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Review Article

The Outcome of Fertility-Sparing and Nonfertility-Sparing Surgery for the Treatment of Adenomyosis. A Systematic Review and Meta-analysis

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ABSTRACT **Objective:** The purpose of this systematic review was to identify the operative issues and specific dysmenorrhea and menorrhagia outcomes in women who had undergone fertility-sparing surgery, as well as determine the expected outcome for extirpative surgery.

Data Sources: PROSPERO (ID no. 125692). Search was conducted for eligible studies up to March 31, 2019, on MEDLINE/PubMed (1966−2019), Scopus/Elsevier (1950−2019), and Google Scholar (up to 2019). The search terms applied for the search strategy were as follows: adenomyosis, adenomyomas, uterus-sparing surgery, fertility-sparing surgery, pain, dysmenorrhea, menorrhagia, uterine volume, adenomyotic volume, case-control studies, cohort studies, and prospective studies.

Methods of Study Selection: A total of 443 studies were initially identified. Exclusion criteria was as follows: (1) inadequate description of preoperative adenomyosis or absence of postoperative histology confirmation of adenomyosis, (2) no statement of use of a standardized instrument for measurement of pain, bleeding, or adenomyotic/uterine volume, (3) follow-up <12 months postoperatively, (4) study population <20 women, and (5) non-English language.

Tabulation, Integration, and Results: Nineteen studies with a total of 1843 patients with adenomyosis were included. Twelve studies were further analyzed in the meta-analysis. Complete excision of adenomyosis was associated with improvement in pain, menorrhagia, and reduction of uterine volume by a factor of 6.2, 3.9, and 2.3, respectively; the partial excision of adenomyosis was associated with improvement in pain, menorrhagia, and reduction of uterine volume by a factor of 5.9, 3.0, and 2.9, respectively; the studies with a mixed volume of patients with complete and partial excision of adenomyosis reported improvement in pain, menorrhagia, and reduction of uterine volume by a factor of 4.0, 6.3, and 5.1, respectively.

Conclusion: The surgical treatment of adenomyosis results in the satisfactory control of pain and bleeding, as well as in the reduction of uterine volume. Further research is warranted to investigate the long-term control of symptoms to identify any parameters related to the recurrence of adenomyosis, as well as to compare the conservative surgical treatment of adenomyosis with other treatment options. Journal of Minimally Invasive Gynecology (2019) 00, 1−23. © 2019 AAGL. All rights reserved.

Keywords: Adenomyosis; Bleeding; Menorrhagia; Pain; Uterus-sparing surgery

Introduction

Rationale

Uterine adenomyosis is a condition characterized by the presence of endometrial glands along with endometrial stroma and a variable degree of smooth muscle hyperplasia within the myometrium [1−3]. The histologic appearance of adenomyosis is chimeric: depending on the depth and the extent of myometrial invasion, the disease can be either

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diffuse or localized (focal), whereas the texture of the lesions can range from mostly solid to mostly cystic [1−3]. Currently, no consensus has been reached regarding the classification of adenomyosis, and the disease can be classified as internal or external adenomyosis or adenomyomas [4,5]. Based on the degree of invasion of the disease, the adenomyotic variants include the following: (1) diffuse disease, in which the foci of ectopic endometrial mucosa are scattered throughout the uterine musculature, (2) focal disease, in which the affected area is markedly restricted and embedded within the myometrium, and (3) exomyometrial types, which can take the forms of polypoid adenomyomas, adenomyomas of the endocervical type, and retroperitioneal adenomyomas [1,5−8]. However, in numerous cases, adenomyosis can be silent and asymptomatic. Clinically, it has been associated with menorrhagia, dysmenorrhea, and chronic pelvic pain, and it may be associated with subfertility depending on the extent, location, and composition of the lesion [1−3,9]. In terms of treatment, this usually comprises a step-up strategy, starting with conservative symptomatic (nonhormonal and hormonal) medication, followed by conservative surgical techniques (uterus-sparing techniques: endometrial ablation and surgical removal of adenomyotic tissue), and escalating in hysterectomy in older women with resistant disease [1−3].

Uterus-sparing surgical treatment of adenomyosis includes the complete or partial excision of the lesion, but there are numerous nonexcisional techniques that have been attempted to control the symptoms [2,3]. Complete excision of adenomyosis, or adenomyomectomy, is normally used in cases of focal adenomyosis or cystic adenomyomas, but it also is associated with surgical techniques in which all the clinically recognizable nonmicroscopic lesions of diffuse adenomyosis are removed during an extirpative surgery. Partial excision of adenomyosis or cytoreductive surgery is usually associated with cases of diffuse adenomyosis in which the removal of nonmicroscopic lesions is only partial because further tissue excision could lead to a "functional hysterectomy." All endometrial resection/ablation techniques (e.g., uterine artery occlusion), which mainly do not involve excision of myometrium, are classified into the group of nonexcisional techniques [2,3]. These techniques aim to control the symptoms of adenomyosis, prevent early recurrences, and offer an optimal uterine environment for conception and pregnancy.

The purpose of this systematic review was to identify the operative issues and specific dysmenorrhea and menorrhagia outcomes in women who underwent fertility-sparing surgery, as well as determine the expected outcome for extirpative disease.

Methods

Protocols and Registration

The current review was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews. All data included in the review are deidentified, and therefore, institutional review board permission was not sought. The review was registered in PROSPERO (ID no. 125692). The aim of this review was to study the outcome of the surgical treatment of women with adenomyosis; the type of conservative surgery should be either complete adenomyomectomy, partial adenomyomectomy, or a type of nonexcisional technique. The patients were observed with respect to the postoperative outcome of (1) pain/dysmenorrhea, (2) bleeding/menorrhagia, and (3) adenomyotic/uterine volume. This review included only randomized controlled trials, cohort studies, and case-control studies; the studies had to report a follow-up of at least 12 months after surgery.

Eligibility Criteria

Studies were included in this review if they met the following criteria: (1) a clear statement of preoperative diagnosis of adenomyosis and a postoperative histology confirmation, (2) a clear statement of use of specific ultrasound or magnetic resonance imaging (MRI) diagnostic criteria for adenomyosis, (3) use of specific standardized symptoms (pain, bleeding) reporting instruments (e.g., Visual Analog Scale [VAS]) and/or preoperative and postoperative standardized measurement of uterine volume, and (4) full description of the operative technique described meticulously in the text of the study.

Exclusion criteria were as follows: (1) case reports or small case series (<20 patients), (2) studies in which the primary and the secondary outcomes were not adequately or clearly described, (3) studies with no preoperative ultrasound/MRI diagnosis or postoperative histology for all patients, and (4) studies not written in English.

Information Sources

For the constellation of this systematic review, 2 reviewers (ML and TM) independently searched for eligible studies up to March 31, 2019, on the MEDLINE/PubMed (1966−2019) and Scopus/Elsevier (1950−2019) databases and Google Scholar (up to 2019). Studies from abstracts volumes or publications in non−peer-reviewed journal were not included.

Search

The review was restricted to published research articles that reported the surgical uterus-sparing management of women with adenomyosis and the postoperative description of their symptoms during at least a medium-term follow-up. The search terms applied for the search strategy were as follows: adenomyosis, adenomyomas, uterus-sparing surgery, fertility-sparing surgery, pain, dysmenorrhea, dyspareunia, bleeding, menorrhagia, uterine volume, adenomyotic volume, case-control studies, cohort studies, and

Table 1

MeSH Term Search and Terms for Google Scholar Search

Source	Search terms
MEDLINE/PubMed	#1 (ablation[MeSH] OR resection[MeSH]) AND ((“adenomyosis”[MeSH]) OR (“adenomyoma”[MeSH])) #2 (“hysterectomy”[MeSH]) AND ((“adenomyosis”[MeSH]) OR (“adenomyoma”[MeSH])) #3 (Outcome[All Fields] AND (“hysterectomy”[MeSH])) AND ((“adenomyosis”[MeSH]) OR (“adenomyoma”[MeSH])) #4 (“conservative treatment”[MeSH Terms] OR (“conservative”[All Fields] AND “treatment”[All Fields]) AND (“adenomyosis”[MeSH]) #5 ((“fertility”[MeSH]) AND (“surgery”[Subheading] OR “surgical procedures, operative”[MeSH Terms] AND “operative”[All Fields]) OR “operative surgical procedures”[All Fields] OR “surgery”[All Fields] OR “general surgery” [MeSH Terms])) AND ((“adenomyosis”[MeSH]) OR (“adenomyoma”[MeSH])) #6 (“surgery”[Subheading] OR “surgical procedures, operative”[MeSH Terms] OR (“surgical” [All Fields] AND “procedures”[All Fields] AND “operative”[All Fields]) OR “operative surgical procedures”[All Fields] OR “surgery”[All Fields]) AND ((“adenomyosis”[MeSH]) OR (“adenomyoma”[MeSH])) #7 ((“fertility”[MeSH]) AND (“therapy”[Subheading] OR “treatment”[All Fields] OR “therapeutics”[MeSH])) AND ((“adenomyosis”[MeSH]) OR (“adenomyoma”[MeSH]))
Google Scholar	#1 (fertility) AND (surgery) AND (adenomyosis) #2 (outcome) AND (hysterectomy) AND (adenomyosis)

prospective studies. The literature search in MEDLINE/PubMed was conducted using specific medical subject heading terms (MeSH) (Table 1). The literature search in Scopus and Google Scholar was conducted with a specific combination of keywords (Table 1). All the review articles published on adenomyosis during the same period were consulted, and their reference lists were searched for possible additional sources.

Study Selection

Two authors (TM and ML) independently performed an initial screening of the study titles/abstracts and excluded all irrelevant publications. In case of a disagreement, a third author (GFG) was consulted, and a decision was reached after discussion. The studies were then checked for full eligibility. Studies that reported no use of standardized instruments of pain, bleeding, or quality of life measurements, studies that had follow-up <12 months, and small case series/case reports were excluded. All other studies were included in the review. All studies that reported measurable and comparable postoperative outcomes were included in the meta-analysis.

Data Collection Process: Data Items

Data were extracted using a Microsoft Excel data sheet. Specific data items searched in each study were as follows: (1) the presence of preoperative ultrasound/MRI criteria for the diagnosis of adenomyosis, (2) a full description of a uterus-sparing technique, (3) a preoperative and postoperative estimation of adenomyotic/uterine volume, (4) a description of a specific standardized reporting instrument for pelvic pain or dysmenorrhea, (5) a description of a specific standardized reporting instrument for menorrhagia, (6) the rates of reoperation, and (7) a report of immediate- and middle-term complications. The following parameters were evaluated for cases and controls in the studies: (1) the number of individuals included in the study, (2) the demographics (age, body mass index [BMI], gravidity, and parity), (3) preoperative measurements (adenomyotic/uterine volume [cm^3], pain score, bleeding score), (4) length of follow-up (months), (5) postoperative measurements (pain score, pain score reduction [%], bleeding score, bleeding score reduction [%]), (6) intraoperative and postoperative complications, and (7) reoperation rates. All categorical data were expressed in means and standard deviations (SDs).

A data extraction form was completed, and all data from the eligible studies were entered into Review Manager (RevMan 5.3 software; The Cochrane Collaboration, Copenhagen, Denmark). The systematic review description process was performed according the recommendations for the reporting of Meta-analysis of Observational Studies in Epidemiology [10] and the PRISMA guidelines [11].

