OUTCOME OF POSTOPERATIVE INTENSIVE CARE ADMISSION AFTER EMERGENCY COLORECTAL CANCER SURGERY DOES NOT DIFFER FROM OTHER EMERGENCY COLORECTAL SURGERY

CHAPTER 5

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Abstract

Background: Emergency presentation of colorectal carcinoma (CRC) is associated with a high morbidity and mortality, frequently requiring postoperative care on the intensive care unit (ICU). We here sought to determine whether CRC influences the short-term outcome of patients admitted to the ICU after emergency colorectal surgery.
Methods: We compared CRC patients who were admitted to the ICU after emergency colorectal surgery with a defined group of patients undergoing acute surgery for other colorectal diseases. We used the National Intensive Care Evaluation registry to identify all patients with unplanned admission to the ICU after emergency colorectal surgery between January 2007 and August 2012 in the Netherlands.
Results: 11,495 patients were admitted to the ICU after emergency colorectal surgery, of whom 13.7% had CRC. On ICU admission, CRC patients had a lower prevalence of confirmed infection (22.3%) than patients with non-malignant disease (41.0%). Patients with CRC had a shorter ICU length of stay (median 2.3 days) than patients without CRC (median 2.8 days). In addition, CRC patients had a lower ICU mortality (10.3 versus 12.9%). Hospital length of stay and mortality did not differ between groups. In a multivariate analysis in-hospital mortality was associated with high age, low body weight, high severity of illness at ICU admission, chronic comorbidities and metastasized carcinoma. CRC as reason for surgery, gender and organizational level of ICU were not associated with mortality.
Conclusion: The diagnosis of CRC does not influence in-hospital mortality of patients admitted to the ICU after emergency colorectal surgery.

Introduction

Colorectal cancer (CRC) is a common disease worldwide. In the United States CRC is the third most frequently diagnosed cancer and the second leading cause of cancer-related death [1]. In the Netherlands CRC is the second most common malignancy with an incidence of more than 57 per 100,000 population per year [2]. A subset of patients with CRC require acute surgery, e.g. after intestinal obstruction and/or perforation; the proportion of CRC patients with an acute presentation varied between 8-25% in different studies [3-6]. Acute presentation of CRC is associated with higher postoperative morbidity and mortality [5-9]. As a consequence, unlike after elective CRC operations, postoperative care after emergency CRC surgery is frequently provided on Intensive Care Units (ICUs).

We recently used the National Intensive Care Evaluation (NICE) registry, which prospectively collects data from all ICU admissions in 80 Dutch ICUs [10], to study the outcome of unplanned ICU admissions of 15,211 cancer patients in these ICUs during a four-year period [11]. In unplanned non-surgical cancer patients both ICU mortality and in-hospital mortality were almost twice as high as in unplanned non-surgical patients without cancer. In contrast, ICU mortality did not differ between unplanned surgical cancer patients and unplanned surgical non-cancer patients (9.0% and 8.9% respectively). In-hospital mortality was slightly higher in unplanned surgical cancer patients (17.4% and 14.6% respectively). This previous investigation did not stratify patients according to type of cancer or type of surgery [11].

Gender has been reported to influence treatments and outcome of patients with CRC [12]. Several studies have reported a longer survival of women after CRC resection when compared to men [12-15]. On the other hand, females with CRC more often present with an emergency, possibly because women undergo endoscopic screening less frequently than men [12, 15]. A possible gender effect on postoperative survival after emergency CRC surgery has not been studied thus far. Notably, gender may impact on the occurrence of complications and the type of therapeutic interventions while on the ICU. Although overall ICU mortality does not seem to differ between sexes [16, 17], men are more likely to develop sepsis [17-19]. Additionally, men are more likely to receive invasive therapeutic procedures while on the ICU [16, 20].

Knowledge of the short-term outcome of patients admitted to the ICU after emergency CRC surgery and how this relates to the outcome of patients receiving postoperative ICU care after unforeseen colorectal surgery for reasons not related to cancer is limited. We here sought to determine whether CRC is an important factor in the short-term outcome of patients admitted to the ICU after emergency colorectal surgery. Therefore, the specific aims of the present study were (1) to compare short-term outcomes of unplanned ICU admissions after emergency surgery for CRC with those in unplanned ICU admissions after emergency colorectal surgery for other reasons, and (2) to study factors that influence short-term outcomes in this acute CRC surgical population. For this we analyzed all ICU admissions in the Netherlands collected in the NICE registry from January 2007 through August 2012.

