Surgical Oncology 35 (2020) 126–131

Contents lists available at ScienceDirect

Surgical Oncology

journal homepage: http://www.elsevier.com/locate/suronc

Non-curative gastrectomy for advanced gastric cancer does not result in additional risk of postoperative morbidity compared to curative gastrectomy

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ARTICLE INFO

Keywords:
Gastric cancer
Non-curative gastrectomy
Morbidity
Population-based

ABSTRACT

Background: Non-curative gastrectomy (nCG) for gastric cancer can be considered in selected cases to relieve symptoms. The aim of this study was to evaluate postoperative morbidity and mortality in patients who underwent nCG and compare these results with an intended curative gastrectomy (CG).

Materials and methods: All patients who underwent both nCG and CG in the Netherlands were included from the Dutch Upper GI Cancer Audit (2011–2016). In this population-based cohort study postoperative morbidity, mortality, readmissions and short-term oncological outcomes were appraised. Propensity score matching (PSM) was applied to create comparable groups of patients who underwent nCG versus CG, using patient and tumor characteristics.

Results: Of the 2202 eligible patients, 115 patients underwent nCG and 2087 underwent CG. After PSM, 115 nCG-patients were matched to 227 CG-patients. More conversions from laparoscopic to open surgery occurred during nCG (10·4 versus 2·6%, $p = 0{\cdot}007$). Although postoperative mortality was higher after nCG in the original cohort (9·6 versus 4·8%, $p = 0{\cdot}026$), after PSM there was no difference between groups (9·6 versus 7·0%, $p = 0{\cdot}415$). Postoperative morbidity, re-interventions and readmission rates did not differ significantly between groups. Resection of additional organs (30·4 versus 11·5%, $p < 0{\cdot}001$) and R+ resections (65·2 versus 12·3%, $p < 0{\cdot}001$) occurred more frequently during nCG.

Conclusions: nCG does not lead to additional postoperative risks compared to CG in patients with similar characteristics, and may be considered in fit patients with advanced gastric cancer. However, randomized trials evaluating potential (survival) benefits of nCG should be awaited.

1. Introduction

Gastric cancer is in fifth place on the list of most common types of malignancies worldwide and the third leading cause of cancer-related death [1]. In the Netherlands, approximately 500 out of 1200 newly diagnosed gastric cancer patients undergo curative treatment each year [2,3]. Curative treatment consists of gastrectomy with lymphadenectomy, preferably combined with perioperative chemotherapy [4,5]. Due to evolving preoperative staging modalities, such as 18 F-fluorodeoxyglucose positron emission tomography with computed tomography and staging laparoscopy, metastatic or irresectable disease might become an increasing entity. Patients with non-resectable or metastasized gastric cancer generally do not undergo surgical resection [6], but receive palliative systemic chemotherapy or best supportive care, leading to a median survival of 8 months [4,7]. In selected cases, non-curative gastrectomy (nCG) is considered to relieve symptoms, such as obstruction, pain or bleeding. In contrast to asymptomatic patients, symptom relief may outweigh the surgical risks in symptomatic patients.

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https://doi.org/10.1016/j.suronc.2020.08.018
Received 3 April 2020; Received in revised form 30 July 2020; Accepted 19 August 2020
Available online 21 August 2020

Some retrospective studies suggest that nCG increases survival compared to palliative chemotherapy, whereas a recent Asian trial (REGATTA), which randomly assigned asymptomatic patients with a single non-curable factor (metastasis to liver, peritoneum or para-aortic lymph nodes) to either solely chemotherapy or gastrectomy (without resection of metastases) followed by chemotherapy, found no benefit of gastrectomy [7–10]. However, it is well known that the Asian gastric cancer population differs from the Western population, as the latter present with more advanced tumors and less favorable patient characteristics, such as overweight, making it difficult to extrapolate these results. To date, the effect of nCG on long-term survival for Western patients is unknown. Moreover, nCG is known for its high mortality and morbidity rates and before making firm statements on long-term outcomes, it is relevant to evaluate short-term outcomes, such as mortality.

Little is known about the safety of non-curative resections compared to curative resections. The aim of this study is to investigate whether the postoperative outcomes differ between non-curative and curative gastrectomy (CG) to contribute to the existing literature supporting that nCG could be considered a valid option for selected patients suffering from advanced gastric cancer.

