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RESEARCH ARTICLE

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Minimally invasive versus open gastrectomy for gastric cancer. A pooled analysis of two European randomized controlled trials

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Abstract

Introduction: Minimally invasive techniques have shown better short term and similar oncological outcomes compared to open techniques in the treatment of gastric cancer in Asian countries. It remains unknown whether these outcomes can be extrapolated to Western countries, where patients often present with advanced gastric cancer.

Materials and Methods: A pooled analysis of two Western randomized controlled trials (STOMACH and LOGICA trial) comparing minimally invasive gastrectomy (MIG) and open gastrectomy (OG) in advanced gastric cancer was performed. Postoperative recovery (complications, mortality, hospital stay), oncological outcomes (lymph node yield, radical resection rate, 1-year survival), and quality of life was assessed.

Results: Three hundred and twenty-one patients were included from both trials. Of these, 162 patients (50.5%) were allocated to MIG and 159 patients (49.5%) to OG. A significant difference was seen in blood loss in favor of MIG (150 vs. 260 mL, $p < 0.001$), whereas duration of surgery was in favor of OG (180 vs. 228.5 min, $p = 0.005$). Postoperative recovery, oncological outcomes and quality of life were similar between both groups.

Conclusion: MIG showed no difference to OG regarding postoperative recovery, oncological outcomes or quality of life, and is therefore a safe alternative to OG in patients with advanced gastric cancer.

KEYWORDS
advanced gastric cancer, minimally invasive gastrectomy

Jennifer Straatman and Richard van Hillegersberg contributed equally to this study.

1 | INTRODUCTION

With the introduction of neoadjuvant chemotherapy, survival rates for advanced gastric cancer have improved. For advanced gastric cancer, surgery with perioperative chemotherapy, is the preferred treatment. Most guidelines recommend a radical gastrectomy with a D2 lymphadenectomy.[1,2] However, in these guidelines, no recommendations are given regarding the use of minimally invasive techniques in the treatment of advanced gastric cancer.

Previous Asian studies indicate that the implementation of minimally invasive techniques showed better short-term outcomes, such as less postoperative complications and faster postoperative recovery.[3–5] However, in Asian countries gastric cancer has a higher incidence and screening programs ensure most patients are treated in early stages of disease, commonly without systemic therapy and more often with partial gastrectomy.[6,7] Patients in Western countries often present with gastric cancer in advanced stages and commonly receive multimodality treatment.[2] Furthermore, obesity is more prevalent in the Western population compared with the Asian population and it is elusive whether results from Asian studies regarding minimally invasive techniques can be extrapolated to the Western population.

Recently, two randomized controlled trials were completed in Europe, comparing short term outcomes of minimally invasive gastrectomy (MIG) versus open gastrectomy (OG) for gastric cancer; the STOMACH trial (surgical technique: open vs. minimally invasive gastrectomy after chemotherapy) and the LOGICA trial (laparoscopic vs. open gastrectomy for gastric cancer).[8,9] Both trials have a relatively small cohort compared to some Asian trials, additionally the STOMACH trial had to readjust the sample size due to slow accrual. Questions arose whether the trial was underpowered with regard to the conclusions that were drawn. Together these trials result in the largest randomized European cohort of patients undergoing open and MIG for gastric cancer. The aim of this study was to assess short-term outcomes and quality of life in this pooled European cohort.

2 | METHODS

2.1 | Study design

A pooled analysis was made of two recently published Western randomized controlled trials; The STOMACH trial and the LOGICA trial. Primary outcome of this pooled analysis was the number of resected lymph nodes in MIG compared to OG in patients with gastric cancer. With advanced gastric cancer being defined as cT2-4a, N0-3, M0, or cT1N+. The full protocols and results were published previously.[8–11] As the introduction and start of these trials were at the same time, both research groups agreed to use the same case report forms to analyze the pooled data of the completed trials.

The STOMACH trial was a non-inferiority, multicenter, international, randomized trial that took place between January 2015 and June 2018 powered for non-inferiority with regard to quality of oncological resection (radical resection and lymphadenectomy). The LOGICA trial was a superiority, multicenter, Dutch national, randomized trial that took place between February 2015 and August 2018 and powered for superiority with regard to duration of hospital admission.

2.2 | Patients

Patients were eligible for participation in both trials if they had histologically proven clinically resectable gastric cancer. In the STOMACH trial patients in whom a total gastrectomy was performed and neoadjuvant chemotherapy was given were included. In the LOGICA trial also patients in whom a distal gastrectomy was performed were included and neoadjuvant chemotherapy was not an inclusion criterion. All patients were at least 18 years of age. If previous surgery of the stomach had occurred patients were excluded from the trials. Quality control took place through video approval by the trial principal investigators or site visits.

2.3 | Outcomes

Primary outcome of the STOMACH trial was oncological outcomes measured as the number of resected lymph nodes and radicality. Primary outcome of the LOGICA trial was length of hospital stay. Both studies assessed intraoperative outcomes such as operation duration, intraoperative complications, and blood loss, as well as postoperative outcomes such as postoperative morbidity and mortality, disease-free survival, overall survival, and quality of life as secondary outcomes. Quality of life was measured by the EORTC-QLQ-C30 and EORTC-QLQ-STO22 questionnaires at baseline, postoperatively, 3 months, 6 months, and 1 year.[12,13] A full overview of the study outcomes, outcome definitions and ways of data collection can be found in the previously published study protocols.[10,11]

2.4 | Statistics

The two cohorts of patients were pooled and grouped into MIG and OG. Analyses were performed based on the intention-to-treat principle. Baseline characteristics of the two arms were compared by means of the student's *t*-test, the Mann–Whitney *U* test and the chi-square test depending on the distribution of the data. All study outcomes except survival were evaluated with the same statistical tests as mentioned above. Survival was evaluated by Kaplan–Meier curves with the log rank test. Quality of life scores were calculated and analyzed at specific time-points and by generalized linear models. Scores were measured in a scale from 0 to 100 with 100 being the best overall health score. Subgroup analyses were performed for total gastrectomy, patients who underwent neoadjuvant chemotherapy, and advanced gastric cancer.

