MMJ

*Malta Medical Journal*, 33 (1): Pages (2021)
http://mmsjournals.org/index.php/mmj

ORIGINAL ARTICLE

# Anterior resection syndrome: Contributing factors and its impact on quality of life

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## BACKGROUND

In Europe, colorectal cancer is the second most common cancer in women and third most common in men. Around half of all colorectal cancer cases affect the rectum. Surgery is the main curative therapy for rectal cancer however this is associated with bowel functional disturbances post anterior resection. The wide spectrum of symptoms following resection and restitution of rectum is what constitutes anterior resection syndrome. The aims of the study were to evaluate the incidence of anterior resection syndrome, identify correlation with clinical variables and its impact on quality of life.

## METHODS

Adult patients who had undergone anterior resection between January 2014 and December 2016 were recruited. Variable factors for low anterior resection syndrome (LARS) were collected retrospectively from clinical records. Data was collected using validated questionnaires, namely LARS scale and EORTC QLQ-C30. Statistical analysis included ordinal logistic regression, one-way ANOVA and Scheffe post-hoc test.

## RESULTS

Between January 2014 and December 2016, 179 patients underwent undergone anterior resection, with 55 patients fulfilling the inclusion criteria. Symptoms of LARS were identified in 51% of patients ($n$=27); with 23% ($n$=13) classified as minor and 28% ($n$=15) as major. Ordinal logistic regression showed that distance from anal verge ($p$=0.02), preoperative radiotherapy ($p$=0.01) and presence of stoma ($p$=0.02) were significantly associated with LARS. Patients with major LARS experienced a significant decrease in their quality of life.

## DISCUSSION

Following anterior resection, patients may suffer from LARS adversely impacting their quality of life. Identification of factors contributing to LARS and its impact on the quality of life allows for better patients stratification in treatment groups and provision of individualised management plan.

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## Introduction

In Europe, colorectal cancer is the second most common cancer in women after breast cancer and third most common cancer in men following lung and prostate cancer. It accounts to 9.7% of all cancers worldwide with 1.8 million new cases diagnosed annually. Around half of all colorectal cancer cases affect the rectum.[1] Surgery is the main curative therapy for rectal cancer. This involves either an abdominal perineal resection (AP) or a sphincter-sparing resection. Improvements in pre-operative staging and surgical techniques have led to the advent of low and ultra-low anterior resection, both being sphincter sparing surgeries for patients who might have otherwise undergone an AP resection. Hence for patients in whom a negative distal margin can be achieved, low anterior resection is preferred as it maintains bowel continence and avoids a permanent colostomy. However, bowel functional disturbances constitute a major problem for many surviving rectal cancer patients following anterior resection. The wide spectrum of symptoms following resection and restitution of rectum is what constitutes low anterior resection syndrome (LARS).[2]

Studies have shown that anterior resection syndrome may be attributed to sphincter injury, denervation during pelvic dissection associated with altered rectal sensation, low coloanal anastomosis as well as reduced capacity and compliance of rectal remnant.[3] Anterior resection syndrome constitutes fecal incontinence or urgency, frequent or fragmented bowel movements, emptying difficulties and increased intestinal gas. Although most of the functional impairments are clinically recovered following one year after surgery, long term studies report the presence of bowel dysfunction for years following resection. This dysfunction varies in its symptoms and severity and may have significant impact on patient's quality of life.[4-5] Hence, the aims of the study were to evaluate the incidence of anterior resection syndrome, identify correlation between anterior resection syndrome and clinical variables and evaluate the impact of anterior resection syndrome on quality of life.

## Materials and Methods

All adult patients, under the care of all surgical firms at the national acute hospital in Malta, who had undergone anterior resection for rectal cancer between January 2014 and December 2016 were included. Approval from data protection unit at Mater Dei hospital was sought to obtain access to patient's details and files for data collection. Approval from local research ethics committee and the patients' caring consultants was obtained. The study was also registered with ClinicalTrials.gov.

