

VALIDATION OF THE SLOVENIAN VERSION OF THE LOW ANTERIOR RESECTION SYNDROME SCORE FOR RECTAL CANCER PATIENTS AFTER SURGERY

POTRDITEV SLOVENSKE VERZIJE VPRAŠALNIKA O SINDROMU NIZKE SPREDNJE RESEKCIJE REKTUMA PRI BOLNIKIH Z RAKOM DANKE PO OPERACIJI

Jan GROSEK^{1*}, Jurij Aleš KOŠIR¹, Jerica NOVAK², Mirko OMEJC¹, Aleš TOMAŽIČ¹, Gregor NORČIČ¹

¹University Medical Centre Ljubljana, Department of Abdominal Surgery, Zaloška cesta 7, 1000 Ljubljana, Slovenia

²Institute of Oncology Ljubljana, Division of Surgery, Zaloška cesta 2, 1000 Ljubljana, Slovenia

Received: Oct 12, 2018

Accepted: Jul 3, 2019

Original scientific article

ABSTRACT

Purpose: The purpose of this study was to translate the low anterior resection syndrome (LARS) score into Slovenian and to test its validity on Slovenian patients who underwent low anterior rectal resection.

Keywords:

low anterior resection, low anterior resection syndrome, rectal cancer, bowel function, quality of life

Methods: The LARS score was translated from English into Slovenian and then back-translated following international recommendations. The Slovenian version of the LARS questionnaire was completed by patients who underwent low anterior rectal resection between 1 January 2006 and 31 December 2010 at the University Medical Centre Ljubljana. An anchor question assessing the impact of bowel function on lifestyle was included. To assess test-retest reliability, some of the patients answered the LARS score questionnaire twice.

Results: A total of 100 patients (66.7%) of the 150 patients who were contacted for participation, were included in the final analysis. A total of 58 patients reported major LARS score. The LARS score was able to discriminate between patients who received radiotherapy and those who did not ($p < 0.001$), and between total and partial mesorectal excision ($p < 0.001$). Age was not associated with a greater LARS score ($p = 0.975$). There was a perfect fit between the QoL category question and the LARS score in 66.0% of cases and a moderate fit was found in 24.0% of the cases, showing good convergent validity. Test-retest reliability of 51 patients showed a high intraclass correlation coefficient of 0.86.

Conclusions: The Slovenian translation of the LARS score is a valid tool for measuring LARS.

IZVLEČEK

Namen: Prevod in potrditev vprašalnika o sindromu nizke sprednje resekcije rektuma (vprašalnik LARS).

Ključne besede:

nizka sprednja resekcija rektuma, sindrom nizke sprednje resekcije, rak danke, funkcionalne težave, kvaliteta življenja

Metode: Študija, ki je vključevala 100 slovenskih bolnikov, je potekala februarja in marca 2018. Vprašalnik LARS je bil preveden v slovenščino iz angleščine po mednarodnih priporočilih. Sodelovali so pacienti, ki so bili zaradi raka danke na Univerzitetnem kliničnem centru v Ljubljani operirani v obdobju od 1. januarja 2006 do 31. decembra 2010 in pri katerih je bila narejena sfinkter ohranjujoča nizka sprednja resekcija rektuma. Poleg vprašalnika LARS so pacienti odgovorili tudi na dodatno vprašanje o vplivu težav s črevesjem na kvaliteto svojega življenja.

Rezultati: Vprašalnik z dodatnim vprašanjem smo poslali 150 pacientom, v raziskavo jih je bilo vključenih 100. Pri 58 bolnikih so rezultati potrdili prisotnost zelo izrazitega sindroma nizke sprednje resekcije. Vprašalnik LARS zanesljivo loči bolnike, ki so bili pred operacijo obsevani, od tistih, ki tovrstnega zdravljenja niso prejeli ($p < 0,001$). Prav tako zanesljivo razlikuje tudi med pacienti, pri katerih je bil narejen delni ali popolni izrez mezorektuma ($p < 0,001$). Starost ni povezana z rezultati vprašalnika LARS ($p = 0,975$). 51 naključno izbranim pacientom smo vprašalnik poslali dvakrat. Popolno skladnost med vprašanjem o kvaliteti življenja in izidom vprašalnika LARS smo ugotovili v 66,0 %, zmerno skladnost pa v 24,0 %, kar kaže dobro konvergenčno veljavnost testa. Testiranje in ponovno testiranje sta potrdili visoko zanesljivost slovenskega prevoda vprašalnika s korelacijskim koeficientom znotraj skupine, ki je znašal 0,86.

