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ORIGINAL ARTICLE

Development and external validation of a nomogram and online tool to predict bowel dysfunction following restorative rectal cancer resection: the POLARS score

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ABSTRACT

Objective Bowel dysfunction is common following a restorative rectal cancer resection, but symptom severity and the degree of quality of life impairment is highly variable. An internationally validated patient-reported outcome measure, Low Anterior Resection Syndrome (LARS) score, now enables these symptoms to be measured. The study purpose was: (1) to develop a model that predicts postoperative bowel function; (2) externally validate the model and (3) incorporate these findings into a nomogram and online tool in order to individualise patient counselling and aid preoperative consent.

Design Patients more than 1 year after curative restorative anterior resection (UK, median 54 months; Denmark (DK), 56 months since surgery) were invited to complete The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30 version3 (EORTC QLQ-C30 v3), LARS and Wexner incontinence scores. Demographics, tumour characteristics, preoperative/postoperative treatment and surgical procedures were recorded. Using transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) guidelines, risk factors for bowel dysfunction were independently assessed by advanced linear regression shrinkage techniques for each dataset (UK:DK).

Results Patients in the development (UK, n=463) and validation (DK, n=938) datasets reported mean (SD) LARS scores of 26 (11) and 24 (11), respectively. Key predictive factors for LARS were: age (at surgery); tumour height, total versus partial mesorectal excision, stoma and preoperative radiotherapy, with satisfactory model calibration and a Mallow's Cp of 7.5 and 5.5, respectively.

Conclusions The Pre-Operative LARS score (POLARS) is the first nomogram and online tool to predict bowel dysfunction severity prior to anterior resection. Colorectal surgeons, gastroenterologist and nurse specialists may use POLARS to help patients understand their risk of bowel dysfunction and to preoperatively highlight patients who may require additional postoperative support.

Significance of this study

What is already known on this subject?

- Restorative rectal cancer surgery commonly affects bowel function and this frequently results in significant impairment to quality of life.
- Optimal patient-centred care requires these symptoms to be routinely assessed through patient-reported outcome measures (PROMs), with clinical intervention where possible.
- Recently, a simple PROM that assesses postoperative bowel dysfunction following an anterior resection has been internationally validated. The PROM is called the Low Anterior Resection Syndrome (LARS) score. It is highly acceptable to patients and has excellent psychometric properties. However, this information is only available in the postoperative setting, once patients have become symptomatic.
- Currently, clinicians and patients have a lack of awareness about postoperative bowel dysfunction. Clinicians fail to manage patients' expectations by providing insufficient preoperative information and frequently investigations and treatment of symptoms are limited.

What are the new findings?

- The two largest international LARS datasets have been used to develop and validate the Pre-Operative LARS score (POLARS) score in accordance with TRIPOD guidelines.
- The POLARS score is the first nomogram and online tool to predict bowel dysfunction preoperatively.

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INTRODUCTION

Survival from rectal carcinoma has almost tripled over the past 40 years, with 5-year survival exceeding 55% across Europe.[1 2] This has been attributed to optimal surgery by total mesorectal excision (TME),[3] in conjunction with multidisciplinary team management[4 5] and selective multimodal therapy.[6] Furthermore, the widespread introduction of circular stapling devices has

Significance of this study

How might it impact on clinical practice in the foreseeable future?

- In routine practice, POLARS has the potential to provide patients and healthcare teams with a practical means of preoperatively highlighting patients at significant risk of postoperative bowel dysfunction. We anticipate this will inform multidisciplinary team discussions and enable patient-tailored consent. High-risk patients should understand the consequences of bowel dysfunction and that colostomy formation is one of the several strategies for managing LARS.
- POLARS may have an important medicolegal role by providing evidence that an appropriate preoperative discussion about postoperative bowel dysfunction has taken place.
- POLARS can be used in clinical trials to identify the high-risk patients most likely to require clinical intervention. It could also serve as a stratification tool within relevant randomised clinical trials.

reduced the need for permanent colostomies and a restorative anterior resection is currently regarded as the optimal procedure for the majority of patients with rectal cancer.[7]

Following a restorative anterior resection, 70%–90% of patients report bowel dysfunction.[8 9] However, 1 year after surgery up to 30% of patients report resolution of bowel dysfunction with no major impact on quality of life.[8 10] In contrast, over 40% become 'toilet dependent'[11] and report that bowel dysfunction has a devastating consequence on work, social and physical functioning as well as global quality of life.[8 10 12] The priority of follow-up has been to perform surveillance for cancer recurrence and healthcare professionals have widely held the belief that postoperative bowel dysfunction cannot be improved.[13] Therefore, these side effects of treatment are frequently missed or overlooked.[13] Encouragingly, recent studies suggest that incremental improvements in bowel dysfunction can be achieved[14] and the results of the optimising radiotherapy bowel injury therapy (ORBIT) study demonstrate that a detailed clinical algorithm of targeted treatment strategies can improve radiotherapy-induced symptoms.[15]

