Management of Heterotopic Pregnancy
Experience From 1 Tertiary Medical Center

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Abstract: The objective of this study is to summarize the experiences of our department in the management of heterotopic pregnancy (HP) and to analyze the influence of different treatment modality on the viable intrauterine pregnancy.

There were 64 patients diagnosed as HP in the Department of Gynecology and Obstetrics in our hospital between January 2003 and June 2014, 52 HP patients with viable intrauterine pregnancy were included and analyzed in our study. Interventions included expectant management, surgical management and transabdominal sonographic guided transvaginal aspiration of ectopic gestational embryo (embryo aspiration) management.

Main outcome measures are maternal outcome and pregnancy outcome.

In expectant management group, 4 patients suffered rupture of ectopic pregnancy, 6 patients transferred to surgical management, 1 patient suffered a fever of 40.4 °C, the abortion rate was 5% (1/20). In surgical management group, emergency surgery was performed in 9 patients with unstable hemodynamics and 3 patients with stable hemodynamics, 1 patient suffered uterine rupture 5 weeks later and dead fetus was demonstrated, 1 patient suffered urinary retention postoperative, the abortion rate was 14.8% (4/27). In embryo aspiration management group, 1 patient needed another embryo aspiration, all patients were eventful and no abortion was observed.

In our retrospective study, transabdominal sonographic guided aspiration of ectopic gestational embryo has the best maternal outcome and the lowest abortion rate, surgical management group shows the highest abortion rate, and expectant management presents the worst maternal outcome.

INTRODUCTION
Heterotopic pregnancy (HP) refers to the simultaneous presence of intrauterine pregnancy (IUP) and ectopic pregnancy (EP), which is very rare but a potentially life-threatening condition. HP can be spontaneous or the consequence of assisted reproductive technology (ART), the spontaneous incidence of HP in general population is thought to be about 1 in 30,000, but with the widespread of ART, the incidence of HP in woman with ART raises to about 0.09% to 1.00%.

Clinical presentations of HP are untypical, common presentations include vaginal bleeding, acute abdominal pain, and hypovolemic shock, while 1 report points out that about 50% HP patients can be totally asymptomatic. Human beta chorionic gonadotropin is unimportant in the establishment of HP due to the co-existence of the IUP. Transvaginal sonographic examination plays an important role in the diagnosis of HP, which presents as an IUP co-existed with a separated adnexal mass, gestational sac, or ring sign. However, even transvaginal sonographic examination has performed, the EP may also be missed or misdiagnosed as hemorrhagic corpus luteum cyst. In fact, it is estimated that about 58.93% to 73.75% cases of HP are not confirmed before surgery. So, it is a consensus that an early and accurate diagnosis of HP is often difficult.

Management of HP is still controversial. According to literatures, treatment modalities of HP include expectant management, surgical management, and sonographic guided embryo aspiration with or without embryo-killing drugs. However, due to the rarity of HP, most publications about HP are case report or small case series, treatment experiences are limited, so there is no consensus on the preferred treatment modality of HP.

The objective of this retrospective study is to summarize the experiences of our department in the management of HP and to analyze the influence of different treatment modality on the viable IUP.

MATERIALS AND METHODS
There were 64 patients diagnosed as HP in the Department of Gynecology and Obstetrics in our hospital between January 2003 and June 2014. The diagnostic criteria of HP were: in expectant management patients, HP was diagnosed mainly on the presence of an IUP and typical EP sonographic characteristics; in other patients, HP was diagnosed based on the intraoperative findings and histological examination of suspected EP
tissues. All medical records and sonographic pictures are collected and reviewed carefully to exclude the misdiagnosis. Since 1 objective of our study is to retrospectively analyze the influence of different treatment modality on the viable IUP, 12 patients without viable IUP before treatment are excluded, thus 52 patients are finally included in our study.

Patients are divided into 3 groups according to the treatment modality they received, those are expectant management group, surgical management group, and transabdominal sonographic guided transvaginal aspiration of ectopic gestational embryo (embryo aspiration) management group. All patients except those unconscious were well informed about their situation and the potential advantages and disadvantages of each treatment modality, the final treatment modality was confirmed based on the presentations, hemodynamic situation, and patients’ choice. Basic demographics, such as pregnancy history, conception mode, gestational age, clinical presentations, location, sonographic characteristic, and hemodynamics situation, of all patients are presented in Tables 1–3.