Methods

Ethics statement

The Dutch National Intensive Care Evaluation (NICE) initiative is officially registered according to the Dutch Personal Data Protection Act. The need for ethical committee approval is waived

by the Central Committee on Research Involving Human Subjects, because the study was purely observational and because only anonymous patient data were used.

Patient data

The database of the NICE registry was used in this observational study [10]. In 1996 the NICE foundation started collecting data on patients admitted to Dutch ICUs. The participating ICUs (covering 80% of Dutch ICUs) provide information on all ICU admissions with the aim to assess and compare the performance of the ICUs and to improve the quality of care. For each ICU admission variables are collected that describe patient characteristics, severity of illness during the first 24 hours of ICU admission, and the ICU and in-hospital mortality and length of stay [10]. The data are encrypted such that all patient-identifying information, including name and patient identification number, are untraceable. The recorded variables are used to calculate probabilities of death for each patient using the Acute Physiology and Chronic Health Evaluation (APACHE) IV prognostic model [21]. Data for the current study were collected from all consecutive admissions to the 80 ICUs between January 1st 2007 and August 1st 2012. In the Netherlands, ICUs are categorized by organizational level 1, 2 or 3. Medical care is covered by certified intensivists for 24 hours per day, seven days per week in level 2 and 3 ICUs. The minimal volume of care per year is 3000 treatment days in level 3 and 1500 treatment days in level 2 ICUs. In level 1 ICUs, medical care is offered by intensivists at daytimes, while other medical specialists may be responsible at night and during weekends.

Selection of patients

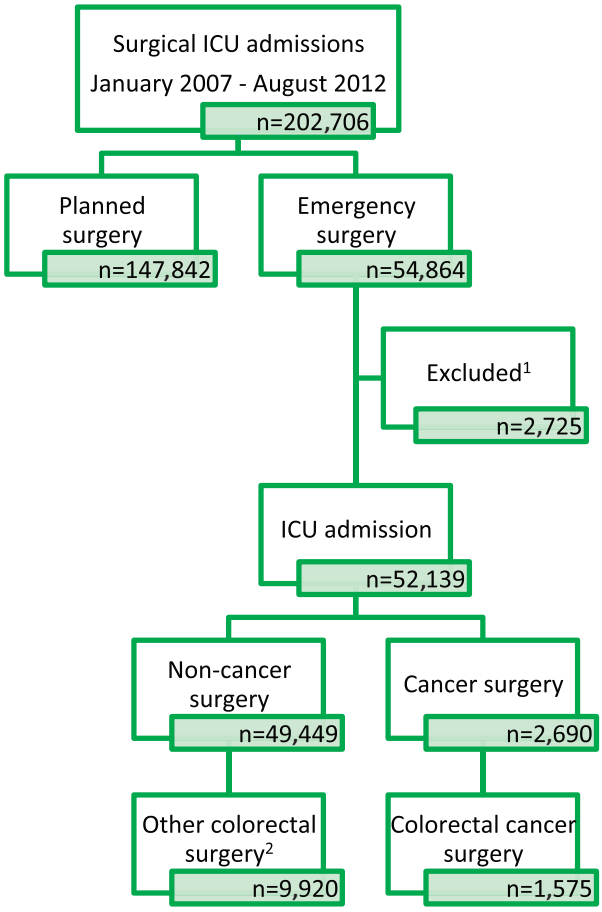
Patient selection was done according to Figure 1. Patients admitted to the ICU for emergency colorectal surgery were identified by selecting for (a) admission type (surgical and unplanned), (b) type of surgery (colorectal) and (c) indication (CRC or non-malignant disease, i.e. diverticular disease, fistula or abscess, gastrointestinal obstruction, perforation or rupture, or peritonitis). Patients with inflammatory bowel disease were excluded from the current analysis because they are likely to be younger and to use immune suppressive medication [22-24]; patients with gastrointestinal vascular ischemia were excluded because they are more likely to have significant comorbidities and a grim prognosis if acute surgery is needed [25-28]. In addition, surgery for complications of previous surgical procedures were excluded. According to the APACHE IV exclusion criteria, patients younger than 16 years, patients whose ICU stay was less than 4 hours, patients who were admitted from or discharged to another ICU, patients with burns and, patients admitted after transplant operations (except for hepatic and renal transplantation) were excluded from the multivariate logistic regression analyses [21].