Risk of Bias in Individual Studies

Two independent reviewers (ML and TM) evaluated each study for any risk of bias using the Newcastle-Ottawa Coding Quality Assessment Scale (NOS) for the assessment of cohort and case-control studies, and the corresponding form of NOS for cross-sectional studies. The NOS form includes 3 main domains: selection, comparability, and outcome (cohort and cross-sectional studies), or selection, comparability, and outcome (case-control studies). The NOS domains are composed of items that should be evaluated, and in cases in which a study meets the predefined criteria, the study must fulfill higher quality criteria and score a star in the given domain. Regarding the domain “Selection” in the NOS for cohort studies, the items “representativeness of the exposed cohort” and “selection of the non-exposed cohort” were evaluated as fulfilled if the recruitment of the study population was performed in a

consecutive way (either prospectively or retrospectively); the items "ascertainment of exposure" and "demonstration the outcome was not present at start" were evaluated as fulfilled if all the included patients had the condition (symptomatic adenomyosis), and they were subsequently exposed to the standard intervention described in the study (excision of adenomyosis). The domain "Comparability of cohorts on the basis of the design" in the NOS for cohort studies was evaluated as fulfilled if all patients in both cohorts of intervention were allocated according to a matched design. For the domain "Outcome" in the NOS for cohort studies, the item "Assessment of outcome" was evaluated as fulfilled if there was an independent blind assessment stated in the paper or if there was a stated medical record linkage; the item "Adequate follow-up for outcomes to occur" was fulfilled if there was a postoperative follow-up of at least 12 months; and the item "Adequacy of follow-up of cohorts" was fulfilled in the studies in which both exposed and nonexposed cohorts had similar rates of loss during follow-up and a loss of <10% of the initial study cohort.

Summary Measures

The principal summary measures were the rates of postoperative improvement in women with adenomyosis in terms of pain, menorrhagia, and adenomyotic/uterine volume. Postoperative results were expressed as difference of preoperative and postoperative means.

Synthesis of Results: Risk of Bias across Studies, Additional Analysis

The degree of dysmenorrhea and menorrhagia, as well as uterine volume before and after the operation, was recorded in each intervention group. Chi-square and Fisher exact tests were used as appropriate to examine the significance of differences between various groups for the outcomes. A p-value less than .05 was defined as indicating statistical significance. Meta-analysis was performed for a follow-up period of 12 months. Standardized mean differences and 95% confidence intervals for the outcomes were calculated, using the DerSimonian-Laird random effects model [12]. Indices expressed in median values and ranges were transformed into mean and variance (SD) using the formula proposed by Hozo et al [13]. To address the heterogeneity among the studies, Cochran Q test was applied, which is included in each meta-analysis function because it forms part of the DerSimonian-Laird random effects pooling method [12]. Gavanghan et al [14] suggested that Q has low power as a comprehensive test of heterogeneity, especially when the number of studies is small (i.e., in most meta-analyses). Conversely, Q has too much power as a test of heterogeneity if the number of studies is large, as clearly demonstrated by Higgins et al [15]. In view of the low methodologic quality of most studies that have been performed, there is a tendency to advise using random effect models [16]. The quantity I2 describes the percentage of total variation across studies, which is due to true heterogeneity rather than chance, thus quantifying the effect of heterogeneity and providing a measure of the degree of inconsistency in the results of the studies, where 0% indicates no observed heterogeneity and larger values show more heterogeneity. The high I2 values in this review showed that most of the variability in this study is due to heterogeneity rather than chance. Statistical analyses were performed using MedCalc for Windows, v.12.7 (MedCalc software, Mariakerke, Belgium). In general, if a funnel plot for the number of analyzed studies as a function of the discriminatory power of the meta-analysis demonstrates a symmetric funnel-shaped distribution for the respective data sets, it suggests that publication bias is unlikely to be present. In our study, however, given the constrictions of only a few articles analyzed and subsequently a limited number of data sets available, the derived funnel plots appeared asymmetric, indicating that publication bias was most likely to be present (Comprehensive Meta Analysis v.3.3.070; Biostat Inc., Englewood, NJ) (Supplementary Figs. S1−S3).

Results

Study Selection

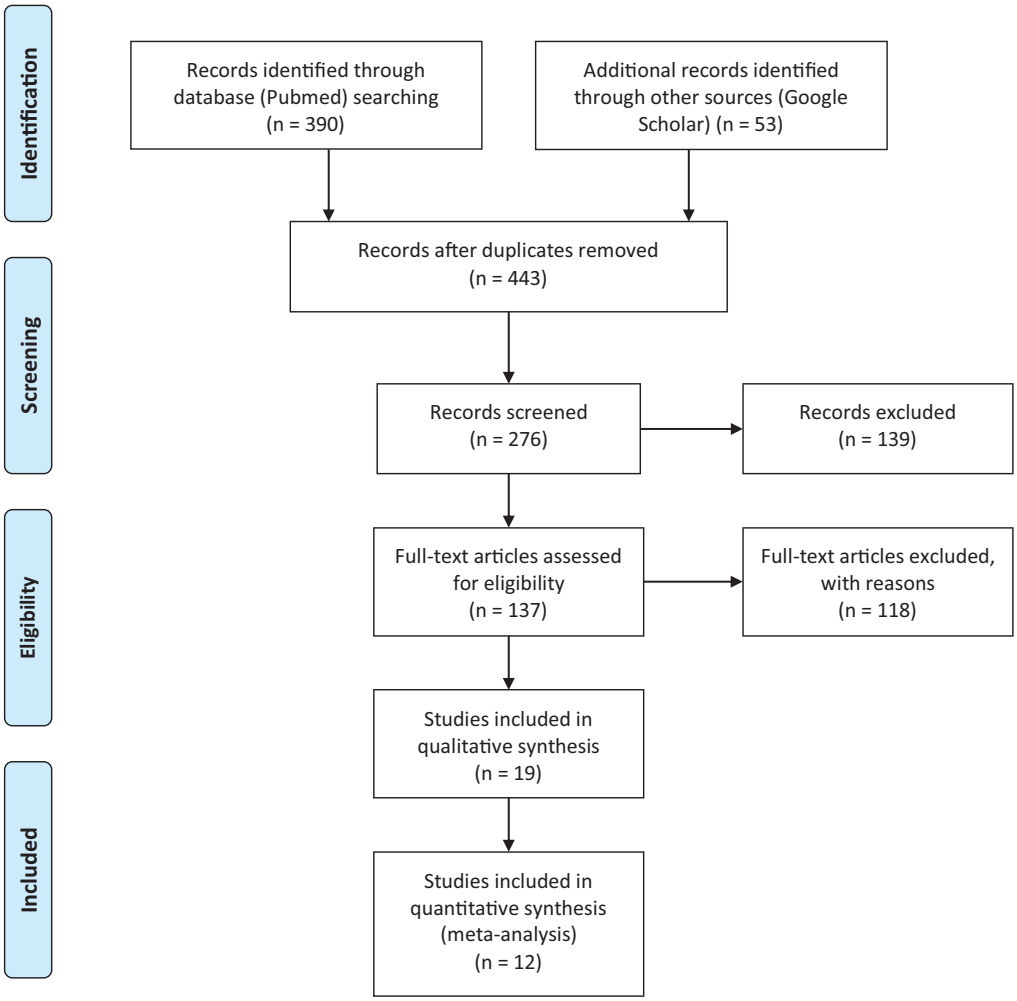
The initial PubMed search indicated 3063 articles dealing with surgical treatment and adenomyosis; additional Google Scholar and Scopus search elicited another 19 530 articles (Table 1; Fig. 1). A total of 443 studies were identified as suitable for further screening, and 137 full-text articles were assessed for eligibility, with 115 studies excluded for the following reasons: (1) inadequate description of preoperative adenomyosis or absence of postoperative histology confirmation of adenomyosis (n = 55), (2) no statement of use of a standardized instrument for measurement of pain, bleeding, or adenomyotic/uterine volume (n = 38), (3) follow-up <12 months postoperatively (n = 12), (4) study population <20 women (n = 20), and (5) non-English language (n = 14). Nineteen studies were included in qualitative synthesis, and another 12 studies were included in the meta-analysis.

Study Characteristics

Nineteen studies (n = 1843 patients with adenomyosis) were selected for qualitative review. The main characteristics of the included studies are shown in Table 2; these studies were published from 7 different countries with publication dates from 2009 to 2018, the time span of the studies ranged from 12 to 123 months and the years 1998 to 2016. The study designs were as follows: 18 cohort studies (6 prospective, 12 retrospective) and 1 prospective observational study. Five studies (n = 612 patients) reported uterus-sparing treatment of adenomyosis with complete excision

Fig. 1

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart of the study.



of adenomyosis or adenomyomectomy [17−21]. There were 2 distinct surgical approaches in this group: the traditional "wedge" or classical excisional technique [17,19,21] and a variation of the "flap" method, including studies where triple-flap or double-flap methods were applied [18,20]. Seven studies (n = 559 patients) reported uterus-sparing treatment of adenomyosis with partial excision of adenomyosis or adenomyomectomy [22−28]. In 5 studies, the traditional wedge or classical excisional technique was used [22,23,25,27,28]; 1 study described the double-flap method [26]; in another study, a hysteroscopic endomyometrial approach under ultrasound guidance was used [24]. Three studies (n = 373 patients) reported uterus-sparing treatment of adenomyosis without defining the type of excision of adenomyosis or adenomyomectomy [29−31]. Three studies (n = 256 patients) reported treatment of adenomyosis with hysterectomy [31−34]. One study (n = 43 patients) reported treatment of adenomyosis with hysteroscopic endomyometrial resection [35] (Table 2).

Regarding the use of standardized instruments for preoperative and postoperative measurement of pain and bleeding, it was found that a VAS score for pain was used in 13 studies [17,18,20,22−26,28−31,33]; a chronic pain-grade questionnaire investigating pain intensity, degree of effect on activities, and lack of energy in 1 study [19]; a verbal numeric rating scale and an analgesic usage score in 2 studies [21,27]; a 4-grade ordinal scale in 1 study [33]; and a quality of life questionnaire in 1 study [34]. For measurement of menorrhagia, the Mansfield-Voda-Jorgensen menstrual bleeding scale was used in 4 studies [17,21,23,24], a pictorial blood assessment chart in 3 studies [25,28,30], a VAS score for bleeding in 2 studies [20,31], a 5-point scale according to menses duration and anemia degree in 1 study [18], the menstrual product use of pads/day in 1 study [26],

Table 2

Characteristics of the Studies Included in the Systematic Review (PICOS)

