Predicting mortality within 90 days of first intervention in patients with left-sided obstructive colon cancer

Burghgraef, T.A.; Bakker, I.S.; Veld, J.V.; Wijsmuller, A.R.; Amelung, F.J.; Bemelman, W.A.; ... ; Dutch Snapshot Res Grp

ORIGINAL CONTRIBUTION

Predicting Mortality Within 90 Days of First Intervention in Patients With Left-Sided Obstructive Colon Cancer

Thijs A. Burghgraef, M.D.[1,2] • Ilsalien S. Bakker, M.D., Ph.D.[2] • Joyce V. Veld, M.D., Ph.D.[3,4] • Arthur R. Wijsmuller, M.D., Ph.D.[2] • Femke J. Amelung, M.D., Ph.D.[5] Willem A. Bemelman, M.D., Ph.D.[3] • Frank Ter Borg, M.D., Ph.D.[6] Jeanin E. van Hooft, M.D., Ph.D.[4,7] • Peter D. Siersema, M.D., Ph.D.[8] Pieter J. Tanis, M.D., Ph.D.[9] • Esther C.J. Consten, M.D., Ph.D.[1,2]

On behalf of the Dutch Snapshot Research Group*
1 Department of Surgery, Meander Medical Center, Amersfoort, the Netherlands
2 Department of Surgery, University Medical Center Groningen, Groningen, the Netherlands
3 Department of Surgery, Amsterdam University Medical Centers, University of Amsterdam, Amsterdam, the Netherlands
4 Department of Gastroenterology and Hepatology, Amsterdam University Medical Centers, Amsterdam, the Netherlands
5 Department of Surgery, Jeroen Bosch Hospital, Den Bosch, the Netherlands
6 Department of Gastroenterology and Hepatology, Deventer Hospital, Deventer, the Netherlands
7 Department of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, the Netherlands
8 Departments of Gastroenterology and Hepatology, Radboud University Medical Center, Nijmegen, the Netherlands
9 Department of Surgery, Amsterdam University Medical Centers, University of Amsterdam, Cancer Center Amsterdam, Amsterdam, the Netherlands

BACKGROUND: Acute resection for left-sided obstructive colon carcinoma is thought to be associated with a higher mortality risk than a bridge-to-surgery approach using decompressing stoma or self-expandable metal stent, but prediction models are lacking.

OBJECTIVE: This study aimed to determine the influence of treatment strategy on mortality within 90 days from the first intervention in patients presenting with left-sided obstructive colon carcinoma.

DESIGN: This was a national multicenter cohort study that used data from a prospective national audit.

SETTINGS: The study was performed in 75 Dutch hospitals.

PATIENTS: Patients were included if they underwent resection with curative intent for left-sided obstructive colon carcinoma between 2009 and 2016.

INTERVENTIONS: First intervention was either acute resection, bridge to surgery with self-expandable metallic stent, or bridge to surgery with decompressing stoma.

MAIN OUTCOME MEASURES: The main outcome measure was 90-day mortality after the first intervention. Risk factors were identified using multivariable logistic analysis. Subsequently, a risk model was developed.

RESULTS: In total, 2395 patients were included, with the first intervention consisting of acute resection in 1848 patients (77%), stoma as bridge to surgery in 332 patients (14%), and stent as bridge to surgery in 215 patients

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*A full list of collaborators is included under the Acknowledgment.

Correspondence: Esther C.J. Consten, M.D., Ph.D., Department of Surgery, University Medical Center Groningen, Hanzeplein 1, 9713 GZ Groningen, the Netherlands. E-mail: e.c.j.consten@umcg.nl

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(9%). Overall, 152 patients (6.3%) died within 90 days from the first intervention. A decompressing stoma was independently associated with lower 90-day mortality risk (HR, 0.27; 95% CI, 0.094–0.62). Other independent predictors for mortality were age, ASA classification, tumor location, and index levels of serum creatinine and C-reactive protein. The constructed risk model had an area under the curve of 0.84 (95% CI, 0.81–0.87).

LIMITATIONS: Only patients who underwent surgical resection were included.

CONCLUSIONS: Treatment strategy had a significant impact on 90-day mortality. A decompressing stoma considerably lowers the risk of mortality, especially in older and frail patients. The developed risk model needs further external validation. See **Video Abstract** at http://links.lww.com/DCR/B975.

PREDICCIÓN DE LA MORTALIDAD A 90 DÍAS POSTERIORES A LA PRIMERA CIRUGÍA EN PACIENTES CON CÁNCER DE COLON OBSTRUCTIVO DEL LADO IZQUIERDO

ANTECEDENTES: Se cree que la resección aguda para el carcinoma de colon obstructivo del lado izquierdo está asociada con un mayor riesgo de mortalidad que un enfoque puente a la cirugía que utiliza un estoma de descompresión o un stent metálico autoexpandible, pero faltan modelos de predicción.

