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The effect of temporary uterine artery ligation on laparoscopic myomectomy to reduce intraoperative blood loss: A retrospective case–control study

Daiki Hiratsuka, Wataru Isono *, Akira Tsuchiya, Asuka Okamura, Akihisa Fujimoto, Osamu Nishii

Department of Obstetrics and Gynaecology, University Hospital Mizonokuchi, Teikyo University School of Medicine, 5-1-1, Futago, Takatsu-Ku, Kawasaki, Kanagawa 213-8507, Japan

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ABSTRACT

Objective: To reduce intraoperative blood loss in laparoscopic myomectomy, uterine artery occlusion or temporary uterine artery clipping have been employed. Recently, in addition to these techniques, temporary uterine artery ligation has been reported as a new method that has less invasive effects on fertility and needs no special devices to be used. This study aimed to evaluate the effect of temporary uterine artery ligation to minimize intraoperative blood loss during laparoscopic myomectomy.

Study Design: This was a retrospective case-control study at the department of Obstetrics and Gynaecology, University Hospital Mizonokuchi, Teikyo University School of Medicine. A total of 264 patients with uterine leiomyoma who underwent laparoscopic myomectomy were enrolled in this study. We divided the patients into two groups, those who underwent temporary uterine artery ligation (52 patients) and those who did not (212 patients) and compared the operation time, blood loss volume, and other indexes. Second, to identify influential factors, we assessed the effects of 11 representative factors on massive blood loss or a prolonged operation time using multivariate analysis.

Results: The intraoperative blood loss volume was decreased by approximately half with the addition of temporary uterine artery ligation (75.1 ± 73.6 ml vs. 158.5 ± 233.2 ml, $p = 0.011$), but the operation time was longer (200.5 ± 46.9 min vs. 160.1 ± 51.3 min, $p < 0.001$). Among the 264 patients, 25 patients (9/52 in the case group and 16/212 in the control group) had a prolonged operation time (≥ 240 min), and 24 patients (1/52 in the case group and 23/212 in the control group) experienced massive blood loss (≥ 400 ml). In the multivariate analysis, high body mass index, concomitant surgery and temporary uterine artery ligation showed a positive association with a prolonged operative time, and the presence of single leiomyoma showed a negative association. Concomitant surgery and the presence of large leiomyoma showed a positive association with massive blood loss, and temporary uterine artery ligation showed a negative association.

Conclusions: By performing temporary uterine artery ligation during laparoscopic myomectomy, the volume of intraoperative blood loss could be decreased, especially in patients with large leiomyomas. However, because this procedure prolongs the operation time, there is still room for improvement.

1. Introduction

Uterine leiomyomas are the most common oestrogen-dependent benign tumours in women of reproductive age [1–4]. Since even relatively small uterine leiomyomas can cause symptoms such as hypermenorrhoea, decreased fertility, and increased miscarriage, myomectomy is the most popular treatment for women who desire to preserve their fertility. Currently, except for hysteroscopic myomectomy (HM) for submucosal leiomyoma, laparoscopic myomectomy (LM) has become the most popular treatment because of several advantages,

List of abbreviations: HM, hysteroscopic myomectomy; LM, laparoscopic myomectomy; TUAL, temporary uterine artery ligation; LC, laparoscopic cystectomy; HP, hysteroscopic polypectomy; OR, odds ratio; CI, confidence interval; GnRH, Gonadotropin releasing hormone; MRI, Magnetic resonance imaging.

* Corresponding author.
E-mail address: tetuken2010@gmail.com (W. Isono).

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Table 1
Patient characteristics.

