NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of hysteroscopic removal of uterine fibroids with power morcellation

Uterine fibroids are non-cancerous growths that develop in or around the womb (uterus). This procedure is done for fibroids inside the womb, using general, local or spinal anaesthesia. A thin tube with a camera on the end (hysteroscope) is inserted through the vagina and cervix and into the womb. Instruments are passed through the hysteroscope to cut the fibroid into small pieces (morcellation). The pieces of fibroid are removed through the hysteroscope. The aim is to reduce symptoms caused by fibroids.

Contents

Abbreviations

Word or phrase	Abbreviation
Confidence interval	CI
Food and Drug Administration	FDA
Health Related Quality of Life	HRQOL
International Federation of Gynecology and Obstetrics	FIGO
Manufacturer and User Facility Device Experience database	MAUDE
Uterine Fibroid Symptom and Quality of Life	UFS-QOL

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and professional opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in November 2020.

Procedure name

- Hysteroscopic removal of uterine fibroids with power morcellation

Professional societies

- Royal College of Obstetricians and Gynaecologists
- British Society for Gynaecological Endoscopy.

Description of the procedure

Indications and current treatment

Uterine fibroids (also known as uterine leiomyomas or myomas) are benign tumours of the uterus. They can be asymptomatic or cause symptoms including heavy periods or bleeding between periods. They can be associated with fertility problems and miscarriage.

Treatment depends on whether the fibroids cause symptoms, and if the person would like to become pregnant in the future. For symptomatic fibroids, treatment options include medication, interventional radiology and surgery. Interventional radiology treatments include uterine artery embolisation and MRI-guided focused ultrasound. Surgery includes hysterectomy, myomectomy, endometrial ablation techniques and myolysis.

What the procedure involves

Hysteroscopic morcellation aims to remove uterine fibroids under visual guidance using a hysteroscope inserted into the uterus. Hysteroscopic morcellation is intended to reduce the risks of traumatic injury to the uterus and the risk of inadvertent fluid overload associated with traditional procedures. An intended advantage of the procedure over thermal ablation techniques is avoiding the risk of thermal injury.

Hysteroscopic removal of uterine fibroids with power morcellation is usually done with the patient under general or spinal anaesthesia, typically as a day-case procedure. A hysteroscope is inserted into the uterus through the cervix and saline is pumped thorough a small channel in the hysteroscope to distend the uterus. A morcellator is passed through the hysteroscope and used to cut and simultaneously aspirate the morcellated fibroid tissue. The aspirated tissue can be collected for histological analysis.

Different devices are available for this procedure.

Efficacy summary

Improvement in symptoms and patient satisfaction

In a non-randomised comparative study of 29 patients with submucosal fibroids, a satisfactory outcome (when the patient subjectively reported reduced menstrual bleeding and considered the operation to have improved menstrual symptoms at 3-month follow up) was reported for 93% of patients who had hysteroscopic morcellation and 85% of those who had loop resection (p=0.841). A satisfactory

outcome was reported for all patients when uterine fibroid protrusion was more than 60% (Lee M, 2016).

In a case series of 73 patients with submucosal fibroids, 84% (54/73) of patients were satisfied with the procedure, 6% (4/73) were neutral and 9% (6/73) were dissatisfied. Failure to control abnormal uterine bleeding was reported in 33% (24/73) of patients, with persistence of at least 1 symptom in 21% (15/73) of patients and recurrence of symptoms in 18% (13/73) of patients (Maheux-Lacroix S, 2017).

In a randomised controlled trial of 74 patients with fibroids or polyps, comparing an office setting with an ambulatory setting, the overall UFS-QOL symptom score improved from 67.5 (±15.4) at baseline to 22.3 (±22.6) at 12-month follow up ($p<0.01$). Overall, 89% of patients were satisfied or very satisfied and 96% of patients would recommend the treatment to other patients with similar symptoms (Rubino R, 2015).

Fibroid volume reduction

In a systematic review of 498 patients with fibroids or polyps, the total removal rate was higher for hysteroscopic morcellation than conventional resectoscopy (96% compared with 86%, OR 4.28, 95% CI 1.68 to 10.9, $p=0.002$; $I^2=0\%$; 3 studies) (Yin X, 2018).

In a systematic review of 650 patients with fibroids or polyps, hysteroscopic morcellation was associated with lower odds of incomplete removal of lesions when randomised trials were meta-analysed (OR 0.12, 95% CI 0.03 to 0.54, $p=0.006$; $I^2=0\%$; 3 studies). This effect was not statistically significant in observational studies or when all studies were compared (Shazly S, 2016).

In a case series of 278 patients with fibroids or polyps, the mean percentage of fibroids removed was 87% (Scheiber M, 2016).

In a case series of 244 patients with fibroids, polyps or other intrauterine pathology, complete resection of fibroids was reported for 66% (63/95) of patients. The completeness of resection of pathology was associated with symptom resolution for fibroids ($p=0.005$). Increasing fibroid size was negatively correlated with complete removal. (Arnold A, 2016).

In the case series of 73 patients, 100% of pathology was removed in 71% (49/69) of patients. Less than 50% of pathology was removed in 1 patient, 50% to 74% was removed in 13% (9/69) of patients, and 75% to 99% was removed in 15% (10/69) of patients. A second procedure was needed for 4 patients because the maximum saline deficit was reached before the resection was complete; these patients all had submucosal fibroids of 40 mm or larger (Maheux-Lacroix S, 2017).

In the randomised controlled trial of 74 patients with fibroids or polyps, comparing an office setting with an ambulatory setting, the overall percentage of pathology removal for fibroids was 96% and 64% of fibroids had 100% removal (Rubino R, 2015).

Quality of life

In the randomised controlled trial of 74 patients with fibroids or polyps, comparing an office setting with an ambulatory setting, the overall HRQOL score improved from 38.7 (±23.3) at baseline to 83.9 (±24.4) at 12-month follow up ($p<0.01$) (Rubino R, 2015).

Subsequent surgery

In the case series of 73 patients, 27% (20/73) of patients had further related surgery: 19% (14/73) had operative hysteroscopy (11 fibroid resections, 1 polyp resection, 2 endometrial ablations), 12% (9/73) had a hysterectomy and 3% (2/73) had laparoscopic myomectomy. Multivariate cox proportional hazards analysis showed a total pathology size of 50 mm or more was associated with an increased risk of needing a subsequent surgical procedure (hazard ratio 2.9, $p=0.02$) (Maheux-Lacroix S, 2017).

In a case series of 320 patients with submucosal fibroids, 17% (53/320) had a repeat morcellation procedure 3 months after the initial procedure because of incomplete resection. Of the 130 patients with FIGO type 0 fibroids, 14% (18/130) of patients had a hysterectomy within 3 years of the procedure. A hysterectomy was done within three years in 9% (11/126) of patients with FIGO type 1 fibroids and 18% (11/63) of patients with FIGO type 2 fibroids (Vidal-Mazo C, 2019).

In the case series of 244 patients with fibroids, polyps or other intrauterine pathology, 6% (5/85) of women with fibroids had a subsequent hysterectomy (Arnold A, 2016).

Pregnancy

Pregnancy was reported in 1 patient who had hysteroscopic morcellation of fibroids, 2 patients who had removal of polyps and 2 who had removal of pregnancy products in the case series of 244 patients with fibroids, polyps of other intrauterine pathology (Arnold A, 2016).

Pregnancy was reported in 71% (44/62) of patients in a case series of 62 patients with intrauterine pathology and infertility or recurrent pregnancy loss. The mean time to pregnancy was 8 months after the procedure. Of the 50 pregnancies in 44 patients, 39 (78%) resulted in a live birth, with 1 pregnancy ongoing at the last follow up. Of the 67 lesions in patients who became pregnant, 14 (21%) were

fibroids. Of the 31 lesions in patients who did not become pregnant, 5 (16%) were fibroids (Bhalani V, 2016).

Safety summary

Unspecified operative and postoperative complications

There was no statistically significant difference in the rate of operative and postoperative complications between hysteroscopic morcellation and conventional resection in the systematic reviews of 650 patients and 498 patients respectively with fibroids or polyps (Shazly S, 2016; Yin X, 2018).

Prolapsed fibroid

Pain caused by a prolapsed fibroid was reported in 3% (2/73) of patients in the case series of 73 patients. This happened 1 and 2 months respectively after the initial procedure and both were successfully treated by combined vaginal and hysteroscopic resection of the remaining fibroid (Maheux-Lacroix S, 2017).

A prolapsed submucosal fibroid was reported in 1% (3/255) of patients at 2 to 12 weeks after surgery in the case series of 244 patients. One patient needed unplanned emergency surgery and a blood transfusion for haemorrhage, with vaginal resection of the prolapsed submucosal fibroid. The second patient had offensive vaginal discharge, which resolved after the prolapsed submucosal fibroid was removed vaginally. The third woman had a 60 mm prolapsed submucosal fibroid detected on laparoscopic hysterectomy for persistent abnormal uterine bleeding (Arnold A, 2016).

Bowel damage

Bowel damage was reported in 12 patients who had hysteroscopic morcellation in a review of the Food and Drug Administration (FDA) Manufacturer and User Facility Device Experience (MAUDE) database: 2 of these patients needed temporary colostomies and were admitted into the intensive care unit. The review estimated that approximately 180,000 hysteroscopic morcellation procedures had taken place during the study period (Haber K, 2015).

Death

Death was reported in 2 patients who had hysteroscopic morcellation in the review of the FDA MAUDE database. One patient had multiple comorbidities such as chronic hypertension and obesity; the patient desaturated during anaesthesia and was diagnosed with pulmonary embolism and died. The second patient was an elderly woman who ‘was not well’; she was readmitted the day after her procedure and died shortly after. An exact cause of death was not reported (Haber K, 2015).

Fluid deficit or fluid overload

Fluid overload that needed treating by intubation and admission to the intensive care unit was reported in 11 patients in the review of the FDA MAUDE database. Uncomplicated fluid overload that resolved spontaneously or with conservative treatment was reported in 19 patients in the same review (Haber K, 2015). Hysteroscopic morcellation was halted in 1 patient because of an imminent fluid overload in the randomised controlled trial of 60 patients who had hysteroscopic morcellation or conventional hysteroscopic resection (Van Dongen H, 2008).

In the systematic review of 650 patients with fibroids or polyps, hysteroscopic morcellation was associated with a smaller fluid deficit when randomised trials were meta-analysed (weighted mean difference -36.16, 95% CI -60.66 to -11.67, p=0.004; I2=0%; 2 studies). This effect was not statistically significant in observational studies or when all studies were compared (Shazly S, 2016).

In the non-randomised comparative study of 29 patients with submucosal fibroids, the mean fluid deficit was 1,005 ml for hysteroscopic morcellation and 225 ml for loop resection (p=0.003) (Lee M, 2016).