Zaključek: Slovenski prevod vprašalnika LARS smo potrdili kot notranje skladno, zanesljivo in natančno orodje za oceno funkcionalnih težav s črevesjem pri pacientih po operaciji raka danke in tudi vpliv teh na kvaliteto njihovega življenja.

*Corresponding author: Tel. + 386 41 808 063; E-mail: jan.grosek@kclj.si

1 INTRODUCTION

Rectal carcinoma is one of the most common forms of cancer in both men and women in the Western world and one of the most common causes of death (1-3). The substantial improvement in rectal cancer survival rates is the result of earlier diagnosis, advances in surgical techniques and improved delivery of radiotherapy. Sphincter-preserving low anterior resection (LAR) with total or partial mesorectal excision has become the gold standard treatment for mid and low rectal cancers (3). Many patients who undergo a LAR for rectal cancer suffer major defecation dysfunction due to nerve and sphincter damage combined with poor neorectal capacity (4). The term Low Anterior Resection Syndrome (LARS) was introduced to describe this complex range of symptoms and the LARS score (LARSS) was defined to assess the severity of complaints and its negative impact on the quality of life (QoL) of patients (4). These patients typically fall into one of two categories: those with faecal incontinence, frequency, and urgency, and those with constipation and feelings of incomplete emptying. Some report features of both (4). The prevalence of LARS varies considerably, ranging from 19% to 90% of patients who undergo rectal resections (5-8).

Several risk factors have been proposed for the development of LARS following surgery for rectal cancer, including age, female sex, surgical technique (mesorectal excision, intersphincteric resection, type of anastomosis and construction of temporary stoma), prolonged presence of defunctioning ileostomy, neoadjuvant and/or adjuvant therapy, and postoperative complications (anastomosis leak, abscess) (9, 10). The level of anastomosis seems to be the most important risk factor (9, 10).

The impact of the surgical procedure on QoL is often underestimated by the treating physicians (6). QoL questionnaires can provide detailed information about the consequences of treatment and have been reported to improve the treatment of patients (6).

One of the most commonly used questionnaires to evaluate bowel function is the LARSS (11). This self-administered questionnaire was developed in Denmark specifically for rectal cancer patients who underwent curative low anterior resection with or without radiotherapy for non-disseminated disease (11). The LARSS evaluates the five most bothersome issues that patients with LARS have: incontinence for flatus, incontinence for liquid stool, frequency, clustering and urgency (11). The LARSS has already been validated in many European and Asian countries (12-15). Reproducibility of the questionnaire was confirmed with test-retest studies, which have all yielded an intraclass correlation coefficient higher than the acceptable level of 0.80 (12-15).

In 2015, 388 patients were diagnosed with rectal cancer in Slovenia (1, 2). Slovenian colorectal cancer patients report poorer physical, cognitive and social functioning and other symptoms that occur frequently, such as constipation, diarrhea and financial difficulties (16). However, LARS has not been evaluated in the Slovenian rectal cancer population, as LARSS has not been validated in Slovenian yet.

Aiming at validating the Slovenian version of the LARSS, the objective of the study was to assess some of its psychometric characteristics in the group of Slovenian patients who underwent sphincter-preserving rectal resections due to rectal adenocarcinoma.

2 METHODS

2.1 Participants

The electronic database of a tertiary medical centre was used to find patients with rectal cancer that were treated with curative surgical resection in the period between 1 January 2006 and 31 December 2010. All patients, 18 years and older, operated for rectal adenocarcinoma within 15 cm of the anal verge were intended to be included. Exclusion criteria were the presence of a stoma, known disseminated or recurrent disease, inability to read and write in Slovenian or any psychiatric conditions that might intervene with the questionnaire evaluation. In February and March 2018 questionnaires regarding bowel function were sent to all eligible 150 patients identified in our database, who had undergone either a curative total mesorectal excision (TME) or a curative partial mesorectal excision (PME) (Figure 1). All included patients have signed an informed consent for participation in the study. Demographic and clinical information was obtained from the electronic database.

2.2 Study Instrument

2.2.1 Description of the LARSS

Bowel function was assessed with the LARSS. The questionnaire includes 5 questions that evaluate gastrointestinal symptoms. The questions and scoring algorithm of the LARSS in Slovene language are shown in Table 1. The score values were assigned to possible answers in order to calculate the LARSS, which was divided into "no LARS" (score of 0-20 points), "minor LARS" (21-29 points) and "major LARS" (30-42 points) (11). All questions had to be answered for inclusion in our analysis.

