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Laparoscopic Transient Uterine Artery Occlusion and Myomectomy for Symptomatic Uterine Myoma as an Alternative to Hysterectomy

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Additional information is available at the end of the chapter

Abstract

Objective: To compare the clinical outcomes of laparoscopic transient uterine artery ligation plus myomectomy (LTUAL) to simple laparoscopic myomectomy (LM) for symptomatic myomas.

Methods: A comparative observational study was adopted; 167 patients with a diagnosis of symptomatic uterine myoma were retrospectively observed. And 84 patients underwent LTUAL and LM, 83 patients underwent LM only. Operative time, blood loss, gonadal hormone level, uterine artery resistance index, menorrhagia, pregnancy rate, and recurrence rate of myoma were evaluated.

Results: The intraoperative blood loss in the LTUAL group was lower than in the LM group. The menstrual blood volume (MBV) and the menstrual period of the LTUAL group were unchanged after operation relative to the prediseased volume. No significant difference was found in the resistance index of the uterine artery blood flow, the recurrence rate, and the fertility rate between the LTUAL and the LM groups.

Conclusions: LTUAL and LM are a promising surgical treatment for symptomatic uterine myoma and did not produce any appreciable adverse effect on fertility.

Keywords: Laparoscopic, Uterine artery occlusion, Myomectomy, Uterine myoma

1. Introduction

Uterine myomas are the most common benign tumor of the female reproductive system. It is estimated that they occur in up to 35% of women 35 years of age [1]. Most of these myomas are asymptomatic, although some may cause symptoms that require a definite treatment. Approximately 30% of women with myomas have been reported to have menstrual abnormalities, most often menorrhagia. Dysmenorrhea also may occur. Acute pain can occur with red degeneration, necrosis, and torsion of a pedunculated myoma. Large myomas can also stimulate urinary tract compression, resulting in symptoms such as urinary frequency and urgency. Myomas may also cause infertility and miscarriage [2].

There are many therapeutic strategies, but the management of women with symptomatic uterine myomas depends on the patient's age, the reasons for treatment, the issue of fertility preservation, and the patient's preference. Although hysterectomy has long been considered a good choice if women have completed childbearing, there are many other therapeutic approaches available for preservation of the uterus, because psychologically, the uterus has been regarded as the regulator and controller of important physiologic functions, a sexual organ, a source of energy and vitality, and a maintainer of youth and attractiveness. Some of these therapies include uterine artery embolization (UAE), MRgFUS (magnetic resonance-guided focused ultrasound surgery), and ultrasound-guided ablation (VizAblate™ [Gynasonics, Redwood City, CA, USA] and Acessa™ [Halt Medical, Inc., Brentwood, CA, USA] procedures). The standard treatment for symptomatic uterine fibroids has always been myomectomy. Myomectomy has been traditionally performed by laparotomy, but over the past decade, laparoscopic and hysteroscopic techniques have been developed. The surgery can now be performed laparoscopically and hysteroscopically. Laparoscopic surgery has seen significant improvement in its techniques and instruments, and has been developed and used in the management of various kinds of benign diseases. Although some concerns about the role of laparoscopic myomectomy (LM) as a treatment option for symptomatic uterine myomas are still present, it is still widely used for symptomatic subserosal fibroids and can even be used for intramural fibroids, depending on the position of the fibroid and the skills of the surgeon. Many comparison studies have evaluated the safety and feasibility of abdominal myomectomy and LM [3]. These studies showed that LM is clearly associated with shorter hospitalization, faster recovery, less expense, less pain, less blood loss, less fever, and fewer surgical complications compared with abdominal myomectomy. Pregnancy rates and recurrence rates appear to be comparable between LM and abdominal myomectomy [3]. Therefore, the use of LM can be considered as one of the choices in the management of women with symptomatic uterine myomas.

Myomectomy is a challenging procedure for gynecologists and can result in excessive blood loss. In general, it is suitable only for patients who have a few relatively small myomas or myomas that are primarily below the serosa [4]. The relative contraindications of LM include a history of multiple, large, intrauterine wall myomas [5]. With recent technique advances, LM can be performed as the treatment for relatively large uterine fibroids. However, the challenges

of increased operation time and the high risk of blood loss still remain [6]. Several methods to control blood loss during LM are available, including the use of dilute vasopressin, hypotensive anesthesia, and administration of GnRH agonists. Until now, there is no single method to completely control intraoperative blood loss and prevent postoperative exudation from the uterine incisional wound.

