ORIGINAL ARTICLE

Uterine artery embolization for treatment of symptomatic fibroids; a single institution experience

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Abstract

Background: Uterine fibroids are the most common reproductive tract tumours in females. Uterine artery embolization (UAE) is a fertility-sparing procedure for treatment of symptomatic fibroids. We evaluated the efficacy and safety of UAE in the treatment of 118 patients with symptomatic uterine fibroids in a single Academic Centre in the West of Ireland to determine whether fibroid and uterine size affect clinical outcomes and complications.

Methods: This was a retrospective cohort of 118 patients who underwent UAE for treatment of symptomatic fibroids between November 2006 and August 2011. Diagnosis of fibroids in symptomatic patients was established by magnetic resonance imaging (MRI) and/or transabdominal ultrasonography (US). Three different embolic agents were used. All patients had at least one follow-up using MRI, at three and/or 12 months. A non-validated questionnaire was used to report patient satisfaction with regards to symptoms improvement on a yes-or-no basis.

Results: Mean fibroid volume, uterine size and dominant fibroid size were significantly reduced at three months and one year follow-up ($p = 0.00$) and that was tallied with symptoms improvement ($p < 0.05$). Overall patient satisfaction at three months was 84% falling to 75.9% by 12 months (all $p < 0.05$). Few complications were reported (2.5%). No significant difference was observed in safety or efficacy for different embolic agents.

Conclusion: The study confirms the safety and efficacy of UAE in the treatment of symptomatic fibroids. Hippokratia 2014; 18 (3): 258-261.

Keywords: Uterine fibroid embolization, menorrhagia, leiomyoma

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Introduction

Uterine fibroids are the most common reproductive tract tumour in females showing increasing prevalence with age[1]. They are incidentally diagnosed during a clinical or ultrasound (US) examination and cause no symptoms. If symptomatic, they commonly cause menorrhagia, dysmenorrhoea and non-bleeding bulk-related symptoms.

Uterine artery embolisation (UAE) has been approved by the National Institute for Clinical Excellence (NICE) for the treatment of uterine fibroids and relieving symptoms[2]. UAE is a minimally invasive procedure, performed under local anaesthetic and requires an overnight hospital stay. A number of different embolic materials and techniques are available at varying costs, yet the best method of achieving effective embolisation is unclear. Technical failure is uncommon and a repeat procedure is rarely required. Despite unpredictable complications with UAE, the risk of long-term sequelae is low.

We aimed to evaluate the efficacy and complication rates of UAE in our institution in order to determine whether fibroid volume, tumour size and dominant fibroid size affect therapeutic efficacy and complications.

Methods

In this retrospective study, 118 women underwent UAE for treatment of symptomatic fibroids between November 2006 and August 2011. Institutional ethical approval has been taken for the study from the local ethics committee at University Hospital Galway. All patients were counselled about the risks and benefits of UAE and informed consent was obtained. Patients were all symptomatic and refused hysterectomy when indicated. Exclusion criteria included current pregnancy, endometrial polyps or hyperplasia, pelvic malignancies or infections and presence of any contraindications for angiography. All patients underwent gynaecologic examination, magnetic resonance imaging (MRI) and/or trans-abdominal US (GE 200, GE, USA, Convex probe, 2.5-5 MHz). The fibroid volume was calculated using a prolate ellipse formula (length x depth x width x 0.5233). All patients had at least one follow-up using MRI, at three and/or 12 months. A non-validated questionnaire was used to report patient satisfaction with regards to symptoms improvement on a yes-or-no basis.

The primary outcome was safety based on assessment

of peri- and post-operative complications. Complications were graded with respect to severity using the complication classification developed by the Society of Interventional Radiology (SIR)[3]. General side effects (GSEs) such as post embolisation syndrome (PES) not requiring readmission, natural fibroid expulsion and vaginal discharge were considered a normal consequence of the embolisation process.

