Additional benefit of hemostatic sealant in preservation of ovarian reserve during laparoscopic ovarian cystectomy: a multi-center, randomized controlled trial

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STUDY QUESTION: Is hemostasis by hemostatic sealant superior to that achieved by bipolar coagulation in preserving ovarian reserve in patients undergoing laparoscopic ovarian cystectomy?

SUMMARY ANSWER: Post-operative ovarian reserve, determined by serial serum anti-Müllerian hormone (AMH) levels, was significantly less diminished after ovarian hemostasis when hemostatic sealant was used rather than bipolar coagulation.

WHAT IS KNOWN ALREADY: Hemostasis achieved with bipolar coagulation at ovarian bleeding site results in damage to the ovarian reserve.

STUDY DESIGN, SIZE, DURATION: A prospective, multi-center randomized trial was conducted on 100 participants with benign ovarian cysts, between December 2012 and October 2013.

PARTICIPANT/MATERIALS, SETTING, METHODS: Participants were randomized to undergo hemostasis by use of either hemostatic sealant (FloSeal™) or bipolar coagulation during laparoendoscopic single-site (LESS) ovarian cystectomy. The primary end-point was the rate of decline of ovarian reserve calculated by measuring serum AMH levels preoperatively and 3 months post-operatively.

MAIN RESULTS AND THE ROLE OF CHANCE: Age, parity, socio-demographic variables, preoperative AMH levels, procedures performed and histologic findings were similar between the two groups of patients. There were also no differences in operative outcomes, such as conversion to other surgical approaches, operative time, estimated blood loss, or perioperative complications between the two groups. In both study groups, post-operative AMH levels were lower than preoperative AMH levels (all \( P < 0.001 \)). The rate of decline of AMH levels was significantly greater in the bipolar coagulation group than the hemostatic sealant group (41.2% [IQR, 17.2–54.5%] and 16.1% [IQR, 8.3–44.7%], respectively, \( P = 0.004 \)).

LIMITATIONS, REASONS FOR CAUTION: Some caution is warranted because other ovarian reserve markers such as serum markers (basal FSH and inhibin-B) or sonographic markers were not assessed.

WIDER IMPLICATIONS OF THE FINDINGS: The present study shows that the use of a hemostatic sealant during laparoscopic ovarian cystectomy should be considered, as hemostatic sealant provides the additional benefit of preservation of ovarian reserve.

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Key words: ovarian cystectomy / ovarian cysts / ovarian reserve / AMH

† T.S. and S.-H.L. contributed equally to this paper.
Introduction

Laparoscopy has become the gold standard for surgical treatment of benign ovarian cysts and is usually performed by stripping the ovarian cyst wall, followed by bleeding control of the ovarian wound ground using bipolar coagulation. However, hemostasis achieved with bipolar coagulation could result in damage to the ovarian reserve (Tsolakidis et al., 2010; Coric et al., 2011; Hirokawa et al., 2011; Var et al., 2011; Sonmez et al., 2013) and decrease the response of the ovaries to hormonal stimulation for assisted reproductive technologies (Esinler et al., 2006; Almog et al., 2010; Benaglia et al., 2010). It is thought that excessive use of bipolar coagulation for hemostasis purposes may result in thermal destruction of normal ovarian follicles. Some cases of premature ovarian failure have also been reported after bilateral ovarian cystectomy (Busacca et al., 2006; Di Prospero and Micucci, 2009; Hwu et al., 2011).

To avoid damage to healthy ovarian tissue, hemostasis using various topical hemostatic agents has been introduced to control post-cystectomy ovarian wound bleeding (Angioli et al., 2009; Ebert et al., 2009). Among these, FloSeal (Baxter Healthcare Corporation, Deerfield, IL, USA) is a hemostatic sealant composed of a gelatin-based matrix and thrombin solution. Upon coming into contact with blood after application at a bleeding site, the gelatin particles swell and tamponade the bleeding. The bulk of the gelatin matrix-thrombin composite has the effect of slowing the blood flow and providing exposure to a high thrombin concentration, thus hastening clot formation. This treatment may be particularly suitable for use in post-cystectomy ovarian wound bleeding, where there is a superficially pervasive focus of bleeding.