Author, yr	Country	Start	Finish	Duration, months	Population	Intervention	Outcomes	Design
Complete excision of adenomyosis/adenomyomectomy								
Kwack et al, 2018 [17]	South Korea	Jun 2011	Jul 2016	73	Diffuse/focal adenomyosis	Laparoscopic/laparotomic occlusion of the uterine artery and adenomyomectomy	(1) Dysmenorrhea, (2) bleeding	Retrospective cohort
Chong et al, 2016 [18]	South Korea	Aug 2008	May 2011	37	Diffuse/focal adenomyosis	Laparoscopic/robotic adenomyomectomy with uterine artery ligation	(1) Pain, (2) menorrhagia	Retrospective cohort
Dai et al, 2012 [19]	China	Oct 2005	Nov 2010	62	Adenomyosis	Laparotomic local excision for uterine adenomyomas	(1) Pain, (2) bleeding, (3) recurrence	Prospective cohort
Osada et al, 2011 [20]	USA	June 1998	Aug 2008	123	Diffuse adenomyosis	Excision of diffuse adenomyosis	(1) Pain, (2) bleeding, (3) fertility outcome	Prospective cohort
Wang et al, 2009 [21]	Taiwan	N/A	N/A	N/A	Local adenomyosis	Group A: (1) excision of local adenomyosis, group B: (2) excision of local adenomyosis + postop GnRH	(1) Pain, (2) bleeding	Prospective cohort
Partial excision of adenomyosis								
Yu et al, 2018 [22]	China	Nov 2005	Nov 2015	120	Diffuse/focal adenomyosis	Laparoscopic adenomyomectomy	Identify predictors of unsuccessful operation for adenomyosis	Retrospective cohort
Jun-Min et al, 2018 [23]	China	Jan 2012	Nov 2014	34	Diffuse/focal adenomyosis	Laparotomy. Modified excision of diffuse adenomyosis	(1) Bleeding, (2) dysmenorrhea, (3) uterine volume	Retrospective cohort
Xia et al, 2017 [24]	China	Oct 2012	Oct 2014	24	Diffuse/focal adenomyosis	Ultrasound-guided resectoscopic adenomyomectomy	(1) Bleeding, (2) dysmenorrhea, (3) uterine volume	Retrospective cohort
Yang et al, 2017 [25]	China	Jan 2009	Dec 2013	60	Diffuse/focal adenomyosis	Laparoscopic uterine artery occlusion, partial adenomyomectomy, pelvic plexus ablation	(1) Pain, (2) bleeding,(3) uterine volume	Prospective cohort
Huang et al, 2015 [26]	China	Mar 2011	Feb 2014	47	Diffuse/focal adenomyosis	Group A: laparoscopic adenomyomectomy, group B: double-flap method	(1) Bleeding, (2) dysmenorrhea, (3) uterine volume	Retrospective cohort
Wang et al, 2009 [27]	Taiwan	1999	2003	N/A	Diffuse adenomyosis	Excision of diffuse adenomyosis	(1) Pain, (2) pregnancy	Retrospective cohort
Kang et al, 2009 [28]	South Korea	Jul 2003	Oct 2005	27	Diffuse/focal adenomyosis	Laparoscopic partial resection of adenomyosis and uterine artery occlusion	(1) Pain, (2) menorrhagia	Retrospective cohort
Studies with cases of partial and complete excision of adenomyosis								
Lin et al, 2018 [29]	Taiwan	Jan 2005	Dec 2014	120	Diffuse/focal adenomyosis	Laparoscopy/laparotomy: uterus-sparing treatment of adenomyosis. Control group: with GnRH, intervention group: GnRH + (levonorgestrel-releasing intrauterine system)	(1) Bleeding, (2) dysmenorrhea	Retrospective cohort

Table 2

Continued

Author, yr	Country	Start	Finish	Duration, months	Population	Intervention	Outcomes	Design
Liu et al, 2014 [30]	China	Jul 2003	Jul 2009	72	Diffuse/focal adenomyosis	Laparoscopic bilateral uterine artery occlusion and partial resection of adenomyosis	(1) Bleeding, (2) pain	Retrospective cohort
Kitade et al, 2018* [31]	Japan	2003	2013	120	Focal adenomyosis	Laparoscopy; group A: (1) wedge resection of focal adenomyosis, group B: (2) double-flap method for focal adenomyosis	(1) Bleeding, (2) pain	Prospective cohort
Hysterectomy								
Ajao et al, 2018* [32]	USA	2008	2012	48	Adenomyosis	Total abdominal hysterectomy	(1) Pain, (2) bleeding, (3) improvement in quality of life	Retrospective cohort
Berner et al, 2014 [33]	Norway	Sep 2008	Sep 2010	24	Preoperative cyclic pelvic pain	Laparoscopic supracervical hysterectomy	(1) Pelvic pain	Prospective observational single center
Liu et al, 2017 [34]	China	Jan 2012	Dec 2012	12	Adenomyosis	Group A: HIFU, group B: hysterectomy	(1) Quality of life score	Retrospective cohort
Endomyometrial ablation/resection								
Philip et al, 2018 [35]	France	Dec 2012	May 2016	41	Adenomyosis	Global endometrial ablation with NovaSure	(1) Bleeding, (2) dysmenorrhea	Prospective cohort

GnRH = gonadotropin-releasing hormone; HIFU = HIFU = high-intensity focused ultrasound; N/A = nonapplicable; PICOS = population, intervention, comparison, outcomes, and study design.

* Start and/or finish date not provided.

and a direct measurement of blood loss during menses in 1 study [30]. Preoperative and postoperative estimation of the volume of the adenomyotic lesion was indirectly performed in most studies, sonographically measuring the volume of the uterus [18−20,22−28,30], and in 1 study sonographically measuring the maximal size of the adenomyotic lesion [17] (Table 3).

Risk of Bias within Studies: Risk of Bias across Studies

The evaluation of the included studies with NOS for risk of bias yielded the following results (Table 4): all studies but 1 [32] were evaluated as fully representative of patients with adenomyosis because they had consecutive recruitment from the community; all studies with a nonexposed cohort were evaluated as fully representative of patients with adenomyosis because they had consecutive recruitment from the community; similarly, all studies had full ascertainment of exposure (surgery for adenomyosis), and it was clearly demonstrated that the study outcome (symptom relief) was not present at the start of the study because all studies were based on hospital surgical records. Regarding the comparability between exposed and nonexposed individuals, all studies presented a design matching the 2 groups about the presence of adenomyosis, but there was no adjustment in any study for the confounders, such as age, parity, or BMI. Regarding the outcome, none of the cohort studies used an independent postoperative blind assessment, all cohort studies had a follow-up linked with hospital records, 3 cohort studies had an inadequate follow-up length or an inadequate percentage of study population followed up [17,26,29], and another 3 studies had a loss to follow-up rate >10% [26,29,30].

Overall, at NOS evaluation, 3 studies were assessed with 8 stars [21,25,27], 2 studies were assessed with 7 stars [17,30], 11 studies were assessed with 6 stars [18−20,22−24,26,28,30,31,33,35], and 2 studies were assessed with 5 stars [29,32].

Results of Individual Studies

In general, all studies demonstrated a clear improvement of all clinical manifestations of adenomyosis after surgical intervention. For reasons of homogeneity of reporting the results, the clinical outcome at the follow-up of 12 months was selected for presenting the parameters under investigation. Postoperative pain was improved by 45% to 90%, postoperative menorrhagia by 48% to 92%, and uterine volume was diminished by 25% to 87% (Supplementary Table S1).

After complete excision of adenomyosis, the postoperative measurement of pain improved by 70% to 90%, the postoperative measurement of menorrhagia by 70% to 92%, and the reduction of uterine volume was reduced by 65% (Supplementary Table S1). Common complications in this group of surgery were blood loss (36−372 mL), uterine hematomas, and febrile morbidity, and there were 3 cases of serious complications (small bowel perforation, epigastric artery, and ileus) (Table 5). Conception, full-term, and total delivery rates were 26.9%, 76.7%, and 85.1%, respectively (Supplementary Table S2).

After partial excision of adenomyosis, the postoperative measurement of pain improved at a rate ranging from 41% to 90%, whereas the postoperative measurement of menorrhagia improved from 48% to 89%; the reduction of uterine volume was reduced by 25% to 87% (Supplementary Table S1). Common complications in this group of surgery were blood loss (24−169 mL), and febrile morbidity (0.5%) (Table 5). Conception, full-term, and total delivery rates were 50.0%, 66.7%, and 73.3%, respectively (Supplementary Table S2).

In the group of studies in which it was not clear whether the patients included were treated with partial or complete excision of adenomyosis, the postoperative measurement of pain improved at a rate ranging from 45% to 72%, the postoperative measurement of menorrhagia at 60%, and the reduction of uterine volume reduced by 58% (Supplementary Table S1). A common complication in this group was blood loss (86−245 mL) (Table 5). Conception, full-term, and total delivery rates were 16.4%, 70.8%, and 70.8%, respectively (Supplementary Table S2).

After hysterectomy, the postoperative measurement of pain improved by 84% (Supplementary Table S1).

After endomyometrial ablation, the percentage of women who had dysmenorrhea and menorrhagia reduced from 70% to 33% and 86% to 14%, respectively (Supplementary Table S1).

Recurrences of adenomyosis were reported in 3.3% (n = 61/1843, 37/612 [6.0%] cases who had complete excision, 14/559 [2.5%] cases who had partial excision, and 11/43 [25.5%] cases who had endometrial ablation). Hysterectomy was finally performed in 1.0% (n = 19/1843, 5/612 [0.8%] cases who had complete excision, 14/559 [0.7%] cases who had partial excision, 3/373 [0.8%] cases who had nonspecific excision, and 8/43 [18/6%] cases who had endometrial ablation) (Table 5).

Synthesis of Results: Additional Analysis

The studies that used standardized instruments for reporting pain and menorrhagia were used for further meta-analysis. Six studies were excluded from the meta-analysis because the symptoms were reported as a percentage of the study population and not as an arithmetic mean of the symptoms score or because the standardized instruments used in these studies were not suitable for transformation for further process along with the rest of the studies [17,19,24,30,32,35].

After meta-analysis of the available studies, it was found that the complete excision of adenomyosis was associated with improvement in pain, menorrhagia, and reduction of uterine volume by a factor of 6.2, 3.9, and 2.3, respectively;

Table 3

Instruments Used for Measurement of Symptoms and Type of Intervention in the Studies Included in the Systematic Review

Author, yr	Cases/controls	Pain measurement	Bleeding measurement	Volume measurement	Description of operative technique
Complete excision of adenomyosis/adenomyomectomy					
Kwack et al, 2018 [17]	Cases	Dysmenorrhea: 11-point scale (0 = no pain, 10 = worst pain imaginable)	MVJ menstrual bleeding scale	Maximal size of adenomyosis (cm, mean, standard deviation)	Diffuse adenomyosis and lesions >5 cm/laparotomy: temporary atraumatic occlusion of uterine artery. Perpendicular bisection from fundus to isthmus—opening of endometrial cavity. Excision of adenomyotic lesion through visual and tactile sensation. Preservation of 5-mm myometrium adjacent to endometrium and 5-mm-thick uterine serosa. Endometrial lining closed with interrupted 3-0 Polysorb; myometrial defects closed with interrupted 1-0 Polysorb. Serosal incision closed with continuous 3-0 Polysorb.
	Controls				Focal adenomyosis and lesions <5 cm/laparoscopy: temporary atraumatic occlusion of uterine artery with endoscopic vascular clip. Deep incision on uterine wall with monopolar diathermy over the adenomyotic lesion until endometrium visually exposed. Complete excision of adenomyoma. Preservation of 5-mm myometrium adjacent to endometrium and 5-mm-thick uterine serosa. Suturing the defect area with 3 layers. Single interrupted suture, continuously nonlocking suture, continuously interlocking suture.
Chong et al, 2016 [18]	Cases	VAS score	5-point scale. 0 = no anemia/menses <4 days; 1 = no anemia/menses 4 to 7 days; 2 = no anemia/menses >1 week; 3 = anemia/menses <4 days; 4 = anemia/menses 4 to 7 days; 5 = anemia and menses >7 days	Estimated uterine volume $0.5233 \times D1 \times D2 \times D3$	Robotic or laparoscopy: double-flap method. Uterine artery ligation with bipolar diathermy. Intramyometrial injection of vasopressin solution. Vertical incision with monopolar hook or Harmonic scalpel over the adenomyotic lesion. Exposure of endometrial cavity. Removal of adenomyotic tissue completely by using monopolar hook or Harmonic scalpel. Closure of the endometrial cavity with 2-0 Vicryl. The left serosal flap sutured to the right muscular layer with Monosyn 0. Right serosal flap adhered to the left serosa with interrupted sutures.
Dai et al, 2012 [19]	Cases	Chronic pain-grade questionnaire: pain intensity (0−100), degree of effect on activities (0−100), lack of energy (0−6)	N/A	Estimated uterine volume ($\Pi = 3.14$) $V = (L \times T \times W) \times \Pi/6$	Laparotomy, oxytocin local injection, surgical enucleation of the adenomyotic tissue, tactile examination of the uterus until full enucleation of the adenomyosis was performed or uterus reduced to $6 \times 5 \times 4$ cm. 2-0 absorbable sutures to the myometrium without penetrating endometrium. For deep adenomyoma cavities, layer by layer suture; 1-0 continuous suture for the uterine serosa.
Osada et al, 2011 [20]	Cases	Yes. VAS score	VAS score	Not performed	Triple-flap method. Laparotomy. Rubber tourniquet around proximal cervix. Bisection of uterus at sagittal plane until uterine cavity. Adenomyotic tissues grasped with forceps and excised leaving 1 cm of myometrium from the serosa

