

## Incidence of amenorrhea and premature ovarian failure in women who underwent uterine fibroid embolization: single centre study

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### Abstract

**Purpose:** To retrospectively determine the incidence of amenorrhea and premature ovarian failure in women who underwent uterine fibroid embolization (UFE) in King Fahad Specialist Hospital in Dammam (KFSH-D).

**Patients and methods:** All women who had undergone UFE in KFSH-D from August 2007 to October 2015 were included for a total of 82 patients. Follow up consisted of a questionnaire inquiring about symptoms, improvement after the procedure and whether menstruation resumed or not. The pre-procedure and post-procedure pelvis MRI as well as UFE images and reports were reviewed for all patients.

**Results:** We were able to contact 67 patients and one patient (1.5 %) was found to have amenorrhea. She was 52 years old at the time of UFE and had irregular period. Menstruation did not resume following UFE along with menopausal symptoms including night sweats, mood swings and irritability, likely due to premature ovarian failure (POF). The rest of patients had normal resumption of menses.

**Conclusion:** The incidence of amenorrhea is less than what's reported in the literature could be due to advances in UFE since its introduction as a treatment for uterine fibroids, these include advances in image quality, tans-catheter embolization equipments/techniques and embolic material used in UFE.

### Introduction

Uterine Fibroid Embolization (UFE) has been accepted as an alternative to surgical treatment of uterine fibroids (UF) [1- 5]. UFE is a relatively safe and minimally invasive procedure; however, several complications have been linked to it [6, 7]. Permanent amenorrhea and premature ovarian failure (POF) are the common complications with reported incidence of up to 3% in women younger than 45 years and 7%-14% in women older than 45 years [3- 5, 8, 9]. Permanent amenorrhea is defined as lack of resumption of menstruation after embolization, with menstruation not resuming for 12 or more months [1- 3, 10]. While POF is defined as the presence of permanent amenorrhea along with elevated follicle stimulating hormone (FSH) levels (> 40 IU/L) and clinical symptoms suggestive of menopause including hot flashes, night sweats, mood swings, vaginal dryness and irritability [2, 11].

The articles addressing amenorrhea and premature ovarian failure associated with UFE are scanty, with only a few studies from the Middle East. Moreover, we want to find out whether there has been a possible change in the incidence of amenorrhea due to advances in UFE since its introduction as a treatment for uterine fibroids.

### Patients and methods

The institutional review board (IRB) at King Fahad Specialist Hospital in Dammam (KFSH-D) approved the study. A retrospective case study was conducted concerning 82 patients who underwent uterine fibroid embolization in KFSH-D from August 2007 to October 2015. The patients were contacted over the phone by the two investigators and oral informed consent was taken. The patients answered a questionnaire titled 'Incidence of amenorrhea after Uterine Fibroid Embolization' inquiring about symptoms, menstrual cycle before the procedure, improvement after the procedure, whether the cycle resumed after the procedure; and if it hadn't resumed how many cycles were missed.

Any patient who reported amenorrhea were further asked about clinical symptoms suggestive of menopause including hot flashes, night sweats, mood swings, vaginal dryness and irritability. Women with amenorrhea will be excluded if they: Underwent other gynecologic interventions (including hysterectomy, myomectomy, hysteroscopic treatment or dilatation and curettage) or are on hormonal therapy (Oral Contraceptive Pills) since these are confounding variables and could affect the resumption of menses. Patients with amenorrhea will be further assessed by FSH level to confirm the presence of premature ovarian failure, as well as pelvic ultrasound to assess endometrial thickness.

The available pre-procedure and post-procedure pelvis magnetic resonance imaging were reviewed and a note was made of the size of the uterine fibroid, right and left ovary. The UFE images and reports of all patients were reviewed as well and a record was made if the embolization was unilateral or bilateral, size and amount of embolic material and whether uterine artery to ovarian artery anastomosis was detected.

### **UFE Technique**

Uterine artery embolization was performed by the unilateral femoral approach using local anesthesia. The common femoral artery was accessed by using the modified Seldinger technique and an initial aortogram was done by placing a pig tail catheter at the level of the renal arteries to aid in delineating the arterial anatomy. Subsequently, super selective cannulation of the uterine artery was achieved using a micro catheter and embolization particles are injected until blood flow significantly slows or stops.

Bilateral uterine artery embolization was successfully performed in 77 patients (93.9 %) of the 82 patients. Only five patients had unilateral embolization performed.

The embolic material consisted of micro-spheres in 61% of patients and polyvinyl alcohol in 31.1 % and a combination of both in 7.7 % of cases. The size of embolic material varied, ranging from 100-300 to 700-900µm.

### **Results**

Of the 82 patients, twelve (14.6%) were lost to follow up and three (3.7%) deceased due to reasons unrelated to UFE. A total of 67 patients were included into this study. The age of patients ranged from 27 to 53 years old (Mean, 39.5). All women were middle eastern and pre-menopausal. The mean menstrual cycle length was 28.31 days, with a range of 20 – 33 days and mean duration of bleeding was 8.58 days, with a range of 4 to 20 days (Table 1). Symptoms included heavy and/or prolonged period (85 %), dysmenorrhea (76 %), increase in abdominal girth (37 %) and frequent urination (32 %). Of the 67 patients 43 (64.2 %) had regular periods and 24 had irregular periods (35.8 %) (Table 2). Sixty-six patients had normal resumption of menses following the procedure with mean of 53.5 days for the period to resume. Most patients reported satisfactory improvement of their symptoms (Table 3). In this study we found that only one patient (1.5 %) had amenorrhea following UFE. The patient was 52 years old at the time of the procedure and had irregular menses. Menstruation did not resume following UFE for more than 12 months along with menopausal symptoms including hot flashes, night sweats, mood swings and irritability (Table 4). Following the procedure, the patient reported no improvement in her complain of pelvic pain and hence has undergone a hysterectomy. Therefore, FSH level and pelvic ultrasound were not performed.