The specific symptoms reported after an anterior resection of the rectum vary widely, from daily episodes of incontinence and urgency to obstructed defecation and constipation.[9] The spectrum of symptoms associated with postoperative bowel dysfunction and the associated bowel-related quality of life impairment has been termed anterior resection syndrome.[9] This broad definition of anterior resection syndrome has made it difficult to accurately evaluate patient symptoms and comparison of outcomes between patients has been challenging. However, a key step forward in the management of anterior resection syndrome has been the development of a patient-reported outcome measure (PROM) called the Low Anterior Resection Syndrome (LARS) score. This score was developed on the basis of patient-reported symptoms. The LARS score can accurately measure the severity of postoperative bowel dysfunction and it has been proven to correlate well with quality of life measures.[8 12 16]

The purpose of this study was to personalise the preoperative consent process by: (1) identifying the risk factors for postoperative bowel dysfunction according to the LARS score; (2) developing a model that predicts the LARS score; (3) externally validating the model in a separate international dataset and (4) incorporate the findings into a nomogram and online tool that can be useful in clinical practice by offering individualised information for decision-making at the time of patient consent or during preoperative patient discussions.

METHODS

Data and participants

A retrospective cohort study was performed in 12 UK centres and nationally across Denmark (DK). Eligible patients received a standardised postal invitation to complete the LARS score, as well as two other questionnaires that are not reported in this study (EORTC QLQ-C30 v3 and the Wexner incontinence score). The questionnaires were dispatched and returned between July 2013–February 2014 and February 2009–July 2009 for the UK and DK, respectively.

In both datasets, the inclusion criteria were an anterior resection performed for a diagnosis of rectal adenocarcinoma between 0 and 15 cm from the anal verge. The exclusion criteria were an incomplete cancer resection, recurrence, metastatic disease, intestinal stoma or patients whose bowel continuity had been restored for <12 months, dementia or previous use of translators in clinical consultation. In DK, a well-maintained national registry identified all eligible patients. In the UK, research nurses at each centre identified a consecutive series of eligible patients for each participating consultant surgeon. For consultants practicing for >12 years, the search was truncated at January 2001.

The study received approval from the Central Denmark Regional Committee on Biomedical Research Ethics, UK National Research Ethics Committee approval (13/WM/0059) and it was registered on the UK National Institute of Health Research portfolio (UKCRN ID 14499).

Outcome

In order to predict the risk of postoperative bowel dysfunction, we used the LARS score; the only PROM designed specifically to quantify bowel dysfunction following an anterior resection. It has been shown to reliably and consistently evaluate bowel symptoms.[12] Developed in Danish,[12] it is now internationally validated,[17] with validated translations in Chinese,[18] English,[19] German,[17] Spanish[17] and Swedish.[17] Validation is also underway for Portuguese, Dutch, Tamil, Turkish, Thai, Greek and Mandarin.

The LARS score is a quick simple self-administered questionnaire that objectively measures patient symptoms, without any subjective quality of life questions. It consists of five questions: incontinence of flatus; incontinence of liquid stool; frequency; clustering and urgency (see online supplementary appendix 1). Each item is individually weighted and a summative score is derived (range 0–42).[12] Based on appropriate psychometric properties, this scoring tool classifies patients into three severity groups: no LARS (0–20 points), minor LARS (21–29 points) and major LARS (30–42 points).[12]

Predictors

All candidate predictors were selected on the basis of detailed literature reviews and clinical evidence,[8–10] within the confines of data availability, all risk factors previously reported to contribute to bowel dysfunction were used. The following data were extracted from the medical records of each patient: age at surgery; gender; time since surgery; partial or total mesorectal

excision (PME vs TME); defunctioning stoma; tumour, node, metastasis stage by pathology report;[20] tumour height (distance from anal verge on MRI or rigid sigmoidoscopy in centimetres); timing and type of radiotherapy and chemotherapy. Low rectal carcinoma was defined as a tumour ≤6 cm from the anal verge. A PME was performed on selected upper rectal tumours that mobilised sufficiently such that the mesorectum could be transected at least 5 cm below the tumour without the need to mobilise the 'lateral ligaments'.[21]

Missing values

Prior to data analysis, the primary outcome data were inspected for missing values. In order to include them in the analyses, multiple imputation procedures were developed and a suitable imputed dataset was generated for the final analysis. The UK and Danish patients with missing predictor variables were excluded.

Statistical analysis

The continuous predictors were time since surgery, tumour height and age at surgery and as categorical predictors gender, defunctioning stoma, PME versus TME, tumour stage (≤pT2 vs >pT2), nodal stage, the use of preoperative and postoperative chemotherapy and radiotherapy. Variables were compared between the two datasets using SE, ORs with 95% CIs, χ^2, Mann-Whitney U test and t-test, where appropriate. The preimputation and postimputation datasets were compared with Kruskal-Wallis equality-of-populations rank test.

