Study Title:

Constipation after elective laparoscopy for benign gyneacological indications – a prospective observational study

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Background:

laparoscopy, general anesthetic, fasting, reduced mobility and most significantly opiate use may all impact a patient's bowel habits resulting in post-operative constipation. Anecdotally some patients report difficulty with constipation postoperatively, but despite an extensive literature review, rates of constipation in patients undergoing laparoscopy for benign gynaecological disorders have not been well described.

Due to the nature of minimally invasive surgery, patients are commonly discharged home the same or second post-operative day and may not be reviewed by their surgeon for up to six weeks. Patients are often given little or no information on post-operative constipation and are left to manage the problem without guidance. Further analgesia may be used exacerbating the problem. In some instances, this leads to representations to hospital or general practitioner and rarely admission to hospital.

Post-operative constipation rates will vary according to the patient demographic as well as the procedure being performed. In one study, patients undergoing orthopedic procedures had rates of constipation of up to 58% of patients with the mean day of first defecation being the fourth post operative day[1]. Another study in patients undergoing pelvic floor reconstructive surgery, patients not using laxatives also had a mean day of first defecation of day four with 44% of patients requiring an enema to relieve constipation[2]. The use of opiates for the management of post operative pain is common and some patients may be using opiates for symptom relief pre-operatively. Opioid induced constipation has been reported in 81% of daily users and 46% of patients using opiates three times per week[3]. The type of pure opioid does not significantly influence the prevalence of constipation[3].

There is no standard definition of post-operative constipation. Patients may have different impressions of what defines constipation. It may encompass infrequent stools, stools that are hard or pellet like, or stools that are difficult to evacuate. The widely accepted ROME IV criteria for functional or opiate induced constipation aims to provide a more encompassing definition

of constipation[4]. However, its usefulness in acute post-operative constipation is limited given the definition requires the presence of symptoms in >25% of defecations. This may lead to inaccuracies when the condition is acute and may be transient in nature

We believe studying the incidence of post-operative constipation will enable the provision of better education and treatment as well as inform future research to improve the care of patients undergoing planned laparoscopy.

Objective:

We hypothesize that post-operative constipation in patients undergoing laparoscopy for benign gynecological disorders is an underappreciated complication of surgery and causes distress to the patient.

Our primary objective is to define the incidence of new onset constipation in patients undergoing elective laparoscopy.

Primary Objective: Constipation in patients undergoing laparoscopic surgery for benign gynaecology

The incidence of post-operative constipation, based on a modified ROME IV criteria; Defined as two or more of:

- Passage of first stool after the third post operative days from surgery
- Straining to pass stool
- Lumpy or hard stools (form 1 or 2 on Bristol stool form scale)
- Sensation of anorectal blockage
- Sensation of incomplete emptying
- Use of manual maneuvers to facilitate bowel motion
- Use of laxatives or enemas to facilitate bowel movements

Secondary Outcomes:

- Level of distress or bother caused by post-operative constipation
- Opiate use – pre/intra/ and post operatively
- Laxative use – pre and post operatively
- Time to bowels return to normal pre-op status
- Unplanned presentations to medical practitioner – Emergency department, general practitioner due to constipation
- Incidence of pre-operative constipation (functional or opiate induced constipation) as per Rome IV criteria (see below)
- Incidence of post-operative constipation that is persistant at three months follow up (as per ROME IV criteria)

Methods

The planned study will be a prospective observational study. Recruited participants will be provided with a pre-operative questionnaire to assess participant demographic, baseline bowel habit, laxative and analgesia use in the week prior to their procedure (Appendix One). The presence of pre-existing constipation will be defined by the ROME IV criteria

The participant will undergo their planned procedure. The participant's surgery and post-operative care will not be affected by their enrolment in this trial. Treating clinicians (surgeons, residents, anesthetists and nursing staff) should not alter their routine management.

Following planned surgery, the participant will complete a second questionnaire in the second post-operative week (Appendix Two). The postoperative questionnaire post-operative bowel habit, the use of opiates (via patient tablet count), laxative use and any unplanned presentation to a medical practitioner for constipation. A third questionnaire will be sent at three months post operatively. This survey will consist of the same questions in the first survey and will ensure that bowel habit has returned to normal or if constipation is persistent.

