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ABSTRACT

Background: Quality of gastric cancer surgery is crucial for favorable prognosis. Generally, prospective trials lack quality control measures. This study assessed surgical quality and a novel D2-lymphadenectomy photo-scoring in the LOGICA-trial.

Methods: The multicenter LOGICA-trial randomized laparoscopic versus open total/distal D2-gastrectomy for resectable gastric cancer (cT1-4aN0-3M0) in 10 Dutch hospitals. During the trial, two reviewers prospectively analyzed intraoperative photographs of dissected nodal stations for quality control, and provided centers weekly feedback on their D2-lymphadenectomy, as continuous quality-enhancing incentive. After the trial, these photographs were reanalyzed to develop a photo-scoring for future trials, rating the D2-lymphadenectomy dissection quality (optimal-good-suboptimal-unevaluable). Interobserver variability was calculated (weighted kappa). Regression analyses related the photo-scoring to nodal yield, recurrence and 5-years survival.

Results: Between 2015 and 2018, 212 patients underwent total/distal D2-gastrectomy (n = 122/n = 90), and 158 (75%) received neoadjuvant chemotherapy. R0-resection rate was 95%. Rate of ≥15 retrieved lymph nodes was 95%. Moderate agreement was obtained in stations 8 + 9 ($\kappa = 0.522$), 11p/11d ($\kappa = 0.446$) and 12a ($\kappa = 0.441$). Consensus was reached for discordant cases (30%). Stations 8 + 9, 11p/11d and 12a were rated 'optimal' in 76%, 63% and 68%. Laparoscopic photographs could be rated better than open (2% versus 12% 'unevaluable'; 73% versus 50% 'optimal'; $p = 0.042$). The photo-scoring did not show associations with nodal yield ($p = 0.214$), recurrence ($p = 0.406$) and survival ($p = 0.988$).

Conclusions: High radicality and nodal yield demonstrated good quality of D2-gastrectomy. The prospective quality control probably contributed to this. The photo-scoring did not show good performance, but can be refined. Laparoscopic D2-gastrectomy was better suited for standardized surgical photo-evaluation than open surgery.

1. Introduction

D2-gastrectomy is the mainstay of curative multimodality treatment for gastric cancer, resulting in 36–45% 5-years survival [1–4]. High quality of surgery is crucial for achieving a favorable prognosis [5]. However, a uniform definition of 'surgical quality' of D2-gastrectomy is lacking. Important quality indicators are R0-resections, lymph node yield and uneventful hospital stay, since they are independently associated with survival [5–7]. Furthermore, international guidelines dictate the quality target of ≥15 retrieved lymph nodes [1,8,9]. However, this target does not incorporate the location of retrieved lymph nodes, which may also be important because each nodal station in

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D2-lymphadenectomy can contain metastases [10–13]. For example, compliance to D2-lymphadenectomy evaluates each station separately, and may be a quality indicator [13–15]. Additionally, different centers still attain a wide variety in nodal yield [16]. These aspects underline the need for 'high-quality' D2-gastrectomy and improved standardization of its surgical technique, which is essential for quality control of gastric cancer treatment, in trials, proctoring, (inter)national comparison and audits.

In general, prospective trials often lack uniform evaluation metrics and do not incorporate quality-enhancing measures during a trial. Several previous studies evaluated surgical quality of and compliance to D2-gastrectomy [13,15,17–21]. However, solid comparison is complicated as these studies used multiple quality assessment methods, applied different surgical participation criteria, showed variations in obtained results and only one incorporated prospective feedback rounds during the trial. Improved methodological recommendations for future clinical trials are warranted.

The LOGICA-trial incorporated pre-trial hands-on proctoring, clearly defined participation criteria, standardized surgical procedures, and implemented a prospective quality control during the trial. This study's objective was to assess the surgical quality and quality control of D2-gastrectomy in the LOGICA-trial, and to validate two potential quality indicators: (1) a new D2-lymphadenectomy photo-scoring system and (2) compliance to D2-lymphadenectomy.

2. Methods

This study is a post-hoc analysis of the multicenter randomized controlled LOGICA-trial. The LOGICA-trial randomized between a laparoscopic versus open approach for total or distal D2-gastrectomy for resectable gastric cancer (cT1-4aN0-3M0), and found no significant differences in surgical and oncological outcomes including quality of life. The LOGICA study protocol and results were published previously, detailing the inclusion and exclusion criteria, staging and standardized (surgical) treatment procedures [22,23]. Institutional review board approval was obtained at all ten Dutch participating hospitals. All LOGICA-patients were eligible for inclusion and signed written informed consent.

2.1. Staging and treatment

The multidisciplinary tumor board determined the staging and treatment according to Dutch national guidelines, as previously published [1,22]. All patients with advanced disease stage (cT3-4 and/or cN+) who were deemed medically and physically fit underwent perioperative chemotherapy as standard of care. Total or distal D2-gastrectomy was performed depending on tumor location, histological subtype and disease stage, and combined with Roux-en-Y reconstruction and total omentectomy [22]. D2-lymphadenectomy was defined according to the 5th Japanese Gastric Cancer Association (JGCA) guidelines and consisted of nodal stations no. 1–9, 11p/11d and 12a for total gastrectomy and no. 1, 3, 4d/4sb, 5–9, 11p and 12a for distal gastrectomy (Supplementary Fig. 1) [3]. Enhanced Recovery After Surgery (ERAS) was routinely applied during postoperative recovery [24].