Model development was performed according to TRIPOD guidance.[22] The LARS scores were treated as continuous data and analysed using linear regression techniques. Model development used statistical criteria according to several stepwise selection and shrinkage techniques. The final model selection applied shrinkage and selection method for linear regression (LASSO).[23] LASSO performs backward selection of variables in combination with a penalty on the absolute value of the regression coefficients, such that some are set to zero whereas others are shrunk towards smaller (absolute) values. Compared with standard backward selection, the additional shrinkage improves model performance by avoiding overfitting, optimism and miscalibration. LASSO estimations were performed and reported for each dataset separately. Mallows' Cp was used to select the optimal combination of model parameters, focusing on simultaneous elimination of bias and variance, in order to achieve the best available predicted score.[24] The coefficients selected were according to the model with the lowest Cp; ideally this is less than or equal to the number of parameters (p) in the regression.[25] A value much greater than p (twofold or more) indicates substantial bias in the model.

Sample size

There are no generally accepted approaches to estimate the sample size requirements for derivation and validation studies of risk prediction models, however, we ensured that the study met suggested requirements of having at least 10 events per candidate variable for the derivation of a model and at least 100 events for validation studies.[22]

Model validation

Conventional receiver operating characteristic curves are not widely available for models with continuous outcomes, therefore, the predictive ability of the UK model was compared against the Danish model using calibration approaches, which included a statistical comparison using the Somer's D test and the Harrel's D statistic.[26] Although the LASSO is expected to show less overoptimism than backward elimination, we still corrected for overoptimism in calibration and discrimination performance using bootstrap resampling.[27] A medium-scale simulation (5000 replications) of the UK data model was undertaken regarding the root mean square error, that is, the SD of the errors of the model.

Pre-Operative LARS score nomogram and online prediction tool

The LASSO findings were used to generate a nomogram (or alignment chart), which is intended to be a simplified tool for clinicians; enabling a predicted LARS score for any combination of key predictor variables. This may be difficult to access during clinical practice and therefore the model formula was also coded into a web-compatible electronic JAVA script. Finally, model performance was evaluated by six clinicians (NJB, KJE, RG-J, TJ, SL, BJM) according to five randomly selected scenarios that were inputted into the model and evaluated for clinical appropriateness.

RESULTS

Participants

A flow diagram summarising the identified eligible patients and the study participants is shown in figure 1. The development and validation datasets included 463 UK and 938 Danish patients, respectively. The demographics and tumour characteristics between cohorts were clinically comparable, as shown in table 1. The UK patients were older at the time of surgery (1.3 years) and compared with Danish patients the tumour height was lower by 1.4 cm (95% CI 1.1 to 1.7, p<0.001).

LARS scores were provided by 1401 patients, the mean (range) age was 64 (29–92) years and 42% (586/1401) were female. The mean (range) tumour height was 9.9 cm (0–15 cm) from the anal verge, 63% (885/1401) received a defunctioning stoma which was subsequently reversed. All defunctioning stomas were reported as ileostomies, with no reported colostomies. A TME was performed in 67% and a PME in 33% (473/1392) of patients. Outcome data were reported 4.9 (2.0) years after surgery. The mean (SD) LARS score was 25.0 (11.6), with no LARS reported by 33.7% (472/1401), minor LARS by 23.3% (327/1401) and major LARS by 43.0% (597/602) of patients. The mean LARS score was statistically higher in the UK patients compared with the Danish patients (UK: 26.0 (11.4) vs DK: 24.5 (11.6), p=0.014). However, categorical (by type) comparison did not significantly differ between cohorts, as shown in table 2.

Missing data

The overall response rate of the LARS PROM was 80% (493/579) and 87% (938/1078) for the UK and DK, respectively. Missing responses were identified in 12 UK questionnaires, hence 2.6% (12/463) of responses. These were handled by multiple imputation techniques. The LARS score did not significantly differ between the reference data and the postimputation dataset; mean (SD) of 26.11 (11.39) and 26.04 (11.46) (p=0.92). The imputation dataset was used for all of the UK cohort analysis. The Danish dataset had no missing responses. Predictor variables were missing for 41 UK patients (73% (30/41) due to TME status) and 224 Danish patients (90% (201/224) due to node or T stage status). The missing data are listed in table 1. Hence, data available for regression analysis included 422 UK patients and 737 Danes.

