



Introduction of minimally invasive surgery for distal and total gastrectomy: a population-based study



E.C. Gertsen^a, H.J.F. Brenkman^a, M.F.J. Seesing^a, L. Goense^{a, b}, J.P. Ruurda^a,
R. van Hilleberg^{a, *}, on behalf of the Dutch Upper Gastrointestinal Cancer Audit (DUCA) group

^a Department of Surgery, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands

^b Department of Radiation Oncology, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands

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ABSTRACT

Background: Minimally invasive gastrectomy has been introduced in Western populations during the last decade. As minimally invasive distal gastrectomy (MIDG) versus total gastrectomy (MITG) are procedures with a different complexity, outcomes may differ. The aim of this population-based cohort study was to evaluate the safety of MIDG and MITG.

Materials and methods: All patients who underwent potentially curative gastrectomy for gastric adenocarcinoma were included from the Dutch Upper GI Cancer Audit (2011–2016). Propensity score matching was applied to create comparable groups of patients receiving open distal gastrectomy (ODG) versus MIDG and open total gastrectomy (OTG) versus MITG, using patient and tumor characteristics. Postoperative outcomes and short-term oncological outcomes were appraised.

Results: Of the 1970 eligible patients, 1138 underwent distal gastrectomy and 832 underwent total gastrectomy. For distal gastrectomy, 390 ODG were matched to 288 MIDG patients. Although overall postoperative morbidity and mortality were similar, patients who underwent MIDG encountered less intra-abdominal abscesses (4% vs. 1%, $p = 0.039$) and wound complications (6% vs. 2%, $p = 0.021$). The median hospital stay was shorter after MIDGs (9 vs. 7 days, $p < 0.001$). For total gastrectomy, 323 OTG patients were matched to 258 MITG patients. Overall postoperative morbidity, mortality and hospital stay were similar, whereas the anastomotic leakage rate was higher after MITGs (11% vs. 17%, $p = 0.030$). Short-term oncological outcomes between both groups were equal for distal and total gastrectomy.

Conclusion: Benefits of MIG during the early introduction were demonstrated for distal gastrectomy but not for total gastrectomy. An increased anastomotic leakage rate was encountered for MITG.

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Introduction

Gastric cancer is the fifth most common type of malignancy worldwide and the third leading cause of cancer-related death [1]. In the Netherlands, approximately 1200 new gastric cancer patients are identified yearly, of which nearly 500 undergo curative treatment [2,3].

Gastrectomy with lymphadenectomy is the cornerstone of curative treatment for gastric cancer, potentially combined with

perioperative chemotherapy [4,5]. Open gastrectomy is the standard surgical procedure worldwide [3,6]. Several Asian trials have demonstrated benefits of minimally invasive gastrectomy, including decreased postoperative morbidity and shorter hospital stay [7]. Minimally invasive gastrectomy has been performed increasingly in the Netherlands, representing 58% of all gastrectomies in 2016 [8]. Recently, it was demonstrated by a Dutch research group that in a Western population-based cohort study, overall morbidity and mortality occurring after minimally invasive gastrectomy were similar with open gastrectomy, but minimally invasive gastrectomy embraced the additional advantages of fewer wound complications and shorter hospitalization [9].

In Western countries, total gastrectomy and distal gastrectomy are the most frequently performed types of gastric resection [3]. It

* Corresponding author. Department of Surgery, Division Cancer Center, University Medical Center Utrecht, Heidelberglaan 100, Utrecht, 3508 GA, The Netherlands.

E-mail address: R.vanHilleberg@umcutrecht.nl (R. van Hilleberg).

is known that total gastrectomy is a more extensive and difficult procedure compared to distal gastrectomy, resulting in longer operative time, more estimated blood loss and a higher risk of postoperative complications [10–13]. Because most Western studies did not make a distinction between distal and total gastrectomy [14,15], the aim of the present study is to evaluate the safety of the introduction of minimally invasive distal gastrectomy (MIDG) and minimally invasive total gastrectomy (MITG) in the Netherlands.

