



# Nationwide population-based cohort study to assess risk of surgery for adhesive small bowel obstruction following open or laparoscopic rectal cancer resection

P. Andersen<sup>1,3</sup> , K. K. Jensen<sup>4</sup>, R. Erichsen<sup>1,2</sup>, T. Frøslev<sup>2</sup>, P.-M. Krarup<sup>4</sup> , M. R. Madsen<sup>3</sup>, S. Laurberg<sup>1</sup> and L. H. Iversen<sup>1</sup>

<sup>1</sup>Section of Coloproctology, Department of Surgery, and <sup>2</sup>Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, <sup>3</sup>Department of Surgery, Herning Regional Hospital, Herning and <sup>4</sup>Digestive Disease Centre, Bispebjerg Hospital, University of Copenhagen, Copenhagen, Denmark  
Correspondence to: Mr P. Andersen, Section of Coloproctology, Department of Surgery, Aarhus University Hospital, Tage-Hansens Gade 2, DK-8000 Aarhus C, Denmark (e-mail: peterand82@hotmail.com)

**Background:** Laparoscopic surgery has been reported to reduce the formation of adhesions following colorectal surgery. The aim of this nationwide cohort study was to investigate the risk of surgery for adhesive small bowel obstruction (SBO) following open and laparoscopic rectal cancer resection.

**Methods:** Patients undergoing rectal cancer resection between 2005 and 2013 were identified in the Danish Colorectal Cancer Group database. The primary outcome of surgery for adhesive SBO was identified in the Danish National Patient Registry. The risk of surgery for adhesive SBO was estimated as the cumulative incidence proportion, treating death as a competing risk. Cox proportional hazards regression analysis with multivariable adjustment was used to compute hazard ratios (HRs). The secondary outcome was 30-day mortality after surgery for adhesive SBO.

**Results:** Of 7657 patients, 340 (4.4 per cent) underwent surgery for adhesive SBO. The 5-year risk of surgery for adhesive SBO was 4.5 per cent among 4472 patients undergoing open resection and 3.0 per cent among 3185 patients having a laparoscopic resection. Laparoscopic rectal resection was associated with a lower risk of subsequent operation for adhesive SBO (adjusted HR 0.65, 95 per cent c.i. 0.50 to 0.86;  $P=0.002$ ). The adjusted HR of mortality after adhesive SBO was 0.84 (0.37 to 1.91;  $P=0.671$ ) comparing patients with previous laparoscopic and open resection.

**Conclusion:** Laparoscopic rectal cancer resection was associated with a decreased risk of surgery for adhesive SBO. There was a substantial difference in 30-day mortality after surgery for adhesive SBO based on the surgical approach used at the time of rectal resection.

## Funding information

Program for Clinical Research Infrastructure (PROCRIN)

Paper accepted 12 May 2017

Published online 24 July 2017 in Wiley Online Library (www.bjsopen.com). DOI: 10.1002/bjs5.5

## Introduction

Mechanical small bowel obstruction (SBO) occurs in approximately 9 per cent of patients undergoing abdominal surgery, and adhesive SBO accounts for just over half of these events<sup>1</sup>. Adhesions develop after abdominal surgery as a result of peritoneal trauma and subsequent inflammation<sup>2</sup>. Among patients undergoing abdominal surgery, those with a rectal resection have the highest adhesion-related readmission rates<sup>1,3,4</sup>, and adhesiolysis-related procedures are associated with high inpatient expenditure<sup>5</sup>.

Worldwide, the surgical approach in rectal cancer treatment has changed towards increasing use of laparoscopy. The established benefits of laparoscopic resection, as opposed to open rectal cancer resection, include better short-term postsurgical outcomes in terms of duration of hospital stay, shorter time to first defaecation and fewer wound infections, whereas long-term disease-free and overall survival rates are similar<sup>6</sup>.

Much of the literature related to surgery for adhesive SBO is based on colorectal surgery for various indications, with conflicting results. Some studies<sup>4,7–10</sup> have suggested an advantage for laparoscopic surgery, whereas others<sup>11–14</sup>

have found no difference in the risk of adhesive SBO after open or laparoscopic surgery. Only two studies<sup>4,15</sup> have compared the risk of surgery for adhesive SBO following laparoscopic or open rectal surgery. Both suggested an advantage for laparoscopic surgery.

The present study aimed to investigate the risk of surgery for adhesive SBO following open and laparoscopic approaches for rectal cancer resection in a nationwide, population-based design with long-term follow-up.

## Methods

A population-based nationwide cohort study was conducted in the setting of the entire Danish population (5.7 million people) in the period 2005–2013. Data were linked between registries by the Central Personal Registry number, a unique identifying number assigned to all Danish citizens and residents since 1968<sup>16</sup>, allowing for unambiguous data linkage and ensuring complete follow-up of patients.

The study was approved by the Danish Data Protection Agency (record number 2014-41-3456) and is reported according to the STROBE guidelines<sup>17</sup>.

## Data sources

The Danish Colorectal Cancer Group (DCCG) database is nationwide and records information (diagnostics, treatment, postoperative complications within 30 days, and pathology) on all patients with a first-time diagnosis of colorectal adenocarcinoma using a prospectively developed database<sup>18</sup>. DCCG has a patient completeness rate of more than 99 per cent<sup>19</sup> and registration began in May 2001. DCCG links to the Danish Civil Registration System<sup>20</sup>, which tracks vital status and residence information, and was updated on 17 October 2015 at initiation of the study.

