A randomized controlled study comparing harmonic versus electrosurgery in laparoscopic myomectomy

Pietro Litta, M.D.,[a] Sara Fantinato, M.D.,[a] Francesco Calonaci, M.D.,[b] Erich Cosmi, Ph.D., M.D.,[a] Marco Filippeschi, M.D.,[c] Irene Zerbetto, M.D.,[b] Felice Petraglia, M.D.,[b] and Pasquale Florio, Ph.D., M.D.[b]

[a] Department of Gynecological Science and Human Reproduction, University of Padua, School of Medicine, Padua; [b] Department of Pediatrics, Obstetrics and Reproductive Medicine, Section of Obstetrics and Gynecology, University of Siena, Siena; and [c] Section of Obstetrics and Gynecology, San Giuseppe Hospital, Empoli, Italy

Objective: To compare the effectiveness and safety of harmonic scalpel versus electrosurgery to reduce blood loss during laparoscopic myomectomy.
Design: Prospective randomized controlled study.
Setting: Tertiary referral centers for gynecological care.
Patient(s): One hundred sixty consecutive premenopausal women with symptomatic uterine leiomyomata who were assigned to one of the two treatment groups (a total of 80 patients in each group): treatment with electrosurgery devices with a vasoconstrictive solution (50 mL of saline solution and 0.5 mL of epinephrine [1/2 vial of 1 mg/mL]; group A) or harmonic scalpel (group B).
Intervention(s): Laparoscopic myomectomy.
Main Outcomes Measure(s): The global operative time, the time spent for myoma enucleation and for suturing uterine wall defects, and intraoperative blood loss as well as the surgical difficulty degree and postoperative pain at 24 and 48 hours after the laparoscopic procedure.
Result(s): No relevant intra- or postoperative complications were observed in either group. The degree of pain 24 hours after surgery was significantly lower in patients in whom the harmonic scalpel was used. The degree of surgical difficulty did not differ between groups, but the global operative time was significantly shorter in the harmonic scalpel group.
Conclusion(s): The use of the harmonic scalpel for laparoscopic myomectomy is associated with low total operative time, low intraoperative blood loss, and low postoperative pain, with no increase in surgical difficulty. (Fertil Steril® 2010;94:1882–6. ©2010 by American Society for Reproductive Medicine.)

Key Words: Bleeding, fibroid, hemorrhage, laparoscopy, leiomyoma, miomectomy, operative time, pain, Ultracision

The standard treatment of leiomyomas is hysterectomy for patients who have completed childbearing and myomectomy for those wishing to preserve fertility. The accomplishment of myomectomy by laparoscopy has been often questioned for the excessive blood that it may cause and, as direct consequence, for the length of the operating time due to hemostasis, which requires a meticulous time-consuming technique (1–3). The occurrence of discrete blood loss associated with the dissection of huge fibroids may render myomectomy a more technically challenging procedure than hysterectomy, so that in up to 20% of cases there may be a requirement for transfusion and/or for conversion of myomectomy to hysterectomy (1, 4, 5).

Various electrosurgical devices have been introduced in clinical practice to achieve a safe and faster hemostasis, and, in recent years, researchers have been looking for new instruments with less thermal spread in the effort to reduce both operating time and complications (2, 6). The Harmonic Scalpel Ultracision (Ethicon Endosurgery, Cincinnati, OH) is an ultrasonic surgical instrument that, vibrating at 55,000 cycles per second, enhances the blade's ability to cut and coagulate blood vessels. It dissects tissues, causing no eschar build-up on the blade, less thermal damage to surrounding tissue, no smoke in the operative field, and minimization of accidental injury (7, 8).

In the present prospective randomized controlled study, we compared the effectiveness of harmonic scalpel versus electrosurgery to reduce blood loss during laparoscopic myomectomy.

