Short-term outcomes after elective colon cancer surgery: An observational study from the Norwegian registry for gastrointestinal and HPB surgery, NoRGast.

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ABSTRACT

Background: To describe the real burden of major complications after elective surgery for colon cancer in Norway, and to assess which predictors that are significantly associated with the short-term outcome.

Methods: An observational, multi-centre analysis of prospectively registered colon resections registered into the Norwegian Registry for Gastrointestinal Surgery, NoRGast, between January 2014 and December 2016. A propensity score-adjusted subgroup analysis for surgical access groups was attempted, with laparoscopic resections grouped as intention-to-treat.

Results: Out of 1812 resections, 14.0% of patients experienced a major complication within 30 days following surgery. The over-all reoperation rate was 8.7%, and rate of reoperation for anastomotic leak was 3.8%. Twenty patients (1.1%) died within 30 days after surgery. Higher age was not a significant predictor of major complications, including 30-day mortality. After correction for all co-variables, open access surgery was associated with higher rates of major complications (OR 1.67 (CI 1.22-2.29), p=0.002), higher 30-day mortality (OR 4.39 (CI 1.19-16.13) p=0.026) and longer length-of-stay (HR 0.58 (CI 0.52-0.65) p<0.001).

Conclusions: Our results indicate a low complication burden and high rate of uneventful patient journeys after elective surgery for colon cancer in Norway. Age was not associated with higher morbidity or mortality rates. Open access surgery was associated with an inferior short-term outcome.

Key words: Short-term outcomes, colon cancer, elective surgery, laparoscopy

INTRODUCTION

In 2012 Norway reported the world's 6th highest incidence of colorectal cancer (1), and the incidence has for the past decades been steadily increasing. (2) The prognosis following surgical treatment is excellent, with a 5-year relative survival rate of 84 % after resection for non-metastatic disease. (3) Even the oldest and most frail patients will often be offered surgery with curative intent. While the potential gain from uneventful surgery is large, the consequences of major complications may be devastating with loss of function and impaired quality of life that are at best temporary. There is also a growing interest for the negative impact from non-fatal major surgical complications on long-term cancer survival. (4-6) Given its high incidence rate and potentially good prognosis, a nationwide high-quality surgical service for colon cancer is a vital concern for public health.

While surgery for most other cancer forms (including rectal cancer) is centralized, surgery for malignant tumours of the colon is still performed in general hospitals in Norway. The Norwegian Colorectal Cancer Registry (NCCR) continuously surveys the oncological outcomes on national and hospital level, but includes only limited data for major complications and risk factors. Randomized controlled trials (RCTs) and selected single-centre series should be complemented by data that illustrate real-life outcomes for all patients and all surgeons. The novel Norwegian Registry for Gastrointestinal surgery (NoRGast) is a prospective registry for colorectal, upper gastrointestinal and hepato-pancreato-biliary (HPB) surgery that offers readily available outcome data for a national cohort and includes core case-mix factors for risk adjustment (7). The registry is procedure-based, and all formal HPB or gastrointestinal resections are eligible for inclusion. Data is entered by a health care professional through a secured web portal. All Norwegian hospitals, ranging from large tertiary colorectal, upper GI or HPB units to small general hospitals performing less than 20 colonic resections per year are invited to contribute. Contribution was initially voluntarily, but as the registry received status as a national quality registry in 2016 the registration has since been made mandatory.

The aim of this study was to describe the real-life complication burden after elective resections for colonic cancer in Norway, and to assess factors that influence the short-term outcome.

METHODS

NoRGast started data collection in 2014 and holds by entry of 2018 data for over 17.000 resections for both malignant and benign disease. The dataset includes patient baseline data, procedural characteristics and outcomes prospectively registered by the operating unit under index admission and at a 30-day follow-up. This is described in more detail elsewhere. (7) ERAS has been endorsed by all hospitals following a series of national symposia. However, this registry does not hold any data that assess the degree of compliance to standard protocols.

Data from all colonic resections performed between 01.01.2014 and 01.12.2016 were retrieved from the NoRGast database. The included resections were grouped by NCSP-codes (8) as "ileocecal resections and right hemicolectomies" (JFB 20-21-30-31-33-34), "resections of the transverse colon and left hemicolectomies" (JFB 40-41-43-44), "sigmoid resections" (JFB 46-47-53-54-60-61) and "subtotal, total and other colectomies" (JFB 50-51-63-64 and JFH 00-01-10-11). Only resections performed for confirmed or strongly suspected colonic neoplasia were included. These were identified by having a corresponding ICD-diagnosis (9) denoting cancer or neoplasia (C18.0-9, C19, D01.0-1, D12.0-7, D37.2-4 or K63.5). Non-scheduled surgery, defined by start of anaesthesia between 4 PM and 8 AM or performed during weekends and public holidays, was excluded. Tumour stage is not recorded in the registry and was accordingly not included in this analysis.

All patients included in NoRGast have given written consent to have their data stored in the registry, and the register holds a data storage licence from the Norwegian Data Authority. The study was approved by both the Regional Ethics Committee and the Data Protection Officer, and performed within the limits and regulations of the written consent already obtained.

Severe pulmonary disease (FEV1 < 50% and or vital capacity < 60%) and severe cardiac disease (NYHA class 3 or 4, or severe arrhythmia requiring mechanical support) were defined in concordance with the modified Estimation of Physiologic Ability and Surgical Stress (mE-PASS) definitions (10). Weight loss was defined as weight loss of any size

calculated from patient-reported weight 6 months prior to surgery and scaled weight upon admission. Surgical access modality was analysed as intention-to-treat, comparing all intended laparoscopic resections (completed or converted to open procedure) to primarily open resections. CRP and albumin levels used in the modified Glasgow Prognostic Score (mGPS) were measured within three weeks preoperatively.

