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Clinical outcomes in bariatric surgery

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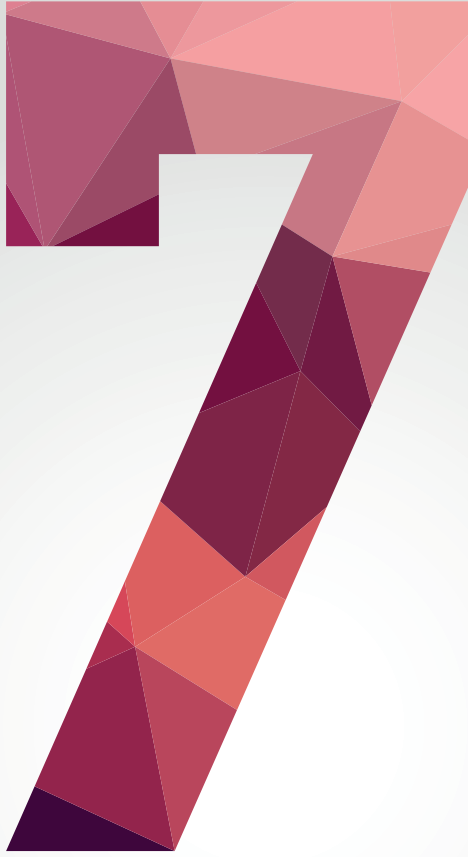


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Obesity as a determinant of perioperative and postoperative outcome in patients following colorectal cancer surgery: A population-based study (2009-2016)

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ABSTRACT

BACKGROUND

Obesity is an increasing problem worldwide that can influence perioperative and postoperative outcomes. However, the relationship between obesity and treatment-related perioperative and short-term postoperative morbidity after colorectal resections is still subject to debate.

STUDY

Patients were selected from the DCRA, a population-based audit including 83 hospitals performing colorectal cancer (CRC) surgery. Data regarding primary resections between 2009 and 2016 were eligible for analyses. Patients were subdivided into six categories: underweight, normal weight, overweight and obesity class I, II and III.

RESULTS

Of 71,084 patients, 17.7% with colon and 16.4% with rectal cancer were categorized as obese. Significant differences were found for the 30-day overall postoperative complication rate ($p < 0.001$), prolonged hospitalization ($p < 0.001$) and readmission rate (colon cancer $p < 0.005$; rectal cancer $p < 0.002$) in obese CRC patients. Multivariate analysis identified BMI 30 kg/m^2 as independent predictor of a complicated postoperative course in CRC patients. Furthermore, obesity-related comorbidities were associated with higher postoperative morbidity, prolonged hospitalization and a higher readmission rate. No significant differences in performance were observed in postoperative outcomes of morbidly obese CRC patients between hospitals performing bariatric surgery and hospitals that did not.

CONCLUSION

The real-life data analysed in this study reflect daily practice in the Netherlands and identify obesity as a significant risk factor in CRC patients. Obesity-related comorbidities were associated with higher postoperative morbidity, prolonged hospitalization and a higher readmission rate in obese CRC patients. No differences were observed between hospitals performing bariatric surgery and hospitals that did not.

INTRODUCTION

The World Health Organization (WHO) has recognized obesity as a pandemic disease that contributes to rising healthcare costs worldwide.^{1,2} Up to one-third of the Western population is currently overweight or obese.³⁻⁵

Not only is obesity considered to be of growing concern in the aetiology of colorectal cancer (CRC), but there is also a rising awareness of possible treatment-related morbidity and mortality after colorectal resections in obese patients.^{6,7} One study, which included almost 12,000 rectal cancer patients, showed a significant association between obesity and postoperative morbidity.⁸ However, findings in the international literature are often contradictory and inconclusive, due to limited study populations.^{9,10}

The aim of this population-based study was to evaluate the influence of obesity on perioperative and short-term postoperative outcomes in patients surgically treated for primary CRC in a nationwide registry. In addition, hospitals performing both bariatric and colorectal surgery and those performing only colorectal surgery were compared to test a possible association between surgical experience with obese patients and the outcomes of these CRC patients.

MATERIAL AND METHODS

DATA SOURCE

Data were derived from the Dutch ColoRectal Audit (DCRA), formerly known as the Dutch Surgical Colorectal Audit (DSCA). The DCRA collects information on patients, tumours, treatment, perioperative and short-term outcome characteristics (<30 days) of all patients undergoing surgical resection for primary CRC in the Netherlands.⁶

PATIENT SELECTION

For this study, no ethical approval or informed consent was required under Dutch law. All patients registered in the DCRA undergoing primary colorectal tumour resection between 1 January 2009 and 31 December 2016, were evaluated. Minimal data requirements were date of birth, body mass index (BMI), date of operation, type of surgery, tumour specifications and 30-day morbidity. All patients were examined preoperatively by an anaesthesiologist no more than 2 working days before the elective operation. Body weight and height were measured by the anaesthetist as standard procedure by all elective operations.

In addition to demographics and the American Society of Anesthesiologists (ASA) classification¹¹, an extensive set of comorbidities were registered in the DCRA. The Charlson Comorbidity Index (CCI)¹² was used as a composite comorbidity score.^{13, 14}

OUTCOME PARAMETERS

The primary endpoint of this study was a severe adverse postoperative event captured by a composite measure: complicated postoperative course. A complicated postoperative course was defined as prolonged hospitalization (>14 days postoperative) or Clavien-Dindo Classification of Surgical Complications (CD) grade III or higher.¹⁵ It includes complications requiring surgical, endoscopic and/or radiological interventions (CD grade III), life-threatening complications requiring admission to an intensive care unit (CD grade IV) or death (CD grade V).¹⁶

Secondary endpoints included any perioperative and postoperative complications, defined as a surgical or non-surgical complication occurring within 30 days after the primary resection, not classified as CD grade III or higher. In the DCRA, perioperative complications, postoperative complications, wound infections, wound dehiscence and intra-abdominal complications, such as postoperative bleeding, ileus, infection, abscess or anastomotic leakage, were registered when a re-intervention was performed. Non-surgical complications were defined as cardiac, thromboembolic, pulmonary, infectious, neurological or other.

