

# Low anterior resection syndrome (LARS) after sphincter-sparing rectal cancer surgery.

## Incidence and risk factors



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### Low anterior resection syndrome (LARS) after sphincter-sparing rectal cancer surgery. Incidence and risk factors

**BACKGROUNDS:** *Low anterior resection syndrome (LARS) was defined with symptoms such as frequency, incontinence, urgency, and constipation in patients who underwent Sphincter-Sparing Rectum Surgery (SSRC). In this study, LARS rates and risk factors of the patients who underwent SSRC were investigated.*

**MATERIAL METHOD:** *The medical records of patients with SSRC at general surgery department were examined retrospectively. Clinical characteristics, neoadjuvant chemo-radiotherapies, distal resection levels, open/laparoscopic procedures, post-operative complications, and pathological outcomes were recorded. LARS scoring system defined by Emmertsen and Laurberg was used to calculate LARS scores.*

**RESULTS:** *The number of eligible patients was 129. The rectal resection was performed by either low anterior resection (LAR) or very low anterior resection (VLAR). VLAR was used to specify that had anastomosis <5cm to the anal verge. The median follow-up time was 12 (1-30) months. LARS were detected in 60 (%47) patients. LARS rates were significantly higher in the patients underwent VLAR (n: 35 9% vs. 48%<0,001). In univariate analysis, the level of distal resection, open surgeries, neoadjuvant RT, and diversion with temporary stoma were significantly different in LARS group. However, in multivariate analysis, distal resection level was the only significant risk factor for LARS.*

**CONCLUSION:** *Low anterior resection syndrome (LARS) was frequently seen in patients who underwent sphincter-sparing rectum surgery (SSRS). It was detected that distal resection levels were the most important risk factor for the development of LARS. This result showed that LARS should not be disregarded in patients underwent SSRS.*

**KEY WORDS:** Bowel Dysfunction, Cancer, Incontinence, LARS, Rectum

### Introduction

Rectal carcinomas are one of the most common malignancies of the gastrointestinal tractus. Approximately 35% of colonic cancers are located in the rectum and rectosigmoid junction <sup>1</sup>. Since the early 19th century,

rectal cancers had been treated with rectal resections <sup>2</sup>. From the first described in 1979 by Heald, Total Mesorectal Excision (TME) is the gold standard resection technic for rectal cancer treatment <sup>3</sup>. Low Anterior Resection (LAR) with rectal reconstruction was used for most of the rectal surgeries. In addition to TME, using neoadjuvant radiotherapy (NRT) decreased the locoregional recurrences. Especially last two decades, as a result of TME and RT, the overall survival of rectal cancer patients was significantly increased <sup>2</sup>. In addition to this, LAR with rectal reconstruction rates of rectal cancer surgeries were also increased. Therefore, researchers were started to study on bowel dysfunctions and quality of life parameters of patients who underwent rectal surgery. TME and NRT lead to functional problems such as urinary, sexual, and bowel disorders, which disturb the quality of life. Recently Low Anterior Resection Syndrome

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(LARS) is a commonly described bowel disorder that occurred after rectal surgery<sup>4</sup>. However, it is less discussed in the literature and usually ignored in clinical practice. In previous studies, different rates of LARS were reported with a huge spectrum. Therefore, in this study, we aimed to evaluate the rate of LARS among patients underwent rectal surgery in a single center.

## Material and Method

Data regarding patients underwent rectal cancer surgery between Jan./2016-Dec./2020 in Marmara University Hospital's General Surgery Department were analyzed retrospectively. Patients underwent rectal resection and anastomosis and still living without stoma at the date of the study were included in the study. Patients underwent abdominoperineal resection (APR), transanal minimally invasive surgery (TAMIS), patients who still live with a protective stoma, and Hartman's stoma were excluded from the study.

Demographics including age, gender, body mass index (BMI), comorbidities, NRT, the surgical procedure, type of surgery (open or laparoscopic), protective ostomy during index operation, pathological results were recorded. The rectal resection was performed by either low anterior resection (LAR) or very low anterior resection (VLAR). VLAR was used to specify that had anastomosis <5cm to the anal verge. All patients were invited to the hospital to evaluate the LARS score. The time from surgery to the time of the study was recorded as follow-up time. The follow-up time of patients who had a diverting stoma was calculated from the second surgery. Low Anterior Resection Syndrome (LARS) were described as urgency, defecation frequency, and incontinence of wind and liquid stool, and LARS score was evaluated by Laurberg and Emmertsen according to these parameters, in which 0-20 score described as No LARS, 21-29 described minor LARS, and 30-42 score was described major LARS<sup>5</sup>. In this study, patients were examined in two groups, LARS group, and No LARS group.

