# Risk Factors Associated with Low Anterior Resection Syndrome. A Cross-Sectional Study

**DR LIM SEE LIANG**

DISSERTATION SUBMITTED IN PARTIAL FULLFILMENT OF THE

REQUIREMENTS FOR DEGREE OF MASTER OF MEDICINE

(GENERAL SURGERY)


UNIVERSITI SAINS MALAYSIA

2020

# TABLE OF CONTENTS

# ACKNOLEDGEMENTS

First and foremost, I would like to express my deepest gratitude to God for showering me his blessing throughout my research work to complete the study successfully.

I would like to extend my sincere gratitude to my research supervisor, Dr. Wan Zainira Wan Zain (General Surgeon, Hospital Universiti Sains Malaysia) for giving me the opportunity to do this research under her guidance. Her vision, motivation, and sincerity have inspired me to successfully complete this thesis. I would also like to extend my heartfelt thanks to Dato' Dr Ahmad Shanwani Mohamed Sidek (Consultant Colorectal and General Surgeon, Hospital Raja Perempuan Zainab II), my external supervisor who have so much shared his wisdom in assisting me completing my research.

I am thankful for the amazing support shown by all the lecturers and colleagues from Department of Surgery, HUSM. Also, I express my heartful thanks to my parents and wife whom without their prayers and love I would not be here today.

# LIST OF ABBREVIATIONS

| | |
|---|---|
| AR | Anterior Resection |
| CRC | Colorectal Cancer |
| LAR | Low Anterior Resection |
| LARS | Low Anterior Resection Syndrome |
| NT | Neoadjuvant therapy |
| TNM | Tumour, Nodal, Metastasis |
| TME | Total Mesorectal Excision |
| ULAR | Ultra-Low Anterior Resection |

## Abstrak

***Latar Belakang:*** Hasil onkologi selepas pembedahan barah rektum telah meningkat baik dengan ketara dalam beberapa dekad kebelakangan ini dengan penyakit berulang yang lebih rendah and kelangsungan hidup yang lebih panjang dari keseluruhan. Walau bagaimanapun, kelebihan hasil onkologi yang diperolehi telah membayangi fungsi usus selepas pembedahan, di mana kebanyakan gejala agak teruk tetapi kurang dilaporkan. Sebilangan besar pesakit mengalami gejala usus setelah pembedahan, termasuk inkontinensi kentut and najis, bungan najis yang kerap dan tidak terkawal, atau rasa membuang najis yang tidak lengkap. Gabungan symptom di atas selepas pembedahan barah rektum dengan preservasi spinkter dikenali sebagai *Low Anterior Resection Syndrome (LARS).*

***Tujuan:*** Tujuan kajian ini adalah untuk mengenal pasti kelaziman dan faktor-faktor yang berkaitan dengan *LARS.*

***Kaedah:*** Ini adalah kajian keratan rentas dari dua hospital tertiari rujukan dengan unit kolorectal di Kelantan. Semua pesakit menghidap penyakit barak rektum yang telah menjalani reseksi anterior rendah antara Januari 2011 hingha Disember 2020 layak dimasukkan ke dalam kajian. Semasa menjalani rawatan susulan di klinik, pesakit akan diminta untuk melengkapkan soal selidik berdasarkan temu ramah (skor LARS) untuk menilai fungsi usus selepas pembedahan barah rektum. Pesakit seterusnya akan dikelompokkan kepada dua kohort yang berasingan- mereka yang mempunyai gejala utama and mereka yang tidak mempunyai gejala atau hanya gejala ringan. Faktor-faktor akan dibandingkan berdasar kepada golongan gejala LARS utama.

***Keputusan:*** Sebanyak 76 pesakit menghidap penyakit barah rektum yang telah menjalani reseksi anterior rendah dan memenuhi syarat dari klinik direkrut ke dalam

kajian. Terdapat 25 (32.8%) pesakit dengan LARS utama, 10 (13.1%) pesakit LARS minor, dan 41 (53.9%) pesakit tanpa LARS. Paras tumor dari dubur menunjukkan hubungan ( P =0.039) dengan perkembangan LARS utama. Pesakit yang mempunyai tumor kurang dari 8cm dari dubur meningkatkan risiko LARS sebanyak tiga kali ganda berbanding dengan tumor pesakit yang melebihi 8cm ke atas *(Adjusted OR (95% CI) = 3.11 (1.06,9.13))*

***Kesimpulan:*** Kami mengenal pasti paras tumor rendah sebagai faktor yang signifikan yang memberi kesan negatif terhadap fungsi usus selepas pembedahan. Kelaziman LARS yang tinggi menekankan keperluan kajian mengenai faktor-faktor yang menyumbang kepada LARS dan kepentingan memahami patofisiologi LARS supaya kita dapat meningkatkan fungsi usus pesakit dan kualiti kehidupan mereka selepas pembedahan barah rektum.