2.2.2 Translation to Slovenian Language

The translation procedure followed international guidelines, and included independent forward and back-translations, as well as adaptive testing of the final Slovenian version (17-20). Two independent professional translators, both native Slovenian speakers, produced the forward translation (English to Slovenian). The translators discussed any discrepancies between the two versions until a final consensus was reached. This was then back-translated (Slovenian to English) by a third independent native English translator. The third translator was not familiar with the original version. For approval of the final Slovenian version, the back-translated English version was screened for equivalence to the original English version. The final version was checked and accepted by the team conducting the study.

2.3 Psychometric Validation

2.3.1 Reliability

Test-retest reliability, a measure of consistency and the ability to achieve consistent results over different points in time, were obtained from a randomly-selected subgroup of participants who were mailed the LARSS questionnaire twice. A period of 14 days was considered long enough so that the participants could not recollect any of their previous responses, but also potentially short enough to remain stable in terms of symptoms, which is essential when evaluating reliability (21). To confirm stability of the bowel function study, the subjects were asked the following question in the second questionnaire: *“Compared to the last time you completed the questionnaire, did you experience any change in bowel function?”*. Subjects who confirmed a change in bowel function were excluded from the test-retest evaluation.

2.3.2 Validity

Convergent validity is an agreement between measures that are assumed to be related, which is assessed by different methods. The convergent validity of the Slovenian LARSS was tested by adding an extra question to investigate the association between LARSS and QoL (*“Overall, how much does your bowel function affect your quality of life?”*), and was sent with the LARSS questionnaire (22). The available responses were *“No impact”, “A little”, “Some”, “A lot”*.

Discriminant validity evaluates the ability to discriminate between groups with known differences. Discriminative validity was assessed by comparison of the following groups in the LARS numerical score: presence or absence of radiotherapy, type of surgery (TME/PME), older or younger than the mean age of the participants in the study (i.e. 73.5 years).

2.3.3 Statistical Tools

The T-test, Mann-Whitney U test or the chi-squared test were used to detect any differences between respondents and non-respondents. The LARSS was computed and categorized into three groups: no LARS (0-20 points), minor LARS (21-29 points) or major LARS (30-42 points). The values of impact of bowel function on QoL were categorized into three groups for the analysis of convergent validity: *“no”, “minor” or “some/major”*. The association between the LARSS and QoL was illustrated as a percentage of *“perfect”, “moderate” or “no fit”* between the groups. The same LARS-group and QoL-group (eg. no LARS/no impact on QoL) were treated as a perfect fit, a mismatch in one category as moderate and a mismatch for more than one category as a no fit. The difference in the LARS numerical score between the three categories of QoL was tested with the Kruskal-Wallis test, and post-hoc comparisons were made with the Mann-Whitney U test. The sensitivity and specificity of the LARSS was computed with a cut-off value of 30 points predicting some/major impact of bowel function on QoL.

For discriminant validity testing, we used the non-parametric Wilcoxon rank sum test to compare patients with different age, type of surgery and radiation therapy. Test-retest reliability was examined graphically by means of a Bland-Altman plot. The ICC was calculated and the difference in the LARS numerical score between the first and second test was compared by using the Wilcoxon test. Furthermore, the percentage of perfect, moderate and no fit between the value of the first and second test was calculated for each question of the LARSS. When a participant gave the same answer (chose the same category) in both tests, it was treated as a perfect fit. A mismatch in one category was treated as a moderate fit and it was a no fit when there was a mismatch in more than one category.

All p values < 0.05 were considered statistically significant. The statistical analysis was performed using IBM SPSS Statistics, version 24 (IBM Corp. Armonk, NY, USA).

Table 1. The Slovenian version of Low Anterior Resection Syndrome Score (LARSS) (11).

| | |
|---|----|
| 1. Se vam kdaj zgodi, da ne morete zadržati uhajanje vetrov? | |
| - Ne, nikoli | 0 |
| - Da, manj kot enkrat na teden | 4 |
| - Da, vsaj enkrat na teden | 7 |
| 2. Se vam kdaj zgodi, da vam po nesreči uide nekaj tekočega blata? | |
| - Ne, nikoli | 0 |
| - Da, manj kot enkrat na teden | 3 |
| - Da, vsaj enkrat na teden | 3 |
| 3. Kako pogosto odvajate blato? | |
| - Več kot 7-krat na dan (na 24 ur) | 4 |
| - Od 4- do 7-krat na dan (na 24 ur) | 2 |
| - Od 1- do 3-krat na dan (na 24 ur) | 0 |
| - Manj kot enkrat na dan (na 24 ur) | 5 |
| 4. Se vam kdaj zgodi, da morate ponovno na blato v eni uri po zadnjem odvajanju blata? | |
| - Ne, nikoli | 0 |
| - Da, manj kot enkrat na teden | 9 |
| - Da, vsaj enkrat na teden | 11 |
| 5. Ali kdaj občutite tako hudo siljenje na blato, da morate steči na stranišče? | |
| - Ne, nikoli | 0 |
| - Da, manj kot enkrat na teden | 11 |
| - Da, vsaj enkrat na teden | 16 |