The Accordion system for grading postoperative complications is used in the registry. (11) Briefly, any percutaneous, angiographic or endoscopic intervention is classified as Accordion grade 3, reoperation with new access to the abdomen or single organ failure (SOF) as Accordion grade 4, reoperation *and* SOF, or multi-organ failure (MOF) as Accordion grade 5, and death as Accordion grade 6. (11) Only the highest graded complication is scored for any given patient. The primary outcome was any major complication (defined as Accordion grade 3 or higher) occurring within 30 days after index surgery with separate sub-analyses for reoperation, anastomotic leak (AL) and mortality. All major complications occurring during transfer- or readmission stays within 30 days were also included. AL was defined as reoperation with anastomotic dehiscence as the primary intraoperative finding. Only resections where a new anastomosis was fashioned were included in analysis of AL rates. Deep infection near the anastomosis was classified as AL if discovered upon reoperation, but classified as accordion grade 3 (and omitted from AL definition) if solely percutaneous drainage was performed.

For univariable analyses Pearson chi-square or Fischer exact test (as fit) was used for categorical data, and two-sided t-test was used for continuous variables. Unadjusted odds ratios (OR) were computed for crude effect measure. A backward, step-wise method for binary logistic regression was used to further explore associations between predictors and outcomes, with adjusted OR (aOR) estimated for effect size. Only predictors with a p-value <0.05 in univariable analysis for each outcome were included. To assess the regression model for possible multicollinearity the variance inflation factor was computed. For subgroup analyses comparing outcomes for access modality, a propensity score correcting for skewness in baseline characteristics was calculated. (12) The propensity score was then included in a second binary logistic regression together with access modality, age and gender. Correction with propensity score in logistic

regression was chosen over propensity score matching due to minor baseline differences in the two access groups. Patients with missing values were selectively excluded from the univariate analyses, and for regression analyses patients with any missing value were excluded. Predictors with a level of missing values above 20% were excluded from analyses. Age was grouped for univariable analyses, but analysed as a continuous variable in regression analyses. Significance level was set to $p<0.05$, and all confidence intervals were 95%. SPSS 24 software (IBM) was used for all analyses.

The manuscript was drafted in accordance with the STROBE guidelines for observational studies. (13)

RESULTS

Data from 2778 colon resections performed between 1 January 2014 and 15 December 2016 were retrieved from the NoRGast database. Of these, 966 patients were excluded for either having a main diagnosis of non-neoplastic disease (n=711), start of anaesthesia between 4 PM and 8 AM indicating non-scheduled surgery (n=108) or both (n=147), leaving 1812 eligible patients for further analysis. See flowchart (Figure 1). A total of 960 resections (53.0%) were completed by laparoscopic technique, 109 resections (10,2% of all commenced as laparoscopy) were converted to open technique, and 743 (41.0%) were primarily open procedures. Sixteen surgical units contributed data, of which five were large academic hospitals and the remaining units general hospitals with a varying annual number of colonic resections. The distribution in use of laparoscopy is grouped by annual hospital volume and shown in Table 1. The contributing hospitals perform approximately 60 % of the annual number of colonic resections in Norway. The median number of included resections from each unit was 138 (range 24-365) and the median frequency of laparoscopic access 69.0% (range 28-100). Preoperative weight loss suffered from a high number of missing values (47%) due to lacking registration of patient-reported weight 6 months prior to surgery, and was excluded from further analysis. The rate of missing values was 16.9% for the modified Glasgow Prognostic Score (mGPS), 7.0% for BMI and all other variables had a missing value rate of less than 2%.

Of the 1812 resected patients, 249 (14.0%) experienced a major complication (Table 2, Figure 2). Of these 249 patients, 20 (1.1%) died (i.e. Accordion grade 6). Another 17 patients (0.9%) had a grade 5 complication; 171 patients (9.4%) had grade 4, and 46 patients (2.5%) a grade 3 complication. In univariable analysis, older age, male gender, higher ECOG-, mGPS- or ASA-scores and open surgery were all associated with a higher complication rate. In a multivariable model, the higher complication rates observed with higher mGPS (aOR mGPS 0 to 2: 1.82 (CI 1.17-2.82)) and ASA-scores (aOR ASA 1 to 3: 2.27 (CI 1.06-4.87)) as well as open access technique (aOR 1.55 (CI 1.15-2.10)) remained statistically significant. The crude incidences of reinterventions and organ failure stratified by access type are shown in Figure 3.

A total of 158 patients (8.7%) had a reoperation within 30 days (Table 3). Of these, 146 patients had a reoperation during the index stay and 26 patients following primary discharge, but within 30 days from index surgery. Main finding at reoperation was AL in 62 (39.2%) patients, wound dehiscence in 32 (20.3%), intraabdominal bleeding in 11 (7.0%) and deep infection not in proximity to the anastomosis in 9 (5.7%) patients. In 39 patients (24.7%) there were other findings, and in five patients (3.2%) there were no specific findings upon reoperation. Male gender, open access and resection type were significant single predictors for undergoing a reoperation. In multivariable analysis, only male gender (aOR 1.48 (CI 1.06-2.06)) and resection type remained statistically significant.