In expectant management group, patients were under strict observation on any signs of the rupture of EP, such as the progression of abdominal pain and unstable hemodynamic presentations. Transvaginal sonographic re-examinations were performed weekly to monitor the changes of EP mass and clues of hemoperitoneum. When the rupture of EP was suspected, rapid enlargement of EP mass was demonstrated or cardiac activity was presented, surgery was performed immediately to have good maternal results.

In surgical management group, emergency surgery, either laparotomy or laparoscopy, was performed to those patients with unstable hemodynamic situations and to those rupture of EP were suspected. To those patients with stable hemodynamic situations, selective surgery was performed. Antibiotic was applied preoperatively and postoperative for 2 days to avoid infection.

In embryo aspiration management group, patients received transvaginal sonographic re-examinations postoperative weekly to monitor the changes of EP mass and clues of hemoperitoneum. If enlargement of EP mass was demonstrated, another embryo aspiration or surgery would be performed. And if there was any sign of rupture, surgery was needed to rescue patient’s life.

The luteal support strategy of all patients was determined by ART experts.

The endpoint of follow-up was the termination of this pregnancy. Maternal outcome and pregnancy outcome were main therapeutic measurements. Other therapeutic measurements included the transfer to other treatment modality, operation time, blood transfusion, and complications.

This retrospective study was approved by the Medical Ethics Committee of our hospital, all patients and (or) their husbands were well informed about their situation, and written informed consents were received before treatment.

RESULTS

Maternal outcome and pregnancy outcome of patients in expectant management group were showed in Table 1. Four patients suffered rupture of EP during hospitalization, the rupture rate was 20% (4/20). Among them, 3 patients suffered tubal rupture and another patient suffered uterine corner rupture, emergency surgery was performed timely in these 4 patients. One patient showed cardiac activities of the EP and another patient showed gradual enlargement of ectopic gestational sac during weekly sonographic re-examinations, surgery was performed in both patients. One patient suffered a fever of 40.4°C, she was uneventful after the application of antibiotic for 3 days. One patient ended up with abortion during observation 1 week later, the total abortion rate was 5% (1/20) during observation. Three patients, with ongoing living IUP before check out, lost follow-up because of the change of contact information.

Maternal outcome, pregnancy outcome, and operative data in surgical management group were presented in Table 2. Emergency surgery was performed in 9 patients with unstable hemodynamics; among them, 6 patients needed blood transfusion, 2 patients suffered abortion during follow-up; the abortion rate in patients with unstable hemodynamics was 22.22% (2/9).

This three patients with stable hemodynamics received emergency surgery because of the rupture of EP. Two patients with stable hemodynamics suffered abortion postoperative, the abortion rate was 11.11% (2/18). Total abortion rate in surgical management group was 14.8% (4/27) during observation. One patient suffered uterine rupture 5 weeks later after corner resection, dead fetus was demonstrated in the following surgery. One patient suffered a complication of urinary retention. Two patients lost follow-up with viable IUP because of the change of contact information.

Maternal outcome and pregnancy outcome of patients in embryo aspiration management group were showed in Table 3. One patient showed obvious enlargement of the ectopic gestational sac by weekly sonographic re-examination 1 week later, another procedure was performed to avoid the rupture of ectopic gestational sac. The other 4 patients were all eventful. No abortion was observed in this group.

DISCUSSION

An early and accurate diagnosis of HP is often difficult and challenging due to the rarity of HP, the delay or failure of diagnosis may lead to potential life-threatening conditions such as the rupture of EP, hypovolemic shock or even loss of life, so the early and accurate diagnosis of HP is extremely critical. Though the sensitivity of transvaginal sonographic examination, ranged from 26.3% to 92.4%, in the definitive diagnosis of HP is still debatable, a routine transvaginal sonographic examination at 4 to 6 weeks after ART to exclude EP and HP is recommended. So, an early transvaginal sonographic examination is recommended in early pregnancy, especially those patients conceived via ART or those with other risk factors.

Unlike those patients with EP only, most HP patients are conceived via ART and have a strong desire to preserve the viable IUP, so the key point of treatment is to preserve the viable IUP and to resolve the EP, this makes the treatment of HP difficult and challenging.