STATISTICAL ANALYSIS

Patients were subdivided into different weight categories, as defined by the World Health Organization: underweight (BMI < 18.5 kg/m²), normal weight (BMI 18.5 – 24.9 kg/m²), overweight (BMI 25.0 – 29.9 kg/m²), obesity class I (BMI 29.9 – 34.9 kg/m²), obesity class II (BMI 35.0 – 39.9 kg/m²), obesity class III (BMI ≥ 40.0 kg/m²).¹⁷

Differences in patient and treatment characteristics for the different weight categories were assessed using Mann-Whitney *U* test for categorical variables and an independent sample t-test for continuous variables. Obese patients (BMI ≥ 30.0 kg/m²) were compared with normal-weight patients (BMI 18.5 – 24.9 kg/m²).

To evaluate hospital outcomes, a multivariate logistic regression was performed. The regression included gender, age, comorbidity-related scores (CCI score, ASA score), tumour location, pathological tumour stage, surgery setting (elective or urgent/emergency), preoperative tumour complications, additional resection due to tumour

invasion or to metastases as single factors. The variable BMI has been left out of the standard case-mix correction.⁶

The risk of postoperative complication was calculated using multivariate logistic regression analysis. Comorbidity-related scores and BMI were entered in the multivariate analysis to evaluate the effects of obesity and its associated comorbidities on postoperative outcome. Next to the p-values calculated with the Mann-Whitney *U* test, are the odds ratios (OR) stated. An OR is a measure of association between an exposure and an outcome.¹⁸

Comparisons were made between hospitals performing both bariatric and colorectal surgery and those performing only colorectal surgery. Analyses were performed to identify whether obese patients with CRC were more frequently referred to hospitals performing bariatric surgery and if patients were equally distributed (with regard to patient characteristics) among both types of hospitals.

R version 3.4.2 was used for statistical analysis in combination with the “Companion to Applied Regression”-package (car 2.1-5), “A Grammar of Data Manipulation”-package (dplyr 0.7.4), “Data Visualization for Statistics”-package (sjmisc 2.6.2) and “Labelled Data Utility Functions”-package (sjlabelled 1.0.4).

RESULTS

BASELINE CHARACTERISTICS

A total of 83 participating hospitals entered 77,819 unique patient records, including 55,892 (71.8%) colon cancer and 21,595 (27.8%) rectal cancer patients. The 332 (0.4%) patients with an unknown tumour, were excluded. In total, 50,876 (91.0%) colon cancer and 20,208 (93.6%) rectal cancer patients for whom a computable preoperative BMI could be calculated, were eligible for final analysis. **Table 1a** and **Table 1b** show the baseline characteristics of CRC patients in the different weight categories, during the study period (2009 – 2016).

OBESE COLON CANCER (OCC) PATIENTS

Of the 50,876 colon cancer patients, 9016 (17.7%) patients were obese as shown in **Table 1a**. OCC patients were significantly younger (mean 69.4 years; SD \pm 9.9, $p < 0.001$) compared with normal-weight colon cancer (NCC) patients (mean 70.5 years; SD \pm 11.5, $p < 0.001$) and overweight colon cancer patients (mean 70.6 years; SD \pm 10.2, $p < 0.001$) (**Table 1a**).

Table 1a: Patient, tumour and treatment characteristics of colon cancer patients combined with postoperative complications. Legend: *Mortality is shown as Clavien-Dindo classification grade V; **Clavien-Dindo classification grade \geq III combined with prolonged hospital stay; red values are column percentage values; green values are row percentage values. Abbreviations: ASA, American Society of Anesthesiologists risk score.

	Total		Normal weight 18.5 – 24.9 kg/m ²		Overweight 25.0 – 29.9 kg/m ²		Obesity > 30.0 kg/m ²		p-value
	N	%	N	%	N	%	N	%	
Number of colon cancer patients									
	50,876	100.0	20,755	40.8	20,212	39.7	9,016	17.7	<0.001
Patient characteristics									
Gender	23,759	46.7	10,690	45.0	7,987	33.6	4,431	18.6	<0.001
Age	7,297	14.3	3,289	45.1	2,580	35.4	1,276	17.5	<0.001
60 – 70 years	15,424	30.3	5,762	37.4	6,248	40.5	3,171	20.6	<0.001
70 – 80 years	17,522	34.4	6,736	38.4	7,336	41.9	3,166	18.1	<0.001
\geq 80 years	10,613	20.9	4,958	46.7	4,045	38.1	1,396	13.2	<0.001
ASA score	37,944	74.6	16,005	42.2	15,409	40.6	5,909	15.6	<0.001
I - II	11,898	23.4	4,307	36.2	4,445	37.4	2,904	24.4	<0.001
III	897	1.8	372	41.5	313	34.9	184	20.5	<0.001
IV - V	11,755	23.1	4,323	36.8	4,721	40.2	2,558	21.8	<0.001
Charlson score	13,692	26.9	4,721	36.5	5,535	40.4	2,901	21.2	<0.001
\geq 2	20,755	40.8	-	-	-	-	-	-	-
Body mass index	20,212	39.7	-	-	-	-	-	-	-
18.5 – 24.9 kg/m ²	6,881	13.5	-	-	-	-	-	-	-
25.0 – 29.9 kg/m ²	1,603	3.2	-	-	-	-	-	-	-
30.0 – 34.9 kg/m ²	532	1.0	-	-	-	-	-	-	-
35.0 – 39.9 kg/m ²	17,590	34.6	7,131	40.5	6,727	38.2	3,423	19.5	<0.001
\geq 40.0 kg/m ²									
Abdominal surgical history									
Yes	22,272	43.8	9,461	42.5	8,553	38.4	3,795	17.0	<0.001
Tumour characteristics									
Tumour location	8,584	16.9	3,487	40.6	3,421	39.9	1,502	17.5	0.191
Right colon									
Transversum / left colon									