Some 1663 patients (91.8 %) had a new anastomosis fashioned at index surgery, of whom 62 (3.7%) had a reoperation with AL as primary finding (Table 4). The only significant predictor of AL requiring reoperation was resection type (aOR for AL with ileocecal and right hemicolectomies as reference: transversal and left hemicolectomies 2.46 (CI 1.23-4.93) and subtotal, total and other colectomies 2,20 (CI 1.40-8.83)).

Twenty patients died within 30 days, yielding an overall 30-day mortality rate of 1.1% (Table 5). Older age, higher WHO-ECOG-, mGPS- or ASA-score, pulmonary comorbidity, cardiac comorbidity and open access were significant predictors in univariable analysis. After multivariable analysis only open access (aOR 2.87 (CI 1.08-7.59)), severe pulmonary disease (aOR 4.95 (CI 1.83- 13.31)) and severe cardiac disease (aOR 2,92 (CI 1.09-7.82)) remained statistically significant predictors of death. Fourteen of the 20 patients who died did not undergo a reoperation. The mortality rate at 30 days was 1.9% (14 out of 743) after open surgery and 0.6% (6 out of 1069) after laparoscopic surgery (p = 0.008).

Some 177 patients (9.8%) were readmitted within 30 days; either to index hospital (n=160) or another hospital (n=17). The readmission rates among patients who had a anastomosis fashioned during index surgery was 9.6% (160 out of 1664) compared to 11.5% (17 out of 148) of those who did not have a new anastomosis. . A total of 26 patients had a reoperation during the readmission stay, of whom 7 also had a reoperation during the index stay. The overall LoS was mean 7.4 days and median 5

days (IQR 4-8), with median LoS for laparoscopic and open resections of 4 days (IQR 3-6) and 7 days (IQR 5-11), respectively.

At the time of surgery, 452 patients (25.0%) in the cohort were older than 80 years. Of these, 82.5% did not experience any major complication, and 30-day mortality was 2.2%. After covariable adjustment, age was not a statistically significant predictor for major complications. A high fraction of patients had a new anastomosis fashioned and this did not differ between age groups. There was a lower rate of AL requiring reoperation (3.1%) observed in the >80 group, but higher age was not associated with lower AL rate (OR 0.98, CI (0.96-1.00) p=0.063).

Open access technique was associated with an inferior outcome when compared to laparoscopic access. Several baseline characteristics differed between the surgical access groups, with a trend indicating that patients operated upon with open technique were somewhat more high-risk than those who underwent a laparoscopic procedure (Table 6). Therefore, we performed a regression analysis of access as a predictor adjusted with a propensity score correcting for baseline differences between the two surgical access groups (Table 7). A difference in disfavour of open technique remained statistically significant for rate of any major complication (aOR 1.67 (CI 1.22-2.29)), 30-day mortality (aOR 4.39 (CI 1.19-16.13)) and LoS (aHR 0.58 (0.52-0.65)).

DISCUSSION

Population-based data for the complication burden and magnitude of impact from risk factors may aid clinicians and patients in decision-making and provide essential backdrops for interpretation of clinical trials. This multi-centre study from both low- and high-volume units throughout Norway reveals a low rate of major complications, with low overall rates of reoperation, anastomotic leak (AL) requiring reoperation and mortality within 30 days.

A high proportion (86.0%) of this unselected cohort did not experience any kind of major complication. When compared to other population-based publications our results are in line with reports from the Swedish (8.0 % reoperations, 4.2 % AL and 1.4% mortality) (14), and Danish (4.3% AL and 1.4 % mortality) (15), national colorectal cancer registries. A recent retrospective single-centre study from Sweden reported an AL rate of over 7.0% for colonic resections. (16) Notably, AL rates are not directly comparable due to diverging definitions, as AL rates in NoRGast do not include micro leakages that do not necessitate a reoperation. AL requiring only percutaneous drainage would within our registry be classified as Accordion 3 together with any other endoscopic or percutaneous intervention (including drainage of pleural effusion). Data from a Dutch national report (17) however, corresponds to a rate of reoperations due to AL of 6.4% and an overall mortality rate of 3.4% after elective colonic surgery, which are both somewhat higher than in the current study.

The overall LoS in our unselected material was short, in line with single centre reports from specialized Enhanced Recovery After Surgery (ERAS) units and fast-track programs, and shorter than several population-based studies. (18-21). The readmission rate of 9,8% is not exceeding readmission rates in reports with longer primary LoS (22, 23) and hence seems acceptable, reflecting an overall reasonable discharge policy. The conversion rate of 10.2% of all commenced laparoscopy is in line with recent reports from other unselected cohorts (24, 25).

Age has both traditionally and in recent publications been linked to complicated and prolonged postoperative hospital stays (26), but comparable complication rates and

survival after surgical treatment of octogenarians have also been published. (27, 28) This study showed no association between higher age and major complications, including mortality. The tendency of a low rate of AL requiring reoperation among the oldest has been observed in other publications (17). These non-inferior outcomes among the oldest may partly be due to younger patients receiving more extensive surgery. One may further assume that octo- and nonagenarians undergoing surgery have been carefully selected and that the rather crude indicators in the registry have not fully captured their low risk profile. Nevertheless, our results indicate that such a selection results in a comparatively good outcome in those accepted for surgery.

