



The Advantages and Disadvantages of Uterine Artery Embolization in Women with Adenomyosis: What's New?

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Abstract

Purpose of Review This review will examine the use of uterine artery embolization (UAE) for the management of adenomyosis (AUB-A) and evaluate its advantages and disadvantages.

Recent Findings In the last 5 years, 8 articles have described UAE for the management of AUB-A. These include 2 prospective and 5 retrospective studies and 1 systematic review and meta-analysis. There are no randomised controlled trials for UAE as a treatment of adenomyosis. Recent data report a reduction in heavy menstrual bleeding (HMB) in 80–88% of patients and a reduction in dysmenorrhoea in 76–80% of those undergoing UAE. Quality of life is reported to be significantly improved and uterine volumes reduced following treatment. Disadvantages of UAE include post-procedural pain, adenomyoma extrusion, pyomyoma, Asherman syndrome, and requirement for further intervention including subsequent hysterectomy for management of pain or bleeding.

Summary Initial non-randomised data support uterine artery embolization as an effective modality for the conservative management of AUB-A. The advantages of UAE include avoidance of abdominal surgery, significant improvement in symptoms, and quality of life scores and preservation of reproductive potential. To date, most data are retrospective with no randomised controlled studies and a few prospective analyses. Randomised controlled data are needed to comprehensively evaluate UAE as conservative treatment for AUB-A and to compare efficacy, cost, and durability of both medical and surgical treatments.

Keywords Adenomyosis · Uterine artery embolization · Interventional radiology · Heavy menstrual bleeding · Dysmenorrhoea

Introduction

Adenomyosis is a condition in which endometrial glands and stroma are found in the myometrium with subsequent inflammation and myometrial hypertrophy [1]. The condition was first described in the early twentieth century. It is a recognised structural cause of abnormal uterine bleeding in the current FIGO classification system (the 'A' in the PALM-COEN classification system) [2, 3]. Women with adenomyosis usually present with heavy menstrual bleeding,

dysmenorrhoea, and mass-related symptoms. Other symptoms may include non-menstrual pelvic pain and subfertility [4, 5]. The exact prevalence of adenomyosis is difficult to determine, as histological confirmation is considered the gold standard [6]. Histological findings of specimen after hysterectomy for benign indications reveal adenomyosis in 10 to 25% of uteri. Yet, in selected populations, the prevalence could be up to 80% [7–10]. Advancements in imaging modalities have improved non-invasive diagnosis of adenomyosis with sensitivities and specificities of 65.0% and 97.5% and 77.5% and 92.5% for ultrasound and MRI, respectively [11].

Management of adenomyosis can be defined as medical, surgical, and radiological with the specific treatment modality, or combination treatment depending on symptom profile and patient preference. Hormonal and non-hormonal medical therapy is most often considered the first-line treatment. The most studied method is the use of LNG-IUS for symptomatic adenomyosis [6]. Surgical

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intervention in the form of hysterectomy has traditionally been reserved for those who are refractory to medical therapy, have completed their families, or who suffer from predominantly mass-related symptoms. An alternative method is uterine artery embolization for women who desire uterine preservation or wish to avoid surgery.

Methodology

We performed a literature search in the PubMed and Cochrane databases between 2016 and 2021. Search terms included “adenomyosis” and “uterine artery embolization” in sequence and in combination. The search was limited to studies published in English language. A total of 118 articles were identified and screened for inclusion based on publication title and abstract. The bibliographies of relevant studies were screened for additional publications. A total of 8 studies were identified including 2 prospective, 5 retrospective, and a systematic review and meta-analysis. These studies are summarised in Table 1.

What Is Uterine Artery Embolization?

UAE for the management of benign leiomyoma (AUB-L) was first described by Ravina et al. in the mid-1990s [12]. Our knowledge of this application has expanded markedly with the findings of long-term reductions in symptom severity scores and improvement in quality-of-life scores of up to 64% and 23%, respectively [13]. Randomised controlled studies comparing UAE to other procedures for management of AUB-L continue to demonstrate treatment superiority with low rates of subsequent hysterectomy [14].