Patients were recruited from data recorded in operation record sheets. Patients were excluded if they met the below criteria:

- colon cancer >15cm from anal verge
- permanent stoma
- known disseminated or recurrent disease
- patient without restitution of bowel continuity after one year

All patients were sent a letter by ordinary mail which contained an information sheet and a consent form describing the study aim and declaration of its confidentiality. It also contained 2 validated questionnaires: LARS scale questionnaire and EORTC QLQ-30.[6-7]

The LARS score is a validated five-score questionnaire focusing on bowel symptoms. According to the score patients are grouped into non-LARS (if score obtained is 0-20

points), minor LARS (21-29 points) and major LARS (30-42 points).[6] Hence, it enables quantification of the severity of intestinal and defecatory dysfunction following anterior resection. The EORTC QLQ-30 is a validated 30-item questionnaire designed to assess quality of life in cancer patients. The higher the score was suggestive of better quality of life and better functioning level.[7]

Participants were asked to return the consent form and the questionnaire in a paid self-addressed envelope. Patients who failed to answer the questionnaire were contacted by phone and encouraged to participate to increase the response rate.

The following data on patients' demographic (age, sex, comorbidities), tumour related factors (distance from anal verge, histological and MRI based TNM staging) and stoma related data (presence, type, time before closure) were collected. iSoft Clinical Manager (iCM) and electronic case summaries were used to collect clinical variables. The cancer staging was based on American Joint Commission on Cancer (AJCC) Tumor Node metastasis (TNM) classification system. Analysis was performed using IBM SPSS® Statistics. The relationship between possible risk factors and the severity of LARS as the dependent variable was analysed using ordinal logistic regression. Categorical variables were assessed using one-way ANOVA. Scheffe post-hoc test was used for analysis of variance. Statistical significance was set at $p<0.05$. The study has been reported in line with the STROCSS criteria.

## Results

179 patients had anterior resection between January 2014 and December 2016; out of which 124 patients failed to fit the inclusion criteria hence, 57 patients were eligible to participate. Only 1 patient failed to return the questionnaire and one questionnaire was invalid as several answers were selected simultaneously. Thus the study population was composed of 55 patients (Figure 1).

Table 1 shows the demographic and therapeutic characteristics of the studied participants. Most of the participants were male (69%, *n*=38) and had an overall mean age of 65 years. One quarter of the patients were diabetic (25%, *n*=14), 71% (*n*=39) received neoadjuvant therapy whilst 44% (*n*=44) had adjuvant therapy as decided by the multidisciplinary team. In most patients rectal cancer was between 5-10cm from anal verge (60%, *n*=33). Most patients had T3 disease with no lymph node involvement. (Table 2). Sixty-four percent of procedures (*n*=35) were performed using an open technique, with laparoscopy being employed in one third of patients. Four percent of patients (*n*=2) required conversion to open with adhesion being the reasons for conversion. A defunctioning stoma was created in 51% of patients (*n*=28) with the majority of these having loop ileostomy. Stoma reversal was performed with a mean of 215 days after primary surgery.

LARS symptoms were identified in 51% of patients (*n*=27); classified as minor in 23% of patients (*n*=13) and major in 28% of patients (*n*=15) (Figure 2). The mean time from surgery to patients assessment of LARS though the questionnaire was 995 days.