MATERIALS AND METHODS

From January 9, 2006, to October 31, 2008, 182 consecutive ambulatory premenopausal women with symptomatic uterine leiomyomata were enrolled in the study after ultrasound assessments. There was always an interval period ranging from weeks to several months between the time when the women consentedto be in the trial, randomization, and myomectomy. This interval provided women with time to consider their decision and change their minds if they wished to opt out of the study. At the end of the selection, only 160 patients were enrolled for laparoscopic myomectomy. Ethical approval was obtained from the Local Ethical Committee, and informed consent was obtained from patients before randomization.

Randomization was achieved using sealed, opaque envelopes containing computer-generated block randomization numbers, and envelopes were opened on the hospital site the day before surgery. Thus, each subject was

Received June 23, 2009; revised August 16, 2009; accepted August 18, 2009; published online October 12, 2009.

P.L. has nothing to disclose. S.F. has nothing to disclose. F.C. has nothing to disclose. E.C. has nothing to disclose. M.F. has nothing to disclose. I.Z. has nothing to disclose. F.P. has nothing to disclose. P.F. has nothing to disclose.

Reprint requests: Pasquale Florio, M.D., Ph.D., Resident Assistant, Department of Pediatrics, Obstetrics and Reproductive Medicine, Section of Obstetrics and Gynecology, University of Siena, Policlinico "Le Scotte" Viale Bracci, 53100 Siena, Italy (FAX: 39-0577-233-454; E-mail: florio@unisi.it).

Copyright ©2010 American Society for Reproductive Medicine, Published by Elsevier Inc.
0015-0282/$36.00
doi:10.1016/j.fertnstert.2009.08.049

assigned to one of the two treatment groups, with a total of 80 patients in each group. The selection was based on the use during laparoscopic surgery of electrosurgery devices (group A) or harmonic scalpel (group B). Each woman's age, parity, and body mass index (BMI) were assessed, and transvaginal ultrasound and blood sampling were performed. All the surgeons involved in the current protocol were skilled in both procedures, and the decision between the two approaches was made preoperatively according to the randomization.

The main indications for myomectomy were abnormal uterine bleeding, unexplained infertility lasting more than 3 years, recurrent abortion during the first trimester, and pelvic pain. The diagnosis of unexplained infertility was made after exclusion of endocrine abnormalities and tubal and male factor infertility factors with a complete hormonal assay, a hysterosalpingogram, and a semen analysis; we excluded patients whose partners presented with severe oligoasthenospermia. Inclusion criteria were symptomatic subserous or intramural myomas with sizes ranging from 4 to 10 cm and the number of myomas ranging from one to five.

Exclusion criteria were a documented significant cardiopulmonary disease defined as a history of cardiac failure, myocardial infarction, unstable angina, acute or recent vascular thrombosis, asthma or pulmonary obstructive disease poorly controlled, or contraindicating prolonged Trendelenburg position; prior pelvic or abdominal radiation therapy; or inadequate bone marrow, renal, and hepatic function. Previous abdominal surgery was not considered a contraindication for the laparoscopy. Other exclusion criteria were intramural leiomyoma of ultrasound diameter <4 cm or >10 cm, more than five myomas, presence of submucosal fibroids as confirmed by hysteroscopy, pattern of hyperplasia with cytologic atypia in the endometrial biopsy performed in case of menometrorrhagia, abnormal Papanicolaou test, or positive urine pregnancy test result. Patients (9/182; 5%) with submucosal fibroids were excluded from the study because the standard minimally invasive surgical procedure for treating them is hysteroscopic myomectomy (9), in order to avoid the risks of opening the uterine cavity and of intrauterine adhesions (10) and to prevent excessive myometrial bleeding.

