MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2020; 26: e921185
DOI: 10.12659/MSM.921185

Received: 2019.11.05
Accepted: 2019.12.17
Published: 2020.01.01

Use of Laparoscopic Slip Knot with Purse-String Suture in Surgical Management of Unruptured Heterotopic Interstitial Pregnancies

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCEF 1 Ruilin Lei*
ABCD 1 Jinxiao Liang*
CDE 1 Xiaoting Ling
BDG 1 Jing Xu
CDF 2 Sihua Liang
AEG 1 Hui Zhou
ACG 1 Bingzhong Zhang

1 Department of Gynecologic Oncology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Guangdong, P.R. China
2 Operating Room, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, Guangdong, P.R. China

* Ruilin Lei and Jinxiao Liang contributed equally to this work

Corresponding Authors: Hui Zhou, e-mail: zhouhuisysu@163.com, Bingzhong Zhang, e-mail: zhbzhong@sysu.edu.cn
Source of support: Departmental sources

Background: The aim of this study was to investigate the advantages and disadvantages of using laparoscopic slip knot with purse-string suture technique in the surgical management of unruptured heterotopic interstitial pregnancies compared with other surgical strategies.

Material/Methods: We retrospectively analyzed data on 13 patients with unruptured heterotopic interstitial pregnancies who underwent laparoscopy in our hospital between May 2012 and August 2018. The control group consisted of 10 patients who underwent cornual resection or cornuostomy with conventional sutures and knots. The study group consisted of 3 patients whose surgical plans involved use of the slip knot with purse-string suture technique followed by cornuostomy. We evaluated the surgical records and video to comparatively analyze their operation duration, intraoperative blood loss, and pregnancy outcomes.

Results: The average volume of intraoperative blood loss was 76.67±25 ml in the study group and 215.00±110 ml in the control group. On average, the intraoperative blood loss volume in the study group was 138 ml less than in the control group and the difference was statistically significant ($P<0.05$). There was no statistically significant difference in the live birth rate and operation time between the 2 groups ($P>0.05$). The duration of hemostasis in the study group was 11 min shorter than in the control group, while the duration of cornual electrocoagulation in the study group was 18.5 s shorter. Both groups achieved thorough hemostasis without the help of vasopressin and avoided use of embryo-killing drugs such as methotrexate. Neither group required second surgery or developed postoperative complications such as uterus rupture or persistent ectopic pregnancy.

Conclusions: This strategy is safe and reliable for gestational sac clearance while simultaneously preventing any potential harm to the intrauterine embryo. It is particularly suitable for unruptured HIP patients who have a strong desire to preserve their intrauterine embryos.

MeSH Keywords: Laparoscopy • Pregnancy, Ectopic • Pregnancy, Heterotopic • Suture Techniques

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/921185

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Background

Interstitial pregnancy (IP) refers to an ectopic pregnancy in which the gestational sac implants itself in the interstitial part of the fallopian tube [1]. The main surgical treatments are cornual resection [2] and cornuostomy [3]. Hemorrhage can occur if the gestational sac is improperly incised or ruptured; therefore, it is critical to control intraoperative bleeding and to thoroughly excise the lesion. Effective measures to control intraoperative blood loss are intramuscular injection of vasopressin [4], cornual loop ligature [5], and occluding the ascending branch of the uterine artery [6]. To prevent persistent ectopic pregnancy, cornual resection and local injection of methotrexate (MTX) [7,8] are recommended.

Heterotopic interstitial pregnancy (HIP) is a rare form of pregnancy that involves the coexistence of an ectopic interstitial pregnancy and intrauterine pregnancy, and it is one of the most life-threatening types of ectopic gestations [9]. Such patients often have a strong desire to preserve their intrauterine embryos; hence, it is fundamental to avoid procedures that potentially affect fetal development [3]. Therefore, the current management method of IP may not be suitable for HIP; for instance, vasopressin can increase the risk of miscarriage due to its physiologic actions in promoting contractions in smooth muscles [10], arterioles, and capillaries. In addition, exposure to MTX during the first trimester can lead to development of "fetal-MTX syndrome" [11], which is a serious congenital malformation syndrome characterized by growth deficiency, microcephaly, craniosynostosis, facial deformities, and limb defects. Electrocoagulation is an important method to achieve hemostasis during surgery, but the damage it causes to the myometrium can increase the risk of subsequent rupture [4]. Moreover, some studies have suggested that electric currents can disturb the endogenous electric fields of fetuses, which can lead to developmental abnormalities or malformations [12,13]. Cornuostomy is an attractive alternative to cornual resection because it preserves the normal uterine myometrium [14].