**Figure 1** Flow chart of patient selection

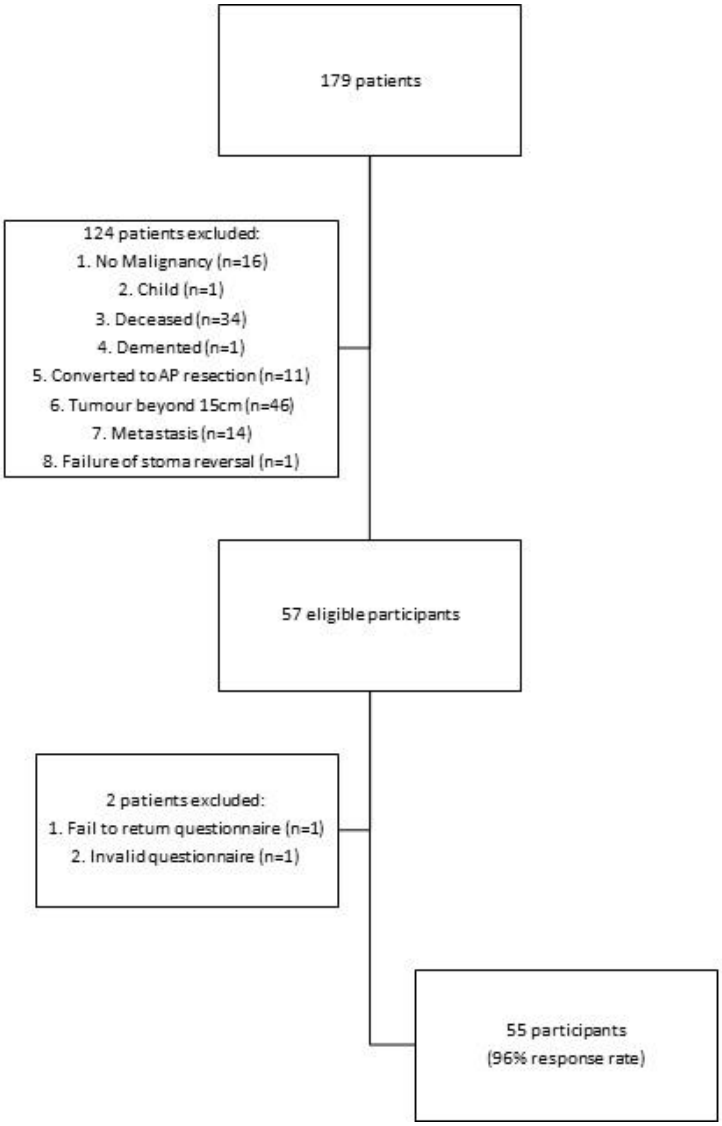
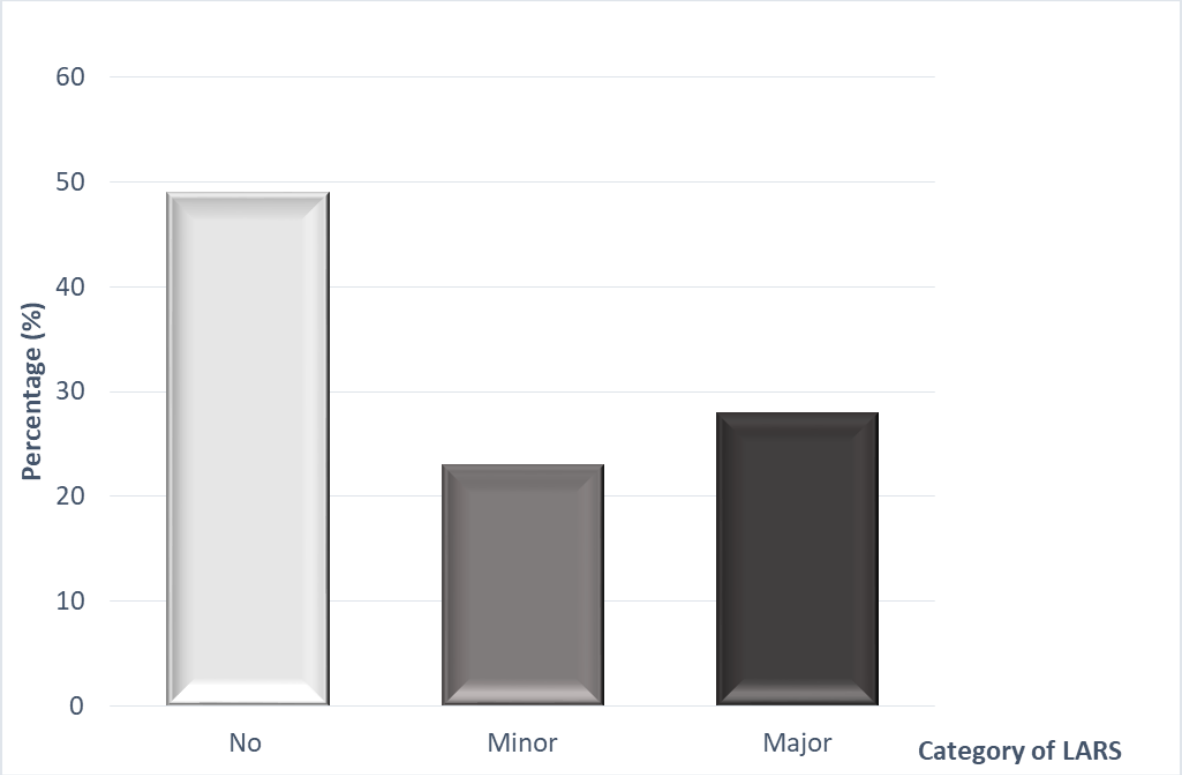