Women underwent [1] pelvic examination; [2] preoperative transvaginal ultrasound evaluation (Real Time Ultrasound Scan Equipment, Siemens Sonoline ELEGRA Millenium Edition, [Erlangen, Germany] with a transvaginal probe at 4.5–7.0 MHz) to determine the number, location, and size of the myomas; and [3] diagnostic hysteroscopy to exclude the presence of submucous myomas. Uterine and leiomyoma sizes were evaluated by measuring the three main diameters (D1, D2, D3) and applying the formula of the ellipsoid (D1 $\times$ D2 $\times$ D3 $\times$ 0.52). An arithmetic mean of the sizes was used in cases of more that two leiomyomata. The ultrasonographer was unaware of treatment assignment.

Surgical Procedures

The operation took place under general anesthesia with nasogastric tube insertion and a bladder catheter installed during the operation. Laparoscopic myomectomies were performed with a 10-mm telescope (Karl Storz, Tuttlingen, Germany) through one optic trocar located in the umbilicus and lateral trocars placed fairly high, two fingers above the anterosuperior iliac spines, and outside the rectus abdominis muscles. The left trocar was 12 mm in size to allow the myoma drill and morcellator to be inserted; central and right lateral trocars were 5 mm in size. Number, size, and location of myomas were noted; the course of ureters, especially in the case of broad ligament myomas, was traced.

In patients to be treated by electrosurgery (group A), a vasoconstrictive solution composed of 50 mL of saline solution and 0.5 mL of epinephrine (1/2 vial of 1 mg/mL) was used to infiltrate through a 22-gauge needle the serosa and/or myometrium overlying and just around the leiomyoma before uterine incision. Before each infiltration, repeated aspirations were performed to prevent intravascular injection. A monopolar needle (cut blend set at 50 W) was used to incise transversely the serosa overlying the myoma until its pseudocapsule was reached. After the identification of the cleavage plane, the myoma was then fixed with a myoma drill (Karl Storz). Traction and countertraction movements were applied, together with the use of Endo Shears scissors (Tyco U.S. Surgical, Norwalk, CT) and bipolar forceps that were used for simultaneously coagulating, cutting the connective tissue bridges, and gradually enucleating the fibroid from the uterine wall.

In patients in group B, the Harmonic Scalpel Ultracision (10 mm in size) was used to incise the serosa overlying the myoma and the surrounding connective tissue bridges to excise it and for hemostasis. It was placed through either of the parallel ports, with a forceps through the ipsilateral sheath to gently provide countertraction against the myometrial wall and to help the identification of tissue planes and rinse blood from the surgical site. An initial transverse elliptical incision was done, allowing resection of myometrium covering the myoma. Once the myoma was exposed, countertraction was accomplished with the use of a myoma drill; the myometrium was pushed away, and the harmonic scalpel blade was placed with the flat surface on the myoma to cut and coagulate simultaneously.

Uterine wall suture was performed in all cases in one or two layers with Polysorb 0 GS-21 (Polysorb, USSC, Norwalk, CT) interrupted sutures and intracorporeal knots. Myomas were extracted by a tissue morcellator (Storz). Hemostasis control was performed at the conclusion of the surgical procedure, when all operative samples were weighed and submitted for pathologic examination.

Outcomes Measurement

Systolic/diastolic blood pressure and heart rate were recorded in each subject 5 minutes before and 15, 30 and, 45 minutes after myoma enucleation. The global operative time (computed from the insertion of trocars to the end of uterine wall suture) and the time of enucleating myomas and of suturing the uterine wall defect were recorded. Intraoperative blood loss was evaluated as the balance between the aspirated and the irrigated liquid.

Surgical difficulty degree was evaluated subjectively by the same operator with the use of a visual analog scale (VAS), varying linearly from 1 (low difficulty) to 10 (high difficulty). The length of postoperative ileus was evaluated by asking the patients when they recovered the ability to pass gas, and 24 hours after surgery a blood sample was performed and the variation in hemoglobin (δHb) levels was calculated for each woman. The postoperative pain (assessed 24 and 48 hours after the surgical procedure) was evaluated using a VAS, and the severity of the pain was expressed as a score ranging from 0 to 10.

