



# Long-Term Outcomes of Uterine Artery Embolization Using Gelatin Sponge Particles Alone for Symptomatic Fibroids

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**OBJECTIVE.** The purpose of this study was to evaluate the long-term outcomes of uterine artery embolization using only gelatin sponge particles for symptomatic fibroids.

**MATERIALS AND METHODS.** As part of an ongoing study of the procedure for fibroids, prospective data of the initial 96 consecutive women treated between December 1997 and December 2001, were collected in January 2005. It had been more than 3 years since embolization in all cases. The follow-up period ranged from 4 to 60 months (mean, 37.4 months). On the basis of serial questionnaires, we investigated the cumulative rates of symptom control, gynecologic interventions, and overall failure, using the Kaplan-Meier product limit estimator. Symptom control was defined as meaning patients whose symptoms had improved as indicated on the last questionnaire and who had not undergone any further gynecologic intervention because of symptoms. Overall failure was defined as meaning the patients who indicated that there had been no symptom improvement or recurrence or that they had undergone further gynecologic interventions.

**RESULTS.** Of all 96 women, 16 (17%) were lost to follow-up during the period. Cumulative rates of symptom control were 96.9% at 1 year, 89.5% at 3 years, and 89.5% at 5 years. Cumulative rates of complications related to the gynecologic intervention and overall gynecologic interventions were 2.1% and 4.2%, respectively, at 1 year, 2.1% and 5.4% at 3 years, and 2.1% and 10.5% at 5 years. Cumulative rates of overall failure were 4.2% at 1 year, 12.7% at 3 years, and 12.7% at 5 years. Major complications were noted in 3.1% (3/96). Of these three women, two required hospitalization for transvaginal resection of sloughing fibroids and one developed sexual dysfunction. Two women became pregnant, but both pregnancies resulted in miscarriage.

**CONCLUSION.** Uterine artery embolization using gelatin sponge particles alone can achieve long-term symptom control for fibroids in most cases.

**Keywords:** embolization, fibroids, gelatin sponge particles, genitourinary tract imaging, uterine artery, women's imaging

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Uterine artery embolization has been widely recognized as a safe and effective treatment for symptomatic uterine fibroids and an alternative to major surgery, including hysterectomy and myomectomy, because this minimally invasive treatment can contribute to improved symptoms with few major complications. A number of articles have reported rates of improvement in clinical symptoms associated with uterine fibroids of approximately 80–90% on short- and middle-term follow-up [1–8]. However, reports describing long-term outcomes of embolization have been limited [9, 10]. Moreover, in those papers dealing with long-term outcomes, the primary embolic agents used were polyvinyl alcohol particles [9, 10]. To our knowledge, no report has presented the long-term outcomes of uterine artery embolization using

gelatin sponge particles alone for symptomatic fibroids. The purpose of this study was to evaluate the long-term outcomes, including symptom control, symptom recurrence, additional gynecologic interventions, complications, overall failure, and pregnancy after uterine artery embolization using gelatin sponge particles alone for symptomatic uterine fibroids.

#### Materials and Methods

As part of an ongoing study of uterine artery embolization using gelatin sponge particles alone as the primary treatment for symptomatic uterine fibroids at our institution, prospective data of the initial 96 consecutive women who underwent the procedure between December 1997 and December 2001, were collected in January 2005, and analysis was completed in April 2005. It had been more than 3 years since embolization in all patients, more than

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4 years for 49 patients, and more than 5 years for 16 patients. We informed all patients of the potential benefits and risks of uterine artery embolization for uterine fibroids and using gelatin sponge particles as the sole embolic agent for the procedure. Oral and written informed consent was obtained from all patients before the procedure. We also instructed all women to inform us of any adverse reactions should these occur. The institutional ethics committee approved the procedure.

