

In-bag manual versus uncontained power morcellation for laparoscopic myomectomy: randomized controlled trial

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Objective: To evaluate whether manual in-bag morcellation could be efficiently proposed as alternative to the uncontained power technique.

Design: Randomized controlled trial.

Setting: Academic hospital.

Patient(s): One hundred fifty-two premenopausal women eligible for myomectomy were screened, and 104 were randomized.

Intervention(s): Patients were randomized into two groups. In the experimental group, "in-bag" protected morcellation was performed. In the control group, patients were treated by uncontained power myoma removal.

Main Outcome Measure(s): The primary endpoint was the comparison of morcellation operative time (MOT). The secondary endpoints were the comparisons of total operative time (TOT), simplicity of morcellation (as defined by the surgeon using a visual analogue scale scale), intraoperative blood loss, rate of complications, and postoperative outcomes.

Result(s): A sample size of 51 per group ($n = 102$) was planned. Between March 2014 and January 2015, patients were randomized as follows: 53 to the experimental group and 51 to the control group. Most demographic characteristics were similar across groups. MOT was observed to be similar in both study groups (16.18 ± 8.1 vs. 14.35 ± 7.8 minutes, in the experimental and control groups, respectively). Fibroid size was identified as the principal factor influencing morcellation time (Pearson coefficient 0.484 vs. 0.581, in the experimental and control groups, respectively). No significant difference in TOT, simplicity of morcellation, delta Hb, postoperative pain, and postoperative outcomes were observed between groups.

Conclusion(s): The protected manual in-bag morcellation technique represents a time-efficient and feasible alternative, which does not interfere with surgical outcomes in women undergoing laparoscopic myomectomy.

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Key Words: Fibroid, in-bag morcellation, myomectomy, power morcellation, sarcoma

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Uterine leiomyomas are frequent benign neoplasms, with an estimated incidence of 20%–80% in reproductive-age women, de-

pending on diagnostic modality, symptomatology, or race (1, 2). When symptomatic, they adversely affect women's quality of life, causing

menorrhagia, anemia, and loss of fertility (2). Thus, in symptomatic women desiring offspring, conservative surgery is mandatory to improve general well-being and achieve pregnancy.

Compared with the open approach, laparoscopic myomectomy decreases morbidity and length of hospitalization (3). While recent years have seen a wide diffusion and increasing use of laparoscopy, the long-term sequelae of such a practice are still to be investigated.

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A current example of possible sequelae relates to the use of the power morcellator, an instrument with a fast rotating cylindrical knife, which divides large masses of tissue, allowing extraction of smaller fragments through the abdominal cavity (4). The chief issue related to its use is the risk of dissemination of tissue fragments and the occurrence of peritoneal leiomyomatosis or, even worse, the spreading of unsuspected uterine sarcomas within the pelvis and the abdomen, significantly worsening the patient's long-term survival.

In April 2014 the Food and Drug Administration (FDA) published a press release discouraging the use of power morcellation owing to potential upstaging of uterine sarcoma, despite the rarity of this circumstance, which is reported to range from 0 to 0.49% in patients with presumed fibroids (4, 5).

To date, no diagnostic modalities are available to preoperatively differentiate benign from malignant uterine tumors (6–8), and this is the main concern about the current management of sarcoma. The validation of alternative surgical techniques for the safe removal of surgical specimens (myomas or the entire uterus) is vital.

The aim of this prospective randomized controlled trial (RCT) was to verify whether a "protected extracorporeal in-bag" morcellation by flat knife or scissors coring could be efficiently proposed in alternative to the standard intracorporeal uncontained power technique.

MATERIALS AND METHODS

An unblinded RCT was conducted at the Department of Obstetrics and Gynecology, University "Magna Graecia" of Catanzaro.

The methodology was in accordance with the guidelines of the Declaration of Helsinki on Human Experimentation and of Good Clinical Practice. The study protocol was approved by the Ethical Committee of the Department of Gynecology and Obstetrics (University 'Magna Graecia' of Catanzaro) and submitted to the website for clinical trials (www.clinicaltrials.gov, identifier number NCT02086435). The purpose of the protocol, in light of U.S. FDA recommendations, was carefully explained, and written informed consent was obtained from each patient.

Between March 2014 and January 2015, premenopausal women with heavy menstrual bleeding or patients already diagnosed with fibroids from referral sources and undergoing a myomectomy were enrolled in the study. Inclusion criteria were the following: age between 18 and 40 years, body mass index (BMI) 18–40 kg/m², heavy menstrual bleeding, and the presence of at least one myoma measuring 4 cm or more in diameter (but no myoma measuring >10 cm, according to our clinical practice on eligibility for laparoscopy).

