678 789	100.0% -17.96 [-27.89, -8.04]	\bullet
	Test for overall effect: Z	= 3.55 (P = 0.0004)	= 9270	-100 -50 0 50 100 Favours [ICG] Favours [control]
C	;	ICG Control	Odds Ratio	Odds Ratio
	Study or Subgroup	Events Total Events Total Wei	ght M-H. Fixed, 95% Cl	M-H. Fixed, 95% Cl
	Chen QY 2020	20 129 21 129 18.	.3% 0.94 [0.48, 1.84]	
	Clanchi F 2020	5 37 5 37 4.	.4% 1.00 [0.26, 3.79]	
	Huang ZN 2021	10 94 12 94 11.	.0% 0.81 [0.33, 1.99]	
	Kwon IG 2019	5 40 4 40 3.	.0% 1.29 [0.32, 5.19]	
		1 14 8 65 2. 50 74 75 04 00	0% 0.55 [0.06, 4.77]	
	Lee 5 2022	6 61 6 75 E	0% 1.25 [0.20, 1.00]	
	Liu X 2020	12 28 15 29 9	8% 0.65 [0.30, 4.11]	_
	Lu A 2021	1 20 10 20 0.	8% 0.17 [0.02, 1.07]	
	Park SH 2020	1 20 14 00 0.	.6% 0.77 [0.12 5.00]	
	Park SH 2020 Tian Y 2022	2 27 3 32 2		
	Park SH 2020 Tian Y 2022 Ushimaru Y 2019	2 27 3 32 2. 2 84 3 84 3	0% 0.66 [0.11, 4.05]	
	Park SH 2020 Tian Y 2022 Ushimaru Y 2019 Wei M 2022	2 27 3 32 2. 2 84 3 84 3. 15 107 12 88 11.	.0% 0.66 [0.11, 4.05] .6% 1.03 [0.46, 2.34]	
	Park SH 2020 Tian Y 2022 Ushimaru Y 2019 Wei M 2022	2 27 3 32 2 2 84 3 84 3 15 107 12 88 11.	.0% 0.66 [0.11, 4.05] .6% 1.03 [0.46, 2.34]	
	Park SH 2020 Tian Y 2022 Ushimaru Y 2019 Wei M 2022 Total (95% CI)	2 27 3 32 2 2 84 3 84 3 15 107 12 88 11. 715 826 100.	.0% 0.66 [0.11, 4.05] .6% 1.03 [0.46, 2.34] .0% 0.78 [0.57, 1.05]	•
	Park SH 2020 Tian Y 2022 Ushimaru Y 2019 Wei M 2022 Total (95% CI) Total events Heterogeneity: Chi2.	2 27 3 32 2 2 84 3 84 3 15 107 12 88 11. 715 826 100. 129 178 5 45 df = 11 (P = 0.91); P = 0.94	.0% 0.66 [0.11, 4.05] .6% 1.03 [0.46, 2.34] .0% 0.78 [0.57, 1.05]	• •
	Park SH 2020 Tian Y 2022 Ushimaru Y 2019 Wei M 2022 Total (95% Cl) Total events Heterogeneity: Chi ² Test for overall affect	$\begin{array}{cccccccccccccccccccccccccccccccccccc$.0% 0.66 [0.11, 4.05] .6% 1.03 [0.46, 2.34] .0% 0.78 [0.57, 1.05] .0% 0.78 [0.57, 1.05]	
	Park SH 2020 Tian Y 2022 Ushimaru Y 2019 Wei M 2022 Total (95% CI) Total events Heterogeneity: Chi ² Test for overall effec	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	0.% 0.66 [0.11, 4.05] 6.% 1.03 [0.46, 2.34] .0% 0.78 [0.57, 1.05] ⊢.	01 0.1 1 10 100 Favours [ICG] Favours [control]
	Park SH 2020 Tian Y 2022 Ushimaru Y 2019 Wei M 2022 Total (95% CI) Total events Heterogeneity: Chi ² Test for overall effec	2 27 3 32 2 2 84 3 84 3 15 107 12 88 11. 715 826 100. 129 178 = 5.45, df = 11 (P = 0.91); P = 0% t: Z = 1.66 (P = 0.10)	0.% 0.66 [0.11, 4.05] 6% 1.03 [0.46, 2.34] .0% 0.78 [0.57, 1.05] ⊢ 0.	01 0.1 1 10 100 Favours [ICG] Favours [control]