In the case series of 278 patients with fibroids or polyps, the mean fluid deficit was 287 ml (Scheiber M, 2016).

In the case series of 244 patients with fibroids, polyps or other intrauterine pathology, the median fluid deficit for patients with fibroids was 880 ml (range 20 to 2,536) (Arnold A, 2016).

Hysterectomy

Hysterectomy was reported in 6 patients in the review of the FDA MAUDE database: 3 were because of excessive blood loss, 2 were at the patient's request after the diagnoses of uterine perforation and a failed endometrial ablation, and 1 was because of device failure (see below) (Haber K, 2015).

Uterine perforation

Uterine perforation that needed no additional surgery or treatment was reported in 28 patients in the review of the FDA MAUDE database (Haber K, 2015).

Pelvic infection

Pelvic infection was reported in 4 patients in the review of the FDA MAUDE database (Haber K, 2015).

Postoperative bleeding

Postoperative bleeding that could be controlled with non-invasive measures was reported in 6 patients in the review of the FDA MAUDE database (Haber K, 2015).

Device failure

Device failure, including metal shavings and broken pieces of device visualised in the uterine cavity, poor visualisation, failure of outflow, and a defective device that would not activate, was reported in 25 patients in the review of the FDA MAUDE database. In 1 reported case the blade fell into the uterine cavity, could not be retrieved and a hysterectomy was done (Haber K, 2015).

Disseminated peritoneal leiomyomatosis

Disseminated peritoneal leiomyomatosis was described in 1 patient in a case report. The patient had a total laparoscopic hysterectomy at least 4 years after hysteroscopic morcellation of fibroids. At the time of the hysterectomy, the patient had an approximate 14-week size, globular retroverted uterus with multiple fibroids and severe adhesive disease. There were numerous individual deposits throughout the peritoneum and omentum that appeared to be consistent with fibroids. In addition, there was leiomyomatous disease on the ovaries bilaterally and a large cyst on the left ovary. Pathology from surgery showed a benign serous cystadenoma, endometriosis, and diffuse peritoneal leiomyomatosis (Benton A, 2018).

Other

Hospital admission because of an unknown cause was reported in 3 patients in the review of the FDA MAUDE database (Haber K, 2015). Self-resolving dyspnoea was reported in 1 patient in the case series of 73 patients (attributed to anaesthesia without any evidence of fluid overload) (Maheux-Lacroix S, 2017).

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, professional experts did not describe any anecdotal adverse events. They considered that the following was a theoretical adverse event: potential theoretical risk of spread of malignant tissue via tubal ostia into peritoneum.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to hysteroscopic removal of uterine fibroids with morcellation. The following databases were searched, covering the period from their start to 20 October 2020: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The inclusion criteria shown in the following table were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with uterine fibroids.
Intervention/test	Hysteroscopic removal of uterine fibroids with power morcellation.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on about 2,000 patients from 2 systematic reviews, 2 randomised controlled trials (1 is also included in the systematic review and the

other compares 2 different healthcare settings), 1 non-randomised comparative study, 3 cohort studies, 2 case series and 1 case report (Yin X, 2018; Shazly S, 2016; Van Dongen H, 2008; Lee M, 2016; Maheux-Lacroix S, 2017; Vidal-Mazo C, 2019; Scheiber M, 2016; Arnold A, 2016; Rubino R, 2015; Bhalani V, 2016; Benton A, 2018). In addition, there is a review of 119 adverse events reported on the FDA MAUDE database (Haber K, 2015).

Other studies that were considered to be relevant to the procedure but were not included in the main summary of the key evidence are listed in the appendix.

Summary of key evidence on hysteroscopic removal of uterine fibroids with power morcellation

Study 1 Yin X (2018; published online 2019)

Study details

Study type	Systematic review and meta-analysis
Country	Not reported for individual studies
Recruitment period	Search date: 1 May 2019
Study population and number	n=498 (5 studies); 215 hysteroscopic morcellation, 183 conventional resectoscopy Patients with endometrial polyps or fibroids
Age	Mean ranged from 37 to 51 years
Patient selection criteria	3 databases (Web of Science, PubMed and Medline), were searched, to identify all relevant studies that evaluated hysteroscopic tissue removal system efficacy and safety for the treatment of endometrial polyps or myomas, compared with conventional resectoscopy. Additional publications that had not been identified in the electronic searches were examined manually. The search was limited to English language publications. The following search strategy was used for the literature search: ("hysteroscopic" or "hysteroscopy" or "hysteroscopic surgery") AND ("myoma" or polyps"). Studies were included in the analysis if they were retrospective, observational and prospective randomised controlled trials and if the patients had endometrial lesions including endometrial polyps or submucous fibroids, the intervention comprised of hysteroscopic tissue removal systems while the control group had conventional resectoscopy with monopolar or bipolar electrosurgical system, at least 1 of 5 outcomes were reported (success rate, fluid deficit, operation time, complications and complete removal). Studies were excluded if the identified publication described a non-comparative study or was a letter, case report, or review. Additionally, if the outcomes 'data of interest' were not described clearly, the study was also excluded.
Technique	Hysteroscopic morcellation devices: Truclear (Smith & Nephew, US), Myosure (Hologic, US), Intrauterine Bigatti Shaver (Karl Storz, Germany). Conventional resectoscopy: 2 studies used a 26 Fr bipolar electrosurgical system (Karl Storz SE & Co KG), 1 study used an 8.5 mm bipolar resectoscope (Gynecare Versapoint), and 2 studies used an 8.6 mm monopolar resectoscope (Olympus Corp).
Follow-up	Not reported.
Conflict of interest/source of funding	One of the authors is a consultant for Karl Storz SE & Co KG and the developer of the Intrauterine Bigatti Shaver. Another author is a consultant for Karl Storz SE & Co KG. No financial industry support was received for this study.

Analysis

Study design issues: Systematic review and meta-analysis. Data was extracted from the included studies using a standard 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses' data extraction form. If the

relevant data was not clear, the corresponding author of the original trial was contacted by email for missing or further information. The risk of bias was assessed in accordance with the Cochrane Handbook for Systematic Reviews of Interventions. Data synthesis was done using Rev Man 5.2 (Cochrane Collaboration, London, UK). Continuous data was presented as mean value and standard deviation, and the weighted mean difference and 95% confidence interval (CI) was calculated. Dichotomous data was expressed as odds ratios (ORs) with 95% Cis. The heterogeneity in outcomes across trials was assessed using the chi-squared and I^2 tests. An I^2 value of more than 50% was considered to indicate substantial heterogeneity, which prompted use of a random effects model for the analysis. Otherwise, a fixed effects model was applied. Publication bias was assessed with a funnel plot.

Study population issues: Of the 5 studies, 3 reported fibroids as the primary lesion.

One study of 84 patients with polyps was also included in the Shazly S et al., 2016 systematic review.

Key efficacy findings

Number of patients analysed: 498

Operation time

There was no statistically significant difference in operation time between hysteroscopic morcellation and conventional resectoscopy (mean difference −0.33 minutes, p=0.83; 5 studies).

Operation time for polypectomy only was statistically significantly shorter for hysteroscopic morcellation than conventional resectoscopy (mean difference -2.93min, 96% CI -4.25 to -1.61, p<0.0001; 3 studies).

There was no statistically significant difference for fibroid complete removal time (p=0.46).

Total removal rate

The pooled results showed that the success rate was higher with hysteroscopic morcellation than with conventional resectoscopy, (147/154 [95.5%] compared with 107/124 [86.3%]; odds ratio 4.28, 95% CI 1.68 to 10.91; p=0.002; I^2=0%, p=0.83; 3 studies).

Key safety findings

Fluid deficit

All 5 studies showed that the fluid deficit was higher with hysteroscopic morcellation than with conventional resectoscopy (mean difference 158.98 mL, 95% CI 41.4 to 276.5; p=0.008), but no fluid overload syndrome was reported. Fluid deficit was statistically significantly higher for fibroids treated by hysteroscopic morcellation (p=0.02), but not for polyps (p=0.88).

The authors noted that a possible explanation for the higher fluid deficit in the hysteroscopic morcellation group could be that 1 of the studies used a fast and high pressure fluid pumping device to maintain a clear view, and to prevent bleeding inside the uterine cavity.

Complications

Four studies reported intraoperative and postoperative complication rates, including perforation, via falsa and bleeding. There was no statistically significant difference between hysteroscopic morcellation and conventional resectoscopy (odds ratio 0.31, 95% CI 0.08 to 1.19; p=0.09).

Study 2 Shazly S (2016)

Study details

Study type	Systematic review and meta-analysis
Country	France, the Netherlands, Spain, Belgium, UK
Recruitment period	Search date: August 2015
Study population and number	n=650 (238 hysteroscopic morcellation, 412 electrosurgical resection); 7 studies Patients with endometrial polyps or submucous fibroids
Age	Mean age ranged from 38 to 55 years
Patient selection criteria	Studies that compared electrosurgical resection with hysteroscopic morcellation for treating uterine cavitary lesions were included. Randomised controlled trials and prospective and retrospective studies were considered eligible. Case reports, case series, and noncomparative studies were excluded. There were no limitations based on foreign language or date of publication.
Technique	Devices: Truclear (Smith & Nephew, US) and Myosure (Hologic, US).
Follow-up	Range from none to 3 months
Conflict of interest/source of funding	None for authors of the systematic review.

Analysis

Study design issues: Systematic review and meta-analysis. The main outcomes were total procedure time, fluid deficit between fluid instillation and collection, and complete removal of the lesion. Analyses of long-term outcomes and pain scores were not possible because of insufficient data. The Newcastle-Ottawa scale was used to assess observational studies and the Cochrane Risk of Bias Tool was used to assess randomised controlled trials. Of the 7 included studies, 4 were randomised controlled trials (1 of which included patients with fibroids) and 3 were retrospective observational studies (2 of which included patients with fibroids).

Study population issues: An endometrial polyp was the primary lesion in 4 studies. One study included only patients with submucous fibroids, whereas the remaining 2 studies included patients with both polyps and fibroids. The documented polyp sizes ranged from 9.2 to 17 mm and 9.7 to 25.4 mm for fibroids. Abnormal uterine bleeding was the most common presentation followed by infertility.

One study of 84 patients with polyps was also included in the Yin X et al., 2018 systematic review.