Table 3

Continued

Author, yr	Cases/controls	Pain measurement	Bleeding measurement	Volume measurement	Description of operative technique
					and the endometrium. Endometrial lining closed with interrupted 3-0 Vicryl. On 1 side of uterus, the myometrium and serosa are approximated in the anteroposterior plane with interrupted 2-0 Vicryl. The contralateral uterine wall brought over the reconstructed wall to cover the suture line.
Wang et al, 2009 [21]	Cases	(1) VNRS-6, (2) AUS	MVJ menstrual bleeding scale	Not performed	Minilaparotomy, ultraminilaparotomy, or laparoscopy: routine local injection of vasopressin. Adenomyotic lesions meticulously dissected; excision of all nonmicroscopic lesions performed by palpation. Horizontal sutures and locking sutures for closure of myometrium. Continuous 5-0 for uterine serosa. Postoperatively, 6-course monthly regimen of GnRH agonist therapy.
	Controls				Same surgical intervention with no medical treatment postoperatively.
Partial excision of adenomyosis					
Yu et al, 2018 [22]	Cases	VAS score	N/A	Estimated uterine volume ($\Pi = 3.14$) $V = (L \times T \times W) \times \Pi/6$	Laparoscopic adenomyomectomy: incision on uterine wall with monopolar diathermy or scissors. Gradual dissection of the adenomyoma with scissors, monopolar diathermy and/or bipolar diathermy without penetrating the endometrium. 8 patients: laparoscopic presacral neurectomy.
Jun-Min et al, 2018 [23]	Cases	VAS score	MVJ menstrual bleeding scale	Estimated uterine volume $V = (L \times T \times W) \times 0.5236$	Laparotomy. Longitudinal incision of uterus through myometrium and endometrium. U-shaped resection of the adenomyotic tissues to a thickness of 3 mm of inner myometrium on both sides. Approximation and closure of residual endometrial lining and myometrium of bisected uterus with 3-0 sutures. Closure of serosa with modified serosal layer 2-0 suture.
Xia et al, 2017 [24]	Cases	VAS score	MVJ menstrual bleeding scale	Estimated uterine volume $V = (L \times T \times W) \times 0.523$	TCR resectoscope (12° optic) equipped with 3 × 5-mm loop. 0.9% NaCl as irrigant. Continuous transabdominal ultrasound guidance. Cutting loop to resect the lesions repeatedly and progressively with standard electroresection. Hysteroscopic evaluation of endometrial defects, hypervascularization, strawberry pattern, or cystic hemorrhagic lesions on endometrial surface. Procedure stop when (1) estimated fluid deficit >1 L, (2) any complication occurred.
Yang et al, 2017 [25]	Cases	VAS score	PBAC	Ultrasound-measured uterine volume	Uterus-sparing: laparoscopic uterine artery occlusion, partial adenomyomectomy and pelvic plexus ablation.
	Controls				Uterus-sparing: laparoscopic uterine artery occlusion, partial adenomyomectomy without pelvic plexus ablation.

Table 3

Continued

Author, yr	Cases/controls	Pain measurement	Bleeding measurement	Volume measurement	Description of operative technique
Huang et al, 2015 [26]	Cases	VAS score	The menstrual product use of ≥5 pads/day was defined as menorrhagia; mild (5−7 pads/day), moderate (7−9 pads/day), and severe (>9 pads/day)	Estimated uterine volume $V = (L \times T \times W) \times 0.5233$	Laparoscopic double-flap: midline incision on fundal serosal surface by scissors/monopolar. Sagittal direction until cavity. Adenomyomatous tissues identified and grasped with forceps and excised from surrounding myometrium. Myometrial thickness of 1 cm below the serosa or above the endometrium secured. Endometrial lining approximated with interrupted 3-0 Vicryl. For myometrium and serosa 2-0 Vicryl. The first flap from the side wall of the uterus (including the serosa and the myometrium) brought into second flap in the other side of uterine wall. The second flap in the other side of uterine wall brought to cover first flap. Serosal surface of the underlying flaps stripped: only myometrial tissue flaps overlapped.
	Controls				Conventional laparoscopic adenomyomectomy
Wang et al, 2009 [27]	Cases	(1) VNRS-6, (2) AUS	N/A	Ultrasound maximal diameter (mm) of the uterus	"Cytoreductive" surgery: adenomyotic lesions meticulously dissected; excision of all nonmicroscopic lesions performed by palpation of the uterus. Horizontal sutures and locking sutures for closure of myometrium. Continuous 5-0 for uterine serosa. Postoperatively with/without medical treatment with 6-month GnRH agonist.
	Controls				No surgical intervention. Medical treatment with 6-month GnRH agonist.
Kang et al, 2009 [28]	Cases	VAS score	Pictorial blood loss assessment chart was used to measure menstrual blood loss	Estimated uterine volume $V = (L \times T \times W) \times 0.523$	Laparoscopy. Uterine artery occluded with PlasmaKinetic forceps. In case of diffuse adenomyosis, the diseased part was removed as much as possible. Myometrium and serosa were repaired in 1 or 2 layers, with interrupted figure-of-eight suture or single stitch with polyglycolic acid suture 0.
Studies with cases of partial and complete excision of adenomyosis					
Lin et al, 2018 [29]	Cases	VAS score	N/A	N/A	Laparotomy/laparoscopy with uterine manipulator. Vertical incision of pelvic resection of the uterine wall. Focal adenomyomectomy: separation of the normal myometrium from the adenomyoma, and excision of lesion. Cytoreductive surgery for diffuse adenomyosis: massive removal of adenomyotic foci including an amount of healthy myometrium. Endometrial cavity and uterine wall were closed with absorbable suture or a knotless tissue closure device. Multilayer closure of the myometrium. After surgery insertion of an LNG-IUS.
	Controls				Same surgical intervention without LNG-IUS insertion postoperatively.

Table 3

Continued

Author, yr	Cases/controls	Pain measurement	Bleeding measurement	Volume measurement	Description of operative technique
Liu et al, 2014 [30]	Cases	VAS score	PBAC	Estimated uterine volume $V = (L \times T \times W) \times 0.523$	Laparoscopy. Uterine artery isolated and occluded with bipolar forceps (Gyrus ACMI Inc., UK) or PlasmaKinetic forceps (Gyrus ACMI Inc.) under direct vision. Focal adenomyosis dissected with monopolar incision. Adenomyotic tissue excised to access healthy myometrium via a monopolar incision, or with scissors until normal tissue reached. Diffused adenomyosis: forceps or a suction tube to demarcate between the normal myometrium from adenomyosis, then the diseased part removed as completely as possible. When uterine cavity was entered, figure-of-eight sutures for closure, leaving as little dead space as possible. Myometrium and serosa with continuous inverting zero polyglycolic acid sutures (Safil, B. Braun, Rubi, Spain).
Kitade et al, 2018 [31]	Cases	VAS score	VAS score	N/A	Laparoscopic wedge excision: adenomyosis <5 cm with outbound spatial pattern. V-shaped notch with monopolar electrosurgery/scissors to remove adenomyotic nodule and surrounding serosa. Remaining muscle layer sutured from base of the muscularis in 2 to 4 layers. Double-flap method: transverse incision reaching the endometrial cavity; resection of adenomyotic tissue en bloc. The remaining serosal tissue serving as the upper and lower flaps, which are overlapped and sutured. Any perforations to the endometrium sewn up with 2/0 suture. Inner side of the lower serosal flap sutured with 1/0 and the upper fringe of the serosal flap sutured continuously.
Hysterectomy					
Ajao et al, 2018 [32]	Cases	10 questions for symptoms and impact to quality of life	Survey: 10 questions for symptoms and impact to quality of life	N/A	Hysterectomy
Berner et al, 2014 [33]	Cases	VAS score. 4-grade ordinal pain scale (no, weak, moderate, severe)	N/A	N/A	Laparoscopic subtotal hysterectomy
Liu et al, 2017 [34]	Cases	Quality of life symptoms	N/A	N/A	Total abdominal hysterectomy
Endomyometrial ablation/resection					
Philip et al, 2018 [35]	Cases	VAS score	Validated nonstandardized questionnaire	N/A	Outpatient department under general or locoregional anesthesia. Hysteroscopy and curettage—endometrial cancer exclusion. NovaSure. A control hysteroscopy performed at the end of procedure to assess the quality of destruction.

AUS = Analgesic Usage Score; GnRH = gonadotropin-releasing hormone; L = craniocaudal length of the uterus; LNG-IUS = levonorgestrel-releasing intrauterine system; MVJ = Mansfield-Voda-Jorgensen; N/A = nonapplicable; PBAC = pictorial blood assessment charts; T = dorsoventral thickness of the uterus; TCR = transcervical resection; VNRS-6 = Verbal Numeric Rating Scale; VAS = Visual Analog Scale; W = lateral width of the uterus.

Table 4

Evaluation of the Included Studies with NOS for Risk of Bias

Author, yr	Selection				Comparability	
	Representativeness of exposed cohort	Selection of nonexposed cohort	Ascertainment of exposure	Demonstration that outcome not present at start	Adenomyosis symptoms	Other factors
Complete excision of adenomyosis/adenomyomectomy						
Kwack et al, 2018 [17]	Retrospective cohort study; consecutive selection therefore truly representative *	Drawn from same community as exposed cohort *	All participants exposed to study intervention *	Outcome of interest not present at start *	Yes *	Not matched –
Chong et al, 2016 [18]	Retrospective cohort study; consecutive selection therefore truly representative *	N/A –	All participants exposed to study intervention *	Outcome of interest not present at start *	N/A –	N/A –
Dai et al, 2012 [19]	Prospective cohort study; consecutive selection therefore truly representative *	N/A –	All participants exposed to study intervention *	Outcome of interest not present at start *	N/A –	N/A –
Osada et al, 2011 [20]	Prospective cohort study; consecutive selection therefore truly representative *	N/A –	All participants exposed to study intervention *	Outcome of interest not present at start *	N/A –	N/A –
Wang et al, 2009 [21]	Prospective cohort study; consecutive selection therefore truly representative *	Drawn from same community as exposed cohort *	All participants exposed to study intervention *	Outcome of interest not present at start *	Yes *	Not matched –
Partial excision of adenomyosis						
Yu et al, 2018 [22]	Retrospective cohort study; consecutive selection therefore truly representative *	N/A –	All participants exposed to study intervention *	Outcome of interest not present at start *	N/A –	N/A –
Jun-Min et al, 2018 [23]	Retrospective cohort study; consecutive selection therefore truly representative *	N/A –	All participants exposed to study intervention *	Outcome of interest not present at start *	N/A –	N/A –
Xia et al, 2017 [24]	Retrospective cohort study; consecutive selection therefore truly representative *	N/A –	All participants exposed to study intervention *	Outcome of interest not present at start *	N/A –	N/A –
Yang et al, 2017 [25]	Prospective cohort study; consecutive selection therefore truly representative *	Drawn from same community as exposed cohort *	All participants exposed to study intervention *	Outcome of interest not present at start *	Yes *	Not matched –