Although the use of FloSeal for ovarian hemostasis during laparoscopic ovarian cystectomy may preserve ovarian reserve, no data on its effectiveness were available at the commencement of this study. Therefore, we conducted a multi-center, randomized controlled trial to investigate whether hemostasis by use of FloSeal was superior to that achieved by bipolar coagulation in preserving ovarian reserve. This was assessed by comparing the rate of decline of post-operative serum anti-Müllerian hormone (AMH) levels in patients undergoing laparoscopic ovarian cystectomy for benign ovarian cysts.

Materials and Methods

Study design and subjects

This study was conducted prospectively between December 2012 and October 2013 at three institutions (CHA Gangnam Medical Center, Seoul, Korea; Kangbuk Samsung Hospital, Seoul, Korea; National Health Insurance Service Ilsan Hospital, Goyang, Korea). Women who were planning to undergo laparoscopic ovarian cystectomy for benign ovarian cysts were invited to participate. Inclusion criteria were: age between 18 and 45 years, maximum cyst diameter between 3 and 10 cm, regular menstrual bleeding (defined as cycle length between 21 and 45 days) and appropriate medical status for laparoscopic surgery (American Society of Anesthesiologists Physical Status classification 1 or 2). Exclusion criteria were: any suspicious finding of malignant ovarian diseases, post-menopausal status, pregnancy, lactation, baseline serum AMH <0.50 ng/ml, any other endocrine disease (such as thyroid dysfunction, hyperprolactinemia or Cushing’s syndrome) or use of hormonal treatments in the 3 months before enrollment.

Subjects were randomly assigned to a hemostatic sealant group or hemostatic bipolar coagulation at a 1:1 ratio using a random permuted-block randomization algorithm with stratification according to participating institution via an interactive Web-based response system (http://www.randomization.com). Randomization took place when a study nurse called the coordinating center just before general anesthesia on the day of surgery. The protocol was approved by the Institutional Review Board of each participating institution and registered with ClinicalTrials.gov (Identifier: NCT01857466). The study was performed in accordance with the protocol, and all subjects provided written informed consent before participation.

Study treatment

One surgeon from each participating center performed all the surgeries at that institution. Participating surgeons had comparable surgical skills and experience and a preference for laparoendoscopic single-site (LESS) surgery. After the introduction of general anesthesia, the subject was placed in the Trendelenburg position, and a single multi-channel port was inserted through the umbilicus. The use of various ports and laparoscopic instruments was allowed when performing the LESS surgery based on the surgeon’s preference. Before initiating ovarian cystectomy, the ovary was completely freed by obuse and sharp dissection. After identifying a cleavage plane between the cyst wall and ovarian cortex, the ovary was pulled slowly and gently in opposite directions by means of twoatraumatic grasping forceps. Once the whole cystic wall was separated from the ovarian cortex, hemostatic sealant or bipolar coagulation was applied for hemostasis. In the hemostatic sealant group, sites of bleeding were covered with FloSeal under direct vision with a laparoscopic applicator (Supplementary data, Movie S1), and the ovarian cortex was closed on itself, followed by a 2-min wait for the FloSeal to act. Bleeding sites were then reexamined by irrigation. In the bipolar coagulation group, hemostasis of the ovarian parenchyma was achieved with selective minimal bipolar coagulation (20–30 watt current) without excessive coagulation of the surgical defect to avoid damaging the ovary. In both groups, residual ovarian tissue was not sutured, and ovarian edges were left to heal by secondary intention (Candiani et al., 2005). However, ovarian suture was allowed for additional ovarian hemostasis and was recorded. No chemical or mechanical hemostats except for FloSeal or bipolar coagulation were allowed in either group.

Total operative time was defined as the time from skin incision to skin closure. Estimated blood loss (EBL) was calculated by the anesthesia unit as the difference between the total amounts of suction and irrigation. A blood sample was taken within 24 h following surgery, and hemoglobin decrease was defined as the difference between preoperative hemoglobin levels and that at post-operative day 1. Subjects were discharged from the hospital after bowel activity restoration, ambulation, no post-operative fever and no need for narcotic analgesics. Length of hospital stay was defined as the time from operation to discharge. All intraoperative and post-operative complications arising within 3 months of surgery were recorded. All subjects were scheduled for follow-up appointments at 1-week, 1-month and 3-month post-surgery.