**Table 1** Patients' demographic and therapeutic characteristics

| | Frequency (*n*=55) | Percentage (%) |
|---|---|---|
| **Gender** | | |
| Male | 38 | 69 |
| Female | 17 | 31 |
| **Mean Age (years)** | 65 years | |
| **Diabetes mellitus** | | |
| Yes | 14 | 25 |
| No | 41 | 75 |
| **Hypertension** | | |
| Yes | 29 | 53 |
| No | 26 | 47 |
| **Neoadjuvant therapy** | | |
| Pre-operative radiotherapy | 39 | 71 |
| Pre-operative chemotherapy | 26 | 47 |
| **Adjuvant therapy** | | |
| Post-operative radiotherapy | 0 | 0 |
| Post-operative chemotherapy | 24 | 44 |
| **Distance from anal verge (cm)** | | |
| <5 | 1 | 2 |
| 5-10 | 33 | 60 |
| 10-15 | 21 | 38 |
| **Surgical technique** | | |
| Open | 35 | 64 |
| Laparoscopic | 18 | 33 |
| Conversion to open | 2 | 4 |
| **Presence of stoma** | | |
| Ileostomy | 26 | 47 |
| Colostomy | 2 | 4 |
| No stoma | 27 | 49 |

**Figure 2** Stratification of patients according to LARS symtoms




### *3.1 Association*

Our logistic analysis showed a significant association of LARS with distance from anal verge (OR3.55, 95% CI 1.22-10.28; *p*=0.02), preoperative radiotherapy (OR 4.66, 95% CI 1.44-15.15; *p*=0.01) and presence of stoma (OR3.36, 95%CI 1.21-9.30; *p*=0.02). No significant association was found between gender, diabetes mellitus, tumour staging, surgical technique and interval from stoma reversal (Table 2).

### *3.2 Quality of life*

The larger difference in mean quality of life scores was between the Major LARS group and each of the other two groups as demonstrated in Figure 3. One-way ANOVA analysing quality of life by LARS showed that these differences in quality of life score are statistically significant. The Scheffe post-hoc test ascertained that the significant difference lies between the No LARS and the Major LARS groups (*p*<0.0005; 95% CI 0.81 - 1.94) and between the Minor LARS and the Major LARS groups (*p*<0.01; 95% CI 0.39 - 1.64) (Figure 4).