ICG fluorescence imaging-guided lymphadenectomy could reduce the tumor recurrence rate after surgery, with the recurrence rate 8.1% and 17.0% in the ICG and control groups, respectively. And another two studies also got the similar results (21, 22). However, Wei M et al. (28) pointed out that the tumor recurrence rates were similar between the two groups after surgery, with the recurrence rate 13.1% and 15.9% in the ICG and control groups, respectively. According to the pooled analysis, ICG fluorescence imaging-guided lymphadenectomy could reduce the overall recurrence rate (P= 0.02). However, the 2-year OS rates were comparable between the ICG and control groups (P = 0.43). Nevertheless, this result does not indicate that ICG fluorescence imaging-guided lymphadenectomy cannot improve the prognosis of GC patients, because there were only two studies reported survival results, and the follow-up period was shorter, without 5-year survival rate. So more studies with longer follow-up are necessary and expected.

Our study has some limitations. Firstly, there were only two RCTs in the included studies, which may increase the risk of selective bias. Therefore, more high-quality RCTs are expected to provide more credible evidence on this issue. Secondly, due to the limitations of data acquisition and language understanding, only English studies were included in this meta-analysis, which may also increase the risk of selective bias. Thirdly, the uses of ICG, including the dosage, injection method, injection time and



Forest plots showing the assessment of oncological outcomes including (A) overall recurrence rate, (B) 2-year OS rate. *ICG*, indocyanine green; *OS*, overall survival.



ICG imaging system, were all different in these studies, which probably led to heterogeneity in the outcomes.

Conclusions

Despite the limitations of the included studies, this metaanalysis indicates that ICG fluorescence imaging-guided lymphadenectomy could increase the number of retrieved LNs, reduce intraoperative blood loss and the overall recurrence rate without increasing operative time and overall complications. It is very valuable for complete LNs dissection in radical gastrectomy for GC. Nevertheless, more high-quality prospective studies and RCTs are necessary to confirm this conclusion.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

Author contributions

ZL made substantial contributions to conception and design for this work. BD, AZ, and ZL collected all the data. BD and ZL were the major contributors in writing the manuscript. YZ, WY, and LL performed critical revision for important intellectual content. All authors read and approved the final manuscript.

Funding

This work was supported by Scientific Research Project of Southwest Medical University (No.2020ZRQNB026).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* (2021) 71:209–49. doi: 10.3322/caac.21660

2. Japanese Gastric Cancer Association. Japanese Gastric cancer treatment guidelines 2018 (5th edition). *Gastric Cancer* (2021) 24:1–21. doi: 10.1007/s10120-020-01042-y

3. Li Z, Song M, Zhou Y, Jiang H, Xu L, Hu Z, et al. Efficacy of omentumpreserving gastrectomy for patients with gastric cancer: A systematic review and meta-analysis. *Front Oncol* (2021) 11:710814. doi: 10.3389/fonc.2021.710814

4. Li ZL, Zhao LY, Zhang WH, Liu K, Pang HY, Chen XL, et al. Clinical significance of lower perigastric lymph nodes dissection in siewert type II/III adenocarcinoma of esophagogastric junction: A retrospective propensity score matched study. *Langenbecks Arch Surg* (2022) 407:985–98. doi: 10.1007/s00423-021-02380-w

5. Ko CS, Jheong JH, Jeong SA, Kim BS, Yook JH, Yoo MW, et al. Comparison of standard d2 and limited lymph node dissection in elderly patients with advanced gastric cancer. *Ann Surg Oncol* (2022) 29:5076–82. doi: 10.1245/s10434-022-11480-w

