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[Intervention Review]

In-bag manual versus uncontained power morcellation for laparoscopic myomectomy

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ABSTRACT

Background

Uterine leiomyomas, also referred to as myomas or fibroids, are benign tumours arising from the smooth muscle cells of the myometrium. They are the most common pelvic tumour in women. The estimated rate of leiomyosarcoma, found during surgery for presumed benign leiomyomas, is about 0.51 per 1000 procedures, or approximately 1 in 2000.

Treatment options for symptomatic uterine leiomyomas include medical, surgical, and radiologically-guided interventions. Laparoscopic myomectomy is the gold standard surgical approach for women who want offspring, or otherwise wish to retain their uterus. A limitation of laparoscopy is the inability to remove large specimens from the abdominal cavity through the laparoscope. To overcome this challenge, the morcellation approach was developed, during which larger specimens are broken into smaller pieces in order to remove them from the abdominal cavity via the port site. However, intracorporeal power morcellation may lead to scattering of benign tissues, with the risk of spreading leiomyoma or endometriosis. In cases of unsuspected malignancy, power morcellation can cause unintentional dissemination of malignant cells, and lead to a poorer prognosis by upstaging the occult cancer.

A strategy to optimise women's safety is to morcellate the specimens inside a bag. In-bag morcellation may avoid the dissemination of tissue fragments.

Objectives

To evaluate the effectiveness and safety of protected in-bag extracorporeal manual morcellation during laparoscopic myomectomy compared to intra-abdominal uncontained power morcellation.

Search methods

On 1 July 2019, we searched; the Cochrane Gynaecology and Fertility Group Specialized Register of Controlled Trials, CENTRAL, MEDLINE, Embase, PsycINFO, CINAHL, LILACS, PubMed, Google Scholar, and two trials registers.

We reviewed the reference lists of all retrieved full-text articles, and contacted experts in the field for additional and ongoing trials.

Selection criteria

We included all randomised controlled trials comparing in-bag extracorporeal manual morcellation versus intracorporeal uncontained power morcellation during laparoscopic myomectomy in premenopausal women.

Data collection and analysis

We followed standard Cochrane methods.

Two review authors independently reviewed the eligibility of trials, extracted data, and evaluated the risk of bias. Data were checked for accuracy.

The summary measures were reported as risk ratios (RR) or mean differences (MD) with 95% confidence interval (CI).

The outcomes of interest were a composite of intraoperative and postoperative complications, operative times, ease of morcellation, length of hospital stay, postoperative pain, conversion to laparotomy, and postoperative diagnosis of leiomyosarcoma. Results for the five main outcomes follow.

Main results

We included two trials, enrolling 176 premenopausal women with fibroids, who underwent laparoscopic myomectomy.

The experimental group received in-bag manual morcellation, during which each enucleated myoma was placed into a specimen retrieval bag, and manually morcellated with scalpel or scissors. In the control group, intracorporeal uncontained power morcellation was used to reduce the size of the myomas.

No intraoperative complications, including accidental morcellation of the liver, conversion to laparotomy, endoscopic bag disruption, bowel injury, bleeding, accidental injury to any viscus or vessel, were reported in either group in either trial.

We found very low-quality evidence of inconclusive results for total operative time (MD 9.93 minutes, 95% CI -1.35 to 21.20; 2 studies, 176 participants; $I^2 = 35\%$), and ease of morcellation (MD -0.73 points, 95% CI -1.64 to 0.18; 1 study, 104 participants). The morcellation operative time was a little longer for the in-bag manual morcellation group, however the quality of the evidence was very low (MD 2.59 minutes, 95% CI 0.45 to 4.72; 2 studies, 176 participants; $I^2 = 0\%$). There were no postoperative diagnoses of leiomyosarcoma made in either group in either trial.

We are very uncertain of any of these results. We downgraded the quality of the evidence due to indirectness and imprecision, because of limited sites in high-income settings and countries, small sample sizes, wide confidence intervals, and few events.

Authors' conclusions

There are limited data on the effectiveness and safety of in-bag morcellation at the time of laparoscopic myomectomy compared to uncontained power morcellation. We were unable to determine the effects of in-bag morcellation on intraoperative complications as no events were reported in either group. We are uncertain if in-bag morcellation improves total operative time or ease of morcellation compared to control. Regarding morcellation operative time, the quality of the evidence was also very low and we cannot be certain of the effect of in-bag morcellation compared to uncontained morcellation. No cases of postoperative diagnosis of leiomyosarcoma occurred in either group. We found only two trials comparing in-bag extracorporeal manual morcellation to intracorporeal uncontained power morcellation at the time of laparoscopic myomectomy. Both trials had morcellation operative time as primary outcome and were not powered for uncommon outcomes such as intraoperative complications, and postoperative diagnosis of leiomyosarcoma.

Large, well-planned and executed trials are needed.

PLAIN LANGUAGE SUMMARY

In-bag manual versus uncontained power morcellation for laparoscopic myomectomy

Review question

Cochrane authors reviewed the effectiveness and safety of in-bag manual morcellation compared to uncontained power morcellation during laparoscopic myomectomy. The primary outcome of the review was a composite of intraoperative (during surgery) complications.

Background

Myomectomy is a surgical procedure to remove uterine fibroids — also called leiomyomas. These common, non-cancerous growths usually develop in the uterus during childbearing years, but they can occur at any age. In laparoscopic myomectomy, which is a minimally invasive procedure, the surgeon accesses and removes the fibroids through several small abdominal incisions.

Laparoscopic myomectomy is the gold standard for women with uterine leiomyomas, but it is difficult to remove large fibroids through the small incisions and tubes (laparoscopes). To overcome this challenge, surgeons developed a technique to break the large fibroids into smaller pieces (morcellation).

However, power morcellation (using a drill-like instrument to cut up the fibroids) inside the abdomen may lead to the scattering of the tissues. These tissues may be benign (such as fibroids or endometriosis), but they may also be tissues from an undiagnosed cancer. A strategy to optimise women's safety is to cut up larger fibroids with a scalpel or scissors, inside a bag.

Study Characteristics

We included two randomised controlled trials, which enrolled 176 premenopausal women undergoing laparoscopic myomectomy; they were randomised to receive either in-bag manual morcellation (87 women) or uncontained power morcellation (89 women). The literature was searched to 1 July 2019.

Key results

Neither study reported complications during or after surgery, including no diagnoses of leiomyosarcoma, for women in either group.

We are very uncertain whether in-bag morcellation reduces the total time of the operation, or improves the ease of morcellation. The evidence suggests that the morcellation operative time was slightly longer when the surgeon used in-bag morcellation. However, the quality of the evidence is very low and we cannot be certain of any of these results.

Quality of the evidence

The evidence was of very low quality. The main limitations were indirectness (both trials took place in high-income settings and countries, therefore, our findings are limited to this type of setting), and imprecision (both trials had small sample sizes and wide confidence intervals).

SUMMARY OF FINDINGS

Summary of findings 1. Any type of in-bag morcellation versus uncontained power morcellation during laparoscopic myomectomy

Any type of in-bag morcellation versus uncontained power morcellation during laparoscopic myomectomy

Patient or population: premenopausal women undergoing laparoscopic myomectomy for uterine fibroids

Setting: university hospitals in Italy

Intervention: any type of in-bag morcellation

Comparison: uncontained power morcellation

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with uncontained power morcellation	Risk with any type of in-bag morcellation				
Composite intraoperative complications	No intraoperative complications occurred in either group in either trial.			176 (2 RCTs)	⊕○○○ Very low ^{a,b}	The evidence is very uncertain about the effect of in-bag morcellation on composite intraoperative complications.
Total operative time (minutes)	The mean total operative time for the control group was 94.41 minutes	The mean total operative time for the intervention group was 105.1 minutes (ranging from 96.96 to 113.24 minutes)	MD 9.93 (-1.35 to 21.20)	176 (2 RCTs)	⊕○○○ Very low ^{a,c}	The evidence is very uncertain about the effect of in-bag morcellation on total operative time
Morcellation operative time (minutes)	The mean morcellation operative times for the control group was 10.26 minutes	The mean morcellation operative times for the intervention group was 12.83 minutes (ranging from 9.47 to 16.18 minutes)	MD 2.59 (0.45 to 4.72)	176 (2 RCTs)	⊕○○○ Very low ^{a,c}	The evidence is very uncertain about the effect of in-bag morcellation on morcellation operative time
Ease of morcellation (scale 1 to 10; 1 = very difficult, 10 = very easy)	The mean ease of morcellation score for the control group was 7.5	The mean ease of morcellation score for the intervention group was 6.77	MD -0.73 (-1.64 to 0.18)	104 (1 RCT)	⊕○○○ Very low ^{a,c}	The evidence is very uncertain about the effect of in-bag morcellation on ease of morcellation
Postoperative diagnosis of	There were no postoperative diagnoses of leiomyosarcoma made in either group in either trial.			176 (2 RCTs)	⊕○○○ Very low ^{a,b}	The evidence is very uncertain about the effect of in-bag morcellation

tion on postoperative diagnosis of leiomyosarcoma.

leiomyosarcoma

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **MD:** Mean Difference

GRADE Working Group grades of evidence

High certainty. We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty. We are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty. Our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

Very low certainty. We have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

^adowngraded once for indirectness; all the included trials took place in high-income settings and countries

^bdowngraded twice for very serious imprecision; zero events, small sample size

^cdowngraded twice for very serious imprecision; small sample size, wide confidence interval

BACKGROUND

Description of the condition

Uterine leiomyomas, also called myomas, or fibroids, are benign tumours arising from the smooth muscle cells of the myometrium. They are the most common pelvic tumour in women. Uterine fibroids arise in women of reproductive age; and symptoms include menorrhagia, pain, miscarriage, and infertility (Wallach 2004). The estimated rate of leiomyosarcoma found at surgery for presumed benign fibroids is about 0.51 per 1,000 procedures, or approximately 1 in 2000 (Pritts 2015).

Uterine fibroids are described according to their location in the uterus, although many fibroids have more than one location designation. The International Federation of Gynecology and Obstetrics (FIGO) classification system for fibroid location is as follows (Munro 2011):

1. intramural myomas (FIGO type 3, 4, 5);
2. submucosal myomas (FIGO type 0, 1, 2);
3. type 0: completely within the endometrial cavity;
4. type 1: extend less than 50% into the myometrium;
5. type 2: extend 50% or more into the myometrium;
6. subserosal myomas (FIGO type 6, 7);
7. cervical myomas (FIGO type 8).

The estimated incidence of uterine fibroids is about 20% to 80% in women of reproductive age (Donnez 2015). The incidence rates of fibroids are typically found to be two to three times greater in black women than in white women (Baird 2003). Other risk factors include reproductive and endocrine factors, nulliparity, early menarche, prenatal exposure to diethylstilbestrol, and obesity (Pavone 2018). Use of long-acting progestin-only contraceptives (e.g. depot medroxyprogesterone) appear to protect against the development of leiomyoma (Wise 2004).

Relief of symptoms is the major goal in the management of women with significant symptoms. Asymptomatic myomas can be managed by reassurance and careful follow-up. It is estimated that at least 50% of fibroids are asymptomatic (Divakar 2008).

The type of intervention is individualised, based on the type and severity of symptoms, size and location of myomas, patient age, reproductive plans, and obstetric history.

