Low Anterior Resection Syndrome Score

Development and Validation of a Symptom-Based Scoring System for Bowel Dysfunction After Low Anterior Resection for Rectal Cancer

Katrine J. Emmertsen, MD,*† and Søren Laurberg, MD*†

Objective: The aim of this study was to develop and validate a scoring system for bowel dysfunction after low anterior resection (LAR) for rectal cancer, on the basis of symptoms and impact on quality of life (QoL).

Background: LAR for rectal cancer often results in severe bowel dysfunction (LAR syndrome [LARS]) with incontinence, urgency, and frequent bowel movements. Several studies have investigated functional outcome, but the terminology is inconsistent hereby complicating comparison of results.

Methods: Questionnaires regarding bowel function was sent to all 1143 LAR patients eligible for inclusion identified in the national Colorectal Cancer Database. Associations between items and QoL were computed by binomial regression analyses. The important items were selected and regression analysis was performed to find the adjusted risk ratios. Individual score values were designated items to form the LARS score, which was divided into “no LARS,” “minor LARS,” and “major LARS.” Validity was tested by receiver operating characteristic (ROC) curve and Spearman’s rank correlation and discriminant validity was tested by Student t tests.

Results: A total of 961 patients returned completed questionnaires. The 5 most important items were “incontinence for flatus,” “incontinence for liquid stools,” “frequency,” “clustering,” and “urgency.” The range (0–42) was divided into 0 to 20 (no LARS), 21 to 29 (minor LARS), and 30 to 42 (major LARS). The score showed good correlation and a high sensitivity (72.54%) and specificity (82.52%) for major LARS. Discriminant validity showed significant differences between groups with and without radiotherapy (P<0.0001), tumor height more or less than 5 cm (P=0.0001), and total mesorectal excision/ partial mesrectal excision (P=0.0163).

Conclusions: We have constructed a valid and reliable LARS score correlated to QoL—a simple tool for quick clinical evaluation of the severity of LARS.


During the past decades, treatment and cure of rectal cancer have improved markedly. These advancements have resulted in more patients receiving sphincter-preserving surgery with a low colorectal or a coloanal anastomosis to avoid permanent colostomy. Unfortunately, many of these patients develop severe bowel dysfunction resulting in incontinence for flatus and/or feces, urgency, and frequent bowel movements. This combination of symptoms after LAR is referred to as LAR syndrome (LARS) and can be associated with a negative impact on quality of life (QoL).1,2

In a recent Cochrane review on the effect of reconstruction on morbidity after colorectal surgery for rectal cancer, the conclusion was that the addition of enterocutaneous fistula and morbidities was a significant burden and a consequence of the reconstructive surgery.3 Unfortunately, the use of many different scales for reporting the function made a meta-analysis impossible. For instance, fecal incontinence was reported using 7 different scales. Therefore the results were reported in tabular form and discussed qualitatively only.4

To be able to assess the functional outcome after surgery and to compare results from different surgical approaches and from different studies, it is important that uniform terminology and scales are used. The Wexner incontinence score, the Rockwood Fecal Incontinence Severity Index, or the St Marks’ Fecal Incontinence Grading Score are used in several studies to assess the incontinence in LARS patients.5–12 Although very useful in assessing simple incontinence, they are much too narrow and specific for assessing the complicated dysfunctions in LARS, which in many cases include fragmentation and urgency.13 Also these scores do not incorporate the degree of subjective bother or impact on QoL. A scoring system based purely on quantification of symptoms, without considering the degree of subjective bother, could give a wrong impression of the impact on the patient’s life. A scoring system used for the assessment of the function should therefore be constructed by taking incidence and subjective bother impact on QoL for each symptom into consideration.

The objective of this study was to develop and validate a scoring system based on the symptoms and impact on QoL to evaluate bowel dysfunction after LAR.

