TITLE PAGE**Feasibility and safety of laparoscopic Complete Mesocolic Excision (CME) for right-sided colon cancer: short-term outcomes. A randomized clinical study.**

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Mini-Abstract

We evaluated the feasibility and safety of laparoscopic complete mesocolic excision (CME) with operative time, intraoperative blood loss and other complications, conversion rate, and anastomotic leak as primary endpoints and overall postoperative complications as the secondary endpoint. Compared to conventional resection, CME had a significantly longer operative time with a higher number of lymph nodes and longer surgical specimens. There were no differences in terms of intraoperative blood loss, conversion rate, leakage, or other postoperative complications.

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Structured Abstract

Objective: The aim of this prospective clinical study is compare short-term outcome of laparoscopic right hemicolectomy using the Complete Mesocolic Excision (CME group) with patients who underwent conventional right-sided colonic resection (NCME group).

Summary Background Data: Although CME with central vascular ligation in laparoscopic right hemicolectomy is associated with a significant decrease in local recurrence rates and improvements in cancer-related 5-year survival, there may be additional risks associated with this technique because of increased surgical complications. As a result, there is controversy surrounding its use.

Methods: In this randomized controlled trial, several primary endpoints (operative time, intraoperative blood loss, other complications, conversion rate, and anastomotic leak) and secondary endpoints (overall postoperative complications) were evaluated. In addition, we evaluated histopathologic data, including specimen length and the number of lymph nodes harvested, as objective signs of the quality of CME, related to oncological outcomes.

Results: The CME group had a significantly longer mean operative time than the NCME group (216.3 min versus 191.5 min, $p=0.005$). However, the CME group had a higher number of lymph nodes (23.8 versus 16.6; $p<0.001$) and larger surgical specimens (34.3 cm versus 29.3 cm; $p=0.002$). No differences were reported with respect to intraoperative blood loss, conversion rate, leakage, or other postoperative complications.

Conclusions: In this study laparoscopic CME were a safe and feasible technique with improvement in lymph nodes harvesting and length of surgical specimens with no increase of surgical intraoperative and postoperative complications.

Keywords: Laparoscopic colonic resection – laparoscopic complete mesocolic excision – colon cancer – right-sided colon cancer – laparoscopic surgery

Background

Since first description in 1982 by Heald Total Mesorectal Excision (TME) has become the standard of surgical resection in treatment of rectal cancer. The use of TME dramatically reduced local recurrences and improved oncological outcomes [1]. With the diffusion of laparoscopic approach for management of colon cancer several studies demonstrated an increase of recurrences in right-sided colon cancer resections due, probably, to an inadequate lymph nodes dissection [2]. In 2009 Hohenberger et al [3] proposed Complete Mesocolic Excision (CME) with Central Vascular Ligation (CVL) for laparoscopic right hemicolectomy according to principles of TME for rectal cancer. The original study reported a significant decrease in local recurrence, from 6.5% to 3.6%, and improvements in the cancer-related 5-year survival. Nevertheless, this technique seems to expose patients to a higher risk of surgical complications, and several reports have shown that patient outcomes remain controversial [4]. On the basis of these considerations, the aim of this study was to evaluate the feasibility and safety of laparoscopic CME for right-sided colon cancer in a referral surgical department for colorectal surgery. To the best of our knowledge, there are no published randomized clinical trials comparing laparoscopic CME and standard laparoscopic right hemicolectomy.

