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RESEARCH

Quality of Life in Patients Affected by Endometrial Cancer: Comparison Among Laparotomy, Laparoscopy and Vaginal Approach

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Abstract The aim of this study is to verify if the surgical approach (laparoscopy/laparotomy/vaginal) in stage-I endometrial cancer treatment, may have effects on intra- and post-operative outcomes and on the patient's quality of life. The study group consisted of patients with histological diagnosis of type-I endometrial adenocarcinoma, stage-I. They were divided into three groups according to surgical approach chosen (laparotomic/laparoscopic/vaginal). Every patient answered a telephone health survey (SF-36) at 30 and 180 days post-surgery. Surgical-operating times, hospitalization length and short/long-term complications after surgery were also compared. The SF-36 survey revealed a better performance status in patients who underwent laparoscopy as compared to those who received laparotomy or vaginal surgery. We found significantly better results considering General Health, Physical Functioning, Role-Physical and Bodily Pain in the laparoscopy group after 30 and 180 days. Patients who underwent laparoscopy had significantly shorter hospitalization and less post-operative complications even if laparoscopy required significantly longer surgical-operating times compared to vaginal surgery. Our data confirm the superiority of the laparoscopic approach respect to the laparotomic and vaginal ones both in term of hospitalization length and post-operative complications.

Keywords Endometrial cancer · Laparotomic surgery · Laparoscopic surgery · Vaginal surgery · Quality of life · Complications

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Introduction

EC (Endometrial cancer) is the most common gynecological neoplasia of the female genital tract in the developed Countries. The greatest incidence of EC is found in post-menopausal women [1], despite in some cases it occurred also in pre-menopausal ones with known risk factors such as obesity, diabetes, hypertension and previous Tamoxifen use [2–4].

Over the last two decades no variation in the incidence of EC was reported [4]. It is estimated that there are 88,068 cases in Europe and 40,102 in North America each year. The concept of Quality of Life (QoL) is well established and comprehensible, yet open to interpretation. A 1948 WHO definition states that : "Quality of life is defined as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns." The subjective perception of a person's state of health and the effects that surgery may have on their QoL are of particular interest to clinicians and patients alike. This fact, along with clinical effectiveness, provide a measure of the quality of care. In the last 10 years, the SF-36 is the most frequently used indicator

of QoL since it is one of the most appropriated tool for health analysis [5].

The SF-36 Health Survey is composed of 36 multiple choice questions which yield an eight-scale profile of both physical and mental health. The physical component of the survey addresses items related to the patient's Physical Functioning (PF), Role-Physical (RP), Bodily Pain (BP), and General Health (GH). The mental component of the survey assesses items regarding Vitality (VT), Social Functioning (SF), Role-Emotional (RE) and Mental Health (MH). In addition, the SF-36 survey includes a self-evaluated health transition item referring to a change in the patient's health. This value is not used in scoring the eight scales but rather provides useful informations on the change in health status in the 6 months prior to answering the survey. The aim of the present study was to evaluate perioperative complications and postsurgical QoL of patients treated by laparoscopy or laparotomy or vaginal approach for surgical staging of type I EC.

Materials and Methods

A retrospective-observational study on 81 patients with histological diagnosis of EC-endometrioid type, 1st FIGO stage, referred between 2003 and 2011 at the Department of Surgical Sciences (OB/GYN Unit of the University of Parma-Italy) was conducted.

For all patients, we considered the 2009 revised guidelines for FIGO stage [6], adapting to these last staging all cases treated before the 2009 and staged according to 1988 FIGO guidelines [7].

All women enrolled in the study were surgically treated, according to FIGO guidelines, by total hysterectomy with bilateral salpingo-oophorectomy plus peritoneal washing. Pelvic lymph nodes removal was performed according to grading (grade 3 or grade 2 with estimated myometrium invasion more than 50 %) and preoperative imaging features (bulky lymph nodes, myometrium invasion more than 50 %, estimated tumor size larger than 3 cm) [8].

After an adequate counselling, bilateral salpingo-oophorectomy was not performed in premenopausal patients who desire to avoid iatrogenic menopause.

Patients who underwent VAG surgery were affected by grading 1 or 2 without suspicious of lymph nodes involvement or myometrium invasion more than 50 % at preoperative imaging; according this, they do not received lymphadenectomy.

All patients were divided into three Groups each of 27 women according to the surgical approach chosen: Group-0, patients who underwent laparoscopy (VDL); Group-1, patients who underwent laparotomy (LPT) and Group-2, patients who had vaginal surgery (VAG).

