Short-Term Results of Transcatheter Uterine Artery Embolization Using Lipiodol and Gelfoam Cubes for Symptomatic Uterine Leiomyoma

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To evaluate the effectiveness and safety of transcatheter uterine artery embolization (UAE) using lipiodol-gelfoam cube mixture for the treatment of symptomatic uterine leiomyomas.

Fifty women with symptomatic uterine leiomyomas underwent transcatheter bilateral UAE using lipiodol and gelfoam cubes. Ultrasonography was used to assess the size of uterus and the dominant fibroids before, at 4 month and 1 year after UAE. A questionnaire was obtained to assess patients' clinical outcome.

Menorrhagia improved significantly or mildly in 37 (92.5%) of 40 patients at 4 months after embolization and 20 (95%) of 21 patients at 1 year after embolization. Bulk-related symptoms improved significantly or mildly in 24 (89%) of 27 patients at 4 months after embolization and in 13 (93%) of 14 patients at 1 year after embolization. The uterine and dominant fibroids volumes decreased by 35% and 51% at 4 months and 43% and 67% at 1 year respectively. Pain control was achieved easily by oral analgesics. One patient was readmitted because of sepsis and ulceration of the urinary bladder.

UAE could be performed using a combination of lipiodol and gelfoam cubes with clinical results comparable to that obtained by traditional embolizers.

Key words: Arteries, therapeutic embolism; Leiomyoma; Uterine neoplasms

Transcatheter uterine artery embolization, a recognized treatment of uterine leiomyoma, was first reported in 1995 by Ravina [1]. In most reports of uterine artery embolization for uterine fibroids, polyvinyl alcohol (PVA) is the most commonly used permanent embolizer with established clinical and imaging success [2-7]. There have been a few reports of using absorbable gelfoam cubes with satisfactory results but some have argued it as a sole embolic agent for UAE for uterine leiomyoma [8]. Gelfoam and lipiodol have been used as effective and cheap embolic agent for hepatocellular carcinoma (HCC). The purpose of our study is to evaluate whether UAE performed using gelfoam cubes and lipiodol as embolizers, obtains comparable results to that of polyvinyl alcohol.

MATERIALS AND METHODS

Patient selection

Fifty women (aged 27 to 51 years; mean 40.1 years) with symptomatic uterine leiomyomas underwent artery embolization using gelfoam cubes and lipiodol during a 35-month period. This therapeutic trial was approved by our institutional review board. Patients were referred by experienced gynecologists, who determined that the leiomyomas were the sole or the major cause of symptoms and required treatment. All the patients were premenopausal and their major clinical problems include menorrhagia, pain, or bulk related symptoms. The patients were informed of all therapeutic options, potential benefits and risks of uterine artery embolization.
**Patient preparation**

Patients were admitted for pre-operative evaluation one day before the procedure. Complete blood count, laboratory studies (i.e., pregnancy test), chest radiographs were performed for all the patients. One gram of cefazolin was given intravenously just before angiography.

**Embolization procedure**

After local anesthesia using 2% lidocaine, all the patients underwent access of the common femoral artery. A 6 French (Fr) vascular sheath was used. At first, a 4 Fr pigtail catheter was inserted to the renal artery level. A mapping aortogram was obtained after injection of Ioversol (Optiray; Mallinckrodt Medical, Quebec, Canada). A 5 F angiocatheter (Roberts uterine curve; Cook, Bloomington, U.S.) was exchanged for catheterization of the internal iliac artery[9]. Selective catheterization of left uterine artery was performed by pulling down the performed upward curve of the catheter. The catheter tip was positioned at about 1 cm beyond the junction of the descending and horizontal portions, and the tip conformed to the arch segment of uterine artery to avoid vascular spasm. No microcatheter was needed for further advancement. The gelfoam cubes, each measuring about 1 mm$^2$, were cut from a gelatin sponge sheet (Gelfoam Sponge; Pharmacia, Michigan, USA) during the angiographic procedure. The gelfoam cubes were then soaked in a cub, half filled with equal mixture of saline and contrast medium. The embolization procedure was first carried out by infusing about 5-10 ml lipiodol (lipiodol ultra-fluide, Guerbet, France) according to the vascularity of the fibroids until the forward flow in the uterine artery became sluggish. Then, the distal descending uterine artery was occluded slowly with gelfoam cubes. The catheter was then flushed with normal saline for a few times at the end of the embolization. The catheter was gradually withdrawn into the iliac artery while keeping negative pressure by a hand-held syringe, to avoid any incidental embolization by embolizers left in the catheter. The catheter was maneuvered into right internal iliac artery, and a similar embolization procedure was repeated. No antibiotics were given after the embolization procedure.

