

Uterine Artery Embolisation for Treatment of Fibroids: Experience in Chinese Women

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ABSTRACT

Twelve women with symptomatic fibroids were treated with transcatheter uterine artery embolisation with the use of polyvinyl alcohol (PVA) particles. For the nine women who were due for follow-up, reduction in uterine volume and dominant fibroid size were observed on magnetic resonance imaging. All the nine women had normal luteinising hormone (LH) and follicle stimulating hormone (FSH) levels before the procedure and during the follow-up. Seven of the nine women reported noticeable symptomatic improvement during the follow-up. Pain experienced was of variable level, but well controlled. Adequate analgesia is essential for the procedure. Longer follow-up and prospective fertility studies are required to evaluate the long-term effects before this procedure could be safely extended to younger age groups.

Keywords: Leiomyoma, magnetic resonance imaging, therapeutic embolisation, uterine arteries, uterus.

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INTRODUCTION

Uterine fibroids are the commonest benign tumours in women of reproductive age, and a common incidental finding at routine pelvic examination and imaging. Conservative treatment is appropriate in asymptomatic patients unless the fibroids are very large. For symptomatic or large fibroids, myomectomy and hysterectomy have been the mainstay of treatment. Transcatheter selective bilateral uterine artery embolisation is a good alternative for the treatment of fibroids in those patients who wish to retain their uterus and refuse surgery, and for those patients who are of high surgical risk.

Uterine artery embolisation as a primary therapy for fibroids was first advocated by Ravina et al in 1994^(1,2). Partial and complete resolution of symptoms was achieved in 14 of the 16 patients treated. Subsequent large-scale studies demonstrated good results without major complications⁽³⁻⁸⁾. The effect of uterine artery

Table I. Counselling on uterine artery embolisation for fibroids.

Benefits

1. Avoid risks of major surgery
2. Preserve uterus
3. Shorter hospital stay
4. All fibroids treated in a single session
5. Can be repeated if necessary

Problems

1. Complications of embolisation
 - Pelvic pain
 - Post-embolisation syndrome
 - Infection
 - Groin haematoma
 - Massive necrosis of fibroid
 - Most are self-limiting and can be controlled by conservative means
 - Occasionally may lead to hysterectomy if massive necrosis occurs
2. Failure of procedure
 - Chance from other series - about 15%
 - Persistent symptoms
 - No reduction in fibroid size
3. Need for longer follow-up to determine long term success
4. More frequent visits for imaging and blood-taking
5. Effect on fertility not exactly known though pregnancy after the procedure have been reported

embolization in a Chinese population has not been documented. In October 1998, we began to perform uterine artery embolization to treat symptomatic fibroids. This is the report of our initial experience.

PRE-OPERATIVE ASSESSMENT, MATERIALS AND METHODS

Women with symptoms attributable to the uterine fibroids and considered suitable for embolisation by the gynaecologists were included in this study. They were considered suitable for embolisation if they had a large uterine fibroid with symptoms warranting surgical treatment, but who wished to retain their uterus, refused surgery, or were of high surgical risk e.g. previous abdominal surgery, medical problems, obesity. Exclusion criteria included uncontrolled bleeding diathesis, pregnancy, chronic pelvic inflammatory disease, and asymptomatic fibroids. Pap smears and/or endometrial