METHODS

The Danish Colorectal Cancer Group has prospectively registered all patients diagnosed with rectal cancer in Denmark since May 2001. The database contains information on patient characteristics, stage of disease, and treatment. Through this database, patients eligible for inclusion were identified. The inclusion criterion was curative LAR for nondisseminated rectal cancer during the period of May 2001 to April 2007. According to national guidelines, LAR includes all patients receiving a total mesorectal excision (TME) or a partial mesrectal excision (PME) for rectal cancer with the creation of an anastomosis. Through cross-checking with the National Patient Registry, patients eligible for this study were identified. The exclusion criteria were the following: disseminated or recurrent disease, younger than 18 years, previous cancer excluding spinocellular and basocellular carcinoma of the skin, mental dementia, and the inability to read and understand the Danish language. Data on the patients’ mental states and their language abilities were not available through registries and was therefore obtained by contacting their general practitioners.

Of 2557 patients meeting the inclusion criteria, 1414 patients met the exclusion criteria. The remaining 1143 patients were contacted by mail during the spring of 2009 and asked to participate in the study (Fig. 1). The study was approved by the Regional Committee on Biomedical Research Ethics and supported by the Danish Cancer Foundation.

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DEVELOPMENT OF THE BASIC QUESTIONNAIRE

The primary draft of the questionnaire was based on a thorough review of the literature, a review of the available questionnaires/scoring systems, a panel of experts, and a pilot testing. The questionnaire was then validated by test–retest reliability and semistructured interviews.

Literature Review

Medline was searched by using the MeSH term “Rectal cancer” and the terms “bowel function” and “functional outcome.” The papers were reviewed regarding the questionnaires and solitary items used in each study. A comprehensive list of possible items was generated on the basis of this literature.

Available Questionnaires/Scoring Systems

The Wexner score, the St Marks’ incontinence score, and the Cleveland constipation score were assessed and incorporated in the draft so that each score can be calculated from the answered questionnaire.13–15 Other available questionnaires in Danish and English regarding bowel function were reviewed, and questions regarded relevant for LARS patients were added to the draft of the questionnaire. These include the Fecal Incontinence Severity Index,12 the Fecal Incontinence Quality of Life scale16 the Inflammatory Bowel Disease Questionnaire17 the Irritable Bowel Syndrome Quality of Life instrument18 and many others.

Panel of Experts

The primary draft of questions was sent to a group of 7 experts on bowel function and/or questionnaires. The experts consisted of four colorectal surgeons, one gastroenterologist, and one oncologist all with special interests within the field of colorectal function and/or cancer, and to one epidemiologist with major experience in questionnaire studies and development. Each item was discussed at a conference, and a second draft of the questionnaire was formed on the basis of these discussions. The second draft was mailed to the experts for further comments and revisions until all were satisfied.

Pilot Testing

Randomly selected eligible patients were approached in the day clinic. They were asked to read the questionnaire and then go through a semistructured interview addressing each question with regard to relevance, importance, and wording. They were also asked whether they could think of anything else important that was missing in the draft. After the first 10 interviews, the questionnaire was revised according to the results, and the second round of pilot testing was performed in a similar fashion. This second test was performed on 15 patients and gave no reason for further changes.

Test–Retest Reliability

A revision of patient charts identified 35 patients who had undergone curative LAR for rectal cancer at the Colorectal Surgical Unit, Aarhus University Hospital, Denmark, in the period of January 2006 to October 2007. These were contacted by mail and asked to participate in the testing of the questionnaire. Of the 35 eligible patients, 29 returned the questionnaires. These patients were then sent the second questionnaire and all patients returned this questionnaire with a mean interval of 14 days.