Methods

Between January 2015 and December 2019, 134 patients who underwent to laparoscopic right colonic resection were enrolled in this study and randomly allocated to receive conventional right-sided colonic resection or CME. Between January 2015 and December 2019, 134 patients who underwent laparoscopic right colonic resection were enrolled in this prospective study and were randomly allocated to receive either conventional right-sided colonic resection or CME. We performed an analysis of preoperative data, intraoperative procedures, and postoperative results (Table 1). We compared the short-term outcomes in patients who underwent laparoscopic right hemicolectomy using the CME and CVL technique (CME group) to those in patients who underwent conventional right-sided colonic resection (not CME, NCME group). Computerized randomization was performed by our department, and the information regarding planned procedures was sent to the surgical team on the morning of the surgery. The allocated procedure was not concealed to the investigators or patients (Fig. 1). This clinical study is referred to as the LaCoMEStaR (Laparoscopic Complete Mesocolic Excision versus Standard Right hemicolectomy) study, which was publicly registered (number ISRCTN71842827). The randomization was successfully performed because all surgical procedures were performed in a high-volume center by two surgeons experienced in colorectal resections and laparoscopic CME (more than 35 procedures)

before the beginning of the study in order to obtain proficiency in the standard technique. Only in two cases was there was a technical crossover between the two groups. In particular, in two patients allocated to undergo CME, complete exposure of the superior mesenteric vessels did not occur despite subsequent dissection involving the Fredet fascia. These patients were thus excluded from the final analysis.

Preoperative data

We collected preoperative data; all patients eligible for inclusion underwent a complete clinical study [5] in order to evaluate their performance status and American Society of Anesthesiology (ASA) score. In all cases, we performed a colonoscopy for the diagnosis and a computed tomography contrast-enhanced abdominal scan for tumoral staging [6, 7]. Inclusion criteria were age ≥ 18 years, right-sided colon cancer, no distant metastasis, and written informed consent. Exclusion criteria were open surgery, right colonic resections for inflammatory bowel disease (IBD), and associated major surgical procedures. We excluded five patients with IBD, two patients with synchronous right-sided rectal cancer managed with a combined procedure and transanal extraction of the specimen, and two patients who underwent laparoscopic treatment for colonic neoplasm and liver metastasis in the same surgical step.

Surgical procedure

The patient was placed on the operating table in the light Trendelenburg position with the legs apart. No patients underwent bowel preparation before the surgical procedure. Instead, we administered preoperative oral antibiotics. To induce pneumoperitoneum, we used both the trans-umbilical open technique and a Veress needle in the left subcostal region with an optical 10-mm trocar in the left peri-umbilical region [8, 9]. We positioned the other three trocars in the left hypochondrium (5 mm), left flank (12 mm), and suprapubic region (12 mm). We chose to position two 12-mm trocars to create the possibility of using the laparoscopic endostapler alternately from the left side and from the suprapubic trocar, respectively, for the section of the terminal ileum and the transverse colon.

Here, we describe the surgical details of CME. The procedure started with traction of the caecum and the terminal ileum to detect the ileum-colic vessels. This was the first fundamental step in performing CVL and, subsequently, CME, because in this phase we identified the ileocolic vessels with ligation at the origin from the superior mesenteric vessels. We continued with the dissection of the Toldt's fascia between the visceral

peritoneum of the ascending colon and the Gerota fascia. After a medial-to-lateral and bottom-up dissection, and preparation of the last ileal loop, we removed the lymph nodes and adipose tissue covering the duodenum and the head of the pancreas, with the identification of the fusion fascia of Fredet [10], complete detachment of the mesocolon, and ligation at the origin of the right colic vessels, gastrocolic trunk of Henle, and right branch of the middle colic vessels. We used a 45-mm endostapler (Echelon Flex® Endopath stapler, Ethicon or EndoGIA®; Medtronic Inc., Minneapolis, MN, USA) to section the terminal ileum and transverse colon. We performed an extracorporeal anastomosis or a side-to-side intracorporeal anastomosis with endo-stapler and a double-line continuous resorbable barbed suture and intra-corporeal knotting. In these last patients, at the end of the procedure, surgical specimens were removed through a mini-laparotomy on a suprapubic 12-mm trocar.