Table 4

Continued

Author, yr	Selection								Comparability			
	Representativeness of exposed cohort		Selection of nonexposed cohort		Ascertainment of exposure		Demonstration that outcome not present at start		Adenomyosis symptoms		Other factors	
Huang et al, 2015 [26]	Retrospective cohort study; consecutive selection therefore truly representative	*	Drawn from same community as exposed cohort	*	All participants exposed to study intervention	*	Outcome of interest not present at start	*	Yes	*	Not matched	–
Wang et al, 2009 [27]	Retrospective cohort study; consecutive selection therefore truly representative	*	Drawn from same community as exposed cohort	*	All participants exposed to study intervention	*	Outcome of interest not present at start	*	Yes	*	Not matched	–
Kang et al, 2009 [28]	Retrospective cohort study; consecutive selection therefore truly representative	*	N/A	–	All participants exposed to study intervention	*	Outcome of interest not present at start	*	N/A	–	N/A	–
Studies with cases of partial and complete excision of adenomyosis												
Lin et al, 2018 [29]	Retrospective cohort study; consecutive selection therefore truly representative	*	Drawn from same community as exposed cohort	*	All participants exposed to study intervention	*	Outcome of interest not present at start	*	N/A	–	Not matched	–
Liu et al, 2014 [30]	Retrospective cohort study; consecutive selection therefore truly representative	*	N/A	–	All participants exposed to study intervention	*	Outcome of interest not present at start	*	N/A	–	N/A	–
Kitade et al, 2018 [31]	Prospective cohort study; consecutive selection therefore truly representative	*	N/A	–	All participants exposed to study intervention	*	Outcome of interest not present at start	*	N/A	–	N/A	–
Hysterectomy												
Ajao et al, 2018 [32]	Retrospective cohort study, the exposed cohort is not truly representative of the women with adenomyosis in the community because of the high rate of nonresponders	–	High rate of nonresponders	–	All participants exposed to study intervention	*	Outcome of interest not present at start	*	Nonexposed group: not matched	–	Not matched	–
Berner et al, 2014 [33]	Prospective observational study; consecutive selection therefore truly representative	*	Drawn from same community as exposed cohort	*	All participants exposed to study intervention	*	Outcome of interest not present at start	*	Nonexposed group: not matched	–	Not matched	–

Table 4

Continued

Author, yr	Selection								Comparability				Outcome								NOS score
	Representativeness of exposed cohort		Selection of nonexposed cohort		Ascertainment of exposure		Demonstration that outcome not present at start		Adenomyosis symptoms		Other factors		Assessment: independent of blind		Assessment: record linkage		Enough follow-up		Follow-up: adequacy of cohorts		
Liu et al, 2017 [34]	Retrospective cohort study; consecutive selection therefore truly representative	*	Drawn from same community as exposed cohort	*	All participants exposed to study intervention	*	Outcome of interest not present at start	*	Nonexposed group: not matched	–	Not matched	–									
Endomyometrial ablation/resection																					
Philip et al, 2018 [35]	Prospective cohort study; consecutive selection therefore truly representative	*	N/A	–	All participants exposed to study intervention	*	Outcome of interest not present at start	*	N/A	–	N/A	–									
													Postop assessment not blind	–	Postop assessment linked to hospital records	*	Main follow-up results 7 months <12 months	–	100% at 7 months	*	7(*)/10(*)
													Postop assessment not blind	–	Postop assessment linked to hospital records	*	Follow-up adequate (36 months)	*	100% at 12 months	*	6(*)/10(*)
													Postop assessment not blind	–	Postop assessment linked to hospital records	*	Follow-up adequate (>12 months)	*	<10% lost to follow-up at 12 months	*	6 (*)/10(*)
													Postop assessment not blind	–	Postop assessment linked to hospital records	*	Follow-up adequate (36 months)	*	100% at 12 months	*	6(*)/10(*)
													Postop assessment not blind	–	Postop assessment linked to hospital records	*	Follow-up adequate (12 months)	*	100% at 12 months	*	8(*)/10(*)
													Postop assessment not blind	–	Postop assessment linked to hospital records	*	Follow-up adequate (>12 months)	*	100% at 24 months	*	6(*)/10(*)
													Postop assessment not blind	–	Postop assessment linked to hospital records	*	Follow-up adequate (24 months)	*	<10% lost to follow-up at 24 months	*	6(*)/10(*)
													Postop assessment not blind	–	Postop assessment linked to hospital records	*	Follow-up adequate (>12 months)	*	100% at 12 months	*	6(*)/10(*)
													Postop assessment not blind	–	Postop assessment linked to hospital records	*	Follow-up adequate (60 months)	*	<10% lost to follow-up at 60 months	*	8(*)/10(*)

Table 4

Continued

Outcome								NOS score
Assessment: independent of blind		Assessment: record linkage		Enough follow-up		Follow-up: adequacy of cohorts		
Postop assessment not blind	–	Postop assessment linked to hospital records	*	Inadequate (65% lost at 12 months)	–	<35% lost to follow-up at 12 months	–	6(*)/10(*)
Postop assessment not blind	–	Postop assessment linked to hospital records	*	Follow-up adequate (36 months)	*	100% at 36 months	*	8(*)/10(*)
Postop assessment not blind	–	Postop assessment linked to hospital records	*	Follow-up adequate (12 months)	*	100% at 12 months	*	6(*)/10(*)
Postop assessment not blind	–	Postop assessment linked to hospital records	*	Inadequate (<60% lost at 24 months)	–	>50% lost to follow-up at 12 months	–	5(*)/10(*)
Postop assessment not blind	–	Postop assessment linked to hospital records	*	Follow-up adequate (36 months)	*	<5% lost to follow-up at 36 months	*	6(*)/10(*)
Postop assessment not blind	–	Postop assessment linked to hospital records	*	Follow-up adequate (36 months)	*	<5% lost to follow-up at 36 months	*	6(*)/10(*)
Postop assessment not blind		–		Postop assessment linked to hospital records	*	Follow-up adequate (12 months)	*	<5% lost to follow-up at 12 months
*	5	(*)/10(*)						
Postop assessment not blind	–	Postop assessment linked to hospital records	*	Follow-up adequate (12 months)	*	N/A	–	6(*)/10(*)
Postop assessment not blind	–	Postop assessment linked to hospital records	*	Follow-up adequate (12 months)	*	<5% lost to follow-up at 12 months	*	7(*)/10(*)
Postop assessment not blind	–	Postop assessment linked to hospital records	*	Follow-up adequate (36 months)	*	<5% lost to follow-up at 36 months	*	6(*)/10(*)

NA = nonapplicable; NOS = Newcastle-Ottawa Scale; * = the study fulfills NOS criterion; - = the study does not fulfill NOS criterion.

Table 5

Intraoperative and Postoperative Complications after Surgery for Adenomyosis

Author, yr	n	Follow-up (months)	Estimated blood loss	Hematoma	Febrile morbidity	Other serious complications	Recurrence	Hysterectomy
Total	1843			6/1843 (3.3%)	10/1843 (5.4%)	3/1843 (1.6%)	63/1843 (3.4%)	21/1843 (1.1%)
Complete excision of adenomyosis/adenomyomectomy								
Kwack et al, 2018 (laparoscopic group) [17]	108	13.8 ± 13.1	222.7 ± 231.1	0	0	Small bowel perforation (1/116, 0.9%)	10 (8.6%)	1/116 (0/9%)
Kwack et al, 2018 (laparotomy group) [17]	116		155.3 ± 116.2	0	0	Epigastric artery bleeding at trocar site (1/108, 0.9%)	11 (10.2%)	2/108 (1.8%)
Chong et al, 2016 [18]	33	52 (38–76)	36.1 ± 37.4	0	3/33 (10%)	Ileus (1/33, 3.3%)	4/33 (12%)	0
Dai et al, 2012 [19]	86	24.8 ± 17.3	–	0	0	0	6/86 (7.0%)	2/86 (2.3%)
Osada et al, 2011 [20]	104	123	372.0 ± 314.4	6/105 (5.8%)	0	0	4/105 (3.8%)	0
Wang et al, 2009 [21]	165	24	–	0	0	0	0	0
Partial excision of adenomyosis								
Yu et al, 2018 [22]	49	55	–	0	0	0	12/49 (24.5%)	4/49 (8.2%)
Yu et al, 2018 [22]	37	12	80.0 ± 35.2	–	4/37 (10.8%)	–	0	2/37 (5.4%)
Jun-Min et al, 2018 [23]	198	24	–	0	1/198 (0.5%)	0	2/198 (1%)	0
Xia et al, 2017 [24]	51	24	24.2 ± 18.5	0	0	0	0	0
Yang et al, 2017 [25]	50	36	169.4 ± 61.9	0	0	0	0	0
Huang et al, 2015 [26]	52	36	150.6 ± 45.5	0	0	0	0	0
Wang et al, 2009 [27]	98	12	–	0	0	0	0	0
Kang et al, 2009 [28]	28	36	–	0	0	0	0	0
Studies with cases of partial and complete excision of adenomyosis								
Lin et al, 2018 (surgery + LNG-IUS) [29]	54	24	189.6 ± 195.2	–	–	–	–	–
Lin et al, 2018 (surgery only) [29]	61	24	207.0 ± 218.8	–	–	–	–	–
Liu et al, 2014 [30]	182	36	86.1 ± 36.3	–	–	–	–	3/179 (1.7%)
Kitade et al, 2018 (wedge resection) [31]	76	36	172.1 ± 175.2	–	–	–	–	–
Kitade et al, 2018 (diffuse) [31]			245.3 ± 232.3	–	–	–	–	–
Hysterectomy								
Ajao et al, 2018 [32]	171	62	–	–	–	–	–	–
Berner et al, 2014 [33]	19	12	–	–	–	–	–	–
Liu et al, 2017 [34]	66	12	–	–	–	–	–	–
Endomyometrial ablation/resection								
Philip et al, 2018 [35]	43	36	–	–	–	–	11/43 (25.5%)	8/43 (19%)

LNG-IUS = levonorgestrel-releasing intrauterine system.

the partial excision of adenomyosis was associated with improvement in pain, menorrhagia, and reduction of uterine volume by a factor of 5.9, 3.0, and 2.9, respectively; the studies with a mixed volume of patients with complete and partial excision of adenomyosis reported improvement in pain, menorrhagia, and reduction of uterine volume by a factor of 4.0, 6.3, and 5.1, respectively. Hysterectomy is associated with improvement of pain by a factor of 2.2 (Table 6; Figs. 2–4).

Discussion

Summary of Evidence

Conservative surgical treatment of adenomyosis results in high rates of control of symptoms, especially regarding pain (>70% at 12 months) and bleeding (>70% at 12 months), and in many cases, it facilitates conception without endangering the outcome of pregnancy. Hysterectomy for adenomyosis appears to be a terminal option for these patients and is associated with equally good outcomes regarding pain and bleeding.

Overall, the results of this review suggest that the uterus-sparing treatment of adenomyosis is associated with an improvement of symptoms of pain and bleeding by a factor of 5.3 and 3.7, respectively. Uterine volume after conservative surgery is estimated to be reduced by a factor of 3.1. There seem to be no significant differences between the types of conservative surgery, although a direct comparison cannot be easily performed in the setting of this review.

Complications during surgery and early postoperative period are usually associated with the type of approach (laparotomy or laparoscopy), and they do not appear to be extraordinary. Flap approaches are not associated with extra morbidity, and there are no reports indicating that hematomas, postoperative dehiscence of the uterine scar, or adhesions are increased, either after laparotomy or laparoscopy. The most probable explanation is that all these techniques are reported from centers of surgical excellence, where extensive surgical experience in all surgical techniques increases the possibility of a good postoperative outcome: intraoperative bleeding is reduced, surgical knots are secure and adequately tight to diminish the risk of dead space between the approximated uterine flaps, and the risk of damaging neighboring organs is equally reduced. An important question remains: is the generalization of the results of this type of surgery applicable to surgeons who have limited experience? Another issue is whether the variations of surgical approaches can be considered as a homogeneous group: for example, how similar are the "triple-flap" and "double-flap" methods in terms of tissue extraction and, more importantly, tissue restoration. Studies specifically designed to answer these questions are still not available.