Outcome measures and sample size

The primary aim of the current trial was to test whether hemostasis by hemostatic sealant (FloSeal) is superior to that by bipolar coagulation in preserving ovarian reserve in patients undergoing laparoscopic ovarian cystectomy. Serum AMH level was chosen as the best marker to evaluate the impact of laparoscopic cystectomy on ovarian reserve and was measured before randomization and at post-operative 3 months in all subjects. The outcome measure was the rate of decline in AMH level from before surgery to 3 months post-surgery: decline rate (%) = 100 × [preoperative AMH level – post-operative AMH level]/preoperative AMH level. Blood samples were obtained from patients to measure the serum AMH level. The serum was separated from the whole blood, transferred 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.

At the time of the study design, because of the lack of publications describing changes in AMH level after LESS ovarian cystectomy, we conducted a pilot study to identify the sample size needed at one participating institution (CHA Gangnam Medical Center). AMH level was measured before surgery and 3 months post-surgery in 20 patients who underwent LESS ovarian cystectomy with hemostasis by bipolar coagulation (mean ± SD, 40 ± 33%). Arbitrarily, we considered a relative 20% difference in AMH level between the two surgical techniques to be clinically relevant. Assuming a significance level of 5% and power of 80% and allowing for a 12% dropout rate, we estimated that 50 subjects would be needed per group (one-sided test). A one-sided test was used in the power calculation because previous studies have suggested that bipolar coagulation for ovarian hemostasis might decrease postoperative ovarian reserve (Tsatalidis et al., 2010; Coric et al., 2011; Hirokawa et al., 2011; Var et al., 2011; Sonmez et al., 2013); in contrast, there is no evidence that application of hemostatic sealant decreases ovarian reserve.

Statistical analysis
SPSS 13.0 (SPSS, Inc., Chicago, IL, USA) was used for all statistical analyses. All analyses were performed according to the intention-to-treat principle. Qualitative data are presented as frequency. In cases of quantitative variables, after the normality of the data was checked, mean ± SD and median (range) were used to describe normal and non-normal distribution, respectively. Baseline clinical characteristics and study outcomes between the two groups were compared using Student’s t-test or the Mann–Whitney test for continuous variables and the χ² test or Fisher’s exact test for categorical variables, as appropriate. The Wilcoxon signed-rank test was used to compare serum AMH levels before and after surgery in the same group. All P-values were two-sided and considered statistically significant if P < 0.05.

Results
Enrollment took place from December 2012 through July 2013, and the 3-month follow-up was concluded in October 2013. Of the total 118 patients who were invited to participate in the study, 13 declined participation, and 5 were ineligible for the study because of baseline AMH level <0.50 ng/ml; thus, 100 subjects underwent randomization (Fig. 1). The characteristics of patients who declined participation were similar to those of the study participants (data not shown). There were 50 subjects randomly assigned to the bipolar coagulation group or the hemostatic sealant group. None of the study participants changed groups or stopped participating in the study after randomization or before surgery. All procedures were completed by LESS surgery. In two patients (4%) assigned to the bipolar group, additional hemostasis using ovarian suture was required to control ovarian bleeding and prevent ovarian thermal damage by excessive bipolar coagulation. In three patients (6%) assigned to the hemostatic sealant group, bipolar coagulation was required in addition to FloSeal application to control ovarian bleeding.

The baseline demographic characteristics of the two groups are described in Table I. The mean age and body mass index of the study subjects were 31.2 ± 5.8 years and 20.8 ± 2.6 kg/m², respectively. The preoperative tumor marker levels, maximum diameter of ovarian cysts
and bilaterality of lesions were similar between the two study groups. In Table II, the surgical results are compared between the two groups. Ovarian pathology, the procedures performed, operative time, estimated blood loss, hemoglobin decrease, intraoperative and perioperative complications, and length of hospital stay were all similar between the two groups.

