Double-stapled anastomosis versus mucosectomy and handsewn anastomosis in ileal pouch-anal anastomosis for ulcerative colitis or familial adenomatous polyposis (Protocol)

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TABLE OF CONTENTS

[Intervention Protocol]

Double-stapled anastomosis versus mucosectomy and handsewn anastomosis in ileal pouch-anal anastomosis for ulcerative colitis or familial adenomatous polyposis

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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

The purpose of this review is to compare outcomes following double-stapled anastomosis (DST) versus handsewn anastomosis techniques in individuals undergoing ileal pouch-anal anastomosis (IPAA) for ulcerative colitis (UC) or familial adenomatous polyposis (FAP).

BACKGROUND

Description of the condition

Inflammatory bowel disease comprises Crohn's disease and ulcerative colitis (UC). The annual incidence of UC has been reported as 24.3 per 100,000 person-years in Europe, 6.3 per 100,000 person-years in Asia and the Middle East, and 19.2 per 100,000 person-years in North America (Molodecky 2012). The age at diagnosis of UC shows a characteristic biphasic distribution with two peaks (the first between 20-30 years of age and the second between 50-70 years of age) (Tozun 2009). The mean age at diagnosis of UC is 32.0 ± 13.4 years (Abdul-Baki 2007).The main indications for the surgical management of UC include fulminant colitis with toxic megacolon, massive bleeding, intractable disease, development of dysplasia or carcinoma and failed medical treatment (Nicholls 2009). The curative surgical management of individuals with UC usually includes the resection of the entire diseased colon with end ileostomy or ileal pouch anal anastomosis.
Familial adenomatous polyposis (FAP) is a genetically transmitted disease, responsible for 0.05% to 1% of colorectal cancer cases (Church 2011). Individuals with FAP are at a very high risk of developing colorectal cancer: 100% of affected individuals will develop colorectal cancer during their life time (Clark 2009). FAP is characterized clinically by the presence of a large number (from 100 to 1000) of adenomatous polyps that are present across the

entire colon. Patients with FAP usually undergo surgery (panproctocolectomy) to remove all the affected colonic and rectal mucosa (Fry 2012) to prevent development of cancer. This is followed by an end ileostomy (including a continent ileal reservoir (Kock pouch)) or ileal pouch anal anastomosis.

Description of the intervention

Parks was the first to describe restorative proctocolectomy (Parks 1978), which is the preferred surgical technique in individuals with UC or FAP in terms of functional outcome, quality of life and development of pathology. Restorative proctocolectomy is also referred to as ileal pouch-anal anastomosis (IPAA) and pelvic pouch in the literature (Tekkis 2008; Fry 2012). According to the current literature, two main surgical techniques are used to perform IPAA: mucosectomy and handsewn anastomosis; and double-stapled anastomosis (DST). Both approaches have their own advantages and disadvantages. DST results in a mucosal cuff of anal transitional zone (ATZ) tissue, often with a small rectal cuff (Remzi 2012), which necessitates frequent clinical and endoscopic surveillance, whereas mucosectomy and handsewn anastomosis is associated with a risk of alteration in anorectal function from potential sphincter damage during mucosal dissection (Heppell 1997; Tekkis 2008). To date, of multiple studies that reviewed the outcomes of DST in IPAA in individuals with UC, only two are systematic reviews with meta-analyses (Schluender 2006; Lovegrove 2006).

The ileal pouch is formed by folding the terminal ileum into various shapes, the most common shape being used a 'J' shape. During DST, a mechanical side-to-side anastomosis is constructed at the level of the common ileal wall, and the pouch is anastomosed to the anus using a double-stapled technique (Cima 2011). In the handsewn IPAA technique, a handsewn anastomosis is formed between the pouch and anus after the mucosectomy of the rectal stump (Scott-Conner 2006).

How the intervention might work

For handsewn technique with mucosectomy, all colorectal mucosa is removed which would otherwise leave a risk of further inflammatory disease, dysplasia or cancer in UC, but the manipulation of the anal canal and the excision of the anal transition zone (ATZ) can hamper the anal sensation and anal physiology leading to postoperative functional/continence problems.

In stapling technique, although it is technically simple and is associated with better functional outcome compared to the handsewn technique, the persistence of residual rectal mucosa carries the risk of disease recurrence and development of malignancy and thus requires frequent and regular surveillance of the pouch.

