Uterine artery embolization (UAE) compared with myomectomy for the management of uterine fibroids: a systematic review and meta-analysis

Emily Williams¹, Stephen Walker², Siobhan Quenby³, and Joshua Odendaal²

June 29, 2022

Abstract

Background Uterine artery embolization (UAE) and myomectomy are uterus-sparing treatments for uterine fibroids. Each carries a different risk and efficacy profile. Despite this there is a lack of direct comparison between the two techniques making treatment choice decisions difficult. Objectives To compare the therapeutic efficacy and complications of UAE versus myomectomy. Search strategy A systematic search of The Cochrane Library, Medline, and EMBASE databases was conducted using a pre-defined search strategy. The review was prospectively registered on PROSPERO (CRD42021259347). Selection Criteria All randomised controlled trials and cohort studies published between January 1995 and August 2021 directly comparing UAE and myomectomy were included. Data Collection and Analysis Meta-synthesis of raw data was performed using Review Manager 5.4.1 from the Cochrane Collaboration. A pooled estimate of efficacy was established using a fixed-effect model. Main results 8 studies were identified. UAE was associated with lower complication rates (OR 0.56; 95% CI 0.40-0.79), increased improvement in bleeding (OR 1.61 95% CI 1.07-2.43) and a shorter total recovery time (7.72 days versus 36.63 days). Whilst myomectomy was associated with a higher post-procedure quality of life (mean difference -10.56; 95% CI -15.34 - -5.79) and lower re-intervention rate (OR 5.16; 95% CI 2.41-11.04). No significant difference in procedural failure rate was seen (OR 0.67; 95% CI 0.30-1.50). Given concerns with UAE and future fertility limited post-procedure fertility outcomes were identified. Conclusions: Given differences in efficacy profiles a personalised approach to treatment discussions should be maintained. Funding: None Keywords: Uterine artery embolization, myomectomy, uterine fibroid

Word count for abstract: 245 Word count for main text: 3284 (excludes abstracts, in-text references, tables, graphs, figures, acknowledgements, reference list and appendices)

Co-authors: Emily Williams, BSc. University of Warwick Medical School. Email: Emily.williams.1@warwick.ac.uk. 07446983225. (Corresponding author)

Stephen Walker, BSc. University of Warwick Medical School. Email: stephen.g.walker@warwick.ac.uk

Siobhan Quenby, MD FRCOG. Email: s.quenby@warwick.ac.uk Tommy's National Centre for Miscarriage Research, University Hospitals Coventry & Warwickshire, Coventry CV2 2DX, United Kingdom.

Joshua Odendaal, MBBS BSc(Hons) MRCOG. Email: joshua.odendaal@warwick.ac.uk Division of Biomedical Sciences, Clinical Sciences Research Laboratories, Warwick Medical School, University of Warwick, Coventry CV2 2DX, United Kingdom.

Shortened title: UAE vs myomectomy for uterine fibroids **Tweetable abstract:** Myomectomy is associated with improved quality of life compared to greater symptomatic control with UAE.

¹University of Warwick

²University of Warwick Warwick Medical School

³Warwick Medical School

Abstract

Background

Uterine artery embolization (UAE) and myomectomy are uterus-sparing treatments for uterine fibroids. Each carries a different risk and efficacy profile. Despite this there is a lack of direct comparison between the two techniques making treatment choice decisions difficult.

Objectives

To compare the therapeutic efficacy and complications of UAE versus myomectomy.

Search strategy

A systematic search of The Cochrane Library, Medline, and EMBASE databases was conducted using a pre-defined search strategy. The review was prospectively registered on PROSPERO (CRD42021259347).

Selection Criteria

All randomised controlled trials and cohort studies published between January 1995 and August 2021 directly comparing UAE and myomectomy were included.

Data Collection and Analysis

Meta-synthesis of raw data was performed using Review Manager 5.4.1 from the Cochrane Collaboration. A pooled estimate of efficacy was established using a fixed-effect model.

Main results

8 studies were identified. UAE was associated with lower complication rates (OR 0.56; 95% CI 0.40-0.79), increased improvement in bleeding (OR 1.61 95% CI 1.07-2.43) and a shorter total recovery time (7.72 days versus 36.63 days). Whilst myomectomy was associated with a higher post-procedure quality of life (mean difference -10.56; 95% CI -15.34 - -5.79) and lower re-intervention rate (OR 5.16; 95% CI 2.41-11.04). No significant difference in procedural failure rate was seen (OR 0.67; 95% CI 0.30-1.50). Given concerns with UAE and future fertility limited post-procedure fertility outcomes were identified.