The Danish National Patient Registry (NPR) was established in 1977 and contains data on all hospital admissions and discharges, diagnoses and procedures<sup>21</sup>. Diagnoses are coded by treating physicians at the time of discharge using ICD-10 (1994 to present). Surgical procedures are recorded according to the Danish Classification of Surgical Procedures from 1977 to 1995, and according to the Nordic Medico-Statistical Committee Classification of Surgical Procedures (NOMESCO) since 1996.

## Cohort

The cohort was defined as patients undergoing intended curative resection (rectal resection, rectal resection including a colostomy, extralevator abdominoperineal excision (ELAPE) and abdominoperineal excision (APE))

for rectal adenocarcinoma (located within 15 cm of the anal verge), as recorded in the DCCG database from 1 January 2005 to 31 December 2013. Patients were included at the date of first rectal cancer resection and categorized according to surgical approach as open or laparoscopic. If laparoscopic surgery was converted to open surgery, the surgical approach was categorized as open. In 2004, only 2 per cent of patients underwent laparoscopic rectal resection<sup>22</sup>, but thereafter laparoscopic surgery was gradually implemented nationwide<sup>19</sup>. Therefore the study was initiated from 1 January 2005, when the laparoscopic rate for rectal cancer resection was 6.2 per cent. During the study period, allocation to open or laparoscopic rectal cancer resection was dependent on surgeon and/or departmental preference.

## Outcomes

The primary outcome was the patient's first-time surgery for adhesive SBO. Only operations for adhesive SBO performed more than 30 days after rectal cancer resection were included to avoid any surgery related to early post-operative bowel obstruction<sup>23</sup>. For the primary outcome, duration of hospital stay, time from admission to adhesive SBO surgery, and time from adhesive SBO surgery to discharge according to surgical approach at rectal cancer resection were evaluated. For evaluation of potential bias from misclassification of the study outcome (*Table S1*, supporting information), surgery for adhesive SBO was identified in the NPR by three different algorithms: using surgery codes for division of adhesions causing bowel obstruction and lysis of adhesions (main algorithm), as reported previously in a study regarding surgery for adhesive SBO following colonic cancer resection<sup>24</sup>; a more sensitive algorithm in which the main algorithm was supplemented with surgery codes for small bowel resection, anastomosis without bowel resection, and small bowel stomas together with diagnosis codes for SBO; and a more specific algorithm in which the main algorithm was supplemented with diagnosis codes for SBO (*Table S2*, supporting information).

Validation of the outcome algorithms was performed by medical record review approved by the Danish Health Authority (record number 3-3013-1255/1) (Appendix S1) and reasons for SBO surgery other than adhesions were also identified (*Table S3*, supporting information). The positive predictive value (PPV) of adhesive SBO for each of the three algorithms is also shown in *Table S3* (supporting information).

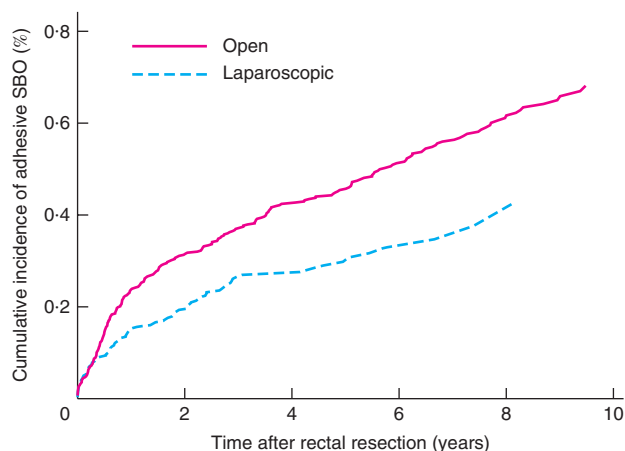
The secondary outcome was 30-day mortality following surgery for adhesive SBO according to surgical approach at the time of rectal cancer resection.

