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The impact of chronic obstructive pulmonary disease on intensive care unit admission and 30-day mortality in patients undergoing colorectal cancer surgery: a Danish population-based cohort study

Research year report

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Preface

This study was carried out during my research year at Department of Clinical Epidemiology, Aarhus University Hospital, Denmark (September 2011-September 2012)

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Abbreviations:

CCI	Charlson Comorbidity Index
CI	Confidence interval
COPD	Chronic Obstructive Pulmonary Disease
CPR	Civil registration number
CRC	Colorectal Cancer
DCR	Danish Cancer Registry
DNRP	Danish National Registry of Patients
HR	Hazard ratio
ICD	International Classification of Diseases
ICU	Intensive Care Unit

Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) may increase risk of postoperative complications and thus mortality after colorectal cancer (CRC) surgery, but the evidence is sparse.

Methods: We conducted this nationwide population-based cohort study in Denmark (5.5 million inhabitants). The study encompassed all patients undergoing CRC surgery in the period 2005-2009, identified through medical databases. We categorized CRC patients according to presence/absence of a history of COPD. We assessed the frequency of admissions to intensive care units (ICUs), treatment with mechanical ventilation, and reoperation. We computed 30-day mortality among patients with and without COPD using the Kaplan-Meier method. We used Cox regression to compute hazard ratios (HRs) for death among COPD patients compared with patients without COPD, controlling for confounding factors.

Results: We identified 13,029 CRC surgery patients. Of these, 1,040 (8.0%) had a history of COPD. Among COPD patients, 30.6% were admitted postoperatively to the ICU and 2.2% were treated with mechanical ventilation. In patients without COPD, the corresponding proportions were 19.0% and 1.1%. The reoperation frequency was 10.6% among COPD patients, compared to 8.1% among patients without COPD. Thirty-day mortality was 14% (95% confidence interval (CI): 12.1%-16.3%) among CRC patients with COPD and 5.9% (95% CI: 5.4%-6.3%) among CRC patients without COPD, corresponding to an adjusted HR of 1.6 (95% CI: 1.3-1.9).

Conclusion: COPD is a strong predictor for ICU admission and mortality after CRC surgery.

Introduction

Colorectal cancer (CRC) is a common disease, arising at a median age of approximately 70 years.[1,2] Surgical resection of the tumour has the potential to cure early-stage disease.[3] When the disease is more advanced, resection is combined with chemotherapy and/or radiation.[3] Although treatment is effective, mortality remains high.[3] Overall 30-day mortality after CRC resection has been estimated at approximately 10%, with an even higher rate among elderly patients.[4,5]

Many CRC patients have concurrent chronic diseases, including chronic obstructive pulmonary disease (COPD). Evidence is accruing that COPD is associated with substantially increased mortality after various types of surgery. Much of this evidence originates from studies of patients undergoing surgery for perforated peptic ulcers, cardiac procedures, and hip fractures [6,7,8], but the evidence for an association with postoperative colorectal cancer surgery is limited. [4,9-10] The former studies have mainly included COPD as a covariate in analyses for other purposes like hospital variation in mortality[4], have combined several types of cancer or lung diseases[9,11], or focused only on men.[10] They have all indicated that COPD may be an important predictor for postoperative mortality.

A primary reason for increased postoperative mortality among COPD patients may be respiratory failure, leading to more frequent and longer intensive care unit (ICU) admissions.[12,13] In addition, patients with a high comorbidity burden generally have been found to be at increased risk of surgical complications, leading in turn to a need for reoperation[14], but none of the former studies have examined the risk of postoperative admission to intensive care. We conducted a nationwide population-based cohort study to investigate in detail the impact of COPD on ICU admissions, need for mechanical ventilation, occurrence of reoperation, and 30-day mortality following CRC surgery.

Method

Setting

This cohort study was conducted in Denmark, a country with 5.5 million inhabitants.[15]

All Danish citizens have equal access to tax-funded medical care, and all CRC surgery is performed in public hospitals.

Since 1968, everyone living in Denmark has been assigned a civil registration number (CPR number) by the Danish Civil Registration System (CRS).[16] The CRS is updated daily and contains information on gender, date of birth, and vital status. We used the CPR number to link individual-level data among registries.