In the NCME group, after traction of the caecum and terminal ileum, we identified and ligated the ileum-colic vessels, with no exposure of the superior mesenteric vessels and with no dissection of the pre-duodeno-pancreatic tissue. Often, in these cases, it was not necessary to ligate at the origin of the right colic vessels or gastrocolic trunk because of the surgical dissection in the context of the mesentery.

Evaluation of surgical outcomes

We evaluated the feasibility and safety of laparoscopic CME within a follow-up period of 30-days (short-term outcome). Several primary endpoints were evaluated (operative time, intraoperative blood loss, other complications, conversion rate, and anastomotic leak) and secondary endpoints (overall postoperative complications by the Clavien-Dindo classification, with particular attention to the reoperation rate [Grade IIIB] and admission to the intensive care unit [ICU] [Grade IV]) [11]. In addition, we evaluated histopathologic data, including specimen length and lymph nodes harvested, as objective signs of the quality of CME, related to oncological outcomes. The number of reported lymph glands was contingent upon both the technical prowess of the surgeon and the diligence and techniques of the pathologist. Therefore, we involved a team of three pathologists experienced in colorectal cancer (more than 250 colorectal cancer examinations with lymph-node detection) who were blinded to the method of surgery (CME or NCME). The pathologists used a standardized report for the pathological analysis, detailing the length of the specimen, size, and location of cancer, the margin from the tumor, the number and involvement of lymph nodes, grading of the neoplasm, and the pathological staging of the disease. The surgical specimen was fixed in 10% formalin solution and then processed routinely for paraffin embedding. Conventional methods of visual inspection and palpation were used to identify the

nodes. There were no differences amongst the pathologists in terms of the number of nodes identified. We did not use a specific technique for a special fat clearance in the lymph-node detection. Tumor tissue genotyping was used instead as the routine approach in the oncological management of these patients because of its ability to guide first-line chemotherapy most effectively (e.g. identification of KRAS and/or BRAF) and identify recurrences (e.g. circulating tumor DNA). Statistical analysis was performed with SPSS 25.0 (SPSS Inc., Chicago, IL, USA) in a blinded manner, reviewed by an external statistician. Quantitative variables were expressed as mean (range) and categorical variables as count (percentage). Continuous data were analyzed with the Student's t-test and categorical variables were compared with the Chi-squared test. A p-value <0.05 was considered statistically significant. A power analysis determined that 59 patients would be required to demonstrate a clinically acceptable 30-minute difference in operative time between the CME and NCME groups at a significance level of 5% and power of 80%. Furthermore, 44 patients would be required in each group to demonstrate a clinically acceptable difference (5) in the number of lymph nodes between the CME and NCME groups at a significance level of 5% and power of 80%.

Results

Between January 2015 and December 2019, we collected data from 132 patients (70 male and 62 female) who underwent laparoscopic right colonic resection and were eligible for this study. The main demographic characteristics of the included patients are reported in Table 2. The mean age was 67.8 years (range 26–88), with a significant difference between the CME and NCME groups (70.2 years versus 65.3 years, $p<0.05$). For other variables such as sex, BMI, ASA classification, and anastomosis technique, no statistically significant differences between the groups were seen. Table 3 lists the operative outcomes of all patients. The CME group had a significantly longer mean operative time than that in the NCME group (216.3 min versus 191.5 min, $p=0.005$). However, the CME group had a higher number of lymph nodes (23.8 versus 16.6, $p<0.001$) and larger surgical specimens (34.3 cm versus 29.3 cm, $p=0.002$). No differences were reported with respect to intraoperative blood loss, conversion rate, leakage, or other postoperative complications. In terms of intraoperative blood loss, no patient in either group underwent intraoperative blood transfusion. In the postoperative period, five patients in the CME group and four patients in the NCME group required blood transfusions. In the CME group, we observed two conversions to open surgery (3%) because of voluminous cancer with infiltration of the parietal peritoneum. In the NCME group, three conversions were due to visceral

adhesions (n=2) or lesion in the colonic flexure (n=1). No conversion was linked to difficult mesocolic dissection or vascular injuries. We also registered two cases of intraoperative complications in the CME group: one case of jejunal perforation repaired with laparoscopic sutures, and one colonic perforation during dissection with no cancer dissemination. In the NCME group, there was one case of colonic perforation of the hepatic flexure with conversion to open surgery.