To those patients with stable hemodynamic situation and asymptomatic, expectant management could be considered. The main advantage of expectant management is that it avoids all potential complications related to the surgery and transabdominal sonographic guided transvaginal aspiration of ectopic gestational embryo. Nevertheless, expectant management should not be considered in patients with viable EP or unstable hemodynamic situation. As the risks of continued growth and rupture of EP still exist, failures of expectant management have been reported. In our research, 20% patients in expectant management group suffered rupture of EP eventually, 1 patient presented cardiac activities of EP and another
| Patient No. | Gravity, Parity, Abortion, and Ectopic Pregnancy Mode of Conception | Gestational Age at Diagnosis, d | Clinical Presentations | Location of Ectopic Pregnancy | Fetal Heart Beats of Ectopic Pregnancy | Diameters of Gestational Mass, mm | Treatment of the Ectopic Pregnancy | Maternal Outcome | Secondary Treatment | Pregnancy Outcome |
|------------|---------------------------------------------------------------|-------------------------------|-----------------------|-------------------------------|--------------------------------------|------------------------------------|---------------------------------|----------------|------------------|------------------|
| 1          | /C3 G1P0A0 IVF-ET                                             | 50 Abdominal pain             | Right tube            | Abdominal pain and vaginal bleeding | 57 Expectant, Tubal rupture with hemoperitoneum up to 800 mL | Emergency laparotomy and salpingectomy | Term delivery, CS                |                |                  |                  |
| 2          | /C3 G1P0A0 IVF-ET                                             | 53 Abdominal pain and vaginal bleeding | Left tube            | Abdominal pain and vaginal bleeding | 53 Expectant, Tubal rupture, Right tube | Emergency laparotomy and salpingectomy | Lost follow-up, live fetus with normal NT 1 wk later |                |                  |                  |
| 3          | /C3 G1P0A0G1P0A0 IVF-ET                                      | 39 Abdominal pain and vaginal bleeding | Right tube            | Abdominal pain and vaginal bleeding | 39 Expectant, Tubal rupture, Right tube, Right corner | Emergency laparotomy and salpingectomy | Lost follow-up, live twin pregnancy 3 wk postoperative |                |                  |                  |
| 4          | /C3 G1P0A0G1P0A0 IVF-ET                                      | 47 Pregnancy of unknown etiology | Right tube            | Right corner and shock, hemoperitoneum up to 1200 mL | 47 Expectant, Right corner rupture and shock, hemoperitoneum up to 1200 mL | Emergency laparotomy and right corner incision, 350 mL CRBC was transfused | Emergency laparotomy and right corner incision, 350 mL CRBC was transfused |                |                  |                  |
| 5          | /C3 G1P0A0G1P0A0 IVF-ET                                      | 46 Abdominal pain and vaginal bleeding | Right tube            | Abdominal pain and vaginal bleeding | 46 Expectant, Right tube | Transvaginal sonography showed heart beats of ectopic pregnancy | Term delivery, CS                |                |                  |                  |
| 6          | /C3 G1P0A0G1P0A0 IVF-ET                                      | 54 Abdominal pain and Right tube | Right tube            | Abdominal pain and Right tube | 54 Expectant, Right tube | Emergency laparotomy and salpingectomy | None |                  |                  |
| 7          | /C3 G1P0A0G1P0A0 IVF-ET                                      | 50 Abdominal pain             | Right tube            | Abdominal pain and vaginal bleeding | 50 Expectant, Right tube | Emergency laparotomy and salpingectomy | None |                  |                  |
| 8          | /C3 G1P0A0G1P0A0 IVF-ET                                      | 50 Abdominal pain             | Right tube            | Abdominal pain and vaginal bleeding | 50 Expectant, Right tube | Emergency laparotomy and salpingectomy | None |                  |                  |
| 9          | /C3 G1P0A0G1P0A0 IVF-ET                                      | 54 Abdominal pain and Right tube | Right tube            | Abdominal pain and Right tube | 54 Expectant, Right tube | Emergency laparotomy and salpingectomy | None |                  |                  |
| 10         | /C3 G1P0A0G1P0A0 IVF-ET                                      | 37 Abdominal pain and Right tube | Right tube            | Abdominal pain and Right tube | 37 Expectant, Right tube | Emergency laparotomy and salpingectomy | None |                  |                  |
| 11         | /C3 G1P0A0G1P0A0 IVF-ET                                      | 50 Abdominal pain             | Right tube            | Abdominal pain and vaginal bleeding | 50 Expectant, Right tube | Emergency laparotomy and salpingectomy | None |                  |                  |
| 12         | /C3 G1P0A0G1P0A0 IVF-ET                                      | 49 Spontaneous pregnancy      | Right tube            | Right tube | 49 Expectant, Right tube | Emergency laparotomy and salpingectomy | None |                  |                  |
| 13         | /C3 G1P0A0G1P0A0 IVF-ET                                      | 63 Abdominal pain and Right tube | Right tube            | Abdominal pain and Right tube | 63 Expectant, Right tube | Emergency laparotomy and salpingectomy | None |                  |                  |
| 14         | /C3 G1P0A0G1P0A0 IVF-ET                                      | 44 Abdominal pain and Right tube | Right tube            | Abdominal pain and Right tube | 44 Expectant, Right tube | Emergency laparotomy and salpingectomy | None |                  |                  |
| 15         | /C3 G1P0A0G1P0A0 IVF-ET                                      | 51 Abdominal pain             | Right tube            | Abdominal pain and vaginal bleeding | 51 Expectant, Right tube | Emergency laparotomy and salpingectomy | None |                  |                  |
| 16         | /C3 G1P0A0G1P0A0 IVF-ET                                      | 50 Abdominal pain             | Right tube            | Abdominal pain and vaginal bleeding | 50 Expectant, Right tube | Emergency laparotomy and salpingectomy | None |                  |                  |
| 17         | /C3 G1P0A0G1P0A0 IVF-ET                                      | 50 Abdominal pain             | Right tube            | Abdominal pain and vaginal bleeding | 50 Expectant, Right tube | Emergency laparotomy and salpingectomy | None |                  |                  |
| 18         | /C3 G1P0A0G1P0A0 IVF-ET                                      | 51 Abdominal pain             | Right tube            | Abdominal pain and vaginal bleeding | 51 Expectant, Right tube | Emergency laparotomy and salpingectomy | None |                  |                  |
| 19         | /C3 G1P0A0G1P0A0 IVF-ET                                      | 50 Abdominal pain             | Right tube            | Abdominal pain and vaginal bleeding | 50 Expectant, Right tube | Emergency laparotomy and salpingectomy | None |                  |                  |
| 20         | /C3 G1P0A0G1P0A0 IVF-ET                                      | 50 Abdominal pain             | Right tube            | Abdominal pain and vaginal bleeding | 50 Expectant, Right tube | Emergency laparotomy and salpingectomy | None |                  |                  |