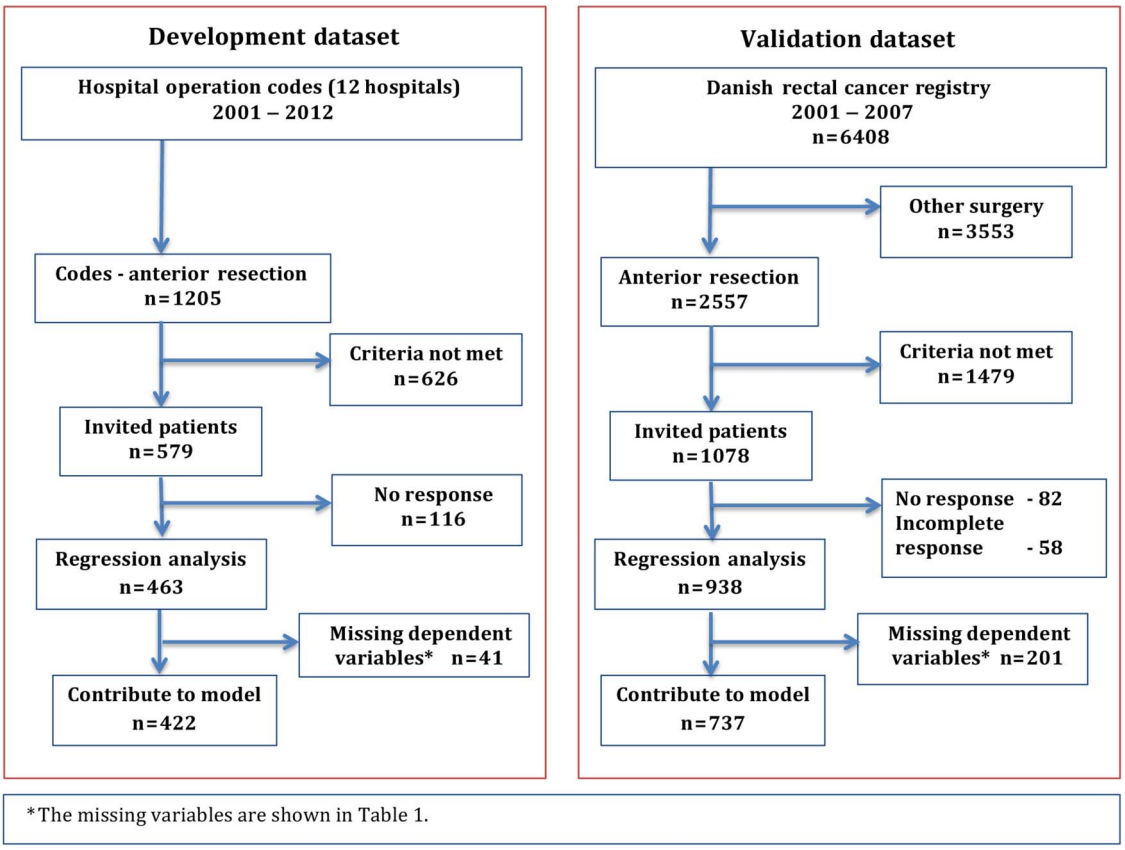

Figure 1 Diagram representing patient flow in the development (UK) and validation (Denmark) datasets.

Model development

Following univariate analysis, we applied LASSO methods in the two cohorts separately. Figure 2 shows selected predictors and their regression coefficients for both the development and validation models and online supplementary appendix 2 reports the regression analysis for each variable by ordinary least squares (OLS). LASSO identified tumour height, TME status and preoperative radiotherapy in both cohorts. In addition, LASSO identified age at surgery, male gender and presence of stoma for the Danish cohort as contributive model predictors. The minimum Mallow's Cp statistic was highly acceptable and comparable between models (Cp: 7.5 vs 5.5).[25]

Model evaluation

In this case, we first derived the fitted values from the UK and DK models separately using the UK data (training dataset), and we then estimated the two statistics using the DK dataset (test dataset). Somer's D was found to be 0.26 for the UK and 0.28 for the DK model (diff: −0.19 (−0.21 to −0.11)) and Harrell's C was 0.615 against 0.625 (diff: −0.006 (−0.009 to −0.003)) suggesting small predictive differences. The values for each model were then compared with calibration plots (figure 3). The results suggest the predicted LARS values were commensurate, in quality and magnitude, between the UK and Danish cohorts.

To enhance the model's generalisability, the study inclusion criteria were deliberately broad; patients of all ages (range 29–92 years) were included in both cohorts. However, the robustness or frailty of patients aged over 80 years varies widely, these factors are likely to influence treatment decisions and functional outcomes considerably.[28] For these practical reasons, the nomogram is truncated at age 80 years, implying that 24 (5.1%) UK patients and 33 (3.5%) Danish patients were excluded in this section.

Nomogram and online tool

Figure 4 shows the nomogram to predict bowel dysfunction, that is, predict the LARS score. To demonstrate its straightforward application, we considered five plausible clinical scenarios, as shown in table 3. These were regarded as highly clinically appropriate outcomes by all six raters.

The web-compatible electronic JAVA script applied the model formula: POLARS Score = 44.9561 + (−0.2117 × age) +(−1.014 × gender) + (−1.9655 × PME) + (0.6374 × height) +(0.7817 × stoma) + (3.3049 ×Pre - Operative Radiotherapy)

Available at: **http://www.pelicancancer.org/bowel-cancer-research/polars**. The codes for each variable are: (1) gender—0=male, 1=female. (2) Age—continuous variable/age as an integer. (3) TME=1, PME=0. (4) Tumour height (distance from the anal verge)—integer 0–15. (5) Defunctioning ileostomy—0=no, 1=yes. (6) Preoperative radiotherapy—0=no, 1=yes.

