

5. THE BIOLOGY AND PATHOLOGY OF OVARIAN TUMOURS

INTRODUCTION TO OVARIAN CARCINOMA TYPES

These guidelines address the common types of ovarian malignancies, which fall into the category known as surface epithelial/stromal tumours. Collectively, they comprise almost 60% of all ovarian tumours and up to 90% of primary ovarian cancers in Australia. They are a heterogeneous group, many with homologues within the Müllerian duct derivatives and related structures. The terms commonly given to these tumours in the ovaries (eg serous, mucinous, endometrioid, clear cell and transitional cell) reflect this homology. This is a more important reason for grouping them together than their supposed common histogenesis and is the rationale for establishing common principles of tumour grading, staging and treatment for malignancies of the female genital tract. Such homologous tumours have been reported elsewhere in the female pelvis, quite commonly in the broad ligaments and widespread throughout the peritoneal cavity, and even in testicular and para-testicular tissues in men. Considering them as a single neoplastic spectrum, and as intrinsically ‘ovarian’, has led to blurring of well-defined patterns of genesis, metastasis, pathological correlates, therapeutic responses and clinical outcomes.

PRECURSOR LESIONS AND PATTERNS OF CARCINOGENESIS

There is good circumstantial evidence that ovarian epithelial/stromal malignancies arise, by progressive transformation, from the glandular cells of benign epithelial precursors (inclusion cysts or benign tumours). Serosal inclusions, surface proliferations, metaplasias or endometriosis in the ovary (and elsewhere) represent possible precursor lesions for surface epithelial/stromal tumours. The nature and distribution of these lesions are central to understanding such tumours, for they demonstrate the Müllerian potential of the surface ‘epithelium’ of the ovary that, in turn, may dictate the relative frequency and histological range of the neoplasms that develop. In this regard, very considerable research effort has been directed to the specific properties and dynamics of the surface epithelium of the ovaries, on the unproven assumption that such efforts will reveal the pathogenetic pathways of ovarian carcinoma – the characteristics of the ‘cancer prone ovary’.¹

BORDERLINE TUMOURS

There is uncertainty about the role of benign and so-called borderline or proliferating epithelial tumours (these latter two epithets are used interchangeably and also equate to the widely used term, ‘of low malignant potential or LMP’) as precursor lesions for epithelial malignancies. It seems that non-serous carcinomas regularly arise from

pre-existing benign neoplastic lesions (i.e. from 'benign' through 'proliferating' to 'malignant'), with an extended transit time, via a multi-step adenoma-carcinoma sequence, which usually preserves evidence of the pre-existing lower grade neoplasms. There is equally good circumstantial evidence that many high-grade (poorly differentiated) serous carcinomas arise de novo from non-neoplastic epithelial precursor lesions while most low grade (well differentiated) serous carcinomas arise from pre-existing proliferating neoplasms, but with a foreshortened transit time. Indeed evidence seems to indicate entirely different genetic mutational pathways for the development of proliferating (borderline) serous tumours and high-grade invasive serous carcinomas.²⁻⁴ It is speculated that the series of molecular genetic events necessary for this transformation may occur rapidly or more slowly.⁵ In the former event the transition from non-neoplastic inclusion cyst to carcinoma might occur in the absence of a benign tumour phase or, alternatively, it might not be appreciated pathologically. In the latter event, a benign or proliferating tumour might result, followed by a carcinoma only after further steps and only in some patients.

These concepts, if proven, have important consequences for the screening strategies for ovarian carcinoma in women, particularly in those at increased genetic risk of ovarian cancer, as the majority of women with germline mutations in BRCA1 /BRCA2 have high grade serous cancers that arise de novo, are often multifocal and appear to have a short sojourn time with rapid progression (*see chapter 2 on Risk factors for ovarian cancer, chapter 3 – Screening for ovarian cancer, chapter 4 – Familial aspects of ovarian cancer, and chapter 9 – The management of borderline ovarian tumours*).