The procedure involves occlusion of subsidiaries of the uterine vessels using digital subtraction angiography (DSA) [15]. The embolization particles used are usually tris-acryl gelatin microspheres (TAGM) or non-spherical polyvinyl alcohol particles (PVA). The latter is associated with lower procedural radiation with comparable symptom response [15, 16]. Transfemoral access has been traditionally used. However, recent data shows that radial artery access results in less pain, shorter procedure times, and reduced length of stay following UAE [17, 18]. Occlusion of the blood supply to the uterus and the target lesion/s leads to hypoxia, ischaemia, and necrosis of the proliferative ectopic glandular tissue with minimal disruption to the surrounding normal tissue [19]. Subsequent resorption and remodelling results in decreased AUB-A-associated symptoms.

AUB-A Symptom Control Following UAE

Table 2 summarises the data on clinical response following UAE for AUB-A. Dysmenorrhoea is the hallmark symptom of adenomyosis and is reported in up to 90% of symptomatic patients [20•]. In a prospective evaluation of 115 women with dysmenorrhoea who underwent UAE, moderate improvement in symptoms was observed in 64 (55.7%) and a marked improvement in 31 (27.0%) cases 12 months following UAE [21]. A systematic review and meta-analysis in 2007 supports those findings. The authors reviewed 30 studies including 1049 patients with adenomyosis (pure AUB-A and mixed AUB-A/L) between 1999 and 2016. They found improvement in up to 93.9% of patients at 12-month follow-up [22]. Long-term data from this study showed that although initial response rates were similar, patients who had combined AUB-A and AUB-L had a sustained response to treatment compared with those who had AUB-A alone [22]. It might be due to the more diffuse infiltration of AUB-A compared to AUB-L and could explain the greater likelihood of symptom deterioration in the longer term. There are many different methods to quantify reductions in dysmenorrhoea following UAE and this heterogeneity clouds data interpretation and perhaps overestimates treatment response. A retrospective study that employed visual analogue scales (VAS) with clearly defined “improvement” parameters to assess post-procedural dysmenorrhoea demonstrated a reduction in dysmenorrhoea in 80.4% of people at 12-month follow-up ($n = 56$) [23]. This is supported by a retrospective analysis of 115 people who underwent UAE for the management of AUB-A. The authors reported a reduction in VAS pain scores from 7.45 to 1.32 (mean reduction 6.13, $p < 0.001$) at extended follow-up (mean follow-up 22.5 months, range 6–84 months) [20•].

UAE is also associated with significant improvement and reduction in HMB. Retrospective studies revealed improvement in abnormal bleeding in 70.9% ($n = 227$) of women 12 months after UAE, an effect that is sustained for 5 years [19]. These promising data have been reproduced in multiple studies with improvements in HMB between 70.9 and 88.0% of cases (Table 2) [20•, 23, 24, 25••]. This is further supported by a meta-analysis of data from 4 studies involving 111 participants that shows improved bleeding profiles in 81.3% of patients after a mean follow-up of 32 months [22].

Of the studies we reviewed, 4 specifically examined the effect of UAE on uterine volume, as a marker of mass-related symptoms, determined by MRI. A prospective study involving 115 patients demonstrated a progressive mean reduction in uterine volume of 28.0% ($p = 0.02$), 37.0% ($p = 0.02$) and 51.0% ($p = 0.005$) at 3,