Semistructured Interviews

Through revision of patient lists over 5 consecutive days in the day center at the Colorectal Surgical Unit, Aarhus University Hospital, Denmark, 6 former rectum cancer patients were identified and asked to participate. The inclusion and exclusion criteria were as previously described. The patients included 2 women and 4 men and had a mean age of 68.5 years hereby reflecting the population of the Danish rectal cancer patients. The bowel function questionnaires and a list of exploratory questions regarding the questionnaire (see Table 1) were sent to the patients some days before the interview, and the patients were asked to consider and evaluate each question accordingly. Each patient was then interviewed face-to-face for 30 to 45 minutes. The interview was based on the questions in Table 1, but the interviewer and the patient were not restricted to the questions and could elaborate freely on the subject.

STATISTICAL ANALYSIS

The test–retest reliability of the questionnaire was assessed by the Cohen’s Kappa with a kappa value of less than 0.4 regarded as poor or moderate agreement, 0.4 to 0.75 as fair to good agreement, and more than 0.75 as excellent agreement. For all ordinal outcomes (24 of 27 questions), weighted kappa with linear weights were used taking into account the degree of disagreement between the first and the second answer. A nonweighted kappa was used for nominal and dichotomous outcome. The threshold for considering a question as
TABLE 1. The Questions for the Semistructured Interviews

<table>
<thead>
<tr>
<th>General questions for the semi-structured interview</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did you find any question difficult to understand?</td>
</tr>
<tr>
<td>Were any questions transgressing/taboo-breaking for you?</td>
</tr>
<tr>
<td>Did you miss any questions you think could be relevant for exploring the bowel function after the operation?</td>
</tr>
<tr>
<td>Is the layout good? Is structure of the questionnaire logical? Is the font and size easily readable?</td>
</tr>
<tr>
<td>Do you have any additional comments to the questionnaire?</td>
</tr>
<tr>
<td>For each question, the patient is asked:</td>
</tr>
<tr>
<td>Is this question easy/difficult to understand?</td>
</tr>
<tr>
<td>How easy/hard did you find it to place yourself in one of the answering categories?</td>
</tr>
<tr>
<td>Do you have any suggestions on how the question should be better phrased?</td>
</tr>
</tbody>
</table>

Valid and reliable was set at $\alpha \geq 0.4$. Reliability was tested on the original answering categories. All statistical analyses were performed using STATA 10 (StataCorp LP, College Station, TX).

ITEM SELECTION FOR THE LARS SCORE

The score was developed on the basis of the questionnaire results from a randomly selected half of the study population ($n = 483$). The primary results were reviewed and for all valid and reliable questions, the response options were summarized into 3 to 4 options depending on the distribution of answers and the relative risks (RRs). The impact on QoL was assessed by a single question—“On overall, how much is your QoL influenced by your bowel dysfunction?” with the response options “not at all,” “a little,” “some,” or “a lot.” These options were then combined into 2 groups reporting no/minor or some/major impact on QoL. The questions were correlated to the impact on QoL, and the associations were calculated by binomial regression analyses. Binomial regression, like logistic regression, is a type of generalized linear model. The response is the logarithm of the probability of the event adjusted for covariates (in logistic regression the response is the log odds ratio), which allows the parameters to be interpreted as functions of RRs. All items not significantly associated with impact on QoL were excluded from the multivariate model. The criterion for including an item in the multivariate analysis was $P < 0.05$. Hence, items were grouped into 4 different areas known to be associated with LARS (incontinence, emptying difficulties, urgency, and frequency). For each group, multivariate analysis was performed and the RR for each item was computed making corrections for the other independent variables in the group. The items for the scale were selected on the basis of the highest adjusted RRs and on an estimation of clinical importance. An adjusted RR $> 2.5$ ($P < 0.05$) within each group was the criterion for inclusion into the multivariate analysis for the final score, regardless of the exact significance. Finally, the multivariate analysis was repeated with the chosen variables, and the corrected RRs were computed. To make an additive model based on the sum of scores, the logarithmic values of the RRs were calculated, multiplied with 10, and rounded off to get a score value for each symptom. The individual maximal scores for each symptom were added to make the maximal LARS score. The LARS score was plotted against the impact on QoL, and on the basis of this plot and mean values of LARS score, the range of the score was divided into groups of “no LARS,” “minor LARS,” and “major LARS.”

