



Review Article

Laparoscopic Excision Versus Ablation for Endometriosis-associated Pain: An Updated Systematic Review and Meta-analysis

Jyotsna Pundir, MD*, Kireki Omanwa, MRCOG, Elias Kovoor, MD, Vishal Pundir, MS, Gillian Lancaster, PhD, and Peter Barton-Smith, MD

From the Centre for Reproductive Medicine, St Bartholomew's Hospital, West Smithfield, London, United Kingdom (Dr. J. Pundir), Department of Obsterics and Gynaecology, University of Nairobi, Nairobi, Kenya (Dr. Omanwa), Maidstone and Tunbridge Wells NHS Trust, Kent, United Kingdom (Drs. Kovoor and V. Pundir), Institute of Primary Care and Health Sciences, Keele University, Newcastle, United Kingdom (Dr. Lancaster), and Princess Grace Hospital, London, United Kingdom (Dr. Barton-Smith).

ABSTRACT The aim of this study was to update the evidence on the surgical management of endometriosis-associated pain. Does laparoscopic excision offer any benefits over laparoscopic ablation? This is a systematic review and meta-analysis in which we searched MEDLINE, Embase, Institute for Scientific Information conference proceedings, the International Standard Randomised Controlled Trial Number registry, the Register and Meta-register for randomized controlled trials, the World Health Organization trials search portal, the Cochrane Library, and the British Library of electronic theses. Three randomized controlled trials were included, which enrolled 335 participants with a sample size per study ranging from 24 to 178 participants. Of these 3 studies, data from 2 could be pooled for meta-analysis. The primary outcome measure was the reduction in the visual analog scale score for dysmenorrhea. The secondary outcome measures included the reduction in the visual analog scale score for dyspareunia, dyschezia, and chronic pelvic pain and the reduction in Endometriosis Health Profile-30 core pain scores. The meta-analysis showed that the excision group had a significantly greater reduction in symptoms of dysmenorrhea (mean difference [MD] = 0.99; 95% confidence interval [CI], -0.02 to 2.00; p = .05) and dyschezia (MD = 1.31; 95% CI, 0.33-2.29; p = .009) compared with ablation. The symptoms of dyspareunia showed a nonsignificant benefit with excision (MD = 0.96; 95% CI, -0.07 to 1.99; p = .07). Data from 1 study showed a significant reduction in chronic pelvic pain (MD = 2.57; 95% CI, 1.27 - 3.87; p = .0001) and Endometriosis Health Profile-30 core pain scores (MD = 13.20; 95%)CI, 3.70–22.70; p = .006) with the excision group compared with the ablation group. The limited available evidence shows that at 12 months postsurgery, symptoms of dysmenorrhea, dyschezia, and chronic pelvic pain secondary to endometriosis showed a significantly greater improvement with laparoscopic excision compared with ablation. Journal of Minimally Invasive Gynecology (2017) ■, ■–■ © 2017 AAGL. All rights reserved.

Keywords: Ablation; Endometriosis; Excision; Laparoscopic; Pain; Vaporization

The evaluation and treatment of endometriosis have evolved alongside the development of minimally invasive surgery in recent decades. This is a direct result of having a relatively simple, low morbidity means of assessing the female pelvis using diagnostic laparoscopy. Although recently

The authors declare that they have no conflict of interest.

1553-4650/\$ - see front matter 0 2017 AAGL. All rights reserved. http://dx.doi.org/10.1016/j.jmig.2017.04.008 we have developed the ability to accurately diagnose and map the presence of deep infiltrating endometriosis in specialist centers with readily accessible transvaginal or transrectal ultrasound [1,2], we still lack the ability to diagnose early-stage disease without diagnostic laparoscopy. Once it has been found, it is recommended in European Society of Human Reproduction and Embryology guidelines to see and treat the lesions when possible [3] because there is evidence that their removal reduces endometriosis-associated pelvic pain and improves spontaneous fertility rates [4-6].

The technique used during laparoscopy for achieving this remains a contentious issue, with many general

Corresponding author: Jyotsna Pundir, MD, Centre for Reproductive Medicine, Second Floor, Kenton and Lucas Wing, St Bartholomew's Hospital, West Smithfield, London EC1A 7BE, UK. E-mail: jyotsnapundir@yahoo.com

Submitted November 17, 2016. Accepted for publication April 19, 2017. Available at www.sciencedirect.com and www.jmig.org

Downloaded for Lib Rary (whippsx.library@bartshealth.nhs.uk) at Barts Health NHS Trust from ClinicalKey.com by Elsevier on May 26, 2017. For personal use only. No other uses without permission. Copyright ©2017. Elsevier Inc. All rights reserved.

gynecologists not seeing and treating or applying only superficial electrosurgical ablation. Those with an interest in endometriosis are more likely to use more comprehensive vaporization techniques with laser, helium gas, or argon plasma therapy through to full surgical excision of lesions.