Primary Outcomes: The rate of LARS among the patients underwent rectal surgery.

Secondary Outcomes: Evaluating the factors may lead to LARS.

## ANALYSIS

SPSS version 24.0 (Spss inc. IBM, Chicago, US) was used for statistical analysis. Data on quantitative variables are presented as median and minimum-maximum and frequencies for qualitative variables. We used the Mann-Whitney U-test for continuous data and the  $\chi^2$  test or Fisher's exact test for categorical data. Univariate analysis was performed to compare the presence or absence of LARS (yes/no) with patient-related variables.

Multivariate analysis was performed of those variables, which showed a statistically significant association on univariate analysis of  $p < 0.05$ .

## Results

Between Jan./2016-Dec./2020, 391 patients underwent rectal cancer surgery. Among them, 187 were excluded because they have APR, tamis and still live with a stoma. Seventy-five patients were lost of follow-up. The remaining 129 patients were included in the study (Fig. 1).

The median LARS score of the entire cohort was 16. We compared the patients described LARS(both minor and major) with those without LARS (no LARS). The patients with No LARS were 69 (53.5%), while 16 (12.5%) patients had minor LARS, and 44 (34%) had major LARS. Age, gender, BMI, comorbidities, T stage, and follow-up time were not significantly different between the two groups (Table I). Laparoscopic procedures were significantly higher among the patients without LARS than those with LARS ( $p: 0.009$ ). Protective stoma during the index operation rate was higher in LARS group than it in no LARS group [respectively, 52%(n: 31) vs. 32% (22),  $p; 0.02$ ].

Neoadjuvant radiotherapy rate was higher in LARS group than it in no LARS group [respectively, 52%(n: 31) vs 32% (n:22),  $p; 0.02$ ].

LAR rate was higher in NO LARS group that it in LARS group [respectively, 91%(n: 63) vs 52%(n: 31)  $p < 0.001$ ]. Furthermore, VLAR rate was higher in LARS

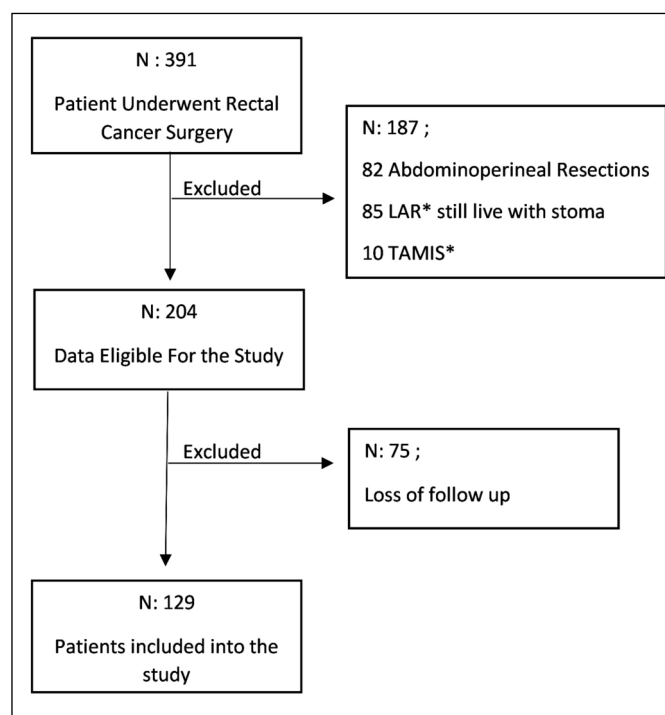


Fig. 1: Patient Flowchart.