Methods

Study design

This population-based cohort study included data from the Dutch Upper GI Cancer Audit (DUCA), a prospective nationwide registration of all patients undergoing surgery with the intention of resection for gastroesophageal cancer. The DUCA is part of the Dutch Institute for Clinical Auditing (DICA) that organizes national audits in a uniform format. It does so by requiring hospitals that perform gastric cancer surgery (varying from 36 hospitals in 2011 to 22 hospitals in 2016, due to centralization), to annually provide data which include patient and tumor characteristics, items regarding processes of care and clinical and pathological outcomes of surgery. An independent team of data managers performed an in-depth quality investigation on a random data sample, which showed a complete and reliable data entry in all participating hospitals [3]. This study was approved by the scientific committee of the DUCA and no ethical approval or informed consent was required under Dutch law.

Patient population

All patients who underwent elective gastrectomy with curative intent for gastric adenocarcinoma (cT1–4a-x, N0–3-x, M0–x) in the period 2011–2016 were included from the DUCA. Patients in which no lymphadenectomy was performed or no Roux-en Y or Billroth reconstruction was created, were excluded, as were the patients with registered data not compatible with gastrectomy. Patients were staged and treated according to the Dutch national guidelines [4]. Staging consists of gastroscopy and computed tomography (CT) of the thorax and abdomen [16]. Before its recent implementation in the nationwide guidelines in July 2016 [16], ¹⁸F fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT and staging laparoscopy were not routinely performed. Treatment with curative intent was defined as gastrectomy and lymphadenectomy, with or without perioperative chemotherapy, which was only offered to patients with an advanced tumor (cT2+ or N+) deemed fit enough to tolerate chemotherapy according or comparable to the MAGIC trial [5,17]. As recommended in the Dutch national guidelines, the surgical procedure consisted of (sub)total gastrectomy with, if deemed necessary (in case of advanced stage), a modified D2 lymphadenectomy (without pancreaticosplenectomy), according to the Japanese Gastric Cancer Treatment Guidelines [18]. Subtotal gastrectomies consisted of distal gastrectomies with the exception of a few. Tumors were classified according to the 7th edition of the American Joint Committee on Cancer TNM staging system [19].

Outcome measures

Patient, tumor and hospital characteristics were appraised. Postoperative outcomes (e.g. morbidity, re-interventions, mortality and recovery) and histopathological characteristics were

analyzed. Overall morbidity was divided into four groups: i) intra-abdominal complications including anastomotic leakage; ii) wound complications including infection/abscess and fascia dehiscence; iii) non-surgical complications including pulmonary, cardiac, thromboembolic, neurologic and urologic complications; iv) other complications (Tables 3 and 4). All complications were scored according to the standards of the DUCA, provided via online information [20].

Statistical analysis

A propensity score matched analysis was used to balance observed covariates between open and minimally invasive surgery for both the distal and total gastrectomy group. To enhance matching, missing patient and treatment-related characteristics were imputed. Missing data were considered at random and handled using imputation with the iterative Markov chain Monte Carlo method (5 iterations) [19]. The frequency of missing values per variable before imputation is presented in Tables 1 and 2.

In the current study, the propensity score was the conditional probability to undergo open or minimally invasive surgery based on all the patient and treatment-related characteristics mentioned in Tables 1 and 2. Propensity scores were calculated for all patients using a non-parsimonious multivariable logistic regression model. First 1:1 nearest-neighbor matching without replacement was performed within a caliper width of 0.25 multiplied by the standard deviation of the logit propensity score. Then a second-level match (1:2) was added among the remaining patients. Balance in patient and treatment-related characteristics was measured using the standardized mean difference; differences of less than 10% represent adequate balance [20].

IBM SPSS Statistics version 23.0 (IBM, Armonk, New York, USA) and R 3.1.2 open-source software (<http://www.R-project.org>; 'MatchIt' and 'optmatch' packages) were used for statistical analysis. To identify differences in postoperative and histopathological outcomes, categorical parameters were compared using the Chi-square test, and the student's t-test was used for continuous variables. Logarithmic transformation was applied for variables with a non-parametric distribution. Statistical significance was acknowledged when the p-value was below 0.05.

