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Minimally Invasive versus Open Approach for Right-Sided Colectomy: A Study in 12,006 Patients from the Dutch Surgical Colorectal Audit

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Keywords

Laparoscopy · Colon cancer · Right colectomy

Abstract

Background: There is ongoing debate whether laparoscopic right colectomy is superior to open surgery. The purpose of this study was to address this issue and arrive at a consensus using data from a national database. Methods: Patients who underwent elective open or laparoscopic right colectomy for colorectal cancer during the period 2009-2013 were identified from the Dutch Surgical Colorectal Audit. Complications that occurred within 30 days after surgery and 30-day mortality rates were calculated and compared between open and laparoscopic resection. Results: In total, 12,006 patients underwent elective open or laparoscopic surgery for right-sided colorectal cancer. Of these, 6,683 (55.7%) underwent open resection and 5,323 (44.3%) underwent laparoscopic resection. Complications occurred within 30 days after surgery in the laparoscopic group in 26.1% of patients and in 32.1% of patients in the open group (p < 0.001). Thirty-day

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E-Mail karger@karger.com www.karger.com/dsu mortality was also significantly lower in the laparoscopic group (2.2 vs. 3.6% p < 0.001). **Conclusion:** In this non-randomized, descriptive study conducted in the Netherlands, open right colectomy seems to have a higher risk for complications and mortality as compared to laparoscopic right colectomy, even after correction for confounding factors.

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Introduction

Laparoscopic colorectal surgery has grown in popularity ever since it was first described in 1991 [1]. Since then, several randomized trials have indicated that laparoscopic surgery can be applied safely for treating both malignant and benign diseases. Generally accepted advantages of laparoscopy include reduced blood loss, fewer adhesions, less pain, decreased risk of long-term incisional hernia formation, shorter hospital stay, better cosmetic effects and faster return to normal activities [2–5]. Specific advantages of laparoscopic colorectal

Robbert J.I. Bosker, MD Department of Surgery, Deventer Hospital PO Box 5001, NL-7400 GC Deventer (The Netherlands) E-Mail r.bosker@dz.nl surgery as compared with conventional colorectal surgery include shorter duration of post-operative paralytic ileus, better pulmonary function and improved quality of life [6–9].

However, some authors have stated that these results could not be applied to right-sided colectomy [10, 11]. Conversely, some recent studies have shown that mortality and morbidity were significantly lower after laparoscopic right-sided colectomy compared to mortality and morbidity after open surgery [12, 13].

The purpose of this study was to address this controversy and provide a recommendation for daily practice in colon surgery. Therefore, patient outcomes for morbidity and mortality in both elective laparoscopic and open right colectomy for colon cancer were compared using a national database in the Netherlands.

Material and Methods

Database

For this study, data was derived from the Dutch Surgical Colorectal Audit (DSCA), a national, web-based and interactive database in the Netherlands [14]. All Dutch Hospitals performing colectomies were included in this database. The database included information on patient and tumour characteristics, diagnostics, procedures and short-term outcomes of patients undergoing a resection for primary colorectal carcinoma. The dataset is based on evidence-based guidelines and annually verified with the Netherlands Cancer Registry data. From January 2009 until December 2013, 48,757 patients were included in the DSCA database [15].

Patient Selection

For the present analysis, patients who underwent elective right colectomy for cancer were selected (n = 15,018). After exclusion of patients with missing data on 30-day post-operative mortality (n = 304, 2.0%) and patients who underwent an acute resection (n = 2,708, 18.0%), 12,006 patients were included for the present analysis.

Included Variables

Thirty-day mortality was considered the primary outcome (dichotomous variable). For all included patients, the vital status was known. Date of resection and date of death (if applicable) were used to compose the variable vital status 30 days after surgery. Thirty-day post-operative complications were analyzed as secondary outcome. The occurrence of 30-day complications was registered for 11,925 of the 12,006 (99.3%) included patients.

Complications were scored on the following categories: surgical, pulmonary, cardiac, thrombo-embolic, infectious, neurologic or other.

In addition, data on demographics, tumour characteristics and procedure characteristics of all patients included the following:

1. Demographics: age, gender, body mass index (BMI), pre-operative morbidity (cardiac, vascular, diabetes, pulmonary, neurologic, gastrointestinal, urogenital, thrombotic, muscular, endocrine, infectious, malignancies, previous abdominal surgery), pre-operative condition as measured using the American Society of Anesthesiologists (ASA) score.

- 2. Tumour characteristics: histological type, histopathological results according to the TNM classification.
- 3. Procedure characteristics: type of resection, conversion (early/ late), and inter-operative complications.