## ABSTRACT

***Introduction:*** Oncological outcomes following rectal cancer surgery have improved significantly over recent decades with lower recurrences and longer overall survival. However, these survival advantages have greatly overshadowed functional outcomes of surgery, which are poor for many patients and consistently under-reported. Many of the patients experienced several bowel symptoms after surgery, which include flatus and faeces incontinence, frequent bowel opening, urgency or sense of incomplete defecation. This combination of such symptoms after sphincter preserving surgery is referred as Low Anterior Resection Syndrome (LARS).

***Aim:*** The aim of this study is to identify the prevalence and risk factors associated with development of LARS.

***Methods:*** This is a cross-sectional study from 2 tertiary hospitals with colorectal unit in Kelantan. All patients who were diagnosed with rectal cancer and had undergone sphincter-preserving low anterior resection at the participating hospitals between January 2011 and December 2020 were eligible. Upon clinic follow up, patients were asked to complete an interviewed based simple questionnaire (LARS score) designed to assess bowel dysfunction after rectal cancer surgery. Patients were grouped into two separate cohorts—those with major LARS scores and those with mild/no LARS symptoms. Categorical outcomes were compared for the major LARS group.

***Results:*** A total of 76 patients who fulfilled subject criteria recruited from clinic from those who had sphincter preserving rectal surgery for rectal cancer in participating hospital. There were 25 (32.8%) patients with major LARS, 10 (13.1%) patients minor LARS, and 41 (53.9%) patients with no LARS. Height of tumour from anal verge showed the association (P value =0.039) with development of major LARS. Those

patients with less than 8cm tumour from anal verge increased risk of LARS by three times compared to those with 8cm and above (Adjusted OR (95% CI) = 3.11 (1.06,9.13)).

***Conclusion:*** We identified low tumour height as a significant risk factor which has negative impact on bowel function after surgery. The high prevalence of LARS emphasizes the need of study regarding risk factor and importance of understanding pathophysiology of LARS, in order for us to improve patient bowel function and quality of life after rectal cancer surgery

# CHAPTER 1: INTRODUCTION

## 1.1 Literature Review

Colorectal cancer is one of the leading cancers worldwide and the second most common cancer in Malaysia (13.2%) as reported in Malaysia National Cancer Registry Report 2007-2011(1). Left-sided carcinoma is the commonest form and constitutes 81.8% of all notified cases. Historically, abdominal perineal resection was the gold standard for treating low-lying rectal cancers. During the past decades, treatment and cure of rectal cancer have improved markedly with the advent of better surgical techniques and equipment as well as neoadjuvant therapy. Low anterior resection (LAR) with total mesorectal excision has become the preferred procedure in suitable patients with mid and low rectal cancers, with the intention to preserve sphincter and avoid permanent stoma (2).

A recent meta analysis found the estimated prevalence of major Law Anterior Resection Syndrome (LARS) was 41% (95% CI 34 -48). Radiotherapy used in either a neoadjuvant or adjuvant setting was the most consistently assessed variable affecting major LARS and reached statistical significance in 8 of the studies. Tumour height and hence anastomotic level was the second most commonly analysed variable and 6 of the 11 studies identified a statistically significant association with the development of major LARS. Four studies looked at the presence of an ileostomy and duration prior to reversal, all of which found an increased risk of major LARS (3).

The prevalence of LARS in another study showed low and ultralow anastomotic heights and post-operative chemotherapy were independent clinical predictors for

LARS occurrence at 1 year. Obstructive presenting symptoms and ultralow anastomoses were independent predictors at 2 years. Temporary diversion ileostomy was a recurring independent predictor of LARS occurrence at the 2–5-year time. It appears that defunctioning the colon may have long term effects on evacuatory function following anterior resection (4).