All intra- and postoperative complications were recorded. A 6-month postoperative follow-up was done.

Statistical Analysis

All data were analyzed with Prism software (GraphPad Software Inc., San Diego) and expressed as mean $\pm$ SD. The Kolmogorov-Smirnov test was used to evaluate whether values had a Gaussian distribution to choose between parametric and nonparametric statistical tests. A sample-size calculation was computed by using a two-tailed test with an α-level of 0.01 and 99% power. The primary study objective was to establish whether the amount of intraoperative blood loss changes with laparoscopic myomectomy by electrosurgery and vasoconstriction agent compared with harmonic scalpel surgery. Based on previous data reporting that mean ($\pm$SD) intraoperative blood loss after laparoscopic myomectomy and vasoconstriction agent was 143.9 $\pm$ 48.1 mL (11), a sample size of 78 patients per group was chosen to compute the statistical significance between the groups for an intraoperative blood loss difference of at least 25 mL between groups.

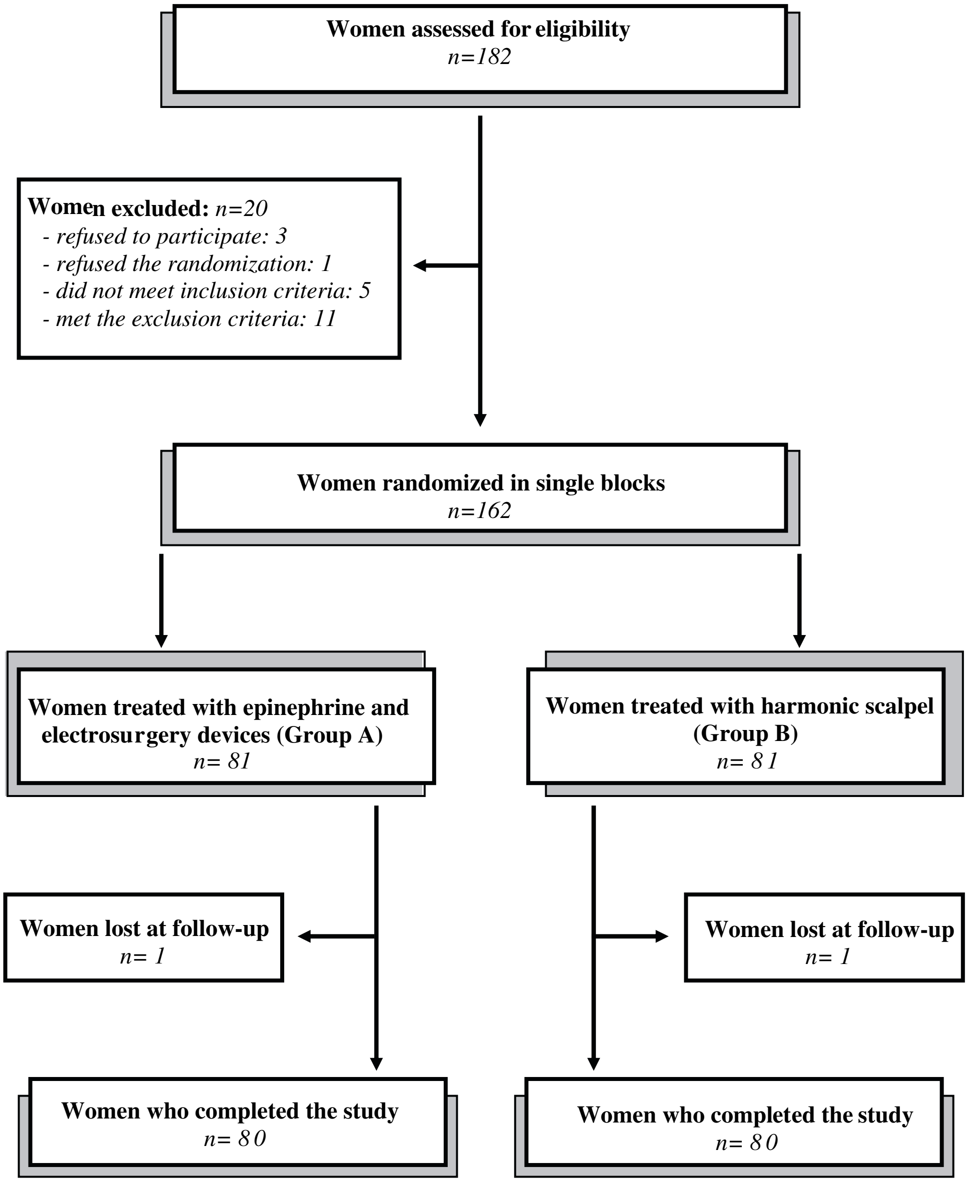
The unpaired *t*-test was used to compute statistical significance, and χ^2 and Fisher's exact tests were used to analyze differences between proportions. $P<.05$ was considered statistically significant.