All women were premenopausal and had one or more clinical symptoms associated with uterine fibroids, including menorrhagia ( $n = 82$ ), pain during menstruation ( $n = 26$ ), and bulk-related symptoms ( $n = 75$ ). The mean age of the women was 42.5 years (range, 32–52 years). Three women (3%) were 32–34 years, 16 (17%) were 35–39 years, 45 (47%) were 40–44 years, 27 (28%) were 45–49 years, and five (5%) were 50 years or older. All patients were Asian. Nine women (9%) had previously undergone myomectomy, 33 (34%) were receiving gonadotropin-releasing hormone agonists, and five (5%) had been taking birth-control pills. Of 96 women, 83 had no plans for future pregnancy. In principle, we excluded women desiring future pregnancy from our indication for this treatment because data on pregnancy after embolization are not yet sufficient; however, 13 women who desired future pregnancy underwent uterine artery embolization because their gynecologist judged these women to have no other treatment option except hysterectomy or difficult myomectomy or because the women refused major surgery. Gynecologists diagnosed the tumors as uterine fibroids in all women. It was confirmed that a Papanicolaou test before the procedure was negative in all women and an endometrial biopsy was negative in women with abnormal uterine bleeding before the procedure.

We performed baseline MRI in all women before uterine artery embolization and confirmed that the tumors were uterine fibroids. We assessed the maximal diameter and tumor volume of the largest fibroid, the location of the largest fibroid, and the number of fibroids greater than 1 cm in size per patient; and we calculated the uterine volume using the baseline MRI. Tumor and uterine volumes were calculated using the formula of a prolate ellipse (length  $\times$  depth  $\times$  width  $\times$  0.5233). We routinely performed unenhanced and contrast-enhanced MRI at 1 week, 4 months, and 1 year after the procedure. After 1 year, when patients had residual or new problems related to fibroids and embolization, we contacted them and performed unenhanced and contrast-enhanced MRI as necessary. Complete devascularization of the tumor was assessed using contrast-enhanced MRI 1 week after embolization [11].

All uterine artery embolization procedures were performed using a unilateral femoral approach as

previously described [6]. A microcatheter was used in all but four patients. The embolic agent used was gelatin sponge particles measuring approximately 500–1,000  $\mu\text{m}$ , which were cut from gelatin sponge sheets (Spongel, Yamanouchi) by the operators using a scalpel and small scissors, as previously described [6]. The embolic agents were mixed with saline, contrast medium (iopamidol), and antibiotics (cefazolin sodium, 1 g) and slowly infused into the uterine arteries. The end point of embolization was complete or near stasis in the ascending uterine artery. No supplemental embolic agents were used in any patient. Postprocedural cramping was mainly managed using morphine hydrochloride and naproxen, as previously described [6].

Baseline clinical symptoms were assessed in all women using an oral questionnaire before the procedure. Each woman was followed up at 1 week, 4 months, and 1 year after the procedure; and we obtained a response to a written questionnaire at 4 months, 1 year, and then annually after uterine artery embolization. The written questionnaires included items regarding changes in symptoms, complications, additional gynecologic interventions, and pregnancy. When additional information was required, we surveyed the patients by telephone. When patients underwent further gynecologic interventions, including hysterectomy, myomectomy, transvaginal tumor resection, dilatation and curettage, or repeated embolization or angiography after embolization, thereafter we did not obtain serial questionnaires and assess changes in symptoms, complications, and pregnancy because these further gynecologic interventions could have affected these items.

Changes in symptoms were classified as follows: markedly improved, moderately improved, slightly improved, no change, and worsened, compared with preprocedural conditions. When patients responded that symptoms were markedly, moderately, or slightly improved compared with baseline status, we regarded them as showing improvement in symptoms. Thus, we classified change in symptoms into three grades: improved, no change, and worsened. When women had undergone gynecologic interventions after uterine artery embolization, the information was obtained from the gynecologist, questionnaires, or medical record. We assessed the number and causes of gynecologic interventions performed after embolization during the follow-up period.

Cumulative rates of overall gynecologic interventions and complications related to gynecologic interventions were calculated using the Kaplan-Meier product limit method. Women who did not undergo any further gynecologic intervention during the follow-up period after embolization were classified into one of four groups: symptom control, primary failure, symptom recurrence, or lost to follow-up, on the

basis of responses to serial questionnaires or at routine or unanticipated hospital visits.