Preoperative AMH levels were also similar between patients in the two study groups (3.26 ng/ml [IQR, 2.01–5.04 ng/ml] in the bipolar coagulation group and 3.20 ng/ml [IQR, 2.32–6.07 ng/ml] in the hemostatic sealant group) \((P = 0.659)\) (Table III). At 3-month post-surgery, serum AMH levels of the bipolar coagulation and hemostatic sealant groups fell to 2.04 ng/ml (IQR, 1.00–3.56 ng/ml) \((P < 0.001)\) and 2.67 ng/ml (IQR, 1.34–5.13 ng/ml) \((P < 0.001)\), respectively. Therefore, the rate of decline of serum AMH level was 41.2% (IQR, 17.2–54.5%) in the bipolar coagulation group versus 16.1% (IQR, 8.3–44.7%) in the hemostatic sealant group. Serum AMH levels decreased significantly more in the bipolar coagulation group than in the hemostatic sealant group \((P = 0.004)\) (Fig. 2).

### Discussion

We undertook a multi-center, randomized controlled trial to test the hypothesis that the use of hemostatic sealant for ovarian hemostasis would help preserve ovarian reserve to a greater extent than bipolar coagulation. We found that laparoscopic ovarian cystectomy decreased ovarian reserve, as determined by AMH levels, independent of the method used to obtain hemostasis of the ovarian tissue. However, ovarian reserve was significantly less diminished after ovarian hemostasis when hemostatic sealant was used rather than bipolar coagulation (16.1 versus 41.2%, respectively; \(P = 0.004)\).

Ovarian reserve is defined as the functional potential of the ovary, which reflects the number and quality of antral follicles left in the ovary, and is correlated with response to ovarian stimulation using exogenous gonadotrophins (Broekmans et al., 2006; Esinler et al., 2006; Benaglia et al., 2010). Over the years, various tests and markers for

<table>
<thead>
<tr>
<th>Table I  Baseline characteristics.</th>
<th>Bipolar coagulation group ((n = 50))</th>
<th>Hemostatic sealant group ((n = 50))</th>
<th>(P)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>31.2 ± 5.7</td>
<td>31.3 ± 6.1</td>
<td>0.860</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>20.5 ± 2.6</td>
<td>21.2 ± 2.6</td>
<td>0.146</td>
</tr>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nulliparous</td>
<td>40 (80%)</td>
<td>40 (80%)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Parous</td>
<td>10 (20%)</td>
<td>10 (20%)</td>
<td></td>
</tr>
<tr>
<td>Preoperative CA125 (IU/ml)</td>
<td>24.4 (6.2–151.9)</td>
<td>18.3 (4.3–208.3)</td>
<td>0.166</td>
</tr>
<tr>
<td>Preoperative CA19–9 (IU/ml)</td>
<td>19.1 (0.6–161.3)</td>
<td>12.5 (3.4–172.7)</td>
<td>0.182</td>
</tr>
<tr>
<td>Maximum diameter of ovarian cyst (cm)</td>
<td>6.18 ± 1.8</td>
<td>5.97 ± 2.3</td>
<td>0.262</td>
</tr>
<tr>
<td>Abdominal surgical history</td>
<td>7 (14%)</td>
<td>8 (16%)</td>
<td>0.779</td>
</tr>
<tr>
<td>Bilaterality of lesion</td>
<td>13 (26%)</td>
<td>8 (16%)</td>
<td>0.326</td>
</tr>
<tr>
<td>Preoperative hemoglobin (mg/dl)</td>
<td>12.8 ± 1.0</td>
<td>12.8 ± 1.1</td>
<td>0.528</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table II  Surgical results.</th>
<th>Bipolar coagulation group ((n = 50))</th>
<th>Hemostatic sealant group ((n = 50))</th>
<th>(P)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathology</td>
<td></td>
<td></td>
<td>0.302</td>
</tr>
<tr>
<td>Endometrioma</td>
<td>28 (56%)</td>
<td>28 (56%)</td>
<td></td>
</tr>
<tr>
<td>Mature cystic teratoma</td>
<td>11 (22%)</td>
<td>16 (32%)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>11 (22%)</td>
<td>6 (12%)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Surgical approach</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single-port laparoscopy (LESS)</td>
<td>50</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Multi-port laparoscopy</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Ovarian surgery</td>
<td></td>
<td></td>
<td>0.326</td>
</tr>
<tr>
<td>UOC</td>
<td>37 (74%)</td>
<td>42 (84%)</td>
<td></td>
</tr>
<tr>
<td>BOC</td>
<td>13 (26%)</td>
<td>8 (16%)</td>
<td></td>
</tr>
<tr>
<td>USO or BSO</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Adhesiolysis</td>
<td>15 (30%)</td>
<td>12 (24%)</td>
<td>0.326</td>
</tr>
<tr>
<td>Additional ovarian hemostasis (a)</td>
<td>2 (4%)</td>
<td>3 (6%)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Operative time (min)</td>
<td>62.8 ± 29.9</td>
<td>68.9 ± 27.7</td>
<td>0.205</td>
</tr>
<tr>
<td>Estimated blood loss (ml)</td>
<td>67.3 ± 49.9</td>
<td>55.9 ± 45.4</td>
<td>0.218</td>
</tr>
<tr>
<td>Hemoglobin drop (mg/dl)</td>
<td>1.85 ± 0.81</td>
<td>1.69 ± 0.84</td>
<td>0.228</td>
</tr>
<tr>
<td>Transfusion</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Post-operative complications</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
<td>3 (2–4)</td>
<td>3 (2–5)</td>
<td>0.894</td>
</tr>
</tbody>
</table>

