Current Concepts in the Management of Endometrial Carcinoma

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Endometrial carcinoma should be treated by hysterectomy and bilateral salpingo-oophorectomy, if feasible.

INTRODUCTION

Endometrial carcinoma is the most common gynaecological malignant disease in developed countries.[1,2] The incidence is increasing worldwide, most likely related to the ageing population. The majority of patients are postmenopausal, with the peak age of occurrence between 60 to 69 years.[3] Following a meeting of the International Federation of Gynecology and Obstetrics (FIGO) in 1988, endometrial carcinoma has since become a surgically staged disease. (Table 1) Up to 83.2% of the patients present at stages I and II of the disease. The overall 5-year survival rate is 80%, and that for surgical stage Ia and Ib disease is 91%.[3]

PRESENTATION AND DIAGNOSIS

Many patients with endometrial carcinoma present with irregular vaginal bleeding or postmenopausal bleeding. Some may also have coexisting risk factors, such as nulliparity, obesity, diabetes mellitus, hypertension, polycystic ovarian syndrome, use of unopposed oestrogen, or familial conditions like hereditary non-polyposis colorectal cancer (HNPCC).

An initial investigation by transvaginal ultrasound (TVS) is a simple and non-invasive test to exclude endometrial carcinoma. Using 5 mm as the cut-off to define abnormal endometrial thickening, 96% (95% confidence interval [CI] 94%-98%) of women with endometrial carcinoma, and 92% (95% CI 90%-93%) of women with cancer polyp or atypical hyperplasia, had thickened endometrium.[4] However, a recent study showed that 34% of patients with type II (see below, under "Prognostic Factors") endometrial carcinoma had thin or indistinct endometrial thickness on ultrasound.[5] Moreover, a meta-analysis on the use of endometrial thickness in prediction of endometrial cancer showed that the detection rate was 63% (95% CI 58%-69%) with a 10% false-positive rate, or 96% (95% CI 94%-98%) with a 50% false-positive rate. This implies that 4% of the patients with endometrial carcinoma would still be missed even with a false-positive rate as high as 50%.[6]

Endometrial aspiration is an effective diagnostic method, which can be done with simple devices like the Pipelle aspirator, and the Novak, Vabra and Karman curettes. A meta-analysis showed that endometrial biopsy by Pipelle sampling achieved detection rates of 99.6% and 91% for endometrial carcinoma in postmenopausal and premenopausal

Table 1. FIGO stage of endometrial carcinoma

Stage*	
I	Tumour confined to the corpus
IA	Tumour limited to the endometrium
IB	Invasion to less than half of the myometrium
IC	Invasion equal to or more than half of the myometrium
II	Tumour involving cervix
IIA	Endocervical glandular involvement only
IIB	Cervical stromal invasion
III	Tumour limited to the pelvis
IIIA	Tumour invades the serosa of the corpus uteri and/or adnexae and/or positive cytological findings
IIIB	Vaginal metastases
IIIC	Metastases to pelvic and/or para-aortic lymph nodes
IV	Tumour invades local structures or metastases in distant sites
IVA	Tumour invasion of bladder and/or bowel mucosa
IVB	Distant metastases, including intra-abdominal metastasis and/or inguinal lymph nodes

* Each stage is subdivided in grade 1, 2 and 3 based on tumour grade.

women, respectively.[7] Another systematic quantitative review demonstrated that the probability of endometrial cancer was 81.7% (95% CI 59.7%-92.9%) for a positive test and 0.9% (95% CI 0.4%-2.4%) for a negative test on endometrial biopsy.[8]

Hysteroscopy with endometrial biopsy or dilatation and curettage (D&C) is another method used to diagnose endometrial carcinoma. A meta-analysis involving 26,346 patients found that a positive finding in hysteroscopy (pooled likelihood ratio [LR] 60.9; 95% CI 51.2-72.5) increased the probability of cancer to 71.8% (95% CI 67.0%-76.6%), while a negative hysteroscopy result (pooled LR 0.15; 95% CI 0.13-0.18) reduced the probability of cancer to 0.6% (95% CI 0.5%-0.8%).[9] The concern about peritoneal spillage of tumour cells during hysteroscopy has been raised. Studies have shown that although there might be spread of tumour cells in the abdominal cavity during the procedure, no significant effect was found in the patients' prognosis.[10,11] Longer follow-up is certainly needed to confirm these findings.

