

# Laparoscopic surgical staging of endometrial cancer: does obesity influence feasibility and perioperative outcome?

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## Summary

**Aim:** Laparoscopic treatment of early-stage endometrial cancer is the gold standard to reduce perioperative morbidity. Obesity is a well-known risk factor for endometrial cancer and anesthesiological and surgical complications. The authors' aim was to examine the effect of body mass index (BMI) on perioperative parameters and complications in laparoscopically-treated patients with endometrial cancer. **Materials and Methods:** A consecutive series of patients affected by endometrial cancer and their demographic and clinicopathological data were collected. Patients were divided in 41 non-obese (BMI  $\leq$  29.9) and 34 obese (BMI  $\geq$  30) groups. All patients had been preoperatively evaluated with hysteroscopic procedures and toraco-abdominal computed tomography (CT) and had been submitted to laparoscopic radical hysterectomy according to Querleu-Morrow, pelvic lymphadenectomy, peritoneal washing, and bilateral adnexectomy. **Results:** There was no statistically significant difference in blood loss, number of lymph nodes removed, and hospital stay between the groups, but there was a trend towards a lengthening of surgical time in the obese women. There were no major intraoperative and postoperative complications. **Discussion:** This study demonstrates that laparoscopic approach is feasible and safe in obese women evaluating the anesthesiological risk.

**Key words:** Radical laparoscopic hysterectomy; Endometrial cancer; Obesity.

## Introduction

Endometrial cancer is the most common gynecological neoplasia in the developed world and it constitutes six to nine percent of all cancer in women. Seventy-five percent of endometrial cancer are diagnosed at an early stage [1-3].

More than 40% of cases of endometrial cancer can be caused by obesity and more than 50% of women with early-stage endometrial cancer are obese.

Obese patients frequently have metabolic syndrome, diabetes, hypertension, cardiovascular disease, and other comorbidities that increase their anesthesiological risk.

Recommended treatment is abdominal hysterectomy and bilateral adnexectomy, while performing also pelvic lymphadenectomy is still controversial. Some authors demonstrated that lymphadenectomy does not improve overall and disease-free survival [4, 5].

Recently, laparoscopy is becoming the standard care in presumed early-stage endometrial cancer [2, 6, 7] since overall and disease-free survival are comparable to laparotomic surgery, while hospital stay and surgical morbidity are decreased by minimally-invasive surgery [8, 9]. High performance of laparoscopic surgery in the oncological field has also been extended to cases of obese women, but it constitutes a controversy among authors [10, 11]. The randomized trial LAP2 study found that the only difference in the outcome of laparoscopically-treated patients with endometrial cancer related to obesity was the rate of conversion to laparotomy. The conversion rate increased from 17.5% in patients with body mass index (BMI) of 25 to 57.1% in BMI higher than 40 [12]. On the contrary, reduction of postoperative complications, wound infection, thrombosis, ileus, and hospital

stay may give even greater advantages in obese than in general population.

The purpose of study is to evaluate the feasibility of total radical laparoscopic hysterectomy (TRLH) and the surgery-related morbidity in obese women with endometrial cancer.

## Materials and Methods

A consecutive series of 75 patients with early-stage endometrial cancer underwent laparoscopic surgery at the Department of Woman and Child Health-University of Padua, and were operated by the same expert surgeon. BMI was calculated using a standard BMI chart (patients' height and weight). The authors divided the patients into two groups obese (BMI  $\geq$  30) and non-obese (BMI  $\leq$  29.9). The non-obese group consisted of 41 patients and the obese group of 34 patients. The study was restricted to those patients under 75 years of age who had presumed endometrial carcinoma up to Stage 2 (Stage FIGO 2009) and lombo-aortic lymphadenectomy was never performed.

The authors also collected age, parity, menopausal status, BMI, grading, histological type, number, and positivity of pelvic lymph nodes.

