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REVIEW ARTERIAL INTERVENTIONS

Uterine Artery Embolisation for Women with Giant Versus Non-giant Uterine Fibroids: A Systematic Review and Meta-analysis

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Abstract

Background Evidence supporting uterine artery embolisation (UAE) for giant fibroids (≥ 10 cm and/or uterine volume ≥ 700 CC) remains sparse. We performed a systemic review and meta-analysis of UAE outcomes for symptomatic giant versus non-giant fibroids.

Methods The literature was systematically reviewed. Research studies of UAE as an adjunct to surgery, and those not using peri-operative MRI were excluded. Primary outcomes were fibroid size and uterine volume reduction, procedure time, length of hospital stay, reinterventions, patient symptom improvement/satisfaction and complications.

Results We identified four observational studies (839 patients; giant = 163, non-giant = 676). Both groups demonstrated reduction in fibroid size and uterine volume after UAE, with equivocal difference in uterine volume reduction (Mean difference (MD) − 0.3 95% confidence interval (CI) − 3.8 to 3.1, $p = 0.86$) and greater reduction in non-giant dominant fibroid size (MD − 5.9 95% CI − 10.3 to − 1.5, $p < 0.01$). Giant fibroids were associated with 5.6 min longer mean operative time (MD 5.6 min 95% CI 2.6–8.6, $p < 0.01$) and 4.8 h longer mean hospital stay (MD 4.8 h 95% CI 1.1–8.6, $p = 0.01$). Patient symptoms/satisfaction outcomes were summarised, but too heterogeneous for meta-analysis. Major complication and reintervention rates were low, with a statistically higher rate of major complications (Odds ratio (OR) 4.7 95% CI 1.5–14.6, $p < 0.01$) and reinterventions (OR 3.6 95% CI 1.7–7.5, $p < 0.01$) in giant fibroids.

Conclusions Current evidence shows UAE is a safe and effective option to treat giant fibroids. However, the limited available data indicate a relatively higher risk of complications and reinterventions when compared with non-giant fibroids. Patients should be selected, counselled and managed accordingly.

Level of Evidence Level III, Systematic review of retrospective cohort studies.

Keywords Uterine · Leiomyoma · Fibroid · Embolisation · Giant · Non-giant

Introduction

Uterine artery embolisation (UAE) is a minimally invasive treatment for symptomatic uterine fibroids and is routinely offered to women alongside surgery (myomectomy and hysterectomy). The benefits of UAE in comparison with surgery are clear, including the use of conscious sedation rather than general anaesthetic, faster recovery post-procedure and fertility preservation [1, 2]. Previous randomised controlled trials such as EMMY and REST have

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demonstrated level 1 evidence for the use of UAE in the treatment of the majority of fibroid sizes [3, 4]. However, the evidence for the use of UAE specifically in giant fibroids, defined as fibroids larger than or equal to 10 cm and/or women with a fibroid uterine volume greater than 700 cc, remains sparse, and the results are variable [5–7].

Studies have suggested a greater risk of complications in giant uterine fibroids compared to non-giant fibroids, including an increased risk of infection, sepsis and uterine necrosis necessitating hysterectomy [8, 9].

The aim of study was to perform a systematic review and meta-analysis of the clinical outcomes, including quality of life and symptom improvement, fibroid and uterine volume reduction, procedure time, length of hospital stay, as well as complications and reinterventions following UAE for giant and non-giant fibroids.

Methods

Design and Study Selection

The study conformed with Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) standards [10]. The study methodology was specified prior to data extraction and registered with the international prospective register of systematic reviews (PROSPERO) (Registration number: CRD42019118989). We planned to include comparative studies of uterine artery embolisation for women with symptomatic giant uterine fibroids ($\geq$ 10 cm dominant fibroid diameter and/or uterine volume $\geq$ 700 cm^3) versus non-giant fibroids ($\leq$ 10 cm dominant fibroid diameter and/or uterine volume $\leq$ 700 cm^3). Only studies using magnetic resonance (MR) imaging to evaluate fibroid characteristics were included. Patients who had previous medical and/or surgical management for fibroids were included. We excluded case reports, case series and studies of UAE as an adjunct prior to surgery.