Why it is important to do this review

Both approaches have advantages and disadvantages. The handsewn technique with mucosectomy is probably more challenging but should guarantee a definitive cure to the disease. On the other hand it is likely to be burdened by worse functional results. Double-stapled anastomosis appears to be effective, to have an acceptable safety profile and convenient in individuals with UC and FAP, but clinical evidence of its efficacy and safety is still lacking especially in terms of functional outcome, quality of life and the risk of developing subsequent dysplasia in the ATZ. This review should assess if one technique could be considered superior to the other in terms of benefit for the patient, in the short as well in the long run.

There may be a concern about introducing bias in this study by including patients of UC and FAP both. Although UC and FAP differ completely in their aetiology, clinical course and presentation, from a surgical point of view, both these conditions are treated with restorative proctocolectomy and the ultimate outcome in terms of functional results and quality of life as well as development of pathology, especially recurrence or development of cancer are paramount irrespective of its primary aetiology. Therefore, it has been decided to include both patients suffering from UC and FAP for this review. We will investigate potential bias by performing subgroup analysis for patients with UC and FAP.

OBJECTIVES

The purpose of this review is to compare outcomes following double-stapled anastomosis (DST) versus handsewn anastomosis techniques in individuals undergoing ileal pouch-anal anastomosis (IPAA) for ulcerative colitis (UC) or familial adenomatous polyposis (FAP).

METHODS

Criteria for considering studies for this review

Types of studies

This review will include randomised clinical trials (RCTs) irrespective of their publication status or language.

Types of participants

General population (children and adults), irrespective of race, gender, socioeconomic status, health status or geographical location, who have undergone IPAA for UC or FAP.

Types of interventions

Studies that compare mucosectomy and handsewn versus DST in IPAA. Different terms are used in the literature for this surgical procedure (e.g. restorative proctocolectomy and pelvic pouch) (Spencer 2011).

Types of outcome measures

Primary outcomes

- Functional outcomes (stool frequency, seepage, pad usage, incontinence)
- Quality of life
- Rectal cuff and ATZ pathology (dysplasia, inflammation and neoplasia)

Secondary outcomes

- 30-day postoperative overall mortality
- Surgical postoperative complications (anastomotic leak, pelvic sepsis, anastomotic stricture, pouch-related fistula, small bowel obstruction, pouchitis, ileal pouch failure)
- Anorectal physiology
- Impotence

Search methods for identification of studies

A systematic comprehensive search will be undertaken to identify all relevant studies and articles regardless of language or publication status (published, unpublished, and ongoing). We will search a wide range of databases and other sources in order to identify relevant studies.

Electronic searches

We will develop detailed search strategies for each database to be searched (listed below) in order to identify studies relevant to this review. Appendix 1 presents the strategies for CENTRAL, Medline and Embase developed by the CCCG TSC.

- The Cochrane Colorectal Cancer Group's Trials Register (to present)
- The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*, current issue)
- MEDLINE via OVID (1950 to present)
- EMBASE via OVID (1974 to present)
- ISI Web of Knowledge (limited to Conference Proceedings) (1990 to present)

Searching other resources

We will search the Meta Register of Controlled Clinical Trials (http://www.controlled-trials.com/mrct) for ongoing trials on the topic of interest. We will manually check the reference lists of all included studies to identify any additional studies.
We will contact organisations, researchers and experts known to be involved in the field by electronic mail in an effort to trace unpublished or ongoing studies.

Data collection and analysis

Selection of studies

We will import the records obtained from each database into the bibliographic software package, EndNote 8.02 (EndNote 8.02), and merge them into one core database to remove duplicate records. We will enter the records of all potentially relevant reports identified when searching other (non-electronic) sources (reference lists of relevant trials, reviews, articles and textbooks) manually into EndNote. Two review authors (RC and UM) will independently and in duplicate assess the titles and abstracts of all reports of trials identified as outlined above. We will obtain hard copies of the full text of studies that possibly fulfil the inclusion criteria. We will resolve disagreements between authors by discussion. Where resolution is not possible, a third review author (JS) will be consulted. Further information will be requested from the authors of papers that contain insufficient information before a decision about eligibility is made. If more than one publication of a trial is identified, we will review all the publications and the paper with the first publication date will be included as the primary version. We will conduct data extraction and a quality assessment of all studies meeting the inclusion criteria. We will record the studies rejected at this or subsequent stages, and the reasons for exclusion, in a table of excluded studies.