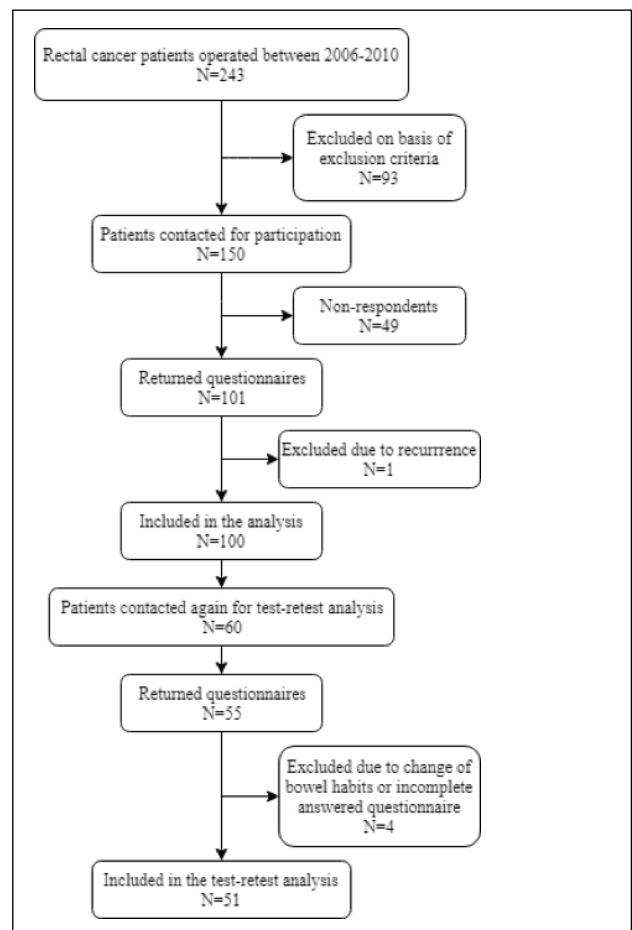
3 RESULTS

3.1 Study Participants Characteristics

Out of 150 patients eligible for the study, 101 responded, yielding a 67.3% response rate. Out of these patients, one experienced recurrence and was excluded from the analysis. The final sample therefore included 100 participants. Clinical and demographic data is shown in Table 2. After 14 days, the same questionnaire was sent to 60 randomly-selected participants. Out of those, 55 (93.6%) participants responded. One participant returned an incomplete questionnaire and three participants reported a change in bowel function. Overall, 51 participants were included in the test-retest analysis (Figure 1).

Table 2. Patient characteristics.

| | N=100 |
|---|-------------|
| Males, n (%) | 69 (69) |
| Age in years at time of survey, mean (SD) | 73.5 (10.6) |
| Age in years at time of operation mean (SD) | 63.4 (10.5) |
| Tumour stage | |
| T0-T2, n (%) | 52 (52) |
| T3-T4, n (%) | 48 (48) |
| Years since operation, mean (SD) | 9.7 (1.4) |
| Type of surgery | |
| TME, n (%) | 69 (69) |
| PME, n (%) | 31 (31) |
| Tumour level in cm, mean (SD) | 9.4 (3.3) |
| Radiotherapy, n (%) | 57 (57) |
| Chemotherapy, n (%) | 69 (69) |

**Figure 1.** Study flowchart. A total of 100 patients were included in the analysis. Of those, 51 were included in the test-retest analysis.

There were no statistically significant differences between respondents and non-respondents in type of surgery ($p=0.900$), age at the time of surgery ($p=0.916$), age at the time of the survey ($p=0.992$), radiotherapy ($p=0.726$), chemotherapy ($p=0.247$), colonoscopic tumour level ($p=0.760$), number of positive lymph nodes ($p=0.086$), years since operation ($p=0.608$) or tumour stage ($p=0.356$).

Respondents and non-respondents differed with regard to gender ($p=0.042$). Women were less likely to respond to the questionnaire as there were 24 (48%) women among the non-respondents and 31 (31%) women among the respondents.