The exclusion criteria were age over 40 years, presence of uterine neformation suspicious for malignancy, acute or chronic psychiatric disorders, use of drugs during the 6-month period before enrollment date that affect cognitive ability or state of consciousness and alertness, presence of calcified fibroids at ultrasound examination (for which the effort to morcellate them mechanically may outweigh the

amount of time saved), presence of ovarian cysts or adnexal lesions, previous endometrial hyperplasia, abnormal PAP test, positive pregnancy test, previous laparotomic pelvic surgery, major medical conditions, or hepatic, renal, and cardiovascular disorders or other concurrent medical illnesses.

On admission for each enrolled patient, clinical and biochemical assessments were performed. Anamnestic information regarding menstrual cycle characteristics (age at menarche; regularity, quantity, and duration of menstruation; presence of dysmenorrhea; parity; and previous abortion status) were noted. Anthropometric measurements (age, height, weight, BMI) were also recorded.

All subjects underwent venous blood sampling for hematological (including ferritin) and coagulation evaluation. Blood samples were obtained in the morning between 08:00 and 09:00 a.m. following an overnight fast and bed rest. In all women, a gynecological inspection and an instrumental evaluation were performed. Transvaginal ultrasound was performed by the same experienced operator (D.L.) who assessed uterine size and morphology and ovarian characteristics. Presence, location (intramural, submucosal, or subserosal myoma), and size of fibroids were described; additionally, vascularization by echo-color Doppler was also assessed. Fibroids were measured in three perpendicular planes, and size was determined, while volume was calculated using the ellipsoid formula.

Standard preoperative workup included a serum dosage of CA125 and LDH isoenzymes 3-4-5 to exclude cases at increased risk for malignant uterine disease. If there was a suspicion of neoplastic fibroid degeneration, magnetic resonance imaging, hysteroscopy, and endometrial biopsy were also performed, according to our standard clinical practice.

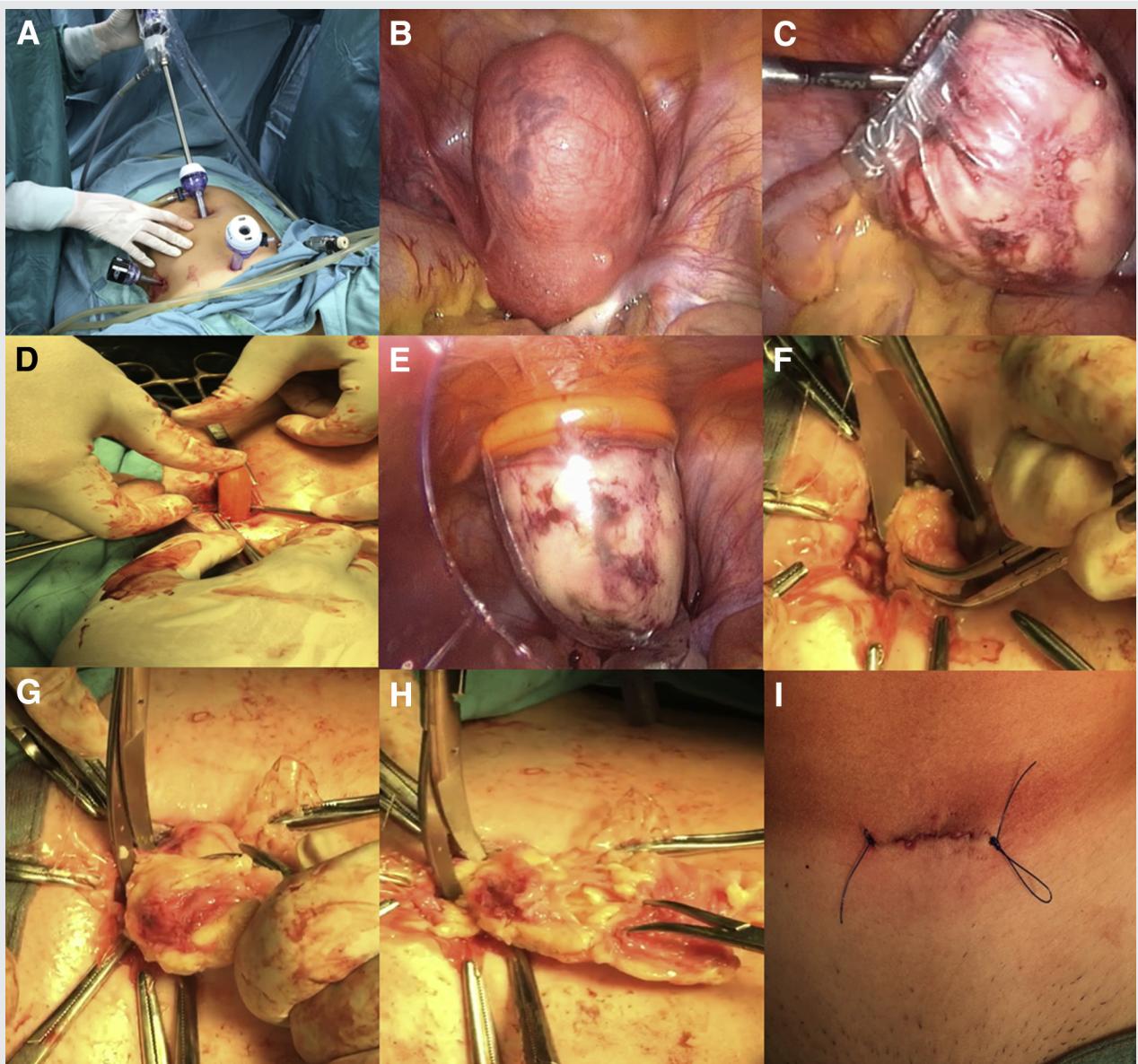
All eligible patients were randomized 1:1 by computer software to one of two independent treatment arms (experimental and control) by a blinded nurse. The experimental group included patients treated with manual "protected" removal by in-bag extracorporeal morcellation by knife or scissors coring; the control group included patients treated with standard uncontained power morcellation, using a reusable electronic device.