After uterus-sparing surgery for adenomyosis, the conception rates appear to be satisfactory, early pregnancy wastage does not seem to be increased, pregnancies seem to continue without significant complications, and the viable term delivery rates seem to be satisfactory. Morbid variations of placentation rates (placenta previa, placenta percreta) do not seem to be increased. Cesarean section is usually preferred as a method of delivery, although there are cases of vaginal delivery without complications [17]. However, in a nonsystematic review, Osada [36] described 23 cases of uterine rupture out of 2365 women who underwent adenomyomectomy (1.0%). The author concluded that the factors that could be related to uterine rupture after uterus-sparing surgical treatment of adenomyosis seem to be the method of removal of adenomyotic tissue, the degree of remnants of adenomyosis left postoperatively, the method of reconstructing the uterine wall, postoperative complications (infection, hematoma), and the interval between the procedure and conception [36].

Another question remains: what is the optimal surgical technique for the uterus-sparing treatment of adenomyosis? In summary, the following surgical approaches have been proposed: (1) classical excision of adenomyotic tissue after longitudinal incision of the uterus, (2) wedge resection [29,31], (3) a variation of the flap method [18,20,26,31], and (4) U-shaped resection of the adenomyotic tissue [23]. In addition, the following additional techniques used for bleeding control have been described: (1) temporary atraumatic occlusion of the uterine artery [17], (2) ligation of the uterine artery [17], (3) injection of vasopressin solution into the myometrium [18,21], (4) injection of oxytocin into the myometrium [19], (5) use of a rubber tourniquet around the proximal uterine cervix [20], and (6) ablation of the pelvic plexus [25]. Thus, the surgeon should individualize the treatment to the patient's needs. Preoperative imaging with ultrasound and MRI can indicate with precision the location and extent of the disease in the index patient. The localized lesions should preferably be excised completely using an approach similar to myomectomy. On the other hand, diffuse lesions should be treated by a method that secures (1) the maximal removal of adenomyotic tissue and (2) optimal functional restoration of the integrity of the uterine wall. In cases of diffuse but not extended adenomyosis, the surgeon should bear in mind the objectives of complete removal of the adenomyotic tissue and of the reconstruction of the uterus; a more aggressive approach is associated with a better outcome in terms of control of symptoms and early recurrence. Laparoscopy is the method of choice for surgical approach. Accompanying techniques such as temporary uterine artery occlusion facilitate the procedure and diminish blood loss. However, open surgery still offers several advantages: the tactile recognition of adenomyotic tissue, the digital manipulation of the endometrial cavity to remove nearby adenomyosis without further trauma of the

Table 6

Preoperative and Postoperative Uterine Size, Menorrhagia, and Pelvic Pain/Dysmenorrhea Rates, from the Studies Included in Meta-analysis

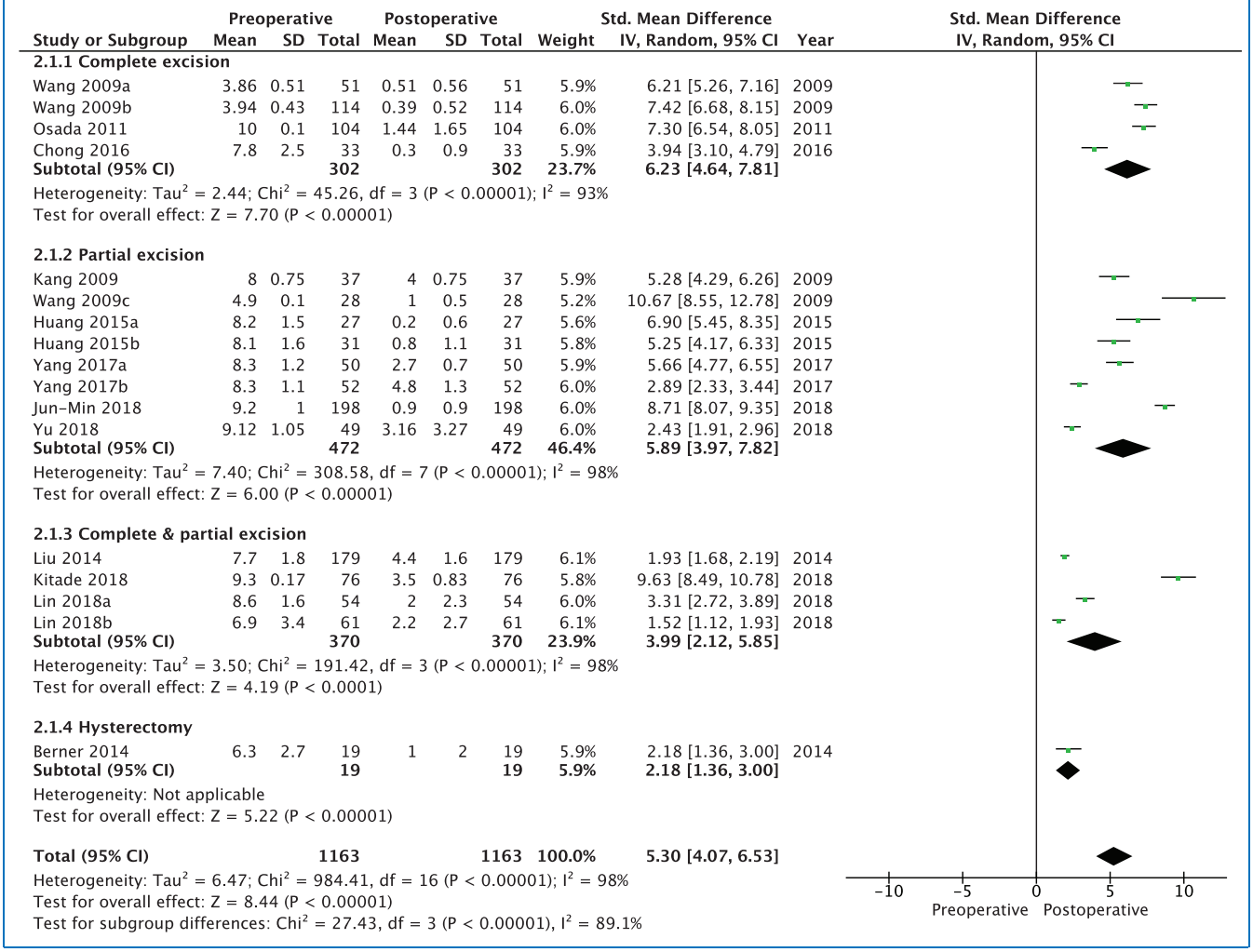
Author, yr	n	Follow-up (months)	Age	Preop uterine volume (cm^3)	Postop uterine volume (cm^3)	p-value	Uterine volume reduction (%)
Complete excision of adenomyosis/adenomyomectomy							
Chong et al, 2016 [18]	33	52 (38–76)	39.4 ± 4.3	199.1 ± 75.8	70.0 ± 31.6	<.01	64.84
Osada et al, 2011 [20]	104	123	37.6 ± 6.9	–			–
Wang et al, 2009 (surgery only) [21]	51	24	37.0 ± 4.8	–	–		–
Wang et al, 2009 (surgery + GnRH) [21]	114	24	38.9 ± 3.8	–	–		–
Partial excision of adenomyosis							
Yu et al, 2018 [22]	49	55	40.6 ± 5.2	–	–		–
Jun-Min et al, 2018 [23]	198	24	36.2 ± 8.6	338.47 ± 62.73	42.86 ± 10.26	<.01	87.33
Yang et al, 2017 (with plexus ablation) [25]	50	36	40.4 ± 3.7	200.4 ± 55.3	134.0 ± 28.6	<.01	–
Yang et al, 2017 (without plexus ablation) [25]	52	36	39.6 ± 4.0	202.3 ± 54.5	133.0 ± 35.1	<.01	34.25
Huang et al, 2015 (double-flap) [26]	46	12	37.1 ± 6.6	209.1 ± 117.5	45.8 ± 4.9	<.01	78.09
Huang et al, 2015 (conventional) [26]	48	24	36.6 ± 5.9	198.5 ± 82.6	59.7 ± 24.1	<.01	69.92
Wang et al, 2009 [27]	28	36	34.3 ± 2.1	101.7 ± 9.2	76.0 ± 9.2	<.01	25.3
Kang et al, 2009 [28]	37	12	42	224.7 ± 48.7	91.6 ± 28.4	<.01	59.2
Studies with cases of partial and complete excision of adenomyosis							
Lin, 2018 (surgery + LNG-IUS) [29]	54	24	38.8 ± 5.1	–	–		–
Lin et al, 2018 (surgery only) [29]	61	24	38.5 ± 5.3	–	–		–
Liu et al, 2014 [30]	182	36	40.6 ± 6.2	218.5 ± 31.8	91.2 ± 18.6	<.01	58.26
Kitade et al, 2018 [31]	76	36	36 (28–39)	–	–		–
Hysterectomy							
Berner et al, 2014 [33]	19	12	43.7 ± 4.8	–	–		–

Preop pain score	Postop pain score	p-value	Pain reduction (%)	Preop bleeding score	Postop bleeding score	p-value	Bleeding reduction (%)
7.8 ± 2.5	0.8 ± 1.5	<.01	89.74	2.5 ± 1.8	0.2 ± 0.6	<.01	92
10.0	1.67	<.01	83.3	10.0	2.87	<.01	71.3
3.86 ± 0.51	1.14 ± 0.87	<.01	70.4	3.08 ± 1.44	0.91 ± 0.77	<.01	70.4
3.94 ± 0.43	0.78 ± 0.84	<.01	79.18	3.68 ± 1.03	0.91 ± 0.77	<.01	75.27
9.12 ± 1.05	4.11 ± 3.54	<.01	54.9	–	–		–
9.2 ± 1.0	0.9 ± 1.1	<.01	90.21	38.7 ± 19.8	3.9 ± 1.8	<.01	89.92
8.3 ± 1.2	2.6 ± 0.9	<.01	68.67	122.6 ± 34.2	62.2 ± 13.4	<.01	50.73
8.3 ± 1.1	5.0 ± 1.4	<.01	41.25	132.6 ± 36.8	61.8 ± 13.5	<.01	53.39
8.2 ± 1.5	0.4 ± 0.9	<.01	97.5	8.1 ± 1.3	3.8 ± 0.6	<.01	49.38
8.1 ± 1.6	2.0 ± 2.1	<.01	90.12	8.2 ± 1.5	4.6 ± 1.1	<.01	48.78
4.9 ± 0.1	1.8 ± 1.1	<.01	77.5	–	–		–
8 (7–10)	4 (3–6)	<.01	50.0	158 (316–255)	59 (19–76)	<.01	62.65
8.6 ± 1.6	2.4 ± 2.8	<.01	72.09	–	–		–
6.9 ± 3.4	2.6 ± 3.0	<.01	62.31	–	–		–
7.7 ± 1.8	4.2 ± 1.5	<.01	45.45	146 (128–235)	58 (29–78)	N/A	60.27
9.3 (9–10)	3.5 (1–6)	N/A	53.76	–	–		–
6.3 ± 2.7	1.0 ± 2.0	<.01	84.12	–	–		–

GnRH = gonadotropin-releasing hormone; LNG-IUS = levonorgestrel-releasing intrauterine system; N/A = nonapplicable.

