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Controversies in the Surgery of Endometrial Cancer

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1. Introduction

Endometrial cancer represents over 96% of uterine cancer and is the most common gynecologic cancer in the developed countries with an estimated prevalence of 142,200 women diagnosed in 2011 worldwide[1].

This cancer affects mainly postmenopausal women, 95% of cases occurring in patients over 40 years of age; nonetheless up to 14% of patients are premenopausal, and 5% of cases occurs under the age of 40 years.

The 26th Annual Report of the International Federation of Gynecology and Obstetrics (FIGO) states that 83% of endometrial cancer patients are diagnosed and treated at early stage (FIGO I and II) with 5 year actuarial survival rates ranging from 85% to 91%[2].

Different treatments plans can be proposed for cancer of uterine corpus, but the standard treatment for this disease has been and remains hysterectomy.

The FIGO (Fédération Internationale de Gynécologie Obstétrique) staging system for this pathology has been recently reviewed and approved at the TNM UICC Core Group meeting in Geneva at the beginning of May 2008[3] and subsequently adopted by the American Joint Committee on Cancer (AJCC).

The proposed changes to the staging for endometrial cancer are linked to the data provided by the FIGO Annual Report and confirmed by other publications (Table 1).

The surgical treatment for most patients affected by endometrial cancer includes the thorough a surgical exploration of the abdominal cavity with collection of free peritoneal fluid/ peritoneal washing for cytologic evaluation, total extrafascial hysterectomy with bilateral salpingoophorectomy. The traditional abdominal access is laparotomic with vertical midline incision. The removal of pelvic/paraortic lymph nodes is also required to perform an adequate staging according to FIGO guidelines.

Usually this cancer belongs to perimenopausal age, a small percentage of cases affecting younger women.

Most premenopausal patients have a favorable disease-free survival rate (93%) compared to older patients (86%), with a higher rate of low-grade and low-stage disease.

The overall good prognosis in young women affected by early stage endometrial cancer makes fertility-sparing management an attractive option to this group of patients.

Stage I*	Tumor confined to the corpus uteri
IA	No or less than half myometrial invasion
IB	Invasion to or more than half of the myometrium
Stage II*	Tumor invades cervical stroma, but does not extend beyond the uterus**
Stage III*	Local and/or regional spread of the tumor
IIIA	Tumor invades the serosa and/or adnexae***
IIIB	Vaginal and/or parametrial involvement
IIIC	Metastases to the pelvic and/or para-aortic lymph nodes
IIIC1	Positive pelvic nodes
IIIC2	Positive para-aortic lymph nodes with or without positive pelvic lymph nodes
Stage IV*	Tumor invades bladder and/or bowel mucosa, and/or distant metastases
IVA	Tumor invasion of bladder and/or bowel mucosa
IVB	Distant metastases, including intraabdominal metastases and/or inguinal lymph nodes

* Either G1, G2, or G3
** Endocervical glandular involvement only should be considered as Stage I and no longer as Stage II
*** Positive cytology has to be reported separately without changing the stage.

Table 1. Endometrial Cancer: New FIGO Staging.

The progressive increasing incidence of endometrial cancer in the last few decades combined with the increase of absolute number of under forty's with childbearing desire have forced clinicians to consider fertility-sparing options in treatment of this pathology.
These strategies include endocrine treatment and surgical ovarian preservation.
Fertility-sparing endocrine treatment is founded on the use progestational agents. The clinical staging system proposed by the FIGO in 1971 is still applicable for patients who attempt for a medical fertility sparing option (table 2).

Stage characteristics

I	Carcinoma is confined to the corpus
IA	Length of the uterine cavity is 8 cm or less
IB	Length of the uterine cavity is more than 8 cm

Histologic subtypes of adenocarcinoma

G1	Highly differentiated adenomatous carcinoma
G2	Differentiated adenomatous carcinoma with partly solid areas
G3	Predominantly solid or entirely undifferentiated carcinoma
II	Carcinoma involves the corpus and cervix
III	Carcinoma extends outside the uterus but not outside the true pelvis
IV	Carcinoma extends outside the true pelvis or involves the bladder or rectum

Table 2. Corpus Cancer Clinical Staging, FIGO 1971.

The use of progestational agents is still a subject of investigation in young patients with early stage disease [4,5,6] and it has been shown to have reasonable success particularly in women with low-grade disease [7]. A recent multicenter phase II study of treatment with medroxyprogesterone acetate for endometrial carcinoma and for atypical hyperplasia in young women by Ushijima and colleagues found a complete response in 55% and 82% of cases respectively, with a 47% recurrence rate observed during the 2-year follow up period.

Progestational uterine-preserving treatment is a reasonable option in women affected by early stage, low-grade endometrial cancer, but these patients should be widely counseled about the high recurrence risk observed in cases responding to progestins (about 50% of cases), and thus recommended to close follow-up because of the substantial rate of recurrence.[4]

MRI, with its high soft tissue contrast resolution and multiplanar capability, has been evaluated in several series. Most of them reported data on the prediction of deep myometrial invasion. In these series the sensitivity of the radiological procedure ranges between 71% to 83%, the specificity between 74% to 96% with Negative and Positive Predictice Values between 86%-97% and 80%-91% respectively.[8 9 10]

If the requirement for conservative treatment is no myometrial invasion, then MRI is a poor screening test with an NPV of only 46%[11].