**Table 2** Histopathological staging and MRI staging of patients with rectal tumour

| | Frequency (n=55) | Percentage (%) |
|---|---|---|
| **Pathological stage, T** | | |
| T0 | 10 | 18 |
| T1 | 4 | 7 |
| T2 | 16 | 29 |
| T3 | 23 | 42 |
| T4 | 2 | 4 |
| **Pathology, N** | | |
| N0 | 33 | 60 |
| N1 | 17 | 31 |
| N2 | 5 | 9 |
| **MRI stage, T** | | |
| No MRI | 8 | 15 |
| T0 | 2 | 4 |
| T1 | 0 | 0 |
| T2 | 16 | 29 |
| T3 | 27 | 49 |
| T4 | 2 | 4 |
| **MRI stage, N** | | |
| N0 | 26 | 47 |
| N1 | 13 | 24 |
| N2 | 8 | 15 |

**Figure 3** Box plot demonstrating quality of life based on LARS score category

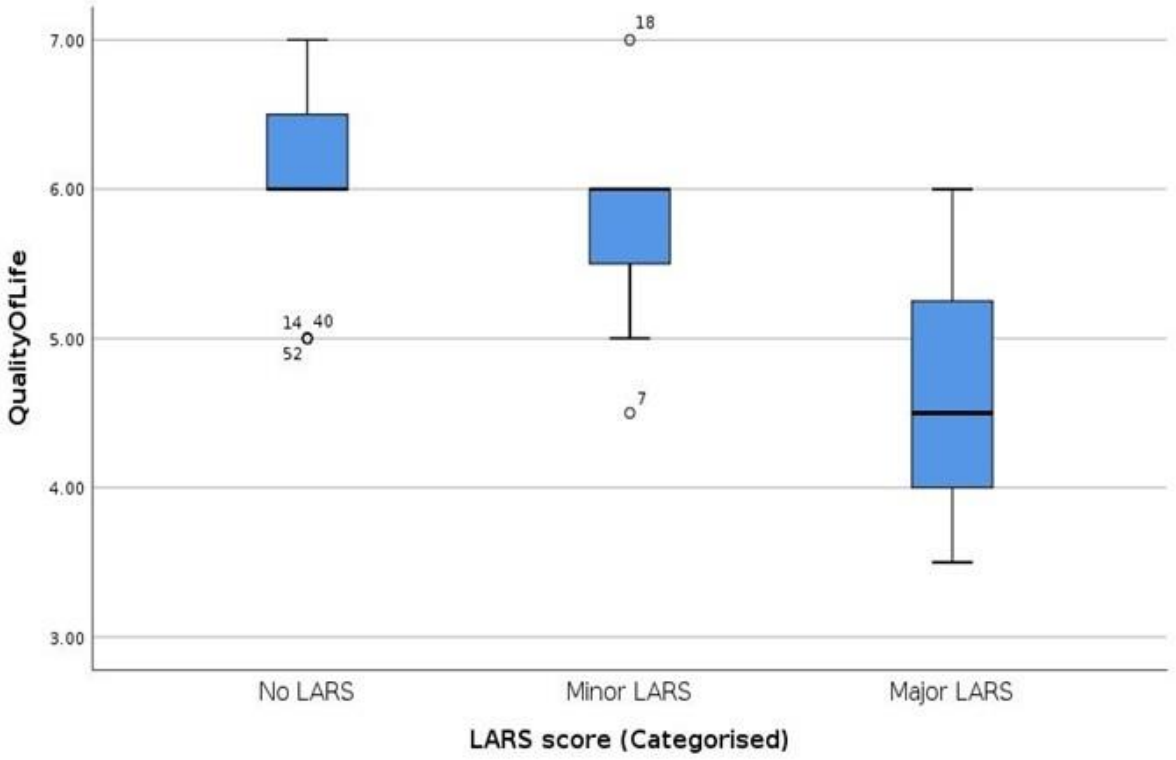



**Figure 4** Scheffe post-hoc test demonstrating quality of life according to different LARS categories.

QualityOfLife
Scheffe

| (I) LARS score (Categorised) | (J) LARS score (Categorised) | Mean Difference (I-J) | Std. Error | Sig. | 95% Confidence Interval | |
|---|---|---|---|---|---|---|
| | | | | | Lower Bound | Upper Bound |
| No LARS | Minor LARS | .35714 | .24724 | .360 | -.2659 | .9802 |
| | Major LARS | 1.37143* | .22388 | .000 | .8072 | 1.9356 |
| Minor LARS | No LARS | -.35714 | .24724 | .360 | -.9802 | .2659 |
| | Major LARS | 1.01429* | .24970 | .001 | .3851 | 1.6435 |
| Major LARS | No LARS | -1.37143* | .22388 | .000 | -1.9356 | -.8072 |
| | Minor LARS | -1.01429* | .24970 | .001 | -1.6435 | -.3851 |

*. The mean difference is significant at the 0.05 level.

