

SUBMITTED VERSION

This is the pre-peer reviewed version of the following article:

Kheng-Seong Ng, Marc A Gladman

Patient reported and physician recorded bowel dysfunction following colorectal resection and radical cystectomy: a prospective, comparative study

Colorectal Disease, 2020; OnlinePubl:1-32

which has been published in final form at <http://dx.doi.org/10.1111/codi.15041>. This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Use of Self-Archived Versions.

© This article is protected by copyright. All rights reserved [Wiley]

PERMISSIONS

<https://authorservices.wiley.com/author-resources/Journal-Authors/licensing/self-archiving.html>

Submitted (preprint) Version

The submitted version of an article is the author's version that has not been peer-reviewed, nor had any value added to it by Wiley (such as formatting or copy editing).

The submitted version may be placed on:

- the author's personal website
- the author's company/institutional repository or archive
- not for profit subject-based preprint servers or repositories

Self-archiving of the submitted version is not subject to an embargo period. We recommend including an acknowledgement of acceptance for publication and, following the final publication, authors may wish to include the following notice on the first page:

"This is the pre-peer reviewed version of the following article: [FULL CITE], which has been published in final form at [Link to final article using the DOI]. This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Use of Self-Archived Versions."

The version posted may not be updated or replaced with the accepted version (except as provided below) or the final published version (the Version of Record).

There is no obligation upon authors to remove preprints posted to not for profit preprint servers prior to submission.

1 April, 2020

<http://hdl.handle.net/2440/123961>

Title: Patient reported and physician recorded bowel dysfunction following colorectal resection and radical cystectomy: a prospective, comparative study

Authors: Kheng-Seong Ng MBBS (Hons I), PhD, FRACS ¹
Marc A Gladman PhD, MRCOG, FRCS (Gen Surg) FRACS ²

Kheng-Seong Ng National Health and Medical Research Council
(NHMRC) Colorectal Research Fellow

Marc A Gladman Professor of Colorectal Surgery

Published Colorectal Dis. 2020 Mar 16. doi: 10.1111/codi.15041. Online ahead of print.

Institution: ¹ Academic Colorectal Unit, Sydney Medical School - Concord, University of Sydney, Australia

²Gastrointestinal & Enteric Neuroscience Research Group, Adelaide Medical School, Faculty of Health & Medical Sciences, The University of Adelaide, Australia

Supportive Foundations:

Dr. Kheng-Seong Ng has been supported by an NHMRC Postgraduate Research Scholarship, and a Royal Australian College of Surgeons (RACS) Foundation of Surgery Research Scholarship

Category: Original article

Conflicts: No conflicts of interest exist.

Word Count: 3146

Author Contributions:

KSN was involved in study conception and design, data acquisition, data analysis and interpretation, drafting and critical review of the manuscript, final approval of manuscript.

MAG was involved in study conception and design, data acquisition, data analysis and interpretation, drafting and critical review of the manuscript, final approval of manuscript.

Address for correspondence:

Professor Marc A Gladman
S234 Helen Mayo South,
Frome Road,
The University of Adelaide
Adelaide, South Australia 5005
Tel: +61 8 8313 5035
E-mail: marc.gladman@adelaide.edu.au

ABSTRACT

Aim:

Bowel dysfunction following anterior resection (AR) is termed ‘low anterior resection syndrome (LARS)’. It is unclear whether such dysfunction occurs following other bowel/pelvic operations as well. This study aimed to characterise and compare bowel dysfunction following AR, right hemicolectomy (RH) and radical cystectomy (RC).

Method:

A prospective study of consecutive patients undergoing AR, RH, and RC (2002–2012) was performed at a tertiary referral centre in Sydney, Australia. Outcome measures included: (i) patient-reported (satisfaction with bowel function, self-described bowel function, and self-reported change in bowel function); (ii) objective assessment of bowel function using validated criteria to identify symptoms and stratify patients into those with constipation and/or faecal incontinence (FI); and (iii) health-related quality of life (SF-36v2).

Results:

Of 743 eligible patients, 70% participated (AR: $n=338$, mean age 69.6yrs [SD11.9], 59% male; RH: $n=150$, 75.8yrs [SD10.5], 54% male; RC: $n=34$, 71.1yrs [SD14.1], 71% male). AR patients were three times more likely to report change in bowel function post-surgery, and self-judged their bowel function as ‘abnormal’ more frequently (64%) than following RH (35%) and RC (35%) ($P<0.01$). AR patients were four times more likely to meet criteria for *concomitant* constipation and FI. Patients with *concomitant* constipation and FI had lower physical and mental SF-36v2 scores ($P<0.001$).

Conclusion:

Bowel dysfunction occurred after RH and RC but rates were higher following AR. This suggests that LARS occurs due to a direct impact of partial/complete loss of the rectum rather than just due to loss of bowel length and/or the consequence(s) of pelvic dissection.

WHAT DOES THIS PAPER ADD TO THE LITERATURE?

This paper has used patient-reported and objective measures to confirm that rates of bowel dysfunction following anterior resection are significantly higher than those following other abdomino-pelvic surgical procedures, suggesting that such dysfunction occurs due to the direct impact of rectal resection rather than just loss of bowel length and/or pelvic dissection.

INTRODUCTION

Bowel dysfunction following anterior resection (AR) of the rectum, termed 'low anterior resection syndrome' (LARS)[1-6], is characterised by bowel frequency, evacuatory dysfunction, and faecal urgency/incontinence. Rates of such bowel dysfunction range between 3.2 and 79.3%[7-9]. However, it is unclear whether bowel dysfunction only occurs / is higher following AR or whether it occurs following other abdominopelvic procedures too, as no previous studies have reported comparative data. This is all the more pertinent given that high rates of bowel dysfunction have been demonstrated amongst community-dwellers, the majority who have never undergone surgery[10-12].