Description of the intervention

Interventions for symptomatic uterine fibroids include medical therapy, interventional radiology, and surgery (Donnez 2015; Giarrè 2019). Surgical approach includes myomectomy or hysterectomy. Myomectomy is a surgical procedure to remove uterine fibroids. In laparoscopic myomectomy, a minimally invasive procedure, the surgeon accesses and removes the fibroids through several, small, abdominal incisions (Donnez 2015).

Compared with a laparotomy, laparoscopic myomectomy is associated with significantly less subjectively reported postoperative pain, lower postoperative fever, and shorter hospital stay (Bhave Chittawar 2014).

A limitation of laparoscopy is the inability to remove large specimens from the abdominal cavity through the

laparoscope. To overcome this challenge, the morcellation approach was developed, during which larger specimens are broken into smaller pieces, in order to remove them from the abdominal cavity (Senapati 2015). Until 2014, intra-abdominal, or intracorporeal power morcellation (also known as electromechanical morcellation), was the primary method of uterine fibroid morcellation used during laparoscopic myomectomy. With power morcellator, electrical energy is transformed into mechanical power, which cuts the specimen into many small pieces, which then can be easily removed through a 12 mm to 20 mm laparoscopic access port (Glaser 2018). However, to reduce the risk of injury to other structures, this method should only be used by experienced operators.

Following a highly publicised case of morcellation, where a woman was postoperatively diagnosed with leiomyosarcoma, the US Food and Drug Administration (FDA) released a warning statement, in 2014, discouraging the use of power morcellation, in order to reduce the risk of unintentionally spreading undiagnosed leiomyosarcoma cancer cells throughout the abdominal cavity (Wright 2015). The FDA updated the warning in 2020. In the 2020 safety communication, the FDA recommends performing laparoscopic morcellation for myomectomy or hysterectomy only with a tissue containment system, and performing these procedures only in appropriately selected patients (FDA 2020).

Distributed between December 2014 and February 2015, a survey of the American Association of Gynecologic Laparoscopists Minimally Invasive Gynecologic Surgery Fellowship program faculty, showed that intra-abdominal power morcellation was used commonly before the FDA warning; after 2014, gynaecologists adapted their management strategies (Desai 2015). For example, there are several reports of morcellation performed in a contained isolation system, such as an insufflated bag (Siedhoff 2017).

How the intervention might work

Preoperative diagnosis of uterine sarcoma is very difficult, and currently, its diagnostic accuracy is not satisfactory. Although the use of multiple predictors, including age, serum lactate dehydrogenase (LDH) values, LDH5/LDH1 ratio ultrasound, magnetic resonance imaging (MRI), and endometrial cytology, is beneficial in the clinical setting, no test can definitely exclude leiomyosarcoma preoperatively (Mollo 2018).

Performing intracorporeal power morcellation at the time of laparoscopic myomectomy may lead to a scattering of benign tissues, with the risk of spreading leiomyoma or endometriosis. Dispersed tissue fragments can implant on abdominal organ surfaces and lead to several complications, including inflammation and infection (Siedhoff 2017).

In cases of unsuspected malignancy, power morcellation can cause unintentional dissemination of malignant cells and a poorer prognosis by upstaging the occult cancer. It is worth noting that cancer cells may be spread during open myomectomy and with laparoscopic myomectomy, even before morcellation.

A strategy to optimise women's safety is to morcellate the specimens inside a bag. In-bag morcellation may avoid the dissemination of tissue fragments at the time of laparoscopic myomectomy, compared to intra-abdominal uncontained power morcellation.

Why it is important to do this review

For women who require myomectomy, the laparoscopic approach is considered the gold standard, because of intraoperative and postoperative benefits, and the minimal access route. Since currently, there are no accurate diagnostic modalities to differentiate benign from malignant uterine tumours, it is important to validate alternative surgical techniques for the safe removal of the specimens during laparoscopic myomectomy.

This review aims to investigate the potential benefits and safety of in-bag manual morcellation versus uncontained power morcellation for women undergoing laparoscopic myomectomy.

OBJECTIVES

To evaluate the effectiveness and safety of protected in-bag extracorporeal manual morcellation during laparoscopic myomectomy compared to intra-abdominal uncontained power morcellation.

METHODS

Criteria for considering studies for this review

Types of studies

We included all randomised controlled trials (RCT) comparing in-bag extracorporeal manual morcellation versus intracorporeal uncontained power morcellation at the time of laparoscopic myomectomy. We did not include trials evaluating procedures other than laparoscopic myomectomy, such as hysteroscopic myomectomy.

Types of participants

We included premenopausal women undergoing laparoscopic myomectomy.

Types of interventions

The experimental intervention was extracorporeal in-bag manual morcellation.

The comparator was intracorporeal uncontained power morcellation.

Types of outcome measures

Primary outcomes

1. Composite intraoperative complications included at least one of the following:
 - a. accidental morcellation of the liver;
 - b. conversion to laparotomy;
 - c. endoscopic bag disruption;
 - d. bowel injury;
 - e. bleeding;
 - f. accidental injury to any viscus or vessel.

Secondary outcomes

1. Total operative time, in minutes
2. Morcellation operative time, in minutes. This was defined as the time from when the myoma was clamped and subjected to intracorporeal morcellation, or positioned within a bag for

- extracorporeal in-bag morcellation, to the moment when the last fragment of myoma was removed from the surgical field.
3. Ease of morcellation, defined by the surgeon as one (very difficult) to 10 (very easy)
4. Postoperative length of stay, in days
5. Postoperative pain expressed on a visual analogue scale (VAS), from one (little pain) to 10 (intense pain)
6. Conversion to laparotomy (related only to morcellation or bag issues)
7. Postoperative diagnosis of leiomyosarcoma
8. Postoperative complications, including:
 - a. abscesses
 - b. ileus
 - c. sepsis
 - d. blood transfusion

Search methods for identification of studies

We searched for all published and unpublished RCT, without language restrictions, and in consultation with the Gynaecology and Fertility (CGF) Group Information Specialist.

Electronic searches

We searched the following electronic databases, trial registers, and websites:

1. The CGF Group Specialized Register of Controlled Trials; PROCITE platform (searched 1 July 2019; [Appendix 1](#));
2. Cochrane Central Register of Controlled Trials; Ovid (CENTRAL; 2019, Issue 5) (searched 1 July 2019; [Appendix 2](#));
3. MEDLINE; Ovid – Epub ahead of print, In-process & Other non-indexed citations platform (1946 to 1 July 2019; [Appendix 3](#));
4. Embase; Ovid (1980 to 1 July 2019; [Appendix 4](#));
5. PsycINFO; Ovid (1806 to 1 July 2019; [Appendix 5](#));
6. CINAHL (Cumulative Index to Nursing and Allied Health Literature; EBSCO; 1961 to 1 July 2019; [Appendix 6](#)).

We combined the MEDLINE with the Cochrane highly sensitive search strategy for identifying randomised trials, from Chapter 6 of the *Cochrane Handbook of Systematic Reviews of Interventions* (Lefebvre 2011). We combined the Embase, PsycINFO and CINAHL searches with trial filters developed by the Scottish Intercollegiate Guidelines Network (SIGN; sign.ac.uk/search-filters.html).

Search terms were: endobag, containment bag, morcellation bag, bowel bag, containment system, myoma, myomata, fibroids, myomectomy, laparoscopy.

Searching other resources

Other electronic sources of trials included the following.

1. Trial registers for ongoing and registered trials:
 - a. ClinicalTrials.gov (clinicaltrials.gov);
 - b. The World Health Organization International Trials Registry Platform search portal (apps.who.int/trialsearch/).
2. LILACS and other Spanish and Portuguese language databases: Latin American and Caribbean Health Science Information database (1982 to June 2019), found in the Virtual Health Library Regional Portal (VHL; pesquisa.bvsalud.org/portal/).

3. PubMed and Google Scholar, for recent trials not yet indexed in the major databases.

We handsearched reference lists of all retrieved full-text articles and all relevant conference proceedings. We personally contacted experts in the field requesting additional relevant data, so unpublished studies could be included. We also handsearched relevant journals and conference abstracts that are not covered in the CGF register, in liaison with the Information Specialist.

We did not apply any language or date restrictions to the searches. We included a PRISMA flow chart to present the results of the search and the process of screening and selecting studies for inclusion in the review.

Data collection and analysis

We conducted data collection and analysis in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2019).

Selection of studies

We used Covidence software for selection of studies, data extraction, and assessment of risk of bias of included studies (Covidence). Two review authors (FZ, GS) independently conducted an initial screen of titles and abstracts identified by the search. We excluded studies with clearly irrelevant titles or abstracts. We retrieved full-text articles of all potentially eligible studies; two review authors (FZ, GS) independently assessed them. We recorded the reason for exclusion for any study that we excluded following a review of the full text. Disagreements or doubts were resolved by discussion with a third review author (RV).

Data extraction and management

For eligible studies, two review authors (FZ, GS) extracted data using a data extraction form in Covidence (Covidence). We resolved discrepancies through discussion with a third review author (RV).

FZ and RV are co-authors of one of the trials included in the full review (Venturella 2016). FZ and RV were not involved in data extraction and management of this trial; it was independently assessed by GS and AR.

Data extracted included study characteristics and outcome data. We entered data into Review Manager 5 software and checked for accuracy (Review Manager 2014). When information regarding any of the above was unclear, we attempted to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors (GS, FZ) independently assessed risk of bias for each study, using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2019). We resolved any disagreement by discussion and by involving an additional assessor (RV).

FZ and RV are co-authors of one of the trials included in the full review (Venturella 2016). FZ and RV were not involved in assessment of risk of bias of this trial; it was independently assessed by GS and AR.

We reported the assessment of risk of bias graphically, as a summary of risk of bias for each trial, and as percentages across all

included studies. For details of the domains we assessed for risk of bias, see Appendix 7.

Co-authors of included trials were not involved in the assessment of eligibility or risk of bias of those trials.

Measures of treatment effect

We expressed dichotomous data as Mantel-Haenszel risk ratio (RRs) with 95% confidence intervals (CIs), using the random-effects model of DerSimonian and Laird, and combined them in meta-analyses using Review Manager 5 software.

Graphically, we displayed increased risk of a particular outcome in the meta-analyses to the right of the centre line, and decreased risk of an outcome to the left of the centre line.

For continuous outcomes, we extracted means (with or without standard deviation) and imported the values into Review Manager 5. We reported the summary measures as summary mean difference (MD) with 95% confidence intervals (CIs), using the random-effects model of DerSimonian and Laird. If similar outcomes were reported on different scales, we calculated the standardized mean difference (SMD).

Unit of analysis issues

The analysis was per women randomly assigned. We conducted intention-to-treat (ITT) analysis when possible.

Dealing with missing data

For missing data from any of the included studies, we contacted the study authors to supply relevant missing information. If missing data were not provided, we conducted ITT analysis, if possible. For dichotomous data, the denominator represented the number of women entering the trial, and we assumed that the outcome did not occur. If data for continuous outcomes were lacking, we only used the available data because we were unable to impute missing values.

Assessment of heterogeneity

We assessed the characteristics of included studies to decide whether the participants, interventions, and outcomes were sufficiently similar for meta-analysis to be appropriate.