TABLE I

N : 129	No LARs (n: 69)	LARs (n:60)	p
Age (Median)(Years)	60(31-82)	59(37-82)	0.12
Gender			
Male	39 (65%)	41(59%)	0.52
Female	21 (35%)	28(41%)	
BMI (Median)(kg/m <sup>2</sup> )	26(18-35)	27(19-44)	0.87
Comorbidity (%)	30(44%)	35(58%)	0.09
ProtectiveStoma During Index Operation	22(32%)	31(52%)	<b>0.02</b>
Laparoscopic Procedure	18(26%)	5(8%)	<b>0.009</b>
Follow Up (Median)(Months)	12(1-30)	10(1-23)	0.06
Stage T4	12(17%)	5(8%)	0.13
Resection Level			
LAR	63 (91%)	31 (52%)	<b>&lt;0.001</b>
VLAR*	6 (9%)	29 (48%)	
Neoadjuvant RT	17(25%)	33(55%)	<b>&lt;0.001</b>

Legend: BMI: Body Mass Index; LARs: Low Anterior Resection Syndrome; Significant p values in bold letters; \*Anastomosis Below 5 cm

TABLE II - Multivariate Analysis

	B	S.E.	Wald	df	p	Exp(B)
Neoadjuvant RT	,725	,480	2,285	1	0,131	2,065
Resection Level (LAR/VLAR)	-2,253	,575	15,382	1	<b>&lt;0,001</b>	,105
ProtectiveStoma During Index Operation			1,108	2	0,575	
Open/ Laparoscopic Approaches			5,638	2	0,06	
Constant	2,665	1,165	5,233	1	,022	14,374

Legend: LAR: Low Anterior Resection; VLAR: Very Low Anterior Resection; RT: Radiotherapy; Significant p values in bold letters

group that it in NO LARS group [ respectively, 9%(n: 6) vs 48% (n: 29),  $p < 0.001$ ].

We performed a multivariate analysis to factor that have significance in the Univariate analyzes. Laparoscopic procedures, protective ostomy during index operation, NRT, and operation types (LAR/VLAR) were examined. The multivariate analysis showed that level of anastomosis was the only significant factor for LARS development among the study groups ( $p < 0.001$ ) (Table II)

## Discussion

This study showed that LARs was observed in 47 % of patients underwent rectal surgery in a single center. Furthermore, multivariate analysis showed that a lower level of anastomosis was the only significant factor for LARS among the study groups.

Data regarding LARS after rectal cancer treatment was reported with very different rates in different studies (10%-80%)<sup>6-8</sup>. Furthermore, it is not often discussed in clinical practice. These complications can have a major impact on patients' psychological, social, and emotional functioning, as well as in their overall well-being. This study, with relatively high number of consecutive

patients, might fill this gap and highlights the less discussed issue of LARS.

This study has some limitations that need to be acknowledged. First, the retrospective design. Second, the study population is a cohort of surviving rectal cancer patients who were treated in a single center. Therefore, results may not be generalizable to all patients undergoing rectal cancer surgery. Finally, procedure subgroups were not randomly assigned and differed in their tumor stages as well as their treatments.

The relation between age and LARS was shown many differences in the previous studies. Some studies were not found any correlation between age and LARS<sup>9</sup>. However, there are those who were argued that the development of LARS increases with age<sup>10</sup>, while there were also studies that found higher rates of LARS in younger patients<sup>11</sup>. In this study, there wasn't any significant relation between age and LARS in the two groups. The impact of gender on the development of LARS was controversial. Bregendahl et al. showed that the female gender was a risk factor for LARS after neoadjuvant therapy<sup>11</sup>. For all that, there were studies that the male gender was a significant risk factor for LARs<sup>12</sup>. Nevertheless, this study found no significant relation between gender and LARs. In previous studies, no clearly reported data

