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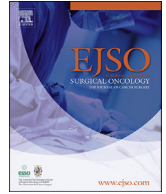
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Risk factors for a permanent stoma after resection of left-sided obstructive colon cancer – A prediction model



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ABSTRACT

Introduction: In patients with left-sided obstructive colon cancer (LSOCC), a stoma is often constructed as part of primary treatment, but with a considerable risk of becoming a permanent stoma (PS). The aim of this retrospective multicentre cohort is to identify risk factors for a PS in LSOCC and to develop a pre- and postoperative prediction model for PS.

Materials and methods: Data was retrospectively obtained from 75 hospitals in the Netherlands. Patients who had curative resection of LSOCC between January 1, 2009 to December 31, 2016 were included with a minimum follow-up of 6 months after resection. The interventions analysed were emergency resection, decompressing stoma or stent as bridge-to-elective resection. Main outcome measure was presence of PS at the end of follow-up. Multivariable logistic regression analysis was performed to identify risk factors for PS at primary presentation (T_0) and after resection, in patients having a stoma in situ (T_1). These risk factors were used to construct a web-based prediction tool.

Results: Of 2099 patients included in the study (T_0), 779 had a PS (37%). A total of 1275 patients had a stoma in situ directly after resection (T_1), of whom 674 had a PS (53%). Median follow-up was 34 months. Multivariable analysis showed that older patients, female sex, high ASA-score and open approach were independent predictors for PS in both the T_0 and T_1 population. Other predictors at T_0 were sigmoid location, low Hb, high CRP, cM1 stage, and emergency resection. At T_1 , subtotal colectomy, no primary anastomosis, not receiving adjuvant chemotherapy and high pTNM stage were additional predictors. Two predictive models were built, with an AUC of 0.74 for T_0 and an AUC of 0.81 for T_1 .

Conclusions: PS is seen in 37% of the patients who have resection of LSOCC. In patients with a stoma in situ directly after resection, 53% PS are seen due to non-reversal. Not only baseline characteristics, but also treatment strategies determine the risk of a PS in patients with LSOCC. The developed predictive models will give physicians insight in the role of the individual variables on the risk of a PS and help in informing the patient about the probability of a PS.

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1. Introduction

Emergency resection (ER) for left-sided obstructive colon cancer (LSOCC) often leads to a Hartmann's procedure with end colostomy

[1,2]. In case of resection with primary anastomosis, surgeons often create a temporary defunctioning ileostomy in the emergency setting. These stomas might reduce the risk of anastomotic leakage, but up to 35% are not closed, leaving a patient with a permanent stoma (PS) [3–5]. Patients with a PS may suffer from different types of stoma related complications. The choice for an ileostomy or a colostomy remains a subject of debate. It is known that an ileostomy is often associated with high-output stoma, increasing the risk of dehydration and metabolic complications, especially in elderly patients [5–8]. A colostomy is more often associated with parastomal herniation, skin care problems and stoma retractions [7–9].

Alternatively, a decompressing stoma can be constructed as a bridge to elective surgery (BTS) [10,11]. Due to the ileocecal valve, preferably a decompressing colostomy is constructed. Reversal of a decompressing stoma often requires a 3-stage procedure, and several studies have shown that 10–30% of these decompressing stomas become permanent [4,10,11]. BTS can also be accomplished by endoscopic insertion of a self-expandable metallic stent (SEMS). Data concerning the risk of PS after stenting in LSOCC is heterogeneous [3,12,13].

Multiple studies have been conducted to evaluate risk factors for PS in patients with rectal cancer surgery [14–17]; however, such studies in LSOCC remain scarce. Rectal cancer studies found that American Society of Anaesthesiologists (ASA) score, advanced cancer and open surgery are all potential pre-intervention risk factors for a PS [14,16,17]. Our Dutch Snapshot Research Group found that after ER in LSOCC, anaemia, impaired kidney function, and metastatic disease at presentation were all risk factors for non-closure of a temporary decompressing stoma [3]. However, it is unclear whether these risk factors also apply following a BTS approach. Furthermore, the risk profile for PS might have changed in the postoperative setting for those patients with a stoma present after resection. Therefore, the aim of the current study was to identify risk factors for a PS at initial presentation, as well as after resection, in LSOCC.

2. Materials and methods

2.1. Design

This national cohort study was performed by the Dutch Snapshot Research Group (DSRG) according to a predefined protocol [2,18]. Data of 3153 patients who had a resection for LSOCC between January 1, 2009, to December 31, 2016 were retrieved from the Dutch Colorectal Audit (DCRA). Surgical residents from the DSRG extended this database with additional disease, procedural and outcome data from the original patient files in 75 Dutch hospitals. Data entry was performed from August 2017 to December 2017. The institutional review board of the Amsterdam University Medical Centre, the Netherlands, approved this study.