Discussion

In the present randomized clinical trial, there were no significant differences in terms of bleeding and blood transfusion between the two groups. In the CME group, we observed a significantly longer mean operative time, a higher number of lymph nodes, and larger surgical specimens. In the pathological examination, we considered the length of the surgical specimen and the distance of the tumor from the margin, which was greater than 5 cm in all cases. We only reported the total length of the specimen because with CVL, this implied a greater mesocolic resected area, though this is not a certainty because it could be argued that the two variables (length of the specimen and mesocolic resected area) are not necessarily co-linear. In the CME group, 25.2% of patients had positive lymph nodes (pT1 and pT2), while in the NCME group, only 17.8% of patients had positive lymph nodes. Therefore, the difference in positive lymph nodes between the two groups (CME and NCME) was statistically significant, and CME probably reduced the understaging of right-sided colon cancer. To prove with certainty that the CME reduced the understaging of right-sided colon cancer we seemingly should perform NCME resection, followed immediately by resection of additional mesentery by CME technique or detailed anatomic analysis of the resected mesentery demonstrating that some patients had positive nodes only in areas that would be considered part of the CME resection, but not the NCME resection. Both these conditions were not admitted in the clinical practice. However, the explanation of our positive results could be related to the careful research of embryological landmarks such as the fascia of Toldt and the fusion fascia of Fredet. All colorectal surgeons are familiar with the fascia of Toldt, which allows correct dissection between the ascending colon and retroperitoneum. The fusion fascia of Fredet is described as the embryological adhesion plane between the right colon and duodenal-pancreatic block. This recognition is fundamental for adequate CME and safe CVL, with identification of the superior mesenteric vein and gastrocolic trunk. Garcia-Granero et al. [10] recently described the importance of this landmark in a series of cadaveric dissections and in a group of consecutive laparoscopic right colectomies, and concluded that the fusion fascia of Fredet was essential for correct CME and lymphadenectomy, and for reducing the intraoperative risk of bleeding and other complications. In the CME

group, we prospectively described the dissection along the pancreatic-duodenal block, with complete detachment of the mesocolon and CVL, and these data were retrospectively confirmed by a thorough review of the surgical video in order to obtain a rigorous group classification. In the 67 patients in the CME group, we did not observe significant intraoperative bleeding. In laparoscopic right hemicolectomy, correct embryological sharp dissection with preservation of the visceral fascia and complete removal of the regional lymph nodes could be supported by the use of advanced energy devices and accurate vision systems, such as 3D or 4K [12, 13]. In the CME group, we observed two visceral intraoperative complications: a jejunal perforation and a colon perforation. These are uncommon complications, and both were observed in patients with history of previous surgery. The jejunal perforation occurred in a patient with cancer of the ascending colon and a previous median laparotomy for open splenectomy, performed in a trauma emergency. In this case, we found severe adhesion syndrome in the left abdominal quadrants, with difficult trocar placement. During this maneuver, we observed a millimetric jejunal perforation, which was repaired with intracorporeal sutures. A colon perforation occurred in a patient with cancer localized in the caecum and a history of laparotomic cholecystectomy (20 years prior), with severe adhesions between the colonic flexure and hepatic margin. These rare complications were due to adhesion syndrome, and had no relationship with the execution of CME. In the present study, we also considered secondary endpoints, such as postoperative complications, and found no differences between the two groups. Among the major complications, we reported two cases of reoperation (Grade IIIb sec. by the Clavien-Dindo classification) in the CME group due to postoperative acute cholelithiasis and one anastomotic leakage approached by laparoscopy [14]. In the NCME group, we observed two cases of anastomotic leakage and a patient who developed intraabdominal collection. In contrast, many other authors have found that CME was associated with more postoperative surgical complications than NCME, probably caused by extensive dissection and visceral lesions. On this basis, Strey et al. [15] attempted to describe a standardized surgical procedure, with identification of the “critical views”, in order to improve the quality of CME and reduce the surgical complication rate. In the present prospective study, we also collected histological data, such as the specimen length and the number of harvesting lymph nodes, which are objective signs of quality of CME and are directly related to oncological outcomes. Laparoscopic surgery has deepened the field of colonic resection. Several randomized studies have demonstrated surgical safety and good oncological outcomes with the laparoscopic technique versus traditional open resection [16, 17]. However, with the worldwide spread of the laparoscopic approach, more and more authors have described an increase in local recurrences in patients with right-sided colon cancer [2]. In 2009, Hohenberger et al. [3] introduced the concept of CME and CVL. These techniques