Conclusions: Given differences in efficacy profiles a personalised approach to treatment discussions should be maintained.

Funding: None

Keywords: Uterine artery embolization, myomectomy, uterine fibroid

Main text
Funding

None.

Introduction Uterine fibroids are benign tumours of the uterine muscle, and are the most common type of tumour amongst women of reproductive age^[1]. Symptomatic uterine fibroids are a common and significant health problem affecting as many as 1 in 3 women in the UK, and have a lifetime prevalence of around 30%^[2]. Fibroids can cause severe symptoms such as menorrhagia, pelvic pressure, pain, and also impact upon the mental health and sexual functioning of those who have them. Fibroids can also cause infertility. In cases like these, treatment is often required to improve symptoms^[3]. Two common uterine-conserving treatments for uterine fibroids are UAE and myomectomy. UAE is a comparatively newer technique and is limited to tertiary centres with the appropriate expertise. The British Medical Journal (BMJ) recommends both UAE and myomectomy as first-line treatments for fibroids where uterine preservation is desired. According to this algorithm, UAE is only recommended for those not desiring future fertility^[4]. Other studies such as Vercellini et al., 1998^[5] also favour myomectomy for fertility preservation. However, in 2013, the Royal College of Obstetricians and Gynaecologists (RCOG) stated that there is no robust evidence comparing

the two for fertility and pregnancy outcomes^[6]. There are a few randomised controlled trials (RCTs) comparing UAE with hysterectomy^[7, 8, 9, 10, 11]. There are some recent systematic reviews that compare UAE with surgical treatment as a whole [12, 13], however it is hard to assess the differences between UAE and myomectomy specifically where generic 'surgery' headings are used. At the time the current RCOG guidance was created for fibroids, only two RCTs had been undertaken that directly compared UAE and myomectomy [14, 15], since then another RCT has been published, the FEMME 2020 trial [16]. The decision between UAE and myomectomy can have a significant effect on the quality of life of those who suffer with uterine fibroids, including symptom control, fatigue, and feeling of general health. This study aims to review and meta-analyse the data to assess whether there are any significant differences in outcomes which may help guide future management algorithms. Methods Core outcome sets No core outcome sets were used in this study. Patient and public involvement No patients or public were involved in this study. Data sourcesThe protocol for this systematic review was developed in line with PRISMA-P guidance^[17] and prospectively registered on the Prospero database (Reference number CRD42021259347). Ethical approval was not required to undertake this review. A systematic search of The Cochrane Library, Medline, and EMBASE databases was conducted using a pre-defined search strategy (Appendix S1) to gather all studies comparing UAE versus myomectomy in patients with symptomatic uterine fibroids. Study SelectionArticles were screened by two independent reviewers. Any discrepancies were resolved by consensus. Articles were included if they were published in a peer-reviewed journal, published in English from 1995 onwards, and were comparing UAE with myomectomy as treatment for women with symptomatic fibroids. Papers were excluded if they were abstracts, letters, opinion pieces or reviews. RCTs, cohort studies, and case-controlled studies were included. A citation search of the selected articles was performed to identify any further relevant studies. Data extractionData from each paper was entered into a bespoke designed data extraction table. This included data such as the type and size of fibroid, as well as patient demographic data. Outcome data was extracted which included: Technical failure, re-intervention rates, haemorrhage, infection, length of stay in hospital, mental health/mood, sexual functioning, resolution of symptoms, improvement in menorrhagia, post-procedural quality of life score, time taken to return to normal activities, number of patients who had complications Assessment of Study Quality/Bias The papers were assessed for risk of bias using the Newcastle-Ottawa scale (NOS) for cohort studies and Cochrane RoB2 tool for RCTs [19]. The NOS compares across three domains: selection, comparability, and exposure. The Cochrane RoB2 tool assesses for bias across six domains: randomisation, assignment to an intervention, adherence to an intervention, missing outcome data, measurement of the outcome, and selection of reported result. Data analysis Dichotomous data were presented as odds ratio with 95% confidence intervals (CIs) and continuous outcome measures by weighted mean differences and 95% CIs. Meta-synthesis of raw data was performed using Review Manager 5.4.1 from the Cochrane Collaboration^[20]. Weighted mean scores were undertaken for 'length of stay in hospital' and 'time taken to return to activities' as these were continuous outcomes for which both papers gave no information on CIs. The I² test was used to test for heterogeneity between studies and sensitivity analyses were undertaken for results which gave an I² of over 50%. Results An electronic search of The Cochrane Library, Medline, and EMBASE databases was conducted on August 21st 2021. This produced 485 results, 180 from Medline, 253 from Embase, and 52 from The Cochrane Library. (Table S1) There were 15 papers included for full-text review and four were removed as they did not report myomectomy data separately from hysterectomy^[8, 10, 11, 21], one was removed as it was a sub-analysis of the REST trial that focused on imaging outcomes^[22], and four papers were removed as they were systematic reviews ^[12, 23, 24, 25]. Two more papers were added from citation reviews [26, 27]. In total there were eight studies included in this metaanalysis and systematic review. There were five cohort studies [26, 27, 28, 29, 30] and three RCTs [14, 15, 16]. The characteristics of the included studies are shown in Table 1. Bias assessments are shown in Appendices S2 and S3. Three of the cohort studies were undertaken at a single institution^[26, 27, 30] and two were undertaken as multi-centre studies [28, 29]. There were a total of 625 women in the cohort, and 489 in the myomectomy cohort. Inclusion criteria were similar across the eight studies, with all of them requiring symptomatic uterine fibroids. Siskin et al., 2006; Mara et al., 2007 and Goodwin et al., 2006 all specified maximum FSH levels for their participants, to ensure that they were not already menopausal at the time of the study. Manyonda et al., 2012 also specified that only pre-menopausal women were to be included. However, Razavi et al., 2003 specified that for inclusion in the study the women must be seeking symptomatic relief, not seeking treatment for fertility problems. All of the studies reported key demographic data such as age of the participants. For two of the papers [14, 15] it was possible to perform comparison, and there was found to be no significant difference in age between the UAE and myomectomy cohorts [OR=-0.76, 95% CI (-1.99, 0.47)] (Appendix S4). There were 12 outcomes that were deemed comparable between the papers, five of these were related to technical aspects of the procedure, such as infections and need to re-intervene at a later date. The remaining seven were related to the quality of life of the women in the respective studies, such as mental health and sexual functioning. These are outlined below.