Statistical analysis

Categorical variables are presented as percentages and continuous variables are presented as mean and standard deviation (SD), or in case of non-normally distributed variables as median and interquartile range (IQR). Standardized mortality ratios (SMRs) were calculated by dividing the actual in-hospital mortality by the expected mortality as calculated by the APACHE IV prognostic model. The chi-squared test was used to compare categorical data, and the student's T test (for normally distributed variable) or Mann-Whitney U-test (non-normally distributed variables) were used for other variables when comparing two groups.

Type of colorectal surgery and outcome: to assess the associations between the type

Figure 1: Patient selection



Data were collected from all consecutive admission to 80 ICUs between January 1st 2007 and August 1st 2012.

[1] Excluded because ICU admission was done for logistical reasons (NICE registry definition: admission could have been postponed for 12 hours).

[2] Diverticular disease, fistula or abscess, gastrointestinal obstruction, perforation or rupture, or peritonitis.

of colorectal surgery, i.e. cancer vs. non-cancer, and in-hospital mortality multivariate logistic regression analyses were performed. In order to adjust for underlying case-mix differences ,the APACHE IV severity of illness score (consisting of the APACHE IV acute physiology score (APS) and comorbidities), gender, age (dichotomized as below or above 70 years), level of ICU, BMI (i.e. categorized as normal range, underweight and overweight), chronic comorbidities (i.e.

Table 1a: Patients admitted in the ICU after emergency colorectal surgery

	Colorectal Cancer Surgery 1,575 (13.7%)	Other Colorectal Surgery 9,920 (86.3%)	*p*
Age			
Median	74	71	
Interquartile Ranges	65-81	59-79	*<0.001*
<70 y (%)	37.6	46.3	*<0.001*
≥70 y (%)	62.4	53.7	*<0.001*
Mean BMI (SD)	**25.6 (8.3)**	**25.6 (6.1)**	***0.862***
Underweight (BMI <18.5) (%)	4.3	5.4	
Normal range (BMI 18.5-25.0) (%)	47.6	47.7	
Overweight (≥25.00) (%)	48.1	46.9	
Chronic comorbidity (%)			
Chronic renal failure[1]	4.1	7.2	*<0.001*
COPD	10.9	10.5	*0.456*
Heart failure	4.3	3.6	*0.088*
Diabetes	14.2	12.5	*0.031*
Neurologic disorder[2]	1.5	1.4	*0.655*
Cirrhosis	0.26	1.2	*<0.001*
Metastasized neoplasm	28.7	8.6	*<0.001*
Hematological malignancy	1.2	1.7	*0.085*
Level of ICU[3] (%)			***<0.001***
level 1	35.8	26.8	
level2	48.6	50.4	
level3	14.5	21.8	
Admission source[4] (%)			***<0.001***
Same Hospital	91.7	84.0	
Other hospital	6.8	14.3	

CRC = Colorectal cancer, [1] Includes chronic dialysis, [2] Includes previous cerebrovascular accident,
[3] Level one being lowest level and level three the highest level of ICU in the Netherlands, [4] Rest is missing.

COPD, Heart failure, neurologic disorder, neoplasm, and hematological malignancy), and acute comorbidities (i.e. confirmed infection, mechanical ventilation, vasopressors, and acute renal failure) were included in the model as covariates [21, 29].

Results were considered statistically significant if p-values were below 0.05. All statistical analyses were performed using PASW statistics 19 (SPSS, Chicago).

Results

Patients

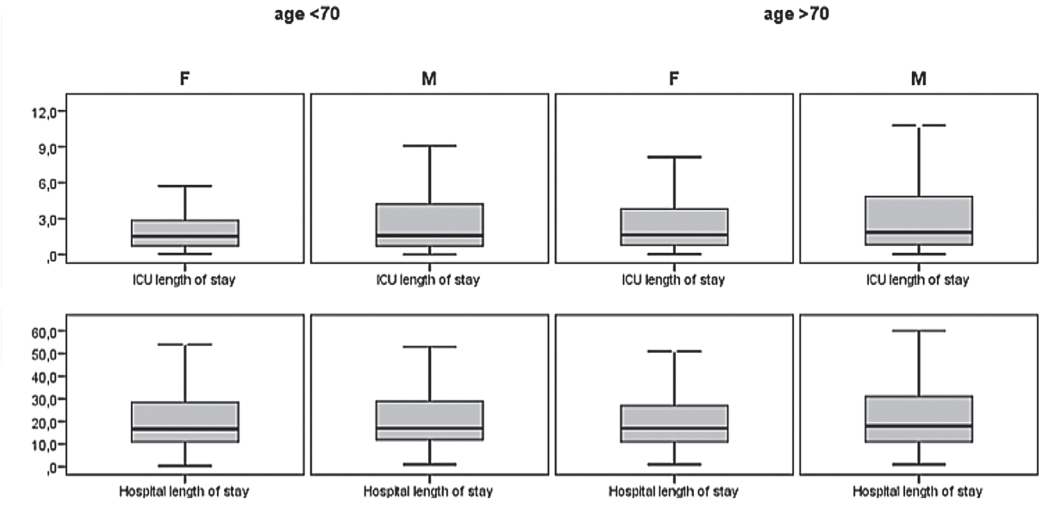
From January 2007 to August 2012, 11,495 patients were admitted to the participating ICUs after unplanned colorectal surgery (Figure 1, Table 1a). Of these, 1,575 (13.7%) had a diag-