All = artificial insemination by husband, CRBC = concentrated red blood cells, CS = cesarean section, IVF-ET = in vitro fertilization and embryo transfer, NT = nuchal translucency thickness.
Parent refused to surgical management; a = misdiagnosed as threatened abortion; b = those patients were concomitant with ovarian hyper-stimulation syndrome; c = edecestus was done in those patients to exclude the rupture of ectopic pregnancy; d = the patient was hospitalized for severe ovarian hyper-stimulation syndrome; e = typical sonography characteristics of ectopic pregnancy were showed during regular ultrasound examination.
| Case No. | Gravity, Parity, Abortion, and Ectopic Pregnancy | Mode of Conception at Diagnosis, d | Clinical Presentations | Location of Ectopic Pregnancy | Diameters of Gestational Mass, mm | Fetoplacental Hemodynamics Situation | Treatment of the Ectopic Pregnancy | Blood Loss, mL | Operation Time, min | Blood Transfusion | Maternal Outcome | Pregnancy Outcome |
|----------|------------------------------------------------|----------------------------------|------------------------|-------------------------------|----------------------------------|------------------------------------|-----------------------------------|----------------|----------------|----------------|----------------|----------------|
| 1        | G1P0A0 IVF-ET                                  | 43                               | Abdominal pain          | Right tube                    | Unknown                          | Unknown                            | Unstable Emergency laparotomy      | 50, 500 mL    | 73             | CRBC and 600 mL plasma | Uneventful Term delivery, CS |                    |
| 2        | G2P0A0E1 IVF-ET                               | 35                               | Abdominal pain          | Left tube                     | –                                | Undescribed                      | Unstable Emergency laparoscopy and salpingotomy | 50, 800 mL    | 65             | CRBC and 200 mL plasma | Uneventful Term delivery |                    |
| 3        | G3P0A1E1 IVF-ET                               | 40                               | Abdominal pain and shock| Right tube                    | –                                | 27                                | Unstable Emergency laparoscopy and salpingotomy | 50, 1500 mL   | 95             | None             | Uneventful Term delivery, CS |                    |
| 4        | G1P0A0 IVF-ET                                 | 46                               | Vaginal bleeding and shock| Right tube                    | –                                | Undescribed                      | Unstable Emergency laparoscopy and salpingotomy | 50, 800 mL    | 90             | CRBC and 1400 mL CRBC and 400 mL plasma | Uneventful Term delivery | Lost follow-up with live intrauterine pregnancy |
| 5        | G1P0A0 IVF-ET                                 | 46                               | Vaginal bleeding and abdominal pain| Right tube                    | –                                | 80                                | Unstable Emergency laparoscopy and salpingotomy | 30, 500 mL    | 50             | None             | Uneventful Term delivery, CS |                    |
| 6        | G1P0A0 IVF-ET                                 | 52                               | Abdominal pain and shock| Left tube                     | –                                | Undescribed                      | Unstable Emergency laparoscopy and salpingotomy | No estimate, 1200 mL  | 40             | CRBC and 1600 mL CRBC | Uneventful Term delivery | Abortion |
| 7        | G2P0A1 IVF-ET                                 | 35                               | Shock                   | Left tube                     | –                                | 54                                | Unstable Emergency laparoscopy and salpingotomy | 50, 1500 mL   | 80             | CRBC and 900 mL whole blood | Uneventful Term delivery |                    |
| 8        | G3P0A2 IVF-ET                                 | 58                               | Shock                   | Right tube                    | Unknown                          | Unknown                            | Unstable Emergency laparoscopy and salpingotomy | 50, 1750 mL   | 90             | CRBC and 800 mL CRBC and 650 mL plasma | Uneventful Term delivery, CS |                    |
| 9        | G1P0A0 IVF-ET                                 | 37                               | Vaginal bleeding and abdominal pain| Left tube                     | –                                | 25                                | Unstable Emergency laparoscopy and salpingotomy | 50, 800 mL    | 50             | None             | Uneventful Term delivery | Abortion |