The intervention was UAE for symptomatic giant fibroids and the comparator was UAE for symptomatic non-giant uterine fibroids. Primary outcome measures were dominant fibroid volume reduction and uterine volume reduction, operation time, length of hospital stay, reintervention rate, post-operative patient satisfaction and symptomatic improvement and complication rate. Post-operative complications were classified using the Society of Interventional Radiology (SIR) classification system for complications by outcome [11].

Literature Search Strategy

Two authors (OL and NP) independently conducted an online literature search (1995—present day), using PubMed, MEDLINE, EMBASE and CENTRAL (Cochrane Central Register of Controlled Trials). The final search was on 30 January 2019. The search did not use language restrictions. We also searched bibliographic lists. The search strategy used is outlined in Appendix 1.

Selection of Studies

Titles and abstracts were reviewed by two authors (OL, NP). Full texts were screened against the inclusion criteria when required. Any discrepancies were resolved by a third author (MH).

Data Extraction and Management

A data extraction spreadsheet was created and piloted (OL, NP) for recording:

- Study characteristics; (first author, country of origin, year published, study type, study period, definitions of terminology pertaining to the study).
- Patient demographics; (number of patients, age, inclusion/exclusion criteria, previous or present medical/surgical treatment, fibroid burden.
- Procedural data; (pre-operative/post-operative protocol, imaging, operative technique and equipment).
- Outcome data; (patient-related outcomes, complications, imaging outcomes, operative/post-operative data).

Assessment of Risk of Bias

Included studies were independently quality assessed (OL and NP) for risk of bias using the Newcastle–Ottawa Scale (NOS).

Analysis

For dichotomous outcome measures (complication rates and reintervention rate), the odds ratio (OR) was used. Odds ratios were presented with the 95% confidence interval (CI). OR was defined as the odds of an event in the giant fibroid cohort compared to the non-giant fibroid cohort. An OR less than one indicated a favourable result for the giant fibroid cohort. For continuous outcome measures (operative time, length of hospital stay, dominant fibroid volume and uterine volume), the mean difference (MD) was used. The mean value with the standard deviation was used to describe fibroid and uterine size.

The patient was the unit of analysis. Authors were contacted where data were missing or required clarification.

Review Manager 5.3 software (Review Manager. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used for statistical analysis. The Mantel–Haenszel fixed effect model was used. A random effects model was used where significant between-study heterogeneity existed.

Heterogeneity between studies was assessed using the Cochrane Q score and by calculating I^2. Heterogeneity was classified as low (0–25%), moderate (25–75%) or high (75–100%).

Sensitivity analyses were performed to test the robustness of our findings against arbitrary decisions made by authors.

Results

The literature searching identified 673 articles. Titles, abstracts and full texts were reviewed. Four relevant studies were identified to include in our analysis (Fig. 1) [12–15]. All were retrospective cohort studies reporting a total of 843 patients (giant n = 163, non-giant n = 676).

Characteristics of included studies are summarised in Table 1. Comparison of patient demographics was reported in two of the four included studies [12, 14]. One study did not report a protocol [15]. Angiographic endpoints were comparable (defined as sluggish contrast flow in uterine artery). Follow-up reporting was variable among included studies.

The study by Prollius et al. described 'giant' as a uterine volume of > 780 cm^3 [15]. The authors decided to include this relevant study as the small uterine volume variation of 80 cm^3 which was felt to be satisfactory. In the study by Berczi et al. [13], seven patients underwent peri-operative ultrasound (USS) instead of MR due to claustrophobia. The authors included this study after deciding that this small number of USS data points was acceptable.

Methodological Appraisal

Risk of bias of included studies assessed using the Newcastle–Ottowa Scale (NOS) is shown in Table 2. The risk of bias was low in two studies (Katsumori and Choi) and moderate in two studies (Berczi and Prollius) [12–15].

Outcome Analysis

Outcomes are given in Fig. 2.

Dominant Tumour Size Reduction

Two included studies reported this outcome [12, 14]. UAE resulted in effective mean tumour size reduction in both groups, giant: 48.0% ± 19.9; non-giant: 53.2% ± 24.3. Analysis of 365 patients indicated that patients with giant fibroids experienced significantly less tumour size reduction effect than patients with non-giant fibroids (MD − 5.89 95% CI − 10.31 to − 1.47, p = 0.009). Low inter-study heterogeneity was indicated (I^2 = 0%, p = 0.86).