A recent Cochrane review concluded that there was lowquality evidence that laparoscopic excision and ablation were similarly effective in relieving pain [7]. However, this review only included 1 trial from the medical literature. These data have been used in European Society of Human Reproduction and Embryology guidelines for endometriosis as grade C evidence advising that clinicians may consider both ablation and excision of peritoneal endometriosis to reduce endometriosis-associated pain [3]. Because there have been more studies identified on this subject, our study sought to systematically rereview and update the existing evidence related to the impact of laparoscopic excision on endometriosisassociated pelvic pain compared with laparoscopic ablation or vaporization to further guide clinical practice.

Materials and Methods

Literature Search Methodology

We searched MEDLINE (1950-October 2014) and Embase (1980-October 2014). The search also included ISI conference proceedings as well as databases for the registration of ongoing and archived randomized controlled trials (RCTs), namely, the International Standard Randomised Controlled Trial Number registry, the Register and Meta-register for RCTs (http://www.controlled-trials.com), and the World Health Organization trials search portal (i.e., the International Clinical Trials Registry Platform, apps.who.int/trialsearch/Trial). A combination of Medical Subject Headings and text words were used to generate 2 subsets of citations: 1 including studies of "endometriosis" and the second "excision, ablation, diathermy, vaporisation, vaporization." These subsets were combined using "AND" to generate a subset of citations relevant to our research question. We also searched the Cochrane Library for RCTs and the British Library of electronic theses online service (http://ethos.bl.uk) with the search term of "endometriosis." The reference lists of all known primary and review articles were examined to identify cited articles not captured by the electronic searches. No language restrictions were placed on any of our searches. The searches were conducted independently by J.P. and V.P.

Study Selection

The PICOS (Population Intervention Controls Outcomes Type of Studies) study protocol for the review was followed. Studies were selected if the target population was women undergoing laparoscopic surgery for endometriosis with any excision technique and were compared with women with any ablative or vaporization technique. The primary outcome measure was reduction in dysmenorrhea, and the secondary outcome measures were a reduction in dyspareunia, dyschezia, pelvic pain, chronic pelvic pain, and quality of life Endometriosis Health Profile-30 (EHP-30) pain scores. We included all randomized and nonrandomized trials in this systematic review. Studies were selected in a 2-stage process. First, the titles and abstracts from the electronic searches were scrutinized by 2 reviewers independently (J.P. and V.P.), and the full articles of all citations that were likely to meet the predefined selection criteria were obtained. We wrote to the corresponding authors in cases in which data were not clear or reported or a full article was not available for the details. Second, final inclusion or exclusion decisions were made on examination of the full articles. Any disagreements about inclusion were resolved by consensus or arbitration by a third reviewer (E.K.).

Assessment of Methodological Quality and Data Extraction

Each study included was assessed for sequence generation, allocation sequence concealment, blinding, incomplete outcome data, selective outcome reporting, and other potential sources of bias. The selected studies were assessed for methodological quality using the components of study design that are related to internal validity. The assessment of methodological quality was based on the guidelines in the Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0). The selected studies were assessed for methodological quality using the components of study design that are related to internal validity [8]. Two reviewers (V.P. and K.O.) completed data extraction and quality assessment [9]. Information on the method of randomization, allocation concealment, blinding, intention-to-treat analysis, and follow-up rates was sought by examining the full-text articles. Study characteristics and participant features were extracted from each study.

Statistical Analysis

From each study, outcome data were extracted by 2 reviewers (J.P. and K.O.). For continuous estimates, the mean difference (MD) with the 95% confidence interval (CI) was calculated using the inverse-variance method. We considered $p \le .05$ to be statistically significant. The results from individual studies were pooled using random effects models because we assumed that the observed estimates of treatment effect would vary across studies because of real differences in the treatment effect in each study caused by study characteristics (as well as sampling variability) [10]. Heterogeneity of the exposure effects was evaluated graphically using forest plots [11] and statistically using the I^2 statistic [12]. A chi-square test for heterogeneity was also performed, and the p values are presented. Exploration of causes of heterogeneity was planned using variations in features of population, exposure, and study quality. We adhered to published guidance for conducting systematic reviews throughout (i.e., The Cochrane Handbook). Statistical

Downloaded for Lib Rary (whippsx.library@bartshealth.nhs.uk) at Barts Health NHS Trust from ClinicalKey.com by Elsevier on May 26, 2017.