The non-inferior short-term (non-oncological) outcomes after laparoscopic surgery for colon cancer were confirmed in early RCTs (29, 30). A recent Japanese RCT reported lower morbidity after laparoscopy. (31) While several observational studies and long-term follow-ups after RCTs indicate a non-inferior long-term survival (32-34), a large population-based European retrospective study even reported enhanced survival after laparoscopy. (35) A meta-analysis on both short- and long-term outcomes after RCTs suggests that laparoscopy may be preferred due to superior short-term results. (36) A large retrospective report including more than 200.000 patients in the US reported, similar to our study, diverging results for morbidity, mortality, rate of routine discharge and LoS, and concluded with benefits from a laparoscopic approach. (21) Although the guidelines from the Norwegian Gastrointestinal Cancer Group do not clearly recommend either access modality over the other (37), the Norwegian Colorectal Cancer Registry (NCCR) measures laparoscopy rate as a quality indicator. (3, 37) The rate of procedures commenced as laparoscopy in our study (59%) is in line with national cohorts from the NCCR for 2014 (52%) and 2015 (56%). (3)

The association between surgical access and diverging outcomes in our data is strong. The over-all rate of major complications was almost twice as high in the open access group, and the distribution in severity of complications did not differ between the access groups (Figure 2). Data on tumour stage are not included in this registry (NoRGast). In a Norwegian national cohort of colon cancer resections from 2007-2010, 11.7% presented as T4-tumours, of which 84.3% were removed by open access. (38). Although the limitations of laparoscopic technique have gradually reclined, there is a possibility of a

higher proportion of large-sized and T4 tumours in the open access group. Tumour size and stage could both affect the choice of access and choice of restoration, and contribute to morbidity and hence represents a possible confounder. There was a lower rate of new anastomosis fashioned in the open surgery group versus the laparoscopy group (95.0% vs 87.2%) in the current cohort, which may partly be due to inter-access differences in resection types performed. There was a larger proportion of sigmoid resections in the laparoscopy group and more transverse, left sided and total/subtotal colectomies done by open access. As these latter subtypes of colonic resections were associated with a higher complication rate, resection type was included in the basis of the propensity score correction. Its skewing effect on outcomes was hence adjusted for but still did not affect the lower complication rate following laparoscopic surgery. Furthermore, the lower rate of primary reconstruction resulted in a lower proportion of patients under risk for AL, and would in theory diminish the risk of major adverse advents in the open resection group. Our results must be interpreted with caution due to possible patient selection bias between access modalities not revealed by the case-mix factors registered. However, the observed large inter-unit variation in use of laparoscopy (range 28-100, Table 1) cannot be explained by patient or tumour factors alone, and must to some extent be a result of diverging attitudes between the units regarding the routine use of laparoscopic access .

Some limitations need to be addressed. The included resections were registered from 16 separate surgical departments throughout Norway, and this material does not constitute a complete national cohort. In 2015 altogether 28 units reported more than 20 resections for colonic malignancies to the NCCR (3). The study period included the sparse start of the registry and most units had not been reporting for two full years. The completeness of data on unit level was therefore necessarily variable and impossible to assess. No attempt was hence made to analyse the results on hospital level. Non-scheduled surgery performed within office hours was not possible to identify, and might be a confounder adding additional burden to the open access group. Considering the low complication rates, the variable coverage rate on an institutional level may raise the suspicion of selection bias. Although unlikely, this cannot be completely refuted until more complete cohorts are gathered.

CONCLUSIONS

Our data indicate low complication rates and a high fraction of uneventful patient journeys after scheduled surgery for colon cancer in Norway when compared to reports from other national registers in countries of similar population. Age was not associated with higher morbidity or mortality rates. Within the limitations of an observational study and in absence of stratification for tumour stage, our data show the use of open access technique to be associated with higher complication rates.

Conflicts of interest:

On behalf of all authors: The authors constitute the board of the NoRGast registry. No other conflicts of interest are declared.

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Table 1: Distribution of annual resection volume per hospital unit and use of laparoscopy

Resections per year[1]	Hospital units (n)	Resections (n)[2]	Laparoscopy (% (range))[3]
< 50	5	256	80 (62-100)
50-100	7	772	64 (41-100)
> 100	4	784	47 (28-80)
Total	16	1812	67 (28-100)

[1] Annual number of resections for colon cancer (source: Colorectal Cancer Registry of Norway, National report 2015, reference 3), [2] Number of resections in the current cohort operated upon in a hospital unit within the corresponding volume group, [3] Percentage of resections in the current cohort performed with laparoscopy (ITT) within the corresponding volume group, with unit range in brackets.

Table 2: Univariable and multivariable analyses of association between the predictors and any major complication (Accordion score 3-6) within 30 days

				Univariable		Multivariable	
		n	rate (%)	OR (CI[1])	p[2]	adjusted OR (CI[1])	p[3]
All patients		1812	14,0				
Age group	<65	475	12,6	ref	0,049	-	-
	65-80	885	13,0	1,03 (0,74-1,43)			
	>80	452	17,5	1,46 (1,02-2,11)			
Gender	female	959	12,3	ref	0,026	-	-
	male	853	15,9	1,35 (10,4-1,76)			
WHO ECOG-score	0 or 1	1529	14,1	ref	0,058	-	-
	> 1	245	19,6	1,41 (0,99-2,02)			
mGPS	0	1080	13,7	ref	0,004	ref	0,022
	1	278	15,7	1,12 (0,77-1,64)		0,97 (0,66-1,42)	
	2	146	25,3	2,02 (1,32-3,09)		1,82 (1,17-2,82)	
ASA-score	I	121	6,6	ref	<0,001	ref	0,021
	II	994	12,8	1,94 (0,92-4,07)		1,50 (0,70-3,18)	
	III	650	19,5	3,17 (1,50-6,66)		2,27 (1,06-4,87)	
	IV	46	15,2	2,54 (0,86-7,45)		2,12 (0,68-6,44)	
Severe pulmonary disease	no	1681	13,7	ref	0,132	-	-
	yes	130	18,5	1,43 (0,90-2,27)			
Severe cardiac disease	no	1611	13,6	ref	0,134	-	-
	yes	200	17,5	1,35 (0,91-2,00)			
Weight class (BMI)	< 18,5	69	14,5	0,98 (0,48-1,97)	0,744	-	-
	18,5-25	683	15,8	ref			
	25-30	650	13,1	0,84 (0,62-1,15)			
	>30	283	15,9	0,98 (0,66-1,45)			
Access	Laparoscopy	1069	10,5	ref	<0,001	ref	0,004
	Open	743	19,1	2,02 (1,54-2,64)		1,55 (1,15-2,10)	
Resection type[4]	IC and RHC	1032	13,5	ref	0,003	-	-
	SR	476	11,1	0,81 (0,58-1,13)			
	TRR and LHC	196	19,9	1,60 (1,08-2,37)			
	SC/TC and oth.	108	21,3	1,74 (1,06-2,85)			