| 10       | G1P0A0 IVF-ET                                 | 59                               | Vaginal bleeding and abdominal pain| Right tube                    | +                                | 63                                | Stable Laparoscopy and salpingotomy | 50, 500 mL    | 40             | None             | Uneventful Term delivery, CS | Lost follow-up, live fetus with normal NT |
| 11       | G2P0A0E1 IVF-ET                               | 91                               | Asymptomatic            | Left uterus corner            | +                                | 71                                | Stable Emergency laparoscopy and uterus corner resection | 800          | 145            | None             | Uneventful Term delivery | Uterine rupture Dead fetus 5 wk later |
| 12       | G3P0A0E2 IVF-ET                               | 42                               | Asymptomatic            | Left uterus corner            | +                                | 31                                | Stable Laparoscopy | 50           | 25             | None             | Uneventful Term delivery |                    |
| 13       | G4P0A1E2 IVF-ET                               | 52                               | Asymptomatic            | Right uterus corner           | +                                | 19                                | Stable Laparoscopy and uterus corner resection | 30           | 25             | None             | Uneventful Term delivery, CS |                    |
| 14       | G1P0A0 IVF-ET                                 | 47                               | Vaginal bleeding and abdominal pain| Left tube                     | +                                | Undescribed                      | Stable Laparoscopy and salpingotomy | 30           | 35             | None             | Uneventful Term delivery, CS |                    |
| 15       | G1P0A0 IVF-ET                                 | 53                               | Asymptomatic            | Left tube                     | +                                | 17                                | Stable Laparoscopy and salpingotomy | 100          | 55             | None             | Uneventful Term delivery, CS |                    |
| 16       | G3P0A1E1 IVF-ET                               | 41                               | Asymptomatic            | Right tube                    | –                                | 29                                | Stable Laparoscopy and salpingotomy | 50           | 60             | None             | Uneventful Term delivery, CS |                    |
| 17       | G1P0A0 IVF-ET                                 | 37                               | Abdominal pain          | Left tube                     | –                                | 59                                | Stable Emergency laparoscopy and left salpingotomy, right tubal ligation | 100, 500 mL   | 110            | None             | Uneventful Term delivery, CS |                    |
| 18       | G5P1A1E2 IVF-ET                               | 51                               | Asymptomatic            | Right tube                    | –                                | 46                                | Stable Laparoscopy and salpingotomy | 20, 50 mL     | 40             | None             | Uneventful Term delivery, CS |                    |
| 19       | G1A0P0 IVF-ET                                 | 48                               | Abdominal pain          | Right tube                    | –                                | 67                                | Stable Laparoscopy and salpingotomy | 20, 150 mL    | 70             | None             | Uneventful Term delivery, CS |                    |
| 20        | G2P0A1 IVF-ET                                 | 46                               | Abdominal pain          | Right tube                    | –                                | 24                                | Stable Laparoscopy and salpingotomy | 80           | 50             | None             | Postoperative fever (38.6) Term delivery, CS (partial placenta previa) | Abortion |
| 21       | G4P1A2 IVF-ET                                 | 41                               | Vaginal bleeding and abdominal pain| Bilateral tube                 | Right: 43; left: 18               | Stable Laparoscopy and salpingotomy | 30           | 65             | None             | Urinary retention |                    |
### Management of Heterotopic Pregnancy