Data extraction and management

Two review authors (ST and RC) will extract data independently, and disagreements will be resolved by a consensus meeting with a third review author (UM). We will test the data extraction sheet before hand. The form will be used to collect information such as trial characteristics (year of publication, country of the study, methodological quality items of the study); participant characteristics (numbers, age range, sex), intervention characteristics, comparator characteristics and outcome characteristics. The form will also be used to record any adverse events reported in the trials. If necessary, we will contact study authors to obtain missing data.

Assessment of risk of bias in included studies

We will assess the potential risk of bias for each trial and summarise this using the criteria and the 'Risk of bias' table described in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* Version 5 (Higgins 2011). We will classify studies into three categories according to the approach provided in Section 8.7 of the *Cochrane Handbook for Systematic Reviews of Interventions* Version 5 (Higgins 2011).

Measures of treatment effect

We will perform analyses using the Review Manager 5 statistical package (Review Manager 5) recommended by The Cochrane Collaboration and using Chapter 9 of the *Cochrane Handbook for Systematic Reviews of Interventions* as a guide (Higgins 2011). Statistical analyses of dichotomous variables will be performed by using odds ratios (OR) as the summary statistics; time-to-event analyses will be conducted by calculating the hazard ratio (HR). We will report study results with their associated 95% confidence intervals (CI).

Unit of analysis issues

We will analyse included studies according to the unit of randomisation.

Dealing with missing data

We will not exclude studies on the basis of missing data, and we will use the methods outlined in Chapter 16 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) for imputing missing data. When necessary, we will attempt to contact the authors and ask them for more information. We will make explicit the assumptions about the reasons why the data are missing. We will analyse only available data for the data judged to be 'missing at random'; missing data will be ignored. For data judged to be 'not missing at random', we will perform a sensitivity analysis to assess how changes in the assumptions made may affect the results. We will address the potential impact of missing data on the findings in the 'Discussion' section of the review.

Assessment of heterogeneity

We will assess heterogeneity according to the approach provided in Section 9.5 of the *Cochrane Handbook for Systematic Reviews of Interventions* Version 5 (Higgins 2011). If sufficient studies are included in the review, we will use the Chi^2 test and I^2 measurement to assess heterogeneity. An I^2 value of greater than 50% will be used as an indicator of moderate-to-high heterogeneity (Higgins 2003).

Assessment of reporting biases

We will use funnel plots in analyses including 10 or more studies for a given outcome in order to assess small study effects. As there can be several explanations for funnel plot asymmetry, we will interpret these results carefully (Sterne 2011).

Data synthesis

Data will be synthesised using Review Manager 5 software, according to The Cochrane Collaboration statistical guidelines. We will attempt the pooling of trials only if at least two trials with comparable protocols in the same indication and with similar outcome measurements are available. As we expect considerable heterogeneity in the included studies, we will use a random-effects model as a primary method of meta-analysis. In the event that no meta-analysis for any primary outcome is possible we will present a narrative synthesis.

Subgroup analysis and investigation of heterogeneity

If adequate data are available, we aim to perform subgroup analyses in different groups of individuals with ulcerative colitis (UC) or familial adenomatous polyposis (FAP), undergoing ileal pouch-anal anastomosis (IAPP).

Sensitivity analysis

If sufficient trials are included in the review, we will undertake sensitivity analyses of methodological items of study quality and of potential sources of heterogeneity specified a priori, as follows: excluding/including unpublished studies, excluding/including studies with unclear or inadequate allocation concealment, excluding/including studies with unclear or inadequate blinding of outcomes assessment and excluding/including studies with unclear or inadequate completeness of follow up. Sensitivity analyses will also be performed to test how the different assumptions about the missing data and data extracted from trials to assess the potential impact on the results. We will report any post-hoc decisions regarding choice of analysis.

