study in Thai patients



**KEYWORDS** 

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Factors determining low anterior resection

syndrome after rectal cancer resection: A

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### Summary Background/Objective: Defective defecation function, also known as low anterior resection syndrome (LARS), is a common problem after surgical treatment of rectal cancer that has a detrimental effect on quality of life. This study aimed to look for the incidence of LARS in low anterior resection patients whose native rectum could not be kept and determine factors influencing major LARS. Methods: Rectal cancer patients who underwent tumor removal with mesorectal excision and colorectal anastomosis by a colorectal surgeon during the years 2004–2013 were asked to participate a structured interview using the verified version of the Low Anterior Resection Score questionnaire. Clinical parameters were analyzed against the incidence of major LARS. The cut-off anastomotic level that corresponded to the risk of major LARS was calculated by using a receiver operating characteristic curve. Anorectal physiology was compared between those with major LARS and those without LARS by anorectal manometry. Results: This study included 129 patients (67 men and 62 women). Incidences of minor LARS (LAR score 21–29) and major LARS (LARS score $\geq$ 30) score 21een those with major LARS and those univariate analysis, factors associated with major LARS were extent of operation, presence of temporary ostomy, and chemoradiation therapy. Major LARS was found at 28.2% in those who underwent low anterior resection, which was significantly higher than the incidence of 5.2% in the anterior resection group (p < 0.01). Radiation therapy was the only factor independently associated with major LARS at an odds ratio of 6.55 (95% confidence interval: 2.37-18.15). The receiver operating characteristic curve plot between sensitivity and specificity of the anastomotic level in determining major LARS showed an area under the curve of 0.73. The cut-off anastomotic level that best predicted major LARS was at 5 cm, which gave

Conflicts of interest: All contributing authors declare no conflicts of interest.

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a negative predictive value of 89%. Individual defecation symptoms that were significantly associated with major LARS included pain on defecation, difficulty holding stool, and needing to use a pad. Anorectal manometry showed a significant difference in the resting anal pressure and squeeze pressure, which suggests that derangement in sphincteric function caused by surgery and postoperative adjuvant treatment may contribute to the LARS.

*Conclusion:* LARS is a significant problem found in about one third of rectal cancer patients after colorectal anastomosis. Symptoms of concern include pain on defecation and decreased ability to hold. Risk of having major LARS increases with adjuvant treatment and lower anastomotic level.

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### 1. Introduction

Colorectal cancer (CRC) is one of the leading cancers worldwide. In Thailand, the cancer ranks within the top five and is responsible for 15% of all cancers in men and 11% in women.<sup>1</sup> Survival of CRC has markedly improved recently with an overall 5-year survival rate at ~70%.<sup>2</sup> In Songklanagarind Hospital, the major tertiary care unit and referral center in southern Thailand, a recent study reported that the 5-year survival rate of Stage I–III CRC was 73%.<sup>3</sup>

Low anterior resection (LAR) with a total mesorectal excision (TME) is the current gold standard surgical technique that is generally used for the mid and some lower level rectal cancers.<sup>4,5</sup> Recent advances in surgical techniques and neoadjuvant therapy have reduced the tumor recurrence rate after resection and, at the same time, provided a better chance to preserve the sphincter in rectal cancer patients whose tumor is situated in the lower rectum.<sup>6</sup> Unfortunately, anatomical preservation of the sphincter does not always mean perfect restoration of anorectal functions, as many patients who undergo a LAR for rectal cancer suffer major defecation dysfunction, including incontinence, urgency, and clustering of stools. Such symptoms are defined as LAR syndrome (LARS) or anterior resection syndrome<sup>7,8</sup> and are usually associated with a negative impact on long term quality of life.<sup>9</sup>

A variety of studies have reported an incidence of LARS of between 19% and 52% in patients receiving a LAR, depending on syndrome classification as well as the period and intensity of follow-up.<sup>10-13</sup> Recent studies have addressed factors determining LARS, such as age, sex, surgical technique (mesorectal excision, intersphinteric resection, and temporary stoma), type of anastomosis, adjuvant therapy, neoadjuvant therapy, and postoperative complications (e.g., anastomosis leakage).<sup>6,7</sup> However, no consensus has vet been drawn regarding the major risk factors for LARS. Some studies have attempted to identify LARS risk factors, but have not indicated the statistical significance of the identified factors. Some recent studies have suggested that the level of anastomosis could be a crucial factor determining poor continence outcome. However, most studies have been limited in various ways and no significant conclusion could be reached.<sup>11,13,14</sup> It is generally agreed that a low level of anastomosis tends to increase the risk of a worse outcome, which can be explained by the disturbance of normal physiology of rectal capacity and reduced rectal compliance after a LAR. However, there has been to date no study examining the relationship between anastomosis cut-off level and good continence.

In this study, we aimed to evaluate functional outcomes after LAR and anterior resection (AR) in patients with rectal cancer and address the incidence of LARS by using a standard questionnaire. Factors determining significant LARS, especially anastomosis level, were analyzed. In addition, anorectal manometric profiles were compared between the major LARS group and the normal one, in order to determine the pathophysiology of LARS.

## 2. Methods

Patients who were diagnosed with rectal cancer and had undergone a tumor resection with mesorectal excision in either AR or LAR method at our institution between 2004 and 2013 who met the inclusion criteria were asked to participate in the study. For analysis, LARs in this study were subgrouped into: conventional LAR (LAR, those with colorectal anastomosis); and extended LAR (ELAR: those with coloanal anastomosis). The indication for colostomy in this study was the preference of the attending surgeon, which generally depended on difficulty of the anastomosis as determined by height of the anastomosis from the anorectal ring, type of pelvis, and body build of the patient. All included patients had a postoperative follow-up period of at least 12 months, had completed their adjuvant treatment and had had their protective ostomy closed. Patients with a distant metastasis at the time of diagnosis, who had not had their ostomy closed prior to being considered for the study and/or had local recurrence after surgery and had neoadjuvant therapy were not included. All participants consented to a structured interview wherein they completed a questionnaire to assess their defecation functions. The questionnaire consisted of two parts, an LAR scoring part and an additional "stool diary" to look for any abnormal stooling behaviors (stool diary created by one of the authors, K.T.). The LAR score used the translated-to-Thai version of the questionnaire proposed by Emmertsen and Laurberg.<sup>15</sup> Validation of the translated questionnaire was done before the study.

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