Study population

We used the Danish Cancer Registry (DCR) to identify all CRC patients diagnosed in the period from January 1, 2005 through December 31, 2009. This period was chosen because ICU admissions have been recorded since 2005. The DCR, established in 1943, captures all incident cancer cases in Denmark through notification from hospital departments, specialists, and autopsy reports.[17] DCR data include CPR number, month and year of cancer diagnosis, and tumor spread at diagnosis. We classified CRC stages as localized (Duke's A and B), regional (Duke's C), metastasized (Duke's D), or unknown (see Appendix I).

We used the CPR number to link the CRC patients to the Danish National Registry of Patients (DNRP), in order to identify date of CRC surgery. The DNRP, a nationwide registry established in 1977, maintains records on 99.4% of all discharges from Danish hospitals.[18] Emergency room and outpatient clinic visits have been included since 1995 and ICU admissions including mechanical ventilation since 2005.

Data in the DNRP include CPR number, hospital, department, discharge diagnoses, and surgical and diagnostic procedures. Diagnoses were coded according to the *International Classification of Diseases*, 8th revision (ICD-8) until 1993 and 10th revision (ICD-10) thereafter. Hence, our study cohort consisted of patients who underwent CRC surgery (see Appendix I for surgical procedure codes). We categorized CRC surgery as either open surgery, laparoscopic resection, or other surgery. We also categorized surgeries as acute or elective because emergency surgery has been shown to be associated with increased mortality.[4]

COPD patients

Within the cohort of CRC surgery patients, we searched the DNRP for any inpatient COPD diagnosis since 1977. In addition, we identified and included patients diagnosed with COPD in outpatient specialist clinics and emergency rooms since 1995 (ICD codes are provided in Appendix I).

Outcomes: admission to intensive care, mechanical ventilation, reoperation, and death

We obtained data from the DNRP on ICU admissions,[19] use of mechanical ventilation, and reoperations within 30 days following surgery (Procedure codes are provided in Appendix I). We used these as markers of surgical complications.[20] To investigate 30-day mortality, CRS data were used to follow patients from date of CRC surgery until death, emigration, 30 days postoperatively, or the end of the study period, whichever came first.

Comorbidities

We used Charlson Comorbidity Index (CCI) scores to assess comorbidity levels in the study cohort. The CCI score is computed as the sum of points (between 1 and 6) assigned to each of the 19 diseases included in the score (see Appendix I).[21] Information on comorbid diseases was obtained from the DNRP, including all inpatient and outpatient diagnoses within 5 years prior to the CRC surgery date. Patients were classified into three groups according to their CCI score: 0 points (‘‘low comorbidity level’’); 1-2 points (‘‘moderate comorbidity level’’); and 3 or more points (‘‘severe comorbidity level’’). We excluded chronic pulmonary disease and CRC from the CCI, because these comprise the exposure and the patient population under study. In addition to the CCI score, our analyses included data on alcohol-related diseases and obesity (see Appendix I).

Statistical analyses

We calculated frequencies of covariates (including categories of demographic characteristics, CCI scores, types of admission, types of surgery, and cancer stages) according to the presence or absence of COPD. We computed the proportion of patients who were admitted to the ICU, received mechanical ventilation, and underwent reoperation within 30 days after surgery. We used Jeffrey’s method to compute 95% confidence intervals (CIs) for the proportions.[22] We estimated and plotted 30-day mortality by COPD status for all CRC surgery patients and for those with colon and rectal cancer separately, using the Kaplan-Meier method. We used a Cox regression model to estimate

hazard ratios (HRs) with 95% CIs for death, in order to compare mortality among patients with and without COPD.

We adjusted for the following potential confounders: age, gender, type of admission, stage of cancer, presence/absence of alcohol-related diseases, obesity, and CCI score. CRC patients without COPD constituted the comparison group. In order to examine any potential differences in the influence of COPD on particular subgroups, we also repeated the regression analyses stratified by age, gender, CCI score, admission type, surgery type, and CRC stage.

All statistical analyses were performed using STATA software (version 11.0 StataCorp LP, College Station, TX).

Results

Descriptive data

We identified 13,029 CRC surgery patients, of whom 1,040 (8.0%) had a COPD diagnosis. The proportion of patients with COPD was slightly higher among patients with colon cancer (8.4% of 8,574 colon cancer patients) compared to patients with rectal cancer (7.2% of 4,455 rectal cancer patients).

CRC patients with COPD were older and had a higher CCI score than CRC patients without COPD. Gender, admission type, surgery type, and CRC stage at time of diagnosis were similar in patients with and without COPD (Table 1).