A cross-sectional study conducted from 2001 to 2009 in two acute-care teaching hospitals in Barcelona. The questionnaire was sent to 329 patients (response rate of 57.7%), the study population included 184 patients. There were 44 (23.9%) patients with no LARS, 36 (19.6%) with minor LARS and 104 (56.2%) with major LARS. In the univariate analysis, total mesorectal excision ($P$ = 0.0008), protective ileostomy ($P$ = 0.002), preoperative and postoperative radiotherapy ($P$ = 0.0000), postoperative chemotherapy ($P$ = 0.0046) and age ($P$ = 0.035) were significantly associated with major LARS, whereas in the multivariate analysis, total mesorectal excision (odds ratio [OR] 2.18, 95% confidence interval [CI] 1.02-4.65), preoperative radiotherapy (OR 4.33, 95% CI 2.03-9.27) and postoperative radiotherapy (OR 9.52, 95% CI 1.74-52.24) were independent risk factors for major LARS (5).

Another cross-sectional study by assesses bowel dysfunction after low anterior resection with and without neoadjuvant therapy (NT) for rectal cancer. Major LARS was observed in 41% among 938 patients included in that study using LARS score. The study observed an increased risk of major LARS after TME in patients receiving neoadjuvant compared to patients without neoadjuvant therapy and this persisted after adjusting for possible confounding variables. (6).

## 1.2 Study rationale

Oncological outcomes following rectal cancer surgery have improved significantly over recent decades. However, these survival advantages have greatly overshadowed functional outcomes of surgery, which are poor for many patients and consistently under-reported (7). Unfortunately, anatomical preservation of the sphincter does not always mean a perfect restoration of anorectal functions. Many of these patients develop severe bowel dysfunction resulting in incontinence for flatus and/or faeces, 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 (8).

LARS has a major impact on quality of life (QoL), with many patients describing debilitating social limitations and developing psychiatric disorders. Recent studies have addressed factors contributing to LARS, such as age, sex, surgical technique (mesorectal excision and temporary stoma), type of anastomosis, adjuvant therapy, neoadjuvant therapy, and postoperative complications (e.g., anastomosis leakage) (9).

Since patients who undergo a sphincter-sparing rectal resection are at risk of developing LARS, peri-operative efforts should be made to prevent LARS. The aim of this study is to identify the prevalence and risk factors associated with development of LARS in our local setting. It is hoped that identification of clinical risk factors that predispose to the occurrence of LARS will facilitate understanding of pathogenesis and perhaps serve as a platform for the design and execution of future research.

# CHAPTER 2: STUDY PROTOCOL

## 3.1 Documents submitted for ethical approval

# Research Title:
# Risk Factors Associated With Low Anterior Resection Syndrome. A Cross-Sectional Study

**Revised Protocol**

Principal Investigator

Dr. Lim See Liang

Department of General Surgery

Health Campus, Universiti Sains Malaysia (USM)

Supervisor:

Dr. Wan Zainira Wan Zain

Department of General Surgery

Health Campus, Universiti Sains Malaysia (USM)

Co-Supervisor:

Dato' Dr. Ahmad Shanwani Bin Mohammed Sidek

Department of General Surgery

Hospital Raja Perempuan Zainab II

## Introduction

Colorectal cancer is one of the leading cancers worldwide and the second most common cancer in Malaysia (13.2%) as reported in Malaysia National Cancer Registry Report 2007-2011 (1). Left-sided carcinoma is the commonest form and constitutes 81.8% of all notified cases. Historically, abdominal perineal resection was the gold standard for treating low-lying rectal cancers. During the past decades, treatment and cure of rectal cancer have improved markedly with the advent of better surgical techniques and equipment as well as neoadjuvant therapy. Low anterior resection with total mesorectal excision (LAR) has become the preferred procedure in suitable patients with mid and low rectal cancers, with the intention to preserve sphincter and avoid permanent stoma (2).

## Problem statement & Study rationale

Oncological outcomes following rectal cancer surgery have improved significantly over recent decades. However, these survival advantages have greatly overshadowed functional outcomes of surgery, which are poor for many patients and consistently under-reported (7). Unfortunately, anatomical preservation of the sphincter does not always mean a perfect restoration of anorectal functions. Many of these patients develop severe bowel dysfunction resulting in incontinence for flatus and/or faeces, 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 (8).