nosis of CRC. Patients with CRC were older (median age 74 years) than patients admitted for unplanned colorectal surgery for non-malignant disease (median age 71 years) (p<0.001) and there were slightly more men in the former group (51.4% and 49.9% respectively, Table 1b). With regard to chronic comorbidity, differences between both patient groups were modest, with the CRC group harboring more patients with diabetes and fewer patients with chronic renal failure and cirrhosis. Of patients with CRC 28.7% had metastasized disease; notably, 8.6% of the unplanned colorectal surgical patients without CRC had a metastasized malignancy from another (not colorectal) origin. Patients with benign colorectal disease were more often admitted to the ICU from another hospital (14.3% versus 6.8% of patients with CRC, p<0.001). Both patient groups were predominantly admitted to a level 2 ICU; however, patients with benign colorectal disease more often were admitted to a level 3 ICU when compared with patients with CRC.

Acute comorbidity and admission laboratory results

Clear differences existed between patient groups with regard to acute comorbidity (Table 2a). Patients undergoing emergency surgery for other reasons than CRC had a higher prevalence of confirmed infection and sepsis (both p<0.001 versus CRC patients), more frequently had acute renal failure (p<0.001), and more often required mechanical ventilation (p<0.001) and vasopressors (p=0.007). APACHE IV scores were similar in both patient-groups (Table 2a). With regard to laboratory results on the first day after admission, differences between groups were

Figure 2: ICU and hospital length of stay for unplanned CRC patients admitted to the ICU for emergency colorectal surgery stratified according the age (< 70 and > 70 years) and gender



Data are expressed as box-and-whisker diagrams depicting the smallest observation, lower quartile, median, upper quartile and largest observation.

Table 1b: Patients admitted in the ICU after emergency colorectal surgery separated by gender

	Colorectal Cancer Surgery			Other Colorectal Surgery		
	Female 765 48.6%	Male 810 51.4%	*p*	Female 4,968 50.1%	Male 4,952 49.9%	*p*
Age						
Median	76	72	*<0.001*	74	69	*<0.001*
Interquartile Ranges	66-83	64-80		61-81	58-77	
<70 y (%)	32.4	42.8	*<0.001*	40.4	52.2	*<0.001*
≥70 y (%)	67.6	57.2	*<0.001*	59.6	47.8	*<0.001*
Mean BMI (SD)	**25.5 (6.7)**	**25.7 (9.7)**	***0.831***	**25.8 (6.5)**	**25.5 (5.6)**	***0.614***
Underweight (BMI <18.5) (%)	6.3	2.5		6.7	4.1	
Normal range (BMI 18.5-25.0) (%)	46.6	48.5		45.8	49.7	
Overweight (≥25.00) (%)	47.1	49.0		47.5	46.2	
Chronic comorbidity (%)						
Chronic renal failure[1]	3.2	4.9	*0.138*	6.1	8.2	*<0.001*
COPD	9.2	12.5	*0.035*	10.0	11.0	*0.001*
Heart failure	3.5	5.1	*0.139*	3.4	3.8	*0.171*
Diabetes	13.5	14.9	*0.428*	13.7	11.3	*<0.001*
Neurologic disorder[2]	1.6	1.5	*0.525*	1.3	1.5	*0.494*
Cirrhosis	0.1	0.4	*0.625*	1.0	1.3	*0.103*
Metastasized neoplasm	28.8	28.6	*1.000*	7.8	9.4	*0.002*
Hematological malignancy	0.8	1.5	*0.239*	1.3	2.0	*0.003*
Level of ICU[3] (%)			***0.066***			***0.010***
level 1	35.8	35.7		28.4	25.1	
level2	47.5	49.6		50.3	50.5	
level3	16.3	13.3		20.5	23.2	
Admission source[4] (%)			***0.165***			***0.398***
Same Hospital	91.4	92.0		84.3	83.7	
Other hospital	7.6	6.0		13.8	14.7	

[1] Includes chronic dialysis, [2] Includes previous cerebrovascular accident, [3] Level one being lowest level and level three the highest level of ICU in the Netherlands, [4] Rest is missing.

modest at best and clinically not relevant (Table 2a). In accordance with the higher prevalence of acute renal failure in patients undergoing emergency surgery for other reasons than CRC, peak plasma creatinin levels were higher in this group than in patients with CRC (Table 2a, p<0.001).

