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A cross-sectional review of reporting variation in post-operative bowel dysfunction following rectal cancer surgery.

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Contributions: DGJ and NY conceptualised the idea and had input to the study design. SJC and WB performed searches and collected data. SJC and NC performed statistical analysis. All authors contributed to the final writing of the manuscript. SJC and WSB contributed equally to this work and are joint first authors. DGJ is the study guarantor.

Abstract

Background: Postoperative bowel dysfunction affects quality of life after sphincter-preserving rectal cancer surgery, but the extent of the problem is not clearly defined due to inconsistent outcome measures used to characterise the condition.

Objective: The purpose of this study was to assess variation in reporting of postoperative bowel dysfunction and make recommendations for standardisation in future studies. **If possible, a quantitative synthesis of bowel dysfunction symptoms was planned.**

Data Sources: MEDLINE and EMBASE databases and the Cochrane Library were queried between 2004-2015.

Study Selection: The studies selected reported at least one component of bowel dysfunction following resection of rectal cancer.

Main Outcome Measures: The main outcome measures were reporting, measurement and definition of post-operative bowel dysfunction.

Results: Of 5428 studies identified, 234 met inclusion criteria. Widely reported components of bowel dysfunction were incontinence to stool (227/234; 97.0%), frequency (168/234; 71.8%) and incontinence to flatus (158/234; 67.5%). Urgency and stool clustering were reported less commonly, with rates of 106/234 (45.3%) and 61/234 (26.1%). Bowel dysfunction measured as a primary outcome was associated with better reporting (OR: 3.49; 95% CI: 1.99–6.23; P<0.001). Less than half of the outcomes were assessed using a dedicated research tool (337/720; 46.8%), with the remaining descriptive measures infrequently defined (56/383; 14.6%).

Limitations: Heterogeneity in the reporting, measurement and definition of post-operative bowel dysfunction precluded pooling of results and limited interpretation.

Conclusion: Considerable variation exists in the reporting and definition of postoperative bowel dysfunction. These inconsistencies preclude reliable estimates of incidence and meta-analysis. A recently validated scoring tool for postoperative bowel dysfunction, the LARS score, should be endorsed for future studies.

Introduction

Rectal cancer is common in Europe and America, with at least one third of all colorectal cancers arising from the rectum[1, 2]. The standard approach following rectal cancer surgery is to restore gastrointestinal continuity (sphincter-sparing surgery) if feasible and safe to do so. However, loss of the normal rectal reservoir function can result in severe post-operative bowel dysfunction. The resulting syndrome, Low Anterior Resection Syndrome (LARS), can severely impact on quality of life (QoL) and is estimated to affect 50% - 90% of patients[3-5].

LARS syndrome is a constellation of symptoms that characterizes disordered postoperative defecation, including incontinence, urgency, frequency and stool clustering. A number of instruments exist to measure functional bowel outcomes, including the Wexner and Kirwan scores, but these are limited to one or few functional components[6, 7]. The “LARS Score” has recently emerged as a validated tool for measuring multiple functional components as a composite outcome[8].

Inconsistent assessment of outcomes leads to unreliable estimates of adverse events, which may misdirect surgical management and future research. Furthermore, the absence of universally accepted definitions of adverse events leads to heterogeneity, which precludes accurate meta-analysis. To maximise the value of conclusions drawn from research studies, outcome measures must be reported and defined consistently. The purpose of this study was to explore the reporting practices of authors investigating bowel dysfunction following rectal cancer surgery and so help standardize future work. Specifically, we sought to explore the selection, measurement, and definition of functional bowel outcomes. We hypothesized that significant heterogeneity would exist in all of these domains.

Materials and Methods

Study Design

This study was performed according to a pre-planned protocol and registered prospectively on the PROSPERO database of systematic reviews. The subsequent report is produced in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA)[9].

Searches

A search strategy (Suppl 1) was executed to identify all studies reporting at least one component of postoperative bowel dysfunction (including frequency, urgency, clustering and incontinence) following resection of rectal cancer. Two independent investigators performed systematic searches of MEDLINE (via OvidSP), EMBASE (via OvidSP), and the Cochrane Library. Searches were performed on a single day (8th July 2015) and stored offline for inspection. Studies identified via the initial search were screened for relevance and content prior to full inspection, with discrepancies addressed by re-examination until consensus was achieved. Reference lists from identified systematic reviews were inspected for studies of potential interest.