Vaginal route was preferred in cases in which lymphadenectomy was preoperatively estimated not necessary, high BMI, contraindication to general anesthesia or concomitant pelvic organ prolapse [9]. Laparoscopy was preferred in nulliparous, younger and in diabetic women while laparotomy was preferred in patients with history of endometriosis and/or high number of previous abdominal surgery because of the estimated increased risk of pelvic adhesions.

Women with FIGO stage≥II were excluded from the study in order to avoid a possible bias in the perceived QoL due to adjuvant-chemotherapy treatment.

For each patient we collected data about general features (age, weigh, height, BMI) at time of diagnosis, type of surgical approach (VDL, LPT, VAG), surgical-operating time, histopathological grading of EC, adjuvant-radiotherapy received, length of hospitalization.

In addition, the remote pathological anamnesis was carefully evaluated, focalizing on possible comorbidities such as hypertension, diabetes mellitus (DM), osteo-muscular and cardiovascular pathologies, and any diagnoses of depression which could influence and modify the patient's QoL.

The QoL was evaluated by telephone interviews administering the SF-36 Health Survey 30 days and 180 days after the end of therapy (surgical and/or radiation). The survey consists of eight scales with 36 multiple choice questions.

The Physical Functioning area was investigated with questions aimed to clarify the levels and types of limitations such as heavy lifting, stair climbing, bending over, kneeling, and walking short distances.

In the scales Role-Physical and Role-Emotional questions pertained to limitations, reduced tolerance and difficulties encountered in performing household tasks and other usual activities. The questions distinguished between limitations due to physical or mental health.

Concerning Bodily Pain the questions measured the magnitude, the inconvenience and the repercussions on normal activities.

The General Health was analyzed by questions concerning both positive and negative health aspects, thereby avoiding skewing caused by questions with homologous polarity.

Four bipolar type questions were asked on Vitality

The Social Functioning area was analyzed by questions on the quality and quantity of social activity performed.

Mental Health was studied by questions which addressed each of the main dimensions of mental health (anxiety, depression, loss of behavioral/emotional control and psychological wellbeing).

The evaluation of the change in the patient's health (CS) was assessed by asking the patients to rate the level of change in their general health in the last 6 months and in relation to the period prior to surgery or radiation therapy. The question was not included in the calculation of the score from the eight-scale multiple question survey but it provide useful

information on the change in the state of health in the 6 months prior to the telephone interview. At the end of each questionnaire each patient was asked to indicate any complications encountered at immediate post-operative, medium-term and late-term period.

The answers were then analyzed in order to construct numeric scales which qualify the 8 concepts of health. The points for each concept were assigned according to the guidelines of the SF-36 Health Survey Questionnaire [5].

The raw scores obtained for each area were then transformed into a scale from 0 to 100 in order to make them comparable.

All the enrolled patients have been properly informed about the aim of the study and they consented trough a written consent form the use of data respecting their privacy (Italian law 675/96). After verbal consultation of local ethical committee, our Study was defined exempt by IRB. Approval from the local institutional review board for health sciences was not required for observational studies, since the clinical management and/or surgical approach were not modified by the investigators.

The scores were then analyzed the ANalysis Of VAriance (ANOVA), the non-parametric ANOVA, the Kruskal-Wallis, the chi square and the Fischer exact test, using the PASW statistics (formerly SPSS) software version 19 for Windows.

Results

Results

The study population consisted of 81 patients whose general characteristics are illustrated in Table 1. The three groups were homogeneous with regards to median age ($p = 0.45$), BMI ($p = 0.38$) and comorbidities (statistically non-significant for diabetes mellitus, depression, osteo-muscular pathologies and arterial hypertension). The comparison of surgical-operation times (OT), resulted statistically different in the three groups (OT Group-0 vs OT Group-1: $p = 0.006$, OT Group-2 vs OT Group-0: $p < 0.001$, OT Group-2 vs OT Group-1: $p < 0.001$), showing a median time of 150 min in Group-0 (70–260 min); 195 min in Group-1 (90–260 min) and 90 min in Group-2 (45–185 min).

Considering surgical FIGO stage, 22 patients were IA and 5 IB in Group-0, 23 IA and 4 IB in Group-1, 26 IA and 1 IB in Group-2.*[p:n.s]*

Concerning EC grading, grading I was detected in 20 patients of Group-0, in 19 of Group-1 and in 23 of Group-2, grading II-III was detected in the remaining cases.*[p:ns]*

Selective pelvic lymphadenectomy was performed in 6 cases of Group-0 and in 4 cases of Group-1.*[p:ns]* Peritoneal cytology was negative in all cases.