The secondary outcome was treatment efficacy including resolution of symptoms and patient-reported satisfaction. Other efficacy outcomes included technical success, reduction in fibroid/uterine size (as determined by MRI) and further treatments required for unresolved fibroid symptoms. Efficacy and safety were analysed for associations with fibroid and uterine size and volumes.

Normality tests were carried out to determine data distribution for age and size. Age and weight were transformed into categorical variables by their mean values. Wilkoxon tests for paired samples, Spearman's correlation and chi-square tests for univariate analysis were used where appropriate. Missing data were excluded in the calculations. Statistical tests were two-tailed with a significance level set at $p<0.05$ and confidence interval (CI) at 95%. Analyses were performed using Statistical Package for the Social Sciences (SPSS) version 15.0 (SPSS Inc., Chicago, IL, USA).

The procedure was performed by a Consultant Interventional Radiologist or a Senior Registrar under supervision. The technique is well described elsewhere[4,5]. In brief, particles are delivered by catheter to the uterine artery and they block off the vascular supply to the fibroid. Particles included a) Embosphere® (sizes 500-900 μm) (Biosphere Medical, MA), (n = 87, 73.7%) b) Embozene® (sizes 500-900 μm) (CeloNova Biosciences, Newnan, GA), (n = 28, 23.7%) c) polyvinyl alcohol (PVA) (sizes 710-1,000 μm) (Boston Scientific/Target Therapeutics, Cork Ltd, Cork, Ireland), (n = 3, 2.5%).

Results

Baseline demographics and presenting symptoms are shown in Table 1. Three and six patients had previously undergone UAE and myomectomy respectively. One and nine patients had used GnRH analogues and the Mirena coil® respectively.

Primary outcome

The majority of the UAEs were technically uneventful (n = 115, 97.4%). Two procedures were difficult (a unilateral instead of standard bilateral UAE and a right femoral artery injury requiring subsequent angioplasty). The majority of subjects had no intraoperative complications (90%). Three out of 118 patients (2.5%) declined PCA, as they were symptoms free. The mean length of stay was 2.38 ± 0.8 days (1-8 days). One hundred five out of 118 (89%) patients were discharged home following their overnight stay. One patient was treated with antibiotics for groin haematoma; another patient was investigated for suspected pulmonary embolus (PE), which was not confirmed. One patient developed an acutely ischaemic limb from a non-specific undetermined reaction. Therefore, complications were reported for three out of 118 patients (2.5%) (SIR Class D). There were no SIR Class E or F complications. No significant difference was observed in safety for different embolic agents (One-way Anova, p = 0.23).

Table 1: Baseline characteristics of patients who underwent uterine artery embolisation (UAE) for treatment of symptomatic fibroids.

Parameters	Mean±SD	Range
Age (years)	43.46 ± 5.62	24-55
Weight (kg)	76.51±18.34	52-124
Preop Hb (g/dl)	11.52 ± 2.43	9.8 - 14.9
Smoking History	N	(%)
Smokers	88	74.6
Non-smokers	30	25.4
Race		
Caucacian	113	95.8
Non-Caucacian	5	4.2
Symptoms		
No symptoms	9	7.2
Mennorhagia	109	92.8
Dysmennorhea	29	24.6
Urinary pressure	29	24.6
Pelvic mass	19	16.1
Fatigue	7	5.9

UAE: uterine artery embolisation, SD: standard deviation.

Secondary outcomes

Mean uterine size, fibroid volume and dominant fibroid size was significantly reduced at three months (p = 0.00). These changes were associated with significant symptom improvement, including menorrhagia (58 out of 69, 84%) and bulk related symptoms (62 out of 69, 90%) (all p's < 0.05). Mean fibroid volume and dominant fibroid size were further reduced after one year (p = 0.00); however mean uterine size increased, although this was still reduced compared to the pre-UAE size (p < 0.05) (Table 2). No fibroid size change was observed in four out of 49 (9.7%) patients. At 12 months, follow-up was available for 62 out of 118 patients and in those menorrhagia was present only in 24.1% (p < 0.05). Volumetric response (VR) (%) appeared to be associated with symptoms improvement at three and 12 months but this was not significant. Improvements in menorrhagia at three and 12 months were unrelated to initial fibroid volume and fibroid size. Little difference, although significant was observed for VR between smokers and non-smokers [Wilkoxon test, 44.5 (95% CI: 36.8-52.09) vs 47

Table 2: Changes in fibroid volume, uterine size and dominant fibroid size at different evaluation points following uterine artery embolisation (UAE) for treatment of symptomatic fibroids.