Intuitively, LARS is considered to occur as a consequence of the partial/complete loss of the rectum, although loss of bowel length and / or the consequences of pelvic dissection may provide alternative explanations for the observed bowel dysfunction. Accordingly, bowel dysfunction following (i) right hemicolectomy (RH), which results in loss of bowel length but without pelvic dissection, and (ii) radical cystectomy (RC), which involves (radical) dissection of pelvic viscera but without rectal resection or loss of bowel length, may provide useful comparison rates for more accurate interpretation of the those following AR. Such knowledge may also shed light on its potential underlying pathoetiology of LARS and whether partial/complete resection of the rectum (with its critical role in the storage/evacuation of faeces) is the key driver of bowel dysfunction following AR.

Recently, efforts have been made to arrive at a consensus definition for LARS[6] and a symptom scoring tool[2] has been developed to objectively assess severity. However, the LARS score does not directly report on important patient-reported outcome measures

(PROMs), such as patient-reported descriptions of bowel function or satisfaction with it, or impact on quality of life. Consequently, a novel opportunity exists to robustly document these outcomes following AR and in comparison to other abdominopelvic procedures. Therefore, this study aimed to objectively measure rates of bowel dysfunction, including PROMs, and health-related quality of life (HRQoL), in the setting of a prospective, comparative study following AR, RH, and RC to test the hypothesis that rates of bowel dysfunction would be significantly higher after AR.

MATERIALS AND METHODS

Study design and participants:

A prospective study of consecutive patients who underwent surgery between 2002 and 2012 (inclusive) at a tertiary referral centre in Sydney, Australia was performed. The study population was identified from prospectively maintained electronic databases and included those who had previously undergone: (i) AR for colon/rectal adenocarcinoma; (ii) RH for colon adenocarcinoma; and (iii) RC for lower urological tract malignancy. All patients who were alive and without a stoma at the time of study were included. Patients were contacted by postal mail in 2013 and sent a self-administered questionnaire for prospective assessment of their post-operative bowel function and HRQoL. AR was defined as a restorative proctectomy with anastomosis within 15cm from the anal verge[13, 14]. In our institution, even sigmoid cancers are treated typically with a high anterior resection, involving high ligation of the inferior mesenteric artery, splenic flexure mobilisation, and anastomosis to the mid-upper rectum.

Clinical assessment of post-operative bowel symptoms

The questionnaire comprised seven sections and incorporated questions designed to provide *subjective/patient-reported* and *objective* symptom-based assessment of post-operative bowel function. Clinicopathological details of the patient's index surgery were obtained from relevant databases[15].

Patient-reported outcome measure (PROM) assessment

A 7-point Likert scale (0 to 6) was used to subjectively assess satisfaction with bowel function, with the anchors of '0' referring to complete dissatisfaction, and '6' referring to complete satisfaction. An *a priori* decision was made to interpret scores of 4 to 6 as 'satisfied', a score of 3 as 'ambivalent', and scores of 0 to 2 as 'dissatisfied'.

Other patient-reported measures recorded included:

- (i) the need to seek medical attention for post-operative bowel dysfunction;
- (ii) self-described post-operative bowel function (normal, constipated, diarrhoea, or variable); and
- (iii) self-reported change in bowel function post-surgery.

Objective symptom assessment

Postoperatively, bowel function was objectively assessed using standardised criteria based on validated scoring systems, specifically Rome III criteria[16] for diagnosis of functional bowel disorders, Cleveland clinic (Wexner) constipation score[17], and modified Cleveland clinic (Vaizey) incontinence score[18]. These criteria and scoring systems were used to document individual symptoms of bowel dysfunction, of which 18 were identified (see ‘Results’).

To reflect the physiologic function of the rectum, i.e. the *storage* and *evacuation* of faeces, these objective symptoms were stratified into two broad categories of dysfunction. Symptoms of *storage dysfunction* included: (i) bowel frequency – >3 bowel movements per day; (ii) loose stools – Bristol type 6 or 7 stools during $\geq 75\%$ of bowel movements; (iii) incontinence to solid stool $\geq 1/\text{month}$; (iv) incontinence to liquid stool $\geq 1/\text{month}$; (v) incontinence to flatus $\geq 1/\text{month}$; (vi) need to wear a pad/plug for faecal soiling $\geq 1/\text{month}$; (vii) faecal urgency – the inability to defer defaecation for 15 minutes $\geq 1/\text{month}$; (viii) poor stool/gas discrimination – stool mistaken for gas $\geq 1/\text{month}$; and (ix) need for constipating medications $\geq 1/\text{month}$. Symptoms of *evacuation dysfunction* included the following, occurring for at least 25% of defaecations: (i) excessive straining at stool; (ii) sensation of incomplete emptying following a bowel movement; (iii) sensation of anorectal obstruction during a bowel movement; (iv) unsuccessful

bowel movement attempts; (v) need to digitate (either per anus or per vagina) to help complete a bowel movement; (vi) need for an enema or suppository to facilitate a bowel movement; (vii) need for toilet revisiting due to incomplete evacuation; (viii) evacuation attempts lasting >10 minutes, and (ix) hard stools – Bristol type 1 or 2 stools.