For personal use only. No other uses without permission. Copyright ©2017. Elsevier Inc. All rights reserved.

analyses were performed using RevMan 5.2.7 software (Cochrane Collaboration, Oxford, UK).

Results

Literature Search

The process of literature identification and selection is summarized in Fig. 1. Of the 502 publications identified by the search, 13 were selected during the initial screening. After examination of the full articles, 10 were excluded (Table 1) [5-7,13-19]. Therefore, 3 studies satisfied the selection criteria and were included in this review [20-22]. These 3 studies were randomized trials. We did not find any nonrandomized trials addressing this subject.

Study Characteristics

The 3 included RCTs enrolled 335 participants. In total, 167 women were randomized to treatment with excision,

and 168 women were randomized to ablation. Overall, 222 (66.3%) women completed the follow-up of the study protocol, 114 (68.2%) in the excision arm and 108 women in the ablation arm (64.3%), with a similar rate of follow-up in both arms. The sample size per study varied across the trials and ranged from 24 to 178 participants. Of these 3 studies, 2 were published as full articles [20,21], and 1 was a doctoral thesis dissertation examined and accepted at the University of Surrey, Guildford, UK [22].

The characteristics and methodological quality of the included trials are summarized in Tables 2 and 3, respectively. The inclusion and exclusion criteria, sample size, treatment protocol, and all outcomes reported are included. The risk of bias from the included studies is represented in Figs. 2 and 3. Our judgments about each risk of bias item, presented as percentages across all included studies, are shown in Fig. 2 and for each risk of bias item for each included study in Fig. 3. All 3 studies had a parallel design. The method of randomization was performed by



Downloaded for Lib Rary (whippsx.library@bartshealth.nhs.uk) at Barts Health NHS Trust from ClinicalKey.com by Elsevier on May 26, 2017. For personal use only. No other uses without permission. Copyright ©2017. Elsevier Inc. All rights reserved.

4

Table 1	
Reason of exclusion of studies in the s	stematic review of laparoscopic excision versus ablation for endometriosis-associated pain
Study	Reason for exclusion
Abbott et al, 2003	Prospective observational cohort study for women up to 5 years after laparoscopic excision of endometriosis
Abbott et al, 2004	Comparison of diagnostic laparoscopy with full excisional surgery
Duffy et al, 2014	Cochrane review
Healey et al, 2014	Same cohort, reported 5-year follow-up data
Jacobson et al, 2004	Cochrane review (withdrawn subsequently)
Michalopoulos et al, 2012	Review
Suchetha et al, 2012	Retrospective observational data
Wood and Mehar, 1996	Observational data on excision
Yeung et al, 2013	A pilot feasibility study for a randomized study of excision versus ablation
Yeung et al, 2009	Review

computer-generated random numbers in 1 study [21] and by random sequence generation in blocks of 10 in 2 studies [20,22]. Allocation concealment was in place in 2 studies [21,22]. All studies claimed they were double-blinded; however, it was not clear in the methodology of the study of Wright et al [20]. All trials addressed incomplete outcome data. The follow-up duration was 6 months in 1 study [20] and 12 months in the remaining 2 studies [21,22]. The follow-up rate varied between 58% and 100%. All studies performed a priori power calculation to determine the sample size needed for the outcome of pelvic pain.

Description of Studies

The study of Wright et al included 24 women [20]. It compared excisional with ablative treatment for revised American Society for Reproductive Medicine (rASRM) stage 1 (mild endometriosis) [23] endometriosis in the management of chronic pelvic pain. Participants completed a questionnaire detailing symptoms related to chronic pelvic pain (pelvic pain, dysmenorrhea, dyspareunia, dyschezia, constipation, diarrhea, cramps exercise pain, back pain, and fatigue) and rated their pain on a ranked ordinal scale preoperatively and after 6 months after surgery. Signs were assessed by the patient rating the amount of discomfort felt during palpation (uterine mobility, tenderness, adnexal pain, ultrasound scan, and pouch of Douglas). The group used 3-mm monopolar diathermy scissors with a combination of 90 W pure cut and 50 W coagulation for excision and a coagulation current of 50 W with the closed end of a pair of 3-mm monopolar laparoscopic scissors for ablation. The study reported that both treatment modalities produced good symptomatic relief and a reduction in pelvic tenderness (67%). There was no significant difference between the 2 procedures for any of the individual questionnaire items. A high pain score before treatment was suggested to be a good predictor of appreciable improvement after surgery.