In this paper, we propose a safe and effective surgical strategy that can thoroughly remove the interstitial gestational tissue while minimizing adverse effects on the fetus in the uterine cavity. This strategy uses a slip knot with purse-string suture technique followed by cornuostomy. We retrospectively analyzed the data collected from 13 cases of unruptured heterotopic interstitial pregnancies treated by laparoscopic surgery in our hospital to investigate the effectiveness of the treatment and pregnancy outcomes. This study was approved by the Ethics Committee of Sun Yat-sen Memorial Hospital (approval number SYSEC-KY-KS-2019-130). All patients provided written informed consent prior to study commencement.

Material and Methods

Patients

From among the 24 000 IVF-ET procedures performed at our center during the last 6 years, only 13 patients were eligible for this study. We retrospectively analyzed the data from these 13 patients with unruptured HIP who underwent laparoscopy in our hospital between May 2012 and August 2018, and all the patients were recruited after assisted reproductive techniques. Ten patients who underwent cornual resection or cornuostomy with conventional sutures and knots were selected as the control group; the other 3 were selected as the study group, whose surgical plans involved the slip knot with purse-string suture technique followed by cornuostomy. A transvaginal ultrasound scan was performed on the third postoperative day or before discharge to confirm the fetal viability of intrauterine gestation in each patient who continued with their intrauterine pregnancy. A routine prenatal examination was carried. The 2 groups were followed up until childbirth. We also evaluated surgical videos of the operations to comparatively analyze their operation duration, intraoperative blood loss, and pregnancy outcomes.

Methods

Surgical method: purse-string suture

Surgery was performed under general anesthesia. Surgical incisions were made at the umbilicus, McBurney's point, and Munro's point. Laparoscopic findings included an obvious "ox horn-like" bulge at the interstitium, which showed distension with increased tension, weakened muscular layer, and richer vasculature (Figure 1B), all of which were consistent with observations made by ultrasound (Figure 1A) (ultrasound diagnostic criteria: gestational sac located eccentrically 1 cm from the most lateral edge of the uterine cavity, surrounded by asymmetrical thin (<5 mm) myometrial tissue; presence of 'interstitial line' sign, an echogenic line that extends into the upper regions of the uterine horn and borders the margin of the intramural gestational sac, representing either interstitial portion of the tubes or endometrium [15]). After separating adhesions surrounding the lesion, the fimbriae part of the fallopian tube was raised and closely approached using an ultrasonic scalpel to excise the mesosalpinx from the isthmus of the fallopian tubes to the uterine cornual. Four or 5 stitches of 2/0 absorbable sutures were passed around the relative hypertrophic basal part of the muscle layer at the uterus cornual in a purse-string fashion.

The first and second stitches entered from right to left, at a distance of 5–8 mm, with an approximate depth of 1 mm (Figure 2A); the third stitch entered from anterior of the uterus

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

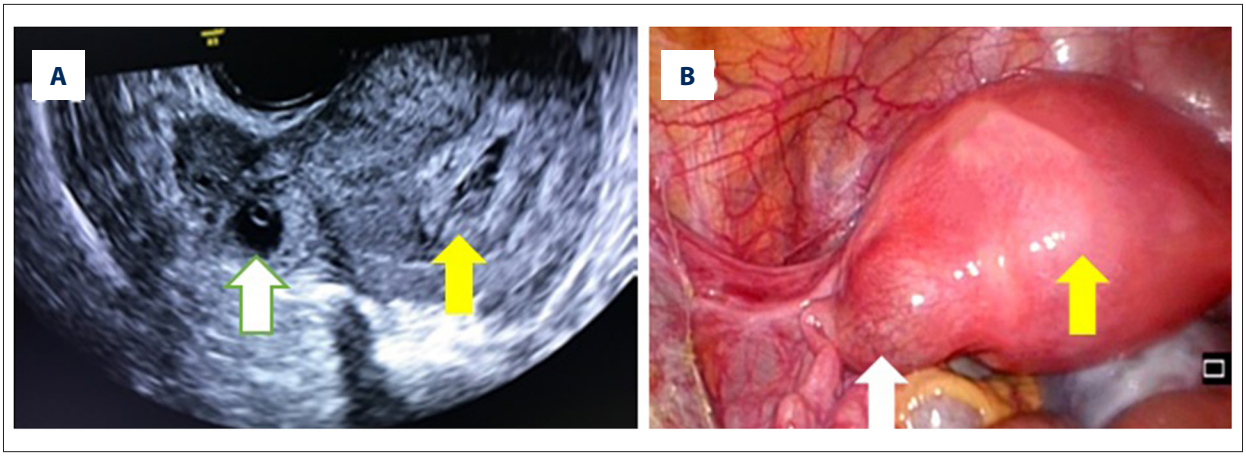

Figure 1. (**A**) Transvaginal ultrasound view: white arrow indicating the interstitial pregnancy (HIP) lesion 25×24×27 mm, CRL 6mm, fetal cardiac activity can be seen, yellow arrow indicating the intrauterine embryo, 18×13×16 mm, CRL 5 mm, primitive cardiac pulsation can be seen; (**B**) Laparoscopic finding of HIP of the patient.