2.2. Hospital participation criteria

The participation criteria mandated that centers performed ≥20 gastrectomies yearly and were experienced in open gastrectomy. Prior to the trial start, each surgical team had completed the European Society of Surgical Oncology hands-on proctoring course on laparoscopic D2-gastrectomy and performed ≥20 laparoscopic gastrectomies before participating [25]. Two surgical videos of laparoscopic D2-gastrectomy were reviewed by the central investigators (RvH/JR) and additional proctoring feedback was provided if applicable.

2.3. Prospective quality control

As continuous quality-enhancing incentive, intraoperative photographs were prospectively taken after dissecting the mid-truncal (stations 7 + 9), left suprapancreatic (station 11p/11d) and right suprapancreatic area (stations 8 + 12a) according to specific instructions (Supplementary Methods). This was implemented from November 2016. Two expert surgeons (RvH/JR; >400 performed gastrectomies combined) analyzed these photographs and provided weekly feedback to individual centers on the quality of their performed D2-lymphadenectomy during the trial.

2.4. The novel D2-lymphadenectomy photo-scoring

After completing the trial, those intraoperative photographs were re-assessed to develop a new uniform D2-lymphadenectomy scoring system for future trials. For this photo-scoring, the dissection quality of stations 8 + 9, 11p/11d and 12a was classified by two reviewers (RvH/JR) independently as optimal, good, suboptimal and unevaluable for blurred or incomplete sight. In case of disagreement, a consensus meeting was held. The intraoperative photographs captured the N2-stations (no. 7–9, 11p/11d and 12a). These N2-stations served as a proxy for surgical quality of the entire D2-lymphadenectomy.

2.5. Histopathological examination

Histopathological examination was performed according to Dutch national guidelines, as previously reported [1,22]. For accurate location of retrieved lymph nodes, individual stations were collected in separate pathology containers (no. 8, 9, 11p/11d and 12a) or clearly marked at the resection specimen (no. 1–7), as elaborated in Supplementary Methods. Pathology reports were acquired via PALGA, The Netherlands nationwide network and registry of histo-/cytopathology [26].

2.6. Compliancy to D2-lymphadenectomy

As sensitivity analysis for the dissection quality of D2-lymphadenectomy, compliancy was post-hoc categorized into compliancy-groups based on histopathological examination and according to previously reported definitions: compliance (all nodal stations with ≥1 retrieved lymph node(s)), minor or major non-compliance (1–2 or ≥3 stations without nodes) and contamination (resected nodal stations beyond D2-lymphadenectomy with ≥1 node(s); thus D2+; stations 10 or 13–16) [3,13,14].

2.7. Outcomes

The surgical quality of D2-gastrectomy was qualified based on radicality and nodal yield over time, rate of ≥15 lymph nodes, and compliancy to D2-lymphadenectomy. Furthermore, the prospective quality control was evaluated, and interobserver variability was assessed for the photo-scoring. To validate the new D2-lymphadenectomy photo-scoring and surgical compliancy as two potential independent quality indicators, these were separately related to nodal yield, recurrence and 5-years overall survival.

2.8. Statistical analysis

Analyses were per protocol. Continuous variables were compared using independent unpaired *T*-tests or Mann-Whitney *U*-tests depending on the data distribution. Categorical variables were compared with X^2-tests, Fisher's exact test if 25% of values counted ≤5 or Kruskal Wallis tests, when appropriate. Factors influencing nodal yield were identified using multivariable linear regression. For interobserver variability, reviewer disagreement was measured using weighted kappa (κ). Overall survival dated from inclusion to death for any reason or lost-to-follow-

up, and was compared with the log-rank test after plotting Kaplan-Meier curves. Factors were related to survival using the multivariable Cox Proportional Hazards Model. A two-sided $\alpha < 0.05$ was considered statistically significant for all tests, which were performed using IBM SPSS Statistics version 27.0 (SPSS Inc. Chicago, USA).

3. Results

Between February 2015–August 2018, 212/227 LOGICA-patients underwent D2-gastrectomy, and 15 patients were excluded as previously reported [23]. Baseline characteristics (n = 212) are displayed in Table 1. Most patients (n = 138; 65%) showed advanced cT-stage (cT3-4). Neoadjuvant chemotherapy was administered to 158 patients (75%). Laparoscopic and open distal gastrectomy were performed in 58 (48%) and 64 (52%) patients, whereas 48 (53%) and 42 (47%) patients underwent laparoscopic and open total gastrectomy.

3.1. Radicality

Histopathological results are listed in Table 2. R0-resection rate was 95% (n = 202/212), and was similar per one-third of the trial time period (94% versus 93% versus 99%; $p = 0.226$), also independent from surgical approach (Supplementary Table 1). Of the 10 R1-patients, 8 patients showed both distal and proximal (n = 4) or only proximal (n = 4) positive resection margins after total gastrectomy, and 2 patients had a positive proximal margin after distal gastrectomy.

Five of the 10 R1-patients (50%) developed disease recurrence during a median follow-up of 21 months [IQR 21–40], either locoregional recurrence localized at the anastomosis after total gastrectomy (n = 1) or distant/peritoneal metastases (n = 4). In contrast, the recurrence rate for the 202 R0-patients was 27%.

