

Incidence of the anterior resection syndrome using low anterior resection score (LARS scale)

Porezekcinio tiesiosios žarnos sindromo dažnis naudojant žemos priekinės tiesiosios žarnos rezekcijos skalę (LARS skalę)

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Background

Up to 90 % of patients undergoing low anterior resection, complain of increased daily bowel movements, urgency for defecation, and a variable degree of incontinence. A symptom-based scoring system for bowel dysfunction after low anterior resection for rectal cancer has recently been validated in Lithuanian population.

Purpose: we aimed to measure the incidence and severity of the anterior resection syndrome (ARS) using LARS and its correlation with selected variables or risk factors.

Methods

LARS score was sent to 183 patients who underwent low anterior resection with TME with coloanal anastomosis from January 1st, 2008 to December 31st, 2012 at the National Cancer Institute. Of them 111 (responsibility was 60.7%) have completed the questionnaire. The variables studied were age, sex, location of the tumour, neoadjuvant radiotherapy, time after treatment.

Results

Of 111 questionnaires 108 were completed properly (59.0%). 27 patients (25%) had no ARS, 26 (24%) had minor ARS and 55 (56%) had major ARS. In univariate analysis age, sex, neoadjuvant radiotherapy, and tumour localization did not have an im-

pact on severity of bowel dysfunction symptoms after low anterior resection with TME. Also there was no difference between female and male patient groups ($p=0.33$), patients who had/had not undergone radiation therapy ($p=0.07$), and those with low or high tumour edge level ($p=0.17$). However, time after operation (< 12 months) was associated to ARS.

Conclusion

More than half of the operated patients presented severe LARS score and only a one fourth did not provide a quantifiable ARS. Timing after surgery was the main factor affecting ARS.

Key words: low anterior resection, low anterior resection syndrome, LARS score, total mesorectal excision

Įvadas

Iki 90 proc. pacientų, operuotų dėl tiesiosios žarnos navikų, skundžiasi padažnėjusio tuštinimosi epizodais, nesulaikomu noru tuštintis, įvairaus laipsnio išmatų nelaikymu. Visai neseniai tuštinimosi sutrikimų skalė šiems simptomams vertinti buvo išversta į lietuvių kalbą ir patvirtinta naudoti klinikinėje praktikoje.

Tyrimo tikslas

Mūsų tikslas buvo nustatyti porezekcinio tiesiosios žarnos sindromo (ARS) pasireiškimo dažnį ir sunkumą pacientams po tiesiosios žarnos rezekcijos bei išsiaiškinti rizikos veiksnius.

Metodai

Porezekcinio tiesiosios žarnos sindromo skalė buvo išsiųsta 183 pacientams, kuriems nuo 2008 m. sausio 1 d. iki 2012 m. gruodžio 31 d. Nacionaliniame vėžio institute buvo atlikta tiesiosios žarnos rezekcija su totaline mezorektaline ekscizija suformuojant žarnos jungtį. Iš jų skalę užpildė 111 (atsakomumas – 60,7 %). Kartu tyrėme šiuos galimus blogesnės tuštinimosi funkcijos rizikos veiksnius: lytis, amžius, naviko aukštis, priešoperacinis spindulinis gydymas, laikas po operacijos.

Rezultatai

Iš 111 užpildytų klausimynų 108 buvo užpildyti tinkamai (59 %). 27 pacientams (25 %) ARS nepasireiškė, 26 (24 %) pasireiškė silpnas ARS, o net 55 (56 %) – ryškus. Išanalizavę rizikos veiksnius nustatėme, jog tik laikas po operacijos buvo lemiamas veiksnyms ARS po operacijos pasireikšti (ilgesnis laikas, ne tokie ryškūs simptomai).

Išvados

Daugiau nei pusei pacientų atsirado ryškus tuštinimosi sutrikimas ir tik ketvirtadalis neturėjo jokių skundų. Laikas, praėjęs nuo operacijos, buvo vienintelis teigiamas veiksnys šiems simptomams susilpnėti.