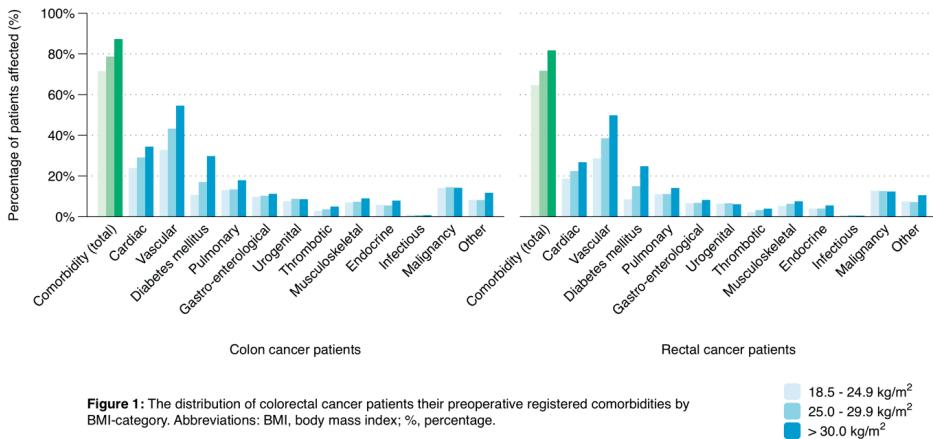
Table 1a: Patient, tumour and treatment characteristics of colon cancer patients combined with postoperative complications. Legend: *Mortality is shown as Clavien-Dindo classification grade V; **Clavien-Dindo classification grade \geq III combined with prolonged hospital stay; red values are column percentage values; green values are row percentage values. Abbreviations: ASA, American Society of Anesthesiologists risk score. (continued)

	Total						Normal weight 18.5 – 24.9 kg/m ²			Overweight 25.0 – 29.9 kg/m ²			Obesity > 30.0 kg/m ²			p-value	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%			
		20,020	39.4	7,807	39.0	8,238	41.1	3,719	18.6	1,454	17.8	730	12.3	61	13.1		461
Preoperative tumour complications	8,159	16.0	3,274	40.1	2,971	49.9	209	44.8	1,149	35.9	1,847	42.7	1,645	19.8	5,019	17.2	0.001
	5,953	11.7	2,067	34.7	186	39.8	467	0.9	1,494	46.7	1,456	33.7	3,108	37.4	12,050	41.2	0.001
	467	0.9	209	44.8	186	39.8	467	0.9	1,494	46.7	1,456	33.7	3,108	37.4	12,050	41.2	0.001
	2,891	5.7	1,494	46.7	1,494	46.7	2,891	5.7	1,494	46.7	1,494	46.7	2,891	5.7	1,494	46.7	0.034
Pathological T classification	4,321	8.5	1,456	33.7	1,847	42.7	1,456	8.5	1,456	33.7	1,847	42.7	1,456	8.5	1,456	33.7	<0.001
	8,317	16.3	3,108	37.4	3,457	41.6	8,317	16.3	3,108	37.4	3,457	41.6	8,317	16.3	3,108	37.4	<0.001
	29,222	57.4	12,050	41.2	11,659	39.9	29,222	57.4	12,050	41.2	11,659	39.9	29,222	57.4	12,050	41.2	0.001
	8,208	16.1	3,826	46.6	2,926	35.6	8,208	16.1	3,826	46.6	2,926	35.6	8,208	16.1	3,826	46.6	0.001
	808	1.6	315	39.0	323	40.0	808	1.6	315	39.0	323	40.0	808	1.6	315	39.0	0.635
Pathological N classification	29,304	57.6	11,707	40.0	11,693	39.9	29,304	57.6	11,707	40.0	11,693	39.9	29,304	57.6	11,707	40.0	<0.001
	12,485	24.5	5,226	41.9	4,947	39.6	12,485	24.5	5,226	41.9	4,947	39.6	12,485	24.5	5,226	41.9	0.006
	8,497	16.7	3,563	41.9	3,354	39.5	8,497	16.7	3,563	41.9	3,354	39.5	8,497	16.7	3,563	41.9	0.031
	590	1.2	259	43.9	218	36.9	590	1.2	259	43.9	218	36.9	590	1.2	259	43.9	0.244
Metastatic disease	5,962	11.7	2,773	46.5	2,189	36.7	5,962	11.7	2,773	46.5	2,189	36.7	5,962	11.7	2,773	46.5	<0.001
Lymph nodes	45,351	89.1	18,514	40.8	18,036	39.8	45,351	89.1	18,514	40.8	18,036	39.8	45,351	89.1	18,514	40.8	0.169
	≥10 retrieved						≥10 retrieved						≥10 retrieved				
Surgical characteristics																	
Setting	7,708	15.2	3,807	49.4	2,683	34.8	7,708	15.2	3,807	49.4	2,683	34.8	7,708	15.2	3,807	49.4	<0.001
Approach	29,249	57.5	11,206	38.3	12,107	41.4	29,249	57.5	11,206	38.3	12,107	41.4	29,249	57.5	11,206	38.3	<0.001
Conversion	3,749	7.4	1,205	32.1	1,498	40.0	3,749	7.4	1,205	32.1	1,498	40.0	3,749	7.4	1,205	32.1	<0.001
Yes							Yes						Yes				
Complications																	

Table 1a: Patient, tumour and treatment characteristics of colon cancer patients combined with postoperative complications. Legend: *Mortality is shown as Clavien-Dindo classification grade V; **Clavien-Dindo classification grade \geq III combined with prolonged hospital stay; red values are column percentage values; green values are row percentage values. Abbreviations: ASA, American Society of Anesthesiologists risk score. (continued)