We used the I^2 statistic to assess heterogeneity in the meta-analysis. We interpreted results of the I^2 statistic as follows (Higgins 2019):

- 0% to 40%: might not be important;
- 30% to 60%: may represent moderate heterogeneity;
- 50% to 90%: may represent substantial heterogeneity;
- 75% to 100%: considerable heterogeneity.

Assessment of reporting biases

We did not investigate reporting biases (such as publication bias) because we included fewer than 10 studies in the meta-analysis.

Data synthesis

We performed statistical analysis using Review Manager 5.3 (Review Manager 2014). We aimed to combine the data in the following comparisons, using a random-effects model:

1. any type of in-bag morcellation versus uncontained power morcellation;
2. in-bag morcellation using a 10 mm bag versus uncontained power morcellation;
3. in-bag morcellation using a 15 mm bag versus uncontained power morcellation.

For comparisons 2 and 3, 10 mm and 15 mm refer to the size of the port.

Subgroup analysis and investigation of heterogeneity

Where data were available, we aimed to conduct subgroup analyses for the comparison 'any type of in-bag morcellation versus uncontained power morcellation' according to the following categories:

1. participants with myoma(s) of less than 5 cm versus those with myoma(s) of 5 cm or greater;
2. participants with single myoma versus those with multiple myomas;
3. participants younger than 45 years versus those aged 45 years and older.

Sensitivity analysis

To examine the stability of study results, we planned to conduct the following sensitivity analyses for the primary outcomes for the comparison 'any type of in-bag morcellation versus uncontained power morcellation':

1. excluding trials published only as an abstract;
2. restricting the analyses to trials with low risk of bias in the first two domains only (i.e. selection bias, see [Appendix 7](#));
3. using fixed-effect instead of random-effects model.

Overall quality of the body of evidence: 'Summary of findings' table

We used the GRADE approach to assess the quality of the body of evidence relating to the following outcomes for the comparison 'any type of in-bag morcellation versus uncontained power morcellation':

1. intraoperative complications;
2. total operative time;
3. morcellation operative time;
4. ease of morcellation;
5. postoperative diagnosis of leiomyosarcoma.

The GRADE approach uses five considerations (study limitations (e.g. risk of bias), consistency of effect, imprecision, indirectness, and publication bias) to assess the quality of the body of evidence for each outcome. The evidence can be downgraded from high quality by one level for serious (or by two levels for very serious) limitations. We used GRADEpro GDT software to import data from Review Manager 5 in order to generate 'Summary of findings' tables ([GRADEpro GDT](#)). A summary of the intervention effect and a measure of quality for each of the above outcomes is presented.

RESULTS

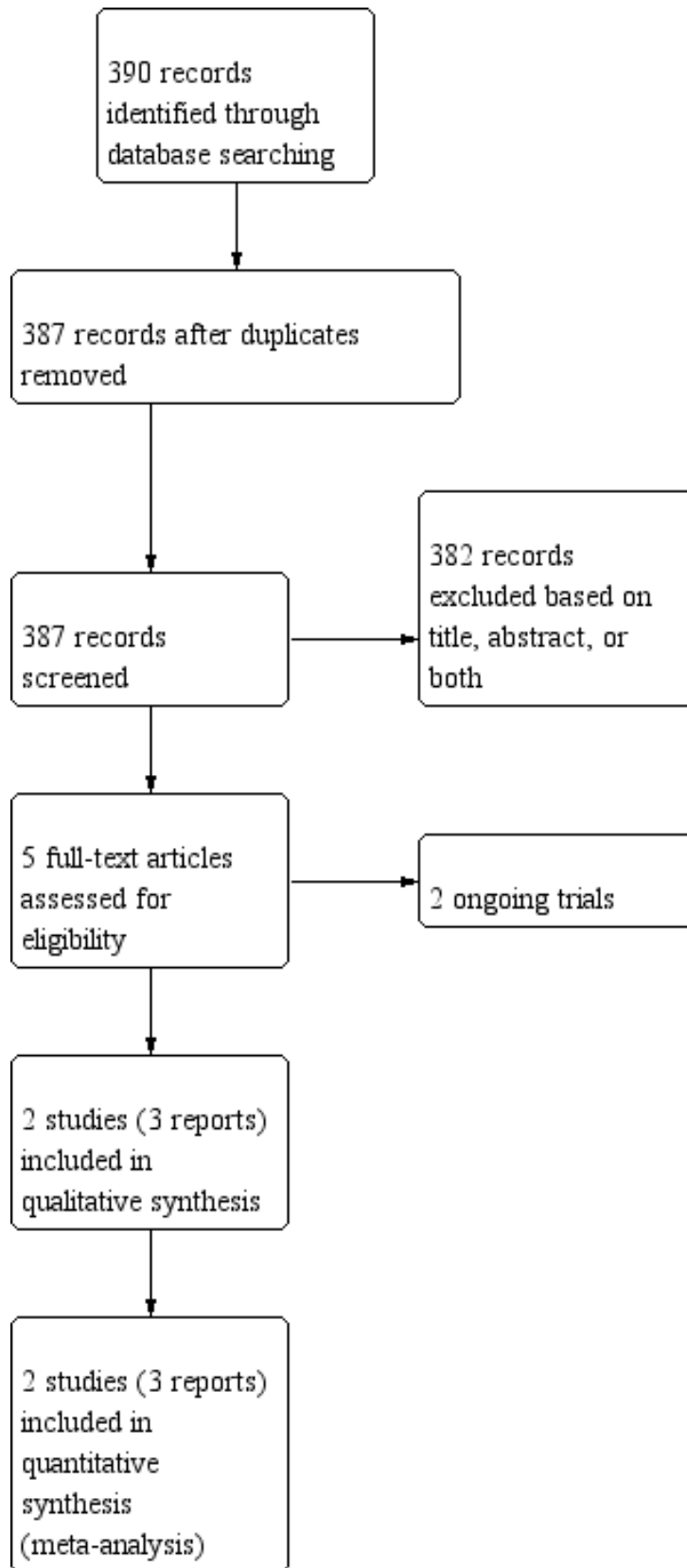
Description of studies

Results of the search

After the initial abstract screening (387 records screened), we assessed five papers for eligibility; we classified two as ongoing trials ([NCT02777203](#) and [NCT03281460](#)); we included two trials, reported in three papers ([Frasca 2018](#); [Venturella 2016](#)).

We included two trials in the meta-analysis, including 176 participants (87 in the intervention group and 89 in the control group; [Frasca 2018](#); [Venturella 2016](#)). See: [Figure 1](#).

Figure 1. Study flow diagram



Included studies

The two trials included women undergoing laparoscopic myomectomy who were randomised to receive either uncontained or in-bag morcellation.

In the control group, intracorporeal uncontained power morcellation was performed with a reusable power morcellator (Rotocut G1, Storz).

In the intervention group, each enucleated myoma was placed into a specimen retrieval bag. The fibroid was tightly grasped with Schroeder tenaculum and extracorporeal manual morcellation was performed with scalpel or scissors, avoiding bag damage.

In both included trials, the primary outcome was the comparison of morcellation operative time, and the final diagnosis of fibroid was obtained after postoperative histological examination of all tissue samples.

Setting

Both included trials were based in Italian university hospital settings, and were single centre trials.

Participants

[Venturella 2016](#) included premenopausal women with heavy menstrual bleeding or patients already diagnosed with fibroids from referral sources and undergoing a laparoscopic myomectomy. Inclusion criteria were: age between 18 and 40 years, body mass index (BMI) 18 kg/m² to 40 kg/m², heavy menstrual bleeding, and the presence of at least one myoma measuring 4 cm or more in diameter (but no myoma measuring >10 cm, according to local practice on eligibility for laparoscopy).

[Frasca 2018](#) included premenopausal patients aged between 18 and 50 years, with an ultrasonographic diagnosis of at least one myoma measuring between 4 cm and 10 cm in mean diameter, and presenting with heavy menstrual bleeding or infertility as indications to laparoscopic myomectomy.

Intervention and comparisons

In [Venturella 2016](#), in the intervention group, each enucleated myoma was placed into a non-rip nylon specimen bag (Endo Catch Gold Auto Suture 10 mm or 15 mm, Covidien), which could hold 220 mL or 1000 mL, according to the size chosen. The central lower 10 mm trocar incision was increased to 30 mm, and a 65-mm reusable sterile pessary was placed inside of the bag, between the myoma and pelvic wall, to create a barrier between the morcellated portion of the myoma and the bag. In this way, the pessary protected the bag from the coring rotational movements of either the knife or the scissors and allowed a more manageable coring. After exteriorisation of the fibroid's surface with the aid of Alexis retractors, it was grasped with Schroeder tenaculum, double tooth, or Backhaus towel forceps and subjected to gradual manual morcellation with scalpel or scissors by cautious C-coring. The surgeons achieved adequate traction on the fibroid by using different instruments, depending on the myoma consistency.

In the control group of [Venturella 2016](#), intracorporeal uncontained morcellation using a power morcellator (Rotocut G1, Storz) was performed.

In the intervention group of [Frasca 2018](#), each enucleated myoma was placed into a specimen retrieval bag (Endo Catch II Auto Suture 10 mm or 15 mm, Covidien). The edges around the bag's opening were then pulled out through the lower central 10 mm trocar incision, previously enlarged to 20 mm, along with the abdominal fascia. The fibroid was tightly grasped with Schroeder tenaculum and extracorporeal manual morcellation was performed with scalpel or scissors, while the first assistant carefully pulled on the edges of the bag to move it away from the blade, avoiding bag damage. At the end of morcellation, the endoscopic bag was retrieved through the port incision and filled with water to identify bag disruptions.

In the control group of [Frasca 2018](#), intra-abdominal uncontained power morcellation was performed with the reusable power morcellator Rotocut G1, Storz.

Outcomes

Primary outcome

Both included trials reported on the primary outcome of composite intraoperative complications.

Secondary outcomes

Both included trials reported on total operative time, morcellation operative time, ease of morcellation, postoperative length of stay, postoperative pain, conversion to laparotomy, postoperative diagnosis of leiomyosarcoma, and postoperative complications.

Funding

Neither trial disclosed their funding sources.

Declarations of interest

Both trials declared that none of the authors had any conflicts of interest.

Excluded studies

We did not exclude any studies after full-text review.

Ongoing studies

[NCT02777203](#) and [NCT03281460](#) were reported as completed on clinicaltrials.gov, but we were unable to find any published data. It was unclear if the intervention group was manual in-bag morcellation, or in-bag morcellation with device. We were unable to contact the principal investigator in order to obtain more information on this trial.