Uterine Volume Reduction

Two studies were included in this analysis [12, 14]. UAE resulted in uterine volume reduction in both groups, giant:

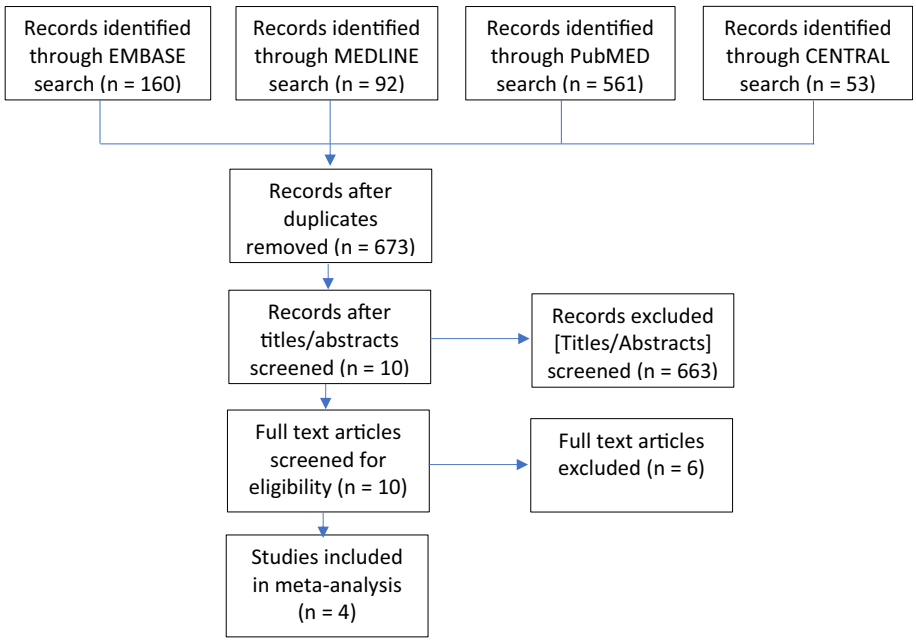


Fig. 1 PRISMA study flow diagram

Table 1 Study characteristics and baseline demographics

Author	Country	Year	Journal	Study period	Study type	Total patients	Non-giant	Giant
Berczi et al. [13]	Hungary	2015	CVIR	4 years 8 months	RCS	303	262	41
Choi et al. [14]	Republic of Korea	2013	JVIR	6 years 1 months	RCS	323	260	63
Prollius et al. [15]	South Africa	2004	BJOG	NR	RCS	61	49	12
Katsumori et al. [12]	Japan	2003	ARRS	NR	RCS	152	105	47

Age (mean years)	Embolic agent	Peri-operative protocol	Success rate	FU protocol	Duration of FU (mean months)		Percentage of cohort FU (%)	
					Clinical	Imaging	Clinical	Imaging
42.3 (24–54)	Non-spherical PVA particles 500–700 μm and 355–500 μm diameter	Pre and post-operative antibiotics. IV Opioid, PO NSAID. Observed overnight	NR (Unilateral embolisation: N: 7.3% versus G: 0%)	Follow-up interviews in post-operative clinic.	N: 7.6 ± 4.9 versus G: 8.98 ± 6.7	NR	N: 91.2 versus G: 87.8	NR
N: 37.3 (± 5.6) versus G: 37.1 (± 5.6)	PVA alcohol particles or foam embolisation particles (250–710 μm) operators' preference	NR	N: 100% versus G: 98.4%	MRI within 3 Months. Questionnaire at 1, 3 and 12 months.	Short-term: N: 2.9 ± 0.8 versus G: 3.0 ± 0.9 Mid-term: N: 32.3 ± 15.4 versus G: 34.1 ± 16.4	Short-term: N: 3.1 versus G: 3.1 Mid-term: N/A	Short-term: N: 100 versus G: 100 Mid-term: N: 75.4 versus G: 74.6	No comparative data. All patients had MR follow-up: 88% within 3 months 12% within 4–11 months
40 (19–62)[a]	Polyvinyl alcohol particles	Pre and post-operative antibiotics. Admitted 1 day pre-operatively.	NR 1 failed procedure. No comparative data available	MRI at 3 and 12 months post-operatively.	NR	NR	N: 100 versus G: 100	NR
42.5 (31–52)	Gelatin sponge particles 500–1000 μm, contrast and antibiotics (1 g cefazolin, cefamezin)	2 days of post-operative IV antibiotics followed by 2 days oral antibiotics. Oral NSAIDs 2 weeks post-operatively	NR 1 failed procedure. 1 unilateral embolisation. No comparative data available	MRI at 1 week, 4 and 12 months post-operatively. Questionnaire at 4 months, 1 and 2 years.	No comparative data. Study mean: 17.5 No sig. difference between cohorts stated in text.	NR	No comparative data. No sig. difference stated in text. > 4 Months: 63.2 > 12 Months: 32.2	Limited comparative data. 1 week: N: 99% versus G: 100% 4 months: NR 12 months: NR