**Table 1** Characteristics of patients undergoing surgery for rectal cancer in Denmark, 2005–2013

	Open resection (n = 4472)	Laparoscopic resection (n = 3185)	P‡
Age (years)			0.197
≤ 64	1709 (38.2)	1178 (37.0)	
65–75	1628 (36.4)	1141 (35.8)	
> 75	1135 (25.4)	866 (27.2)	
Sex ratio (M : F)	2789 : 1683	1909 : 1276	0.031
CCI score			0.104
0 (none)	3458 (77.3)	2407 (75.6)	
1 (mild)	522 (11.7)	381 (12.0)	
2 (moderate)	336 (7.5)	254 (8.0)	
≥ 3 (severe)	156 (3.5)	143 (4.5)	
Smoking status			< 0.001
Active smoker	820 (18.3)	600 (18.8)	
Former smoker	1611 (36.0)	1142 (35.9)	
Non-smoker	1226 (27.4)	978 (30.7)	
Missing	815 (18.2)	465 (14.6)	
BMI (kg/m <sup>2</sup> )			< 0.001
< 25	1620 (36.2)	1444 (45.3)	
25–30	1415 (31.6)	1026 (32.2)	
> 30	608 (13.6)	369 (11.6)	
Missing	829 (18.5)	346 (10.9)	
Previous abdominal surgery			0.098
No	3249 (72.7)	2368 (74.3)	
Yes	1223 (27.3)	817 (25.7)	
Procedure			< 0.001
Rectal resection	2520 (56.4)	1959 (61.5)	
Rectal resection + colostomy	715 (16.0)	400 (12.6)	
ELAPE*	253 (5.7)	369 (11.6)	
APE†	984 (22.0)	457 (14.3)	
Stoma at rectal resection			< 0.001
No	1040 (23.3)	894 (28.1)	
Yes	3432 (76.7)	2291 (71.9)	
Blood loss (ml)			< 0.001
≤ 150	723 (16.2)	2177 (68.4)	
151–300	1125 (25.2)	531 (16.7)	
> 300	2509 (56.1)	371 (11.6)	
Missing	115 (2.6)	106 (3.3)	
Fascial dehiscence			< 0.001
No	4324 (96.7)	3148 (98.8)	
Yes	148 (3.3)	37 (1.2)	
Wound infection			< 0.001
No	4154 (92.9)	3056 (95.9)	
Yes	318 (7.1)	129 (4.1)	
Anastomosis*			< 0.001
Yes			
No leakage	2238 (50.0)	1691 (53.1)	
Leakage	282 (6.3)	268 (8.4)	
No anastomosis	1952 (43.6)	1226 (38.5)	
(y)pT status			< 0.001
0–3	3904 (87.3)	2947 (92.5)	
4	471 (10.5)	186 (5.8)	
Missing	97 (2.2)	52 (1.6)	
Year of surgery			< 0.001
2005–2007	2136 (47.8)	310 (9.7)	
2008–2010	1492 (33.4)	1019 (32.0)	
2011–2013†	844 (18.9)	1856 (58.3)	

Only patients alive 30 days after surgery were included in the study. Values in parentheses are percentages. CCI, Charlson co-morbidity index; (EL)APE, (extralevator) abdominoperineal excision. \*Indicates anastomotic leak among the entire cohort of patients, including those without an anastomosis.

†Patients diagnosed with rectal cancer in 2011–2013; however, 114 patients underwent subsequent rectal cancer resection in 2014. ‡ $\chi^2$  test.



**Fig. 1** Crude cumulative incidence of surgery for adhesive small bowel obstruction (SBO) after open or laparoscopic rectal resection

### Co-variables

Co-variables were selected from the DCCG database and included age, sex, smoking status, BMI, surgical procedure, stoma formation at rectal resection, intra-operative blood loss, fascial dehiscence, postoperative wound infection, anastomotic leak, (y)pT status and year of surgery. Co-morbidity was assessed using the Charlson co-morbidity index (CCI)<sup>25</sup> and categorized as none (score 0), mild (score 1), moderate (score 2) or severe (score 3 or more).

Information on previous abdominal surgery (from 1977), including gynaecological, urological and vascular surgery, was collected from the NPR using surgery codes.

### Statistical analysis

Continuous data were transformed into categorical variables and presented as absolute numbers and percentages. Differences in characteristics among patients undergoing laparoscopic or open rectal cancer resection were compared by means of the  $\chi^2$  test.

Patients were followed from 30 days after the date of open or laparoscopic rectal cancer resection until surgery for adhesive SBO, death, emigration or end of follow-up (17 October 2015), whichever came first. The absolute risk of surgery for adhesive SBO was estimated as the cumulative incidence proportion at 1, 3 and 5 years, treating death as a competing risk<sup>26</sup>. Cox proportional hazards regression analysis was used to calculate hazard ratios (HRs), comparing laparoscopic and open approaches. HRs were adjusted for the co-variables listed in *Table 1*, except blood loss, fascial dehiscence, wound infection and anastomotic leak, which may be considered intermediate steps on the

causal pathway between surgical approach and operation for adhesive SBO. Analyses were also made adjusting for all co-variables shown in *Table 1*.

To evaluate subgroup differences in risk of surgery for adhesive SBO, stratification by all available co-variables listed in *Table 1* was performed. As sensitivity analyses, HRs and adjusted HRs were calculated for the two alternative algorithms for adhesive SBO using similar methodology.

Because 21.2 per cent of patients had missing data for one or more of the characteristics (*Table 1*), multiple imputation was used to impute missing values, assuming data were missing at random<sup>27</sup> (*Table S4*, supporting information), and 20 data sets were imputed. Apart from the co-variables listed in *Table 1*, surgery for adhesive SBO and the Nelson–Aalen cumulative baseline hazard were included in the multiple imputation model. The imputed values were used in all regression analyses. To evaluate the robustness of the findings, complete case analyses were also made.

According to surgical approach, duration of hospital stay, time from admission to surgery, and time from surgery to discharge after surgery for adhesive SBO were compared using Student's *t* test.

In the analysis of the impact of surgical approach at rectal cancer resection on 30-day mortality after surgery for adhesive SBO, patients were followed from date of adhesive SBO surgery until death, immigration or end of follow-up (17 October 2015), whichever occurred first. Thirty-day mortality was estimated using the Kaplan–Meier method, and mortality was compared between patients who initially underwent laparoscopic *versus* open rectal cancer resection using Cox proportional hazards regression analysis, adjusting for age, CCI, smoking status and (y)pT status. Statistical analyses were performed using STATA/IC™ version 14.0 (StataCorp, College Station, Texas, USA).  $P < 0.050$  was considered significant.