2. Materials and methods

2.1. Study design

In this population-based study, data of all patients undergoing surgery for gastric cancer were included from the Dutch Upper GI Cancer Audit (DUCA), which is a prospective nationwide registration. The DUCA is part of the Dutch Institute for Clinical Auditing (DICA), performing national audits in a uniform format. Hospitals are required to annually provide data that include patient and tumor-related characteristics, items regarding processes of care and clinical and pathological outcomes of surgery. A complete and reliable data entry was demonstrated by an independent team of data managers which performed an in-depth quality investigation [3]. This study was approved by the scientific committee of the DUCA and no ethical approval or informed consent was required under Dutch law.

2.2. Patient population

Between 2011 and 2016 all patients who underwent elective gastrectomy for gastric adenocarcinoma were extracted from the DUCA database. Tumors were classified according to the 7th edition of the American Joint Committee on Cancer TNM staging system [11]. Patients in which a prophylactic gastric resection was performed were excluded, as were patients in whom essential data were missing. According to the Dutch national guidelines, patients were staged with gastroscopy and computed tomography (CT) of the thorax and abdomen [12]. In patients with ≥cT2 or cN+, cM0 stage disease and who were deemed fit enough, curative treatment with perioperative chemotherapy equal or similar to the MAGIC trial regimen was started, followed by surgical resection [5, 13]. Surgical resection consisted of (sub)total gastrectomy, with a modified D2 lymphadenectomy (without pancreaticosplenectomy) according to the Japanese Gastric Cancer Treatment Guidelines [14]. In case of non-curative treatment, (sub)total gastrectomy with limited lymphadenectomy was performed.

2.3. Definition

The DUCA registers the intent of surgery as determined by the surgical team at two time points: (1) before the start of surgery, and (2) at the end of surgery. To evaluate outcomes of non-curative gastrectomy from a clinical decision-making point of view, this study defined non-curative gastrectomy as surgery with non-curable intent at one or both time points: patients in whom M1 disease or irresectability was preoperatively known or intraoperatively found. A curative gastrectomy was defined as not having the intent for non-curable surgery at both time points. At first, due to expected differences, three groups were created that consisted of (1) curative patients, (2) patients in whom cM1 disease was preoperatively known and (3) patients in whom irresectability or M1 disease was intraoperatively found. Since no significant differences were found between the non-curative groups, the two non-curable groups were merged for all analyses. As the DUCA registry lacks data on reasons for performing non-curative or palliative gastrectomy, it was chosen to name this latter group non-curative gastrectomy as palliative gastrectomy might imply treatment of symptoms.

2.4. Outcome measures

Patient characteristics (age, Body Mass Index (BMI), sex, American Society of Anesthesiologists (ASA) classification and comorbidities), treatment characteristics (neoadjuvant treatment, type of procedure and type of resection), postoperative characteristics (morbidity, re-interventions, mortality and recovery) and tumor-specific characteristics (TNM stage, Lauren classification, tumor differentiation, additional resections, radicality of the resection, and lymph node yield) were appraised. The conversion rate was assessed in both groups and was defined as any minimally invasive intended procedure, that was converted to an open procedure. Postoperative complications that were assessed included intra-abdominal complications (anastomotic leakage, abscesses, bleeding, pancreatic complications, chyle leakage and trauma of the gut), wound complications (infection/abscess and fascia dehiscence), non-surgical complications (including pulmonary, cardiac, thromboembolic, neurologic and urologic complications) and other complications. The definition of postoperative mortality and readmissions were: death during the initial hospital stay or within 30 days after surgery and readmissions within 30 days after discharge, respectively. All complications were scored according to the definitions of the DUCA that were online provided for all registrars [15].

2.5. Statistical analysis

Propensity score matching (PSM) was used to balance observed preoperative covariates between curative versus non-curative gastrectomy. In order to perform matching, missing patient and treatment-related characteristics were imputed. Missing data regarding inclusion and exclusion criteria were not imputed, resulting in exclusion of patients. Missing data were considered at random and handled using imputation with the iterative Markov chain Monte Carlo method (5 iterations) [16]. The frequency of missing values per variable before imputation are presented in Table 1.

