Review FIGO staging in vulval and endometrial cancer

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Key content:

- FIGO staging for vulval and endometrial cancer was last amended in May 2009 and is now based on surgical pathology.
- Staging should be of benefit without significantly increasing morbidity.
- Other factors such as tumour type and grade and any comorbidities also contribute to survival.

Learning objectives:

- To understand the principles of cancer staging.
- To be aware of the appropriate preoperative preparation.
- To be able to stage vulval and endometrial cancer once the histopathology is available.

Ethical issues:

- Surgery should be of benefit regarding survival or in guiding appropriate treatment.

Keywords computed tomography / hysterectomy / lymphadenectomy / magnetic resonance imaging / ultrasound

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Introduction

The International Federation of Gynecology and Obstetrics (FIGO) was established on 26 July 1954 to represent 42 international societies; it now has 113 member associations internationally. The work of FIGO covers many areas of obstetrics and gynaecology and it has had patronage of the *Annual Report on Results of Treatment in Gynecologic Cancer* since 1954. The first gynaecological staging systems pre-date FIGO; that for cervical cancer was published by the League of Nations in 1920. **Box 1** shows the functions of cancer staging.

The original FIGO staging classifications were based on clinical examination to assess the anatomical extent of the disease. The staging of vulval and endometrial cancer is now based on surgical pathology. Any staging system needs to be reliable, unambiguous and practical in a wide range of environments. Each component of surgical staging must have a therapeutic benefit or provide information that affects treatment planning sufficiently to ensure that any benefit outweighs surgical morbidity. Performing a surgical procedure with recognised morbidity without patient benefit is unethical, except with informed consent within clinical research.

This article reviews the staging of vulval and endometrial cancer because both have changed recently. Ongoing reviews of staging of all cancers are important so that non-contributory staging investigations can be abandoned and beneficial investigations introduced.

Vulval cancer

Vulval cancer is uncommon, comprising 4% of all gynaecological malignancies.[2] Just over 1000 cases are diagnosed in the UK every year, making vulval cancer the 20th most common cancer among women.[3] It is mainly a disease of older women, with the incidence increasing with age: 80% of vulval cancers occur among women over the age of 60 years. Known risk factors include human papillomavirus, which is associated with approximately 30% of cases, and immunosuppression. Vulval intraepithelial neoplasia is a precursor of vulval cancer and lichen sclerosus is associated with 33% of cases.

Tumours most commonly occur on the labia majora, but are also found on the labia minora, clitoris and perineum; 90% are squamous lesions, with melanoma being the next most common cell type. Melanomas are more likely to affect the clitoris or labia minora and are staged, as for other melanomas, by Breslow's classification.[4] Other vulval cancers are uncommon and include:

- adenocarcinoma from Paget's disease
- verrucous carcinoma
- Bartholin gland carcinoma
- basal cell carcinoma.

Staging of vulval cancer

(See **Table 1**.) Surgical staging was introduced for vulval cancer in 1988 and has been modified over time, most recently in May 2009. The modifications have focused on subdividing stage III disease according to the number and nature of lymph node metastases, and downstaging to stage II tumours that extend into adjacent perineal structures but where there is no involvement of the inguinofemoral lymph nodes. These changes reflect the fact that the number of lymph nodes involved is a more significant prognostic factor than fully resected local disease.

Full staging of vulval cancer involves histological examination of the vulval specimen, with clear surgical margins, and of the inguinal and femoral lymph nodes (**Figure 1**). Approximately 30% of women with locally operable tumours will have nodal involvement at the time of surgery. The histological type of the tumour affects the likelihood of lymph node involvement.[5]

Radical groin lymphadenectomy is associated with significant morbidity; however, nodal metastasis in vulval cancer is the main prognostic factor and locoregional control of disease is a key requirement of treatment. This was achieved previously by systematic inguinofemoral node dissection. Recently, sentinel node biopsy (the sentinel node receives the primary lymphatic flow from the tumour) has been introduced to reduce morbidity. Studies have shown negative predictive values of 95–100%.[6]