Radiotherapy was performed in all cases with grading 3 or FIGO stage IB.

Adnexa-sparing surgery was performed in 2 cases of Group-0 (7.4 %), in 3 cases of Group-2 (11.1 %) while in none of Group-1.[p:n.s]

The median length of post-operative hospitalization was 3 days (2–5) in Group-0, 6 days (3–10) in Group-1 and 4 days (3–8) in Group-2. The length of hospitalization for the three groups was significantly different between Group-0 vs Group-1 ($p < 0.001$), between Group-0 vs Group-2 ($p = 0.006$) and between Group-2 vs Group-1 ($p < 0.001$).

The comparisons of immediate post-operative (48 h after surgery) complications in the three groups were non-significantly dissimilar for the four types of complications analyzed (nausea/vomiting, fever, altered sensitivity in inferior limbs, urinary burning).

The prevalence of medium and long term complications were statistically increased in Group-2: we found a significant increase in de-novo urge incontinence ($p = 0.004$) and cystocele/rectocele ($p = 0.041$). Among the groups, no statistical differences were found in term of stress incontinence, infections, lower limb edema.

Table 1 Study population: general features

	Group 0	Group 1	Group 2	*p*
Age mean; IIQ [aa]	67 (44–77)	63 (49–77)	62 (41–82)	n.s.
BMI mean; IIQ [kg/h^2]	28.3 (19.5–37.5)	28.3 (19.1–41.2)	29.4 (20.6–45.3)	n.s.
Diabetes mellitus n.;%	2 (7.4)	7 (25.9)	7 (25.9)	n.s.
Depression n.;%	3 (11.1)	3 (11.1)	4 (14.8)	n.s.
Osteomuscular pathologies n.;%	14 (51.8)	22 (81.4)	17 (62.9)	n.s.
Hypertension n.;%	14 (51.8)	12 (44.4)	8 (29.6)	n.s.

The scores obtained from the SF-36 survey for the eight scales analyzed are detailed reported in Fig. 1 concerning 30 days after treatment and in Fig. 2 concerning the 180 days.

The assessment of General Health at 1 month and 6 months showed a significant difference between Group-0 vs Group-2 ($p = 0.009$). The comparisons between the other groups were not significantly dissimilar.

The comparisons of the Physical Functioning after 1 month in all three types of surgical approaches were significantly different between Group-0 vs Group-1 ($p < 0.001$), between Group-0 vs Group-2 ($p = 0.013$) and between Group-2 vs Group-1 ($p = 0.014$). However, after 6 months, statistically significant differences were only present between Group-0 vs Group 1 ($p < 0.001$). The evaluation of the Role-Physical after 1 and 6 months in the three types of surgical approaches was only statistically significant between Group-0 and Group-1 vs Group-2. The comparison of the Bodily Pain after 1 and 6 months in the three groups was only significantly different between Group-0 vs Group-1 ($p = 0.048$). The analysis of the change in General Health of the patients before and after surgery showed an improvement in all three groups, with significance between Group-0 vs Group-1 and Group-2 ($p = 0.02$). The examination of Vitality, Role-Emotional, Mental Health, and Social Functioning did not show any significant differences between the three surgical approaches. We considered osteo-muscular pathologies a possible bias in the evaluation of Physical Functioning and therefore decided to remove 28 affected patients from the total sample. We then reexamined the results 1 month after surgery and we found statistical differences between Group-0 vs Group-1 ($p < 0.001$), between Group-0 vs Group-2 ($p = 0.008$) and between Group-2 vs Group-1 ($p = 0.011$). The analysis after 6 months was significantly different between Group-0 vs Group-1 ($p < 0.001$) and between Group-0 vs Group-2 ($p = 0.034$). The comparison between Group-1 and Group-2 resulted not significantly different ($p = 0.138$). Again to eliminate any bias in the analysis of the Role-Physical, we excluded patients suffering from any mood disorders. The data at 1 and 6 months post-surgery were significantly different between Group-0 vs Group-1 ($p < 0.001$) and between Group-2 vs Group-1 ($p = 0.015$). There was no significant difference between Group-0 vs Group-2 ($p = 0.454$).

Discussion

The aim of the study was to evaluate the QoL, using the SF-36 survey, in patients affected by stage I EC-endometroid type who underwent either laparotomic, laparoscopic or vaginal surgical staging.