### Results

A total of 7845 patients underwent rectal cancer resection between 2005 and 2013. Of these, 188 died within the 30-day postoperative period after resection, leaving 7657 patients for the analysis. The patient characteristics listed in *Table 1* show data before multiple imputation. Open resection was performed in 4472 patients (58.4 per cent) and laparoscopic resection in 3185 (41.6 per cent). Patients undergoing open or laparoscopic resection were comparable according to age, CCI score and previous abdominal surgery. Patients who had a laparoscopic resection were more often women, non-smokers, with a lower BMI, and were more likely to have undergone rectal resection or

**Table 2** Crude and adjusted hazard ratios for surgery for adhesive small bowel obstruction after rectal cancer resection

	Crude HR	P	Adjusted HR	P
Age (years)				
≤ 64	1.00 (reference)		1.00 (reference)	
65–75	1.02 (0.81, 1.29)	0.869	1.06 (0.84, 1.35)	0.618
> 75	0.75 (0.56, 1.01)	0.055	0.71 (0.52, 0.98)	0.036
Sex				
M	1.00 (reference)		1.00 (reference)	
F	1.04 (0.84, 1.29)	0.712	1.04 (0.83, 1.31)	0.721
CCI score				
0 (none)	1.00 (reference)		1.00 (reference)	
1 (mild)	0.97 (0.69, 1.38)	0.882	0.99 (0.70, 1.41)	0.963
2 (moderate)	0.95 (0.69, 1.38)	0.828	0.91 (0.59, 1.42)	0.689
≥ 3 (severe)	1.13 (0.63, 2.01)	0.683	1.04 (0.58, 1.87)	0.903
Smoking status				
Active smoker	1.00 (reference)		1.00 (reference)	
Former smoker	0.50 (0.39, 0.66)	< 0.001	0.57 (0.43, 0.75)	< 0.001
Non-smoker	0.45 (0.34, 0.60)	< 0.001	0.51 (0.38, 0.68)	< 0.001
BMI (kg/m <sup>2</sup> )				
< 25	1.00 (reference)		1.00 (reference)	
25–30	0.65 (0.50, 0.84)	0.001	0.66 (0.51, 0.86)	0.002
> 30	0.59 (0.41, 0.84)	0.004	0.57 (0.40, 0.83)	0.003
Previous abdominal surgery				
No	1.00 (reference)		1.00 (reference)	
Yes	1.25 (0.99, 1.58)	0.055	1.22 (0.95, 1.55)	0.113
Surgical approach				
Open	1.00 (reference)		1.00 (reference)	
Laparoscopic	0.62 (0.49, 0.79)	< 0.001	0.65 (0.50, 0.86)	0.002
Procedure				
Rectal resection	1.00 (reference)		1.00 (reference)	
Rectal resection + colostomy	1.71 (1.27, 2.29)	< 0.001	1.58 (1.13, 2.21)	0.007
ELAPE	1.22 (0.78, 1.91)	0.376	1.09 (0.68, 1.76)	0.710
APE	1.59 (1.23, 2.06)	< 0.001	1.32 (1.00, 1.78)	0.054
Stoma at rectal resection				
No	1.00 (reference)		1.00 (reference)	
Yes	1.77 (1.34, 2.33)	< 0.001	1.43 (1.04, 1.97)	0.027
(y)pT status				
0–3	1.00 (reference)		1.00 (reference)	
4	1.22 (0.84, 1.79)	0.299	1.00 (0.68, 1.47)	1.00
Year of surgery				
2005–2007	1.00 (reference)		1.00 (reference)	
2008–2010	0.80 (0.62, 1.03)	0.085	0.88 (0.68, 1.15)	0.351
2011–2013	0.76 (0.57, 1.01)	0.056	0.95 (0.68, 1.33)	0.771

Values in parentheses are 95 per cent confidence intervals. Hazard ratios (HRs) were mutually adjusted for all co-variables shown in the table. CCI, Charlson co-morbidity index; (EL)APE, (extralevator) abdominoperineal excision.

ELAPE. Intraoperative blood loss, stoma at rectal cancer resection, fascial dehiscence, wound infection, anastomotic leak and more advanced tumour stage were more common in open than in laparoscopic resection. Throughout the study period an increasing proportion of patients were operated on laparoscopically.

Some 340 of 7657 patients (4.4 per cent) had surgery for adhesive SBO following rectal cancer resection. Median follow-up was 5.0 (i.q.r. 2.6–7.6) years for patients undergoing open resection and 3.5 (2.3–5.2) years for those having laparoscopic resection. Median time from 30 days after rectal cancer resection to surgery for adhesive SBO was 1.5

(0.5–4.0) and 0.9 (0.2–2.3) years for open and laparoscopic resection respectively.

The 1-, 3- and 5-year risk of adhesive SBO surgery in patients undergoing open resection was 2.4 (95 per cent c.i. 2.0 to 2.8), 3.7 (3.2 to 4.3) and 4.5 (3.9 to 5.2) per cent respectively, compared with 1.5 (1.1 to 2.0), 2.7 (2.1 to 3.3) and 3.0 (2.4 to 3.7) per cent in those having a laparoscopic resection (*Fig. 1*).