The histological diagnosis was obtained by hysteroscopic procedures [13-16], clinical examinations consisted in total body computed tomography (CT) and blood tests. Exclusion criteria included: a documented significant cardiopulmonary disease defined as a history of cardiac failure, myocardial infarction, unstable angina, acute or recent vascular thrombosis, poorly-controlled asthma or pulmonary obstructive disease, or contraindicating prolonged Trendelenburg position; prior pelvic or abdominal radiation therapy; or inadequate bone marrow, clotting factor, renal, and hepatic function.

All women were surgically treated according to the method previously described in other papers by the same authors [9]. All patients underwent laparoscopic surgery under general anesthesia, short-course antibiotic therapy with third-generation cephalosporin and thromboprophylaxis, and with dalteparin sodium 100 UI/kg/die for 30 days.

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The feasibility of TRLH and pelvic lymphadenectomy was assessed in terms of conversion to laparotomy, surgical time (from the beginning of pneumoperitoneum to suturing of the skin), estimated blood loss (EBL), and length of postoperative hospital stay. Complications during days of admission up to 30 days after discharge were recorded from medical charts.

Statistical analysis was conducted with SPSS 19.0. Continuous variables are expressed as mean value  $\pm$  standard deviation and were compared using non-parametric Mann-Whitney U test. Categorical variables are expressed as number (percentages).

A  $p$  value  $< 0.05$  is considered statistically significant.

## Results

Overall, 75 laparoscopic radical hysterectomies, bilateral adnexectomies, peritoneal washing, and pelvic lymphadenectomies were performed for early-stage endometrial cancer. The mean age was 64.1 years (range 36 - 75) and the two groups were homogeneous for age, parity, and menopausal status. There were 34 (45.3%) obese patients ( $\text{BMI} \geq 30$ ); while 41 (54.7%) were normal or over-weight ( $\text{BMI} \leq 29.9$ ). The average BMI was 29.3 with the heaviest patient having a BMI of 64. Seven patients were morbidly obese with a  $\text{BMI} \geq 40$ . Pelvic lymph nodes were positive only in eight patients (10.7%) (Table 1). There was no statistically significant difference in surgical time between the two groups, even if in the obese group there was a longer surgical time 197 ( $\pm 9.17$ ) minutes vs 166 ( $\pm 10.1$ ); intraoperative blood loss was comparable in the two groups and not clinically relevant: 30 ml ( $\pm 32$ ) in the non-obese and 62 ml ( $\pm 74$ ) in the obese, as well as hospital stay, 3.35 days ( $\pm 1.74$ ) vs 3.16 ( $\pm 1.2$ ), respectively. Systematic lymphadenectomy was successfully performed in all patients in both groups and the mean number of pelvic lymph nodes removed were not statistically different 15.39 ( $\pm 7.63$ ) vs 17.5 ( $\pm 8.83$ ) (Table 2). There were no severe intra-postoperative complications in both groups. In the obese group there was only one case of vaginal cuff dehiscence 12 days after surgery; seven (9.3%) cases of lymphorrhea, four in obese and three in non-obese group, two cases of lower leg lymphedema, and one patient had deep vein thrombosis. In 71 cases, uterus, adnexa, and lymph nodes were removed by endobag through the vaginal route, while in four cases through an extended umbilical incision because of uterus oversize (range 350 - 510 g).

## Discussion

Currently, many retrospective studies report that laparoscopic approach includes several advantages for women as minor risk of blood loss, necessity of transfusion, postoperative pain, and length of hospital stay compared to open surgery, in the treatment of early-stage endometrial cancer [17].

In obese women who constitute a high-percentage of women suffering from endometrial cancer, it is controversial if this approach is feasible, cost-effective, and safe. Several issues as higher rate of complications, conversion to laparotomy, reduced feasibility of lymphadenectomy, lengthening of surgical time, as well as hospital stay are often debated [6, 18-26]. Enhancement