Risk of bias in included studies

See: [Figure 2](#) and [Figure 3](#)

Figure 2. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies

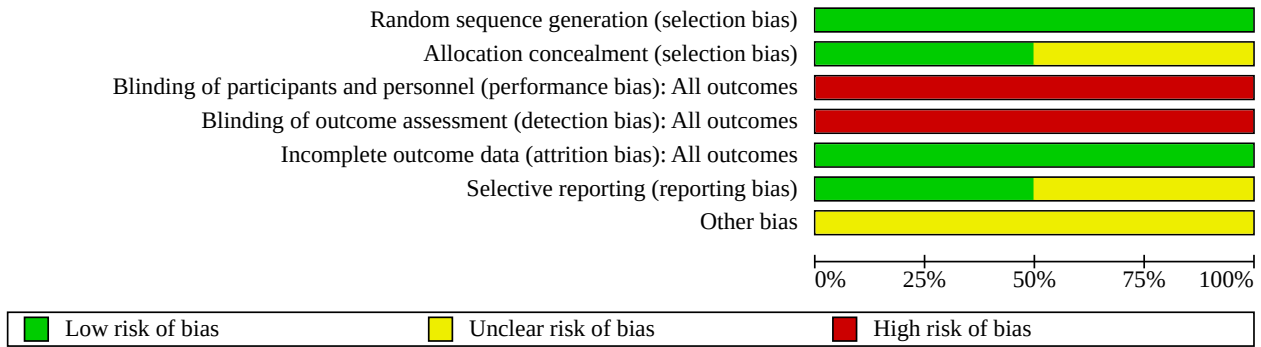


Figure 3. 'Risk of bias' summary: review authors' judgements about each 'Risk of bias' item for each included study

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias): All outcomes	Blinding of outcome assessment (detection bias): All outcomes	Incomplete outcome data (attrition bias): All outcomes	Selective reporting (reporting bias)	Other bias
Frasca 2018	+	?	-	-	+	?	?
Venturella 2016	+	+	-	-	+	+	?

Overall, the trials were at low risk of bias, with low risk of bias in random sequence generation, incomplete outcome data, and selective reporting. However, blinding was not feasible in either trial given the intervention, resulting in our assessment of a high risk of bias in performance bias and detection bias.

Allocation

Random sequence generation

We considered risk of selection bias to be low for random sequence generation, because both included trials used computer-generated sequences.

Allocation concealment

Venturella 2016 used sealed opaque envelopes for allocation concealment; Frascà 2018 did not report any information regarding allocation concealment, therefore, we assessed unclear risk of bias for this domain.

Blinding

Both trials were unblinded. Women and staff were aware of the intervention to which they were allocated due to its nature. Therefore, we assessed this domain at high risk

Incomplete outcome data

We assessed both trials at low risk of attrition bias because they reported no losses to follow-up.

Selective reporting

We considered the risk of reporting bias as low in Venturella 2016. We did not note any deviations from the original protocol.

Frascà 2018 was not registered in a trial register, or was the original protocol available; therefore, we considered it as unclear risk of bias for reporting bias.

Other potential sources of bias

Venturella 2016 and Frascà 2018 did not provide enough information to enable us to adequately assess the presence of other forms of bias; as such, we deemed them as unclear risks of bias.

Effects of interventions

See: **Summary of findings 1** Any type of in-bag morcellation versus uncontained power morcellation during laparoscopic myomectomy

See **Summary of findings 1** for the main comparison "any type of in-bag morcellation versus uncontained power morcellation".

Comparison 1. Any type of in-bag morcellation versus uncontained power morcellation

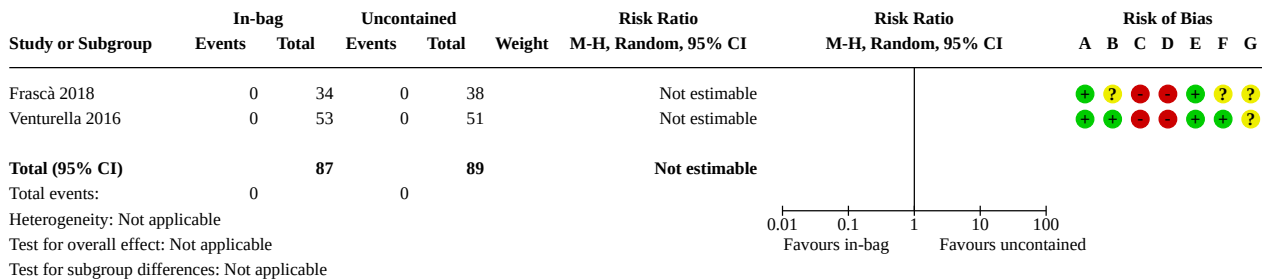
Both trials compared extracorporeal in-bag manual morcellation versus intracorporeal uncontained power morcellation (Frascà 2018; Venturella 2016).

Primary Outcome

1.1. Composite intraoperative complications

No intraoperative complications, including accidental morcellation of the liver, conversion to laparotomy, endoscopic bag disruption, bowel injury, bleeding, or accidental injury to any viscus or vessel, occurred in either group in either trial (Analysis 1.1; Figure 4). Therefore meta-analysis was not possible.

Figure 4. Forest plot of comparison: 1 Any type of in-bag morcellation versus uncontained power morcellation, outcome: 1.1 Composite intraoperative complications



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

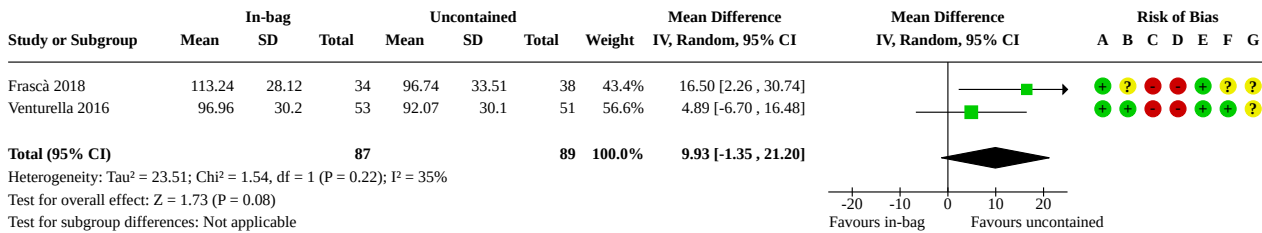
Secondary Outcomes

1.2. Total operative time

The results for total operative time were inconclusive between the in-bag and uncontained morcellation groups (mean difference (MD) 9.93 minutes, 95% confidence interval (CI) -1.35 to 21.20;

2 studies, 176 participants; I² = 35%; very low-quality evidence; Analysis 1.2; Figure 5). The evidence suggests that if mean total operative time with uncontained morcellation is 94 minutes, the mean total operative time with in-bag morcellation is 9.93 minutes longer (1.35 minutes shorter to 21.20 minutes longer).

Figure 5. Forest plot of comparison: 1 Any type of in-bag morcellation versus uncontained power morcellation, outcome: 1.2 Total operative time



Risk of bias legend

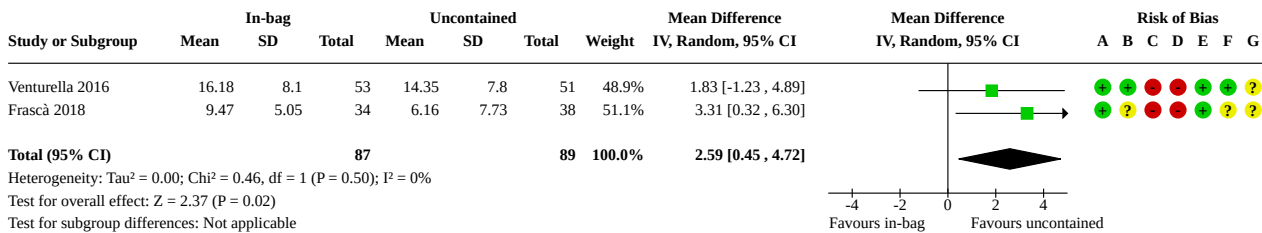
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

1.3. Morcellation operative time

The morcellation operative time was longer in the in-bag manual morcellation group than in the uncontained power morcellation group, however the quality of the evidence was very low and we cannot be certain of the effect. (MD 2.59 minutes, 95% CI

0.45 to 4.72; 2 studies, 176 participants; I² = 0%; very low-quality evidence; Analysis 1.3; Figure 6). The evidence suggests that if mean morcellation operative time with uncontained morcellation is 10 minutes, the mean morcellation operative time with in-bag morcellation is 2.59 minutes longer (between 0.45 minutes and 4.72 minutes longer)

Figure 6. Forest plot of comparison: 1 Any type of in-bag morcellation versus uncontained power morcellation, outcome: 1.3 Morcellation operative time



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

1.4. Ease of morcellation

The results for ease of morcellation were inconclusive between the in-bag and uncontained morcellation groups (MD -0.73 points, 95% CI -1.64 to 0.18; 1 study, 104 participants; very low-quality evidence; Analysis 1.4). The evidence suggests that if the mean score for the ease of uncontained morcellation group is 7.5 points, then the mean score for ease of in-bag morcellation is -0.73 points lower (1.64 points lower to 0.18 points higher).

that if the mean postoperative length of stay with uncontained morcellation is 3 days, then the mean postoperative length of stay with in-bag morcellation is 0.03 days longer (0.42 days shorter to 0.49 days longer).

1.5. Postoperative length of stay in days

The results for length of postoperative length of stay were inconclusive between the in-bag morcellation and uncontained morcellation groups (MD 0.03 days, 95% CI -0.42 to 0.49; 2 studies, 176 participants; I² = 75%; Analysis 1.5). The evidence suggests

1.6. Postoperative pain

The results for postoperative pain were inconclusive between the in-bag morcellation and uncontained morcellation groups (MD 0.22 points, 95% CI -0.50 to 0.94; 2 studies, 176 participants; I² = 63%; Analysis 1.6). The evidence suggests that if the mean postoperative pain score for the uncontained morcellation group is 2 points, the mean postoperative pain for the in-bag morcellation group is 0.22 points higher (0.50 points lower to 0.94 points higher).

1.7. Conversion to laparotomy

There were no laparotomy conversions reported for either group in either trial. Therefore meta-analysis was not possible

1.8. Postoperative diagnosis of leiomyosarcoma

There were no postoperative diagnoses of leiomyosarcoma reported for either group in either trial. Therefore meta-analysis was not possible

1.9. Postoperative complications

The results for postoperative complications were inconclusive between the in-bag morcellation and uncontained morcellation groups (risk ratio (RR) 0.80, 95% CI 0.16 to 4.12; 2 studies, 176 participants; $I^2 = 0\%$; [Analysis 1.9](#)). If the chance of postoperative complications in the uncontained morcellation group is assumed to be 3%, the chance of postoperative complications in the in-bag morcellation group would be between 1% and 14%.

Subgroup analyses

1. Participants with myoma(s) of less than 5 cm versus those with myoma(s) of 5 cm or greater

Neither of the included trials reported stratified data on myoma(s) of less than 5 cm versus those with myoma(s) of 5 cm or greater.

2. Participants with single myoma versus those with multiple myomas

Neither of the included trials reported stratified data on participants with single myoma versus those with multiple myomas.

3. Participants younger than 45 years versus those aged 45 years and older

Neither of the included trials reported stratified data on participants younger than 45 years versus those aged 45 years and older.

Sensitivity analyses

1. Excluding trials published only as an abstract

Neither of the included trials were published only as an abstract.

2. Restricting the analyses to trials with low risk of bias in the first two domains only

We only assessed one trial at low risk of selection bias ([Venturella 2016](#)). For morcellation operative time, the results were inconclusive between the in-bag morcellation and uncontained morcellation groups (MD 1.83, 95% CI -1.23 to 4.89; 1 study, 104 participants; low-quality evidence).

The analysis did not lead to a change in conclusions for the other outcomes for which there were data.

3. Using fixed-effect instead of random-effects model

Using a fixed-effect model, uncontained morcellation showed a shorter total operative time than in-bag morcellation (MD 9.52, 95% CI 0.53 to 18.51; 2 studies, 176 participants; $I^2 = 35\%$; very low-quality evidence; [Analysis 2.1](#)).