Key efficacy findings

Number of patients analysed: 650 (238 hysteroscopic morcellation, 412 electrosurgical resection)

Incomplete removal of lesion – submucosal fibroids and polyps

- All studies (4 studies; 203 morcellation, 212 resection): odds ratio=0.29, 95% CI=0.05 to 1.53, p=0.14

- Randomised controlled trials (3 studies; 169 morcellation, 163 resection): odds ratio=0.12, 95% CI=0.03 to 0.54, p=0.006; I^2=0%
- Retrospective observational studies (1 study; 34 morcellation, 49 resection): odds ratio=1.24, 95% CI 0.49 to 3.13

Number of insertions – submucosal fibroids and polyps

- All studies (2 studies [both randomised controlled trials]; 74 morcellation, 70 resection): weighted mean difference=-3.04, 95% CI=-7.86 to 1.78, p=0.22

Procedure time – submucosal fibroids only

- All studies (2 studies [both retrospective observational studies]; 62 morcellation, 221 resection); weighted mean difference=-13.44, 95% CI -38.13 to 11.25, I^2=97%

Key safety findings

Fluid deficit (ml) – submucosal fibroids and polyps

- All studies (3 studies, 4 cohorts; 129 morcellation, 286 resection): weighted mean difference=-170.33, 95% CI=-382.04 to 41.38, p=0.18
- Randomised controlled trials (2 studies; 74 morcellation, 70 resection): weighted mean difference=-36.16, 95% CI=-60.66 to -11.67, p=0.004; I^2=0%
- Retrospective observational studies (1 study, 2 cohorts; 55 morcellation, 216 resection): weighted mean difference=-269.55, 95% CI -607.82 to 68.71

Operative and postoperative complications – submucosal fibroids and polyps

- All studies (3 studies; 140 morcellation, 148 resection): weighted mean difference=0.72, 95% CI=0.20 to 2.57, p=0.62
- Randomised controlled trials (2 studies; 106 morcellation, 99 resection): weighted mean difference=0.41, 95% CI=0.07 to 2.49, p=0.33
- Retrospective observational studies (1 study; 34 morcellation, 49 resection): weighted mean difference=1.52, 95% CI 0.40 to 5.71

Study 3 Van Dongen H (2008) – included in 2015 overview

Study details

Study type	Randomised controlled trial
Country	The Netherlands
Recruitment period	2005 to 2006
Study population and number	n=60 (30 hysteroscopic morcellation [10 fibroids] versus 30 conventional hysteroscopic resectoscopy [12 fibroids]) Women with intrauterine polyps or submucous fibroids (type 0 or 1).
Age	Mean 49 years
Patient selection criteria	Intrauterine polyp or type 0 or type 1 submucous fibroid smaller than 30 mm in diameter and an indication for removal (abnormal uterine bleeding, dysmenorrhoea, infertility). Exclusion criteria were type 2 fibroids, suspicion of malignancy before surgery, or contraindications for hysteroscopic surgery.
Technique	All procedures were done in an inpatient setting with the patients under general or spinal anaesthesia. Hysteroscopic morcellator (Smith and Nephew, USA) was used with normal saline solution for distension and irrigation. Conventional resectoscopy used sorbitol (4%) for distension and irrigation.
Follow-up	Not reported
Conflict of interest/source of funding	Financial support was received from Smith and Nephew, USA.

Analysis

Study design issues: Randomisation was done using sealed opaque envelopes. The procedures were done by 6 residents in training for obstetrics and gynaecology. The primary outcome measure was the operating time, defined as the time between the introduction of the hysteroscope until the removal of the instrument at the end of the procedure. Intention-to-treat analysis.

Study population issues: There were no significant differences in baseline characteristics (age, median parity, menopausal state, indication for surgery, preoperative diagnosis, size of intrauterine abnormality) between the groups. Most patients had polyps rather than fibroids – the results were not separated by indication.

Other issues: The authors noted that no learning curve was observed. They also noted that approximately 20% of resectoscopy procedures had to be taken over by the trainer, compared with 3% of the morcellator procedures. This study is included in the systematic review by Shazly (2016).

Key efficacy findings

Number of patients analysed: 60 (30 hysteroscopic morcellation, 30 conventional resectoscopy)

Mean operating time (minutes)

- Hysteroscopic morcellation=10.6 (95% CI 7.3 to 14.0)
- Conventional resection=17.0 (95% CI 14.1 to 19.9), p=0.008

Median number of insertions

- Hysteroscopic morcellation=1 (range 1–2)
- Conventional resection=7 (range 3–50)

Multiple linear regression analysis showed that operating time increased significantly, in both groups, when volume of intrauterine lesions increased.

Key safety findings

Mean total distension fluid used (ml)

- Hysteroscopic morcellation=3413 (95% CI 2209 to 4617)
- Conventional resection=5050 (95% CI 4106 to 5994), p=0.041

Mean total fluid deficit (ml)

- Hysteroscopic morcellation=409 (95% CI 229 to 589)
- Conventional resection=545 (95% CI 406 to 684), p=0.224

Complications

- 1 patient allocated to conventional resectoscopy did not undergo the intended procedure because of a perforation during cervical dilation.
- Hysteroscopic morcellation was aborted prematurely in 1 patient with submucous type 1 fibroid because of an imminent fluid overload.
- Histological analysis of the specimens revealed that 2 patients in the hysteroscopic morcellation group had malignant endometrial carcinoma (both were diagnosed with fibroid type 0 before the surgery). Both patients were treated primarily with the hysteroscopic morcellator and subsequently (after diagnosis) had a radical hysterectomy with bilateral salpingo-oophorectomy.

Study 4 Lee M (2016)

Study details

Study type	Non-randomised comparative study
Country	China
Recruitment period	2011 to 2014
Study population and number	n=29 (15 hysteroscopic morcellation, 14 hysteroscopic monopolar loop resection) Patients with submucosal fibroids
Age	Not reported
Patient selection criteria	All patients who had hysteroscopic resection of submucosal fibroids were selected and case notes reviewed.
Technique	Hysteroscopic morcellation device: Myosure (Hologic, US). Normal saline was used as the distending medium. Loop resection: monopolar energy was used and glycine was the distending medium.
Follow-up	3 months
Conflict of interest/source of funding	None

Analysis

Follow-up issues: no losses to follow-up were described. Two patients from the morcellation group and 1 from the conventional group were excluded due to the need for multiple procedures including endometrial ablation or laparoscopic ovarian cystectomy during the same operation. One patient in the conventional resection group had a uterine perforation that needed surgical repair and was excluded from data analysis.

Study design issues: Retrospective, single centre non-randomised comparative study. The choice of procedure was dependent on the operator. Those patients with prolonged operating time because of multiple operations for other indications or complications were excluded from the final analysis. Postoperatively, a satisfactory outcome was considered when the patient subjectively reported reduced menstrual bleeding and considered the operation to have improved menstrual symptoms at 3-month follow-up.

Study population issues: The mean size of fibroids resected was 3.3 cm (range 2 to 5 cm) for the conventional technique and 3.5 (range 1.5 to 6 cm) for hysteroscopic morcellation (p=0.470).

Study is also included in systematic review by Yin X et al. (2018).

Other issues: All hysteroscopic morcellation procedures were done between 2013 and 2014 after the procedure was introduced in the department.

Key efficacy findings

Number of patients analysed: 25 (13 hysteroscopic morcellation, 12 conventional hysteroscopic resection)

Duration of procedure (minutes)

- Hysteroscopic morcellation=36.6 (range 17 to 72)
- Loop resection=53.6 (range 39 to 102), p=0.005

Mean difference in haemoglobin levels before and 3 months after procedure (g/l); n=9 in both groups

- Hysteroscopic morcellation=+17.0 (range -4 to +40)
- Loop resection=+21.5 (range +1 to +44), p=0.235

Satisfactory outcome

- Hysteroscopic morcellation=93.3%
- Loop resection=84.6%, p=0.841

Satisfactory outcome when uterine fibroid protrusion >60%

- Hysteroscopic morcellation=100%
- Loop resection=100%

Comparison of outcomes for small and large fibroids

Fibroid size	Hysteroscopic morcellation	Loop resection	p value
Small (3 cm or less)	n=9	n=5	
Duration of procedure (mins)	27.6 (14 to 45)	53.4 (29 to 76)	0.019
Patient satisfaction	9 (100%)	4 (80%)	0.797
Large (more than 3 cm)	n=4	n=7	
Duration of procedure (mins)	57 (40 to 66)	65 (39 to 102)	0.527
Patient satisfaction	3 (75%)	6 (85.7%)	0.788

Key safety findings

Mean fluid deficit (ml)

- Hysteroscopic morcellation=1,005 (range 40 to 2,600)

- Loop resection=225 (range 0 to 1,000), p=0.003

Mean fluid deficit (ml) for small fibroids (3 cm or less)

- Hysteroscopic morcellation (n=9) = 634.4 (range 40 to 1,600)
- Loop resection (n=5) = 80 (range 0 to 200), p=0.019

Mean fluid deficit (ml) for large fibroids (more than 3 cm)

- Hysteroscopic morcellation (n=4) = 1,839 (range 556 to 2,600)
- Loop resection (n=7) = 328.6 (range 0 to 1,000), p=0.024

Complications

- Hysteroscopic morcellation: no intraoperative or postoperative complications that could lead to an extended hospital stay.
- Loop resection: 1 uterine perforation

No patient in either group developed any complication associated with excessive fluid absorption.

Study 5 Maheux-Lacroix S (2017)

Study details

Study type	Cohort study
Country	Australia
Recruitment period	2011 to 2016
Study population and number	n=73 Women with abnormal uterine bleeding associated with benign submucosal fibroids
Age	Mean 43 years
Patient selection criteria	Inclusion criteria: women with abnormal uterine bleeding who had a hysteroscopic resection by mechanical morcellation of a benign submucosal fibroid confirmed at histopathology. Abnormal uterine bleeding was defined by having at least 1 of the following International Federation of Gynecology and Obstetrics (FIGO) standardised symptoms: heavy menstrual bleeding, inter-menstrual bleeding, post-coital bleeding, or post-menopausal bleeding. Exclusion criteria included viable pregnancy, active pelvic infection, an in situ intra-uterine device, concomitant endometrial ablation or resection, and malignancy or pre-malignancy (endometrial hyperplasia) at histopathology.
Technique	Device: Myosure LITE or XL (Hologic, US) Paracervical or cervical block with local anaesthesia with or without epinephrine was used according to surgeons' preferences. All resected specimens were sent for histologic examination.
Follow-up	Mean 32 months (range 6 to 54)
Conflict of interest/source of funding	One author is the recipient of a Training Award from the Fonds de Recherche Quebec-Sante. One author is a paid consultant for Hologic and is a member of their Medical Advisory Committee in Australia. He has no shares or equity in the company.

Analysis

Follow-up issues: Patients with a minimum of 6 months after their index surgery were contacted by email (2 attempts) or phone (2 attempts). There were 92 women eligible for the study but 19 were lost to follow-up, leaving 73 (79%) included in the analysis.