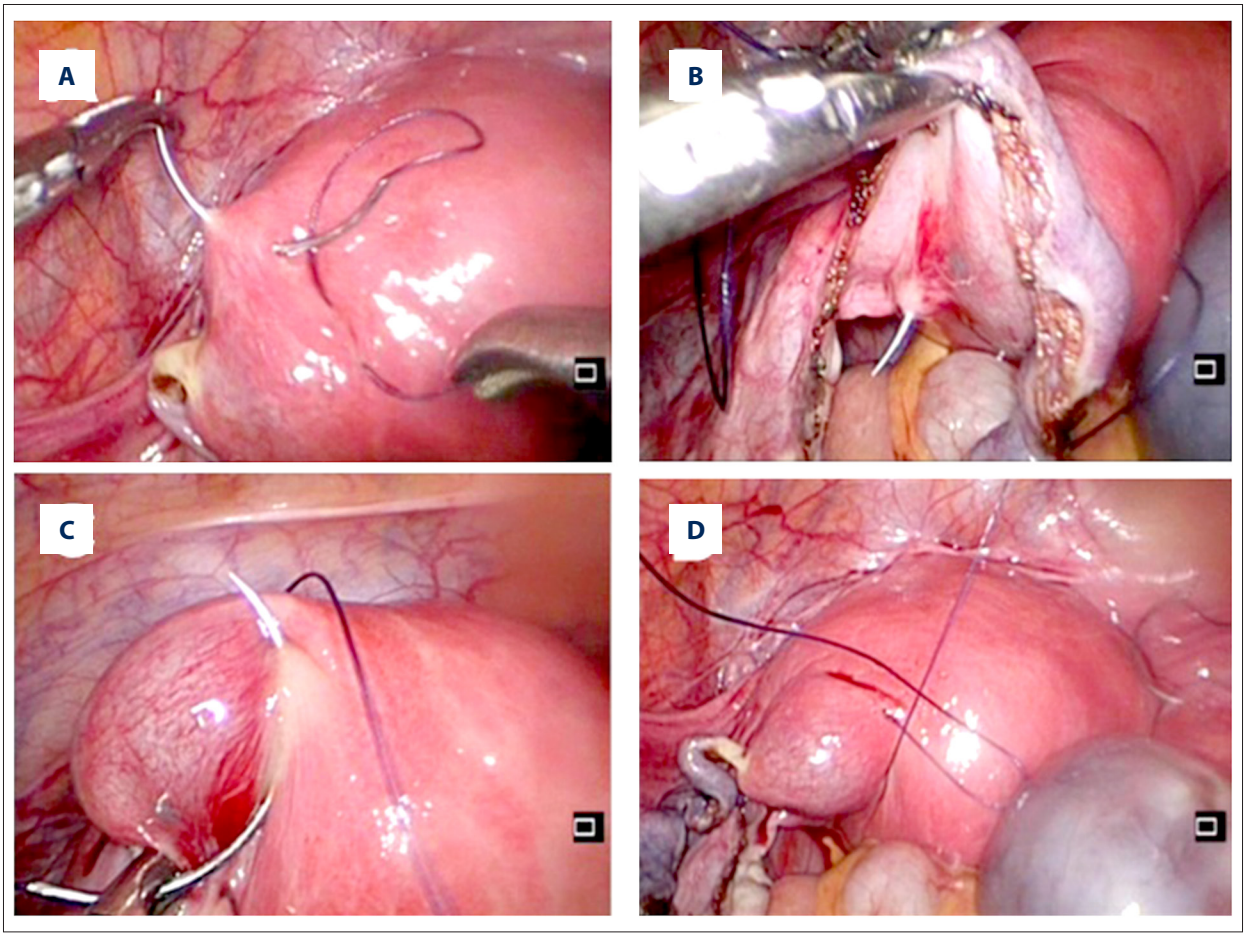

Figure 2. Steps of laparoscopic purse-string suture. (**A**) The first and second stitches entered from right to left. (**B**) The third stitch entered from anterior of the uterus cornual and passed through the coverings of the broad ligament. (**C**) The fourth stitch was executed with the left hand holding the instruments as the needle entered from left to right. (**D**) Final outcome of the laparoscopic purse-string suture.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

