

EMMY Trial: A Randomised Comparative Study of Uterine Artery Embolisation Versus Hysterectomy for Management of Symptomatic Uterine Fibroids

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ABSTRACT

Introduction: Symptomatic uterine fibroids are disabling and are associated with significant morbidity that affects many women of childbearing age. Study aimed to evaluate the safety of uterine artery embolization (UAE) compared with hysterectomy.

Material and Methods: The Embolization versus hysterectomy (EMMY) study is a randomized controlled trial on 100 subjects who were randomly assigned (1:1) to UAE or hysterectomy, using a computer-based minimization scheme. The main end point was the abolition of menorrhagia with follow-up period being two years.

Results: The mean age was 43.2 years (UAE group) and 44.1 years (hysterectomy group). UAE was successfully performed in 44 patients (procedural success rate: 88%). UAE procedures on average took shorter than hysterectomy procedures (78 vs 98 minutes, $P = .062$). Patients subject to UAE had significantly less blood loss than those undergoing hysterectomy (32.0 and 444.0 mL, respectively; $P = .001$). In the UAE group, During hospital stay febrile morbidity was significantly less common in the UAE group (3 patients) than after hysterectomy (10 patients) $P = .00384$.

Conclusion: UAE has lower complications rate and reduced length of hospital stay.

Keywords: EMMY Trial, Uterine Artery, Embolisation Versus Hysterectomy, Symptomatic Uterine Fibroids

INTRODUCTION

Uterine fibroids (leiomyomas) are commonest benign smooth muscle tumors arising from the myometrium.^{1, 2} These lesions have unknown etiology, but are oestrogen and progesterone-dependent tumours. They occur very rarely prior to menarche, usually occur in reproductive life, and often regress in size after menopause. Risk factors include age, obesity, nulliparity, early menarche, alcohol, and hypertension.^{3, 4}

Studies showed that around 70% of women will have one or more uterine fibroids by the age 50. Symptoms include abnormal uterine bleeding, pelvic pain, obstructive effects on bladder or rectum, and infertility.⁵⁻⁷

Prolonged menstrual bleeding is the most common symptom for which patients visit hospital, which may cause iron deficiency anemia. Uterine Artery Embolization (UAE) is used to treat for heavy menstrual bleeding caused by uterine fibroids. When the conservative therapies for symptomatic fibroids fail, hysterectomy provides the ultimate solution for symptomatic relief.⁶⁻⁸

The EMMY trial is used to assess the safety and efficacy of UAE compared to hysterectomy for treating symptomatic uterine fibroids. Since Ravina et al. described uterine artery embolisation (UAE) in 1995, it has received considerable attention in the international media and on the Internet as a new treatment for uterine fibroids, arguably replacing hysterectomy as the standard treatment. Although UAE has been investigated in several case series and one small preconsent semi-randomised trial, the superiority of UAE in terms of safety and benefits remains questionable since proper randomised controlled data (RCT) are still lacking.³⁻⁶ We carried this study to compare UAE and hysterectomy in treating Uterine fibroids.

Materials and Methods:

This Embolization versus hysterectomy (EMMY) study was conducted on 100 subjects carried out at Mallareddy Narayana Hospital, Suraram, Hyderabad from April 2018 to November 2019.

Inclusion Criteria

1. Patients with uterine fibroids confirmed by ultrasonography;
2. Patients with menorrhagia, among other possibly fibroid-related signs and symptoms;
3. Patients scheduled for a hysterectomy.

Exclusion Criteria

1. Patients with renal failure, active pelvic infection, or clotting disorders were clinically established;
2. Patients allergic to contrast material;
3. Patients with uterine malignancy;

The study subjects were randomly divided into UAE and hysterectomy groups after obtaining institutional ethical

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committee approval and written informed consent. All patients underwent a pelvic ultrasound to measure the largest fibroid in three dimensions, longitudinal (D1), anterior-posterior (D2), and transverse (D3).

Methodology

Uterine Artery Embolization

Under local or epidural/ spinal anesthesia, UAE was performed. Femoral artery was accessed either unilaterally or bilaterally. A 4-F or 5-F catheter was inserted into the femoral artery up to the aortic bifurcation and embolization was carried out. Into each uterine artery, Polyvinyl alcohol particles (PVA) mixed with contrast medium and saline, was injected until parenchyma filling of the fibroids had stopped (target embolization), or until the main uterine artery was blocked with stasis of contrast (selective embolization).