OBJETIVO: Determinar la influencia de la estrategia de tratamiento sobre la mortalidad dentro de los 90 días desde la primera intervención utilizando un modelo de predicción en pacientes que presentan carcinoma de colon obstructivo del lado izquierdo.

DISEÑO: Un estudio de cohorte multicéntrico nacional, utilizando datos de una auditoría nacional prospectiva.

ENTORNO CLINICO: El estudio se realizó en 75 hospitales holandeses.

PACIENTES: Se incluyeron los pacientes que se sometieron a una resección con intención curativa de un carcinoma de colon obstructivo del lado izquierdo entre 2009 y 2016.

INTERVENCIONES: La primera intervención fue resección aguda, puente a cirugía con stent metálico autoexpandible o puente a cirugía con estoma descompresor.

PRINCIPALES MEDIDAS DE VALORACIÓN: La principal medida de resultado fue la mortalidad a los 90 días después de la primera intervención. Los factores de riesgo se identificaron mediante análisis logístico multivariable. Posteriormente se desarrolló un modelo de riesgo.

RESULTADOS: En total se incluyeron 2395 pacientes, siendo la primera intervención resección aguda en 1848 (77%) pacientes, estoma como puente a la cirugía en 332 (14%) pacientes y stent como puente a la cirugía en 215 (9%) pacientes. En general, 152 pacientes (6,3%) fallecieron dentro de los 90 días posteriores a la primera intervención. Un estoma de descompresión se asoció de forma independiente con un menor riesgo de mortalidad a los 90 días (HR: 0,27, IC: 0,094–0,62). Otros predictores independientes de mortalidad fueron la edad, la clasificación ASA, la ubicación del tumor y los niveles índice de creatinina sérica y proteína C reactiva. El modelo de riesgo construido tuvo un área bajo la curva de 0,84 (IC: 0,81–0,87).

LIMITACIONES: Solo se incluyeron pacientes que se sometieron a resección quirúrgica.

CONCLUSIONES: La estrategia de tratamiento tuvo un impacto significativo en la mortalidad a los 90 días. Un estoma descompresor reduce considerablemente el riesgo de mortalidad, especialmente en pacientes mayores y frágiles. Se desarrolló un modelo de riesgo, que necesita una mayor validación externa. Consulte **Video Resumen** en http://links.lww.com/DCR/B975. *(Traducción—Dr. Ingrid Melo)*

KEY WORDS: Acute resection; Bridge to surgery; Decompressing stoma; Left-sided obstructive colon carcinoma; Mortality; Self-expandable metal stent.

Colorectal cancer is the third most commonly diagnosed cancer worldwide, with more than 1.9 million new global cases in 2019.[1] Although a majority of patients are diagnosed with mild symptoms or at an early stage after a positive fecal immunochemical test in a national screening program, 9% to 13% of patients present with acute colonic obstruction, which accounts for 85% of the emergency colectomies for colon cancer.[2,3]

Emergency resection is commonly used for left-sided obstructive colonic cancer (LSOCC); however, it is associated with high mortality risk.[3,4] Therefore, decompression of the colonic obstruction using a decompressing stoma (DS) or a self-expandable metal stent (SEMS) as a bridge to surgery (BTS) has been suggested as an alternative strategy for curative treatment of LSOCC. As concerns have been raised regarding the long-term oncological safety of colonic stenting, SEMS placement is not recommended as a standard treatment in various international guidelines.[5,6] Although DS as BTS is increasingly used, emergency resection remains the preferred approach in most Dutch hospitals.[7]

Previous studies suggested that short-term mortality rates increased after emergency resection, especially in older patients with comorbidities.[4] This led to the recommendation of BTS over emergency resection for elderly patients (older than 70 years) with ASA class III or IV.[4,8] Nevertheless, there is still conflicting evidence regarding the impact of a BTS approach on mortality in LSOCC, and

prediction models have to our knowledge not been published.[9–12] Therefore, this study aimed to determine the association between treatment and mortality within 90 days from the first intervention for patients presenting with LSOCC using a prediction model.

MATERIALS AND METHODS

Design

This study used data from a national collaborative research project initiated by the Dutch Snapshot Research Group. This project has been described in detail previously.[7] In short, prospectively collected short-term data from patients who underwent resection of LSOCC between 2009 and 2016, registered in the mandatory Dutch ColoRectal Audit, were merged with long-term data using a retrospective medical record review collected by 75 of 77 Dutch hospitals.