Preliminary histological diagnosis is mandatory before radical treatment and a chest X-ray is a routine staging requirement. For tumours >2 cm in diameter, computed tomography (CT) of the chest, abdomen and pelvis may be appropriate to detect disease above the inguinal ligament, which could change the planned treatment. Other preoperative investigations include a full blood count, biochemical profile, electrocardiogram and

Box 1
The functions of cancer staging

- To allow meaningful international comparisons of survival for individual cancers
- To allow comparison of different treatment modalities
- To facilitate research into treatment efficacy by ensuring that participants in trial arms are comparable, thus aiding comparison of treatment strategies
- To enable clinicians to counsel patients accurately about treatment options, treatment-specific morbidity and prognosis[1]

Stage	Criteria
	Primary tumour cannot be assessed
	No evidence of primary tumour
0	Carcinoma *in situ* (pre-invasive)
I	Tumour confined to vulva or vulva and perineum, greatest dimension ⩽2 cm
IA	Tumour confined to vulva or vulva and perineum, greatest dimension ⩽2 cm, stromal invasion of ⩽1.0 mm
IB	Tumour confined to vulva or vulva and perineum, greatest dimension ⩽2 cm, stromal invasion >1.0 mm with negative nodes
II	Tumour of any size with extension to adjacent perineal structures (lower third of urethra, lower third of vagina, anus), with negative lymph nodes
III	Tumour of any size with or without extension into adjacent perineal structures, with positive inguinofemoral lymph nodes
IIIA	With 1 lymph node metastasis, any size, or 2 lymph node metastases <5 mm
IIIB	With ⩾2 lymph node metastases >5 mm or ⩾3 lymph node metastases <5 mm
IIIC	Positive nodes with extracapsular spread
IVA	Tumour invades any of the following: • bladder mucosa • rectal mucosa • upper urethral mucosa or is fixed to bone and/or bilateral regional lymph node metastases
IVB	Any distant metastasis including pelvic lymph nodes

Shaded areas indicate recent changes

Table 1
FIGO staging for vulval cancer

a cervical smear if this is appropriate. Comorbidity assessment is important in this elderly population.

Stage-based survival is shown in **Table 2**. Data for survival from vulval melanoma are difficult to obtain because of its rarity. The most recent data suggest a survival rate of 91% for stage I and 31% for higher stage tumours.[7]

Endometrial cancer

Endometrial cancer is the most common gynaecological malignancy in the developed world, particularly among postmenopausal women. The incidence rises from 2/100 000 women per year among those under 40 years of age to 40–50/100 000 among women between the ages of 60–89 years. There are two broad categories of endometrial cancer: type 1 and type 2. Type 1 is a slow-growing malignancy, thought to be linked to estrogen and obesity through the peripheral conversion of androstenedione to estrone in body fat, and it accounts for approximately 80% of cases. Type 2 is a more aggressive, faster growing malignancy which does not appear to have any connection with estrogen and which accounts for approximately 10% of cases. Compared with type 1, the prognosis for type 2 endometrial cancer is less favourable and presentation can occur at a more advanced stage.

Endometrioid carcinoma is thought to progress through a premalignant stage of complex atypical hyperplasia in most cases, whereas papillary serous and clear-cell carcinomas arise as a result of a sequence of genetic mutations.[1] Women often present early, as postmenopausal bleeding is recognised by both women and clinicians as an important abnormality. However, 25% of cases present in the perimenopausal years, causing diagnostic delays. The National Institute of Health and Clinical Excellence (NICE) recognises this and in their guidance advises that women over the age of 45 years should have an endometrial biopsy during investigation of abnormal uterine bleeding.[8]