2.2. Population

Patients were included from the DCRA in case of (1) clinical signs of an ileus, (2) confirmation of obstruction on CT with a distended colon proximal to the obstruction, (3) tumour localization at the splenic flexure, descending colon or sigmoid, and (4) histologically proven cancer. The exclusion criteria were (1) unknown follow-up data, (2) palliative intention, (3) free air on CT, (4) double tumour, (5) stoma at the time of initial presentation with LSOCC, (6) missing stoma data, and (7) survival/follow-up less than 6 months. Patients who were treated with Emergency resection, DS as BTS and SEMS as BTS were included. Patients were categorized by having a PS or not having a PS at the end of follow-up.

2.3. Primary outcome and definitions

Primary outcome was having a PS at the end of follow-up, with a minimum follow-up of 6 months after tumour resection. Risk factors for PS were analysed for two different patient scenarios, T₀ and T₁. T₀ was defined as the initial presentation with LSOCC within the above defined overall population. The T₁ population comprised all patients with a stoma in situ directly after tumour resection. Thus, patients with both (new) defunctioning stomas as well as the primarily placed decompressing stomas are included. All patients with bowel continuity after resection from the T₀ population are thereby excluded. This was done to identify risk factors for non-closure of the stoma.

2.4. Predictive variables

Based on presumed association with PS, and literature, the following variables were included for univariable analysis of the T₀ population: age, sex, body mass index (BMI; <18.5 vs. 18.5–25.0 vs. 25.0–30.0 vs. >30.0), American Society of Anaesthesiology (ASA) classification (1–2 vs. 3–4), tumour location (splenic flexure vs. descending colon vs. sigmoid), preoperative haemoglobin (Hb; >7.0 vs. ≤7.0 mmol/l), preoperative C-Reactive Protein (CRP; <10 vs. 10–50 vs. >50 mg/l), preoperative creatinine (<110 vs. 110–200 vs. >200 μmol/l), cT stage (T1–3 vs. T4), cM stage (0 vs. 1), Treatment in high caseload hospital, interval between presentation and first intervention (≤1 day vs. >1 day), type of procedure (ER vs. SEMS as BTS vs. decompressing stoma as BTS), and surgical approach (laparoscopic vs. open surgery). For the T₁ population, the following variables were analysed: age, sex, BMI, ASA, tumour location, interval between presentation and first intervention, type of procedure (segmental resection vs. subtotal colectomy), surgical approach, neo-adjuvant treatment during bridging interval, (par) enteral feeding until resection, primary anastomoses, pTNM stage (1–3 vs. 4), post-operative complications, and adjuvant chemotherapy. BMI was categorized according to the standard ‘Centres for disease control and prevention’ definition [19]. Cut-off levels of Hb and creatinine were selected based on clinical references. For preoperative CRP the first category was determined based on clinical reference values and the other categories based on a q-q plot of CRP vs PS. For “Treatment in high caseload hospital”, the cut-off was selected using the median. Hospitals with 20 or more LSOCC resections annually were scored as high caseload hospital.

2.5. Statistical analysis

Baseline characteristics were separately analysed for the T₀ and T₁ populations using descriptive statistics. Continuous values were shown as means (standard deviations, SDs) or median (minimum, maximum). Logistic regression was used for univariable analysis of the primary outcome parameter in the two populations separately. All variables with a p-value <0.1 in univariable analysis were included in the multivariable model with a backward stepwise approach. The multivariable logistic regression model was tested for multicollinearity. Missing data was imputed using multiple imputation in SPSS, if data was missing at random. Finally, cross-validation and bootstrapping were performed to correct for optimism. We used the AUC guidelines where 0.7 to 0.8 is considered acceptable, 0.8 to 0.9 is considered excellent, and more than 0.9 is considered outstanding [20].

The independent predictive variables were subsequently used to construct a web-based predictive tool (Evidencio, Haaksbergen, the Netherlands). This graphic regression model is constructed using statistics in which predictive variables are implemented into an equation. Both models were cross-validated with a 10-fold

cross-validation (cv). The average cvAUC was calculated including the corresponding bootstrap bias corrected 95% CI. Furthermore, a sensitivity analysis of our regression models was performed using split-sample validation. A 0.8–0.2% split ratio and a balanced split method were used to avoid oversampling resulting in an equal proportion of stoma cases in each group. A p-value of <0.05 was considered statistically significant. Analyses were performed using IBM SPSS version 27 and R version 4.1.2 (R foundation, Austria).

3. Results

3.1. Patient characteristics

From 3153 patients in the original study population, 1054 were excluded (Fig. 1). A total of 2099 patients were included in the T₀ population, of whom 779 (37%) had a PS after at least 6 months of follow-up. The median (IQR) follow-up was 34 (19–54) months. Baseline characteristics of the T₀ population are displayed in Table 1. Patients in the PS group were older (<0.001), had a higher ASA score (<0.001), more sigmoid tumours (<0.001), more often Hb < 7 mmol/L (<0.001), creatinine >200 µmol/L (<0.002) or CRP >10 (<0.001), and more often metastases at presentation (<0.001), and underwent open surgery (<0.001) and ER (<0.001).