Ovarian preservation in young patients, preferably in early stage, low grade cases, may be considered taking into account the potential risk of missing occult ovarian metastases or coexisting synchronous ovarian primary tumors [12,5] and the potential risk of endocrine stimulation of residual microscopic endometrial cancer foci [13,14,15,16]

Twenty-three coexisting synchronous epithelial ovarian tumors and 3 metastatic disease were reported in a cohort of 102 women younger than 45 years with endometrial cancer, thus ovarian cancer accounting for 25% of the study cohort. In this report, 4 patients (15%) had normal preoperative imaging of the adnexa, and 4 (15%) had benign appearing ovaries at the time of intraoperative assessment. Recent results of a Surveillance, Epidemiology, and End Results Database (SEER) analysis on ovarian preservation applied to 402 out of 3269 evaluable premenopausal women with stage I endometrial cancer (12%) showed that ovarian preservation may be safe and had no effect on either cancer-specific survival or overall survival. However, it must be considered that young patients could harbor a genetic predisposition to multiple site primary cancer [17].

The Lynch syndrome is an autosomal-dominant cancer susceptibility syndrome associated with early-onset colon, rectal, ovary, small bowel, ureter/renal pelvis, and endometrial cancer. This syndrome occurs in nearly 10% of endometrial cancer patients less than 50 years of age, compared to the 2% to 5% of all endometrial cancer cases, and the risk of ovarian cancer in patients affected by HNPCC is 10% to 12%.

The omission of a bilateral salpingo-oophorectomy should be carefully counseled in these young high-risk patients, and all the known devices should be used to best define their effective risk of ovarian cancer, such as genetic evaluation of mismatch repair defects or BRCA1 and BRCA2 germ line gene mutations.

However in the preoperative counseling the clinician has to make the patient clearly understanding that a negative genetic evaluation does not eliminate the risk of synchronous or metachronous ovarian cancers.

Usually, overall surgical cure rates for endometrial cancer are high but, unfortunately, up to 25% of affected patients have a poor prognosis when the disease is widely spread at diagnosis or characterized by poor clinical-pathological risk factors such as high grade of histological differentiation, deep myometrial invasion or unfavorable histology (clear cells / serous papillary pattern). Treatment planning must be tailored depending on tumor grade, depth of myometrial invasion, and extension to cervical stroma: these factors are directly related to the risk of regional lymph node and distant metastasis, influencing overall prognosis.

Laparotomic surgery has been considered the standard surgical approach in patients affected by endometrial cancer. This surgery must include an initial exploration of the abdominal and pelvic cavities, peritoneal free fluid or washing collection for cytology, biopsy of any suspicious extra uterine lesion, total extrafascial hysterectomy with bilateral salpingo-oophorectomy. In order to complete the surgical staging, the dissection of pelvic and para-aortic lymph nodes are recommended by FIGO.

Vaginal hysterectomy has often been defined as the simplest and least morbid approach and different studies found similar treatment outcomes in stage I endometrial cancer patients treated with vaginal or laparotomic hysterectomy [18,19,20]. Still, limitations to vaginal approach are the lack of exploration and of cytological evaluation of the abdominal cavity, difficulty in performing salpingo-oophorectomy and the inability to perform a thorough evaluation of lymph nodes [19]. This surgical approach should be considered a valid alternative for high-risk patients with co-morbidities that can contraindicate abdominal procedures.[21,22]

In the latest years, hysterectomy and bilateral salpingo-oophorectomy performed by a laparoscopic-assisted-vaginal (LAVH) or total laparoscopic (TLH) approach have increasingly been integrated in the standard practice of endometrial cancer patients. These techniques are able to overcome some of the limitations of the vaginal approach.

Initial case reports and small single-institution retrospective series described laparoscopic technique and demonstrated its feasibility during the early '90s [23,24,25]; subsequently larger series, randomized small size trial, and finally a multi-institutional randomized controlled trial, evaluated the feasibility and survival outcomes of laparoscopy in endometrial cancer patients [26,27,28,29]. A small prospective trial [26] randomized 70 patients with FIGO stage I-III endometrial carcinoma to radical vaginal or laparoscopy-assisted simple hysterectomy or simple or radical abdominal hysterectomy with or without lymph node resection. The laparoscopic group showed significantly lower blood loss and transfusion rates, while the number of pelvic and para-aortic lymph nodes, duration of surgery, and incidence of postoperative complications were similar for both groups. A significantly shorter hospital stay was found in the laparoscopic group, in accordance with other Authors [35,36]. No significant differences were observed between the laparoscopic and laparotomy groups in terms of disease recurrence rate and long-term survival (97.3% vs. 93.3% and 83.9% vs. 90.9%, respectively).

The conclusion of this study was that laparoscopic staging combined with laparoscopically assisted vaginal hysterectomy can be recommended for the treatment of women with endometrial cancer, offering a less invasive approach that is associated with less intraoperative and postoperative morbidity.

Results of a large randomized trial (LAP II trial) from the Gynecologic Oncology Group (GOG) comparing laparoscopic hysterectomy with comprehensive surgical staging to the traditional laparotomy technique were recently published [29,30].

The study enrolled 2616 patients with clinical stage I to IIA uterine cancer and randomized 920 patients to the open arm, and 1,696 to laparoscopy. The conversion rate from laparoscopy to open procedure was 26%; it increased with increasing patient obesity. Median number of removed pelvic nodes was similar between each technique, while a statistically significant higher para-aortic node dissection rate was observed in the laparotomy group (97% versus 94%). Most importantly, the frequencies of patients found to have positive lymph nodes were the same in both groups (9%). The rate of postoperative complications, median blood loss, and median length of hospital stay were significantly lower in the laparoscopy group, despite the relatively high conversion rate.

The authors concluded that laparoscopic surgical staging is an acceptable and possibly a better option, particularly when the surgery can be successfully completed laparoscopically, even if the results specific to long-term oncologic outcomes are not known.

Age and obesity have been suggested as relative contraindications to laparoscopic surgery. Similar conclusions where reached by Scribner et al. [31]

The authors concluded that, with the growth of an aging patient population, the laparoscopic management of endometrial cancer is a viable option.