The study of Healey et al [21] randomized 178 women of reproductive age presenting with pelvic pain and visually proven endometriosis. Women with rASRM endometriosis stage 1 to 3 were included. The study recruited 89 women in each arm of excision and ablation. Out of these 178 women, 95 women completed the study at 12 months, 54 women in the excision arm and 49 women in the ablation arm. Each subject's endometriosis was scored and staged with the use of the rASRM system and the superficial/deep categorization [24] at the end of the operation. Both groups were comparable regarding baseline patient characteristics. Women completed a questionnaire rating their various pains using visual analog scales (VASs) preoperatively and at 3, 6, 9, and 12 months after surgery. The study did not specify the method of excision and ablation because they allowed individual consultants to use their preferred method. Of the excision group, 87% subjects had positive histology for endometriosis. The study reported no significant difference in reduction in overall VAS pain scores at 12 months after surgery between ablation and excision. They suggested that because of the nonsignificant trends seen in this study, a larger study may find a difference in outcomes looking at dyspareunia, rectal pain, or dyschezia. Subjects were also stratified on the basis of superficial and deep endometriosis. No significant differences were found in changes in VAS score among women with deep endometriosis undergoing excision or ablation.

The doctoral thesis of Barton-Smith [22] was a randomized blinded trial of CO_2 laser vaporization versus harmonic scalpel excision of rASRM stage 1 to 3 (i.e., superficial and deep infiltrating endometriosis) and excluded rASRM stage 4 (i.e., severe disease). Pelvic pain was recorded preoperatively and at 3, 6, and 12 months after surgery. The hypothesis was that thorough vaporization should not be inferior to excision. The study recruited 133 women and randomized 66 to excision and 67 to ablation. Ninety-five women completed the study at 12 months, 48 in the excision group and 47 in the ablation group. Histology was taken in 65 of 133 cases (49%), 49 from the excision group and 16 from the vaporization group. Overall, 54 of the 65 cases had histology positive for endometriosis, showing a successful

Table 2

Characteristics of the studies included in the review of laparoscopic excision versus ablation for endometriosis-associated pain

Author

number						
of cases	Inclusion criteria	Exclusion criteria	Excision	Ablation	Method of assessment	Outcomes reported
Barton-Smith, 2010 N = 95	Severity of disease: rASRM stages 1-3 Women with pelvic pain; >18 years old; absence of contraindications to both treatments and consenting to participate	 Pregnant, breast-feeding, unwilling to discontinue hormonal treatment for 6 months postoperatively, other conditions causing pelvic pain (e.g., gastrointestinal or genitourinary). Patients who had received additional treatment for endometriosis within 3 months of surgery. rASRM stage 4/severe disease 	At recruitment n = 66 By 12 months n = 48 Excision with Endo-Surgery LCS-C5 or ACE Harmonic Scalpel	At recruitment n = 67 By 12 months n = 47 Vaporization with CO ₂ standardized – 300 mm focal length and 30 W power with a 2.5-mm Swiftlase spot	 Data collection preoperatively and at 3, 6, and 12 months postoperatively. EHP-30 core pain domain (EHP-30 HRQoL), pain score between 0 and 100 where 0 is the best possible state. Pain also assessed by 10-cm VAS for dysmenorrhea, dyspareunia, chronic pelvic pain, and dyschezia. HRQoL with the EHP-30 core domains for control and powerlessness, emotional well-being, social support, self-image, and sexual intercourse; each with a 0-100 score where 0 is the best and 100 the worst possible outcome. 	Follow up: at 3, 6, and 12 months Primary outcome: EHP 30 HRQoL Other outcomes: VAS for dysmenorrhoea, dyspareunia, chronic pelvic pain, and dyschezia HRQoL: EHP-30 Whether women took hormonal treatment, had subsequent surgery, or became pregnant
Healey et al, 2010 N = 103	Severity of disease: rASRM system and also the superficial/deep categorization at the end of the operation. Women with a history of dysmenorrhea, dyspareunia, or cyclical pelvic pain; >18 years old; informed consent; and English speaking.	Not using or planning to use hormonal therapy. On laparoscopy, no obvious endometriosis; obvious endometriosis involving muscle levels of bowel, bladder, or ureter. rASRM stage 4/severe disease	At recruitment n = 89 By 12 months n = 54 Excision Method not specified	At recruitment n = 89 By 12 months n = 49 Ablation Method not specified It allowed individual consultants to use their preferred method for ablation.	A questionnaire assessing pain types and severity was completed by women before surgery and every 3 months for 12 months. Pain severity: measured by VASs made up of a 10-cm line marked with "no pain" at the left end and "worst imaginable pain" at the right end. Scores presented as a range from 0 to 10.	Follow-up: at 3, 6, and 12 months Preoperative and postoperative AFS scores. Reduction in VAS score 12 months after the operation: overall pain, pelvic pain, period pain, back pain, rectal pain, thigl pain, abdominal pain, defecation pain, voiding pain, nausea, abdominal bloating, vomiting, and dyspareunia (Continued