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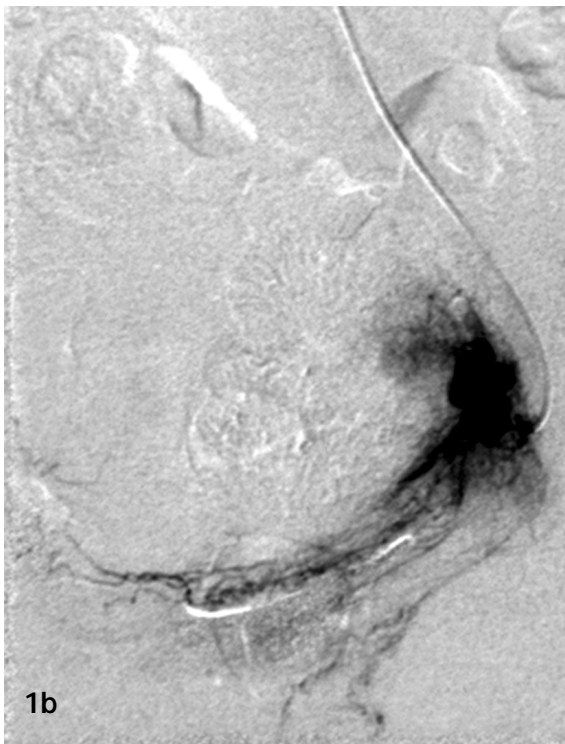
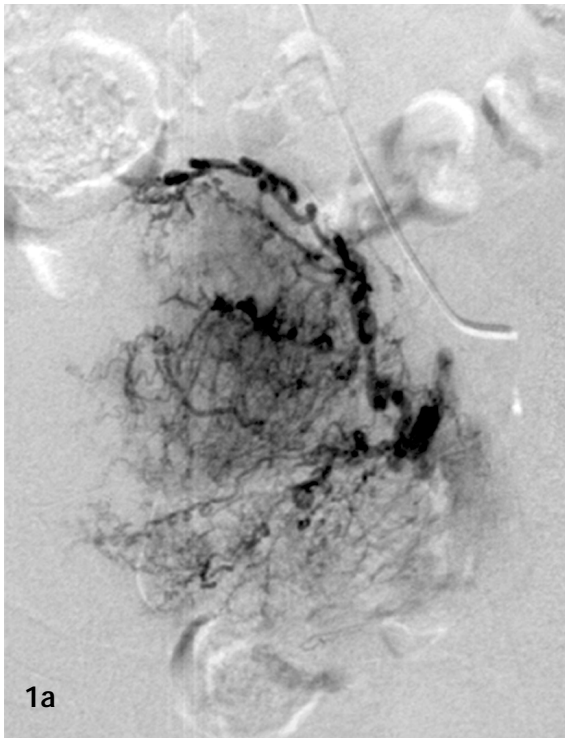


Fig. 1 (a) Digital subtraction angiography of the uterine artery showing abnormal vessels feeding the fibroids. (b) Angiogram after embolisation. The arteries feeding the fibroids were occluded.

biopsies were performed to exclude cervical and endometrial pathology if necessary.

All the women were assessed by a gynaecologist for eligibility to undergo embolisation. Explanation of the procedure, counselling on benefits, risks and alternative treatments were given. Written informed consent was obtained.

Before the procedure, complete blood picture, gonadotrophin levels and clotting profiles were checked. The size and number of the fibroids and volume of the uterus were assessed by magnetic resonance imaging of the pelvis. They were advised to use contraception in the cycle before the procedure. The date of the last menstrual period was confirmed on the day of the procedure, and urine pregnancy test was performed if there was any uncertainty with the dates.

The women were followed up regularly after the procedure and they were asked to fill out questionnaires after three months for symptomatology and to determine whether they were satisfied with the technique. Complete blood picture and gonadotrophin levels were checked at three and six months.

The sizes of the uterus and fibroids were assessed clinically and with MR pelvis before the procedure, and at three and six months. The studies were performed with a Siemens 1.0 T Magnetom Expert machine utilising a phased array body coil. T2 weighted turbo spin echo sequence was used to acquire images in transverse and sagittal planes. The three maximal dimensions (length, width and antero-posterior diameter) of the uterus and the dominant fibroid were measured using the electronic planimetry available with the machine. The volume was calculated by multiplying the products of the dimensions with 0.523, presuming that the uterus and the fibroids were oval.

A single dose of 750 mg cefuroxime (Zinacef, Glaxo Wellcome, Middlesex, England) was administered intravenously as prophylactic antibiotics before each procedure.

Angiography and embolisation via the right femoral artery approach using local anaesthesia were performed on a digital angiographic unit. Four or five Fr Cobra-1 or Sidewinder-1 catheters (Radiofocus, Terumo Corporation, Tokyo, Japan) were used to catheterise both internal iliac arteries in turn. Both uterine arteries were then identified and selectively catheterised and the blood supply to the uterus and fibroids demonstrated on angiography. 300-500 μ m polyvinyl alcohol particles (Contour emboli, Boston Scientific, Medi-Tech Target, Target Therapeutics, Fermont, USA) were used for embolisation of the uterine arteries bilaterally, until stasis or near stasis was achieved (Fig. 1).