The term ‘anterior resection syndrome’ (ARS) has been used to describe the diverse and interchangeable evacuatory symptoms that may occur following distal

colorectal resection. Symptoms range from obstructed defaecation to urgency to incontinence and have been quoted as occurring between 0 and 74 % of patients. A pragmatic definition of anterior resection syndrome is disordered bowel function after rectal resection, leading to detriment in quality of life (7).

The estimated prevalence of LARS ranging from 19-52% (10). This variability arises from the use of different data collection tools that are not specific to LARS and this has made any meta-analysis impossible. The LARS score was thus developed to allow for the collection of comparable data which would make such a meta-analysis possible and allow for a more accurate estimation of the true prevalence of LARS. The LARS score is a validated scoring system that is specific for LAR patients, taking into account impact of bowel dysfunction on overall quality of life (11).

LARS has a major impact on quality of life (QoL), with many patients describing debilitating social limitations and developing psychiatric disorders (12). Recent studies have addressed factors contributing to LARS, such as age, sex, surgical technique (mesorectal excision and temporary stoma), type of anastomosis, adjuvant therapy, neoadjuvant therapy, and postoperative complications (e.g., anastomosis leakage) (11).

Since patients who undergo a sphincter-sparing rectal resection are at risk of developing LARS, peri-operative efforts should be made to prevent LARS. The aim of this study is to identify the prevalence and risk factors associated with development of LARS. It is hoped that identification of clinical risk factors that predispose to the

occurrence of LARS will facilitate understanding of pathogenesis and perhaps serve as a platform for the design and execution of future research.

## Research question

1. What is the prevalence of low anterior resection syndrome (LARS) among patients underwent sphincter preserving rectal surgery?
2. What are the risk factors associated with the development of LARS?

## General Objective

To identify the prevalence of low anterior resection syndrome among patients underwent sphincter preserving rectal surgery and variable clinical factors associated with it.

## Specific Objective

1. To identify prevalence and severity of low anterior resection syndrome using LARS score among rectal cancer patients underwent sphincter preserving rectal surgery.
2. To determine the association between various risk factors and the development of LARS.

**Literature review**

A recent meta analysis found the estimated prevalence of major LARS was 41% (95% CI 34 -48). Studies that were included used the LARS score as their primary collection tool. Radiotherapy used in either a neoadjuvant or adjuvant setting was the most consistently assessed variable affecting major LARS and reached statistical significance in 8 of the studies. Tumour height and hence anastomotic level was the second most commonly analyzed variable and 6 of the 11 studies identified a statistically significant association with the development of major LARS. Four studies looked at the presence of an ileostomy and duration prior to reversal, all of which found an increased risk of major LARS (3).

The prevalence of ARS in one study showed low and ultralow anastomotic heights and post-operative chemotherapy were independent clinical predictors for ARS occurrence at 1 year. Obstructive presenting symptoms and ultralow anastomoses were independent predictors at 2 years. Temporary diversion ileostomy was a recurring independent predictor of ARS occurrence at the 2–5-year time. It appears that defunctioning the colon may have long term effects on evacuatory function following anterior resection (4).

A cross-sectional study conducted from 2001 to 2009 in two acute-care teaching hospitals in Barcelona. The questionnaire was sent to 329 patients (response rate of 57.7%), the study population included 184 patients. Predictors of LARS were assessed by univariate and multivariate analyses. There were 44 (23.9%) patients with no LARS, 36 (19.6%) with minor LARS and 104 (56.2%) with major LARS. In the univariate analysis, total mesorectal excision (P = 0.0008), protective ileostomy (P = 0.002),

preoperative and postoperative radiotherapy (P = 0.0000), postoperative chemotherapy (P = 0.0046) and age (P = 0.035) were significantly associated with major LARS, whereas in the multivariate analysis, total mesorectal excision (odds ratio [OR] 2.18, 95% confidence interval [CI] 1.02-4.65), preoperative radiotherapy (OR 4.33, 95% CI 2.03-9.27) and postoperative radiotherapy (OR 9.52, 95% CI 1.74-52.24) were independent risk factors for major LARS (5).