Technical failure

Technical failure did not significantly differ between groups [OR=0.67, 95% CI (0.30, 1.50)] (Figure 1, A). Five papers commented on rates of failure [14, 15, 26, 27, 29] however Narayan et al., 2010 gave their results as an adjusted OR and this could not be meta-analysed with the other data. None of the studies gave a specific definition for 'technical failure' however they did give examples of what was considered to be a failed procedure. In this review, the need for conversion for hysterectomy mid-procedure, and any repeat surgery to correct immediate complications were also considered under this outcome.2. Re-intervention rates Re-intervention rates varied significantly between groups [OR=5.16, 95% CI (2.41, 11.04)] (Figure 1, B), with myomectomy having lower rates of re-intervention post-procedurally compared with UAE. Four studies reported on this [14, 15, 27, 30]. One study, Razavi et al., 2003, did show lower re-intervention rates in its UAE cohort, with there being five out of 62 patients in the UAE cohort, and four out of 40 in the myomectomy cohort. Manyonda et al., 2012 found that there was unsuspected adenomyosis in three of the six patients who underwent a hysterectomy at re-intervention in the UAE group, which offers a potential explanation for the need for re-intervention in these cases. 3. Haemorrhage There was a significantly lower rate of haemorrhage in the UAE cohorts compared with the myomectomy ones [OR=0.22, 95% CI (0.06, 0.77)] (Figure 1, C), this was demonstrated in all three studies that commented on this outcome. 4. Infection

Infection rates did vary significantly between UAE and myomectomy cohorts [OR=0.20, 95% CI (0.06, 0.72)] (Figure 1, D), with the data favouring the UAE group.

5. Length of stay in hospital A weighted mean was calculated for the number of days spent in hospital for both the UAE and myomectomy cohorts across the five studies which recorded this in their study (Figure 2, K). It was found that the UAE group had a mean number of 1.28 days (range 0-2.5) in hospital, whereas the myomectomy group had a mean number of 3.49 days (range 2.5-6) in hospital. 6. Mental health/mood

Changes in mental health/mood post-procedurally did not vary significantly between UAE and Myomectomy [OR=-0.13, 95% CI (-5.3, 5.04)] (Figure 2, F) This data included two studies reporting their results at 6 months post-op and at 12 months. [14, 29]).