A propensity score was calculated for each patient using a non-parsimonious multivariable logistic regression model based on all patient and treatment-related characteristics presented in Tables 1 and 2. In this context, the propensity score represents the conditional probability to undergo non-curative or curative gastrectomy. First, 1-to-1 nearest-neighbor matching without replacement was performed – using a caliper width of 0·25 multiplied by the standard deviation of the logit propensity score – to generate matched pairs of cases. Accordingly, a second level of matches (2:1) was added to the control group (curative gastrectomy). Balance in patient and treatment-related characteristics was assessed using the standardized difference of the mean; a differences of less than 10% indicates adequate covariate balance [17].

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. Categorical parameters (postoperative and histopathological outcomes) were compared using the Chi-square test (or Fisher's Exact test in case of cell counts less than 5), and for continuous variables the student's t-test was used. For variables with a non-parametric distribution logarithmic transformation was applied. A p-value below 0·05 was considered statistically significant.

Table 1
Baseline characteristics of the patients who underwent elective gastrectomy for gastric cancer.

	Original cohort (*n* = 2202)				Propensity score matched group* (*n* = 342)		
	Curative gastrectomy *n* = 2087 (%)	Non-curative gastrectomy *n* = 115 (%)	*SMD*	Initial missing values (%)	Curative gastrectomy *n* = 227 (%)	Non-curative gastrectomy *n* = 115 (%)	*SMD*
Age, years (mean ± SD)	68·5 ± 11·6	71·1 ± 11·4	22·4	3 (0·1)	71·5 ± 11·0	71·0 ± 11·4	4·5
BMI, kg/m2 (mean ± SD)	25·4 ± 4·4	25·0 ± 4·4	9·0	51 (2·3)	25·2 ± 4·8	25·0 ± 4·3	4·3
Gender (male, %)	1309 (62·7)	71 (61·7)	2·1	0 (0·0)	136 (59·9)	71 (61·7)	4·1
ASA-classification			28·1	21 (0·9)			0·0
I-II	1455 (69·7)	65 (56·5)			129 (56·8)	66 (57·4)	
III-IV	613 (29·4)	48 (41·7)			98 (43·2)	49 (42·6)	
Comorbidities				0 (0·0)			
Cardiac	645 (30·9)	32 (27·8)	6·5		65 (28·6)	32 (27·8)	2·2
Vascular	844 (40·4)	39 (33·9)	12·2		80 (35·2)	39 (33·9)	2·1
Diabetes	355 (17·0)	21 (18·3)	2·7		42 (18·5)	21 (18·3)	2·6
Pulmonary	341 (16·3)	15 (13·0)	8·2		28 (12·3)	15 (13·0)	3·0
cT-stage			53·8	550 (25·0)			3·6
T1-2	603 (28·9)	11 (9·6)			22 (9·7)	11 (9·6)	
T3-4	962 (46·1)	76 (66·1)			153 (67·4)	76 (66·1)	
Tx	522 (25·0)	28 (24·3)			52 (22·9)	28 (24·3)	
cN-stage			56·6	344 (15·6)			9·5
N0	1082 (51·8)	30 (26·1)			70 (30·8)	30 (26·1)	
N+	757 (36·2)	66 (57·4)			124 (54·6)	66 (57·4)	
Nx	248 (11·9)	19 (16·5)			33 (14·5)	19 (16·5)	
cM-stage			248·1	101 (4·6)			102·9
M0	1986 (95·2)	78 (67·8)			227 (100·0)	78 (67·8)	
M1	0 (0·0)	37 (32·2)			0 (0·0)	37 (32·2)	
Mx	101 (4·8)	0 (0·0)			n.a.	n.a.	
Neoadjuvant chemotherapy[a]			44·9	4 (0·2)			2·1
Yes	1229 (58·9)	41 (35·7)			83 (36·6)	41 (35·7)	
No	821 (39·3)	72 (62·6)			144 (63·4)	72 (62·6)	
Type of procedure (open, %)	1361 (65·2)	81 (70·4)	12·6	0 (0·0)	162 (71·4)	82 (71·3)	0·0
Type of resection			10·1	0 (0·0)			2·0
Total gastrectomy	901 (43·2)	44 (38·3)			88 (38·8)	44 (38·3)	
Distal gastrectomy	1186 (56·8)	71 (61·7)			139 (61·2)	71 (61·7)	