**Clinical follow-up**

The general well-being of the patients was evaluated by the referring gynecologists at 4 months and 1 year after UAE. The radiologist also interviewed the patients by telephone. The questions included improvement of symptoms, complications and side effects. The most frequent complaint of symptomatic leiomyoma was abnormal uterine bleeding. The symptoms related to bulky uterus were urinary frequency, pressure sensation, and sensation of mass was also mentioned. The subjective change of menorrhagia and bulk-related symptoms were evaluated on the basis of responses to a five-point symptom scale (significant improvement, slight improvement, no change, slight deterioration, significant deterioration). A clinical successful result was defined as significant or slight improvement of symptoms. Patient satisfaction was similarly defined.

Most patients tolerated the procedure well, but moderate to severe cramp-like pelvic pain was the major symptom immediately after the procedure. The post-UAE pain was controlled by intravenous Meperidine and oral acetaminophen or non-steroid anti-inflammatory drugs. None of our patients received patient-controlled analgesia pump for post-operative pain control. Post procedure pain was evaluated by Visual Analog scale (VAS) [10]. A one-week oral medication for pain control after discharge was prescribed for the patients. At the last clinical visit, usually 6 months after UAE, we asked the patients would they recommend such procedure to other women with symptomatic uterine leiomyomas.

Ultrasoundography was performed by gynecologists before and after uterine artery embolization in all women. The uterine volume, size and number of leiomyomas were recorded. The uterine volume was measured using the formula of length $\times$ width $\times$ depth $\times$ 0.5233 as a prolate ellipse. The largest fibroid was defined as the dominant fibroid and its pre- and post-embolization volume was measured. Reduction ratio of the uterine and fibroid volume after uterine artery embolization was calculated with the paired sample t-test. A $p$-value of .05 was considered statistically significant.

**RESULTS**

Patient characteristics were summarized in Table 1. Bilateral embolization of the uterine arteries were accomplished in 48 (96%) of the 50 patients. In the remaining two patients, unilateral UAE was performed, because of tortuosity of the uterine arteries. Both of them were satisfied with the result of UAE in the follow-up period. The duration of the procedure ranged from 35 to 100 min (mean 43 min). The results of charting of the post-procedure pain were shown in table 2. The mean of total dose of Meperidine given during the admission course was 52mg (range 25 to 175mg). Forty women were given
2000mg of acetaminophen orally, and the other 10 women were given 1000mg of naproxen, in four portions during a 7-day period before the patients came back to our outpatient clinic. With the combined use of oral medication, pain control was achieved in all patients. The post procedure pain usually subsided within 1 to 7 days. Thirty (88%) of 34 of patients got pain relief within 3 days. Six and 10 patients experienced nausea and vomiting respectively, but their symptoms subsided within a few days receiving no further medication. The mean hospitalization duration was 1.6 ± 1.5 days (range, 1-9 days).

The uterine diameter and dominant fibroid diameter before UAE ranged from 5.7cm to 12.2cm and 2.6cm to 10.8cm. There was a mean reduction in uterine volume of 35% (range from 8.4% to 56.4%) and 43% (range from 17.7% to 73%) at 4 months and 1 year after UAE. The mean reduction in dominant fibroid volume was 51% (range from 4.3% to 100%) and 67% (range from 17.4% to 100%) at 4 months and 1 year after UAE (Table 3). Statistical analysis with paired sample t test demonstrated that the reduction of both uterine volume and dominant fibroid volume was statistically significant ($P = 0.015$ and 0.029).

Menorrhagia improved significantly or slightly in 37 (92.5%) of 40 patients at 4 months after embolization and 20 (95%) of 21 patients at 1 year after embolization. Bulk-related symptoms improved significantly or slightly in 24 (89%) of 27 of patients at 4 months after embolization and in 13 (93%) of 14 of patients at 1 year after embolization (Table 3).