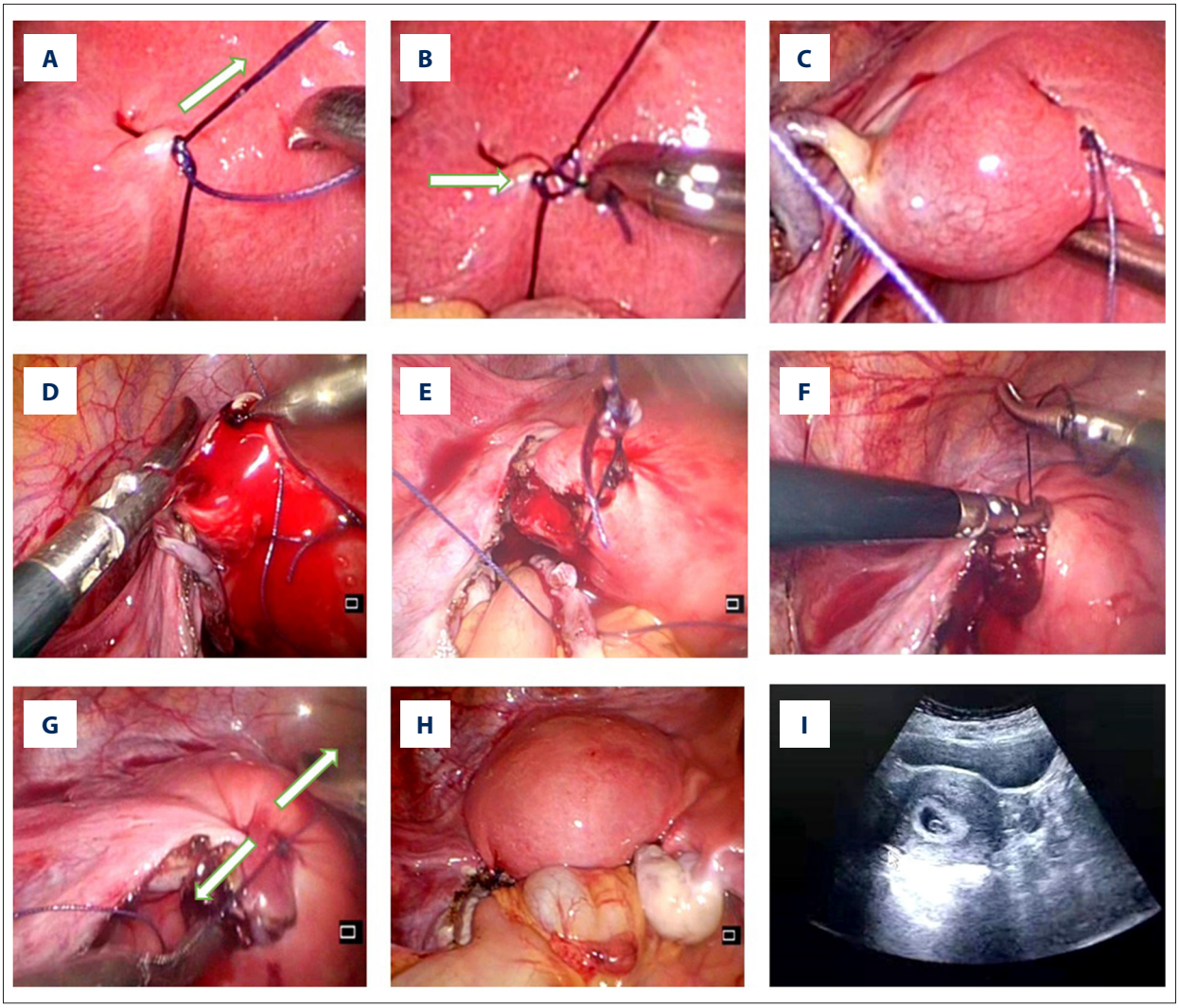

Figure 3. (**A–G**) Steps in making a slip knot; corresponding to Steps 1 to 9 in the main text; (**G**) The arrow shows the direction of force to pull the suture; (**H**) Uterus after the operation, with thorough hemostasis; (**I**) Postoperative ultrasonography checkup showed a surviving embryo.

cornual, passed through the coverings of the broad ligament, and exited posteriorly with difficulty (Figure 2B); the fourth stitch was executed with the left hand holding the instruments as the needle entered from left to right. Gentle movements are essential when the needle emerges to avoid tearing the tissue (Figure 2C, 2D).

It is advised to completely include the interstitial-cornual tissue in the circular loop of purse-string suture during the process of purse-string suturing. In contrast to conventional suture methods in which greater stitching depth suggests the inclusion of more ligated structures, purse-string suturing uses a shallow stitching depth to allow greater inclusion of tissue structures. This is because greater stitching depth in the purse-string suture excludes tissues from the ligature loop, leading to incomplete hemostasis, and it can even result in rupture of the lesion, subsequently affecting the precision and speed of the operation due to blood obstructing the surgical view. However, an excessively shallow stitching depth can cause laceration or slippage of tissue.