Results

Study population

During the study period, 2154 patients underwent a gastrectomy with curative intent for gastric adenocarcinoma in the Netherlands. Of these patients, 184 patients were excluded, because no lymphadenectomy was performed (n = 72) or no Roux-en Y or Billroth reconstruction was made (n = 99). In addition, patients who were registered as minimally invasive thoracic surgery were excluded (n = 3), as were the patients of whom it was unclear or deviant where the anastomosis was located (n = 10). Of the 1970 remaining patients, 1138 underwent distal and 832 underwent total gastrectomy. After propensity score matching, 390 ODG patients were matched to 288 MIDG patients (Table 1). In the total gastrectomy group, 581 patients remained after PSM, 323 receiving OTG and 258 receiving MITG (Table 2).

In both the distal and total gastrectomy group, most of the patients were male and had an ASA II classification. The most common cT-stage was cT3 tumor, the majority of the patients was staged as N0-stage, and around 50% of patients in both groups was treated with neoadjuvant chemotherapy.

Table 1

Baseline characteristics of the original and propensity score matched cohort of patients who underwent distal gastrectomy.

Patient characteristics	Original cohort (n = 1138)			Missing values (%)	PSM cohort ^a (n = 678)		
	ODG n = 761 (%)	MIDG n = 377 (%)	SMD		ODG n = 390 (%)	MIDG n = 288 (%)	SMD
Age, years (mean ± SD)	70.6 ± 11.0	69.8 ± 11.0	7.0	0 (0)	70.4 ± 10.9	70.4 ± 10.7	0.5
BMI, kg/m² (mean ± SD)	25.3 ± 4.2	25.3 ± 4.3	0.4	35 (3)	25.3 ± 4.1	25.4 ± 4.2	0.7
Gender			7.7	0 (0)			0.4
Male	465 (61)	216 (57)			243 (62)	176 (61)	
Female	296 (39)	161 (43)			147 (38)	112 (39)	
ASA-classification			4.2	14 (1)			1.6
I	91 (12)	41 (11)			49 (13)	36 (13)	
II	404 (54)	217 (58)			213 (55)	160 (56)	
III	246 (33)	110 (30)			121 (31)	88 (31)	
IV	10 (1)	5 (1)			7 (2)	4 (1)	
Comorbidities				0 (0)			
Cardiac	259 (34)	119 (32)	5.3		130 (33)	99 (34)	3.4
Vascular	312 (41)	180 (48)	13.5		164 (42)	135 (47)	5.9
Diabetes	126 (17)	81 (22)	12.0		67 (17)	58 (20)	3.8
Pulmonary	131 (17)	59 (16)	4.3		70 (18)	50 (17)	<0.1
cT-stage			1.2	307 (27)			4.7
T1	56 (10)	37 (13)			36 (9)	42 (15)	
T2	201 (37)	94 (33)			153 (39)	87 (30)	
T3	268 (49)	141 (50)			184 (47)	150 (52)	
T4	24 (4)	10 (4)			17 (4)	9 (3)	
cN-stage			1.0	162 (14)			<0.1
N0	438 (68)	219 (67)			261 (69)	196 (70)	
N1	170 (26)	76 (23)			99 (26)	63 (22)	
N2	35 (5)	27 (8)			18 (5)	18 (6)	
N3	6 (1)	5 (2)			3 (1)	4 (1)	
Neoadjuvant treatment				0 (0)			
None	379 (50)	169 (45)	10.0		177 (45)	137 (48)	7.0
Chemotherapy	379 (50)	203 (54)	8.1		212 (54)	150 (52)	7.0
Chemoradiotherapy	2 (<1)	5 (1)	9.2		1 (<1)	1 (<1)	<0.1
Year of surgery				0 (0)			
2011	127 (17)	13 (3)	40.4		24 (6)	13 (5)	7.2
2012	152 (20)	4 (1)	184.4		10 (3)	4 (1)	3.4
2013	178 (23)	30 (8)	57.0		57 (15)	30 (10)	1.9
2014	142 (19)	91 (24)	12.8		137 (35)	85 (30)	4.0
2015	93 (12)	105 (28)	34.8		93 (24)	82 (29)	1.9
2016	69 (9)	134 (36)	55.2		69 (18)	74 (26)	4.4
Volume			55.1	0 (0)			4.3
0–20	476 (63)	136 (36)			167 (43)	113 (39)	
>20	285 (38)	241 (64)			223 (57)	175 (61)	

ASA: American Society of Anesthesiologists, BMI: Body Mass Index, MIDG: Minimally Invasive Distal Gastrectomy, ODG: Open Distal Gastrectomy, PSM: Propensity Score Matched, SMD: Standardized Mean Difference.