Reikšminiai žodžiai: tiesiosios žarnos rezekcija, porezekcinis tiesiosios žarnos sindromas, porezekcinio tiesiosios žarnos sindromo skalė, totalinė mezorektalinė ekscizija

Introduction

In the last 3 decades advances in rectal cancer treatment have achieved a reduction in the locoregional recurrence rate. During this period low anterior resection with total mesorectal excision (TME) became a gold standard for rectal cancer treatment. Most of the patients (up to 90%) operated with preservation of the sphincter will develop an alteration of intestinal and defecatory functions. The dysfunction varies in its symptoms and severity, and it manifests as urgency, incontinence and fragmented defecation, with bowel movements that are repeated, incomplete or difficult. The set of these symptoms constitutes what is known as the anterior resection syndrome (ARS) [1]. The syndrome is attributed to rectal sphincter injury, denervation during pelvic dissection [2, 3], the low coloanal anastomosis,

the impaired capacity and compliance of the remnant of the rectum, and the loss of rectal sensation [1]. Furthermore, urinary and sexual dysfunction may occur in 10–35% of patients [4].

A symptom-based scoring system for bowel dysfunction after low anterior resection for rectal cancer has recently been developed and validated by *Emmertsen* [5]. Since then, the LARS score has been translated and validated in several languages, including Lithuanian language [6, 7].

The aim of this study was to study the incidence, distribution and severity of ARS among our rectal cancer patients treated by anterior resection using the LARS score. Also we aimed to confirm its quantitative correlation with the risk factors which are known to be connected with ARS.

Patients and methods

Patients

All of the patients treated in our hospital for rectal cancer with a curative purpose by anterior resection of the rectum from January 2008 to December 2012 were included in this study. An Ileostomy takedown was performed on an average of 3 months following primary surgery. Patients were questioned at least 6 months after the ileostomy takedown, from August to November, 2013. To all patients a letter by mail containing the request to take part in the study, an informative note describing its aim and a declaration of its confidentiality was sent. It also contained the LARS scale questionnaire in Lithuanian. The patients who failed to answer the questionnaire appropriately were excluded. Questionnaires were sent to 183 patients. 111 (60.7%) of them, 69 males and 39 females, responded (mean age 66.9 years). Three patients failed to complete the questionnaire. 108 (59.0%) fully completed questionnaires were the object of our final analysis.

Patients with T3 (with any N stage) cancer or node-positive T1 or T2 cancer, underwent short-course radiotherapy prior to surgery (5x5Gy). Patients who had T3 tumour with an endangered circumferential margin or T4 tumour (any N), underwent long-course radiotherapy with two cycles of 5-FU based chemotherapy before surgery. The operative procedure included midline laparotomy, high ligation of the inferior mesenteric vessels, mobilization of the splenic flexure, colorectal resection with TME, and a double stapled coloanal anastomosis. All the patients had negative distal and circumferential margins on subsequent histological examination.

LARS scale (Table 1)

The LARS score consists of five items concerning the following: incontinence for flatus, incontinence for liquid stool, frequency of bowel movements, clustering of stools, and urgency. Each symptom of bowel dysfunction is weighed according to its impact on the quality of life. The calculated score ranges from 0 to 42, with a score of 0–20 representing no ARS, a score of 21–29 representing minor ARS, and a score of 30–42 representing major ARS.

Statistical analysis

The results were analysed using the SPSS 17.0 statistical package (Chicago, IL). Data are described in terms of absolute and relative frequencies in percentages and averages with standard deviation for continual variables, or the median and interquartile range if the data distribution made this advisable. Firstly possible risk factors with the LARS category were analysed in univariate analysis. This had the purpose of identifying statistically significant variables using the Student t-test (Mann–Whitney U test) or Pearson's χ^2 (Fisher's test).

Results

Clinical and demographic data of the patients are shown in Table 2. 80 (74.1%) of the patients had cancer in the middle third, and 28 patients (25.9%) – in the lower third of the rectum. 53 patients (49.1%) underwent neoadjuvant radiotherapy.