Using these symptom phenotypes, patients were then formally classified as having (a) storage dysfunction; and/or (b) evacuation dysfunction. Storage dysfunction was diagnosed when either incontinence to solid or liquid stool, or two or more symptoms of storage dysfunction were reported. Evacuation dysfunction was diagnosed when two or more symptoms of evacuation dysfunction were reported. This progression of grouping individual symptoms into two symptom ‘domains’ allowed stratification of patients into those with (i) storage dysfunction alone; (ii) evacuation dysfunction alone; (iii) concomitant storage and evacuation dysfunction; and (iv) no dysfunction – criteria not met.

Quality of Life Assessment

HRQoL was assessed in all patients using the SF-36v2[®] Health Survey[19]. The SF-36v2 is a generic health outcome measure, comprising a physical composite score (PCS), which identifies limitations in physical functioning and/or restrictions due to bodily pain (reflected by low PCS scores), and a mental composite score (MCS), which identifies psychological distress, and/or social and role disability due to emotional problems (reflected by low MCS scores)[19] [20].

This study was approved by the Sydney Local Health District Human Research Ethics Committee (LNR/12/CRGH/39).

Statistical analysis

Descriptive statistics and univariate analyses using *t*-test, Mann-Whitney test and contingency (Chi-square) analysis for parametric, non-parametric, and categorical data, respectively, were conducted to assess patient and clinical characteristics and the crude association with study outcomes. Age-adjusted odds ratios were obtained by multivariate logistic regression modelling. HRQoL measures (PCS and MCS) were compared between the three study groups using the ANOVA test, and adjusted for age by multivariate linear regression. For all tests, a P-value of <0.05 was significant (SPSS version 21; SPSS Inc., Chicago, IL, USA).

RESULTS

Study Population Characteristics

Anterior resection:

Of the 754 patients who underwent AR over the study period, 476 were alive and met the inclusion criteria. Of these, 338 subjects (71.0%) participated (mean age 69.6yrs [SD11.9], 58.9% male). Demographic characteristics and pertinent factors in the medical histories are presented in Table 1. The mean duration from the patient's surgery to their questionnaire was 5.0yrs (SD 2.7). The clinicopathological features of the study population are presented in Table 2. Of patients who underwent AR in the study period, two subsequently underwent pelvic exenteration for local cancer recurrence and were excluded from the study; no patients had a stoma formed for post-operative bowel dysfunction.

The gender distribution, tumour site, anastomotic heights, method of surgery, proportions receiving neoadjuvant radiotherapy and adjuvant chemotherapy, and proportions with a temporary diverting ileostomy, were similar between study participants and non-responders. However, study participants were younger at the time of surgery (64.7 vs. 68.5 years, $P<0.001$), had lower ASA scores ($P<0.001$), had lower rates of anastomotic leaks (1.8% vs. 4.3%, $P=0.02$), and had lower proportions of N- and M-positive cancers (31.1% vs. 48.0%, $P<0.001$).

'Control' groups: Right hemicolectomy and Radical cystectomy

Of 225 alive patients who underwent RH surgery and met the inclusion criteria, 150 patients (66.7%) participated. Comparisons of this group's characteristics with the AR group are presented in Tables 1 and 2. RH patients were significantly older (mean age 75.8yrs [SD10.5] vs. 69.6yrs [SD11.9], $P<0.001$).

Of the 42 alive RC patients, 34 patients (81.0%) participated. Comparisons of their data with the AR group are presented in Table 1 and Table 2. The AR and RC patients were age and sex matched (mean age: RC 71.1yrs [SD14.1] vs. AR 69.6yrs [SD11.9]; $P=0.50$) (Table 1). No RC patients received pelvic radiotherapy.

'PROM' Assessment

Anterior resection:

Patient-reported assessment of post-operative bowel function is presented in Table 3. Almost three-quarters (72.1%) expressed satisfaction with their current bowel function (satisfaction scores 4 to 6). Yet, over one-third ($n=123$, 36.4%) had sought medical attention for post-operative bowel dysfunction, whilst two-thirds of patients self-judged their own bowel habit as 'abnormal'. The majority (59.8%) of patients felt their bowel function had changed since surgery, with most reporting increased bowel frequency (23.3%) and looser stools (10.8%).

'Control' groups: Right hemicolectomy and Radical cystectomy

Satisfaction with post-operative bowel function was similar between RH and AR patients (median 5 [IQR 4-6] vs. 5 [IQR 3-6], $P=0.22$). However, RH patients reported significantly lower rates of seeking medical attention (20.0% vs. 36.4%, $P<0.001$) and change in bowel function post-surgery (30.7% vs. 59.8%, $P<0.001$). Patients were more likely to describe their bowel habit as 'normal' (65.3%) following RH compared with AR (36.4%) ($P<0.001$) (Table 3).

Satisfaction with post-operative bowel function was similar following RC compared to AR (median 4.5 [IQR 3-6] vs. 5 [IQR 3-6], $P=0.62$). AR patients were three times more likely to self-report change in bowel function following surgery compared with RC patients (OR3.01,

95%CI 1.44–6.29). Patients were more likely to describe their bowel habit as ‘normal’ (64.7% vs. 36.4%, $P=0.002$) following RC compared with AR (Table 3).

Objective Symptom Assessment

Anterior resection:

Objectively, at least one symptom of bowel dysfunction was reported by 314 patients (92.9%). Each patient reported a mean of 6 (SD 3.5) symptoms. The frequencies of individual symptoms reported are presented in Table 4. Notably, of the top ten individual symptoms reported, six were reflective of evacuation dysfunction. Following stratification, 173 patients (51.2%) reported coexisting evacuation ***and*** storage dysfunction, 79 patients (23.4%) met criteria for evacuation dysfunction ***alone***, and 36 patients (10.7%) met criteria for storage dysfunction ***alone***.