Symptom control was defined as meaning that women responded that symptoms had improved on the last questionnaire and they had not undergone any further gynecologic intervention for symptoms, including complication-related symptoms, during the follow-up period. Primary failure was defined to mean symptoms had not improved or had worsened after embolization, based on the response to the last questionnaire or at the last routine or unanticipated hospital visit, or when the patient underwent further gynecologic intervention because of failure of symptom control without transient improvement in symptoms. Symptom recurrence was defined as meaning patients responded that symptoms had not improved or had worsened even though there was previous improvement after embolization or new symptoms had developed; this response was assessed by the last questionnaire obtained or at the last routine or unanticipated hospital visit, or when the patient underwent gynecologic intervention for recurrent symptoms, including complication-related symptoms. Patients were defined as lost to follow-up when responses to questionnaires could not be obtained. We considered these patients censored at this point, and their last responses on serial questionnaires were considered to indicate patient status. Overall failure of uterine artery embolization was defined as meaning primary failure, symptom recurrence, or performance of further gynecologic interventions. We calculated the cumulative rates of symptom control, primary failure, symptom recurrence, and overall failure of uterine artery embolization using the Kaplan-Meier product limit method.

Regarding adverse events, we defined complications in hospital as meaning patients required unanticipated imaging assessment, an increased level of care, or unanticipated treatment, or reported persistent disability or injury associated with the procedure. After discharge, we defined complications as meaning patients required unanticipated hospital visits, unanticipated imaging assessment, unanticipated medical treatment, or repeated hospitalization associated with adverse events. These events are cited in the systematic evaluation of complications after uterine artery embolization for symptomatic fibroids reported by Spies et al. [12]. Complications of uterine artery embolization were classified into six grades, as previously reported [12, 13]: grade A, no therapy, no consequence; grade B, nominal therapy, observation, no consequence; grade C, required therapy, unanticipated minor hospitalization for less than 48 hr; grade D, major therapy, unplanned increased level of care, unanticipated prolonged hospitalization for more than 48 hr; grade E, permanent adverse sequelae;

and grade F, death. We defined grades A and B as minor complications and grades C–F as major complications. If a patient had two or more complications, we counted all of the complications.

When amenorrhea occurred and continued for two or more consecutive cycles until 1 year after embolization, we regarded it as a complication. Amenorrhea was investigated by serial questionnaires or at the time of routine or unanticipated hospital visits. In this study, permanent amenorrhea was defined as amenorrhea that occurred after embolization and continued for 12 or more months without resumption of menstruation. Transient or permanent amenorrhea was defined as amenorrhea that occurred after embolization and continued for two or more consecutive cycles. The age at onset of permanent amenorrhea and transient or permanent amenorrhea was assessed, and cumulative rates of onset of permanent amenorrhea and transient or permanent amenorrhea were measured using the Kaplan-Meier product limit method.

We investigated menopausal symptoms, including hot flashes, night sweats, and so on, by serial questionnaires or at the time of routine or unanticipated hospital visits. The age at onset of menopausal symptoms was assessed, and cumulative rates of onset of menopausal symptoms were measured using the Kaplan-Meier product limit method.

**Results**

Baseline MRI showed the following results: The mean maximal diameter of the largest tumor was 8.6 cm (range, 2–16.3 cm). The mean largest tumor volume was 322 mL (range, 4–1,601 mL). The largest fibroid was located in the submucosal area in 36 women, in the intramural area in 50, and in the subserosal area in 10. The number of fibroids per woman ranged from 1 to 30 (mean, 6.5). Mean uterine volume was 962 mL (range, 180–2,506 mL). All but one patient successfully underwent bilateral uterine artery embolization. Unilateral uterine artery embolization was performed in one patient because the contralateral uterine artery was absent. Thus, the technical successful rate was 99%. No repeated angiography, uterine artery embolization, or ovarian artery embolization was performed in any patient.

Contrast-enhanced MRI was obtained 1 week after embolization in all but one woman. It showed that 89% (85/95) of the largest fibroids were completely infarcted and that all fibroids were completely infarcted in 79% (75/95) of patients. One woman with asthma underwent contrast-enhanced CT instead of contrast-enhanced MRI.