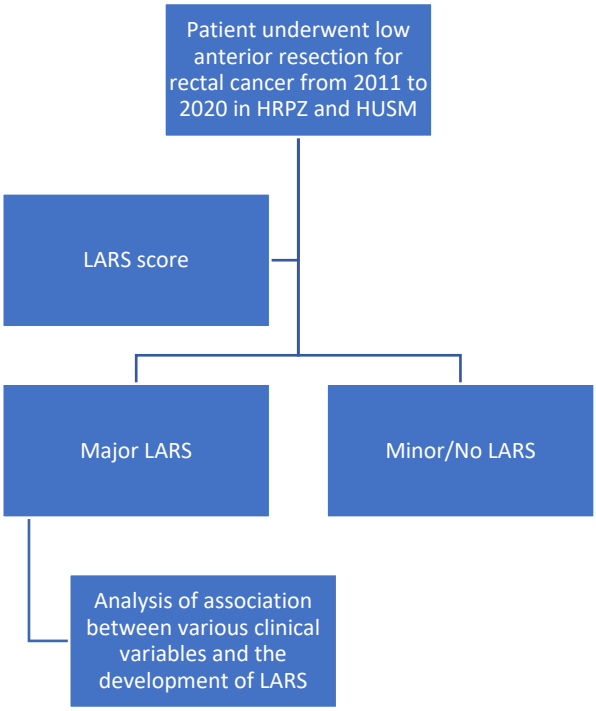
Another cross-sectional study assesses bowel dysfunction after low anterior resection with and without neoadjuvant therapy (NT) for rectal cancer. Major LARS was observed in 41% among 938 patients included in that study using LARS score. The study observed an increased risk of major LARS after TME in NT+ patients compared to NT - patients and this persisted after adjusting for possible confounding variables. In addition, more NT+ patients reported that bowel dysfunction affected their quality of life compared with NT – patients (6).

Hughes, Cornish et al aim to identify the incidence and risk factors for the development of bowel dysfunction following rectal cancer surgery. The study showed 56% had major LARS symptoms, 18% had minor symptoms and 26% had no LARS symptoms. Neoadjuvant radiotherapy, predominantly long-course chemoradiotherapy (LCCRT), was an independent risk factor for development of major LARS symptoms, while restoration of bowel continuity within 6 months was protective (2).

Above studies either meta-analysis or cross-sectional study have shown prevalence of LARS in their respective study centre, and their symptoms were further classified to major, minor or no LARS. Radiotherapy and tumour height were the most

consistently assessed variables, both showing a consistent negative effect on bowel function. In this study, apart from the established risk factors, we are going to assess the relationship other possible factors that might lead to development of LARS which include: approach of surgery, duration defunctioned with stoma, post-operative complications.

**Conceptual framework**




The above diagram illustrates the workflow of this study. This study is a cross-sectional study carried out for patients who underwent low anterior resection for rectal cancer from 1st January 2011 until 31st December 2020 at Colorectal Unit HRPZ II and HUSM. The outcome was divided into 2 groups; major LARS and minor/no LARS. Preoperative, perioperative and post-operative values are recorded to evaluate the association between various clinical variables and the development of LARS.

## Research design

This is a cross-sectional study from 2 tertiary hospitals with colorectal unit. All patients who were diagnosed with rectal cancer and had undergone sphincter-preserving low anterior resection at the participating hospitals between January 2011 and December 2020 were eligible. The data of these patients will be retrieved from Record unit and operation theatre HRPZ II & HUSM. On entry into the study, patients were asked to complete an interviewed based simple questionnaire designed to assess bowel dysfunction after rectal cancer surgery in colorectal clinic during follow up, which will take about 5 minutes. The rest of clinical variables will be retrieved from patient case notes and electronic records.

## Study area

1. Hospital Raja Perempuan Zainab II, Kota Bharu, Kelantan.
2. Hospital Universiti Sains Malaysia, Kota Bharu, Kelantan.

Both hospitals are tertiary hospital and referral centre in Kelantan state of Malaysia with colorectal units which perform majority of surgery for patient with rectal cancer in Kelantan, Malaysia.

## Study duration

Period of data collection will be from 1st June 2020 until 31st Dec 2020.