 Li Z, Jiang H, Chen J, Jiang Y, Liu Y, Xu L. Comparison of efficacy between transabdominal and transthoracic surgical approaches for siewert type II adenocarcinoma of the esophagogastric junction: A systematic review and metaanalysis. Front Oncol (2022) 12:813242. doi: 10.3389/fonc.2022.813242

7. Reinhart MB, Huntington CR, Blair LJ, Heniford BT, Augenstein VA. Indocyanine green: Historical context, current applications, and future considerations. *Surg Innov* (2016) 23:166–75. doi: 10.1177/1553350615604053

8. Li Z, Zhou Y, Tian G, Liu Y, Jiang Y, Li X, et al. Meta-analysis on the efficacy of indocyanine green fluorescence angiography for reduction of anastomotic leakage after rectal cancer surgery. *Am Surg* (2021) 87:1910–9. doi: 10.1177/0003134820982848

9. Park JH, Berlth F, Wang C, Wang S, Choi JH, Park SH, et al. Mapping of the perigastric lymphatic network using indocyanine green fluorescence imaging and tissue marking dye in clinically advanced gastric cancer. *Eur J Surg Oncol* (2022) 48:411–7. doi: 10.1016/j.ejso.2021.08.029

10. Osterkamp J, Strandby RB, Nerup N, Svendsen M, Svendsen LB, Achiam MP. Time to maximum indocyanine green fluorescence of gastric sentinel lymph nodes and feasibility of combined indocyanine green/sodium fluorescein gastric lymphography. *Langenbecks Arch Surg* (2021) 406:2717–24. doi: 10.1007/s00423-021-02265-y

11. Jung MK, Cho M, Roh CK, Seo WJ, Choi S, Son T, et al. Assessment of diagnostic value of fluorescent lymphography-guided lymphadenectomy for gastric cancer. *Gastric Cancer*. (2021) 24:515–25. doi: 10.1007/s10120-020-01121-0

12. Ekman M, Girnyi S, Marano L, Roviello F, Chand M, Diana M, et al. Nearinfrared fluorescence image-guided surgery in esophageal and gastric cancer operations. *Surg Innov* (2022) 29(4):540–9. doi: 10.1177/15533506211073417

13. Chen QY, Xie JW, Zhong Q, Wang JB, Lin JX, Lu J, et al. Safety and efficacy of indocyanine green tracer-guided lymph node dissection during laparoscopic

radical gastrectomy in patients with gastric cancer: A randomized clinical trial. JAMA Surg (2020) 155:300-11. doi: 10.1001/jamasurg.2019.6033

14. Cianchi F, Indennitate G, Paoli B, Ortolani M, Lami G, Manetti N, et al. The clinical value of fluorescent lymphography with indocyanine green during robotic surgery for gastric cancer: A matched cohort study. *J Gastrointest Surg* (2020) 24:2197–203. doi: 10.1007/s11605-019-04382-y

15. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol* (2005) 5:13. doi: 10.1186/1471-2288-5-13

16. Huang ZN, Su-Yan, Qiu WW, Liu CH, Chen QY, Zheng CH, et al. Assessment of indocyanine green tracer-guided lymphadenectomy in laparoscopic gastrectomy after neoadjuvant chemotherapy for locally advanced gastric cancer: Results from a multicenter analysis based on propensity matching. *Gastric Cancer*. (2021) 24:1355–64. doi: 10.1007/s10120-021-01211-7

17. Kwon IG, Son T, Kim HI, Hyung WJ. Fluorescent lymphography-guided lymphadenectomy during robotic radical gastrectomy for gastric cancer. *JAMA Surg* (2019) 154:150–8. doi: 10.1001/jamasurg.2018.4267