The crude HR for adhesive SBO surgery, comparing patients undergoing laparoscopic and open rectal resection, was 0.62 (95 per cent c.i. 0.49 to 0.79;  $P < 0.001$ ) (*Table 2*). After adjustment for co-variables, the HR was 0.65 (95 per

cent c.i. 0.50 to 0.86;  $P = 0.002$ ). When adjustment was also made for blood loss, fascial dehiscence, wound infection and anastomotic leak, the results were similar (adjusted HR 0.65, 0.48 to 0.88;  $P = 0.006$ ).

Table 2 also shows HRs of surgery for adhesive SBO for the co-variables included in the analyses. Age above 75 years, non and former smoker, and increasing BMI were factors associated with lower risk of surgery for adhesive SBO. Conversely, rectal cancer resection with a colostomy, APE and stoma at rectal cancer resection were all factors associated with increased risk of surgery for adhesive SBO. Complete case analysis yielded results similar to those presented in Table 2 (data not shown).

In subgroup analysis, surgical approach seemed to have no impact in patients who smoked (Table 3). It appeared that surgical approach primarily had an impact on risk of surgery for adhesive SBO in patients without wound infection, fascial dehiscence or anastomotic leak. Otherwise, no substantial difference in risk of surgery for adhesive SBO was found among subgroups of patients.

Sensitivity analyses using the two additional algorithms for identifying adhesive SBO yielded results that were not substantially different from those of the main algorithm (Table S1, supporting information).

For adhesive SBO surgery, the median length of hospital stay was 5 days shorter among patients previously operated on laparoscopically for rectal cancer than in those who had open operations, and the time from adhesive SBO surgery to discharge was 3 days shorter. The time from hospital admission to day of surgery for adhesive SBO did not differ significantly according to surgical approach (Table 4).

Use of a laparoscopic approach in surgery for adhesive SBO among patients with a previous open rectal cancer resection was 4.0 per cent (10 of 249), compared with 11 per cent (10 of 91) in patients who had previously undergone a laparoscopic resection.

### Mortality analysis of patients undergoing surgery for adhesive small bowel obstruction

Of the 340 patients with rectal cancer who subsequently had surgery for adhesive SBO, 32 (9.4 (95 per cent c.i. 6.8 to 13.1) per cent) died within 30 days. The 30-day mortality rate in patients who had surgery for adhesive SBO following previous open resection was 9.7 (6.6 to 14.1) per cent *versus* 8.9 (4.5 to 17.0) per cent in patients in those who initially had a laparoscopic resection. The adjusted HR for death after adhesive SBO was 0.84 (0.37 to 1.91;  $P = 0.671$ ), comparing patients having previous laparoscopic or open resection for rectal cancer.

**Table 3** Subgroup analysis of risk of surgery for adhesive small bowel obstruction according to surgical approach at rectal cancer resection

	Adjusted hazard ratio		P
	Open	Laparoscopic	
Age (years)			
≤ 64	1.00 (reference)	0.71 (0.47, 1.09)	0.117
65–75	1.00 (reference)	0.65 (0.42, 1.02)	0.062
> 75	1.00 (reference)	0.56 (0.31, 1.03)	0.064
Sex			
F	1.00 (reference)	0.59 (0.39, 0.90)	0.014
M	1.00 (reference)	0.72 (0.50, 1.02)	0.067
CCI score			
0 (none)	1.00 (reference)	0.64 (0.47, 0.86)	0.004
1 (mild)	1.00 (reference)	0.74 (0.33, 1.69)	0.479
2 (moderate)	1.00 (reference)	0.75 (0.25, 2.23)	0.604
≥ 3 (severe)	1.00 (reference)	0.34 (0.08, 1.48)	0.153
Smoking status			
Active smoker	1.00 (reference)	0.91 (0.58, 1.43)	0.681
Former smoker	1.00 (reference)	0.53 (0.31, 0.89)	0.017
Non-smoker	1.00 (reference)	0.56 (0.30, 1.03)	0.063
BMI (mg/kg <sup>2</sup> )			
< 25	1.00 (reference)	0.54 (0.38, 0.79)	0.001
25–30	1.00 (reference)	0.86 (0.51, 1.45)	0.580
> 30	1.00 (reference)	0.81 (0.31, 2.09)	0.665
Previous abdominal surgery			
No	1.00 (reference)	0.78 (0.56, 1.06)	0.118
Yes	1.00 (reference)	0.40 (0.23, 0.70)	0.001
Procedure			
Rectal resection	1.00 (reference)	0.50 (0.34, 0.74)	0.001
Rectal resection + colostomy	1.00 (reference)	0.53 (0.27, 1.06)	0.072
ELAPE	1.00 (reference)	1.92 (0.64, 5.71)	0.244
APE	1.00 (reference)	0.92 (0.54, 1.57)	0.748
Stoma at rectal resection			
No	1.00 (reference)	0.38 (0.19, 0.74)	0.005
Yes	1.00 (reference)	0.74 (0.55, 1.00)	0.050
(y)pT status			
0–3	1.00 (reference)	0.67 (0.51, 0.89)	0.006
4	1.00 (reference)	0.35 (0.11, 1.10)	0.073
Year of surgery			
2005–2007	1.00 (reference)	0.83 (0.49, 1.40)	0.485
2008–2010	1.00 (reference)	0.59 (0.38, 0.91)	0.016
2011–2013	1.00 (reference)	0.67 (0.42, 1.06)	0.090
Blood loss (ml)			
≤ 150	1.00 (reference)	0.65 (0.41, 1.02)	0.061
151–300	1.00 (reference)	0.71 (0.39, 1.30)	0.263
> 300	1.00 (reference)	0.70 (0.38, 1.29)	0.251
Fascial dehiscence			
No	1.00 (reference)	0.67 (0.51, 0.88)	0.004
Yes	1.00 (reference)	1.30 (0.07, 25.21)	0.863
Wound infection			
No	1.00 (reference)	0.61 (0.46, 0.82)	0.001
Yes	1.00 (reference)	1.68 (0.66, 4.27)	0.272
Anastomotic leak			
No	1.00 (reference)	0.40 (0.25, 0.63)	< 0.001
Yes	1.00 (reference)	1.05 (0.47, 2.34)	0.897
No anastomosis	1.00 (reference)	0.86 (0.59, 1.26)	0.453

