# Hemodynamics of Uterine and Intraovarian Arteries in Ovarian Hyperstimulation Syndrome During Culdocentesis and Persistent Ascites for Predicting Pregnancy Rate

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***Objective.*** To investigate the effects of culdocentesis on uterine and intraovarian hemodynamics and the association between persistent ovarian hyperstimulation syndrome (OHSS) and successful pregnancy.

***Methods.*** Women who were admitted to our hospital with severe OHSS and received the transvaginal culdocenteses were included. All patients were divided according to the amounts of ascites removed (patients with < 2000 mL ascites and patients with ≥ 2000 mL ascites); and their pulsatility index (PI) and maximum peak systolic velocity (MPSV) of uterine and intraovarian arteries were compared. The correlation between the persistent ascites and successful pregnancy was evaluated.

***Results.*** A total of 25 patients and 82 culdocenteses (49 culdocenteses in patients with < 2000 mL ascites and 33 culdocenteses in patients with ≥ 2000 mL ascites) were included. The uterine artery PI value decreased significantly after culdocentesis. Uterine artery PI value reduced after performance of 38 of 49 (78%, < 2000 mL ascites) and 25 of 33 (76%, ≥ 2000 mL ascites) culdocenteses. Uterine MPSV value and the PI and MPSV values of intraovarian arteries did not reduce significantly after culdocentesis. PI and MPSV values before or after culdocenteses between both groups were not different. Persistent ascites was related to higher rate of pregnancy.

***Conclusions.*** Culdocentesis improved uterine perfusion, but did not improve intraovarian perfusion. The improvement of uterine perfusion was not related to the amount of ascites removed. Persistence of ascites was related to successful pregnancy. **(Mid Taiwan J Med 2001;6:30-5)**

**Key words**

culdocentesis, intraovarian artery, maximum peak systolic velocity, ovarian hyperstimulation syndrome, pulsatility index, uterine artery

## INTRODUCTION

Ovarian hyperstimulation syndrome (OHSS) is a life-threatening complication of ovarian stimulation. Paracentesis or culdocentesis has been used to reduce dyspnea and improve the general condition of patients with severe ascites [1]. Most studies concerning OHSS and paracentesis have dealt with the description of the clinical course and the serum biochemical changes [1,2]. Few investigators have described the uterine and

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ovarian hemodynamic changes after paracentesis or culdocentesis. Because uterine perfusion is related to fetal development [3], it is important to investigate whether culdocentesis improves uterine perfusion.

Chen et al initially demonstrated the hemodynamic changes of uterine and intraovarian arteries after paracentesis in patients with OHSS [4]. In our series, we evaluated the effects of transvaginal culdocentesis on the hemodynamics of the uterine and intraovarian arteries. To our knowledge, this is the largest survey. Furthermore, no previous investigators have demonstrated the relationship between persistent ascites and final pregnancy rate. Herein we demonstrated the correlation between the persistent ascites and successful pregnancy.

## MATERIALS AND METHODS

Women who were admitted to our hospital, accepted controlled ovarian hyperstimulation (COH) for *in vitro* fertilization, and developed OHSS in our unit were included. The diagnosis of severe OHSS was based on the definition proposed by Schenker and Weinstein [5]. The ovarian stimulation protocol for *in vitro* fertilization (IVF) using gonadotrophin-releasing hormone agonist (GnRH-a) and gonadotrophins was as previously described [6]. In brief, the ovaries were stimulated using follicle stimulating hormone (FSH, Metrodin; Serono, Rome, Italy) or human menopausal gonadotrophin (HMG, Pergonal, Serono, Rome, Italy). The women also underwent the long protocol down-regulation of the gonadotrophin releasing hormone agonist suppression (Leuprolide acetate depot, Takeda Chemical Industries, Ltd., Japan) from the midluteal phase (menstrual days 21–23).

Individualized injections of gonadotrophin continued until there were two or more follicles ≥18 mm; then the human chorionic gonadotrophin (HCG, 10,000 IU, Profasi; Serono) was administered. Oocytes were retrieved transvaginally 34–36 hours after administration. The oocytes were cultured, inseminated and transferred as previously described [6]. The luteal phase was supported with HCG (1,500 IU/day, Pregnyl; Organon, Oss, the Netherlands) on days 1, 4 and 7 post embryo transfer (ET) and progesterone (Duphaston, 15 mg/day, oral, Solvay Co., Holland) from day 9 post ET.

All patients with tense ascites, dyspnea or progressive oligouria underwent transvaginal culdocentesis. Double lumen ovum pick-up needle (K-2538; Cook, Australia) and suction unit (Craft DUO/VAC, Rocket of London) with negative pressure of 300 mm-Hg were used for ascites aspiration. After the aseptic procedure and systemic analgesic (diazepam, 10 mg, and meperidine, 50 mg, intravenously) administration, transvaginal ultrasound needle-guided aspiration of the ascites was done using a transvaginal transducer (5 MHz; Aloka, Japan). Vital signs were monitored during and after culdocentesis. Removal of ascites was performed until no further fluid was obtained; a maximum of 3500 mL was aspirated. According to the amount of aspirated ascites, the patients were divided into two groups: patients with < 2000 mL ascites and patients with ≥ 2000 mL ascites.