3.2 Psychometric Validation

3.2.1 Reliability

Figure 2 shows a Bland-Altman plot of agreement between the first and second LARSS. The 95% limits of the agreement were -10.84 to 12.48.

The intraclass correlation coefficient was 0.86 (95% CI: 0.78-0.92). No statistically significant difference was found between the first and second LARS numerical score ($p=0.270$).

The percentages with 95% CI of perfect, moderate and no fit between the first and second response to each of the LARSS questions are shown in Table 3.

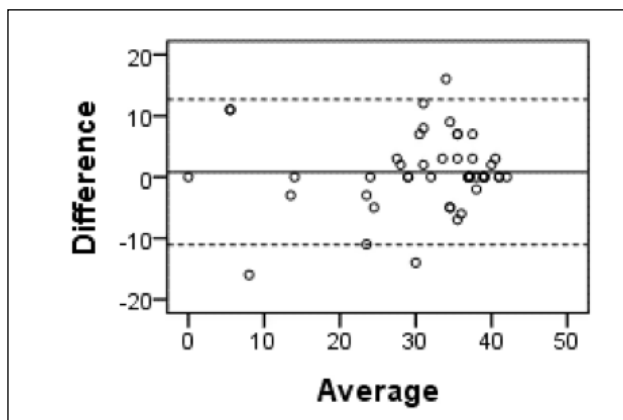


Figure 2. Bland-Altman plot illustrating the difference between the numerical LARSS values at the first and second test (solid line denotes mean difference, dashed lines denote limits of agreement).

Table 3. Agreement between responses at the first and the second LARS test for each question of the LARSS.

| | Perfect | Moderate | No |
|----|------------------|------------------|--------------|
| Q1 | 78.4 (66.7-90.1) | 15.7 (5.4-26.0) | 5.9 (0-11.6) |
| Q2 | 72.5 (59.9-85.2) | 25.5 (13.1-37.9) | 2.0 (0-5.9) |
| Q3 | 78.4 (66.7-90.1) | 19.6 (8.3-30.9) | 2.0 (0-5.9) |
| Q4 | 76.5 (64.4-88.5) | 17.6 (6.8-28.5) | 5.9 (0-12.6) |
| Q5 | 78.4 (66.7-90.1) | 19.6 (8.3-30.9) | 2.0 (0-5.9) |

* Percentages with 95% CI are shown

3.2.2 Validity

A comparison between the QoL groups and the LARSS groups is summarized in Table 4. The agreement between the two groups is the highest (55%) in the major LARS and some/major impact of bowel function on QoL.

Table 4. Fit between the QoL category and the LARSS category.

| Impact of bowel function on QoL | No LARS (0-20 points) | Minor LARS (21-29 points) | Major LARS (30-42 points) |
|---------------------------------|-----------------------|---------------------------|---------------------------|
| No | 3 (3%) | 2 (2%) | 0 (0%) |
| Minor | 8 (8%) | 8 (8%) | 3 (3%) |
| Some/major | 10 (10%) | 11 (11%) | 55 (55%) |

The percentages of perfect, moderate and no fit between the LARS and QoL groups with 95% confidence intervals are shown in Table 5. No fit was found in 10% of the data.

Table 5. Fit between the LARSS group and the QoL group.

| Fit | n% (95% CI) |
|----------|------------------|
| No | 10.0 (4.0-16.0) |
| Moderate | 24.0 (14.5-32.5) |
| Perfect | 66.0 (56.5-75.4) |

A box plot illustrating the association between QoL groups and the LARS numerical score is shown in Figure 3. QoL groups differ statistically significant in the LARS numerical score ($p<0.001$). The post-hoc difference was found between the some/major impact of bowel function in the QoL group, and the no ($p=0.002$) and minor impact group ($p<0.001$). The group with minor impact of bowel function on QoL did not have a statistically significant difference from the group with no impact on QoL with regard to the LARS numerical score ($p=0.353$).

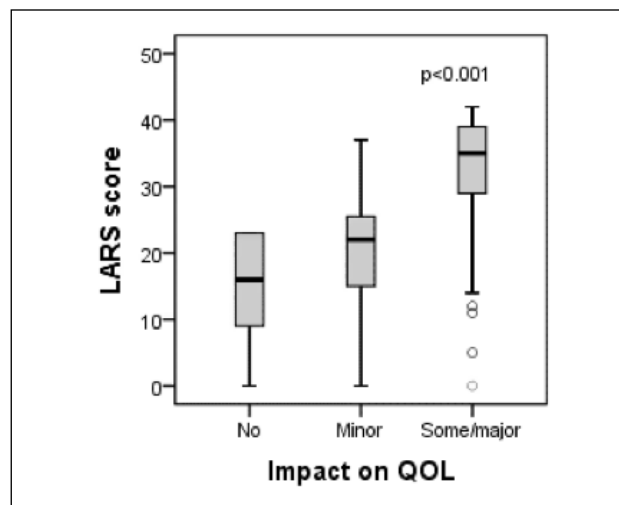


Figure 3. Box plot showing the relationship between the LARSS and the QoL group.