Table 1. — *Clinical and pathological features of patients.*

	No. patients	BMI $\leq 29$	BMI $\geq 30$
Age	64.1 ( $\pm 9.2$ )	63.7 ( $\pm 10.95$ )	66.32 ( $\pm 6.17$ )
Nulliparous	18 (24%)	11 (26.8%)	7 (20.6%)
Menopause	63 (84%)	33 (80.5%)	30 (88.2 %)
Stage IA	35 (46.7%)	17 (41.5%)	18 (53%)
Stage IB	30 (40%)	16 (39%)	14 (41.2%)
Stage II	4 (5.3%)	3 (7.3%)	1 (2.9%)
Stage III	5 (6.7%)	5 (12.2%)	0
Stage IVB	1 (1.3%)	0	1 (2.9%)
G1	36 (48%)	13 (31.7%)	23 (67.6%)
G2	31 (41.3%)	20 (48.8%)	11 (32.4%)
G3	8 (10.7%)	8 (19.5%)	0
Endometrioid histotype	67 (89.3%)	33 (80.48%)	34 (100%)
Other histotypes	8 (10.7%)	8 (19.52%)	0

Table 2. — *Perioperative outcome in women with BMI  $\leq 29.9$  and  $\geq 30$ .*

	Patients Mean	n. 75 Range	BMI $\leq 29.9$ Mean $\pm$ DS	BMI $\geq 30$ Mean $\pm$ DS	$p$ value
Surgical time (min)	178.89	85-300	166.11 ( $\pm 10.1$ )	197.05 ( $\pm 9.17$ )	0.11
Blood loss (ml)	44	5-300	30 ( $\pm 32.94$ )	62.37 ( $\pm 74.09$ )	0.07
Lymph nodes (number)	15.4	6-40	15.39 ( $\pm 7.63$ )	17.56 ( $\pm 8.83$ )	0.39
Hospital stay (days)	3.27	1-10	3.35 ( $\pm 1.742$ )	3.16 ( $\pm 1.214$ )	0.79

of already impaired cardiopulmonary dysfunction due to Trendelenburg and high intra-abdominal pressure are challenges for both the anesthesiologist and surgeon. Moreover technical limits due to intra-abdominal fat, can lengthen the surgical time and increase the risk of atelectasis, reduction of functional residual capacity and hypercapnia, and worsen cardiac overload [27]. This data as in other studies show among the evaluated parameters only a lengthening of surgical time in obese women. In these cases, it is necessary to underline that recommending laparoscopic surgery implies a close collaboration between surgeon and anesthesiologist.

A randomized trial has confirmed that in patients with endometrial cancer, quality of life is significantly better during perioperative period after TRLH compared to total abdominal hysterectomy [28]. In a retrospective study comparing laparoscopic and laparotomic procedures in obese women, with or without pelvic lymphadenectomy, laparoscopic approach is safe and feasible with low-risk of serious complications [29]. As in the group of Kohler *et al.* [21], the authors managed to perform pelvic lymphadenectomy in all patients with complete surgical staging, fulfilling the standard of oncologic surgery, confirming that only in the hands of skilled surgeons laparoscopic approach has allowed to perform a complete surgical staging with a good outcome of the patients. According to some authors, laparoscopic surgery is not cost-effective because of increased laparotomic conversion rate [12, 30]. In a randomized study, Bijen *et al.* [30] proved that obese women having a BMI of class II (35-39.99), are at high-risk for conversion to laparotomy. In the present consecutive series, even if limited, there was no laparotomic conversion in the obese group. Such a conversion rate can be influenced by the experience of

the surgeon and by not performing para-aortic lymphadenectomy. In the recently published data of Farthing *et al.*, as well as this present study, the feasibility and cost-effectiveness of laparoscopic approach in obese women was confirmed by the low-risk of wound infection, wound dehiscence, post incisional hernia, and intensive care admission [19]. Furthermore, length of hospital stay is not different in obese vs non-obese patients and it has already been demonstrated that quick recovery of laparoscopic treatment decreases the costs of admission compared to laparotomy [20].

## Conclusions

Surgical staging is the main prognostic factor in oncological field. Laparoscopic surgery is proved safe and feasible also in case of obese women, but this is attainable only with a close collaboration between surgeon and anesthesiologist.