VALIDITY OF THE LARS SCORE

The validity of the LARS score was tested on the other half of the study population ($n = 478$). The sensitivity and specificity of the LARS score in predicting the impact on QoL was assessed by receiver operating characteristic (ROC) curves of the score versus groups reporting no/minor or some/major impact on QoL. For each group, the mean and standard deviation of the LARS score was calculated, and score differences between groups were tested by the Kruskal-Wallis test. A 3-by-3 table depicting LARS-group versus the impact on QoL (no, little, and some/major) was used to assess the prediction model by calculating the percentage of perfect fit, moderate fit, and no fit.

The validity was also evaluated by testing whether the score was able to show differences between groups of patients on the basis of clinical variables. This was tested by Student $t$ tests with unequal variance—our hypothesis was that patients receiving radiotherapy and patients with low tumors (0–5 cm from the anal verge) would have higher scores. Also patients receiving a TME would have higher scores than those resected with a PME.

RESULTS

Validity of the Questionnaire

The test–retest reliability indicated kappa values of 0.46 to 0.95 hereby showing fair to good/excellent agreement in all 27 questions. The semistructured interviews showed some difficulties in the exact interpretation of 7 of the questions, some being ambiguous and one missing an important response category. These questions were not used in the LARS score. Overall, the questionnaire was found highly reproducible and valid in LAR patients.

The LAR Patients

Among the 1143 patients included in the study, 1061 (92.8%) responded. Of those, 42 replied that they had been through a reoperation with creation of a permanent colostomy and could therefore not participate. In total, 961 had completed the full questionnaire and were eligible for participation in this study. The distribution was 405 women and 556 men, with a mean age of 68.5 (range: 36.5–95.3) years. The mean age at the time of the operation was 63.8 (range: 33.9–91.6) years, and mean follow-up time was 55.5 months (range: 24.0–95.9) months. Of the total cohort, 573 patients had received a TME. Patient characteristics and treatment data are shown in Table 2.

Item Selection

The 5 most important items were “incontinence for flatus,” “incontinence for liquid stool,” “frequency of bowel movements,” “clustering of stools,” and “urgency.” All items showed significant correlation to impact on QoL and were designated score values accordingly (see Table 3). The range of the score was 0 to 42 with the limits of 0 to 20 (no LARS), 21 to 29 (minor LARS), and 30 to 42 (major LARS).

Validity of the LARS Score

The ROC curve (Fig. 2) showed an area under the curve $= 0.8525$ and a high sensitivity (72.5%) and specificity (82.52%) for identifying patients with a major impact on QoL with a cut off at 30 points. The prediction model showed perfect fit in 62.21%, moderate fit in 31.94%, and no fit in 5.85% (see Table 4).