The parameters recorded were the type of anesthesia, type of UAE, amount of PVA vials used, amount of blood loss, procedure duration and complications.

Hysterectomy

Different procedures used were abdominal hysterectomy, either by median or a pfannenstiell incision, laparoscopically assisted vaginal hysterectomy (LAVH), and laparoscopic hysterectomy. The parameters recorded were antibiotics used, anesthesia type, hysterectomy type, removal of the cervix, ovaries, duration of procedure and any complications.

Follow-up

We followed up to two years with elimination of menorrhagia as the primary end point. UAE was judged comparable to hysterectomy when menorrhagia resolved in at least 75% of patients, with uterus preservation and no considerable difference in major complications among both procedures.

STATISTICAL ANALYSIS

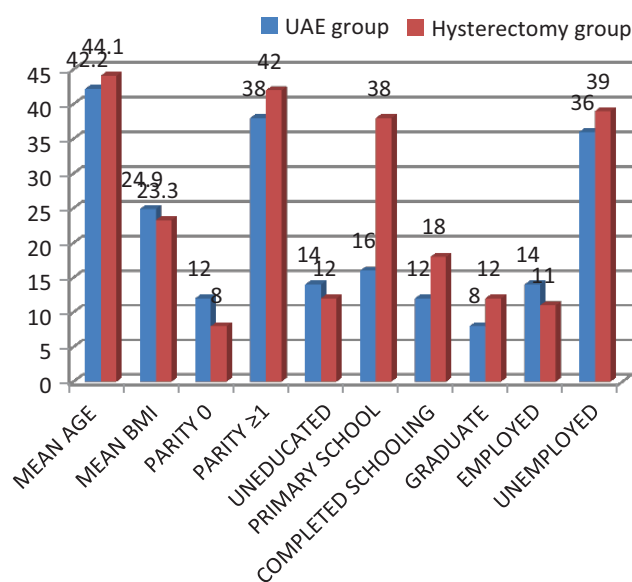
Analyses were done using SPSS Version 20 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: USA, IBM Corp). Differences in baseline characteristics were tested with multiple logistic regression analysis. Differences in complications between groups were expressed in absolute numbers, rates, and relative risks (RR) with 95% CI. Differences in hospital stay were tested with the Mann-Whitney U test. Differences in categorical data were compared with χ^2 -tests or Fisher exact tests if appropriate.

RESULTS

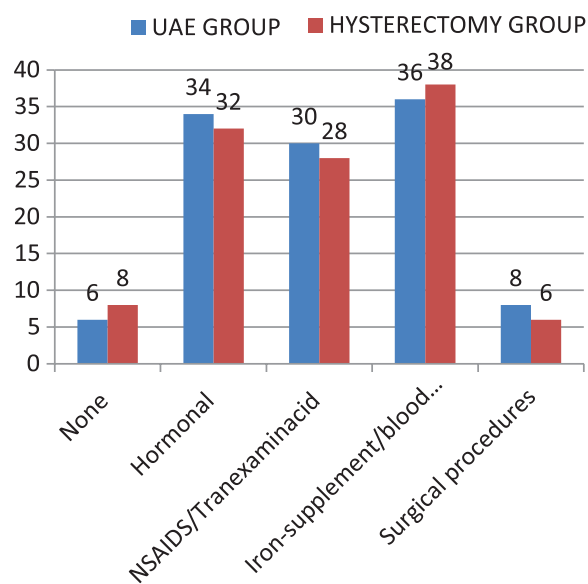
Our sample of 100 subjects were randomized: 50 each allocated for UAE and hysterectomy. The mean age was 43.2 years (UAE group) and 44.1 years (hysterectomy group) (Table 1 and Graph 1).

Most of the patients (80%) had already received one or more treatments for symptomatic uterine fibroids before study enrollment. Patients suffered from menorrhagia for a median of 24 months. Other symptoms besides menorrhagia were prevalent. The majority of women had multiple fibroids (Table 2 and Graphs 2 & 3).