Percentages may not add up to 100% due to rounding.

^a Dataset after imputation.

Postoperative outcomes

For distal gastrectomy, the postoperative outcomes of the original and the PSM cohort of the patients are shown in Table 3. Results are henceforth given from the propensity score analysis. In 24 patients (9%) conversion of MIDG to ODG occurred, due to extent of the tumor (18%), limited accessibility (73%) or intraoperative complications (9%). Although overall postoperative morbidity (37% vs. 34%, $p = 0.422$) and mortality (both 3%, $p = 0.817$) were similar, patients who underwent MIDG encountered less intra-abdominal abscesses (4% vs. 1%, $p = 0.039$), chyle leakage (2% vs. <1%, $p = 0.036$), wound infections (6% vs. 2%, $p = 0.021$) and fascia dehiscence (2% vs. 0%, $p = 0.034$). In addition, significant less neurological complications (i.e. delirium) were found in the MIDG group (5% vs. 2%, $p = 0.041$). The anastomotic leakage rate (3% vs. 3%) and number of re-interventions (12% vs. 11%) were equal between the groups. The median hospital stay was shorter after MIDG (9 vs. 7 days, $p < 0.001$), whereas the median ICU stay was equal (both 0 days).

For total gastrectomy, Table 4 presents the postoperative outcomes of the original and the PSM cohort. Conversions occurred in 11% of patients undergoing MITG, caused by extent of the tumor

(41%), limited accessibility (44%) or intraoperative complications (15%). After PSM, overall postoperative morbidity (45% vs. 47%, $p = 0.643$) and mortality (6% vs. 8%, $p = 0.291$) were similar between OTG and MITG, whereas the anastomotic leakage rate was higher after MITG (11% vs. 17%, $p = 0.030$). On the other hand, less chyle leakage was seen in the MITG group (5% vs. 1%, $p = 0.016$). Wound complications, medical complications and re-interventions were similar between the OTG and MITG group. Although the length of hospital stay was similar between both groups (both 10 days, $p = 0.608$), the median ICU stay was shorter in the MITG group (1 day vs. 0 days, $p = 0.001$).

Surgical and histopathological outcomes

For distal gastrectomy (Supplementary file S1), the median lymph node yield was 19 nodes after ODG and 21 nodes after MIDG ($p = 0.214$). A radical resection was realized in 93% after ODG and 94% after MIDG ($p = 0.634$).

After total gastrectomy (Supplementary file S2), the median lymph node yield was similar between OTG and MITG (21 vs. 22 nodes, $p = 0.425$). In 89% of the patients in both groups, a radical resection was achieved ($p = 0.911$).

Table 2
Baseline characteristics of the original and propensity score matched cohort of patients who underwent total gastrectomy.