Immediately before surgery, each patient received 2 g IV of antibiotic prophylaxis (Ceftriaxone). No treatment for thrombosis prophylaxis was administered on the day of surgery.

All laparoscopic myomectomies were performed by two experienced surgeons (F.Z., M.M.), who were informed about the patient's group only at the time of morcellation. Surgeons followed the same standardized procedures for each intervention. After induction of anesthesia, in both groups, a uterine manipulator was positioned and pneumoperitoneum, through the introduction of the Veress needle, was obtained. Laparoscopic myomectomy was carried out according to our described standard technique (9), but using Monocryl suture CT 0 (Ethicon) instead of Vicryl CT 2-0 (Fig. 1A). During each surgical intervention, a careful and systematic inspection of the uterus, ovaries, and entire pelvis was performed (Fig. 1B).

In the experimental group, each enucleated myoma was placed within a rip-stop nylon specimen bag (Endo Catch

FIGURE 1



Experimental technique: manual “protected” removal by in-bag extracorporeal morcellation. (A) Four standard laparoscopic accesses were created; (B) pelvis was inspected, and standard laparoscopic myomectomy was performed; (C) each enucleated myoma was placed within a rip-stop nylon specimen; (D, E) the central lower 10 mm trocar incision was upsized to 30 mm, and a 65-mm reusable sterile pessary was placed inside of the bag, between the myoma and pelvic wall; (F–H) after exteriorization of the fibroid’s surface, it was grasped and subjected to gradual morcellation with scalpel or scissors by cautious C-coring; (I) the skin incision was closed.

Venturella. In-bag morcellation for uterine myoma. *Fertil Steril* 2016.

Gold Auto Suture 10 or 15 mm, Covidien), which could hold 220 mL or 1,000 mL according to the size chosen (Fig. 1C). The central lower 10 mm trocar incision was upsized to 30 mm, and a 65-mm reusable sterile pessary was placed inside of the bag, between the myoma and pelvic wall (Fig. 1D and E), to create a “barrier” between the morcellated portion of the myoma and the bag. In this way, the pessary protected the bag from the coring rotational movements of either the knife or the scissors and allowed a more manageable coring.

After exteriorization of the fibroid’s surface with the aid of Alexis retractors, it was grasped with Schroeder tenaculum, double tooth, or Backhaus towel forceps and subjected to gradual morcellation with scalpel or scissors by cautious C-coring (Fig. 1F–1I). Fibroid adequate traction was allowed by using different instruments, depending on the myoma consistency. In the control group, standard intracorporeal un-contained morcellation using a power morcellator (Rotocut G1, Storz) was performed (9). The final diagnosis of fibroid

was obtained only after postoperative histological examination of all tissue samples.

At 3 and 24 hours (h) after surgery, blood sample and vital parameters (heart rate and blood pressure) were assessed to quantify postoperative blood loss.

In the first 24 h after surgery, all patients received IV analgesics. Patients received 4,000 units low molecular weight heparin (Enoxaparin sodium) administered SC 24 h after surgery and then once daily for 4 weeks.

The primary endpoint was the comparison of morcellation operative time (MOT) in the experimental and control groups; it was defined as the time interval beginning from the moment in which, once the hemostasis of the uterine breach had been secured, the myoma was clamped and subjected to intracorporeal morcellation or positioned within a rip-stop nylon specimen bag for extracorporeal morcellation to the moment when the last fragment of myoma was considered removed from the surgical field.