	Total		Normal weight 18.5 – 24.9 kg/m ²		Overweight 25.0 – 29.9 kg/m ²		Obesity > 30.0 kg/m ²		p-value
	N	%	N	%	N	%	N	%	
Peroperative complications	1,312	2.6	486	37.0	538	41.0	268	20.4	0.011
Bleeding	205	0.4	73	35.6	80	39.0	50	24.4	0.080
Bowel injury	351	0.7	124	35.3	150	42.7	69	19.7	0.196
Ureter/urethral injury	89	0.2	36	40.4	28	31.5	22	24.7	0.112
Bladder injury	61	0.1	23	37.7	25	41.0	12	19.7	0.926
Total	15,173	29.8	5,898	38.9	5,995	39.5	2,984	19.7	<0.001
Postoperative complications	7,595	14.9	2,847	37.5	3,029	39.9	1,579	20.8	<0.001
Surgical complications	2,820	5.5	1,116	39.6	1,109	39.3	521	18.5	0.012
Pulmonary complications	1,791	3.5	698	39.0	684	38.2	373	20.8	0.507
Cardiac complications	341	0.7	125	36.7	134	39.3	76	22.3	0.631
Thromboembolic complications	1,897	3.7	715	37.7	752	39.6	395	20.8	0.497
Infectious complications	727	1.4	298	41.0	286	39.3	122	16.8	0.056
Neurological complications	4,219	8.3	1,608	38.1	1,708	40.5	808	19.2	<0.001
Total	1,935	3.8	729	37.7	785	40.6	381	19.7	0.014
Anastomotic leakage	241	0.5	113	46.9	90	37.3	33	13.7	0.167
Bleeding	4,402	8.7	1,651	37.5	1,737	39.5	923	21.0	<0.001
Grade III-IV	1,610	3.2	669	41.6	614	38.1	269	16.7	<0.001
Grade V	8,740	17.2	3,531	40.4	3,408	39.0	1,590	18.2	<0.001
>14 days	9.4	\pm 8.8	9.4	\pm 8.7	9.3	\pm 8.8	9.7	\pm 9.1	-
Duration (mean/days/SD)	11,228	22.1	4,491	40.0	4,380	39.0	2,096	18.7	<0.001
Severe complicated course**	2,604	5.1	1,000	38.4	1,032	39.6	522	20.0	0.005
Readmission									

This group also had a higher ASA-score and were associated with more preoperative comorbidities (OCC 87.3% vs NCC 71.6%, $p < 0.001$). In particular, cardiac, vascular, diabetes, and pulmonary comorbidities were recorded significantly more frequently (**Fig. 1**). Colon tumours were seen significantly more in the right colon and had a significantly lower pathological and clinical tumour stage. OCC patients were mostly operated using a laparoscopic approach (OCC 61.8% [5575 of 9016] versus NCC 54.0% [11,206 of 20,755], $p < 0.001$), but less frequently underwent an emergency procedure (OCC 10.6% [957 of 9016], NCC 18.3% [3807 of 20,755], $p < 0.001$). In 11.0% of OCC and 5.8% of NCC patients, a laparoscopic conversion was needed. Furthermore, more perioperative complications were seen in the OCC group ($p \frac{1}{4} 0.011$), but for the specific complications bleeding, bowel injury, ureter/urethral and bladder injury, no significant differences were observed.



In total, 33.1% ($n = 2984$) of the OCC patients developed a postoperative complication compared with 28.4% ($n = 5898$) of the NCC patients. Significant differences in surgical complications ($p < 0.001$) and pulmonary complications ($p < 0.001$) were seen in the OCC group. Furthermore, significant differences were observed in postoperative re-interventions performed for anastomotic leakage ($p < 0.014$) and for severe complicated course in the OCC group ($p < 0.001$). The higher number of total postoperative and surgical complications in combination with a higher CD grade and prolonged hospitalization resulted in more OCC patients with a severe complicated postoperative course. Regarding the percentage of mortality (CD grade V), a slight but significant difference was seen in favour of the OCC group: 3.0% [269 of 9016] versus 3.2% [669 of 20,755] in the NCC group ($p < 0.001$).

Table 1b: Patient, tumour and treatment characteristics of rectal cancer patients combined with postoperative complications. Legend: *Mortality is shown as Clavien-Dindo classification grade V; **Clavien-Dindo classification grade \geq III combined with prolonged hospital stay; red values are column percentage values; green values are row percentage values. Abbreviations: ASA, American Society of Anesthesiologists risk score.

	Total			Normal weight 18.5 – 24.9 kg/m ²			Overweight 25.0 – 29.9 kg/m ²			Obesity > 30.0 kg/m ²			p-value
	N	%		N	%		N	%		N	%		
Number of rectal cancer patients	20,208	100.0		8,186	40.5		8,377	41.5		3,322	16.4		<0.001
Patient characteristics													
Gender	7,426	36.7	Female	3,305	44.5		2,560	34.5		1,357	18.3		<0.001
Age	4,429	21.9	< 60 years	1,903	43.0		1,725	38.9		700	15.8		<0.001
	7,001	34.6	60 – 70 years	2,637	37.7		2,967	42.4		1,298	18.5		<0.001
	6,286	31.1	70 – 80 years	2,500	39.8		2,663	42.4		1,038	16.5		0.088
	2,481	12.3	\geq 80 years	1,143	46.1		1,020	41.1		280	11.3		<0.001
ASA score	16,713	82.7	I - II	6,957	41.6		6,999	41.9		2,498	14.9		<0.001
	3,274	16.2	III	1,132	34.6		1,290	39.4		795	24.3		<0.001
	152	0.8	IV - V	74	48.7		51	33.6		22	14.5		0.046
Charlson score	4,158	20.6	1	1,479	35.6		1,787	43.0		827	19.9		<0.001
	4,440	22.0	\geq 2	1,646	37.1		1,866	42.0		857	19.3		<0.001
Body mass index	8,186	40.5	18.5 – 24.9 kg/m ²	-	-		-	-		-	-		-
	8,377	41.5	25.0 – 29.9 kg/m ²	-	-		-	-		-	-		-
	2,684	13.3	30.0 – 34.9 kg/m ²	-	-		-	-		-	-		-
	488	2.4	35.0 – 39.9 kg/m ²	-	-		-	-		-	-		-
	150	0.7	\geq 40.0 kg/m ²	-	-		-	-		-	-		-
Abdominal surgical history	6,096	30.2	Yes	2,396	39.3		2,445	40.1		1,133	18.6		<0.001
Tumour characteristics													
Distance anal verge	5,290	26.2	<5 cm	2,187	41.3		2,141	40.5		869	16.4		0.112
	6,340	31.4	5-10 cm	2,623	41.4		2,623	41.4		980	15.5		0.011