3 | RESULTS

Six hundred and eighty-six patients were eligible for inclusion, 347 patients were not included in the trial due to a decline of participation, screening failure, language barrier, disseminated disease, or other reasons. A total of 321 were included from both trials; 96 from the STOMACH trial and 225 from the LOGICA trial. Of these, 162 patients (50.5%) were allocated to MIG and 159 patients (49.5%) to OG. A flow chart of the included patients is depicted in Figure 1.

Baseline characteristics such as age, gender, American Society of Anesthesiologists (ASA) classification were similar between both groups except for body mass index (BMI). Mean BMI was 26.4 ± 4.7 kg/m^2 in the minimally invasive group versus 25.1 ± 3.9 kg/m^2 in the open group (p = 0.005).

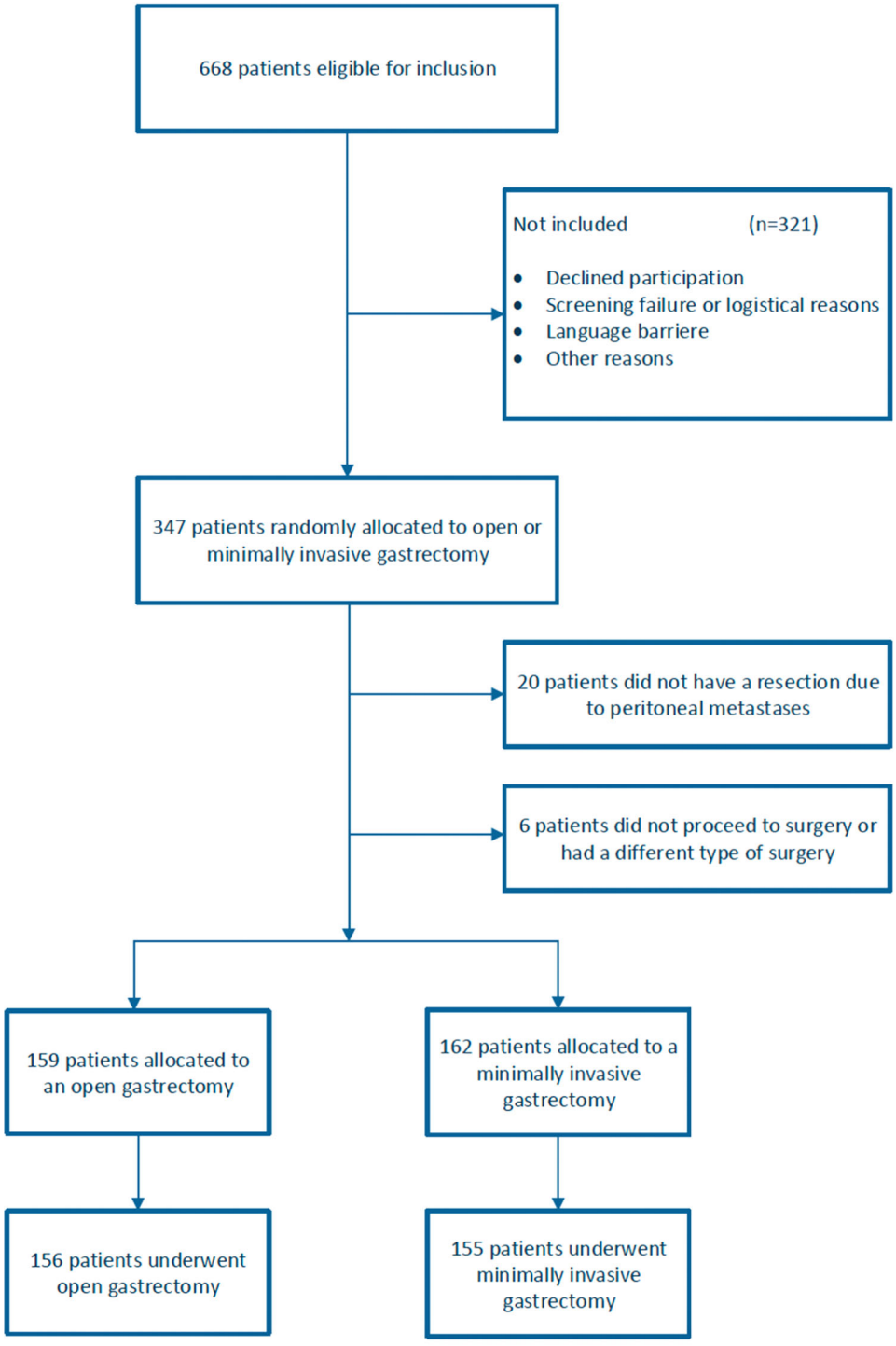

FIGURE 1 Flow chart of included patients.

A total of 307 out if 321 patients had clinical locally advanced gastric cancer. There were no significant differences in clinical TNM stage between both groups.

In the open group, more patients received neoadjuvant chemotherapy compared to the patients in the minimally invasive group, 136 patients (85.5%) versus 124 patients (76.5%) ($p = 0.047$).