The secondary endpoints were the comparisons of these two techniques in terms of [1] total operative time (TOT; skin-to-skin); [2] simplicity of morcellation (expressed on the visual analog scale [VAS] scale where 1 defines very bad simplicity and 10 excellent simplicity); [3] intraoperative blood loss (defined as the variation in hemoglobin concentrations between 24 h postoperative and preoperative blood sample); [4] postoperative hospital stay (number of days of hospitalization after surgery); [5] postoperative pain (measured on the VAS scale where 1 stands for a little pain and 10 for intense pain); and [6] postoperative complications (blood transfusion and/or laparotomy conversions). In the experimental group, at the end of each morcellation, the bag was filled with water and checked for integrity.

To estimate the sample size required, we analyzed our data, which consisted of a large population of women who underwent laparoscopic myomectomy; the average time of morcellation by the standard technique was 15.0 (5.8; mean [SD]) minutes. We assumed as clinically significant a difference greater than or equal to 15% in operating time between experimental and standard techniques. Based on these estimates, using a two sided α of 0.05% and a β of 0.20 (power of 80%), we calculated a required sample size of 90 women (45 per group). Considering a dropout rate of 10%–15% in each arm, we established the requirement for the randomization of 104 women to detect a potential 15% difference in morcellation time between groups.

Results were expressed as mean \pm SD. The normal distribution of continuous variables was evaluated with the Kolmogorov-Smirnov test (Lillifors variant). Continuous variables were analyzed by the use of *t*-test for paired and unpaired data, the test of variance analysis of variance for repeated measures, and the Bonferroni test for post hoc analysis, if necessary and appropriate. For analysis of categorical variables, the χ^2 -test and Fisher's exact test were used, when necessary. Using a Kaplan-Meier estimator, we generated cumulative hazard curves to estimate events. The statistical analysis of the results was conducted using the Statistical Package for the Social Sciences software (SPSS 20, SPSS Inc.).

RESULTS

Between March 2014 and January 2015, 152 patients eligible for myomectomy were evaluated. Forty-seven patients did not meet inclusion criteria and were excluded. One-hundred four patients were considered eligible for inclusion in the study protocol and randomized to two treatment arms: 53 assigned to the experimental and 51 to the control group.

In Table 1, the demographic characteristics of enrolled women are shown. No significant difference between groups in term of age, BMI, parity, and number and size of myoma was detected. At the end of the enrollment, we treated eight patients with three myomas (four patients for each group), 26 women with two myomas (15 and 11 in the experimental and control groups, respectively), and 70 patients with one fibroid (34 and 36 in the experimental and control groups, respectively). The mean weight of the surgical specimens did not differ between groups (336.32 ± 215.32 vs. 312.45 ± 203.78 g, in the experimental and control groups, respectively; $P=.13$).

All the removed fibroids were able to be contained in the chosen bag in the experimental group. In particular, 13 fibroids ranging from 4 to 5 cm were placed into a 10 mm bag, and 11 fibroids measuring 5–6 cm, 14 measuring 6–7 cm, six measuring 7–8 cm, and seven measuring 8–9 cm were morcellated into a 15-mm bag.

As detailed in Table 2, no significant increase in MOT was observed in the experimental group (16.18 ± 8.1 vs. 14.35 ± 7.8 minutes, in the experimental and control groups, respectively; $P=.41$). On subanalysis of data, fibroid size represented the principal parameter influencing MOT (Pearson coefficient 0.484 vs. 0.581, in the experimental and control groups, respectively; $P<.001$).

Compared with controls, no significant ($P=.24$) increase in TOT was observed in the experimental group (96.96 ± 30.2 vs. 92.08 ± 30.1 minutes, in the experimental and control groups, respectively).

Regarding simplicity of morcellation, surgeons did not note any significant differences between in-bag and uncontaminated morcellation (6.77 ± 2.1 vs. 7.50 ± 2.1 ; $P=.27$ in the experimental and control groups, respectively). Correlation analysis among variables potentially linked to simplicity of morcellation revealed the most significant factor to be represented by the size of the myoma (Pearson coefficient -0.799 ; $P<.001$) in the control group, whereas BMI (Pearson

TABLE 1

Anthropometric, clinical, and sonographic basal parameters.

Parameter	Experimental group (n = 53)	Control group (n = 51)	P value
Age, y	31.74 ± 5.6	32.45 ± 6.1	.54
BMI, kg/m ²	22.17 ± 2.7	23.28 ± 3.5	.07
Parity	1.05 ± 1.1	1.26 ± 1.1	.37
Myoma dimension, cm	61.05 ± 12.6	59.37 ± 13.9	.52
Myoma	1.37 ± 0.6	1.43 ± 0.6	.62

Note: Data are expressed as median \pm SD.