After resection, 824 (39%) of the 2099 patients did not have a stoma in situ. The remaining 1275 were included in the T₁ analysis (Table 2). Of those 1275 patients with a stoma in situ directly after tumour resection, 674 (53%) still had a PS after at least 6 months of follow-up. Patients in whom the stoma was never closed were older (<0.001), more often female (<0.011), had higher ASA score (<0.001), more often open surgery (<0.001), ER (<0.001), and subtotal colectomies performed (<0.001), less often underwent

primary anastomoses (<0.001), had a higher rate of resection related complications (0.016), higher pTNM stage (<0.001), and less often received adjuvant chemotherapy (<0.001). Sub-analysis of the male and female population was performed to further analyse possible confounders. Female patients in the PS group more frequently had a history of abdominal surgery compared to male patients at T₁ (OR 2.64, 95% CI 1.89–3.69), in particular urogenital operations (OR 12.48, 95% CI 5.91–26.53).

3.2. Logistic regression analysis

In the univariable analysis at T₀, age, female sex, high ASA-score, BMI <18.5, sigmoid tumours, low Hb, high creatinine, high CRP, presence of metastasis, open approach and ER were associated with a PS based on a p-value <0.10. All variables except for BMI and creatinine remained independently associated with PS (p-value <0.05) in the multivariable regression analysis (Table 3). Moreover, the multicollinearity analysis showed tolerance values of >0.4, which is acceptable.

The univariable analysis of the 1275 patients at T₁ showed age, female sex, high ASA-score, BMI <18.5, open approach, ER, subtotal colectomy, no primary anastomosis, resection related complication, no adjuvant chemotherapy, and high pTNM stage to be risk factors for a PS. In multivariable analysis, BMI <18.5, ER and resection related complications appeared not associated with PS. All other variables were independent predictors for PS (Table 4).

3.3. Predictive model

Two regression models were built (T₀ and T₁). They were developed using the independent predictors of the multivariable

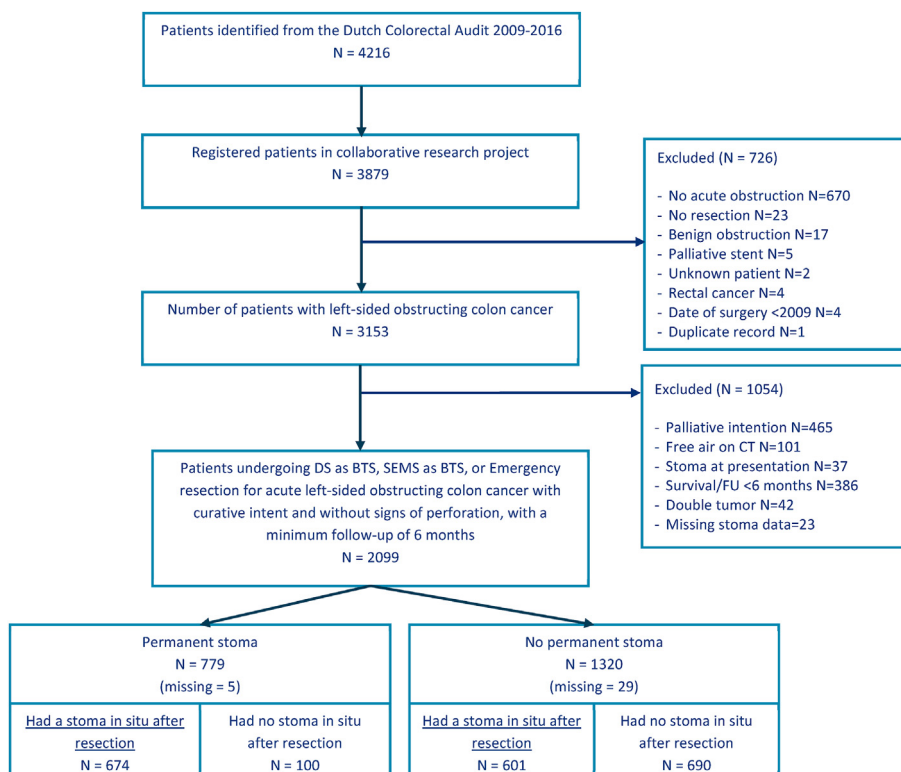


Fig. 1. Patient flow of study participants.

CT: computed tomography, FU: follow up, BTS: bridge to surgery, SEMS: self-expandable metal stent, DS: Decompressing stoma.

Table 1
Baseline characteristics at T₀, with a minimum follow-up of 6 months*.