Intensive care unit admission, mechanical ventilation, and reoperation within 30 days after surgery

Among CRC patients with COPD, 30.6% (95% CI: 27.7%-33.5%) were admitted to the ICU within 30 days after surgery, compared with 19.0% (95% CI: 18.3%-19.7%) of patients without COPD.

CRC patients with COPD also received more mechanical ventilation treatment (2.2%; 95% CI: 1.4%-3.3%) than patients without COPD (1.1%; 95% CI: 0.9%-1.3%) and more frequently underwent reoperation (10.6% (95% CI: 8.8%-12.6%) vs. 8.1% (95% CI: 7.6%-8.6%)).

Similar results were seen when colon cancer and rectal cancer were considered separately (Table 2).

In the analysis by year of CRC surgery we found that the frequency of ICU admission declined from 41.5% in 2005 to 22.3% in 2009 (Table 3). Among patients without COPD, 23.9% were admitted to the ICU in 2005 and 14.8% were admitted in 2009. Thus, while the frequency of ICU

admission declined over time among CRC patients with and without COPD, the frequency continued to be highest among COPD patients.

In contrast we found that the frequency of treatment with mechanical ventilation increased from 1.2% in 2005 to 2.3% in 2009 among COPD patients. In patients without COPD the frequency increased from 0.9% to 1.3%. Finally, the frequency of reoperation declined in COPD patients from 14.5% to 8.5% over the study period. It also declined in patients without COPD from 9.6% in 2005 to 8.5% in 2009 (Table 3).

Mortality

Thirty-day mortality after CRC surgery was 14.0% (95% CI: 12.1%-16.3%) among patients with COPD and 5.9% (95% CI: 5.4%-6.3%) among patients without COPD, corresponding to an adjusted HR of 1.6 (95% CI: 1.3-1.9). Mortality in patients with COPD started to diverge from that in patients without COPD approximately three days after surgery (Figure 1).

Thirty-day mortality in colon cancer patients with COPD was 16.4% (95% CI: 13.9%-19.3%) and in those without COPD it was 6.8% (95% CI: 6.3%-7.4%), corresponding to an adjusted HR of 1.7 (95% CI: 1.4-2.1).

Thirty-day mortality was 8.8% (95% CI: 6.1%-12.4%) in rectal cancer patients with COPD and 4.1% (95% CI: 3.5%-4.7%) in rectal cancer patients without COPD. The adjusted HR was 1.3 (95% CI: 0.8-1.9) (Table 4).

Stratified analyses

Stratified analyses showed that COPD had a particularly strong impact on 30-day mortality among patients under age 70 (HR = 1.9; 95% CI: 1.1-3.5), among men (HR = 1.8; 95% CI: 1.4-2.4), and among patients undergoing elective surgery (HR = 2.1; 95% CI: 1.7-2.8) or laparoscopic surgery (HR = 2.5; 95% CI: 1.4-4.5) (Table 5).

Discussion

Key findings

In this nationwide population-based study, we found that CRC surgery in patients with COPD was more frequently complicated by ICU admission, mechanical ventilation, and reoperations, compared to CRC patients without COPD. Even after extensive adjusting for comorbidity level, COPD remained clearly associated with increased mortality.

Other studies

To our knowledge, this is the first study to focus specifically on the impact of COPD on postoperative mortality and in particular intensive care treatment among CRC patients. Nonetheless, our mortality results accord with those of a study that investigated hospital differences in mortality after CRC surgery among patients in Danish hospitals.[4] In that study, presence of COPD was associated with a 71% increase in 30-day mortality compared to CRC patients without COPD. Other studies investigating the impact of COPD on mortality after surgery, have also demonstrated an association.[6,7,9-11] For example, Ried *et al*. found that 6.1% of patients with COPD died within 30 days of cardiac surgery, compared to 0.8% of patients without COPD.[7] Moreover, a Danish study by Christensen *et al.* reported that 30-day mortality after surgery for peptic ulcer was 44% among COPD patients and 25% among patients without COPD.[6]

Potential mechanisms

Several physiological mechanisms may explain our findings. Previous studies have shown that COPD patients suffer more often from respiratory complications, such as pneumonia, after surgery than patients without COPD. [23,24] This is supported by our finding of an association between COPD and an increased frequency of ICU admission and mechanical ventilation.