Percentages may not add up to 100% due to rounding. *Dataset after imputation. SMD of more than 10% indicate inadequate covariate balance. ASA: American Society of Anesthesiologists, BMI: Body Mass Index, n.a. not applicable, MIG: Minimally Invasive Gastrectomy, SMD: Standardized Mean Difference. a. In both groups <2% received neoadjuvant chemoradiotherapy.

3. Results

3.1. Study population

Between 2011 and 2016, 2237 patients underwent elective (sub) total gastrectomy for gastric adenocarcinoma in the Netherlands. Patients were excluded (n = 35), in case prophylactic or unknown resection was performed (n = 6) or when essential data was missing (n = 29). A total of 2087 patients underwent curative gastrectomy, whereas 115 patients underwent non-curative resection. Locations of the primary tumor in the original cohort were as follows: fundus (7·7%), corpus (30·9%), antrum (41·0%), pyloric (8·8%), whole stomach (5·7%), residual stomach (4·1%) and unknown (2·0%). In general, the CG group consisted of fitter patients (lower age, ASA classification and tumor stages) of whom the majority underwent neoadjuvant chemotherapy. In the CG group, 50% completed neoadjuvant chemotherapy, in the nCG this percentage was only 25%. Using PSM, 227 curative gastrectomy patients were matched to the 115 non-curative gastrectomy patients (Table 1). After PSM the balance among the two treatment groups improved substantially, creating two groups with comparable, nevertheless more frail patients. Regarding clinical M-stage, PSM was unable to create a balance, due to the fact that the curative group did not consist of M1 patients. The 67.8% M0 patients in the nCG were patients preoperatively known with a cT4b tumor or patients in whom irresectable or metastatic disease was intraoperatively found.

3.2. Postoperative outcomes

In Table 2 postoperative outcomes of both the original and the PSM cohort of patients are demonstrated. In the PSM cohort, conversion occurred in 10·4% of non-curative patients versus 2·6% in the curative group ($p = 0·007$), either caused by irresectability (in the majority of cases; 58·2%), accessibility or intraoperative complications. Regarding intra-abdominal and non-surgical complications, re-interventions, readmissions and hospital stay, no significant differences were found. A higher mortality rate was demonstrated after nCG compared to CG in the original cohort (9·6 versus 4·8%, $p = 0·026$), which was not found after PSM (9·6 versus 7·0%, $p = 0·415$).

3.3. Surgical and histopathological outcomes

Patients in the non-curative group had significantly more advanced disease, with more pT4 tumors and more pN + stage disease, more diffuse tumors and more additional organs were resected (Table 3). During nCG more (partial) splenectomies (6·1 versus 1·8%, $p = 0·002$), hepatectomies (3·5 versus 1·2%, $p = 0·061$) pancreatectomies (10·4 versus 2·5%, $p < 0·001$) and resections of the mesocolon (7·8 versus 2·7%, $p = 0·002$) were performed, in comparison with CG. In addition, less favorable oncological outcomes (R+ resections, less lymph nodes) were found in the nCG group.

4. Discussion

This population-based study evaluated postoperative outcomes after

Table 2
Postoperative outcomes of the patients who underwent elective gastrectomy for gastric cancer.