7. Sexual functioning There was no significant difference in sexual functioning between UAE and myomectomy [OR=-6.33, 95% CI (-12.93, 0.27)] (Figure 2, G). This data included two studies [14, 29]).8. Resolution of symptoms Resolution of symptoms did not vary significantly between groups [OR=1.72, 95% CI (0.91, 3.27)] (Figure 2, H). Three papers reported on this [15, 28, 30]. All these papers used different scoring systems, however, the result had little statistical heterogeneity (I² 0%) implying consistency in the finding. 9. Improvement in menorrhagia There was a significant difference in improvement of menorrhagia between UAE and myomectomy groups [OR=1.61, 95% CI (1.07, 2.43)] (Figure 2, I). Siskin et al.,2006 found a reduction in mean menorrhagia bleeding at 6 months of 52.1% with UAE, and 43.7% with myomectomy. Razavi et al., 2003 found a reduction in menorrhagia was 64% for their myomectomy group and 92% for their UAE group. 10. Post-procedural quality of life score. Post-procedural quality of life scores 12 months post-operatively were significantly higher in the myomectomy cohort in comparison to the UAE cohort [OR=10.56, 95% CI (-15.34, -5.79)] (Figure 2, J). 11. Time taken to return to normal activities UAE group took a weighted mean of 7.7 days (range 7.5-8) to return to normal activities, whereas the myomectomy group took 36.6 days (range 36-37) (two studies [27, 28] (Figure 2, L)). 12. Complications It was found that there was a significantly higher rate of complications in the myomectomy group in comparison to the UAE group