allow performance of a wider lymphadenectomy with a better pathological staging and lower rate of local recurrence. On the other hand, several authors have reported that CME was associated with a higher rate of intraoperative complications and postoperative morbidity [18]. A recent meta-analysis by Wang et al. [19] considered intraoperative blood loss and surgical complications as measures of CME safety, and concluded that CME was associated with significantly more adverse events than NCME. Many authors assigned intraoperative bleeding to vascular injuries during the central dissection of the superior mesenteric vessels and/or gastrocolic trunk [20, 21]. Hohenberger et al. [3] described a significant increase in cancer-related survival (82.1% to 89.1%) with the use of CME. Several studies that reported better results for CME in terms of large bowel length, area of mesentery, and total lymph nodes presented with an internal selection bias due to the inclusion of both open and laparoscopic CME [22, 23]. A meta-analysis by Wang et al. [19] identified this heterogeneity and described the differences due to the pathological evaluation of surgical specimens among different hospitals. The effect of CME on oncological outcomes has been reported by many authors, with controversial results attributable to the positive role of adjuvant chemotherapy. A recent review by Alhassan et al. [24] included 14 studies evaluating perioperative, histological, and oncological outcomes. In all cases, CME provided an embryological plane dissection to allow an extensive resection of the colonic mesentery. The authors instead stressed the differences between CME and D3-lymphadenectomy because both techniques ensured similar lymph nodes harvesting, but CME was superior in terms of bowel length and area of resected mesentery. This could influence oncological outcomes. Other studies compared the oncological results of CME with an historical control group that had an internal bias related to the patient selection and progressive improvement of chemotherapy [18, 25, 26]. A recent single-center study by An et al. [27] showed no differences between CME and NCME in the 5-year disease-free survival rate, but the overall survival was better in the CME group. We can infer from this that a greater mesentery area and lymph node field results in improved survival rates, but better data are needed to finally validate these results [28]. To the best of our knowledge, this is the first randomized clinical trial on the use of CME in laparoscopic right colonic resection. Correct randomization is crucial for an accurate result analysis. In this single-center study, we involved a surgical team that was experienced in laparoscopic colorectal surgery, with standardization of the technique and a low possibility of crossover between the two arms. In the description of the surgical procedures, the only differences concerned the induction of the pneumoperitoneum and the type of anastomosis. The dissection was performed precisely as described in the methods session, and was subsequently confirmed through a careful viewing of the videos. At the same time, our study had several limitations. First, it was a single-center study and the limited number of Italian patients could

represent a potentially bias in terms of preoperative characteristics (BMI distribution, comorbidity, ASA score, and previous surgery) and postoperative results. In the present study, the mean BMI was 25.5 kg/m², and although the mean BMI did not differ between the CME and NCME groups, the range of BMI did differ. A high BMI can increase the difficulty of laparoscopic surgery and/or the rate of conversion to open surgery and complications, but in the present study, BMI did not influence the feasibility and safety of laparoscopic CME. Second, we only recorded the surgical and postoperative outcomes over a short-term period in the assessment of the feasibility and safety of the CME technique, and there was a lack of oncological outcomes over a long-term follow up. Furthermore, we measured the specimen length and number of lymph nodes, but we did not report the length of the vascular pedicle and the area of the resected mesentery.