Length of stay and mortality

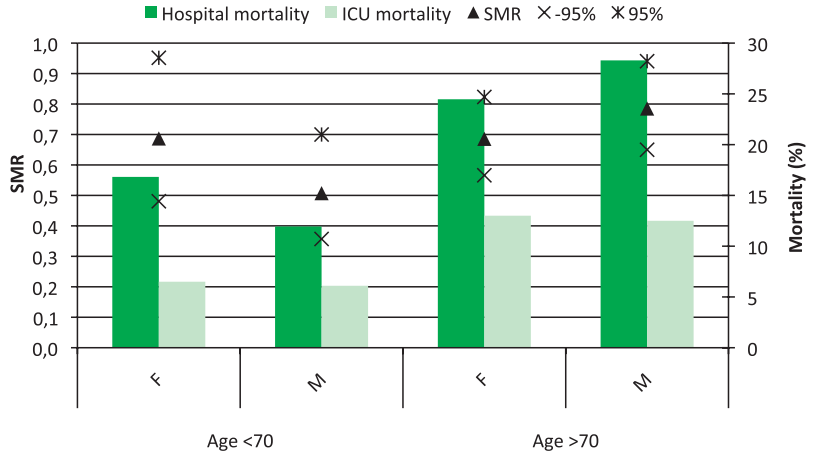
Patients with CRC had a shorter length of stay on the ICU (median 2.1 days) than patients with benign colorectal disease (median 2.8 days)(p<0.001), while hospital length of stay did not

differ between patient groups (median 19 days, Table 2a). Similarly, patients with CRC had a lower ICU mortality (10.3% vs 12.9%, p=0.004), whereas in-hospital mortality was not different between groups (22.5 and 21.7% respectively, p=0.523). Multivariate analysis showed that high APACHE IV score, high age, low body weight, COPD, chronic heart failure, metastasized carcinoma, hematologic malignancy, mechanical ventilation, treatment with vasopressors and acute renal insufficiency were all independently associated with in-hospital mortality (Table 3). On the other hand, surgery for CRC and organizational level of the ICU were not associated with in-hospital mortality.

Influence of gender

To obtain insight into a possible influence of gender on the outcome of emergency colorectal surgery in cancer patients, we studied differences between males and females in this group and (as a reference) in the group of non-CRC unplanned surgery (Tables 1b, 2b). Severity of illness, age, body weight index and acute and chronic co-morbidities were comparable in male and female patients. In patients without cancer, but not in CRC patients, ICU mortality and in-hospital mortality were higher in female patients. In the multivariate analysis, gender was not associated with in-hospital mortality (Table 3). Considering that women were relatively older than men in both patient groups (Table 1b), we also determined ICU and hospital length of stay in men and women with CRC aged below or above 70 years admitted for unplanned colorectal surgery (Figure 2). Clearly, gender did not influence length of stay in either age cohort. Finally, we assessed the impact of gender on ICU and hospital mortality in CRC patients stratified according to age (below or above the age of 70; Figure 3). This analysis showed that older

Figure 3: ICU and hospital mortality of unplanned CRC patients admitted to the ICU for emergency colorectal surgery stratified according the age (< 70 and > 70 years) and gender



CRC = Colorectal cancer. Bars indicate hospital mortality (dark green) and ICU mortality (light green). Triangles indicate SMR (standardized mortality ratio) with 95% confidence intervals.