Questionnaires will be distributed via a third party online service (Survey Monkey) to be completed on there own electronic device or via a written survey. After consent has been obtained the patient will receive a text message sent via The Royal Women's Hospital email browser with a link to complete the pre-operative questionnaire (Appendix 3). Participants will be sent a text message with a link to the post-operative questionnaire two weeks after their surgery. Participants who have not completed the post-operative questionnaire one week after this text message will be sent a reminder text message (ie at 3 weeks after surgery). Participants will also have the option of completing a printed questionnaire that may be returned in person or via a reply paid envelope. Patients who have not completed the survey will be invited to complete this retrospectively at the routine six week post-operative review.

At the completion of the survey patients suffering from significant constipation will be advised to seek assistance from there general practitioner or attend the emergency department at The Royal Women's Hospital.

Setting:

- This is a single center study performed by the Gynaecology 2 unit at The Royal Women's Hospital, Melbourne, Victoria. Australia
- The Royal Womens hospital is a tertiary level obstetrics and gynaecology hospital located in one of Australia's capital cities. The Gynaecology 2 unit is a minimally invasive Gynaecology unit that has a specific focus on endometriosis.

Particpants:

Study participants will be those already planned for elective surgery. They will be identified and recruited pre-operatively by the treating gynaecologist, gynaecology trainee or appointed research assistant in the Gynaecology 2 clinic, the pre-admission clinic or at the time of admission for surgery at The Royal Women's Hospital.

Inclusion Criteria:

- Planned laparoscopic surgery for benign gyneacological indications
- Aged >/= 18 years

Exclusion Criteria:

- Non consent
- Non English speaking
- Known chronic bowel conditions (such as inflammatory bowel disorders, bowel malignancy – active or previously treated, diverticular disease) with exception of IBS
- Planned bowel shaving or bowel resection
- Intra-operative bowel injury
- Bowel preparation prior to surgery
- Planned hysterectomy
- Conversion to laparotomy

Study timeframe:

We will recruit until we reach our sample size of 100 particpants. There are approximately 5-10 cases of laparoscopic treatment of endometriosis per week. Allowing for patients who choose not to participate in the study, cancelled lists and drop-outs, we estimate 25% will agree to participate and return the surveys. we calculate we would need 6 months to reach our goal of 100 patients.

Additional Variables:

Information about additional variables will be collected using a data collection sheet (Appendix 4). The data collection sheet will be completed by the treating surgeon, or operating registrar at the time of surgery for day procedures or on the day of discharge for those planned for admission to hospital. The additional variables were chosen as they were considered to be additional factors that may increase the risk of post operative constipation. The data from the collection sheet will be collated with the patients survey results so that a secondary multivariant analysis may be performed

Sample size calculations:

No previous studies have been identified that examined post-operative constipation in patients undergoing laparoscopic treatment of benign gynecological conditions. We feel that a sample size of 100 patients will be adequate to represent of this population

Potential Bias

- Selection Bias – We will aim to recruit all eligible patients booked for laparoscopic surgery to this study. Particpants with pre-existing constipation issues may be more likely to participate in the study. Assessing pre-operative bowel function will help us identify this and analyze based on different subgroups. The use of technology such as Survey Monkey on an electronic device may potentially select those participants who are more computer literate. Providing the option of completing the survey via paper copy aims to reduce this effect

- Recall bias - Our survey relies on subjective data collection. By collecting data at three different time periods (prior to surgery, at the initial post operative period, and at three months) we aim to reduce the effect of recall bias on our data.
- Attrition bias – Participants who have difficulty with constipation are possibly more likely to continue with the proposed study follow up than those who do not. We plan to use a recall system via text message as well as a simple to use survey with an aim to diminish losses to follow up. Participants will be prompted to complete surveys at the six week follow up.
- Assessor bias – with a focus on constipation treating teams may increase counselling on constipation and management to the participants decreasing the true incidence.

Confidentiality and Data Protection

Consenting participants will be allocated a unique patient identifier and all data will be recorded in this de-identified manner. All information will be kept secure: all paperwork from the project will be kept in a locked room and all computerized information will be kept in a database that is password protected. All information will be kept for a period of 7 years after the project is completed, at which time hard copy records will be shredded and computer files deleted. In any publication, information will be provided in such a way that participants cannot be identified. This will be ensured by providing summarized data or else by referring to individual results by their study number.