As 10 patients did not proceed to surgery due to metastases or progression of disease at restaging following neoadjuvant treatment, 155 patients underwent MIG and 156 patients OG. In the minimally invasive group 95 patients (58.6%) underwent total gastrectomy, and 92 patients (57.9%) in the open group ($p = 0.420$). D2 lymphadenectomy was performed in 139 patients (89.7%) in the minimally invasive group and 142 patients (91%) in the open group ($p = 0.451$). An overview of baseline characteristics and pathologic outcome is depicted in Tables 1 and 2.

3.1 | Intraoperative outcomes

A significant difference was seen in blood loss and for the duration of surgery. Median duration of surgery was 228.5 min in the minimally invasive group versus 180 min in the open group ($p = 0.005$). Median blood loss was 150 mL during MIG versus 260 mL during OG ($p < 0.001$).

Intraoperative complications occurred in 14 patients (8.0%) after MIG and in 14 patients (8.9%) after OG ($p = 0.788$). Intraoperative bleeding was reported when the patient needed a blood transfusion. An overview of all operative outcomes is depicted in Table 3.

3.2 | Postoperative recovery

Postoperative recovery was similar between both groups. Median hospital stay was 7.0 in the minimally invasive group and 8.0 in the open group ($p = 0.117$).

In 67 patients (41.4%) in the minimally invasive group a postoperative complication occurred and in 66 patients (41.5%) in the open group ($p = 0.978$). In patients who experienced postoperative complications, median hospital stay was 10.0 after MIG and 11.0 after OG ($p = 0.248$). Anastomotic leakage occurred in 14 patients (8.6%) in the minimally invasive group and in 16 patients (10.1%) in the open group ($p = 0.705$). Postoperative death occurred in 5 patients (3.1%) in the minimally invasive group versus 10 patients (6.3%) in the open group ($p = 0.978$). An overview of morbidity and mortality is depicted in Table 4.

3.3 | Oncological outcome

No differences were seen in complete oncological resection (Table 2). The median lymph node yield was 32 (24–46) in both groups ($p = 0.661$). In the minimally invasive group 146 patients (94.2%) had a radical R0 resection in comparison to 144 patients (92.3%) in the open group ($p = 0.786$). There was no difference in 1-year survival between both groups. After MIG, 129 patients (83.8%) were still alive 1-year postoperatively versus 129 patients (82.7%) after OG ($p = 0.879$).

TABLE 1 Baseline characteristics.

Parameter	OG		MIG		p-value
Patients (*n*, %)	159	49.5%	162	50.5%	
Gender (male, %)	103	64.8%	96	59.3%	0.358
Age (years, mean ± SD)	65.5	11.8	65.4	12.3	0.926
BMI (kg/m^2, mean ± SD)	25.1	3.9	26.4	4.7	0.005
Weight loss (yes, %)	89	56.0%	77	47.5%	0.136
ASA classification					
ASA I	20	12.6%	11	6.8%	0.116[a]
ASA II	96	60.4%	113	69.8%	
ASA III	43	27.0%	38	23.5%	
Smoking	50	32.3%	45	30.0%	0.539
Alcohol (Y/N)	66	42.6%	71	44.7%	0.734
Medical history					
Cardiovascular	85	53.5%	81	50.0%	0.577
Gastrointestinal	45	28.3%	42	25.9%	0.707
Endocrine	38	23.9%	44	27.2%	0.524
Previous abdominal surgery	50	31.6%	39	24.5%	0.171
Preoperative workup and staging					
Gastroscopy location[b]					
Proximal	28	17.6%	28	17.5%	0.984[a]
Middle	60	37.7%	59	36.9%	
Distal	71	44.7%	73	45.6%	
Clinical T-stage					
cT1	8	5.0%	9	5.6%	0.736[a]
cT2	37	23.3%	45	27.8%	
cT3	99	62.3%	91	56.2%	
cT4	15	9.4%	17	10.5%	
Clinical N-stage					
N0	74	46.5%	82	50.6%	0.613[a]
N1	78	49.1%	76	46.9%	
N2	6	3.8%	4	2.5%	
N3	1	0.6%	0	0.0%	
Neoadjuvant therapy	136	85.5%	124	76.5%	0.047

Abbreviations: MIG, minimally invasive gastrectomy; OG, open gastrectomy.

[a]Additional post hoc testing between groups, adjusted with Bonferroni correction revealed no significant differences between groups.

[b]Two patients missing in the MIG group.

TABLE 2 Pathological outcomes.

Parameter	OG (n = 156)		MIG (n = 155)		p Value
Tumor type					
Intestinal	89	57.1%	70	45.8%	0.138*
Diffuse	58	37.2%	77	50.3%	
Mixed	6	3.8%	4	2.6%	
Other	3	1.9%	4	2.6%	
(y)pathological T stage					
(y)pT0	13	8.3%	8	5.2%	0.441*
(y)pTis	2	1.3%	3	1.9%	
(y)pT1	22	14.1%	21	13.5%	
(y)pT2	17	10.9%	18	11.6%	
(y)pT3	68	43.6%	57	36.8%	
(y)pT4	34	21.8%	48	31.0%	
(y)pathological N stage					
(y)pN0	74	47.4%	63	40.6%	0.157*
(y)pN1	29	18.6%	26	16.8%	
(y)pN2	29	18.6%	26	16.8%	
(y)pN3	24	15.4%	40	25.8%	
(y)pathological M stage					
(y)pM1	5	3.1%	7	4.3%	0.138
Mandard					
1	15	9.6%	10	7.0%	0.281*
2	12	7.7%	8	21.7%	
3	39	25.0%	25	30.4%	
4	34	21.8%	35	32.2%	
5	29	18.6%	37	34.8%	
Missing	27	17.3%	40	27.8%	
Number of retrieved LN	32	(24–46)	32	(24–45)	0.661
Radicality					
R0	144	92.3%	146	94.2%	0.786
R+	6	3.8%	8	5.2%	
Missing	6	3.8%	1	0.6%	

Abbreviations: MIG, minimally invasive gastrectomy; OG, open gastrectomy.