DISCUSSION

This study has achieved stated objectives by using two large independent but comparable international datasets, to identify, develop and validate a tool that predicts for long-term bowel dysfunction. The key variables identified from both cohorts were age, gender, tumour height from the anal verge, use of defunctioning ileostomy, preoperative radiotherapy and a TME compared with a partial, mesorectal excision.

Several studies have reported that the closer the tumour is to the anal verge the greater the risk of bowel dysfunction,[12 29–31] particularly when a restorative intersphincteric resection is performed.[32] Similarly, TME and preoperative radiotherapy are

Table 1 Comparison between the inclusion criteria and predictor variables in the development dataset (UK) and the validation dataset (Denmark)

N	Development UK (n=463)	Validation Denmark (n=938)	Data set comparison	
			Difference mean (SE)	OR (95% CI)*
Patients contributing to model	422	737		
Inclusion criteria	The same inclusion criteria			
Recruitment period	2001–2012	2001–2007		
Time from surgery to LARS score, years				
Mean (SD)	5.2 (2.4)	4.7 (1.7)	0.49 (0.11)‡	
[range]†	[1.5–12.4]	[2.0–8.1]		
Age at surgery, years				
Mean (SD)	64.9 (10.0)	63.6 (10)	1.25 (0.56)‡	
[range]	[29–92]	[34–91]		
Gender				
Male, n (%)	279 (60.3)	536 (57.1)		1.06 (0.96 to 1.16)
Tumour height				
Mean (SD), cm	9.0 (3.3)	10.4 (2.9)	−1.4 (0.17)§	
[range]	[1–15]	[1–15]		
Missing	1	7		
pT-stage				
T1 and 2, n (%)	242 (53)	308 (41)		0.81 (0.72 to 0.90)
T3, n (%)	199 (43)	418 (56)		1.28 (1.13 to 1.44)§¶
T4, n (%)	18 (4)	19 (3)		
Missing	4	201		
pN-stage				
Negative	306 (69)	550 (74)		0.94 (0.87 to 1.01)
Positive	136 (31)	191 (26)		
Missing	21	197		
Defunctioning stoma				
n, (%)	362 (80)	513 (55)		1.46 (1.36 to 1.58)§
Missing	0	0		
Surgery				
TME	343 (80)	555 (59)		1.36 (1.26 to 1.45)§
PME	90 (20)	383 (41)		
Missing	30	0		
Radiotherapy, n (%)				
Preoperative	145 (32)	191 (20)		1.55 (1.29 to 1.87)§
Postoperative	3 (0.7)	2 (0.2)		
Preoperative radiotherapy				
None	314 (68)	747 (80)		
Short course	60 (13)	95 (10)		
Long course	85 (19)	96 (10)		
Missing	4	0		
Chemotherapy, n (%)				
Preoperative	88 (19)	76 (8)		4.91 (3.73 to 6.46)§
Postoperative	148 (32)	62 (7)		2.36 (1.78 to 3.15)§

*ORs are reported for the discrete data with the development dataset as the reference value.
†14 missing values.
‡<0.05.
§<0.001.
¶OR by ≤pT2 vs >pT2.
LARS, Low Anterior Resection Syndrome; PME, partial mesorectal excision; TME, total mesorectal excision.

well-established risk factors.[8 29–31 33] Constructing a colonic J pouch or transverse coloplasty has been reported to improve anorectal function, particularly in the first postoperative year, but the sparse reports of long-term follow-up suggest that beyond 1 year a reservoir does not significantly improve function compared with an end-to-end anastomosis.[34] Anastomotic leak has also been shown to increase the risk of bowel dysfunction,[8] however, this information is not available preoperatively and cannot contribute to a preoperative model.

Fashioning a stoma, a defunctioning ileostomy in all reported cases, was found to significantly impair bowel function in the group overall. This association has been reported previously.[35] The pathophysiology is believed to relate to disuse colitis and a prolonged period without restoration of bowel continuity, which may lead to irreversible colon and rectal atrophy.[36] Short chain fatty acid enemas and timely stoma reversal are established treatments,[37] however, they are of limited efficacy, and other strategies are required.

Table 2 Comparison between the outcome variable (LARS score) for the development (UK) and the validation (Denmark) datasets

	UK	Denmark	
N	463	938	p Value
LARS score mean (SD)	26.0 (11.4)	24.5 (11.6)	0.014*
LARS categories n (%)			
Zero score	22 (4.8)	48 (5.1)	0.096†
No	116 (25.1)	286 (30.5)	
Minor	106 (22.9)	221 (23.6)	
Major	219 (47.3)	383 (40.8)	

*Mean difference 1.51 (95% CI 0.22 to 2.80).
†Pearson $\chi^2(3)=6.35$.
LARS, Low Anterior Resection Syndrome.