The follow-up period ranged from 4 to 60 months (mean, 37.4 months). Serial questionnaires were obtained from 100% of patients at 1 year after embolization, 89% at 2 years, 86% at 3 years, 79% at 4 years, and 67% at 5 years. Of all 96 women, 16 (17%) were lost to follow-up during the follow-up period (Table 1). Of these 16 patients, 10 were lost to follow-up at 2 years, four at 3 years, one at 4 years, and one at 5 years. We confirmed that all 16 patients indicated improvement in symptoms and had not undergone any further gynecologic interventions at the last questionnaires obtained or at the last routine or unanticipated hospital visit.

Table 1 shows the outcomes after uterine artery embolization.

**Primary Failure**

Improvement in symptoms was observed in all patients who responded to the initial questionnaires (Table 2).

**Symptom Recurrence**

Nine women developed symptom recurrence (Tables 1 and 3). Of these nine women, five underwent gynecologic interventions for symptom recurrence, including complication-related symptoms. A 42-year-old woman taking antiplatelet drugs for cerebral disease reported improvement in severe menorrhagia after embolization. However, she underwent hysterectomy because of recurrent uterine bleeding 11 months after embolization, as previously reported [14]. A 32-year-old woman who had undergone abdominal myomectomy 5 years earlier underwent uterine artery embolization for menorrhagia and bulk-related symptoms caused by uterine fibroids. Baseline MRI showed the uterus was 2,247 mL because of multiple fibroids. Her symptoms improved markedly after the procedure, but dysmenorrhea and bloating reoccurred 2 years after embolization. These symptoms corresponded to

rapid regrowth of multiple residual viable fibroids and rapid occurrence of new fibroids, which were confirmed by enhanced MRI. Forty-two months after embolization, she underwent abdominal hysterectomy.

A 39-year-old woman with bulk-related symptoms caused by an intramural fibroid 11.8 cm in maximal diameter underwent uterine artery embolization. Two years after embolization, all symptoms had resolved and MRI showed that the tumor was completely infarcted. However, genital bleeding and menorrhagia developed gradually thereafter. MRI 3 years after embolization showed endometrial thickness of more than 2 cm, suggesting endometrial polyps or hyperplasia, and the fibroid was completely infarcted. Subsequently, she underwent dilatation and curettage under hysteroscopic guidance, and the histopathologic examination indicated endometrial polyp.

A 48-year-old woman with a single submucosal tumor measuring 12 cm in diameter and a 42-year-old woman with a single submucosal tumor measuring 7.5 cm in diameter

**TABLE 1: Patient Outcomes After Embolization**

Outcome	No. of Patients
Additional gynecologic intervention	
Primary failure of symptom control <sup>a</sup>	0
Symptom recurrence <sup>a</sup>	5
Other <sup>a</sup>	2
No additional gynecologic intervention	
Symptom control	69
Primary failure of symptom control	0
Symptom recurrence	4
Lost to follow-up	16

<sup>a</sup>Reason additional interventions were performed.

**TABLE 2: Cumulative Outcomes After Uterine Artery Embolization**

Outcome	% After Embolization <sup>a</sup>				
	1 yr	2 yr	3 yr	4 yr	5 yr
Primary failure of symptom control	0	0	0	0	0
Symptom recurrence	3.1	5.5	10.5	10.5	10.5
Gynecologic interventions	4.2	4.2	5.4	10.5	10.5
Complication-related gynecologic interventions	2.1	2.1	2.1	2.1	2.1
Symptom control	96.9	94.5	89.5	89.5	89.5
Overall failure of uterine artery embolization	4.2	6.5	12.7	12.7	12.7

<sup>a</sup>Cumulative rates using Kaplan-Meier product limit method.

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**TABLE 3: Symptom Recurrence After Uterine Artery Embolization**

Patient Age (yr)	Recurrent Symptoms	Cause of Recurrence	Time of Recurrence <sup>a</sup> (mo)	Time of Intervention <sup>a</sup> (mo)	Treatment
42	Uterine bleeding	Suspected residual viable fibroid	11	11	Abdominal hysterectomy
32	Bulk-related symptoms	Regrowth of multiple fibroids	24	42	Abdominal hysterectomy
39	Menorrhagia	Endometrial polyp	24	36	Dilatation and curettage
35	Bulk-related symptoms	Regrowth of uninfarcted fibroid	29	—	Medication (30 mo) <sup>b</sup>
47	Dysmenorrhea	Adenomyosis	30	—	Medication (36 mo) <sup>b</sup>
39	Menorrhagia	Regrowth of multiple fibroids	24	—	Medication (36 mo) <sup>b</sup>
39	Bulk-related symptoms	Suspected regrowth of fibroids	36	—	None
48	Pain	Sloughing fibroid	4	4	Transvaginal tumor resection
42	Pain	Sloughing fibroid	7	7	Transvaginal tumor resection

Note—Dash (—) indicates no additional gynecologic interventions during the follow-up period.