Study design issues: Prospective, multicentre cohort study. The main aim was to assess the need for repeat surgical intervention after the procedure. Other outcomes included patient satisfaction, symptom resolution, postoperative complications and predictors of negative outcomes. Medical records including medical notes, operation report and histopathology results were reviewed to confirm the nature and indication for subsequent surgery. A failure to control abnormal uterine bleeding was defined as either the persistence or the recurrence of at least one of the following symptoms: heavy menstrual bleeding, inter-menstrual bleeding, post-coital bleeding or post-menopausal bleeding).

Study population issues: Of the 19 patients who were lost to follow-up, 12 (63%) were nulliparous compared with 23 (31%) in the included group (p=0.0114). All other baseline characteristics were similar. Patients had

type 0, 1 or 2 fibroids. More than 1 fibroid was removed in 28% of patients and 14% (10/73) also had a polyp removed. The mean total size of pathology at the time of index surgery was 42 mm.

Key efficacy findings

Number of patients analysed: 73

4 patients needed a second procedure because the maximum saline deficit was reached before the resection was completed. These patients all had submucosal fibroids of 40 mm or more.

Percentage of pathology removed

- 100%=71% (49/69)
- 75 to 99%=15% (10/69)
- 50 to 74%=13% (9/69)
- <50%=1% (1/69)

Patient satisfaction

- Satisfied=84% (54/73)
- Neutral=6% (4/73)
- Dissatisfied=9% (6/73)

Failure to control abnormal uterine bleeding=33% (24/73)

- Persistence of at least 1 symptom=21% (15/73) [reported in paper as 23%]
- Recurrence of symptoms=18% (13/73) [reported in paper as 20%]

Any subsequent related surgery=27% (20/73)

- Operative hysteroscopy=19% (14/73) (11 resection of fibroid, 1 resection of polyp, 2 endometrial ablation)
- Hysterectomy=12% (9/73)
- Laparoscopic myomectomy=3% (2/73)

Estimated cumulative incidence of subsequent related surgery by size of fibroid

	Estimated cumulative incidence (%) ± standard deviation		
Pathology size	**1 year**	**2 years**	**3 years**
All	15±4	23±5	30±6
<50 mm	10±4	15±5	21±6
50 mm and above	25±9	38±10	54±17

Multivariate cox proportional hazards analysis showed a total pathology size of 50 mm or more was associated with an increased risk of needing a subsequent surgical procedure (hazard ratio 2.9, p=0.02). Having 2 or more fibroids resected was also associated with an increased risk but it did not reach statistical significance (hazard ratio 1.8, p=0.1). There was no association found when comparing type 2 fibroids to other pathology (p=0.57).

For women who had a hysterectomy, multiple fibroids were reported and histopathologically confirmed in all cases and adenomyosis in 66% (6/9) of patients.

Key safety findings

Postoperative complications=7% (5/73)

- Pain caused by a prolapsed fibroid=2.7% (2/73) (1 and 2 months respectively after initial procedure; both patients had an incomplete resection that was successfully treated by combined vaginal and hysteroscopic resection of the remaining fibroid)
- Pelvic infection=2.7% (2/73) (treated with antibiotics)
- Self-resolving dyspnoea=1.4% (1/73) (attributed to anaesthesia without any evidence of overload)

Study 6 Vidal-Mazo C (2019)

Study details

Study type	Cohort study
Country	Spain
Recruitment period	2013 to 2018
Study population and number	n=320 (353 myomas) Premenopausal patients with submucosal fibroids and symptoms of abnormal uterine bleeding or infertility
Age	Mean 43 years
Patient selection criteria	Patients with 1 or more submucosal fibroids confirmed by hysteroscopy and pathological study. Indications for hysteroscopy included anormal uterine bleeding and infertility. Fibroids of FIGO type 0, 1 and 2 were included. Fibroids larger than 5 cm were excluded.
Technique	Device: Myosure The procedures were done in office and patients were discharged at the end of the procedure. Oral sedation was used with paracervical anaesthesia. Patients were instructed to take an oral analgesic before the procedure. No patient had prophylactic antibiotics. In case of incomplete resection, a re-morcellation was offered 3 months later. All resected samples were sent for histological examination.
Follow-up	Up to 5 years
Conflict of interest/source of funding	None

Analysis

Follow-up issues: All patients had a follow up visit 3 to 6 months after the procedure and were invited to attend an annual review. There were 99 women remaining to be evaluated (31%) in the second year. In the third year, 176 (55%) patients had not been evaluated and at the fourth and fifth year of follow-up, 75% of patients had not yet completed the study.

Study design issues: Prospective cohort study. The aim of the study was to evaluate the clinical recurrence of submucosal fibroids after hysteroscopic morcellation, and to study the characteristics associated with clinical recurrence after 5 years of follow-up. The FIGO classification was used to characterise the fibroids; if there were more than 1, the fibroid of greater hysteroscopic complexity was classified, and the size was calculated as the total sum of all fibroids.

Study population issues: Of the 319 patients with reported FIGO fibroid type, 130 (41%) had type 0, 126 (40%) had type 1 and 63 (20%) had type 2 fibroids. The mean size of submucosal fibroid was 24.6 mm. Abnormal uterine bleeding was the indication in 290 (91%) patients and infertility in 30 (9%).

Key efficacy findings

Number of patients analysed: 320

16.6% (53/320) of patients had a repeat morcellation procedure 3 months after the initial procedure because of incomplete resection.

Outcomes by fibroid type, n (%)

Type	Post procedure	2 year review	3 year review	4 year review	5 year review
FIGO 0	n=130				
Not evaluated	1 (0.8%)	33 (25.4%)	61 (46.9%)	93 (71.5%)	114 (87.7%)
Discharged	109 (83.9%)	87 (66.9%)	64 (49.2%)	32 (24.6%)	14 (10.8%)
Hysterectomy	6 (4.6%)	7 (5.4%)	5 (3.8%)	0 (0%)	0 (0%)
Recurrence	14 (10.8%)	3 (2.3%)	0 (0%)	5 (3.8%)	5 (3.8%)
FIGO 1	n=126				
Not evaluated	1 (0.8%)	38 (30.2%)	64 (50.8%)	90 (71.4%)	105 (83.3%)
Discharged	88 (69.8%)	74 (58.7%)	58 (46%)	35 (27.8%)	21 (16.7%)
Hysterectomy	4 (3.2%	7 (5.6%)	0 (0%)	1 (0.8%)	0 (0%)
Recurrence	27 (26.2%)	7 (5.6%)	4 (3.2%)	0 (0%)	0 (0%)
FIGO 2	n=63				
Not evaluated	1 (1.6%)	28 (44.4%)	51 (81%)	57 (90.5%)	62 (98.4%)
Discharged	35 (55.6%)	25 (39.7%)	7 (11.1%)	6 (9.5%)	1 (1.6%)
Hysterectomy	6 (9.5%)	4 (6.4%)	1 (3.2%)	0 (0%)	0 (0%)
Recurrence	21 (33.3%)	6 (9.5%)	3 (4.8%)	0 (0%)	0 (0%)

Key safety findings

The paper states that there were no complications related to surgery or clinical follow up.

Study 7 Scheiber M (2016)

Study details

Study type	Case series
Country	US (34 centres)
Recruitment period	Not reported
Study population and number	n=278 (187 fibroids [33%], 372 polyps [67%]) Women with indications for hysteroscopic myomectomy or polypectomy
Age	Mean 44 years
Patient selection criteria	Inclusion criteria: age 18 to 65 years, identification of intrauterine pathology using ultrasound, saline infusion sonography, or hysteroscopic examination, with polyps of any size or submucosal fibroids 6 cm or less in diameter. Exclusion criteria: pregnancy, intrauterine device in situ at the time of the procedure, current use of anticoagulant or antiplatelet medication in addition to low-dose aspirin, active pelvic inflammatory disease or pelvic/vaginal infection, known or suspected coagulopathy or bleeding disorder, increased fluid overload risk (such as history of predisposing cardiac, hepatic, or renal dysfunction), or other comorbid condition that, in the opinion of the investigator, could limit the ability to participate or affect the scientific integrity of the study.
Technique	Device: MyoSure Hysteroscopic Tissue Removal System (Hologic Inc., US) General anaesthesia was used for 71% of procedures. Of the 278 patients, 250 were treated in an ambulatory surgery centre or hospital outpatient department and 28 were treated in physician offices.
Follow-up	Not reported
Conflict of interest/source of funding	The 2 authors received compensation for speaking engagements by Hologic Inc. Neither author had any other potential conflicts of interest, financial or otherwise.

Analysis

Study design issues: Prospective, single-arm, multicentre registry. The aim of the study was to assess the feasibility of hysteroscopic morcellation across a diverse set of facilities, including both surgical and office-based settings. The primary efficacy endpoint was the percentage of lesions removed. Secondary outcomes included procedure time, cutting time, fluid deficit, and the need for mechanical cervical dilation. A 5-point Likert scale was used to evaluate physician postoperative satisfaction with the morcellation system, with a score of 5 indicating ‘‘very satisfied,’’ and a score of 1 indicating ‘‘very dissatisfied.’’ The safety endpoint assessed the incidence of adverse events observed before discharge from the recovery room or reported by the patient after discharge. Study physicians were asked to report the occurrence of specific adverse events, which were cramping, nausea, pain, haemorrhage, pulmonary distress, cervical tearing, fibroid recurrence, vaginal bleeding, vomiting, fluid overload, infection, reaction to anaesthetic agents, and uterine perforation.

Study population issues: Most patients (73%) were premenopausal. Of the 278 patients, 74% were treated for abnormal uterine bleeding, and 15% were treated for infertility. The mean fibroid diameter was 2.2 cm (range

0.3 to 5.5 cm). Fibroids were most commonly located in the anterior section of the uterus (26% of the total). Polyps were most commonly located in the posterior uterus (24% of the total).

Key efficacy findings

Number of patients analysed: 278

Operative parameters and observations

Parameter	All sites	n	Office	n	Ambulatory surgical centre or hospital outpatient department	n	p value
% pathology removed, by patient	95.4±13.2	278	96.8±14.1	28	95.2±13.1	250	0.5436
% polyp removed, by lesion	99.3±5.8	331	99.3±6.1	27	99.9±0.4	304	0.0900
% fibroid removed, by lesion	86.8±24.1	157	94.8±17.6	18	85.8±24.7	139	0.1368
Resection time, min	6.0±9.0	229	8.9±15.6	21	5.8±8.1	208	0.0978
Time in post-anaesthesia care unit, min	55.4±37.1	207	36.8±24.7	16	57.0±37.5	191	0.0263
Physician satisfaction score 4 to 5, %	95	278	89	28	96	250	0.1470

Of 245 patients for whom cervical dilation information was recorded, mechanical dilation was done in 215 patients (87.7%) and mean dilation was 0.9 cm (range 0.3 to 2.8 cm).