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TABLE 2**Primary and secondary endpoints.**

End-points	Experimental group (n = 53)	Control group (n = 51)	P value
Morculation operating time, min	16.18 ± 8.1	14.35 ± 7.8	.41
Total operative time, min	96.96 ± 30.2	92.07 ± 30.1	.24
Intraoperative blood loss, delta Hb	1.38 ± 0.8	1.32 ± 0.8	.71
Complications, n (%)	0 (0)	1 (2)	.30
Simplicity of morculation, VAS scale	6.77 ± 2.6	7.50 ± 2.1	.27
Hospital stay, d	3.24 ± 0.6	3.41 ± 0.6	.19
Postoperative pain, VAS scale	1.56 ± 0.9	1.62 ± 0.9	.73

Note: Data are expressed as median ± SD unless otherwise indicated.

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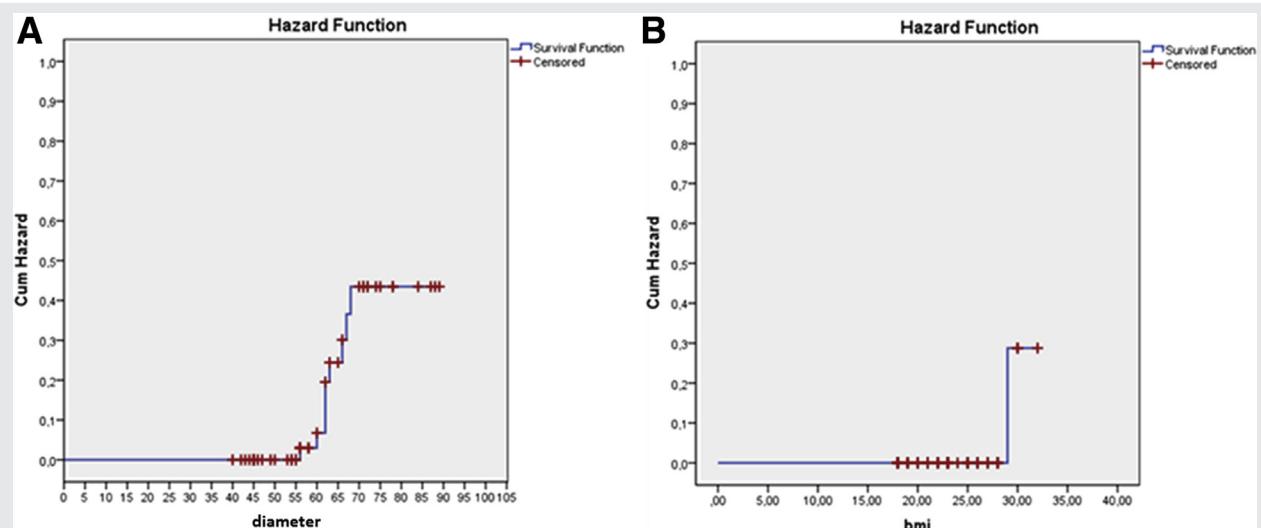
coefficient -0.826 ; $P < .001$) was the most influential factor in the experimental group.

Considering only cases belonging to the control group, by applying the Kaplan-Meier estimator (evaluating the diameter of myoma as a time function and assuming a VAS score of 5 as an event), we found that all cases presenting with a myoma measuring less than 55 mm in diameter were assigned a VAS score equal to or greater than 6, while in the event of a myoma presenting with a diameter greater than 65 mm, the probability of being assigned a VAS score of 5 or less approached 45% (Fig. 2A).

On the other hand, when introducing the variable BMI in the time function of Kaplan-Meier estimator, we found that in the experimental group all cases with $BMI < 29$ received a VAS score of 6 or more, while in women with $BMI \geq 29$, the risk of a VAS score of 5 or less was 30% (Fig. 2B).

No significant difference in terms of delta Hb (1.38 ± 0.8 vs. 1.32 ± 0.8 g/dL, in the experimental and control groups, respectively; $P = .71$) and postoperative hospital stay (3.25 ± 0.6 vs. 3.41 ± 0.6 days, in the experimental and control groups, respectively; $P = .18$) were detected.

No difference ($P = .73$) in the number of analgesic vials used was observed (1.62 ± 0.9 vs. 1.57 ± 0.9 , in the experimental and control groups, respectively), nor in postoperative pain reported by patients (1.56 ± 0.9 vs. 1.62 ± 0.9 points in the experimental and control groups, respectively; $P = .73$). Similarly, the in-bag morculation was not related to specific intraoperative complications, like the standard technique in our study population. Only one case of pre-pneumoperitoneum was encountered as a minor complication in the control group. No cases of visible bag disruptions were recorded in the experimental group, nor

FIGURE 2

Kaplan-Meier estimators. (A) in the control group, evaluating the diameter of the myoma as a time function and assuming a VAS score of 5 as an event, in the presence of a myoma with a diameter greater than 65 mm the probability of being assigned a VAS score of 5 or less approached 45%; (B) in the experimental group, when introducing the variable BMI in the time function of the Kaplan-Meier estimator, in women with $BMI \geq 29$, the risk of a VAS score of 5 or less was 30%.