| Case No. | Ectopic Pregnancy Situation | Treatment of the Ectopic Pregnancy | Operation Time (min) | Blood Loss, mL | Material Outcome | Blood Transfusion | Outcome |
|----------|----------------------------|-----------------------------------|----------------------|----------------|----------------|------------------|----------|
| 22       | Right tube                 | Salpingectomy and salpingostomy   | 30                   | None           | Term delivery, CS | None             | None     |
| 23       | Left tube                  | Salpingectomy and salpingostomy   | 24                   | Stable         | Uneventful      | None             | Term delivery, CS |
| 24       | Left tube                  | Salpingectomy and salpingostomy   | 35                   | Stable         | Uneventful      | None             | Term delivery, CS |
| 25       | Right tube                 | Salpingectomy and salpingostomy   | 25                   | Stable         | Uneventful      | None             | Term delivery, CS |
| 26       | Right tube                 | Salpingectomy and salpingostomy   | 41                   | Stable         | Uneventful      | None             | Term delivery, CS |
| 27       | Left tube                  | Salpingectomy and salpingostomy   | 35                   | Stable         | Uneventful      | None             | Term delivery, CS |

**Note:** CRBC = concentrated red blood cells, CS = cesarean section, IVF-ET = in vitro fertilization and embryo transfer, NT = nuchal translucency thickness, PROM = premature rupture of membrane.

1 patient showed the enlargement of EP mass. Those facts suggest that regular ultrasonographic re-examinations and close observations are essential for patients chosen expectant management. Once there are any clues indicating rupture or enlargement of EP, other rescue treatment is recommended to have a good maternal outcome.

Surgical management, either laparotomy or laparoscopy, is a feasible treatment modality for HP. To those patients with unstable hemodynamic situation or with any signs indicating rupture of the EP, emergency surgery is strongly recommended to rescue the patient. Selective surgery is only suitable for those HP patients with stable hemodynamic situation. Surgical removal of the EP mass includes salpingectomy, salpingostomy, cornual resection, oophorectomy, and even total abdominal hysterectomy. Surgical management gains the advantage of complete removal of the EP mass, while there might be a higher abortion rate of the IUP. In our research, total abortion rate in surgery management group was up to 14.8%, obviously higher than the other 2 groups.

Transabdominal sonographic guided aspiration of ectopic gestational embryo with or without embryo-killing drug, which is thought to be minimally invasive, has been performed as treatment modality of EP for years, its safety and effectiveness have been well demonstrated. The difficulty of this treatment modality in the management of HP depends on the location of the ectopic gestational sac, it should be attempted only when the ectopic gestational sac is clearly visualized. Both potassium chloride and hyperosmolar glucose can be used as embryo-killing drugs in the management of HP, while methotrexate (MTX) should be avoided because of its teratogenic effects on the viable IUP. Since rupture of the EP after this procedure have been reported, repeated sonographic examination and strict observation are strongly advised till the ectopic gestational sac becomes stable. And if the enlargement of EP is demonstrated, a repeat procedure or change to surgery management is recommended.