Key safety findings

- Mean fluid deficit=287±453 ml
- Adverse events=1.8% (5/278) of patients (3.6% in office setting and 1.6% in ambulatory surgical centre or hospital outpatient department, p=0.4143); 4 patients had mild cervical trauma and 1 patient had moderate postoperative pedal oedema. All adverse events were described as mild and resolved spontaneously.

Study 8 Arnold A (2016)

Study details

Study type	Cohort study
Country	Australia
Recruitment period	2013 to 2015
Study population and number	n=244; 255 procedures (102 fibroids, 98 polyps, 22 mixed pathology, 16 pregnancy tissue, 17 preinvasive or invasive endometrial abnormalities) Women who had hysteroscopic removal of intrauterine pathology
Age	Median 44 years (range 22 to 82)
Patient selection criteria	Women aged ≥18 years needing a hysteroscopic procedure involving resection of endometrial pathology were included in the study. Exclusion criteria included viable pregnancy, active pelvic infection, and an intrauterine contraceptive device remaining in situ.
Technique	MyoSure Lite or MyoSure XL device (Hologic, US).
Follow-up	Median 3.6 months
Conflict of interest/source of funding	One author is a paid consultant for Hologic and is a member of their speakers' bureau. He has no shares or equity in the company. One author received a travel grant from Hologic to present this study at a meeting. No funding was received to conduct this study.

Analysis

Study design issues: Prospective cohort study. Surgical data included the need for and extent of cervical dilatation; pathology type, size, and location; percentage of pathology removed, noted as complete (100% of abnormal tissue removed visually) or as an estimated visual assessment of tissue removal, defined as 75% to 99%, 50% to 74%, and <50% and surgical vision, defined as 100%, 75% to 99%, 50% to 74%, and <50% by the operating surgeon; fluid deficit; and any intraoperative complications. When there were multiple pathologies within the endometrial cavity, all pathologies were combined to calculate the size of total pathology. Postoperative data included final pathological diagnosis, resolution of symptoms when seen at follow-up as indicated clinically, and whether further surgery was planned or had been done.

Study population issues: The most common indication for treatment was abnormal bleeding (82%), followed by infertility (6%) and retained products of conception (4%); the indication was not reported for 8% of patients.

Key efficacy findings

Number of patients analysed: 244 (255 procedures)

Complete resection of fibroids=66% (63/95) of patients

The reasons for incomplete resection of fibroids included maximal fluid deficit reached in 13 (41%), technical issues in 2 (6%), poor vision in 6 (19%), calcified pathology in 3 (9%), and no documented reason in 8 (25%).

Procedure information

Variable	Fibroids (n=102)	Polyps (n=98)	Mixed pathology (n=22)	Pregnancy tissue (n=16)	Preinvasive or invasive (n=17)	p value
Final histology, n (%)	29 (28) type 0; 38 (37) type 1; 17 (17) type 2; 18 (18) not documented		16 (73) polyps and fibroids; 4 (18) benign endometrium ; 1 (4.5) septum; 1 (4.5) adenomyoma	16 products of conception	9 (53) preinvasive; 8 (47) invasive	
Median duration of activation of morcellation device, min:s (range)	4:33 (0:09 to 22:45)	0:28 (0:02 to 9:50)	2:03 (0:23 to 13:18)	1:16 (0:17 to 8:33)	0:56 (0:22 to 3:16)	<0.001
Median size of pathology, mm (range)	40 (10 to 150)	20 (3 to 70)	30 (10 to 80)	25 (8 to 45)	20 (5 to 70)	<0.001
Median saline deficit, ml (range)	880 (20 to 2,536)	200 (10 to 2,500)	525 (40 to 2,440)	900 (70 to 2,500)	256 (40 to 1,900)	<0.001
Complete resection of pathology, n (%)	63 (66); 18 (62) type 0; 27 (71) type 1; 11 (65) type 2	91 (92)	16 (76)	13 (87)	15 (88)	

Completeness of resection data was missing for 12 procedures (7 fibroids, 3 polyps, 1 mixed pathology and 1 pregnancy tissue)

Complete resection of pathology was statistically significantly more likely for polyps compared with fibroids (92% vs 66%; p<0.001). The completeness of resection of pathology was associated with symptom resolution for fibroids (p=0.005), but not for polyps (p=0.431).

Multivariable logistic regression analysis was done for possible factors associated with incomplete resection of a fibroid, including total size of pathology, size of the largest fibroid, operator skill level, and subtype of fibroid (0, 1, or 2). The size of the largest leiomyoma (p<0.005) and the seniority of the surgeon (p<0.012) were the only statistically significant factors associated with the likelihood of complete resection with a single procedure. Increasing leiomyoma size was negatively correlated with complete removal.

Completeness of resection of fibroids according to fibroid size

- <20 mm=90%
- 20 to 29 mm=89%
- 30 to 39 mm=83%
- ≥40 mm=48%

Pregnancy

Pregnancy occurred in 5 women to the time of follow-up (2 who had polyp removal, 2 who had removal of pregnancy products, and 1 who had fibroid removal).

Repeat procedures

3 women, who had completely resected pathology, had a repeat procedure at 12 to 18 months after the initial procedure because of new pathology. An additional 6 women had a repeat procedure scheduled after incomplete removal of pathology at the first operation, and 1 woman, who had 15 fibroids, had 3 procedures over an 8 week period to completely resect pathology.

Hysterectomy

6% (5/85) of women with a fibroid had a subsequent hysterectomy. Of the 5 women, 2 had a complete submucous fibroid resection but persistent symptoms of abnormal uterine bleeding. Final pathology showed intramural fibroids with no submucous component. The other 3 women had an incomplete fibroid resection at the primary hysteroscopic procedure, and all 3 had laparoscopic hysterectomy, with diffuse leiomyomatosis in 1, a 60-mm prolapsed submucosal fibroid in 1, and intramural fibroids in 1.

Key safety findings

- There were no intraoperative complications
- Postoperative complications=1% (3/255)

All 3 patients with postoperative complications had incomplete removal of fibroid at the index surgery and then sustained a prolapsed submucosal fibroid at 2 to 12 weeks after surgery. One patient needed unplanned emergency surgery and a blood transfusion for haemorrhage, with vaginal resection of the prolapsed submucosal fibroid. The second patient had offensive vaginal discharge, which resolved after the prolapsed submucosal fibroid was removed vaginally. The third woman had a 60 mm prolapsed submucosal fibroid (mentioned above) detected on laparoscopic hysterectomy for persistent abnormal uterine bleeding.

Study 9 Rubino R (2015) – included in 2015 overview

Study details

Study type	Randomised controlled trial (comparing an office setting against an ambulatory surgical centre)
Country	US
Recruitment period	Not reported
Study population and number	n=74 patients (42 fibroids, 66 polyps) Pre or peri-menopausal women with submucosal fibroids or polyps and abnormal uterine bleeding
Age	Mean 41 years
Patient selection criteria	Intrauterine polyps or submucosal fibroids which were compatible with office-based treatment based on 1 or more of the following criteria: 1 or more polyps, with at least 1 of the polyps ≥1.5 cm and ≤3.0 cm diameter with a broad based attachment to the uterine wall; up to 2 type 0 or type 1 fibroids with at least 1 of them being ≥1.5 cm and none of them being >3.0 cm; polyps plus up to 2 type 0 or type 1 fibroids with at least 1 of the fibroids being ≥1.5 cm and ≤3.0 cm and none of the fibroids being >3.0 cm. Exclusion criteria: known or suspected cancer; contraindication or allergy to local anaesthetic; history of chronic narcotic use; previous uterine artery embolisation; presence of intrauterine device at the time of the procedure; active pelvic inflammatory disease or pelvic/vaginal infection; type 2 submucosal fibroids, fundal type 1 fibroids, submucosal fibroids >3.0 cm or highly vascularised fibroids.
Technique	All procedures were done using the Myosure hysteroscopic tissue removal system (Hologic, US).
Follow-up	12 months
Conflict of interest/source of funding	Study was sponsored by Hologic Inc.

Analysis

Study design issues: patients were randomised to have the procedure either in an 'office' setting or in an ambulatory surgical centre. Different levels of analgesia were used in each setting. Each patient completed the Health Related Quality of Life (HRQOL) questionnaire and the Uterine Fibroid Symptom and Quality of Life (UFS-QOL) questionnaire prior to treatment and 12 months after treatment.

Study population issues: In this study, 61% (66/108) of the abnormalities in the 74 patients were polyps. Patient reported outcome data are not presented separately for those women with fibroids only.

Key efficacy findings

Number of patients analysed: 74

Percentage pathology removal for fibroids

- Overall=95.9%±6.8% (range 75%–100%)
- Office setting=94%±8.6% (range 75%–100%)
- Ambulatory surgical centre=99.8%±0.4% (range 99%–100%)

Proportion of fibroids with 100% removal

- Overall=63.6%
- Office setting=52%
- Ambulatory surgical centre=83.3%

Mean resection time (seconds)

- Overall=143.0±293.3
- Office setting=189.3±376.9
- Ambulatory surgical centre=82.2±77.4

UFS-QOL symptom severity (higher scores indicate more severe symptoms) and HRQOL scores (higher scores indicate better quality of life)

	Overall	Office	surgical centre
UFS-QOL symptom score before procedure	67.5±15.4	68.3±16.3	66.4±14.0
UFS-QOL score at 12-months follow-up	22.3±22.6	39.1±24.7	38.2±21.1
UFS-QOL symptom severity improvement	45.2±23.2 p<0.01	42.7±24.0 p<0.01	48.3±21.6 p<0.01
HRQOL score before procedure	38.7±23.3	39.1±24.7	38.2±21.2
HRQOL score at 12-months follow-up	83.9±24.4	81.1±28.1	87.6±17.9
HRQOL improvement	45.5±25.1 p<0.01	42.3±25.3 p<0.01	49.4±24.3 p<0.01

Patient satisfaction (proportion of patients who reported that they were 'satisfied' or 'very satisfied')

- Overall=89.2%
- Office setting=88.6%
- Ambulatory surgical centre=96.9%

Proportion of patients who would recommend treatment to other patients having similar symptoms

- Overall=95.9%
- Office setting=95.5%
- Ambulatory surgical centre=100%

Key safety findings

- Adverse events=2.7% (2/74; 1 patient experienced pain that was described as mild and 1 patient had diarrhoea and food poisoning).