Statistical Analysis

Patients were categorized into 2 groups according to the reported surgical procedure: open or laparoscopic resection. Next, demographic, tumour and procedure characteristics were compared between these 2 groups using independent Student *t* tests and Mann-Whitney test for normally and skewed distributed continuous variables, respectively, and chi-square tests for categorical variables.

To study the association between the type of resection and 30-day post-operative mortality and complications, 2 logistic regression models were used with 30-day mortality (dichotomous) or 30-day complications (dichotomous) as dependent variable and type of resection (open or laparoscopic) as independent variable. The results of the logistic regression were presented as OR with 95% CI. To study the influence of other factors on the association between type of resection and post-operative mortality complications, 2 multivariate regressions were performed in which potential confounding factors were included as co-variables. These variables were age (continuous), gender (dichotomous), ASA score (dichotomous, I/II vs. III/IV) resection R0-R2 (categorical), BMI (continuous), previous abdominal surgery (dichotomous), tumour location (dichotomous), pre-operative co-morbidity (dichotomous), and N classification. These potential confounders were selected based on previous literature and/ or based on their significant contribution to the univariate model when they were entered one by one (an effect over >10% on the regression coefficient of type of surgery was used as cut-off value). In addition, since effect modification by T classification was anticipated, regression models were stratified according to T classification (T1-3 vs. T4). The OR with 95% CI from these multivariable regression models was presented as the outcome of our study. All analyses were performed in IBM SPSS version 22.0. A *p* value of <0.01 was considered statistically significant.

Results

Demographic, Tumour and Procedure Characteristics.

In this study, we analyzed 12,006 patients of whom 6,683 (55.7%) patients underwent open right-sided colon resection and 5,323 (44.3%) laparoscopic right-sided colon resection. Demographic and clinical characteristics are shown in Table 1. When comparing both patient groups, there were significantly more females in the laparoscopic resection group as was a small, but statistically significant, higher mean age and BMI. In addition, preoperative malignancies, previous abdominal surgery, high ASA score (≥III), blood transfusion during hospital

 Table 1. Baseline patient characteristics and tumour characteristics

	Open	Laparoscopio	c <i>p</i> value		Open	Laparoscopic	<i>p</i> value
n (%)	6,683 (55.7)	5,323 (44.3)		Number of lymph			
Patient characteristics				nodes, mean (SD)	18.02 (9.9)	18.08 (8.4)	0.71
Age, years, mean (SD)	72.9 (10.5)	71.6 (10.5)	< 0.001	Number of positive	1 = 4 (2 (2)	1 20 (2 15)	0.001
Age ≥ 65 years, %	79.6	77.7	< 0.001	lymph nodes, mean (SD)	1./4 (3.6)	1.39 (3.15)	<0.001
Gender, male, %	45.2	48.0	0.002	1 classification, %		6.4	
BMI, gem, mean (SD)*	25.9 (4.4)	26.3 (4.3)	< 0.001		4.4	6.4	
BMI ≥30, %	15.9	16.6	0.34	12	14.9	18.7	<0.001
Preoperative				13	62.3	63.2	<0.001
co-morbidity, %				14	17.2	10.3	
Cardiac	31.3	31.1	0.89	1x	1.0	0.8	
Vascular	40.0	40.9	0.32		0.2	0.2	
Diabetes	17.7	17.4	0.72	N classification, %			
Pulmonary	14.6	14.0	0.38	0	59.8	64.2	
Neurological	16.0	15.9	0.83	l	23.6	22.1	
Gastrointestinal	11.0	10.5	0.34	2	16.1	13.4	< 0.001
Urogenital	8.9	82	0.22	Nx	0.4	0.4	
Thrombotic	4 1	4 2	0.22	Pre-operative complications			
Muscular	7.0	8.1	0.02	tumour, %			
Endocrine	67	6.9	0.02	None	74.6	71.1	
Infectious	0.8	0.9	0.70	Faecal peritonitis	0.2	0.1	
Malignancies	16.0	12.7	<0.70	Abscess	0.9	0.3	
Dravious abdominal	10.0	12.7	<0.001	Ileus	2.5	1.4	< 0.001
	40.5	25.9	<0.001	Anaemia	16.4	22.4	
ASA score (%III V)	40.3	33.0 24.1	<0.001	Other	5.5	4.8	
ASA score (%111- v)	27.2	24.1	<0.001	Conversion, %			
Tumor and procedure chara	acteristics			No	na	87.9	
Histological type, %				Early	na	6.3	
Adenocarcinoma	89.5	90.9		Late	na	5.8	
Mucinous tumours	7.3	6.1	0.03	Intraoperative complications			
Signet ring cell	1.3	0.9		None	98.4	98.0	
Other	2.0	2.1		Yes (bleeding, injury			
R0–R2 resection, %				other abdominal organ	ι,		
R0	96.8	98.6		perforation bowel)	2.0	1.6	0.56
R1	2.0	1.0	< 0.001				
R2	1.2	0.4		* >10% missing cases.			