‘Control’ groups: Right hemicolectomy and Radical cystectomy

Fewer symptoms were reported per patient following RH compared with AR, with a mean of 4 symptoms (SD 3) reported following RH. When compared to RH patients, AR patients were: (i) almost four times more likely to report toilet revisiting (OR3.63, 95%CI 2.41–5.43) or bowel frequency (OR3.53, 95%CI 2.24–5.59); (ii) three times more likely to report solid stool incontinence (OR3.16, 95%CI 1.70–5.89), evacuation time >10 minutes (OR2.72, 95%CI 1.25–5.95), sensation of incomplete emptying (OR2.60, 95%CI 1.75–3.86), or use of pads/plugs for faecal soiling (OR2.54, 95%CI 1.26–5.15); and (iii) twice more likely to use constipating medications (OR2.35, 95%CI 1.11–4.93), report unsuccessful evacuation attempts (OR1.85, 95%CI 1.22–2.79), liquid stool incontinence (OR1.85, 95%CI 1.17–2.94), or excessive straining (OR1.57, 95%CI 1.06–2.31) (Table 4). When categorised into symptom domains, AR patients were almost four times more likely to report ***combined*** evacuation and

storage dysfunction (age adjusted OR3.31, 95%CI 1.95–5.65), and twice as likely to report evacuation dysfunction *alone* (age adjusted OR1.89, 95%CI 1.04–3.43) (Table 4).

Fewer symptoms were reported per patient following RC compared with AR (a mean of 4.5 [SD 3.6] symptoms reported per RC patient). AR patients were five times more likely to report bowel frequency (OR4.90, 95%CI 1.86–12.99), and three times more likely to report toilet revisiting (OR3.17, 95%CI 1.52–6.62) and sensation of incomplete emptying (OR2.59, 95%CI 1.27–5.29), compared with RC patients. Patients were over three times more likely to report *combined* evacuation and storage dysfunction (age adjusted OR3.43, 95%CI 1.40–8.40) following AR compared with RC patients (Table 4).

Factors influencing post-operative bowel function in AR patients

On univariate analysis, patients with lower anastomoses (P=0.001) were less satisfied with their bowel function, as were patients who had previously been diverted with a loop ileostomy (P=0.001). On multivariate modelling, only anastomotic height persisted to be independently associated with post-operative satisfaction. Specifically, patients with lower anastomoses were less likely to be satisfied, with patients undergoing a low (6–10cm from the anal verge) or ultra-low (1–5cm) anastomosis being half as likely to report satisfaction with their post-operative bowel function (low: adjusted OR0.47, 95%CI 0.24–0.89; ultra-low: adjusted OR0.50, 95%CI 0.23–1.08).

Compared with patients reporting no dysfunction, patients who met the criteria for evacuation *and* storage dysfunction were more likely to have: lower anastomoses and tumour heights (P<0.01), had previous diverting ileostomies (57.8% vs. 24.0%, P<0.001), received

neoadjuvant radiotherapy (8.7% vs. 2.0%, $P<0.01$), and undergone previous anal surgery (11.6% vs. 2.0%, $P<0.05$).

Quality of Life Assessment

There was no significant difference in age-adjusted PCS scores between the three study groups (adjusted B -0.48, 95%CI -1.31 – 0.36; $P=0.263$), but age was strongly associated with PCS (adjusted B -0.23, 95%CI -0.30 – -0.16; $P<0.001$). Similarly, there was no difference in MCS scores between the three groups, either before or after age-adjustment (mean MCS – AR: 51.6 [SD9.8], RH: 50.8 [SD10.6], RCL 51.8 [SD10.8]; adjusted B -0.14 [95%CI -1.00 – 0.73; $P=0.757$]).

While there were no differences in PCS and MCS scores between the three patient groups, HRQoL was associated with presence of bowel dysfunction. When the patients across the groups were combined, PCS scores were significantly lower in those patients reporting combined evacuation and storage dysfunction (mean 44.1[SD9.9] vs. 47.8[SD10.0]; $P<0.001$), as were MCS scores (mean 49.5 [SD10.7] vs. 52.9 [SD9.4]). These findings persisted after adjusting for age (PCS: adjusted B -3.91 [95%CI -5.59 – -2.23], $P<0.001$; MCS: adjusted B -3.51 [95%CI -5.25 – -1.76], $P<0.001$).

DISCUSSION AND CONCLUSIONS

This study contributes to the existing literature on LARS by including prospective, comparative data, including PROMs / HRQoL for the first time. It confirms that rates of bowel dysfunction are significantly higher following AR than other bowel/pelvic procedures. This strongly suggests that LARS is, in the most, due to the direct consequences of partial/complete loss of the rectum. In this study, 60% of AR patients noted a change in bowel function postoperatively. By comparison, reported change in bowel function was less following RH and RC, as were rates of seeking medical attention for bowel dysfunction. Further, patients were more likely to self-judge their bowel function as 'normal' following RH and RC compared to following AR. Objectively, over 90% of patients experienced at least one symptom of dysfunction following AR, while patients suffered fewer symptoms following RH and RC. Consequently, lower proportions of RH and RC patients met criteria for evacuation and/or storage dysfunction.

This study assessed PROMs of patient satisfaction, the need to seek medical attention for bowel dysfunction, self-described post-operative bowel function, and self-reported change in bowel function following surgery. The assessment of PROMs with respect to bowel (dys)function following AR in this study is an important contribution to this topic and reflects a desire in general contemporary clinical practice to focus on *patients, their* disease, and the impact of *their* treatment on daily life[21-23]. This study demonstrated that the majority (72%) of AR patients were satisfied with their post-operative bowel function, a finding which corroborates with results from other studies[24-26]. Despite the high rates of patient-reported satisfaction, 60% noted changes in bowel habit following surgery (typically to frequent, loose stools). A similar proportion self-judged their own bowel habit as 'abnormal', leading over one-third of study participants to seek medical attention for post-operative bowel dysfunction. These assessments provide strong evidence that AR impacts substantially on bowel function as

perceived by patients themselves.