Obese patients have also been suggested to be poor laparoscopic candidates due to difficulties in establishing pneumoperitoneum, poorer visualization, inability to tolerate steep Trendelenburg positioning needed to facilitate the surgery, and difficulties with ventilation. It is important to mention that complete surgical staging is more difficult in obese patients regardless of the surgical approach.

In a study of Eltabbakh et al. comparing LAVH and abdominal approach in women with BMI between 28 and 60 [32] laparoscopic conversion was required only in 8% of patients: laparoscopic surgery was associated with a longer operative time (195

minutes vs. 138 minutes), more pelvic nodes (mean 11 vs. 5), less pain medicine requirement, and shorter hospital stay (2.5 vs. 5.6 days) were recorded.

Total laparoscopic hysterectomy has also been shown to be feasible in heavier patients [33]. In the prospective GOG series, there was ≥80% success rate with patients with a BMI of 27 or less, but even at a BMI of 35, 65% could have successful laparoscopic surgery. [34]

In conclusion, the surgical approach and the technique used to remove the uterus with the ovaries does not represent a source of controversy since the comprehensive surgical pathological evaluation should be accomplished with different approaches. [25]

Minimal access surgery is being applied increasingly in gynecological oncology and is now a commonplace in the surgical treatment of endometrial cancer.

The widespread adoption of laparoscopy has been slow due to the prolonged learning curve needed to become proficient in such a technique. The development of robotic surgery has facilitated the use of laparoscopy due to the faster and easier learning curve.

In robotic surgery, the main surgeon sits at the surgeon console located away from the patient, places his index fingers and thumbs in the master rings and along with foot pedals is able to control all the robotic instruments held by the patient-side cart through a computer-based technology. Endometrial cancer is particularly suited for robotic surgery for several reasons. The majority of women with endometrial cancers are obese and at greater risk for postoperative wound complications, and would benefit from a minimally invasive procedure with smaller incisions, resulting in less risk for wound problems. However, at the same time obesity increases the degree of difficulty of management via laparoscopy: the level of difficulty of operating in an obese patient via robotic surgery is minimal. In a retrospective comparison of obese women and morbidly obese women undergoing traditional laparoscopic approach vs. robotic-assisted approach, better surgical outcomes were observed in the group undergoing robotic-assisted laparoscopy. [35]

Actually there are no published data of survival in endometrial cancer patients treated with robotic system that has been introduced in clinical practice short time ago. However, early case series thus far reported suggests that robotic surgery for endometrial cancer is feasible and safe. The use of robotic-assisted laparoscopy for the management of endometrial cancer is expected to be rapid, paralleling the growth that has been observed with radical prostatectomy.

Another important issue in the management of endometrial cancer is the tailoring of "radicality" according to the "clinical stage" of the disease.

Radical hysterectomy is the standard of care of early stage cervical cancer (IA2–IB1), but its role in endometrial cancer remains unclear [36]. A radical surgical approach to endometrial cancer requires the uterus to be removed with parametria, paracolpos, and an adequate vaginal cuff, and ensures wider tumor-free resection margins than those obtained with total abdominal hysterectomy. The main goals of the radical surgical approach for stage I endometrial cancer are a better local control of the disease and a reduction in the use of adjuvant radiation with its possible related complications.

A multicenter randomized Italian trial [37] aimed to determine whether a modified radical (Piver– Rutledge class II) hysterectomy can improve survival and loco regional control compared to the standard extrafascial (Piver–Rutledge class I) hysterectomy. The Authors randomized 520 early stage endometrial cancer patients and evaluated the difference between Class I vs. Class II group in terms of loco regional control, disease-free and overall survival, and treatment-related morbidity.

Intraoperative and postoperative complications rates were similar in the two arms, but there were slight imbalances with respect to urinary complications. Although class II hysterectomy turned out to be feasible in most patients enrolled onto our study (only 19 of the 279 assigned to class II underwent class I hysterectomy), it was far longer (20 min) and was associated with greater blood loss (50 ml) than class I.

The univariate and multivariate estimates of the HRs of recurrence confirm that class II hysterectomy offers no benefit.

The identification of spread to draining lymph node basins is considered of outmost importance since it can change the prognosis and modify the use of postoperative therapies. However no consensus exists regarding the role and the extension of lymphadenectomy in the primary surgical setting and more controversial is the therapeutical role of this procedure.

In women submitted to systematic lymphadenectomy without clinical suspect of nodal metastasis, pelvic lymph node involvement may be assessed in 8 to 28% of patients. [38, 39].

The risk of pelvic and/or paraortic nodal metastases [2] depends on hystotype, myometrial invasion and hystological grade of differentiation, ranging from 0% up to 20% in M0G1 and M3G3 patients (see Table 3).

Myometrial invasion	P-A-(%)	P+A-(%)	P-A+(%)	P+A+(%)
Unknown	97.42	1.81	0.17	0.60
M0	94.20	3.40	0.60	1.80
M≤50%	93.88	4.56	0.62	0.94
M>50%	73.90	18.41	1.56	6.14

P-, P+: negative, positive pelvic nodes;
A-, A+: negative, positive aortic nodes;
M0: no myometrial invasion
M≤50%: myometrial invasion ≤50%
M>50%: myometrial invasion >50 %.

Table 3. Carcinoma of the corpus uteri. Patients treated in 1999-2001. Lymhnodal status (a).

Even if there is no evidence that risk/benefit balance is in favor of lymphadenectomy however this procedure can cause potentially significant morbidity in approximately 11% of cases [40].

The relevance of lymph node status is of outmost importance for the prognosis of this disease. For this reason this procedure represents a fundamental step in staging the disease [3]. The main risks attributable to nodal dissections include increased operative time, potential for blood loss associated with vascular injuries eventually requiring blood transfusion, genitofemoral

nerve injury with resulting numbness and paresthesias over medial thighs, lymphocysts formation, and lymphedema.