Table 1b: Patient, tumour and treatment characteristics of rectal cancer patients combined with postoperative complications. Legend: *Mortality is shown as Clavien-Dindo classification grade V; **Clavien-Dindo classification grade \geq III combined with prolonged hospital stay; red values are column percentage values; green values are row percentage values. Abbreviations: ASA, American Society of Anesthesiologists risk score. (continued)

	Total						Normal weight		Overweight		Obesity		p-value
	18.5 – 24.9 kg/m ²		25.0 – 29.9 kg/m ²		> 30.0 kg/m ²								
	N	%	N	%	N	%	N	%	N	%	N	%	
Preoperative tumour complications													
≥ 10 cm	8,040	39.8	3,126	38.9	3,433	42.7	1,380	17.2	<0.001				
Bleeding	2,448	12.1	985	40.2	997	40.7	421	17.2	0.513				
Obstruction/ileus	572	2.8	298	52.1	196	34.3	54	9.4	<0.001				
Abscess	107	0.5	56	52.3	27	25.2	18	16.8	<0.001				
Other	846	4.2	386	45.6	342	40.4	94	11.1	<0.001				
Clinical T classification													
cT1	649	3.2	242	37.3	284	43.8	119	18.3	0.044				
cT2	4,760	23.6	1,812	38.1	2,066	43.4	828	17.4	<0.001				
cT3	11,462	56.7	4,656	40.6	4,764	41.6	1,872	16.3	0.468				
cT4	1,923	9.5	896	46.6	676	35.2	279	14.5	<0.001				
cTx/unknown	1,414	7.0	580	41.0	587	41.5	224	15.8	0.933				
Clinical N classification													
cN0	8,119	40.2	3,286	40.5	3,365	41.4	1,343	16.5	0.943				
cN1	6,314	31.2	2,515	39.8	2,646	41.9	1,050	16.6	0.624				
cN2	4,059	20.1	1,660	40.9	1,655	40.8	673	16.6	0.673				
cNx/unknown	1,716	8.5	725	42.2	711	41.4	256	14.9	0.212				
Pathological T classification													
(y)pT0-1	1,854	9.2	712	38.4	809	43.6	316	17.0	0.012				
(y)pT2	6,252	30.9	2,481	39.7	2,620	41.9	1,078	17.2	0.001				
(y)pT3	9,389	46.5	3,814	40.6	3,883	41.4	1,534	16.3	0.805				
(y)pT4	944	4.7	455	48.2	323	34.2	126	13.3	<0.001				
(y)pTx/unknown	1,769	8.8	724	40.9	742	41.9	268	15.1	0.271				
Pathological N classification													
pN0	12,869	63.7	5,249	40.8	5,308	41.2	2,105	16.4	0.749				
pN1	4,675	23.1	1,860	39.8	1,962	42.0	781	16.7	0.668				

Table 1b: Patient, tumour and treatment characteristics of rectal cancer patients combined with postoperative complications. Legend: *Mortality is shown as Clavien-Dindo classification grade V; **Clavien-Dindo classification grade \geq III combined with prolonged hospital stay; red values are column percentage values; green values are row percentage values. Abbreviations: ASA, American Society of Anesthesiologists risk score. (continued)

	Total		Normal weight 18.5 – 24.9 kg/m ²		Overweight 25.0 – 29.9 kg/m ²		Obesity > 30.0 kg/m ²		p-value
	N	%	N	%	N	%	N	%	
pN2	2,325	11.5	926	39.8	972	41.8	391	16.8	0.885
pNx/unknown	339	1.7	151	44.5	135	39.8	45	13.3	0.175
Metastatic disease	1,429	7.1	657	46.0	554	38.8	184	12.9	<0.001
Lymph nodes	15,619	77.3	6,262	40.1	6,482	41.5	2,632	16.9	0.025
Surgical characteristics									
Setting	294	1.5	139	47.3	108	36.7	34	11.6	0.002
Approach	12,796	63.3	5,150	40.2	5,385	42.1	2,105	16.5	<0.001
Conversion	1,323	6.5	341	25.8	602	45.5	372	28.1	<0.001
Complications									
Peroperative complications	783	3.9	262	33.5	338	43.2	169	21.6	<0.001
Bleeding	149	0.7	59	39.6	57	38.3	30	20.1	0.538
Bowel injury	142	0.7	53	37.3	62	43.7	23	16.2	0.515
Ureter/urethral injury	123	0.6	45	36.6	43	35.0	32	26.0	0.021
Bladder injury	46	0.2	14	30.4	22	47.8	8	17.4	0.190
Total	7,604	37.6	2,874	37.8	3,159	41.5	1,452	19.1	<0.001
Postoperative complications	3,953	19.6	1,419	38.9	1,509	41.3	668	18.3	0.195
Surgical complications	855	4.2	341	39.9	334	39.1	159	18.6	0.056
Pulmonary complications	540	2.7	204	37.8	211	39.1	117	21.7	0.409
Cardiac complications	109	0.5	41	37.6	47	43.1	20	18.3	0.994
Thromboembolic complications	982	4.9	353	35.9	390	39.7	220	22.4	0.025
Infectious complications	241	1.2	84	34.9	109	45.2	43	17.8	0.530
Neurological complications									

Table 1b: Patient, tumour and treatment characteristics of rectal cancer patients combined with postoperative complications. Legend: *Mortality is shown as Clavien-Dindo classification grade V; **Clavien-Dindo classification grade \geq III combined with prolonged hospital stay; red values are column percentage values; green values are row percentage values. Abbreviations: ASA, American Society of Anesthesiologists risk score. (continued)