Age-adjusted generic HRQoL scores were similar between the three patient groups studied. The SF-36v2 has been utilised in the assessment of HRQoL outcomes for over 200 diseases and conditions[27], yet it proved insufficiently sensitive to discriminate the impact of varying degrees of bowel dysfunction between the patient groups. It is unclear whether the use of another HRQoL measure, such as the EORTC-QLQ questionnaire, would have yielded different results[28]. Importantly, bowel dysfunction, regardless of what type of surgery was performed, impacts deleteriously on HRQoL. In the present study, patients with combined evacuation and storage dysfunction had significantly lower age-adjusted PCS and MCS scores compared to those without, a finding that corroborates well with those of previous studies[29, 30].

Rather than employing the LARS questionnaire, which was developed for and specifically measures bowel dysfunction following low anterior resection[2], a more comprehensive objective assessment of symptoms following other operations, i.e. RH and RC was performed. Moreover, as the LARS score only assesses 'storage dysfunction' of the rectum (i.e. incontinence, urgency, frequency etc), this study used questions from validated questionnaires to assess bowel dysfunction globally i.e. Rome III criteria for functional bowel disorders, the Wexner score for constipation and Vaizey score for incontinence. Used in combination, they provide a comprehensive interrogation of the wide-ranging symptoms that comprise bowel dysfunction. This initiative was validated by the high rates of symptoms of evacuatory dysfunction observed by three-quarters of AR patients in this study. This is another important contribution to the existing literature, particularly considering that a recent systematic review demonstrated that evacuatory dysfunction was assessed in only one-third of studies

investigating bowel dysfunction post AR[6].

In contrast to patients following AR, long-term bowel function following RH has been poorly documented. The current study demonstrates favourable outcomes for RH patients. Previously, it has been proposed that resection of the right colon might have deleterious effects on bowel function, on the basis that loss of the ileocecal valve may lead to changes in colonic motility, absorption, and microflora[31]. Our study suggests that only one-third of RH patients experience change in bowel habit or judge bowel function to be abnormal post-operatively, compared to two-thirds of patients following AR.

Only one previous study has directly compared bowel function following RH and AR[32]. In that study performed over 20 years ago, stool frequency was once to twice each day in 78% of patients following RH, but only 45% following AR. Incontinence was more significant following AR, and defaecatory problems occurred in <4% of RH patients compared to almost one-third of AR patients[32]. Despite that study using non-validated tools of symptom assessment, their findings are in keeping with ours and confirm that bowel dysfunction is more common following AR than right-sided resections, suggesting that LARS is due to more than just 'loss of bowel length'.

Bowel function has rarely been investigated following RC, although the possibility of sensorimotor disturbance to the rectum secondary to traction injury, pelvic scarring, and iatrogenic tissue/neural damage has been postulated in a previous study[33, 34]. The results of our study support these previous assertions by demonstrating substantial rates of symptoms such as excessive straining (56%) and unsuccessful evacuation attempts (41%) following RC. Yet, the present study demonstrates that symptomatology of bowel dysfunction is still greater

following AR than RC, with more symptoms reported per patient following AR. This gives weight to the argument that LARS is due to more than just 'pelvic dissection'.

Overall, the current study demonstrated that patients were four times more likely to meet pre-defined criteria for *concomitant* evacuation and storage dysfunction, three times more likely to meet criteria for evacuation (\pm storage) dysfunction and twice as likely to meet criteria for storage dysfunction, following AR than both RH and RC. Rates of certain individual symptoms were notably higher in patients following AR, with patients five times more likely to report bowel frequency compared with RC patients, and three times more likely to report toilet revisiting compared with both RH and RC patients.

The results of this study should be interpreted in the context of non-operative controls as well, although age- and sex-matched comparison is challenging between separate studies. Rates of incontinence to liquid and solid stool amongst AR patients in our study was 32% and 23%, respectively, compared to 9% and 2% found in a previous survey of Australian residents[35]. Direct assessment of individual symptoms allowed rates of patients meeting symptom-based criteria for functional bowel disorders in our study to be measured, and found that 48% of AR patients met Rome III criteria for functional constipation; by comparison, in a separate study of Australian healthcare seekers, functional constipation was diagnosed in 8% of adults[11].

This study was limited by certain factors. This study used arbitrary (but pragmatic) definitions for evacuation and storage dysfunctions, based on the number of symptoms described. The number of patients in the RC group was also substantially less than in the AR and RH groups, reflecting the number of cystectomies performed in our hospital during the decade of interest; this impacts on the reliability of our group comparisons. Finally, whilst comparison between

the three patient cohorts (AR, RH, and RC) was age-controlled, other confounding factors could potentially exist that have not been accounted for. For example, there were varying rates of temporary ileostomy and pelvic radiotherapy between the three groups, reflecting fundamental differences in the way that the corresponding malignancies are managed. Similarly, the operative approach varied between the three groups; most notably all RC patients underwent an open operation. Consequently, these factors could have contributed to varying rates of bowel dysfunction post-operatively.

In conclusion, this study confirms that bowel habit is altered, abnormal, and leads to medical attention being sought in a greater proportion of patients following AR than following RH and RC. Patients suffered more symptoms of bowel dysfunction following AR than RH and RC with a greater proportion meeting criteria for evacuation dysfunction and/or storage dysfunction. This suggests that the development of bowel symptoms following AR is, at least in part, due to partial/complete loss of the rectum rather than loss of bowel length and pelvic dissection.