Data Procurement

Procurement of additional data was performed using a web-based tool developed by Medical Research Data Management (Deventer, the Netherlands) to guarantee and adhere to privacy regulations. Data entry was performed by surgical residents under the supervision of 1 or 2 consultant surgeons between August 2017 and December 2017. Discrepancies and missing values identified by the coordinating researcher were communicated back to the participating local residents for verification or completion of the data. The final data set was pseudonymized. The study design and drafting of the article were in accordance with the Strengthening the Reporting of Observational studies in Epidemiology statement. This observational study was approved by the medical ethics committee of the Academic Medical Center in Amsterdam, which waived the need for informed consent.

Patients

Eligibility criteria were 1) primary tumor location at the splenic flexure, descending colon, or sigmoid; 2) diagnosis of colonic obstruction based on at least 1 clinical sign of obstruction (bloated abdomen, nausea, and/or vomiting), combined with radiological signs on CT (dilated colon with or without small-bowel distention); and 3) resection of the primary tumor with curative intent. For the purpose of the present study, patients were excluded if they 1) presented with clinically overt perforation and/or free air on abdominal CT, 2) were found to have a case of a synchronous second colorectal cancer, 3) were treated with palliative intent, and 4) had an unknown follow-up status. Therapeutic strategies were categorized as acute resection, DS as BTS, or SEMS as BTS.

Primary Outcome and Predictive Variables

The primary outcome was all-cause 90-day mortality from the first intervention, which was acute resection, DS, or SEMS. The following baseline characteristics were considered as potential predictors of the primary outcome: age, sex, BMI, ASA class, surgical approach (open/laparoscopic), tumor location (sigmoid, splenic flexure, descending colon), creatinine and C-reactive protein levels at the time of presentation, cT stage (T1–3 vs T4), cM stage, interval between presentation and first intervention (≤1 vs >1 d), and type of first intervention. We used cutoff points for BMI according to the standard definition of the Centers for Disease Control and Prevention.[13] The age cutoff of 70 years was used according to international guideline recommendations, with an additional cutoff at 80 years.[6] For serum creatinine and C-reactive protein levels, 2 cutoff points were identified. The first cutoff was based on the reference values, whereas the second was based on the qq plot of index serum levels versus 90-day mortality. If acute resection was performed despite initial BTS intervention (SEMS or DS), analysis was performed according to the intention-to-treat principle. Acute resection within 2 days after the initial BTS intervention was registered as a proxy for clinical failure of BTS.

Statistical Analysis

Data were analyzed using R version 3.6.1. Categorical or dichotomous variables were presented as numbers with percentages. Continuous variables were shown as mean and SD or median and interquartile range (IQR), depending on the distribution. A multivariable logistic regression was performed using a backward model. Missing data were imputed using multiple imputation if data were missing at random or completely at random. The logistic regression model was evaluated for assumptions and adjusted if necessary. *P* values and HRs were used to interpret the results. A CI that was either below or above 1 was interpreted as significant. In addition, internal validation was performed using bootstrapping by drawing a random sample of 150 patients from the original study population. Calibration was evaluated by plotting the observed number of deceased patients to the predicted number of deceased patients. The performance of the model was tested by calculating the area under the curve (AUC) of the receiver-operating characteristic curve after correcting for optimism based on the calibration plot. Finally, a web-based tool and a risk stratification table were built to visualize the predicted risk (Evidencio, Haaksbergen, the Netherlands).

RESULTS

Patient Characteristics

A total of 3153 patients were entered in the initial database, of whom 758 patients were excluded: 115 patients because of free air on the CT scan, 168 patients with a synchronous second colorectal cancer, 414 patients with palliative

intent treatment, 15 patients who underwent local excision of the primary tumor, and 46 patients with unknown follow-up status at 90 days. This resulted in 2395 patients who were included for final analysis. The first intervention was an acute resection in 1848 patients (77%), DS followed by resection in 332 patients (14%), and SEMS followed by resection in 215 patients (9%; Fig. 1). Patients in the SEMS group were significantly older, patients in the DS group had a significantly higher rate of cT4 tumors, and patients in the acute resection group were significantly less frequently operated on using a laparoscopic approach. Final resection was performed after a median of 36 days (IQR, 22–65) after the first intervention in the DS group and after a median of 19 days (IQR, 8–30) in the SEMS group. Resection within 2 days from a bridging intervention occurred in none of the patients in the DS group and in 26 patients (12.1%) in the SEMS group. The number of clinically overt perforations after SEMS was 5 of 332 patients (1.5%; Table 1).

Logistic Regression Analysis

Overall, 152 patients (6.3%) died within 90 days of the first intervention. The 90-day mortality rate was 7.3% for patients undergoing acute resection, 1.5% for DS as BTS, and 5.6% for SEMS as BTS (Table 1). Univariable analysis showed an increased risk of mortality for patients older than 80 years, patients with ASA classification III or IV, patients presenting with creatinine levels >110 μmol/L, or patients with C-reactive protein (CRP) levels >50 mg/L. Patients with an ASA class of I or those who had been treated with DS as BTS had a decreased risk of mortality (Table 2).