**Tables and Notes:**
- **Table I**: Baseline characteristics.
- **Table II**: Surgical results.
- **Table III**: Ovarian reserve by assessment of AMH levels pre- and post-operatively.
- AMH, anti-Müllerian hormone; IQR, interquartile range.
- LESS, laparoendoscopic single-site surgery; UOC, unilateral ovarian cystectomy; BOC, bilateral ovarian cystectomy; USO, unilateral salpingo-oophorectomy; BSO, bilateral salpingo-oophorectomy.
- Some participants received additional ovarian hemostasis because, despite the application of the allocated method for ovarian hemostasis, ovarian bleeding did not stop.
ovarian reserve have been reported. Assessment of ovarian reserve includes measurement of levels of serum markers, such as basal FSH, inhibin-B and AMH, and ultrasonographic markers, such as ovarian volume and antral follicle count (Broekmans et al., 2006; Var et al., 2011). Of these, serum AMH level has recently been accepted as the most reliable and easily measurable marker for post-operative assessment of ovarian reserve (Seifer et al., 2002; Fanchin et al., 2003; McIlveen et al., 2007; Kwee et al., 2008); it is menstrual cycle-independent, consistent cycle-to-cycle, and is unaffected by the use of oral contraceptive pills or gonadotrophin-releasing hormone agents (Seifer and Maclaughlin, 2007). In a recent systematic review by Somigliana et al., evidence deriving from the evaluation of eleven studies addressing AMH level modifications after surgical excision of endometriomas consistently supported a surgery-related damage to ovarian reserve (Somigliana et al., 2012). Therefore, in this trial, we used serum AMH level as a marker to evaluate the impact of laparoscopic cystectomy on ovarian reserve.

Preserving ovarian reserve is of paramount importance during ovarian surgery. However, the safety of cystectomy for ovarian cysts has been questioned due to occasional damage to the ovary caused by surgery. Therefore, after laparoscopic stripping of the ovarian cyst wall, bleeding control of the ovarian wound ground is important. To achieve ovarian hemostasis, direct compression of the ovarian wound, ovarian sutures, and bipolar coagulation of the bleeding ground are widely used. In most cases, direct compression alone is insufficient. In contrast, ovarian sutures are useful, but can result in additional damage to healthy tissue and an increase in intra-ovarian pressure in ischemic regions. Additionally the inflammatory effect of suture materials on ovarian tissue has not been evaluated. Bipolar coagulation of the ovarian wound after cystectomy is an effective ovarian hemostasis method but can potentially harm the surrounding healthy ovarian tissue. In this study, we provide new evidence that ovarian hemostasis by hemostatic sealant is a promising strategy to control post-cystectomy ovarian wound bleeding and preserve ovarian reserve.