## Study population

The study subjects are patients who diagnosed with rectal cancer and had undergone sphincter-preserving low anterior resection at the participating hospitals.

**Subject criteria**

Inclusion criteria

- Age 18 years and above
- Had restored bowel continuity for at least 12 weeks
- Patient with rectal cancer with AR/LAR/ULAR performed

Exclusion criteria

- Patient with stoma (unable to assess bowel function)
- Recurrent disease
- Intellectual disability

**Sample size estimation**

Sample size for this study was calculated by using PS Power and Sample Size Calculations Version 3.0 software.

The total samples in which the corrected samples obtained after included the 10% drop out rate (Corrected sample size = calculated sample size + ( 0.1 x calculated sample size)). The detail calculation and output from PS Power and Sample Size Calculations Version 3.0 software for both objectives were as follows;

Based on Objective 2: To determine the association between various clinical variables and the development of LARS among rectal cancer patients

P0: Proportion of rectal cancer patients with mild LARS = 0.25 (expert opinion)

P1: Proportion of rectal cancer patients with severe LARS = 0.56 (Gomez,2017)

Corrected sample size, n= (38 x 2) + 10% dropout

= 76 + 8 = 84

Thus, the total samples required in this study will be 84 patients.

**Sampling method and subject recruitment**

Sampling method for selecting the patients in this study will be simple random sampling.

**Research tool**

1. Low anterior resection syndrome score (11)(13)

   LARS score is a simple five-question tool that was first created in 2012 in Denmark and has been validated in English translation in 2015 by Therese Juul. Obtained with permission.

   On European society of coloproctology website, LARS scoring instructions are available together with the Bowel Function Questionnaire in 24 languages and Malay language was one of the translated versions. All the patient will be interviewed only by principal investigator to reduce the risk of bias.

   The duration to complete the questionnaire will take less than 5 minutes.

**Operational definition**

Low anterior resection syndrome is a constellation of symptoms, such as faecal incontinence or urgency, frequent or fragmented bowel movements, emptying difficulties, and increased intestinal gas, that occurs after a sphincter-sparing resection (ie, anterior resection) of the rectum.

**Data collection method**

The LARS score questionnaire will be directed to patient during clinic follow up.

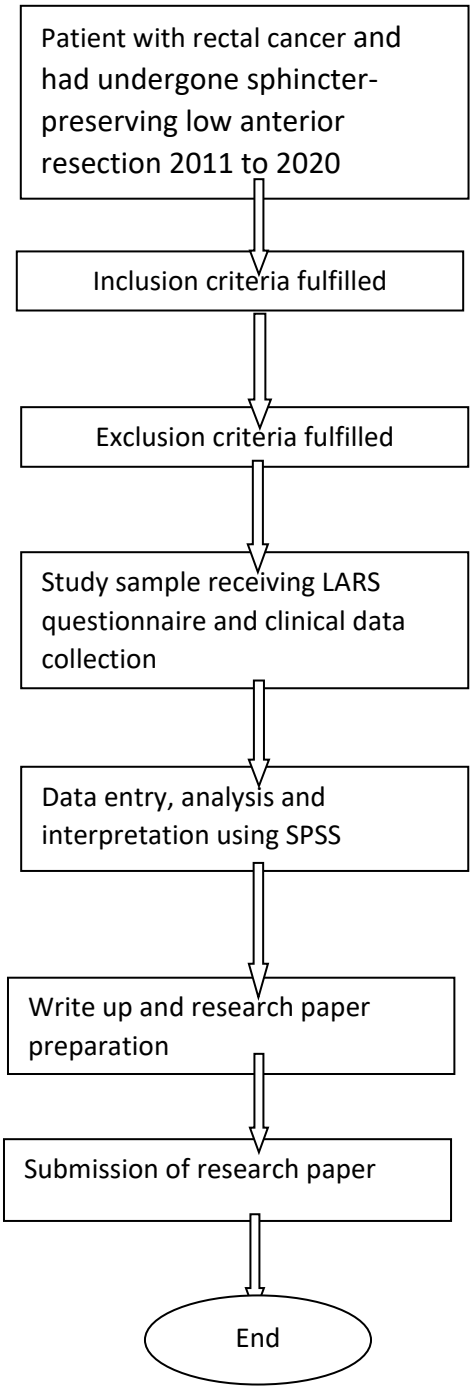
Clinical data from the questionnaires were collected and inserted into a LARS database. Patients were grouped into two separate cohorts—those with major LARS scores and those with mild/no LARS symptoms. Categorical outcomes were compared for the major LARS group.