MTX is widely used in the conservative management of EP due to its highly effective to halt trophoblast proliferation. But evidence of MTX-related teratogenicity has already been observed in surviving intrauterine fetus after failed medical abortion or other treatment. Though there are researches showed good therapeutic effect and no negative pregnancy outcomes with medical treatment of MTX, we hold the attitude that the use of MTX, no matter systematically or locally, should be avoided in the treatment of HP.

One report pointed out that about 31.4% HP were end up with natural spontaneous abortion, in our research, the total abortion rate is 26.56% (17/64) in all HP patients, which is lower than previous reported, we speculate the reason is that part of HP are missed before diagnosis. Clayton pointed out that 63.3% of IUP kept on living when HP cases were treated properly and the miscarriage rate of HP patient underwent surgery was up to 31.25% (25/80). While in our research, at least 78.85% (41/52) HP patients finally delivered 1 or more babies and the abortion rate in surgery management group was 25.93% (7/27) at the most. We speculate this owns to the multi-team endeavor of gynecologist and experts in ART in our center.

Due to the rarity of HP, it is difficult to conduct a randomized controlled trial. The limitation of our retrospective study is that patients enrolled in each group are indeed uncomparable in some basal clinical characteristics, it is difficult to point out which is the preferred treatment modality for most HP patients, so the treatment of HP should be individualized, and more researches are needed to be performed.
| Patient No. | Gravity, Parity, Abortion and Ectopic Pregnancy | Mode of Conception | Gestational Age at Diagnosis, d | Clinical Presentations | Location of Ectopic Pregnancy | Fetal Heart Beats of Ectopic Pregnancy | Diameters of Gestational Mass, mm | Treatment of the Ectopic Pregnancy | Maternal Outcome | Pregnancy Outcome |
|------------|---------------------------------|-------------------|-------------------------------|------------------------|-------------------------------|-------------------------------------|-----------------------------------|----------------------------------|----------------|------------------|
| 1          | G1P0A0                          | IVF-ET            | 54                            | Asymptomatic           | Left tube                     | +                                   | 38                                | Transabdominal sonographic guided transvaginal aspiration of gestational sac (twice) | Uneventful    | Preterm delivery, CS (severe preeclampsia) |
| 2          | G2P0A1                          | IVF-ET            | 42                            | Vaginal bleeding and abdominal pain | Left tube                     | +                                   | 41                                | Transabdominal sonographic guided transvaginal aspiration of gestational sac | Uneventful    | Term delivery, CS (POPP) |
| 3          | G3P0A1E1                        | IVF-ET            | 44                            | Asymptomatic           | Left tube                     | +                                   | 22                                | Transabdominal sonographic guided transvaginal aspiration of gestational sac | Uneventful    | Preterm delivery |
| 4          | G6P0A5                          | IVF-ET            | 45                            | Abdominal pain         | Left tube                     | +                                   | Undescribed                      | Transabdominal sonographic guided transvaginal aspiration of gestational sac | Uneventful    | Term delivery, CS (severe preeclampsia) |
| 5          | G1P0A0                          | IVF-ET            | 45                            | Asymptomatic           | Right tube                    | +                                   | 32                                | Transabdominal sonographic guided transvaginal aspiration of gestational sac | Uneventful    | Term delivery, CS (DCDA) |

CS = cesarean section, DCDA = double chorion double amniotic sac, IVF-ET = in vitro fertilization and embryo transfer, POPP = persistent occipito transverse position.

This patient had another transabdominal sonographic guided transvaginal aspiration of gestational sac for the enlargement of the ectopic gestational sac showed by regular sonographic re-examination 1 week later.
CONCLUSIONS

In our retrospective study, transabdominal sonographic guided aspiration of ectopic gestational embryo has the best maternal outcome and the lowest abortion rate, surgical management group shows the highest abortion rate, and expectant management presents the worst maternal outcome.

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