3.4 | Quality of life

3.4.1 | Overall health scores

A response compliance was achieved of 80% in the STOMACH trial and 64% in the LOGICA trial for all PROMs. No differences were observed in health-related quality of life (HRQoL) scores between MGI and OG (Figure 2). The median EORTC-QLQ-C30 overall health score 1 year postoperatively was 66.7 (50–83.3) in the minimally invasive group and 66.7 (58.3–83.3) in the open group (p = 0.196). An overview of quality-of-life scores is depicted in Figure 2.

3.4.2 | EORTC-QLQ-C30 separate domain scores

In the EORTC-QLQ-C30 questionnaire, no statistically significant differences were observed between the minimally invasive and open group for the different functional scales; physical functioning, role functioning, emotional functioning, cognitive functioning, and social functioning (Figure 2).

EORTC-QLQ-C30 symptom scales showed no differences between both groups (Figure 2), generalized linear models also revealed no differences in trends over time between the groups.

3.4.3 | EORTC-QLQ-STO22 separate domain scores

The EORTC-QLQ-STO22 is a gastric cancer specific module. The measured domains include; dysphagia, pain, reflux, dietary restrictions, anxiety, dry mouth, taste, and body image. No significant differences were seen between both groups (Figure 2).

3.5 | Subgroup analyses

Subgroup analyses were performed of patients who underwent total gastrectomy, distal gastrectomy, had advanced gastric cancer, and who underwent neoadjuvant chemotherapy. In all subgroup analyses, no differences were seen between OG and MIG for postoperative complications, admission duration, lymphadenectomy, radicality, and survival (Table 5).

4 | DISCUSSION

This pooled European cohort of two randomized controlled trials evaluated postoperative outcomes of MIG versus OG. No differences were seen regarding postoperative morbidity, oncological outcomes, nor quality of life. MIG was associated with a longer operating time but with less intraoperative blood loss. These results are in line with previous studies and support that MIG is a safe alternative to OG for the surgical treatment of gastric cancer.[8,9,14–17]

MIG has increasingly been adopted worldwide. A recent study demonstrated a 4-fold increase in minimally invasive distal gastrectomy (9% vs. 39%) and a 5.5-fold increase in minimally invasive total gastrectomy (6% vs. 33%).[18] Until recently, high-level evidence supporting MIG was retrieved from trials performed in the Asian population, which differ significantly from the Western population.[2,14–17,19] The STOMACH and LOGICA trials were the first Western randomized controlled trials on this subject.[8,9] The current study included all patients from the STOMACH and LOGICA trial. As the same case report forms and definitions were used in both trials,

TABLE 3 Operative outcomes.

Parameter	OG (*n* = 156)		MIG (*n* = 155)		*p* Value
Type of resection					
Total gastrectomy	92	57.9%	95	58.6%	0.420[a]
Distal gastrectomy	64	40.3%	59	36.4%	
No gastrectomy	3	1.9%	8	4.9%	
Lymphadenectomy					
D1	0	0.0%	1	0.6%	0.451[a]
D1+	14	9.0%	15	9.7%	
D2	142	91.0%	139	89.7%	
Duration of surgery (median, IQR)	180	(150–225)	228.5	(179–269)	0.005
Blood loss (median, IQR)	260	(150–500)	150	(50–300)	<0.001
Additional resection required					
Splenectomy	9	5.7%	3	1.9%	0.072
Pancreatectomy	1	0.6%	2	1.2%	0.573
Feeding jejunostomy	23	15.6%	21	13.5%	0.606
Peroperative complications	14	8.9%	13	8.0%	0.788
Bleeding	9	5.7%	9	5.6%	0.793[a]
Bowel perforation	1	0.6%	0	0%	
Other	4	2.5%	4	2.5%	
Conversion from MI to open			10	6.2%	NA
SMEQ score	55	(29.5–70)	55	(40–78.5)	0.211

Abbreviations: MIG, minimally invasive gastrectomy; OG, open gastrectomy.
[a]Additional post hoc testing between groups, adjusted with Bonferroni correction revealed no significant differences between groups.

the pooled data could be analyzed in detail. The outcomes of the current study are in line with the primary outcomes of the separate trials, with no statistically significant difference between MIG and OG in the median length of hospital admission (7 vs. 8 days, $p = 0.117$), median number of resected lymph nodes (32 vs. 32 nodes, $p = 0.661$), and radical resection rate (94.2% vs. 92.3% R0, $p = 0.786$). These results confirm that MIG and OG are equivalent on important outcomes such as postoperative recovery and complete oncological resection. Even when taking into account the average higher BMI in the MIG population in these studies.

While previous studies have found minimally invasive techniques to have shorter hospital stay in comparison to open techniques, this study did not show a significant difference between both groups. A recent pooled analysis of 18 studies comparing MIG with OG for advanced gastric cancer showed a significant difference in hospital stay in favor of MIG.[20] However, only one of these studies showed an overall shorter hospital stay in comparison to the outcome of this cohort.[21] All other studies reported similar or overall longer hospital stay in both groups. An explanation for these outcomes might be the application of enhanced recovery after surgery protocols in our cohort resulting in overall fast postoperative recovery. A higher use of postoperative analgesia after OG may have resulted in faster recovery as well. This is supported by a secondary analysis of the LOGICA cohort, showing that patients in the

TABLE 4 Morbidity and mortality.