## Discussion

In our study, more than half the patients who underwent anterior resection for rectal cancer presented with anterior resection syndrome. Of these, 28% of these experienced major symptoms even after one year post operatively. Although functional bowel changes are more severe in the initial 12 months postoperatively, after which stabilisation in symptoms is achieved, this study demonstrates that the symptoms experienced in LARS are not transient with its effects persisting following one year post operatively. This is comparable to other international studies.[4,8-10]

Literature demonstrates multiple factors which may contribute to LARS. These include the patient's age,[3] gender,[3,8,11] surgical techniques,[11-12] presence of stoma,[9,11,13-14] level of anastomosis[4,11,15] and radiotherapy.[9,11] Consistent with other literature, our study showed that distance from anal verge ($p$=0.02), preoperative radiotherapy ($p$=0.01) and presence of stoma ($p$=0.02) are significantly associated with LARS. Pre-operative radiotherapy and presence of stoma may not have a direct causal relationship to LARS but may be a co-variant of the distance from anal verge. Patients who have a rectal tumour at low distance from anal verge are more likely to have a protective temporary stoma to secure anastomosis and receive neo-adjuvant therapy hence further contributing to LARS. Conversely, patients who have distal sited tumours have a decrease in rectal capacity and reservoir following resection whilst radiotherapy is known to cause pelvic nerve damage, suggesting their independent aspect in contributing to LARS.

LARS was noted to exert significant impact on patient's quality of life. Our study showed that the perception of quality of life was significantly worse in patients who were classified to have major LARS compared to those who did not suffer from LARS or had minor LARS symptoms. This is consistent with the study by Juul et al. which assessed the effect of LARS across multiple European countries.[16]

The strengths of the study include the use of validated scores for classification of LARS and quality of life increasing the validity of the results. This study had a response rate of 96% suggesting adequate representation of the population studied. As the study was performed by filling in an anonymous questionnaire, the patients were more likely to express their symptoms rather than by patient's interview; hence being representative of the true incidence of LARS and its impact on quality of life. Nevertheless, the limitations of this study include its retrospective study design and the small study population.

This study adds to the understanding of the contributing factors leading to LARS, the long term effects of this syndrome post-operatively and its impact on quality of life. Based on our study findings, the factors contributing to LARS are noted to be largely non-modifiable. Hence, adequate consideration should be given in the pre-operative counselling and post-operative identification of the syndrome and management of bowel dysfunction.

## Conclusion

With the improved surgical techniques, colorectal procedures which achieve adequate surgical margin and total mesorectal excision are the current surgical standard for rectal carcinoma. However restoration of bowel continuity does not mean satisfactory bowel function. More than half the patients who had anterior resection suffer from LARS at least one year after surgery. Given its impact on patient's quality of life, pre-operative counselling on bowel dysfunction is crucial in patients who are scheduled to undergo anterior resection. Additionally, patients should be adequately evaluated during postoperative follow-up to enable early identification of the syndrome and provide a patient-tailored management approach.

## Summary box

**Facts already known:**

- In Europe, colorectal cancer is the second most common cancer in women and third most common in men.
- Around half of all colorectal cancer cases affect the rectum.
- Anterior resection is a sphincter sparing surgery for the treatment of rectal cancer.

**New findings:**

- The effects of low anterior resection syndrome (LARS) are not transient with its effects persisting 1 year post operatively.
- The distance from anal verge, preoperative radiotherapy and presence of stoma are significantly associated with LARS.
- Patients suffering from major LARS have a significant decrease in their quality of life

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