Patient characteristics	Original cohort (n = 832)			Missing values (%)	PSM cohort ^a (n = 581)		
	OTG n = 518 (%)	MITG n = 314 (%)	SMD		OTG n = 323 (%)	MITG n = 258 (%)	SMD
Age, years (mean ± SD)	65.9 ± 12.4	66.0 ± 12.0	0.3	3 (<1)	66.2 ± 12.1	65.9 ± 12.1	0.3
BMI, kg/m² (mean ± SD)	25.4 ± 4.5	25.5 ± 4.8	4.2	13 (2)	25.6 ± 4.7	25.6 ± 5.0	0.3
Gender			21.5	0 (0)			0.8
Male	357 (69)	183 (58)			214 (66)	164 (64)	
Female	161 (31)	131 (42)			109 (34)	94 (36)	
ASA-classification			15.7	3 (<1)			0.3
I	100 (19)	45 (14)			57 (18)	44 (17)	
II	296 (58)	182 (58)			188 (58)	153 (59)	
III	117 (23)	84 (27)			77 (24)	60 (23)	
IV	2 (<1)	3 (1)			1 (<1)	1 (<1)	
Comorbidities				0 (0)			
Cardiac	139 (27)	94 (30)	6.8		87 (27)	68 (26)	1.7
Vascular	190 (37)	122 (39)	4.5		131 (41)	102 (40)	1.2
Diabetes	66 (13)	54 (17)	11.8		40 (12)	39 (15)	6.2
Pulmonary	75 (15)	60 (19)	11.8		52 (16)	41 (16)	0.5
cT-stage			12.1	184 (22)			2.4
T1	33 (8)	12 (5)			24 (7)	14 (5)	
T2	98 (25)	53 (21)			84 (26)	60 (23)	
T3	234 (59)	170 (68)			186 (58)	169 (66)	
T4	30 (8)	18 (7)			29 (9)	15 (6)	
cN-stage			0.6	124 (15)			2.0
N0	241 (56)	143 (51)			163 (53)	127 (51)	
N1	128 (30)	91 (33)			98 (32)	80 (32)	
N2	51 (12)	37 (13)			41 (13)	36 (14)	
N3	8 (2)	9 (3)			7 (2)	8 (3)	
Neoadjuvant treatment				1 (<1)			
None	168 (33)	86 (27)	11.7		107 (33)	73 (28)	0.9
Chemotherapy	335 (65)	219 (70)	11.0		206 (64)	177 (69)	1.7
Chemoradiotherapy	14 (3)	9 (3)	1.0		10 (3)	8 (3)	2.3
Year of surgery				0 (0)			3.6
2011	81 (16)	0 (0)	n.a.		0 (0)	0 (0)	n.a.
2012	95 (18)	9 (3)	92.6		15 (5)	9 (4)	3.5
2013	116 (22)	53 (17)	14.7		89 (28)	53 (21)	9.8
2014	90 (17)	94 (30)	27.4		89 (28)	69 (27)	3.0
2015	65 (13)	80 (26)	29.6		63 (20)	61 (24)	3.6
2016	71 (14)	78 (25)	25.7		67 (21)	66 (26)	6.7
Volume			39.7	0 (0)			1.2
0-20	342 (66)	145 (46)			163 (51)	124 (48)	
>20	176 (34)	169 (54)			160 (50)	134 (52)	

ASA: American Society of Anesthesiologists, BMI: Body Mass Index, MITG: Minimally Invasive Total Gastrectomy, n.a.: not applicable, OTG: Open Total Gastrectomy, PSM: Propensity Score Matched, SMD: Standardized Mean Difference.

Percentages may not add up to 100% due to rounding.

^a Dataset after imputation.

Discussion

This is the first population-based cohort study to evaluate the safety of minimally invasive surgery for distal and total gastrectomy in a Western population. MIDG was associated with less intra-abdominal abscesses and wound complications and a shorter hospital stay compared to ODG. After MITG, the anastomotic leakage rate was significantly higher in comparison with OTG. Remarkably, the frequently reported shorter hospitalization after minimally invasive surgery was not demonstrable for MITG. Overall postoperative morbidity, mortality, radicality and lymph node yield were similar between minimally invasive and open surgery for both distal and total gastrectomy. Finally, this study demonstrates a diminished rate of chyle leakage after minimally invasive surgery for both distal and total gastrectomy, and less neurological complications after MIDG compared with ODG.

Due to its greater complexity, total gastrectomy is more often associated with a higher risk of complications, especially concerning anastomotic complications [12,13]. This is probably caused by a more technically challenging anastomotic technique involving the esophagus, combined with a different anatomical position and

vascularization. This difference stresses the importance of separate analysis for distal and total gastrectomy.