In general, if a patient is suspected to have endometrial carcinoma, endometrial aspiration should be performed as first-line investigation because it has higher sensitivity than TVS. TVS can be used as a screening tool when endometrial aspiration is not feasible, for example in a patient who is never sexually active or whose cervix is stenotic. A positive ultrasound finding is an indication for endometrial sampling for histological diagnosis. If endometrial aspiration or TVS are inconclusive, or if there is a high clinical suspicion despite negative result, diagnostic hysteroscopy with endometrial biopsy or D&C should be performed.

INVESTIGATION

Preoperative assessment includes investigations such as blood tests to assess the patient's general fitness for surgery, and chest X-ray to exclude lung metastasis. Other imaging techniques have also been advocated for pre-operative staging.

Computed tomography (CT) has a limited value in detecting nodal involvement and myometrial invasion,[12,13] while magnetic resonance imaging (MRI) is useful in assessing myometrial invasion and has a sensitivity and specificity of 50% to 90%.[14-16] The sensitivity and specificity of MRI in detecting cervical invasion is 60% to 70% and 80% to 90%, respectively; such knowledge enables the surgeon to plan the extent of the operation.[16,17] A recent trial comparing the effectiveness of positron emission tomography (PET) with MRI and CT showed that although PET had a higher sensitivity in detecting extra-uterine lesions, there was no difference in the specificity.[18] PET was also insensitive in identifying lymph nodes less than 1 cm in diameter, limiting its routine use in pre-operative evaluation of endometrial carcinoma.

PROGNOSTIC FACTORS

There are several variables that influence the patient's outcomes. (Table 2) Among these, the FIGO stage, differentiation grade (tumour grade 1, 2 or 3 for each FIGO stage) and histological type of the disease correlate most with the patient's prognosis.[3,19-21]

The patient's FIGO stage is the strongest prognostic factor. The 5-year disease-free survival has been demonstrated to be roughly 85% for stage I, 75% for stage II, 45% for stage III, and 25% for stage IV.[20-22] In the FIGO staging system, the tumour is graded based on the architectural features. Tumours with ≤5% solid growths are classified as grade 1,

those with 6% to 50% as grade 2, and those with >50% and those non-endometrioid carcinomas as grade 3. The presence of grade 3 nuclear features, including marked nuclear pleomorphism, coarse chromatin and prominent nucleoli, increases the tumour grade by one.[23] Increasing tumour grade worsens the survival even within the same stage of the disease.[3] (Table 3)

Myometrial invasion is also a component of the staging system. It is recognized as an independent factor of the patient's outcome. It has been shown that the 5-year survival rates were 94% for stage I diseases confined to the endometrium, and 91%, 84% and 59% for those involving the inner third, the middle third and the outer third of the myometrium, respectively.[24] A Gynecologic Oncology Group (GOG) study showed that the frequency of lymph node involvement increased with the histological grade and the depth of myometrial invasion.[19] In that study, the incidence of para-aortic and pelvic lymph node metastasis was ≤5% for grade 1 or 2 tumours confined to the inner third of the myometrium without extra-uterine spread. However, the incidence of pelvic and aortic node metastasis rose to 34% and 23% respectively when the tumours were grade 3 diseases involving the outer third of the myometrium.

The histological type of the tumour calls for particular attention. Endometrial carcinoma has been classified into two types: type I and type II.[25] Type I tumours constitute about 80% of endometrial carcinoma. Compared with type II tumours, type I tumours tend to occur in premenopausal and perimenopausal women. They are predominantly endometrioid carcinoma (EC), and are usually preceded by endometrial hyperplasia. They tend to be low-grade with minimal myometrial invasion. Patients with this type of tumours tend to have a favourable prognosis. Uterine papillary serous (UPSC) and clear cell (CC) carcinomas belong to type II tumours and are more frequently associated with high nuclear grade, deep myometrial invasion, lympho-vascular permeation, lymph node metastasis and abnormal p53 expression.[26-28] Even when compared with patients with grade 3 EC (G3EC), more patients with UPSC and CC had stage III to IV diseases (52% and 36% vs 29%; $p<0.0001$).[29]