Metastatic tumours from other sites are not addressed specifically in these guidelines, the exception being pseudomyxoma peritonei. This is an uncommon condition associated with both intra-abdominal and ovarian mucinous tumours, and is now thought to be almost always metastatic from the appendix. Correct assignment of this condition to the category of metastatic low-grade mucinous carcinoma (as it must be), has important implications for the remaining proliferating mucinous tumour group, relegating such tumours from being 'of low malignant potential' to benign/atypical and, at worst, premalignant (see below).

INTRAOPERATIVE CONSULTATION AND MANAGEMENT (INCLUDING FROZEN SECTION REPORTING)

Intraoperative pathological consultation is of value in cases where clinical management decisions may be altered depending on the histological type and grade of tumour, e.g. young women for whom continuing fertility is crucial. An experienced gynaecological pathologist should be able to assist with gross examination alone of the fresh specimen, while in other circumstances or with doubtful cases, a 'working' diagnosis can be made by either frozen section (FS), or cytological 'scrape' preparation.⁶ The latter technique, when the pathologist is familiar with the expected cytological appearances, has the advantage of not requiring a cryostat (i.e. can be offered to those patients who are HIV or HCV positive). Both techniques are prone to sampling and diagnostic error.

Specific intraoperative recommendations from the pathologist may include the following:

- removal of the appendix in all cases of pseudomyxoma peritonei, even if clinically normal
- endometrial curettage if conservative therapy is planned for an endometrioid ovarian tumour of any degree of proliferation
- careful examination of the large bowel if a mucinous ovarian carcinoma is diagnosed (most are metastatic rather than primary)

Frozen section (FS) is more reliable in separating benign from borderline tumours than borderline tumours from carcinomas. The former, however, is not a distinction that impacts on patient management. Sampling error is a significant problem in the latter differentiation, particularly in non-serous neoplasms, which are more heterogeneous, with benign, borderline and carcinomatous components often coexisting in the same lesion.⁷

Clinicians should be aware that a single sample may not provide adequate material for the histopathologist whereas, further sampling for paraffin sections may result in upgrading of a FS diagnosis of benign to borderline tumour (not significant) or of a high-grade borderline tumour to invasive carcinoma (significant). If any doubt is expressed by the pathologist on FS, the more conservative diagnosis must be the 'working' diagnosis for immediate patient management.

Guideline - Sampling of suspected borderline tumours	Level of Evidence	Refs
It is recommended to sample several areas from any suspected borderline ovarian tumour (eg highly complex cystic tumours) to reduce sampling error, especially for tumours that are, or appear to be, mucinous or which are over 1kg.	III-3	7

Fresh material can be taken for molecular and ploidy studies and for research (with patient consent), if appropriate. Consent is best obtained before rather than after surgery. Tumour impression smears or 'scrape' preparations may be made for subsequent comparison with peritoneal washing cytology.

SURGICAL CUT UP

It is desirable, in early FIGO stage cases, to mark the surface of the ovary/mass (eg with Alcian Blue) so that this can later be identified histologically as distinct from cyst lining epithelium. In cases of prophylactic oophorectomy in 'high-risk' patients, great care must be taken in the handling of the ovaries. The serosal surface layer is very fragile and may be the site of macroscopically invisible carcinoma-in-situ or lesser 'dysplastic' changes that should be documented.^{1,8} **In these cases, the entire ovary (and associated tube, if also removed) should be blocked for examination.**

PATHOLOGY BLOCK SELECTION

For suspected borderline tumours the accepted standard is one block of tumour per centimetre of maximum diameter of the 'solid' ovarian mass (i.e. exclude 'cysts' in measurement). This is to detect small areas of high-grade invasive carcinoma, which might otherwise be missed, and is particularly important in mucinous tumours.

In cases of pseudomyxoma peritonei the **entire appendix should be submitted**.

Transverse sections are best (apart from the actual tip), to allow assessment of degree of penetration through the wall of any tumour. Free mucin from the abdomen should be sampled in several blocks. A similar approach is merited in malignant mucinous tumours as signs of intra-abdominal dissemination and of appendiceal primaries may be very subtle macroscopically.