Inclusion Criteria

Eligible studies included adult patients (18 years and older) undergoing resection of rectal cancer via open, laparoscopic or laparoscopic-assisted approaches. Only manuscripts published between January 2004 and July 2015 in the English language were included to capture studies relevant to modern clinical practice. Letters, technical notes, study protocols and other grey literature were excluded due to the high likelihood of incomplete data.

Definitions

Bowel dysfunction was defined according to components of the LARS Score described by Emmertson et al. The LARS Score is a validated instrument for measuring post-operative bowel dysfunction following surgery for rectal cancer, and incorporates 5 symptoms of postoperative bowel dysfunction: stool frequency, urgency, clustering, and stool and flatus incontinence. **This collective of symptoms has been show to correlate strongly with post-operative bowel function on the basis of symptoms and quality of life following low anterior resection. As such, these form the basis upon which reporting of bowel dysfunction is assessed through this review[8].**

Data Extraction

A single investigator performed raw data extraction, with a randomly selected sample of 20% of manuscripts chosen for validation by a second investigator. Data extracted included: study design (randomized vs. non-randomized), reporting of defecatory outcomes (frequency, urgency, stool clustering, stool and flatus incontinence), outcome status (primary vs. non-primary), dedicated assessment instrument (name) country of origin (determined according to corresponding author affiliation), year of publication, study population size and funding arrangements.

Outcome Measures

The study assessed three key outcomes. Firstly, reporting of bowel dysfunction was measured according to components of the LARS score. The components were summarised according to binary groups: “<50% reported” (less than or equal to two reported components) and “>50% reported” (greater than or equal to three reported components). The groups were used as a proxy for describing “poor” and “good” completeness of reporting respectively. **Secondly,** for each reported outcome, **the presence of a dedicated measurement instrument and its validity were**

assessed. Instruments were considered ‘validated’ if evidence of internal and external validation existed in current literature, and ‘non-validated but published’ if only a description of its properties existed. **Thirdly, presence** of a formal definition **and its respective assessment criteria was assessed**. Outcomes measured using validated or non-validated but published instruments were considered defined because the respective assessment criteria had previously been described. Global quality of life tools incorporating bowel components were considered relevant instruments only if raw data for individual defecatory components were reported. If sufficient homogeneity existed, we planned to summarize incidences of individual functional bowel outcomes using formal statistical methods. **If this was not possible we planned to provide a simple, descriptive summary of current evidence, whilst recognising the attendant limitations.**

Statistical Analysis

Descriptive statistics were used for simple comparisons. The Chi-squared test (χ^2) was used to compare differences between categorical groups or if assumptions of the χ^2 test were violated, Likelihood Ratios were calculated as per convention. Differences were considered to be statistically significant if $p<0.05$. Adjusted binary logistic regression was used to test the impact of confounding variables. The binary outcome target was completeness of reporting of bowel dysfunction (<50% reported components vs. >50% reported components). Explanatory variables entered into the model were deemed to be relevant factors that may affect completeness of reporting. The analysis produced an odds ratio (OR) and 95% confidence intervals (95%), such that values greater than 1 indicated a higher likelihood of complete reporting. The analysis was performed using Statistical Package for the Social Sciences (SPSS) version 22.0 (SPSS Inc, IBM, Chicago, IL).

Results

Characteristics of included manuscripts

Of 5428 studies initially identified, 234 studies met the criteria for inclusion (Figure 1). Of 234 included studies, 32/234 (13.7%) were randomised and most studies tested post-operative bowel function as a primary outcome (144/234; 61.5%). The median study population size was 70 (interquartile range: 35-127), with a total representative population of 45,115 across all studies. Funding arrangements were commonly not reported (n=122/234; 52.1%), with the remaining studies funded by non-industry sources (n=66/234; 28.2%) or not at all (n=46/234; 19.7%) (Table 1).