Lymphovascular invasion is associated with poor survival, more recurrence and lymph node metastasis.[30] Tumour size less than 2 cm had also been correlated with better 5-year survival rate and less lymph node metastasis.[31] Other independent prognostic factors include age,[32] race,[33] and diabetes mellitus.[34] On the other hand, the presence of oestrogen and progesterone receptors in endometrial cancer tissues is associated with more favourable clinical outcomes.[35-36] Recent advances in molecular science have drawn the focus to the genetic and epigenetic changes in carcinogenesis. Certain genes have been identified as potential prognosticators. For example, PTEN and beta-catenin mutations are independent predictors of earlier stage, better disease grade and negative lymph node involvement,[37-39] while p53 and HER-2/neu mutations are associated with advanced disease stage, poor histological grade, lymph node metastasis and poor clinical outcomes.[39-44]

Table 2. Independent prognostic factors in endometrial carcinoma

FIGO stage
Histological grade
Myometrial invasion
Histological type
Vascular space invasion
Tumour size
Patients' factors (eg, age, race, presence of diabetes mellitus)
Steroid receptor status
DNA ploidy and other biological markers (eg, microsatellite instability, PTEN, p53, Bcl-2, K-ras)

Table 3. Overall survival (%) at 5 years for different stages of endometrial carcinoma for patients treated in 1999–2001

	Stage I	Stage II	Stage III	Stage IV
Surgical grade 1	92.9	86.0	78.6	49.2
Surgical grade 2	89.9	80.0	67.3	26.5
Surgical grade 3	78.9	66.0	46.4	13.4

Adapted from reference 3.

TREATMENTS

The management algorithm of patients with stage I and occult stage II endometrial carcinoma is summarized in Figure 1. In essence, endometrial carcinoma should be treated by hysterectomy and bilateral salpingo-oophorectomy if feasible, because patients undergoing surgery with or without radiotherapy have a 5-year survival rate of 80% to 90%, as compared with 40% to 50% only for those receiving radiotherapy alone.[45-46] In addition, because there may be difficulty in determining the stage of the disease pre-operatively and intra-operatively, adjuvant radiotherapy may be required after the final histological diagnosis is made, in order to eradicate any occult lymph node metastasis and to prevent vaginal vault recurrence. Different modes of treatment are further elaborated below.

Surgery

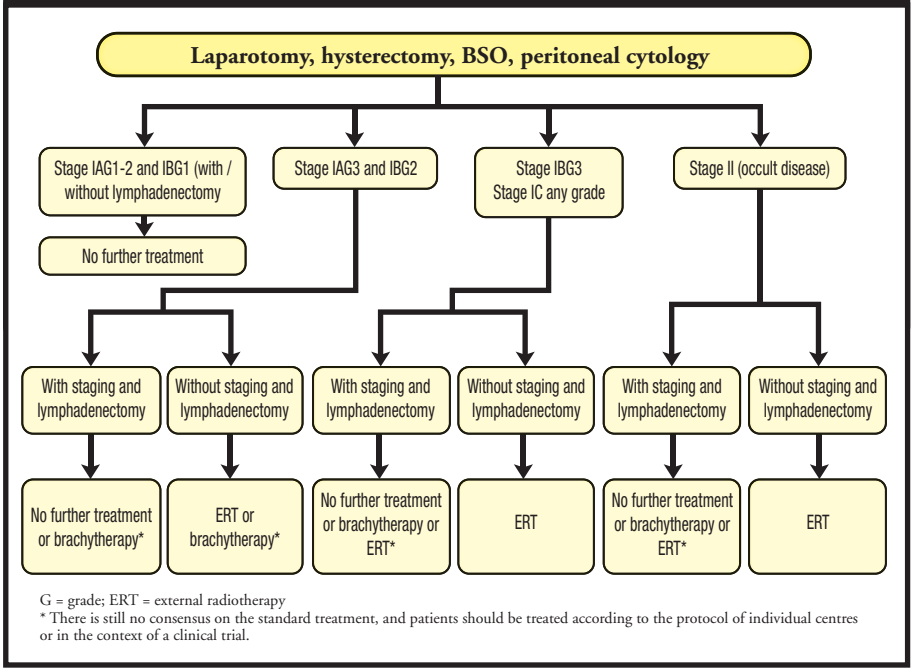
The standard surgical treatment is total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAHBSO). Peritoneal washings, lymphadenectomy and biopsy of any suspicious lesions are performed at the same time for the purpose of staging. Omentectomy is also performed in selected cases such as in UPSC. For most patients, these procedures serve both staging as well as therapeutic purposes.