Postoperative recovery and complications					
Parameter	OG (*n* = 156)		MIG (*n* = 155)		*p* Value
Admission duration (days) (median, IQR)	8	(6-11)	7	(6-9.75)	0.117
Uncomplicated	7	(5-8)	7	(5-8)	0.181
Complications	11	(9-15)	10	(7-17)	0.248
Days till start oral intake (median, IQR)	1	(1-4)	1	(1-4)	0.968
Postoperative complications	66	41.5%	67	41.4%	0.978
CD 1	7	4.4%	11	6.8%	0.399[a]
CD 2	28	17.6%	29	17.9%	
CD 3a	7	4.4%	8	4.9%	
CD 3b	10	6.3%	5	3.1%	
CD 4	4	2.5%	9	5.6%	
CD 5	10	6.3%	5	3.1%	
Anastomotic leak	16	10.1%	14	8.6%	0.705
1-Year survival	129	82.7%	129	83.8%	0.879

Abbreviations: MIG, minimally invasive gastrectomy; OG, open gastrectomy.
[a]Additional post hoc testing between groups, adjusted with Bonferroni correction revealed no significant differences between groups.

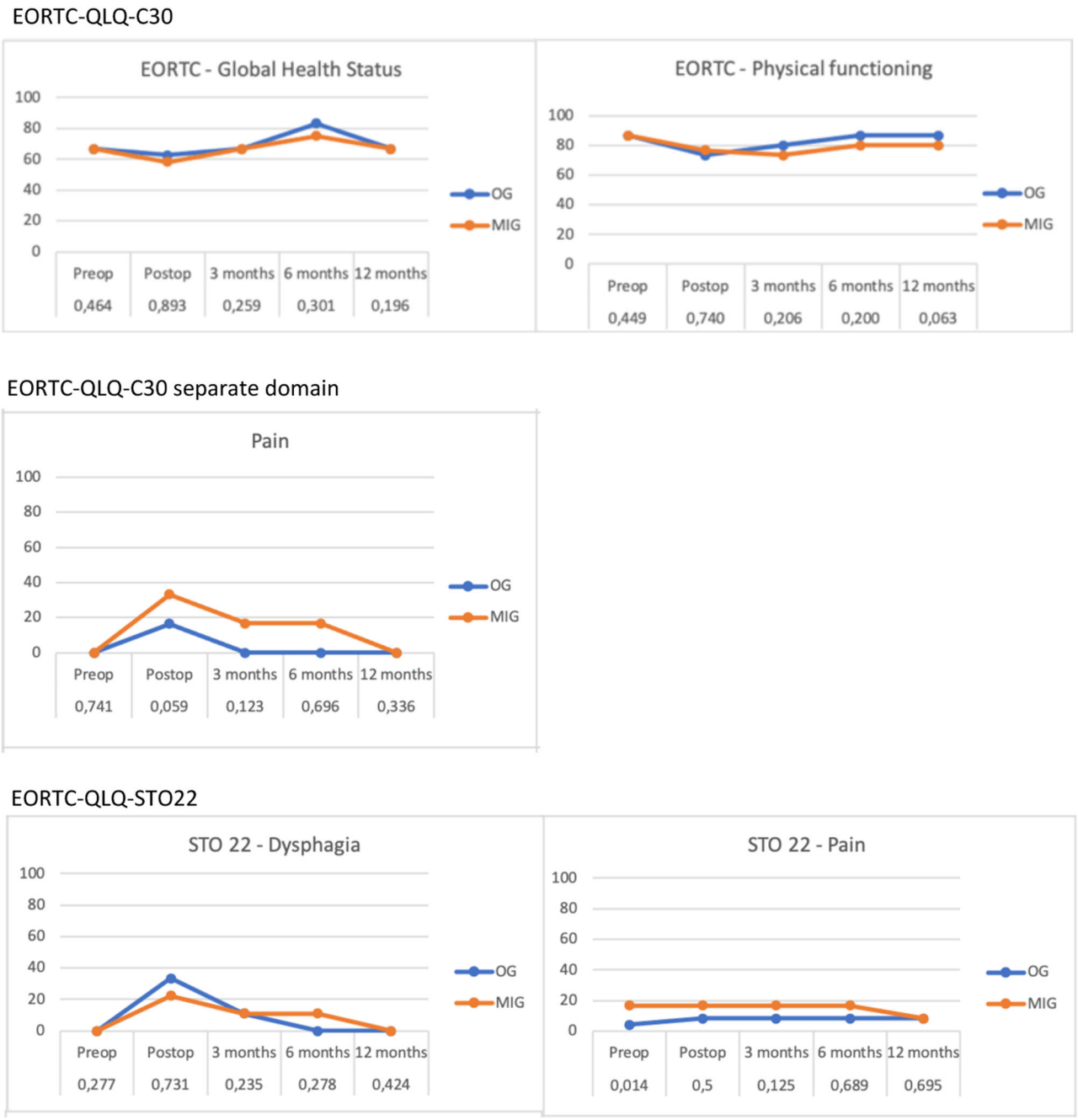

FIGURE 2 Health-related quality of life.

MIG group did not need epidural analgesia and had a significantly lower consumption of opioids.[22] Long-term complications associated with open abdominal surgery are incisional hernias.[23] It is expected that there will be less incisional hernias after MIG in comparison to OG. Long-term complications from the STOMACH and LOGICA cohort has to be awaited.