Pundir et al. Excision versus Ablation for Endometriosis Associated Pain

Indometriosis Associated Pain

ARTICLE IN PRESS

Mean change in questionnaire pain, fatigue. Signs: uterine cramps exercise pain, back adnexal pain, ultrasound dyspareunia, dyschezia, scan, pouch of Douglas. constipation, diarrhea, Symptoms: pelvic pain, AFS = American Fertility Society; EHP-30 = Endometriosis Health Profile-30; HRQoL = health-related quality of life; rASRM = revised American Society of Reproductive medicine criteria; VAS = visual analog scale. mobility, tenderness, Follow-up: 6 months Outcomes reported dysmenorrhea, scores and 6 months after surgery. Questionnaire preoperatively questionnaire rating the symptoms on a ranked amount of discomfort ordinal scale of 1-5. Signs: patients rate the Method of assessment during palpation. Symptoms: with a current of 50 W. The closed could be seen. All visible until the peritoneum was lesions were coagulated. monopolar laparoscopic destroyed and an eschar ablation at coagulation Coagulation continued end of a pair of 3-mm Monopolar diathermy scissors was used. Ablation n = 12 performed in cutting mode. combination of 90 W pure cut and 50 W coagulation; diathermy scissors with a majority of the surgery Monopolar excision with 3-mm monopolar Excision n = 12 uterosacral nodularity or infiltrating deep disease disease: ovarian cyst or Evidence of advanced Exclusion criteria history of dysmenorrhea, pelvic pain, or backache dyspareunia, dyschezia, Severity of disease: rASRM 1: mild, Inclusion criteria Women with a superficial Wright et al, of cases number Continued Author N = 242005

correlation between visual inspection and histologic analysis in 83% of cases. The proportion of women showing pain improvement was not statistically significant between the 2 groups although there was a trend toward excision being superior (excision group: 85.4% and vaporization group: 72.9%). However, the extent of pain improvement in the reduction of EHP-30 pain scores was significantly better for excision compared with vaporization at 12 months for both superficial and deep disease. VAS scores were significantly improved at 12 months in all pain domains for excision, whereas vaporization showed significant improvements for dysmenorrhea and dyspareunia but not for dyschezia. Improvement in chronic pelvic pain was significantly better in excision compared with vaporization. Analysis of deep disease alone revealed that, unlike excision, vaporization did not show a significant improvement in EHP-30 pain scores at 12 months.

We could not include results from Wright et al [20] in this meta-analysis because of incomplete data. We pooled the data from the remaining 2 studies in this meta-analysis where possible [21,22].

Primary Outcome Measure

Reduction in VAS Score for Dysmenorrhea

Pooling of the results of the 2 studies [21,22] showed that the excision group had a significantly greater reduction in VAS scores of dysmenorrhea compared with ablation (MD = 0.99; 95% CI, -0.02 to 2.00; p = .05; Fig. 4). There was no significant heterogeneity between the studies $(I^2 = 4\%; \chi^2 = 1.04, p = .31).$

Secondary Outcome Measures

Reduction in VAS Score for Dyspareunia

Pooling of the results of these 2 studies [21,22] showed that the excision group had a significantly greater reduction in VAS scores of dyspareunia compared with ablation (MD = 0.96; 95% CI, -0.07 to 1.99; p = .07; Fig. 5). There was no significant heterogeneity between the studies ($I^2 = 0\%$; $\chi^2 = 0.31$, p = .58).

Reduction in VAS Score for Dyschezia

Pooling of the results of these 2 studies [21,22] showed that the excision group had a significantly greater reduction in VAS scores of dyschezia compared with ablation (MD = 1.31; 95% CI, 0.33-2.29; p = .009; Fig. 5). There was no significant heterogeneity between the studies ($I^2 = 0\%$; $\chi^2 = 0.26$, p = .61).

Reduction in VAS Score for Chronic Pelvic Pain

One study reported on chronic pelvic pain [22], which showed a significant reduction in chronic pelvic pain with

Downloaded for Lib Rary (whippsx.library@bartshealth.nhs.uk) at Barts Health NHS Trust from ClinicalKey.com by Elsevier on May 26, 2017. For personal use only. No other uses without permission. Copyright ©2017. Elsevier Inc. All rights reserved.

Table 2

Pundir et al. Excision versus Ablation for Endometriosis Associated Pain

Table 3

Quality of studies included in the systematic review of laparoscopic excision versus ablation for endometriosis-associated pain

Author	Method of randomization	Allocation concealment	Blinding	Intention-to-treat analysis	Follow-up rate (%)	Design
Barton – Smith 2010	Random sequence generation in blocks of 10	Yes	Double	Yes	77	Randomized double blind
Healey et. al., 2010	Computer-generated random numbers	Yes	Double	Yes	58	Randomized double blind
Wright et. al., 2005	Random sequence generation in blocks of 10	ND	ND	ND	100	Randomized double blind
ND = not documented.						

the excision group compared with the ablation group (MD = 2.57; 95% CI, 1.47-3.67; p < .00001; Fig. 5).