[OR=0.56, 95% CI (0.40, 0.79)] (Figure 1, E). Five papers provided data on the number of participants experiencing complications^[14, 15, 27, 28]. 'Complications' included events such as infections, haematomas, post-embolisation syndrome, bowel obstructions, rash, transfusions, pain, readmissions, and adhesions. Discussion Main findings Both UAE and myomectomy are uterine-sparing treatment options for fibroids. UAE offers a minimally invasive approach, however myomectomy is generally favoured as first line treatment for fibroids that require further treatment than hormonal or analgesic medications^[4]. There are several studies that compare UAE to all surgical managements of fibroids [10, 11, 12, 13, 23, 24, 25]. But very few of these papers separate results for different surgical techniques, so they could not be included in this review. A few literature reviews that do compare UAE and myomectomy do not include more recent RCT data that would have an impact on the findings. A review by Jun et al., 2012 that compared UAE with surgical treatments only included one RCT that had myomectomy data. Since then, there have been two large RCT trials with more data specifically for UAE versus myomectomy [14, 16]. Further to this, the 2014 Cochrane review for outcomes of different treatments for uterine fibroids included only two studies that compared UAE and myomectomy^[23]. In this review we included eight studies, which to the best of our knowledge means it is the largest meta-analysis of UAE versus myomectomy. There were no significant differences found between the UAE and myomectomy groups for numbers of technical failures, mental health scores, and sexual functioning. UAE was associated with lower complication rates (OR 0.56; 95% CI 0.40-0.79), increased improvement in bleeding (OR 1.61 95% CI 1.07-2.43) and a shorter total recovery time (7.7 days versus 36.6 days). Whilst myomectomy was associated with a higher post-procedure quality of life (mean difference -10.56; 95% CI -15.34 - -5.79) and lower re-intervention rate (OR 5.16; 95% CI 2.41-11.04). No significant difference in procedural failure rate was seen (OR 0.67; 95% CI 0.30-1.50). It was expected that UAE is associated with a lower risk of haemorrhage, infection, stay in hospital, and recovery time. This is because it is less invasive, and similar results have been reported in UAE vs surgery meta-analyses [11, 23]. Furthermore, 'surgery' (including myomectomy) has been associated with a lower rate of re-interventions [11, 25], and higher post-procedural quality of life score [21]. In our review we found that UAE had a lower risk of complications compared with myomectomy, however, other papers have found that UAE is associated with higher numbers of complications compared with 'surgery' [10, 25]. Whereas Jun et al., 2012 found no difference in complications incidence, and less 'major complications' in UAE cohorts. These differences are also likely to be explained by separating out myomectomy from other surgical procedures. The 'improvement in menorrhagia' outcome had high heterogeneity ($I^2=71\%$). So a sensitivity analysis was undertaken (Appendix S5) where Razavi et al., 2003's paper was removed, which improved the heterogeneity. This may be because each author measured the outcome differently, with Goodwin et al., 2006 and Siskin et al., 2006 measuring a reduction in bleeding score, and Razavi et al., 2003 measured the percentage of patients that had a 'successful' reduction in menorrhagia. Strengths and limitationsThe RCTs included within this study did not blind patients to the intervention, increasing their risk of bias. However, this is a limitation which was found to be acceptable given that patients needed to be able to give informed consent to the procedure. Furthermore, Manyonda et al., 2012 and 2020 had some deviations from the initial randomisation with some patients receiving a different intervention. Four of the cohort studies were deemed to have issues with comparability between UAE and myomectomy groups (Table S1). These included problems such as a large difference in cohort sizes [29], and the presence of potential confounding variables such as obesity and smoking ^[26]. Siskin 2006 evaluated the gynaecological histories between the cohorts as well as looking at demographic information and surgical histories. Overall, there were no papers that presented a significant risk of bias, and therefore all eight were included in the data analysis. In regards to bias assessment, two of cohort studies had a low risk of bias (Goodwin et al., 2006 and Siskin et al., 2006), and three had a medium risk of bias (Narayan et al., 2010, Broder et al., 2002, and Razavi et al., 2003). One RCT was determined to have a low risk of bias (Mara et al., 2007), and the other two were found to have a medium risk (Manyonda et al., 2012 and 2020). The aspects of bias that were most prevalent in the studies was in the study selection and availability of follow-up data for all participants. Although four of the eight papers did use the Uterine Fibroid Symptom and Quality of Life (UFS-QOL) score^{[31][14, 16, 28, 29]}, to assess quality of life outcomes, most studies reported their results in different formats, and some papers did not give data for each outcome on the UFS-QOL scoring framework. There were some outcomes that could not be meta-analysed and this was a limitation of our study. Two studies did give data for patient satisfaction [26, 29], although Narayan et al., 2010 gave their results in odds ratio and Broder et al., 2002 gave theirs in percentages of participants satisfied. This meant it was not possible to meta-analyse. Three papers did report on pain [27, 28, 29], Siskin et al., 2006 reported pain scores as a change from baseline, and Goodwin et al., 2006 reported it as a mean score. Although both used the UFS-QOL framework they presented their results differently and because of this they could not be meta-analysed. Razavi et al., 2003 reported on pain as a percentage of patients with resolution of pain. There was difficulty in assessing post-procedural complications between the papers. Some gave complication rates as 'early' or 'late' [15, 28], whilst others gave 'occurrence of adverse events' [14, 27] without indication of when they occurred. Some papers elaborated on specific complications such as 'infection' or 'haematoma' [14, 28], however others just reported how many patients had a 'complication', and gave examples within the text. Because of this, in this review outcomes were reported both under a generic 'complication' heading and specific ones where possible. Interpretation Mara et al., 2007 and Siskin et al., 2006 gave data on pregnancies, labours, and miscarriages. With Mara et al., 2007 also giving data on live birth. They found five births in the UAE group (out of 26 who tried to conceive) and 19 births in the Myomectomy group (out of 40 who tried to conceive). Some of the papers noted that they did not include women who wanted to get pregnant in the UAE cohort due to ethical reasons [14, 28, 29] . Therefore, pregnancy and fertility outcomes could not be compared. Current NHS treatment algorithms for fibroids do suggest that there are hesitations for use of UAE in those who may wish to become pregnant [3,5]. Therefore, this is a key comparator for the two treatment modalities that needs to be explored further, especially given that fibroids do largely affect pre-menopausal women. The findings of this study suggest that guidelines for the treatment of uterine fibroids should be based upon the individual preferences of the patients. It would be hard to make a treatment algorithm based on the findings, as there is no clear 'better' treatment. Rather, there are risks associated with both treatments that need to be balanced with the goal of reducing symptoms and increasing the quality of life of the patient. There is a hesitancy for use of UAE over myomectomy within current guidelines that may need to be re-assessed to ensure the best options are offered to those seeking treatment for uterine fibroids. Patients should be given the data in a clear format that shows which outcomes are associated with each treatment option, and healthcare professionals should aid the patient in this decision using an appropriate evidence-base. Conclusions Both UAE and myomectomy are safe and effective treatment options for uterine fibroids. They both offer a high rate of technical success, and offer significant improvement in sexual functioning, mental health, and general quality of life. However, there is a higher chance of requiring re-interventions if UAE is chosen. UAE offers lower rates of haemorrhage and infection, and allows for patients to leave hospital faster, and return to activities of daily life faster than those who have myomectomy. More research needs to be undertaken to compare fertility and birth outcomes, as there is a mixed picture in the literature and few studies have explored these outcomes. Future research on this topic could potentially benefit from a standardised method of reporting outcomes, including follow-up times, so that more accurate comparisons can be made.

Acknowledgements

None

Disclosure of interests There are no patent ownership, stock ownership, consultancies, speaker's fees, shares, personal, political, intellectual or religious interests to disclose

Contribution to Authorship

Initial idea: EW

Data extraction, analysis: JO, SW, EW

Manuscript preparation: JO, EW

Manuscript revisions: SQ Project supervision: SQ, JO Ethics approval No ethical approval was required for this project as per the NHS Research Ethics Service guidelines.