During the procedure 0.05-0.1 mg fentanyl (Fentanyl Janssen, Janssen Pharmaceutica, Belgium) intravenously were administered to all except one patient (Table IV). Three women were sedated with 3 - 4 mg midazolam (Dormicum, Roche, Basal, Switzerland) intravenously. Five non-sedated women were given 100 mg indomethacin suppositories (Lifepharm, Milan, Italy). After the procedure, analgesia e.g. intramuscular pethidine (Antigen

Table II. Summary of patient demographic information and presenting symptoms.

Patient no.	Age (years)	Gynaecologic History	Inclusion criteria	Symptoms
1	38	Myomectomy Bowel adhesion Adenomyosis	Wish to retain uterus Bowel adhesion Refuse operation	Pelvic pain Menorrhagia with anaemia Frequency, tenesmus & distension
2	41	Detrusor instability	Wish to retain uterus Refuse operation	Frequency and tenesmus Pelvic mass
3	45	None	Wish to retain uterus	Frequency and distension
4	42	None	Wish to retain uterus Refuse operation	Pelvic pain Menorrhagia with anaemia Frequency & distension
5	40	None	Wish to retain uterus Refuse operation	Frequency
6	44	None	Wish to retain uterus	Frequency & distension Suprapubic mass Menorrhagia with anaemia
7	38	Male infertility No plan for pregnancy	Wish to retain uterus	Pelvic pain Frequency, retention of urine & distension
8	41	None	Refuse operation	Suprapubic mass Pelvic pain Tenesmus and distension
9	32	Chronic rheumatic heart disease with mitral valve replacement on warfarin menorrhagia	Wish to retain uterus	Menorrhagia and anaemia
10	44	None	Refuse operation	Menorrhagia and dysmenorrhoea
11	50	None	Refuse operation	Menorrhagia and anaemia
12	46	None	Alternative to operation	Menorrhagia

Pharmaceuticals Limited, Tipperary, Ireland) were given when they were observed in the ward. The pain was quantified with the use of the visual analogue scale (VAS). The scale range from 0 to 10, with 0 being no pain and 10 being most intense and unbearable pain. The visual analogue scale is a simple and efficient self-report of pain intensity that has no descriptive bias^(9,10).

RESULTS

Twelve Chinese women (aged 32-50 years; mean, 41.8 years) with symptoms related to uterine fibroids were included in this prospective study (Table II). All of them were premenopausal; five were married, and completed childbearing; seven were single, and had not been pregnant before. All wished to retain their uterus and refused operation. One of them had predominantly adenomyosis on MR study. One of the women had metallic-mitral valve replacement for chronic rheumatic heart disease, and hence ultrasound, instead of MRI, was used for pre- and post-treatment assessment. None of them had plans for future pregnancy.

The presenting symptoms of the women are summarised in Table II. The equivalent fundal height

was from 12 to 18 weeks of gestation. All of them had normal luteinising hormone (LH) and follicle stimulating hormone (FSH) levels.

All the 12 women underwent successful bilateral transcatheter uterine artery embolisation. Mild extravasation of contrast from a uterine artery was observed during the procedure in one woman without major consequence. Computed tomography of pelvis was performed immediately and no pelvic haemorrhage was found.

11 of the 12 women experienced pain during embolisation (Table IV). The amount of pain experienced varied. Nine of them were non-sedated and three were sedated. Five of the nine non-sedated women were also given rectal indomethacin; (With indomethacin, VAS: 0, 1, 7, 10 and 10; without indomethacin, VAS: 3, 6, 8 and 9). The three sedated women did not receive indomethacin (VAS: 5, 5, and 8).

They all had satisfactory control of post-procedure pain with systemic analgesia provided. Six women experienced nausea and vomiting during the first two days after the procedure. Three also had low-grade fever and leucocytosis on days 2-3, day three and day five respectively. Three had small amount of blood