Variable	Group	Total n (%)	T ₀ - Initial presentation with acute LSOCC (n = 2099)		
			No permanent stoma n (%)	Permanent stoma n (%)	p
Total	n (%)	2099	1320 (62.9)	779 (37.1)	
Age	Mean (SD)	68.73 (11.60)	66.28 (11.37)	72.89 (10.76)	<0.001
Sex	Male	1141 (54.4)	737 (55.8)	404 (51.9)	0.08
	Female	958 (45.6)	583 (44.2)	375 (48.1)	
ASA score	I-II	1495 (71.2)	1028 (77.9)	467 (59.9)	<0.001
	III-IV	583 (27.8)	279 (21.1)	304 (39.0)	
	Missing	21 (1.0)	13 (1.0)	8 (1.0)	
BMI (kg/m²)	18.5–25.0	864 (41.2)	553 (41.9)	311 (39.9)	0.37
	<18.5	40 (1.9)	20 (1.5)	20 (2.6)	
	25.0–30.0	669 (31.9)	426 (32.3)	243 (31.2)	
	>30.0	215 (10.2)	132 (10.0)	83 (10.7)	
	Missing	311 (14.8)	189 (14.3)	122 (15.7)	
Tumor location	Sigmoid	1447 (68.9)	865 (65.5)	582 (74.7)	<0.001
	Splenic flexure	274 (13.1)	192 (14.5)	82 (10.5)	
	Descending colon	378 (18.0)	263 (19.9)	115 (14.8)	
Hemoglobin at presentation (mmol/L)	>7.0	1749 (83.3)	1126 (85.3)	623 (80.0)	<0.001
	≤7.0	196 (9.3)	96 (7.3)	100 (12.8)	
	Missing	154 (7.3)	98 (7.4)	56 (7.2)	
Creatinine at presentation (umol/L)	≤110	1648 (78.5)	1048 (79.4)	600 (77.0)	0.002
	110–200	236 (11.2)	136 (10.3)	100 (12.8)	
	>200	19 (0.9)	5 (0.4)	14 (1.8)	
	Missing	196 (9.3)	131 (9.9)	65 (8.3)	
CRP at presentation (mg/L)	≤10	828 (39.4)	579 (43.9)	249 (32.0)	<0.001
	10–50	808 (38.5)	494 (37.4)	314 (40.3)	
	>50	296 (14.1)	148 (11.2)	148 (19.0)	
	Missing	167 (8.0)	99 (7.5)	68 (8.7)	
cT stage	cT1–cT3, cTx	2007 (95.6)	1264 (95.8)	743 (95.4)	0.68
	cT4	92 (4.4)	56 (4.2)	36 (4.6)	
cM stage	cM0, cMx	1914 (91.2)	1232 (93.3)	682 (87.5)	<0.001
	cM1	185 (8.8)	88 (6.7)	97 (12.5)	
Treatment in high caseload hospital	No	533 (25.4)	335 (25.4)	198 (24.7)	0.98
	Yes	1566 (74.6)	702 (74.6)	581 (74.6)	
Interval between presentation and first intervention	≤1 day	1185 (56.5)	755 (57.2)	430 (55.2)	0.37
	>1 day	914 (43.5)	565 (42.8)	349 (44.8)	
Approach	Laparoscopic	352 (16.8)	281 (21.3)	71 (9.1)	<0.001
	Open	1733 (82.6)	1034 (78.3)	699 (89.7)	
	Missing	14 (0.7)	5 (0.4)	9 (1.2)	
Treatment	Emergency resection	1649 (78.6)	974 (73.8)	675 (86.6)	<0.001
	DS as BTS	262 (12.5)	198 (15.0)	64 (8.2)	
	SEMS as BTS	188 (9.0)	148 (11.2)	40 (5.1)	

ASA: American Society of Anesthesiology, CRP: C-Reactive Protein, cT: clinical Tumor stage, cN: clinical lymph node metastasis stage, cM: clinical metastasis stage, BMI: Body Mass Index, SEMS: Self Expandable Metal Stent, DS: Decompressing Stoma, BTS: Bridge to Surgery followed by resection, p: p-value, NA: not applicable. *: Median (IQR) 34 (19–54) months.

logistic regression analysis in Tables 3 and 4. After correction for optimism, the T₀-model showed a cvAUC of 0.74 (Fig. 2) whereas the T₁-model showed a cvAUC of 0.81 (Fig. 3). Finally, two graphical web-based predictive models were developed to predict the risk of PS at T₀ and at T₁ (Supplementary Fig. 1 and Supplementary Fig. 2, respectively).

4. Discussion

This national cohort study on LSOCC revealed an overall PS rate of 37%, and found that patient and disease related factors, as well as treatment related factors were associated with the risk of PS. Among patient related factors were age, sex, and ASA-score. Disease related factors included tumour location, Hb level, CRP level and presence of metastasis. Risk factors for PS related to surgical treatment were open approach, ER, subtotal colectomy and no primary anastomosis. The predictive model developed for T₀ (initial presentation) demonstrated an acceptable cvAUC of 0.74, whereas the predictive model of T₁ (having a stoma in situ directly after resection) showed an excellent cvAUC of 0.81.