The total major complication rate was 8 % (4/50), including permanent amenorrhea (1/50), urosepsis (1/50) and vaginal myomas expulsion (2/50). Four patients experienced transient amenorrhea initially, and had normal follicle stimulating hormone (FSH) levels after UAE. Their normal menstruation resumed within 3 months. One patient went into permanent menopause at the age of 51 with an elevated serum FSH level at 6 months after UAE. One patient developed urosepsis (Escherichia coli) associated with endometritis, which subsided at 9 days after intravenous antibiotic therapy. Two patients experienced vaginal myomas expulsion at the 3rd and 4th weeks after UAE. One of them [11] was admitted again due to sepsis and ulceration of urinary bladder which was found in cystoscopic examination. On post-embolization day 42, a large necrotic tissue that protruded to the cervical os was twisted out easily at an office visit with negligible bleeding. The pathological examination revealed extensive coagulative and necrotic tissue measuring $6.1 \times 4.9 \times 2.2$ cm. Four months after the procedure, ultrasonography indicated that reduction of uterine volume was 22.4% and the dominant fibroid had been completely removed. Another patient also experienced vaginal myoma expulsion and was removed earlier without obvious side effect.

No patient got pregnant after the embolization during the follow-up period. No mortality was encountered. No patient underwent secondary surgical intervention for residual uterine leiomyoma. Forty patients

### Table 1. Patient characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>n (%)</th>
<th>Mean ± SD (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>50</td>
<td>40.1 ± 5.4 (27–51)</td>
</tr>
<tr>
<td>Hospitalization (days)</td>
<td>50</td>
<td>1.6 ± 1.5 (1–9)</td>
</tr>
<tr>
<td>Menopause</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Myomectomy</td>
<td>8 (16)</td>
<td></td>
</tr>
<tr>
<td>Laparoscopy</td>
<td>3 (6)</td>
<td></td>
</tr>
<tr>
<td>No. of myoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 dominant</td>
<td>43 (86)</td>
<td></td>
</tr>
<tr>
<td>&gt; 1</td>
<td>7 (14)</td>
<td></td>
</tr>
<tr>
<td>Bilateral UAE</td>
<td>48 (96)</td>
<td></td>
</tr>
<tr>
<td>Time of procedure(minutes)</td>
<td>50</td>
<td>43.6 ± 10.2 (35–100)</td>
</tr>
<tr>
<td>Meperidine dose (mg)</td>
<td>34 (68)</td>
<td>52 ± 12 (25–175)</td>
</tr>
<tr>
<td>acetaminophen</td>
<td>40 (80)</td>
<td></td>
</tr>
<tr>
<td>naproxen</td>
<td>10 (20)</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Post procedure pain was evaluated by Visual Analog Scale (VAS)

<table>
<thead>
<tr>
<th>VAS Grade</th>
<th>No of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Severe pain</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>Moderate pain</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>2</td>
<td>Mild pain</td>
<td>5</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>0</td>
<td>No pain</td>
<td>16</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>50</td>
</tr>
</tbody>
</table>

### Table 3. Outcome after uterine artery embolization.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>4 months post-UAE (n = 40)</th>
<th>1 years post-UAE (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction of Uterus (%)</td>
<td>35 (8.4-56.4)</td>
<td>43 (17.7-73)</td>
</tr>
<tr>
<td>Myoma (%)</td>
<td>51 (4.3-100)</td>
<td>67 (17.4-100)</td>
</tr>
<tr>
<td>Symptom resolution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menorrhagia (%)</td>
<td>92.5 (37 of 40 patients)</td>
<td>95 (20 of 21 patients)</td>
</tr>
<tr>
<td>Bulk-related symptoms (%)</td>
<td>89 (24 of 27 patients)</td>
<td>93 (13 of 14 patients)</td>
</tr>
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</table>

*Symptoms improved significantly and slightly.*
(100%) commented that they would like to recommend this procedure to others with symptomatic fibroids.

**DISCUSSION**

In our series, UAE using gelfoam cubes and lipiodol results in an appreciable improvement of symptoms. The reduction of both uterine and leiomyomas are significant and the results can be maintained in the follow-up period, without evidence of tumor regrowth.

**Symptoms improvement**

In reported series of UAE using PVA particles,
menorrhagia improved in 81-94% of patients, and bulk-related symptoms improved in 64-96% of patients [2-5]. In a series of 60 patients reported by Katsumori et al [12] who used gelfoam cubes, described a similar satisfactory outcome. Our study using a combination of gelfoam cubes and lipiodol obtained improvement of menorrhagia and bulk-related symptoms at 1 year in 95% and 93% of patients respectively.