Access to SurveyMonkey's technology resources is only permitted through secure connectivity (e.g., VPN, SSH) and requires multi-factor authentication. SurveyMonkey's information systems and technical infrastructure are hosted within world-class, SOC 2 accredited data centers. Physical security controls at the data centers include 24x7 monitoring, cameras, visitor logs, entry requirements, and dedicated cages for SurveyMonkey hardware.

Funding:

Nil funding was sourced for the completion of the trial. Registrars participating in the trial are allocated paid research time as part of their employment agreement.

Conflict of interest: None declared

Reference:

1. Park, J, 2016. Constipation in Patients following Orthopedic Surgery: Incidence and Influencing factors. *Korean Journal of Adult Nursing*, 28(6), 637-645.
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3. Bell, T, 2009. The prevalence, severity, and impact of opioid-induced bowel dysfunction: results of a US and European patient survey (PROBE 1). *Pain Medicine*, 10(1), 35-42
4. Lacy, B, 2016. Bowel Disorders. *Gastroenterology*, 150, 1393-1407.
5. Security statement, Survey Monkey. 2019. [ONLINE] Available at : https://www.surveymonkey.com/mp/legal/security/. [Accessed 5 February 2019]. LAST UPDATED: APRIL 11TH, 2018

Appendix 1

Proposed Patient Questionnaire – PreOP

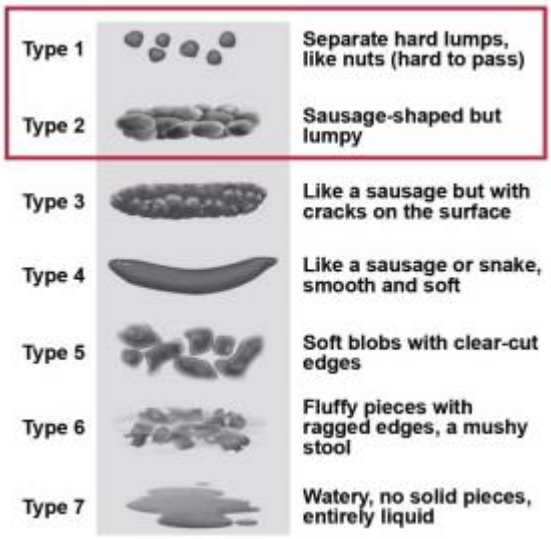
Thank you for your participation in this research titled "Constipation after elective laparoscopy for benign gynaecological indications". This research is aimed at improving care to our patients undergoing surgery. You have been chosen to participate in this study as you are undergoing an elective laparoscopy at The Royal Womens Hospital.

First, we would like to ask you some questions about yourself:

1. What is your date of birth
2. The reason for your planned surgery
    a. Pelvic pain or suspected endometriosis
    b. An ovarian cyst
    c. Infertility
    d. Other – please specify
3. Do you suffer from any chronic bowel disorder?
    a. No
    b. Yes – please specify
4. Do you suffer from any chronic medical condition?
    a. No
    b. Yes – please specify
5. Have you ever had a laparoscopic (key-hole) procedure before?
    a. No
    b. Yes
6. Do you take regular medication?
    a. No
    b. Yes - please specify
7. Please enter height and weight

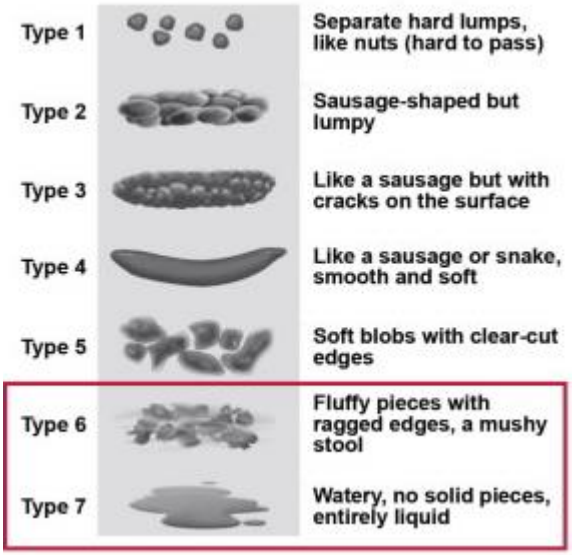
The following questions are to describe your usual bowel habits. Pick the response that best fits your typical habit.