When the specimen includes a macroscopically normal contralateral ovary, this should be blocked in its entirety, as microscopic tumour is often found and affects both staging and assessment of likely primary site, where this is in doubt.

Macroscopically negative omentum often has microscopic deposits (22%) and these are commonly the only evidence for upstaging the patient and mandating adjuvant therapy. It is therefore recommended that a minimum of 4 blocks be submitted from macroscopically normal omenta in patients with no other macroscopic evidence of high stage disease.⁹

HISTOPATHOLOGY REPORTING

There is little scientific analysis of methods of histological typing of ovarian carcinomas, this still being based essentially on pattern recognition. Where there are mixed epithelial types identified, the percentages should be estimated, but no evidence exists on the best method of achieving this or on the clinical significance of mixed versus 'pure' types. Epithelial tumour type is a recognised prognostic variable for carcinomas, but it is unclear if this is independent of grade or stage. There is early evidence of some variation in chemo-responsiveness by histological type. A small percentage of tumours, despite expert assessment, will remain unclassifiable, although clearly 'Müllerian.'

NOTES ON HISTOLOGICAL TYPE OF THE PERITONEAL METASTASES

It should be noted if a significant component of the metastatic tumour is of a different histological type from the primary, especially one that is thought to have a worse prognosis or response to chemotherapy.¹⁰

RECOMMENDED GRADING SYSTEM FOR INVASIVE CARCINOMAS

There have been various methods for the histological grading of invasive carcinomas, many have been vague and showed poor reproducibility or were only limited to one carcinoma sub-type. The recently developed Universal Grading System addresses some of these limitations.¹¹ Although still cumbersome, it is said to be reproducible by the authors, and may be modified to compensate for variation from microscope to microscope (see below).

Guideline - Grading system for invasive carcinomas	Level of Evidence	Refs
The use of the Universal Grading System is recommended and addresses some of the limitations of other methods for histological grading. There is good predictive power across most stages and types.	III-3	11,12

The specific components of the Score must be recorded as well as the final grade, as different components have different prognostic value depending on stage.¹² The scoring system is summarised below:

Architectural pattern	Score
Predominantly glandular	1
Predominantly papillary	2
Predominantly solid	3
Nuclear pleomorphism	
Slight	1
Moderate	2
Marked	3
Mitotic activity in most active region (originally expressed as mitotic figures per 10 high-power fields where 1 HPF = 0.345 mm²):	
0-3/mm ²	1
4-8/mm ²	2
>8/mm ²	3
Add these three scores together for an individual tumour to give final grade.	
3-5	Grade 1
6-7	Grade 2
8-9	Grade 3

NB. Clear cell carcinomas and transitional cell carcinomas are not graded.

Key point:

- Good reproducibility in assessing mitotic activity requires careful attendance to a strict protocol, good quality sections and ongoing quality assurance feedback.¹³

GRADING OF PSEUDOMYXOMA PERITONEI

The cytological atypia and architectural features of the mucin-secreting cells in the peritoneal deposits and/or in the free floating mucinous ascites (histological or cytological assessment) have been found to correlate strongly with prognosis and a categorisation on this basis is recommended.^{14,15}

The peritoneal mucin may vary in features, which can have prognostic significance.¹⁶ It is not yet clear if this is independent of the cellular features as above. In pseudomyxoma peritonei, the tumours should be classified based on the resemblance of the peritoneal deposits to benign or borderline ovarian cystadenomas (peritoneal adenomucinosis) or to carcinoma (peritoneal mucinous carcinomatosis) as the prognosis has been found to differ accordingly.^{14,15}

CATEGORISATION OF BORDERLINE (PROLIFERATING) TUMOURS

Borderline tumours are distinguished from benign by the presence of at least two of the following four features in any one area of a tumour: 'budding' architectural pattern, multi-layering, at least mild nuclear atypia and increased mitoses. A small area of atypia (<10% of available material is a useful watershed) should not be sufficient to put the tumour into the borderline category¹⁷ remembering that the distinction between benign and proliferating has no bearing on clinical outcome.