The surgical safety and oncologic outcomes of MIDG compared with conventional ODG were previously evaluated in two large Asian trials. In the CLASS-01 trial, a Chinese multicenter trial of 1039 patients with advanced cancer, the overall postoperative morbidity rate was comparable between the MIDG (15.2%) and ODG (12.9%) group. Moreover, no significant differences were reported for anastomotic leakage (1.9% vs. 0.6%), postoperative mortality (0.4% vs. 0%) or short-term oncological outcomes. However, patients that underwent MIDG had a shorter postoperative hospital stay. Results of the KLASS-01 trial, a Korean multicenter trial including 1384 patients with early cancer, demonstrate a lower postoperative morbidity rate (13.7% vs. 18.9%) and shorter hospitalization (7.2 vs. 8.0 days) after MIDG. No difference in anastomotic leakage (0.7% vs. 1.0%) or postoperative mortality (0.6% vs. 0.3%) was reported. However, the lymph node yield was less favorable for MIDG in this trial (40.5 vs. 43.3 lymph nodes). In comparison to both Asian trials, the current study found similar postoperative morbidity and mortality rates between MIDG and ODG (with advantages of

Table 3

Postoperative outcomes of the original and propensity score matched cohort of patients who underwent distal gastrectomy.

Postoperative outcomes	Original cohort (n = 1138)			PSM cohort (n = 678)		
	ODG n = 761 (%)	MIDG n = 377 (%)	p-value	ODG n = 390 (%)	MIDG n = 288 (%)	p-value
Conversions	–	33 (9)	–	–	24 (9)	–
Morbidity	269 (35)	127 (34)	0.580	143 (37)	97 (34)	0.422
Intra-abdominal complications						
Anastomotic leakage ^a	25 (3)	16 (4)	0.414	10 (3)	10 (3)	0.490
Abscess	30 (4)	7 (2)	0.062	16 (4)	4 (1)	0.039
Bleeding	11 (1)	5 (1)	0.872	5 (1)	4 (1)	0.904
Pancreatitis, leakage or fistula	1 (<1)	2 (1)	0.217	1 (<1)	1 (<1)	0.829
Chyle leakage	14 (2)	2 (1)	0.077	9 (2)	1 (<1)	0.036
Trauma of the gut	6 (1)	7 (2)	0.110	4 (1)	4 (1)	0.665
Wound complications						
Infection/abscess	36 (5)	6 (2)	0.008	22 (6)	6 (2)	0.021
Fascia dehiscence	15 (2)	0 (0)	0.006	6 (2)	0 (0)	0.034
Non-surgical complications						
Pulmonary ^b	97 (13)	42 (11)	0.436	45 (12)	35 (12)	0.806
Cardiac ^c	44 (6)	19 (5)	0.606	22 (6)	15 (5)	0.806
Thromboembolic ^d	5 (1)	7 (2)	0.062	1 (<1)	4 (1)	0.088
Neurologic ^e	34 (5)	11 (3)	0.207	20 (5)	6 (2)	0.041
Urologic ^f	24 (3)	20 (5)	0.076	15 (4)	15 (5)	0.394
Other	89 (33)	45 (35)	0.645	37 (26)	35 (36)	0.090
Re-interventions^g	96 (13)	50 (13)	0.758	46 (12)	32 (11)	0.783
Mortality^h	34 (5)	12 (3)	0.300	11 (3)	9 (3)	0.817
Recovery						
ICU stay (median, IQR)	0 (0–54)	0 (0–40)	<0.001	0 (0–44)	0 (0–56)	<0.001
Hospital stay (median, IQR)	9 (1–124)	7 (2–164)	<0.001	9 (3–124)	7 (2–164)	<0.001
Readmissions ⁱ	72 (10)	44 (12)	0.246	38 (10)	31 (11)	0.664

ICU: Intensive Care Unit, IQR: interquartile range, MIDG: Minimally Invasive Distal Gastrectomy, ODG: Open Distal Gastrectomy, PSM: Propensity Score Matched.