Characteristic	Average ± SD (Minimum - Maximum), Number
Age	**37.2 ± 4.8 (22–48), n = 264**
Body mass index (kg/m^2)	**21.9 ± 3.5 (15.7–35.4), n = 264**
Parity	**0.2 ± 0.5 (0–3), n = 264**
Operation time (minutes)	**168.0 ± 52.9 (61–311), n = 264**
Blood loss (ml)	**142.1 ± 214.0 (0–2150), n = 264**
Size of dominant leiomyoma (cm, by MRI)	**7.1 ± 2.5 (2–18), n = 264**
Weight of resected leiomyoma (g)	**148.7 ± 134.4 (2–940), n = 253**
Number of resected leiomyomas	**3.2 ± 3.0 (1–22), n = 264**
Size of resected dominant leiomyoma (cm)	**6.1 ± 2.1 (1–16), n = 264**
Type of dominant leiomyoma	
Submucosal leiomyoma	**n = 19**
Subserosal leiomyoma	**n = 61**
Intramuscular leiomyoma	**n = 184**
Location of dominant leiomyoma	
Anterior wall	**n = 131**
Posterior wall	**n = 126**
Fundus	**n = 1**
Lateral wall	**n = 2**
Cervix	**n = 4**
Symptoms	
Menstrual disorder	**n = 162**
Abdominal abnormality	**n = 62**
Infertility	**n = 41**
No symptoms	**n = 32**
Adhesion/Endometriosis	**n = 76**
Endometriosis positive	**n = 64**
Endometriosis negative	**n = 12**
Gynaecological operation history	**n = 21**
Endometrium perforation	**n = 52**
Preoperative Hb level (g/dL)	**12.9 ± 1.2 (7.5–15.2), n = 264**
Postoperative Hb level (g/dL)	**10.7 ± 1.1 (7.5–13.6), n = 264**
Autologous blood donation	**n = 145**
Blood transfusion	**n = 23**

The representative patient characteristics that were obtained from the medical records are summarized in this table. For each item, we calculated the averages and standard deviations, the minimal and maximal values, and the count data from the medical records. The weight of the resected leiomyoma was defined as the total weight of the resected leiomyoma. The number of resected leiomyomas and the size of resected dominant leiomyomas were measured during the operation. The size of the leiomyoma was determined by the maximal diameter. In some cases, multiple symptoms occurred in a single patient.
Abbreviations: Avg.: Average, SD: Standard deviation, Min.: Minimum, Max.: Maximum, BMI: Body mass index, MRI: Magnetic resonance imaging.

including superior aesthetic results, faster recovery and a shorter hospital stay [5,6]. However, when treating large and multiple leiomyomas, it may be difficult to control the amount of bleeding that occurs during LM [7]. Therefore, surgeons may perform procedures to minimize bleeding and ensure that LM can be performed safely. Uterine artery occlusion, during which bilateral uterine arteries are permanently coagulated or ligated, is one way to minimize bleeding during LM [8–11]. However, it remains unclear whether permanent uterine artery occlusion causes infertility or perinatal complications [8–11]. To address patient concerns about infertility or perinatal complications, we developed the Temporary uterine artery ligation (TUAL) technique to block the uterine blood supply, which is a new method that can be used to prevent massive intraoperative bleeding. TUAL may be less invasive than "permanent" uterine artery ligation. Additionally, the use of special devices is unnecessary for this procedure because only multifilament sutures are used, unlike during temporary uterine artery clipping [12–15]. Therefore, in this report, we introduce our TUAL technique and analyse the effect of this procedure on patients who underwent LM.

2. Methods

2.1. Data collection and statistical analysis

This study was reviewed and approved by the Human Ethical Committee of the University of Teikyo Hospital (Trial registration number: 20–094). The deidentified medical records of 264 female patients who underwent LM from October 1, 2016, to March 31, 2022, were reviewed retrospectively. Of these patients, 52 patients underwent TUAL to prevent massive blood loss during LM. This study also included 45 patients with concomitant surgeries, including laparoscopic cystectomy (LC) (n = 27), HM (n = 9), hysteroscopic polypectomy (HP) (n = 8), laparoscopic salpingo-oophorectomy (n = 2), laparoscopic adenomyomectomy (n = 1) and laparoscopic salpingostomy (n = 1). Among the 264 patients, we extracted the pertinent patient characteristics, operation time and blood loss volume, which are further described below. The statistical analyses were performed using JMP version 12 for Windows (SAS Institute, Inc., Tokyo, Japan) to determine the correlations between the patient characteristics and the surgical complications. The odds ratios (ORs) and 95% confidence intervals (CIs) were estimated to determine the strengths of the correlations. Results with a p value of < 0.05 were considered statistically significant.