stay and R1–R2 resections were significantly more frequent in patients who underwent open resection. The number of lymph nodes removed was the same in both groups. Pathological data showed significantly more positive lymph nodes, more T4 and more N2 classifications in open resection as compared to laparoscopic resection.

Post-Operative Complications

Within 30 days after surgery, significantly more patients who underwent an open resection showed postoperative complications as compared to patients in the laparoscopic surgery group (Table 2). Especially, surgical complications leading to a re-intervention were more prevalent in patients who underwent an open procedure. Table 3 presents the results of the logistic regression analyses of type of resection in relation to 30-day post-operative complications. After adjustment for potential confounders, patients who underwent open surgery had a statistically significant 1.34 (95% CI 1.24–1.45) higher odds of complications within 30 days after surgery as compared to patients in the laparoscopic surgery group. The odds were somewhat higher for patients with T4 tumours as compared to patients with T1–3 tumours (1.50 [1.16–1.93] vs. 1.32 [1.20–1.45]), but the confidence intervals overlapped.

Post-Operative Mortality

In total, 353 (2.9%) patients died within 30 days after resection, 115 of the 5,323 patients who underwent laparoscopic resection died (2.2%) and 238 of the 6,683 pa-

Right-Sided Colectomy in 12,006 Patients

Groningen 190 - 6/19/2019 3:04:17 PM

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Table 2. Complications within 30 days after surgery

Total population	Open, <i>n</i> (%)	Laparoscopic, <i>n</i> (%)	<i>p</i> value	
Complication <30 days	2,135 (32.1)	1,380 (26.1)	<0.001	
Re-intervention for surgical complication	815 (12.3)	524 (9.9)	< 0.001	
Anastomotic leakage	312 (4.7)	214 (4.1)	0.09	
Pulmonary	319 (4.8)	252 (4.8)	0.67	
Cardiac	213 (3.2)	132 (2.5)	0.022	
Thromboembolic	39 (0.6)	25 (0.5)	0.40	
Infectious	194 (2.9)	116 (2.2)	0.01	
Neurologic	68 (1.0)	65 (1.2)	0.28	
Other	320 (4.8)	203 (3.8)	0.01	
≥ 2 complications	356 (5.3)	236 (4.4)	0.025	
Blood transfusion	1,247 (20.3)	774 (15.2)	< 0.001	
Readmission within 30 days	204 (8.7)	181 (6.6)	< 0.001	

Table 3. Risk of complications within 30 days after surgery

	Laparoscopic	Open	<i>p</i> value
Complications <30 days of surgery, <i>n</i> (%)	1,380 (26.1)	2,135 (32.1)	< 0.001
Logistic regression models		OR (95% CI)	
Not adjusted	1		
Total population		1.34 (1.24–1.45)	< 0.001
T1-3		1.30 (1.20-1.42)	< 0.001
Τ4		1.48 (1.18-1.85)	0.001
Adjusted for ASA score, age, gender, R1–R2 resection, BMI, previous			
abdominal surgery, co-morbidity, N classification	1		
Total population		1.34 (1.23-1.47)	< 0.001
T1-3		1.32 (1.20-1.45)	< 0.001
T4		1.50 (1.16–1.93)	0.002

tients who underwent open resection died (3.6%). Table 4 shows the results of the logistic regression analyses of type of resection in relation to mortality. After adjustment for potential confounders, patients who underwent open surgery had a 1.42 (95% CI 1.10–1.83) higher odds of mortality within 30 days after surgery as compared to patients who underwent laparoscopic surgery. In addition, the odds were higher in patients with T4 tumours (3.03 [1.33–6.93]) as compared to patients with T1–3 tumours (1.30 [0.99–1.71]).

Discussion

In the present study, we investigated the risk of open and laparoscopic right colectomy on 30-day postoperative complications and mortality. After adjustment for potential cofounders, patients who underwent a right, open colectomy had a significantly 1.34 and 1.42 higher odds of complications and mortality respectively. In addition, the odds for mortality in patients presented with a T4 tumour were higher as compared to patients with a T1–3 tumour, i.e. 3.03 and 1.30, respectively.