However, a possible explanation for the higher frequency of ICU admissions among COPD patients, compared to patients without this condition, could be that some hospitals previously admitted COPD patients routinely to the ICU after CRC surgery. Most hospitals have abandoned this practice, as indicated in our study, which found the most pronounced decline in number of ICU admissions from 2005-2009 among COPD patients.

Another consideration is that postoperative complications may depend on the severity of COPD.

It has been demonstrated that the most common causes of death in patients with mild COPD are lung cancer and cardiovascular disease, while patients with moderate to severe COPD more often

have respiratory disease as cause of death in addition to cardiovascular disease.[25] This could explain their increased need for mechanical ventilation and their increased mortality. Furthermore, patients with severe COPD who experience exacerbations are usually treated with glucocortiocoids, which slow wound healing.[26] This could account for some postoperative complications experienced by COPD patients.

Although patients with COPD are less likely to receive laparoscopic surgery, those who do undergo this type of surgery have higher mortality than patients without COPD. One possible reason for increased mortality could be perioperative hypoventilation when the pressure in the abdomen is increased during laparoscopic surgery, especially since patients with COPD already have decreased lung capacity.

Methodological considerations

In this nationwide, population-based study we have complete follow up, allowing almost complete elimination of the risk of selection bias. We used the cancer registry, where 92%-98% of all the CRC patients are registered.[27]

One concern was that COPD may be underreported in the DNRP, in which case we have included some true COPD patients in the comparison cohort which was assumed to be free of COPD. Such misclassification would have caused us to underestimate the true association. However, Osler *et al.* found a COPD prevalence of 11.2% in their cohort which accords with our findings, although they included both patients with a previous hospital admission with COPD or medical treatment for COPD.[4] This may imply that underreporting of COPD is not a major problem in our study. Furthermore, the coding of COPD in the DNRP has been demonstrated to have a 92% positive predictive value.[28]

Unfortunately, we lacked detailed data on severity of COPD in the DNRP and we were therefore unable to evaluate e.g. mortality differences by severity of COPD.

We controlled for several important sources of confounding, such as obesity, alcohol-related diseases, and other comorbidity. A validation study has reported high positive predictive values of the DNRP coding of all diseases included in the CCI.[29] Nonetheless it is likely that particularly obesity and alcohol-related diseases are underreported in the DNRP and that our results therefore might be affected by residual confounding.

Conclusion

We found an increased need for ICU admission, mechanical ventilation, and reoperation after CRC surgery in COPD patients, compared with patients without COPD. In addition, COPD was associated with increased 30-day mortality after CRC surgery. These findings were more pronounced for colon cancer than for rectal cancer. Our findings underscore the need for close post-operative surveillance of CRC patients with COPD.

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Table 1. Characteristics of patients undergoing colon and rectal cancer surgery by presence/absence of a previous diagnosis of chronic obstructive pulmonary disease (COPD), Denmark, 2005-2009.

	Colon cancer				Rectal cancer			
	COPD	**%**	**No COPD**	**%**	**COPD**	**%**	**No COPD**	**%**
Total	720	100	7,854	100	320	100	4135	100
Age group (years)								
40-59	31	4.3	1,314	16.7	24	7.5	919	22.2
60-69	118	16.4	2,164	27.6	64	20.0	1,366	33.0
70-79	293	40.7	2,483	31.6	137	42.8	1,172	28.3
80+	278	38.6	1,893	24.1	95	29.7	678	16.5
Gender								
Female	369	51.3	3,976	50.6	127	39.7	1,594	38.6
Male	351	48.7	3,878	49.4	193	60.3	2,541	61.4
Charlson score								
0	409	56.8	5,981	76.2	194	60.6	3,297	79.7
1-2	236	32.8	1,478	18.8	92	28.8	640	15.5
3+	75	10.4	395	5.0	34	10.6	198	4.8
Type of admission								
Elective	489	67.9	5,503	70.1	276	86.3	3,704	89.6
Acute	230	32.1	2,335	29.7	41	12.8	411	9.9
Unknown	1	0.1	16	0.2	3	0.9	20	0.5
Type of surgery								
Open	491	68.2	5,171	65.8	171	53.4	2,166	52.4
Laparoscopic	151	21.0	1,920	24.5	39	12.2	607	14.7
Other	78	10.8	763	9.7	110	34.4	1,362	32.9
Cancer stage								
Localized	318	44.2	3,039	38.7	128	40	1,475	35.7
Regional	150	20.8	2,081	26.5	78	24.4	1,434	34.7
Metastasized	155	21.5	1,756	22.3	53	16.6	626	15.1
Unknown	97	13.5	978	12.5	61	19.0	600	14.5

Table 2. Characteristics of the treatment of patients undergoing colon and rectal cancer surgery by presence/absence of a previous diagnosis of chronic obstructive pulmonary disease (COPD), Denmark, 2005-2009.