Table 2a: Admission parameters, severity of illness and mortality for patients admitted in the ICU after emergency colorectal surgery

	Colorectal Cancer Surgery (1,575)	Other Colorectal Surgery (9,920)	*p*
Acute comorbidity (%)			
GI bleeding	1.7	1.2	*0.098*
Confirmed infections	22.3	41.0	*<0.001*
Pneumonia	1.4	1.2	*0.333*
Sepsis	9.2	19.6	*<0.001*
CPR	0.8	0.8	*0.515*
Cardiac dysrhythmia	8.2	8.4	*0.437*
Vasopressors	42.8	46.1	*0.007*
Immunodeficiency	4.7	8.2	*<0.001*
Mechanical ventilation 24hrs	51.8	61.3	*<0.001*
Acute renal failure	7.3	12.2	*<0.001*
Laboratory results day 1 (Median and IQR)			
Hematocrit (lowest, liter/liter)	0.29 (0.25-0.34)	0.30 (0.25-0.34)	*0.797*
Leukocytes (highest $x10^9$/liter)	11.5 (11.9-17)	11.6 (7.4-17)	*0.902*
Leukocytes (lowest $x10^9$/liter)	8.2 (4-12.5)	8.4 (4.4-13.1)	*0.003*
Thrombocytes (lowest $x10^9$/liter)	230 (157-299)	204 (141-292)	*<0.001*
Albumen (lowest gram/liter)	17 (12-22)	18 (12-23)	*0.566*
Creatinin (max, micromole/liter)	87 (66-126)	99 (70-152)	*<0.001*
PaO2/FiO2 ratio	254 (186-337)	236 (168-320)	*<0.001*
Severity of illness and mortality			
APACHE IV score (IQR)	70 (54-88)	69 (57-87)	*0.616*
ICU lengths of stay (IQR)	2.1(0.9-5.7)	2.8 (1.1-7.4)	*<0.001*
Hospital length of stay (IQR)	19 (12-32)	19 (11-35)	*0.359*
ICU mortality (%)	10.3	12.9	*0.004*
Hospital mortality (%)	21.7	22.5	*0.523*
APACHE IV SMR (±95% CI)	0.69 (0.57-0.81)	0.91(0.81-1.01)	*<0.001*

IQR = Interquartile ranges

patients of both genders had a significantly higher ICU and hospital mortality. Most notably, whereas ICU mortality was similar in men and women in both age cohorts, hospital mortality was lower in men aged below 70 years but higher above 70 years when compared to women within the respective age cohorts.

Discussion

To the best of our knowledge our study is the first to specifically address postoperative care and outcome of CRC patients who are admitted to the ICU after emergency colorectal surgery. Our survey comprised 1,575 CRC patients who received postoperative care in one of 80 partici-

pating ICUs after unplanned surgery during a five-year and seven-month period, and who were compared with 9,920 patients who received postoperative care after unplanned colorectal surgery for other reasons during the same period in the same ICUs. Our main findings are that CRC patients had fewer acute comorbidities, fewer infections, a shorter length of ICU stay and a lower ICU mortality, while hospital length of stay and mortality did not differ between groups. In accordance, in a multivariate analysis, low body weight, high age, chronic comorbidities and high severity of illness at ICU admission, but not CRC, gender or organizational level of ICU were associated with in-hospital mortality.

In spite of improved surgical techniques and perioperative care colorectal surgery remains to account for the greatest share of adverse events in general surgical patients, contributing a disproportionate part of morbidity, mortality and length of stay in this group [30]. Postoperative complication rates and mortality after CRC surgery are as high as 20-40% and 5% respectively [31-34]. Emergency surgery for CRC bears an even greater risk for postoperative complications and mortality. In a Dutch study, the risk of developing any postoperative complication among colon cancer patients was significantly higher for those undergoing emergency surgery (odds ratio 3.6) [35]. Similarly, emergency surgery was identified as an important risk factor for mortality amongst CRC patients, bearing a 2.5-fold increased risk of death [34]. Moreover, in an investigation that examined > 30,000 colorectal resections in 142 US hospitals mortality was 1.9% after nonemergency surgery versus 15.3% after emergency operations [36]. In accordance, in our cohort of patients after unplanned CRC surgery, we found high ICU mortality and in-hospital mortality of 10% and 22% respectively. Importantly, the high mortality was also found in patients after unplanned colorectal surgery for non-cancer diagnoses.

Our findings differ from a previous study comparing outcome of Dutch patients after unplanned ICU admission for cancer versus non-cancer reasons [11]. In that study medical cancer patients had a strongly increased hospital mortality (40.6%) when compared with medical non-cancer patients (23.7%); mortality was also higher in unplanned surgical patients with cancer compared with surgical patients without cancer (17.4% vs. 14.6%) [11]. This earlier study contained all types of cancer [11]. In the current analysis in patients with CRC only, the risk of mortality was not higher in patients with cancer as compared with patients with non-cancer reasons for colorectal surgery requiring ICU admission, such as treatment for diverticular disease, fistula, abscesses, gastrointestinal obstruction, perforation or rupture. Interestingly, ICU mortality was even lower in patients with CRC compared with patients after colorectal surgery for other reasons. This lower mortality may be explained by higher acute comorbidities, such as infections and renal failure, in patients admitted to the ICU after non-cancer surgery.