Recently, a major development in overcoming this problem is the laparoscopic uterine artery occlusion (LUAO) [7], which was introduced in 2001. This procedure can result in remarkably decreased blood loss in LM [8], and it has expanded the application of LM greatly, such as the large, multiple, and deep myomas located in the uterus. However, the possible side effects of LUAO, such as the increased abortion rate and preterm delivery [9, 10], lack further verification in literature. As a result, we have developed a new approach to LUAO: laparoscopic transient uterine artery ligation (LTUAL). In this study, we attempt to elucidate this new approach and evaluate the possible results of LTUAL and LM on outcomes such as ovary function, recurrence rates, and fertility compared with traditional LM.

2. Materials and methods

2.1. Patients

A comparative observational study was adopted. Between January 1, 2006, and June 31, 2008, 167 patients with a diagnosis of symptomatic uterine myoma and who were hospitalized at Southwest Hospital in Chongqing, China, for LM were enrolled in this study.

Per the inclusion criteria, all patients had symptoms attributable to myomas, including menorrhagia, bulge sensation, pain, and urinary frequency, with the most common being menorrhagia. The diagnosis was confirmed by ultrasonography or computed tomography scan. All the patients preferred not to undergo a hysterectomy. The exclusion criteria eliminated women who were older than 43 years or had an additional gynecologic disease such as adenomyoma, genital malignant tumor, genital malformation, premature ovarian failure, polycystic ovary, fallopian tubes adhesion or imperforation, or sactosalpinx. Women whose husbands had abnormal results of the seminal fluid test were also excluded.

The institutional review board of our institution approved the study, and all participants provided written informed consent before entry. All patients in this study were thoroughly notified of the benefits, curative effects, potential risks, and uncertain fertility issues related to uterine artery occlusion. Eighty-four patients who accepted LTUAL were placed in the LTUAL group and treated with LTUAL and LM. Eighty-four patients who refused LTUAL were placed in the LM group and received LM only. There was no difference in the age, the body mass index, the maximal diameter, and the location and number of myomas between the two groups (Table 1).

| Characteristic | LTUAL (n = 84) | LM (n = 83) | <i>P</i> value |
|------------------------------------|-------------------|------------------|----------------|
| Age, y | 32.5 (25–43) | 32 (26–43) | 0.936 |
| Body mass index, kg/m ² | 22.65 (18.1–27.7) | 23.1 (18.4–27.1) | 0.927 |
| Pregnancy history, n | | | |
| Nullipara | 52 (61.9%) | 59 (71.1%) | |
| Multipara | 32 (38.1%) | 24 (28.9%) | |
| Symptoms, n | | | |
| Menorrhagia | 61 (72.6%) | 56 (67.5%) | 0.468 |
| Bulge sensation | 52 (61.9%) | 48 (57.8%) | 0.591 |
| Pain | 19 (22.6%) | 30 (36.1%) | 0.055 |
| Urinary frequency | 16 (19.0%) | 21 (25.3%) | 0.331 |
| Myomas | | | |
| Diameter, cm | 5.8 (3–12) | 5.9 (3–11) | 0.504 |
| Location, n | | | 0.973 |
| Subserous | 22 (26.2%) | 20 (24.1%) | |
| Intrauterine wall | 32 (38.1%) | 28 (33.7%) | |
| Submucosal, n | 7 (8.3%) | 9 (10.8%) | |
| Multiple, n | 23 (27.4%) | 26 (31.3%) | |
| Average multiple number | 4 (2–13) | 3.5 (2–8) | 0.87 |

Table 1. Basic characteristics of the enrolled women.

2.2. Operative procedures

All procedures were performed under general endotracheal anesthesia. The LTUAL technique was performed like the LUAO previously described [7], except that the uterine artery was transiently ligated by a slipknot with a surgical silk suture. The successful artery ligation could be confirmed as previously described [8]. Next, the LM progress was performed as previously described [8]. Last, the slipknot was removed and the uterine arteries were recanalized. Finally, the fallopian tube perfusion test was performed to exclude patients with broken uterine walls or obstructed fallopian tubes. Blood loss was estimated by calculating the blood volume of the suction machine during surgery.