CVIR Cardiovascular and interventional radiology, *JVIR* Journal of vascular and interventional radiology, *BJOG* British journal of obstetrics and gynaecology, *ARRS* American roentgen ray society, *RCS* Retrospective cohort study, *NR* Not recorded, *N* Non-giant, *G* Giant, *FU* Follow-up

[a]Median age

Table 2 Risk of bias analysis using Newcastle–Ottawa scale (NOS)

Author	Selection				Comparability	Outcome			
	Representativeness	Selection	Ascertainment of exposure	Records outcome absence pre-intervention	Comparability of cohorts	Assessment of outcome	Appropriate follow-up period	Cohort follow-up achieved	NOS total (/9)
Katsumori et al.	*	*	*	*	**	*	*		8
Prollius et al.	*	*	*	*		*	*	*	7
Choi et al.	*	*	*	*	**	*	*		8
Berczi et al.	*	*	*	*		*	*	*	7

38.6% ± 16.2; non-giant: 37.5% ± 18.7. Analysis of 365 patients did not find a significant difference between the giant and non-giant fibroid groups (MD − 0.31 95% CI − 3.76 to 3.14, $p = 0.86$). There was evidence of considerable heterogeneity between studies ($I^2 = 85\%$, $p = 0.01$).

Operative Time

Two studies reported this outcome [12, 14]. Analysis of 365 patients indicated a significantly longer operative time for giant fibroids (Choi paper: non-giant fibroids group 44.9 ± 12.7 min, giant fibroid group 49.0 ± 13.3 min; Katsumori paper: non-giant fibroids group 46.6 ± 14.3 min, giant fibroid group 55.3 ± 15.8 min; MD 5.58 min 95% CI 2.58–8.57, $p = 0.0003$). Moderate heterogeneity was indicated ($I^2 = 49\%$, $p = 0.16$).

Length of Hospital Stay

Two studies reported this outcome [12, 14]. Analysis of 365 patients indicated a significantly longer hospital stay for giant fibroids (Choi paper: non-giant fibroids group 2.4 ± 1.0 days, giant fibroid group 2.6 ± 1.5 days; Katsumori paper: non-giant fibroids group 3.8 ± 0.8 days, giant fibroid group 4.0 ± 1.6 days; MD 4.84 h 95% CI 1.06-8.61, $p = 0.01$). Low heterogeneity was indicated amongst included studies ($I^2 = 0\%$, $p = 0.96$).

Reintervention Rate

All studies reported this outcome. The reintervention rates (Table 3) were 2.51% (non-giant) and 8.59% (giant). Analysis of 843 patients found a significantly higher reintervention rate associated with embolisation of giant fibroids (OR 3.57 95% CI 1.70–7.49, $p = 0.0008$). There was low heterogeneity among the included studies ($I^2 = 0\%$, $p = 0.44$).

Patient Satisfaction

Two studies reported this outcome [12, 13]. We were unable to pool these studies for analysis due to heterogeneity of the questionnaires used. Table 4 shows the data from included studies.