The advantage of a minimally invasive approach for colon surgery has been demonstrated by several multicentre studies [2–5]. However, most studies do not differentiate between left- and right-sided resections. Most surgeons appreciate the advantages of the laparoscopic approach for left colectomies, but this seems a debatable matter for the right-side approach [10, 11].

This non-randomized observational study was therefore designed to address this issue. This study describes daily practice in the Netherlands. The laparoscopic approach is performed in 44% of all elective right colectomies in the Table 4. Risk of death within 30 days after surgery

	Laparoscopic	Open	<i>p</i> value
Mortality <30 days of admission, n (%)	115 (2.2)	238 (3.6)	<0.001
Logistic regression models		OR (95% CI)	
Not adjusted	1		
Total population		1.67 (1.34-2.10)	< 0.001
T1-3		1.57 (1.23-2.01)	< 0.001
T4		288 (1.41-5.88)	0.004
Adjusted for ASA score, age, gender, R1–R2 resection, BMI, previous			
abdominal surgery, co-morbidity, N classification	1		
Total population		1.42 (1.10-1.83)	0.007
T1-3		1.30 (0.99–1.71)	0.06
T4		3.03 (1.33-6.93)	0.009

Netherlands. The reason that a decade after large prospective randomised clinical trials looking at laparoscopic versus open surgery, the uptake of laparoscopic right colectomy is still less than 50% is not clear from the database. We think this might have to do with the surgical culture in different groups. Due to privacy rules, investigators only have access to an anonymous version of the DSCA. Therefore, we were not able to see if there are differences in uptake and variation in results between different hospitals, which would have been of added value to our study.

Some surgeons argue that an open right colectomy can be performed through a small transverse incision, the same size that is necessary for extracting the specimen and for making the anastomosis in laparoscopic surgery. Perhaps nowadays when more intra-corporal anastomoses are being made, there is a higher uptake of laparoscopic surgery. On the other hand, recently in 2012, an article was published by a Dutch group, which concluded that laparoscopic and transverse right colectomy were one and the same [11].

The group of patients selected for laparoscopic surgery seems to have a slightly more favourable set of characteristics. This could lead to potential selection bias, and may be more difficult cases were operated open. However, the differences between the 2 groups are very small and significant only due to the large number of patients but probably clinically less relevant. When looking at the short-term oncological outcomes, the number of lymph nodes removed is the same in both groups, but there are more R1 and R2 resections in the open group. This could also be due to selection bias or the quality of the surgery.

An interesting finding of this study is the difference in 30-day post-operative complications and mortality. Patients who underwent open right colectomy had a 1.34 and 1.42 higher odds ratio of complications and mortality respectively. In addition, the risk of mortality is highest in patients with a T4 tumour.

The higher mortality rate in the open group compared to the laparoscopic group is in agreement with results from other studies [12, 16, 17]. A systematic review and meta-analysis by Arezzo et al. [12] representing 3,049 patients observed a mortality of 1.2% in the laparoscopic group compared to 3.4% in the open group.

The Danish population based-study is the only population-based study that analyzed the data for colon and rectal cancer separately [16]. This group reported a drop in mortality in all colon resections from 7.8 in 2001–2002 to 2.8% in 2011. They concluded that the implementation of laparoscopic surgery might be the main factor for this observation.

A drawback to this conclusion might be a selection of patients as a reason for this finding. Patients excluded from laparoscopic surgery might have had a higher risk profile and therefore a worse outcome. As shown in our data, more patients with T4 tumours were selected for open surgery. The latter is put in different perspective by a previous study of McCloskey et al. [18]. They reported that the positive effect of laparoscopy might be stronger in more high-risk patients than in low-risk patients. In our study, patients selected for open surgery had significantly higher BMI, a history of having undergone abdominal surgery and a higher ASA classification. However, after correction for these confounding factors, patients who underwent an open procedure still had a 1.34 higher OR for complications and a 1.42 higher odds for mortality.

The DSCA only provides short-term outcome. Therefore, we are not able to determine the effects of the onco-

Groningen 190 - 6/19/2019 3:04:17 PM logic outcome. The fact that we are not able to provide information on long-term outcome is a limitation to our study and means that our results should be interpreted with care.