For respondents in the validation group reporting no impact on QoL ($n = 121$) the mean LARS score was 12.98 (SD 10.3), for those reporting minor impact on QoL ($n = 164$) the mean score was 23.24 (SD 9.4), and for those reporting some/major impact on QoL ($n = 193$) the mean score was 32.75 (SD 7.75) (Fig. 3). Differences in LARS score between groups were highly significant ($P < 0.001$, Kruskal-Wallis test). The Student’s $t$-test showed significant differences between group means with and without radiotherapy ($P < 0.0001$), tumor height ($P = 0.0031$) and TME/PME ($P = 0.0193$).
TABLE 2. Patient and Treatment Characteristics of Participants (n = 961)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Development Group (N = 483)</th>
<th>Validation Group (N = 478)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>274 (56%)</td>
<td>282 (59%)</td>
</tr>
<tr>
<td>Female</td>
<td>209 (44%)</td>
<td>196 (41%)</td>
</tr>
<tr>
<td>Age at time of survey, years (range)</td>
<td>68.0 (37.8–93.1)</td>
<td>68.9 (36.5–95.3)</td>
</tr>
<tr>
<td>T stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>38 (8%)</td>
<td>37 (8%)</td>
</tr>
<tr>
<td>T2</td>
<td>109 (23%)</td>
<td>96 (20%)</td>
</tr>
<tr>
<td>T3</td>
<td>222 (46%)</td>
<td>214 (45%)</td>
</tr>
<tr>
<td>T4</td>
<td>10 (2%)</td>
<td>11 (2%)</td>
</tr>
<tr>
<td>N stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>278 (58%)</td>
<td>276 (58%)</td>
</tr>
<tr>
<td>N1</td>
<td>73 (15%)</td>
<td>67 (14%)</td>
</tr>
<tr>
<td>N2</td>
<td>37 (8%)</td>
<td>28 (6%)</td>
</tr>
<tr>
<td>Age at time of operation, years (range)</td>
<td>63.4 (34.2–89.0)</td>
<td>64.3 (33.9–91.6)</td>
</tr>
<tr>
<td>Follow-up time, months (range)</td>
<td>55.0 (24.0–95.9)</td>
<td>56.0 (24.2–95.7)</td>
</tr>
<tr>
<td>TME</td>
<td>285 (59.0%)</td>
<td>288 (60.3%)</td>
</tr>
<tr>
<td>Distance to anal verge, cm (±SD)</td>
<td>10.4 (±2.8)</td>
<td>10.4 (±2.9)</td>
</tr>
<tr>
<td>Temporary diverting stoma</td>
<td>243 (50.3%)</td>
<td>279 (57.9%)</td>
</tr>
<tr>
<td>Radio-/chemotherapy</td>
<td>103 (21.4%)</td>
<td>98 (20.6%)</td>
</tr>
</tbody>
</table>

*In 224 patients, there was no record of T stage.
†In 202 patients, there was no record of N stage.

TABLE 3. The LARS Score

<table>
<thead>
<tr>
<th>Item</th>
<th>N</th>
<th>%</th>
<th>RR</th>
<th>P</th>
<th>Adjusted RR</th>
<th>LogRR</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incontinence for Flatus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>97</td>
<td>19.8</td>
<td>1</td>
<td></td>
<td>1.00</td>
<td>0.00</td>
<td>0</td>
</tr>
<tr>
<td>&lt; once a week</td>
<td>127</td>
<td>25.9</td>
<td>2.03</td>
<td>0.029</td>
<td>1.50</td>
<td>0.40</td>
<td>4</td>
</tr>
<tr>
<td>≥ once a week</td>
<td>267</td>
<td>54.4</td>
<td>4.67</td>
<td>&lt;0.001</td>
<td>1.93</td>
<td>0.66</td>
<td>7</td>
</tr>
<tr>
<td>Incontinence for liquid stools</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>264</td>
<td>53.8</td>
<td>1</td>
<td></td>
<td>1.00</td>
<td>0.00</td>
<td>0</td>
</tr>
<tr>
<td>&lt; once a week</td>
<td>184</td>
<td>37.5</td>
<td>2.27</td>
<td>&lt;0.001</td>
<td>1.36</td>
<td>0.30</td>
<td>3</td>
</tr>
<tr>
<td>≥ once a week</td>
<td>43</td>
<td>8.8</td>
<td>3.22</td>
<td>&lt;0.001</td>
<td>1.38</td>
<td>0.33</td>
<td>3</td>
</tr>
<tr>
<td>Frequency of bowel movements</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;7 times a day</td>
<td>35</td>
<td>7.1</td>
<td>3.07</td>
<td>&lt;0.001</td>
<td>1.46</td>
<td>0.38</td>
<td>4</td>
</tr>
<tr>
<td>4–7 times a day</td>
<td>147</td>
<td>29.9</td>
<td>1.97</td>
<td>&lt;0.001</td>
<td>1.18</td>
<td>0.17</td>
<td>2</td>
</tr>
<tr>
<td>1–3 times a day</td>
<td>268</td>
<td>54.6</td>
<td>1</td>
<td></td>
<td>1.00</td>
<td>0.00</td>
<td>0</td>
</tr>
<tr>
<td>&lt; once a day</td>
<td>41</td>
<td>8.4</td>
<td>1.42</td>
<td>0.128</td>
<td>1.68</td>
<td>0.52</td>
<td>5</td>
</tr>
<tr>
<td>Clustering of stools</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>85</td>
<td>17.3</td>
<td>1</td>
<td></td>
<td>1.00</td>
<td>0.00</td>
<td>0</td>
</tr>
<tr>
<td>&lt; once a week</td>
<td>222</td>
<td>45.2</td>
<td>4.32</td>
<td>&lt;0.001</td>
<td>2.49</td>
<td>0.91</td>
<td>9</td>
</tr>
<tr>
<td>≥ once a week</td>
<td>184</td>
<td>37.5</td>
<td>10.30</td>
<td>&lt;0.001</td>
<td>2.86</td>
<td>1.05</td>
<td>11</td>
</tr>
<tr>
<td>Urgency</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>144</td>
<td>29.3</td>
<td>1</td>
<td></td>
<td>1.00</td>
<td>0.00</td>
<td>0</td>
</tr>
<tr>
<td>&lt; once a week</td>
<td>221</td>
<td>45.0</td>
<td>4.19</td>
<td>&lt;0.001</td>
<td>2.89</td>
<td>1.06</td>
<td>11</td>
</tr>
<tr>
<td>≥ once a week</td>
<td>126</td>
<td>25.7</td>
<td>10.10</td>
<td>&lt;0.001</td>
<td>4.76</td>
<td>1.56</td>
<td>16</td>
</tr>
</tbody>
</table>