Values in parentheses are 95 per cent confidence intervals. Hazard ratios were adjusted for sex, age, Charlson co-morbidity index (CCI), smoking status, BMI, previous abdominal surgery, procedure, stoma at rectal resection, (y)pT status and year of surgery. (EL)APE, (extralevator) abdominoperineal excision.

**Table 4** Comparison of duration of hospital stay for surgery for adhesive small bowel obstruction following open and laparoscopic rectal cancer resection

	Open rectal resection (n = 4472)	Laparoscopic rectal resection (n = 3185)	P†
Surgery for adhesive SBO	249 (5.6)	91 (2.9)	
Duration of hospital stay (days)*	16.0 (9.0–31.0)	11.0 (7.0–26.0)	0.037
Time from admission to surgery (days)*	3.0 (1.0–7.0)	2.0 (1.0–5.0)	0.456
Duration of postoperative stay (days)*	11.0 (6.0–21.0)	8.0 (5.0–19.0)	0.073

Values in parentheses are percentages unless indicated otherwise; \*values are median (i.q.r.). SBO, small bowel obstruction. †Student's *t* test.

## Discussion

Patients undergoing laparoscopic resection for rectal cancer had a 5-year risk of needing surgery for adhesive SBO of 3.0 per cent, compared with 4.5 per cent in those who had an open rectal resection. After adjustment for potential confounders, the relative risk of adhesive SBO surgery was 35 per cent lower following laparoscopic compared with open rectal cancer resection. The median length of hospital stay after surgery for adhesive SBO following laparoscopic rectal resection was also shorter than that for open resection. Although the crude 30-day mortality rate after adhesive SBO surgery was lower for patients who had previously undergone laparoscopic rectal cancer surgery (8.9 per cent *versus* 9.7 per cent for open resection), the adjusted estimates were too imprecise to draw any firm conclusions.

The findings of this study are similar to those in other reports<sup>4,15</sup>. One<sup>15</sup> of these studies reported that after 10 years the need for further operation for adhesive SBO was 7 per cent (5 of 74 patients) following open rectal resection *versus* 0 per cent (0 of 74) after laparoscopic surgery. The other report<sup>4</sup> examined the risk of surgery for SBO including adhesive SBO following rectal resection in a Swedish population-based study. Among 3523 patients undergoing anterior resection, the 5-year risk of SBO or adhesive SBO after open anterior resection was 2.8 per cent, compared with 1.6 per cent after laparoscopic surgery. In multivariable analysis comparing open with laparoscopic surgery, a non-significant odds ratio of 1.8 was found. Notably, only 2 per cent of the anterior resections in that study were performed laparoscopically.

Other large population-based studies<sup>7,8,10</sup> have assessed the risk of surgery for SBO, including adhesive SBO, after colorectal surgery for various indications, and have again drawn similar conclusions of a reduced risk following an initial laparoscopic approach. A recent Danish study<sup>24</sup> using methodology similar to that in the present study found a 3-year risk of surgery for adhesive SBO of 1.2 per cent among patients undergoing laparoscopic surgery for colonic cancer compared with 1.5 per cent following open surgery. The findings of the present study suggest that rectal cancer resection leads to more episodes of subsequent

surgery for adhesive SBO than colonic cancer surgery. None of these previous studies examined the outcome of surgery for SBO or adhesive SBO to evaluate the effect of potential misclassification bias, nor did they consider duration of hospital stay or 30-day mortality following surgery for adhesive SBO.

Not all studies are in agreement with the present finding, however. At least four other smaller, non-population-based studies<sup>11–14</sup> found no difference in risk of surgery for SBO or adhesive SBO according to surgical approach in colorectal surgery, although one study<sup>12</sup> evaluated only colonic resections.

Based on the stratified analyses, the present study suggests that surgical approach had an impact primarily among patients with no wound infection, fascial dehiscence or anastomotic leak, suggesting that in those with these postoperative complications the effect of the peritoneal inflammation related to the complications is more likely to influence adhesion development than the surgical approach. In addition, postoperative complications may lead to subsequent surgery, which may further increase the risk of adhesion development.