1. In the last 3 months, how often did you have hard or lumpy stools that looked like Type 1 or 2 in the picture below? (Percent of all bowel movements)
    a. Select 0-100% (range will be in 10% increments)



2. Did you have hard or lumpy stools (like type 1 or 2) when you were not taking drugs for diarrhea
    a. No or rarely
    b. Yes
3. In the last 3 months, how often did you have fewer than three bowel movements a week without taking a laxative medication or enema? (Percent of weeks)
    a. Select 0-100%
4. In the last 3 months, how often did you strain during bowel movements? (Percent of bowel movements)
    a. Select 0-100%
5. In the last 3 months, how often did you have a feeling of incomplete emptying after bowel movements? (Percent of bowel movements)
    a. Select 0-100%
6. In the last 3 months, how often did you have a sensation that the stool could not be passed (was blocked), when having a bowel movement? (Percent of bowel movements)
    a. Select 0-100%
7. In the last 3 months, how often did you press on or around your bottom, or remove stool with your fingers, in order to have a bowel movement? (Percent of bowel movements)
    a. Select 0-100%
8. Did any of the symptoms of constipation in the prior questions begin more than 6 months ago?
    a. Yes
    b. No
9. To assist in passing of bowel motion I use laxative medication: yes or no
    a. No
    b. Yes
        i. Never
        ii. Occasionally – once or twice a week
        iii. Usually – most days

10. The level of bother or distress caused by my bowel habits – please give a number between 1 (not at all) to 10 (a great deal).
11. Do you use Opiod pain killers (eg codeine, morphine, endone, oxycontin, tapentadol):
    a. No
    b. Yes
        i. Which Opiate pain killers do you use
            1. Tramadol (eg Tramal)
            2. Codeine (e.g Panadeine forte)
            3. Morphine
            4. Oxycodone (e.g endone, oxytcontin)
            5. Other
        ii. How often do you use opiate pain killers
            1. Occasionally – less thank weekly
            2. Weekly
            3. One or two days per week
            4. Three or more days, but not daily
            5. Daily
12. Have any of the constipation symptoms listed in the previous questions changed since you started taking prescription medication for pain?
    a. Yes
    b. No
13. In the last 3 months, how often did you have mushy or watery stools that looked like Type 6 or 7 in the picture below when you were not using drugs or other treatment for constipation? (Percent of all bowel movements)
    a. Select 0-100%



14. Did you have mushy and watery stools (like Type 6 or 7) when you were not using drugs or other treatment for constipation?
    a. No or rarely
    b. Yes

If you are experiencing significant difficulties with constipation or other bowel problems then please seen advice from your treating doctor, you general practitioner or present to the emergency department at The Royal Womens Hospital

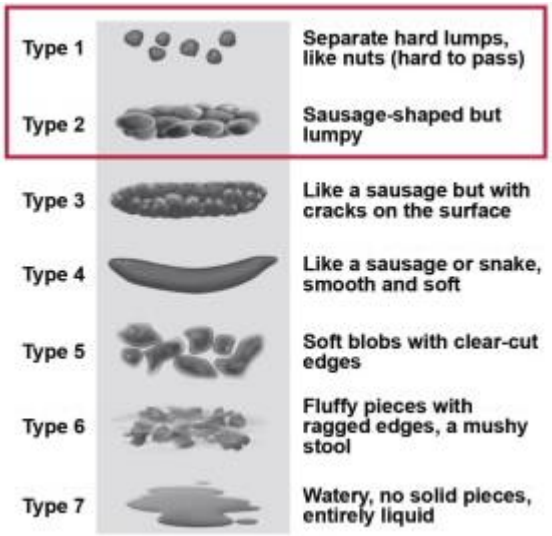
Appendix 2

Proposed patient Questionnaire – Post op

Thank you for your participation in this research titled "Constipation after elective laparoscopy for benign gynaecological indications". This research is aimed at improving care to our patients undergoing surgery. You have been chosen to participate in this study as you are undergoing an elective laparoscopy at The Royal Womens Hospital.