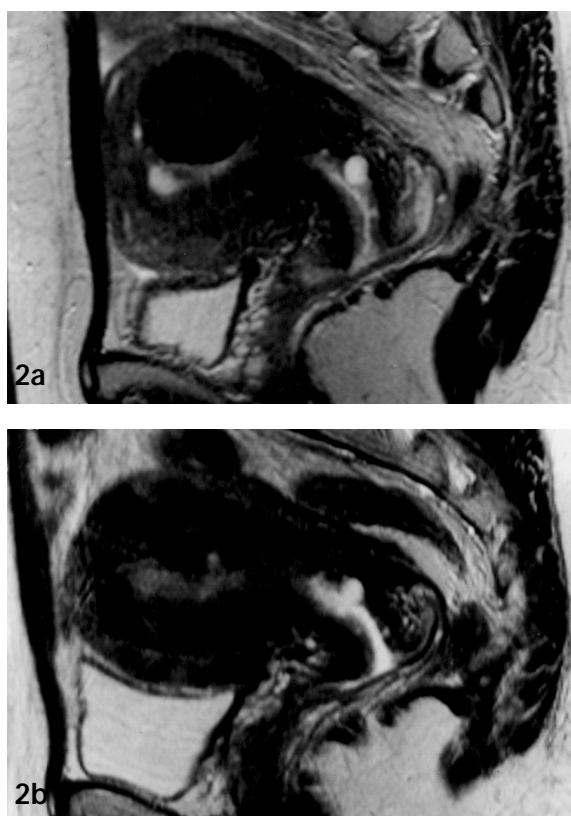


Fig. 2 MR features of uterine fibroid before and after embolization. (a) T2-weighted sagittal image demonstrates a large mural fibroid before embolization. Incidental nabothian cysts are noted in cervix. (b) T2-weighted sagittal image 6 months after the embolization. The size of the fibroid has decreased.

Table III. Presenting symptoms.

Symptoms	No.
Pressure symptoms	8
Frequency & Urgency	7
Menorrhagia	7
Anaemia	5
Pelvic pain	4
Abdominal mass	3
Tenesmus	3

stained vaginal discharge during the first 2-3 days. All these symptoms were self-limiting. No purulent vaginal discharge was observed in any of the women. Fibroid necrosis or severe infection was not found in any of them. The duration of hospital stay ranged from two to seven days (Median 4 days).

For the nine women due for three or six months clinical follow-up, seven women reported noticeable symptomatic improvement during the follow-up. When analysed by symptom type, five of eight women with pressure symptoms improved (3 slightly, 1 significantly, and 1 with complete resolution). Three of the four women with pelvic pain improved (1 slightly,

Table IV. Procedural pain control.

Patient no.	Sedation	Analgescic	Visual analogue scale
1	Midazolam 3mg ivi	Fentanyl 0.1mg ivi	5
2	nil	Fentanyl 0.1mg ivi	3
3	nil	Fentanyl 0.1mg ivi	9
4	Midazolam 4mg ivi	Fentanyl 0.1mg ivi	5
5	nil	Fentanyl 0.1mg ivi	8
6	Midazolam 3mg ivi	Fentanyl 0.1mg ivi	8
7	nil	Fentanyl 0.05mg ivi Indomethacin supp 50mg	1
8	nil	Fentanyl 0.05mg ivi Indomethacin supp 50mg	0
9	nil	Fentanyl 0.1mg ivi Indomethacin supp 100mg	10
10	nil	Indomethacin supp 50mg	10
11	nil	Fentanyl 0.1mg ivi	6
12	nil	Fentanyl 0.1mg ivi Indomethacin supp 100mg	7

1 significantly, and 1 with complete resolution). Three of the four women with menorrhagia improved subjectively (2 slightly and 1 significantly). Significant improvement in haemoglobin level was observed in the two women with anaemia. (Haemoglobin level rising from 7 to 11.3 g/dL and from 8.1 to 12 g/dL). The patient with adenomyosis had significant improvement in pain and menorrhagia subjectively, though the haemoglobin level did not differ.

All of the patients had normal LH and FSH levels during the follow-up.

For those women due for three or six months MRI reassessment (Table V), reductions in dominant fibroid size were observed in six out of the eight women who presented with fibroids. (At three months: mean reduction 41.5%; range 19.6 - 56.5%. At six months: mean reduction 50.3%; range 23.4-79.7%) (Fig. 2).

Reductions in uterine volume was observed in the woman who presented with adenomyosis and uterine enlargement predominantly (Patient no. 1). The reduction was 28.5% at 3 months and 21.5% at six months.