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were transfusion, laparotomic conversion or injury to organs, or hemorrhage or wound infection recorded in either group.

DISCUSSION

In women of reproductive age, with ovarian reserve compatible with the achieving of pregnancy (10), laparoscopic myomectomy is often preferred to laparotomic owing to the substantial advantages of the minimally invasive approach over laparotomy. Among the other advantages, smaller incisions, minimal blood loss, better visibility of the operative field, less postoperative infections, adhesions, and postoperative pain have been reported (11).

In the last years, the power tissue morcellator has assumed a pivotal role in specific gynecologic procedures, such as myomectomy, since it allows the removal of very large uterine fibroids through small laparoscopic incisions and averts a posterior culdotomy, resulting in faster healing and recovery time. However, the use of a power morcellator is under scrutiny by the medical community and the FDA, since it can cause undetected cancer cells to spread and because it may also lead to parasitic fibroids (5).

The current study is the first reported RCT comparing manual in-bag extracorporeal morcellation with the uncontained power technique in patients undergoing laparoscopic myomectomy. In our study population, the in-bag procedure was related to neither higher morcellation operating time nor higher total operative time compared with the uncontained technique, with fibroid size representing the principal parameter influencing morcellation time.

In the hands of experienced surgeons, the new technique is at least comparable to the standard procedure and even superior to such in the event of fibroids larger than 7 cm. However, the presence of obesity distances the myoma from the skin surface, thus making extracorporeal exposure and coring through a 30-mm skin incision more difficult.

Our results appear to suggest that in-bag morcellation may represent an efficient alternative to the power technique. It does not interfere with surgical outcomes while allowing a bagged removal of fibroids, thus significantly minimizing the “unprotected” handling of tissues in the pelvic cavity. Although the clinical impact of this surgical step is not yet clear, the importance of handling tissue with the goal of minimal spread, at least that strictly related to the morcellation step, is addressed with the bagging technique.

This is an important finding for all laparoscopic surgeons, considering that since 1993 (11–13), power morcellation has represented the gold standard in minimally invasive surgeries. Recently, a public awareness campaign was launched after the electromechanical morcellation of a uterus with presumed benign fibroid, which was ultimately ascertained to be a leiomyosarcoma. The campaign culminated in a black box warning issued from the FDA for electromechanical morcellators (5).

In a 2015 systematic review and meta-analysis, Bogani et al. (14) showed that morcellation increased the overall (62% vs. 39%; odds ratio [OR], 3.16 [95% confidence interval {CI}, 1.38, 7.26]) and intra-abdominal (39% vs. 9%; OR, 4.11

[95% CI, 1.92, 8.81]) recurrence rates of unexpected uterine leiomyosarcoma as well as the death rate (48% vs. 29%; OR, 2.42 [95% CI, 1.19, 4.92]) (13). Nevertheless, no between-group difference in the cumulative extra-abdominal recurrence (OR, 0.34 [95% CI, 0.07, 1.59]) rate was observed (14).

On the other hand, according to a recent cost-effectiveness analysis, “eliminating morcellation as a treatment for myomas is not cost-effective under a wide variety of probability and cost assumptions and performing laparotomy for all patients who might otherwise be candidates for morcellation is a costly policy from a societal perspective” (15). Moreover, Siedhoff et al. (16) recently published their study on a decision tree constructed to compare outcomes for a hypothetical cohort of premenopausal patients undergoing hysterectomy for presumed myoma. In this population, the risk of leiomyosarcoma morcellation was found to be balanced by procedure-related complications that are associated with laparotomy, including death (16).

Researchers agree that patients must be informed about the possibility of a nonidentified sarcoma and the possible impact on prognosis resulting from its morcellation, although it is a difficult process since the risks are vague or unquantified owing to limited available data. Innovative multimodal protocols are urgently needed for the detection of occult cancers before surgery, since preoperative differential diagnosis between uterine myoma and sarcoma remains extremely difficult owing to similarities in clinical presentation. At the present moment, the reliability and reproducibility of intraoperative frozen sections for determination of the biological behaviour of myometrial tumors (17) are controversial, given the risks of sampling and interpretation errors.

Thus, to reduce the risk of dispersion of occult cancerous tissues within the abdominal cavity, manual coring within an endoscopic bag (during which the myoma is placed in a bag laparoscopically and fragmented within the bag external to the pelvis) has been proposed as a feasible and reproducible technique by many investigators (18–24).