The following data were recorded from patient case notes

- Demographic: age at surgery: gender, race
- Emergency/ Elective
- Pre-operative variables
    - Tumour staging
    - Tumour height
    - neo-adjuvant CCRT : long course/short course
- Intra-operative variables
    - Laparoscopic or open surgery
    - procedure duration
    - height of the anastomosis
    - formation of a stoma:

        - before surgery or during surgery
    - anterior resection/ low anterior resection /ultra-low anterior resection
- Post-operative variables
    - time defunctioned with a stoma
    - adjuvant chemotherapy
    - adjuvant radiotherapy
- Complication
    - Anastomotic leak
    - pelvic abscess
    - post-operative ileus
    - anastomotic stricture

**Study flowchart**



**Data analysis**

Data will be entered and analysed using SPSS version *22*. Descriptive statistics will be used to summarise the socio-demographic characteristics of subjects. Numerical data will be presented as mean (SD) or median (IQR) based on their normality distribution. Categorical data will be presented as frequency (percentage). Each specific objective will be analyzed descriptively. All the variables for testing the associated factors will be analyzed using Multiple Logistic Regression analysis.

**Expected result(s):**

Table 1: Demographic Characteristics among Rectal Cancer Patients

| Category | Mean (SD) | Frequency (%) |
|---|---|---|
| Age at surgery | | |
| Gender | | |
| Male | | |
| Female | | |
| Race | | |
| Malay | | |
| Chinese | | |
| Indian | | |
| Others | | |
| Type of surgery | | |
| Emergency | | |
| Elective | | |

Table 2: Associated Risk Factors with Low Anterior Resection Syndrome among Rectal Cancer Patients using Multiple Logistics Regression

| Variable | b | Adjusted OR (95% CI) | Wald statistic (df) | p value[a] |
|---|---|---|---|---|
| Age at surgery | | | | |
| Gender | | | | |
| Male | | | | |
| Female | | | | |
| Race | | | | |
| Malay | | | | |
| Chinese | | | | |
| Indian | | | | |
| Others | | | | |
| Type of surgery | | | | |

| | | | | |
|---|---|---|---|---|
| Emergency | | | | |
| Elective | | | | |
| Pre-operative variables | | | | |
| Intra-operative variables | | | | |
| Post-operative variables | | | | |
| Complication | | | | |

**Gantt chart & milestone**

| | **2019** | | | | | | | **2020** | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **J** | **J** | **A** | **S** | **O** | **N** | **D** | **J** | **F** | **M** | **A** | **M** | **J** | **J** | **A** | **S** | **O** | **N** |
| Proposal preparation and presentation | | | | | | | | | | | | | | | | | | |
| Ethics approval | | | | | | | | | | | | | | | | | | |
| Data collection and entry | | | | | | | | | | | | | | | | | | |
| Data analysis and interpretation | | | | | | | | | | | | | | | | | | |
| Research Report writing up | | | | | | | | | | | | | | | | | | |
| Submission of draft and revision | | | | | | | | | | | | | | | | | | |
| Submission of research study | | | | | | | | | | | | | | | | | | |

**Ethical consideration(s):**

1. **Subject vulnerability and risk**

   Participant included are 18 years old and above and those with intellectual disability are excluded, as they probably can't answer questionnaire. Risk of participant in this study also minimal. Taking part in this study would not change patient current management of the disease. Patient or participant will not get any personal benefit nor detriment in this study. However, patient will be given full freedom to participate or not without affecting his/her medical condition management and care.

2. **Declaration of absence of conflict of interest**

   This study is absence of conflict of interest

3. **Patient's consent**

   Written consents are prepared in both English and Malay language. Patients will also be explained that any information is kept confidential. The use of a translator will be available for any other patients who are not well commanded in English or Malay language. After all the explanations are given, the patients will sign or use thumbprints once they agree with the study. Patients are given the option to stop being a part of this study at any time.