The median time from rectal cancer resection to surgery for adhesive SBO was shorter in patients operated on laparoscopically. This might suggest that surgeon's threshold for adhesive SBO surgery is lower in patients who previously had laparoscopic surgery owing to fewer and less severe adhesions<sup>28</sup>. The finding of shorter stays after surgery for adhesive SBO in patients who had previously undergone a laparoscopic resection is also interesting, with shorter hospital stay possibly reflecting fewer, less severe, adhesions<sup>29</sup>.

Multivariable analysis revealed a number of co-variables associated with surgery for adhesive SBO, including age 75 years or less, smoking, low BMI, rectal resection with a colostomy, APE and any stoma at rectal resection. Younger age has been associated with surgery for adhesive SBO in other studies<sup>7,10</sup>, possibly explained by an increased tendency towards conservative management of the adhesions in older patients.

Smoking has previously been shown to be a significant risk factor for postoperative adhesions and intestinal

obstruction<sup>30</sup>, and postsurgical peritoneal adhesion formation is increased in mice given nicotine in the perioperative period<sup>31</sup>.

The main strengths of this study include a nationwide population, the size of the cohort, virtually complete registration to the DCCG database, high data accuracy and long-term follow-up<sup>18</sup>. As only patients with intended curative rectal cancer resection were included in the study in order to create a homogeneous study cohort, it seems unlikely that a significant number of patients would have developed adhesive SBO as a result of recurrent intra-peritoneal disease.

This study has limitations. Only surgery for adhesive SBO was evaluated, and it could be speculated that conservatively managed adhesions might be more common following laparoscopic than open rectal resection, owing to fewer and less severe adhesions<sup>29</sup>. No information on the use of neoadjuvant therapies in relation to rectal cancer treatment was available, although these treatments might affect the risk of adhesive SBO. The specific interaction between neoadjuvant therapies and surgical approach to rectal cancer, in terms of the subsequent development of adhesive SBO, is worthy of further examination. In the present study, laparoscopic operations that were converted to an open approach were categorized as open surgery. This may have introduced additional bias, as some of the factors responsible for conversion might also have contributed to adhesion formation, subsequently increasing the risk of later surgery for adhesive SBO.

Despite these limitations, laparoscopic rectal cancer resection was associated with a decreased risk of subsequent surgery for adhesive SBO compared with open resection. This reduction in a material risk should be disclosed to patients with rectal cancer when helping them make a decision about surgery.

## Acknowledgements

The study was supported by the Program for Clinical Research Infrastructure (PROCRIN) established by the Lundbeck Foundation and the Novo Nordisk Foundation. *Disclosure*: The authors declare no conflict of interest.

## References

- ten Broek RP, Issa Y, van Santbrink EJ, Bouvy ND, Kruitwagen RF, Jeekel J *et al.* Burden of adhesions in abdominal and pelvic surgery: systematic review and meta-analysis. *BMJ* 2013; **347**: f5588.
- Hellebrekers BW, Kooistra T. Pathogenesis of postoperative adhesion formation. *Br J Surg* 2011; **98**: 1503–1516.
- Parker MC, Wilson MS, Menzies D, Sunderland G, Clark DN, Knight AD *et al.*; Surgical and Clinical Adhesions Research (SCAR) Group. The SCAR-3 study: 5-year adhesion-related readmission risk following lower abdominal surgical procedures. *Colorectal Dis* 2005; **7**: 551–558.
- Angenete E, Jacobsson A, Gellerstedt M, Haglund E. Effect of laparoscopy on the risk of small-bowel obstruction: a population-based register study. *Arch Surg* 2012; **147**: 359–365.
- Sikirica V, Bapat B, Candrilli SD, Davis KL, Wilson M, Johns A. The inpatient burden of abdominal and gynecological adhesiolysis in the US. *BMC Surg* 2011; **11**: 13.
- Vennix S, Pelzers L, Bouvy N, Beets GL, Pierie JP, Wiggers T *et al.* Laparoscopic versus open total mesorectal excision for rectal cancer. *Cochrane Database Syst Rev* 2014; (4)CD005200.
- Burns EM, Currie A, Bottle A, Aylin P, Darzi A, Faiz O. Minimal-access colorectal surgery is associated with fewer adhesion-related admissions than open surgery. *Br J Surg* 2013; **100**: 152–159.
- Klaristenfeld DD, McLemore EC, Li BH, Abbass MA, Abbas MA. Significant reduction in the incidence of small bowel obstruction and ventral hernia after laparoscopic compared to open segmental colorectal resection. *Langenbecks Arch Surg* 2015; **400**: 505–512.
- Reshef A, Hull TL, Kiran RP. Risk of adhesive obstruction after colorectal surgery: the benefits of the minimally invasive approach may extend well beyond the perioperative period. *Surg Endosc* 2013; **27**: 1717–1720.
- Aquina CT, Probst CP, Becerra AZ, Iannuzzi JC, Hensley BJ, Noyes K *et al.* Missed opportunity: laparoscopic colorectal resection is associated with lower incidence of small bowel obstruction compared to an open approach. *Ann Surg* 2016; **264**: 127–134.
- Alvarez-Downing M, Klaassen Z, Orringer R, Gilder M, Tarantino D, Chamberlain RS. Incidence of small bowel obstruction after laparoscopic and open colon resection. *Am J Surg* 2011; **201**: 411–415.
- Bartels SA, Vlug MS, Hollmann MW, Dijkgraaf MG, Ubbink DT, Cense HA *et al.*; Collaborative LAFA Study Group. Small bowel obstruction, incisional hernia and survival after laparoscopic and open colonic resection (LAFA study). *Br J Surg* 2014; **101**: 1153–1159.
- Saklani AP, Naguib N, Shah PR, Mekhail P, Winstanley S, Masoud AG. Adhesive intestinal obstruction in laparoscopic vs open colorectal resection. *Colorectal Dis* 2013; **15**: 80–84.
- Taylor GW, Jayne DG, Brown SR, Thorpe H, Brown JM, Dewberry SC *et al.* Adhesions and incisional hernias following laparoscopic versus open surgery for colorectal cancer in the CLASICC trial. *Br J Surg* 2010; **97**: 70–78.
- Ng SS, Leung KL, Lee JF, Yiu RY, Li JC, Hon SS. Long-term morbidity and oncologic outcomes of laparoscopic-assisted anterior resection for upper rectal