The evaluation of an oncology patient's QoL is an important value that is strictly linked with the quality of the oncological treatment.

The laparoscopic surgery is currently the most appropriate approach for the treatment of early stage EC [10, 11], even if no clear evidences in order to define the best surgical management are still available for the treatment of advanced stages (often treated by laparotomic approach as for the non-endometrial corpus uteri malignancies) [12–14].

Several Authors demonstrated both retrospectively [5, 15, 16], and prospectively [17, 18], that laparoscopic surgery

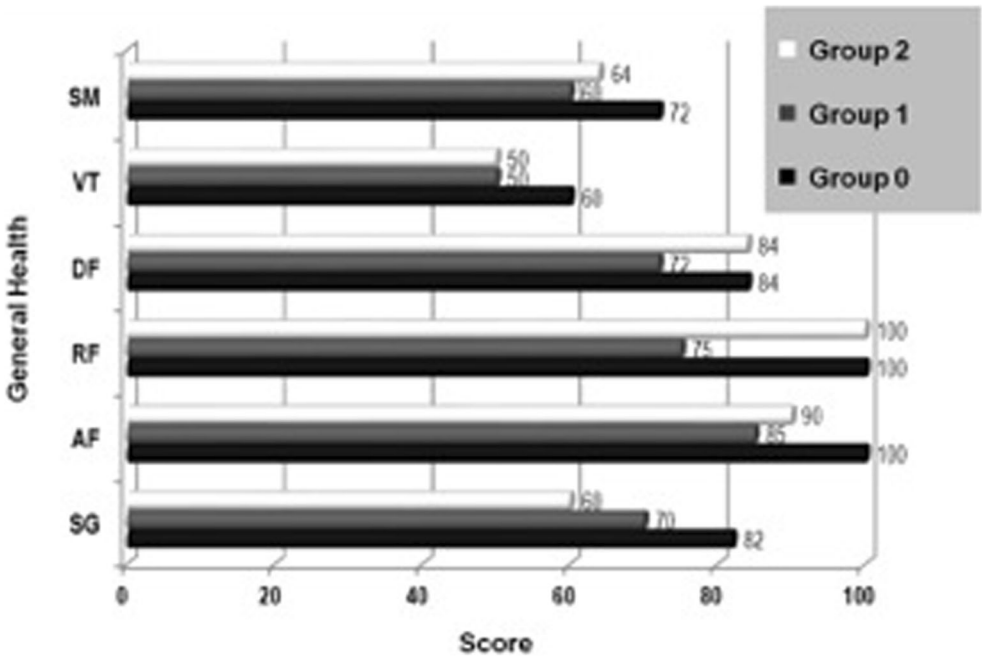

Fig. 1 Graphical representation of the results obtained for each health scale in the three patient groups 1 month after surgery (30 days)

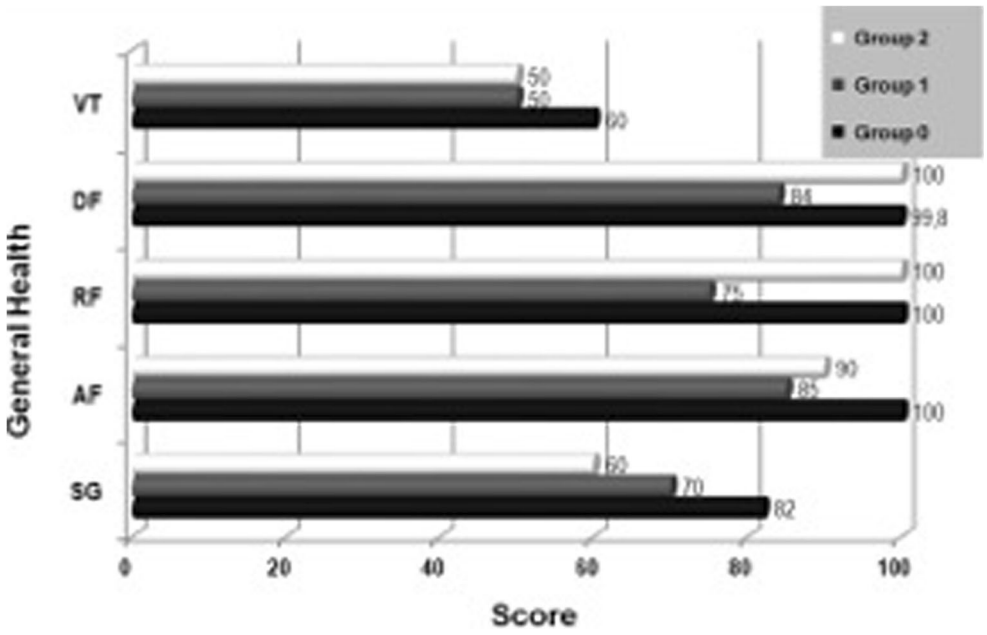

Fig. 2 Graphical representation of the results obtained for each health scale in the three patient groups 6 month after surgery (180 days)