Gastric cancer is one of the most prevalent malignancies in Asia, but its incidence is low in Western countries.[24] In Asia, screening programs for the detection of gastric cancer exist and most diagnoses are made at an early stage of disease resulting in more patients who undergo primary surgery.[25] Patients who received neoadjuvant therapy are relatively underrepresented in previous Asian trials, and therefore there was no solid evidence to support MIG for these patients' subgroups.[26] In the current study, subgroup analyses for patients who received neoadjuvant therapy and those patients who underwent primary resection showed no difference between MIG and OG regarding oncological outcomes and postoperative outcomes. These results implicate that MIG can be performed safely for patients with advanced gastric cancer, patients who undergo total gastrectomy and patients who are submitted to neoadjuvant therapy.

Several studies have showed similar survival outcomes in MIG and OG, which is in line with the recent analysis of 3-year survival in

TABLE 5 Subgroup analyses.

Postoperative outcomes					
Advanced gastric cancer[a]	**OG (*n* = 151)**		**MIG (*n* = 156)**		***p* Value**
Admission duration (days) (median, IQR)	8	(6–11)	7	(6–10)	0.161
Uncomplicated	7	(5–8)	7	(5–8)	0.267
Complications	11	(9–15.25)	10	(7–17.25)	0.265
Postoperative complications	62	41.00%	64	41.00%	0.447[b]
CD 1	6	4.0%	10	6.4%	
CD 2	26	17.2%	27	17.3%	
CD 3a	7	4.6%	8	5.1%	
CD 3b	10	6.6%	5	3.2%	
CD 4	4	2.6%	9	5.8%	
CD 5	9	6.0%	5	3.2%	
Anastomotic leak	15	9.9%	14	9.0%	0.774
Number of retrieved LN (median, IQR)	32	(24–46)	33	(24–45)	0.780
Radicality					
R0	136	90.1%	140	89.7%	0.639
R+	6	4.0%	8	5.1%	
Missing	9	6.0%	8	5.1%	
Survival 1 year	123	81.5%	124	79.5%	0.663
Neoadjuvant chemotherapy	**OG (*n* = 136)**		**MIG (*n* = 124)**		***p* Value**
Admission duration (days) (median, IQR)	8	(6–11)	7	(6–9)	0.164
Uncomplicated	7	(5–8)	7	(5–8)	0.279
Complications	11	(9–15)	9	(7–17)	0.185
Postoperative complications	51	37.5%	49	39.5%	0.519[b]
CD 1	6	4.4%	9	7.3%	
CD 2	24	17.6%	21	16.9%	
CD 3a	5	3.7%	6	4.8%	
CD 3b	8	5.9%	4	3.2%	
CD 4	3	2.2%	7	5.6%	
CD 5	5	3.7%	2	1.6%	
Anastomotic leak	11	8.1%	10	8.1%	0.994
Number of retrieved LN (median, IQR)	32	(23.25–45)	32	(24–45)	0.926
Radicality					
R0	123	90.4%	112	90.3%	0.847
R+	6	4.4%	6	4.8%	
Missing	7	5.1%	6	4.8%	
Survival 1 year	116	85.3%	102	82.3%	0.506
Total gastrectomy	**OG (*n* = 92)**		**MIG (*n* = 95)**		***p* Value**
Admission duration (days) (median, IQR)	9	(7–12)	8	(7–11)	0.173
Uncomplicated	8	(6.25–9)	7	(6–8)	0.251
Complications	11	(9–15)	11	(8–19)	0.504
Postoperative complications	44	47.8%	46	48.4%	0.639[b]
CD 1	3	3.3%	5	5.3%	
CD 2	21	22.8%	21	22.1%	
CD 3a	4	4.3%	6	6.3%	
CD 3b	7	7.6%	4	4.2%	
CD 4	3	3.3%	7	7.4%	
CD 5	6	6.5%	3	3.2%	
Anastomotic leak	13	14.1%	14	14.7%	0.906
Number of retrieved LN (median, IQR)	35.5	(26.25–48)	33	(25–43)	0.323
Radicality					
R0	81	88.0%	87	91.6%	0.661
R+	5	5.4%	7	7.4%	
Missing	6	6.5%	1	1.1%	
Survival 1 year	72	78.3%	79	83.2%	0.396
Distal gastrectomy	**OG (*n* = 64)**		**MIG (*n* = 59)**		***p* Value**
Admission duration (days) (median, IQR)	6	(5–8)	6	(4.50–7)	0.600
Uncomplicated	5	(4.75–7)	6	(4–7)	0.820
Complications	10	(5.75–17.75)	7	(6.50–11.50)	0.335
Postoperative complications	22	34.4%	19	32.2%	0.904[b]
CD 1	4	6.3%	5	8.5%	
CD 2	7	10.9%	7	11.9%	
CD 3a	3	4.7%	2	3.4%	
CD 3b	3	4.7%	1	1.7%	
CD 4	1	1.6%	2	3.4%	
CD 5	4	6.3%	2	3.4%	
Anastomotic leak	3	4.7%	0	0.0%	

TABLE 5 (Continued)

Distal gastrectomy	OG ($n = 64$)	MIG ($n = 59$)	p Value
Number of retrieved LN (median, IQR)	28 (23–38)	29 (18–40)	0.545
Radicality			
R0	63 98.4%	58 98.3%	0.954
R+	1 1.6%	1 1.7%	
Survival 1 year	57 89.1%	50 84.7%	0.477

Abbreviations: MIG, minimally invasive gastrectomy; OG, open gastrectomy.

[a]Advanced gastric cancer is defined as cT2-4a, N0-3, M0, or cT1N+.

[b]Additional post hoc testing between groups, adjusted with Bonferroni correction revealed no significant differences between groups.

the STOMACH trial.[20,27,28] A recent study from Tsekrekos et al. showed a better survival after laparoscopic surgery. However, this survival benefit was exclusively seen in patients who underwent distal gastrectomy and no difference was demonstrated in the total gastrectomy group.[29]

Long-term survival and long-term quality of life of the STOMACH and LOGICA trial has to be awaited.