The sensitivity (95% CI) of the LARSS, of 30 points or more, for distinguishing between the some/major impact of bowel function on QoL group from the other two QoL groups was 72.4 (60.9-82.0) and the specificity was 87.5 (67.6-97.3).

Patients who received radiotherapy had a higher statistically significant LARSS than those who did not ($p<0.001$). Patients that had a TME operation had a higher statistically significant LARSS than those that had a PME operation ($p<0.001$). Patients below or equal to the mean age of 73.5 years did not differ from those above the

mean age in LARSS ($p=0.975$). Differences between the groups are illustrated in Figure 4.

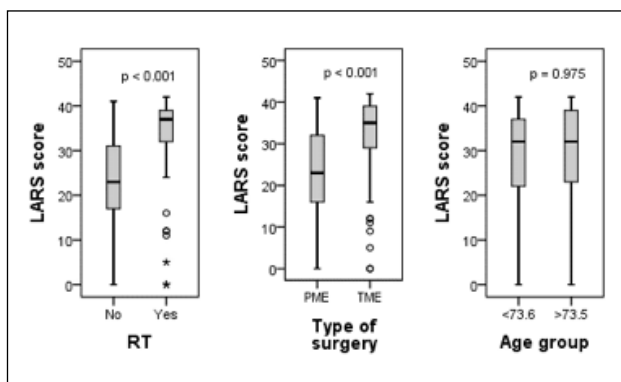


Figure 4. The LARSS in clinical subgroups: radiotherapy, type of surgery and age.

4 DISCUSSION

In our study we have provided a cross-culturally adapted Slovenian translation of the LARSS and demonstrated its validity and reliability. We observed that the Slovenian version of the LARS questionnaire was easily understood and applied. The results of our study are similar to those presented in previous validations. As such, we believe that the Slovene LARSS is a cross-culturally equivalent instrument to the original version.

The test-retest reliability has been found to be excellent, with the total score measuring 0.86, which indicates low measurement error for the questionnaire. There were no statistically significant differences between the numerical value of the LARSS for the first and second test. These results are comparable to the Danish, Lithuanian, Dutch and English results (12, 13, 15, 23). Proof of correctness and equivalence between the Slovenian and the previously validated questionnaires was provided by the high internal consistency of the translated questionnaire and the excellent test-retest reliability observed in results.

To provide equivalence between the English and the Slovenian version of the LARSS, rigorous translation and cross-cultural adaptation processes were followed. An extra QoL category question was added to validate the Slovenian LARSS. The share of our patients with a “perfect fit” between the LARSS and QoL is higher (66%) in comparison to other reports, ranging from 41% to 63% (12, 13, 15, 24). No fit between the LARSS and QoL was also higher in our study compared to other studies, in which it measured up to 8% (12, 13, 15, 25). All of the patients, where there was no fit, reported no LARS and some or major impact of bowel function on their quality of life. This could mean that the questionnaire lacks an important aspect of bowel function that has an impact on QoL. It is possible though, that patients reported some or major

impact of bowel function on QoL due to problems unrelated to passing stool, such as abdominal pain or bloating.

Finally, the LARSS was higher in patients who underwent neoadjuvant radio-chemotherapy and had TME, which is in accordance with the results of other studies (10, 26-29). Radiotherapy and the type of surgery are the most consistently reported factors associated with major LARS. It has been shown that radio-chemotherapy has negative effects on anorectal function by causing damage to the sphincter mechanism and nearby nerves, thus causing decreased rectal sensation and incontinence (23, 24).

The limitation of our study is that it is a unicentric study at a tertiary referral centre. To gain a better picture of functional complaints in Slovenian patients, a multicentric study is needed. On the other hand, one of the strengths is the high response rate. There was a difference between respondents and non-respondents regarding the sex of the population. Women were significantly less likely to respond to the questionnaire. Other studies did not show a difference in LARSS regarding sex, so we believe our results are a good representation of the population (25). However, it could be hypothesized that the non-respondents have better or worse anorectal function than the respondents. The patients in our study had their operations 7 years prior to completing the questionnaire, and as such, the results represent the situation after the initial postoperative phase, when bowel function has already stabilized.