Conclusion

This prospective study considered patients who underwent laparoscopic right colectomy in a single high-volume university hospital from January 2015 to December 2019, and all procedures were performed by an experienced colorectal and laparoscopic surgical team in order to achieve a standardized technique. Moreover, data from both the CME and NCME groups were collected during the same period, with no bias linked to significant surgical and technological improvements. In this single-center randomized clinical trial, we found that in experienced hands laparoscopic CME and CVL is a safe and feasible technique, associated with greater nodal harvest without a significant increase in perioperative complications. On the basis of these short term data it is unknown whether there is oncologic benefit associated with the technique, and there is greater expense (due to increased operative time), thus it would seem appropriate to recommend the procedure for selected patients. Multi-center randomized controlled trials with larger numbers of patients and long-term follow up are needed to validate the surgical and oncological results of laparoscopic CME for right-sided colon cancer.

Abbreviations: CME (Complete Mesocolon Excision); NCME (Not Complete Mesocolon Excision); CVL (Central Vascular Ligation); TME (Total Mesorectal Excision); ICU (Intensive Care Unit)

Declarations

Ethics approval and consent to participate

Consent to publish was given by University of Palermo.

Consent to publish

All patients consented to publish their data.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

The datasets used and/or analysed during the current study are available from the Department of Surgical, Oncological and Oral Sciences, University of Palermo, Via L. Giuffrè 5 - 90127 Palermo, on reasonable request. The registration number is ISRCTN71842827.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

All authors contributed significantly to the present research. All authors read and approved final manuscript.

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Table 1. Database with analysis of patients preoperative data, intraoperative procedures and postoperative results

Preoperative data	Intraoperative procedures	Postoperative results
Demographic data	Operative time	Overall complications rate
Previous abdominal surgery	Intraoperative blood loss	Reoperation rate
ASA score	Other complications	Specimen length
Tumor location	Conversion rate	pTNM

Table 2. Details of patients preoperative characteristics.

	<i>CME (n. 67)</i>	<i>NCME (n. 65)</i>	<i>Total (n. 132)</i>	<i>P value</i>
	<i>Median (range) or %</i>	<i>Median (range) or %</i>	<i>Median (range) or %</i>	
<i>Age (years)</i>	70.2 (44 - 85)	65.3 (26 - 88)	67.8 (26 - 88)	0.023
<i>Gender</i>				
<i>M</i>	38 (56.7%)	34 (52.3%)	72 (54.5%)	
<i>F</i>	29 (43.3%)	31 (47.7%)	60 (45.5%)	
<i>Body Mass Index</i>	24.9 (20.2 - 30.5)	26.2 (19.0 - 34.7)	25.5 (19.0 - 34.7)	0.285
<i>BMI distribution</i> <i>n. of patients (%)</i>				
< 25	33 (49,5%)	28 (43,1%)	61 (46.2%)	
25 - 30	31 (46.3%)	33 (50.7%)	64 (48.5%)	
> 30	3 (4.5%)	4 (6.1%)	7 (5.3%)	
<i>Comorbidity</i>	67 (100%)	64 (99.9%)	131 (99%)	1.000
<i>Cardiovascular diseases</i>	51 (75%)	46 (71.4%)	97 (73.5%)	0.98
<i>Lung diseases</i>	17 (25%)	12 (19%)	29 (22%)	0.719
<i>Renal</i>	3 (5%)	6 (9.5%)	9 (6.8%)	0.98
<i>Diabetes</i>	13 (20%)	18 (28.6%)	31 (23.5%)	0.719
<i>Others</i>	7 (10%)	24 (37%)	31 (23.5%)	0.067
<i>Previous surgery</i>	11 (16.4%)	13 (20%)	24 (18.2)	0.98
<i>ASA score</i>				0.684
ASA 2	5 (7.5%)	6 (9.2%)	11 (8.3%)	
ASA 3	57 (85.1%)	54 (83.1%)	111 (84.1%)	
ASA 4	5 (7.5%)	5 (7.7%)	10 (7.6%)	
<i>Tumor location</i>				0.495
<i>Cecum</i>	18 (26.9%)	29 (44.6%)	47 (35.6%)	
<i>Ascending</i>	33 (49.2%)	26 (40%)	59 (44.7%)	
<i>Hepatic flexure</i>	12 (18%)	7 (10.8%)	19 (14.4%)	
<i>Proximal transverse</i>	4 (5.9%)	3 (4.6%)	7 (5.3%)	