With the advent of laparoscopic surgery, laparoscopic-assisted vaginal hysterectomy (LAVH) and total laparoscopic hysterectomy (TLH) have become more and more popular. A randomized study involving 70 patients with stage I to III diseases compared the outcomes between LAVH and TAH. It was shown that LAVH was better than TAH in terms of peri-operative blood loss (229.2 ± 190.2 mL vs 594.2 ± 629.9 mL, respectively; p=0.003), transfusion rates (1/37 vs 11/33, respectively; p=0.005), duration of infusion therapy (1.6 ± 0.76 days vs 2.8 ± 1.9 days, respectively; p=0.003), duration to first bowel movement (2 ± 0.57 days vs 2.4 ± 0.75 days, respectively; p=0.02) and hospital stay (8.6 ± 2.7 days vs 11.7 ± 3.8 days, respectively; p<0.001). No difference was observed in the yield of pelvic and para-aortic lymph nodes, duration of surgery, incidence of postoperative complications, and the overall and recurrence-free survival rates.[47]

There has also been a randomized study comparing LAVH with TLH, which showed that the mean total operating time was significantly shorter in the TLH than in the LAVH group in experienced hands (184.0 ± 46.0 minutes vs 213.2 ± 39.4 minutes; p=0.003). Further analysis showed that the hysterectomy phase was shorter in the TLH group only in overweight (68.1 ± 9.3 minutes vs 77.9 ± 9.8 minutes for LAVH; p=0.005) and obese patients (62.1 ± 9.9 minutes vs 87.7 ± 13.1 minutes for LAVH; p<0.0001), indicating that TLH might benefit obese patients. There was no significant difference in the estimated blood loss, intra-operative and post-operative complications, as well as the recurrence rate.[48] Therefore, although TAHBSO and staging are the gold standard of treatment, LAVH and TLH should be considered as alternatives if expertise and facilities are available.

For diseases involving the cervix apart from occult stage II disease, radical hysterectomy with parametrial removal has been advocated as it can result in better survival rates when compared with simple hysterectomy.[49,50] Total laparoscopic radical

Figure 1. Management plan for patients with stage I and occult stage II endometrial carcinoma



G = grade; ERT = external radiotherapy
* There is still no consensus on the standard treatment, and patients should be treated according to the protocol of individual centres or in the context of a clinical trial.

hysterectomy is a potential alternative to open surgery, though experience is lacking.[51,52]

For more advanced or recurrent diseases, cytoreduction should be considered in suitable candidates. A study involving 33 stage IIIC and nine stage IV patients reported that optimal cytoreduction (residual tumour ≤2 cm) could only be achieved in 72% of patients.[53] The median survival was 17.8 months and 6.7 months for patients with optimal and sub-optimal cytoreduction, respectively (p=0.001). Another study involving 65 stage IVB patients showed that optimal cytoreduction (residual tumour ≤1 cm) could be achieved in 55.4% of patients.[54] In a study from the same centre, which involved 35 patients with recurrence of endometrial carcinoma, reported that optimal cytoreduction (no gross residual tumour) could be achieved in 65.7% of patients. The median survival time for those who had cytoreduction was 28.0 months, as compared to 13.0 months for those being treated non-surgically (p<0.0001). Patients who underwent complete salvage cytoreduction had a median post-recurrence survival time of 39.0 months, compared to 13.5 months for those with gross residual diseases (p=0.0005).[55] Pelvic exenteration may also be considered in certain patients with central recurrence, but this surgical procedure can lead to both physical and psychological morbidity.