Surgical method: slip knot technique

(1) After adjusting the length of the suture on both ends, tie a single knot under loose tension (Figure 3A), then make another single knot in the opposite direction. Both knots should be kept loose (Figure 3B). (2) Hold one end of the suture with the left hand using forceps, take this end as the main tension line by pulling the suture in a straight and upright manner while keeping the suture loose on the right hand. The suture end on the right side should naturally rest on the main tension line (Figure 3B). (3) Place the suture knots gently onto the surface of the uterus

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

(without tightening it) (Figure 3C). (4) Following the preparation of the slip knot, cut open the ectopic mass along the cornual and expand the incision, then completely excise the gestational sac (Figure 3D) and remove the fallopian tubes closely along the uterus using an ultrasonic scalpel. (5) Raise the main tension line and push the slip knot towards the uterus with force to tighten the loop, then pull shut the knot to immediately achieve hemostasis (Figure 3E, 3F). (6) Observe the wound incision. If there is on-going bleeding, the knot can be suitably tightened. (7) Increase traction on the loose end, then both the main traction line and the loose end will intertwine with one another. As both hands pull the suture tightly in the opposite direction to the equal tension, the slip knot will securely become a square knot (Figure 3G). (8) Make a third knot and prevent this knot from slipping. (9) If the wound area is wide or is seeping blood, more sutures can be sewn to strengthen the hold, or electrocoagulation can be used for hemostasis.

It should be noted that: (1) To produce a qualified slip knot, place different pulling forces on both ends of the suture and differentiate clearly between the main tension line and the loose end to allow the knot to slide down and rest upon the main tension line. If both ends of the suture are pulled with equal forces, it will produce a square knot. In the process of tightening the suture, a square knot will be locked and it cannot slide further down the "main tension line". (2) Once the ectopic mass is cut open, blood often gushes out of the wound, or can even spurt. Given that the purse-string suture and slip knot are made beforehand, the surgeon should be mentally prepared for such scenarios and should remain calm while cleaning the wound. After the gestational tissues are thoroughly cleared, the purse-string suture must be immediately tightened to stop the bleeding. (3) For larger ectopic masses, it may be appropriate to slightly tighten the purse-string suture first before excision to minimize blood loss. However, this can cause some parts of the gestational sac to be trapped in the ligation, which will affect subsequent surgical procedures. (4) The length of the incision needs to be adequate to aid in voiding the gestational tissue.

Statistical analysis

The data were analyzed using SPSS 16.0 statistical software. Measurement data are presented as $\bar{\chi}\pm s$; data between groups were subjected to *t* test and non-parametric test (Mann-Whitney U test); numerical data are presented as percentages; comparisons among groups were subjected to chi-square test (Fisher's exact test). Differences with <0.05 were considered as statistically significant.

Analysis of surgical recordings

To review the available surgical video (2 cases from the study group, 2 cases from the control group), we timed every procedure stepwise in seconds and derived the average value from 3 readings for each video.

Results

Results of statistical analysis

All patients had a history of infertility and accepted IVF-ET, and 100% choose cesarean section for delivery (Table 1). The average volume of intraoperative blood loss was 76.67±25.166 (50~100) ml in the study group and 215.00±110.680 (50~400) ml in the control group, and the difference was statistically significant ($P<0.05$). There was no significant difference in live birth rate and operation time between the 2 groups ($P>0.05$, Table 2). In the control group, 3 patients had an abortion within 7 to 10 weeks. Among these 3 patients, fetal heartbeats were not detected in 2 cases before surgery. Also, patients in the study group (slip knot with purse-string suture) did not require a pelvic drainage tube after the operation. Pituitrin and drugs like MTX were not used in either group.

Analysis result of surgical video

On average, the control group required 659 s to achieve wound closure, while the study group only required 15 s. This is because the study group did not require stitches or knot-tying during wound closure, as the procedure only demanded the tightening of the slip knot. Hence, the average accumulated duration for cornual electrocoagulation was 2 s in the study group and 21 s in the control group. The total time to achieve hemostasis was 17 s in the study group and 680 s in the control group, with a significant difference of 663 s (equivalent to almost 11 min) (see Table 3).

Postoperative complications

Neither group needed a second surgery nor developed postoperative complications such as hemorrhage, persistent ectopic pregnancy, and uterus rupture.

Discussion

Heterotopic pregnancy (HP) is a condition in which both intrauterine and extrauterine pregnancies occur simultaneously [16]. It is rare in spontaneous pregnancy (incidence rate, 1 in 10 000–50 000), but is relatively common (0.3–1%) in pregnancies that arise from assisted conception [17,18]. With interstitial pregnancy comprising only 2.4% of ectopic pregnancies [19], Heterotropic interstitial pregnancies (HIP) are exceedingly rare. Investigations concerning surgical treatment for HIP have been reported, mainly under titles such as "cornual resection

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 1. Summary of patients with unruptured heterotopic interstitial pregnancies who were treated by laparoscopic method.