Reporting Defecatory Dysfunction

The most widely reported components of bowel function were incontinence to stool (227/234; 97.0%), frequency (168/234; 71.8%) and incontinence to flatus (158/234; 67.5%). Urgency and stool clustering were reported less commonly, with rates of 106/234 (45.3%) and 61/234 (26.1%) respectively. Only 52/234 (22.2%) manuscripts reported all five components and 104/234 (44.4%) reported fewer than 50% of components (Table 2). Bowel dysfunction measured as a primary outcome was associated with improved completeness of reporting (OR=3.49; CI: 1.99-6.23; $p<0.001$). Conversely, publication in the preceding five years (2010-2015) was associated with fewer reported components (OR=0.56; CI: 0.32 to 0.98; $p=0.037$) (Table 3).

Measurement of Defecatory Dysfunction

Fifteen dedicated instruments were identified, including nine validated (Table 4). A total of 337/720 (46.8%) individual outcomes were measured, of which validated instruments accounted for 295/337 (87.5%). The remaining outcomes were assessed

using descriptive methods (383/720; 53.2%). Most validated instruments used measurements of incontinence, including the Wexner Score and Faecal Incontinence Severity Index (FISI)[10]. Urgency and clustering were less commonly measured using a validated tool. The Kirwan Score was the second most commonly used instrument, but no clear evidence of adequate validation was identified. **At the time of data abstraction, the LARS score was reported in only seven studies.**

Defining Defecatory Dysfunction

Of the outcomes measured using descriptive methods, only 56/383 (14.6%) were defined in the manuscripts. Definitions were most commonly reported for clustering (20/51; 39.2%) and urgency (30/89; 33.7%). Frequency (4/130; 3.8%), incontinence to stool (2/83; 2.4%) and incontinence to flatus (0/30; 0.0%) were less commonly defined. Considerable variability existed between reported definitions, particularly concerning urgency and clustering (Table 5).

Incidence of Defecatory Dysfunction

A high level of heterogeneity in reporting precluded a formal analysis of symptom-specific incidence. Included studies comprised a broad mix of procedure types, operative approaches and ranges of follow up. Of 80 studies reporting the Wexner score, 13/80 (16.3%) reported an average score greater than 10 (follow up: 12-60 months), indicating significant post-operative incontinence in a minority of cohorts. Conversely, of 16 studies using the Kirwan system, 8/16 (50.0%) studies reported a modal score of at least 1 (follow up: 6-21 months), indicating at least some level of post-operative incontinence in half of these cohorts. Incidences of urgency, frequency and clustering varied significantly between studies. Urgency was reported at average rates between 0–83.8% (follow up: 3-60 months) and stool clustering between 15–94.4% (follow up: 6-56 months). The average number of bowel

movements across studies was reported between 2–10.33 per 24 hours (follow up: 3-76.5 months).

Discussion

This study assessed variation in reporting of post-operative bowel dysfunction after sphincter-preserving surgery for rectal cancer, **including choice of outcome, method of measurement, and criteria for definition.** The results demonstrated substantial variation in reporting of five key elements of defecation. Some outcomes were measured using dedicated instruments. The remainder was poorly and inconsistently defined. A high level of heterogeneity in published studies precluded an a priori analyses of symptom-specific incidence**..**

Post-operative bowel dysfunction reduces QoL for patients who have undergone sphincter-preserving surgery for rectal cancer[3]. A conglomerate of other post-operative functional complications, including deranged bladder and sexual function, may accompany this. An appreciation of post-operative functional complications amongst clinicians is essential to optimise QoL, yet the impact of disordered defecation appears inadequately understood. Chen and colleagues recently described a discrepancy in clinicians' and patients' perspective of post-operative bowel dysfunction, highlighting a poor understanding of symptoms that genuinely matter to patients and the impact on patients' QoL[11]. The study highlighted that clinicians overestimate the impact of incontinence for liquid stool and frequency and underestimate the impact of urgency and clustering. The results of the current study provide further evidence to support this discrepancy, with urgency and stool clustering infrequently reported relative to stool incontinence and frequency.

A variety of instruments for reporting post-operative bowel dysfunction were identified. Some of these are validated, such as the Wexner and FISI instruments, whereas others are only described in the literature. The Kirwan instrument is commonly used as a measure of incontinence, yet the authors found no published evidence of internal or external validation in rectal cancer patients during this study. Most instruments are limited to reporting one or a small number of bowel symptoms relevant to LARS. This is problematic because measurement of a single symptom is not adequate to appreciate the true impact. The impact of LARS is heterogeneous and limiting the range of outcomes measured probably underestimates the extent of the problem. In addition, variation in choice and definition of functional outcomes is problematic and makes comparisons between studies difficult. This precludes reliable meta-analysis and restricts the value of the evidence. The LARS score has emerged as a comprehensive measure of five key components of bowel dysfunction. It accounts for incidence and severity of symptoms using proportional scoring criteria according to their impact on QoL. Only a small number of studies have utilised the LARS score to date, but its use is growing in popularity.