Table 1
Baseline characteristics.

Characteristic	Entire study cohort n = 212 (100%)	Intraoperative photographs cohort n = 111 (100%)
Age (median; in years, [IQR])	70 [61–76]	68 [60–75]
Gender		
Female	80 (*38*)	36 (*32*)
Male	132 (*62*)	75 (*68*)
BMI (median; in kg/m2 [IQR])	25 [23–29]	25 [22–29]
ASA classification		
0	20 (*9*)	16 (*14*)
1	140 (*66*)	66 (*60*)
2	52 (*25*)	29 (*26*)
Tumor location		
Proximal	27 (*13*)	16 (*14*)
Middle	65 (*31*)	26 (*23*)
Distal	120 (*57*)	69 (*62*)
Clinical T-stage		
cT1	13 (*6*)	8 (*7*)
cT2	61 (*29*)	28 (*25*)
cT3	120 (*57*)	65 (*59*)
cT4	18 (*8*)	10 (*9*)
Clinical *N*-stage		
cN0	116 (*55*)	64 (*58*)
cN+	96 (*45*)	47 (*42*)
Clinical M-stage		
cM0	212 (*100*)	111 (*100*)
Lauren classification		
Intestinal type[a]	124 (*60*)	63 (*59*)
Diffuse type	84 (*40*)	45 (*41*)
Extent of gastrectomy		
Total gastrectomy[b]	90 (*43*)	52 (*46*)
Distal gastrectomy	122 (*57*)	59 (*54*)
Surgical approach		
Open	106 (*50*)	60 (*54*)
Laparoscopic	106 (*50*)	51 (*46*)
Neoadjuvant chemotherapy		
Yes	158 (75)	93 (84)
No	54 (25)	17 (16)

IQR = interquartile range. BMI = Body Mass Index (kg/m^2). ASA = American Society of Anesthesiologists.
Percentages may not add up to 100% due to rounding.
Intraoperative photographs were taken of the D2-lymphadenectomy as elucidated in the Methods section.
[a] The Lauren mixed type tumors were categorized among the intestinal type. There were 4 missings.
[b] One patient underwent total gastrectomy plus esophageal resection with cervical esophagostomy due to extensive tumor growth.

Table 2
Histopathological results regarding radicality and lymph node yield.

Histopathological characteristic		Entire study cohort n = 212 (100%)	*p*-value
Radicality			
R0		202 (*95*)	
R1[a]		10 (*5*)	
R0-resections over time: per one-third part of the trial period			
First one-third		94%	0.226
Second one-third		93%	
Third one-third		99%	
Positive resection margins [a]			
Proximal only		6 (3)	
Both proximal and distal		4 (2)	
Distal only		0 (0)	
Lymph node yield	(median [IQR])	29 [21–39]	
Lymph node yield over time: per one-third part of the trial period			
First one-third	(median [IQR])	29 [24–42]	0.407
Second one-third	(median [IQR])	30 [21–40]	
Third one-third	(median [IQR])	28 [21–35]	
Removal of ≥15 lymph nodes		202 (95)	

Disease recurrence after D2-gastrectomy[b]	**Recurrence; yes n = 212** (100%)
Recurrence stratified for resection margin status (radicality)	
R0-resections	55/202 (27)
R1-resections [c]	5/10 (50)
Recurrence stratified for removal of ≥15 lymph nodes	
Patients with ≥15 lymph nodes	56/202 (28)
Patients with <15 lymph nodes	4/10 (40)
Recurrence stratified for the D2-lymphadenectomy photo-scoring [d]	
Optimal	19/67 (28)
Good	7/17 (41)
Suboptimal	3/12 (25)
Unevaluable	0/8 (0)

IQR = interquartile range. Percentages may not add up to 100% due to rounding. There were no missings in this Table.
[a] Of these 10 R1-resections, 8 patients underwent total gastrectomy and 2 patients underwent distal gastrectomy.
[b] The median follow-up for recurrence was 21 months [IQR 12–40 months].
[c] Of the 10 R1-patients, 5 patients (50%) developed disease recurrence, either locoregional recurrence localized at the anastomosis after total gastrectomy (n = 1) or distant/peritoneal metastases (n = 4).
[d] Recurrence was not significantly related to the D2-lymphadenectomy photo-scoring ($p = 0.406$).

3.2. Lymph node yield

Median nodal harvest yielded 29 nodes per patient [IQR 21–39], and was similar per one-third of the trial time period (29 [24–42] versus 30 [21–40] versus 28 [21–35] nodes; $p = 0.407$), also independent from surgical approach (Fig. 1). Furthermore, median lymph node yield did not differ over time as well separately per nodal station for no. 8 + 9 (3 versus 3 versus 4 nodes; $p = 0.820$), 11p/11d (2 versus 2 versus 1 nodes; $p = 0.324$) and 12a (1 versus 1 versus 1 node; $p = 0.628$).