Many believe that nodal dissection should be reserved for those with sufficient risk of nodal disease. Most important factors related to incidence of nodal metastases are tumor grade and depth of myometrial invasion as we can see analyzing data of GOG 33 study [38]. Patients with grade 1 lesion with inner part of myometrium involved showed a 3% risk of nodal metastasis defined by the Authors "negligible". Patients with grade 3 lesions with deep myometrial invasion showed a 34% risk of nodal localizations.

Clear cell tumors and serous papillary tumors are more often affected by nodal metastasis (30-50% of risk independently by prognostic factors on surgical specimen) [41].

Usually the risks related to nodal resection are acceptable, if this procedure is managed by skilled and well trained physicians, and this procedure deeply influences the use of postoperative treatment: less indications for radiation therapy or use of vaginal cuff brachytherapy instead of whole pelvic external irradiation [42] [43]. Without nodal information, physicians must rely on uterine factors to estimate the probability for nodal disease and pelvic failure to determine the need for postoperative radiation. This estimation can result in a substantial increase in the use of radiation.

The advantages of systematic lymphadenectomy are evidenced in some retrospective studies. Other observational studies, however, have not shown any such benefit. Until 2011 no class I evidence paper had been published.

MRC ASTEC trial [44] enrolled 1408 women with proven endometrial carcinoma from 85 centers in four countries.

This randomized trial did not showed any evidence of benefit with systematic lymphadenectomy for endometrial cancer in terms of overall, disease-specific, and recurrence-free survival. Overall morbidity was low, but there was a substantial increase in the incidence of lymphedema in the lymphadenectomy group compared with standard surgery. The Authors concluded that the balance of risks and benefits for systematic iliac and obturator lymphadenectomy does not favor this intervention, with no clear evidence of benefit in terms of overall or recurrence-free survival and increased risk of lymphedema. These results suggest that lymphadenectomy in patients affected by endometrial cancer, whose neoplasm is preoperatively diagnosed as confined to the corpus, has no therapeutic effect and is therefore not justified as a therapeutic procedure. Nevertheless this surgical procedure is required for surgical staging in order to identify those patients who will have benefit from adjuvant treatment.

It must be noted that this trial received a number of criticisms concerning the inclusion of a large number of women at low risk of nodal metastases and variable extent of nodal dissection between recruiting centers.

An Italian randomized prospective study [45] recruited 514 patients with preoperative FIGO stage I endometrial carcinoma (Stage IB with grade 1 lesions were excluded from randomization), randomly assigned to undergo pelvic systematic lymphadenectomy or no lymphadenectomy whose anatomical and numerical extent was clearly defined in the study design. No lack of consistency between the centers and uniformly high nodal counts were detected.

According to the Authors, pelvic systematic lymphadenectomy did not change the natural history of the disease since the pattern of disease recurrence, was similar between the two groups. However, pelvic lymphadenectomy did allow for a more accurate prognosis on the basis of the pathological lymph node assessment and, in this trial, provided for approximately 10% of the upstaging to surgical stage IIIC (P < .001).

The role of para-aortic lymphadenectomy is another field of debate: the anatomic extent and level of dissection remain ill defined for patients undergoing para-aortic node sampling or systematic dissection. [46,47,48,49]

Reports that address the routes of lymphatic dissemination in endometrial cancer have suggested that the principal connections are between the uterine corpus and the external iliac and obturator basins [50,51,52]. A direct route may exist from the corpus to the paraaortic node-bearing basins by the lymphatic channels adjacent to the gonadal vessels within the infundibulopelvic ligament [51,52]. Other reports have also suggested a potential direct lymphatic communication between the external iliac and obturator basins and the paraaortic node-bearing tissue [48,53]. Therefore, an a priori assertion exists that the paraaortic node-bearing tissue in the region of the origin and insertion of the gonadal arteries and veins, respectively, would be favored sites for nodal involvement.

In absence of metastatic pelvic nodes, isolated positive para-aortic nodes are identified in a small number of patients. The historical data from GOG 33 showed that isolated para-aortic nodal metastases occurred in 2% of patients. These data also suggest that when positive, outcomes are improved in patients who have complete surgical resection of para-aortic nodes. This effect may be simply be a consequence of better staging rather than a true therapeutic effect. Another explanation may be that extensive lymphadenectomy reflects overall better care. The use of Radiation therapy responding to positivity of para-aortic nodes may be another explanation of better survival in patients submitted to this procedure [54].

The risks of paraortic nodal involvement are essentially the same that predicts the pelvic nodal spread (depth of myometrial invasion, nuclear grading, and the presence of lymph-vascular space involvement) [46,55]. Mariani et al. showed that patients at high risk for para-aortic nodal disease (based on invasion >50%, palpable positive pelvic nodes, positive adnexa) who did not have para-aortic dissection or who had biopsy only and who were managed as though para-aortic nodes were positive had 5-year survival of 71% compared to 85% for those patients with positive para-aortic nodes who did undergo complete resection [56].

At the present time, the superior extent of para-aortic dissection should be at least to the level of the inferior mesenteric artery (IMA). The Mayo Clinic group retrospectively in their series observed that the routinely performed lymphadenectomies only up to the IMA potentially miss 38% to 46% of patients with positive para-aortic nodes because of the high rate of isolated involvement above the IMA. Furthermore, 63% of patients in Mayo's series with positive lymph nodes below the IMA also had positive nodes above the IMA that would have escaped detection if the dissection had been limited to the lower node basins. Thus, the node-bearing tissue between the IMA and the renal vessels appears in their experience of outmost importance for the assessment of the extent of disease and thus for determination of overall treatment dispositions. [56] This extended para-aortic dissection is feasible laparoscopically as well laparotomically [57]. Prospective data describing the frequency of high para-aortic/renal nodes are awaited.