Toh et al [13] compared the outcome of UAE in 3 diagnostic categories—submucosal leiomyoma, intramural leiomyoma, and adenomyosis which were categorized by magnetic resonance imaging (MRI). In their study, the group of patients with submucosal myomas obtained 81% of symptoms resolution. In contrast, the group of patients with adenomyosis got only 25% of symptom-free. In our study using sonography as an imaging tool, separation of different subgroup of uterine myoma could not be achieved. Since the relatively poor tissue contrast and spatial resolution of ultrasound images, there may be undetected adenomyosis in our series. We suggest that part of slightly lower rate may result from the undetected adenomyosis.

**Volume reduction of Uterine and dominant myoma**

In previous reports, UAE was performed with PVA and volume reduction rates for the dominant myoma and uterus are 49% to 78% and 34% to 52%, respectively [2-5]. In our report, the dominant fibroids and uterine volumes decreased by 67% and 43% at 1 year respectively and the results have demonstrated outcomes similar to that of PVA.

In our preliminary result, UAE using gelfoam cubes and lipiodol could be a safe intervention for symptomatic myoma. At 4 months or at 1 year after embolization, the mean decrease of myoma volume was more dramatic than that of the uterine volume. The major effect of ischemic atrophy occurred in the uterine myomas is probably due to the development of collateral vessels to the uterus, while myoma blood supply was blocked permanently. Weintraub et al [14] also described that color Doppler imaging showed a marked decrease in blood flow to the myoma after UAE. Katsumori et al [15] also reported similar findings by MRI.

**Post-embolization pain**

Post-procedural cramping was more significant in patients undergoing UAE with PVA than in our study. Most of the patients in our series experienced no significant or only mild post-embolization pain and the pain could be released by intramuscular injection of meperidine or by oral NSAIDs which made the control of post embolization pain more easily. In a previous report, intensive postoperative pelvic pain was well-managed using a patient-controlled analgesia pump (PCA) in 85% of women [5]. The size of the polyvinyl alcohol is considered an important factor that may induce pain which was inversely proportional to the clinical symptom [16]. The particle of the gelfoam cube is bigger than the polyvinyl alcohol which may be the reason for this phenomenon. We think that further investigation is required.

**Morbidity and Mortality**

Our study showed a 8% complication rate, without mortality, comparable to that of UAE using PVA [17] and gelfoam cubes only reported by Katsumori et al [12].

Approximately 5% of patients began menopause after UAE [18], and the condition was more common in women over the age of 45 [2, 5, 19, 20]. In our study, menopausal symptoms with continued amenorrhea occurred only in a 51 years old patient. Transient or permanent amenorrhea would come from non-target organ embolization, which may damage the collateral blood circulation between the ovaries and the uterus. Patients with feeble ovary function would be more susceptible to non-target embolization. Therefore, more care should be taken for perimenopausal patients.

Non-target embolization may do harm to the blood circulation of bladder wall [11]. In addition, difficulty in urination due to post-procedural pain and bed-ridden status can increase the risk of urinary tract infection. Accordingly, early recognition of patients with symptoms of urinary tract infection or positive urinalysis, and prompt initiation of treatment are important to prevent progression of infection.

Passage of leiomyoma tissue was the common complication and appeared to occur only in leiomyomas in contact with the endometrial surface [21, 22]. In the series of Spies et al [17], they reported a 2.5% passage of leiomyomas tissue in 400 patients. Vaginal myoma expulsion occurred in 2 of our patients. One had developed sepsis and focal bladder ulceration. After administration of appropriate antibiotics and timely expulsion of the necrotic myoma vaginally, symptoms of dysuria, leucorrhoea, and cramping resolved completely. Huang et al [16] recommended that hysteroscopy should be performed before UAE if a large submucosal myoma was suspected, in order to avoid uterine adhesion following myoma expulsion and infection. Patient selection for UAE or myomec-
tomy needs better pre-procedure evaluation.