<sup>a</sup>After embolization.

<sup>b</sup>Parentheses indicate the time patients underwent medication for symptom recurrence after embolization.

had severe pain due to sloughing fibroids, which blocked the uterine cervical canal at 4 and 7 months after embolization, respectively. Both patients successfully underwent transvaginal tumor resection, as previously described [6, 14].

Of 73 women who did not undergo further gynecologic interventions and were not lost to follow-up after embolization, four women indicated symptom recurrence, and 69 indicated on the last questionnaire that symptoms had improved (Tables 1 and 3). A 35-year-old woman who had undergone abdominal myomectomy 5 years earlier underwent uterine artery embolization for menorrhagia and bulk-related symptoms caused by multiple uterine fibroids. Although the symptoms improved after embolization, she experienced recurrent bulk-related symptoms 29 months after embolization. Serial MRI showed that a large subserosal fibroid being fed by the ovarian artery was not infarcted at all and had increased rapidly during the follow-up period, although other multiple fibroids were infarcted and decreased in volume. She has been monitored with medication 43 months after embolization.

A 47-year-old woman with multiple fibroids accompanied by diffuse adenomyosis underwent embolization and symptoms improved markedly. However, because she had recurrent dysmenorrhea at 30 months after embolization, she was being monitored with medication 3 years after embolization. A 39-year-old woman with menorrhagia, pain, and bulk-related symptoms due to multiple fibroids underwent embolization and all symptoms improved. However, she developed recurrent menorrhagia 24 months after embolization. Serial MRI showed small viable fibroids that

gradually increased in size, which were thought to be the cause of the recurrent symptoms. She was being monitored with medication 3 years after embolization.

A 39-year-old woman who had undergone abdominal myomectomy 5 years earlier underwent uterine artery embolization because she had bulk-related symptoms caused by multiple uterine fibroids. Enhanced MRI 1 week after embolization showed that all but one 2.5-cm intramural fibroid were infarcted. Enhanced MRI 1 year after embolization showed that the fibroid measured 3.5 cm. Although the symptoms had improved after embolization, she experienced recurrent bulk-related symptoms 36 months after embolization. She was being monitored without medication 3 years after embolization. Therefore, cumulative rates of symptom recurrence were 3.1% at 1 year, 5.5% at 2 years, 10.5% at 3 years, 10.5% at 4 years, and 10.5% at 5 years (Table 2). The intervals between the procedure and symptom recurrence ranged from 4 to 36 months (mean, 21.2 months; 95% confidence interval [CI], 12.6–29.8 months).

### Symptom Control

Cumulative symptom control rates were 96.9% at 1 year, 94.5% at 2 years, 89.5% at 3 years, 89.5% at 4 years, and 89.5% at 5 years (Table 2 and Fig. 1).

### Complications

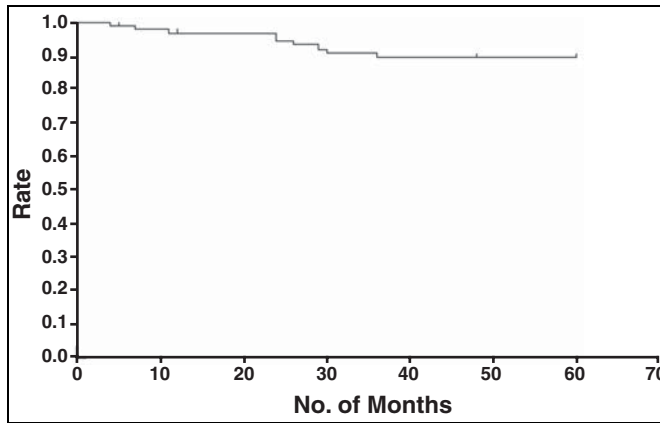
Twenty-five complications (26.0%, 25/96), occurring in 21 women (21.9%, 21/96), were noted (Table 4). However, 22 of 25 complications were minor, requiring no therapy or nominal therapy. Major complications requiring major therapy, an unplanned increased level of

care, or unanticipated prolonged hospitalization (> 48 hr) or including permanent adverse sequelae were noted in 3.1% (3/96) of patients.