Patient Symptom Improvement

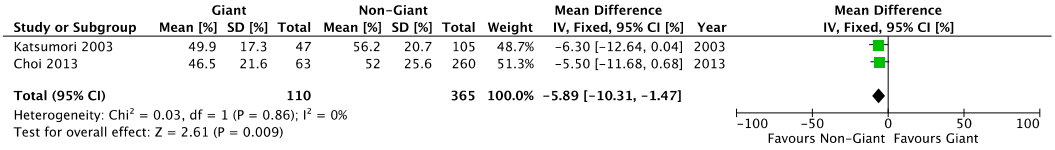
All studies reported this outcome [12–15]. The symptom improvement data collection tools utilised in the studies were too heterogenous to allow meta-analysis to be performed. Table 4 shows the data from included studies. Regardless of the assessment tool utilised, data from both groups showed good overall patient satisfaction with the procedure, and effective post-operative symptom improvement.

Post-operative Complications

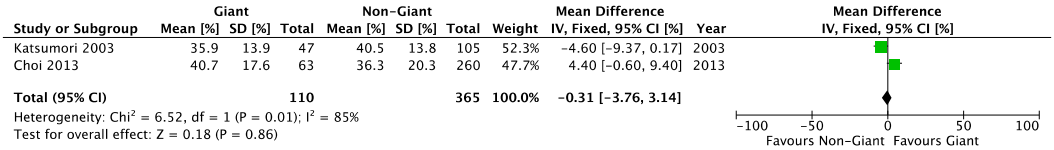
All included studies reported this outcome. The complication rates were 17.99% for non-giant and 23.03% for giant fibroids. Pooled analysis of 843 patients found a non-significant increase in the post-operative complication rate associated with embolisation of giant versus non-giant fibroids (OR 1.45 95% CI 0.94–2.24, $p = 0.09$). Moderate heterogeneity may have existed amongst included studies ($I^2 = 29\%$, $p = 0.24$).

Minor Post-operative Complications

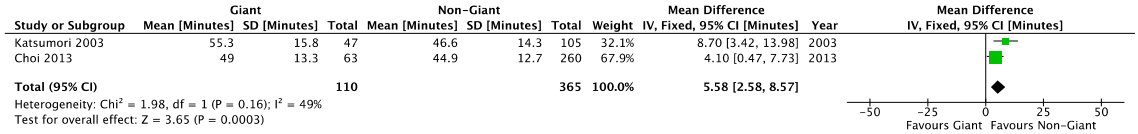
All included studies reported this outcome. Minor complication rates were 17.1% and 19.0% following embolisation of non-giant and giant fibroids, respectively. Analysis of 843 patients did not indicate a significant difference between groups (OR 1.22 95% CI 0.77–1.94,