Study 10 Bhalani V (2016)

Study details

Study type	Case series
Country	US (2 clinics)
Recruitment period	Not reported
Study population and number	n=62 Women with intrauterine pathology and infertility or recurrent pregnancy loss
Age	Mean 37 years (range 28 to 46)
Patient selection criteria	Inclusion criteria: women aged 45 years or less (or over 45 if using egg donation at the time of hysteroscopic intervention), documented history of infertility for at least 6 months if aged 35 years or more or at least 12 months if aged less than 35 years, recurrent (2 or more) clinical pregnancy losses, postoperative follow-up at least 6 months with documented efforts to conceive, or confirmed fetal heartbeat or other pregnancy verification within 6 months of procedure.
Technique	Device: Myosure Hysteroscopic Tissue Removal System (Hologic Inc., US).
Follow-up	At least 6 months
Conflict of interest/source of funding	2 authors have previously received remuneration from Hologic Inc., the device manufacturer.

Analysis

Study design issues: Retrospective case series, from 2 private infertility clinics. The main outcomes were the incidence of pregnancy and subsequent live births during follow-up. Secondary outcomes included mean time to pregnancy, age at pregnancy, lesion size and number, and proportion of pathology removed. The authors noted that the total number of fibroids identified was insufficient to correlate with pregnancy outcomes.

Study population issues: Diagnosed reasons for infertility were diverse and often multifactorial. Ovarian dysfunction (55%), male factor (31%) and endometriosis (16%) were more commonly identified than strictly uterine factors (8%). Indications for treatment included polyps as well as fibroids. There were 98 lesions in the 62 patients, most of which (75%) were polyps. There were only 19 fibroids (the number of patients is unclear because at least 1 patient had multiple fibroids). No patient had concurrent polyps and fibroids. Fibroids were classified as type 0 (74%) and type 1 (26%) according to the FIGO classification.

Key efficacy findings

Number of patients analysed: 62

Percentage of fibroid tissue removed during hysteroscopic morcellation=95.5%

Fertility outcomes

Fertility outcomes	Site 1 (n=33)	Site 2 (n=29)	Total (n=62)	p value
Pregnancy, number (%)	22 (67)	22 (76)	44 (71)	0.7737
Mean time to pregnancy, months (±standard deviation)	11.9±7.6	4.9±4.3	8.4±7.0	0.0005
Range, number (%)				
1 to 3 months	1 (3)	11 (38)	12 (27)	0.0007
4 to 6 months	5 (15)	4 (18)	9 (20)	0.9999
7 to 12 months	8 (24)	5 (23)	13 (30)	0.5477
>12 months	8 (24)	2 (9)	10 (23)	0.0880
Mean age at pregnancy, years	37.5±3.9	35.7±4.1	36.8±4.0	0.0582
Pregnant, age >35 years, number (%)	17 (77)	9 (41)	26 (59)	0.0130
Outcome, number (% of pregnancies)	n=24	n=26	n=50	
Live birth, living child	21 (88)	18 (69)	39 (78)	0.1754
Stillbirth, antepartum (>20 weeks)	2 (8)	0 (0)	2 (4)	0.2253
Spontaneous abortion (≤20 weeks)	1 (4)	6 (23)	7 (14)	0.1004
Ectopic pregnancy	0 (0)	1 (4)	1 (2)	0.9999
Ongoing at last follow-up	0 (0)	1 (4)	1 (2)	0.9999

Pathology observations in patients who became pregnant

Lesion characteristic	Site 1 (35 lesions)	Site 2 (32 lesions)	Total (67 lesions)
Lesion type, number (% of all lesions)			
Fibroid	5 (14)	9 (28)	14 (21)
Polyp	27 (77)	20 (63)	47 (70)
Other (for example, synechia)	3 (9)	3 (9)	6 (9)
Mean lesion size, cm			
Fibroid	2.1±1.2	2.2±1.5	2.1±1.3
Polyp	1.4±0.8	1.5±0.9	1.4±0.8
Amount of lesion removed, %			
Fibroid	94.0±13.2	97.1±7.6	95.8±9.9
Polyp	100	100	100

Lesion parameters in patients who conceived compared with those who remained infertile after hysteroscopic morcellation

Lesion characteristic	Pregnant (n=44)	Not pregnant (n=18)	p value
Lesion type, number (% of all lesions)	n=67 lesions	n=31 lesions	
Fibroid	14 (21)	5 (16)	0.7843
Polyp	47 (70)	26 (84)	0.2130
Other (for example, synechia)	6 (9)	0 (0)	0.1724
Multiple polyps present, number (% of patients)	5 (11)	4 (22)	0.2297
Mean lesion size, cm			
Fibroid	2.1±1.3	2.5±0.9	0.5427
Polyp	1.4±0.8	1.3±1.1	0.6992
Fibroid location, number (% of fibroids)	n=14 fibroids	n=5 fibroids	
Anterior	4 (29)	2 (40)	0.9999

Fundal	2 (14)	0 (0)	0.9999
Lateral wall	2 (14)	1 (20)	0.9999
Lower uterine segment	3 (21)	1 (20)	0.9999
Posterior	3 (21)	1 (20)	0.9999
Polyp location, number (% of polyps)	n=47 polyps	n=26 polyps	
Anterior	10 (21)	7 (27)	0.5787
Fundal	9 (19)	7 (27)	0.5565
Lateral wall	10 (21)	4 (15)	0.7576
Lower uterine segment	7 (15)	3 (12)	0.9999
Posterior	11 (23)	5 (19)	0.7739
Amount of lesion removed, %			
Fibroid	95.8±9.9	100±0.0	0.0039
Polyp	100±0.0	100±0.0	0.9999

Key safety findings

No intraoperative or perioperative adverse events were recorded for any patient.

Study 11 Haber K (2015)

Study details

Study type	Review of US Food and Drug Administration (FDA) Manufacturer and User Facility Device Experience (MAUDE) database
Country	US
Recruitment period	Database search=June 2014
Study population and number	n=119 events Women who had hysteroscopic surgery to remove an intrauterine polyp or fibroid with a reciprocating morcellator.
Age	Not reported
Patient selection criteria	The database was searched for the following key words: 'Myosure', 'Truclear', 'hysteroscopic reciprocating morcellator', 'Interlace' and 'hysteroscope', 'Myosure' and 'hysteroscopy', 'Smith & Nephew' and 'hysteroscope'.
Technique	The Truclear hysteroscopic morcellator (Smith & Nephew, USA) and the Myosure tissue removal system (Hologic, USA) were used.
Follow-up	Not reported
Conflict of interest/source of funding	Not reported

Analysis

Study design issues: Reports were reviewed individually for annotations of patient injury or death and were categorised by date reported, date of occurrence, type of morcellation device, type of complication, brief description and who reported the incident. Each company was contacted to provide an estimate of the number of units sold to date in the USA as a surrogate of the number of procedures performed. Duplicate reports were identified and removed.

Limitations of the FDA MAUDE database include the potential submission of incomplete, inaccurate, untimely, unverified, or biased data. In addition, the incidence or prevalence of an event cannot be determined from this reporting system alone because of under-reporting of events, inaccuracies in reports, lack of verification that the device caused the reported event, and lack of information about frequency of device use.

Study population issues: Women treated for polyps were also included.

Key efficacy findings

No efficacy findings were reported.

Key safety findings

Adverse events reported on FDA MAUDE database

Major complications	Truclear	Myosure	Total
Death	0	2	2
Bowel damage	3	9	12
Admission to intensive care unit	1	13	14
Hysterectomy	1	5	6
Unknown cause of admission	1	2	3
Total	6	31	37

Minor complications	Truclear	Myosure	Total
Uncomplicated fluid overload (resolved spontaneously or with intravenous Lasix)	1	18	19
Pelvic infection	0	4	4
Uterine perforation (needing no additional surgery or treatment)	6	22	28
Postoperative bleeding (controlled with non-invasive measures)	1	5	6
Device failure	9	16	25
Total	17	65	82

2 patients with bowel damage needed temporary colostomies and were admitted into the intensive care unit.

2 patients had a hysterectomy ‘per patient request’ after the diagnoses of uterine perforation and a failed endometrial ablation. 3 patients needed hysterectomy because of excessive blood loss.

11 patients with fluid overload needed intubation and admission to the intensive care unit.

Device failure included metal shavings and broken pieces of device visualised in the uterine cavity, poor visualisation, failure of outflow, and a defective device that would not activate. In 1 reported case, the blade fell into the uterine cavity and could not be retrieved. A hysterectomy was done and the patient did well postoperatively.

Of the 2 deaths, 1 was in a patient with multiple comorbidities such as chronic hypertension and obesity; the patient desaturated during anaesthesia and was diagnosed with pulmonary embolism and died. The second patient was an elderly woman who ‘was not well’; she was readmitted the day after her procedure and died shortly after. An exact cause of death was not reported.

It is estimated that approximately 80,000 Myosure devices have been sold since FDA approval in 2009 and an estimated 100,000 Truclear procedures have been done since 2004.

Estimated complication rate=0.07% (119/180,000); 0.1% for the Myosure hysteroscopic morcellator and 0.02% for the Truclear device.

Study 12 Benton A (2018)

Study details

Study type	Case report
Country	US
Recruitment period	Procedure was done in 2013
Study population and number	n=1 Patient with disseminated peritoneal leiomyomatosis after hysteroscopic fibroid morcellation
Age	Age at time of procedure not reported
Patient selection criteria	Not applicable
Technique	Mechanical hysteroscopic myomectomy
Follow-up	Not reported (period between procedure and referral was at least 4 years).
Conflict of interest/source of funding	None

Key safety findings

The patient presented for laparoscopic hysterectomy in the setting of infertility and known uterine fibroids. As part of her infertility work-up and treatment, the patient had a laparoscopy, which showed a pelvis free of fibroids, and a mechanical hysteroscopic myomectomy in 2013. The pathology report from the procedure was consistent with leiomyoma. The patient was unable to conceive and she continued to have heavy menstrual bleeding and developed symptomatic anaemia. She had a repeat dilation and curettage without hysteroscopy in 2017 and a large posterior fibroid was noted.

She then had a total laparoscopic hysterectomy, bilateral salpingectomy, and left oophorectomy. At the time of the procedure, the patient had an approximate 14-week size, globular retroverted uterus with multiple fibroids and severe adhesive disease. There were numerous individual deposits throughout the peritoneum and omentum that appeared to be consistent with fibroids. In addition, there was leiomyomatous disease on the ovaries bilaterally and a large cyst on the left ovary. Pathology from surgery returned showing a benign serous cystadenoma, endometriosis, and diffuse peritoneal leiomyomatosis.

The authors concluded that hysteroscopic mechanical morcellation of symptomatic fibroids can cause intraperitoneal spillage of intrauterine contents, which could result in intra-abdominal pathology.