regarding a correlation between associated comorbidities and LARS. In this study, we didn't find a difference between two groups on patients' comorbidities. However, Bolton et al. found a linear correlation between American Society of Anaesthesiologists (ASA) Classification score and LARS prevalence<sup>13</sup>. Recently, studies showed that the primary tumour's T stage was not a significant risk factor for LARS<sup>14,15</sup>, we also showed that T4 stage was not a risk factor for LARS. In previous studies, it was shown that the surgical approach (open or laparoscopic) was not a risk factor for LARS<sup>12,16</sup>. In addition, minimally invasive rectal resection procedures such as Transanal Endoscopic Microsurgeries (TEM) and Transanal Minimal Invasive Surgery (TAMIS) were not a significant factor for LARS. Palmieri et al. showed that TEM and TAMIS were not related to bowel dysfunctions after surgery<sup>17</sup>. However, in this study, laparoscopic procedures were significantly higher in no LARS group, in which the majority of the patients were diagnosed with rectosigmoid junction tumour, and subsequently laparoscopic anterior resection was performed. Many previous studies showed that LARS prevalence in patients with a temporary stoma was higher than in patients with no ostomies<sup>18</sup>. In this study, the associated protective stoma with the index operation was significantly higher in LARS group. This may be explained by the diverting ostomies were usually performed to patients with lower anastomosis and who received preoperative NRT. For this reason, we think that there was no relation between diverting stoma itself with LARS. NRT was found an important risk factor in most of the previous studies for LARS<sup>20,21</sup>. Even in short course NRT, Chen et al. reported a significant relation between LARS and preoperative radiotherapy<sup>22</sup>. In this study, despite a significant difference in univariate analysis, NRT was not found a significant risk factor in the multivariate analysis. Furthermore, distal resection level was the only significant risk factor for the LARS development in multivariate analysis. These results showed that distal level anastomosis is the most important factor in LARS occurrence and this statement was emphasized in previous studies<sup>16,23</sup>.

According to these results, we thought that, patients underwent distal rectal resections with reconstructions, regardless of whether NRT was received or not, were at risk for the development of LARS. Therefore, these patients should be informed about these clinical situation and, should be referred early for treatment options. Especially the patients with major LARS, try various treatment options such as dietary changes, medical treatments, and pelvic floor exercises. Some of these patients may have benefits from these treatments. In addition to this, Anorectal Biofeedback is one of the most used treatment modalities for LARS<sup>24,25</sup>. In our department, some of our patients also were included in the Biofeedback program, and the results of these processes will be published in further studies.

## Conclusion

LARs was a common problem that affected the quality of life in patients underwent rectal cancer surgery with reconstructions. The more distal anastomosis is a clear risk factor for LARS occurrence. Early diagnosis and treatment should be kept in mind for these patients.

## Riassunto

La sindrome da resezione anteriore bassa del retto (LARS) nei pazienti sottoposti a chirurgia del retto con risparmio dello sfintere (SSRC) è definita per sintomi quali frequenza, incontinenza, urgenza e costipazione. In questo studio sono stati studiati i tassi di LARS e i fattori di rischio dei pazienti sottoposti a SSRC.

**MATERIALE-METODO:** Sono state esaminate retrospettivamente le cartelle cliniche dei pazienti trattati con SSRC presso il reparto di chirurgia generale. Sono state registrate le caratteristiche cliniche, le chemio-radioterapie neo/adiuvanti, i livelli della resezione distale, le procedure laparotomiche versus laparoscopiche, le complicanze postoperatorie e gli esiti patologici. Per calcolare i punteggi LARS è stato utilizzato il sistema di punteggio LARS definito da Emmertsen e Laurberg.

**RISULTATI:** Il numero di pazienti eleggibili allo studio sono stati 129. La resezione rettale è stata eseguita mediante resezione anteriore bassa (LAR) o resezione anteriore molto bassa (VLAR). VLAR è stato utilizzato per specificare che aveva un'anastomosi <5 cm al margine anale. Il tempo medio del follow-up è stato di 12 (1-30) mesi. I LARS sono stati rilevati in 60 pazienti (% 47). I tassi di LARS sono risultati significativamente più alti nei pazienti sottoposti a VLAR (n: 35,9% vs. 48% <0,001). Nell'analisi univariata sono risultati significativamente differenti, il livello di resezione distale, gli interventi chirurgici laparotomici, la RT neoadiuvante e la stomia temporanea nel gruppo LARS. Tuttavia, nell'analisi multivariata, il livello di resezione distale è risultato l'unico fattore di rischio significativo per LARS.

**CONCLUSIONE:** La sindrome da resezione anteriore bassa (LARS) è stata osservata frequentemente in pazienti sottoposti a chirurgia del retto con conservazione dello sfintere (SSRS). È stato rilevato che i livelli di resezione distale rappresentano il fattore di rischio più importante per lo sviluppo di LARS. Questo risultato ha mostrato che la insorgenza della LARS non dovrebbe essere ignorata nei pazienti sottoposti a SSRS.

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