Reduction in VAS Score for Pelvic Pain

One study reported on pelvic pain [21], which showed no significant difference between the excision and ablation groups (MD = -0.10; 95%, CI -1.30 to 1.10; p = .87; Fig. 5).

Reduction in EHP-30 Core Pain Score

Only 1 study reported on this outcome [22]. This study showed that the excision group had significantly more reduction in EHP-30 core pain scores compared with ablation (MD = 13.20; 95% CI, 5.15-22.25; p = .001; Fig. 5).

Discussion

Our systematic review identified and included 3 RCTs and pooled the data from 2 RCTs with a comparative meta-analysis of laparoscopic excision versus ablation in alleviating endometriosis-associated pain symptoms. We could not include results from Wright et al [20] in the meta-analysis because of incomplete data. We pooled the data from the remaining 2 studies in this meta-analysis where possible [21,22]. The current Cochrane review [7] also excluded the study of Wright et al [20] from metaanalysis because of incomplete data and pooled data from only 1 RCT [21].

Both the excision and ablation of endometriosis have been shown to improve pain symptoms versus controls in randomized studies at 12 months after surgery [4,13]. The main symptom of endometriosis is dysmenorrhea, which Sutton et al [4] reported as the worst pain symptom women complained of and Abbott et al [13] reported as the most common symptom on follow-up in their respective RCTs. Therefore, dysmenorrhea was selected as the primary outcome. In this meta-analysis, dysmenorrhea, dyschezia, and chronic pelvic pain, all important symptoms of endometriosis, have shown significantly greater improvement from excision compared with ablation at 12 months after surgery. The symptom of dyspareunia showed a trend toward benefit although it did not reach statistical significance. Healey et al [21] gave no definition for pelvic pain in his article, whereas Barton-Smith [22] defined chronic pelvic pain as pelvic pain lasting for greater than 6 months not related to menstruation in order to differentiate it from dysmenorrhea. Many



Downloaded for Lib Rary (whippsx.library@bartshealth.nhs.uk) at Barts Health NHS Trust from ClinicalKey.com by Elsevier on May 26, 2017. For personal use only. No other uses without permission. Copyright ©2017. Elsevier Inc. All rights reserved.

Fig. 3

The risk of bias summary for studies included in the review of laparoscopic excision versus ablation for endometriosis-associated pain.



definitions define chronic pelvic pain as including cyclical pain, and, if Healey et al's definition also included cyclical menstruation pain, then the definitions are heterogeneous and are not comparable in a meta-analysis. Therefore, we did not pool these data and reported them separately. Healey et al showed no significant improvement in any area between the 2 modalities although it did show a trend toward a greater reduction in dyspareunia, rectal pain, and defecation pain in the excision group compared with the ablation group.

Strengths and Limitations

In general, both trials were sufficiently powered, well designed, and had acceptable risk of bias summaries. Both included an investigation of dysmenorrhea, the most common symptom of endometriosis, and measured it in the same way as for the secondary outcome measures of dyspareunia and dyschezia, resulting in a more than reasonable number of outcomes to compare. Both groups had more deep infiltrating disease cases in their excision groups compared with their ablation groups, thus reducing the risk of bias in comparing the 2 trials.

This meta-analysis could only pool data for VAS scores for pain symptoms of dysmenorrhea, dyspareunia, and dyschezia. It included quality of life data from only 1 study [22] that revealed significantly greater improvements in quality of life for excision compared with ablation in all EHP-30 domains at 12 months.

The main limitation of this review remains the inclusion of only 3 studies from the systematic review and 2 studies for pooling the results for meta-analysis. Some outcomes were reported in only 1 study. The existing meta-analysis performed by the Cochrane group on which major national and international guidelines for the management of endometriosis-associated pain are based includes only 1 study. Therefore, the reason for writing this updated review article was to provide better evidence than that currently available because a 1-study meta-analysis is not only pointless but can be misleading. The inclusion of 2 studies for a meta-analysis is also not ideal, but it is the best evidence we have for this important aspect of endometriosis. Furthermore, this updated review changes the results and conclusion of the previous Cochrane review and therefore will provide valuable information to update the evidence-based guidelines. This will lead to change in practice and therefore more effective management of endometriosis-associated pain, which has been a long-awaited outcome for clinicians. There is a precedent because we have all practiced for many years according to the 2-study meta-analysis on the management of endometrioma published by the Cochrane group. We attempted to include both randomized and nonrandomized studies with a hope to include more studies, but we found no such studies in the literature. This highlights the difficulty in conducting such surgical trials addressing the research question and the dilemma faced by the clinicians who practice evidence-based medicine and are currently forced to adopt practice based on the current Cochrane review including 1 study. This updated review will provide further information on this difficult research question, which is a very common clinical situation faced by many gynecologists.