Multivariable regression analysis showed that age was independently associated with mortality within 90 days after the first intervention, with an HR of 3.19 (95% CI, 1.85–5.76) for patients of 70 to 80 years and 7.10 (95% CI, 4.12–12.87) for patients older than 80 years. ASA classification III or IV was also associated with an increased mortality risk, with a HR of 2.62 (95% CI, 1.76–3.93) and 8.14 (95% CI, 4.12–12.87), respectively. Other independent factors associated with increased mortality risk were tumor location in the splenic flexure (HR, 1.89 [95% CI, 1.15–3.05]), serum creatinine level of >200 μmol/L (HR, 3.74 [95% CI, 1.51–8.68]), and serum CRP level of >50 mg/L (HR, 2.67 [95% CI, 1.64–4.40]) at presentation. Regarding treatment strategy, DS as BTS was independently associated with a decreased risk of mortality (HR, 0.27 [95% CI, 0.094–0.62]), whereas SEMS as BTS was not if compared to acute resection (Table 2).

Development of a Predictive Risk Model

Based on internal validation using bootstrapping, correction for overfitting was performed. The AUC was 0.85 (95% CI, 0.82–0.87) for the full model using all risk factors and was 0.84 (95% CI, 0.81–0.87) after correcting for optimism (Fig. 2). The calibration plot after correcting for optimism is shown in Supplemental Figure 1 at http://links.lww.com/DCR/B976. The predicted risk based on the developed risk score is shown in Figure 3, which illustrates the substantial increase in absolute risk of mortality in the presence of multiple risk factors, with the red areas illustrating patients with more than 30% predicted risk of dying within 90 days from first intervention. Additionally, we constructed a web-based tool to assess the risk according to provided patient characteristics. This tool can be accessed at https://www.evidencio.com/models/share/2477 and a screenshot of the web-based tool is shown in Supplemental Figure 2 at http://links.lww.com/DCR/B976.

DISCUSSION

This nationwide cohort study presents that the construction of DS as BTS in patients presenting with LSOCC is associated with a significant reduction in 90-day mortality from

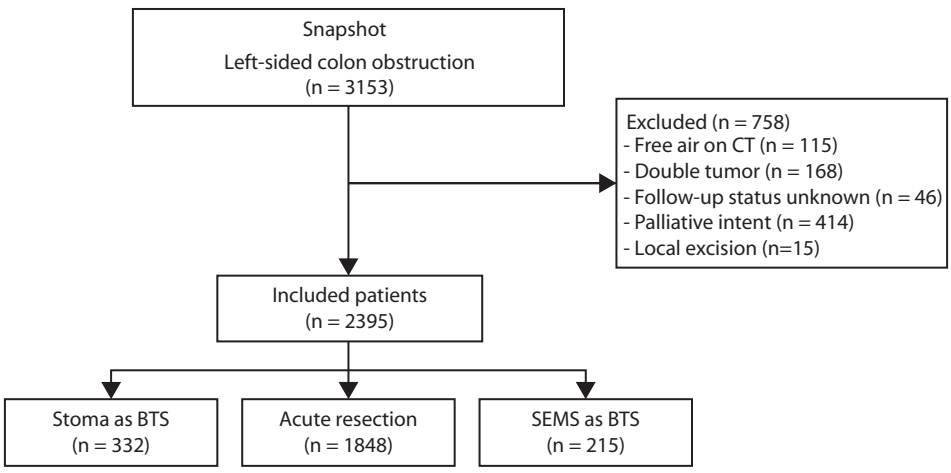

FIGURE 1. Patient flow of study participants. BTS = bridge to surgery; SEMS = self-expandable metal stent.