18. Lan YT, Huang KH, Chen PH, Liu CA, Lo SS, Wu CW, et al. A pilot study of lymph node mapping with indocyanine green in robotic gastrectomy for gastric cancer. *SAGE Open Med* (2017) 5:2104799444. doi: 10.1177/2050312117727444

19. Lee S, Song JH, Choi S, Cho M, Kim YM, Kim HI, et al. Fluorescent lymphography during minimally invasive total gastrectomy for gastric cancer: An effective technique for splenic hilar lymph node dissection. *Surg Endosc.* (2022) 36:2914–24. doi: 10.1007/s00464-021-08584-x

20. Liu M, Xing J, Xu K, Yuan P, Cui M, Zhang C, et al. Application of nearinfrared fluorescence imaging with indocyanine green in totally laparoscopic distal gastrectomy. *J Gastric Cancer*. (2020) 20:290–9. doi: 10.5230/jgc.2020.20.e25

21. Lu X, Liu S, Xia X, Sun F, Liu Z, Wang J, et al. The short-term and long-term outcomes of indocyanine green tracer-guided laparoscopic radical gastrectomy in patients with gastric cancer. *World J Surg Oncol* (2021) 19:271. doi: 10.1186/ s12957-021-02385-1

22. Maruri I, Pardellas MH, Cano-Valderrama O, Jove P, Lopez-Otero M, Otero I, et al. Retrospective cohort study of laparoscopic ICG-guided lymphadenectomy in gastric cancer from a Western country center. *Surg Endosc.* (2022). doi: 10.1007/s00464-022-09258-y

23. Park SH, Berlth F, Choi JH, Park JH, Suh YS, Kong SH, et al. Near-infrared fluorescence-guided surgery using indocyanine green facilitates secure infrapyloric lymph node dissection during laparoscopic distal gastrectomy. *Surg Today* (2020) 50:1187–96. doi: 10.1007/s00595-020-01993-w

24. Puccetti F, Cinelli L, Genova L, Battaglia S, Barbieri LA, Treppiedi E, et al. Applicative limitations of indocyanine green fluorescence assistance to laparoscopic lymph node dissection in total gastrectomy for cancer. *Ann Surg Oncol* (2022) 29(9):5875–82. doi: 10.1245/s10434-022-11940-3

25. Romanzi A, Mancini R, Ioni L, Picconi T, Pernazza G. ICG-NIR-guided lymph node dissection during robotic subtotal gastrectomy for gastric cancer. a single-centre experience. *Int J Med Robot.* (2021) 17:e2213. doi: 10.1002/rcs.2213

26. Tian Y, Lin Y, Guo H, Hu Y, Li Y, Fan L, et al. Safety and efficacy of carbon nanoparticle suspension injection and indocyanine green tracer-guided lymph node dissection during robotic distal gastrectomy in patients with gastric cancer. *Surg Endosc.* (2022) 36:3209–16. doi: 10.1007/s00464-021-08630-8

27. Ushimaru Y, Omori T, Fujiwara Y, Yanagimoto Y, Sugimura K, Yamamoto K, et al. The feasibility and safety of preoperative fluorescence marking with indocyanine green (ICG) in laparoscopic gastrectomy for gastric cancer. *J Gastrointest Surg* (2019) 23:468–76. doi: 10.1007/s11605-018-3900-0

28. Wei M, Liang Y, Wang L, Li Z, Chen Y, Yan Z, et al. Clinical application of indocyanine green fluorescence technology in laparoscopic radical gastrectomy. *Front Oncol* (2022) 12:847341. doi: 10.3389/fonc.2022.847341

29. Yoon BW, Lee WY. The oncologic safety and accuracy of indocyanine green fluorescent dye marking in securing the proximal resection margin during totally laparoscopic distal gastrectomy for gastric cancer: A retrospective comparative study. *World J Surg Oncol* (2022) 20:26. doi: 10.1186/s12957-022-02494-5