To our knowledge, this is the first study analysing risk factors for

a PS after resection of LSOCC, in which different treatment strategies are compared. Moreover, this study analysed predictive variables both at presentation and after resection of the primary tumour, thus also analysed risk factors for non-closure of a stoma. Overall PS rate in the current study was 37%, with the highest PS rate after ER, which is in line with previous studies [21,22]. In the emergency setting, a Hartmann's procedure is often performed in patients with sigmoid tumours [1]. The current results confirm that tumour location in the sigmoid is an independent risk factor for PS. With regard to disease characteristics, presence of metastases is a strong independent risk factor for a PS (Table 3 and Table 4). Patients with stage IV disease might initially receive a temporary stoma. However, if their disease progresses or they receive systemic therapy for longstanding control of disease, further surgical treatment to restore bowel continuity is often avoided.

Patient characteristics such as old age and high ASA score, often represent frail health status, and the clinical condition might further deteriorate in those with an inflammatory response as reflected by high CRP levels and/or anaemia. Patients who are in poor clinical condition are less likely to receive an anastomosis after resection. This might explain why these variables are independent

Table 2
Baseline characteristics at T₁, with a minimum follow-up of 6 months*.

Variable	Group	Total n (%)	T ₁ - Stoma in situ after resection of LSOCC (n = 1275)		
			No permanent stoma	Permanent stoma	p
Total n (%)	—	1275 (100)	601 (47)	674 (53)	—
Age	Mean	69.79	65.83	73.32	<0.001
Sex	Male	701 (55.0)	353 (58.7)	348 (51.6)	0.011
	Female	574 (45.0)	248 (41.3)	326 (48.4)	
ASA score	I-II	856 (67.1)	456 (75.9)	400 (59.3)	<0.001
	III-IV	407 (31.9)	140 (23.3)	267 (39.6)	
	Missing	12 (0.9)	5 (0.8)	7 (1.0)	
BMI (kg/m²)	18.5–25.0	537 (42.1)	256 (42.6)	281 (41.7)	0.372
	<18.5	25 (2.0)	7 (1.2)	18 (2.7)	
	25.0–30.0	403 (31.6)	195 (32.4)	208 (30.9)	
	>30.0	133 (10.4)	63 (10.5)	70 (10.4)	
	Missing	177 (13.9)	80 (13.3)	97 (14.4)	
Tumor location	Sigmoid	967 (75.8)	456 (75.9)	511 (75.8)	0.980
	Splenic flexure	132 (10.4)	63 (10.5)	69 (10.2)	
	Descending colon	176 (13.8)	82 (13.6)	94 (13.9)	
Interval between presentation and first intervention	≤1 day	739 (58.0)	359 (59.7)	380 (56.4)	0.078
	>1 day	533 (41.8)	239 (39.8)	294 (43.6)	
	Missing	3 (0.2)	3 (0.5)	0 (0)	
Approach	Laparoscopic	161 (12.7)	109 (18.2)	52 (7.8)	<0.001
	Open/Conversion	1103 (87.3)	490 (81.8)	613 (92.2)	
Treatment	Emergency resection	1050 (82.4)	465 (77.4)	585 (86.8)	<0.001
	DS as BTS	171 (13.4)	114 (19.0)	57 (8.5)	
	SEMS as BTS	54 (4.2)	22 (3.7)	32 (4.7)	
Neoadjuvant therapy during bridging interval	No	1248 (97.9)	586 (97.5)	662 (98.2)	0.376
	Yes	27 (2.1)	15 (2.5)	12 (1.8)	
(Par)enteral feeding during bridging interval	No	1246 (97.7)	587 (97.7)	659 (97.8)	0.90
	Yes	29 (2.3)	14 (2.3)	15 (2.2)	
Type of resection	Segmental resection	1210 (94.9)	587 (97.7)	623 (92.4)	<0.001
	Subtotal colectomy	64 (5.0)	13 (2.2)	51 (7.6)	
	Missing	1 (0.1)	1 (0.2)	0 (0)	
Primary anastomosis	No	1001 (78.5)	393 (65.4)	608 (90.2)	<0.001
	Yes	274 (21.5)	208 (34.6)	66 (9.8)	
	Missing	0 (0)	0 (0)	0 (0)	
Resection related complications	No	742 (58.2)	371 (61.7)	371 (55.0)	0.016
	Yes	533 (41.8)	230 (38.3)	303 (45.0)	
pTNM stage**	I-III	1134 (88.9)	562 (93.5)	572 (84.9)	<0.001
	IV	141 (11.1)	39 (6.5)	102 (15.1)	
Able to receive adjuvant chemotherapy	No	726 (56.9)	270 (44.9)	456 (67.7)	<0.001
	Yes	549 (43.1)	331 (55.1)	218 (32.3)	

ASA: American Society of Anesthesiology, BMI: Body Mass Index, SEMS: Self Expandable Metal Stent, DS: Decompressing Stoma, BTS: Bridge to Surgery followed by resection, pTNM: pathological TNM stage, p: p-value, NA: not applicable. *: Median (IQR) 31 (18–50) months **: cM is also used to identify metastases for pTNM staging.

risk factors for a PS. This is in line with rectal cancer studies, identifying comparable variables to be independently associated with PS after rectal cancer surgery [7,9,23–25].