Using a fixed-effect model did not lead to different results in the other outcomes for which there were data.

Comparison 2. In-bag manual morcellation using a 10-mm bag versus uncontained power morcellation

Both of the included trials used both 10-mm and 15-mm bags.

Neither of them reported stratified data on in-bag manual morcellation using a 10-mm bag versus uncontained power morcellation. We found no trials evaluating in-bag manual morcellation using only a 10-mm bag.

Comparison 3. In-bag manual morcellation using a 15-mm bag versus uncontained power morcellation

Both of the included trials used both 10-mm and 15-mm bags.

Neither of them reported stratified data on in-bag manual morcellation using a 15-mm bag versus uncontained power morcellation. We found no trials evaluating in-bag manual morcellation using only a 15-mm bag.

DISCUSSION

Summary of main results

This Cochrane Review aimed to evaluate the effectiveness and safety of protected in-bag extracorporeal manual morcellation compared to intracorporeal uncontained power morcellation during laparoscopic myomectomy in premenopausal women with uterine fibroids.

We only found two trials that met our inclusion criteria. Both trials measured morcellation operative time as a primary outcome and were not powered for uncommon outcomes, such as intraoperative complications, or postoperative diagnosis of leiomyosarcoma.

Our review showed there are limited data on the effectiveness and safety of protected in-bag morcellation at the time of laparoscopic myomectomy compared to uncontained power morcellation.

We were unable to determine the effects of in-bag morcellation on intraoperative complications.

Morcellation operative time was longer in the in-bag group, but only by about 2.5 minutes. However, the quality of the evidence was very low and we cannot be certain of the effect ([Analysis 1.3](#)).

The results were inconclusive for ease of morcellation, postoperative length of stay, postoperative pain, and postoperative complications. There were no reports of intraoperative complications, conversions to laparotomy, or postoperative diagnosis of leiomyosarcoma.

Given the very low-quality evidence in the review it is difficult to draw any conclusion on effectiveness and safety of in-bag compared to uncontained power morcellation during laparoscopic myomectomy.

Our findings are summarised in [Summary of findings 1](#) for the main comparison (i.e. any type of in-bag morcellation versus uncontained power morcellation).

We found no trials that looked at in-bag morcellation using a 10-mm bag or a 15-mm bag versus uncontained power morcellation.

Overall completeness and applicability of evidence

Based on our findings, it is evident that there is a paucity of data for effectiveness and safety of protected in-bag compared to uncontained power morcellation during laparoscopic myomectomy.

Both included trials used in-bag extracorporeal manual morcellation; neither used in-bag power morcellation. There were no trials comparing intracorporeal in-bag morcellation with intracorporeal uncontained morcellation.

All of the included trials took place in high-income settings and countries, therefore, our findings are limited to this type of setting.

Overall, even though the findings of the review draw into question the use of in-bag morcellation at the time of laparoscopic myomectomy, we feel that the overall quality of the evidence is too low to support one method over another.

Further high-quality research is required to draw definitive conclusions.

Quality of the evidence

In this Cochrane Review, we identified and included data originating from two randomised controlled trials, involving a total of 176 participants (premenopausal women undergoing laparoscopic myomectomy).

The two included randomised studies were both relatively small, and blinding was not possible. [Frasca 2018](#) was not registered in a trial register; see [Figure 2](#) and [Figure 3](#) for a summary of the risks of bias.

For the comparison 'any type of in-bag morcellation versus uncontained power morcellation', we assessed the evidence to be very low quality. We assessed indirectness as serious, and imprecision as very serious. We downgraded the evidence for indirectness because all the included trials took place in high-income settings and countries, therefore, our findings are limited to this type of setting; and for imprecision because both trials had small sample size and wide confidence intervals, with no events in the primary outcome ([Summary of findings 1](#)).

Quality of the evidence was also limited by the substantial statistical heterogeneity for two outcomes, postoperative length of stay ($I^2 = 75\%$), and postoperative pain ($I^2 = 63\%$).

Potential biases in the review process

We aimed to reduce the risk of publication bias by conducting systematic searches of multiple databases as well as trials registries to identify unpublished and ongoing studies. We contacted trial authors for (more) information when necessary. However, it is

possible that our searches did not identify all unpublished studies. We were unable to develop a funnel plot due to the small number of included studies.

FZ and RV are co-authors of one of the included trials ([Venturella 2016](#)). They were not involved in the assessment of eligibility or risk of bias for this trial. It was assessed by GS and AR.

Agreements and disagreements with other studies or reviews

The evidence presented in this review may be the first in the literature comparing in-bag and intracorporeal uncontained power morcellation during laparoscopic myomectomy. To the best of our knowledge there are no other reviews evaluating this topic.

AUTHORS' CONCLUSIONS

Implications for practice

This review raises important questions regarding the use of in-bag morcellation at the time of laparoscopic myomectomy. There are limited data on the effectiveness and safety of in-bag morcellation compared to uncontained power morcellation.

We were unable to determine the effects of in-bag morcellation on intraoperative complications as no events were reported in either group. We are uncertain if in-bag morcellation increases total operative time or ease of morcellation. Morcellation operative time was slightly longer in the in-bag morcellation group, but the quality of the evidence was very low and we cannot be certain of the results. No cases of postoperative diagnosis of leiomyosarcoma were reported in either group.

Implications for research

This review found limited evidence on the effectiveness and safety of protected in-bag morcellation compared to intracorporeal uncontained power morcellation during laparoscopic myomectomy, and encourages further research. Future trials should look at core clinical outcomes, including intraoperative and postoperative complications, postoperative pain, and postoperative diagnosis of leiomyosarcoma. Future studies should include a clear protocol for in-bag morcellation so that it can be easily evaluated and replicated. They should be larger, multicentred, and high-quality.

ACKNOWLEDGEMENTS

As part of the pre-publication editorial process, this review was commented on by five peers. The authors are grateful to the following peer reviewers: Rik van Eekelen, Anne Lethaby, Mbaka Fon Nji (consumer), Sarah Armstrong, Elena Kostova (Managing editor).

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Frasca 2018

Study characteristics

Methods	Unblinded single-centre randomised controlled trial, conducted at the Gynecology and Human Reproduction Physiopathology of Sant'Orsola-Malpighi University Hospital of Bologna, Bologna, Italy
Participants	Premenopausal women aged between 18 and 50 years, with an ultrasonographic diagnosis of at least one myoma measuring between 4 cm and 10 cm in mean diameter, and presenting a heavy menstrual flow or infertility as indications to laparoscopic myomectomy.
Interventions	Sample size: 72 women (34 in the intervention group and 38 in the control group) In the control group, intra-abdominal uncontained power morcellation was performed with the reusable power morcellator Rotocut G1, Storz. In the intervention group (extracorporeal in-bag manual morcellation), each enucleated myoma was placed within a specimen retrieval bag (Endo Catch II Auto Suture 10-mm or 15-mm, Covidien). The edges around the bag's opening were then pulled out through the lower central 10-mm trocar incision, previously enlarged to 20 mm, along with the abdominal fascia. The fibroid was tightly grasped with Schroeder tenaculum and manual morcellation was performed with scalpel or scissors, while the first assistant carefully pulled on the edges of the bag to move it away from the blade, avoiding bag dam-

Frasca 2018 (Continued)

age. At the end of morcellation, the endoscopic bag was retrieved on the edges of the bag to move it away from the blade, avoiding bag damage, retrieved through the port incision, and filled with water to identify eventual bag disruptions.

Outcomes	The primary outcome was the comparison of morcellation operative times.
Notes	Dates: November 2015 to October 2016 Conflict of interest: none Funding source: not reported Clinical Trial Registration: not registered.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unblinded intervention
Blinding of outcome assessment (detection bias) All outcomes	High risk	Unblinded intervention
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Unclear risk	The study was not registered on ClinicalTrials.gov or on any other trial registry, and original protocol was not available
Other bias	Unclear risk	Insufficient reporting to determine presence of other forms of bias

Venturella 2016
Study characteristics

Methods	Unblinded single-centre randomised controlled trial, conducted at the Department of Obstetrics and Gynecology, University "Magna Graecia" of Catanzaro, Catanzaro, Italy
Participants	Sample size: 104 women (53 in the intervention group and 51 in the control group) Premenopausal women with heavy menstrual bleeding or women already diagnosed with fibroids from referral sources and undergoing a laparoscopic myomectomy. Inclusion criteria were the following: age between 18 and 40 years, body mass index (BMI) 18 kg/m ² to 40 kg/m ² , heavy menstrual bleeding, and the presence of at least one myoma measuring 4 cm or more in diameter (but no myoma measuring >10 cm, according to local practice on eligibility for laparoscopy).

Venturella 2016 (Continued)

Interventions	<p>In the intervention group (extracorporeal in-bag manual morcellation), each enucleated myoma was placed within a rip-stop nylon specimen bag (Endo Catch Gold Auto Suture 10-mm or 15-mm, Covidien), which could hold 220 mL or 1000 mL according to the size chosen. The central lower 10-mm trocar incision was increased to 30 mm, and a 65-mm reusable sterile pessary was placed inside the bag, between the myoma and pelvic wall, to create a barrier between the morcellated portion of the myoma and the bag. In this way, the pessary protected the bag from the coring rotational movements of either the knife or the scissors and allowed a more manageable coring. After exteriorisation of the fibroid's surface with the aid of Alexis retractors, it was grasped with Schroeder tenaculum, double tooth, or Backhaus towel forceps and subjected to gradual morcellation with scalpel or scissors by cautious C-coring. Fibroid adequate traction was allowed by using different instruments, depending on the myoma consistency.</p> <p>In the control group, intracorporeal un-contained morcellation using a power morcellator (Rotocut G1, Storz) was performed.</p>
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Outcomes	The primary outcome was the comparison of morcellation operative times.
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Notes	<p>Dates: March 2014 to January 2015</p> <p>Conflict of interest: none</p> <p>Funding source: Department of Obstetrics and Gynecology, University "Magna Graecia" of Catanzaro</p> <p>Clinical Trial Registration: NCT02086435</p>
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Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated
Allocation concealment (selection bias)	Low risk	sealed, opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	Unblinded intervention
Blinding of outcome assessment (detection bias) All outcomes	High risk	Unblinded intervention
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Low risk	No deviation from the original protocol
Other bias	Unclear risk	Insufficient reporting to determine presence of other forms of bias

Characteristics of ongoing studies [ordered by study ID]

NCT02777203

Study name	Power morcellation systems for laparoscopic hysterectomy and myomectomy
Methods	Open-label, single centre randomised trial conducted in Illinois, USA
Participants	Premenopausal women undergoing robotic or laparoscopic total or supracervical hysterectomies or myomectomies for the indication of symptomatic uterine fibroids
Interventions	In-bag morcellation with specimen morcellated in the EcoSac400 ECO-T bag
Outcomes	Primary outcome: egg albumin leakage
Starting date	May 2016 to July 2019
Contact information	Charles Miller, Advocate Health Care
Notes	On ClinicalTrials.gov, the trial is reported as completed. It is not clear if the intervention group was manual in-bag morcellation, or in-bag morcellation with device. We could not contact the principal investigator in order to obtain more information on this trial.