Borderline (proliferating) tumours are not traditionally graded, although a simple grading of the architectural and cellular changes into low-grade and high-grade has considerable merit and may substitute for the plethora of confusing terms surrounding these neoplasms. The latter (high-grade) subgroup would include lesions up to 'carcinoma-in-situ' (so-called micropapillary serous carcinomas and 'intraepithelial carcinomas' of mucinous type), as discussed below.

SEROUS

An appreciation of serous borderline tumours is the key to understanding of where, in the scheme of ovarian neoplasms, this controversial group stands. Their historical importance¹⁷ is based on a long-term clinical outcome intermediate between benign and frankly malignant tumours, yet good evidence exists that, when confined to the ovaries, patient outcome is no different from that of benign neoplasms.¹⁸ Surgical pathological stage and sub-classification of extraovarian disease into invasive and non-invasive implants are the most important prognostic indicators for serous borderline tumours.

Survival for stage I tumours is 99.5%; survival for advanced stage tumours with non-invasive implants is 95.3%.

Guideline - Prognostic indicators for serous borderline tumours	Level of Evidence	Refs
When considering the prognostic indicators for serous borderline tumours, surgical pathological stage and sub-classification of extra-ovarian disease into invasive and non-invasive implants are the most important indicators.	IV	18

It is irrefutable that the clinical outcome for the patient depends on the presence and nature of the extra-ovarian lesions rather than the biological potential of the ‘ovarian’ mass per se. The controversy, which surrounds these tumours some three-quarters of a century after their original description, and remains unresolved, is the nature of the relationship between the ovarian and the extra-ovarian lesions. Some authorities argue fervently for ‘implantation’ as the sole or dominant process by which the peritoneal lesions arise from the ovarian masses, thus giving credence to the low malignant potential of the neoplastic process as a whole. Others propose equally vehemently for a ‘multifocal’ neoplastic process by which the peritoneal lesions arise independently, thus relegating the proliferating ovarian lesions to a subcategory of benign (i.e. ‘non-malignant’), and assessing the peritoneal lesions on their merits as benign, borderline or frankly malignant. It is inappropriate, here, to attempt to resolve this dilemma.

An observable architectural spectrum of proliferation and cellular changes is present within the category of proliferating serous tumours. No generally accepted guidelines for defining this spectrum exist. At the ‘high-grade’ end of the spectrum, however, an attempt to define a specific subcategory of ‘micropapillary serous carcinoma’ (despite the absence of invasive cancer) has been promoted.¹⁹ It is defensible to regard this end of the spectrum as representing serous papillary carcinoma in situ. An important observation is that small areas of invasive carcinoma (microinvasive carcinoma) do not adversely affect outcome in these or other borderline serous tumours. Microinvasion is defined as one or more foci, each no more than 10mm². Other authors have used the similar cut-off of 3mm greatest diameter, which is recommended as it is simpler to apply.^{20,21} These foci must show either single cells or small irregular solid islands of cells. They are usually multiple.

PERITONEAL IMPLANTS OF BORDERLINE SEROUS TUMOURS: NON-INVASIVE VERSUS INVASIVE

The careful histological assessment of extraovarian lesions (peritoneal ‘implants’) with the specific aim of separating out those showing locally invasive malignancy is crucially important as this feature is the predominant determinant of patient outcome. A recent study found that, even in the absence of destructive invasion of normal tissues, where the implants show both a micropapillary pattern and solid tumour islands surrounded by

clefts, the prognosis for the patient is worsened. In their group of 31 such patients, with a mean 5 year follow-up, 6 were dead of disease and 13 were alive with progressive disease.²²

Involved retroperitoneal lymph nodes (20% of such patients) are no less perplexing. Nodal involvement appears to affect intra-abdominal recurrence rates (presumably due to incomplete surgical resection) but not long-term clinical outcome,²³ and is usually a further manifestation of multifocal tumorigenesis, although true metastases from 'invasive peritoneal implants' may account for some cases. While they may be regarded as metastatic, they should not be interpreted as carcinoma and they do not mandate aggressive therapy.