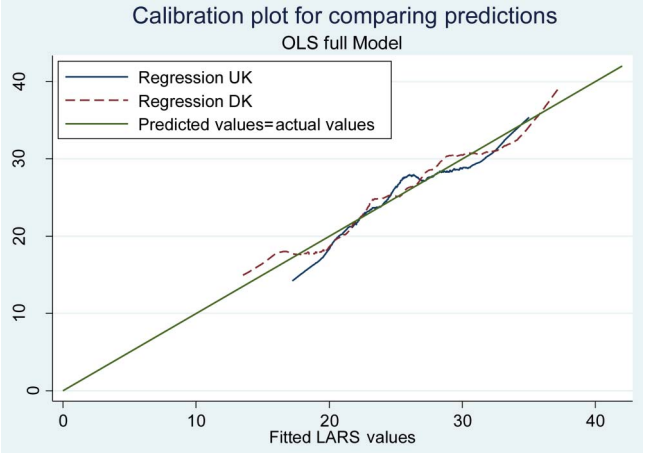

Figure 3 A calibration plot comparing the actual Low Anterior Resection Syndrome (LARS) values with the values predicted by the UK model and the Danish model. DK, Denmark.

The relationship between age and bowel dysfunction was rigorously evaluated. We established that younger patients reported a greater degree of symptom severity. Although this finding is counterintuitive, it has confirmed the findings reported in a binary regression by Bregendahl *et al*.[38] We believe this reflects case selection with some elderly patients, in whom there is underlying sphincter dysfunction or frailty, proceeding to an abdominoperineal excision (APE). It is also plausible that colonic dysmotility, which is associated with ageing,[39] reduces the degree of urgency and bowel frequency resulting in a lower LARS score. This relationship requires further investigation and future studies should also consider patient medication.

This study has the following strengths. First, as the *National Cancer Survivorship Initiative* emphasises, health-related quality of life is one of the most important outcomes from a patient's perspective and patients should be informed and prepared for the consequences of treatment as early as possible,[40] yet in current practice this is frequently overlooked.[13] Second, to our knowledge this is the first tool for predicting postoperative bowel dysfunction in patients with rectal cancer. We have used the LARS score, which is an internationally validated patient-reported outcome measure (PROM) and the model has been developed in a large dataset with external validation in a separate large international dataset. The use of objective statistical methods enabled us to eliminate bias and enhance model validity, and analysis of two cohorts enabled a comparison as well as increased power and robustness. Third, we evaluated various interactions but they neither reached statistical significance nor contributed to the model.

As with any observational study, there were several important factors that we were unable to control. These including socioeconomic status,[41] comorbidities such as depression[42] and the role of self-efficacy, self-management and social support.[43] However, the reasonable CIs for the model predictions when scenarios were evaluated, the calibration plots and the thorough validation we implemented indicate that these models are robust. It is necessary to wait at least 1 year to allow bowel symptoms to stabilise before assessing LARS, which may introduce bias due to dropout from recurrence and death. However, inclusion criteria were clearly defined, participating consultants provided consecutive data and LARS completion rates exceeded 80%. Therefore, these cohorts represent the preoperative sample in closest possible way.

As with most independently collected datasets used for external validation, despite using the same inclusion criteria there were some differences between the two cohorts. The UK patients completed PROMs 6 months later from their date of operation, however, long-term health-related quality of life studies suggest bowel function has stabilised in this group by 36 months and it is unlikely to have impact clinically.[10] Anterior resections were performed for lower tumours (1.4 cm nearer on average to the anal verge) in the UK compared with DK. It has been established that more patients with low rectal cancers receive chemoradiotherapy,[44 45] and are more likely to require defunctioning ileostomies.[46] Additionally, low rectal cancer and radiotherapy appears to be associated with greater bowel dysfunction.[29] Although the tumours were on average lower in the