No complications related to the contained power morcellation technique or the visual evidence of tissue dissemination outside of the isolation bag were described in most studies (23), confirming that the protective technique prevents IP dispersion of tissue fragments (22). Recently, however, spillage of dye or tissue was noted in less than 10% of cases managed with insufflated bag (25), although containment devices were intact in each of these instances, demonstrating that further refinement of this technique is warranted. Several investigators (21–24), moreover, showed that, compared with the standard procedure, the in-bag morcellation was related to longer operating room time (range, 20–114 minutes).

As opposed to our protocol, all these studies referred to a contained power morcellation within an insufflated isolation bag, which probably requires more caution during the procedure to avoid the accidental rupture of the bag when compared with our proposed manual technique. This aspect could probably justify the significant difference between our MOT and those reported by all the other investigators.

Although no significant differences in operative time required for the removal of the surgical specimens from the pelvis have been found in our study population, the

experimental technique here proposed requires a skin incision upsized from 10 to 30 mm instead of the standard 10–15 mm required for the power morcellator. Although it may be performed under the so-called bikini line, it is important to note that the extension of the scar is three times that required by the standard power morcellation procedure. Moreover, the in-bag technique was laborious in overweight and obese women, and its reproducibility remains to be verified in cases presenting with myomas larger than those treated in this RCT (maximum diameter observed, 89 mm).

Despite the randomized fashion of our study, some factors could limit the exploitation of our results. First, all surgeries have been performed by two very experienced surgeons doing a high volume of cases. Our hospital, indeed, is a referral center for women seeking laparoscopic myomectomy throughout the entire region. Therefore, our findings, both in terms of MOT and simplicity of morcellation, may not be generalizable to all surgeons. On the other hand, in peripheral hospitals with no experienced laparoscopic surgeons, it is hard to imagine that a manual coring with blade or scalpel could appear harder to perform than mechanical morcellation.

Moreover, our study was not powered to see differences in rare complications, such as abdominal wall complications or complications related to dissemination of tissue.

Furthermore, no cases with a myoma larger than 10 cm were included in our study, according to our inclusion criteria for eligibility for laparoscopy. It could be speculated that the generally small myomas favored extracorporeal morcellation and mask any real differences between techniques. Actually, among 152 women assessed for eligibility during the study period, just one patient was excluded because her myoma measured 12 cm, and this case was managed as risky because of altered LDH isoenzymes, elevated CA125 values, and increased vascularization.

An important aspect, moreover, threatening the clinical significance of all the studies published on this topic has to be underlined. Morcellation is not the only step that carries the risk of cancer cells spreading during myomectomy. As correctly reported by Nezhat, indeed, “tissue disruption at the time of myomectomy by any method, including laparotomy, carries a small risk of IP dissemination of occult malignant tissue” (26). Myomectomy itself, by definition, is not an oncologically safe procedure, but “en bloc” removal of all myomas would translate to total hysterectomy, which is not indicated in reproductive-age women and will never be the solution to this problem. Especially when infertility is the indication for surgery, moreover, laparoscopy is the best route to perform myomectomy, given the lower rate of adhesions and the minor negative impact on the pelvic architecture (11). For this reason, a new technique able to allow the laparoscopic approach while reducing the dissemination of tissue fragments all over the pelvis (as occurred during mechanical morcellation) is probably a good compromise for balancing the risks and benefits of minimally invasive myomectomy.

CONCLUSIONS

In women affected by uterine fibroids smaller than 10 cm, the protected manual in-bag morcellation may be considered

efficient and feasible since it does not interfere with surgical outcomes nor does it cause longer operative time when compared with the uncontaminated power technique in women undergoing laparoscopic myomectomy.