	Colorectal cancer				Colon cancer				Rectal cancer			
	COPD	% (95% CI)	No COPD	% (95% CI)	COPD	% (95%CI)	No COPD	% (95% CI)	COPD	% (95%CI)	No COPD	% (95% CI)
ICU admission												
No	722	69.4 (66.6-72.2)	9,717	81.0 (80.3-81.7)	482	66.9 (63.4-70.3)	6351	80.9 (80.0-81.7)	240	75.0 (70.0-79.5)	3366	81.4 (80.2-82.6)
Yes	318	30.6 (27.8-33.4)	2,272	19.0 (18.3-19.7)	238	33.1 (29.7-36.6)	1503	19.1 (18.3-20.0)	80	25.0 (20.5-30.0)	769	18.6 (17.4-19.8)
Mechanical ventilation												
No	1017	97.8 (96.8-98.6)	11,858	98.9 (98.7-99.1)	703	97.6 (96.3-98.6)	7760	98.8 (98.5-99.0)	314	98.1 (96.2-99.2)	4098	99.1 (98.8-99.4)
Yes	23	2.2 (1.4-3.2)	131	1.1 (0.9-1.3)	17	2.4 (1.4-3.7)	94	1.2 (1.0-1.5)	6	1.9 (0.8-3.8)	37	0.9 (0.6-1.2)
Reoperation												
No	930	89.4 (87.4-91.2)	11,014	91.9 (91.4-92.3)	640	88.9 (86.4-91.1)	7233	92.1 (91.5-92.7)	290	90.6 (86.9-93.6)	3781	91.4 (90.5-92.3)
Yes	110	10.6 (8.8-12.6)	975	8.1 (7.7-8.6)	80	11.1 (8.9-13.6)	621	7.9 (7.3-8.5)	30	9.4 (6.4-13.1)	354	8.6 (7.7-9.5)

Abbreviation: COPD: Chronic obstructive pulmonary disease

Table 3: Frequency of intensive care unit (ICU) admissions, mechanical ventilation, and reoperations within 30 days of colorectal cancer (CRC) surgery, according to year of surgery and the presence or absence of chronic obstructive pulmonary disease (COPD).

	ICU		Mechanical ventilation		Reoperation	
	COPD	No COPD	COPD	No COPD	COPD	No COPD
2005	69 (41.5)	524 (23.9)	2 (1.2)	19 (0.9)	24 (14.5)	210 (9.6)
2006	72 (32.4)	527 (21.2)	7 (3.2)	36 (1.4)	21 (9.6)	205 (8.2)
2007	65 (31.1)	473 (19.3)	4 (1.9)	19 (0.8)	22 (10.5)	202 (8.3)
2008	61 (27.6)	389 (15.7)	5 (2.3)	24 (1.0)	24 (10.9)	175 (7.)
2009	51 (22.3)	356 (14.8)	5 (2.3)	33 (1.4)	19 (8.6)	182 (7.6)

Numbers in parenthesis are % of all CRC surgeries in each individual year.

Table 4. 30-day mortality and hazard ratios (HRs) after colorectal cancer surgery by presence/absence of chronic obstructive pulmonary disease (COPD), Denmark, 2005-2009.

	Colorectal cancer				Colon cancer				Rectal cancer			
	Deaths	Mortality %	Crude HR	Adjusted HR*	Deaths	Mortality %	Crude HR	Adjusted HR*	Deaths	Mortality %	Crude HR	Adjusted HR*
COPD												
No	701	5.9 (5.4-6.3)	1.00 (ref.)	1.00 (ref.)	533	6.8 (6.3-7.4)	1.00 (ref)	1.00 (ref)	168	4.1 (3.5-4.7)	1.00 (ref)	1.00 (ref.)
Yes	146	14.0 (12.1-16.3)	2.5 (2.1-3.0)	1.6 (1.3-1.9)	118	16.4 (13.9-19.3)	2.6 (2.1-3.1)	1.7 (1.4-2.1)	28	8.8 (6.1-12.4)	2.2 (1.5-3.3)	1.3 (0.8-1.9)