RESULTS

The flow diagram of the clinical trial was reported in Figure 1. After randomization, the two groups were similar for age, parity, BMI; uterine and leiomyoma volume, number of leiomyomas, and volume of largest leiomyoma did not differ between groups (Table 1). The estimated sizes of leiomyomas measured by ultrasound reflected the real size of the tumors removed, and the histopathological examination confirmed the ultrasound diagnosis of uterine leiomyomata.

FIGURE 1

Flow diagram of the clinical trial.



Litta. Laparoscopy, myomectomy, and harmonic scalpel. Fertil Steril 2010.

No relevant intra- or postoperative complications were observed, and all myomectomies were completed laparoscopically. However, the hospital stay was significantly ($P<.0001$) longer in group A than in group B (Table 2), probably because five patients in group A were discharged after 4 days because of fever (temperatures >38°C; Table 2). The time of ileus did not differ significantly between groups, while the degree of pain 24, but not 48, hours after surgery was significantly ($P=.0001$) lower in patients in whom the harmonic scalpel was used (Table 2). The injection of vasoconstrictive solution was associated with a significant ($P<.05$) increase in systolic (basal levels, 116 ± 3.2 mmHg) and diastolic (basal levels, 74 ± 4.1 mmHg) blood pressure and heart rate (basal levels, 68 ± 2.2 bpm) after the myoma enucleation (systolic blood pressure, 123 ± 4.5 mmHg; diastolic blood pressure, 80 ± 5.2 mmHg; heart rate, 78 ± 3.4 bpm) and decreased to baseline values in the remaining periods (data not shown).

No differences were noted with respect to the degree of surgical difficulty and the weight of enucleated myomas, but the global operative time was significantly ($P=.02$) shorter in group B, probably because the intraoperative blood loss and the δHb were both significantly ($P=.004$ and $P=.03$, respectively) lower in group B (Table 2). Blood transfusion was required in none of the cases. At 6 months after surgery, no myoma recurrence was observed at transvaginal ultrasound.

DISCUSSION

Laparoscopic myomectomy is a procedure requiring meticulous dissection, safe anatomical exposure, and effective hemostasis to avoid

TABLE 1

Clinical and anthropometric characteristics of the patients enrolled of the two study groups.