	Original cohort (n = 2202)			Propensity score matched group* (n = 342)		
	Curative gastrectomy n = 2087 (%)	Non-curative gastrectomy n = 115 (%)	p-value	Curative gastrectomy n = 227 (%)	Non-curative gastrectomy n = 115 (%)	p-value
Conversions	68 (3·3)	12 (10·4)	<0·001	6 (2·6)	12 (10·4)	0·007
Morbidity	817 (39·1)	50 (43·5)	0·357	97 (42·7)	50 (43·5)	0·895
Intra-abdominal complications						
Anastomotic leakage[a]	149 (7·1)	10 (8·7)	0·530	17 (7·5)	10 (8·7)	0·696
Abscess	85 (4·1)	6 (5·2)	0·548	11 (4·8)	6 (5·2)	0·881
Bleeding	26 (1·2)	4 (3·5)	0·044	2 (0·8)	4 (3·5)	0·101
Pancreatitis, leakage or fistula	10 (0·5)	1 (0·9)	0·563	0 (0·0)	1 (0·9)	0·336
Chyle leakage	38 (1·8)	3 (2·6)	0·551	4 (1·8)	3 (2·6)	0·691
Trauma of the gut	30 (1·4)	1 (0·9)	0·615	2 (0·8)	1 (0·9)	0·999
Wound complications						
Infection/abscess	62 (3·0)	8 (6·9)	0·018	6 (2·6)	8 (6·9)	0·057
Fascia dehiscence	23 (1·1)	2 (1·7)	0·530	3 (1·3)	2 (1·7)	0·999
Non-surgical complications						
Pulmonary[b]	320 (15·3)	17 (14·8)	0·873	33 (14·5)	17 (14·8)	0·952
Cardiac[c]	126 (6·0)	5 (4·3)	0·456	14 (6·2)	5 (4·3)	0·488
Thromboembolic[d]	28 (1·3)	2 (1·7)	0·720	5 (2·2)	2 (1·7)	0·999
Neurologic[e]	88 (4·2)	3 (2·6)	0·399	12 (5·3)	3 (2·6)	0·253
Urologic[f]	70 (3·4)	6 (5·2)	0·287	8 (3·5)	6 (5·2)	0·455
Other	230 (11·0)	18 (15·7)	0·235	39 (17·2)	18 (15·7)	0·720
Re-interventions	340 (16·3)	22 (19·1)	0·443	37 (16·3)	22 (19·1)	0·513
Mortality	101 (4·8)	11 (9·6)	0·026	16 (7·0)	11 (9·6)	0·415
Recovery						
ICU stay (median, IQR)	0 (0–1)	0 (0–1)	0·917	0 (0–2)	0 (0–1)	0·826
Hospital stay (median, IQR)	9 (7–13)	10 (7–16)	0·197	10 (7–15)	10 (7–16)	0·644
Readmissions	243 (11·6)	16 (13·9)	0·500	30 (13·2)	16 (13·9)	0·858

Percentages may not add up to 100% due to rounding. *Dataset after imputation. Expected count less than 5: Fisher's Exact Test.
ICU: Intensive Care Unit, IQR: interquartile range.
[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.

non-curative gastrectomy for gastric cancer in a Western population in order to provide new information that could guide clinical decision-making. This study demonstrates that postoperative complications and length of hospitalization after nCG and CG are comparable in patients with similar baseline characteristics. Especially, no statistically significant difference in mortality was found between both groups.

Clinical decision-making on whether or not to perform nCG is based on the presence or absence of bothersome symptoms, their direct relation to quality of life (QoL), and the condition of the patient. Other important factors include the number of tumor sites [9,18], risk of postoperative morbidity and mortality and potential survival benefit of nCG.

One of the objectives in favor of performing nCG is that several studies have reported an improved QoL after reducing bothersome symptoms [7,18–22]. These symptoms occur in up to 35% of patients and include obstruction causing nausea/vomiting, hemorrhage or pain [20,22]. In a single center study with 99 patients who underwent gastrectomy with incomplete removal of gross disease (R2 gastrectomy), it was demonstrated that gastrectomy improved bothersome symptoms in only 44% of patients [22]. Another single center cohort study with 151 patients demonstrated that QoL improved for patients who underwent palliative gastrectomy, by means of increased ability to return to normal daily activities and to take oral intake, and less vomiting and gastro-intestinal hemorrhage [18]. Other studies report that severe tumor-related complications occur less frequently in the remaining lifespan of patients who underwent nCG. Also, prevention of further surgery or interventions due to severe tumor-related complications in patients not undergoing resection is desirable [23,24]. Although in the current study, unfortunately, no link could be made to whether patients were symptomatic, the results support that morbidity and mortality is acceptable and even similar to a comparable group with curative intent.