Based on earlier studies, we hypothesized that gender could have an important influence on outcome after CRC surgery [12-15]. Also, gender has been shown to affect ICU care [16, 20, 37]. A large population-based study conducted in Canada demonstrated that older women with critical illness were less likely than critically ill men to be admitted to an ICU and were more likely to die in the ICU or hospital [20]. A prospective study involving 25,998 adult patients admitted to 31 ICUs in Austria also documented gender-related differences in ICU care, with male patients - despite presenting with a lower severity of illness - more likely than female patients to receive a high level of care, as defined by the number of invasive procedures [16]. Although in this investigation women had a higher observed mortality rate than men, there was no difference in outcome after adjustment for the severity of illness [16]. Overall ICU mortality did not differ between sexes in another study [17]. In our current study gender did not impact on

Table 2b: Admission parameters, severity of illness and mortality for patients admitted in the ICU after emergency colorectal surgery separated by gender

	Colorectal Cancer Surgery			Other Colorectal Surgery		
	Female (765)	Male (810)	*p*	Female (4,968)	Male (4,952)	*p*
Acute comorbidity (%)						
GI bleeding	1.4	1.9	*0.558*	0.7	1.7	*<0.001*
Confirmed infections	23.0	21.7	*0.546*	41.1	41.0	*0.439*
Pneumonia	1.2	1.6	*0.524*	1.0	1.4	*0.058*
Sepsis	9.0	9.4	*0.862*	19.6	19.5	*0.501*
CPR	1.0	0.6	*0.411*	0.8	0.8	*0.539*
Cardiac dysrhythmia	8.0	8.4	*0.783*	8.2	8.5	*0.301*
Vasopressors	43.7	41.9	*0.476*	46.1	46.1	*0.489*
Immunodeficiency	4.1	5.3	*0.284*	8.0	8.4	*0.240*
Mechanical ventilation 24hrs	51.2	52.3	*0.687*	61.0	61.5	*0.297*
Acute renal failure	7.1	7.4	*0.846*	11.9	12.5	*0.179*
Laboratory results day 1 (Median and IQR)						
Hematocrit (lowest, liter/liter)	0.29 (0.26-0.32)	0.29 (0.26-0.33)	*0.366*	0.29 (0.25-0.32)	0.30 (0.26-0.34)	*0.614*
Leukocytes (highest x10^9/liter)	11.6 (8.7-17)	10.5 (6.9-14.7)	*0.380*	11.8 (7.6-17)	11.5 (7.4-16.7)	*0.334*
Leukocytes (lowest x10^9/liter)	8.4 (4.3-12.5)	8.0 (4.0-11.1)	*0.032*	8.4 (4.4-13.1)	8.3 (4.4-12.7)	*0.669*
Thrombocytes (lowest x10^9/liter)	236 (164-299)	223 (157-293)	*0.099*	212 (150-292)	196 (141-280)	*<0.001*
Albumen (lowest gram/liter)	16 (12-20)	18 (14-22)	*0.013*	17 (12-21)	18 (14-23)	*0.001*
Creatinin (max, micromole/liter)	76 (59-108)	97 (74-139)	*<0.001*	87 (63-137)	110 (78-169)	*<0.001*
PaO2/FiO2 ratio	256 (186-350)	252 (185-329)	*0.140*	240 (170-327)	232 (166-311)	*0.001*
Severity of illness and mortality						
APACHE IV score (IQR)	72 (58-88)	67 (56-83)	*0.373*	70 (55-89)	69 (53-86)	*0.023*
ICU lengths of stay (IQR)	2.0 (0.9 -5.6)	2.5 (0.9 -5.8)	*0.061*	2.7 (1.0 -7.1)	2.8 (1.1 -7.5)	*0.225*
Hospital length of stay (IQR)	18 (11-30)	18,3 (12 -35)	*0.120*	19 (10-35)	20 (11-36)	*0.275*
ICU mortality (%)	10.8	9.8	*0.507*	14.4	11.4	*<0.001*
Hospital mortality (%)	22.1	21.3	*0.706*	24.5	20.4	*<0.001*
APACHE IV SMR (±95% CI)	0.68 (0.58-0.80)	0.69 (0.59-0.81)	*ns*	0.95 (0.89-1.01)	0.87 (0.81-0.93)	*ns*