## References

- [1] Jemal A., Siegel R., Ward E., Hao Y., Xu J., Thun M.J.: "Cancer statistics, 2009". *Cancer J. Clin.*, 2009, 59, 225.
- [2] Litta P., Bartolucci C., Saccardi C., Codrioni A., Fabris A., Borgato S. *et al.*: "Atypical endometrial lesions: hysteroscopic resection as an alternative to hysterectomy". *Eur. J. Gynecol. Oncol.*, 2013, 1, 51.
- [3] Ferrazzi E., Zupi E., Leone F.P., Savelli L., Omodei U., Moscarini M. *et al.*: "How often are endometrial polyps malignant in asymptomatic postmenopausal women? A multicenter study". *Am. J. Obstet. Gynecol.*, 2009, 200.
- [4] Benedetti Panici P., Basile S., Maneschi F., Alberto Lissoni A., Signorelli M., Scambia G. *et al.*: "Systematic pelvic lymphadenectomy vs no lymphadenectomy in early stage endometrial carcinoma. A randomized clinical trial". *J. Natl. Cancer Inst.*, 2008, 100, 1707.
- [5] ASTEC study group: "Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study". *Lancet*, 2009, 373, 125.
- [6] Rabischong B., Larraín D., Canis M., Le Bouëdec G., Pomel C., Jardon K. *et al.*: "Long-term follow-up after laparoscopic management of endometrial cancer in the obese: a fifteen year cohort study". *J. Minim. Invasive Gynecol.*, 2011, 18, 589.
- [7] Wright J.D., Barrena Medel N.I., Fujiwara K., Herzog J.H.: "Contemporary management of endometrial cancer". *Lancet*, 2012, 379, 1352.
- [8] Galaal K., Bryant A., Fisher A., Al-Khaduri M., Kew F., Lopes A.D.: "Laparoscopy versus laparotomy for the management of early stage endometrial cancer 2012 The Cochrane Collaboration". Published by JohnWiley & Sons, Ltd.
- [9] Litta P., Fracas M., Pozzan C., Merlin F., Saccardi C., Sacco G. *et al.*: "Laparoscopic management of early stage endometrial cancer". *Eur. J. Gynaecol. Oncol.*, 2003, 24, 41.
- [10] Oberamair A., Monolitsas T.P., Leung Y., Hammond I.G., McCartney A.J.: "Total laparoscopic hysterectomy versus total abdominal hysterectomy for obese women with endometrial cancer". *Int. J. Gynecol. Cancer*, 2005, 15, 319.
- [11] Uchenna C., Acholonu Jr, Shao Chun R.: "Laproscopy for the management of early stage endometrial cancer: from experimental to standard of care". *J. Minim. Invasive Gynecol.*, 2012, 19, 434.
- [12] Walker J.L., Piedmonte M.R., Spirtos N.M., Eisenkop S.M., Schlaerth J.B., Mannel R.S. *et al.*: "Laparoscopy compared with laparotomy for comprehensive surgical staging of uterine cancer: Gynecologic Oncology Group Study LAP2". *J. Clin. Oncol.*, 2009, 27, 5331.
- [13] Litta P., Merlin F., Saccardi C., Pozzan C., Sacco G., Fracas M. *et al.*: "Role of hysteroscopy with endometrial biopsy to rule out endometrial cancer in postmenopausal women with abnormal uterine bleeding". *Maturitas.*, 2005, 50, 117.
- [14] Marchetti M., Litta P., Lanza P., Lauri F., Pozzan C.: "The role of hysteroscopy in early diagnosis of endometrial cancer". *Eur. J. Gynaecol. Oncol.*, 2002, 23, 151.
- [15] Litta P., Merlin F., Pozzan C., Nardelli G.B., Capobianco G., Dessole S. *et al.*: "Transcervical endometrial resection in women with menorrhagia: long term follow-up". *Eur. J. Obstet. Gynecol. Reprod. Biol.*, 2006, 125, 99.
- [16] Chiarelli S., Buriticà C., Litta P., Ciani S., Guarch R., Nogales F.F.: "An immunohistochemical study of morules in endometrioid lesions of the female genital tract: CD10 is a characteristic marker of morular metaplasia". *Clin. Cancer Res.*, 2006, 12, 4251.