More recently a large prospective trial compared the outcomes after complete pelvic lymphadenectomy or combined pelvic and para-aortic lymphadenectomy. The trial was non-randomized and was conducted at two sites, one in which pelvic lymphadenectomy was standard and a second where combined pelvic and para-aortic dissection was standard. More than 600 women were included. The authors report significantly increased overall survival in women undergoing para-aortic dissection and argue that women at intermediate or high risk of disease recurrence should have both pelvic and para-aortic lymphadenectomy [58]. No benefit was seen in low risk patients. Although the groups were

comparable in most respects with a similar proportion of non-endometrioid carcinomas, 77% of women in the pelvic/para-aortic group received systemic chemotherapy compared with only 45% of women in the pelvic node group. These results do not argue convincingly for para-aortic lymphadenectomy in women at higher risk of disease recurrence or distant metastasis but do suggest that this is an area that should be addressed by a properly constructed clinical trial.

A recent Cochrane Review [59] assessed that published data do not support the routine use of pelvic lymphadenectomy in the treatment of endometrial cancer thought to be confined to the uterus at presentation. There was no statistically significant difference in survival between the groups. Meta-analysis indicated no significant difference in overall and recurrence-free survival between women who received lymphadenectomy and those who received no lymphadenectomy (pooled HR = 1.07, 95% CI: 0.81 to 1.43 and HR = 1.23, 95% CI: 0.96 to 1.58 for overall and recurrence-free survival respectively) and, in terms of harmful effects of treatment, women who did not receive lymphadenectomy showed a clear benefit. No good quality data were found which assessed the role of para-aortic lymphadenectomy, or removal of grossly enlarged lymph nodes. Further research is needed to allow more individualized treatment strategies, ensuring that women with more aggressive cancers receive appropriate treatment, whilst not exposing women with a better prognosis to potentially serious side effects. In addition, it is imperative to assess the impact of any intervention on quality of life in any future study, particularly for a cancer with good survival rates.

Although lymphadenectomy continues to be controversial for some, over the last 30 years our knowledge of the lymph node involvement in endometrial cancer has increased and how that information can be used to benefit our patients. Lymphadenectomy in endometrial cancer is certainly diagnostic and it may be also therapeutic if systematic pelvic and para-aortic procedures are performed. At the present time low risk patients can avoid this surgical assessment but there is no general agreement in the definition of the "low risk category". Recent data, and a new molecular staging system could improve our knowledge and would probably lead to a consensus in the near future.

2. Debulking

Endometrial cancer is often diagnosed at a stage I disease (71%) [60]. A low percentage of cases present at an advanced stage, defined by FIGO stage III and IV. Nonetheless, rare histopathologic types of endometrial cancer, such as papillary-serous (4% of cases) and clear cell carcinomas (2% of cases) frequently present at an advanced stage, both accounting for 14% of advanced stage (FIGO III and IV) compared with 4% of early stage (FIGO I and II) endometrial cancer patients [61,62].

The management of endometrial cancer is reviewed in several papers; still, limited evidence is available how to manage patients with advanced stage disease. The treatment of this relatively rare group of patients is frequently individualised and it depends on the surgical ability to resect disease.

In patients with macroscopic intraperitoneal disease it is debated if optimal surgical cytoreduction is indicated, and in these cases options include the resection of the easily removable disease such as uterus, adnexa, and omentum, versus performing a wider cytoreductive effort. Different retrospective studies evaluated the impact of surgical cytoreduction on the outcome of advanced endometrial cancer patients, suggesting that survival correlates with the volume of residual disease.

Goff et al [63] analysed 47 cases of stage IV endometrial cancer, observing a statistically significant improvement of median survival in the cases of no bulky disease at the end of surgery compared to patients not completely cytoreducted (18 vs. 8 months respectively).

Chi et al [64] also found a significatively longer median survival in the subgroup of patients treated with optimal cytoreduction (residual tumor < 2 cm) among 55 cases of stage IV endometrial cancer, compared to patients with residual tumor > 2 cm (31 months vs. 12 months).

Bristow et al [65] defines optimal cytoreduction as largest residual tumor < 1 cm and showed that median survival was 34 months after optimal cytoreduction compared to 11 months when suboptimal cytoreduction was performed, with a residual tumor > 1 cm, and again the difference were statistically significative.

In conclusion, it can be assessed that in all cases with no firm contraindication for surgery, primary treatment should include surgery, with an exception for patients with distant metastases: for these cases there may be a limited role of surgery such as to provide control of vaginal bleeding.

Still, the warranty for an optimal cytoreduction in cases with disease outside the uterus is only based on some retrospective studies made on relative small number of patients, different stage of disease are often included and different definitions of surgical cytoreduction are employed. Thus, these studies are difficult to compare, and no randomized trial has been carried out to confirm the advantage of optimal cytoreduction on survival.

Nonetheless, available data suggest that an optimal cytoreduction in advanced stage endometrial cancer is associated with improved survival of these patients.

3. Refferences

[1] Global cancer statistics. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D.CA Cancer J Clin. 2011 Mar-Apr;61(2):69-90. Epub 2011 Feb 4.

[2] Carcinoma of the corpus uteri. FIGO 26th Annual Report on the Results of Treatment in Gynecological Cancer.Creasman WT, Odicino F, Maisonneuve P, Quinn MA, Beller U, Benedet JL, Heintz AP, Ngan HY, Pecorelli S. Int J Gynaecol Obstet. 2006 Nov;95 Suppl 1:S105-43.

[3] Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. Pecorelli S. Int J Gynaecol Obstet. 2009 May;105(2):103-4.