2.2. Patient characteristics and analysis methods

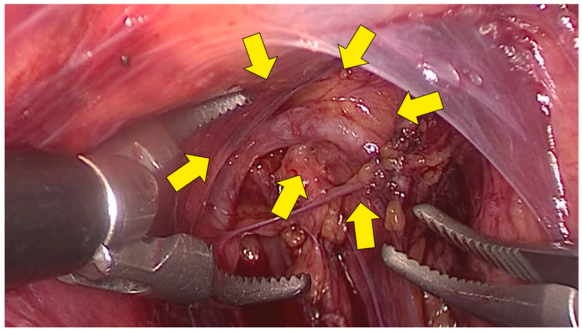
Patient characteristics (shown in Table 1) were obtained from the medical records. First, to identify the effect of performing the concomitant TUAL procedure during LM, we divided all of the patients into two groups, namely, 52 patients who underwent TUAL with LM and 212 patients who did not. The operation time, blood loss volume and other patient characteristics were compared between the two groups using Student's t test.

Second, to detect the factors that affect the difficulty of LM (while controlling for confounding factors), we divided the patients into two groups according to the presence or absence of each factor and performed a multivariate logistic regression analysis. To compare the difficulty of LM, we defined difficult cases as the cases in which the operation time exceeded 240 min (long operation time, 25 cases) or when the intraoperative blood loss exceeded 400 ml (massive blood loss, 24 cases). These values were determined by the averages that were calculated in the 264 patients. Among the 264 patients who underwent LM, we assessed the influence of the following 11 factors: 1) High BMI, defined as a body mass index (BMI) $\geq$ 25 (kg/m^2); 2) Nulliparity, defined as no previous delivery; 3) Gynaecological surgical history; 4) Concomitant surgery, defined as concomitant LC, HM or HP, or other surgery; 5) Single leiomyoma; 6) Large leiomyoma, defined as a dominant leiomyoma with a size $\geq$ 8 cm, as determined by magnetic resonance imaging (MRI); 7) Abdominal adhesion/endometriosis, defined as the presence of abdominal adhesions or endometriosis that was detected by laparoscopic inspection immediately after the start of surgery; 8) Menstrual disorder, defined as hypermenorrhoea or dysmenorrhea; 9) Abdominal pressure, defined as the presence of abdominal pain, frequent urination, constipation or other symptoms; 10) Infertility; and 11) TUAL, defined as a concomitant procedure used to bind the uterine artery. The criteria for a large leiomyoma were determined based on past reports [16,17]. High BMI was defined was according to the Japanese definition of obesity, which is a BMI $\geq$ 25 (kg/m^2) [18].

2.3. Temporary uterine artery ligation procedures

As previously described [19], the basic procedures of LM were performed according to the following steps: 1) An umbilical trocar (12 mm) and three lower abdominal trocars were placed to access the abdominal and pelvic cavities; 2) diluted vasopressin was injected, and a horizontal incision was made using an ultrasonic scalpel; 3) the leiomyomas were then enucleated; 4) two to three layered sutures were placed; and 5) the

(a) The right uterine artery was identified and isolated from the anterior branch of the internal iliac artery.



(b) The right uterine artery was ligated with a multifilament suture. The arrow shows the right uterine artery.

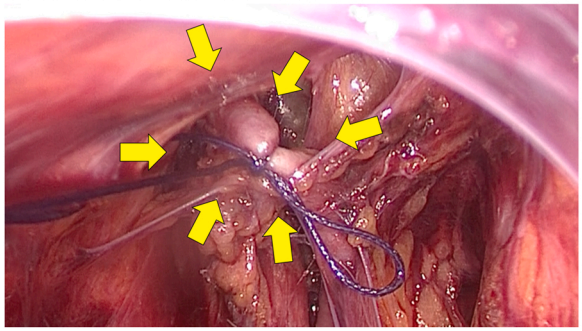


Fig. 1. Temporary uterine artery ligation during the surgical procedure. (a) The right uterine artery was identified and isolated from the anterior branch of the internal iliac artery. (b) The right uterine artery was ligated with a multifilament suture. The arrow shows the right uterine artery.

leiomyomas were removed by using an electrical morcellator or with trans umbilical manual morcellation. In some cases, other laparoscopic and/or hysteroscopic procedures were also performed. All operations were performed under the direct supervision of at least one of two physicians (A.F. and O.N.) who are highly skilled laparoscopy specialists and are accredited by the Japan Society of Gynaecologic and Obstetric Endoscopy and Minimally Invasive Surgery.