Reasons to refrain from nCG are the previously reported high mortality and morbidity rates [7,9,20,22,25–27], of which the latter often results in worsened recovery. In the original cohort, mortality rates after nCG were higher compared to CG, general mortality rates [28,29] and the Asian REGATTA trial [10], which reflects the poor general condition of these patients. Other explanations could be that Western patients present with more advanced tumor stages, whereas no cT4 patients were included in the REGATTA trial. In addition, only patients with a single non-curative factor were included in the Asian study, whereas there might have been patients with multiple non-curative factors in the current study. Moreover, population screening programs in the East allow for more experienced surgeons due to the higher number of gastric cancer patients. Interestingly however, after PSM all complication and recovery rates of nCG-patients were similar to that of CG-patients. These results indicate that postoperative outcomes are not determined by the intent of the procedure, but more likely by the frailty of patients, which was demonstrated to be worse in patients undergoing nCG. The extent of disease was less likely to influence postoperative outcomes, as the pTNM stage was generally higher in the nCG group, while postoperative outcomes were comparable between nCG and CG. In general, a factor that could play a role in reducing postoperative morbidity after nCG is the more frequent implementation of minimally invasive gastrectomy, which has been demonstrated to result in less postoperative complications and shorter hospitalization compared to open procedures [28–30].

Non-curative resection of the primary tumor with the aim of prolonging survival in asymptomatic patients is matter of debate and has not been proven in randomized clinical trials. In colorectal cancer a

Table 3
Histopathological characteristics of the patients who underwent elective gastrectomy for gastric cancer.

	Original cohort (n = 2202)				Propensity score matched group* (n = 342)		
	Curative gastrectomy n = 2087 (%)	Non-curative gastrectomy n = 115 (%)	p-value	Initial missing values (%)	Curative gastrectomy n = 227 (%)	Non-curative gastrectomy n = 115 (%)	p-value
Lauren classification			0·255	453 (20·6)			0·011
Intestinal	901 (54·3)	43 (48·3)			138 (60·8)	51 (44·3)	
Diffuse	643 (38·7)	36 (40·4)			75 (33·0)	51 (44·3)	
Mixed	116 (6·9)	10 (11·2)			14 (6·2)	13 (11·3)	
Tumor differentiation			0·035	331 (15·0)			0·111
Well/moderate	675 (38·2)	29 (27·9)			89 (39·2)	35 (30·4)	
Poor/undifferentiated	1092 (61·7)	75 (72·1)			138 (60·8)	80 (69·6)	
pT-stage			<0·001	0 (0·0)			<0·001
T0	94 (4·5)	1 (0·8)			3 (1·3)	1 (0·8)	
Tis	16 (0·8)	0 (0·0)			0 (0·0)	0 (0·0)	
T1	325 (15·6)	2 (1·7)			23 (10·1)	2 (1·7)	
T2	342 (16·4)	5 (4·3)			35 (15·4)	5 (4·3)	
T3	827 (39·6)	38 (33·0)			107 (47·1)	40 (34·8)	
T4	439 (21·0)	66 (57·4)			59 (26·0)	67 (58·3)	
Tx	44 (2·1)	3 (2·6)			0 (0·0)	0 (0·0)	
pN-stage			<0·001	0 (0·0)			<0·001
N0	926 (44·4)	8 (7·0)			81 (35·7)	9 (7·8)	
N1	400 (19·2)	22 (19·1)			52 (22·9)	24 (20·9)	
N2	338 (16·2)	29 (25·2)			40 (17·6)	31 (27·0)	
N3	369 (17·7)	47 (40·9)			39 (17·2)	34 (29·6)	
Nx	54 (2·6)	9 (7·8)			0 (0·0)	0 (0·0)	
pM-stage			<0·001	151 (6·9)			<0·001
M0	1879 (96·6)	42 (39·6)			217 (95·6)	46 (40·0)	
M1	66 (3·4)	64 (60·4)			10 (4·4)	69 (60·0)	
Additional resections	212 (10·1)	35 (30·4)	<0·001	7 (0·3)	26 (11·5)	35 (30·4)	<0·001
Radicality of the resection			<0·001	45 (2·0)			<0·001
R0	1858 (90·8)	39 (34·4)			199 (87·7)	40 (34·8)	
R+	189 (9·2)	71 (64·5)			28 (12·3)	75 (65·2)	
Lymph node yield (median, IQR)	20 (14–28)	15 (10–22)	<0·001	63 (2·9)	19 (14–28)	15 (8–21)	<0·001
≥ 15 Lymph nodes in the specimen	1479 (73·0)	58 (56·2)	<0·001	63 (2·9)	163 (71·8)	63 (54·8)	0·002
Total positive lymph nodes (median, IQR)	1 (0–5)	6 (2–11)	<0·001	19 (0·8)	2 (0–7)	6 (2–10)	<0·001