[4] J Clin Oncol. 2007 Jul 1;25(19):2798-803. Multicenter phase II study of fertility-sparing treatment with medroxyprogesterone acetate for endometrial carcinoma and atypical hyperplasia in young women. Ushijima K, Yahata H, Yoshikawa H, Konishi I, Yasugi T, Saito T, Nakanishi T, Sasaki H, Saji F, Iwasaka T, Hatae M, Kodama S, Saito T, Terakawa N, Yaegashi N, Hiura M, Sakamoto A, Tsuda H, Fukunaga M, Kamura T.

[5] Outcome of fertility-sparing treatment with progestins in young patients with endometrial cancer. Gotlieb WH, Beiner ME, Shalmon B, Korach Y, Segal Y, Zmira N, Koupolovic J, Ben-Baruch G. Obstet Gynecol. 2003 Oct;102(4):718-25. Review.

[6] Progestin alone as primary treatment of endometrial carcinoma in premenopausal women. Report of seven cases and review of the literature. Kim YB, Holschneider CH, Ghosh K, Nieberg RK, Montz FJ. Cancer. 1997 Jan 15;79(2):320-7.

[7] Hormonal therapy for the management of grade 1 endometrial adenocarcinoma: a literature review. Ramirez PT, Frumovitz M, Bodurka DC, Sun CC, Levenback C. Gynecol Oncol. 2004 Oct;95(1):133-8.

[8] Intraoperative evaluation of depth of myometrial invasion in stage I endometrial adenocarcinoma. Doering DL, Barnhill D, Weiser EB, Burke TW, Woodward JE, Park RC. Obstet Gynecol 1989

[9] Clinical value of intraoperative gross examination in endometrial cancer. Franchi M, Ghezzi F, Melpignano M, Cherchi PL, Scarabelli C, Apolloni C, et al. Gynecol Oncol 2000;76:357

[10] Accuracy of intraoperative frozen-section diagnosis in stage I endometrial adenocarcinoma. .Kucera E, Kainz C, Reinthaller A, Sliutz G, Leodolter S, Kucera H, et al. Gynecol Obstet Invest 2000;49:62

[11] Predictive Value of Magnetic Resonance Imaging in Assessing Myometrial Invasion in Endometrial Cancer. Is Radiological Staging Sufficient for Planning Conservative Treatment? Cade TJ, MBBS, Quinn MA, McNally OM, Neesham D, Pyman J, Dobrotwir A. Int J Gynecol Cancer 2010;20: 1166

[12] Feasibility of ovarian preservation in patients with early stage endometrial carcinoma. Lee TS, Jung JY, Kim JW, Park NH, Song YS, Kang SB, Lee HP. Gynecol Oncol. 2007 Jan;104(1):52-7.

[13] Responses to estradiol in a human endometrial adenocarcinoma cell line (Ishikawa). Holinka CF, Hata H, Kuramoto H, Gurpide E. J Steroid Biochem. 1986 Jan;24(1):85-9.

[14] Association of exogenous estrogen and endometrial carcinoma. Smith DC, Prentice R, Thompson DJ, Herrmann WL. N Engl J Med. 1975 Dec 4;293(23):1164-7.

[15] Increased risk of endometrial carcinoma among users of conjugated estrogens. Ziel HK, Finkle WD. N Engl J Med. 1975 Dec 4;293(23):1167-70.

[16] Coexisting ovarian malignancy in young women with endometrial cancer. Walsh C, Holschneider C, Hoang Y, Tieu K, Karlan B, Cass I. Obstet Gynecol. 2005 Oct;106(4):693-9.

[17] Hereditary colorectal cancer syndromes: molecular genetics, genetic counseling, diagnosis and management. Lynch HT, Lynch JF, Lynch PM, Attard T. Fam Cancer. 2008;7(1):27-39

[18] Evaluation of different surgical approaches in the treatment of endometrial cancer at FIGO stage I. Candiani GB, Belloni C, Maggi R, Colombo G, Frigoli A, Carinelli SG. Gynecol Oncol. 1990 Apr;37(1):6-8.

[19] Vaginal hysterectomy versus abdominal hysterectomy for the treatment of stage I endometrial adenocarcinoma. Massi G, Savino L, Susini T. Am J Obstet Gynecol. 1996 Apr;174(4):1320-6.

[20] Role of vaginal surgery in the 1st stage endometrial cancer. Experience of the Florence School. Scarselli G, Savino L, Ceccherini R, Barciulli F, Massi GB. Eur J Gynaecol Oncol. 1992;13(1 Suppl):15-9.

[21] Use of vaginal hysterectomy for the management of stage I endometrial cancer in the medically compromised patient. Bloss JD, Berman ML, Bloss LP, Buller RE. Gynecol Oncol. 1991 Jan;40(1):74-7.

[22] Lymph node yield from laparoscopic lymphadenectomy in cervical cancer: a comparative study. Fowler JM, Carter JR, Carlson JW, Maslonkowski R, Byers LJ, Carson LF, Twiggs LB. Gynecol Oncol. 1993 Nov;51(2):187-92.

[23] Combined laparoscopic and vaginal surgery for the management of two cases of stage I endometrial cancer. Childers JM, Surwit EA. Gynecol Oncol. 1992 Apr;45(1):46-51.

[24] Laparoscopic lymphadenectomy and vaginal or laparoscopic hysterectomy with bilateral salpingo-oophorectomy for endometrial cancer: morbidity and survival. Magrina JF, Mutone NF, Weaver AL, Magtibay PM, Fowler RS, Cornella JL. Am J Obstet Gynecol. 1999 Aug;181(2):376-81.

[25] Laparoscopic-assisted vaginal hysterectomy for endometrial cancer: clinical outcomes and hospital charges. Gemignani ML, Curtin JP, Zelmanovich J, Patel DA, Venkatraman E, Barakat RR. Gynecol Oncol. 1999 Apr;73(1):5-11.