[1] Values in parenthesis are 95 % confidence intervals. [2] Chi-square tests. [3] Logistic regression analyses. [4] IC: ileocecal resection, RHC: right hemicolectomy, SR: sigmoid resection, TRR: transversal resection, LHC: left hemicolectomy, SC: subtotal colectomy, TC: total colectomy.

Table 3: Univariable and multivariable analyses of association between the predictors and reoperation of any cause within 30 days

			Univariable		Multivariable	
		rate (%)	OR (CI[1])	p[2]	adjusted OR (CI[1])	p[3]
All patients		8,7				
Age group	<65	8,2	ref	0,724	-	-
	65-80	9,3	1,10 (0,77-1,70)			
	>80	8,2	1,00 (0,62-1,59)			
Gender	female	7,4	ref	**0,024**	ref	**0,020**
	male	11,0	1,46 (1,05-2,03)		1,48 (1,06-2,06)	
WHO ECOG-score	0 or 1	9,0	ref	0,602	-	-
	> 1	10,0	0,88 (0,53-1,44)			
mGPS	0	9,0	ref	0,532	-	-
	1	6,8	0,77 (0,46-1,29)			
	2	10,3	1,11 (0,62-2,01)			
ASA-score	I	2,5	ref	0,086		
	II	8,8	3,77 (1,18-12,18)		-	-
	III	10,0	4,37 (1,35-14,14)			
	IV	6,5	2,74 (0,53-14,12)			
Severe pulmonary disease	no	8,7	ref	0,830	-	
	yes	9,2	1,07 (0,58-1,98)			
Severe cardiac disease	no	8,6	ref	0,678	-	-
	yes	10,0	1,11 (0,67-1,84)			
Weight class (BMI)	< 18,5	7,2	0,84 (0,33-2,18)	0,840	-	-
	18,5-25	8,9	ref			
	25-30	8,5	0,98 (0,66-1,44)			
	>30	12,0	1,18 (0,74-1,90)			
Access	Laparoscopy	7,6	ref	**0,039**	-	-
	Open	10,4	1,41 (1,02-1,96)			
Resection type[4]	IC and RHC	8,1	ref	**0,003**	ref	**0,005**
	SR	6,7	0,81 (0,53-1,24)		0,78 (0,51-1,19)	
	TRR + LHC	12,2	1,58 (0,97-2,55)		1,55 (0,96-2,51)	
	SC/TC and oth.	16,7	2,26 (1,30-3,92)		2,20 (1,27-3,84)	

[1] Values in parenthesis are 95 % confidence intervals. [2] Chi-square tests. [3] Logistic regression analyses. [4] IC: ileocecal resection, RHC: right hemicolectomy, SR: sigmoid resection, TRR: transversal resection, LHC: left hemicolectomy, SC: subtotal colectomy, TC: total colectomy.

Table 4: Univariable and multivariable analyses of association between the predictors and reoperation for anastomotic leak (AL) within 30 days

				Univariable		Multivariable	
		Anastomosis[1] (%)	AL rate (%)	OR (CI[2])	p[3]	adjusted OR (CI[2])	p[4]
All patients		91,8	3,8				
Age group	<65	91,8	4,6	ref	0,479	-	-
	65-80	92,1	3,4	0,74 (0,41-1,33)			
	>80	91,4	3,1	0,68 (0,33-1,38)			
Gender	female	91,7	3,0	ref	0,106	-	-
	male	92,0	4,5	1,53 (0,91-2,57)			
WHO ECOG-score	0 or 1	92,3	3,7	ref	0,999	-	-
	> 1	88,6	3,7	1,00 (0,47-2,14)			
mGPS	0	94,3	3,6	ref	0,940	-	-
	1	87,4	3,3	0,80 (0,42-1,97)			
	2	87,0	3,1	0,86 (0,30-2,46)			
ASA-score	I	91,7	1,8	ref	0,726	-	-
	II	93,6	3,8	2,13 (0,51-8,98)			
	III	89,8	4,1	2,34 (0,54-10,03)			
	IV	82,6	0	0			
Severe pulmonary disease	no	91,9	3,7	ref	0,854	-	-
	yes	91,5	3,4	0,91 (0,32-2,55)			
Severe cardiac disease	no	92,1	3,8	ref	0,287	-	-
	yes	89,5	2,2	0,57 (0,21-1,60)			
Weight class (BMI)	< 18,5	78,3	1,9	0,64 (0,08-4,91)	0,367	-	-
	18,5-25	92,4	2,9	ref			
	25-30	93,4	4,6	1,65 (0,90-3,01)			
	>30	92,6	3,8	1,35 (0,62-2,97)			
Access	Laparoscopy	95,0	3,3	ref	0,386	-	-
	Open	87,2	4,2	1,26 (0,75-2,10)			
Resection type[5]	IC and RHC	96,6	2,8	ref	**0,010**	ref	**0,010**
	SR	88,4	3,6	1,28 (0,68-2,42)		1,28 (0,68-2,42)	
	TRR + LHC	92,3	6,6	2,46 (1,23-4,93)		2,46 (1,23-4,93)	
	SC/TC and oth.	60,2	9,2	3,52 (1,40-8,83)		3,52 (1,40-8,83)	