Group	Case No.	Age (yr)	IVF -ET	Gestation (weeks)	Mass size (cm)	Fetal cardiac activity	Method of operation	Operation duration (min)	Blood loss (ml)	Live birth	Gestational age	Type of birth	complication
Control group N=10	1	31	yes	6w	1.5*1.0	Present	**1**	40.0	200.0	Yes	37w3d	CS	No
	2	27	yes	6w2d	1.8*1.2	Absent	**1**	75.0	100.0	No	/	/	/
	3	29	yes	9w	4.0*4.2	Present	**1**	50.0	400.0	Yes	37w1d	CS	PROM
	4	37	yes	7w1d	2.6*1.8	Present	**1**	50.0	300.0	Yes	38w1d	CS	no
	5	36	yes	7w	2.2*1.5	Absent	**1**	90.0	100.0	No	/	/	/
	6	31	yes	8w2d	3.3*2.7	Present	**1**	90.0	300.0	Yes	36w6d	CS	Premature delivery
	7	27	yes	7w3d	1.9*1.5	Present	**1**	40.0	50.0	No	/	/	/
	8	29	yes	7w3d	3.3*2.1	Present	**1**	70.0	200.0	Yes	38w4d	CS	No
	9	37	yes	5w5d	1.3*0.8	Absent	**1**	80.0	200.0	Yes	37w3d	CS	No
	10	40	yes	7w6d	2.5*1.5	Present	**1**	85.0	300.0	Yes	37w1d	CS	Pregnancy hypertension
Study group N=3	11	28	yes	7w2d	3.6*3.1	Present	**2**	40.0	50.0	Yes	38w4d	CS	No
	12	34	yes	6w6d	2.5*2.4	Present	**2**	60.0	80.0	Yes	37w5d	CS	PROM
	13	31	yes	7w5d	3.2*3.3	Present	**2**	70.0	100.0	Yes	38w1d	CS	No

1. Cornual resection or cornuostomy with conventional sutures and knots. **2.** Slip knot with purse-string suture technique followed by cornuostomy. PROM – premature rupture of membranes.

Table 2. Comparison of treatment outcomes between the study group (laparoscopic slip knot with purse-string suture technique followed by cornuostomy) and the control group (conventional suture with cornual resection or cornuostomy).

Variable	Study group (n = 3)	Control group (n=10)	*P*
Operation duration (min)	56.67±15.275 (40~70)	67.00±20.166 (40~90)	0.371
Intraoperative blood loss (ml)	76.67±25.166 (50~100)	215.00±110.680 (50~400)	0.049
Live birth rate, n (%)	100%	70%	0.257

The Mann-Whitney U test was used for p value comparison between the study group and control group in operation duration and intraoperative blood loss; Fisher's exact test was used to get the p value for the live birth rate.

Table 3. Comparison of average time to hemostasis between the study group and the control group.

Time to hemostasis (s)	Study group (n=2)	Control group (n=2)
Average suture duration	0	489
Average duration for knot-tying	15	170
Average accumulated duration for cornual electrocoagulation	2	21
Total time	17	680

Electrocoagulation power: 35 w/h.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

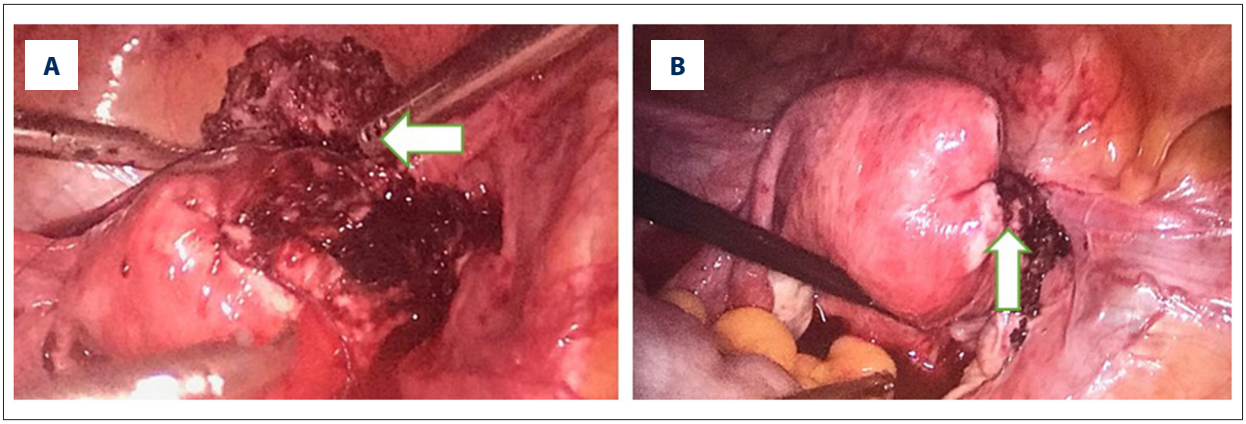

Figure 4. Cornual resection. (**A**) The arrow points to the excised uterine cornual. (**B**) The uterine cornual was removed and the round ligament was severed.

or cornuostomy with conventional suture", which is also the surgical treatment used in the control group in the present study (Figure 4). When dealing with a lesion of a larger mass and richer vascular supply, hemorrhage can happen instantaneously with an incision. This causes an obstructed surgical field, creating greater surgical difficulty and decreased surgical speed and precision, thereby putting mounting pressure on the surgeon. Such scenarios can lead to an incomplete clearance of the ectopic mass or unsecured ligation that require additional suturing, which then lead to prolonged operation duration and bleeding, and can even cause irreversible damage due to excessive cornual resection.