TABLE 1. Baseline characteristics

Variable	All (n = 2395)	DS as BTS (n = 332)	SEMS as BTS (n = 215)	Acute resection (n = 1848)	p
Age, y, n (%)					
<70	1104 (46.1)	183 (55.1)	89 (41.4)	832 (45.0)	<0.001
70–80	453 (18.9)	109 (32.8)	71 (33.0)	658 (35.6)	
>80	838 (35.0)	40 (12.0)	55 (25.6)	358 (19.4)	
Sex, n (%)					
Male	1308 (54.6)	201 (60.5)	121 (56.3)	986 (53.4)	0.047
Female	1087 (45.4)	131 (39.5)	94 (43.7)	862 (46.6)	
ASA score, n (%)					
I	410 (17.1)	46 (13.9)	45 (20.9)	319 (17.3)	<0.001
II	1222 (51.0)	212 (63.9)	114 (53.0)	896 (48.5)	
III	663 (27.7)	69 (20.8)	52 (24.2)	542 (29.3)	
IV	88 (3.7)	5 (1.5)	3 (1.4)	80 (4.3)	
Missing	12 (0.5)	0 (0.0)	1 (0.5)	11 (0.6)	
BMI (kg/m^2), n (%)					
18.5–25.0	988 (41.3)	162 (48.8)	92 (42.8)	734 (39.7)	<0.001
<18.5	52 (2.2)	4 (1.2)	5 (2.3)	43 (2.3)	
25.0–30.0	759 (31.7)	110 (33.1)	71 (33.0)	578 (31.3)	
>30.0	248 (10.4)	32 (9.6)	26 (12.1)	190 (10.3)	
Missing	348 (14.5)	24 (7.2)	21 (9.8)	303 (16.4)	
Tumor location, n (%)					
Sigmoid	1634 (68.2)	224 (67.5)	159 (74.0)	1251 (67.7)	0.01
Splenic flexure	437 (18.2)	54 (16.3)	43 (20.0)	340 (18.4)	
Descending colon	324 (13.5)	54 (16.3)	13 (6.0)	257 (13.9)	
Creatinine at presentation (μmol/L), n (%)					
≤110	1849 (77.2)	248 (74.7)	167 (77.7)	1434 (77.6)	0.005
110–200	293 (12.2)	30 (9.0)	29 (13.5)	234 (12.7)	
>200	28 (1.2)	3 (0.9)	3 (1.4)	22 (1.2)	
Missing	225 (9.4)	51 (15.4)	16 (7.4)	158 (8.5)	
CRP at presentation (mg/L), n (%)					
≤10	900 (37.6)	113 (34.0)	93 (43.3)	694 (37.6)	0.03
10–50	924 (38.6)	121 (36.4)	77 (35.8)	726 (39.3)	
>50	368 (15.4)	55 (16.6)	29 (13.5)	284 (15.4)	
Missing	203 (8.5)	43 (13.0)	16 (7.4)	144 (7.8)	
cT stage, n (%)					
cT1–cT3, cTx, missing	2290 (95.6)	292 (88.0)	209 (97.2)	1789 (96.8)	<0.001
cT4	105 (4.4)	40 (12.0)	6 (2.8)	59 (3.2)	
cN stage, n (%)					
cN0, cNx, missing	2217 (92.6)	289 (87.1)	195 (90.7)	1733 (93.8)	<0.001
cN1–cN2	178 (7.4)	43 (12.9)	20 (9.3)	115 (6.2)	
cM stage, n (%)					
cM0, cMx, missing	2309 (96.4)	314 (94.6)	204 (94.6)	1791 (96.9)	<0.001
cM1	86 (3.6)	18 (5.4)	11 (5.1)	57 (3.1)	
Interval between presentation and first intervention, d, n (%)					
≤1	1344 (56.1)	199 (59.9)	161 (47.9)	984 (53.2)	<0.001
>1	1008 (42.1)	103 (31.0)	48 (22.3)	857 (46.4)	
Missing	43 (1.8)	30 (9.0)	6 (2.8)	7 (0.4)	
Approach, n (%)					
Open	1984 (82.8)	166 (50.0)	126 (58.6)	1692 (91.6)	<0.001
Laparoscopic	411 (17.2)	166 (50.0)	89 (41.4)	156 (8.4)	
Procedure, n (%)					
(Extended) right hemicolectomy	49 (20.4)	8 (2.4)	1 (0.5)	40 (2.2)	0.146
(Extended) left hemicolectomy	705 (29.4)	105 (31.6)	70 (32.6)	530 (28.7)	
Sigmoidectomy	1482 (61.9)	203 (61.1)	137 (63.7)	1142 (61.8)	
Subtotal colectomy	122 (5.1)	11 (3.3)	6 (2.8)	105 (5.7)	
Other	37 (1.6)	5 (1.5)	1 (0.5)	31 (1.7)	
Primary anastomosis, n (%)					
Yes, without deviating stoma	838 (35.0)	114 (34.3)	150 (69.8)	574 (31.1)	<0.001
Yes, with deviating stoma	335 (14.0)	168 (50.6)	12 (5.6)	155 (8.4)	
No	150 (6.3)	49 (14.8)	52 (24.2)	49 (2.7)	
Missing	10 (0.4)	1 (0.3)	1 (0.5)	8 (0.4)	

(*Continued*)

TABLE 1. Continued

Variable	All (n = 2395)	DS as BTS (n = 332)	SEMS as BTS (n = 215)	Acute resection (n = 1848)	p
Acute resection within 2 d after intervention, n (%)	NA	0 (0.0)	26 (12.1)	NA	<0.001
Interval between intervention and resection, d, median (IQR)	NA	36 (22–65)	19 (8–30)	NA	<0.001
Deceased within 90 d, n (%)	152 (6.3)	5 (1.5)	12 (5.6)	135 (7.3)	<0.001
Reason for death, n (%)					
Metastatic disease	10 (0.7)	0	0	10 (7.4)	
Secondary malignancy	3 (2.0)	0	0	3 (2.2)	
Cardiopulmonary complication	47 (30.9)	1 (20.0)	3 (25.0)	43 (31.8)	
Tromboembolic	1 (0.7)	0	0	1 (0.7)	
Surgery-related complication	70 (46.1)	4 (80.0)	9 (75.0)	57 (42.2)	
Unknown	21 (13.8)	0	0	21 (15.6)	

BTS = bridge to surgery; CRP = C-reactive protein; DS = diverting stoma; NA, not available; SEMS = self-expandable metal stent.