[1] Rate of patients who had a new anastomosis fashioned. [2] Values in parenthesis are 95 % confidence intervals. [3] Chi-square tests. [4] Logistic regression analyses. [5] IC: ileocecal resection, RHC: right hemicolectomy, SR: sigmoid resection, TRR: transversal resection, LHC: left hemicolectomy, SC: subtotal colectomy, TC: total colectomy.

Table 5: Univariable and multivariable analyses of association between the predictors and mortality within 30 days

			Univariable		Multivariable	
		rate (%)	OR (CI[1])	p[2]	adjusted OR (CI[1])	p[3]
All patients		1,1	-		-	-
Age group	<65	0,8	ref	0,724	-	-
	65-80	0,7	0,80 (0,23-2,86)			
	>80	2,2	2,66 (0,83-8,56)			
Gender	female	1,3	ref	**0,024**	-	-
	male	0,9	0,75 (0,30-1,84)			
WHO ECOG-score	0 or 1	0,9	ref	0,602	-	-
	> 1	2,4	2,72 (1,03-7,14)			
mGPS	0	0,7	ref	0,532	-	-
	1	1,4	1,96 (0,59-6,55)			
	2	3,4	4,76 (1,54-14,74)			
ASA-score	I	0		0,086	-	-
	II	0,3	I + II: ref			
	III	2,3	III + IV: 9,28 (2,71-31,79)			
	IV	4,3				
Severe pulmonary disease	no	0,8	ref	0,830	ref	**0,002**
	yes	5,4	7,31 (2,87-18,65)		4,95 (1,83-13,31)	
Severe cardiac disease	no	0,8	ref	0,678	ref	**0,033**
	yes	3,5	4,46 (1,76-11,32)		2,92 (1,09-7,82)	
Weight class (BMI)	< 18,5	0	0	0,840	-	-
	18,5-25	1,5	ref			
	25-30	0,8	0,52 (0,18-1,54)			
	>30	1,1	0,72 (0,20-2,64)			
Access	Laparoscopy	0,6	ref	**0,039**	ref	**0,034**
	Open	1,9	3,40 (1,30-8,90)		2,87 (1,08-7,59)	
Resection type[4]	IC and RHC	1,2	ref	**0,003**	-	-
	SR	1,1	0,88 (0,20-3,95)			
	TRR + LHC	1,0	0,90 (0,32-2,58)			
	SC/TC and oth.	0,9	0,79 (0,10-6,17)			

[1] Values in parenthesis are 95 % confidence intervals. [2] Chi-square tests. [3] Logistic regression analyses. [4] IC: ileocecal resection, RHC: right hemicolectomy, SR: sigmoid resection, TRR: transversal resection, LHC: left hemicolectomy, SC: subtotal colectomy, TC: total colectomy.

Table 6: Demographics of analyzed predictors stratified by access modality group

		Laparoscopy	Open	Comparison of access groups
		% of all laparoscopies	% of all open procedures	p[1]
Age group	<65	29,2	21,9	**0,002**
	65-80	46,2	52,6	
	>80	24,6	25,4	
Gender	female	51,6	54,8	0,188
	male	48,4	45,2	
WHO ECOG score	0 or 1	88,7	82,6	**<0,001**
	>1	11,3	17,4	
mGPS	0	77,8	63,6	**<0,001**
	1	13,9	24,8	
	2	8,3	11,7	
ASA score	I	8,7	3,8	**<0,001**
	II	56,3	52,9	
	III	33,1	39,8	
	IV	1,9	3,5	
Severe pulmonary disease	no	94,4	90,6	**0,002**
	yes	5,6	9,4	
Severe cardiac disease	no	90,4	86,9	**0,022**
	yes	9,6	13,1	
Weight class (BMI)	< 18,5	3,5	5,0	0,120
	18,5-25	40,9	40,0	
	25-30	40,0	36,4	
	>30	15,6	18,5	
Resection type[2]	IC + RHC	56,7	57,3	**<0,001**
	SR	30,6	20,1	
	TRR + LHC	8,5	14,1	
	SC, TC and oth.	4,2	8,5	

[1] Chi-square tests. [2] IC: ileocecal resection, RHC: right hemicolectomy, SR: sigmoid resection, TRR: transversal resection, LHC: left hemicolectomy, SC: subtotal colectomy, TC: total colectomy.

Table 7: Propensity score-adjusted odds and hazard ratios for access modality as predictor of outcomes

	Any major complication	Mortality	Length-of-stay
Open access (with laparoscopy as reference)	OR 1,67 (1,22-2,29) **p = 0,002**	OR 4,39 (1,19-16,13) **p = 0,026**	HR 0,58 (0,52-0,65) **p <0,001**

Numbers in parenthesis are 95% confidence intervals. Variables included when computing propensity score: Age, gender, WHO ECOG score, mGPS, ASA score, severe pulmonary and cardiac disease, weight group and resection type. Variables included in propensity score-corrected logistic regression analysis: propensity score, access modality, age and gender.