Before drawing a final conclusion on MIG, data on quality of life, cost-effectiveness and the learning curve of MIG should be taken into account. There was one Asian trial who took quality of life into account; patients with early gastric cancer underwent distal gastrectomy without perioperative chemotherapy who were randomized between MIG and OG.[30] The results of this study demonstrate that at 1-year follow-up, quality of life is comparable between the groups. Based on previous prospective studies, it is not expected that quality of life will deteriorate after 1-year follow-up unless recurrent disease will develop.[31] Recent additional analysis of the LOGICA trial regarding cost-effectiveness demonstrates largely comparable cost-effectiveness between MIG and OG at 1-year follow-up. Finally, centralization of gastric cancer treatment and improvement in the learning curve of MIG could improve overall outcomes for minimally invasive techniques in the Western population.

Besides the long-term outcomes of MIG, other developments in gastric cancer surgery should also be carefully monitored. MIG allows for storage of surgical footage, allowing for quality control, and easy implementation of other visualization techniques such as the application of indocyanine green, and these benefits should be taken into account when assessing the optimal technique. Robot-assisted minimally invasive procedures are gaining popularity worldwide for several high-complex gastrointestinal procedures, such as esophagectomy, pancreaticoduodenectomy, and hiatal hernia repair.[32–34] For gastric cancer, robot-assisted gastrectomy is performed in less than 5% of procedures.[18] Until now, studies from the centers with the largest volumes of robot-assisted gastrectomy demonstrated longer operating time, less blood loss, comparable oncological outcomes, and higher costs as compared to laparoscopic gastrectomy.[35] However, a recent randomized trial by Ojima et al. suggested less postoperative complications following robot-assisted gastrectomy compared to laparoscopic gastrectomy.[36] Along with the technical advances, the implementation of robotic gastrectomy for gastric cancer will most likely increase in the near future.

Strengths of this study include that it is the largest European randomized cohort of patients on OG versus MIG, including two trials with largely comparable perioperative protocols. Secondly, probably due to surgical quality control, surgical quality was high, with a radical resection rate higher than 92% and a median of 32 resected lymph nodes in both treatment arms. Limitations of this study include patients and investigators were not being blinded for the study arm, it was not powered on important outcomes such as survival and quality of life. Finally, despite randomization more patient in the open group received neoadjuvant chemotherapy, which may have influenced the results.

5 | CONCLUSION

The pooled data from two Western randomized controlled trials on MIG versus OG did not show any differences in postoperative recovery and complete oncological resection. In addition, quality of life was not different at 1-year follow-up between both groups. These results support that MIG is a safe alternative to OG for the surgical treatment of patients with advanced gastric cancer.

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CONFLICT OF INTEREST STATEMENT

M. van Berge Henegouwen is consultant for Mylan, Johnson & Johnson, Alesi Surgical, BBraun and Medtronic, and received unrestricted research grants from Stryker. All fees are paid to the institution. For the remaining authors no conflict of interest was declared.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent to be included in the study was obtained from all patients.

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REFERENCES

1. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2021 (6th edition). *Gastric Cancer*. 2023;26:1-25.
2. Smyth EC, Verheij M, Allum W, Cunningham D, Cervantes A, Arnold D. Gastric cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2016;27(suppl 5): v38-v49.
3. Kim W, Kim HH, Han SU, et al. Decreased morbidity of laparoscopic distal gastrectomy compared with open distal gastrectomy for stage I gastric cancer: short-term outcomes from a multicenter randomized controlled trial (KLASS-01). *Ann Surg*. 2016;263(1):28-35.
4. Beyer K, Baukloh AK, Kamphues C, et al. Laparoscopic versus open gastrectomy for locally advanced gastric cancer: a systematic review and meta-analysis of randomized controlled studies. *World J Surg Oncol*. 2019;17(1):68.
5. Chen XZ, Wang SY, Wang YS, et al. Comparisons of short-term and survival outcomes of laparoscopy-assisted versus open total gastrectomy for gastric cancer patients. *Oncotarget*. 2017;8(32): 52366-52380.
6. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015;136(5):E359-E386.
7. Leja M, You W, Camargo MC, Saito H. Implementation of gastric cancer screening—the global experience. *Best Pract Res Clin Gastroenterol*. 2014;28(6):1093-1106.
8. van der Wielen N, Straatman J, Daams F, et al. Open versus minimally invasive total gastrectomy after neoadjuvant chemotherapy: results of a European randomized trial. *Gastric Cancer*. 2021;24(1):258-271.
9. van der Veen A, Brenkman HJF, Seesing MFJ, et al. Laparoscopic versus open gastrectomy for gastric cancer (LOGICA): a multicenter randomized clinical trial. *J Clin Oncol*. 2021;39(9):978-989.
10. Straatman J, van der Wielen N, Cuesta MA, et al. Surgical techniques, open versus minimally invasive gastrectomy after chemotherapy (STOMACH trial): study protocol for a randomized controlled trial. *Trials*. 2015;16:123.
11. Haverkamp L, Brenkman HJ, Seesing MF, et al. Laparoscopic versus open gastrectomy for gastric cancer, a multicenter prospectively