Since 2020, temporary ligation of both uterine arteries has been performed by binding the uterine arteries in some cases, and this is a method for blocking the uterine blood supply without the need for vasopressin injection. At the beginning of the surgery, both uterine arteries were identified, as they run parallel to the ureter, and were isolated from the anterior branch of the internal iliac artery by retrograde tracking of the umbilical ligament (Fig. 1a). This procedure was similar to the technique used in total laparoscopic hysterectomy [20]. These arteries were ligated by using multifilament sutures (1–0 vicryl, Johnson and Johnson Co., LTD, Tokyo, Japan) (Fig. 1b). At the end of the surgery, the sutures were removed.

3. Results

3.1. Patient characteristics

As shown in Table 1, the average age, BMI, and parity of the included patients were 37.2 ± 4.8 (22−48) years old, 21.9 ± 3.5 (15.7–35.4) kg/m^2, and 0.2 ± 0.5 (0−3) parity, respectively. The overall average length of the operation in the 264 patients was 168.0 ± 52.9 (61−311) min, and the average blood loss volume was 142.1 ± 214.0 (0–2150) ml. When concomitant surgeries (such as HM, LC, HP and other surgeries) were performed, the operation time became significantly longer (188.2 ± 57.9 vs. 163.9 ± 50.9 min, p = 0.005), and the blood loss volume increased (215.2 ± 373.6 vs. 127.1 ± 160.4 ml, p = 0.001). The average size of the dominant leiomyoma as measured by MRI and as measured during surgery, the weight of resected leiomyomas and the number of resected leiomyomas were 7.1 ± 2.5 (2−18) cm, 6.1 ± 2.1 (1−16) cm, 148.7 ± 134.4 (2−940) g and 3.2 ± 3.0 (1−22), respectively. When we focused on the location of the dominant leiomyoma, the leiomyomas of the 264 patients could be divided into one of three classifications, including intramuscular leiomyomas (n = 184), submucosal leiomyomas (n = 19) and subserosal leiomyomas (n = 61), or into one of five classifications, including uterine anterior wall (n = 131), uterine posterior wall (n = 126), uterine fundus (n = 1), uterine lateral wall (n = 2) and uterine cervix (n = 4). The representative symptoms were also collected, including menstrual disorder (n = 162), abdominal abnormality (n = 62) and infertility (n = 41), although some patients reported multiple symptoms and others reported no symptoms (n = 32). The average haemoglobin concentrations before and after the operation were 12.9 ± 1.2 (7.5–15.2) and 10.7 ± 1.1 (7.5–13.6), respectively. Autologous blood donations of 400 ml were performed for 145 patients, who wished to prepare and were supposedly at high risk of massive bleeding, such as those who had large leiomyoma or an operation history. Autologous blood transfusions of 400 ml were given to 23 patients, including one patient who required an allogeneic blood transfusion (i.e., 280 ml of red blood cell concentrates) in addition to prepared autologous blood.

Table 2
Comparison of the characteristics of the patients with and without temporary uterine artery ligation.

Index	TUAL	No ligation	P value
Age	**37.2 ± 4.5 (27–45)**	**37.2 ± 4.8 (22–48)**	**0.958**
Body mass index (kg/m^2)	**21.8 ± 3.3 (16.3–33.5)**	**21.9 ± 3.6 (15.7–35.4)**	**0.867**
Parity	**0.1 ± 0.3 (0–1)**	**0.2 ± 0.6 (0–3)**	**0.344**
Gynaecological surgical history	**n = 5/52**	**n = 16/212**	**0.623**
Concomitant procedure	**n = 3/52**	**n = 42/212**	**0.016**
Leiomyoma number	**3.6 ± 3.0 (1–14)**	**3.2 ± 2.9 (1–22)**	**0.336**
Subserous leiomyoma	**n = 12/52**	**n = 49/212**	**0.996**
Dominant leiomyoma size (cm, by MRI)	**7.6 ± 2.4 (3–13)**	**7.0 ± 2.5 (2–18)**	**0.119**
Dominant leiomyoma size (cm, During operation)	**6.5 ± 2.0 (3–12)**	**6.0 ± 2.1 (1–16)**	**0.098**
Adhesion/Endometriosis	**n = 11/52**	**n = 65/212**	**0.176**
Menstrual disorder	**n = 38/52**	**n = 124/212**	**0.053**
Abdominal abnormality	**n = 7/52**	**n = 64/262**	**0.057**
Infertility	**n = 6/52**	**n = 35/212**	**0.038**
Operation time (minutes)	**200.5 ± 46.9 (119–308)**	**160.1 ± 51.3 (61–311)**	**< 0.001**
Blood loss volume (ml)	**75.1 ± 73.6 (0–400)**	**158.5 ± 233.2 (0–2150)**	**0.011**