Female patients had a higher risk of a PS compared to male patients. This might be explained by confounders. One of these confounders is previous abdominal surgery. Previous abdominal surgery was found to be a significant predictor of PS in univariable analysis, but was no longer significant in the multivariable analysis. Further analysis of the data demonstrated that female patients have significantly more previous abdominal surgery compared to male patients. A reason for this might be pregnancy/gynaecology related interventions with related pelvic floor disorders.

The procedural predictive variables open surgery and ER were previously reported as risk factors for a PS [1,22–24]. Probably, open surgery is not causally related to PS and several confounders might play a role in this observed association. Open procedures might have been performed more often by non-GI surgeons, leading to more PS [26]. Also, open surgery might correlate with, ileus, sepsis, or a challenging procedure [26]. All these factors are inherently associated with poor postoperative outcomes, and these conditions might be reasons not to construct a primary anastomosis [27–29]. Studies in diverticulitis also revealed that stomas are less often reversed if index surgery was performed open instead

of laparoscopically [30]. Concerning ER, this strategy in itself also increases the risk of complications and stoma placement [10,22,31–33]. The current results underline the latter, with ER being an independent risk factor for PS in the multivariable analysis at T₀.

Both BTS techniques appeared to decrease the risk of PS. Decompressing the distended bowel will facilitate the construction of a primary anastomosis and reduce the risk of anastomotic leakage, consequently decreasing the risk of a PS.^{29,29} Moreover, patient condition can be optimized during the BTS interval by adequate feeding, which also optimizes surgical conditions with higher chance of primary restoration of bowel continuity.

At T₁, decompressing stoma was associated with lower PS rates in the current analysis. However, in the multivariable analysis no risk reduction was seen. This can be explained by the correlation of decompressing stoma with the variable “primary anastomosis”. If a decompressing stoma is placed as primary intervention, surgeons tend to keep this stoma in situ to protect the primary anastomosis that is made after resection. Apparently, the decompressing stoma that subsequently functions as a protective stoma is often reversed at a later stage. This confirms previous observations [34].

Interestingly, receiving adjuvant chemotherapy was associated with a lower risk of PS. A possible explanation might be that

Table 3
Univariable and multivariable analysis of risk factors for permanent stoma at T₀, with a minimum follow-up of 6 months*.

Variable		Univariable analysis		Multivariable analysis	
		OR (95% CI)	P	OR (95% CI)	P
Age	Mean	1.06 (1.05, 1.07)	<0.001	1.05 (1.04, 1.06)	<0.001
Sex	Male	Reference		Reference	
	Female	1.17 (0.98, 1.40)	0.078	1.31 (1.07, 1.59)	0.008
ASA score	ASA I-II	Reference		Reference	
	ASA III-IV	2.37 (1.95, 2.88)	<0.001	1.84 (1.49, 2.28)	<0.001
BMI	18.5–25.0	Reference		Reference	
	<18.5	1.78 (0.94, 3.36)	0.076		
	25.0–30.0	1.01 (0.82, 1.25)	0.895		
	>30.0	1.12 (0.82, 1.52)	0.477		
Tumor location	Sigmoid	Reference		Reference	
	Splenic flexure	0.64 (0.48, 0.84)	0.001	0.62 (0.46, 0.84)	0.002
	Descending colon	0.65 (0.51, 0.83)	<0.001	0.64 (0.49, 0.83)	0.001
Hemoglobin at presentation (mmol/L)	>7.0	Reference		Reference	
	≤7.0	1.78 (1.34, 2.37)	<0.001	1.40 (1.02, 1.93)	0.040
Creatinine at presentation (umol/L) (first)	≤110	Reference		Reference	
	110–200	1.28 (0.97, 1.69)	0.077		
	>200	4.89 (1.75, 13.65)	0.002		
CRP at presentation (mg/L)	≤10	Reference		Reference	
	10–50	1.54 (1.27, 1.88)	<0.001	1.35 (1.09, 1.67)	0.006
	>50	2.52 (1.94, 3.28)	<0.001	2.20 (1.65, 2.94)	<0.001
cT stage	cT1–3, cTx	Reference			
	cT4	1.09 (0.71, 1.68)	0.64		
Metastases at presentation	cM0, cMx	Reference		Reference	
	Yes	1.99 (1.47, 2.70)	<0.001	2.95 (2.11, 4.11)	<0.001
Treatment in high caseload hospital	No	Reference			
	Yes	1.00 (0.81, 1.22)	0.98		
Interval between presentation and first intervention	≤24 h	Reference			
	>24 h	1.09 (0.91, 1.30)	0.37		
Approach	Laparoscopic	Reference		Reference	
	Open	2.66 (2.02, 3.50)	<0.001	2.03 (1.48, 2.79)	<0.001
Treatment	Emergency resection	Reference		Reference	
	DS as BTS	0.47 (0.35, 0.63)	<0.001	0.64 (0.45, 0.90)	0.01
	SEMS as BTS	0.39 (0.27, 0.56)	<0.001	0.40 (0.27, 0.60)	<0.001