	Total			Normal weight 18.5 – 24.9 kg/m ²			Overweight 25.0 – 29.9 kg/m ²			Obesity > 30.0 kg/m ²			p-value
	N	%		N	%		N	%		N	%		
Postoperative re-interventions													
Total	2,162	10.7		847	39.2		896	41.4		386	17.9		0.252
Anastomotic leakage	723	3.6		283	39.1		325	45.0		109	15.1		0.103
Bleeding	99	0.5		41	41.4		40	40.4		17	17.2		0.990
Clavien-Dindo classification*	1,995	9.9		714	35.8		820	41.1		424	21.3		<0.001
Grade III-IV	386	1.9		180	46.6		127	32.9		66	17.1		<0.001
Grade V	4,423	21.9		1,683	38.1		1,799	40.7		854	19.3		<0.001
Prolonged hospital stay	11.0	\pm 9.7		10.6	\pm 9.6		10.9	\pm 9.6		11.9	\pm 10.3		-
Duration	5,509	27.3		2,087	37.9		2,242	40.7		1,080	19.6		<0.001
Severe complicated course**	1,963	9.7		746	38.0		812	41.4		379	19.3		0.002
Readmission													

Univariate analysis (**Table 2a**) showed a significantly increased risk of postoperative complications in each weight group compared with the NCC group. In particular, an increased risk of postoperative complications was found in class III (BMI ≥ 40.0 kg/m²) OCC patients with an OR of 1.50 (95% confidence interval [CI] 1.26 – 1.78). This relationship remained statistically significant in class III OCC patients (BMI ≥ 40.0 kg/m²) using a multivariate analysis. Factors such as gender, age, tumour location, tumour staging, urgency of operation, preoperative tumour complications, CCI and ASA were entered in the multivariate analysis (**Table 2a**).

OBESSE RECTAL CANCER (ORC) PATIENTS

Of the 20,208 rectal cancer patients, 3322 (16.4%) patients were obese as shown in **Table 1b**. ORC patients were significantly younger (mean 66.7 years; SD \pm 9.8) ($p < 0.001$) and had higher ASA and CCI scores compared with normal-weight rectal cancer (NRC) patients (mean 67.1 years; SD \pm 11.4) (**Table 1b**).

Fig. 1 shows the distribution of comorbidities in the ORC group. ORC patients were associated with more preoperative comorbidities (ORC 81.7% vs NRC 64.7%, $p < 0.001$). Looking at tumour characteristics, the ORC patients were diagnosed with a higher located rectal tumour of >10 cm from the anal verge (ORC 41.5% [1380 of 3322] vs NRC 38.2% [3126 of 8186], $p < 0.001$), and had more preoperative tumour complications: obstruction/ileus ($p < 0.001$) and abscesses ($p < 0.001$). Significant differences in pathological and clinical tumour stage were seen: more cT2 ($p < 0.001$) and cT4 tumours ($p < 0.001$) and (y)pT2 ($p < 0.001$) and (y)pT4 tumours ($p < 0.001$). For surgical characteristics, ORC patients were mostly operated using a laparoscopic approach (ORC 63.4% [2105 of 3322] versus NRC 62.9% [5150 of 8186]). Also, in ORC patients (11.2%) more laparoscopic conversion was needed compared to NRC patients (4.2%). On the other hand, the ORC group less frequently underwent an emergency procedure (ORC 1.0% [34 of 3322]; NRC 1.7% [139 of 8186], $p < 0.001$). Furthermore, more perioperative complications were seen in the ORC group ($p < 0.001$), but for the specific complications bleeding, bowel injury, ureter/urethral and bladder injury, no significant differences were observed, in contrast to the NRC patients.

Of all the ORC patients, 43.7% ($n = 1452$ of 3322) developed a postoperative complication. This was significantly higher in ORC compared with NRC patients (35.1%; $n = 2874$ of 8186). The ORC group developed more postoperative surgical complications ($p = 0.195$), and a significant difference in infectious complications ($p = 0.025$) was seen. Furthermore, no significant difference was observed in postoperative re-interventions performed for anastomotic leakage ($p = 0.103$) and bleeding ($p = 0.988$) in the ORC group, but a significant difference was seen for a severe complicated course ($p < 0.001$).

The increased postoperative complication rate and the higher CD grade in combination with a significantly prolonged hospitalization for the ORC group resulted in more ORC patients with a prolonged hospital stay (ORC 32.5% vs NRC 25.5%).

Univariate analysis (**Table 2b**) showed a significantly increased risk of postoperative complications in each weight group compared with the NRC group. In particular, an increased risk of postoperative complications was found in class II ORC patients with an OR of 1.92 (95% CI 1.60e2.31), remaining significant in the multivariate analysis (standard) (OR 1.96; CI 1.62e2.39).

The same comorbidity-associated factors, as mentioned for the colon cancer patient group, were entered in the multivariate analysis (**Table 2b**).

HOSPITALS PERFORMING AND THOSE NOT PERFORMING BARIATRIC SURGERY

There was a wide variation between hospitals in the number of obese CRC patients treated during the study period. Colon cancer patients were treated in 83 individual hospitals with a range of 49 – 1600 surgical procedures per hospital between 2009 and 2016. This was between 11 and 346 per hospital for OCC patients, with a total of 9016 procedures (**Fig. 2**). All 19 hospitals performing bariatric surgery treated a lower total volume (29.6%) of OCC patients compared with hospitals that do not perform bariatric surgery (2668 vs 6,348, respectively). Besides the number of treated patients, there were no statistically significant differences in preoperative characteristics and postoperative outcomes in OCC patients treated in hospitals offering bariatric surgery and those that do not offer bariatric procedures ($p = 0.754$).

Similar results were seen for rectal cancer patients. The 83 hospitals were jointly responsible for 3322 surgical procedures (range 2 – 132 per hospital) for ORC patients. Fig. 2 shows the distribution in volume and the number of complicated postoperative courses. The 19 hospitals performing bariatric surgery were responsible for 1004 surgical procedures for ORC patients (range 6 – 132 per hospital, 30.2%). No significant difference was seen between treatment in hospitals offering bariatric surgery and hospitals that did not with regard to a complicated postoperative course ($p = 0.149$).