IQR = Interquartile ranges, l.o.s. = length of stay, SMR = standardized mortality ratio

Table 3: Multivariate analysis for hospital mortality

	Odds ratio (CI)
Colorectal Cancer admission	0.87 (0.73-1.03)
Male	1.08 (0.96-1.22)
Age ≥ 70 years	2.41 (2.11-2.74)
APACHE IV score	1.03 (1.02-1.04)
Level of ICU	
Level 1	1.00
Level 2	0.89 (0.75-1.05)
Level 3	1.05 (0.91-1.22)
BMI	
Underweight (BMI <18.5)	1.36 (1.22-1.55)
Normal range (BMI 18.5-25.0)	1.00
Overweight (≥25.00)	0.84 (0.75-0.99)
Chronic comorbidities	
COPD	1.52 (1.29-1.80)
Heart failure	1.74 (1.33-2.30)
Neurologic disorder	1.42 (0.91-2.15)
Metastasized neoplasm	1.94 (1.65-2.29)
Hematological malignancy	1.67 (1.14-2.43)
Acute comorbidities	
Confirmed infection	1.03 (0.93-1.18)
Mechanical ventilation 24hrs	1.39 (1.25-1.66)
Vasopressors	1.31 (1.15-1.50)
Acute renal failure	1.47 (1.25-1.73)

CI = 95% Confidence Interval

ICU or hospital mortality after unplanned ICU admission following emergency CRC surgery.
Our study has some limitations. We extracted data from the NICE registry, which collects data from all ICU admissions to 80 general ICUs in the Netherlands. NICE primarily monitors the performance of ICUs and does not focus specifically on cancer patients. As a consequence thereof, the type of malignancy is only recorded when cancer is the main reason for admission to the ICU; otherwise malignancy is scored as hematological malignancy or metastasized carcinoma without further specification. Hence, the current analysis involves patients of whom CRC was considered one of the maximal two recorded main admission diagnosis by the treating ICU physician. Our study is also limited by the fact that we cannot evaluate the impact of the stage of CRC, which is a major denominator of one-year mortality after colorectal surgery [34], on immediate postoperative outcome, since this information is not collected in the NICE data base. In addition, our survey is limited in that patient follow up was restricted to hospital discharge. Of note, however, the objective of our study was to evaluate the direct outcome of ICU postoperative care after emergency colorectal surgery (i.e. not the impact of emergency CRC surgery on cancer progression and outcome); hence, although we cannot exclude that some

patients died soon after hospital discharge, this limitation in follow up is unlikely to influence our results to an important extent. Finally, a limitation of our study is that we only analyzed the outcome of patients after emergency colorectal surgery who received postoperative care on the ICU. Mortality may differ in patients after unplanned colorectal surgery for CRC or other types of colorectal surgery not requiring ICU admission.

We excluded patients with IBD or ischemic colitis from the reference group receiving postoperative care after emergency colorectal surgery for benign disease, since they differ considerably from CRC patients in various aspects. The proportion of IBD patients going to the ICU is low, many use immune suppressive therapy and the age-peak of incidence of IBD differs strongly from the average age of CRC patients [22-24]. Patients with ischemic colitis have significant comorbidities and are usually treated in a conservative way; if surgery is deemed necessary the outcome is poor with postoperative mortality rates of 37-47%, which at least in part is caused by the underlying widespread vascular occlusive disease rather than by the extent and the complexity of the surgical procedure [25-28]. As such, patients undergoing emergency colorectal surgery for IBD or ischemic colitis are not suitable comparators for patients undergoing unforeseen colorectal surgery for CRC.

In conclusion, we here report that ICU and hospital mortality amongst CRC patients admitted to the ICU after emergency colorectal surgery for all causes is 10.3% and 21.7% respectively. While ICU mortality is slightly lower amongst CRC patients when compared to patients after emergency colorectal surgery for non-malignant disease, hospital mortality is similar in both groups. Factors associated with mortality include high age, low body weight, high severity of illness at ICU admission, chronic comorbidities and metastasized carcinoma. In addition, we show that gender does not influence postoperative outcome after unplanned ICU admission for emergency colorectal surgery. While in the early 1980s the presence of a malignancy was considered a contraindication for admission to an ICU, the success of anti-cancer therapies has created a mind switch amongst clinicians with regard to the use of aggressive supportive therapy in cancer patients [38, 39]. The current study adds to this growing evidence, showing that the diagnosis of CRC should not influence the decision whether or not to provide postoperative ICU care after emergency colorectal surgery.

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