A 35-year-old woman experienced sexual dysfunction after embolization. She reported a significantly decreased intensity of internal orgasm during sexual intercourse. The adverse reaction continued after embolization and was previously reported by us [14]. As we described earlier in this article, a 48-year-old woman with a single submucosal tumor measuring 12 cm in diameter and a 42-year-old woman with a single submucosal tumor measuring 7.5 cm in diameter had sloughing fibroids that blocked the uterine cervical canal and underwent successful transvaginal resection, as previously described [6, 14]. In both women, the outcomes were judged to be major complications because these patients required hospitalization to treat sloughing fibroids.

Cumulative rates of complications related to gynecologic intervention were 2.1% at the 1-, 2-, 3-, 4-, and 5-year follow-ups (Table 2). The interval between the procedure and the complication-related gynecologic intervention ranged from 4 to 7 months (mean, 5.5 months). The age at onset of permanent amenorrhea ranged from 45 to 53 years (mean, 48.9 years; 95% CI, 46.2–51.5 years). Cumulative rates of onset of permanent amenorrhea were 1.1% at 1 year, 2.3% at 2 years, 6.2% at 3 years, 12.2% at 4 years, and 12.2% at 5 years. The age at onset of transient or permanent amenorrhea ranged from 44 to 53 years (mean, 48.5 years; 95% CI, 47.4–49.6 years). Cumulative rates of onset of transient or permanent amenorrhea were 6.4% at 1 year, 10.1% at 2 years, 18.0% at 3 years, 21.2% at 4 years, and 43.7% at 5 years.

**Fig. 1**—Graph shows cumulative rates of symptom control after uterine artery embolization using gelatin sponge particles alone for symptomatic fibroids. Rates were determined using Kaplan-Meier product limit method.



**TABLE 4: Complications After Uterine Artery Embolization**

Complications	No. (%)
Total complications	25 (26.0)
Major	3 (3.1)
Minor	22 (22.9)
No therapy, no consequence	14 (14.6)
Fibroid passing vaginally without intervention	6
Amenorrhea	4
New menopausal symptoms	1
Persistent vaginal discharge	1
Pain	1
Partial defect of uterine wall	1
Nominal therapy, observation, no consequence	8 (8.3)
New menopausal symptoms	2
Fibroid passing vaginally without intervention	1
Vascular injury	1
Prolonged pain	1
Buttock pain	1
Pain due to constipation	1
Hematoma	1
Required therapy, unanticipated minor hospitalization (< 48 hr)	0 (0)
Major therapy, unplanned increased level of care, unanticipated prolonged hospitalization (> 48 hr)	2 (2.1)
Surgery for sloughing fibroids	2
Permanent adverse sequelae	1 (1.0)
Sexual dysfunction	1
Death	0 (0)

The age at onset of menopausal symptoms ranged from 44 to 53 years (mean, 48.6 years; 95% CI, 47.4–49.8 years). Cumulative rates of onset of menopausal symptoms were 8.5% at 1 year, 13.5% at 2 years, 22.7% at 3 years, 31.6% at 4 years, and 31.6% at 5 years.

**Overall Gynecologic Interventions**

Seven women underwent additional gynecologic intervention after embolization, including two women as a result of complications with symptoms and three women for symptom recurrence, as described earlier

(Table 1). The remaining two gynecologic interventions were as follows: A 43-year-old woman with a submucosal fibroid had reported improvement in severe menorrhagia after embolization. However, she underwent a hysterectomy for early uterine cervical cancer 5 months after embolization although the pre-procedural Papanicolaou test was negative. A 50-year-old woman with an intramural fibroid 7 cm in diameter had reported improvement in menorrhagia and anemia for 3 years after embolization. Enhanced MRI obtained 1 year after embolization showed that the tumor was completely nonenhancing and its maximal diameter was 4 cm. However, she underwent a hysterectomy because of uterine prolapse 3 years after embolization. In both women, whom we previously described [14], we judged the outcomes to be caused by other factors than the procedure or uterine fibroids.