Gao et al. proposed that the strategy of "using purse-string suture with ligation followed by cornuostomy to excision of gestational sac" is better than the conventional surgical treatment [20]. However, there are 2 major risks associated with tightening the suture before the gestational tissues are thoroughly cleared: (1) gestational tissue can be partially included in the ligature, which leads to incomplete clearance of the lesion and increases the risk of persistent ectopic pregnancy; and (2) excessive inclusion of tissue (cornual myometrium and gestational sac) into the purse-string suture can spike the tension when tying the knot. This can weaken the knots and necessitate additional stitches or electrosurgery to achieve hemostasis. If there is tension in the cornual during knot-tying, it is possible to make the knot loose, especially when working without the aid of a third surgical incision. The slip knot technique is effective for laparoscopy, as it is well suited for difficult knots and sutures under tension. It is also advantageous due to its adjustability, minimal requirement for assistance, and sturdy nature.

In the present study, the surgical treatment used in the study group – "purse-string suture with slip knot followed by cornuostomy, then finally tightening of the knot" – can effectively overcome the shortcomings of the methods mentioned above. To the best of our knowledge, this is the first study in which the purse-string suture combined slip knot technique was applied in laparoscopic surgeries of unruptured HIP. This strategy increases the surgical success rate, saves time in knot-tying, and minimizes hemorrhage.

From the analysis of the surgical videos, we learned that the control group needed 680 s or longer to achieve hemostasis (including conventional cornual suture and electrocoagulation). The speed of hemorrhage may go up to 30–100 ml/min during the procedure. In contrast, with the purse-string suture and slip knot prepared beforehand, the study group only needed an average of 15 s to achieve hemostasis by tightening the slip knot, which significantly reduced bleeding time and intraoperative blood loss. An average of 11 min was saved from the hemostasis step in the study group compared to that of the control group. Our statistical analysis showed that the intraoperative blood loss volume in the study group was 138 ml less, on average, than that of the control group. This difference was statistically significant ($P<0.05$) and showed a consistent trend with the results of surgical video analysis. The purse-string suture with slip knot technique is more difficult than conventional suturing methods; therefore, there was no statistically significant difference in total operation duration between the 2 groups.

Some reports suggested that lesions greater than 3 cm should be managed with cornual resection [21] to completely remove the interstitial lesion and prevent persistent ectopic pregnancy. However, in a study of uterus rupture in subsequent pregnancy following a history of cornual resection, 2/33 subsequent uterine ruptures were encountered [22]. Another retrospective study on IP showed that of the 10 pregnancies after wedge resection, 3 (30%) patients had uterine rupture and dehiscence in their next pregnancy [23]. In cases where embryos survived the surgical procedure and proceeded with normal development, there was a higher risk of uterus rupture as the

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

uterus expanded rapidly during pregnancy without a sufficient recovery period. However, such a strategy can cause substantial damage to the uterus (Figure 4), which in turn increases the risk of miscarriage and uterus rupture during pregnancy. Gao et al. proposed that laparoscopic cornuostomy is an appropriate treatment for interstitial pregnancy in patients wishing to preserve fertility [24]. According to our experience, our surgical technique is safe and reliable for lesions larger than than 3 cm (and the size of the largest lesion ever encountered in the past was 3.6×3.1 cm). Such a minimally invasive technique will be much more adaptable for larger lesions, which produce greater damage to the uterus.

Therefore, we recommend the purse-string suture with slip knot technique followed by cornuostomy. This technique requires lesser time to achieve hemostasis, thus allowing more time for gestational sac clearance, permits maximum preservation of uterus integrity as it does not remove the cornual (Figure 3H, 3I), and reduces risk of uterus rupture in later stages of pregnancy. Furthermore, the total time needed for cornual electrocoagulation is significantly shortened, which lowers the risk of electrical stimulation of the fetus. This strategy avoids the use of hemostatic drugs and MTX and mechanical stimulation of the uterus (with no need for a pelvic drainage tube). However, this method should not be used with a ruptured HIP as the purse-string suture is more difficult than commonly-used sutures. When the surgical field is blocked by blood, the operation cannot be completed quickly, so a more commonly-used suture is recommended. In addition, this technique can lead to iatrogenic rupture of the lesion during the purse-string suturing process, so the suturing strategy has to be changed to conventional suturing at this time.