The commonly encountered presence of a surface papillary component to the ovarian neoplasm correlates with an increased likelihood of extraovarian lesions being present in the peritoneal cavity, but does not, of itself, adversely affect patient outcome. It is likely that the so-called desmoplastic non-invasive subset of peritoneal lesions is specifically associated with proliferating serous tumours with a surface papillary component.

MUCINOUS

Extending the proliferating or borderline category to ovarian mucinous tumours was based on the assumption that certain non-invasive mucinous neoplasms could be accompanied by extraovarian manifestations, in this case pseudomyxoma peritonei, with adverse consequences for the patient. That is to say, pseudomyxoma peritonei was considered analogous to peritoneal implants of serous borderline tumours. As noted earlier, the majority of researchers in the field currently hold to the view that pseudomyxoma peritonei represents metastatic low grade mucinous carcinoma, most often arising in the appendix, and that concurrent ovarian involvement is also in the nature of metastatic epithelial neoplasia. Proliferating mucinous tumours, unassociated with pseudomyxoma peritonei at presentation, do NOT progress to later produce this condition. The very low risk of progression in these tumours (in the vicinity of 2-5%) is most probably due to tissue sampling which was insufficient to identify areas of invasive carcinoma. As with serous proliferating tumours, there is an observable spectrum of proliferative activity. This statistical risk is clearly greater in those proliferating mucinous tumours with high grade epithelial changes,²⁴ defined as showing more than four layers of nuclei and marked nuclear atypia, but still with no evidence of stromal invasion.

Guideline - Terminolgy in borderline neoplasm	Level of Evidence	Refs
Use of the term 'high grade proliferating' as an alternative to 'carcinoma in situ' or 'intraepithelial carcinoma' within a borderline neoplasm is recommended for mucinous tumours with no evidence of stromal invasion, if they show more than four layers of nuclei and marked nuclear atypia.	IV	24

Approximately 15% of proliferating mucinous tumours show features more closely resembling endocervical than intestinal epithelial differentiation. Of these, 10-15% are associated with small focal extraovarian lesions, akin to the peritoneal implants of serous borderline tumours. The presence of such lesions does not adversely affect patient outcome.

MICROINVASION ARISING IN BORDERLINE TUMOURS

This must not be confused either with frank carcinoma or with carcinoma in situ (see above) although it may overlap with the latter in some cases.

Similar criteria have been applied to both serous and mucinous types. The serous type is easier to identify as single cells, or small invasive papillae with their 'luminal' surface apposed to the stroma, and often apparently within tissue spaces. An inflammatory tissue response is characteristically, but not always, generated. Both serous and mucinous proliferating tumours displaying microinvasion have been found to have a clinical outcome not materially different from those which do not display this feature.²⁵ Thus, while immunostaining (cytokeratins) may assist in identifying such microfoci, their pursuit should be regarded as of academic rather than practical interest.

Note that a desmoplastic or inflammatory response to free mucin may occur and this should not be regarded as evidence of stromal invasion in mucinous proliferating tumours. Similarly, serous tumours may have plaques of desmoplastic fibrosis in the wall, with psammoma bodies. This also does not imply microinvasion.

SIMULTANEOUS ENDOMETRIAL AND OVARIAN CARCINOMAS

In this relatively common situation, the problem is to decide if one or the other or both are primaries, as this affects staging and may affect prognosis. A recent study of endometrioid carcinomas has shown that bilateral ovarian involvement does not necessarily indicate metastatic disease, two of three such cases were primary to the ovary by molecular analysis.²⁶ Furthermore, cases in which the ovary was monoclonal with an endometrial carcinoma, included examples with deep myometrial invasion as well as minimal invasion. Thus, this is also not a useful feature. The study confirmed that the presence of ovarian endometriosis supports the probability that the ovarian tumour is primary. The belief that the overall good prognosis of such tumours implied that most were double primaries received limited support. Approximately 60% of the informative cases were double primaries in a study where both were of the same endometrioid type - a higher percentage would be likely to be double primaries if cases with more disparate histological patterns of differentiation were included. Why independent tumours should so often arise in these two sites is an unanswered question, although a similar phenomenon is observed with independent primary carcinomas in cervix and ovaries.