In total, 95% of patients (n = 202/212) showed ≥15 lymph nodes at histopathological examination (Table 2). The 10 patients with <15

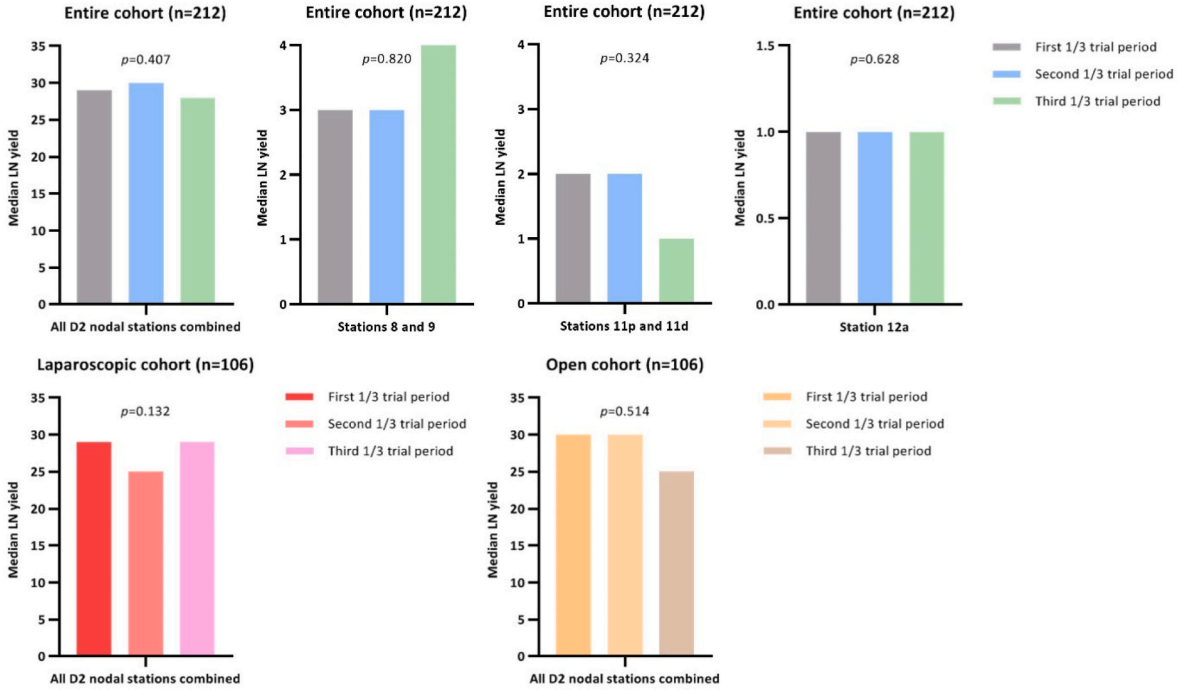

Fig. 1. Median lymph node yield over time (per 1/3 part of the trial period) for all patients (n = 212) and for patient subgroups based on surgical approach (laparoscopic versus open).

retrieved nodes (5%) were equally divided over the laparoscopic and open groups (5 and 5 patients). Patients with <15 nodes showed 40% recurrence rate, compared to 28% recurrences for patients with ≥15 nodes.

3.3. The novel D2-lymphadenectomy photo-scoring

Intraoperative photographs to score the completeness of D2-lymphadenectomy were available for 111/152 patients (73%). Perioperative outcomes of these 111 patients did not differ compared to the remaining patients without (n = 101) intraoperative photographs (Supplementary Table 2).

The reviewers scored 30% disagreement, mostly (55%) differing for 'optimal' versus 'good'. This resulted in moderate agreement (interobserver variability; Fig. 2 and Supplementary Table 3) for stations 8 + 9 (κ = 0.522; 95%CI 0.35–0.70), 11p/11d (κ = 0.446; 95%CI 0.29–0.60) and 12a (κ = 0.447; 95%CI 0.28–0.61).

Thereafter, the reviewers reached consensus for all discordant cases. Using the D2-lymphadenectomy photo-scoring, most nodal stations 8 + 9 (n = 84; 76%), 11p/11d (n = 70; 63%) and 12a (n = 76; 69%) were rated 'optimal' (Figs. 2 and 3). Regarding surgical approach, the intraoperative photographs were less often rated as 'unevaluable' favoring the laparoscopic versus open approach (2% versus 12%; p = 0.042), and more frequently 'optimal' (73% versus 50%; $p = 0.042$).

To validate the photo-scoring as potential quality indicator, it was related to nodal yield, recurrence and survival (Table 2 and Supplementary Tables 4 and 5). No significant associations were found regarding lymph node yield ($p = 0.214$), disease recurrence (28% for