All patients accepted the transvaginal Doppler survey of the uterine and intraovarian arteries before and after culdocentesis as previously described [7]. Sonography was performed with the patients lying in the dorsal supine position. The probe was gently rotated to measure the ascending branch of uterine artery along the lateral border of the uterus. A main vessel within the ovarian stroma was elicited as the intraovarian flow, and the transducer was moved to obtain a clear waveform with equal amplitude. Bilateral uterine and intraovarian arteries were measured and their mean values were used for analysis. The hemodynamics of uterine and intraovarian arteries between the groups before and after culdocenteses were compared. The maximum duration for ultrasound examination was limited to 15 min.

All sonographic surveys were performed by the same operator to eliminate inter-observer variance.

All patients accepted the conservative management, including intravenous fluid and albumin. Albumin was infused according to the serum albumin concentration and the amount of ascites (10 g/L of ascites removed). Hemoconcentration and electrolyte imbalances were corrected using intravenous fluid therapy before culdocentesis in all patients. One week post ET according to the persistence of ascites, all patients were divided into two groups: patients had persistent ascites requiring repeating culdocentesis, and patients had non-persistent ascites. The relationship between persistent ascites and the successful pregnancy was evaluated.

The SAS system was used for statistical analyses. The *t*-test was used to compare the hemodynamic differences between groups with different ascites removal. The pair *t*-test was used to compare uterine and intraovarian hemodynamic changes before and after an intervention in each group. The $\chi^2$ test was used to evaluate the relationship of persistent ascites and pregnancy. A $p$ value of $< 0.05$ was regarded as statistically significant.

## RESULTS

A total of 25 patients and 82 culdocenteses were included (mean ± SD = 3.41 ± 1.31) in this study. Among the Doppler surveys before the 82 culdocentesis, nine (11%) failed to detect uterine and 10 (12%) failed to detect intraovarian artery waveform signals. Among the Doppler surveys after 58 culdocenteses, 12 (15%) failed to detect uterine artery signals and 13 (16%) failed to detect intraovarian artery signals. There were no complications during or after culdocenteses; no injuries occurred to the ovaries or visceral organs and no peritoneal infections were noted in any patient.

During 49 culdocenteses the amount of ascites aspirated was < 2000 mL and during 33 procedures ≥ 2000 mL ascites was aspirated. The mean amounts of ascites in the two groups were 1541.2 ± 251.4 mL and 2424.1 ± 215.2 mL, respectively. The uterine and intraovarian hemodynamic changes before and after culdocentesis are presented in Table 1. The PI and MPSV values before and after culdocenteses in these two groups were not different. The intra-observer variability for all measurements was < 10%.

The individual PI values of uterine and intraovarian arteries before and after culdocentesis in the two subgroups revealed that the uterine artery PI value decreased significantly after culdocentesis ($p$ value < 0.05). The uterine artery PI value decreased after 38 of 49 (78%) procedures of culdocentesis with < 2000 mL ascites removed, and after 25 of 33 (76%) procedures with ≥ 2000 mL ascites removed. In contrast, the PI values of intraovarian artery did not decrease significantly after culdocentesis. The MPSV values of uterine and intraovarian arteries did not decrease significantly after culdocentesis (Table 1).

There were 16 patients with persistent

Table 1. Uterine and intraovarian hemodynamic changes before and after culdocentesis

| | Ascites < 2000 mL (n = 36) | | Ascites ≥ 2000 mL (n = 22) | |
|---|---|---|---|---|
| | Before culdocentesis | After culdocentesis | Before culdocentesis | After culdocentesis |
| Uterine artery* | | | | |
| PI | 1.33 ± 0.21† | 1.30 ± 0.22† | 1.37 ± 0.28† | 1.32 ± 0.27† |
| MPSV | 0.33 ± 0.07 | 0.32 ± 0.07 | 0.34 ± 0.05 | 0.34 ± 0.06 |
| Intraovarian artery* | | | | |
| PI | 0.68 ± 0.07 | 0.68 ± 0.07 | 0.69 ± 0.08 | 0.69 ± 0.09 |
| MPSV | 0.30 ± 0.06 | 0.29 ± 0.06 | 0.30 ± 0.06 | 0.30 ± 0.06 |

*Data are expressed as mean ± SD; †,‡ $p < 0.05$. PI = pulsatility index; MPSV = maximum peak systolic velocity.

and 9 non-persistent ascites. A total of 17 (68%) patients became pregnant. Among the patients with persistent ascites, 14 (88%) became pregnant. Among the patients with non-persistent ascites, only three patients (33%) became pregnant. Persistent ascites was related to higher percentage of successful pregnancies (Fisher's exact test, $p = 0.00986$).