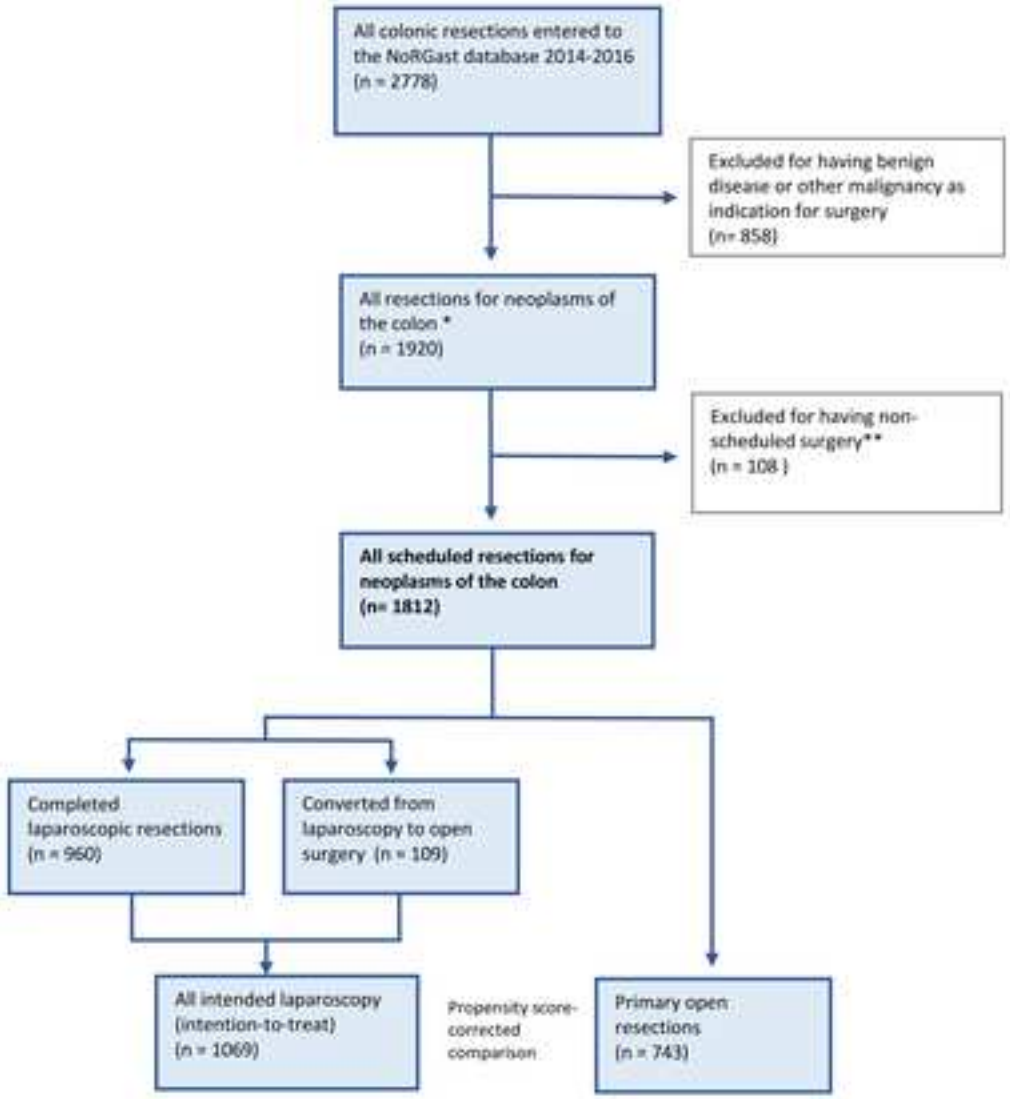
Figure legends

Figure 1: Flowchart for inclusion and categorization according to access modality for sub analyses

Figure 2: The distribution in severity of major postoperative complications presented as cumulative percentages of Accordion grade 3-6. In accordance with the Accordion system, only the highest graded complication is scored for any given patient journey. The cumulative percentages of Accordion score 3-6 are shown in the end of each column. Separate columns are given for the two access groups, and further stratified for age group with a cut-off of 80 years.

Figure 3: Crude incidences of all recorded reinterventions and organ failures within 30 days from index surgery. Notably, in contrast to the Accordion scale where only the most severe complication for each patient journey is graded (Figure 2), all events are here counted under the respective type of reintervention or organ failure group.

Figure 1: Flowchart for inclusion and categorization according to access modality for subanalyses



* defined by ICD-10 codes C18.0-9, C19, D01.0-1, D12.0-7, D37.2-4 or K63.5
** defined by start of anaesthesia between 4 PM and 8 AM or during weekends or public holidays