Table 3. Operative outcomes and short-term complications rate

	<i>CME (n. 67)</i>	<i>NCME (n. 65)</i>	<i>Total (n. 132)</i>	<i>P value</i>
	<i>Median (range) or %</i>	<i>Median (range) or %</i>	<i>Median (range) or %</i>	
<i>Operative time (min)</i>	216.3 (130 – 300)	191.5 (120 – 310)	204 (120 – 310)	0.005
<i>Blood loss (ml)</i>	185 (50 – 350)	200 (50 – 300)	190 (50 – 350)	0.98
<i>Conversion</i>	2 (3%)	3 (4.6%)	5 (2.3%)	0.98
<i>Anastomotic leak</i>	1 (1.5%)	2 (3%)	3 (3.8%)	0.77
<i>Specimen length (cm)</i>	34.3 (21.5 – 67)	29.3 (17.5 – 68)	31.8 (17.5 – 68)	0.002
<i>Lymph nodes (n)</i>	23.8 (12 – 38)	16.6 (5 – 37)	20.3 (5 – 38)	0.001
<i>T stage</i>				0.712
<i>T1</i>	26 (38.8%)	31 (47.7%)	57 (43.2%)	
<i>T2</i>	8 (12%)	9 (13.8%)	17 (12.9%)	
<i>T3</i>	29 (43.3%)	21 (32.3%)	50 (37.9%)	
<i>T4</i>	4 (5.9%)	4 (6.1%)	8 (6%)	
<i>N stage</i>				0.001
<i>N0</i>	33 (49.2%)	41 (63.1%)	74 (56.1%)	
<i>N1</i>	24 (35.8%)	19 (29.2%)	43 (32.6%)	
<i>N2</i>	10 (14.9%)	5 (7.7%)	15 (11.4%)	
<i>M stage</i>				0.98
<i>M0</i>	64 (95.5%)	63 (97%)	127 (96.2%)	
<i>M1</i>	3 (4.5%)	2 (3.1%)	5 (3.8%)	
<i>Intraoperative complications</i>	2 (3%)	1 (1.5%)	3 (2.3%)	0.886
<i>Postoperative complications sec. Clavien-Dindo</i>				
<i>Grade I - II</i>	13 (19.4%)	11 (17%)	24 (18.2%)	0.675
<i>Grade IIIa</i>	2 (3%)	1 (1.5%)	3 (2.3%)	0.886
<i>Grade IIIb</i>	2 (3%) ¹	3 (4.6%) ²	5 (3.8%)	0.98
<i>Grade IV³</i>	6 (8.9%)	7 (10.7%)	13 (9.8%)	0.98
<i>Grade V</i>	2 (2.9%)	1 (1.5%)	3 (2.3%)	0.98

¹two cases of anastomotic leak; ²two cases of anastomotic leak and one patient with intra-abdominal collection. ³In Grade IV complications sec. Clavien-Dindo classification we included all patients that required ICU management in postoperative period.