There are many advantages of UAE using gelfoam cubes. Gelfoam cubes are cheap. It is safe and efficient to use PVA particles as embolic agents for UAE. The primary reason we used gelfoam cube as alternative is that PVA was not available commercially in Taiwan. Gelfoam cube also has been used as a safe and useful embolic agent in UAE for some uterine hemorrhage disorder [23, 24]. Because gelfoam cube is absorbable, there would be little concern of long-term effects on the body. Recanalization of the embolized uterine arteries may be possible and thus repeated embolization may be performed, if the patients suffer from symptomatic residual myoma in the future.

Lipiodol, in conjunction with gelatin sponge particles, is used to encourage complete thrombosis. It has been commonly used safely as an embolic agent and as a carrier of anticancer agents for chemoembolization of hepatic tumors. It also has been used in the treatment of other benign tumors [25], malignancies [26] and arteriovenous fistula in brain [27]. It is safe to use lipiodol with the dose less than 1 ml/kg [28], although a few complications have been reported, such as mild to moderate pulmonary dysfunction on lymphangiography [29], brain infarction after hysterosalpingography, and intracardiac right to left shunting [30]. In our preliminary result, lipiodol could be performed safely in the treatment of symptomatic leiomyomas.

Some issues related to UAE using gelfoam cubes and lipiodol remain to be addressed. First, the size of gelfoam cubes can vary, and they can expand and become gellike in fluid [12]. Ischemic complications attributed to the small size of the embolic agent have been reported when using gelfoam as an embolic agent [31, 32, 33]. The smallest diameter of arteries that can be occluded by gelfoam cubes is remained to be decided. We also do not know how distal the uterine circulation could be occluded by lipiodol, and further histopathology study would be important. Second, there was no control group for comparison in our study. Prospective studies may be needed to differentiate the ischemic effect between single embolic agent of PVA or gelfoam cube and the combination of gelfoam cube and lipiodol. Finally, most patients had no desire for future pregnancy, and no patient get pregnant during our follow-up period. Therefore, we do not know whether gelfoam cube and lipiodol can be recommended for women who plan to get pregnant. Further long-term studies of large series are needed to substantiate these questions.

CONCLUSION

UAE is a minimally invasive procedure applied in the treatment of benign uterine myoma for simple purpose: to relieve symptoms related to myoma and therefore to get better quality of life. We would like to broaden the application of uterine artery embolization as the alternative therapy of symptomatic leiomyomas. With better understanding of the possible complication and the risk of non-target embolization, uterine artery embolization using gelfoam cube and lipiodol could be performed as safely and efficiently as the traditional method.

ACKNOWLEDGMENTS

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REFERENCES

10. Sritatanakul K, Kelvie W, Lasagna L, Calimlim JF, Weis OF, Mehta G. Studies with different types of visu-
31. Hare WSC, Holland CJ. Paresis following internal iliac artery embolization. Radiology 1983; 146: 47-51
以油性碘 Lipiodol 與泡棉 Gelfoam 為栓塞劑經由子宮動脈治療症狀性良性子宮肌瘤的短期結果

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評估利用油性碘 Lipiodol 與泡棉 Gelfoam 為栓塞劑經子宮動脈治療症狀性良性子宮肌瘤的效果與安全性。

共有 50 位婦女接受以油性碘 Lipiodol 與泡棉 Gelfoam 為栓塞劑的子宮肌瘤栓塞手術。術前、術後四個月及術後一年的追蹤均以超音波測量婦女子宮與子宮肌瘤的體積並比較之。同時以問卷詢問因子宮肌瘤所引起的症狀改善的程度。

經血過多有明顯改善與改善者，在追蹤四個月與一年後分別是 92.5%（37/40）與 95%（20/21）。腫瘤壓迫所導致的症狀有明顯改善與改善者，在追蹤四個月與一年後分別是 89%（24/27）與 93%（13/14）。子宮體積在四個月與一年後分別平均減少了 35% 與 43%。主要子宮肌瘤體積在四個月與一年後分別平均減少了 51% 與 67%。子宮肌瘤栓塞術後所引起的腹腔疼痛方面，可藉由口服止痛藥的方式而獲得有效的控制。在併發症方面，有一位病人術後因膀胱潰瘍而導致再次入院。

證明利用油性碘 Lipiodol 與泡棉 Gelfoam 為栓塞劑的子宮肌瘤栓塞手術不僅可以使病人經歷較少的術後疼痛與術後併發症，同時也能獲得很好的滿意度。

關鍵詞：動脈栓塞術 子宮肌瘤