when compared to traditional surgery does not worsen both overall survival (OS) and disease free survival (DFS) [19]. Moreover it offers a quicker post-operative recovery, less hospital stay and a faster return to pre-operative activities. Recently, several Authors, analyzed the QoL of patients with different gynecological cancers [17–20]. Capelli et al. [21] confirmed the efficacy of the SF-36 survey to assess the psycho-physical wellbeing of patients with gynecological malignancies. Zullo et al. [18] gave the same questionnaire to patients with early-stage EC in order to compare the QoL of patients who underwent VDL vs LPT. The results showed that physical and emotional functioning was significantly better in the VDL group respect to LPT group only at 1 month but not at 6 months after surgery. Kornblith et al. showed a significantly earlier return to work in the laparoscopy group when compared to the laparotomy group [22] but he described a smaller difference in the length of time to return to work. Our study is the first in the literature which analyses the QoL in patients who underwent either laparotomy, laparoscopy or vaginal surgery for stage I EC.

The comparative analysis of the three types of surgery demonstrated significant differences for both operative and post-operative features. The absolute shortest surgical-operating time was found in the VAG group (probably because in this group no lymphadenectomy was performed), followed by VDL and then LPT. The post-operative hospitalization length was the least for VDL as compared to vaginal surgery and laparotomy. Late complications (urge incontinence, cystocele/rectocele) were found more frequently in the VAG group with respect to the LPT and VDL groups. Anyway, these findings should be carefully evaluated since probably they could reflect a not underestimable bias linked to patients selection for vaginal approach.

Regarding to short term complications, all groups appeared comparable for the considered outcomes since no significant differences were found.

The analysis of the eight scales of the SF-36 survey showed a significant difference between the three groups for General Health, Physical Functioning, Bodily Pain, and Role-Physical. The surgical approach had no significant impact on Vitality, Role-Emotional, Mental Health and Social Functioning. We believe that those parameters are influenced greatly by the patients' relief of having solved an oncological problem regardless of the surgical approach.

The last question, which analyzed the change in General Health with regards to the type of surgery, showed that 44.4 % of the women who underwent laparoscopy felt a general improvement of General Health while only 29 % of those who underwent laparotomy or vaginal surgery felt the same way. This result may be explained by the fact that the patients' perceived state of health following the resolution of their illness is partly mitigated by the greater "surgical trauma" generated by laparotomy and the greater incidence of post–operative complications after vaginal surgery.

Despite our manuscript represent the first one for its aim and methods, it was not free from bias and limitations: firstly it is a retrospective-observational study and patients were not randomized to one rather than other surgical approach; adnexectomy was not performed in some cases in order to avoid iatrogenic menopause (estrogen deprivation could potentially affect post-surgical QoL); patients who underwent vaginal surgery did not receive lymphadenectomy (potentially at increased risk for suboptimal surgical staging); the large

interval time considered forced us to adapt older FIGO staging to the last one.

Finally, considering that we included in the study patients with different grading (G1–G3) and sub-stage (FIGO 1A and 1B), radiotherapy was performed only in patients estimated at increased risk of recurrence. So, this fact may potentially generate a bias in evaluating post-surgical QoL.

Conclusions

This study, in accordance with those already present in the literature, confirms that laparoscopy is a feasible and safe surgical approach when compared to laparotomy for the stage-1 EC treatment. Vaginal surgery in selected cases may be a valid alternative approach.

Our data confirm the superiority of the laparoscopic surgery with respect to the laparotomic and vaginal ones both in terms of hospitalization length and in terms of long-term post-operative complications development. The reduced invasiveness of laparoscopic approach proves to be beneficial for the physical parameters of the QoL at 30 and 180 days after surgery.

The knowledge of best surgical approach in the sub-cohort of patients affected by osteomuscular disease represent a good and interesting topic which deserve perspective large scale studies. Our little cohort of patients do not have a power to consider them separately.

Conflict of Interest All Authors declare no conflict of interest.