The following questions are to describe your bowel habit **in the first week** following your surgery. Pick the response that best fits your bowel habits after the surgery

1. The time between my surgery and passing my first stool was
    a. Select days post surgery 0-7 or greater
2. In the week following surgery did you have hard or lumpy stools that looked like type 1 or 2 in the picture below
    a. No
    b. Yes
        i. With the first bowel motion after surgery only, then resolved
        ii. With the first and second bowel motion, then resolved
        iii. With the first, second, and third bowel motions, then resolved
        iv. With all bowel motions in the week following surgery



3. In the week following surgery did you strain during bowel movements
    a. No

b. Yes
    i. With the first bowel motion after surgery only, then resolved
    ii. With the first and second bowel motion, then resolved
    iii. With the first, second, and third bowel motions, then resolved
    iv. With all bowel motions in the week following surgery

4. In the week following surgery did you have a feeling of incomplete emptying after bowel movements
    a. No
    b. Yes
        i. With the first bowel motion after surgery only, then resolved
        ii. With the first and second bowel motion, then resolved
        iii. With the first, second, and third bowel motions, then resolved
        iv. With all bowel motions in the week following surgery
5. In the week following surgery, did you have a sensation that the stool could not be passed (was blocked), when having a bowel movement
    a. No
    b. Yes
        i. With the first bowel motion after surgery only, then resolved
        ii. With the first and second bowel motion, then resolved
        iii. With the first, second, and third bowel motions, then resolved
        iv. With all bowel motions in the week following surgery
6. In the week following surgery, did you have to press on or around your bottom, or remove stool with you fingers, in order to have a bowel movement
        i. With the first bowel motion after surgery only, then resolved
        ii. With the first and second bowel motion, then resolved
        iii. With the first, second, and third bowel motions, then resolved
        iv. With all bowel motions in the week following surgery
7. To assist in passing a bowel motion after surgery, I used laxative medication:
    a. No
    b. Yes
        i. With the first bowel motion after surgery only, then resolved
        ii. With the first and second bowel motion, then resolved
        iii. With the first, second, and third bowel motions, then resolved
        iv. With all bowel motions in the week following surgery
8. To assist in passing a bowel motion I required the use of enema medication:
    a. No
    b. Yes
        i. Once only
        ii. More than once
9. For assistance with my bowel motions I visited a health professional: Yes or no, if yes who
    a. No
    b. Yes – if yes who
        i. I contacted my surgeon or treating team

ii. My general practitioner
iii. The Emergency department
iv. The pharmacist
v. A nurse
vi. Other

10. The level of bother or distress caused by my bowels after surgery – please give a number between 1 (not at all) and 10 (a great deal) : - insert scale
11. I used Opiod pain killers/tablets (e.g tramadol, endone, oxycontin, tapentadol, codeine) in the week following surgery
    a. No
    b. Yes
        i. The Opiate I used was:
            1. Tramadol e.g. Tramal
            2. Oxycodone e.g. Endone,
            3. Codeine e.g. Panadeine forte
            4. Tapentadol e.g. Palexia
            5. Other – please specify
        ii. The number of tablets used in the week following surgery – please count the tablets from the packet that was provided to you
            1. Select 1-20
12. The time when I felt my bowel motions returned back to normal after surgery was
    a. Immediately, there was no change in my bowel motions
    b. Within the first three days
    c. Between three to five days
    d. Between five days and a week
    e. Greater than a week

If you are experiencing significant difficulties with constipation or other bowel problems then please seen advice from your treating doctor, you general practitioner or present to the emergency department at The Royal Womens Hospital

Appendix Three

Text message received by patient:

Thank you for your participation in the constipation after laparoscopy study at The Royal Womens hospital. Please click on the link below to be redirected to the before/after surgery questionnaire hosted by Survey Monkey.

This is a reminder message from The Royal Womens Hospital constipation after laparoscopy study. Please click on the link below to be redirected to the before/after surgery questionnaire hosted by Survey Monkey.

Perioperative Data Collection

Constipation at Elective Laparoscopy

Please attach patient Bradma:

Medical co-morbidities:

Indication for laparoscopic surgery:

Operation Details :

- Procedure performed :

- Operating time (from skin incision to close):
- Intraoperative complication: Y / N
    - If yes details:
- EBL (Surgeon estimate):
- rASRM stage of endometriosis :

Perioperative opiate use

- Intraoperative opiate use : (during the procedure and in the recovery)
    - Opiate used: Total drug used:
    - Opiate used : Total drug used:
    - Opiate used: Total drug used:
- Post operative opiate use: (during the patients admission on the ward)
    - Opiate used: Total drug used:
    - Opiate used : Total drug used:
    - Opiate used: Total drug used:

Post-operative inpatient details:

- Immediate post-operative complications:
- Length of stay (days):
- Discharge prescription of opiates and laxatives
    - Opiate prescribed : Dosage
    - Laxative prescribed Y/N