^a Any clinically or radiologically proven anastomotic leakage.^b Pneumonia, pleural effusion, respiratory failure, pneumothorax and/or acute respiratory distress syndrome (ARDS).^c Supra- and ventricular arrhythmia, myocardial infarction and/or heart failure.^d Pulmonary embolism, deep venous thrombosis and/or cerebrovascular accident.^e Acute delirium.^f Acute renal insufficiency, acute kidney failure requiring dialysis, urine tract infection and/or urine retention.^g Re-intervention (radiological/endoscopic/surgical).^h Death during initial hospital admission or within 30 days after surgery.ⁱ Readmission to hospital within 30 days after initial discharge.

MIDG in wound complications and abscesses), and a shorter postoperative hospital stay in favor of MIDG. Fortunately, in contrast to the KLASS-01 trial, the current study found a similar lymph node yield between the two procedures. On the other hand, compared to the Asian trials, the postoperative morbidity and mortality rates were higher in our study [7,21]. Firstly, these discrepancies with the CLASS-01 trial might be clarified by differences in patient characteristics between populations (with more comorbidities and overweight found in the Western population), whereas the discrepancies with the KLASS-01 trial might be explained by differences in tumor characteristics (less advanced tumors in the Korean population) [22]. Secondly, population-based studies frequently reflect other populations compared to randomized trials. Furthermore, Asian centers tend to see a substantially higher number of cases annually due to a higher incidence of gastric cancer. This allows for dedicated specialized gastric surgeons to become more experienced in performing gastrectomies. The shorter postoperative hospital stay compared to the CLASS-01 trial might be explained by the Enhanced Recovery After Surgery (ERAS) program, which most patients were subjected to in the current study [23].

The evidence for the safety, feasibility and benefits of MITG is scarce, in contrast to MIDG. Only a few retrospective, mostly Asian, studies have reported that MITG is safe and feasible [12,13,24,25]. However, the current study shows less advantages of MITG. The frequently reported benefits of minimally invasive surgery, such as less wound infection, less intra-abdominal abscesses and shorter hospital stay were not demonstrated for MITG. Moreover, a higher

rate of anastomotic leakage was found. These findings were also described in a previous study that demonstrated a significantly higher anastomotic leakage rate and a tendency to a higher incidence of re-interventions after MITG [13]. The current findings could be explained by a less steep and more extensive learning curve for MITG compared to MIDG. Minimally invasive gastrectomy has only been introduced in the Netherlands in the past decade and since its introduction, surgeons have been adapting these procedures and are suspected to be halfway through the learning curve. Minimally invasive gastrectomy has been progressively performed with 4% being accomplished in 2011, increasing to 58% in 2016. The findings on MITG imply that more caution should be exercised when performing this procedure. Furthermore, it might be appropriate to organize more dedicated trainings for MITG, especially considering that a previous study concluded that approximately 100 MITGs should be performed to complete the learning curve [26]. In the Netherlands, training of minimally invasive gastrectomy consists of a hands-on course, which is preceded by lectures reviewing anatomy, operative technique and perioperative management for minimally invasive gastrectomy. This course has been adopted as an official European Society of Surgical Oncology Course (ESSO) [27]. After that, a structured proctoring program is offered by expert surgeons starting with a case observation and followed by proctoring on site during the first surgical procedures [28]. There is much discrepancy on the number of procedures required for completion of the learning curve and Western studies on this topic are scarce [26,29].

Following the example of Asian centers and studies, the results

Table 4
Postoperative outcomes of the original and propensity score matched cohort of patients who underwent total gastrectomy.