Table 2b: Univariate and multivariate analyses of rectal cancer patients for a complicated postoperative course. *Multivariate analysis was calculated with CCI-score and ASA-score. Abbreviations: N, number; SD, standard deviation; CI, confidence interval; OR, odds ratio; BMI, body mass index; CCI, Charlson Comorbidity Index; ASA, American Society of Anesthesiologists risk score.

	Normal postoperative course		Complicated postoperative course		p-value	Odds ratio	95% CI
	N	%	N	%			
Rectal cancer patients	11,225	55.5	8,983	44.5	-	-	-
Univariate analysis							
BMI (mean, kg/m ² , SD)	26.0 ± 4.1		26.5 ± 4.4		<0.001	-	-
18.5 – 24.9 kg/m ²	4,780	23.7	3,406	16.9	<0.001	REF	REF
25.0 – 29.9 kg/m ²	4,643	23.0	3,734	18.5	0.780	1.13	1.06 – 1.20
30.0 – 34.9 kg/m ²	1,350	6.7	1,334	6.6	<0.001	1.39	1.27 – 1.51
35.0 – 39.9 kg/m ²	206	1.0	282	1.4	<0.001	1.92	1.60 – 2.31
≥ 40 kg/m ²	69	0.3	81	0.4	0.023	1.65	1.19 – 2.45
Comorbidities	7,608	37.6	6,624	32.8	<0.001	1.33	1.26 – 1.42
Cardiac	2,115	10.5	2,217	11.0	<0.001	1.41	1.32 – 1.51
Vascular	3,839	19.0	3,459	17.1	<0.001	1.20	1.14 – 1.28
Diabetes mellitus	1,416	7.0	1,373	6.8	<0.001	1.25	1.15 – 1.35
Pulmonary	1,156	5.7	1,220	6.0	<0.001	1.37	1.26 – 1.49
Gastro-enterological	721	3.6	690	3.4	0.001	1.21	1.09 – 1.35
Urogenital	615	3.0	676	3.3	<0.001	1.40	1.25 – 1.57
Thrombotic	284	1.4	304	1.5	<0.001	1.35	1.15 – 1.59
Musculoskeletal	662	3.3	572	2.8	0.175	1.09	0.97 – 1.22
Endocrine	478	2.4	370	1.8	0.648	0.97	0.84 – 1.11
Infectious	73	0.4	75	0.4	0.148	1.29	0.93 – 1.78
Malignancy	1,332	6.6	1,226	6.1	<0.001	1.17	1.08 – 1.28
Other	817	4.0	772	3.8	0.001	1.20	1.08 – 1.33
Multivariate analysis*							
BMI (mean, kg/m ² , SD)	26.0 ± 4.1		26.5 ± 4.4		<0.001	-	-
18.5 – 24.9 kg/m ²	4,780	23.7	3,406	16.9	<0.001	REF	REF
25.0 – 29.9 kg/m ²	4,643	23.0	3,734	18.5	0.780	1.11	1.04 – 1.18
30.0 – 34.9 kg/m ²	1,350	6.7	1,334	6.6	<0.001	1.39	1.26 – 1.52
35.0 – 39.9 kg/m ²	206	1.0	282	1.4	<0.001	1.96	1.62 – 2.39
≥ 40 kg/m ²	69	0.3	81	0.4	0.023	1.72	1.23 – 2.42

Table 2a: Univariate and multivariate analyses of colon cancer patients for a complicated postoperative course. *Multivariate analysis was calculated with CCI-score and ASA-score. Abbreviations: N, number; SD, standard deviation; CI, confidence interval; OR, odds ratio; BMI, body mass index; CCI, Charlson Comorbidity Index; ASA, American Society of Anesthesiologists risk score.

	Normal postoperative course		Complicated postoperative course		p-value	OR	95% CI
	N	%	N	%			
Colon cancer patients	33,005	64.9	17,871	35.1	-	-	-
Univariate analysis							
BMI (mean, kg/m ² , SD)	26.2 ± 4.4		26.5 ± 4.7		<0.001	-	-
18.5 – 24.9 kg/m ²	13,724	27.0	7,031	13.8	<0.001	REF	REF
25.0 – 29.9 kg/m ²	13,168	25.9	7,044	13.8	0.294	1.04	1.00 – 1.09
30.0 – 34.9 kg/m ²	4,311	8.5	2,570	5.1	<0.001	1.16	1.10 – 1.23
35.0 – 39.9 kg/m ²	964	1.9	639	1.3	<0.001	1.30	1.17 – 1.44
≥ 40 kg/m ²	301	0.6	231	0.5	<0.001	1.50	1.26 – 1.78
Comorbidities	24,487	48.1	14,782	29.1	<0.001	1.66	1.59 – 1.74
Cardiac	8,111	15.9	5,986	11.8	<0.001	1.55	1.49 – 1.61
Vascular	12,769	25.1	7,916	15.6	<0.001	1.26	1.21 – 1.31
Diabetes mellitus	5,055	9.9	3,338	6.6	<0.001	1.27	1.21 – 1.33
Pulmonary	4,013	7.9	3,190	6.3	<0.001	1.57	1.49 – 1.65
Gastro-enterological	3,058	6.0	2,161	4.2	<0.001	1.35	1.27 – 1.43
Urogenital	2,409	4.7	1,788	3.5	<0.001	1.41	1.32 – 1.51
Thrombotic	1,040	2.0	758	1.5	<0.001	1.36	1.24 – 1.50
Musculoskeletal	2,337	4.6	1,473	2.9	<0.001	1.18	1.10 – 1.26
Endocrine	1,966	3.9	1,121	2.2	0.160	1.06	0.98 – 1.14
Infectious	269	0.5	169	0.3	0.141	1.16	0.96 – 1.41
Malignancy	4,249	8.4	3,022	5.9	<0.001	1.38	1.31 – 1.45
Other	2,714	5.3	1,811	3.6	<0.001	1.26	1.18 – 1.34
Multivariate analysis*							
BMI (mean, kg/m ² , SD)	26.2 ± 4.4		26.5 ± 4.7		<0.001	-	-
18.5 – 25.0 kg/m ²	13,724	27.0	7,031	13.8	<0.001	REF	REF
25.0 – 30.0 kg/m ²	13,168	25.9	7,044	13.8	0.294	1.07	1.02 – 1.11
30.0 – 35.0 kg/m ²	4,311	8.5	2,570	5.1	<0.001	1.21	1.14 – 1.28
35.0 – 40.0 kg/m ²	964	1.9	639	1.3	<0.001	1.38	1.24 – 1.54
≥ 40 kg/m ²	301	0.6	231	0.5	<0.001	1.50	1.25 – 1.79