Table 1 Summary table

Citation	Study design	n	Outcome	Dysmenorrhoea (% of women improved)	HMB (% of women improved)	Uterine volume/mass symptoms	Complications	Follow-up
Guo et al. [24]	Retrospective	76	Effects of ovarian endometriosis on symptom reduction following UAE for adenomyosis	Overall: 57/74 (77.0%) Endo vs. non-endo patients: 47.1% vs. 86.0%, $p=0.001$	Overall: 49/61 (80.3%) Endo vs. non-endo patients: 63.6% vs. 84%, $p=0.263$	N/A	No complications	12 months
Wang et al. [25••]	Retrospective	195	Effects of lesion vascularity on rates of Asherman syndrome following UAE	113/147 (76.8%)	136/159 (85.5%)	Mean volume decrease: 330.8 to 208.4 cm ³ (37.0%)	Oligo/amenorrhoea: 27/195 (13.8%) Ovarian failure: 2/195 (1.0%) Asherman: 25/195 (12.8%)	15 months
Zheng et al. [23]	Retrospective	68	To identify factors to predict responsiveness to UAE for adenomyosis	Overall: 45/56 (80.4%) Complete vs. incomplete necrosis: 94.7% vs. 50.0%, $p < 0.001$	Overall: 33/40 (82.5%) Complete vs. incomplete necrosis: 96.2% vs. 57.1%, $p = 0.004$	N/R	N/R	12 months
Liang et al. [20•]	Retrospective	115	Reduction in dysmenorrhoea, HMB and improvement in UFS-QoL scores	Pain score reduction (VAS): 7.45 to 1.32 Mean reduction 6.13 ($p < 0.0001$)	91/104 (88.0%)	Mean volume decrease: 296 to 198 mL (33.1%)	(Mild) haematoma, endometritis, UTI: 6/115 (5.2%) Amenorrhoea: 15/115 (13.0%), mean age 50.6 Hysterectomy: 6/115 (5.0%)	22.5 months (median)
De Bruijn [22]	Systematic review and meta-analysis	1049	Compare short-term and long-term outcomes following UAE for AUB-A and AUB-AL	Follow-up < 12 months: 254/268 (91.1%) Follow-up > 12 months: 347/410 (84.6%) Overall: 601/678 (88.7%, 95% CI 86.1–91.1)	Follow-up < 12 months: 52/54 (96.3%) Follow-up > 12 months: 246/286 (86.0%) Overall: 298/340 (87.8%, 95% CI 84.3–91.3)	Symptom improvement < 12 months: 27/34 (79.4%) Symptom improvement > 12 months: 90/110 (82.7%) Overall: 117/144 (81.3%, 95% CI 74.8–87.7)	Amenorrhoea: 28/445 (6.3%) Pseudoaneurysm: 2/615 (0.3%) Expulsion of lesion: 10/615 (1.6%) Endometritis: 4/615 (0.7%) DVT: 1/615 (1.6%)	8.9-month mean < 12-month group 35.7-month mean > 12-month group
De Bruijn [30]	Prospective	29	Assessment of symptom severity scores and quality of life following UAE for AUB-A or AUB-AL at 7 years	N/R	N/R	N/R	Hysterectomy: 5/28 (17.9%)	7.4 years (mean)

Table 1 (continued)

Citation	Study design	n	Outcome	Dysmenorrhoea (% of women improved)	HMB (% of women improved)	Uterine volume/mass symptoms	Complications	Follow-up
Zhou et al. [19]	Retrospective	252	Effect of lesion vascularity on success for UAE for AUB-A	Hypervascular at 12 months: 64/74 (86.5%) Isovascular at 12 months: 51/71 (71.8%) Hypovascular at 12 months: 30/51 (58.8%) <i>p</i> = 0.002 <i>Overall at 12 months: 145/196 (74.0%)</i> Hypervascular at 5 years: 51/61 (83.6%) Isovascular at 5 years: 37/55 (67.3%) Hypovascular at 5 years: 19/36 (52.8%) <i>p</i> = 0.005 <i>Overall at 5 years: 107/152 (70.4%)</i>	Hypervascular at 12 months: 68/84 (81.0%) Isovascular at 12 months: 56/82 (68.3%) Hypovascular at 12 months: 37/61 (60.7%) <i>p</i> = 0.024 <i>Overall at 12 months: 161/227 (70.9%)</i> Hypervascular at 5 years: 54/68 (79.4%) Isovascular at 5 years: 35/57 (61.4%) Hypovascular at 5 years: 28/45 (62.2%) <i>p</i> = 0.052 <i>Overall at 5 years: 117/170 (68.8%)</i>	N/R	Failed UAE: 4/264 (6.0%) Ovarian failure: 7/264 (2.7%) Death from PE: 1/264 (0.4%)	5 years
Wang et al. [21]	Prospective	115	Assessment of UAE for management of AUB-A	Markedly improved: 64/115 (55.7%) Moderately improved: 31/115 (27.0%) Slightly improved: 13/115 (11.3%) <i>Overall: 108/115 (93.9%)</i>	N/R	3 months: 28.5% volume reduction (<i>p</i> = 0.02) 6 months: 37.0% volume reduction (<i>p</i> = 0.02) 12 months: 51.0% volume reduction (<i>p</i> = 0.005)	Amenorrhoea: 2/115 (1.7%)	12 months