ASA: American Society of Anesthesiology, CRP: C-Reactive Protein, cT: clinical Tumor stage, cM: clinical Metastasis stage, BMI: Body Mass Index, SEMS: Self-Expandable Metal Stent, DS: Diverting Stoma, BTS: Bridge To Surgery, OR: Odds Ratio, CI: Confidence Interval, p: p-value. *: Median (IQR) 34 (19–54) months.

patients who are not able to receive adjuvant chemotherapy are in poor condition. Patients did not receive adjuvant chemotherapy probably because of postoperative complications, severe comorbidities, malnutrition, or any other reason related to poor health status, and are therefore also less likely to have their stoma reversed.

We build two web-based predictive tools that can be easily used by physicians (supplementary 1 and supplementary 2). Both tools can assist the physician in informing the patient about the probability of a PS. Previous studies have demonstrated that preoperative stoma education leads to better acceptance and management of the stoma [35]. The web-tools will also give physicians insight into the role of the individual variables on the probability of a PS. This is especially relevant considering the fact that several surgical treatment variables appeared to be associated with risk of PS.

The current study has several limitations. Due to the retrospective design, this study is at risk of selection bias. The DCRA database only includes patients who had resection of colon cancer. Thus, patients who had a SEMS or decompressing stoma as BTS but never underwent tumour resection, for instance due to disease progression, were not included. On the contrary, all patients receiving ER were included. However, the impact on the findings might be limited, because patients with palliative treatment in the ER group were excluded. Furthermore, patients who have a stoma in situ at T₁ are more at risk of having certain baseline (T₀) risk factors for a PS. For instance, surgeons are more likely to place a stoma in patients with higher ASA score, to reduce the risk of anastomotic leakage [27]. Also, the reason and considerations why

a stoma became a PS is not documented. Moreover, all patients who died within 6 months or were lost to follow-up within 6 months after resection are excluded. However, if these patients would be included, these patients would not have had enough time to have their stoma reversed. Thus, they would be scored as patients with PS incorrectly. Finally, the minimum follow-up period of 6 months in the current study might be short to definitively conclude that a stoma is permanent. Patients with a stoma who were lost to follow-up after 6 months might still have their stoma reversed elsewhere. However, with a median (IQR) follow-up of 34 (19–54) months, this might concern a limited number of patients.

In conclusion, this study demonstrates that after resection of LSOCC, 37% of the patients are left with a PS. If a stoma is left in situ after resection of LSOCC, 53% of these patients will have a PS. Not only patient and tumour characteristics, but also treatment strategies affect the risk of a PS. This should be taken into account when treating LSOCC. The web-based predictive tools have acceptable to excellent predicting ability and should be further tested in clinical practice.

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Table 4
Multivariable analysis of risk factors for a permanent stoma at T₁, with a minimum follow-up of 6 months*.

		T ₁ - Stoma in situ after resection of LSOCC (n = 1275)			
		Univariable analysis		Multivariable analysis	
		OR (95% CI)	p	OR (95% CI)	p
Age	Mean	1.07 (1.06, 1.08)	<0.001	1.07 (1.05, 1.09)	<0.001
Sex	Male	Reference		Reference	
	Female	1.33 (1.07, 1.67)	0.011	1.50 (1.12, 1.94)	0.002
ASA score	ASA I-II	Reference		Reference	
	ASA III-IV	2.17 (1.70, 2.77)	<0.001	1.50 (1.14, 1.99)	0.004
BMI	18.5–25.0	Reference		Reference	
	<18.5	2.34 (0.96, 5.70)	0.06		
	25.1–30.0	0.97 (0.75, 1.26)	0.83		
	>30.0	1.01 (0.69, 1.48)	0.95		
Tumor location	Sigmoid	Reference		Reference	
	Splenic flexure	0.98 (0.68, 1.41)	0.90		
	Descending colon	1.02 (0.74, 1.41)	0.89		
Interval between presentation and first intervention	≤1 day	Reference		Reference	
	>1 day	0.86 (0.69, 1.08)	0.19		
Approach	Laparoscopic	Reference		Reference	
	Open/Conversion	2.62 (1.85, 3.73)	<0.001	1.58 (1.03, 2.40)	0.035
Treatment	Emergency resection	Reference		Reference	
	DS as BTS	0.40 (0.28, 0.56)	<0.001		
	SEMS as BTS	1.16 (0.66, 2.02)	0.61		
Neoadjuvant therapy during bridging interval	No	Reference		Reference	
	Yes	0.71 (0.33, 1.53)	0.34		
Parenteral feeding during bridging interval	No	Reference		Reference	
	Yes	0.95 (0.46, 1.99)	0.90		
Type of resection	Segmental resection	Reference		Reference	
	Subtotal colectomy	3.70 (1.99, 6.88)	<0.001	4.38 (2.17, 8.82)	<0.001
Primary anastomosis	No	Reference		Reference	
	Yes	0.21 (0.15, 0.28)	<0.001	0.22 (0.15, 0.31)	<0.001
Resection related complications	No	Reference		Reference	
	Yes	1.31 (1.05, 1.64)	0.02		
pTNM stage**	I-III	Reference		Reference	
	IV	2.57 (1.75, 3.78)	<0.001	5.06 (3.19, 8.03)	<0.001
Able to receive adjuvant chemotherapy	No	Reference		Reference	
	Yes	0.39 (0.31, 0.49)	<0.001	0.64 (0.49, 0.86)	0.002