[26] Feasibility of laparoscopic management of presumed stage I endometrial carcinoma and assessment of accuracy of myoinvasion estimates by frozen section: a gynecologic oncology group study. Homesley HD, Boike G, Spiegel GW. Int J Gynecol Cancer. 2004 Mar-Apr;14(2):341-7.

[27] Laparoscopic-assisted vaginal versus abdominal surgery in patients with endometrial cancer--a prospective randomized trial. Malur S, Possover M, Michels W, Schneider A. Gynecol Oncol. 2001 Feb;80(2):239-44.

[28] Analysis of survival after laparoscopy in women with endometrial carcinoma. Eltabbakh GH. Cancer. 2002 Nov 1;95(9):1894-901.

[29] Laparoscopy compared with laparotomy for comprehensive surgical staging of uterine cancer: Gynecologic Oncology Group Study LAP2. Walker JL, Piedmonte MR, Spirtos NM, Eisenkop SM, Schlaerth JB, Mannel RS, Spiegel G, Barakat R, Pearl ML, Sharma SK. J Clin Oncol. 2009 Nov 10;27(32):5331-6.

[30] 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. Kornblith AB, Huang HQ, Walker JL, Spirtos NM, Rotmensch J, Cella D. J Clin Oncol 2009;27:5337–42.

[31] Surgical manangement of early stage endometrial cancer in the elderly: is laparoscopy feasible? Scribner D, Walker J, Johnson G, et al. Gynecol Oncol 2001;83:563–568.

[32] Hysterectomy for obese women with endometrial cancer: laparoscopy or laparotomy. Eltabbakh G, Shamonki M, Moody J Gynecol Oncol 2000;78:329–335

[33] Total laparoscopic hysterectomy for uterine pathology: impact of body mass index on outcomes. O'Hanlan K, Dibble S, Fisher D. Gynecol Oncol 2006;103:938–941

[34] Phase III trial of laparoscopy versus laparotomy for surgical resection and comprehensive surgical staging of uterine cancer: a Gynecologic Oncology Group study. Walker J, Mannel R, Piedmonte M, et al. Gynecol Oncol 2006;101(S1):11–12; abstr 22.

[35] What is the optimal minimally invasive surgical procedure for endometrial cancer staging in the obese and morbidly obese woman? Gehrig PA, Cantrell LA, Shafer A, Abaid LN, Mendivil A, Boggess JF. Gynecol Oncol. 2008 Oct;111(1):41-5.

[36] Randomised study of radical surgery versus radiotherapy for stage Ib-IIa cervical cancer. Landoni F, Maneo A, Colombo A, Placa F, Milani R, Perego P, Favini G, Ferri L, Mangioni C. Lancet. 1997 Aug 23;350(9077):535-40.

[37] Modified radical hysterectomy versus extrafascial hysterectomy in the treatment of stage I endometrial cancer: results from the ILIADE randomized study. Signorelli M, Lissoni AA, Cormio G, Katsaros D, Pellegrino A, Selvaggi L, Ghezzi F, Scambia

G, Zola P, Grassi R, Milani R, Giannice R, Caspani G, Mangioni C, Floriani I, Rulli E, Fossati R. Ann Surg Oncol. 2009 Dec;16(12):3431-41.

[38] Surgical pathologic spread patterns of endometrial cancer. A Gynecologic Oncology Group Study. Creasman WT, Morrow CP, Bundy BN, Homesley HD, Graham JE, Heller PB. Cancer. 1987 Oct 15;60(8 Suppl):2035-41.

[39] The incidence of pelvic lymph node metastasis by FIGO staging for patients with adequately surgically staged endometrial adenocarcinoma of endometrioid histology. Chi DS, Barakat RR, Palayekar MJ, Levine DA, Sonoda Y, Alektiar K, Brown CL, Abu-Rustum NR. Int J Gynecol Cancer. 2008 Mar-Apr;18(2):269-73.

[40] The morbidity of surgery and adjuvant radiotherapy in the management of endometrial carcinoma. Nunns D, Williamson K, Swaney L, Davy M. Int J Gynecol Cancer. 2000 May;10(3):233-238.

[41] Uterine papillary serous carcinoma: patterns of metastatic spread. Goff BA, Kato D, Schmidt RA, Ek M, Ferry JA, Muntz HG, Cain JM, Tamimi HK, Figge DC, Greer BE. Gynecol Oncol. 1994 Sep;54(3):264-8.

[42] Twelve-year experience in the management of endometrial cancer: a change in surgical and postoperative radiation approaches. Barakat RR, Lev G, Hummer AJ, Sonoda Y, Chi DS, Alektiar KM, Abu-Rustum NR. Gynecol Oncol. 2007 Apr;105(1):150-6.

[43] The impact of complete surgical staging on adjuvant treatment decisions in endometrial cancer. Goudge C, Bernhard S, Cloven NG, Morris P. Gynecol Oncol. 2004 May;93(2):536-9.

[44] Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study. ASTEC study group, Kitchener H, Swart AM, Qian Q, Amos C, Parmar MK. Lancet. 2009 Jan 10;373(9658):125-36.

[45] Systematic pelvic lymphadenectomy vs. no lymphadenectomy in early-stage endometrial carcinoma: randomized clinical trial. Benedetti Panici P, Basile S, Maneschi F, Alberto Lissoni A, Signorelli M, Scambia G, Angioli R, Tateo S, Mangili G, Katsaros D, Garozzo G, Campagnutta E, Donadello N, Greggi S, Melpignano M, Raspagliesi F, Ragni N, Cormio G, Grassi R, Franchi M, Giannarelli D, Fossati R, Torri V, Amoroso M, Crocè C, Mangioni C. J Natl Cancer Inst. 2008 Dec 3;100(23):1707-16.