Funding

No funding was received for this project.

References

- 1. Stewart, E., Cookson, C., Gandolfo, R. and Schulze-Rath, R., 2017. Epidemiology of uterine fibroids: a systematic review. BJOG: An International Journal of Obstetrics & Gynaecology, 124(10), pp.1501-1512.
- 2. Royal College of Obstetricians & Synaecologists. 2022. Fibroids. [online] Available at: https://www.rcog.org.uk/en/patients/fertility/female-problems/fibroids/ [Accessed 19 January 2022].
- 3. Younas, K., Hadoura, E., Majoko, F. and Bunkheila, A., 2016. A review of evidence-based management of uterine fibroids. The Obstetrician & Gynaecologist, 18(1), pp.33-42.
- 4. BMJ Best Practice. 2022. Uterine fibroids- treatment algorithm. [online] Available at: https://bestpractice.bmj.com/topics/en-gb/567/treatment-algorithm [Accessed 19 January 2022].
- 5. Vercellini, P., Giorgio Crosignani, P., Mangioni, C., Imparato, E., Ferrari, A. and Giorgi, O., 1998. Treatment with a gonadotrophin releasing hormone agonist before hysterectomy for leiomyomas: results of a multicentre, randomised controlled trial. BJOG: An International Journal of Obstetrics & Gynaecology, 105(11), pp.1148-1154.
- 6. Rcog.org.uk. 2013. Clinical recommendations on the use of UAE in the management of fibroids. [online] Available at: https://www.rcog.org.uk/globalassets/documents/guidelines/23-12-2013_rcog_rcr_-uae.pdf> [Accessed 19 January 2022].
- 7. Hehenkamp, W., Volkers, N., Donderwinkel, P., de Blok, S., Birnie, E., Ankum, W. and Reekers, J., 2005. Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids (EMMY trial): Peri- and postprocedural results from a randomized controlled trial. American Journal of Obstetrics and Gynecology, 193(5), pp.1618-1629.
- 8. Pinto, I., Chimeno, P., Romo, A., Paúl, L., Haya, J., de la Cal, M. et al., 2003. Uterine Fibroids: Uterine Artery Embolization versus Abdominal Hysterectomy for Treatment—A Prospective, Randomized, and Controlled Clinical Trial. Radiology, 226(2), pp.425-431.
- 9. Ruuskanen, A., Hippeläinen, M., Sipola, P. and Manninen, H., 2010. Uterine artery embolisation versus hysterectomy for leiomyomas: primary and 2-year follow-up results of a randomised prospective clinical trial. European Radiology, 20(10), pp.2524-2532.
- 10. Moss, J., Cooper, K., Khaund, A., Murray, L., Murray, G., Wu, O., et al., 2011. Randomised comparison of uterine artery embolisation (UAE) with surgical treatment in patients with symptomatic uterine fibroids (REST trial): 5-year results. BJOG: An International Journal of Obstetrics & Gynaecology, 118(8), pp.936-944.
- 11. Jun, F., Yamin, L., Xinli, X., Zhe, L., Min, Z., Bo, Z. et al., 2011. Uterine artery embolization versus surgery for symptomatic uterine fibroids: a randomized controlled trial and a meta-analysis of the literature. Archives of Gynecology and Obstetrics, 285(5), pp.1407-1413.
- 12. Fonseca, M., Castro, R., Machado, M., Conte, T. and Girao, M., 2017. Uterine Artery Embolization and Surgical Methods for the Treatment of Symptomatic Uterine Leiomyomas: A Systemic Review and Meta-analysis Followed by Indirect Treatment Comparison. Clinical Therapeutics, 39(7), pp.1438-1455.e2.
- 13. Havryliuk, Y., Setton, R., Carlow, J. and Shaktman, B., 2017. Symptomatic Fibroid Management: Systematic Review of the Literature. JSLS: Journal of the Society of Laparoendoscopic Surgeons, 21(3), pp.e2017.00041.