Regarding the role of lymphadenectomy, Kilgore et al found that patients who had undergone multiple-site pelvic node sampling had significantly better survival than patients without node sampling (p=0.0002). This survival benefit existed for both low-risk (disease confined to the corpus) and high-risk (disease in the cervix, adnexa, uterine serosa, or washings) patients (low-risk, p=0.026; high-risk, p=0.0006).[56] The COSA-NZ-UK endometrial cancer study showed that the recurrence rate was 45% for those node-positive patients when compared with 14% for those node-negative patients.[57] The all-cause survival and endometrial carcinoma survival were also significantly better in those who had complete negative lymphadenectomy (35/207 deaths; 22 from cancer) when compared with those without complete lymphadenectomy (226/774 deaths; 118 from cancer) (p<0.01). However, a recent study from the Surveillance, Epidemiology, and End Results (SEER) Program showed that the survival benefit of extensive lymphadenectomy only existed in the intermediate- and high-risk patients (stage IB, grade 3; stage IC and II-IV, all grades). No significant benefit of lymphadenectomy was noted in the low-risk patients (stage IA, all grades; stage IB, grades 1 and 2; p=0.23).[58]

Lymphadenectomy is an essential part of staging which can help predict the prognosis of the patients. However, lymphadenectomy can lead to significant morbidity including lymphoedema (0.7%-4.6%) and lymphocyst formation (1.3%-1.9%); the SEER study showed that there was no significant survival benefit with lymphadenectomy for patients with stage I low-risk disease who have low incidence of node metastasisas. Hence, some centres omit lymphadenectomy for this group of patients and perform it only for those who have tumours with deep myometrial invasion as shown by MRI preoperatively or sectioning of the uterus intraoperatively, those found to have grade 2 or 3 or non-endometrioid tumours by endometrial biopsy preoperatively, and those who have stage II diseases or above.[22,59]

Radiotherapy

Radiotherapy is mainly used as an adjuvant therapy. It has several modalities, including vault brachytherapy, external pelvic irradiation, extended-field irradiation, whole abdominal irradiation, and intraperitoneal ^{32}P. Studies have shown that the 5-year survival rate was more than 90% for patients with stage I to II grade 1 to 2 diseases without radiotherapy, suggesting that radiotherapy might not be necessary for these patients.[60-61]

A prospective study conducted more than 30 years ago compared the outcomes of 540 patients with stage I endometrial carcinoma receiving either postoperative vaginal brachytherapy alone, or brachytherapy with additional pelvic irradiation. The latter group had a significant reduction in vaginal and pelvic recurrences (1.9 % vs 6.9%; p<0.01). However, this group of patients had more distant metastases (9.9% vs 5.4%).[62] The authors in this study concluded that only patients with grade 3 tumours infiltrating more than half of the myometrium could benefit from external radiotherapy.

As for stage III and IV diseases, the use of radiotherapy has been addressed by a recent GOG study, which showed that the 3-year recurrence-free survival rates were 29% and 27%, and the survival rates were 31% and 35%, for type I and type II tumours respectively, after external radiotherapy with or without para-aortic boost.[63] Certainly, the treatment for this group of patients should be individualized and multi-modality treatment is needed.

Evaluation of Surgery With and Without Radiotherapy

Another multi-centre prospective randomized trial, the PORTEC trial, compared surgery (TAHBSO without lymphadenectomy) and adjuvant radiotherapy (whole pelvic radiotherapy) with surgery alone in 714 patients with stage I endometrial carcinoma, including those who had grade 1 disease with ≥50% myometrial invasion, grade 2 disease with any invasion, and grade 3 disease with <50% invasion.[64] Although there was significant difference in the 5-year actuarial locoregional recurrence rates between the radiotherapy and control groups (4% vs 14%, p<0.001), no difference was observed in the actuarial 5-year overall survival rates (81% vs 85%; p=0.31). There were 40 non-irradiated patients who developed vault recurrence, but only four of them died of it. In addition, radiotherapy was associated with more complications (25% vs 6%; p<0.0001).