IQR: interquartile range. The R+ of the PG group consisted of: 44% R1 resections and 21% R2 resections. In the PG group, R0 resections mean that even though the resection was non-curative, in 35% the local resection margins were clear.

retrospective analysis of two phase III studies on metastatic colorectal carcinoma (CAIRO and CAIRO2) showed that resection of the primary tumor resulted in a significant survival benefit [31,32]. However, in both studies comparing different chemotherapeutic regimens, patients were selected after surgical resection of the primary tumor and therefore these results were not corrected for morbidity and mortality that occurred as a result of surgery. For that reason, the CAIRO4 study is conducted which randomly assigns asymptomatic patients for resection of the primary tumor followed by systemic therapy or systemic therapy without resection. Results of this trial are awaited.

For gastric cancer, many studies varying from randomized trials to retrospective cohort studies, demonstrated a survival benefit [7–9,14,18–20,22,33–35], which obviously could be a main argument in favor of performing nCG. Included herein is a meta-analysis that analyzed 14 observational studies with 3003 patients who reported a statistically significant improvement in overall survival of nCG (HR 0·56; 95%CI 0·39–0·80; p < 0·002) compared to patients treated without resection [33]. Moreover, the German AIO-FLOT3 trial demonstrated survival benefit in patients with limited metastatic disease who received neoadjuvant chemotherapy and underwent surgery, compared to patients who were not suitable for surgical resection. Also, it is hypothesized that the tumor might respond to palliative (chemo)therapy better, after a significant portion has been resected [9]. On the other hand, the Asian randomized REGATTA-trial did not find a benefit of nCG over palliative chemotherapy in terms of survival. However, patients in the REGATTA-trial mostly suffered from peritoneal metastases, who may not benefit from nCG [10,20]. Currently, the Dutch COSTA-trial and the German RENAISSANCE trial [36] are evaluating potential benefits of nCG in selected patients and the results from these studies will have to be awaited.

The current study has some limitations, as the results are affected by inherent selection bias that could not be adjusted with PSM. Second, the reason for non-curative gastrectomy (e.g. bothersome symptoms) was not available in the dataset, nor was the location of metastases or number of metastatic sites, which precluded performing several relevant sub analyses. Moreover, emergency resections were excluded, which could have led to the exclusion of some nCG cases but allowed for a more homogeneous population. Last, no link could be made with survival data and QoL, since the DUCA lacks this kind of data.

5. Conclusions

A non-curative intent of surgery does not negatively impact postoperative outcomes compared to CG in patients with similar patient and tumor characteristics. As such, nCG might be considered in patients who are critically evaluated and deemed fit enough for surgery.

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.

CRediT authorship contribution statement

Emma C. Gertsen: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Writing - original draft, Writing - review & editing, Visualization, Project administration. **Hylke J.F. Brenkman:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Writing - original draft, Writing - review & editing, Project administration. **Lucas Goense:** Methodology, Validation, Formal analysis, Writing - review & editing. **Nadia Haj Mohammad:** Validation, Formal analysis, Resources, Writing - review & editing. **Bas L.A. Weusten:** Validation, Formal analysis, Resources, Writing - review & editing. **Richard van Hillegersberg:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Writing - original draft. **Jelle P. Ruurda:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Writing - original draft.

Declaration of competing interest

ECG, HJFB, LG, NHM, BLAW, RvH and JPR have no conflicts of interest or financial ties to disclose.

Acknowledgements

The authors would like to thank all participating centers in the Netherlands for collecting the data and the Dutch Upper GI Cancer Audit (DUCA) for supplying the data for this study. This study was not preregistered in an independent, institutional registry.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.suronc.2020.08.018.

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