Table 1. Lithuanian version of Low anterior resection syndrome score (LARS-LT)

1. Ar kada nors yra buvę, kad negalėjote kontroliuoti dujų susikaupimo (pagadinote orą)?
<input type="checkbox"/> Ne, niekada
<input type="checkbox"/> Taip, rečiau negu kartą per savaitę
<input type="checkbox"/> Taip, mažų mažiausiai (bent) kartą per savaitę
2. Ar kada nors turėjote atsitiktinį vandeningo išsituštinimo pratekėjimą?
<input type="checkbox"/> Ne, niekada
<input type="checkbox"/> Taip, rečiau negu kartą per savaitę
<input type="checkbox"/> Taip, mažų mažiausiai kartą per savaitę
3. Kaip dažnai tuštinatės?
<input type="checkbox"/> Daugiau negu 7 kartus per dieną (24 valandas) (per parą)
<input type="checkbox"/> 4–7 kartus per dieną (24 valandas)
<input type="checkbox"/> 1–3 kartus per dieną (24 valandas)
<input type="checkbox"/> Rečiau negu kartą per savaitę (24 valandas)
4. Ar kada nors tuštinotės vėl, nepraėjus valandai po paskutinio tuštinimosi?
<input type="checkbox"/> Ne, niekada
<input type="checkbox"/> Taip, rečiau negu kartą per savaitę.
<input type="checkbox"/> Taip, mažų mažiausiai kartą per savaitę
5. Ar kada nors turėjote labai skubų poreikį tuštintis, kad privalėjote bėgti į tualetą?
<input type="checkbox"/> Ne, niekada
<input type="checkbox"/> Taip, rečiau negu kartą per savaitę
<input type="checkbox"/> Taip, mažų mažiausiai kartą per savaitę

Table 2. Clinical and demographic characteristics of 108 patients undergoing low anterior resection for rectal cancer

Variables	Absolute number	Per cent
Male	69	63.89
Female	39	36.11
Age (years), mean (SD)	66.93 (9.57)	na
Stage, TNM		
I	30	27.78
II	37	34.26
III	41	37.96
Tumour localization		
Lower third	28	25.93
Middle third	80	74.07
Neoadjuvant radiotherapy	53	49.07
LARS score, mean (SD)	28.23 (11.03)	na
Time after operation (months), mean (SD)	35.2 (15.21; 7 to 65)	na

SD = standard deviation; LARS score = Low Anterior Resection Syndrome score

Table 3. Univariate analysis of risk factor for ARS

Risk factor	LARS score (mean ± SD)	p
Sex		
Male	27.2±9.7	0.33
Female	30.3±10.2	
Age (y)		
<66.5	29.1±11.5	0.45
≥66.5	31.6±8.9	
Distance of tumour from anal verge (cm)		
<10	28.5±9.9	0.17
≥10	31.0±9.1	
Neoadjuvant radiotherapy		
No	30.5±10.6	0.07
Yes	32.3±9.6	
Length of postoperative period (mo)		
<12	30.6±8.7	0.02
≥12	25.9±10.1	

LARS low anterior resection syndrome, SD standard deviation

According to our data 27 patients (25%) had no ARS, 81 (75%) had ARS; of them: 26 (24%) had minor ARS and 55 (56%) had major ARS.

In univariate analysis age, sex, neoadjuvant radiotherapy, and tumour localization did not have an impact on severity of bowel dysfunction symptoms after low anterior resection with TME. LARS score could not

detect differences between female and male patient groups ($p=0.33$), patients who had/had not undergone radiation therapy ($p=0.07$), and those with low or high tumour edge level ($p=0.17$). However, there was significant difference between patients who filled the scale less than 12 month and more than 12 month after the operation (Table 3).

Discussion

With improving surgical techniques of colorectal anastomosis, operations involving removal of rectal tumours with adequate surgical margin and mesorectal have become the current surgical standard for rectal cancer [8]. But restoration of bowel continuity does not always mean a good function. Up to 90 % of patients experience some degree of bowel dysfunction [9].

In our study, more than half of the patients who underwent low anterior resection for rectum cancer presented with major ARS, and only one-fourth had no quantifiable ARS. The overall perception of quality of life was significantly worse in patients with a major ARS. Only time after surgery (less than one year) was significant factor associated with the ARS. Although the functional alterations of the ARS are more intense and apparent in the first 12 months after surgery, after which the symptoms stabilise, the long-term results indicate that the ARS is a permanent alteration with a multifactor physiopathology. In a recent study by Sturiale et al, authors found that ARS is present even in patients 10 years and more after rectal resection [10]. Another study showed no changes in anorectal function between one year and five years after the operation [11]. Furthermore, neoadjuvant radiotherapy before surgery and TME were not associated with worse functional outcomes in our study. This finding is conflicting compared to recent studies on rectal cancer management [12, 13]. In a French study investigating the localization

of rectal tumours, the authors found that an anastomosis more distant from the anal verge did not improve the quality of the life of patients [14]. This corresponds with our findings. In addition, our study did not show any influence on age or sex for ARS. However, in one study the sex and a younger age were shown as factors worsening ARS [15].