- cancer: ten-year results of a prospective, randomized trial. *Dis Colon Rectum* 2009; **52**: 558–566.
- 16 Pedersen CB. The Danish Civil Registration System. *Scand J Public Health* 2011; **39**(Suppl 7): 22–25.
  - 17 von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007; **370**: 1453–1457.
  - 18 Ingeholm P, Gögenur I, Iversen LH. Danish Colorectal Cancer Group Database. *Clin Epidemiol* 2016; **8**: 465–468.
  - 19 Danish Colorectal Cancer Group. [Annual Review 2014.] [http://www.dccg.dk/03\\_Publikation/02\\_arsrapport.html](http://www.dccg.dk/03_Publikation/02_arsrapport.html) [accessed 12 December 2016].
  - 20 Pedersen CB. The Danish Civil Registration System. *Scand J Public Health* 2011; **39**(Suppl 7): 22–25.
  - 21 Lyng E, Sandegaard JL, Rebolj M. The Danish National Patient Register. *Scand J Public Health* 2011; **39**(Suppl 7): 30–33.
  - 22 Danish Colorectal Cancer Group. [Annual Review 2004.] [http://www.dccg.dk/03\\_Publikation/02\\_arsrapport.html](http://www.dccg.dk/03_Publikation/02_arsrapport.html) [accessed 12 December 2016].
  - 23 Masoomi H, Kang CY, Chaudhry O, Pigazzi A, Mills S, Carmichael JC et al. Predictive factors of early bowel obstruction in colon and rectal surgery: data from the Nationwide Inpatient Sample, 2006–2008. *J Am Coll Surg* 2012; **214**: 831–837.
  - 24 Jensen KK, Andersen P, Erichsen R, Scheike T, Iversen LH, Krarup PM. Decreased risk of surgery for small bowel obstruction after laparoscopic colon cancer surgery compared with open surgery: a nationwide cohort study. *Surg Endosc* 2016; **30**: 5572–5582.
  - 25 Thygesen SK, Christiansen CF, Christensen S, Lash TL, Sorensen HT. The predictive value of ICD-10 diagnostic coding used to assess Charlson comorbidity index conditions in the population-based Danish National Registry of Patients. *BMC Med Res Methodol* 2011; **11**: 83.
  - 26 Kim HT. Cumulative incidence in competing risks data and competing risks regression analysis. *Clin Cancer Res* 2007; **13**: 559–565.
  - 27 White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Stat Med* 2011; **30**: 377–399.
  - 28 Dowson HM, Bong JJ, Lovell DP, Worthington TR, Karanjia ND, Rockall TA. Reduced adhesion formation following laparoscopic versus open colorectal surgery. *Br J Surg* 2008; **95**: 909–914.
  - 29 Hull TL, Joyce MR, Geisler DP, Coffey JC. Adhesions after laparoscopic and open ileal pouch–anal anastomosis surgery for ulcerative colitis. *Br J Surg* 2012; **99**: 270–275.
  - 30 Andolf E, Thorsell M, Källén K. Cesarean delivery and risk for postoperative adhesions and intestinal obstruction: a nested case–control study of the Swedish Medical Birth Registry. *Am J Obstet Gynecol* 2010; **203**: 406.e1–406.e6.
  - 31 Condon ET, Cahill RA, O'Malley DB, Aherne NJ, Redmond HP. Evaluation of postoperative peritoneal adhesion formation following perioperative nicotine administration. *J Surg Res* 2007; **140**: 135–138.

### Supporting information

Additional supporting information may be found online in the supporting information tab for this article:

**Appendix S1** Validation of the primary outcome algorithms (Word document)

**Table S1** Sensitivity analysis of the hazard ratio of adhesive small bowel obstruction after open and laparoscopic rectal cancer operation according to the different algorithms defining the study outcome (Word document)

**Table S2** The three algorithms used to identify surgery for adhesive small bowel obstruction (Word document)

**Table S3** Outcome algorithms of adhesive small bowel obstruction validated against the medical record review (Word document)

**Table S4** Characteristics of patients according to missing data (Word document)