The GOG-99 study evaluated the use of radiotherapy after comprehensive surgery with staging and lymphadenectomy in 392 patients with stage IB to C, and stage II (occult) diseases.[65] The patients were further randomized into control and treatment (whole pelvic radiotherapy) groups. The estimated 2-year cumulative incidences of recurrence (CIR) were 12% and 3% for the control and treatment groups, respectively (relative hazard [RH] 0.42; p=0.007). The treatment difference was particularly evident among the following groups: (1) those with grade 2 to 3 diseases, presence of lymphovascular invasion, and outer third myometrial invasion; (2) those aged ≥50 years with any two risk factors listed above; or (3) those aged at least 70 years with any risk factor (2-year CIR 26% vs 6%; RH=0.42). However, there was no difference in the estimated 4-year survival between the control and treatment groups (86% vs 92%, RH=0.86, p=0.557).

In addition, a recent Cochrane meta-analysis showed that post-TAHBSO adjuvant external beam radiotherapy reduced locoregional recurrence (relative risk [RR] 0.28, 95% CI 0.17-0.44, p<0.00001) in patients with stage I disease, but such benefit did not confer an advantage to the risk reduction of distant recurrence and death from all causes or endometrial cancer.[66] A trend towards the reduction in the risk of death from all causes or endometrial cancer was however noted for those with stage IC grade 3 disease.

So far, adjuvant radiotherapy has not been shown to be of survival benefit for those with stage I disease. The possible explanation is that vault recurrence can readily be treated by radiotherapy, with a complete remission rate of up to 89%.[67] Based on the above evidence, it might be reasonable to omit radiotherapy for low-risk patients with stage I disease, especially those younger than 60 years of age. For those with stage I node-negative intermediate- or high-risk disease after comprehensive surgery with lymphadenectomy, whether adjuvant radiotherapy is needed is controversial. This is because although survival outcomes were not compromised even if radiotherapy was not given,[68-70] it can increase the risk of local recurrence. Such practice is subject to individual centres.

On the other hand, some studies have suggested that external irradiation might be replaced by vault brachytherapy for those at low-risk or intermediate-risk without lymph node metastasis after TAHBSO and selected lymphadenectomy.[57,71,72] Such modification might potentially reduce complications related to external radiotherapy. Whether lymphadenectomy has a genuine positive impact on the use of adjuvant radiotherapy is still uncertain. The ASTEC (A Study in the Treatment of Endometrial Cancer) trial, coordinated by the Medical Research Council, UK, is a randomized trial to determine the impact of lymphadenectomy and adjuvant external beam radiotherapy in the treatment of endometrial carcinoma. It is still ongoing and may perhaps provide some answers.

Chemotherapy

Chemotherapy is not the first-line treatment in endometrial carcinoma. A number of trials have been performed evaluating the use of drugs such as cisplatin, carboplatin, paclitaxel, doxorubicin, topotecan and so on, with or without concomitant radiotherapy.

A recent multi-centre phase II study involving 42 patients with cytological or histological diagnosis of advanced or recurrent endometrial carcinoma demonstrated an overall response rate of 59.5% (95% CI 43.3-74.3) when using carboplatin and liposomal doxorubicin as first-line chemotherapy.[73] The major side effects were neutropenia, thrombocytopenia and anaemia.

A recent meta-analysis of six trials demonstrated that progression-free survival was significantly improved when more intensive chemotherapy was used in advanced or recurrent diseases (HR=0.80, 95% CI 0.71-0.90; p=0.004).[74] However, the overall survival was not improved (HR=0.90, 95% CI 0.80-1.03; p=0.12).

Another multi-centre phase II trial investigated the effects of postoperative radiotherapy and cisplatin and paclitaxel in 46 patients having grade 2 or 3 diseases with either >50% myometrial invasion, cervical stromal invasion or pelvic-confined extra-uterine diseases.[75] At 4-year follow-up, the overall survival and disease-free survival were 85% and 81%, and the pelvic, local and distant recurrence rates were 2%, 2% and 19%, respectively. From this study, it was shown that the combination of adjuvant chemotherapy and radiotherapy could provide good local control but not distant metastasis. Therefore, their efficacy should be further explored by larger randomized controlled trials.

Chemotherapy has also been used as an adjunct to surgery in uterine papillary serous carcinoma (USPC) and clear cell carcinoma of corpus, with estimated 5-year overall survival and progression-free survival rates of 79.7% and 55.7%, respectively.[76]

Studies that have been carried out so far have favoured the use of chemotherapy. Further randomized trials are definitely needed in order to define its role and design its regimen in treating endometrial carcinoma.