Fig. 2

Results of the meta-analysis of the studies included in this review with regard to postoperative improvement in pain/dysmenorrhea. CI = confidence interval; SD = standard deviation.



endometrial lining, and the fact that no morcellation is needed, and the secure tightening of the uterine wall flaps in cases in which extended reconstruction is required.

Any comparison between conservative surgery for adenomyosis with nonsurgical approaches is beyond the scope of this review. It is common sense, however, that these 2 alternatives should not be antagonistic but synergistic. Conservative surgery appears to be more suitable as the first option for women with restricted available reproductive time (older nulliparous women or patients with chronic infertility) who are not keen for fertility preservation.

Limitations

The main limitations of this review are as follows: (1) the low quality of the available studies (no randomized controlled trials included), (2) the heterogeneity of the studies regarding the type of operation, (3) the differences between the studies regarding the type of instruments used to quantify the pain and the bleeding, and (4) the differences between the studies in terms of follow-up and rates of lost patients during reexaminations. It appears that questions such as which is the optimum technique for conservative surgical treatment of adenomyosis and whether fertility surgery is better than uterine artery embolization, high-intensity focused ultrasound, or hormonal treatment cannot be readily answered. Studies with follow-up longer than 36 months and clear end points including postoperative bleeding and pain measured with comparable standardized instruments, pregnancy-related outcomes, and rates of recurrences, are needed to evaluate all these surgical approaches in a realistic setting. Moreover, the geographic origin of studies appears to be restricted to Asian/Southeast Asian centers, with sporadic publications from Europe and North America.

Fig. 3

Results of the meta-analysis of studies included in this review with regard to postoperative improvement in bleeding/menorrhagia. CI = confidence interval; SD = standard deviation.

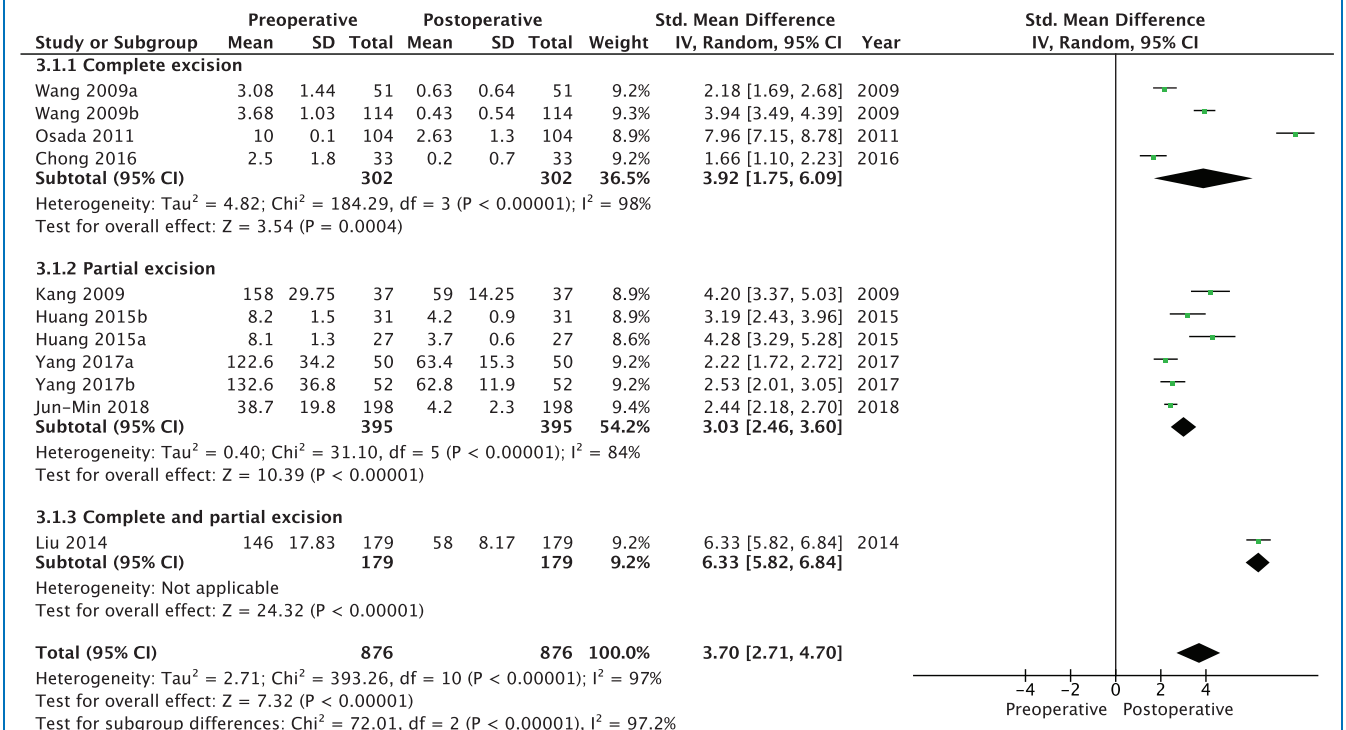
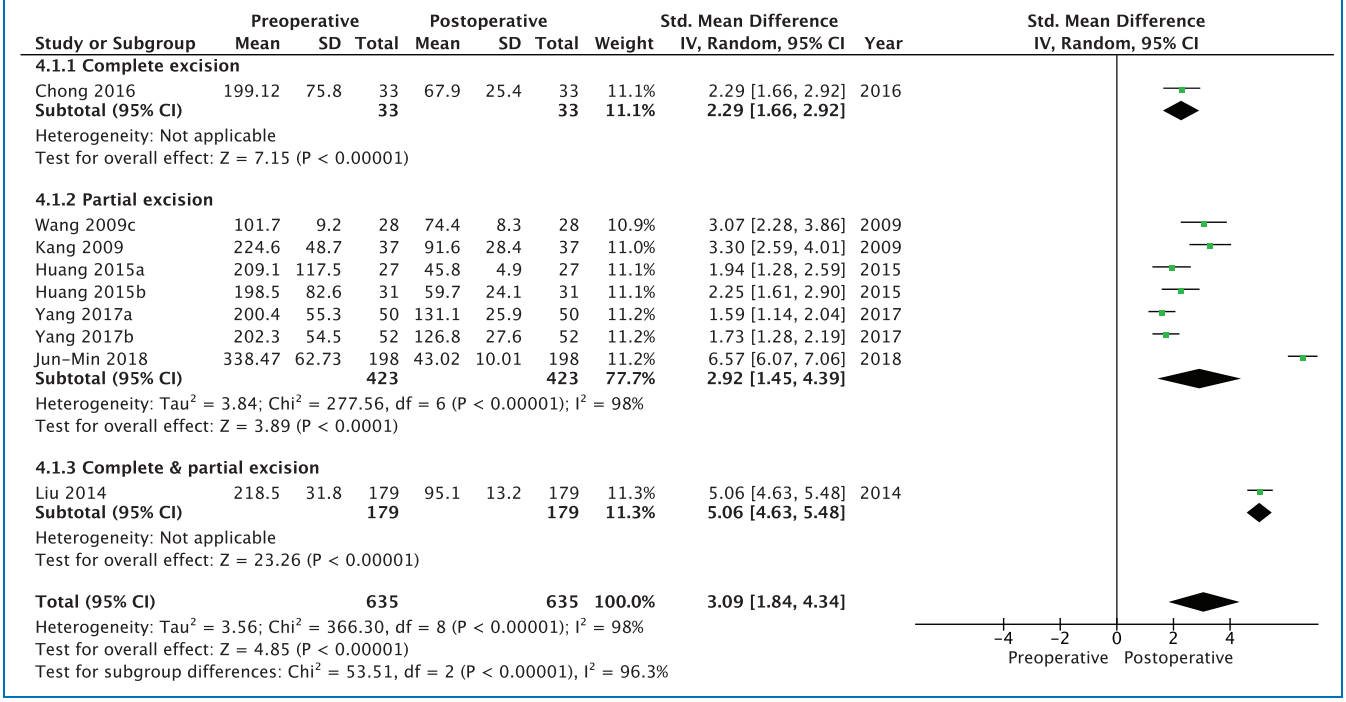


Fig. 4

Results of the meta-analysis of the studies included in this review with regard to postoperative reduction in the uterine volume. CI = confidence interval; SD = standard deviation.



Conclusions

In conclusion, the surgical treatment of adenomyosis results in the satisfactory control of pain and bleeding, as well as in the reduction of uterine volume. Intraoperative and long-term complications are restricted, and the recurrences appear to be decreased in medium-term follow-up. Further research is warranted to investigate the long-term control of symptoms, identify any parameters related to the recurrence of adenomyosis, and compare the conservative surgical treatment of adenomyosis with other treatment options.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.jmig.2019.08.004.

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Supplemental Table 1

Pre-Operative & Post-operative uterine size, menorrhagia, and pelvic pain/dysmenorrheoa rates, from the studies included in the systematic review

Author, Year	n	Follow-up (months)	Age	Parity	Pre-Op Uterine Volume (cm^3)	Post-Op Uterine Volume (cm^3)	Pre-Op Pain Score	Post-Op Pain Score	Pre-Op Bleeding Score	Post-Op Bleeding Score
Complete excision of adenomyosis / Adenomyomectomy										
Kwack, 2018 (Laparoscopic group) (14)	108	13.4 ± 13.1	42.1 ± 4.8	1.7 ± 0.8	Maximal size of adenomyosis (cm, mean SD) =4.3 ± 1.0	N/A	Dysmenorrhea: 36 (33.3%)	Dysmenorrhea: CR: 22 (52.4% PR:19 (45.2%) SeD: 1 (2.4%)	Menorrhagia: 13 (12.0%)	Menorrhagia: CR: 7 (18.0%) PR: 25 (64.1%) SeD: 7 (18.0%)
Kwack, 2018 (Laparotomy group) (14)	116	16.6 ± 10.1	37.5 ± 4.7	0.6 ± 0.8	Maximal size of adenomyosis (cm, mean SD) =6.5 ± 2.1	N/A	Dysmenorrhea: 36 (31.0%)	Dysmenorrhea: CR: 25 (30.1%) PR: 58 (69.9%) SeD: 0 (0%)	Menorrhagia: 10 (8.6%)	Menorrhagia: CR: 11 (14.7%) PR: 53 (70.7%) SeD: 11 (14.6%)
Chong, 2016 (15)	33	52 (38-76)	39.4 ± 4.3	N/A	199.1 ± 75.8g	70.0 ± 31.6g	7.8 ± 2.5	0.8 ± 1.5	2.5 ± 1.8	0.2 ± 0.6
Dai, 2012 (16)	86	24.8 ± 17.3 (6-60)	38 (27-48)	N/A	Grade 0 = 196.8, Grade 1 = 83.3, Grade 2 = 103.7, Grade 3 = 99.1, Grade 4 = 92.0	N/A	Grade 0 = None, Grade 1 = 18, Grade 2 = 17, Grade 3 = 32, Grade 4 = 10	N/A	N/A	N/A
Osada, 2011 (17)	104	123	37.6 ± 6.9	N/A	N/A	N/A	10	1.67	10	2.9
Wang, 2009 (Surgery only) (18)	51	24	37.0 ± 4.8	N/A	N/A	N/A	3.86 ± 0.51	1.1 ± 0.9	3.1 ± 1.4	0.9 ± 0.8
Wang, 2009 (Surgery+GnRH) (18)	114	24	38.9 ± 3.8	-	-	-	3.94 ± 0.43	0.8 ± 0.8	3.7 ± 1.0	0.9 ± 0.8
Partial excision of adenomyosis										
Yu, 2018 (19)	49	55	40.6 ± 5.2	-	-	N/A	9.1 ± 1.0	12m: 3.2 ± 3.3 24 m: 3.3 ± 3.4 36 m: 4.1 ± 3.5	N/A	N/A
Jun-Min, 2018 (20)	198	24	36.2 ± 8.6	-	338.5 ± 62.7	42.9 ± 10.3	9.2 ± 1.0	0.9 ± 1.1	pads: 38.7 ± 19.8	pads:3.9 ± 1.8
Xia, 2017 (21)	51	24	42.5 ± 3.8	≥1: 37/51	N/A	Median weight of resected tissue: 54.4 ± 46.9g	Symptoms Menorrhagia alone 11/51 Dysmenorrhea alone 9/51 Both 31/51	Complete relief: 14 patients (36.84%), Obvious relief: 17 (44.74%). Partial relief: 2 (5.3%) No response: 3 (7.9%). Clinical effectiveness: 33 (86.8%)	Symptoms Menorrhagia alone 11/51 Dysmenorrhea alone 9/51 Both 31/51	Menorrhagia n=42: Complete relief:4 (10.3%) Obvious relief: 10 (25.6%) Partial relief: 19 (48.7%) No response: 6 (15.4%) Clinical effectiveness: 33 (84.6%)
Yang, 2017 (With plexus ablation) (22)	50	36	40.4 ± 3.7	N/A	200.4 ± 55.3	134.0 ± 28.6	8.3 ± 1.2	2.6 ± 0.9	PABC score: 122.6 ± 34.2	PABC score: 62.2 ± 13.4
Yang, 2017 (Without plexus ablation) (22)	52	36	39.6 ± 4.0	-	202.3 ± 54.5	133.0 ± 35.1	8.3 ± 1.1	5.0 ± 1.4	132.6 ± 36.8	61.8 ± 13.5