Cumulative gynecologic interventions rates were 4.2% at 1 year, 4.2% at 2 years, 5.4% at 3 years, 10.5% at 4 years, and 10.5% at 5 years (Table 2). The interval between the procedure and overall gynecologic interventions ranged from 5 to 42 months (mean, 20.3 months; 95% CI, 4.5–36.1 months).

**Overall Failure**

Cumulative rates of overall failure were 4.2% at 1 year, 6.5% at 2 years, 12.7% at 3 years, 12.7% at 4 years, and 12.7% at 5 years (Table 2). The interval between the procedure and overall failure ranged from 4 to 36 months (mean, 21.1 months; 95% CI, 21.9–29.3 months).

**Pregnancy**

Thirteen women wanted to preserve fertility before uterine artery embolization. Their ages ranged from 34 to 48 years (mean, 40 years). Of these 13 women, seven tried to conceive during the follow-up period, but none became pregnant. However, of the remaining 83 women who had not expressed interest in preserving fertility before embolization, two became pregnant. One was parous and the other nulliparous. The former woman with a single submucosal fibroid underwent embolization at 37 years old and became pregnant at 40 years old. MRI before and 1 year after embolization showed the maximal diameters of the tumor were 6 and 2.3 cm, respectively, and the uterine volumes were 312 and 102 mL. The latter woman with multiple fibroids underwent embolization at 37 years old and became pregnant at 41 years old. MRI before and 1 year after embolization showed the maximal diameters

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of the tumor located in the intramural area were 9 and 7 cm, respectively, and the uterine volumes were 517 and 251 mL. Both pregnancies resulted in miscarriage.

### Discussion

Our results suggest that uterine artery embolization using gelatin sponge particles alone for symptomatic uterine fibroids provides long-term symptom control in most patients because the cumulative rates of symptom control were 89.5% at both 3 and 5 years. Marret et al. [9] reported that the crude rate of improvement in clinical symptoms was 83.5% after embolization using polyvinyl alcohol particles on long-term follow-up with a median of 30 months (range, 2–57 months). Therefore, we consider that long-term symptom control after embolization using gelatin sponge particles alone is comparable to that reported by Marret et al. using polyvinyl alcohol particles.

In this study, we assessed the long-term outcomes of uterine artery embolization for symptomatic fibroids using cumulative rates rather than crude rates. We used cumulative rates because we took into account patients lost to follow-up and those who underwent additional gynecologic interventions after embolization, the effective duration of follow-up, and the distribution of outcomes over time [15]. In general, because the crude outcome rates do not consider these factors, they can underestimate the true rates of outcomes rather than cumulative rates, which use life-table analysis or the Kaplan-Meier product limit method [15]. Although 16 of 96 patients were lost to follow-up in our study, we consider that the cumulative rates using the Kaplan-Meier product limit method are a suitable method to assess outcomes.

We assessed change in symptoms on the basis of the patient's responses compared with baseline status at each follow-up point after embolization using serial written questionnaires in this study. Because this method depended on the patient's memory of her baseline status, recall bias might have influenced the outcomes. An objective method of serially assessing symptom severity at baseline and at each follow-up using the same questionnaire format, such as the Uterine Fibroid Symptoms and Quality of Life questionnaire [16], and then statistically comparing the data collected in this manner, is thought to provide more reliable findings. However, during the period that we performed uterine artery embolization in 96 consecutive patients, an appropriate format had

not yet been published, and we did not use such an approach in this study.

Anatomic change, including occurrence of new fibroids or regrowth of existing fibroids during the long term after embolization, is an important issue. In this study, we could not fully assess these changes because our study was an analysis of long-term symptom control using data obtained by serial questionnaires or at routine or unanticipated hospital visits, and we did not routinely perform serial imaging 2 years after embolization in all patients. However, self-reported diagnoses based on serial questionnaires have been considered a good method for assessing recurrence [15], because this method had an excellent match (93%) with diagnoses confirmed by sonography and histology in an article by Marshall et al. [17]. A serial prospective imaging study is warranted regarding detailed anatomic assessment of the occurrence of new fibroids and the regrowth of existing fibroids.