- [17] Zullo F., Palomba S., Falbo A., Costantino M., Tolino A., Zupi E. *et al.*: "A prospective randomized comparison between laparoscopic and laparotomic approaches in women with early stage endometrial cancer: a focus on the quality of life". *Am. Obstet. Gynecol.*, 2005, 193, 1344.
- [18] Eltabbakh G.H., Shamonki M.I., Moody J.M., Garafano L.L.: "Hysterectomy for obese women with endometrial cancer: laparoscopy or laparotomy?". *Gynecol. Oncol.*, 2000, 78, 329.
- [19] Farthing A., Chatterje J., Joglekar Pai P., Dorney E., Ghaem-Maghani S.: "Total laparoscopic hysterectomy for early stage endometrial cancer in obese and morbidly obese women". *J. Obstet. Gynaecol.*, 2012, 32, 580.
- [20] Camanni M., Bonino L., Delpiano E.P.: "Laparoscopy and body mass index: feasibility and outcome in obese patients treated for gynecologic diseases". *Minimal Invasive Gynecol.*, 2010, 576.
- [21] Köhler C., Klemm P., Schau A., Possover M., Krause N., Tozzi R. *et al.*: "Introduction of transperitoneal lymphadenectomy in a gynecologic oncology center: analysis of 650 laparoscopic pelvic and/or paraortic transperitoneal lymphadenectomies". *Gynecol. Oncol.*, 2004, 95, 52.
- [22] Kadar N.: "Laparoscopic pelvic lymphadenectomy in obese women with gynecologic malignancies". *J. Am. Assoc. Gynecol. Laparosc.*, 1995, 2, 163.
- [23] Santi A., Kuhn A., Gyr T., Eberhard M., Johann S., Günthert A.R. *et al.*: "Laparoscopy or laparotomy? A comparison of 240 patients with early stage endometrial cancer". *Surg. Endosc.*, 2010, 24, 939.
- [24] Mourits M.J., Bijen C.B., Arts H.J., ter Brugge H.G., van der Sijde R., Paulsen L. *et al.*: "Safety of laparoscopy versus laparotomy in early stage endometrial cancer: a randomized trial". *Lancet Oncol.*, 2010, 11, 763.
- [25] O'Gorman T., MacDonald N., Mould T., Cutner A., Hurley R., Olaitan A.: "Total laparoscopic hysterectomy in morbidly obese women with endometrial cancer anaesthetic and surgical complications". *Eur. J. Gynaecol. Oncol.*, 2009, 30, 171.
- [26] Eisenhauer E., Wypych K.A., Mehrara B.J.: "Comparing surgical outcomes in obese women undergoing laparotomy, laparoscopy or laparotomy with panniculectomy for the staging of uterine malignancy". *Gynecol. Oncol.*, 2007, 14, 2384.
- [27] Jeremy Dorothy, Zaki-Udin Hassan, Destiny Chau: "Anesthetic implications of obesity in the surgical patient". *Clin. Colon Rectal. Surg.*, 2011, 24, 222.
- [28] Janda M., Gebiski V., Brand A., Hogg R., Jobling T.W., Land R., Manolitsas T.A. *et al.*: "Quality of life after total laparoscopic hysterectomy versus total abdominal hysterectomy for Stage I endometrial cancer (LACE): a randomised trial". *Lancet Oncol.*, 2010, 11, 772.
- [29] Pellegrino A., Signorelli M., Fruscio R., Villa A., Buda A., Beretta P. *et al.*: "Feasibility and morbidity of total laparoscopic radical hysterectomy with or without pelvic lymphadenectomy in obese women with Stage I endometrial cancer". *Arch. Gynecol. Obstet.*, 2009, 279, 655.
- [30] Bijen C.B., de Bock G.H., Vermeulen K.M., Arts H.J., ter Brugge H.G., van der Sijde R. *et al.*: "Laparoscopic hysterectomy is preferred over laparotomy in early endometrial cancer patients, however not cost-effective in the very obese". *Eur. J. Cancer*, 2011, 47, 2158.

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