ASA: American Society of Anesthesiology, BMI: Body Mass Index, SEMS: Self-Expandable Metal Stent, DS: Diverting Stoma, BTS: Bridge to Surgery, OR: Odds Ratio, CI: Confidence Interval, p: p-value. *: Median (IQR) 31 (18–50) months. **: cM is also used to identify metastases in pTNM stage.

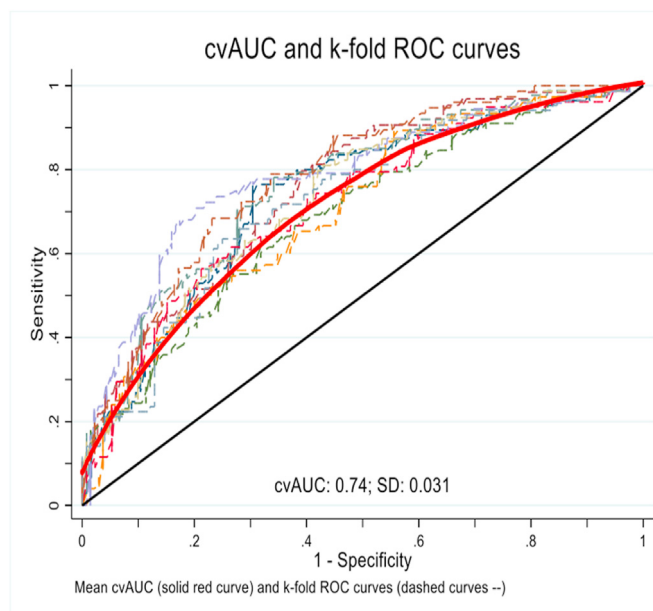


Fig. 2. Receiver operating curve of T₀ model. cvAUC: cross-validated Area Under the Curve. cvAUC: 0.74.

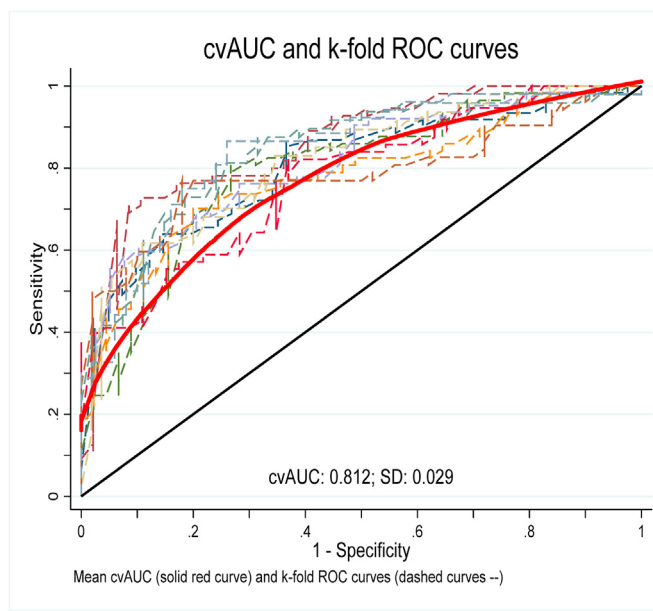


Fig. 3. Receiver operating curve of T₁ model. cvAUC: cross-validated Area Under the Curve. cvAUC: 0.81.

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CRediT authorship contribution statement

Bobby Zamaray: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Data curation, Writing – original draft, Writing – review & editing, Visualization. **J.V. Veld:** Conceptualization, Methodology, Validation, Formal analysis, Resources, Data curation, Writing – original draft, Writing – review & editing. **T.A. Burghgraef:** Conceptualization, Methodology, Resources, Data curation, Writing – review & editing. **R. Brohet:** Methodology, Validation, Formal analysis, Investigation, Resources, Data curation, Writing – review & editing. **H.L. van Westreenen:** Conceptualization, Methodology, Validation, Writing – review & editing, Supervision, Project administration, Funding acquisition. **J.E. van Hooft:** Conceptualization, Methodology, Writing – review & editing, Funding acquisition. **P.D. Siersema:** Conceptualization, Methodology, Writing – review & editing, Funding acquisition. **P.J. Tanis:** Conceptualization, Methodology, Writing – review & editing, Supervision, Funding acquisition. **E.C.J. Consten:** Conceptualization, Methodology, Writing – review & editing, Supervision, Funding acquisition.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejso.2022.12.008>.

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