To the best of our knowledge, this is the only all-encompassing review of reporting practices of post-operative bowel dysfunction, including selection, measurement and definition of outcome measures. A few studies have investigated measurement of post-operative bowel function previously. Chen and colleagues reported a narrative review of anorectal function questionnaires, asessing the appropriateness of key instruments, including the Wexner, Vaizey, MSKCC, LARS and the American Medical System Faecal Incontinence Score (FIS). They highlighted strengths and weaknesses for each instrument, and suggested selective use according to specific context[12]. Scheer and colleagues meta-analysed 43 studies measuring post-operative bowel dysfunction, but were faced with significant challenges when

aggregating data[13]. The pooled incidence of incontinence was 35.2% (95% CI 27.9 – 43.4), but the reliability of this estimate is questionable.

This study was performed as a cross-sectional review of current literature. The time range was intentionally limited to 2004-2015 to reflect current clinical practice and to avoid contamination from surpassed evidence. The five components of bowel dysfunction described by the LARS Score formed the basis of this study as they have previously been shown to correlate well with QoL related to post-operative bowel function in patients undergoing low anterior resection. The LARS score was produced and validated through a systematic consultation process with clinician and patient representatives to identify key components of dysfunction after rectal resection. It is a robust, highly sensitive and highly specific measure for identifying patients with compromised QoL[8].

The current research has its limitations. Although a highly sensitive search strategy was used, it is possible that a minority of eligible studies were missed. To reduce this risk, the authors identified relevant systematic reviews and reviewed reference lists for studies of interest. Secondly, the described results are limited to assessment of five components of post-operative bowel dysfunction. These were chosen according to symptoms described by the LARS Score, and although highly valid, these five symptoms are not exhaustive. Inclusion of other components of bowel dysfunction, such as pad use and need for anti-diarrhoeal agents, may have broadened the results, **and have been used previously in other tools for measuring post-operative bowel dysfunction**. Analysis of symptom-specific incidence was planned, however heterogeneity in reporting, measurement and definition of symptoms precluded formal analysis due to the risk of unreliable and misleading evidence with poor relevance to clinical practice. The descriptive outcomes reported should be interpreted only as a representative summary of current evidence.

Moving forward, this study identifies the need to standardise reporting, measurement and definition of post-operative bowel dysfunction after low anterior resection. Wide uptake of standardised assessment tools would permit future meta-analysis, thus increasing clinicians understanding of LARS and their ability to make effective treatment decisions. A number of validated tools exist, with each having their own respective strengths and weaknesses. The Wexner Score, for example, offers a focussed assessment of incontinence, but is thus limited by a narrow symptom profile by omitting other important components of bowel dysfcuntion[6]. The American Medical System Faecal Incontinence Score has been shown to reliably measure bowel incontinence, but is validated only in non-surgical patients, with unknown cross-applicability[18]. The LARS Score is specific to patients undergoing low anterior resection and benefits from a concise, easy to use structure, making it ideal as a screening tool[12]. However, it lacks depth of detail in each its five component symptoms.

To conclude, there is significant variability in reporting and definition of post-operative bowel dysfunction, which precludes reliable estimates of prevalence and patient impact. A broadly accepted outcome measure may address this deficit and if endorsed widely may permit more accurate meta-analysis of future studies. The recently validated LARS Score is a possible solution and should be the assessment tool of choice in future studies assessing bowel dysfunction following rectal resection.

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Table 1: Characteristics of included studies

Table 2: Number of reported defecatory components (stool frequency, urgency, clustering, stool and flatus incontinence) per included manuscript

Table 3: Adjusted binary logistic regression models for completeness of reporting

Table 4: Summaries and frequency of use of validated bowel dysfunction tools

Table 5: Definitions of non-validated measurement of outcomes

Figure 1: Inclusion and exclusion of manuscripts

Supplement 1: Search strategy to identify studies reporting at least one component of postoperative bowel dysfunction following resection of rectal cancer.