2.3. Follow-up method

The follow-up time ranged 10–40 months. The routine time of interview was 3 and 6 months and at 1, 2, and 3 years after the operation or at any time if any problems arose. All patients were advised to engage in contraceptive measures by the use of condoms for 24 months. After this period, women were free to seek conception.

2.4. Assessment of menstrual patterns

To evaluate the effect of LTUAL on menorrhagia, a questionnaire was sent to each of the patients when compiling their case history. The number of menstrual pads used by each woman was recorded during three menstrual cycles: before the diseased state, during the disease, and after surgery. We set a value of 1 for the menstrual blood volume (MBV) index for the prediseased period for each patient. The diseased MBV index is equal to the number of menstrual pads used during the diseased period divided by the number of menstrual pads used before the diseased period. Once regular menorrhagia recovered at least for 6 months following the operation, the postoperation MBV index was recorded as the diseased MBV index. Because the MBV during the diseased state was mostly irregularly increased in the presence of myomas and was inconsequential for the evaluation of the single effect of LTUAL, we decided to abandon this index. The only comparison was made for the two periods: before the disease occurred and postoperation.

2.5. Recurrence assessment

All patients received an ultrasound examination 3 months after the operation to confirm the effectiveness of the procedure and to exclude the patients with residual myomas; they also received an ultrasound examination at each routine interview. The recurrence was defined when uterine myomas, with a minimum diameter of 0.5 cm, were found in patients without residual myomas.

2.6. Statistical analysis

SPSS 11.5 (SPSS, Inc., Chicago, IL) was used for statistical analysis. Data are presented as mean \pm SD, number (%), and median (range). The difference in means between the groups was tested by using an ANOVA test, if the variable under comparison was not normally distributed. The rank sum test was used. The categorical variables are presented as percentages, and were compared using χ^2 tests or Fisher's exact tests. $P < 0.05$ was considered statistically significant.

3. Results

All 167 patients underwent laparoscopic operations successfully without intraoperative complications, with no cases converting to laparotomy. In the LM group, one patient experienced a 4-hour operation and lost 600 ml of blood during surgery, which necessitated a blood transfusion; later, a wound infection developed, and the patient stayed in the hospital for 21 days for intravenous fluid and antibiotic therapy. Five patients in the LM group received blood transfusions during or after the operation. Two patients in the LTUAL group and four patients in the LM group suffered from urinary tract infections. In addition, one patient in the LTUAL group and four patients in the LM group had a high fever (body temperature $> 38.5^\circ\text{C}$) for more than 3 days and stayed in the hospital for antibiotic therapy for 1 week. There were no severe complications such as ureter, bladder, or bowel injury during the perioperative period. All

pathologic examinations documented the presence of uterine leiomyomas. There was no statistical difference in the average operation time between the LTUAL and the LM groups ($P=0.41$). The transient ligation time in the LTUAL group ranged 55–155 minutes, and the median time was 98.5 minutes. Blood loss was significantly lower in the LTUAL group than in the LM group ($P<0.01$). The mean postoperative hospital stay was 3.8 days (range, 3–21 days).

The results of the menorrhagia assessment are given in Table 2. The MBV, menstrual period, and menstrual cycle were unchanged after surgery in the two groups compared with before the disease occurred ($P>0.05$).

| | LTUAL | LM |
|-----------------------------------|-------------|-------------|
| Volume rank (before disease) | 1.00 ± 0.00 | 1.00 ± 0.00 |
| Volume rank (after surgery) | 1.00 ± 0.00 | 1.00 ± 0.10 |
| <i>P</i> | 0.071 | 0.316 |
| Menstrual period (before disease) | 5 ± 1 | 5 ± 1 |
| Menstrual period (after surgery) | 5 ± 1 | 5 ± 1 |
| <i>P</i> | 0.227 | 0.091 |
| Menstrual cycle (before disease) | 28 ± 2 | 29 ± 3 |
| Menstrual cycle (after surgery) | 28.5 ± 2 | 29 ± 2 |
| <i>P</i> | 0.782 | 0.326 |

Table 2. Menorrhagia evaluation (median ± interquartile range).