To screen for these conditions, transvaginal ultrasound is used as a preliminary to measure endometrial thickness (**Figure 2**). After the menopause, an upper limit of normal of 5 mm gives a negative predictive value of 100% for detecting cancer.[9] In premenopausal women endometrial thickness is less helpful, but ultrasound appearances can help diagnosis. The histopathological diagnosis is then made from outpatient biopsy with or without the aid of outpatient hysteroscopy. Assessment under general anaesthetic is reserved for cases of diagnostic difficulty or as a result of patient

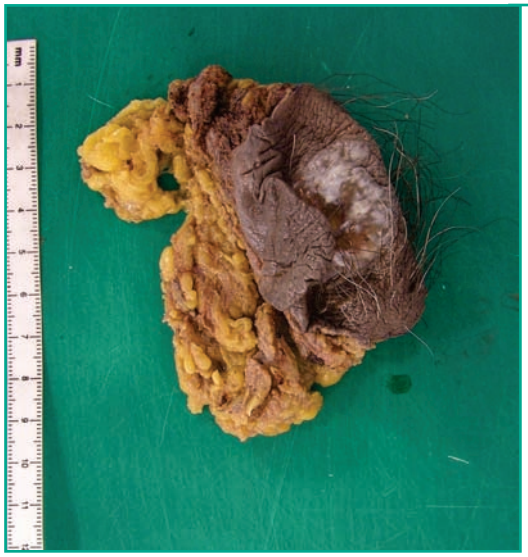

Figure 1
Radical wide local excision of vulval tumour

Stage	5-year survival (%)
I	79
II	59
III	43
IV	13

Table 2
Survival rates by stage for vulval cancer (squamous)

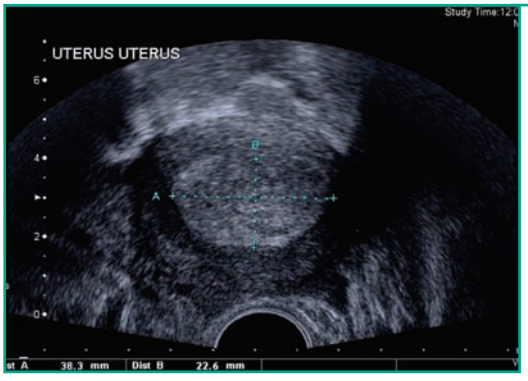

Figure 2
Transvaginal ultrasound scan showing an increased endometrial thickness of 22.6 mm

Table 3
Staging for endometrial cancer

Stage	Criteria
	Primary tumour cannot be assessed
	No evidence of primary tumour
0	Carcinoma *in situ*
I	Tumour confined to uterine body
IA	Tumour limited to endometrium or involves <50% of myometrium
IB	Tumour invades ≥50% of endometrium
II	Tumour invades cervical stroma, does not extend beyond uterus
III	Local and/or regional spread of tumour
IIIA	Tumour invades serosa of uterine body and/or adnexae
IIIB	Vaginal and/or parametrial involvement
IIIC	Metastases to pelvic and/or para-aortic lymph nodes
	IIIC1 positive pelvic nodes
	IIIC2 positive para-aortic lymph nodes with/without positive pelvic lymph nodes
IV	Tumour invades bladder mucosa and/or bowel mucosa and/or distant metastases
IVA	Tumour invasion of bladder and/or bowel mucosa
IVB	Distant metastases, including intra-umbilical metastases and/or inguinal lymph nodes

Shaded areas indicate recent changes

Figure 3
Stage 1A endometrial carcinoma (top right of the uterus)