4. **Privacy and confidentiality**

   Throughout this study, all personal information and data will not be disclosed unless required by law. Subject's confidentiality will be protected; no name or identifying information will be collected. Data will be protected through a

password set to access the database and securely locked. The data is only accessible by researchers involved in this study. The data will be used and remain directly available up to the completion of the study. Thereafter, the data will be compressed with encryption and archived in a flash drive after proper documentation. This is to be destroyed by formatting the flash drive after a 5 years maintenance period determined by the date of its formal closure. We define the formal 15 closure as the submission of a closure report to the National Medical Research Registry of Malaysia. Subject's data and information will be kept confidential and will be known by the research team only. Only aggregated (grouped) results will be presented and submitted to local or international peer-reviewed medical journals and relevant government ministries.

## 5. Publication Policy

An approval from Director General of Ministry of Health, Malaysia will be obtained prior to publication of this research and subject's personal information will be kept confidentially. When publishing or presenting the study results, patient's identity will not be revealed without the expressed consent.

## 6. Community Sensitivities And Benefits

This study may not have immediate benefit to patient or community. However, identifying possible risk factors for development of LARS may help to facilitate understanding of pathogenesis and perhaps serve as a platform for the design and execution of future research.

## 7. Honorarium and incentives

No incentives will be provided to patient. Questionnaire will be conduct in patient routine clinic follow up and question asked is part of patient post operative symptoms review. Patient will not need to travel purposely to participate in this study.

## 8. Other ethical review board approval

National Medical Research Review [NMRR,MOH])

- Status of application – approved

**ATACHMENT A**

## RESEARCH INFORMATION

**Research Title:**

Risk Factors Associated with Low Anterior Resection Syndrome: A cross-sectional study

**Name of investigator and institution:**

Dr Lim See Liang (MMC 62682), Health Campus Universiti Sains Malaysia (USM)

Dr. Wan Zainira Wan Zain (MMC 38667) ,Health Campus Universiti Sains Malaysia (USM)

Dato' Dr. Ahmad Shanwani Bin Mohammed Sidek (MMC 31882), Hospital Raja Perempuan Zainab II

**Name of sponsor**

Self-sponsored

**Introduction**

You are invited to take part voluntarily in a research. This study is regarding low anterior resection syndrome. We are trying to know the prevalence of low anterior resection syndrome in patient underwent sphincter preserving rectal surgery, we will identify it using LARS score. At the same time, we will evaluate variable clinical risk factors associated with development of LARS.It is important that you read and understand this research information before agreeing to participate in this study. You will receive a copy of this form to keep for your records if you agree to participate.

Your participation in this study is expected to take 5 minutes. The expected number of participants is 84 individuals.

**Purpose of the study**

The purpose of this study is to identify the prevalence of low anterior resection syndrome using LARS score among rectal cancer patients post rectal surgery and to determine the association between various clinical variables and the development of LARS

**Participants criteria**

The research team members will discuss your eligibility to participate in this study. It is important that you are completely truthful with the staff.

This study will include individual who are

- Age 18 years and above
- Had restored bowel continuity for at least 12 weeks
- Patient with rectal cancer with AR/LAR/ULAR performed

This study will NOT include individual who are

- Patient with stoma (unable to assess bowel function)
- Recurrent disease
- Intellectual disability

**Study procedure**

You will be interviewed by a doctor. This form contains 5 sections that will enquire about your bowel symptoms after rectal cancer surgery.

It is important that you answer all of the questions asked by the study staff honestly and completely which will take about 5 minutes of your time. Study team will also access your medical records for the information regarding age, race, and operation details.

**Risks**

We do not anticipate any major problems arising from participation in this study. Participation in this study will not affect your treatment, and the risk is minimal. You are free to decline to answer any of the questions that you feel uncomfortable with.

However, we do understand if you are having major LARS, it might cause physical and mental stress. By having LAR syndrome is just collective of bowel symptoms patient might experience after rectal surgery, with various severity in different patients. This questionnaire helps us to understand your symptoms better in order for us to monitor and treat it. We will alert primary doctor regarding your symptoms so they can monitor u more regularly and initiate treatment if necessary. We also will provide psychosocial support by referring to respective team if needed.

**Benefits**

There are unlikely to be direct personal benefits to you from this study. It is hoped that this research will have a beneficial impact by helping us to identify clinical risk factors