N/R, not reported

Table 2 Symptom change

Reference	n	Dysmenorrhoea (% of patients improved)	HMB (% of patients improved)	Uterine volume reduction	Overall symptom improvement	Follow-up
Guo et al. [24]	76	57/74 (77.0%)	49/61 (80.3%)	N/R	N/R	12 months
Wang et al. [25••]	195	113/147 (76.8%)	136/159 (85.5%)	Mean volume decrease: 330.8 to 208.4 cm ³ (37.0%)	N/R	15 months
Liang et al. [20•]	115	Pain score reduction (VAS): 7.45 to 1.32 Mean reduction 6.13 (<i>p</i> < 0.0001)	91/104 (88.0%)	Mean volume decrease: 296 to 198 mL (33.1%)	Symptom score reduction (mean): 57 to 17 (<i>p</i> < 0.0001) QoL score (mean): 45 to 90 (<i>p</i> < 0.0001)	22.5 (median)
Zheng et al. [23]	68	45/56 (80.4%)	33/40 (82.5%)	N/R	N/R	12 months
De Bruijn et al. [22]	1049	601/678 (88.7%, 95% CI 86.1–91.1)	298/340 (87.8%, 95% CI 84.3–91.3)	Decrease in cm ³ : 27.1 cm ³ (95% CI, 5.7–48.5)	877/1049 (83.6%, 95% CI 81.3–85.8)	22.3 months (mean)
Wang et al. [21]	115	Markedly improved: 64/115 (55.7%) Moderately improved: 31/115 (27.0%) Slightly improved: 13/115 (11.3%) Overall: 108/115 (93.9%)	N/R	3 months: 28.5% volume reduction (<i>p</i> = 0.02) 6 months: 37.0% volume reduction (<i>p</i> = 0.02) 12 months: 51.0% volume reduction (<i>p</i> = 0.005)	N/R	12 months
Zhou et al. [19]	252	Overall at 12 months: 145/196 (74.0%)	Overall at 12 months: 161/227 (70.9%)	N/R	N/R	5 years

N/R, not reported

6, and 12 months, respectively [21]. In this cohort, the median baseline uterine volume was 790 cm³ and the most significant reduction in the uterine size observed in the first 3 months follow embolization. The remaining retrospective studies showed similar rates of volume reduction of 33–37% at 12 to 15 months, respectively (Table 2) [20•, 25••]. A systematic review and meta-analysis show improvement in mass-related symptoms (81.3%) with an overall reduction in uterine volume approaching 50% at 24-month follow-up [22]. An example of post-UAE mass reduction is seen in Fig. 1 which demonstrates a marked reduction in adenomyoma volume 6 months after UAE.

Although UAE is a uterine-sparing method, pregnancy following UAE remains controversial with documented complications including intrauterine growth restriction, preterm birth, and increased rates of caesarean [26–28]. Of the studies included in this review, 2 examined pregnancy outcomes with a total of 8 conceptions reported. Of these, 3 underwent elective termination of pregnancy and 2 were complicated by placental insufficiency and preterm birth. The remaining 3 had uncomplicated pregnancies that delivered at term by elective caesarean [20•, 22]. Although we did not encounter studies addressing ongoing fertility following UAE for AUB-A, a systematic review and meta-analysis

(*n* = 353) suggests that UAE does not permanently impact ovarian reserve with no difference in AMH levels detected at 3, 6, and 12 months following UAE for AUB-L [29]. This should be carefully balanced against the documented risk of amenorrhoea, whether secondary to endometrial or ovarian failure.

Predictors of UAE Success

Table 1 shows predictors of AUB-A responsiveness to UAE. In one study, the authors evaluated the impact of UAE on lesion vascularity among 252 patients. Lesion vascularity was classified as hypervascular (abundant vessels centrally and peripherally), isovascular (abundant peripheral vessels and less internal vessels), and hypovascular (a lack of vessels both centrally and peripherally). The vascular supply to the uterus was also assessed and categorised into equal supply (left and right uterine arteries contributing 40–60% of total vascular supply) and unequal supply (one artery dominating with more than 60% of total vascular supply). Patient symptoms including menstrual loss and dysmenorrhoea were evaluated using standardised grading systems with pre-defined markers for improvement. The rates of