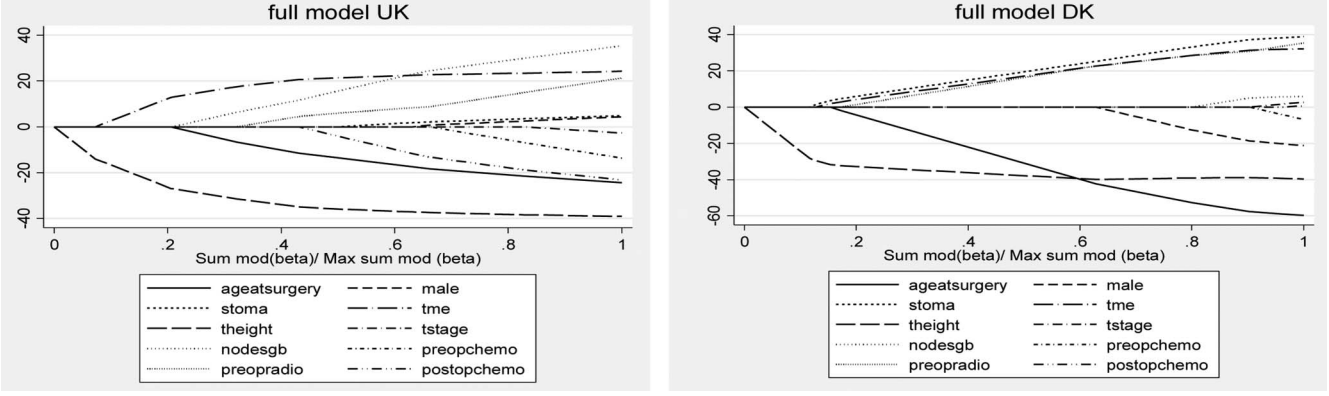

Figure 2 LASSO regression plots. DK, Denmark; LARS, Low Anterior Resection Syndrome; TME, total mesorectal excision.

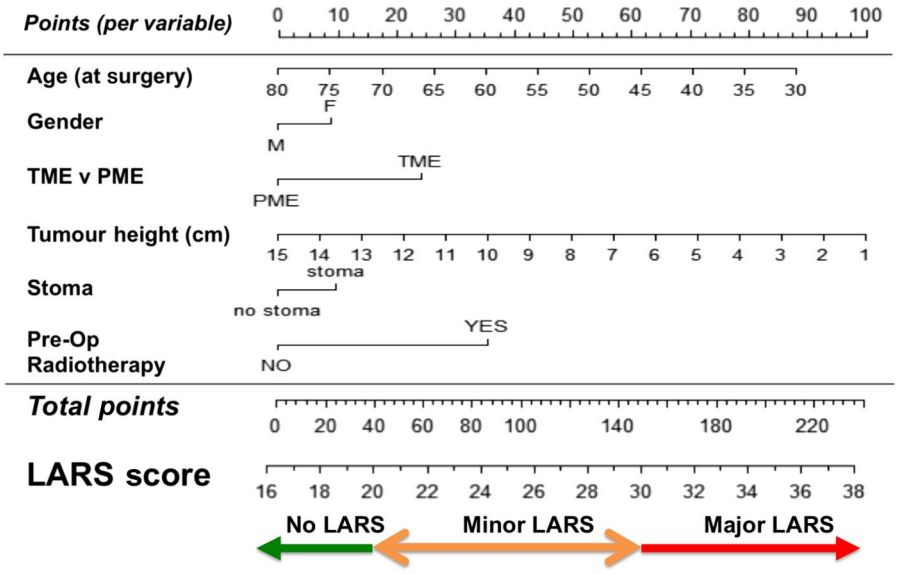

Figure 4 The Pre-Operative LARS (POLARS) score nomogram indicates the risk of postoperative bowel dysfunction among patients due to undergo a restorative anterior resection for rectal cancer. Instructions: locate the patient's age and draw a straight line upwards from the variable to determine how many points towards the predicted LARS score the patient receives for their age. Repeat the process for each of the six variables. Sum the points achieved for each of the predictor variables. Locate the final sum on the Total Points axis. Draw a straight line down to find the patients predicted LARS value. The LARS categories are: No LARS, score <20; minor LARS, 20≤score<30 and major LARS, score ≥30. PME, partial mesorectal excision. TME, total mesorectal excision. LARS, Low Anterior Resection Syndrome. Alternatively, the online calculator may be used via **http://www.pelicancancer.org/bowel-cancer-research/polars**.

Table 3 A series of clinical scenarios inputted into the prediction model in order to generate the expected LARS score (95% CIs)

Scenarios	LARS score UK alone (95% CI)	DK alone
Scenario 1		
Age 65, tumour 8 cm, TME		
Radiotherapy	27 (24.03 to 30.03)	28 (25.80 to 31.20)
No radiotherapy	25 (22.64 to 27.85)	24 (23.14 to 26.06)
Scenario 2		
No radiotherapy, age 65, TME		
Low rectum (4 cm tumour height)	29 (26.09 to 33.85)	29 (26.47 to 31.71)
Mid rectum (8)	25 (26.64 to 27.85)	24 (23.14 to 26.06)
Upper rectum (12)	20 (17.97 to 23.08)	20 (18.97 to 21.24)
Scenario 3		
Radiotherapy, age 65, TME		
Low rectum (2)	31 (27.65 to 35.85)	31 (28.91 to 34.21)
Mid rectum (8)	27 (24.03 to 30.03)	27 (25.28 to 28.86)
Upper rectum (14)	22 (19.28 to 25.34)	22 (20.77 to 24.39)
Scenario 4		
No radiotherapy, TME, 8 cm tumour		
60 years	27 (24.40 to 30.55)	27 (26.14 to 29.74)
70 years	26 (23.57 to 29.66)	26 (24.38 to 28.03)
80 years	25 (24.43 to 28.97)	24 (22.44 to 26.50)
Scenario 5		
No radiotherapy, age 65, tumour 9 cm		
PME	26 (23.33 to 29.16)	26 (24.61 to 28.04)
TME	27 (25.83 to 29.72)	29 (27.83 to 30.28)

DK, Denmark; LARS, Low Anterior Resection Syndrome; PME, partial mesorectal excision; TME, total mesorectal excision.