REFERENCES

1. Bryant CLC, Lunniss PJ, Knowles CH, Thaha MA, Chan CLH. Anterior resection syndrome. *Lancet Oncol* 2012; **13**: e403-e8.
2. 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**: 922-8.
3. Ortiz H, Armendariz P. Anterior resection: do the patients perceive any clinical benefit? *Int J Colorectal Dis* 1996; **11**: 191-5.
4. McDonald PJ, Heald RJ. A survey of postoperative function after rectal anastomosis with circular stapling devices. *Br J Surg* 1983; **70**: 727-9.
5. Pedersen IK, Christiansen J, Hint K, Jensen P, Olsen J, Mortensen PE. Anorectal function after low anterior resection for carcinoma. *Ann Surg* 1986; **204**: 133-5.
6. Keane C, Wells C, O'Grady G, Bissett IP. Defining low anterior resection syndrome: a systematic review of the literature. *Colorectal Dis* 2017; **19**: 713-22.
7. Scheer AS, Boushey RP, Liang S, Doucette S, O'Connor AM, Moher D. The long-term gastrointestinal functional outcomes following curative anterior resection in adults with rectal cancer: a systematic review and meta-analysis. *Dis Colon Rectum* 2011; **54**: 1589-97.
8. Oya M, Sugamata Y, Komatsu J, Ishikawa H, Nozaki M. Poor neorectal evacuation as a cause of impaired defecatory function after low anterior resection: a study using scintigraphic assessment. *Surg Today* 2002; **32**: 111-7.
9. Nesbakken A, Nygaard K, Lunde OC. Outcome and late functional results after anastomotic leakage following mesorectal excision for rectal cancer. *Br J Surg* 2001; **88**: 400-4.
10. Ng KS, Sivakumaran Y, Nassar N, Gladman MA. Fecal Incontinence: Community Prevalence and Associated Factors--A Systematic Review. *Dis Colon Rectum* 2015; **58**: 1194-209.
11. Ng KS, Nassar N, Hamd K, Nagarajah A, Gladman MA. Prevalence of functional bowel disorders and faecal incontinence: an Australian primary care survey. *Colorectal Dis* 2015; **17**: 150-9.
12. Higgins PD, Johanson JF. Epidemiology of constipation in North America: a systematic review. *Am J Gastroenterol* 2004; **99**: 750-9.
13. Sauer R, Becker H, Hohenberger W, Rodel C, Wittekind C, Fietkau R, et al. Preoperative versus postoperative chemoradiotherapy for rectal cancer. *N Engl J Med* 2004; **351**: 1731-40.
14. Sebag-Montefiore D, Stephens RJ, Steele R, Monson J, Grieve R, Khanna S, et al. Preoperative radiotherapy versus selective postoperative chemoradiotherapy in patients with rectal cancer (MRC CR07 and NCIC-CTG C016): a multicentre, randomised trial. *Lancet* 2009; **373**: 811-20.
15. Dent OF, Bokey L, Chapuis PH, Chan C, Newland RC. Trends in short-term outcomes after resection of colorectal cancer: 1971-2013. *ANZ J Surg* 2017; **87**: 39-43.
16. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. *Gastroenterology* 2006; **130**: 1480-91.
17. Agachan F, Chen T, Pfeifer J, Reissman P, Wexner SD. A constipation scoring system to simplify evaluation and management of constipated patients. *Dis Colon Rectum* 1996; **39**: 681-5.
18. Vaizey CJ, Carapeti E, Cahill JA, Kamm MA. Prospective comparison of faecal incontinence grading systems. *Gut* 1999; **44**: 77-80.

19. QualityMetric Incorporated (2011) User's manual for the SF-36v2 Health Survey, 3rd edition (ed Maruish M), Lincoln, RI.
20. Garratt A, Schmidt L, Mackintosh A, Fitzpatrick R. Quality of life measurement: bibliographic study of patient assessed health outcome measures. *BMJ* 2002; **324**: 1417.
21. Nelson EC, Eftimovska E, Lind C, Hager A, Wasson JH, Lindblad S. Patient reported outcome measures in practice. *BMJ* 2015; **350**: g7818.
22. Santana MJ, Haverman L, Absolom K, Takeuchi E, Feeny D, Grootenhuis M, et al. Training clinicians in how to use patient-reported outcome measures in routine clinical practice. *Qual Life Res* 2015; **24**: 1707-18.
23. De-loyde KJ, Harrison JD, Durcinoska I, Shepherd HL, Solomon MJ, Young JM. Which information source is best? Concordance between patient report, clinician report and medical records of patient co-morbidity and adjuvant therapy health information. *J Eval Clin Pract* 2015; **21**: 339-46.
24. Bittorf B, Stadelmaier U, Merkel S, Hohenberger W, Matzel KE. Does anastomotic leakage affect functional outcome after rectal resection for cancer? *Langenbecks Arch Surg* 2003; **387**: 406-10.
25. Nathanson DR, Espat NJ, Nash GM, D'Alessio M, Thaler H, Minsky BD, et al. Evaluation of preoperative and postoperative radiotherapy on long-term functional results of straight coloanal anastomosis. *Dis Colon Rectum* 2003; **46**: 888-94.
26. Matzel KE, Bittorf B, Gunther K, Stadelmaier U, Hohenberger W. Rectal resection with low anastomosis: functional outcome. *Colorectal Dis* 2003; **5**: 458-64.
27. Ware JE, Jr. (2014) SF-36® Health Survey Update.
28. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993; **85**: 365-76.
29. van Heinsbergen M, den Haan N, Maaskant-Braat AJ, Melenhorst J, Belgers EH, Leijtens JW, et al. Functional bowel complaints and quality of life after surgery for colon cancer: prevalence and predictive factors. *Colorectal Dis* 2019
30. Emmertsen KJ, Laurberg S, Rectal Cancer Function Study G. Impact of bowel dysfunction on quality of life after sphincter-preserving resection for rectal cancer. *Br J Surg* 2013; **100**: 1377-87.
31. Ohigashi S, Hoshino Y, Ohde S, Onodera H. Functional outcome, quality of life, and efficacy of probiotics in postoperative patients with colorectal cancer. *Surg Today* 2011; **41**: 1200-6.
32. Ho YH, Low D, Goh HS. Bowel function survey after segmental colorectal resections. *Dis Colon Rectum* 1996; **39**: 307-10.
33. Kramer MW, von Klot CA, Kabbani M, Kabbani AR, Tezval H, Peters I, et al. Long-term bowel disorders following radical cystectomy: an underestimated issue? *World journal of urology* 2015; **33**: 1373-80.
34. Thulin H, Kreicbergs U, Onelov E, Ahlstrand C, Carringer M, Holmang S, et al. Defecation disturbances after cystectomy for urinary bladder cancer. *BJU Int* 2011; **108**: 196-203.
35. Kalantar JS, Howell S, Talley NJ. Prevalence of faecal incontinence and associated risk factors; an underdiagnosed problem in the Australian community? *Med J Aust* 2002; **176**: 54-7.