Variables	Minimum	Maximum	Mean± SD	P Value
Pre-UAE fibroid volume (cc) , n=63	33.2	3153	538.48 ± 580	0.00[a]
Post-UAE fibroid volume at 3 months (cc)	0	1390	308.25 ± 302.1	
Post-UAE fibroid volume at one year (mm)	46	455	208.7 ± 135.3	<0.05 [b]
Pre-UAE uterine size (mm), n=43	60	210	118.6 ± 32.7	0.00[b]
Post-UAE uterine size at 3/12 (mm)	10	151.8	95.75 ± 32.7	
Post-UAE uterine size at one year (mm)	73	147	109.6 ± 29.14	0.00 [b]
Pre-UAE dominant fibroid size (mm), n=73	29	220	88.78 ± 43.32	0.00[a]
Post-UAE dominant fibroid size at 3/12 (mm)	0	170	62.18 ± 41.5	
Post-UAE dominant fibroid size at one year (mm)	30	115	7.15 ± 2.5	0.00[a]

UAE: uterine artery embolisation, SD: standard deviation, [a]: Wilcoxon test, [b]: paired t-test.

(95% CI: 39-55), p < 0.0001]. Interestingly, despite their initial good response at three months, four women had symptom resolution or fibroid regrowth within one year. One patient had a myomectomy in the interim- and ended up with a hysterectomy within two years from the initial UAE. Two patients, age 43 and 45 had further investigation for infertility and underwent ovulation induction. They achieved assisted conception and they were both delivered by caesarean section.

Univariate and multivariate analyses

No significant difference was observed for symptoms improvement at three months and one year between the <mean age and >mean age subgroups. Likewise, neither use of embolic agent nor pre-UAE imaging (MRI or US) predicted symptoms improvement. Smoking or caucacian origin was not associated with symptoms improvement in the univariate or multivariate analysis.

Discussion

Our short-to-midterm 12-month follow-up study confirms the safety and efficacy of UAE for the treatment of symptomatic uterine fibroids. Subjects included symptomatic women, less likely to desire fertility but wished to avoid surgery and also poor surgical candidates. They were primarily referred by Gynecologists; an essential collaboration to optimize the safety and efficacy of UAE[6]. A standardised UAE protocol, pain management and aftercare were available and streamlined by multidisciplinary team. Demographic factors, known to be risk factors for fibroids were recorded from the clinical database, including age, weight, ethnicity, smoking, previous fibroid-related procedures in an attempt to predict adverse effects, however none of those proved significant in the univariate analysis.

Technical failure was low and comparable to other studies[7,8] thanks to operator's high proficiency and the approach of bilateral embolisation, as the only strong predictor of clinical failure appears to be unilateral embolisation.

As the fibroid size is still a matter of debate, the major finding of this study was that mean fibroid volume was significantly reduced by 42.7% at three months and by further 32.5% at one year follow-up. Mean dominant fibroid size was also reduced by 27% at three months and further 68% at 12 months. Likewise, mean uterine size was reduced by ~20% at three months; however this was increased by 14.5% one year after the procedure although still lower by 7.5% compared to the baseline, probably secondary to the development of adenomyosis (Figure 1). These values were rather higher than those reported in most studies[9,10]. Because in those studies, the baseline mean values were higher, the percentage changes