The uterine artery resistance index (RI) was also tested. There was no statistical difference found between the two groups each time, at the preoperative period, and at 3 days, 6 months, and 12 months after surgery in each group ($P>0.05$; Table 3).

| Period | LTUAL (n = 84) | LM (n = 83) | <i>P</i> value |
|----------------|-------------------|-------------------|----------------|
| Before surgery | 0.73 (0.48–0.90) | 0.71 (0.50–0.88) | 0.156 |
| After surgery | | | |
| 3 days | 0.705 (0.49–0.87) | 0.69 (0.53–0.89) | 0.744 |
| 6 months | 0.69 (0.48–0.89) | 0.695 (0.47–0.88) | 0.466 |
| 12 months | 0.69 (0.48–0.87) | 0.70 (0.49–0.86) | 0.882 |

Table 3. Comparison of uterine artery resistance index.

Recurrence rates following the different procedures were examined next. There were six cases confirmed with residual myomas by ultrasonography 3 days after the operations, and these cases were excluded from those subjected to recurrence follow-up for the interference of the

recurrence assessment. The data from the remaining the cases were collected and are presented in Table 4. There was no statistical difference between the LTUAL group and the LM group ($P=0.237$).

The fertility evaluation is presented in Table 4. In the LTUAL group, 31 patients were still using contraception at the 2-year follow-up, and five of the remaining 53 patients have consistently used contraception 2 years later. In the remaining 48 patients seeking pregnancy, the outcomes were as follows: one patient had an ectopic pregnancy that was later subjected to treatment by methotrexate; 15 patients conceived normally, and of these, 9 patients proceeded to full-term pregnancy. In the LM group, 28 patients were still using contraception at the 2-year follow up; 13 patients were currently still using contraception 2 years later. Among the remaining 42 patients attempting to become pregnant, miscarriage occurred in two patients and 16 patients had a normal pregnancy (Table 4), half of whom carried a baby to full-term. There was no statistical difference between the LTUAL and the LM groups ($P=0.495$).

| | LTUAL (n = 84) | LM (n = 83) | <i>P value</i> | OR (95% CI) |
|-----------------------------|-----------------------------|-----------------------------|----------------|---------------------|
| Operation duration, min | 121.92 ± 18.48 ^a | 126.33 ± 27.13 | 0.313 | — |
| Blood loss, ml ^b | 75 (40–190) | 170 (100–600) | 0.001 | — |
| Recurrence, n | 16/82 (19.51%) ^c | 10/79 (12.66%) ^c | 0.237 | 1.673 (0.708–3.950) |
| Pregnancy, n | 15/48 (31.25%) ^d | 16/42 (38.10%) ^d | 0.495 | 0.739 (0.309–1.767) |

Note: OR = odds ratio; CI = confidence interval.

^a Mean ± SD.

^b Precise scale = 5 ml.

^c Patients with residual myomas were excluded.

^d Patients still using contraception were excluded. Total number of women included those who were no longer using contraception and were seeking pregnancy.

Table 4. Surgical parameters and recurrence, pregnancy follow-up data.

4. Discussion

During LM, failure of hemostasis is the primary factor resulting in conversion to laparotomy [11]. However, this problem was addressed by the introduction of LUAO: Liu et al. [7] reported LUAO as a new method for treating symptomatic myomas, but they used this technique as a primary treatment without proceeding to myomectomy, and the recurrence rate was reported as 28.4% within the 4-year follow-up period [12]. In our previous study [8], this technique was used as a supplement for LM first, with the uterine arteries being blocked while the myomas were completely removed. This technique resulted in a remarkable blood loss in the operation and a low recurrence rate, but possible side effects in uterine or ovarian function, especially long-term effects on fertility, need further study.

Because of the possible side effects of LUAO on fertility [9, 10], we developed LTUAL to be used in patients who wish to comply after a thorough explanation of the pros and cons of the procedure. This discussion allowed for the evaluation of the effects of LTUAL on menorrhagia, fertility, and the recurrence rates of myomas.