NCT03281460

Study name	Efficacy of in-bag morcellation (FIBROSAC)
Methods	Open-label, single centre randomised trial conducted in Bron, France
Participants	Women aged 18 years or more undergoing laparoscopic myomectomy or laparoscopic subtotal hysterectomy
Interventions	In-bag morcellation with More-cell-Safe (AMI bag morcellation)
Outcomes	Primary outcome: smooth muscular cells in the peritoneal fluid after morcellation (after morcellation, there will be cytology and immunohistochemistry of peritoneal washing with 500 cc of saline serum)
Starting date	September 2017 to February 2019
Contact information	Gautier Chene, MD. Gynaecology Department, Hôpital Femme Mère Enfant, HCL
Notes	On ClinicalTrials.gov, the trial is reported as completed. It is not clear if the intervention group was manual in-bag morcellation, or in-bag morcellation with device. We could not contact the principal investigator in order to obtain more information on this trial.

DATA AND ANALYSES

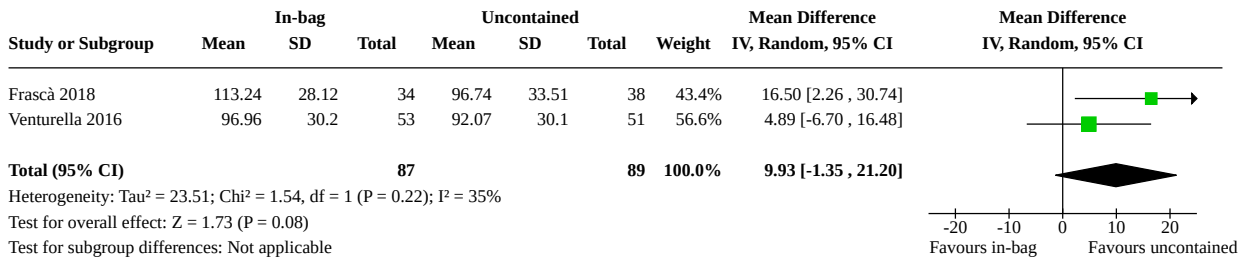
Comparison 1. Any type of in-bag morcellation versus uncontained power morcellation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Composite intraoperative complications	2	176	Risk Ratio (M-H, Random, 95% CI)	Not estimable
1.2 Total operative time	2	176	Mean Difference (IV, Random, 95% CI)	9.93 [-1.35, 21.20]
1.3 Morcellation operative time	2	176	Mean Difference (IV, Random, 95% CI)	2.59 [0.45, 4.72]
1.4 Ease of morcellation	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.5 Postoperative length of stay	2	176	Mean Difference (IV, Random, 95% CI)	0.03 [-0.42, 0.49]
1.6 Postoperative pain	2	176	Mean Difference (IV, Random, 95% CI)	0.22 [-0.50, 0.94]
1.7 Conversion to laparotomy	2	176	Risk Ratio (M-H, Random, 95% CI)	Not estimable
1.8 Postoperative diagnosis of leiomyosarcoma	2	176	Risk Ratio (M-H, Random, 95% CI)	Not estimable
1.9 Postoperative complications	2	176	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.16, 4.12]

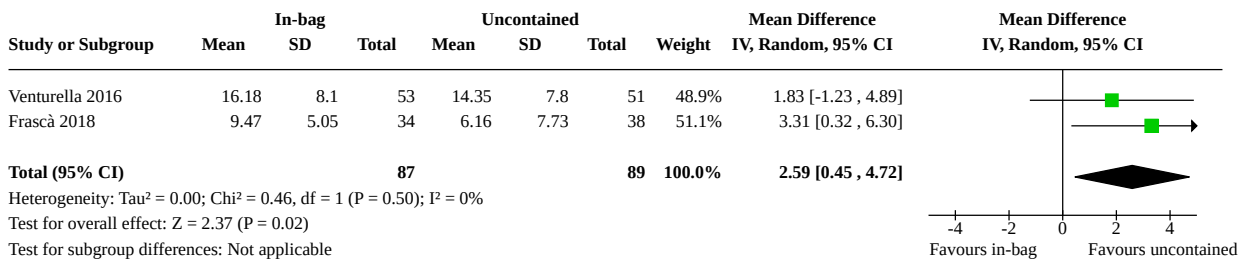
Analysis 1.1. Comparison 1: Any type of in-bag morcellation versus uncontained power morcellation, Outcome 1: Composite intraoperative complications

Study or Subgroup	In-bag		Uncontained		Weight	Risk Ratio	Risk Ratio
	Events	Total	Events	Total		M-H, Random, 95% CI	M-H, Random, 95% CI
Frasca 2018	0	34	0	38		Not estimable	
Venturella 2016	0	53	0	51		Not estimable	
Total (95% CI)		87		89		Not estimable	
Total events:	0		0				
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
Test for subgroup differences: Not applicable							

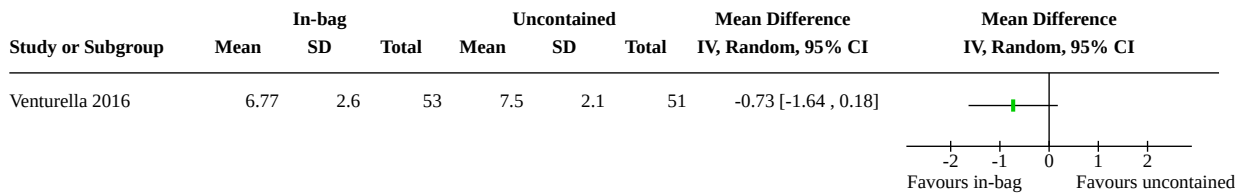
Analysis 1.2. Comparison 1: Any type of in-bag morcellation versus uncontained power morcellation, Outcome 2: Total operative time



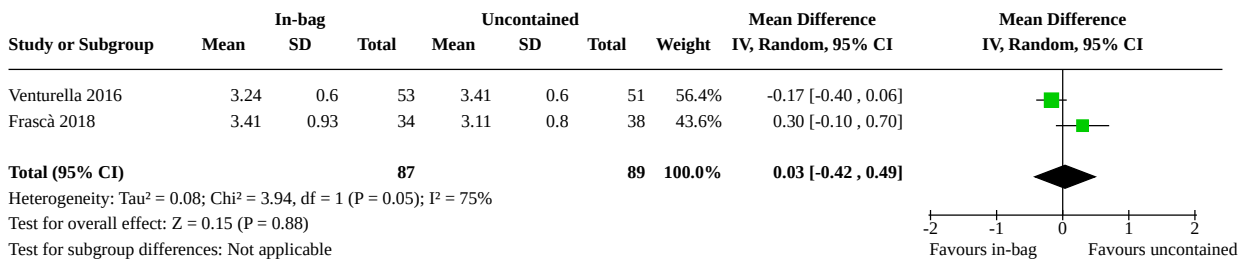
Analysis 1.3. Comparison 1: Any type of in-bag morcellation versus uncontained power morcellation, Outcome 3: Morcellation operative time



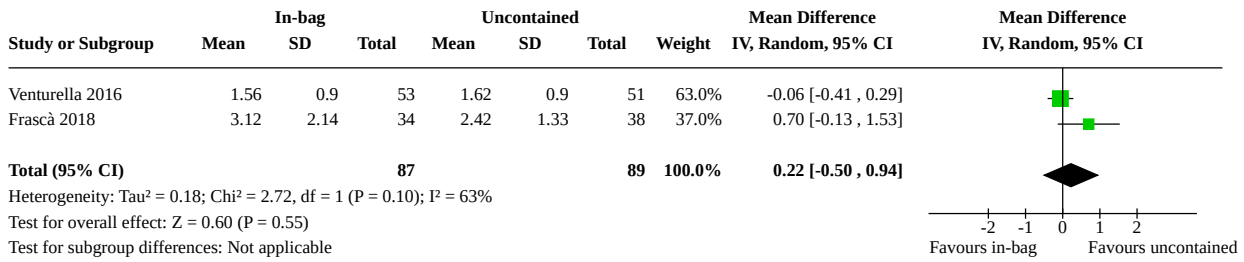
Analysis 1.4. Comparison 1: Any type of in-bag morcellation versus uncontained power morcellation, Outcome 4: Ease of morcellation



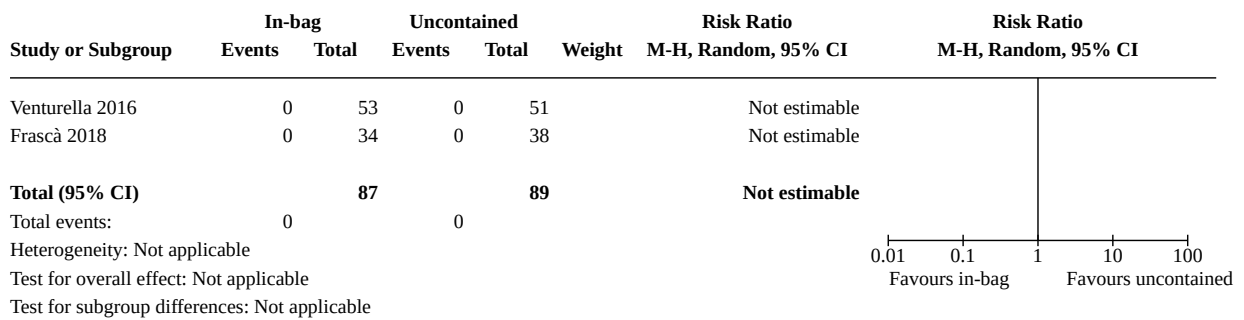
Analysis 1.5. Comparison 1: Any type of in-bag morcellation versus uncontained power morcellation, Outcome 5: Postoperative length of stay



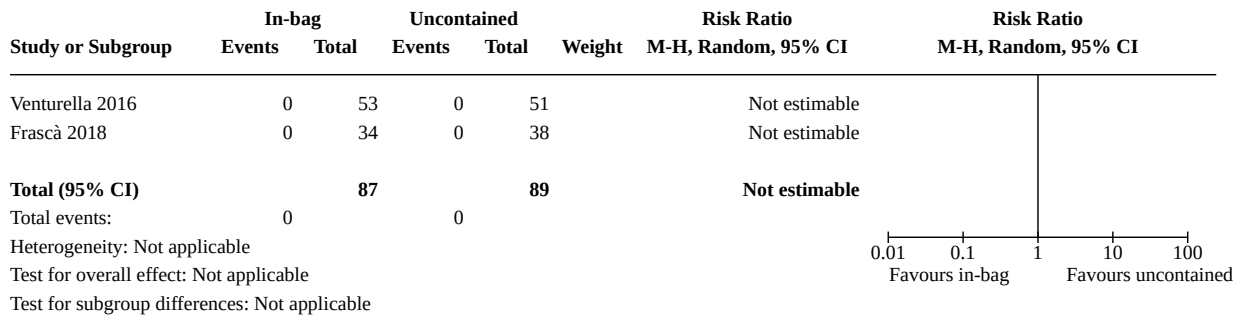
Analysis 1.6. Comparison 1: Any type of in-bag morcellation versus uncontained power morcellation, Outcome 6: Postoperative pain