[46] Analysis of clinicopathologic factors predicting para-aortic lymph node metastasis in endometrial cancer. Nomura H, Aoki D, Suzuki N, Susumu N, Suzuki A, Tamada Y, Kataoka F, Higashiguchi A, Ezawa S, Nozawa S. Int J Gynecol Cancer. 2006 Mar-Apr;16(2):799-804.

[47] Retrospective analysis of selective lymphadenectomy in apparent early-stage endometrial cancer. Cragun JM, Havrilesky LJ, Calingaert B, Synan I, Secord AA, Soper JT, Clarke-Pearson DL, Berchuck A. J Clin Oncol. 2005 Jun 1;23(16):3668-75.

[48] Analysis of FIGO Stage IIIc endometrial cancer patients. McMeekin DS, Lashbrook D, Gold M, Johnson G, Walker JL, Mannel R. Gynecol Oncol. 2001 May;81(2):273-8.

[49] Advanced endometrial cancer: is lymphadenectomy necessary or sufficient? Scott Miller D. Gynecol Oncol. 2006 May;101(2):191-3.

[50] A clinical and pathologic study on para-aortic lymph node metastasis in endometrial carcinoma. Hirahatake K, Hareyama H, Sakuragi N, Nishiya M, Makinoda S, Fujimoto S. J Surg Oncol 1997;65:82–7.

[51] Indispensability of pelvic and paraaortic lymphadenectomy in endometrial cancers. Gynecol Oncol 1997;64:411–7. Yokoyama Y, Maruyama H, Sato S, Saito Y

[52] Lymphatic drainage of the uterus: preliminary results of an experimental study [French]. Lécuru F, Neji K, Robin F, Darles C, de Bièvre P, Taurelle R. J Gynecol Obstet Biol Reprod (Paris) 1997;26:418–23.

[53] Route of lymphatic spread: a study of 112 consecutive patients with endometrial cancer. Mariani A, Webb MJ, Keeney GL, Podratz KC. Gynecol Oncol 2001;81:100–4.

[54] The outcomes of 27,063 women with unstaged endometrioid uterine cancer. Chan JK, Wu H, Cheung MK, Shin JY, Osann K, Kapp DS. Gynecol Oncol. 2007 Aug;106(2):282-8.

[55] The role of pelvic and/or para-aortic lymphadenectomy in surgical management of apparently early carcinosarcoma of uterus. Park JY, Kim DY, Kim JH, Kim YM, Kim YT, Nam JH. Ann Surg Oncol. 2010 Mar;17(3):861-8.

[56] Prospective assessment of lymphatic dissemination in endometrial cancer: a paradigm shift in surgical staging. Mariani A, Dowdy SC, Cliby WA, Gostout BS, Jones MB, Wilson TO, Podratz KC. Gynecol Oncol. 2008 Apr;109(1):11-8.

[57] Laparoscopic paraaortic left-sided transperitoneal infrarenal lymphadenectomy in patients with gynecologic malignancies: technique and results. Köhler C, Tozzi R, Klemm P, Schneider A. Gynecol Oncol. 2003 Oct;91(1):139-48.

[58] Survival effect of para-aortic lymphadenectomy in endometrial cancer (SEPAL study): a retrospective cohort analysis. Todo Y, Kato H, Kaneuchi M, Watari H, Takeda M, Sakuragi N. Lancet. 2010 Apr 3;375(9721):1165-72.

[59] Lymphadenectomy for the management of endometrial cancer (Review) May K, Bryant A, Dickinson HO, Kehoe S, Morrison J The Cochrane Library 2010, Issue 1

[60] F.H. van Wijk, M.E.L. van der Burg, Curt W. Burgeret al. Management of Surgical Stage III and IV Endometrioid Endometrial Carcinoma. An Overview. Int J Gynecol Cancer 2009;19: 431-446

[61] Creasman W, Odicino F, Maisonneuve P, et al. Carcinoma of the corpus uteri. Int J Gynaecol Obstet. 2006;95:S105-S143.

[62] Boruta DM 2nd, Gehrig PA, Groben PA, et al. Uterine serous and grade 3 endometrioid carcinomas: is there a survival difference? Cancer. 2004;101:2214-2221

[63] Goff BA, Goodman A, Muntz HG, et al. Surgical stage IV endometrial carcinoma: a study of 47 cases. Gynecol Oncol. 1994;52: 237-240.

[64] Chi DS, Welshinger M, Venkatraman ES, et al. The role of surgical cytoreduction in Stage IV endometrial carcinoma. Gynecol Oncol. 1997;67:56-60.

[65] Bristow RE, Zerbe MJ, Rosenshein NB, et al. Stage IVB endometrial carcinoma: the role of cytoreductive surgery and determinants of survival. Gynecol Oncol. 2000;78:85-91.
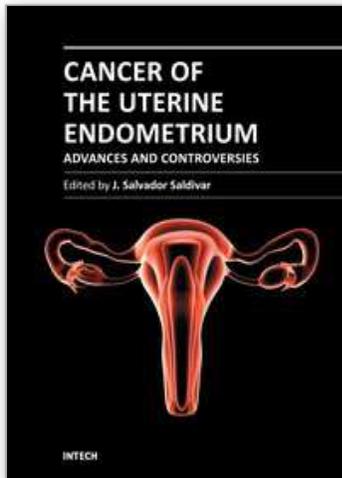
Cancer of the Uterine Endometrium - Advances and Controversies

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The book Cancer of the Uterine Endometrium - Advances and Controversies brings together an international collaboration of authors who share their contributions for the management of endometrial carcinoma. The scope of the text is not basic, but rather aims to provide a comprehensive and updated source of advances in the diagnosis and therapeutic strategies in this field of gynecologic cancer. Each section in the book attempts to provide the most relevant evidence-based information in the biology and genetics, modern imaging, surgery and staging, and therapies for endometrial cancer. It is hoped that future editions will bring additional authors to contribute to this endeavor. To this end, it is our patients who will benefit from this work.

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