DISCUSSION

We have developed a simple and valid scoring system to evaluate bowel function in patients after a LAR for rectal cancer in the clinical setting. The symptoms after LAR are complicated with elements of incontinence, frequent bowel movements, bowel emptying difficulties, and urge. Several studies have demonstrated that up to 50% to 60% of patients experience daily bowel dysfunction with impact on their QoL. In many studies and clinical settings, different validated incontinence scoring systems have been used to evaluate function after LAR. These are far too simple to reflect the complex symptoms after LAR because they do not incorporate the elements of bowel emptying difficulties and urgency. In addition, these scores do not consider the impact on QoL or subjective bother caused by each symptom but merely reflect the incidence. The impact on QoL is important when assessing bowel dysfunction. A mere count of incontinence episodes or daily defecations does not necessarily differentiate between patients with acceptable function and patients in need of further attention. In our opinion, a symptom scoring system should be based on the impact the different symptoms have on the patients’ lives. Most existing scores are based on a linear scale—giving 1 point for a symptom occurring less than once a month, 2 points for occurring less than once a week, 3 points for occurring less than once a day, and 4 points for daily occurrence. However, the bother of a symptom might not be linear. Krogh et al found all items to be nonlinear in their Neurogenic Bowel Dysfunction Score. Therefore, we decided to base our score on the calculated importance of each item and occurrence based on binomial regression models.
and relative risk. Our calculations showed that, also in our population, there was no linear correlation between occurrence and bother of the symptoms.

Furthermore, the various incontinence scores are too generic to be used in a specific population—especially a population of cancer survivors. When exploring function after a specific condition/disease, one must keep in mind that patient populations differ in regard to what affects their QoL the most. It is not reasonable to assume that a specific symptom will affect different patient populations in the same way. We have, in our population of former rectal cancer patients, found “incontinence for flatus” to have a major significant impact on QoL and have therefore included this item with a score of 7 points (of a maximum total of 42). In the Neurogenic Bowel Dysfunction Score, they found “incontinence for flatus” to have only a minor impact on QoL and therefore assigned only 2 points (of a maximum of 47). Therefore, we must conclude that any given symptom will affect a specific population in a specific way.