Conclusions

This strategy is particularly suitable for unruptured HIP patients who have a strong desire to keep their intrauterine embryos. This technique is safe, thorough, rapid in achieving hemostasis, and highly operational, and it minimizes adverse effects and prevents any potential harm to the intrauterine embryo. However, further studies with larger sample sizes and wider clinical applications are needed to validate the advantages of this proposed technique.

References:

1. Tulandi T, Al-Jaroudi D: Interstitial pregnancy: Results generated from the Society of Reproductive Surgeons Registry. Obstet Gynecol, 2004; 103(1): 47–50
2. Jiang Y, Chen J, Zhou H et al: Management and obstetric outcomes of 17 heterotopic interstitial pregnancies. BMC Pregnancy Childbirth, 2018; 18(1): 78
3. Dendas W, Schobbens JC, Mestdagh G et al: Management and outcome of heterotopic interstitial pregnancy: Case report and review of literature. Ultrasound, 2017; 25(3): 134–42
4. Moawad NS, Mahajan ST, Moniz MH et al: Current diagnosis and treatment of interstitial pregnancy. Am J Obstet Gynecol, 2010; 202(1): 15–29
5. Moon HS, Choi YJ, Park YH, Kim SG: New simple endoscopic operations for interstitial pregnancies. Am J Obstet Gynecol, 2000; 182(1 Pt 1): 114–21
6. Tulandi T, Vilos G, Gomel V: Laparoscopic treatment of interstitial pregnancy. Obstet Gynecol, 1995; 85(3): 465–67
7. Khan Z, Lindheim SR: In pursuit of understanding interstitial pregnancies: A rare yet high-risk ectopic pregnancy. Fertil Steril, 2019; 112(2): 246–47
8. Farquhar CM: Ectopic pregnancy. Lancet, 2005; 366(9485): 583–91
9. Parker VL, Srinivas M: Non-tubal ectopic pregnancy. Arch Gynecol Obstet, 2016; 294(1): 19–27
10. Ishikawa H, Unno Y, Omoto A, Shozu M: Local injection of diluted vasopressin followed by suction curettage for cervical ectopic pregnancy. Eur J Obstet Gynecol Reprod Biol, 2016; 207: 173–77
11. Hyoun SC, Običan SG, Scialli AR: Teratogen update: Methotrexate. Birth Defects Res A Clin Mol Teratol, 2012; 94(4): 187–207
12. Xiao-Meng D, Gao J, Sun Q et al: Endogenous electrical fields and its biological significance. Progress in Biochemistry and Biophysics, 2016; 43(08): 731–38
13. Nuccitelli R: Endogenous electric fields in embryos during development, regeneration and wound healing. Radiat Prot Dosimetry, 2003; 106(4): 375–83
14. Uludag SZ, Kutuk MS, Dolanbay M et al: Conservative management of interstitial pregnancies: Experience of a single centre. J Obstet Gynaecol, 2018; 38(6): 848–53
15. Elson CJ: Diagnosis and management of ectopic pregnancy: Green-top guideline No. 21. BJOG, 2016; 123(13): 15–55
16. Alqahtani HA: A case of heterotopic pregnancy after clomiphene-induced ovulation. SAGE Open Med Case Rep,2019; 7(1): 2050313X19873794
17. Ludwig M, Kaisi M, Bauer O, Diedrich K: Heterotopic pregnancy in a spontaneous cycle: Do not forget about it! Eur J Obstet Gynecol Reprod Biol, 1999; 87(1): 91–93
18. Rizk B, Tan SL, Morcos S et al: Heterotopic pregnancies after *in vitro* fertilization and embryo transfer. Am J Obstet Gynecol, 1991; 164(1 Pt 1): 161–64
19. Anderson J, Patterson C, Riley A: Heterotopic interstitial pregnancy: A case report. Case Rep Womens Health, 2018; 17(5): 8–10
20. Gao B, Cheng C, Pan Q et al: Laparoscopic strategy for heterotopic interstitial pregnancy following assisted reproductive techniques. JSLS, 2019; 23(2): pii: e2018.00109
21. Siow A, Ng S: Laparoscopic management of 4 cases of recurrent cornual ectopic pregnancy and review of literature. J Minim Invasive Gynecol, 2011; 18(3): 296–302
22. Svenningsen R, Staff AC, Langebrekke A, Qvigstad E et al: Fertility outcome after cornual resection for interstitial pregnancies. J Minim Invasive Gynecol, 2019; 26(5): 865–70
23. Liao CY, Tse J, Sung SY et al: Cornual wedge resection for interstitial pregnancy and postoperative outcome. Aust N Z J Obstet Gynaecol, 2017; 57(3): 342–45
24. Gao MY, Zhu H, Zheng FY: Interstitial pregnancy after ipsilateral salpingectomy: Analysis of 46 cases and a literature review. J Minim Invasive Gynecol, 2019 [Epub ahead of print]

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]