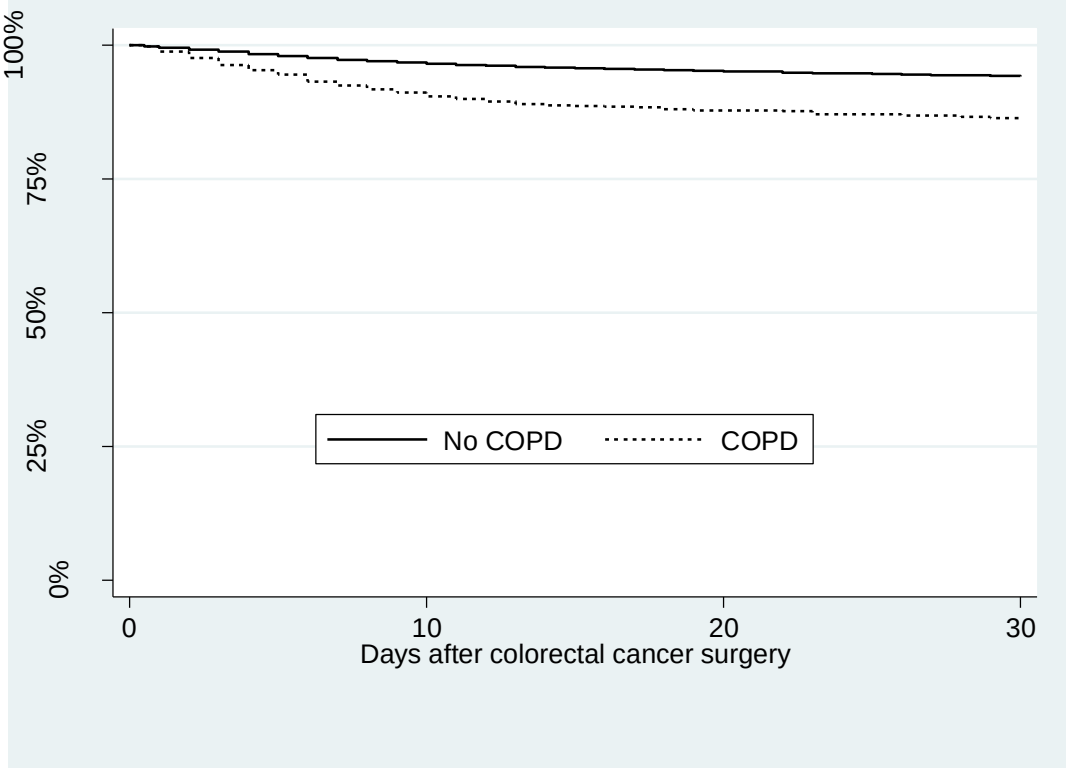
*Adjusted for age, gender, type of admission, cancer stage, obesity and alcohol related diseases and Charlson Comorbidity Index score.

Numbers in parentheses are 95% confidence intervals

Table 5. Crude and adjusted hazard ratios (HRs) after colorectal cancer (CRC) surgery, comparing patients with to those without chronic obstructive pulmonary disease (COPD)

	Colorectal cancer		
	COPD		No COPD
	Crude HR (95% CI)	Adjusted HR (95% CI)	Reference
Stratified by			
Age group (years)			
0-69	2.6 (1.5-4.6)	1.9 (1.1-3.5)	1.0
70+	1.8 (1.5-2.3)	1.6 (1.4-1.9)	1.0
Gender			
Male	2.8 (2.2-3.6)	1.8 (1.4-2.4)	1.0
Female	2.2 (1.7-2.9)	1.5 (1.1-1.9)	1.0
Charlson score			
0	2.6 (2.0-3.4)	2.0 (1.6-2.6)	1.0
1-2	1.8 (1.3-2.4)	1.4 (1.1-1.9)	1.0
3+	1.6 (1.0-2.6)	1.4 (0.9-2.1)	1.0
Type of admission			
Elective	3.3 (2.6-4.1)	2.1 (1.7-2.8)	1.0
Acute	1.7 (1.3-2.3)	1.2 (0.9-1.7)	1.0
Type of Surgery			
Open	2.8 (2.2-3.4)	1.8 (1.5-2.3)	1.0
Laparoscopic	4.2 (2.4-7.3)	2.5 (1.4-4.5)	1.0
Other	1.6 (1.1-2.3)	1.1 (0.7-1.6)	1.0
CRC stage			
Localized	2.8 (2.0-3.8)	1.9 (1.4-2.6)	1.0
Regional	3.3 (2.2-5.1)	2.1 (1.4-3.2)	1.0
Metastasized	2.3 (1.7-3.2)	1.5 (1.1-2.1)	1.0
Unknown	1.8 (1.2-2.7)	1.5 (0.9-2.2)	1.0

Figure 1. Kaplan-Meier 30-day survival curves for colorectal cancer patients with and without chronic obstructive pulmonary disease (COPD).