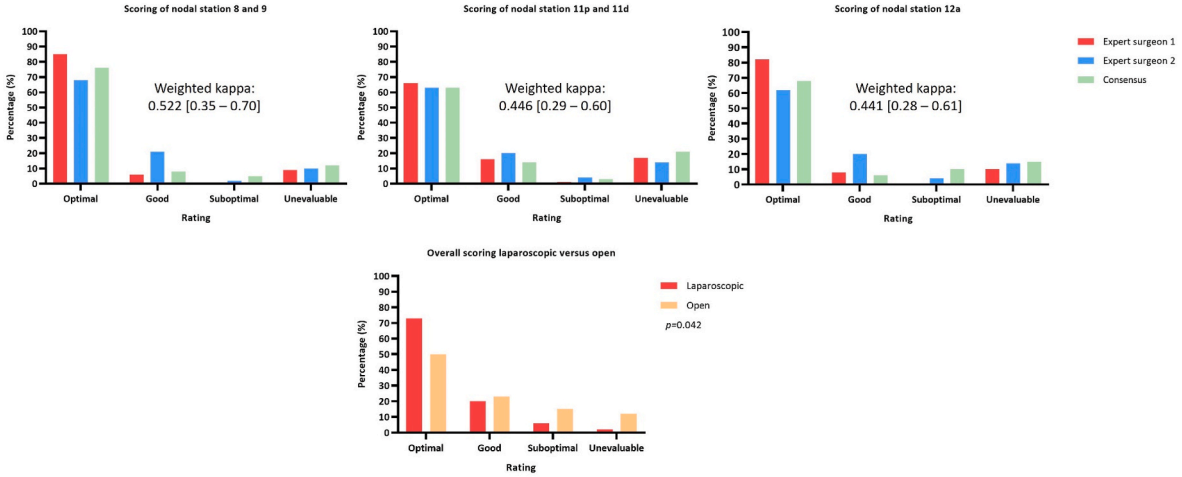

Fig. 2. Results of the new D2-lymphadenectomy photo-scoring system: the initial scoring by both reviewers is given in red/blue and the scoring after reaching consensus for discordant cases in green, including the interobserver variability (weighted kappa). The top row presents the scoring for all patients with available intraoperative photographs (n = 111) per nodal stations 8 + 9, 11p/11d and 12a. The bottom row displays the overall scoring for the laparoscopic (n = 51) versus open approach (n = 60).

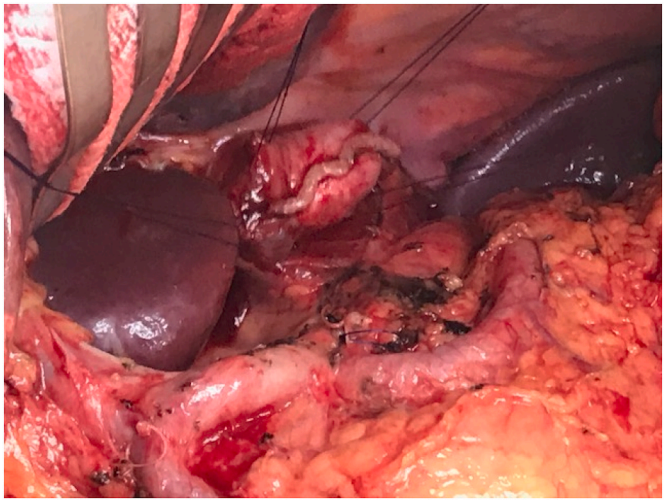

Fig. 3. Example of an intraoperative photograph after dissecting stations 8 + 9, 11 and 12a during open gastrectomy, which was rated 'optimal' in all three lymphadenectomy regions.

'optimal' versus 25% for 'suboptimal'; $p = 0.406$) and overall survival ($p = 0.988$). The photo-scoring did not differ between patients with <15 versus ≥15 lymph nodes (60% versus 60% 'optimal'; $p = 0.623$), and between compliancy-groups ('optimal' scores showed 59% compliance versus 57% non-compliance; $p = 0.812$). Furthermore, perioperative outcomes did not differ when comparing 'optimal' versus 'non-optimal' cases (Supplementary Table 6).

3.4. Sensitivity analysis – surgical compliancy

Based on histopathological assessment, compliancy to D2-lymphadenectomy could be analyzed for 164 patients (Table 3). Compliance (38%) and minor non-compliance (46%) occurred in 84%. Major non-compliance and contamination (D2+) occurred infrequently, both in 13 patients (8% and 8%).

To validate compliancy as quality indicator, it was related to nodal yield, recurrence and survival.

Median lymph node yield was significantly higher ($p < 0.001$) for patients with compliance and contamination (37 [26–46] and 36 [22–40] nodes) compared to minor and major non-compliance (27 [22–34] versus 15 [12–18] nodes).

Although the rate of disease recurrence was 39% for major non-compliance and 27%, 28% and 31% for compliance, minor non-compliance and contamination, no significant association was found between surgical compliancy to D2-lymphadenectomy and disease recurrence ($p = 0.863$).

Median overall survival was 45 months for compliance, 48 months for non-compliance and 30 months for contamination, however the 5-years overall survival was similar (n = 164; $p = 0.804$) (Fig. 4). Subgroup analyses showed comparable survival as well for minor versus major non-compliance (n = 89; $p = 0.891$), and for surgical compliance versus major non-compliance (n = 75; $p = 0.911$).

4. Discussion

This study assessed the surgical quality and prospective quality control in a randomized controlled trial comparing laparoscopic versus open D2-gastrectomy for gastric cancer (LOGICA-trial) as post-hoc analysis. Based on the high and consistent radicality and nodal yield (in total and per station), and low rate of surgical major non-compliance, we consider the surgical quality of D2-gastrectomy to be high. Furthermore, the prospective quality control may be useful as quality-enhancing feedback instrument during trials to continuously stimulate

Table 3
Surgical compliancy to D2-lymphadenectomy.