### **Discussion**

Amenorrhea following UFE is the most common complication with women older than 45 years more prone to amenorrhea.

Amenorrhea and premature ovarian failure following UFE are believed to occur as a result of ‘Non-Target Embolization’. The uterine artery frequently anastomoses with the ipsilateral ovarian artery. When selectively embolizing the uterine artery during UFE, overseen uterine artery-to-ovarian artery anastomoses might serve as a route for non-target embolization of the ovarian artery, which will lead to ovarian ischemia, ovarian failure and eventually amenorrhea.

There are three types of anastomoses:

Type I: the ovarian artery anastomoses with the intramural uterine artery with flow in the tubal artery towards the uterus; Type I is further subdivided into Type Ia in which there is no reflux into the tubal artery

during selective uterine artery angiogram, while in Type Ib there is reflux in to the tubal artery during selective uterine artery angiogram.

Type II: the ovarian artery supplies the fibroid directly.

Type III: the ovarian artery anastomoses with the uterine artery and flow in the tubal artery is towards the ovary which is seen as contrast washout and ovarian blush.

In types Ib and III of ovarian artery to uterine artery anastomosis there is a higher risk of non-target ovarian artery embolization due to reflux / direction of flow in the tubal artery towards the ovary.

UFE images were reviewed and the ovarian artery is not angiographically detected in the amenorrhoeic patient during selective catheterization and embolization of the uterine artery.

Since theoretically the more embolic material used during UFE the higher the chance of non-target embolization. Size of the embolic material is also of importance since if the embolic material is small it is more likely that it could pass through the anastomoses to the ovarian artery.

Five vials of Polyvinyl Alcohol were used during UFE for our patient, and the size used is 350-500µm. The amount and size is not significantly different than those used for the other patients in the study.

One of other the factors that have also been implicated in the causation of POF is endometrial atrophy after UFE. Because of the common arterial blood supply between the myometrium and endometrium, in UFE endometrial perfusion may also be compromised as a result of the decrease in myometrial blood flow occurring after the procedure [12]. A reduction in the thickness of the endometrium compared to endometrial thickness at baseline (<5 mm) would be suggestive of endometrial atrophy.

Since the patient reported no improvement in her complain of pelvic pain which prompted her to seek alternative treatment and underwent hysterectomy, therefore workup including FSH level and pelvis ultrasound were rendered unnecessary and there is no laboratory proof of ovarian failure and menopause.

### Conclusion

We believe that our study supports that age is an important factor with regards to normal resumption of menses following the procedure, with women older than 45 at more risk to have amenorrhea. We also believe that there has been a decrease in the incidence of amenorrhea compared with the reported incidence in the literature probably due to advances in image quality, tans-catheter embolization equipments/techniques and embolic material used in UFE. However, our study is limited as there is no laboratory proof of POF. Although POF is likely the cause of amenorrhea in our patient, endometrial atrophy cannot be entirely excluded as a cause of amenorrhea since pelvis ultrasound was not performed pre and post procedure.

Table 1. Descriptive characteristics

	Mean	median	Standard deviation
Age	39.57	41.0	6.46
Length of the menstrual cycle	28.31	29.0	2.43
Duration of bleeding	8.28	7.0	3.54

Table 2. Pre-embolization symptoms

	Frequency	Percent
Heavy or prolonged period		
Yes	57	85.1%
No	10	14.9%

Pain during menstruation		
Yes	51	76.1%
No	16	23.9%
Frequent urination		
Yes	22	32.8%
No	45	67.2%
Constipation		
Yes	13	19.4%
No	54	80.6%
Increase in abdominal girth		
Yes	25	37.3%
No	42	62.7%
Regular periods		
Yes	43	64.2%
No	24	35.8%

Table 3. Symptoms improvement following UFE on a scale of 0 - 10

Score	Frequency	Percent
0	5	7.5
1	1	1.5
2	2	3.0
3	2	3.0
4	2	3.0
5	4	6.0
6	5	7.5
7	6	9.0
8	11	16.4
9	8	11.9
10	21	31.3
Total	67	100.0

Table 4. Post-embolization symptoms

	Frequency	Percent
Menstruation resumption after UFE		
Yes	66	98.5%
No	1	1.5%
Hot flashes		
Yes	1	1.5%
No	66	98.5%
Mood swings		
Yes	1	1.5%
No	66	98.5%
Night sweats		
Yes	1	1.5%
No	66	98.5%

Irritability		
Yes	1	1.5%
No	66	98.5%
Vaginal dryness		
Yes	0	0 %
No	67	100 %
Hormonal therapy		
Yes	0	0 %
No	67	100%
Amenorrhea		
Yes	1	1.5%
No	66	98.5%

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