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References

1. Berretta R, Merisio C, Melpignano M et al (2008) Vaginal versus abdominal hysterectomy in endometrial cancer: a retrospective study in a selective population. Int J Gynecol Cancer 18:797–802
2. Gizzo S, Di Gangi S, Bertocco A et al (2014) Levonorgestrel intrauterine system in adjuvant tamoxifen treatment: balance of breast risks and endometrial benefits–systematic review of literature. Reprod Sci 21(4):423–431
3. Saccardi C, Gizzo S, Patrelli TS et al (2013) Endometrial surveillance in tamoxifen users: role, timing and accuracy of hysteroscopic investigation: observational longitudinal cohort study. Endocr Relat Cancer 20(4):455–462
4. Patrelli TS, Berretta R, Rolla M et al (2009) Pelvic lymphadenectomy in endometrial cancer: our current experience. Eur J Gynaecol Oncol 30:536–538
5. Brazier JE, Harper R, Jones NM et al (1992) Validating the SF-36 health survey questionnaire: new outcome measure for primary care. BMJ 305(6846):160–164
6. Pecorelli S (2009) Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. Int J Gynaecol Obstet 105:103–104
7. Mikuta JJ (1993) International Federation of Gynecology and Obstetrics staging of endometrial cancer 1988. Cancer 71(4 Suppl): 1460–1463
8. Berretta R, Patrelli TS, Migliavacca C et al (2014) Assessment of tumor size as a useful marker for the surgical staging of endometrial cancer. Oncol Rep 31(5):2407–2412
9. Gizzo S, Burul G, Di Gangi S et al (2013) LigaSure vessel sealing system in vaginal hysterectomy: safety, efficacy and limitations. Arch Gynecol Obstet 288(5):1067–1074
10. Eltabbakh GH (2002) Analysis of survival after laparoscopy in women with endometrial carcinoma. Cancer 95(9):1894–1901
11. Litta P, Fracas M, Pozzan C et al (2003) Laparoscopic management of early stage endometrial cancer. Eur J Gynaecol Oncol 24(1):41–44
12. Berretta R, Patrelli TS, Faioli R et al (2013) Dedifferentiated endometrial cancer: an atypical case diagnosed from cerebellar and adrenal metastasis: case presentation and review of literature. Int J Clin Exp Pathol 6(8):1652–1657
13. Patrelli TS, Gizzo S, Di Gangi S et al (2011) Cervical Mullerian adenosarcoma with heterologous sarcomatous overgrowth: a fourth case and review of literature. BMC Cancer 11:236
14. Patrelli TS, Silini EM, Gizzo S et al (2011) Extragenital Müllerian adenosarcoma with pouch of Douglas location. BMC Cancer 11:171
15. Magrina JF, Weaver AL (2004) Laparoscopic treatment of endometrial cancer: five-year recurrence and survival rates. Eur J Gynaecol Oncol 25(4):439–441
16. Malur S, Possover M, Michels W, Schneider A (2001) Laparoscopic-assisted vaginal versus abdominal surgery in patients with endometrial cancer–a prospective randomized trial. Gynecol Oncol 80(2): 239–244
17. Holub Z, Jabor A, Bartos P et al (2002) Laparoscopic surgery for endometrial cancer: long-term results of a multicentric study. Eur J Gynaecol Oncol 23(4):305–310
18. Zullo F, Palomba S, Russo T et al (2005) A prospective randomized comparison between laparoscopic and laparotomic approaches in women with early stage endometrial cancer: a focus on the quality of life. Am J Obstet Gynecol 193(4):1344–1352
19. Nieboer TE, Hendriks JC, Bongers MY et al (2012) Quality of life after laparoscopic and abdominal hysterectomy: a randomized controlled trial. Obstet Gynecol 119(1):85–91
20. Janda M, Gebski V, Brand A et al (2010) Quality of life after total laparoscopic hysterectomy versus total abdominal hysterectomy for stage I endometrial cancer (LACE): a randomised trial. Lancet Oncol 11(8):772–780
21. Capelli G, De Vincenzo RI, Addamo A et al (2002) Which dimensions of health-related quality of life are altered in patients attending the different gynecologic oncology health care settings? Cancer 95(12):2500–2507
22. Kornblith AB, Huang HQ, Walker JL et al (2009) Quality of life of patients with endometrial cancer undergoing laparoscopic international federation of gynecology and obstetrics staging compared with laparotomy: a Gynecologic Oncology Group study. J Clin Oncol 27(32):5337–5342, Erratum in: J Clin Oncol. 2010 Jun 1;28(16): 2805