Surgical compliancy to D2-lymphadenectomy		n = 164 (100%)[a]
Compliance	(all nodal stations with ≥1 retrieved lymph node(s))	62 (38)
Non-compliance		
Minor non-compliance	(1–2 nodal stations without nodes)	76 (46)
Major non-compliance	(≥3 nodal stations without nodes)	13 (8)
Contamination	(D2+, i.e. stations 10 or 13–16 with ≥1 retrieved lymph node(s))	13 (8)

Compliancy related to surgical quality indicators		**n = 164** (100%)[a]	***p*-value**
Lymph node yield	(median [IQR])		**<0.001**
Compliance		37 [26–46]	
Minor non-compliance		27 [22–34]	
Major non-compliance		15 [12–18]	
Contamination		36 [22–40]	
Disease recurrence			
Compliance		17 (27)	0.863
Minor non-compliance		21 (28)	
Major non-compliance		5 (39)	
Contamination		4 (31)	
Overall survival		Please see Fig. 3.	

Compliancy related to the photo-scoring n = 88 (100%)[b]	Compliance **n = 34 (100%)**	Non-compliance **n = 46 (100%)**	**Contamination n = 8 (100%)**	***p*-value**
The D2-lymphadenectomy photo-scoring				
Optimal	20 (59)	26 (57)	7 (88)	0.812
Good	9 (27)	10 (22)	1 (13)	
Suboptimal	4 (12)	6 (13)	0 (0)	
Unevaluable	1 (3)	4 (9)	0 (0)	

IQR = interquartile range. Bold numbers indicate statistical significance.

[a] There were 48 missings (23%) regarding surgical compliancy to D2-lymphadenectomy, because for these patients the pathology reports did not provide sufficient detail to analyze compliancy. This 'compliancy-unknown'-group showed similar median lymph node yield (29 [IQR 23–39] versus 29 [IQR 21–39] nodes; $p = 0.691$) compared to the remaining cohort.

[b] Intraoperative photographs were available for 111 patients, and there were 23 missings (21%) for compliancy to D2-lymphadenectomy.

surgeons in optimizing their surgical performance. The novel D2-lymphadenectomy photo-scoring showed only moderate agreement between two experienced upper-GI surgeons, and did not show an association with objective quality indicators (nodal yield, recurrence and survival). In addition, laparoscopic D2-gastrectomy was better suited for standardized surgical photo-evaluation than the open approach. Last, the sensitivity analysis to assess quality of nodal dissection in depth showed that compliance to D2-lymphadenectomy was related to nodal yield and may be a valuable quality indicator, but should be further validated as we did not find an association with recurrence and survival.

Radicality rate (95%; despite predominantly advanced cT-stage) and nodal yield (29 nodes [IQR 21–39]) were high and consistent throughout the trial period, independent from surgical approach. Removal of ≥15 lymph nodes is an important quality target in gastric cancer surgery, which was as high as 95% both in the laparoscopic and open LOGICA-groups [1,8,27,28]. Previous prospective gastric cancer trials with mainly advanced cT-stage showed similar radicality rates (90–98%) and nodal range (20–47 nodes) [21,29–32]. Generally, it has been well-established that nodal yield after D2-lymphadenectomy can vary substantially among different surgeons, pathologists and hospitals [16,33–36]. Implementing pre-trial hands-on proctoring, standardized (surgical) protocols, participation criteria and the prospective quality control in the LOGICA-trial has most probably contributed to the high and stable surgical quality. Previous well-designed gastric cancer trials all applied standardized protocols and set a (different number of)