The other main weakness in terms of interpreting pain in these 2 trials is a lack of information on coexisting

Fig. 4

	Excision Ablation			Mean Difference		Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Barton-Smith et. al., 2010	2.94	3.65	48	1.5	2.8	47	56.8%	1.44 [0.13, 2.75]	
Healey et. al., 2010	2.4	3.9	54	2	3.9	49	43.2%	0.40 [-1.11, 1.91]	
Total (95% CI)			102			96	100.0%	0.99 [-0.02, 2.00]	•

Pundir et al. Excision versus Ablation for Endometriosis Associated Pain

Fig. 5

Forest plot of comparison. Excision versus ablation for endometriosis, secondary outcomes. (1) Forest plot of comparison. Excision versus ablation for endometriosis, outcome: dyspareunia. (2) Forest plot of comparison. Excision versus ablation for endometriosis, outcome: dyschezia. (3) Forest plot of comparison. Excision versus ablation for endometriosis, outcome: chronic pelvic pain. (4) Forest plot of comparison. Excision versus ablation for endometriosis, outcome: pelvic pain. (5) Forest plot of comparison. Excision versus ablation for endometriosis, outcome: pelvic pain. (5) Forest plot of comparison. Excision versus ablation for endometriosis, outcome: eHP-30 pain score.



adenomyosis. The presence of coexisting adenomyosis is not recorded in either article and is likely to be a major factor affecting pain score improvements. At the time of both studies, the diagnosis of adenomyosis was generally retrospective in hysterectomy specimens and not by ultrasound. Adenomyosis is now routinely diagnosed on transvaginal ultrasound and even graded on the severity of appearance [25] although this grading is only just beginning to be validated as a prognostic indicator for pain [26].

For most surgeons treating endometriosis of all severities and depths, the preferred technique to be used is excision. This approach is logical because damage-prone adjacent structures like ureters, blood vessels, nerves, and bowel can be dissected free by skilled surgeons to reduce the risk of complications. Furthermore, the depth of disease can be fully assessed by excising around the disease until normal tissue is seen, thus achieving adequate clearance (in other words, the more complex the case, the greater the rationale for using excision as the chosen method). We may also bear in mind that the 2 RCTs for ablation and excision of endometriosis versus no treatment also suggested a possible advantage for excision, showing 80% versus 62.5% with ablation in women showing pain improvement at 6 months [4,13].

The case for excision would undoubtedly be more powerful if both studies were significantly in favor of excision,

9

especially because both trials were sufficiently powered unlike in the Cochrane endometrioma review in which the ambivalent result between excision and ablation came from an underpowered trial [27]. That being said, our meta-analysis suggests that laparoscopic excision significantly reduces dysmenorrhea, dyschezia, and chronic pelvic pain along with a nonsignificant reduction in dyspareunia, which are the most common symptoms of endometriosis.

Conclusion

With only 2 trials able to be included in this meta-analysis and 1 of those trials showing no statistically significant benefit for excision over ablation in any of the outcomes, the evidence cannot be deemed as conclusive. Also, comparative data on outcomes greater than 12 months are lacking. However, at 12 months postsurgery, beyond the time period of the well-documented placebo effect, all the major symptoms of endometriosis (i.e., dysmenorrhea, dyschezia, and chronic pelvic pain) showed a significantly greater improvement and a nonsignificant improvement in dyspareunia with laparoscopic excision compared with ablation in this comprehensive updated systematic review. Further welldesigned and well-conducted multicenter trials with longterm follow-up are warranted to address this issue.