TABLE 2. Univariable and multivariable analyses of risk factors for death within 90 d after the first presentation

	Univariable analysis		Multivariable analysis	
Variable	HR (95% CI)	p	HR (95% CI)	p
Age, y				
<70	Reference		Reference	
70–80	5.02 (2.98–8.93)	<0.001	3.19 (1.85–5.76)	<0.001
>80	12.48 (7.46–22.10)	<0.001	7.10 (4.12–12.87)	<0.001
ASA classification				
II	Reference		Reference	
I	0.20 (0.049–0.56)	<0.001	0.33 (0.080–0.94)	0.07
III	3.66 (2.50–5.41)	<0.001	2.62 (1.76–3.93)	<0.001
IV	12.86 (7.44–22.07)	<0.001	8.14 (4.46–14.75)	<0.001
BMI (kg/m^2)				
18.5–25.0	Reference			
<18.5	1.77 (0.66–3.96)	0.20		
25.0–30.0	1.18 (0.82–1.70)	0.37		
>30.0	1.29 (0.76–2.10)	0.33		
Tumor location				
Sigmoid	Reference		Reference	
Splenic flexure	1.53 (0.97–2.35)	0.07	1.89 (1.15–3.05)	0.01
Descending colon	1.15 (0.74–1.75)	0.78	1.19 (0.73–1.87)	0.47
Creatinine (µmol/L)				
≤110	Reference	Reference	Reference	
110–200	2.65 (1.79–3.87)	<0.001	1.35 (0.87–2.05)	0.17
>200	8.62 (3.82–18.24)	<0.001	3.74 (1.51–8.68)	0.003
CRP (mg/L)				
≤10	Reference	Reference	Reference	
10–50	1.92 (1.27–2.94)	0.002	1.47 (0.95–2.32)	0.09
>50	3.76 (2.41–5.93)	<0.001	2.67 (1.64–4.40)	<0.001
cT stage				
cT1–3, cTx, missing	Reference			
cT4	0.89 (0.34–1.90)	0.79		
Metastases at presentation				
cM0, cMx, missing	Reference			
Yes	1.11 (0.43–2.39)	0.81		
Interval between presentation and first intervention, d				
≤1	Reference		Reference	
>1	1.19 (0.85–1.65)	0.30	1.33 (0.91–1.90)	0.15
Treatment				
Emergency resection	Reference		Reference	
SEMS as BTS	0.86 (0.45–1.52)	0.63	0.94 (0.47–1.74)	0.85
DS as BTS	0.20 (0.070–0.44)	<0.001	0.27 (0.094–0.62)	0.006

BTS = bridge to surgery; CRP = C-reactive protein; DS = diverting stoma; SEMS = self-expandable metal stent.

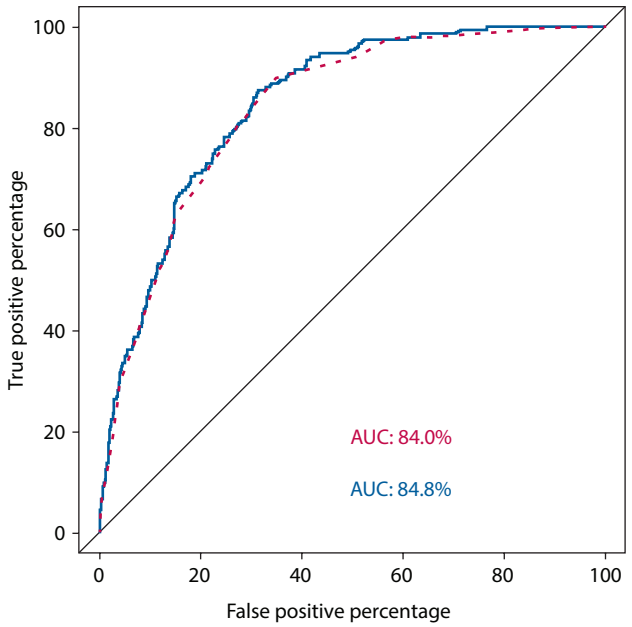

FIGURE 2. Receiver-operating characteristic curve before and after correcting for optimism of the c-statistic (corrected AUC). AUC = area under the curve.

the first intervention compared to acute resection. Besides age and ASA classification as well-known predictors of mortality, tumor location at the splenic flexure, high serum creatinine, and high serum CRP levels at initial presentation were predictive for mortality within 90 days in the emergency setting in this population with nonperforated LSOCC. The developed risk model showed adequate performance with an AUC of 0.84 after internal validation using bootstrapping and subsequent shrinkage. By applying this model, we were able to identify specific high-risk groups with 90-day mortality rates higher than 30% for each age category, depending on the performed treatment strategy.