	Group A (n = 80)	Group B (n = 80)	*P* value
Age, y	37.34 ± 6.24	38.11 ± 6.12	.43
Parity	1.1 ± 0.7	1.1 ± 0.8	1.0
BMI, kg/m^2	25.2 ± 2.4	24.9 ± 2.2	.4
Regular cycles, n (%)	38 (47.5)	34 (42.5)	.80
Metrorrhagia, n (%)	42 (52.5)	46 (57.5)	.83
Uterine volume, cm^3	275.6 ± 35.2	269.8 ± 41.1	.34
Myoma volume, cm^3	82.9 ± 26.2	79.5 ± 21.3	.37
Largest myoma volume, cm^3	41.4 ± 15.2	39.5 ± 17.5	.46
No. of myomas removed	3.35 ± 1.6	3.43 ± 1.61	.73
Type of myomas, n (%)			
Intramural	82 (43.6)	81 (41.1)	.82
Subserosal	92 (48.9)	101 (51.3)	.86
Pedunculated	14 (7.5)	15 (7.6)	.89
Position of myomas, n (%)			
Anterior	55 (29.2)	54 (27.4)	.84
Posterior	74 (39.4)	76 (38.6)	.99
Fundal	31 (16.5)	34 (17.3)	.97
Infraligamentary	11 (5.9)	13 (6.6)	.94

Note: Data are expressed as mean ± SD, unless otherwise stated.

Litta. Laparoscopy, myomectomy, and harmonic scalpel. Fertil Steril 2010.

postoperative complications: excessive hemorrhage remains a major challenge for gynecologic surgeons and is still the most serious event related to laparoscopic myomectomy (1, 2, 5, 12).

In the present study, we found that the use of the harmonic scalpel in myomectomy is associated with shorter global operative time and less intraoperative and total blood loss than epinephrine with electrosurgery as dissector and coagulation devices, according to previous findings (13). The efficacy of the harmonic scalpel was tested without using epinephrine because we wished to stress its usefulness in reducing blood loss and avoiding the putative pharmacological risks related to the use of vasoconstrictors. Indeed, the vasoconstrictive action may not be dissipated during the surgery, and an inaccurate hemostasis may be performed with occulted postoperative bleeding; furthermore, vasoconstriction could damage the surrounding tissue, as reported during vaginal hysterectomy (14).

To explain our results, we have to consider that the mechanisms of the harmonic scalpel action are based on its ability to denature proteins by the transfer of mechanical energy to the tissue, which is sufficient to break tertiary hydrogen bonds, and by the generation of heat from the internal cellular friction, which results from the high-frequency vibration of the tissue. Through this mechanism, it generates heat limited to temperatures around 80°C when a short energy time is used, as a result of the stress and friction it causes in the tissue. Tissue charring and desiccation from the loss of moisture can be minimized, and the limited heat generation also minimizes the zone of thermal injury: vessels are sealed together without bleeding from the surface closest to the blade (7, 8). The spreading of harmonic scalpel cavitationally created vapor is associated with the expansion between tissue planes and their separation, with no destruction of tissue and with enhancement of the visualization of the vascular plane of dissection. In electrosurgery, blood vessels are not significantly coated because of the concomitant reduction in power density as the surface area of contact increases with coaptation.

TABLE 2

Clinical findings related to myomectomy by laparoscopy.

	Group A (n = 80)	Group B (n = 80)	*P* value
Total operative time, min	88.8 ± 35.5	71.8 ± 26.7	.000
Intraoperative blood loss, mL	182.8 ± 116.8	135.2 ± 89.1	.004
Total blood loss, δHb	1.2 ± 0.9	0.9 ± 0.8	.03
Myoma weight, g	139.5 ± 98.2	150.1 ± 158.83	.61
Degree of surgical difficulty	5.2 ± 2.2	5.1 ± 1.8	.75
Postoperative fever, n (%)	5 (2.7)	2 (1.0)	.42
Time of postoperative ileus, hours	20 ± 6	21 ± 5.5	.3
Degree of postoperative pain at 24 h	5.6 ± 0.8	4.4 ± 1.1	.00
Degree of postoperative pain at 48 h	2.5 ± 0.8	2.4 ± 1.1	.2
Hospital stay, d	2.76 ± 1.07	2.27 ± 0.63	.00

Note: Data are expressed as mean ± SD, unless otherwise stated.

Litta. Laparoscopy, myomectomy, and harmonic scalpel. Fertil Steril 2010.