In this study, LTUAL decreased intraoperative blood loss remarkably compared with LM. With the critical problem being tackled, we were able to conduct LM for large, multiple, intrauterine wall and especially submucosal myomas. There was no difference in the duration of the operation between the two groups, because in our experience, LTUAL can be performed within 10 minutes by an experienced gynecologist. However, in the LM group, more time is usually spent trying to maintain the hemostasis of the sutured wounds of the uterine cavity.

A problem related to this study may be the ligation time of the uterine artery. Traditional uterine tourniquets are usually best used for no more than 1 hour [13] to avoid irreversible damage to the uterine myometrium and the risk of embolic events. Although a review showed no embolic phenomena after detorsion in ischemic necrotic twisted adnexa [14], Wang et al. [15] used average occlusion periods of approximately 2 hours without any complications. Our experience would suggest that the occlusion period of the uterine arteries is not a considerable problem because of the intact ovarian and vaginal ascending arteries, which compose part of the triple-extrinsic uterine blood supply system. At the least, our transient ligation period (97.93 ± 19.08 minutes) was verified to be harmless to the myometrium and did not induce any complications.

By the assessment of unchanged uterine RI, menstrual pattern, and the recurrence of myomas, we thought the LTUAL interfered minimally with ovary function, uterine myometrium, and the uterus status, which were important for fertility.

Because of deficiencies associated with our laboratory, we had to study ovarian function indirectly by the indices of uterine artery RI and the menorrhagia change. First, the blood supply of the ovary is the main factor that influences ovarian function. In this type of surgery, the ovarian vessels were untouched; the only operation that could disturb the ovarian blood supply was the LTUAL, because the uterine artery is one of the ramus anastomoticus of ovarian blood supply. We found no differences of the uterine artery RI between the two groups and between different periods. As a result, we verified that the blood supply in the ovaries was not disturbed by LTUAL. Second, no differences in menorrhagia were found between the prediseased state and the postoperative state in the LTUAL and LM groups, so we inferred that LTUAL had minimal interference on ovary function. In our previous study [8] and in the recent literature [12, 16, 17], the recurrence rate using LUAO was low and markedly lower than that reported for abdominal myomectomy and LM [18, 19, 20]. The decreased blood supply to the uterus induced gradual necrosis of the myomas. Lee et al. [21] found a markedly decreased RI index 4 months after LUAO compared with that before surgery. Other similar researches [22, 23] found a shrinking of myomas after LUAO and confirmed that apoptosis was the primary mechanism by which this occurred [23]. In contrast, the recurrence rates appear to be no different between the LTUAL and the LM groups. Thus, minimal interference of LTUAL on the uterine artery and uterine status is confirmed by unchanged menorrhagia and recurrence rate of myomas.

In this study, the gestation rate of patients was evaluated over a 16–36 months follow-up. No difference was found between the LTUAL and the LM groups on the gestation rate, and some patients gave birth to full-term babies; therefore, there is no statistical proof that the LTUAL has any side effect on fertility.

Moreover, the reduced adhesion formation following laparoscopy is another benefit for fertility of these patients. For laparotomy, the postoperative rate of adhesions, which are the most probable risk for infertility, is high (80%) [24]. It has been hypothesized that laparoscopic surgery, by maintaining hemostasis and minimizing peritoneal trauma and inflammation [25], may result in reduced adhesion formation following abdominal and pelvic surgery [26–29]. This lack of adhesions could theoretically help to diminish the risk of infertility. Therefore, we consider LTUAL to be a promising method in patients who wish to preserve fertility.

5. Conclusion

LTUAL preceded by LM provides several benefits to patients and is more in accordance with the modern medical opinion regarding the preservation of the uterus and with limited side effects on ovarian function and fertility. In addition, the procedure is preferable in patients who wish to undergo future pregnancies. However, LTUAL plus LM cannot decrease the recurrence rate of myomas. It must be emphasized that this study was limited by the lack of randomization, and on the basis of this a more rigorous and detailed study should be undertaken. We strongly suggest that a randomized controlled trial is a next step for further verification and discussion.

Nomenclature

LM; laparoscopic myomectomy

LUAO; laparoscopic uterine artery occlusion

LTUAL; laparoscopic transient uterine artery ligation

MBV; menstrual blood volume

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