In 2005, a new instrument for evaluating bowel function after sphincter-preserving surgery was developed—the Memorial Sloan-Kettering Cancer Center Bowel Function Instrument.20 This scoring system takes all aspects of LARS into consideration and has been through thorough validation. Unfortunately, this score is quite comprehensive and time consuming for completing, calculating, and interpreting the results. Therefore, in our opinion, the score is not optimal for use in the clinical setting.

For clinicians in the daily work, it can be time consuming and difficult to make a proper and detailed evaluation of the function of patients coming for their routine follow-up visits at the day clinic. The main aim of these visits is to make sure the patients show no sign of recurrence of their malignant disease. Therefore, dysfunctions are often not diagnosed properly and remain untreated.

That bowel dysfunction is an important matter for most patients is clear from our exceptionally high response rate. The questionnaire was mailed to eligible patients all over Denmark with no particular attachment to our department and with no monetary incentive. Despite this fact, we received replies from 92.8% of the entire cohort and completely filled-in questionnaires from 84%. Along with the questionnaires we received several personal letters thanking us for taking an interest in their problems and for finally drawing attention to this major problem.

The rigorous methodology of the questionnaire development phase, the large cohort, and the high response rate all add to the strength of our study. The score itself was constructed in close cooperation with an experienced statistician, where the mathematics were constantly being reviewed against clinical knowledge. The large cohort made binomial regression analyses possible and permitted us to do corrections for other overlapping independent variables. The dependent variable in our regression analysis was self-reported impact of bowel function on QoL. In the questionnaire, the 4 possible answers were “not at all,” ”a little,” ”some,” and ”a lot.” When using binomial regression analysis, the dependent variable must be dichotomized with only 2 possible outcomes. This simplifies the outcome and does not evaluate specific subareas of QoL, but that lies beyond the aim of this study, and the dichotomization is necessary for the use of this kind of regression analysis. A correlation to more extensive and validated QoL instruments would support the strength of the study.

We are currently collecting data from a large ongoing prospective study on function and QoL in rectal cancer patients where the LARS score is going to be correlated to the EORTC QLQ-C30 (European Organisation for Research and Treatment of Cancer quality of life questionnaires) results with regard to the different domains of QoL.

By developing the instrument on one population and validating it on a similar but separate population, we have ensured that the instrument is valid on similar populations and not just a product of a skewed selection. When validating a score, one must be aware of the risk of circular arguments if development and validation are performed in the same population. Using a separate, but similar population is one
way to test generalizability. Our large cohort made random selection to the development group or validation group possible without compromising the size of the cohort and, thereby, the ability to perform regression analyses.

That a score is mathematically valid does not necessarily mean it is clinically valid and useful. By checking that the score can detect differences in mean scores between groups of patients known to have high/low risk of severe symptoms, we have supported the validity of the score. We found statistically significant differences in mean scores between groups of patients with or without radiotherapy, with high or low tumors and patients receiving a TME or a PME. As shown in numerous studies, the type of bowel reconstruction is of major importance for the functional outcome. Hence, we would have liked to test differences in scores between straight anastomosis, side-to-end anastomosis, and colonic J-pouch. Unfortunately, information on type of anastomosis has not been recorded in the database and was therefore not available. The differences in LARS score after different types of reconstruction will be evaluated in our ongoing prospective study.

The present score was developed and validated on the answers from 961 patients, all having received a LAR 2 to 8 years earlier. This population constitutes 84% of the entire cohort and therefore represents the population quite well. It can be hypothesized that the remaining 16% could be the patients with the worst function—therefore not feeling up to the challenge of answering our questionnaire. It could also be hypothesized that the remaining 16% are the patients with the best function, because their incentive to participate might be lower. This we do not know. Nevertheless, the respondents are very similar to the whole population with regard to gender, age, type of resection, level of anastomosis, and proportion of patients receiving radiotherapy. Therefore, we believe that our cohort is representative for the entire population. Because of the study design, our study population does not include patients in the early postoperative phase. These data were not available from the National Colorectal Cancer Database because of a lag time in the registration of patients and because of the delay between the time our primary data were extracted and the time the questionnaires were sent out. The usefulness of the score on early postoperative symptoms will be evaluated in the upcoming prospective study.