The satisfaction questionnaire showed that seven of the nine women due for clinical follow up had subjective improvement, five reported satisfaction and tolerance to the procedure and agreed to undergo repeated embolization if symptoms recurred and choices of alternative treatments were again available. Seven women agreed that they would recommend this treatment to other women with similar conditions.

Table V. Reduction of dominant uterine fibroid sizes and uterine size* on MRI in the nine women due for 3 or 6 months reassessment.

Patient no.	Pre- treatment Dominant Fibroid volume (ml)	Dominant fibroid volume 3 months (ml)	Dominant fibroid reduction 3 months	Dominant fibroid volume 6 months (ml)	Dominant fibroid reduction 6 months
1*	984.3*	704.0*	28.5%*	772.8*	21.5%*
2	524.5	377.0	28.1%	No follow-up	No follow-up
3	177.0	186.0	-0.1%	183.0	0.0%
4	92.0	40.0	56.5%	18.7	79.7%
5	354.0	284.6	19.6%	271.0	23.4%
6	666.0	260.0	61.0%	233.0	65.0%
7	67.9	31.6	53.5%	36.0	47.0%
8	277.9	192.3	30.0%	176.6	36.5%
Average	393.0		41.5%		50.3%

*This patient had predominantly adenomyosis on MRI. The uterine volume and percentage reduction in size were measured in this case.

DISCUSSION

Uterine fibroid is the commonest tumour of the female genital tract. It is estimated to affect at least 20% of women in reproductive age⁽¹¹⁾. Approximately less than a half of all fibroids are estimated to produce symptoms, which includes pressure symptoms, pain, dysmenorrhoea or menorrhagia⁽¹¹⁾. For decades, hysterectomy and myomectomy have been the standard surgical therapies for symptomatic uterine fibroids. Recently, alternatives such as hysteroscopic and laparoscopic myomectomy have been developed^(12,13). Laparotomy is associated with significant morbidity, while recurrence of fibroids is higher with the laparoscopic approach⁽¹⁴⁾. Hysterectomy becomes inevitable in those patients with recurrence and severe symptoms. Other non-surgical treatments include hormonal treatment such as gonadotrophin releasing hormone analogues⁽¹⁵⁾. However, the inherent side effects of the hormones, and the recurrence of symptoms after cessation of therapy render medical treatment a temporary measure.

Pelvic embolisation has been used in the control of postpartum haemorrhage and treatment of bleeding in gynaecological malignancy⁽¹⁶⁾. In 1995, Ravina et al reported their experience with uterine artery embolisation in the treatment of uterine fibroids^(1,2). Improvement of symptoms had been shown in 14 of the 16 patients treated, with a clinical success rate of 89%. In the series reported by Goodwin et al^(7,8), 81% had moderate or significant improvement in their symptoms. 92% of these patients also had reductions in uterine and dominant fibroid volumes. Overall, the mean uterine and dominant fibroid volume reduction were 42.8% and 48.8%. Several large-scale studies also showed good results and patient satisfaction with very few complications⁽³⁻⁸⁾, though severe injury to the uterus caused by ischaemia or infection was reported in about 1% - 2% of patients.

The effect of uterine artery embolisation in a Chinese population has not been documented. This report describes the results of embolisation treatment in our series of 12 Chinese women with symptomatic fibroids. Seven of the nine patients due for follow up (75%) had subjective improvement. The mean dominant fibroid volume reduction was 41.5% at three months, and 50.3% at six months respectively. No significant complication was found in all women from our series.

Apart from the thorough history and physical examinations, we utilized MRI routinely for pre- and post-procedure imaging evaluation. Compared to ultrasound, MRI is a more objective method to confirm the diagnosis of fibroids. It helps to determine their size and position, and exclude adenomyosis or other conditions. It is less operator-dependent, and allows for more accurate assessment of the uterus and fibroids⁽⁶⁾. Adenomyosis, with symptoms similar to fibroids, is sometimes misdiagnosed as fibroids⁽¹⁷⁾. This together with coincidental adenomyosis, may be possible causes of failure in uterine fibroid embolisation^(8,18). Ultrasound is reported to have a sensitivity of 53% - 89% for adenomyosis where MRI has sensitivity of 88% - 93%⁽¹⁹⁾. Moreover, MRI also helps to depict other pathology in the pelvis, and infarcted fibroids are clearly shown on follow up MRI.