Validity and generalisability of the studies

- The randomised controlled trial comparing hysteroscopic morcellation with conventional resection included a high proportion of patients with polyps rather than fibroids; the results were not reported separately (Van Dongen H, 2008).
- The review of events reported on the MAUDE database used the number of devices sold as a surrogate for the number of procedures done to calculate an approximate complication rate. It also included patients who were treated for polyps as well as those treated for fibroids (Haber K, 2015).
- The randomised controlled trials included only type 0 and type 1 submucous myomas smaller than 3 cm (Van Dongen H, 2008; Rubino R, 2015). Most of the other studies included some patients with type 2 fibroids. Where stated, all studies included submucosal fibroids only.
- Most studies reported a follow-up period of 12 months or less. One study had a mean follow-up of 32 months (Maheux-Lacroix S, 2017). One study reported a follow-up period of up to 5 years, but most patients had not yet reached the 3-year follow-up evaluation (Vidal-Mazo C, 2019).
- Different devices were used for the procedure. Only 1 of the systematic reviews included studies that used the Intrauterine Bigatti Shaver device (Yin X, 2018).
- The indications for treatment varied between studies. One study only included premenopausal patients (Vidal-Mazo C, 2019) and 1 only included pre- or peri-menopausal patients (Rubino R, 2015).
- There are data from the UK, Europe, US, Australia and China.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure (some are not relevant to type 0 and type 1 fibroids).

Interventional procedures

- Ultrasound-guided high-intensity transcutaneous focused ultrasound for symptomatic uterine fibroids. NICE interventional procedures guidance 657 (2019). Available from http://www.nice.org.uk/guidance/IPG657
- Hysteroscopic morcellation of uterine leiomyomas (fibroids). NICE interventional procedures guidance 522 (2015). Available from http://www.nice.org.uk/guidance/IPG522 *[current guidance under review]*
- Magnetic resonance image-guided transcutaneous focused ultrasound for uterine fibroids. NICE interventional procedures guidance 413 (2011). Available from http://www.nice.org.uk/guidance/IPG413
- Uterine artery embolisation for fibroids. NICE interventional procedures guidance 367 (2010). Available from http://www.nice.org.uk/guidance/IPG367
- Magnetic resonance (MR) image-guided percutaneous laser ablation of uterine fibroids. NICE interventional procedures guidance 30 (2003). Available from http://www.nice.org.uk/guidance/IPG30
- Laparoscopic laser myomectomy. NICE interventional procedures guidance 23 (2003). Available from http://www.nice.org.uk/guidance/IPG23

NICE guidelines

- Heavy menstrual bleeding: assessment and management. NICE guideline 88 (2018). Available from http://www.nice.org.uk/guidance/NG88

Additional information considered by IPAC

Professional experts' opinions

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by professional experts, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Two Professional expert questionnaires for hysteroscopic morcellation of uterine fibroids were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme will send questionnaires to NHS trusts for distribution to patients who had the procedure (or their carers). When NICE has received the completed questionnaires, these will be discussed by the committee.

Company engagement

A structured information request was sent to 2 companies who manufacture a potentially relevant device for use in this procedure. NICE received 2 completed submissions. These were considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

- In April 2014, the FDA issued a safety communication that discouraged the use of **laparoscopic power morcellation** during hysterectomy or myomectomy for the treatment of women with fibroids. It stated that the FDA is concerned about women undergoing **laparoscopic power morcellation** for the treatment of uterine fibroids and the risk of inadvertent spread of unsuspected cancer to the abdominal and pelvic cavities. This concern is described in the committee comments of the current guidance.
- Ongoing trials
  - The Hysteroscopic Morcellator Versus the Bipolar Resectoscope for Removal of Larger Intrauterine Polyps, Removal of Submucous Myomas and Removal of Residual Placental Tissue: a Randomized Controlled Trial (NCT01537822); RCT; Belgium and the Netherlands; n=222; Study start date: May 2011; Estimated Study Completion Date: September 2021

References

1. Yin X, Cheng J, Ansari SH et al. (2018) Hysteroscopic tissue removal systems for the treatment of intrauterine pathology: a systematic review and meta-analysis. Facts, Views & Vision in ObGyn 10: 207–13, published online Jul 24 2019
2. Shazly SAM, Laughlin-Tommaso SK, Breitkopf DM et al. (2016) Hysteroscopic morcellation versus resection for the treatment of uterine cavitary lesions: a systematic review and meta-analysis. Journal of Minimally Invasive Gynecology 23: 867–77
3. van Dongen H, Emanuel MH, Wolterbeek R et al. (2008) Hysteroscopic morcellator for removal of intrauterine polyps and myomas: a randomized controlled pilot study among residents in training. Journal of Minimally Invasive Gynecology 15: 466–71
4. Lee MMH, Matsuzono T (2016) Hysteroscopic intrauterine morcellation of submucosal fibroids: preliminary results in Hong Kong and comparisons with conventional hysteroscopic monopolar loop resection. Hong Kong Medical Journal 22: 56–61
5. Maheux-Lacroix S, Mennen J, Arnold A et al. (2018) The need for further surgical intervention following primary hysteroscopic morcellation of submucosal leiomyomas in women with abnormal uterine bleeding. Aust N Z J Obstet Gynaecol 58: 570–75
6. Vidal-Mazo C, Forero-Diaz C, Lopez-Gonzalez E et al. (2019) Clinical recurrence of submucosal myoma after a mechanical hysteroscopic myomectomy: Review after 5 years follow up. European Journal of Obstetrics, Gynecology, and Reproductive Biology 243: 41–45
7. Scheiber MD, Chen SH (2016) A prospective multicenter registry of patients undergoing hysteroscopic morcellation of uterine polyps and myomas. Journal of Gynecologic Surgery 32: 318–23
8. Arnold A, Ketheeswaran A, Bhatti M et al. (2016) A prospective analysis of hysteroscopic morcellation in the management of intrauterine pathologies. Journal of Minimally Invasive Gynecology 23: 435–41
9. Rubino RJ, Lukes AS (2015) Twelve-month outcomes for patients undergoing hysteroscopic morcellation of uterine polyps and myomas in an office or ambulatory surgical center. Journal of Minimally Invasive Gynecology 22: 285–90
10. Bhalani V, Chang A, Adkins C et al. (2016) Fertility outcomes after hysteroscopic morcellation of intrauterine leiomyomas and polyps. The Journal of Reproductive Medicine 61: 327–35

11. Haber K, Hawkins E, Levie M et al. (2015) Hysteroscopic morcellation: review of the manufacturer and user facility device experience (MAUDE) database. Journal of Minimally Invasive Gynecology 22: 110–14

12. Benton A, Sood S, Wagner S et al. (2018) Disseminated peritoneal leiomyomatosis following hysteroscopic leiomyoma morcellation. Journal of Gynecologic Surgery 34: 319–21

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	20/10/2020	Issue 10 of 12, October 2020
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	20/10/2020	Issue 10 of 12, October 2020
MEDLINE (Ovid)	20/10/2020	1946 to October 19, 2020
MEDLINE In-Process (Ovid) & Medline ePub ahead (Ovid)	20/10/2020	October 19, 2020
EMBASE (Ovid)	20/10/2020	1974 to 2020 October 19

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1 Uterine Neoplasms/ and Leiomyoma/ (11317)
2 ((uter* or intrauter*) adj4 (neoplasm* or tumour* or tumor* or growth* or fibroma* or leiomyoma* or leimyoma* or angioleiomyoma* or angiomyoma* or myofibroma* or leyomyoma or lesion*)).tw. (27453)
3 (fibromyoma* or fibroleiomyoma).tw. (710)
4 ((fibroid* or myoma*) adj4 (tumour* or tumor* or uter* or intrauter* or submucos* subseros* or intramural* or pedunculated or cervical)).tw. (6598)
5 or/1-4 (37272)
6 Morcellation/ (277)
7 (hysteroscop* adj5 (morcellat* or cut* or suck* or suction* or remov* or myomectom* or excis* or shav*)).tw. (709)
8 Hysteroscopy/ and uterine myomectomy/ (98)
9 (transcervical adj4 resection).tw. (320)
10 TCRE.tw. (91)
11 Myosure*.tw. (19)
12 Truclear*.tw. (10)
13 Bigatti*.tw. (2)
14 Symphion*.tw. (0)
15 or/6-14 (1337)
16 5 and 15 (550)

17	animals/ not humans/ (4711655)
18	16 not 17 (549)

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the summary of the key evidence. It is by no means an exhaustive list of potentially relevant studies.

Additional papers identified

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in key evidence summary
Bigatti G, Franchetti S, Rosales M et al. (2014) Hysteroscopic myomectomy with the IBS® Integrated Bigatti Shaver versus conventional bipolar resectoscope: a retrospective comparative study. Gynecol Surg 11: 9–18	Retrospective non-randomised comparative study n=127	The results show no difference in terms of cervical dilatation, resection time, and fluid deficit between the 2 groups, but, for fibroids less than 3 cm and type 2 fibroids, the device has been able to treat respectively 94% and 63% of cases in a single step procedure. The overall number of second procedures was statistically significantly less in the hysteroscopic morcellation group than in the conventional resectoscopy group (p=0.0067).	Study is included in systematic review by Yin et al, 2018.
Bigatti G; Ferrario C; Rosales M; et al. (2012) IBS® Integrated Bigatti Shaver versus conventional bipolar resectoscopy: a randomised comparative study. Gynecol Surg 9: 63–72	RCT n=100 (22 patients with fibroids)	There were no complications in the hysteroscopic morcellation group. The smaller IBS device is easier to apply than the conventional resectoscope. Surgery is not interrupted by tissue chips removal making total operating time shorter. It is postulated that resection of fibroids without the use of electrical current could significantly reduce the	Most patients had polyps. Study is included in systematic review by Yin et al, 2018.

		postoperative adhesion formation. Further studies are needed to tailor the indication potential of this approach.	
Bigatti G, Ferrario C, Rosales M et al. (2012) A 4-cm G2 cervical submucosal myoma removed with the IBS® Integrated Bigatti Shaver. Gynecol Surg 9:453–56	Case report n=1	The device was able to remove in a 2-step procedure a very large cervical type 2 submucosal fibroid, considered 1 of the most difficult cases to approach by conventional resectoscopy.	Case report
Bigatti G. (2011) IBS® Integrated Bigatti Shaver, an alternative approach to operative hysteroscopy. Gynecological surgery 8: 187 - 91	Case series n=44 (15 myomas, 2 polyps and myomas) FU=not reported	There were 2 overload complications: 1 was caused by a malfunctioning of the fluid management system. The second complication happened during a 3 cm type 2 fibroid resection.	Studies with more patients or longer follow-up are included.
Cohen S, Greenberg JA. (2011) Hysteroscopic morcellation for treating intrauterine pathology. Reviews in Obstetrics and Gynecology 4: 73–80	Review	Hysteroscopic morcellation allows for the use of smaller diameter hysteroscopes that need less cervical dilation and less anaesthesia than traditional hysteroscopic resection.	No meta-analysis. A more recent systematic review is included.
Emanuel MH, Wamsteker K (2005) The Intra Uterine Morcellator: a new hysteroscopic operating technique to remove intrauterine polyps and myomas. Journal of Minimally Invasive Gynecology 12: 62–6	Non-randomised comparative study n=200 (28 vs 172) FU=3 months	Complete removal of fibroid in a single procedure=93% (26/28). Mean operating time (minutes) • Hysteroscopic morcellation=16.4 (95% CI 12.6 to 20.2) • Conventional resection=42.2 (95% CI 39.7 to 44.7) Fluid loss deficit (ml) • Hysteroscopic morcellation=660.0 (95% CI 418.6 to 901.4)	Included in systematic review by Shazly et al., 2016.