ACKNOWLEDGEMENTS

None

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* *Indicates the major publication for the study*

APPENDICES

Appendix 1. Search strategies

MEDLINE (Ovid) 1946 - 08.11.12 - 271 hits

Search History

1. exp Anastomosis, Surgical/
2. exp Colonic Pouches/
3. exp Anal Canal/su [Surgery]
4. exp Intestinal Mucosa/
5. expProctocolectomy, Restorative/
6. exp Colonic Diseases/su [Surgery]
7. exp Ileum/su [Surgery]
8. exp Colectomy/
9. exp Rectum/su [Surgery]
10. (mucosectom* or anastomos* or ileal* or ileo* or ileum or $anal or anus or rect* or endo* or colon* or mucosa or IPAA or proctocolectom* or colectom* or $pouch).mp.
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12. (ileal or ileo* or ileum or $anal or anus or rect* endo*).mp.
13. 11 and 12
14. exp Suture Techniques/
15. exp Sutures/
16. exp Surgical Staplers/
17. (hand-sewn or handsewn or $sutur* or $stapl*).mp.
18. 14 or 15 or 16 or 17
19. 13 and 18
20. randomized controlled trial.pt.
21. controlled clinical trial.pt.
22. randomized.ab.
23. placebo.ab.
24. clinical trial.sh.
25. randomly.ab.
26. trial.ti.
27. 20 or 21 or 22 or 23 or 24 or 25 or 26
28. humans.sh.
29. 27 and 28
30. 19 and 29

EMBASE (Ovid) 1974 - 10.04.2014 - 355 hits

Search Histoty

1. expileoanal anastomosis/
2. expileorectal anastomosis/
3. exp colon pouch/
4. exp ileum pouch/
5. exp anal canal/su [Surgery]
6. exp intestine mucosa/su [Surgery]
7. expproctocolectomy/

8. exp ileum resection/
9. exp colon resection/
10. exp rectum resection/
11. (mucosectom* or anastomos* or ileal* or ileo* or ileum or $anal or anus or rect* or endo* or colon* or mucosa or IPAA or proctocolectom* or colectom* or $pouch).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
12. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13. (ileal or ileo* or ileum or $anal or anus or rect* endo*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
14. 12 and 13
15. exp suture/
16. (hand-sewn or handsewn or $sutur* or $stapl*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
17. 15 or 16
18. 14 and 17
19. CROSSOVER PROCEDURE.sh.
20. DOUBLE-BLIND PROCEDURE.sh.
21. SINGLE-BLIND PROCEDURE.sh.
22. (crossover* or cross over*).ti,ab.
23. placebo*.ti,ab.
24. (doubl* adj blind*).ti,ab.
25. allocat*.ti,ab.
26. trial.ti.
27. RANDOMIZED CONTROLLED TRIAL.sh.
28. random*.ti,ab.
29. 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28
30. (exp animal/ or exp invertebrate/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans or man or men or wom?n).ti.)
31. 29 not 30
32. 18 and 31

The Cochrane Library 08.11.12 - 295 hits (170 hits in CENTRAL)

#1 MeSH descriptor: [Anastomosis, Surgical] explode all trees
#2 MeSH descriptor: [Colonic Pouches] explode all trees
#3 MeSH descriptor: [Anal Canal] explode all trees and with qualifiers: [Surgery - SU]
#4 MeSH descriptor: [Intestinal Mucosa] explode all trees and with qualifiers: [Surgery - SU]
#5 MeSH descriptor: [Proctocolectomy, Restorative] explode all trees
#6 MeSH descriptor: [Colonic Diseases] explode all trees and with qualifiers: [Surgery - SU]
#7 MeSH descriptor: [Ileum] explode all trees and with qualifiers: [Surgery - SU]
#8 MeSH descriptor: [Colectomy] explode all trees
#9 MeSH descriptor: [Rectum] explode all trees and with qualifiers: [Surgery - SU]
#10 mucosectom* or anastomos* or ileal* or ileo* or ileum or $anal or anus or rect* or endo* or colon* or mucosa or IPAA or proctocolectom* or colectom* or $pouch
#11 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10)
#12 ileal or ileo* or ileum or $anal or anus or rect* endo*
#13 (#11 and #12)
#14 MeSH descriptor: [Suture Techniques] explode all trees
#15 MeSH descriptor: [Sutures] explode all trees
#16 MeSH descriptor: [Surgical Staplers] explode all trees
#17 hand-sewn or handsewn or $sutur* or $stapl*
#18 #14 or #15 or #16 or #17
#19 #13 and #18

CONTRIBUTIONS OF AUTHORS

Jayesh Sagar (JS) and Roberto Cirocchi (RC) were responsibles for the conception of the review. The first draft of the protocol was written by RC, Umberto Morelli, Alberto Arezzo and JS, with comments from Stefano Trastulli and Amilcare Parisi. Massimo Falconi and Mario Morino performed the revision of protocol.

DECLARATIONS OF INTEREST

None known