DISCUSSION

This population-based study on the influence of obesity on perioperative and postoperative outcome in patients during and after CRC resection gives a comprehensive overview of the perioperative and short-term postoperative outcomes of colorectal surgery in obese CRC patients.

Independent analyses and a multivariate logistic regression model, including all obesity-related comorbidities, showed a significantly increased risk factor (OR) in developing a complicated postoperative course for obese CRC patients. This study suggests that obesity and the comorbidities associated with obesity are associated with a higher risk of adverse clinical postoperative outcome, prolonged hospitalization and a higher readmission rate.

Obesity is seen as a potential risk factor for postoperative morbidity, but conflicting results are described in the international literature.^{9, 19} A study by Amri et al. showed no significant association between obesity and complications after colon cancer surgery.¹⁰ Our study, however, confirms the results described in the STARSurg Collaborative study and offers additional perioperative and short-term postoperative information of all CRC hospitals in the Netherlands. Including all Dutch academic, teaching and non-teaching hospitals.⁶ These results are supported by the findings of Smith et al. which showed a significant association between obesity and postoperative complications after rectal cancer resection in a population of almost 12,000 rectal cancer patients.⁸ Also, a recent large, international, multicentre, prospective, cohort study, discussing BMI and postoperative complications after gastrointestinal surgery showed an increased risk of major postoperative complications in overweight and obese patients compared with normal-weight patients.²⁰

Furthermore, various scientific articles suggest a so-called “obesity paradox” for pre-obese and mildly obese surgical patients.^{2, 21, 22} However, this clinical finding is still a point of discussion and such a paradox was not found in this large population-based study.^{23, 24}

Obese CRC patients were generally operated using an open approach, but the literature describes laparoscopic CRC surgery as feasible and safe.²⁵ In the Netherlands, obese CRC patients are mostly operated laparoscopically. Findings in the international literature confirm the association of obese CRC patients with more emergency procedures and laparoscopic conversions.²⁶ Also, significantly more postoperative re-interventions were performed for anastomotic leakage in the OCC group, which was described as an

essential determining factor in a recent observational study.²⁷ Several hypotheses are described in the international literature as a reason for the higher anastomotic leakage rate in the OCC group, e.g. impaired anastomotic microcirculation due to increased abdominal pressure.

As obesity is on the increase, evaluation of care processes in best performing hospitals is of great interest.²⁸ Although, in our study, the experience in the treatment of obese patients, reflected by hospitals offering bariatric surgery, did not result in better postoperative outcomes. Moreover, because participation in the DCRA is mandatory for Dutch hospitals, it was possible to explore hypotheses regarding the underlying mechanisms explaining the observed variation in outcome of obese patients between hospitals. For example, hospitals performing bariatric surgery could have had more experience in the (surgical) treatment of, as well as perioperative care for, obese patients. Although, the analyses did not show different results for CRC surgery between hospitals performing and hospitals not performing bariatric surgery. More in-depth studies are needed to reveal differences in the care processes that lead to better or worse outcomes for obese patients undergoing CRC resection.

The strength of this study was the advantage of population-based data, which reflect daily general practice in the Netherlands. However, some limitations of this population-based study need to be addressed. The combination of the primary inclusion criteria and missing data caused exclusion of 5016 (9.0%) colon cancer and 1387 (6.4%) rectal cancer patients. External third-party data verification showed that weight and height are not typically missing data in patients with an unfavourable postoperative outcome.⁶ Therefore, it can be assumed that the missing data occurred randomly.

Furthermore, the DCRA only provides short-term postoperative surgical and oncological outcomes (<30 days). The content of the DCRA is not only based on mandatory indicators, but also on a dynamic process led by a multidisciplinary team, including colorectal surgeons, oncologists and pathologists, which can lead to new registration of topics based on the team's increasing insights. Information on, e.g. ERAS (enhanced recovery after surgery) and fast-track protocols is currently not registered in the DCRA, but may be added over time. The quality of reported data in the DCRA was influenced over time due to better registration and training of the registrars.⁶ In addition, the start of the national colorectal screening programme in 2014, could have influenced the study results.

The effect of disease-related weight loss was difficult to evaluate. Weight and height of the patient were registered on the day of admission, which was no more than two

working days before the colorectal resection. However, significant weight loss before the primary colorectal resection could be expected due to the disease itself, which is known to be associated with worsened postoperative outcomes.²⁹

We also took bariatric surgery as a proxy for experience in the surgical treatment of obese patients. The development of more specialized hospitals for optimized care, already showed improvement in several quality outcomes, due to increased operative volumes and more specialized care.³⁰⁻³² Surgeons experienced in both bariatric surgery and colorectal surgery might have a better postoperative outcome for (severely) obese patients.³³ It could, therefore, be expected that hospitals performing bariatric surgery could have better results for this specific patient category. However, this study did not find a relationship between experience in the field of bariatric surgery and a favourable postoperative outcome. The assumption in this article, that colorectal surgeons in hospitals offering bariatric surgery by definition have a better experience with obese patients was not sufficient.

CONCLUSIONS

Using real-life data reflecting daily practice in the Netherlands, we identified obesity as an important risk factor in the care process of CRC patients. Obesity-related comorbidities were associated with higher postoperative morbidity, prolonged hospitalization and a higher readmission rate in obese CRC patients. No differences were observed between hospitals performing bariatric surgery and hospitals that did not.

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