References

- Hudelist G, Oberwinkler KH, Singer CF, et al. Combination of transvaginal sonography and clinical examination for preoperative diagnosis of pelvic endometriosis. *Hum Reprod.* 2009;24:1018–1024.
- Holland TK, Cutner A, Saridogan E, Mavrelos D, Pateman K, Jurkovic D. Ultrasound mapping of pelvic endometriosis: does the location and number of lesions affect the diagnostic accuracy? A multicentre diagnostic accuracy study. *BMC Womens Health.* 2013; 13:43.
- Dunselman GA, Vermeulen N, Becker C, et al. European Society of Human Reproduction and Embryology. ESHRE guideline: management of women with endometriosis. *Hum Reprod.* 2014;29:400–412.
- Sutton CJ, Ewen SP, Whitelaw N, Haines P. Prospective, randomized, double-blind, controlled trial of laser laparoscopy in the treatment of pelvic pain associated with minimal, mild, and moderate endometriosis. *Fertil Steril.* 1994;62:696–700.
- Abbott JA, Hawe J, Clayton RD, Garry R. The effects and effectiveness of laparoscopic excision of endometriosis: a prospective study with 2-5 year follow-up. *Hum Reprod.* 2003;18:1922–1927.
- Jacobson TZ, Barlow DH, Koninckx PR, Olive D, Farquhar C. Laparoscopic surgery for subfertility associated with endometriosis. *Cochrane Database Syst Rev.* 2004;4:CD001398.

Journal of Minimally Invasive Gynecology, Vol ■, No ■, ■/■ 2017

- Duffy JM, Arambage K, Correa FJ, et al. Laparoscopic surgery for endometriosis. *Cochrane Database Syst Rev.* 2014;4:CD011031.
- Julian PT Higgins and Sally Green. Cochrane Handbook for systematic reviews of interventions; version 5.1.9. Available at: http://handbook. cochrane.org. Accessed May 8, 2017.
- Berlin JA, Rennie D. Measuring the quality of trials: the quality of scales. *JAMA*. 1999;282:1083–1085.
- Borenstein M, Hedges LV, Higgins JP, Rothstein HR. A basic introduction to fixed-effect and random-effects models for meta-analysis. *Res Synth Methods*. 2010;1:97–111.
- Lewis S, Clarke M. Forest plots: trying to see the wood and the trees. BMJ. 2001;322:1479–1480.
- Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med.* 2002;21:1539–1558.
- Abbott J, Hawe J, Hunter D, Holmes M, Finn P, Garry R. Laparoscopic excision of endometriosis: a randomized, placebo-controlled trial. *Fertil Steril.* 2004;82:878–884.
- Healey M, Cheng C, Kaur H. To excise or ablate endometriosis? A prospective randomized double-blinded trial after 5-year follow-up. *J Minim Invasive Gynecol.* 2014;21:999–1004.
- Michalopoulos G, Makris V, Daniilidis A, et al. Surgical treatment of endometriosis. *Curr Womens Health Rev.* 2012;8:131–137.
- Suchetha M, Prabhu S, Hawthorn R, Jamieson R. Conservative surgical treatment for endometriosis. *BJOG*. 2012;119:231–232.
- Wood C, Maher P. Peritoneal surgery in the treatment of endometriosis—excision or thermal ablation? *Aust N Z J Obstet Gynaecol.* 1996; 36:190–197.
- Yeung PP Jr, Shwayder J, Pasic RP. Laparoscopic management of endometriosis: comprehensive review of best evidence. *J Minim Invasive Gynecol.* 2009;16:269–281.
- Yeung P, Tu F, Bajzak K, et al. A pilot feasibility multicenter study of patients after excision of endometriosis. *JSLS*. 2013;17:88–94.
- Wright J, Lotfallah H, Lovell D, Jones K. A randomised trial of excision vs ablation for the management of mild endometirosis. *Fertil Steril*. 2005;83:1830–1836.
- Healey M, Ang WC, Cheng C. Surgical treatment of endometriosis: a prospective randomized double-blinded trial comparing excision and ablation. *Fertil Steril*. 2010;94:2536–2540.
- Barton-Smith P. An investigation of the surgical treatment of endometriosis [doctoral thesis] 2010. Guildford, UK: University of Surrey; 2010. Available at: http://ethos.bl.uk. Accessed May 8, 2017.
- American Society for Reproductive Medicine. Revised American Society for Reproductive Medicine classification of endometriosis: 1996. *Fertil Steril.* 1997;67:817–821.
- Koninckx PR, Martin D. Treatment of deeply infiltrating endometriosis. Curr Opin Obstet Gynecol. 1994;6:231–241.
- Naftalin J, Hoo W, Pateman K, Mavrelos D, Holland T, Jurkovic D. How common is adenomyosis? A prospective study of prevalence using transvaginal ultrasound in a gynaecology clinic. *Hum Reprod*. 2012;27:3432–3439.
- Naftalin J, Hoo W, Nunes N, Holland T, Mavrelos D, Jurkovic D. Association between ultrasound features of adenomyosis and severity of menstrual pain. *Ultrasound Obstet Gynecol.* 2016;47:779–783.
- Hart R, Hickey M, Maouris P, Buckett W, Garry R. Excisional surgery versus ablative surgery for ovarian endometriomata: a Cochrane Review. *Hum Reprod.* 2005;20:3000–3007.

10