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Impact on ovarian reserve after laparoscopic ovarian cystectomy with reduced port number: a randomized controlled trial

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ABSTRACT

Objectives: Single-port access (SPA) laparoscopic ovarian cystectomy has been reported as a comparable procedure to conventional laparoscopy in terms of operative outcomes. However, whether ovarian function after SPA laparoscopic surgery is similar to conventional laparoscopy is questioned due to the limitations in moving instruments. The aim of this study was to evaluate whether the reduced port number affects the ovarian reserve after laparoscopic ovarian cystectomy.
Study design: This was a randomized controlled trial of 87 women with benign ovarian cyst, who attended a university hospital and were scheduled for laparoscopic ovarian cystectomy. Women were randomized to SPA, two-port access (TPA), or four-port access (FPA) laparoscopic groups. The primary outcome was the serum anti-Müllerian hormone (AMH) levels: preoperative, 1 week, 1 month and 3 months after the operation. Secondary outcomes were operative outcomes.
Results: The mean serum AMH levels of preoperative, 1 week, 1 month and 3 months after laparoscopy were 4.4 ± 2.9, 2.7 ± 2.2, 2.3 ± 1.9, and 2.5 ± 1.5 ng/mL (in the SPA group), 3.6 ± 2.5, 2.3 ± 2.2, 2.6 ± 3.2, and 2.7 ± 2.6 ng/mL (in the TPA group), and 3.9 ± 3.2, 2.4 ± 2.1, 2.5 ± 2.0, and 2.8 ± 2.2 ng/mL (in the FPA group), respectively. There was no statistically significant difference in the serial change of AMH levels among the SPA, TPA and FPA groups.
Conclusions: The laparoscopic ovarian cystectomy with reduced port number does not affect the serial change of ovarian reserve. The SPA or TPA laparoscopy may be the alternative method to conventional laparoscopy in terms of ovarian reserve.

1. Introduction

Single-port access (SPA) laparoscopic surgery has been reported as feasible and comparable with the conventional method in many different fields of surgery [1–4]. In surgical treatment of ovarian cysts, SPA laparoscopic surgery has also been reported as an alternative procedure to conventional laparoscopic ovarian cystectomy or oophorectomy, as far as surgical outcome is concerned [5,6]. The potential advantages of SPA laparoscopic surgery have been considered to be decreased postoperative pain and cosmetic satisfaction, although their results are still controversial [7–9].

In conventional laparoscopic ovarian cystectomy, reduction of ovarian reserve after surgery has been reported: it is attributed to the amount of ovarian tissue removed during the surgery and damage of the ovarian bed by a use of electrocoagulation [10–13]. Considering that SPA laparoscopic surgery has some weaknesses, such as limitation in moving instruments, SPA laparoscopic surgery may have more negative impact on the ovarian reserve than that of the conventional procedures. However, whether the ovarian reserve after SPA laparoscopic surgery is similar to conventional laparoscopy is unknown.

Therefore, this study was conducted to evaluate whether the reduced port number affects the ovarian reserve after laparoscopic ovarian cystectomy. We compared the impact on ovarian reserve after single-port, two-port, and four-port access laparoscopic

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ovarian cystectomies. Ovarian reserve was estimated using anti-Müllerian hormone (AMH), which is acknowledged as the most reliable serum marker.

2. Materials and methods

2.1. Study design and participants

This prospective randomized controlled trial was approved by the institutional review boards and ethics committee of CHA Gangnam Medical Center, CHA University. This study was registered with ClinicalTrials.gov (NCT01631253), and informed consent was gained from all participants.

Between October 2011 and December 2012, women who were scheduled for laparoscopic ovarian cystectomy due to benign ovarian cyst were recruited to participate in this study. The inclusion criteria were as follows: (1) women with presumed benign ovarian cyst by ultrasonography, computed tomography (CT), or magnetic resonance imaging (MRI), (2) aged $\geq$21 and $\leq$45 years, (3) ovarian cyst $\geq$3 cm and $<$10 cm in size, and (4) with regular menstrual cycle (21–35 days) at the time of operation. The exclusion criteria were as follows: (1) women who wanted to receive oophorectomy, (2) previous history of ovarian cyst surgery, (3) any suspicious findings of malignant ovarian diseases, (4) postmenopausal status, (5) women who were pregnant, (6) taking any medication such as oral contraceptive pills or other hormonal agents within 3 months before enrollment, and (7) other endocrine disease.