Here we also found that the harmonic scalpel reduced the operative time because we used it not only for hemostasis but also to simultaneously incise and excise the myoma, thus reducing the need for instrument change. The mechanism by which the harmonic scalpel cuts is known as "power cutting," which is offered by a relatively sharp blade vibrating at 55,500 times per second over a distance of 60–100 μm. By this process, the blade edge may cut tissue by stretching it beyond its elastic limit and, on a more microscopic level, by breaking molecular bands, and such an effect is most easily achieved in high protein density areas such as muscle-rich tissues. Because there is little or no cutting ability with an unpowered blade, the blunt side of the harmonic scalpel can also be used as a blunt dissector, thus reducing the time needed in excising myomas. In contrast, electrosurgery cuts tissue by increasing the temperature of cells above the boiling point of water, causing the water to vaporize, expand, and explode the cells (7, 8). In addition, the reduced generation of smoke that is associated with the use of the harmonic scalpel, with minimal disruption of visualization during the procedure compared with electrosurgery, also reduces the operative time.

Finally, the use of the harmonic scalpel was associated with a low degree of pain intensity, probably because it can avoid stimulation of nerves and muscles, while decreasing trauma to the tissue. Since there is no flow of current to the patient, the harmonic scalpel does not pose the risk of electric nerve or muscle stimulation, probably causing less postoperative pain.

REFERENCES

1. Dubuisson JB, Fauconnier A, Babaki-Fard K, Chapron C. Laparoscopic myomectomy: a current view. Hum Reprod Update 2000;6:588–94.
2. Hurst BS, Matthews ML, Marshburn PB. Laparoscopic myomectomy for symptomatic uterine myomas. Fertil Steril 2005;83:1–23.
3. Falcone T, Bedaiwy M. Minimally invasive management of uterine fibroids. Curr Opin Obstet Gynecol 2002;14:401–7.
4. LaMote AI, Lalwani S, Diamond MP. Morbidity associated with abdominal myomectomy. Obstet Gynecol 1993;82:897–900.
5. Palomba S, Zupi E, Russo T, Falbo A, Marconi D, Tolino A, et al. A multicenter randomized, controlled study comparing laparoscopic versus minilaparotomic myomectomy: short-term outcomes. Fertil Steril 2007;88:942–51.
6. Kongnyuy EJ, Wiysonge CS. Interventions to reduce haemorrhage during myomectomy for fibroids. Cochrane Database Syst Rev 2007;1:CD005355.
7. Kunde D, Welch C. Ultracision in gynaecological laparoscopic surgery. J Obstet Gynaecol 2003;23:347–52.
8. McCarus SD. Physiologic mechanism of the ultrasonically activated scalpel. J Am Assoc Gynecol Laparosc 1996;3:601–8.
9. Di Spiezio Sardo A, Mazzon I, Bramante S, Bettocchi S, Bifulco G, Guida M, et al. Hysteroscopic myomectomy: a comprehensive review of surgical techniques. Hum Reprod Update 2008;14:101–19.
10. Berman JM. Intrauterine adhesions. Semin Reprod Med 2008;26:349–55.
11. Zullo F, Palomba S, Corea D, Pellicano M, Russo T, Falbo A, et al. Bupivacaine plus epinephrine for laparoscopic myomectomy: a randomized placebo-controlled trial. Obstet Gynecol 2004;104:243–9.
12. Sizzi O, Rossetti A, Malzoni M, Minelli L, La Grotta F, Soranna L, et al. Italian multicenter study on complications of laparoscopic myomectomy. J Minim Invasive Gynecol 2007;14:453–62.
13. Ou CS, Harper A, Liu YH, Rowbotham R. Laparoscopic myomectomy technique. Use of colpotomy and the harmonic scalpel. J Reprod Med 2002;47:849–53.
14. England GT, Randall HW, Graves WL. Impairment of tissue defenses by vasoconstrictors in vaginal hysterectomies. Obstet Gynecol 1983;61:271–4.