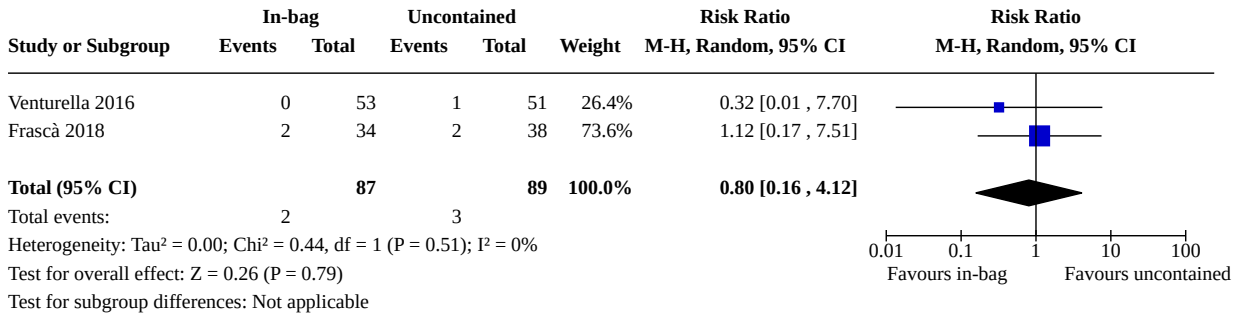
Analysis 1.7. Comparison 1: Any type of in-bag morcellation versus uncontained power morcellation, Outcome 7: Conversion to laparotomy



Analysis 1.8. Comparison 1: Any type of in-bag morcellation versus uncontained power morcellation, Outcome 8: Postoperative diagnosis of leiomyosarcoma



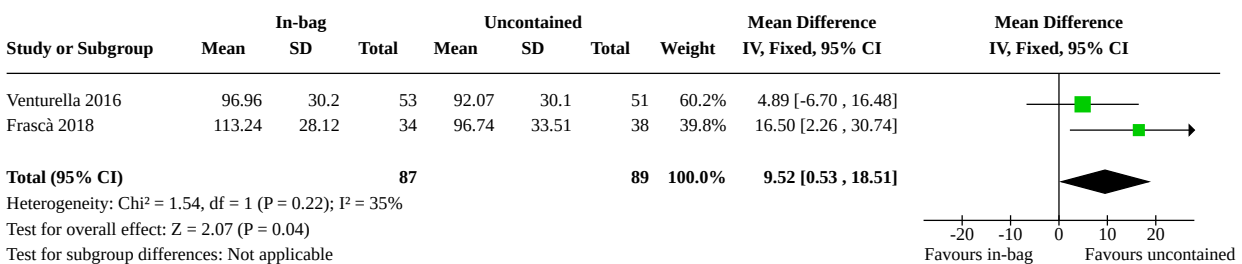
Analysis 1.9. Comparison 1: Any type of in-bag morcellation versus uncontained power morcellation, Outcome 9: Postoperative complications



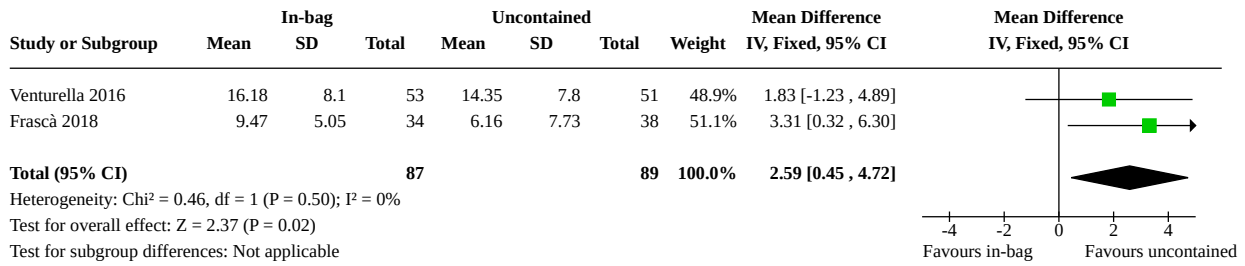
Comparison 2. Sensitivity analysis: fixed-effect model

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Total operative time	2	176	Mean Difference (IV, Fixed, 95% CI)	9.52 [0.53, 18.51]
2.2 Morcellation operative time	2	176	Mean Difference (IV, Fixed, 95% CI)	2.59 [0.45, 4.72]
2.3 Postoperative length of stay	2	176	Mean Difference (IV, Fixed, 95% CI)	-0.05 [-0.25, 0.15]
2.4 Postoperative pain	2	176	Mean Difference (IV, Fixed, 95% CI)	0.05 [-0.27, 0.37]
2.5 Postoperative complications	2	176	Risk Ratio (M-H, Fixed, 95% CI)	0.76 [0.16, 3.68]

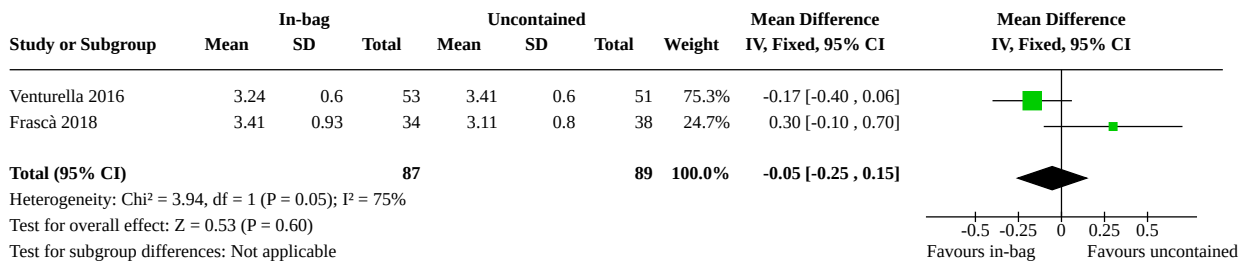
Analysis 2.1. Comparison 2: Sensitivity analysis: fixed-effect model, Outcome 1: Total operative time



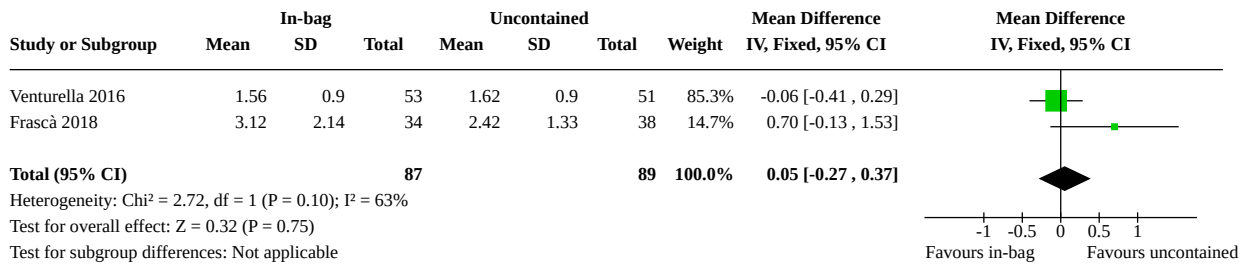
Analysis 2.2. Comparison 2: Sensitivity analysis: fixed-effect model, Outcome 2: Morcellation operative time



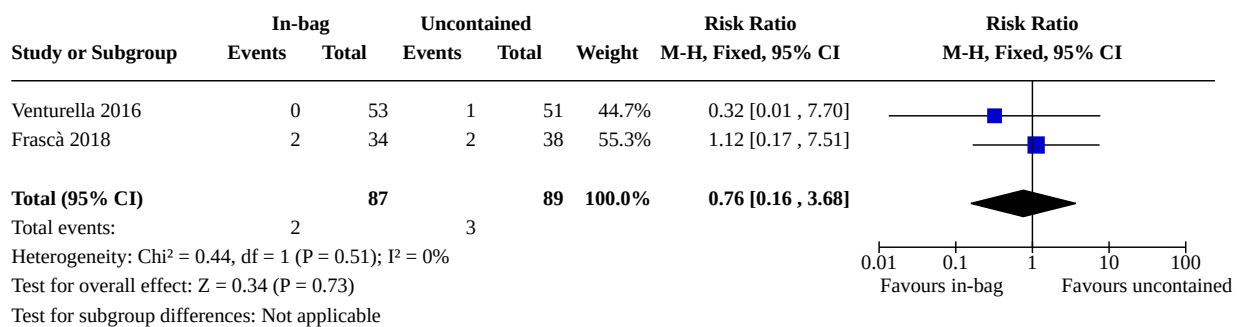
Analysis 2.3. Comparison 2: Sensitivity analysis: fixed-effect model, Outcome 3: Postoperative length of stay



Analysis 2.4. Comparison 2: Sensitivity analysis: fixed-effect model, Outcome 4: Postoperative pain



Analysis 2.5. Comparison 2: Sensitivity analysis: fixed-effect model, Outcome 5: Postoperative complications



APPENDICES

Appendix 1. Cochrane Gynaecology and Fertility specialised register search strategy

Searched 1 July 2019

PROCITE platform

Keywords CONTAINS "uterine fibroids" or "uterine leiomyomas" or "uterine myoma" or "uterine myomas" or "myoma" or "myomas" or "myomata" or "Leiomyoma" or "leiomyomata" or "fibroids" or "myomatous uterus" or "fibroid size" or "fibroid volume" or "fibroids Symptoms" or "fibroids symptoms-scores" or "Leiomyoma-size" or "fibroid" or Title CONTAINS "uterine fibroids" or "uterine leiomyomas" or "uterine myoma" or "uterine myomas" or "myoma" or "myomas" or "myomata" or "Leiomyoma" or "leiomyomata" or "fibroids" or "myomatous uterus" or "fibroid size" or "fibroid volume" or "fibroids Symptoms" or "fibroids symptoms-scores" or "Leiomyoma-size" or "fibroid"

AND

Keywords CONTAINS "morcellation" or "morcellator" or "myomectomy" or "Laparoscopic single-site myomectomy" or "laparoscopic" or "laparoscopic myomectomy" or "laparoscopic procedure" or "laparoscopic surgical treatment" or "laparoscopic surgery" or "laparoscopy" or Title CONTAINS "morcellation" or "morcellator" or "myomectomy" or "Laparoscopic single-site myomectomy" or "laparoscopic" or "laparoscopic myomectomy" or "laparoscopic procedure" or "laparoscopic surgical treatment" or "laparoscopic surgery" or "laparoscopy"

(252 records)

Appendix 2. CENTRAL search strategy

Searched Issue 5 'May 2019' on 1 July 2019

Ovid platform

1 exp leiomyoma/ or exp myoma/ (611)
2 leiomyoma*.tw. (457)
3 myoma*.tw. (654)
4 fibroid*.tw. (958)
5 fibroma*.tw. (122)
6 fibromyoma*.tw. (21)
7 hysteromyoma*.tw. (144)
8 myomectom*.tw. (666)
9 Uterine Myomectomy/ (47)
10 (minimally invasive adj2 procedure*).tw. (514)
11 or/1-10 (2851)
12 Morcellation/ (5)
13 (Morcellat* or Morcelat*).tw. (124)
14 morcellement.tw. (1)
15 morselli?*.tw. (7)
16 morseli?*.tw. (14)
17 morcelli?*.tw. (6)
18 morceli?*.tw. (0)
19 in bag.tw. (2117)
20 spill free.tw. (0)
21 uncontained power.tw. (3)
22 manual.tw. (13656)
23 endobag*.tw. (11)
24 containment bag*.tw. (1)
25 containment system*.tw. (4)
26 bowel bag*.tw. (3)
27 or/12-26 (15831)
28 11 and 27 (68)