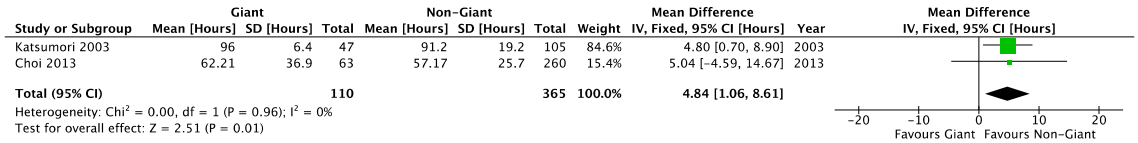
A Dominant tumour size reduction



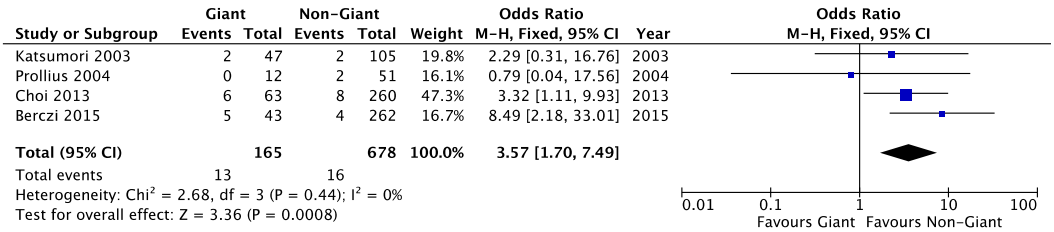
B Uterine volume reduction



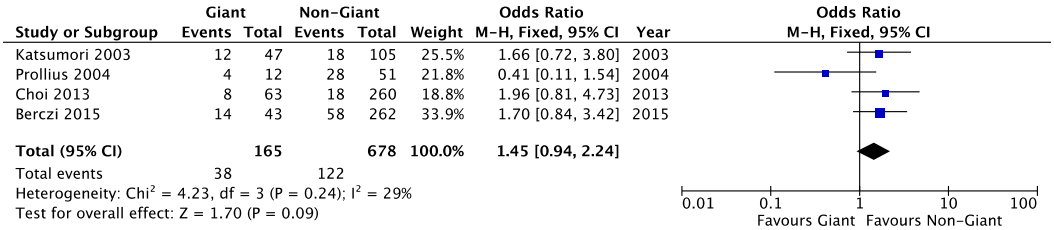
C Operation time



D Length of stay

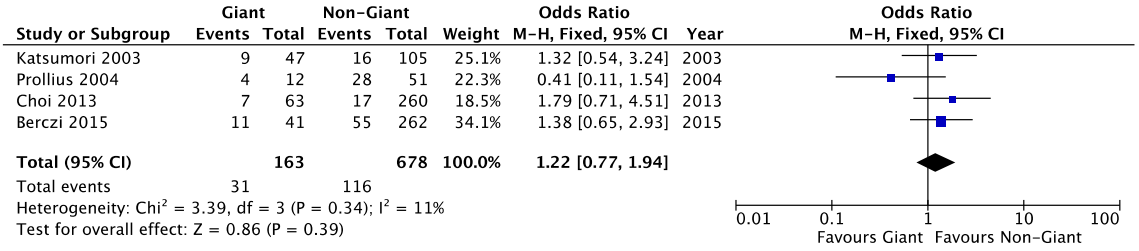


E Reintervention Rate

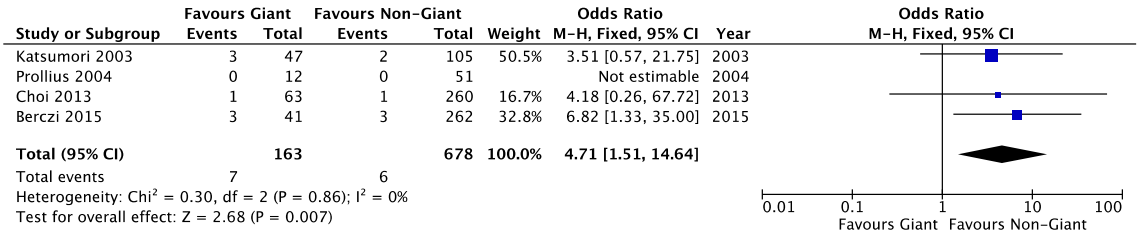


F Postoperative complications (total)

Fig. 2 Forest plots of comparison of **A** dominant tumour size reduction, **B** uterine volume reduction, **C** operation time, **D** length of hospital stay, **E** reintervention rate, **F** post-operative complications (total), **G** post-operative complication (minor), **H** post-operative complications (major). Solid square illustrates the odds ratio or mean difference, and the diamond indicates the pooled effect size. The horizontal line indicates the 95% confidence interval. M–H: Mantel–Haenszel



G Postoperative Complication (minor)



H Postoperative complications (major)

Fig. 2 continued

Table 3 Reported reinterventions and major complications performed post-uterine artery embolisation in non-giant and giant fibroid group

	Non-giant	Giant
Reintervention		
Transvaginal resection	2 (0.300%)	2 (1.23%)
Acute myomectomy	0	1 (0.613%)
Elective myomectomy	8 (1.18%)	6 (3.68%)
Acute hysterectomy	3 (0.444%)	2 (1.23%)
Elective hysterectomy	4 (0.592%)	3 (1.84%)
Major complication		
Uterine infection	2 (0.296%)	3 (1.84%)
Expulsion of fibroid (requiring intervention)	3 (0.444%)	2 (1.23%)
Endocavitatory transformation of fibroid	0	1 (0.613%)
Sexual dysfunction	0	1 (0.613%)
Unstable angina	1 (0.148%)	0

$p = 0.39$). There was minimal indication of between-study heterogeneity ($I^2 = 11\%$, $p = 0.34$).