So far, the score has been developed and validated in a Danish population and in the Danish language. The impact of bowel function on QoL has been shown to differ between different cultures. Therefore, rigorous validation must be performed in other languages and cultures. We are currently working on a validation in English, Swedish, German, Spanish, and French in their respective countries. The nonvalidated English translation of the LARS score and the scoring instructions are seen in Appendix 1 and 2, respectively. Please await validation before use.

In developing this score, we chose to do a comprehensive item reduction from our first comprehensive questionnaire containing 27 questions. This can be argued to reduce the precision of the final score because it only takes 4 aspects of the bowel function into account. Nevertheless, it was our intention to make a simple score that can be filled in and calculated within a few minutes. The form can be filled in by the patients themselves in the waiting room at the day clinic and calculated by the nurse or surgeon in less than 1 minute. This will give a quick evaluation of the patient’s function and indicate for the surgeon whether this should be an area of focus for the consultation in progress.

In conclusion, the score can be used in the daily clinical practice to identify patients with LARS and to monitor and control the effect of treatment of LARS. Furthermore, it can be used in scientific studies to identify different factors’ impact on functional outcome after LAR.

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REFERENCES

APPENDIX 1. Bowel Function Questionnaire

The aim of this questionnaire is to assess your bowel function. Please tick only one box for each question. It may be difficult to select only one answer, as we know that for some patients symptoms vary from day to day. We would kindly ask you to choose one answer which best describes your daily life. If you have recently had an infection affecting your bowel function, please do not take this into account and focus on answering questions to reflect your usual daily bowel function.

Do you ever have occasions when you cannot control your flatus (wind)?
☐ No, never
☐ Yes, less than once per week
☐ Yes, at least once per week

Do you ever have any accidental leakage of liquid stool?
☐ No, never
☐ Yes, less than once per week
☐ Yes, at least once per week

How often do you open your bowels?
☐ More than 7 times per day (24 hours)
☐ 4–7 times per day (24 hours)
☐ 1–3 times per day (24 hours)
☐ Less than once per day (24 hours)

Do you ever have to open your bowels again within one hour of the last bowel opening?
☐ No, never
☐ Yes, less than once per week
☐ Yes, at least once per week

Do you ever have such a strong urge to open your bowels that you have to rush to the toilet?
☐ No, never
☐ Yes, less than once per week
☐ Yes, at least once per week

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APPENDIX 2. LARS Score: Scoring Instructions

Add the scores from each 5 answers to one final score.

Do you ever have occasions when you cannot control your flatus (wind)?
☐ No, never 0
☐ Yes, less than once per week 4
☐ Yes, at least once per week 7

Do you ever have any accidental leakage of liquid stool?
☐ No, never 0
☐ Yes, less than once per week 3
☐ Yes, at least once per week 3

How often do you open your bowels?
☐ More than 7 times per day (24 hours) 4
☐ 4–7 times per day (24 hours) 2
☐ 1–3 times per day (24 hours) 0
☐ Less than once per day (24 hours) 5

Do you ever have to open your bowels again within one hour of the last bowel opening?
☐ No, never 0
☐ Yes, less than once per week 9
☐ Yes, at least once per week 11

Do you ever have such a strong urge to open your bowels that you have to rush to the toilet?
☐ No, never 0
☐ Yes, less than once per week 11
☐ Yes, at least once per week 16

Total Score:

Interpretation:
0–20: No LARS
21–29: Minor LARS
30–42: Major LARS