Previous studies on BTS in patients with LSOCC have also emphasized the ongoing dilemma of the most adequate treatment policy for the individual patient. Transforming emergency surgical tumor resection in elective surgery seems to benefit clinical outcomes, probably because of an improved clinical condition of the patient, adequate oncological staging, laparoscopic surgery, and performing resections during daytime by a dedicated surgical team. Although long-term oncological outcomes seem at least comparable between both BTS strategies and acute resection, reports on short-term outcomes have suggested important differences between the 3 treatment options.[9,12,14–18]

Regarding short-term mortality, the current study demonstrates a risk reduction when performing DS as BTS compared with acute resection, whereas this was not observed for SEMS as BTS. This was also found in a recent systematic review, in which no reduction in mortality was observed in the SEMS as BTS group compared to the emergency surgery group.[14] Studies specifically comparing DS as BTS with SEMS as BTS are scarce. Two small-sized studies and 1 large population-based study revealed no difference in mortality between the 2 groups,[9–11] although long-term overall survival was significantly better after DS in the large population-based cohort.[9] In another population-based study, mortality was similar in the overall population, but higher mortality rates were found in elderly patients with comorbidity after acute resection.[4]

Based on the same data set, we previously published a propensity-matched comparison between DS as BTS and SEMS as BTS.[12] A reduction in 90-day postresection mortality was found (1.7% for DS vs 5.0% for SEMS), although this was not statistically significant ($p = 0.29$). In addition, we performed a propensity-matched comparison between DS as BTS and acute resection, which revealed a

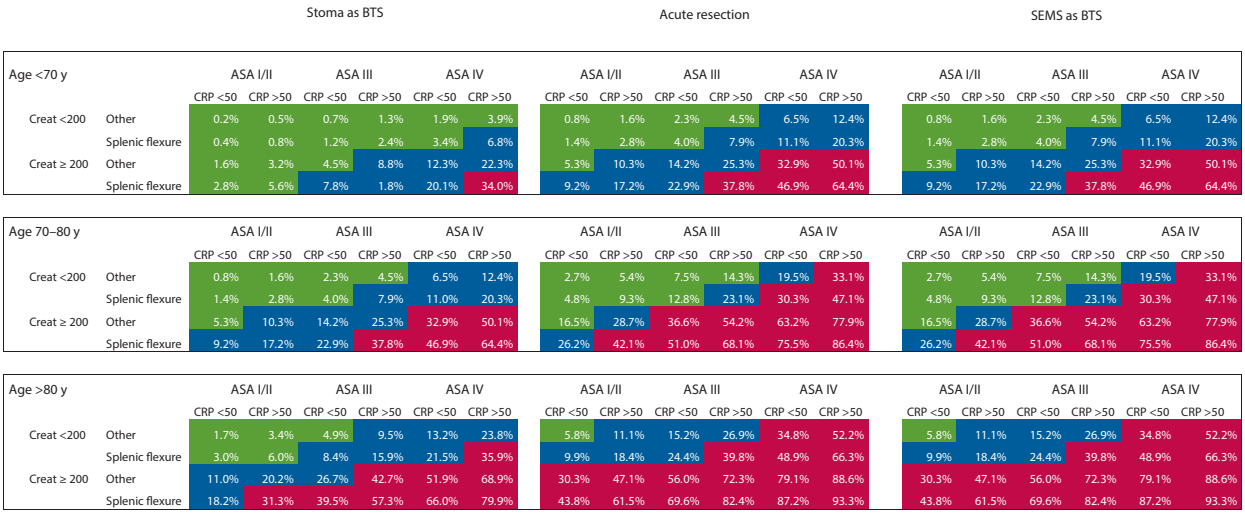

FIGURE 3. Risk stratification based on developed risk score. BTS = bridge to surgery; Creat = serum creatinine level at initial presentation in μmol/L; CRP = C-reactive protein level at initial presentation in mg/L; SEMS = self-expandable metallic stenting.

significantly different 90-day postresection mortality rate in favor of DS (1.7% vs 7.0%; $p = 0.006$).[18] The primary end point in the present study was slightly different because the mortality was determined for the 90-day period since the first intervention. Furthermore, all patients fulfilling inclusion and exclusion criteria could be entered into the multivariable model, which is an advantage compared to propensity-matched analyses that have the inherent problem of losing patients who cannot be matched.