Supplemental Table 1

Continued

Author, Year	n	Follow-up (months)	Age	Parity	Pre-Op Uterine Volume (cm^3)	Post-Op Uterine Volume (cm^3)	Pre-Op Pain Score	Post-Op Pain Score	Pre-Op Bleeding Score	Post-Op Bleeding Score
Huang, 2015 (Double-Flap) (23)	46	12	37.1 ± 6.6	1.1 ± 0.1	209.1 ± 117.5	45.8 ± 4.9	8.2 ± 1.5	12 m: 0.2 ± 0.6, 24 m: 0.4 ± 0.9	8.1 ± 1.3	12 m: 3.7 ± 0.6, 24 m: 3.8 ± 0.6
Huang, 2015 (Conventional) (23)	48	24	36.6 ± 5.9	1.1 ± 0.1	198.5 ± 82.6	59.7 ± 24.1	8.1 ± 1.6	12 m: 0.8 ± 1.1, 24 m: 02.0 ± 2.1	8.2 ± 1.5	12 m: 4.2 ± 0.9, 24 m: 4.6 ± 1.1
Wang, 2009 (24)	28	36	34.3 ± 2.1)	0	101.7 ± 9.2	76.0 ± 9.2	4.9 ± 0.1	1.8 ± 1.1	N/A	N/A
Kang, 2009 (25)	37	12	42 (25-52)	1 (1−2)	224.66 ± 48.7	91.6 ± 28.4	8 (7−10)	4 (3-6)	158 (136−255)	59 (19−76)
Studies with cases of partial & complete excision of adenomyosis										
Lin, 2018 (Surgery + LNG-IUS) (26)	54	24	38.8 ± 5.1	-	-	-	8.6 ± 1.6	2.4 ± 2.8	-	N/A
Lin, 2018 (Surgery only) (26)	61	24	38.5 ± 5.3	-	-	-	2.6 ± 3.0	-	-	-
Liu, 2014 (27)	182	36	40.6 ± 6.2	1 (1−2)	218.5 ± 31.8	91.2 ± 18.6	7.7 ± 1.8	4.2 ± 1.5	146 (128-235)	58 (29-78)
Kitade, 2018 (28)	76	36	36 (28−39)	-	-	N/A	9.3 (9−10)	3.5 (1−6)	N/A	N/A
Hysterectomy										
Ajao, 2018 (29)	171	62	46.6 ± 6.8	2 (0-5)	N/A	N/A	Pain: 98/151, Dyspareunia: 49/151	Pain: 12/98 (12.2%); Dyspareunia: 11/45 (24.4%)	150/171	17/150 (11.3%)
Berner, 2014 (30)	19	12	43.7 ± 4.8	1.6 (1.1)		N/A	VAS score, mean (SD): 6.3 (2.7). Weak: 4 (21.1%) Moderate: 7 (36.8%) Severe: 8 (42.1%)	VAS score, mean (SD):1.0 (2.0), Pelvic pain: None: 12 (63.2%) Weak: 4 (21.1%) Moderate: 2 (10.5%) Severe:1 (5.3%)	N/A	N/A
Liu, 2017 (31)	66	12	45.4 ± 4.3		187.9 (137.2 − 241.6)	N/A	27.9 ± 9.4, Grade 2−3	60.5 ± 8.2	78.4 ml (35.0 −110.0)	N/A
Endomyometrial ablation/Resection										
Philip, 2018 (32)	43	36	46.17 ± 3.74	2.02 ± 1.22	N/A	N/A	Dysmenorrhea 33/43 (76.7) VAS: 5.2 ± 3.3, VAS>4 30/43 (69.8%), VAS<4 13/43 (30.2%)	VAS score>4:12/33 (36.4%); VAS score<4:11/33 (33.3%)	AUB:43/43 (100%); HMB:37/43 (86.0%); IMB:19/43 (44.2%)	AUB: 14/43 (32.6%) HMB:6/43 (14.0%) IMB:9/43 (20.9%) AMENORRHEA: 16/43 (37.2%)

Pre-Op: Pre-Operative Post-Op: Post-Operative; N/A: Non Applicable; CR: Complete Relief; PR: Partial Relief; SeD: Severe Disease; SD: Standard Deviation; PBAC: Pictorial Bleeding Assessment Chart; VAS: Visual Analogue Score; AUB: Abnormal Uterine Bleeding; HMB: Heavy Menstrual Bleeding; IMB: Intermediate Menstrual Bleeding

Supplemental Table 2

Pregnancy rates from the studies included in the systematic review

Author, Year	n	Follow-up (months)	Age	Parity	Patients wishing to conceive (n, %)	Total conceptions (n, %)	Miscarriages (n, %)	Ongoing pregnancies (n,%)	Preterm (n, %)	Full-term (n, %)	Total deliveries (n, %)	*Uterine rupture in pregnancy*
Total	1572				364/1572 (23.1%)	126/364 (34.6%)	23/126 (18.2%)	1/126 (0.8%)	8/112 (7.1%)	83/112 (74.1%)	102/126 (81.0%)	1/126 (0.8%)
Complete excision of adenomyosis / Adenomyomectomy												
Kwack et al, 2018 (Laparoscopic group) (17)	108	13.4 ± 13.1	42.0 ± 4.8	1.7 ± 0.8	108/108 (100%)	2/108 (1.8%)	(0.0%)%)	0/14 (0.0%)	N/A	N/A	11/14 (78.6%)	0%
Kwack et al, 2018 (Laparotomy group) (17)	116				116/116 (100%)	12/116 (10.3%)	3/12 (25.00/2					0%
Chong et al, 2016 (18)	33	52 4	39.4 ± 4.3	-	-	-	-	-	-	-	-	-
Dai et al, 2012 (19)	86	24.8 ± 17.3	38	-	2/86 (2.3%)	2/2 (100.0%)	1/2 (50.0%)	1/2 (50.0%)	0/2 (0.0%)	0/2 (0.0%)	0/2 (0.0%)	0/2 (0.0%)
Osada et al, 2011 (20)	104	123	37.6 ± 6.9	-	26/104 (25%)	16/26 (61.5%)	2/16 (12.5%)	0/16 (0.0%)	0/16 (0.0%)	14/16 (0.0%)	14/16 (87.5%)	0/16 (0.0%)
Wang et al, 2009 (Surgery only) (21)	51	24	37.0 ± 4.8	-	27/51 (52.9%)	20/27 (74.1%)	3/20 (15.0%)	0/20 (0.0%)	2/20 (10.0%)	15/20 (75.0%)	17/20 (85.0%)	0/20 (0.0%)
Wang et al, 2009 (Surgery + GnRH) (21)	114	24	38.9 ± 3.8	-	44/114 (38.6%)	35/44 (79.5%)	3/35 (8.6%)	0/35 (0.0%)	5/35 (14.3%)	27/35 (77.1%)	32/35 (91.4%)	0/35 (0.0%)
Subtotal	612				323/612 (52.8%)	87/323 (26.9%)	12/87 (13.8%)	1/87 (1.1%)	7/73 (9.6%)	56/73 (76.7%)	74/87 (85.1%)	0/87 (0.0%)
Partial excision of adenomyosis												
Yu et al, 2018 (22)	49	55	40.6 ± 5.2	-	-	-	-	-	-	-	-	-
Jun-Min et al, 2018 (23)	198	24	36.2 ± 8.6	-	-	2/2 (100.0%)	0/2 (0.0%)	0/2 (0.0%)	1/2 (50.0%)	1/2 (50.0%)	2/2 (100.0%)	0%
Xia et al, 2017 (24)	51	24	42.5 ± 3.8	≥1: 37/51	-	-	-	-	-	-	-	-
Yang et al, 2017 (With plexus ablation) (25)	50	36	40.4 ± 3.7	-	-	-	-	-	-	-	-	-
Yang et al, 2017 (Without plexus ablation) (25)	52	36	39.6 ± 4.0	-	-	-	-	-	-	-	-	-
Huang et al, 2015 (Double-Flap) (26)	46	12	37.1 ± 6.6	1.1 ± 0.1	6/46 (13%)	-	-	-	-	-	-	-
Huang et al, 2015 (Conventional) (26)	48	24	36.6 ± 5.9	1.1 ± 0.1	4/48 (8.3%)	-	-	-	-	-	-	-
Wang et al, 2009 (27)	28	36	34.3 ± 2.1	0		13/28 (46.4%)	4/13 (30.8%)	0/13 (0.0%)	0/13 (0.0%)	9/13 (0.0%)	9/13 (69.2%)	0/13 (0.0%)
Kang et al, 2009 (28)	37	12	42	1	-	-	-	-	-	-	-	-
Subtotal	587				10/587 (1.7%)	15/30 (50.0%)	4/15 (26.7%)	0/15 (0.0%)	1/15 (6.7%)	10/15 (66.7%)	11/15 (73.3%)	0/15 (0.0%)
Studies with cases of partial & complete excision of adenomyosis												
Lin et al, 2018 (Surgery + LNG-IUS) (29)	54	24	38.8 ± 5.1	-	-	7/54 (13.0%)	3/7 (42.8%)	0/7 (0.0%)	0/7 (0.0%)	4/7 (57.2%)	4/7 (57.2%)	0/7 (0.0%)
Lin et al, 2018 (Surgery only) (29)	61	24	38.5 ± 5.3	-	-	2/61 (3.2%)	0/2 (0.0%)	0/2 (0.0%)	0/2 (0.0%)	2/2 (100.0%)	2/2 (100.0%)	1/2 (50.0%)
Liu et al, 2014 (30)	182	36	40.6 ± 6.2	1 (1−2)	-	-	-	-	-	-	-	-
Kitade et al, 2018 (31)	76	36	36		31/76 (40.7%)	15/31 (48.4%)	4/15 (26.7%)	0/15 (0.0%)	0/15 (0.0%)	11/15 (73.3%)	11/15 (73.3%)	0/15 (0.0%)
Subtotal	373				31/373 (8.3%)	24/146 (16.4%)	7/24 (29.1%)	0/24 (0.0%)	0/24 (0.0%)	17/24 (70.8%)	17/24 (70.8%	1/24 (4.17%)