Local control and long-term survival are the primary therapeutic goals of rectal cancer surgery. However, due to concerns about long term disability, LARS must be taken into appropriate consideration in the management of rectal cancer prior to surgical treatment. Patients should be counselled on what to expect of their functional outcome after the surgery. A nomogram called the Pre-Operative LARS (POLARS) score has already been developed to predict the severity of bowel dysfunction prior to anterior resection (30). It may help rectal cancer patients to already understand the risks of postoperative bowel dysfunction while still in the pre-operative setting.

In conclusion, a valid Slovenian version of the LARS questionnaire is now available and can be used with confidence to identify and follow-up patients who suffer from anorectal disturbances after rectal surgery. The psychometric properties indicate that the Slovenian version of the LARSS is valid, consistent and reliable. This also strengthens the evidence that the LARSS is a strong and valid tool for the assessment of QoL in patients who underwent sphincter-preserving operations for rectal cancer.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ETHICS

Our study was approved by the National Medical Ethics Committee (No. 0120-48/2018/6, from 14. 03. 2018) and all procedures performed in our study were in accordance with the Declaration of Helsinki (1964) and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

FUNDING

There is no financial interest or risk.

REFERENCES

1. CRRS. Cancer in Slovenia 2014. Ljubljana: Institute of oncology Ljubljana, Epidemiology and cancer registry of Republic of Slovenia, 2016.
2. SLORA. Slovenia and cancer [internet] institute of oncology Ljubljana, Epidemiology and cancer registry, 2010. Accessed April 31st, 2019 at: <http://www.slora.si/en>.
3. Grosek J, Velenik V, Edhemovic I, Omejc M. The influence of the distal resection margin length on local recurrence and long-term survival in patients with rectal cancer after chemoradiotherapy and sphincter-preserving rectal resection. *Radiol Oncol.* 2016;51:169-77. doi: 10.1515/raon-2016.0030.
4. Ridolfi TJ, Berger N, Ludwig KA. Low anterior resection syndrome: current management and future directions. *Clin Colon Rectal Surg.* 2016;29:239-45. doi: 10.1055/s-0036-1584500.
5. Ziv Y, Zbar A, Bar-Shavit Y, Igov I. Low anterior resection syndrome (LARS): cause and effect and reconstructive considerations. *Tech Coloproctol.* 2013;17:151-62. doi: 10.1007/s10151-012-0909-3.
6. Juul T, Ahlberg M, Biondo S, Espin E, Jimenez LM, Matzel KE, et al. Low anterior resection syndrome and quality of life: an international multicenter study. *Dis Colon Rectum.* 2014;57:585-91. doi: 10.1097/DCR.0000000000000116.
7. Bryant CL, Lunniss PJ, Knowles CH, Thaha MA, Chan CL. Anterior resection syndrome. *Lancet Oncol.* 2012;13:403-8. doi: 10.1016/S1470-2045(12)70236-X.
8. Pucciani F. A review on functional results of sphincter-saving surgery for rectal cancer: the anterior resection syndrome. *Updates Surg.* 2013;65:257-63. doi: 10.1007/s13304-013-0220-5.
9. Jimenez-Gomez LM, Espin-Basany E, Trenti L, Marti-Gallostra M, Sánchez-García JL, Vallribera-Valls F, et al. Factors associated with low anterior resection syndrome after surgical treatment of rectal cancer. *Colorectal Dis.* 2017;20:195-200. doi: 10.1111/codi.13901.
10. Ekkarat P, Boonpipattanapong T, Tantiphlachiva K, Sangkhathat S. Factors determining low anterior resection syndrome after rectal cancer resection: a study in Thai patients. *Asian J Surgery.* 2016;39:225-31. doi: 10.1016/j.asjsur.2015.07.003.
11. Emmertsen KJ, Laurberg S. Low anterior resection syndrome score development and validation of a symptom-based scoring system for bowel dysfunction after low anterior resection for rectal cancer. *Ann Surg.* 2012;255:922-8. doi: 10.1097/SLA.0b013e31824f1c21.
12. Juul T, Battersby NJ, Christensen P, Janjua AZ, Branagan G, Laurberg S, et al. Validation of the English translation of the low anterior resection syndrome score. *Colorectal Dis.* 2015;17:908-16. doi: 10.1111/codi.12952.