After dividing the 264 patients into two groups according to whether they had TUAL, we compared 15 representative indexes. For each item, we calculated the averages and standard deviations, the minimal and maximal values, and the count data from the medical records. In this analysis, 4 indexes, namely, concomitant surgery, infertility, operation time and blood loss volume, were significantly different between the two groups.
Abbreviations: TUAL: temporary uterine artery binding, BMI: body mass index, MRI: magnetic resonance imaging.

3.2. Effect of temporary uterine artery ligation

Fifty-two patients underwent temporary uterine artery ligation. There were no adverse events, such as bleeding from uterine vessels or ureteral injury, during the procedure.

Comparing the two groups of patients with or without the TUAL procedure, the blood loss volume was decreased by half in the patients who had TUAL compared to the patients who did not (75.1 ± 73.6 vs. 158.5 ± 233.2 ml, p = 0.011) (Table 2). However, the operation time

Table 3
Identification of influential factors for surgical difficulty.

	Total	Long operation time (Total N = 25)			Massive blood loss (Total N = 24)		
Factor	Number	Number	OR (95% CIs)	P value	Number	OR (95% CIs)	P value
High BMI	**40**	**7**	**2.43 (0.94–6.26)**	**0.036**	**3**	**0.78 (0.22–2.76)**	**0.705**
Nulliparity	**227**	**25**	**Impossible to calculate**	–	**20**	**0.80 (0.26–2.48)**	**0.696**
Gynaecological surgical history	**21**	**4**	**2.49 (0.77–8.08)**	**0.119**	**1**	**0.48 (0.06–3.73)**	**0.474**
Concomitant procedure	**45**	**9**	**3.17 (1.30–7.73)**	**0.008**	**10**	**4.18 (1.72–10.16)**	**< 0.001**
Single leiomyoma	**94**	**4**	**0.32 (0.10–0.95)**	**0.031**	**9**	**1.09 (0.46–2.61)**	**0.84**
Large leiomyoma	**113**	**13**	**1.51 (0.66–3.44)**	**0.331**	**18**	**4.58 (1.75–11.95)**	**< 0.001**
Adhesion/Endometriosis	**76**	**9**	**1.44 (0.61–3.43)**	**0.404**	**7**	**1.02 (0.41–2.57)**	**0.966**
Menstrual disorder	**162**	**15**	**0.94 (0.40–2.18)**	**0.884**	**16**	**1.29 (0.53–3.13)**	**0.577**
Abdominal abnormality	**62**	**6**	**1.03 (0.39–2.71)**	**0.949**	**8**	**1.72 (0.70–4.24)**	**0.234**
Infertility	**41**	**5**	**1.41 (0.50–4.00)**	**0.518**	**0**	**Impossible to calculate**	–
Temporary uterine artery ligation	**52**	**9**	**2.56 (1.06–6.19)**	**0.031**	**1**	**0.16 (0.02–1.22)**	**0.045**

A multivariate analysis of 264 patients with LM was performed to examine the influence of the 11 representative factors that were collected from the medical records. The number of patients with each factor, the ORs and 95% CIs for the occurrence of long operation time (≥ 240 min) and massive blood loss (≥ 400 ml) and the p values are shown in the table. High BMI, concomitant surgery, single leiomyoma and TUAL were identified as significant factors for a prolonged operation time. Concomitant surgery, large leiomyoma and TUAL were identified as significant factors for massive blood loss.
Abbreviations: OR: Odds ratio, CI: Confidence interval, BMI: Body mass index, TUAL: Temporary uterine artery ligation.

was increased in the patients who had TUAL compared to those who did not (200.5 ± 46.9 vs. 160.1 ± 51.3 min, $p < 0.001$). Since the values of some variables were not equal between the groups, such as the incidence of concomitant surgery ($p = 0.016$), we also performed a multivariate analysis to evaluate the effect of TUAL on the surgical difficulty without the influence of confounding factors.