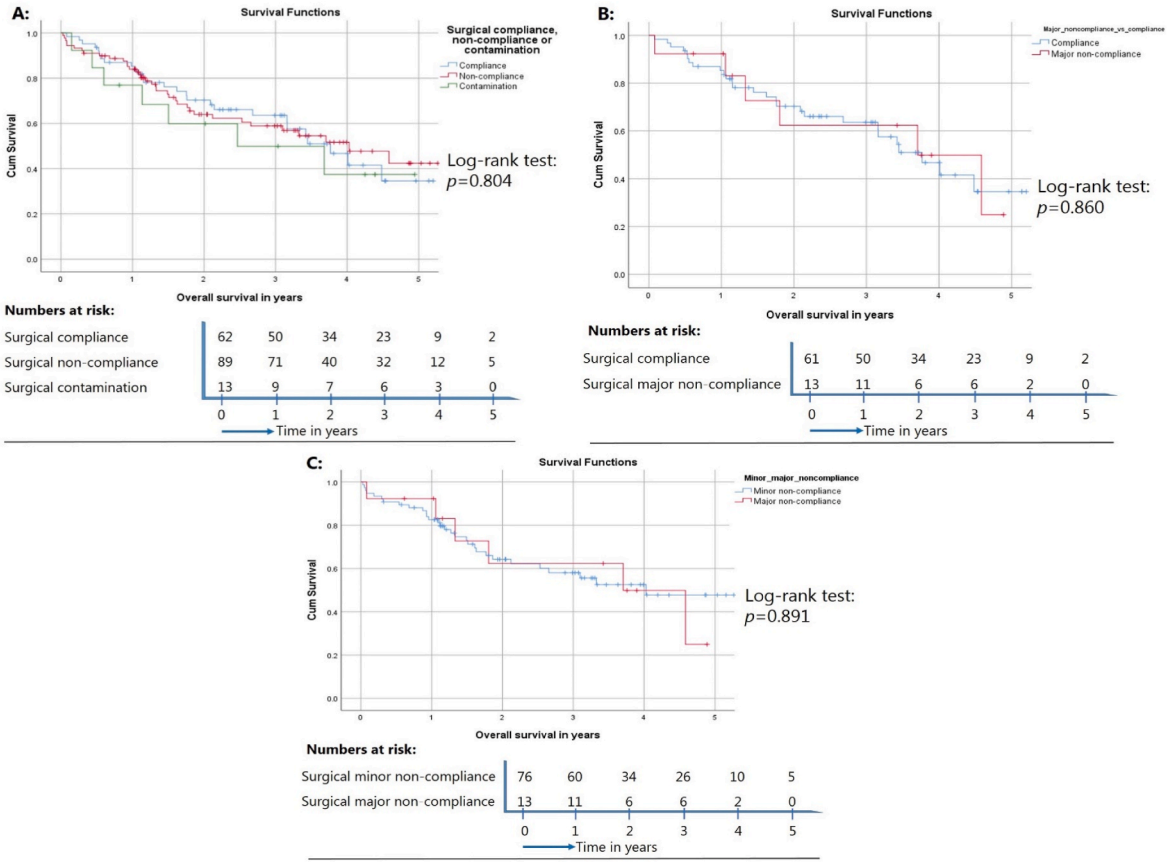

Fig. 4. Overall survival for surgical compliance, (minor/major) non-compliance and contamination in total (A) and in subgroup analyses regarding compliance versus major non-compliance (B) and minor versus major non-compliance (C).

minimum laparoscopic surgical experience, three performed surgical video-review and only one included prospective feedback rounds during the trial [18–20,32,37]. None of these studies incorporated all above-mentioned methods including pre-trial hands-on proctoring as we did in the LOGICA-trial. We strongly recommend implementing these quality measures, which contribute to standardizing surgical quality, optimizing the surgeon's performance and ensuring valid trial results by minimizing learning curve effects and confounding bias.

The prospective quality control in the LOGICA-trial was based on analyses of intraoperative photographs rating the dissection quality of nodal stations 8 + 9, 11p/11d and 12a, resulting in weekly feedback rounds to local centers. We qualified implementing this quality-enhancing instrument as being successful, because our intention was to increase awareness by surgeons to continuously optimize their surgical performance throughout the trial. This might have contributed to the high lymph node yield. Only one previous gastric cancer trial provided frequent prospective feedback to centers based on nodal yield, which showed an increase in nodal yield during their study [15]. This reflects suboptimal results in their initial trial phase, which may have improved by their prospective feedback rounds during the trial, or due to nationwide centralization in that same period [15]. Another previous study used detailed surgical video-review as qualifying prerequisite before starting their trial, but this video-review may also be useful as regular feedback method during a trial [19]. For future trials, we recommend implementing a prospective quality control method with frequent feedback rounds. Furthermore, near-infrared fluorescence-guided surgery (*i.e.,* indocyanine green) can be considered after dissecting nodal stations as quality control for sufficiently removing lymphatic tissue, as previous studies showed its benefit [38–40].

Regarding the D2-lymphadenectomy photo-scoring system, moderate agreement ($\kappa = 0.4–0.6$) was achieved with 70% concordant ratings. This photo-scoring did not show an association with objective quality indicators (nodal yield, recurrence and overall survival). However, several factors might improve interobserver variability and could explain the absence of an association. First, most discordant ratings (55%) differed to minor degree ('optimal'-'good'), which was intuitively scored without clear definitions. This indicates that explicit definitions on the quality of resected nodal regions might increase its performance. Such definitions should include a quantification of (sub)optimal dissected nodal areas based on the JGCA-classification, such as the 'artery covered for 0–10%, 10–30% and >30% with remaining fatty tissue possibly containing residual lymph nodes' [3]. Second, the final view as observed on the intraoperative photographs after completing lymph node dissection served as a proxy for surgical quality of the D2-lymphadenectomy, however we did not analyze the intraoperative process itself during lymph node dissection. Instead of assessing photographs, analyzing short video's may improve orientation and visualization of resected lymphadenectomy regions to possibly capture more detail for quality assessment, as was shown previously [41]. Last, our study was not powered to find a difference for this photo-scoring. Optimizing these aspects could potentially increase the performance of our new D2-lymphadenectomy photo-scoring, warranting its validation in other trials as a potential assessment tool to evaluate and standardize surgical quality in the setting of clinical trials.

The laparoscopic approach was better suited for the D2-lymphadenectomy photo-scoring than open surgery ($p = 0.042$), with less 'unevaluable' (2% versus 12%) and more 'optimal' (73% versus

50%) ratings. This finding may be important for future surgical quality evaluations and proctoring. No previous studies have yet assessed this. Detailed anatomy is challenging to record in open surgery, whereas laparoscopic tools facilitate this with magnified visualization and camera-introduction intra-abdominally. Theoretically, the robot-assisted approach might be superior in this with its three-dimensional and magnified view and stable optical platform controlled by the primary operating surgeon, however additional research is warranted to test this.

Surgical major non-compliance occurred infrequently (8%), and compliance and minor non-compliance accounted for 84% of patients (38% and 46%). Four previous gastric cancer trials assessed surgical compliancy, of which two did not distinguish minor from major non-compliance, complicating detailed comparison [13–15,20]. The other two studies showed higher rates of major non-compliance (20–24%) and slightly lower rates of compliance and minor non-compliance combined (77–80%), supporting the conclusion of high surgical quality in the LOGICA-trial [13,15].