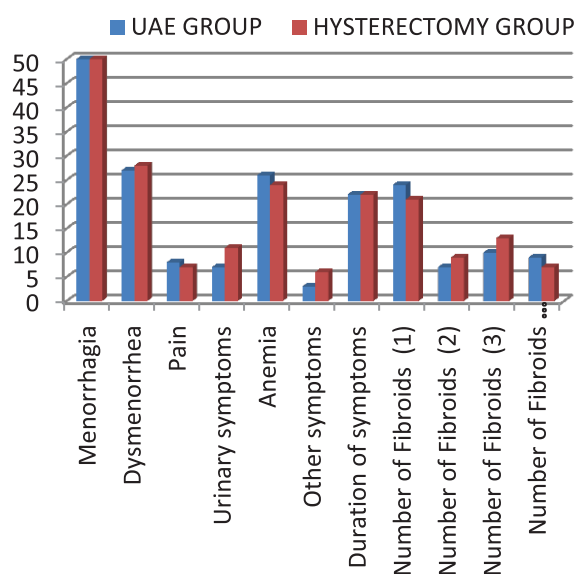
UAE was successfully performed in 44 patients (procedural success rate: 88%). The remaining 12% consisted of



Graph-1: Patient Demographics



Graph-2: Previous Treatment Details



Graph-3: Symptoms, Duration of Symptoms and Number of Fibroids

Characteristic		UAE group (n=50)	Hysterectomy group (n=50)
Mean age		42.2 Years	44.1 Years
Mean BMI		24.9	23.3
Parity	0	12	8
	≥1	38	42
Education	Uneducated	14	12
	Primary school	16	38
	Completed schooling	12	18
	Graduate	8	12
Employment status	Employed	14	11
	Unemployed	36	39

Table-1: Patient demographics

Characteristic	UAE group (n=50)	Hysterectomy group (n=50)
Previous treatment		
None	6	8
Hormonal	34	32
NSAIDS/Tranexaminacid	30	28
Iron-supplement/blood transfusion	36	38
Surgical procedures	8	6
Symptoms		
Menorrhagia	50	50
Dysmenorrhea	27	28
Pain (not during menstruation)	8	7
Urinary symptoms	7	11
Anemia	26	24
Other symptoms	3	6
Duration of symptoms	22 (3-230)	22 (3-230)
Median (range)		
Duration of menstruation Median (range)	22 (3-230)	22 (3-230)
Number of Fibroids		
1	24	21
2	7	9
3	10	13
≥3	9	7

Table-2: Baseline characteristics: symptoms, Previous treatment and Uterus/Fibroid characteristics

Characteristic	UAE group (n=50)	Hysterectomy group (n=50)
Type of UAE		
I. Target embolization		
A. Left uterine artery	42	
B. Right uterine artery	40	
II. Selective embolization		
A. Left uterine artery	5	
B. Right uterine artery	8	
Type of hysterectomy		
A. Abdominal hysterectomy		44
B. Vaginal hysterectomy		36
Mean Duration of procedure (min.)	78±24.5	98±21.6
Mean Blood loss (mL)	32±21.9	442±122.5
Antibiotics administered	18	45

Table-3: Procedural Characteristics

4 patients (8%) with a unilateral procedure (caused by technical failure on the other side) and 2 patients (4%) with bilateral unsuccessful UAE. The bilateral impossibility to embolize resulted from bilateral absence of uterine artery flow to the fibroids (n = 2), bilateral technical failures (n =

1), and a technical failure on the other (n = 1). These patients subsequently underwent hysterectomy, but were analyzed in the UAE group.

Table 3 displays the characteristics of both treatments. In most cases (88%), target embolization was carried out. In

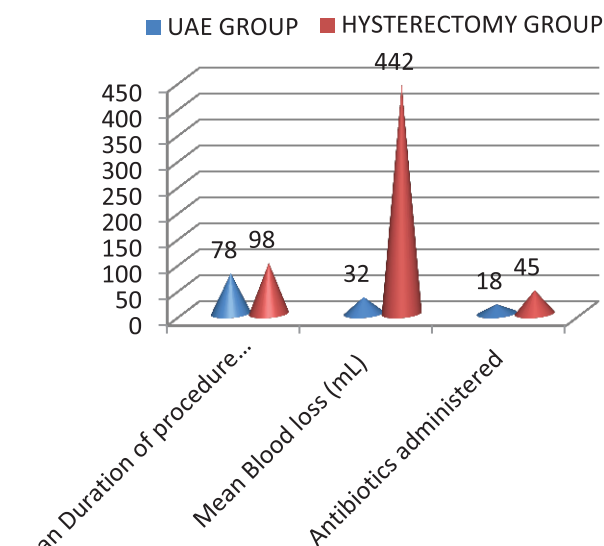
the hysterectomy group, all operations were technically successful. Most hysterectomies were performed