3.3. Factors influencing surgical difficulty

To evaluate significant factors that affect the operation time and blood loss volume, a multivariate analysis of the 11 representative factors was performed (Table 3). According to this analysis, the following three factors were observed more in patients who had a long operation time: 1) high BMI (OR = 2.43, 95% CI 0.94–6.26); 2) concomitant surgery (OR = 3.17, 95% CI 1.30–7.73) and 3) TUAL (OR = 2.56, 95% CI 1.06–6.19). Single leiomyoma (OR = 0.32, 95% CI 0.10–0.95) decreased the risk for a long operative time. However, TUAL was associated with a significantly lower risk of massive blood loss (OR = 0.16, 95% CI 0.02–1.22), while concomitant surgery (OR = 4.18, 95% CI 1.72–10.16) and large leiomyoma (OR = 4.58, 95% CI 1.75–11.95) increased the possibility of massive blood loss. These results confirm that by adding the TUAL procedure to LM, the blood loss volume can be decreased; however, the TUAL procedure made the LM more complex to some extent.

4. Discussion

In this study, we introduced our novel method, TUAL, to prevent massive intraoperative bleeding in LM, and we aimed to evaluate its preventive effect. The addition of TUAL has the potential to prevent massive intraoperative blood loss. The use of this technique decreased the average blood loss amount by approximately 50% (75.1 ± 73.6 vs. 158.5 ± 233.2 ml, $p = 0.011$). When the 24 patients who exhibited over 400 ml of blood loss were categorized as having massive blood loss, the rate was significantly lower (OR = 0.16, $p = 0.045$).

LM has been the most common treatment for patients with uterine fibroids who wish to preserve the uterus [5,6]. Intraoperative bleeding, a major complication, can be effectively treated with the local administration of vasopressin [21]. In addition, there have been several reports regarding the preoperative embolization or permanent ligation of uterine arteries prior to myomectomy [8–11]. Other studies have reported that future fertility could be preserved after the permanent occlusion of uterine vessels because these vessels will recannulate, but it is still unclear whether permanent uterine artery occlusion truly has no detrimental effects on future fertility or livebirth, since adequate follow-up and analysis are difficult [8–11]. However, temporary intraoperative clipping of the uterine artery has also been reported to reduce blood loss and is non-invasive, unlike permanent ligation. However, titanium clips are not designed for removal after insertion, and the removal procedure might cause additional problems, such as vessel injury [12–15]. Recently, temporary uterine artery ligation has been introduced to solve these problems [22,23]. Temporary uterine artery ligation has the advantage of being less invasive and can be introduced at any facility with a technique equivalent to uterine artery identification at total laparoscopic hysterectomy without special equipment. This is the first case–control study that demonstrates the efficacy of temporary uterine artery ligation, which can become a new method of bleeding prevention in LM in the future.

In the analysis of the intraoperative blood loss, the patients who had a large leiomyoma could have increasing blood loss, which is similar to the results of past reports [7,16]. For this reason, the additional TUAL procedure may be recommended for patients with large leiomyomas.

This study found that this additional procedure had one major disadvantage: a possibly increased operation time (approximately 40 min). We evaluated the indexes of the surgical difficulty. We analysed the association of this technique with a long operation time, and 25 patients (9/52 in the case group and 16/212 in the control group) had operative times that were longer than 240 min. Apart from the significance of a high BMI and single leiomyoma, which were similar to findings observed in past reports [24,25], this procedure was also associated with a longer operation time. There is still room for improvement in our technique, since other reports have previously shown that there was no difference in the operation time when adding the haemostatic technique, where temporary clipping of the uterine arteries was performed with a titanium clip [12,13,15]. In addition, the eventual recurrence rate, pregnancy rate, and complications during pregnancy should also be investigated in the future based on the accumulation of cases.

5. Conclusions

By performing the TUAL procedure along with LM, there is a better chance of preventing massive blood loss, especially in patients who have large leiomyomas. On the other hand, because adding this technique leads to an increased operation time, this procedure can be further improved.

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Declarations of interest

None.

Prior presentation

None.

Consent for publication

Written informed consent was obtained from all patients for the publication of the data.

Precis

Temporary uterine artery ligation during laparoscopic myomectomy is a new method to decrease intraoperative blood loss without any special devices.

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