UK cohort, a proportionate difference in clinical management was noted and similarly the reported bowel dysfunction was marginally worse. Furthermore, when the German translation of the LARS score was validated against Danish data, the reported tumour heights were equivalent to the UK (UK—9.0 (SD 3.3) cm; Germany 8.7 (SD 3.5) cm).[17] The frequency of patients receiving stomas and neoadjuvant therapy were similar and the proportion of patients with major and minor LARS was consistent (Germany major LARS 47.8% (99/207), minor LARS 22.9% (42/207)).[17] These differences may explain why stoma reached statistical significance for the Danish cohort only. However, the comparable models and overlapping calibration plots suggest that overall the cohorts are similar.

Finally, advances in medical practice and changes in treatment may decrease the predictive value of the model. For example, small improvements to bowel function and quality of life may be achieved with transanal irrigation, sacral nerve stimulation, pelvic floor exercises, biofeedback and electromyography.[47–52] Advances in radiotherapy appear to reduce collateral tissue damage and may minimise long-term bowel dysfunction.[53] Furthermore, Andreyev *et al*[15] report that implementing a detailed clinical algorithm designed to identify and modify each specific symptom improves post-treatment GI patient-reported outcomes after pelvic radiotherapy. The model should be updated in 5–10 years time to enable reassessment of the impact of these clinical advances.

Applicability of the Pre-Operative LARS score online tool and nomogram

The Pre-Operative LARS score (POLARS) calculates a prediction of the LARS score in order to estimate the patient's post-operative bowel function. The development of a nomogram and the online tool allows the model to be used in clinical practice. This has the potential to personalise care during the multidisciplinary team (MTD) meeting and prior to patient consent.

This information will help to prepare patients for the consequences of treatment. It is increasingly apparent that preoperative patient education and counselling reduce symptoms and improve postoperative quality of life.[40 54–56] We recommend that patients with a score indicating a moderate or high risk of bowel dysfunction (POLARS score >20) should be provided

with the Macmillan Cancer Support patient guide called 'managing late effects of bowel cancer treatment'.[57]

Given the impact that bowel dysfunction has on quality of life, social functioning and employment, it is also important to highlight that from a medicolegal perspective the POLARS score may help to provide evidence that a detailed preoperative discussion about postoperative bowel dysfunction has taken place.

There may also be role for using POLARS in clinical trials that assess postoperative bowel function. This predictive tool may help to identify the high-risk patients most likely to benefit from clinical intervention or it could be included as a stratification criterion during randomisation.

The treatment options for patients with rectal cancer, particularly low rectal cancer, are becoming increasingly complex. The emphasis is on optimal preoperative staging and patient-tailored therapy. We believe POLARS should be used routinely during MDT Meeting to aid decisions. For example, a female aged 65 years with a tumour 5 cm from the anal verge has staging indicating a 'good prognosis tumour' and the oncological gains from preoperative radiotherapy are likely to be marginal.[45 58] Undergoing a TME dissection with preoperative radiotherapy, her predicted LARS score is almost 31, which suggests major LARS. If preoperative radiotherapy were omitted, the predicted LARS score would be 27, which suggests minor LARS. In this context, the functional gains from avoiding treatment may be considerable and surgery alone may be recommended.

Patients with readily resectable cancers may be offered preoperative radiotherapy with a view to achieving a complete clinical response, this controversial approach is called non-operative management or deferral of surgery.[59–61] One-third of these patients may avoid surgery but two-thirds may require surgery despite preoperative radiotherapy.[59] POLARS may inform this discussion by predicting the effect of (potentially avoidable) radiotherapy on bowel dysfunction.

Finally, patients with locally advanced disease require chemoradiotherapy[62 63] and it may be unclear whether restorative resection or an APE is appropriate. There is no clear evidence to suggest a favourable quality of life for one approach over the other.[31 64 65] Therefore, individualised prediction of postoperative bowel function may help to guide this treatment decision.

SUMMARY

This study has achieved the stated aim of developing, and externally validating, a preoperative predictive model. The POLARS model provides patients with an individualised quantifiable measure of their predicted LARS score. Hence, for the first time, a patient with rectal cancer can be preoperatively informed of their likely postoperative bowel function. This will act as an adjunct, but not a substitute, for clinical assessment prior to the MDT discussion and it may help to guide treatment decisions.

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Contributors NJB, GeBo and BJM: conception, design and manuscript draft. NJB and KJE: data extraction. NJB, BJM, RG-J, GrBr, TJ and KJE contributed to patient recruitment. GeBo and NJB: analysis of the data. All authors contributed to revising the article for important intellectual content and approved the final manuscript.

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Development and external validation of a nomogram and online tool to predict bowel dysfunction following restorative rectal cancer resection: the POLARS score

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Notes