		• Conventional resection=741.8 (95% CI 645.9 to 837.7) All patients were symptom free at follow-up.	
Fonge YN, Carter AS, Hoffman MK et al. (2020) Obstetrical outcomes are unchanged after hysteroscopic myomectomy in women with submucosal fibroids. American Journal of Obstetrics and Gynecology MFM 2: 100192	Case control study n=277	Overall, women with submucosal uterine fibroids who have hysteroscopic removal have similar birth outcomes to those who do not.	Only a small proportion of patients had hysteroscopic morcellation.
Friedman JA, Wong JMK, Chaudhari A et al. (2018) Hysteroscopic myomectomy: a comparison of techniques and review of current evidence in the management of abnormal uterine bleeding. Current Opinion in Obstetrics & Gynecology 30: 243-251	Review	Although the hysteroscopic morcellators have been associated with shortened operative time and a decreased learning curve, the data are limited for their use on type 2 fibroids. The evidence suggests that no one technique should be used for all patients, but rather a choice of technique should be taken on a case-by-case basis, depending on the myoma number, size, type, and location.	A systematic review and meta-analysis is included.
Georgiou D, Tranoulis A, Jackson TL (2018) Hysteroscopic tissue removal system (MyoSure) for the resection of polyps, sub-mucosal leiomyomas and retained products of conception in an out-patient setting: A single UK institution experience. European Journal of Obstetrics,	Case series n=124	98% (107/109) of polyps and 74% (14/19) of fibroids were completely resected. 7% (9/124) of women experienced severe pain during the procedure, while 17% and 73% reported moderate and mild pain respectively. 99% (123/124) of women would have the procedure again in the future or recommend it to a friend,	Most of the patients had polyps rather than fibroids.

Gynecology, and Reproductive Biology 231: 147-151		for a similar pathology removal.	
Hamerlynck TWO, Dietz V, Schoot BC (2011) Clinical implementation of the hysteroscopic morcellator for removal of intrauterine myomas and polyps. A retrospective descriptive study. Gynecological Surgery 8: 193-196	Case series n=315 (37 fibroids)	In 37 patients who had hysteroscopic morcellation for fibroids, mean installation time was 9 min, mean operating time 18 min, and median fluid deficit, 440 mL. 8% (3/37) procedures were converted to resectoscopy, related to a type 2 myoma. All procedures were uneventful. Hysteroscopic morcellation for removal of type 0 and 1 myomas ≤3 cm, and removal of polyps appears safe and effective.	Studies with more patients or longer follow-up are included.
Indraccolo U, Bini V, Favilli A (2020) Likelihood of accomplishing an in-patient hysteroscopic myomectomy in a one-step procedure: a systematic review and meta-analysis. BioMed Research International 2020: 4208497	Systematic review and meta-analysis 63 references	There is no single hysteroscopic technique proven to be unequivocally superior to the others for treating submucous fibroids with intramural development in one-surgical step. Nevertheless, despite the heterogeneity found among the clinical series analysed, it seems that all the techniques used to deal with the intramural portion of myomas work better than the slicing technique, achieving a higher rate of procedures accomplished in a single surgical time and a lower number of complications.	Only 1 study on hysteroscopic morcellation was included in the meta-analysis.
Li C, Dai Z, Gong Y et al. (2017) A systematic review and meta-analysis of randomized controlled trials comparing	Systematic review and meta-analysis n=392 (4 trials)	Hysteroscopic morcellation is associated with a higher operative success rate and a shorter operative time among patients with endometrial lesions than is	Only 1 trial included patients with fibroids (Van Dongen et al., 2008)

hysteroscopic morcellation with resectoscopy for patients with endometrial lesions. Int J Gynecol Obstet 136: 6-12		resectoscopy. More high-quality trials are required to validate these results.	
Liang Y, Ren Y, Wan Z et al. (2017) Clinical evaluation of improved MyoSure hysteroscopic tissue removal system for the resection of type II submucosal myomas. Medicine 96: e9363	Case series n=53 FU=6 months	Success rate=96% The low rate of 1-time complete resection for type II submucosal myomas could be improved by combining new apparatus with the MyoSure system. Meanwhile, the advantages of the MyoSure system, including the efficiency and safety, were maintained.	Studies with more patients or longer follow-up are included.
Lukes AS, Roy KH, Presthus JB et al. (2015) Randomized comparative trial of cervical block protocols for pain management during hysteroscopic removal of polyps and myomas. International Journal of Women's Health 7: 833-839	RCT (comparing pain management) n=40 (patients had polyps or fibroids)	Pain during hysteroscopic morcellation of intrauterine polyps and type 0 or 1 myomas can be successfully managed with a local anaesthetic. Two different pain management protocols, a combination para/intracervical block and an intracervical block, were both associated with low pain scores.	Study focuses on pain management, and only a small proportion of the lesions were fibroids.
Miller C, Glazerman L, Roy K et al. (2009) Clinical evaluation of a new hysteroscopic morcellator – retrospective case review. The Journal of Medicine 2: 163–6	Case series n=11 (6 fibroids)	Mean morcellation time for complete resection: • Type 0 fibroids=2 minutes 19 seconds • Type I fibroids=9 minutes 10 seconds Mean fluid deficit (ml): • Type 0 fibroids=205 (range 200–210) • Type I fibroids=1300 (range 500–1900)	Larger studies are included.

Noventa M, Ancona E, Quaranta M et al. (2015) Intrauterine morcellator devices: the icon of hysteroscopic future or merely a marketing image? A systematic review regarding safety, efficacy, advantages, and contraindications. Reproductive Sciences 22: 1289–96	Systematic review n=8 studies	The available evidence allows us to consider intrauterine morcellation devices as a safe, effective, and cost-effective tool for the removal of intrauterine lesions such as polyps, myomas (type 0 and type 1), and placental remnants. Further studies are needed to confirm the available evidence and to validate the long-term safety of procedures for which current data are not exhaustive (placental remnants removal).	No meta-analysis. All relevant studies have been described in the overview, either in the key evidence summary or the appendix.
Ota K, Takahashi T, Kamo N et al. (2020) Successful management of a submucosal fibroid using a hysteroscopic morcellator system in a patient with a history of total proctocolectomy: A case report. Journal of Obstetrics and Gynaecology Research	Case report n=1	Case report of patient with multiple fibroids, including a submucosal type 1 fibroid, who had previously had a total proctocolectomy with intestinal pouch-anal anastomosis for ulcerative colitis. Because there was a high risk of permanent colostomy in the event of a bowel injury, an electrode-free, operative hysteroscopy using the Intrauterine Bigatti Shaver (IBS), a hysteroscopic morcellator system, was used to prevent thermal bowel injury. The fibroid was completely removed with no complications.	Case report – no safety events identified
Pakrashi T, Ressler IB, Sroga JM et al. (2013) Hysteroscopic enucleation of type II submucosal uterine leiomyomas using a TRUCLEAR hysteroscopic morcellator: case	Case report n=1	Case report - complete enucleation of a Type II leiomyoma Hysteroscopic uterine leiomyoma enucleation should only be performed in experienced hands. Inadvertent enucleation of	Case report – no safety events identified

report and review of the literature. Journal of Laparoendoscopic & Advanced Surgical Techniques 23: 378-382		a Type II leiomyoma with a THM device is described, with review of key surgical principles that guided safe resection.	
Rothenberg S, Nayak S, Sanfilippo JS (2014) Clinical use of the intrauterine morcellator: a single academic center's experience. Open Journal of Obstetrics and Gynecology 4: 326–32	Case series n=28 (18% fibroids)	Mean operative time (minutes)=47±20.9 Mean fluid deficit (ml) = 785±956.7 Complication rate=6%	Small study with mixed indications – only 18% of patients had fibroids.
Rubino RJ, Roy KH, Presthus J et al. (2017) Abnormal uterine bleeding control by sequential application of hysteroscopic lesion morcellation and endometrial ablation. The Journal of Reproductive Medicine 62: 102–10	Case series n=26 FU=12 months	Sequential hysteroscopic morcellation and endometrial radiofrequency ablation of intrauterine lesions in women with abnormal uterine bleeding increases amenorrhea rate, alleviates bleeding symptoms, and improves quality of life, with an acceptable safety profile.	Small case series in which hysteroscopic morcellation was followed by endometrial radiofrequency ablation.
Spies JB, Bradley LD, Guido R et al. (2010) Outcomes from leiomyoma therapies. Comparison with normal controls. Obstet Gynecol 116: 641–52	Non-randomised comparative study n=375	At 12 months after treatment, all 3 therapies (hysterectomy, myomectomy, uterine artery embolisation) resulted in substantial symptom relief, to near normal levels, with the greatest improvement after hysterectomy.	Only a small proportion of patients had hysteroscopic myomectomy and it is unclear if any had morcellation.
Vitale SG, Sapia F, Rapisarda AMC et al. (2017) Hysteroscopic morcellation of submucous myomas: a systematic review. BioMed Research International 2017: 6848250	Systematic review n=8 studies	The available studies differ regarding methodology and inclusion and exclusion criteria. Hysteroscopic tissue removal systems reduced operative time compared to traditional resectoscopy in some studies, whereas others did not find	No meta-analysis. All included studies have been described in the overview, either in the key evidence

		significant differences. Despite the availability of few randomised controlled trials and the cost of the instrument, this seems to be a feasible surgical option in terms of operative time and complications. Nevertheless, the type of submucous fibroid remains the biggest challenge: type 0 and 1 are easier to manage than type 2.	summary or the appendix.
Yin X, Cheng J, Ansari SH, et al. (2018) Hysteroscopic tissue removal systems for the treatment of intrauterine pathology: a systematic review and meta-analysis. Facts Views Vis Obgyn. 10: 207–213	Systematic review and meta-analysis n=498 (5 studies)	Hysteroscopic tissue removal systems showed a significantly higher success rate of complete endometrial pathology removal (p=0.002) and a significantly shorter operation time for polyp removal (p<0.0001) compared to conventional resectoscopy. No significant differences, in terms of complications rate, were found (p=0.09). The fluid deficit was significantly higher in the tissue removal system group, compared to conventional resectoscopy (p=0.02).	Of the 5 included studies, 2 used the Integrated Bigatti shaver device.