Treatment failures from uterine artery embolisation may result from unrecognised parasitised fibroid feeders. Nikolic et al reported a case of treatment failure, in which additional arterial flow to the leiomyomata arises from the ovarian artery⁽²⁰⁾. Inadequate infarction of the fibroids caused by under-embolisation may result in failure of symptom control in such a case.

Another potential cause of failure to control symptoms is misdiagnosis of the cause of symptoms. Adenomyosis, endometriosis, dysfunctional uterine

bleeding or other conditions may not respond to embolisation. However, adenomyosis may coexist with uterine fibroids in 10% - 20% of patients, and it is very difficult to prospectively make a diagnosis and exclude them from uterine artery embolisation. Even with the use of MRI, the reported specificity for adenomyosis is only 66%-93%⁽¹⁹⁾. In our series, there was one patient with predominantly adenomyosis on MRI. She had a history of fibroid with myomectomy done in 1997, and was found to have bowel adhesion during the operation. The size of the uterus increased subsequently with symptoms of pelvic pain, menorrhagia with anaemia and pressure. She was considered to be of high surgical risk in the presence of bowel adhesion. She had significant improvement in pain and menorrhagia subjectively after uterine embolisation. Reduction in uterine volume was observed on MRI. There is report on a case of clinical failure of uterine fibroid embolisation due to adenomyosis, despite pathologic evidence of completely infarcted fibroids⁽¹⁸⁾. Further studies on adenomyosis as a cause of treatment failure are required.

One concern about the embolisation procedure is the radiation exposure. Nikolic et al⁽²¹⁾ reported that the mean estimated absorbed ovarian dose during the procedure was 22.34cGy. It is about 30 - 100 times higher than those during conventional diagnostic radiographic examinations, and 12 - 30 times lower than those during radiation therapy for Hodgkin disease of the pelvis⁽²¹⁻³⁰⁾. It is unlikely to result in acute or long-term radiation injury or genetic risk to the patient, on the basis of the known risks of pelvic irradiation for Hodgkin disease^(21,31). Meticulous attention has to be paid to reduce the radiation dose to the patient. Apart from good collimation of the x-ray beam, reduction of the exposure time is also very important. The latter mainly depends on the time needed to catheterise both uterine arteries, and this in turn depends on the experience of the radiologists. All of the radiologists performing this procedure were experienced intervention radiologists and they encountered no technical failure in catheterising both uterine arteries.

The effect of uterine artery embolisation on ovarian function is unclear. There are reports on the hypervascularity of the leiomyomatous uteri, with collaterals between the uterine artery to the ipsilateral ovarian artery, and contralateral ovarian and uterine artery^(32,33). Consequently non-target embolisation of the ovaries is possible during the procedure, and may result in ovarian infarction and subsequent menopause. There are reports on transient and permanent amenorrhoea after uterine artery embolisation^(4,6,34). The incidence of permanent amenorrhoea is less than 2%. It is unclear whether the

amenorrhoea is a sporadic event, as most candidates for the treatment were in their 4th or 5th decade near menopause; or whether there may be effects on ovarian function clinically apparent in few patients. On the other hand, the effect on future fertility and childbearing is also unknown. There are reports on successful pregnancy after the procedure^(2,4), though the pregnancy rate cannot be assessed as most studies do not recruit patients who desire future pregnancy. It is also not known how many patients treated with uterine artery embolisation have attempted to become pregnant. Even if an apparent lower pregnancy rate is shown, it might be difficult to determine whether it is solely due to the effect of the embolisation, as fibroids and any previous myomectomy may also affect the rate of successful pregnancy. In our series, all the women were in the 4th and 5th decades and had no plans for future pregnancy. All had normal LH and FSH levels during the follow-up. Longer follow-up, and further study of ovarian blood supply and physiologic response of the ovaries before and after the procedure is required to assess the possible effect on ovarian function.

CONCLUSION

Transcatheter uterine artery embolisation is an effective alternative treatment for patients with symptomatic fibroids. Symptomatic and radiological improvement were also observed in the one who presented with symptomatic adenomyosis. With adequate analgesia, the procedure may be performed without general anaesthesia, and even without sedation. As the impact on fertility is still unknown, longer follow up and prospective fertility study are required to evaluate the long term effects before this procedure could be safely extended to younger age groups.

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