Complication	UAE group (n=50)	Hysterectomy group (n=50)
Nausea	22	23
Pain	40	45
Febrile morbidity	3	10
Hematoma	10	3
Urinary tract infection	0	2
Anemia requiring transfusion	2	10

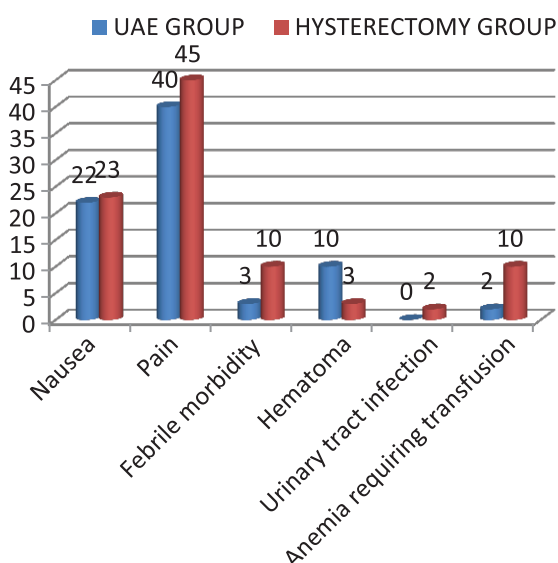
Table-4: Complications following two procedures

Characteristics	UAE group (n=50)	Hysterectomy group (n=50)
Consulted Physician for Pain/Fever	14	18
Patients readmitted for pain/Fever	10	12

Table-5: Follow-up details of Study Subjects



Graph-4: Procedural Characteristics



Graph-5: Complications following two procedures

transabdominally (88.0%). UAE procedures on average took shorter than hysterectomy procedures (78 vs 98 minutes, P = .062). Patients subject to UAE had significantly less blood loss than those undergoing hysterectomy (32.0 and 442.0 mL, respectively; P = .001). Total admission time was significantly (P = .001) shorter in the UAE group (mean 2.0 days) than in the hysterectomy group (mean 5.4 days) (Table 3 and Graph 4).

Table 4 lists complications occurring during and after the procedures. Intraprocedural complications were uncommon in both groups. In the UAE group, During hospital stay febrile morbidity was significantly less common in the UAE group (3 patients) than after hysterectomy (10 patients) P = .00384). Hematomas occurred significantly more frequently after UAE, while the hysterectomy group experienced more urinary tract infections and anemia (Table 4 and Graph 5).

Follow-up

In the UAE group, 24 patients (48%) consulted a physician, mainly for pain and/or fever. In the hysterectomy group, 18 patients (36%) consulted a physician after discharge for various reasons. This difference was not significant (p = 0.2264). Readmissions were significantly more common in the UAE group: 8 patients versus 0 patients in the hysterectomy group (p = .0028). Patients were readmitted for pain (24%), fever (24%), or a combination of both (48%) (Table 5).

DISCUSSION

National Institute of Clinical Excellence (NICE) states that current evidence on UAE is limited because available data are based on selected case series, which are subject to publication and selection bias. The NICE report strongly recommends the initiation of randomised controlled trials. According to the Cardiovascular and Interventional Radiology Society of Europe guidelines, UAE is successful when bilateral UAE was instituted; unilateral UAE was treated as successful procedure if single-sided uterine arterial flow to the fibroids was present. The EMMY randomised trial might give answers to the pending questions of safety and efficacy of UAE compared with hysterectomy. Randomised patients are followed-up for 24 months after the procedure to assess the effect of UAE on menorrhagia (primary endpoint). We believe that UAE should not be implemented as a routine treatment for uterine fibroids causing menorrhagia.⁹⁻¹²

CONCLUSION

Even though our results support UAE, to consider UAE as a good alternative for hysterectomy depends on efficacy, cost, quality of life.

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