2.2. Sample size calculation and randomization

Due to the lack of related published literature, the sample size calculation was based on data of the mean difference in decline of serum AMH level at the third month after surgery between laparoscopic and laparotomic ovarian cystectomy (0.5 ng/mL, SD 0.632 ng/mL) [14]. Considering this difference, at least 25 women were needed in each arm to achieve statistical power of 80% with an alpha of 0.05. Taking into account potential loss of patients to follow-up, a total of 90 patients were recruited.

The patients were randomly allocated to three groups: the single-port access laparoscopy (SPA) group, the two-port access laparoscopy (TPA) group, or the four-port access laparoscopy (FPA) group. Randomization was achieved through the use of 90 sealed opaque envelopes in random blocks previously prepared by a statistician. The envelope containing the group allocation was opened in the operating room by a study nurse, who was not involved in the randomization procedure, before the surgery, allowing the operating equipment to be prepared. This study was open label.

2.3. Operative techniques

All procedures were performed by three laparoscopic surgeons, who had managed more than 100 cases of single-port or two-port laparoscopy since November 2008, and who have performed SPA laparoscopy once for every two conventional laparoscopies for ovarian surgery. All patients underwent the surgery under general anesthesia with endotracheal intubation and were placed in the Trendelenburg position.

For the SPA laparoscopic procedure, a home-made port was used for the umbilical port. The making and settlement of the home-made port have been described previously [15]. For TPA laparoscopic procedure, the umbilical home-made port was used, and one additional 5-mm trocar was inserted in the suprapubic area. For the FPA laparoscopic procedure, one 12-mm trocar in the umbilicus and three ancillary 5-mm trocars (one in the suprapubic area and two in the bilateral lower quadrant areas) were inserted. A 5-mm 0° laparoscope and rigid laparoscopic instruments were used for all laparoscopic procedures. A sharp cortical incision on the ovarian cyst surface was made and a cleavage plane was identified by sharp dissection or hydrodissection. The entire cyst was then enucleated and stripped from the normal ovarian tissue, using bilateral traction, water pressure, and/or sharp dissection. Hemostasis was achieved by selective application of bipolar current. Laparoscopic ovarian suturing was not used in these procedures. The removed cyst was extracted through the umbilicus, using an Endopouch (Ethicon Endo-surgery, Cincinnati, OH). The fascia was sutured with 1–0 Vicryl and the skin was closed using intracutaneous 3–0 Vicryl sutures.

2.4. Outcome measures

The primary outcomes were serum AMH levels measured before surgery, and 1 week, 1 month, and 3 months after surgery. Secondary outcomes were operative outcomes, including operating time, estimated blood loss (EBL), hemoglobin (Hb) drop, adhesiolysis, rupture of cyst, operative complications, conversion rate, and length of hospital stay.

Blood samples were obtained from patients to measure the serum AMH level. The serum was separated from the whole blood, transferred to sterile polypropylene tubes and stored at -70 °C. The serum AMH concentrations were measured by an enzyme immunoassay kit, according to the manufacturer's instructions (Immunotech version, Beckman Coulter, Marseille, France). For AMH, the detection limit of the assay was 0.14 ng/mL, and the intra- and inter-assay coefficients of variation for the AMH assay were below 12.3% and 14.2%, respectively.

The operating time was defined as the interval between skin incision and skin closure. EBL was calculated as the difference between the total amount of suction and irrigation, plus the difference between the total gauze weight before and after surgery. Hb drop was defined as the difference between preoperative Hb and Hb at day 1 after surgery. Operative complications were defined as all intraoperative and postoperative complications arising within 3 months from surgery. Conversion was defined as the use of additional ports or conversion to open surgery. Length of hospital stay was defined as the day from the operation to discharge.

2.5. Statistical analysis

Statistical analysis was performed using SPSS version 13.0 (SPSS, Chicago, IL, USA). $P < 0.05$ was considered statistically significant. All analyses were performed in accordance to the laparoscopic procedure which was initially intended, based on the intention-to-treat analysis. The mean $\pm$ SD or median (IQR) was used to describe the distribution of data after the Kolmogorov–Smirnov normality test. Differences among the three groups were evaluated using the Kruskal–Wallis test or analysis of variance (ANOVA) for continuous variables and a multiple comparison was performed by post hoc test using a least significant difference (LSD) method. For categorical variables, the χ^2 test or Fisher's exact test in case of small number of patients were used. The serial change of variables was evaluated using the ANOVA with repetitive measures and a multiple comparison was performed by post hoc test using a Bonferroni method.

3. Results

Of the 90 women assessed for eligibility, three women were excluded because they declined participation. The remaining 87 women were randomized. Twenty-nine women were allocated