## DISCUSSION

Paracentesis or culdocentesis is the most important treatment for patients with life-threatening OHSS [8]. Drainage of ascites decreases the intra-abdominal pressure, thereby improving venous return, cardiac output and renal perfusion [9]. However, some authors do not recommend paracentesis because of the danger of puncturing and lacerating enlarged ovarian cysts [5], although this procedure was applied safely using ultrasound guidance [10]. However, the main advantage of paracentesis or culdocentesis for treating the OHSS is the high effectiveness in removing the ascites fluid, which results in the rapid relief of symptoms. Furthermore, the removal of ascites may improve renal function, which results in the spontaneous diuresis [8].

Most previous investigators have used transabdominal paracentesis for ascites drainage [4,8], and no investigator has demonstrated the application of transvaginal culdocentesis in patients with OHSS. In our series, we adopted culdocentesis instead of paracentesis. Because of the influence of gravity, we found draining ascites through the cul-de-sac provided an easier approach. Some investigators may have questioned the possible interference of culdocentesis upon embryonic implantation. However, we did not observe significant adverse effects of repeated culdocentesis upon the final outcome compared with paracentesis [4,11].

In our series, we observed that culdocentesis increased uterine perfusion, although the intraovarian flow did not change after culdocentesis. It has been demonstrated that the removal of large amounts of ascites may reduce the intravascular volume, and further induce uterine artery contraction when a patient is not sufficiently hydrated [12]. However, after the adequate hydration, the possibility of insufficient intravascular fluid is decreased. In addition, the decrease of the intraabdominal pressure may contribute to the decreased resistance of uterine artery and improve the uterine perfusion.

We also observed that improvement of uterine perfusion was not related to the amount of ascites removed. Three quarters of the patients had improved uterine perfusion after culdocentesis, and extraction of ascites ≥2000 mL was safe. Most patients with severe OHSS required repeat culdocentesis during the first week post ET. One week post ET, we noted that rapid re-collection of ascites was often related to higher pregnancy rates, whereas patients without persistent ascites often had poor pregnancy outcomes.

The influence of anesthesia upon the embryos was a concern. However, no data have revealed adverse effects upon embryo development [13,14]. Hammadeh et al [14] demonstrated that general anesthesia without nitrous oxide was a suitable alternative to sedation and was recommended for oocyte retrieval. In our laboratory, we routinely use a combination of diazepam (10 mg) and meperidine (50 mg) for general anesthesia during oocyte retrieval. Our experience has revealed its relative safety.

In conclusion, culdocenteses improved uterine perfusion, but did not improve intraovarian perfusion. The improvement of uterine perfusion was not related to the amount of ascites removed. Persistent ascites correlated with the successful pregnancies.

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# 子宮動脈與卵巢動脈血流在卵巢過度刺激症候群病患抽取腹水時之表現及持續性腹水與懷孕率之關聯性

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**背景**　評估卵巢過度刺激症候群之病患於抽取腹水後，對於子宮動脈與卵巢動脈血流變化之影響，亦評估持續性腹水對於預測懷孕率之準確性。

**方法**　以接受卵巢刺激造成卵巢過度刺激及併發腹水之不孕症婦女當作偵測對象，根據抽取腹水之多寡區分爲二組：第一組：抽取腹水< 2000 mL；第二組：抽取腹水≥2000 mL。兩組之子宮與卵巢動脈之脈動係數(pulsatility index，PI)與最大收縮壓流速(maximum peak systolic velocity，MPSV)予以測量並比較。並評估持續性腹水對於預測懷孕率之準確性。

**結果**　共25例病例與82次抽取腹水被規納於此研究，其中第一組佔49次，第二組佔33次，我們發現抽取腹水後會造成子宮動脈之PI值之明顯下降，第一組49次抽取腹水中有38次發現PI值下降(78%)；第二組33次抽取腹水中有25次發現PI值下降(76%)。子宮動脈之MPSV值與卵巢動脈之PI及MPSV值於抽取腹水後並無明顯減低。兩組之PI及MPSV值並無統計學上之差異。同時持續性之腹水與較高之懷孕率有關。

**結論**　抽取腹水可提高卵巢過度刺激症候群病患之子宮動脈血流，卻無法明顯提高卵巢之動脈血流。抽取腹水量之多寡與子宮動脈血流改善之程度並無關聯，腹水之持續存在與否可用於預測胚胎植入後之懷孕率。（中台灣醫誌 **2001;6:30-5**）

**關鍵詞**

抽取腹水，卵巢內動脈，最大收縮壓流速，卵巢過度刺激症候群，脈動係數，子宮動脈

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