The number of patients treated with SEMS in the Netherlands between 2009 and 2016 was relatively low[7] because of disappointing results of the previously performed stent-in I and II trials.[5,19] It has been concluded that colonic stenting requires the expertise of the endoscopist, which was suggested to be insufficient in these studies.[8] However, in the present study, these factors most probably did not contribute to the lack of benefit of SEMS as BTS, as most SEMS were placed in centers with ample experience with stent placement. Nonetheless, the successful placement of a SEMS does not necessarily lead to a successful BTS intervention.[5,20,21] Colonic stents sometimes do not adequately deploy, become obstructed, or even lead to perforation at the stent ends, thereby requiring a secondary acute resection. Our data show that clinical failure was present in 12.1% of the patients who received a SEMS as BTS because they underwent an acute resection within 2 days, whereas none of the patients initially treated with stoma as BTS underwent an acute resection within 2 days.

Besides mortality, other factors are important in clinical decision-making. Stenting is less successful for tumors with longer strictures or for tumors located in the sigmoid or splenic flexure, which tend to have wider angulation distal to the obstruction.[22–25] Furthermore, patients with locally advanced tumors (cT4) may be treated with neoadjuvant therapy, which makes them also less suitable for stenting. Based on our previous study, DS as BTS resulted in more primary anastomoses but a higher postoperative stoma rate. Considering that a stoma as BTS comes with stoma-related morbidity, more reinterventions and longer hospital stay compared to SEMS as BTS were observed.[12] However, the permanent stoma rate was not significantly different between DS and SEMS. Finally, it has been suggested that clinical perforation because of the placement of a SEMS has oncological consequences, which should be taken into consideration during clinical decision-making.[26]

Regarding the observed risk factors for 90-day mortality, tumor location, serum creatinine at presentation, and serum CRP at presentation have not previously been identified as risk factors yet in this specific population of patients with colon cancer. Splenic flexure tumors require an (extended) left colectomy, which is known to be associated with an increased anastomotic leakage rate and risk of mortality.[27] Raised serum CRP and creatinine levels at presentation possibly reflect the clinical condition of the patient in terms of infectious complications because of a distended colon and dehydration, respectively. Combining all these risk factors associated with 90-day mortality into the risk model provides a risk analysis with adequate performance, as reflected by the AUC of 0.84 after shrinkage. This has resulted in a useful tool (https://www.evidencio.com/models/share/2477) in the emergency setting with commonly available parameters that may facilitate clinical decision-making. Although we did perform internal validation using bootstrapping, external validation using an external validation cohort needs to be performed in the future to confirm our results.

Limitations

Some limitations of the present study should be taken into account. First, because acute resection was the most performed treatment strategy, both the DS and SEMS groups were relatively small. Second, the decision-making process in patients who are treated with BTS seems to depend not only on patient and tumor characteristics but also on the hospital of admission. SEMSs are not placed in all Dutch centers, and not all tumors are eligible for stenting. Although this might cause patient selection, this is one of the inherent benefits of DS as BTS because this approach is performed in most hospitals and is effective in almost every patient. Additionally, the construction of a DS is not a complex procedure and can be performed by GI surgeons as well as general surgeons, whereas the placement of a SEMS requires substantial expertise from the gastroenterologist. Third, the database only includes patients undergoing surgical resection because this is one of the requirements of the Dutch ColoRectal Audit database. Therefore, patients who were treated with the initial BTS strategy but did not undergo a secondary resection either because of the progression of the disease, metastasis, or death were not included in the study. This might have introduced selection bias. However, we tried to reduce this bias by excluding patients who underwent emergency resection with palliative intent. Additionally, this prediction model was constructed for the curative setting, and DS or SEMS not followed by resection generally reflects palliative care. Finally, this is a retrospective study, and selection bias or confounding by indication could not be ruled out. However, because it is a nationwide population-based study reflecting clinical practice, it comes with higher external validity than randomized controlled trials. In addition, a randomized controlled trial would be more time-consuming and comes with strict inclusion and exclusion criteria because SEMS in particular is not usable for every LSOCC. However, a prospective randomized controlled trial could provide us with details regarding the number of patients receiving palliative SEMS or stoma as BTS.

CONCLUSION

Patients undergoing resection for LSOCC have a substantial risk of dying within 90 days from the first intervention, with mortality rates higher than 30% in the presence of at least 3 risk factors as identified by the present study. A BTS strategy using DS was independently associated with a lower risk of mortality if compared to acute resection, whereas this was not found for SEMS as BTS. Index levels of creatinine and CRP as well as tumor location were identified as predictors for mortality, as well as age and ASA score. The presented risk model needs further validation in an independent patient cohort, but it seems a useful risk assessment tool for an individual patient with LSOCC and can be valuable in shared decision-making.

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