- 14. Manyonda, I., Bratby, M., Horst, J., Banu, N., Gorti, M. and Belli, A., 2011. Uterine Artery Embolization versus Myomectomy: Impact on Quality of Life—Results of the FUME (Fibroids of the Uterus: Myomectomy versus Embolization) Trial. CardioVascular and Interventional Radiology, 35(3), pp.530-536. 15. Mara, M., Maskova, J., Fucikova, Z., Kuzel, D., Belsan, T. and Sosna, O., 2007. Midterm Clinical and First Reproductive Results of a Randomized Controlled Trial Comparing Uterine Fibroid Embolization and Myomectomy. CardioVascular and Interventional Radiology, 31(1), pp.73-85.
- 16. Manyonda, I., Belli, A., Lumsden, M., Moss, J., McKinnon, W., Middleton, L., et al., 2020. Uterine-Artery Embolization or Myomectomy for Uterine Fibroids. New England Journal of Medicine, 383(5), pp.440-451.
- 17. Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ 2021;372:n160. doi: 10.1136/bmj.n160
- 18. Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al., 2013. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.
- 19. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng H-Y., et al., 2019. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ; 366: 14898.
- 20. Review Manager (RevMan) [Computer program] (2020). The Cochrane Collaboration. Version 5.4.
- 21. Edwards, R., Moss, J., Lumsden, M., Wu, O., Murray, L., Twaddle, S., et al., 2007. Uterine-Artery Embolization versus Surgery for Symptomatic Uterine Fibroids. New England Journal of Medicine, 356(4), pp.360-370.
- 22. Ananthakrishnan, G., Murray, L., Ritchie, M., Murray, G., Bryden, F., Lassman, S., et al., 2012. Randomized Comparison of Uterine Artery Embolization (UAE) with Surgical Treatment in Patients with Symptomatic Uterine Fibroids (REST Trial): Subanalysis of 5-Year MRI Findings. CardioVascular and Interventional Radiology, 36(3), pp.676-681.
- 23. Gupta, J., Sinha, A., Lumsden, M. and Hickey, M., 2012. Uterine artery embolization for symptomatic uterine fibroids. Cochrane Database of Systematic Reviews,.
- 24. Van der Kooij, S., Bipat, S., Hehenkamp, W., Ankum, W., Reekers, J., 2011. Uterine artery embolization versus surgery in the treatment of symptomatic fibroids: a systematic review and metaanalysis. American Journal of Obstetrics and Gynecology, 205(4), pp.317.e1-317.e18.
- 25. Tang, S., Kong, M., Zhao, X., Chen, J., Wang, C., Zhang, H., et al., 2018. A systematic review and meta-analysis of the safety and efficacy of uterine artery embolization vs. surgery for symptomatic uterine fibroids. Journal of Interventional Medicine, 1(2), pp.112-120.
- 26. Narayan, A., Lee, A., Kuo, G., Powe, N. and Kim, H., 2010. Uterine Artery Embolization versus Abdominal Myomectomy: A Long-term Clinical Outcome Comparison. Journal of Vascular and Interventional Radiology, 21(7), pp.1011-1017.
- 27. Razavi, M., Hwang, G., Jahed, A., Modanloo, S. and Chen, B., 2003. Abdominal Myomectomy Versus Uterine Fibroid Embolization in the Treatment of Symptomatic Uterine Leiomyomas. American Journal of Roentgenology, 180(6), pp.1571-1575.
- 28. Siskin, G., Shlansky-Goldberg, R., Goodwin, S., Sterling, K., Lipman, J., Nosher, J., et al., A Prospective Multicenter Comparative Study between Myomectomy and Uterine Artery Embolization with Polyvinyl Alcohol Microspheres: Long-term Clinical Outcomes in Patients with Symptomatic Uterine Fibroids. Journal of Vascular and Interventional Radiology, 17(8), pp.1287-1295.
- 29. Goodwin, S., Bradley, L., Lipman, J., Stewart, E., Nosher, J., Sterling, K., et al., 2006. Uterine artery embolization versus myomectomy: a multicenter comparative study. Fertility and Sterility, 85(1), pp.14-21.

30. Broder, M., Goodwin, S., Chen, G., Tang, LJ., Costantino, MM., Nguyen, MH et al., 2002. Comparison of long-term outcomes of myomectomy and uterine artery embolization. Obstetrics & Gynecology, 100(5), pp.864-868.

31. Spies JB, Warren EH, Mathias SD, Walsh SM, Roth AR, Pentecost MJ. 1999. Uterine fibroid embolization: measurement of health related quality of life before and after therapy. J Vasc Interv Radiol;10:1293–303.