Pelage et al. [18] reported, in a study using contrast-enhanced MRI, that the residual viable component in embolized fibroids can regrow and cause recurrent symptoms over the long term. In our study, serial contrast-enhanced MRI in four of nine women with symptom recurrence showed that the residual viable component in the tumor or new fibroids after embolization increased in size, causing symptom recurrence. We think that this result corresponds to the report of Pelage et al. Therefore, we consider that to avoid recurrent symptoms over the long term, it is necessary to induce complete infarction of all fibroids as much as possible, without complications, by uterine artery embolization, especially for young women. However, we encountered two women with recurrent symptoms due to disorders other than fibroids, such as adenomyosis and endometrial polyps, in our study. This means that recurrent symptoms are not always caused by recurrent fibroids. Therefore, when patients develop symptom recurrence, we think that careful evaluation of the cause is required to perform appropriate treatment.

Spies et al. [12] reported the crude rates of major and minor complications after uterine artery embolization using mainly polyvinyl alcohol particles for fibroids were 4.3% and 7.5%, respectively. In our study, the crude rates of major and minor complications were 3.1% and 22.9%, respectively. The crude rate of major complications was similar to that reported by Spies et al., although the crude rate of minor complications was higher in our study. Cumulative rates of permanent amenorrhea onset

were 1.1% at 1 year, 6.2% at 3 years, and 12.2% at 5 years, whereas cumulative rates of onset of transient or permanent amenorrhea and menopausal symptoms after embolization were 6.4% and 8.5% at 1 year, 18.0% and 22.7% at 3 years, and 43.7% and 31.6% at 5 years, respectively. However, this may not be surprising considering that the age at onset of transient or permanent amenorrhea and the age at onset of menopausal symptoms were a mean of 48.2 and 48.9 years, respectively, and that the baseline age was 40 years or older in 80% (77/96) of women and 45 years or older in 33% (32/96) of women in this study. The mean age at menopause is 51 years, and some symptoms such as hot flashes begin in perimenopause [19]. Therefore, it can be hypothesized that the age at onset of amenorrhea and menopausal symptoms after embolization might be slightly earlier than that in the natural course.

Two women who had not expressed a desire for future pregnancy before embolization became pregnant, but both pregnancies resulted in miscarriage. In contrast, of the 13 women who had wanted before embolization to preserve fertility, seven women tried to conceive during the follow-up period but none became pregnant. We think that these results cannot provide definite conclusions about how uterine artery embolization using gelatin sponge particles alone can affect fertility, because the number of patients is too small and the mean age of the patients was relatively high. Therefore, further investigations regarding fertility after uterine artery embolization using only gelatin sponge particles are required.

The reasons we used gelatin sponge particles as the sole embolic agent for uterine artery embolization are as follows: First, other embolic agents, such as polyvinyl alcohol and trisacryl gelatin microspheres, are not commercially available in Japan. Second, gelatin sponge has been a familiar embolic agent for Japanese interventional radiologists, having been frequently used in embolotherapy for other diseases such as hepatocellular carcinoma. Third, our previous reports [6, 14] suggest that short- and midterm outcomes of uterine artery embolization using gelatin sponge particles alone for fibroids are comparable to those achieved using other embolic agents.

We conclude that uterine artery embolization using gelatin sponge particles alone provides long-term symptom control for fibroids with few major complications in most patients. The outcomes are comparable with previously published reports of embolization using polyvinyl alcohol particles. However,

our study has some limitations. Our study dealt with a limited number of patients and was performed at a single institute during a limited follow-up period. Moreover, 16 patients (17%) were lost to follow-up, although outcomes rates were calculated using the Kaplan-Meier product limit method. Because changes in symptoms were assessed on the basis of patients' responses at each follow-up point compared with the baseline status using serial written questionnaires, recall bias might have influenced the outcomes in this study. This study also cannot provide data regarding anatomic recurrence, including occurrence of new fibroids or regrowth of existing uterine fibroids, over the longer term or regarding fertility issues after embolization. Thus, more detailed studies investigating a much longer term are required.

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