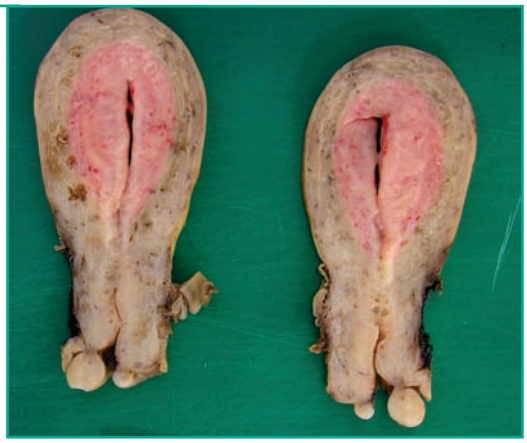

Figure 4
Preoperative CT scan of grade 3 endometrial cancer

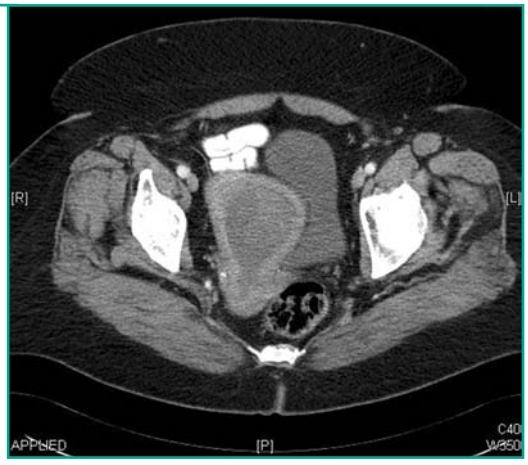

Table 4
Survival rates by stage for endometrial cancer[1]

Stage	5-year survival (%)
I	85
II	75
III	45
IV	25

choice. The pathology report should state the tumour type and the degree of differentiation.

An adverse prognosis is associated with:

- grade 3 tumours (poorly differentiated)
- deep myometrial invasion
- lymphovascular space invasion
- serous papillary tumours
- clear-cell tumours
- cervical involvement
- lymph node involvement.

Staging of endometrial cancer

(See **Table 3**.) As with vulval cancer, the FIGO staging for endometrial cancer changed from clinical to surgical in 1988 and was last amended in May 2009. Full surgical staging comprises a preoperative chest X-ray; total hysterectomy; bilateral salpingo-oophorectomy; and pelvic and para-aortic lymphadenectomy (**Figure 3**). Computed tomography of the chest, abdomen and pelvis is the most useful investigation for defining extrauterine and extrapelvic spread (**Figure 4**). Magnetic resonance imaging (MRI) is the best method of defining myometrial spread. Absence of MRI evidence of deep myometrial penetration has a high negative predictive value for histological deep myometrial penetration, but presence of MRI evidence of deep penetration has a lower positive predictive value.[10]

The recent changes to endometrial cancer staging have involved reducing the substages of stage I from three to two; endocervical glandular involvement has been moved from stage IIA to stage I. The cytology of ascitic fluid or peritoneal washings is no longer part of the staging, but can be reported separately.

International debate continues regarding pelvic lymphadenectomy in endometrial cancer and how this influences staging strategies. North American practice is dominated by full staging to triage those women who are node negative to surveillance only, as they have a good prognosis without adjuvant treatment; women with positive nodes and a worse prognosis are offered adjuvant treatment. However, both the ASTEC[11] and the PORTEC[12] trials have shown that lymph node dissection is not useful for triaging cases and that it confers no therapeutic benefit. Triage is effectively achieved using histological information from the uterine specimen alone, because the therapeutic benefit of adjuvant radiotherapy is seen in both women who have undergone and those who have not undergone systematic lymphadenectomy. Many European centres believe, therefore, that the current evidence shows that the added morbidity of lymph node dissection for full surgical staging, particularly among the elderly and obese, is not justified.

Preoperative ancillary tests, including a full blood count, blood biochemistry, electrocardiogram and chest X-ray, are required. Computed tomography of the chest, abdomen and pelvis may alter treatment planning by revealing extrauterine disease in cases demonstrating adverse cell types on endometrial sampling.

Survival rates by stage of endometrial cancer include all histopathological cell types (see **Table 4**).

Conclusion

The staging of cancer is an integral part of management. Global adherence to FIGO staging ensures meaningful comparison of international data, facilitates research, aids treatment planning and gives accurate information for women with the condition. As clinical practice constantly evolves, regular review of staging is sensible, to ensure that the benefit of the information gained continually outweighs the risk of iatrogenic morbidity.

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