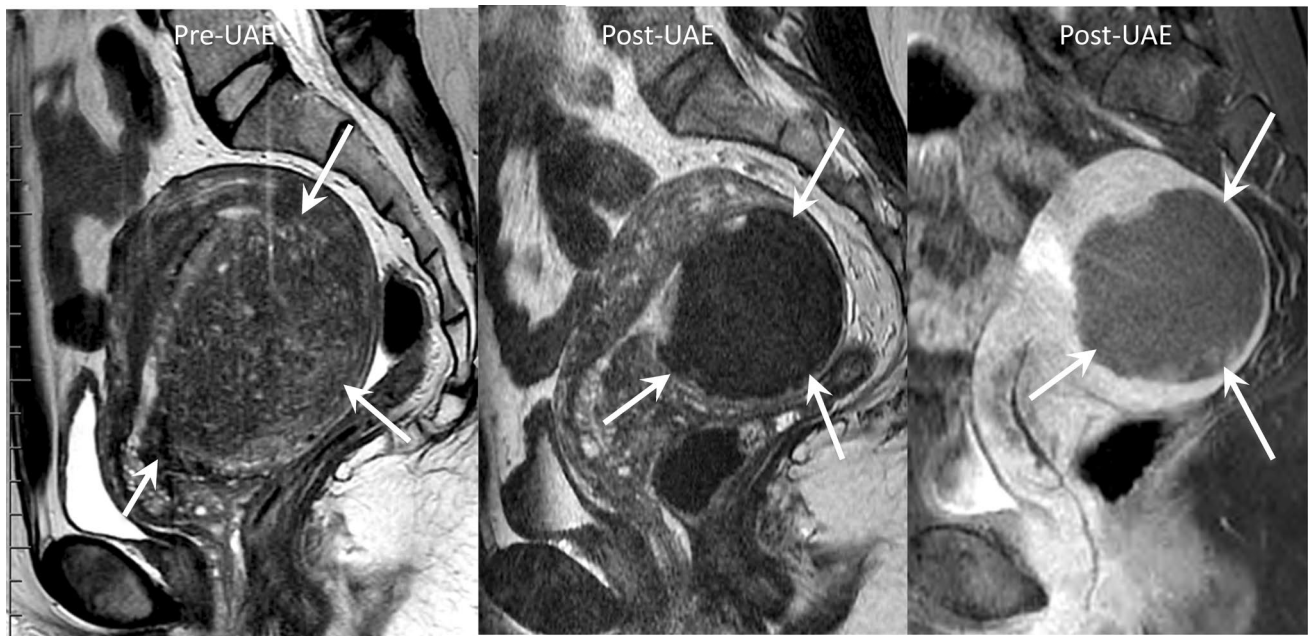


Fig. 1 Forty-five-year-old bank officer GPO0 suffered from severe HMB and dysmenorrhea for many years. Tranexamic acid and norethisterone were not effective. She expelled 2 Mirenas and failed endometrial ablation. MRI showed large focal adenomyosis in the

posterior wall; 6 months post-embolisation MRI showed infarction of focal adenomyosis (arrows) and shrinkage from 272 to 115 ml. Note the normal enhancing and viable myometrium (M). Her periods are now lighter than normal and no longer painful

improvement in dysmenorrhoea and menstrual loss were greater in the hypervascular group when compared to the isovascular and hypovascular groups at 12-month follow-up (Table 2) (86.5% vs. 71.6% and 58.8%, $p=0.002$ and 81.0% vs. 68.3% and 60.7%, $p=0.024$ respectively). These significant differences were not maintained at 5 years with overall improvements in dysmenorrhoea and HMB in 70.4% and 68.8% of cases, respectively [19].

Lesion vascularity has also been identified as a predictor of complications as demonstrated in a retrospective analysis of UAE for AUB-A [25••]. The authors evaluated 195 patients and found a 12.8% risk of Asherman syndrome following UAE. Univariate and multivariate logistic regression showed that those with hypovascular lesions, when accompanied by increased uterine size, had increased rates of post-procedural uterine synechiae ($p=0.019$, OR 0.495, CI 0.275–0.891). The authors postulated that poor vascularity increased the risk of embolic agent reflux into surrounding uterine vasculature with increased global myometrial and endometrial basal layer infarction [25••].

The presence of endometriosis has also been suggested as a predictor of UAE success in the management of AUB-A. In a retrospective study involving 76 patients, the authors examined the impact of ovarian endometriosis on symptom reduction following UAE. They showed that patients without endometriosis had statistically significant improvements in dysmenorrhoea (86.0% vs. 47.1%, $p=0.001$) when compared to those with no imaging evidence of endometriosis.

Differences in reduction of heavy menstrual loss was also observed, but did not reach significance (84.0% vs. 63.6%, $p=0.263$).