TABLES

Table 1. Study population characteristics of anterior resection patients compared with control populations

Patient characteristics	Anterior resection		Right hemicolectomy			Radical Cystectomy		
	N (n=338)	%	N (n=150)	%	P value	N (n=34)	%	P value
Age (years)								
<50	19	5.6	1	0.7	<0.001	4	11.8	0.298
50-59	54	16.0	11	7.3		4	11.8	
60-69	95	28.1	29	19.3		8	23.5	
70-79	89	26.3	51	34.0		6	17.6	
≥ 80	81	24.0	58	38.7		12	35.3	
Male	199	58.9	81	54.0	0.315	24	70.6	0.184
Ethnicity								
North-West European	181	53.6	89	59.3	0.698	29	85.3	0.008
South-East European	84	24.9	32	21.3		2	5.9	
Asian	37	11.0	15	10.0		1	2.9	
Middle Eastern	20	5.9	7	4.7		2	5.9	
Other	16	4.7	7	4.7		0	0	
Employment Status								
Retired	209	61.8	123	82.6	<0.001	24	70.6	0.599
Employed	82	24.3	18	12.1		5	14.7	
Unemployed	20	5.9	6	4.0		2	5.9	
Other	27	8.0	2	1.3		3	8.8	
Alcohol (standard drinks per day)								
0	157	46.4	75	50.3	0.789	16	47.1	0.946
1	103	30.5	42	28.2		10	29.4	
≥ 2	78	23.1	32	21.5		8	23.5	
Body Mass Index (BMI) (n = 307)								
<18.5 (Underweight)	11	3.6	1	0.7	0.230	1	3.3	0.439
18.5 – 25.0 (Normal)	86	28.0	47	33.1		8	26.7	
25.0 – 30.0 (Overweight)	122	39.7	62	43.7		16	53.3	
>30 (Obese)	88	28.7	32	22.5		5	16.7	
Smoking Status								
Current smoker	22	6.5	9	6.0	0.221	7	20.6	0.016
Ex smoker	155	45.9	62	42.0		14	41.2	
Never Smoked	161	47.7	78	52.0		13	38.2	

Bold italics emphasizes significant variables.

Table 2. Clinicopathological features of the study populations

Patient characteristics	AR <i>n</i>=338	RH <i>n</i>=150	RC <i>n</i>=34
	Mean (SD), Percent		
Current age (yrs)	69.6 (11.9)	75.8 (10.5)	71.1 (14.1)
Time since surgery (yrs)	5.0 (2.7)	5.4 (2.8)	5.5 (3.5)
Age at surgery	64.8 (11.8)	70.4 (12.2)	67.1 (14.0)
Male (%)	58.9	54.0	70.6
Anastomotic height (cm)			
1-5	25.3	NA	NA
6-10	24.7		
11-15	50.0		
Tumor height (cm)			
1-5	5.0	NA	NA
6-10	22.2		
11-15	17.2		
>15 (colonic)	55.6		
Diverting ileostomy (%)	45.0	NA	NA
Neoadjuvant radiotherapy (%)	6.2	NA	NA
Anastomotic leak (%)	1.8	0.7	NA
Colonic J-pouch (%)	4.1	NA	NA
Previous anal surgery (%)	9.5	10.0	8.8
Previous vaginal delivery (%)	73.4 (<i>n</i> =139)	82.6 (<i>n</i> =69)	80.0 (<i>n</i> =10)
Previous obstetric trauma (%)	34.5% (<i>n</i> =139)	43.4% (<i>n</i> =69)	50.0% (<i>n</i> =10)
BMI	27.8 (5.8)	27.3 (4.9)	26.3 (4.0)
TNM Stage			
T1-4	68.9	67.3	NA
N-positive	27.8	28.0	
M-positive	3.3	4.7	
ASA			
Class I	22.8	14.0	8.8
Class II	61.1	65.3	73.6
Class III - V	16.0	19.3	17.6
Adjuvant chemotherapy (%)	29.6	22.7	23.5
Laparoscopic surgery (%)	36.1	48.7	0.0
Apical lymph node harvested (%)	76.6	89.3	N/A

BMI – body mass index; ASA – American Society of Anesthesiologists score; * $P < 0.05$; *** $P < 0.001$; NA not applicable / available.