In this study, all the procedures were completed by LESS surgery. We believe that the LESS surgery itself did not affect the post-operative change of ovarian reserve. In the bipolar coagulation group, serum AMH levels declined by 41.2% 3 months post-operatively. This rate is similar to that reported in a recent meta-analysis (Raffi et al., 2012). In this meta-analysis, data from eight studies that assessed 237 patients who underwent laparoscopic ovarian cystectomy using three or four trocars were pooled, revealing a 38% post-operative decline rate in serum AMH level (Raffi et al., 2012). Furthermore, according to a randomized controlled trial comparing post-operative changes in ovarian reserve after single-port (LESS), two-port or four-port laparoscopic ovarian cystectomy, port number in laparoscopic cystectomy did not influence post-operative changes in serum AMH level (Yoon et al., 2014).

Although no research published before start of the present study had compared post-operative changes in AMH levels between hemostatic sealant (FloSeal) and bipolar coagulation groups of patients who underwent laparoscopic ovarian cystectomy, one study has since been published (Sonmez et al., 2013). Mean AMH levels 3 months post-surgery in the hemostatic sealant group in that study were higher than in the bipolar coagulation group, but the difference was not significant (3.07 ± 1.43 versus 2.84 ± 1.12 ng/ml; P > 0.05). However, that study was a single-center study, and only 15 subjects per group were evaluated, there was no intention-to-treat analysis, and no sample size calculations were performed before the study. We believe that an adequate sample size is required to reveal small but definite differences in ovarian reserve.
Our study had several limitations. First, we did not assess other ovarian reserve markers such as serum markers (basal FSH and inhibin-B) or sonographic markers (antral follicle count, peak systolic velocity of the ovarian stroma vasculature and ovarian volume), although serum AMH level has recently been accepted as the most reliable and easily measurable marker for post-operative assessment of ovarian reserve (Seifer et al., 2002; Fanchin et al., 2003; McIlveen et al., 2007; Kwee et al., 2008). Second, we did not use new second-generation bipolar electro-surgical devices, such as LigaSureTM or EnSealTM in the bipolar coagulation group. Furthermore, we did not use other hemostatics such as TisseelTM or TachosilTM in the hemostatic sealants group. Therefore, our results may not applicable to other device settings. Third, we did not collect the serum AMH samples at exact times in the early follicular phase. Although four clinical studies have demonstrated negligible variation of AMH throughout the menstrual cycle (Cook et al., 2000; La Marca et al., 2004, 2006; Hehenkamp et al., 2006), Sowers et al. reported that there were two menstrual patterns of AMH: the ‘aging ovary’ pattern included low AMH levels with little variation while the ‘younger ovary’ pattern included higher AMH levels with significant follicular phase variation (Sowers et al., 2010). One of major concerns raised about this study was inclusion of women up to 45 years of age, who would already have a decreased ovarian reserve as it would be difficult to observe an adverse effect of hemostatic methods in such women. This could have led to groups being more similar to each other and obscuring a significant difference between investigated methods. If the study included only women with a good ovarian reserve, the difference could have been higher. Another concern was the possibility of any potential adverse effects of hemostatic sealant on gametogenesis and post-operative adhesion formation, which could also affect future reproductive potential. More research is needed to resolve these concerns.

In conclusion, we found that use of a hemostatic sealant to control ovarian bleeding during laparoscopic ovarian cystectomy reduced the damage to ovarian reserve compared with bipolar coagulation as determined by pre- and post-operative measurement of serum AMH level. Larger scale, long-term follow-up, randomized controlled trials are required to confirm, or reject, the results of this study.

Supplementary data
Supplementary data are available at http://humrep.oxfordjournals.org/.

Authors’ roles
The study idea was conceived by W.Y.K. The study protocol and analysis were developed by all authors. The first draft was written by T.S. and S.-H.L. W.Y.K. participated in the revision of the paper and critical discussions. All authors approved the final draft.

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Conflict of interest
None declared.

References