Tables and Figures

Included in print:

Table 1: Included Study Characteristics table

Figure 1 : Technical outcomes: Panel A: Technical failure, Panel B: Re-intervention rates, Panel C: Haemorrhage, Panel D: Infection, Panel E: Complication rate

Figure 2: Quality of life outcomes and length of stay: Panel F: Mental health/mood, Panel G: Sexual functioning, Panel H: Resolution of symptoms, Panel I: Improvement in menorrhagia,

Panel J: Post-procedural quality of life score, Panel K: Length of stay in hospital, Panel L: Time taken to return to normal activities Supplementary:

Figure S1: Search terms

Table S1: PRISMA diagram of article selection

Figure S2: Newcastle-Ottawa scores of cohort studies

Figure S3: Cochrane Rob2 scores of RCTs

Figure S4: Age of the participants

Figure S5: Sensitivity analysis, menorrhagia

Tables (to be provided in Main Document as per file upload instructions):

Table 1: Included Study Characteristics table

Study Identifiers			Patients					Outcomes
Study	Study design	Total sample size	Study population	Age	No of fibroids	Size of fibroids	Dominant fibroid type	
Siskin Et al. 2006	Prospective, multicentre, non-randomised Cohort	146	Symptomatic patients > 30 years old. FSH concentration <40 IU/L	UAE mean 43.9, Myomectomy mean 37.8	48.1% of UAE had >10. 18.8% of Myomectomy had >10	UAE mean dominant cm^3 134.84 +/- 159.91 Myomectomy mean dominant cm^3 230.30 +/- 192.62	Intramural 58.4%	Uterine Fibroid QOL Questionnaire, adverse event incidence, time to return to normal activity, and changes in tumor symptom scores, QOL scores, and menorrhagia bleeding scores.
Mara Et al. 2007	RCT	121	age <40 years, USS-verified intramural fibroid at least 4 cm at its largest diameter. FSH concentration <30 IU/L	UAE 32.8 years; Myomectomy mean age, 34.3 years	67.2% had a solitary fibroid. 25.9% had 2-5 fibroids. 6.9% had >5 fibroids	Mean size dominant fibroid: UAE = 62.3mm ± 19.1 (range= 42-107). Myo= 59.8mm ± 16.5 (41-110)	ALL intramural (part of inclusion criteria)	Hospital stay, complications, re-interventions, symptom relief, re-interventions and re-growth of fibroids
Manyonda Et al. 2020	RCT	203	symptomatic patients >18 year	UAE mean 40.2, Myomectomy mean 42.7		UAE mean largest fibroid: 436±594 cm^3. Myo: 446±548	intramural (58%)	Uterine Fibroid QOL Questionnaire, procedual complications
Goodwin Et al. 2006	multicenter,nonrand omized cohort prospective trial	209	age >30, FSH concentration <40 IU/L	UAE mean 43.9. Myomectomy 38.2 years	50.3% had >10 fibroids	UAE mean size- 182.12cm^3. Myo: 226.92	Intramural most common (59.1%)	Quality of life score changes, menstrual bleeding score changes, uterine size differences, time off, and adverse events.
Manyonda Et al. 2012	RCT	163	symptomatic, confirmed by USS 4 cm in diameter, premenopausal	UAE mean 44. Myomectomy 43.2	Not given	UAE mean diameter: 7.7 ± 3.8cm. Myo: 6.53 ± 2.8		QoL measured by a validated questionnaire, hospital stay, rates of complications, and need for reintervention.
Narayan Et al. 2010	Restrospective cohort	89	Women who received UAE or abdominal myomectomy for symptomatic uterine leiomyomata at a single institution	UAE mean 43.6 years. Myomectomy mean 37.4 years	Not given	Not given	Not given	Symptom evaluationswith symptom severity scores, pregnancy rates, and satisfaction with the procedures.
Broder Et al. 2002	Restrospective cohort	102	All women who had UAE or myomectomy at a single institution were invited to take part.	UAE mean 43.5. Myomectomy mean 37.6	Not given	Not given	Not given	Procedure-related complications, changes in symptoms. Length of hospital stay, time until resumption of daily activities, and pain
Razavi Et. al 2003	Restrospective cohort	81	patients who underwent abdominal myomectomy or UAE over the same 30-month period in an academic institution were retrospectively reviewed.	UAE mean 44.2. Myomectomy mean 37.7	Not given	Not given	Not given	Re-intervention rate, symptoms improvement scores, patient satisfaction

Table S1: PRISMA diagram of article selection.

Hosted file

Figure 1.docx available at https://authorea.com/users/492275/articles/575015-uterine-artery-embolization-uae-compared-with-myomectomy-for-the-management-of-uterine-fibroids-a-systematic-review-and-meta-analysis

Hosted file

Figure 2.docx available at https://authorea.com/users/492275/articles/575015-uterine-artery-embolization-uae-compared-with-myomectomy-for-the-management-of-uterine-fibroids-asystematic-review-and-meta-analysis

Hosted file

study characteristics table.xlsx available at https://authorea.com/users/492275/articles/575015-uterine-artery-embolization-uae-compared-with-myomectomy-for-the-management-of-uterine-fibroids-a-systematic-review-and-meta-analysis