Appendix 3. MEDLINE search strategy

Searched from 1946 to 1 July 2019

Ovid platform

In-bag manual versus uncontained power morcellation for laparoscopic myomectomy (Review)

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- 1 exp leiomyoma/ or exp myoma/ (22530)
- 2 leiomyoma*.tw. (13292)
- 3 myoma*.tw. (5704)
- 4 fibroid*.tw. (6159)
- 5 fibroma*.tw. (11713)
- 6 fibromyoma*.tw. (717)
- 7 hysteromyoma*.tw. (75)
- 8 myomectomy*.tw. (3383)
- 9 Uterine Myomectomy/ (797)
- 10 (minimally invasive adj2 procedure*).tw. (6286)
- 11 or/1-10 (48521)
- 12 Morcellation/ (223)
- 13 (Morcellat* or Morcelat*).tw. (1075)
- 14 morcellement.tw. (18)
- 15 morselli?*.tw. (169)
- 16 morseli?*.tw. (404)
- 17 morcelli?*.tw. (104)
- 18 morceli?*.tw. (20)
- 19 in bag.tw. (304)
- 20 spill free.tw. (1)
- 21 uncontained power.tw. (8)
- 22 manual.tw. (88018)
- 23 endobag*.tw. (160)
- 24 containment bag*.tw. (18)
- 25 containment system*.tw. (194)
- 26 bowel bag*.tw. (28)
- 27 or/12-26 (90354)
- 28 11 and 27 (670)
- 29 randomized controlled trial.pt. (484622)
- 30 controlled clinical trial.pt. (93136)
- 31 randomized.ab. (447277)
- 32 randomised.ab. (89197)
- 33 placebo.tw. (204219)
- 34 clinical trials as topic.sh. (187463)
- 35 randomly.ab. (313513)
- 36 trial.ti. (200806)
- 37 (crossover or cross-over or cross over).tw. (80777)
- 38 or/29-37 (1285063)
- 39 exp animals/ not humans.sh. (4593621)
- 40 38 not 39 (1182132)
- 41 28 and 40 (32)

Appendix 4. Embase search strategy

Searched from 1980 to 1 July 2019

Ovid platform

- 1 exp leiomyoma/ or exp myoma/ (34112)
- 2 leiomyoma*.tw. (16126)
- 3 myoma*.tw. (7327)
- 4 fibroid*.tw. (10415)
- 5 fibroma*.tw. (11013)
- 6 fibromyoma*.tw. (283)
- 7 hysteromyoma*.tw. (156)
- 8 myomectomy*.tw. (5982)
- 9 exp myomectomy/ (6601)
- 10 or/1-9 (52909)
- 11 exp morcellation/ (878)
- 12 (Morcellat* or Morcelat*).tw. (2428)
- 13 morcellement.tw. (15)
- 14 (morselli?* or morseli?*)*.tw. (725)
- 15 (morcelli?* or morceli?*)*.tw. (162)

16 in bag.tw. (421)
 17 spill free.tw. (2)
 18 uncontained power.tw. (15)
 19 containment system*.tw. (242)
 20 endobag*.tw. (496)
 21 containment bag*.tw. (43)
 22 bowel bag*.tw. (75)
 23 manual.tw. (117201)
 24 or/11-23 (121583)
 25 10 and 24 (1414)
 26 Clinical Trial/ (949870)
 27 Randomized Controlled Trial/ (552149)
 28 exp randomization/ (82999)
 29 Single Blind Procedure/ (35550)
 30 Double Blind Procedure/ (159063)
 31 Crossover Procedure/ (59560)
 32 Placebo/ (322777)
 33 Randomi?ed controlled trial\$.tw. (205207)
 34 Rct.tw. (32809)
 35 random allocation.tw. (1885)
 36 randomly.tw. (409623)
 37 randomly allocated.tw. (32619)
 38 allocated randomly.tw. (2442)
 39 (allocated adj2 random).tw. (804)
 40 Single blind\$.tw. (22835)
 41 Double blind\$.tw. (191972)
 42 ((treble or triple) adj blind\$.tw. (956)
 43 placebo\$.tw. (285428)
 44 prospective study/ (528556)
 45 or/26-44 (2266761)
 46 case study/ (62005)
 47 case report.tw. (374321)
 48 abstract report/ or letter/ (1061265)
 49 or/46-48 (1487891)
 50 45 not 49 (2215343)
 51 (exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans).ti.) (5737606)
 52 50 not 51 (2061191)
 53 25 and 52 (124)

Appendix 5. PsycINFO search strategy

Searched from 1806 to 1 July 2019

Ovid platform

1 gynecological disorders/ (541)
 2 (leiomyoma* or myoma*).tw. (50)
 3 (fibroid* or fibrom*).tw. (3259)
 4 hysteromyoma*.tw. (2)
 5 myomectomy*.tw. (11)
 6 or/1-5 (3828)
 7 (Morcellat* or Morcelat*).tw. (2)
 8 morcellement.tw. (3)
 9 morselli?*.tw. (66)
 10 morseli?*.tw. (1)
 11 in bag.tw. (21)
 12 or/7-11 (93)
 13 6 and 12 (1)

Appendix 6. CINAHL search strategy

Searched from 1961 to 1 July 2019

EBSCO platform

S45 S21 AND S44 37
 S44 S43 NOT S42 572,660
 S43 S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 598,030
 S42 S40 NOT S41 159,074
 S41 MH (human) 1,942,888
 S40 S37 OR S38 OR S39 179,734
 S39 TI (animal model*) 2,762
 S38 MH (animal studies) 103,970
 S37 MH animals+ 83,361
 S36 AB (cluster W3 RCT) 288
 S35 MH (crossover design) OR MH (comparative studies) 216,690
 S34 AB (control W5 group) 91,629
 S33 PT (randomized controlled trial) 86,878
 S32 MH (placebos) 11,346
 S31 MH (sample size) AND AB (assigned OR allocated OR control) 3,668
 S30 TI (trial) 92,572
 S29 AB (random*) 259,181
 S28 TI (randomised OR randomized) 90,464
 S27 MH cluster sample 3,814
 S26 MH pretest-posttest design 38,773
 S25 MH random assignment 55,270
 S24 MH single-blind studies 12,602
 S23 MH double-blind studies 41,522
 S22 MH randomized controlled trials 83,612
 S21 S7 AND S20 302
 S20 S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 53,377
 S19 TX (bowel bag*) 272
 S18 TX (containment system*) 1,287
 S17 TX (containment bag*) 81
 S16 TX endobag* 42
 S15 TX (manual) 38,598
 S14 TX (in bag) 13,113
 S13 TX (spill free) 97
 S12 TX (uncontained power) 15
 S11 TX morcelli?* or TX morceli?* 38
 S10 TX morselli?* or TX morseli?* 178
 S9 TX Morcellat* or TX Morcelat* 481
 S8 TX morcellement 2
 S7 S1 OR S2 OR S3 OR S4 OR S5 OR S6 6,831
 S6 TX Myomectomy* 1,108
 S5 TX hysteromyoma* or TX fibroma* 1,276
 S4 TX fibroid* or TX fibromyoma* 2,007
 S3 TX leiomyoma* or TX myoma* 4,457
 S2 (MM "Myoma+") 223
 S1 (MM "Leiomyoma") 2,806

Appendix 7. 'Risk of bias' domains

(1) Random sequence generation (selection bias)

For each included study, we described the method used to allocate participants to interventions. We assessed the method as:

1. low risk of bias (any truly random process, e.g. random number table; computer random number generator);
2. high risk of bias (any non-random process, e. g. odd or even date of birth; hospital or clinic record number);
3. unclear risk of bias (insufficient information about the process of sequence generation).

(2) Allocation concealment (selection bias)

For each included study, we described the method used to conceal allocation to interventions prior to assignment. We assessed the method as:

1. low risk of bias (telephone or central randomisation; consecutively numbered sealed opaque envelopes);
2. high risk of bias (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth);
3. unclear risk of bias (insufficient information about the process of allocation concealment).

(3.1) Blinding of participants and personnel (performance bias)

For each included study, we described the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We assessed the method as:

1. low risk of bias (blinding of participants, care providers, and researchers);
2. high risk of bias (no blinding of participants, care providers, and researchers);
3. unclear risk of bias (insufficient information about the process of blinding participants, care providers, and researchers).

(3.2) Blinding of outcome assessment (detection bias)

For each included study, we described the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We assessed the method as:

1. low risk of bias (blinding of outcome assessors);
2. high risk of bias (no blinding of outcome assessors);
3. unclear risk of bias (insufficient information about the process of blinding outcome assessors).

(4) Incomplete outcome data (attrition bias)

For each included study, we described the completeness of data, including attrition and exclusions from the analysis. We assessed the method as:

1. low risk of bias (no missing data, or missing data with clear reasons);
2. high risk of bias (missing data or no reasons given for missing data);
3. unclear risk of bias (insufficient information about the completeness of outcome data).

(5) Selective reporting (reporting bias)

For each included study, we described the completeness of outcomes measured. We assessed the method as:

1. low risk of bias (all prespecified outcomes in the protocol reported in the published article);
2. high risk of bias (not all prespecified outcomes in the protocol reported in the published article);
3. unclear risk of bias (insufficient information about the process of outcome reporting).

(6) Other bias (bias not covered by (1) to (5) above).

For each included study, we described any important concerns we had about other possible sources of bias. We assessed these as:

1. low risk of bias (study free of other bias (e.g. baseline imbalance of groups, blocked randomisation in unblinded trials));
2. high risk of bias (other biases present (these were specified));
3. unclear risk of bias (insufficient information about other sources of bias).

HISTORY

Protocol first published: Issue 6, 2019

Review first published: Issue 5, 2020

CONTRIBUTIONS OF AUTHORS

FZ, RV and GS devised the idea, applied for the review.

FZ, RV and GS drafted the protocol.

FZ, RV, AR and GS approved the final edition.

AR and GS performed review and analysis of pertinent and included trials, risk of bias and data extraction.

FZ, RV, AR and GS approved the final version of the review.

DECLARATIONS OF INTEREST

GS reports no conflict of interest.

AR reports no conflict of interest.

FZ and RV are co-authors of one of the trials included in the full review ([Venturella 2016](#)). They were not involved in the assessment of eligibility or risk of bias for this trial. It was assessed by GS and AR.

SOURCES OF SUPPORT

Internal sources

- Cochrane Gynaecology and Fertility Group, Netherlands

Editorial support

External sources

- None, Other

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We clarified the inclusion criteria as follows:

We included all randomised controlled trials comparing in-bag extracorporeal manual morcellation versus intracorporeal uncontained power morcellation at the time of laparoscopic myomectomy.

We also analysed the results by adopting a fixed-effect model.

INDEX TERMS

Medical Subject Headings (MeSH)

Intraoperative Complications [etiology]; Laparoscopy [adverse effects] [*methods]; Leiomyoma [*surgery]; Length of Stay; Morcellation [adverse effects] [instrumentation] [*methods]; Operative Time; Postoperative Complications [etiology]; Randomized Controlled Trials as Topic; Specimen Handling [instrumentation] [methods]; Uterine Myomectomy [adverse effects] [*methods]; Uterine Neoplasms [*surgery]

MeSH check words

Adult; Female; Humans; Middle Aged; Young Adult