randomized controlled trial (LOGICA-trial). *BMC Cancer*. 2015;15:556.
12. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*. 1993;85(5):365-376.
13. Vickery CW, Blazeby JM, Conroy T, et al. Development of an EORTC disease-specific quality of life module for use in patients with gastric cancer. *Eur J Cancer*. 2001;37(8):966-971.
14. Katai H, Mizusawa J, Katayama H, et al. Survival outcomes after laparoscopy-assisted distal gastrectomy versus open distal gastrectomy with nodal dissection for clinical stage IA or IB gastric cancer (JCOG0912): a multicentre, non-inferiority, phase 3 randomised controlled trial. *Lancet Gastroenterol Hepatol*. 2020;5(2):142-151.
15. Yu J, Huang C, Sun Y, et al. Effect of laparoscopic vs open distal gastrectomy on 3-year disease-free survival in patients with locally advanced gastric cancer: the CLASS-01 randomized clinical trial. *JAMA*. 2019;321(20):1983-1992.
16. Kim HH, Han SU, Kim MC, et al. Effect of laparoscopic distal gastrectomy vs open distal gastrectomy on long-term survival among patients with stage I gastric cancer: the KLASS-01 randomized clinical trial. *JAMA Oncol*. 2019;5(4):506-513.
17. Hyung WJ, Yang HK, Park YK, et al. Long-term outcomes of laparoscopic distal gastrectomy for locally advanced gastric cancer: the KLASS-02-RCT randomized clinical trial. *J Clin Oncol*. 2020;38(28):3304-3313.
18. Gertsen EC, Brenkman HJF, Haverkamp L, Read M, Ruurda JP, van Hillegersberg R. Worldwide practice in gastric cancer surgery: a 6-year update. *Dig Surg*. 2021;38(4):266-274.
19. van der Wielen N, Straatman J, Cuesta MA, Daams F, van der Peet DL. Short-term outcomes in minimally invasive versus open gastrectomy: the differences between East and West. A systematic review of the literature. *Gastric Cancer*. 2018;21(1):19-30.
20. Pang HY, Chen XF, Chen LH, Yan MH, Chen ZX, Sun H. Comparisons of perioperative and long-term outcomes of laparoscopic versus open gastrectomy for advanced gastric cancer after neoadjuvant therapy: an updated pooled analysis of eighteen studies. *Eur J Med Res*. 2023;28(1):224.
21. Khaled I, Priego P, Soliman H, Faisal M, Saad Ahmed I. Oncological outcomes of laparoscopic versus open gastrectomy after neoadjuvant chemotherapy for locally advanced gastric cancer: a retrospective multicenter study. *World J Surg Oncol*. 2021;19:206.
22. van der Veen A, Ramaekers M, Marsman M, et al. Pain and opioid consumption after laparoscopic versus open gastrectomy for gastric cancer: a secondary analysis of a multicenter randomized clinical trial (LOGICA-trial). *J Gastrointest Surg*. 2023;27:2057-2067.
23. Kössler-Ebs JB, Grummich K, Jensen K, et al. Incisional hernia rates after laparoscopic or open abdominal Surgery—a systematic review and meta-analysis. *World J Surg*. 2016;40(10):2319-2330.
24. Rawla P, Barsouk A. Epidemiology of gastric cancer: global trends, risk factors and prevention. *Prz Gastroenterol*. 2019;14(1):26-38.
25. Integraal Kankercentrum Nederland. Slokdarm—en maagkanker in Nederland. 2021.
26. Terashima M, Yoshikawa T, Boku N, et al. Current status of perioperative chemotherapy for locally advanced gastric cancer and JCOG perspectives. *Jpn J Clin Oncol*. 2020;50(5):528-534.
27. Di Carlo S, Siragusa L, Fassari A, et al. Laparoscopic versus open total gastrectomy for locally advanced gastric cancer: short and long-term results. *Curr Oncol*. 2022;29(11):8442-8455.
28. van der Wielen N, Daams F, Rosati R, et al. Three-year survival and distribution of lymph node metastases in gastric cancer following neoadjuvant chemotherapy: results from a European randomized clinical trial. *Surg Endosc*. 2023;37(9):7317-7324.
29. Tsekrekos A, Vossen LE, Lundell L, et al. Improved survival after laparoscopic compared to open gastrectomy for advanced gastric cancer: a Swedish population-based cohort study. *Gastric Cancer*. 2023;26(3):467-477.
30. Kim YW, Baik YH, Yun YH, et al. Improved quality of life outcomes after laparoscopy-assisted distal gastrectomy for early gastric cancer: results of a prospective randomized clinical trial. *Ann Surg*. 2008;248(5):721-727.
31. Avery K, Hughes R, McNair A, Alderson D, Barham P, Blazeby J. Health-related quality of life and survival in the 2 years after surgery for gastric cancer. *Eur J Surg Oncol*. 2010;36(2):148-154.
32. van der Sluis PC, Tagkalos E, Hadzijusufovic E, et al. Robot-assisted minimally invasive esophagectomy with intrathoracic anastomosis (Ivor Lewis): promising results in 100 consecutive patients (the European experience). *J Gastrointest Surg*. 2021;25(1):1-8.
33. Jones LR, Zwart MJW, Molenaar IQ, et al. Robotic pancreatoduodenectomy: patient selection, volume criteria, and training programs. *Scand J Surg*. 2020;109(1):29-33.
34. Brenkman HJF, Parry K, van Hillegersberg R, Ruurda JP. Robot-assisted laparoscopic hiatal hernia repair: promising anatomical and functional results. *J Laparoendosc Adv Surg Tech A*. 2016;26(6):465-469.
35. Kim YM, Hyung WJ. Current status of robotic gastrectomy for gastric cancer: comparison with laparoscopic gastrectomy. *Updates Surg*. 2021;73(3):853-863.
36. Ojima T, Nakamura M, Hayata K, et al. Short-term outcomes of robotic gastrectomy vs laparoscopic gastrectomy for patients with gastric cancer: a randomized clinical trial. *JAMA Surg*. 2021;156(10):954-963.

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