Major Post-operative Complications

All included studies reported this outcome. Major complication rates were 0.88% and 4.29% following embolisation of non-giant and giant fibroids, respectively (Table 3). Analysis of 843 patients shows the rate of major complications to be significantly higher following embolisation of giant fibroids (OR 4.71 95% CI 1.51–14.64, $p = 0.007$). Low heterogeneity was indicated amongst included studies ($I^2 = 0\%$, $p = 0.86$).

Discussion

Principle Findings

Giant fibroids were associated with longer operative time and length of hospital stay. Operative time is expected to be longer in giant fibroids due to the greater tumour bulk requiring embolisation; however, the clinical significance of a 5.6 min mean difference between groups remains uncertain. Extractable data from the included papers was too limited to explain the increased length of hospital stay in patients with giant fibroids, which equated to only a 4.8 h mean difference. Previous data have suggested that uterine volume or fibroid size does not predict pain severity

Table 4 Patient satisfaction and symptom improvement data from included studies

(a) Patient satisfaction

Katsumori et al

	FU Timepoint	Giant	Non-giant	*P value*
Patient satisfaction with procedure and outcomes (score*)	4 m	1.80 ± 0.46	1.97 ± 0.18	0.004
	1 year	1.79 ± 0.50	1.90 ± 0.30	0.247
	2 years	1.83 ± 0.40	1.96 ± 0.20	0.190

*Scores: – 2 markedly dissatisfied | – 1 slightly dissatisfied | 0 neutral | 1 slightly satisfied | 2 markedly satisfied

Berczi et al

		Giant	Non-giant
Would you recommend this to other patients?	Yes	97.2%	98.7%
	No	2.8%	1.3%

Mean FU time (months): Giant: 9 +/– 6.7, Non-giant: 7.6 +/– 4.9

(b) Symptom improvement

Katsumori et al

Symptom (score)*	FU Timepoint	Giant	Non-giant	*P value*
Menorrhagia	4 m	3.36 ± 0.99	3.79 ± 0.55	0.003
	1 year	3.58 ± 0.50	3.79 ± 0.56	0.022
	2 years	3.90 ± 0.32	3.87 ± 0.34	0.835
Bulk symptoms	4 m	3.80 ± 0.41	3.75 ± 0.57	0.874
	1 year	3.75 ± 0.44	3.70 ± 0.70	0.867
	2 years	3.75 ± 0.62	3.87 ± 0.34	0.731

*0 worsened condition | 1 no change | 2 slightly improved | 3 moderately improved | 4 markedly improved

Berczi et al

	Giant	Non-giant	*P value*
Pre-procedural QoL	33.5±24.1	33.5±23.5	0.940
Post-procedural QoL	81.5±23.5	85.6±16.0	0.365

Numerical analog QoL score in post-operative clinic (0 = unbearable; 100 = perfect QOL)

		Giant	Non-giant
Symptom improvement?	Yes	77%	77.8%
	Partially	17.6%	13.9%
	No	5.4%	8.3%

Mean FU time (months): Giant: 9 +/– 6.7, Non-giant: 7.6 +/– 4.9

Choi et al

	FU Timepoint	Giant	Non-giant	*P value*
Symptom scores	Short-term: 3 m	3.1 ± 2.0	3.6 ± 2.0	0.137
	Mid-term: > 1 years	1.9 ± 2.1	2.3 ± 2.3	0.258

10-point visual analogue scale (0 = no symptoms, 10 = worst initial symptoms)

Prollius et al

Percentage improvement at 1 year		Giant	Non-giant	95%CI
Menorrhagia	Volume	91.7	85.7	[– 33.7 to 15.6]
	Clots	66.7	73.5	[– 17.9 to 37.2]
Pressure effects	Discomfort	83.3	57.1	[– 54.8 to 4.5]
	Mass	50	40.8	[– 48.7 to 14.9]
	Deep dyspareunia	50	32.7	[– 43.6 to 13.8]

Determined using 3-point Likert scale: better, same, worse

post-UAE [16]. The overall reduction in operative time and length of hospital stay between the two included papers may reflect increased UAE experience over the decade that separates these studies [12, 14].

No difference in the rate of total complications was identified between groups. Use of the SIR classification system allowed further categorisation. No difference in minor complications was seen; however, a greater prevalence of major complications and reinterventions was identified in the giant fibroid group [11]. Broadly, of the seven major complications within the giant fibroid group, three related to fibroid expulsion requiring intervention/endocavitatory transformation, three related to uterine infection and one patient suffered sexual dysfunction post-UAE.