Surgical compliance resulted in higher nodal yield than minor and major non-compliance (37 versus 27 versus 15 nodes; $p < 0.001$), but was not related to recurrence ($p = 0.863$) or long-term survival ($p = 0.804$), also regarding compliance versus major non-compliance ($p = 0.911$). No previous study related compliance to nodal yield and disease recurrence. Only one previous trial correlated compliance to survival and found significantly better survival for D2-compliancy/-contamination against non-compliant D2-lymphadenectomy, thus comparing "true" D2/D2+ versus D2 of lesser quality [13]. Hence, non-compliance may negatively impact survival. However, in the current study we did not find poorer survival for minor/major non-compliance. It should be mentioned that our study was not powered to detect such a difference. Altogether, surgical compliance takes into account the localisation of retrieved lymph nodes, was related to nodal yield in this study and previously related to survival, and should be further validated as potentially valuable quality indicator for future trials.

A limitation of this study is that the photographs assessment was implemented in November 2016 and 27% showed missings. This decreased statistical power to find associations between the photo-scoring assessment and quality indicators. In addition, it should be mentioned that the N2-stations only (no. 7–9, 11p/11d and 12a) were captured on intraoperative photographs and analyzed, since these nodal stations can be clearly identified on photographs following dissection, showing the vessels originating from the celiac trunk. The N2-stations served as a proxy for surgical quality of the entire D2-lymphadenectomy. However, nodal stations no. 1–6 also have their own oncological impact, especially infrapyloric station 6 which frequently shows metastases, is anatomically challenging to dissect and may be difficult to capture on photographs given its location at the pancreas without a clearly visible vascular structure [10,11]. Future studies validating our photo-scoring system should assess all nodal stations (no. 1–9, 11p/11d and 12a) to determine its value as potential quality indicator in new clinical trials. Third, surgical compliancy could not be assessed for 48 patients (23%), for whom pathology reports contained insufficient detail for stratification over the compliancy-groups. This 'unknown'-group showed similar nodal yield ($p = 0.691$) to the entire cohort. Last, 65% of LOGICA-patients have completed $\geq$5 follow-up years, and the remaining 35% finished at least $\geq$4 years. It is unlikely though that adding a few additional follow-up months would change the conclusions of the survival analyses. Major strengths of this post-hoc analysis are that it sets a sound example for trials how surgical quality can be analyzed, and how to implement proctoring, surgical video-review, standardized procedures and a prospective quality control. Furthermore, this study designed a new D2-lymphadenectomy photo-scoring as quality-enhancing tool for future trials, and was the first to relate surgical compliancy to nodal yield.

5. Conclusions

In conclusion, the surgical quality of D2-gastrectomy in the LOGICA-trial was high. The participation criteria and prospective quality control probably contributed to this. The new D2-lymphadenectomy photo-scoring system did not show good performance in its current form, but it can be refined and should be validated as potential uniform tool for future trials. In addition, laparoscopic D2-gastrectomy was better suited for standardized surgical photo-evaluation than open surgery. Moreover, compliancy to D2-lymphadenectomy may be a valuable surgical quality indicator. Overall, the used evaluation metrics and applied methods in the LOGICA-trial may serve as methodological quality recommendations for future trials.

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Mini abstract

Quality of gastric cancer surgery is crucial for favorable prognosis. High radicality and nodal yield demonstrated good quality of D2-gastrectomy for gastric cancer in the LOGICA-trial. Additionally, for future trials, we recommend implementing the prospective quality control regarding the quality of dissected nodal stations based on analysis of intraoperative photographs.

CRediT authorship contribution statement

Cas de Jongh: Central trial coordinator 2020–2022, study design, Conceptualization, Data curation, Formal analysis, writing of the first draft, and final version of the manuscript. **Lianne Triemstra:** Central trial coordinator 2022-present, study design, Conceptualization, Data curation, Formal analysis, writing and review, of the manuscript. **Arjen van der Veen:** Central trial coordinator 2017–2020, study design, Data curation, patient inclusion, review the manuscript. **Lodewijk AA. Brosens:** Co-investigator, pathologist, Data curation, review of the manuscript. **Grard AP. Nieuwenhuijzen:** Local principal investigator, gastric surgeon, patient inclusion, Data curation, review of the manuscript. **Jan HMB. Stoot:** Local principal investigator, gastric surgeon, patient inclusion, Data curation, review of the manuscript. **Wobbe O. de Steur:** Local principal investigator, gastric surgeon, patient inclusion, Data curation, review of the manuscript. **Jelle P. Ruurda:** Principal investigator, gastric surgeon, study design, Conceptualization, patient inclusion, Data curation, review of the manuscript. **Richard van Hillegersberg:** Central principal investigator, gastric surgeon, study design, Conceptualization, patient inclusion, Data curation, review of the manuscript.

Declaration of competing interest

Richard van Hillegersberg: Consulting or Advisory Role: Intuitive Surgical, Medtronic. Jelle Ruurda: Consulting or Advisory Role: Intuitive Surgical. Lodewijk Brosens: Advisory Role: Bristol Myers Squibb. Grard Nieuwenhuijzen: Consulting or Advisory Role, Medtronic. Research Funding: Dutch Cancer Foundation. Travel, Accommodations, Expenses: Medtronic.

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Appendix A. Supplementary data

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