Figure2

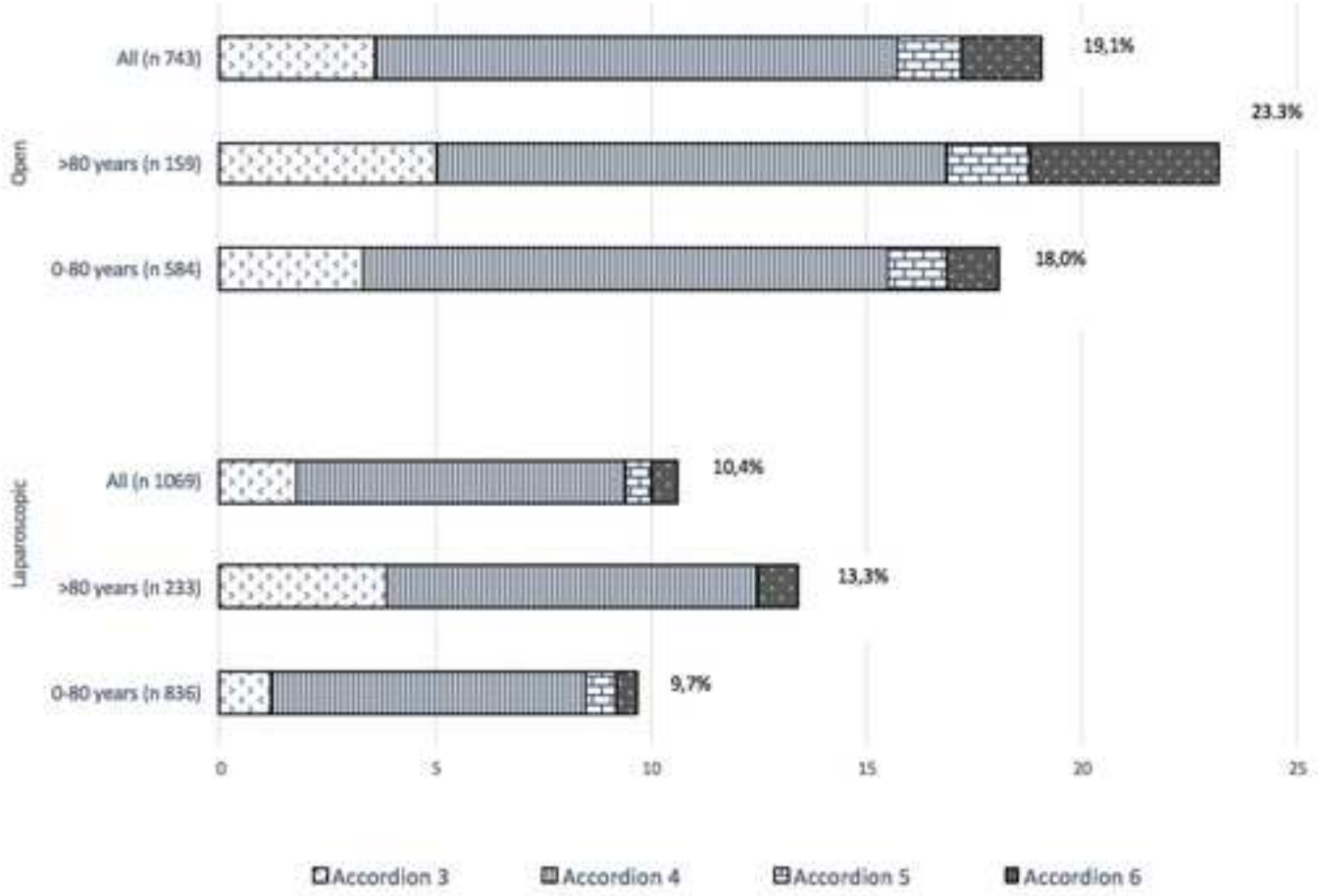


Figure 2: Distribution in Accordion score stratified by access modality group and age.

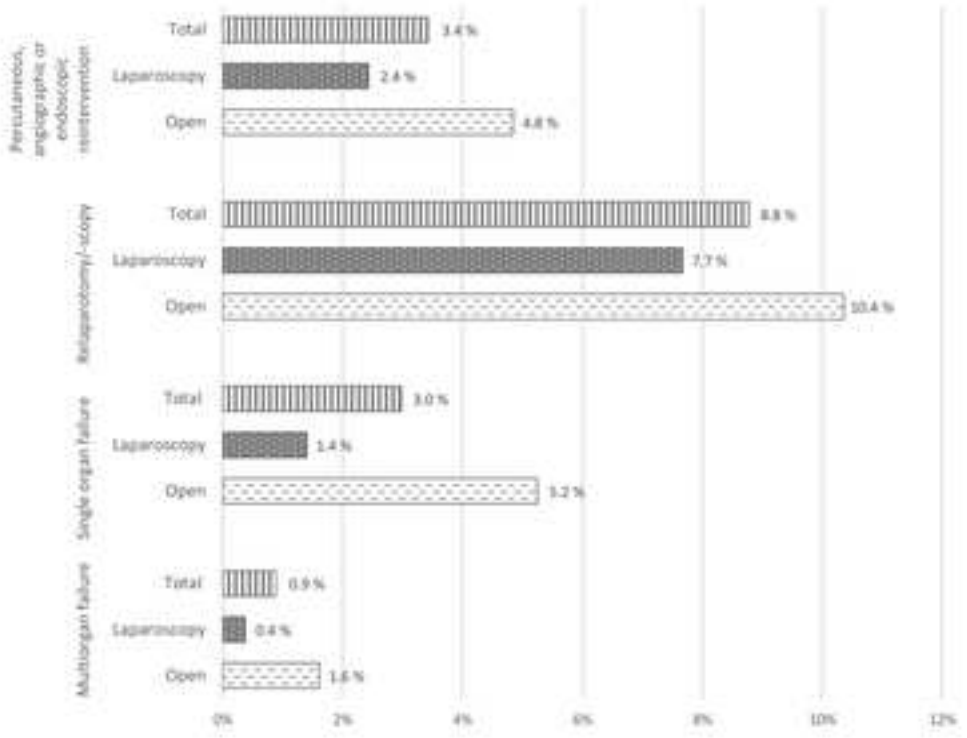


Figure 3: Crude incidences of reinterventions and organ failure stratified by access modality

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