Furthermore, due to the retrospective nature of this study, there might still be some selection bias even if the 2 groups seem comparable after adjustment for confounding factors. For instance, the database does not describe what kind of T4 tumour the surgeon was dealing with. Was it a cecal T4 tumour with only a little serosal involvement or a large tumour invading the duodenum? The same argument could be made about factors such as ASA or co-morbidity, which are subjective and prone to inconsistency. In this non-randomized, observational study in the Netherlands, it was found that open right colectomy leads to a higher complication rate and higher 30-day mortality as compared to laparoscopic right colectomy. This could be because more difficult cases underwent the open surgery, but even after correction for confounding factors it was found that there were more complications and 30-day mortality in the open group.

Disclosure Statement

The authors declare no conflicts of interest.

References

- Jacobs M, Verdeja JC, Goldstein HS: Minimally invasive colon resection (laparoscopic colectomy). Surg Laparosc Endosc 1991;1: 144–150.
- 2 Abraham NS, Young JM, Solomon MJ: Metaanalysis of short-term outcomes after laparoscopic resection for colorectal cancer. Br J Surg 2004;91:1111–1124.
- 3 Gutt CN, Oniu T, Schemmer P, Mehrabi A, Buchler MW: Fewer adhesions induced by laparoscopic surgery? Surg Endosc 2004;18: 898–906.
- 4 Dowson HM, Bong JJ, Lovell DP, Worthington TR, Karanjia ND, Rockall TA: Reduced adhesion formation following laparoscopic versus open colorectal surgery. Br J Surg 2008; 95:909–914.
- 5 Laurent C, Leblanc F, Bretagnol F, Capdepont M, Rullier E: Long-term wound advantages of the laparoscopic approach in rectal cancer. Br J Surg 2008;95:903–908.
- 6 Weeks JC, Nelson H, Gelber S, Sargent D, Schroeder G; Clinical outcomes of Surgical Therapy (COST) Study Group: Short-term quality-of-life outcomes following laparoscopic-assisted colectomy vs open colectomy for colon cancer: a randomized trial. JAMA 2002;287:321–328.

- 7 Veldkamp R, Kuhry E, Hop WC, Jeekel J, Kazemier G, Bonjer HJ, et al: Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial. Lancet Oncol 2005;6:477–484.
- 8 The Clinical Outcomes of Surgical Therapy Study Group, Nelson H, Sargent DJ, Wieand HS, et al: A comparison of laparoscopically assisted and open colectomy for colon cancer. N Engl J Med 2004;350:2050–2059.
- 9 Kuhry E, Schwenk W, Gaupset R, Romild U, Bonjer J: Long-term outcome of laparoscopic surgery for colorectal cancer: a cochrane systematic review of randomised controlled trials. Cancer Treat Rev 2008;34:498–504.
- 10 Braga M, Frasson M, Vignali A, Zuliani W, Di Carlo V: Open right colectomy is still effective compared to laparoscopy: results of randomized trial. Ann Surg 2007;246:1010– 1014.
- 11 Tanis E, Van Geloven AA, Bemelman WA, Wind J: A comparison of short-term outcome after laparoscopic, transverse, and midline right-sided colectomy. Int J Colorectal Dis 2012;27:797–802.
- 12 Arezzo A, Passera R, Ferri V, Gonella F, Cirocchi R, Morino M: Laparoscopic right colectomy reduces short-term mortality and morbidity.

Results of a systematic review and meta-analysis. Int J Colorectal Dis 2015;30:1457–1472.

- 13 Rondelli F, Trastulli S, Avenia N, Schillaci G, Cirocchi R, Gulla N, et al: Is laparoscopic right colectomy more effective than open resection? A meta-analysis of randomized and nonrandomized studies. Colorectal Dis 2012; 14:e447-e469.
- 14 Van Leersum NJ, Snijders HS, Henneman D, Kolfschoten NE, Gooiker GA, ten Berge MG et al: The Dutch surgical colorectal audit. Eur J Surg Oncol 2013;39:1063–1070.
- 15 Annual Report. The Dutch Surgical Colorectal Audit, 2013.
- 16 Iversen LH, Ingeholm P, Gogenur I, Laurberg S: Major reduction in 30-day mortality after elective colorectal cancer surgery: a nationwide population-based study in Denmark 2001– 2011. Ann Surg Oncol 2014;21:2267–2273.
- 17 Kolfschoten NE, Leersum NJ, Gooiker GA, Marang van de Mheen PJ, Eddes EH, Kievit J, et al: Successful and safe introduction of laparoscopic colorectal cancer surgery in Dutch hospitals. Ann Surg 2013;257:916–921.
- 18 McCloskey CA, Wilson MA, Hughes SJ, Eid GM: Laparoscopic colorectal surgery is safe in the high-risk patient: a NSQIP risk-adjusted analysis. Surgery 2007;142:594–597.

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