30. Zhong Q, Chen QY, Huang XB, Lin GT, Liu ZY, Chen JY, et al. Clinical implications of indocyanine green fluorescence imaging-guided laparoscopic lymphadenectomy for patients with gastric cancer: A cohort study from two randomized, controlled trials using individual patient data. *Int J Surg* (2021) 94:106120. doi: 10.1016/j.ijsu.2021.106120

31. Dai W, Zhai ET, Chen J, Chen Z, Zhao R, Chen C, et al. Extensive dissection at no. 12 station during d2 lymphadenectomy improves survival for advanced lower-third gastric cancer: A retrospective study from a single center in southern china. *Front Oncol* (2021) 11:760963. doi: 10.3389/fonc.2021.760963

32. Liang Y, Cui J, Cai Y, Liu L, Zhou J, Li Q, et al. "D2 plus" lymphadenectomy is associated with improved survival in distal gastric cancer with clinical serosa invasion: A propensity score analysis. *Sci Rep* (2019) 9:19186. doi: 10.1038/s41598-019-55535-7

33. Zhang YX, Yang K. Significance of nodal dissection and nodal positivity in gastric cancer. *Transl Gastroenterol Hepatol* (2020) 5:17. doi: 10.21037/tgh.2019.09.13

34. Zhang N, Bai H, Deng J, Wang W, Sun Z, Wang Z, et al. Impact of examined lymph node count on staging and long-term survival of patients with node-

negative stage III gastric cancer: A retrospective study using a Chinese multiinstitutional registry with surveillance, epidemiology, and end results (SEER) data validation. *Ann Transl Med* (2020) 8:1075. doi: 10.21037/atm-20-1358a

35. Komatsu S, Ichikawa D, Nishimura M, Kosuga T, Okamoto K, Konishi H, et al. Evaluation of prognostic value and stage migration effect using positive lymph node ratio in gastric cancer. *Eur J Surg Oncol* (2017) 43:203–9. doi: 10.1016/j.ejso.2016.08.002

36. Omori T, Yamamoto K, Hara H, Shinno N, Yamamoto M, Fujita K, et al. Comparison of robotic gastrectomy and laparoscopic gastrectomy for gastric cancer: A propensity score-matched analysis. *Surg Endosc.* (2022) 36:6223–34. doi: 10.1007/s00464-022-09125-w

37. Lou S, Yin X, Wang Y, Zhang Y, Xue Y. Laparoscopic versus open gastrectomy for gastric cancer: A systematic review and meta-analysis of randomized controlled trials. *Int J Surg* (2022) 102:106678. doi: 10.1016/j.ijsu.2022.106678

38. Rosa F, Alfieri S. Laparoscopic gastrectomy for locally advanced gastric cancer. JAMA Surg (2022) 157:545-6. doi: 10.1001/jamasurg.2021.7582

39. Otsuka R, Hayashi H, Uesato M, Hayano K, Murakami K, Kano M, et al. Comparison of estimated treatment effects between randomized controlled trials, case-matched, and cohort studies on laparoscopic versus open distal gastrectomy for advanced gastric cancer: A systematic review and meta-analysis. *Langenbecks Arch Surg* (2022) 407:1381–97. doi: 10.1007/s00423-022-02454-3

40. Kano K, Yamada T, Yamamoto K, Komori K, Watanabe H, Hara K, et al. Association between lymph node ratio and survival in patients with pathological stage II/III gastric cancer. *Ann Surg Oncol* (2020) 27:4235–47. doi: 10.1245/s10434-020-08616-1

41. Wang JW, Chen CY. Prognostic value of total retrieved lymph nodes on the survival of patients with advanced gastric cancer. *J Chin Med Assoc* (2020) 83:691–2. doi: 10.1097/JCMA.00000000000368

42. Mao M, Zhang A, He Y, Zhang L, Liu W, Song Y, et al. Development and validation of a novel nomogram to predict overall survival in gastric cancer with lymph node metastasis. *Int J Biol Sci* (2020) 16:1230–7. doi: 10.7150/ijbs.39161