Postoperative outcomes	Original cohort (n = 832)			PSM cohort (n = 581)		
	OTG n = 518 (%)	MITG n = 314 (%)	p-value	OTG n = 323 (%)	MITG n = 258 (%)	p-value
Conversions	—	34 (11)		—	27 (11)	—
Morbidity	219 (42)	145 (46)	0.272	144 (45)	120 (47)	0.643
Intra-abdominal complications						
Anastomotic leakage ^a	53 (10)	48 (15)	0.030	34 (11)	43 (17)	0.030
Abscess	26 (5)	16 (5)	0.961	14 (4)	14 (5)	0.541
Bleeding	4 (1)	4 (1)	0.472	1 (<1)	3 (1)	0.217
Pancreatitis, leakage or fistula	3 (1)	2 (1)	0.917	3 (1)	2 (1)	0.842
Chyle leakage	17 (3)	3 (1)	0.034	15 (5)	3 (1)	0.016
Trauma of the gut	8 (2)	4 (1)	0.751	5 (2)	3 (1)	0.692
Wound complications						
Infection/abscess	17 (3)	4 (1)	0.073	10 (3)	4 (2)	0.227
Fascia dehiscence	4 (1)	3 (1)	0.779	2 (1)	3 (1)	0.481
Non-surgical complications						
Pulmonary ^b	89 (17)	63 (20)	0.297	58 (18)	52 (20)	0.502
Cardiac ^c	33 (6)	17 (5)	0.574	27 (8)	13 (5)	0.116
Thromboembolic ^d	8 (2)	9 (3)	0.191	4 (1)	7 (3)	0.195
Neurologic ^e	23 (4)	17 (5)	0.524	13 (4)	14 (5)	0.425
Urologic ^f	13 (3)	9 (3)	0.756	6 (2)	5 (2)	0.944
Other	46 (21)	35 (24)	0.496	33 (23)	27 (23)	0.912
Re-interventions^g	91 (18)	72 (23)	0.059	60 (19)	59 (23)	0.203
Mortality^h	26 (5)	22 (7)	0.233	18 (6)	20 (8)	0.291
Recovery						
ICU stay (median, IQR)	1 (0–93)	0 (0–66)	0.001	1 (0–93)	0 (0–66)	0.001
Hospital stay (median, IQR)	10 (1–207)	9 (2–197)	0.001	10 (1–132)	10 (2–197)	0.608
Readmissions ⁱ	66 (13)	40 (13)	0.999	44 (14)	34 (13)	0.876

ICU: Intensive Care Unit, IQR: interquartile range, MITG: Minimally Invasive Total Gastrectomy, OTG: Open Total Gastrectomy, PSM: Propensity Score Matched.

^a Any clinically or radiologically proven anastomotic leakage.

^b Pneumonia, pleural effusion, respiratory failure, pneumothorax and/or acute respiratory distress syndrome (ARDS).

^c Supra- and ventricular arrhythmia, myocardial infarction and/or heart failure.

^d Pulmonary embolism, deep venous thrombosis and/or cerebrovascular accident.

^e Acute delirium.

^f Acute renal insufficiency, acute kidney failure requiring dialysis, urine tract infection and/or urine retention.

^g Re-intervention (radiological/endoscopic/surgical).

^h Death during initial hospital admission or within 30 days after surgery.

ⁱ Readmission to hospital within 30 days after initial discharge.

of this study might call for further centralization of gastric cancer surgery in the West. In the Netherlands, centers performing gastrectomy should achieve a minimum of 20 gastrectomies a year, but herein no distinction is made between total and distal gastrectomy. Bearing in mind the possible longer learning curve for MITG, it might be justifiable to further increase the annual minimum number of gastrectomies overall per center, or to set a minimum number of annual total gastrectomies per center as well.

As in some other studies, the current study also shows less frequent chyle leakage after MIDG and MITG compared to open resection, which might be explained by the improved visibility during minimally invasive gastrectomy [9,30]. Relating to the higher number of neurological complications (i.e. delirium) following OGD, the explanation might be found in the significantly higher rates of wound complications and higher pain scores associated with open gastrectomy [31–33].

The current study may have some limitations as selection bias or residual confounding, for which PSM cannot adjust, may have affected the results. Furthermore, the current study was not able to report data on anastomosis techniques, surgeon volume, disease progression and survival, as these were lacking from the DUCA.

In conclusion, benefits of minimally invasive gastrectomy during the early introduction can be demonstrated for distal but not for total gastrectomy. Especially, a higher anastomotic leakage rate was found after MITG compared with OTG.

Conflicts of interest statement

E.C. Gertsen, H.J.F. Brenkman, M.F.J. Seesing, L.Goense, J.P.

Ruurda and R. van Hillegersberg have no conflicts of interest or financial ties to disclose.

Human rights statement and informed consent

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. This study was performed with nationwide, anonymous data; thus, informed consent or substitute for it was waived by the ethical review board of the DUCA.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.ejso.2018.08.015>.

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