Two patients underwent transvaginal resection of fibroid material following expulsion of 12 cm submucosal and 19 cm cervical fibroids, respectively [12]. Per-vaginal sloughing of necrotic material post-UAE in such cases is predictable. Pre-procedure planning in conjunction with gynaecology colleagues could have led to elective removal of these devascularised fibroids post-UAE in a controlled manner, reducing the risk of acute cervical occlusion, subsequent uterine infection and the need for emergency surgery [17, 18]. Meticulous post-procedure follow-up for women undergoing UAE for giant fibroids as well as a dedicated management pathway for patients who present with uterine infection may expedite treatment in this patient group, subsequently reducing the requirement for emergency surgery.

Choi et al. described a complication related to endocavitatory transformation of a fibroid on post-procedure imaging; the symptoms experienced by the patient are unclear; however myomectomy was subsequently performed. Two patients from the Berczi et al. cohort underwent acute hysterectomy five and nine weeks post-UAE, respectively, for signs of uterine infection (fever, intractable abdominal pain and raised inflammatory markers) [13]. From the combined data, four patients (1.84%) were described as having uterine infections requiring either antibiotics and/or surgery [12, 13]. A large retrospective study by Rajan et al. which investigated intrauterine infectious complications after UAE identified the proportion of patients requiring either antibiotics and/or surgery as 1.2% [19].

One patient was described by Katsumori et al. as experiencing sexual dysfunction post-UAE [12]. It is debateable whether this should have classified as a major complication given there was no distinct evidence that UAE was the underlying cause and there was no infarction of the cervix on post-procedure MRI. Although there have been case reports of sexual dysfunction post-UAE, a large prospective observational study by Kovascsik et al. found conversely that patients reported improved sexual function and quality of life post-UAE [20, 21].

Limitations

The systematic review process was limited by the lack of randomised controlled trials relating to the use of UAE in the treatment of giant fibroids. The evidence presented, however, reflects the accumulated data which is available in the literature currently. Meta-analysis of operative time, length of hospital stay, dominant tumour size reduction and uterine volume reduction was limited to analysis of two studies.

One major limitation related to the heterogeneous methods used by included studies of assessing symptom severity and quality of life pre- and post-UAE. None of the selected papers utilised the validated uterine fibroid symptom and health-related quality of life (UFS-QoL) questionnaire, instead opting to use their own local questionnaires, which prevented direct comparison between studies [22].

Conclusion

Current evidence shows UAE is a safe and effective option to treat giant fibroids. However, the limited available data indicates a relatively higher risk of complications and reinterventions when compared with non-giant fibroids. Patients should be selected, counselled and managed accordingly.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Informed Consent For this type of study, formal consent is not required. This article does not contain any studies with human participants or animals performed by any of the authors. For this type of study, informed consent is not required. For this type of study, consent for publication is not required.

Appendix 1: Search Strategy

Search No.	Search strategy*
#1	(fibroid emboli*ation).ti,ab
#2	("fibroid emboli*ation").ti,ab
#3	("uterine artery emboli*ation").ti,ab
#4	(uterine artery emboli*ation).ti,ab
#5	(ufe).ti,ab
#6	(1 OR 2 OR 3 OR 4 OR 5)
#7	(giant OR large OR massive).ti,ab
#8	(non-giant OR small).ti,ab
#9	(7 OR 8)
#10	(fibroid*).ti,ab
#11	LEIOMYOMA/
#12	(leiomyoma*).ti,ab
#13	(10 OR 11 OR 12)
#14	(9 AND 13)
#15	(complication*).ti,ab
#16	(reintervention).ti,ab
#17	(reintervention).ti,ab
#18	("uterine volume").ti,ab
#19	(devasculari*ation).ti,ab
#20	(satisfaction).ti,ab
#21	"PATIENT SATISFACTION"/
#22	"INTRAOPERATIVE COMPLICATIONS"/
#23	"POST-OPERATIVE COMPLICATIONS"/
#24	(15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23)
#25	(6 AND 14 AND 24)

*Strategy used to search PubMed, EMBASE, MEDLINE, and Cochrane Central Register of Controlled Trials

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