13. Samalavicius NE, Dulskas A, Lasinskas M, Smailyte G. Validity and reliability of a Lithuanian version of low anterior resection syndrome score. *Tech Coloproctol.* 2016;20:215-20. doi: 10.1007/s10151-015-1424-0.
14. Hou XT, Pang D, Lu Q, Yang P, Jin SL, Zhou Yj, et al. Validation of the Chinese version of the low anterior resection syndrome score for measuring bowel dysfunction after sphincter-preserving surgery among rectal cancer patients. *Eur J Oncol Nurs.* 2015;19:495-501. doi: 10.1016/j.ejon.2015.02.009.
15. Juul T, Ahlberg M, Biondo S, Emmertsen KJ, Espin E, Jimenez LM, et al. International validation of the low anterior resection syndrome score. *Ann Surg.* 2014;259:728-34. doi: 10.1097/SLA.0b013e31828fac0b.
16. Grosek J, Novak J, Kitek K, Bajric A, Majdic A, Kosir JA, et al. Health-related quality of life in Slovenian patients with colorectal cancer: a single tertiary care center study. *Radiol Oncol.* 2019;53:231-7.
17. Guillemin F, Bombardier C, Beaton D. Cross-cultural adaptation of health-related quality of life measures: literature review and proposed guidelines. *J Clin Epidemiol.* 1993;46:1417-32.
18. Stern B, Fabjan TH, Renner-Sitar K, Zaletel-Kragelj. Validation of the Slovenian version of multiple sclerosis quality of life (MSQL-54) instrument. *Zdr Varst.* 2017;56:260-7. doi: 10.1515/sjph-2017-0035.
19. Petek Šter M, Šter B, Petek D, Ceditnik Gorup E. Validation of Slovenian version of Jefferson scale of empathy for students. *Zdr Varst.* 2014;53:89-100. doi: 10.2478/sjph-2014-0010.
20. Ribas Y, Aguilar F, Jovell-Fernández E, Cayetano L, Navarro-Luna A, Muñoz-Duyos A. Clinical application of the LARS score: results from a pilot study. *Int J Colorectal Dis.* 2017;32:409-18. doi: 10.1007/s1007/s
21. Mokkink LB, Terwee CB, Patrick DL, Alonso J, Stratford PW, Knol DL, et al. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. *J Clin Epidemiol.* 2010;63:737-45. doi: 10.1016/j.jclinepi.2010.02.006.
22. Beaton DE, Bombardier C, Guillemin F, Ferraz MB. Guidelines for the process of cross-cultural adaptation of self-report measure. *Spine.* 2000;25:3186-91.
23. Hupkens BJP, Breukink SO, Olde Reuver Of Briel C, Tanis PJ, de Noo ME, van Duijvendijk P, et al. Dutch validation of the low anterior resection syndrome score. *Colorectal Dis.* 2018;20:881-7. doi:10.1111/codi.14228
24. Ho Y, Lee K, Eu K, Seow-Choen F. Effects of adjuvant radiotherapy on bowel function and anorectal physiology after low anterior resection for rectal cancer. *Tech Coloproctol.* 2000;4:13-6. doi: 10.1007/s101510050048.
25. Croese AD, Lonie JM, Trollope AF, Vangaveti VN, Ho YH. A meta-analysis of the prevalence of Low Anterior Resection Syndrome and systematic review of risk factors. *Int J Surg.* 2018;56:234-41.
26. Hughes DL, Cornish J, Morris C, LARRIS Trial Management Group. Functional outcome following rectal surgery-predisposing factors for low anterior resection syndrome. *Int J Colorectal Dis.* 2017;32:691-7. doi: 10.1007/s00384-017-2765-0.
27. Nesbakken A, Nygaard K, Lunde OC. Mesorectal excision for rectal cancer: functional outcome after low anterior resection and colorectal anastomosis without a reservoir. *Colorectal Dis.* 2002;4:172-6.
28. Lewis WG, Martin IG, Williamson ME, Stephenson BM, Holdsworth PJ, Finan PJ, et al. Why do some patients experience poor functional results after anterior resection of the rectum for carcinoma? *Dis Colon Rectum.* 1995;38:259-63.
29. Guren MG, Eriksen MT, Wiig JN, Carlsen E, Nesbakken A, Sigurdsson HK, et al. Quality of life and functional outcome following anterior or abdominoperineal resection for rectal cancer. *Eur J Surg Oncol.* 2005;31:735-42.
30. Battersby N, Bouliotis G, Emmertsen KJ, Juul T, Glynn-Jones R, Branagan G, et al. Development and external validation of a nomogram and online tool to predict bowel dysfunction following restorative rectal cancer resection: the POLARS score. *Gut.* 2018;67:688-96. doi: 10.1136/gutjnl-2016-312695.