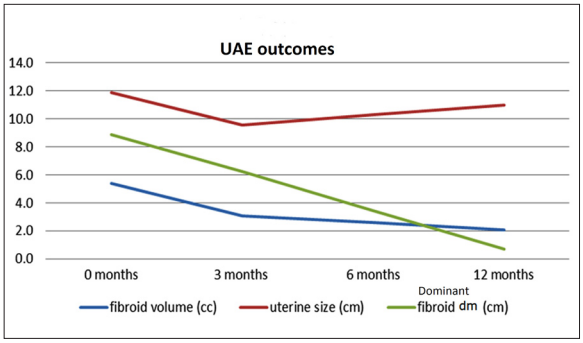

Figure 1: Uterine artery embolisation (UAE) imaging outcomes. Overall patient satisfaction at three months was 84% slightly falling to 75.9% by 12 months (all p < 0.05).

are consistent with the notion that the rate of reduction is volume-dependent (the larger the initial volume, the greater the percentage reduction after UFE)[11]. However, we, in agreement with Katsumori et al, did not identify the baseline fibroid diameter as a risk factor for patients undergoing UAE[12]. Unlike the Katsumori study, baseline size and percent of reduction were significant.

Efficacy was also demonstrated by relief of fibroid-related symptoms, menorrhagia and bulk related symptoms. This compares favorably with the EMMY trial in which the primary endpoint was elimination of menorrhagia in at least 75% of patients[13] and the FIBROID Registry[14]. Likewise, the mean dominant fibroid volume

decreased by 30% to to 46% in 2 randomised controlled trials (RCTs) as reviewed by Gupta et al[15]. However, if the follow up is short, i.e. 6 months, it is likely that positive imaging outcome does not correlate with improvements in symptoms[16]. Neither the success rate nor the probability of complications was affected by the primary fibroid size, in line with a similar study[9].

Embospheres® were predominantly used in this study. Their efficacy and safety has been well demonstrated in a recent study showing improvements of clinical symptoms and quality-of-life (QOL) scores during mid-term follow-up[17]. Since no statistical difference was observed between Embospheres® and Embozenes®, the best method of achieving effective embolisation could not be answered and future RCTs would be required to determine the optimal materials. Following a case of a severe SRI Class-D complication (limb ischaemia), an external investigation failed to show a causal association with use of nanoparticles or catheter fragments. Reassuringly, a recent meta-analysis indicated that UAE has a significantly lower rate of complications compared to surgery[18]. However, this comes at the cost of increased risk of reintervention in the future[19].

Conclusion

In conclusion, the study confirms the safety and efficacy of UAE in the treatment of symptomatic fibroids. Patient satisfaction rates were compared to those reported in similar studies[16,20] suggesting that patients were well informed about the UAE protocol including complications. Conclusions regarding which subgroups of women would be most successfully treated by UAE based on fibroid size could not be possible in the absence of long-term clinical outcome data. Introduction of new imaging techniques for better delineation of fibroids[21] can help towards optimal selection of patients in the base of volume-shrinkage prediction.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgement

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References

1. Edwards RD, Moss JG, Lumsden MA, Wu O, Murray LS, Twaddle S, et al.Uterine-artery embolisation versus surgery for symptomatic uterine fibroids. N Engl J Med. 2007; 356: 360-370.
2. National Institute for Health and Care Excellence (NICE). Uterine artery embolisation for fibroids. 2010; availiable at: http://www.nice.org.uk/IPG367, last accessed:
3. Omary RA, Bettman MA, Cardella JF, Bakal CW, Schwartzberg MS, Sacks D, et al. Quality improvement guidelines for the reporting and archiving of interventional radiology procedures. J Vasc Interv Radiol. 2003; 14: S293-S295.
4 Browne RF, McCann J, Johnston C, Molloy M, O'Connor H, McEniff N. Emergency selective arterial embolisation for control of life-threatening hemorrhage from uterine fibroids. AJR Am J Roentgenol. 2004; 183: 1025-1028.
5. Walker WJ, Barton-Smith P. Long-term follow up of uterine artery embolisation--an effective alternative in the treatment of fibroids. BJOG. 2006; 113: 464-468.
6. Zurawin RK, Fischer JH 2nd, Amir L. The effect of a gynecologist-interventional radiologist relationship on selection of treatment modality for the patient with uterine myoma. J Minim Invasive Gynecol. 2010; 17: 214-221.
7. Nikolic B, Abbara S, Levy E, Imaoka I, Lundsten ML, Jha RC, et al. Influence of radiographic technique and equipment on absorbed ovarian dose associated with uterine artery embolization. J Vasc Interv Radiol. 2000; 11: 1173-1178.
8. Jha RC, Ascher SM, Imaoka I, Spies JB. Symptomatic fibroleiomyomata: MR imaging of the uterus before and after uterine arterial embolization. Radiology. 2000; 217: 228-235.
9. Firouznia K, Ghanaati H, Sanaati M, Jalali AH, Shakiba M. Uterine artery embolization in 101 cases of uterine fibroids: do size, location, and number of fibroids affect therapeutic success and complications? Cardiovasc Intervent Radiol. 2008; 31: 521-526.
10. Pelage JP, Guaou NG, Jha RC, Ascher SM, Spies JB. Uterine fibroid tumors: long-term MR imaging outcome after embolization. Radiology. 2004; 230: 803-809.
11. Bradley EA, Reidy JF, Forman RG, Jarosz J, Braude PR. Transcatheter uterine artery embolisation to treat large uterine fibroids. Br J Obstet Gynaecol. 1998; 105: 235-240.
12. Katsumori T, Nakajima K, Mihara T. Is a large fibroid a high-risk factor for uterine artery embolization? AJR Am J Roentgenol. 2003; 181: 1309-1314.
13. Volkers NA, Hehenkamp WJ, Birnie E, Ankum WM, Reekers JA. Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids: 2 years' outcome from the randomised EMMY trial. Am J Obstet Gynecol. 2007; 196: 519. e1-e11.
14. Spies JB, Cornell C, Worthington-Kirsch R, Lipman JC, Benenati JF. Long-term outcome from uterine fibroid embolization with tris-acryl gelatin microspheres: results of a multicenter study. J Vasc Interv Radiol. 2007; 18: 203-207.
15. Gupta JK, Sinha AS, Lumsden MA, Hickey M. Uterine artery embolization for symptomatic uterine fibroids. Cochrane Database Syst Rev. 2006: CD005073.
16. Hehenkamp WJ, Volkers NA, Donderwinkel PF, de Blok S, Birnie E, Ankum WM, et al. Uterine artery embolization versus hysterectomy in the treatment of symptomatic uterine fibroids (EMMY trial): peri- and postprocedural results from a randomised controlled trial. Am J Obstet Gynecol. 2005; 193: 1618-1629.
17. Marshburn PB, Matthews ML, Hurst BS. Uterine artery embolization as a treatment option for uterine myomas. Obstet Gynecol Clin North Am. 2006; 33: 125-144.
18. Martin J, Bhanot K, Athreya S. Complications and reinterventions in uterine artery embolization for symptomatic uterine fibroids: a literature review and meta analysis. Cardiovasc Intervent Radiol. 2013; 36: 395-402.
19. Moss JG, Cooper KG, Khaund A, Murray LS, Murray GD, Wu O, et al. Randomised comparison of uterine artery embolization (UAE) with surgical treatment in patients with symptomatic uterine fibroids (REST trial): 5-year results. BJOG. 2011; 118: 936-944.
20. Lohle PN, Boekkooi FP, Smeets AJ, Pieters JJ, Vervest HA, Lampmann LE, et al. Limited uterine artery embolization for leiomyomas with tris-acryl gelatin microspheres: 1-year follow-up. J Vasc Interv Radiol. 2006; 17: 283-287.
21. Fallahi A, Pooyan M, Ghanaati H, Oghabian MA, Khotanlou H, Shakiba M, et al. Uterine segmentation and volume measurement in uterine fibroid patients' MRI using fuzzy C-mean algorithm and morphological operations. Iran J Radiol. 2011; 8: 150-156.