Table 3. Comparing medical advice seeking and self-reported bowel habit between anterior resection and right hemicolectomy and radical cystectomy patients

	AR	RH	P-value	OR (95% CI)	RC	P-value	OR (95% CI)
Medical advice sought	36.4	20.0	<0.001	2.35 (1.49 – 3.72)	23.5	0.117	1.91 (0.84 – 4.35)
Self-described bowel habit							
Normal	36.4	65.3	<0.001		64.7	0.002	
Constipated	8.0	8.7			14.7		
Diarrhea	7.4	4.7			0.0		
Variable	48.2	21.3			20.6		
Bowel habit changed since surgery	59.8	30.7	<0.001	3.72 (2.46 – 5.62)	35.3	0.002	3.01 (1.44 – 6.29)

AR – anterior resection; RH – right hemicolectomy; RC – radical cystectomy. ***Bold italics*** emphasises significant variables.

Table 4. Comparing objective symptoms of anterior resection patients versus right hemicolectomy and radical cystectomy patients

	AR	RH	P-value	OR (95% CI)	RC	P-value	OR (95%CI)
Symptom Domains							
Concomitant evacuation and storage dysfunction	51.2	30.0	<0.001	3.54 (2.11 – 5.94)	32.4	0.006	3.46 (1.42 – 8.45)
Evacuation dysfunction only	23.4	21.3	0.005	2.27 (1.28 – 4.03)	23.5	0.120	2.17 (0.82 – 5.77)
Storage dysfunction only	10.7	18.0	0.531	1.23 (0.65 – 2.33)	11.8	0.273	1.98 (0.58 – 6.72)
No dysfunction	14.8	30.7			32.4		
Any evacuation dysfunction	74.6	51.3	<0.001	2.78 (1.86 – 4.15)	55.9	0.020	2.31 (1.13 – 4.76)
Any storage dysfunction	61.8	48.0	0.004	1.75 (1.19 – 2.59)	44.1	0.044	2.05 (1.01 – 4.18)
Individual bowel symptoms							
Bowel frequency	45.9	19.3	<0.001	3.53 (2.24 – 5.59)	14.7	<0.001	4.90 (1.86 – 12.99)
Hard stools	27.8	24.7	0.470	1.18 (0.76 – 1.83)	26.5	0.868	1.07 (0.48 – 2.38)
Excessive straining	53.8	42.7	0.023	1.57 (1.06 – 2.31)	55.9	0.820	0.92 (0.45 – 1.87)
Sensation of incomplete emptying	67.2	44.0	<0.001	2.60 (1.75 – 3.86)	44.1	0.007	2.59 (1.27 – 5.29)
Sensation of anorectal obstruction	29.6	26.7	0.511	1.16 (0.75 – 1.78)	29.4	0.932	1.03 (0.48 – 2.24)
Need to self-digitate	18.6	16.7	0.601	1.15 (0.69 – 1.90)	5.9	0.06	3.66 (0.86 – 15.63)
Unsuccessful evacuation	42.6	28.7	0.003	1.85 (1.22 – 2.79)	41.2	0.873	1.06 (0.52 – 2.17)
Use of enema / suppository	1.2	2.0	0.484	0.59 (0.13 – 2.65)	5.9	0.10	0.19 (0.03 – 1.09)
Evacuation time >10 minutes	13.3	5.3	0.009	2.72 (1.25 – 5.95)	17.6	0.484	0.72 (0.28 – 1.83)
Toilet revisiting	63.0	32.0	<0.001	3.63 (2.41 – 5.43)	35.3	0.001	3.17 (1.52 – 6.62)
Incontinence to liquid stool	31.7	20.0	0.008	1.85 (1.17 – 2.94)	26.5	0.534	1.29 (0.58 – 2.85)
Incontinence to solid stool	23.1	8.7	<0.001	3.16 (1.70 – 5.89)	8.8	0.055	3.10 (0.92 – 10.42)
Incontinence to flatus	59.5	54.7	0.321	1.22 (0.83 – 1.79)	61.8	0.795	0.91 (0.44 – 1.88)
Use of pads / plugs for fecal soiling	15.4	6.7	0.008	2.54 (1.26 – 5.15)	11.8	0.574	1.36 (0.46 – 4.03)
Fecal urgency	44.1	40.0	0.400	1.18 (0.80 – 1.75)	47.1	0.739	0.89 (0.44 – 1.80)
Poor stool / flatus discrimination	23.4	20.7	0.509	1.17 (0.73 – 1.87)	20.6	0.714	1.18 (0.49 – 2.80)
Loose stools	8.9	8.0	0.750	1.20 (0.56 – 2.25)	2.9	0.233	3.21 (0.42 – 24.39)
Need for constipating meds	13.0	6.0	0.004	2.85 (1.36 – 5.95)	2.9	0.067	5.99 (0.80 – 45.45)
Number of symptoms							
Evacuation dysfunction							
≥1	88.8	76.7			76.5		
≥2	74.6	51.3			55.9		
≥3	56.2	37.3			47.1		
≥4	43.8	26.7			32.4		
≥5	28.1	19.3			23.6		
Storage dysfunction							
≥1	81.0	71.3			79.4		
≥2	61.2	48.0			41.2		
≥3	42.3	27.3			32.4		
≥4	31.7	16.7			23.6		
≥5	20.1	10.6			14.8		

AR – anterior resection; RH – right hemicolectomy; RC – radical cystectomy