Hormonal Therapy

The most commonly described hormonal therapy is progestogen. Other hormonal agents such as gonadotropin-releasing hormone analogue (GnRHa), danazol and tamoxifen have not demonstrated a satisfactory effect.[77-79] Although progesterone is associated with minimal toxicity, its use in adjuvant therapy has no effect on the overall survival (OR 1.05; 95% CI 0.88-1.24), relapse of disease (OR 0.81; 95% CI 0.65-1.01) and cancer deaths (OR 0.88; 95% CI 0.71-1.1).[80]

For advanced or recurrent disease, the response rate to progesterone is influenced by the hormonal receptor status, being 5% and 37% respectively, for the progesterone-receptor negative and positive tumours ($p<0.001$); and 7% and 26% respectively, for the oestrogen-receptor negative and positive tumours ($p=0.005$).[81] Two phase II trials using megestrol/medroxyprogesterone and tamoxifen have shown a response rate above 30% in selected groups of patients with advanced diseases.[81-83] In addition, some centres have also used medroxyprogesterone as a fertility-sparing treatment for patients with clinically stage I disease.[84-87] Although successful pregnancies have been reported, the safety of such treatment has to be confirmed by further studies.

CONCLUSION

Significant advances have been made in the management of endometrial carcinoma in the last 2 decades. Imaging tools such as CT, MRI and PET have been more widely used pre-operatively to assist in staging the disease and planning the treatment. Genetic and epigenetic studies can potentially contribute to the development of new prognostic markers, the understanding of the carcinogenesis, and development of potential new anti-cancer therapy. With more experience, the use of laparoscopic surgery can also provide better treatment for patients in terms of less peri-operative morbidity. Nevertheless, this disease remains a challenge to oncologists. There are still a lot of unclear areas waiting to be unravelled, including the need for lymphadenectomy as well as radiotherapy, which may be addressed by the ASTEC study. Until further evidence arises, lymphadenectomy should be performed as a staging procedure, especially for those with deep myometrial invasion or high-grade tumour as shown by preoperative or intraoperative evaulation; adjuvant radiotherapy can be omitted for those with stage I low-risk disease. There is a potential role for chemotherapy and progesterone in advanced or recurrent diseases, although further studies are needed to elucidate their roles.

Practice Points

- The incidence of endometrial carcinoma is increasing worldwide.
- MRI is useful in defining the myometrial invasion and cervical extension. It has a potential role in determining the necessity of lymphadenectomy.
- Uterine papillary serous carcinoma and clear cell carcinoma belong to type II endometrial carcinoma and are associated with poor outcomes.
- Laparoscopic hysterectomy is similar to open hysterectomy in terms of overall and recurrence-free interval.
- The role of lymphadenectomy and radiotherapy has to be further evaluated by randomized controlled trials.
- Chemotherapy may be useful in advanced or recurrent diseases.
- The role of progesterone is limited as a palliative treatment, and the response is influenced by the hormonal receptor status.

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CME Article:

Current Concepts in the Management of Endometrial Carcinoma

Answer True or False to the questions below.

	True	False
1. Endometrial carcinoma is a clinically staged disease.	○	○
2. Spillage of fluid into the peritoneal cavity during hysteroscopy in patients with endometrial carcinoma is associated with a worse prognosis.	○	○
3. Tumours with 6% to 50% solid growths are classified as grade 2.	○	○
4. The frequency of lymph node metastasis is increased with the depth of myometrial invasion.	○	○
5. Type II endometrial carcinoma is associated with endometrial hyperplasia.	○	○
6. The yield of lymph node obtained during laparoscopic operation is significantly less than open operation.	○	○
7. Optimal cytoreduction can be achieved in 50% to 70% of patients with advanced or recurrent diseases.	○	○
8. All studies so far demonstrate no survival benefit of lymphadenectomy for patients with low-risk disease.	○	○
9. Adjuvant radiotherapy can decrease the risk of local and distant recurrence.	○	○
10. Patients with advanced diseases may have a 20% to 30% response rate to medroxyprogesterone.	○	○

ANSWERS

1	2	3	4	5	6	7	8	9	10
F	F	T	T	F	F	T	F	F	T