Appendix I

Colorectal cancer codes	**ICD-10**
Neoplasma malignum coli	DC18
Neoplasma malignum recti	DC20

Colorectal cancer stage definition in the Danish Cancer Registry:	**TNM**
Localized (Duke's A and B)	T0,a,is,1-4,x N0 M0
	T0,a,is,1-2 N0 Mx
	T0,a,is,1 Nx M0,x
Regional (Duke's C)	T0,a,is,1-4,x N1-3 M0
Metastasized (Duke's D)	T0,a,is,1-4,x N1-3 M1,x
	T0,a,is,1-4,x N0 M1
	T0,a,is,1-4,x Nx M1
Unknown	T2-4,x Nx M0,x
	T3-4,x N0 Mx

	ICD 10	**ICD 8**
Chronic obstructive pulmonary disease	DJ40-44	490-92

Charlson Comorbidity score	**ICD 10**	**Score**
Myocardial infarction	I21;I22;I23	1
Congestive heart failure	I50; I11.0; I13.0; I13.2	1
Peripheral vascular disease	I70; I71; I72; I73; I74; I77	1
Cerebral vascular disease	I60-I69; G45; G46	1
Dementia	F00-F03; F05.1; G30	1

~~Chronic pulmonary disease~~	~~J40-J47; J60-J67; J68.4; J70.1; J70.3; J84.1; J92.0; J96.1; J98.2; J98.3~~	~~1~~
Connective tissue disease	M05;M06;M08;M09;M30;M31; M32;M33;M34;M35;M36;D86	1
Ulcer disease	K22.1; K25-K28	1
Mild lever disease	B18; K70.0-K70.3; K70.9; K71; K73; K74; K76.0	1
Diabetes type 1 and type 2	E10.0, E10.1; E10.9 E11.0; E11.1; E11.9	1
Hemiplegia	G81; G82	2
Moderate/severe renal disease	I12; I13; N00-N05; N07; N11; N14; N17-N19; Q61	2
Diabetes with complications	E10.2-E10.8 E11.2-E11.8	2
Any tumour	C00-C75 **except** C18-20	2
Leukaemia	C91-C95	2
Lymphoma	C81-C85; C88; C90; C96	2
Moderate/severe liver disease	B15.0; B16.0; B16.2; B19.0; K70.4; K72; K76.6; I85	3
Metastatic solid tumour	C76-C80	6
AIDS	B21-B24	6

Additional covariates:	**ICD 10**	**ICD 8**
Disease related to alcohol abuse	G62.1; G72.1; G31.2; I42.6; F10 (except F10.0); K29.2; K86.0; Z72.1	291; 303; 577.10
Obesity	E66	277.99

Type of surgery	Nomesco code
Open	JGB00, JGB10,JGB20, JGB30, JGB40, JGB50, JGB60, JGB96, JFB20, JFB30, JFB 33, JFB40, JFB43, JFB46, JFB50, JFB60, JFB63, JFB96, JFH00, JFH10, JFH20, JFH30, JFH33, JFH40, JFH96, JGA00, JGA70
Laparoscopic	JGB01, JGB11, JGB31, JGB97, JFB21, JFB31, JFB34, JFB41, JFB44, JFB47, JFB51, JFB61, JFB64, JFB97, JFH01, JFH11
Other	JGA32-58, JGA73-98, JGW, JFA68(stent), JFA83-84, JFA96-97, JFC, JFF10-13, JFF20-31, JFW

Treatment codes:	
Reoperation after colorectal cancer surgery because of bleeding	KJWD
Reoperation after colorectal cancer surgery because of infection	KJWB, KJWC
Reoperation after colorectal cancer surgery because of insufficient anastomosis	KJWF
Admission to intensive care unit	NABB,NABE
Treatment with mechanical ventilator	BGDA0

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