Another proposed predictor of treatment outcome following UAE can be found in differentiating between pure adenomyosis and mixed adenomyosis with accompanying leiomyomas (AUB-A/L). In a prospective study (2017), Health-Related Quality of Life (HRQOL) and Symptoms Severity (SSS) were evaluated among 29 patients with pure AUB-A ($n=14$) and mixed AUB-A/L ($n=15$) at 7-year follow-up [30]. In this small study, high patient satisfaction ratings of 72% were recorded with no statistically significant differences in HRQOL scores. Symptom Severity Scores, however, were superior in the mixed AUB-A/L groups. Hysterectomy was avoided by 82.0% of women and 74% of cases remained asymptomatic at extended follow-up [30]. These findings were supported by a meta-analysis involving 601 patients that demonstrated a greater improvement in patients with combined disease at long-term follow-up (85.4% vs. 74.0%, $p=0.003$) [22].

Disadvantages of UAE

Uterine artery embolization, although considered a minimally invasive procedure, is not without risks. A 2017 systematic review found 20 publications involving 615 patients that reported complications. The most common

post-procedural symptom was abdominal pain in 67.2% of patients. The pain lasted 2 weeks in 87.4% of cases [22]. Studies looking at varying pain management strategies have failed to identify a superior post-procedural pain protocol and pain should be managed with standard non-steroidal anti-inflammatory drugs, paracetamol, and breakthrough opioid medications [31]. A single randomised controlled trial, however, supports the use of pre-procedural dexamethasone for inflammation suppression and improved pain scores in the first 24 h [32]. Actual complications, including spontaneous expulsion of leiomyomata and endometritis, were reported in 1.6% and 0.7% of cases respectively with a single case of pseudoaneurysm [22].

Persistent amenorrhoea was reported in 13 studies and comprised 6.3% of the total population, all of whom were over 40 years of age. Others reported amenorrhoea rate between 1.7 and 21% with the patient age above 45 in all cases [20•, 25••, 30]. This complication could be due to infarction of the basal endometrium with or without Asherman syndrome as reported rates of proven ovarian failure are lower [19, 25••, 33]. A single-centre study evaluating data from 264 patients reported a peri-procedural death secondary to pulmonary embolism [19]. It is unclear if this was either directly or indirectly associated with the procedure. In general, the absolute risk-related death due to UAE appears low.

Beyond post-procedural complications, another disadvantage of UAE is an ongoing possibility of intervention subsequent to treatment failure. Repeat intervention procedures post-UAE are rare and were reported as 3.0% in only one study [20•]. Hysterectomy rates in the reviewed studies varied between 2.6 and 17.9% at extended follow-up [20•, 22, 30]. Data from the included meta-analysis reports subsequent hysterectomy rates of 2.6% [22].

Conclusion

While UAE remains an accepted conservative treatment option for the management of AUB-L, its application in the management of adenomyosis remains unclear. This is reflected by the relatively small number of publications that have examined the topic in the previous 5 years. Despite limitations in the data available, UAE is a promising conservative treatment modality for women suffering from adenomyosis with HMB, dysmenorrhoea, or mass symptoms. Significant reductions in mass-related symptoms are described in up to 81.3% of patients following UAE for AUB-A [20•, 21, 22, 25••]. This is accompanied by a reduction in HMB and dysmenorrhoea in up to 79.4% and 88.7%, respectively [19, 22].

The advantages of an effective, minimally invasive procedure are centred around avoidance of a major abdominal

procedure; particularly for obese or comorbid patients. UAE is also an alternative option for women who wish to preserve their uterus for personal or reproductive reasons. As demonstrated in this review, there is limited data on pregnancy following UAE for AUB-A and those wishing to pursue pregnancy should be advised of its association with growth restriction and preterm birth. This is reflected in the cautious statements on reproduction following UAE issued by both the American and Australian colleges for Obstetrics and Gynaecology.

Risks of post-procedural pain, Asherman syndrome, amenorrhoea, early menopause, pyomyoma, pseudoaneurysm, and treatment failure have been well documented. There is significant variation in the rates of hysterectomy following UAE for management of AUB-A; however, the most reliable data indicates a rate of 2.6% [22]. UAE remains a safe and effective management strategy for adenomyosis refractory to medical management in appropriately counselled patients.

Advantages

- Minimally invasive
- Uterine preservation
- Alternative option in patients with surgical comorbidities
- Improves dysmenorrhoea, heavy menstrual bleeding, and mass symptoms

Disadvantages

- Risk of treatment failure and subsequent hysterectomy
- Limited data on pregnancy following UAE
- Risk of complications
- Not a definitive procedure

Conclusion

Uterine artery embolization offers a safe and effective conservative treatment modality for the management of adenomyosis.

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Declarations

Conflict of Interest The authors declare no conflicts of interest relevant to this manuscript.

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