The limitations of this study are related to its retrospective nature and the fact that patients underwent rectal resection and TME, later followed by the takedown of the ileostomy over a 5 year period of time, and were then questioned in 2014 after a very different time lapse following initial surgery. Secondly, we introduced only 108 patients – small study size.

Conclusion

To conclude, more than half of the patients operated for cancer of the rectum by anterior resection present an ARS quantified as “major” on the LARS scale, which affects their quality of life. Time after the procedure is the most important independent risk factor for a major ARS. The LARS scale is a simple and quick means of quantifying the ARS and comparing the functional results of different therapeutic or reconstructive strategies following rectal resection. It may also be useful in evaluating the duration of the efficacy of different treatments which have the aim of relieving or improving the ARS.

Conflict of interest: None declared.

REFERENCES

1. Bryant CLC, Lunniss PJ, Knowles CH, Thaha MA, Chan CLH. Anterior resection syndrome. *Lancet Oncol* 2012; 13: 403–8.
2. Efthimiadis C, Basdanis G, Zatagias A, Tzeveleki I, Kosmidis C, Karamanlis E, Harlaftis N. Manometric and clinical evaluation of patients after low anterior resection for rectal cancer. *Tech Coloproctol* 2004; 8: 205–7.
3. Kakodkar R, Gupta S, Nundy S. Low anterior resection with total mesorectal excision for rectal cancer: functional assessment and factors affecting outcome. *Colorectal Dis* 2006; 8: 650–6.
4. Dulskas A, Samalavičius NE. A prospective study of sexual and urinary function before and after total mesorectal excision. *Int J Colorectal Dis* 2016; 31: 1125–30.
5. 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: 922–28.
6. Juu, T, Ahlberg M, Biondo S, Emmertsen KJ, Espin E, Jimenez SM, Matzel KE, Palmer G, Sauermann A, Trenti L, Zhang W, Laurberg S, Christensen P. International validation of the low anterior resection syndrome score. *Ann Surg* 2014; 259: 728–34.
7. Samalavičius 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.
8. Biondo S, Fracalvieri D, Golda T, Frago R, Trenti L, Kreisler E. Update on advances and controversy in rectal cancer treatment. *Tech Coloproctol* 2016; 20: 145–52.

9. Dulskas A, Miliauskas P, Tikuisis R, Escalante R, Samalavicius NE. The functional results of radical rectal cancer surgery: review of the literature. *Acta Chir Belg* 2016; 116: 1–10.

10. Sturiale A, Martellucci J, Zurli L, Vaccaro C, Bruscianno L, Limongelli P, Docimo L, Valeri A. Long-term functional follow-up after anterior rectal resection for cancer. *Int J Colorectal Dis* 2017; 32: 83–8.

11. Floodeen H, Lindgren R, Hallbook O, Matthiessen P. Evaluation of long-term anorectal function after low anterior resection: a 5-year follow-up of a randomized multicenter trial. *Dis Colon Rectum* 2014; 57: 1162–8.

12. 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 Surg* 2016; 39(4): 225–31.

13. Contin P, Kulu Y, Bruckner T, Sturm M, Welsch T, Muller-Stich BP, Huber J, Buchler MW, Ulrich A. Comparative analysis of late functional outcome following preoperative radiation therapy or chemoradiotherapy and surgery or surgery alone in rectal cancer. *Int J Colorectal Dis* 2013; 29: 165–75.

14. Franco-Neto PR, de Queiroz FL, Staino IRFL, Filho AL. Quality of life assessment in the late postoperative period of patients with rectal cancer submitted to total mesorectal excision. *J Coloproctol* 2013; 33: 50–7.

15. Bregendahl S, Emmertsen KJ, Lous J, Laurberg S. Bowel dysfunction after low anterior resection with and without neoadjuvant therapy for rectal cancer: a population-based cross-sectional study. *Colorectal Dis* 2013; 15: 1130–9.