REFERENCES

1. Wallach EE, Vlahos NF. Uterine myomas: an overview of development, clinical features, and management. *Obstet Gynecol* 2004;104:393–6.
2. Donnez J, Hudecek R, Donnez O, Matule D, Arhendt HJ, Zatik J, et al. Efficacy and safety of repeated use of ulipristal acetate in uterine fibroids. *Fertil Steril* 2015;103:519–27.e3.
3. Solnik MJ, Munro MG. Indications and alternatives to hysterectomy. *Clin Obstet Gynecol* 2014;57:14–42.
4. Brölmann H, Tanos V, Grimbis G, Ind T, Philips K, van den Bosch T, et al. Options on fibroid morcellation: a literature review. *Gynecol Surg* 2015;12:3–15.
5. Food and Drug Administration. FDA discourages use of laparoscopic power morcellation for removal of uterus or uterine fibroids. *Food Drug Adm* 2014;17:4. Available at: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm393689.htm>. Accessed April 17, 2014.
6. Park JY, Park SK, Kim DY, Kim JH, Kim YM, Kim YT, et al. The impact of tumor morcellation during surgery on the prognosis of patients with apparently early uterine leiomyosarcoma. *Gynecol Oncol* 2011;122:255–9.
7. Park JY, Kim DY, Kim JH, Kim YM, Kim YT, Nam JH. The impact of tumor morcellation during surgery on the outcomes of patients with apparently early low-grade endometrial stromal sarcoma of the uterus. *Ann Surg Oncol* 2011;18:3453–61.
8. Tan-Kim J, Hartzell KA, Reinsch CS, O'Day CH, Kennedy JS, Menefee SA, et al. Uterine sarcomas and parasitic myomas after laparoscopic hysterectomy with power morcellation. *Am J Obstet Gynecol* 2015;212:594.e1–10.
9. Zullo F, Pellicano M, De Stefano R, Zupi E, Mastrantonio P. A prospective randomized study to evaluate leuprolide acetate treatment before laparoscopic myomectomy: efficacy and ultrasonographic predictors. *Am J Obstet Gynecol* 1998;178:108–12.
10. Venturella R, Lico D, Sarica A, Falbo MP, Gulletta E, Morelli M, et al. OvAge: a new methodology to quantify ovarian reserve combining clinical, biochemical and 3D-ultrasonographic parameters. *J Ovarian Res* 2015;8:21.
11. Zullo F, Falbo A, Iuliano A, Oppedisano R, Sacchinelli A, Annunziata G, et al. Randomized controlled study comparing the Gynecare Morcellex and Roto-cut G1 tissue morcellators. *J Minim Invasive Gynecol* 2010;17:192–9.
12. Steiner RA, Wight E, Tadir Y, Haller U. Electrical cutting device for laparoscopic removal of tissue from the abdominal cavity. *Obstet Gynecol* 1993;81:471–4.
13. Carter JE, McCarus SD. Laparoscopic myomectomy. Time and cost analysis of power vs. manual morcellation. *J Reprod Med* 1997;42:383–8.
14. Bogni G, Cliby WA, Aletti GD. Impact of morcellation on survival outcomes of patients with unexpected uterine leiomyosarcoma: a systematic review and meta-analysis. *Gynecol Oncol* 2015;137:167–72.
15. Bortolotto P, Einerson BD, Miller ES, Milad MP. Cost-effectiveness analysis of morcellation hysterectomy for myomas. *J Minim Invasive Gynecol* 2015;22:820–6.
16. Siedhoff MT, Wheeler SB, Rutstein SE, Geller EJ, Doll KM, Wu JM, et al. Laparoscopic hysterectomy with morcellation vs abdominal hysterectomy for presumed fibroid tumors in premenopausal women: a decision analysis. *Am J Obstet Gynecol* 2015;212:591.e1–8.
17. Tulandi T, Ferenczy A. Biopsy of uterine leiomyomata and frozen sections before laparoscopic morcellation. *J Minim Invasive Gynecol* 2014;21:963–6.
18. McKenna JB, Kanade T, Choi S, Tsai BP, Rosen DM, Cario GM, et al. The Sydney contained in bag morcellation technique. *J Minim Invasive Gynecol* 2014;21:984–5.
19. Cholkeri-Singh A, Miller CE. Power morcellation in a specimen bag. *J Minim Invasive Gynecol* 2015;22:160.
20. Kanade TT, McKenna JB, Choi S, Tsai BP, Rosen DM, Cario GM, et al. Sydney contained in bag morcellation for laparoscopic myomectomy. *J Minim Invasive Gynecol* 2014;21:981.

21. Vargas MV, Cohen SL, Fuchs-Weizman N, Wang KC, Manoucheri E, Vitonis AF, et al. Open power morcellation versus contained power morcellation within an insufflated isolation bag: comparison of perioperative outcomes. *J Minim Invasive Gynecol* 2015;22:433–8.
22. Srouji SS, Kaser DJ, Gargiulo AR. Techniques for contained morcellation in gynecologic surgery. *Fertil Steril* 2015;103:e34.
23. Cohen SL, Einarsson JI, Wang KC, Brown D, Boruta D, Scheib SA, et al. Contained power morcellation within an insufflated isolation bag. *Obstet Gynecol* 2014;124:491–7.
24. Winner B, Porter A, Velloze S, Biest S. Uncontained compared with contained power morcellation in total laparoscopic hysterectomy. *Obstet Gynecol* 2015;126:834–8.
25. Cohen SL, Morris SN, Brown DN, Greenberg JA, Walsh BW, Gargiulo AR, et al. Contained tissue extraction using power morcellation: prospective evaluation of leakage parameters. *Am J Obstet Gynecol* 2015 Sep 6; <http://dx.doi.org/10.1016/j.ajog.2015.08.076> [Epub ahead of print].
26. Nezhat C. The dilemma of myomectomy, morcellation, and the demand for reliable metrics on surgical quality. *JAMA Oncol* 2015;1:78–9.