THE ANATOMICAL PATHOLOGY REPORT

Synoptic reports have been advocated by many authorities,²⁷ as they promote a uniform and complete record of the surgical specimen and highlight prognostic parameters. The report should include:

- the histological type(s) of tumour;
- its grade, including the components of the score;
- the presence of any microinvasion, capsular/surface involvement;
- the presence and types of peritoneal implants; and
- involvement of other structures (fallopian tube, uterine serosa, lymph nodes etc).

Key points:

- It is strongly recommended that a synoptic proforma system be used for epithelial ovarian tumour reports to allow ease of finding and interpreting data consistently on ovarian cancer patients regardless of the laboratory or reporting pathologist.

HISTOPATHOLOGY CHALLENGES AND A CENTRAL REVIEW CENTRE

Studies of gynaecological cancer cases sent for ‘central review’, indicate that the diagnosis is changed in up to 33% of cases, with 12% of patients being given an altered management plan.²⁸ This is a reflection of the diagnostic difficulties in such cases and reinforces the principal of central review by a specialist gynaecological pathologist prior to management planning. The many variations in ovarian cancer types, and in related ovarian conditions, means that few pathologists can have extensive personal experience of all, or can conduct research on rare types, if limited to cases personally diagnosed (*see Foreword, pvii*).

Hence, best practice would suggest the desirability of a mechanism for central pathology review to which unusual, difficult or interesting cases can be referred for further assessment and categorisation. With current rapid improvements in digital technology, it may not be necessary for all, or even most cases, to be sent physically to a central laboratory (*see Appendix 6, p182- Future research needs*).

MOLECULAR BIOLOGY

Many advances in our understanding of molecular genetics of ovarian cancer have been made, but these are not yet affecting clinical practice. The interested reader is referred to the excellent reviews by Russell²⁹ and by Leary and Friedlander.³⁰

The oncogene with most promise of clinical relevance is p53. The p53 gene on chromosome 17p 13.1 is central to the control and regulation of DNA repair in cells.

Deletions and mutations of this gene are common in all human tumours. The protein causes arrest of cell cycle after DNA damage and triggers apoptosis if the damage is too great for repair. There have been many studies to determine the incidence and role of p53 in ovarian tumours. In a number of these studies p53 protein over expression alone was used as an indirect indicator of mutation and caution is needed in interpreting these results as there is not always a good correlation between immunohistochemical assessment of protein levels and mutation analysis to detect changes in the controlling gene segment.^{31,32,33,34,35}

p53 mutation and over expression is commonly observed in invasive serous ovarian tumours with an incidence ranging from 23 – 72%.^{36,37} Mutations are rarely observed in borderline serous ovarian tumours. Most studies suggest that p53 alterations are a late event in the development of ovarian tumours with evidence of loss of p53 function in about 15% of early stage tumours^{38,39} and over 50% of late stage disease.^{40,41} A number of studies have looked at the prognostic significance of p53 status in ovarian tumours but the findings are inconclusive.^{42,43} More recently there have been studies to suggest that p53 mutations are associated with platinum resistance, an area of current interest.⁴⁴

Other genetic mutations seem to operate in histological tumour types other than serous carcinomas. For example PTEN (Phosphatase and tensin homologue deleted on chromosome 10) is frequently altered in endometrioid neoplasms,^{45,46} and K-ras mutations have been identified with progressive frequency in mucinous ovarian tumours of increasing levels of proliferative activity.⁴⁷

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6. MULTIDISCIPLINARY MANAGEMENT OF WOMEN WITH OVARIAN CANCER

The goal of management in women who have epithelial ovarian cancer is to provide the best possible outcome. The major factors that determine outcome are:

- early and accurate diagnosis; and
- surgical care appropriate to the presenting disease

Both elements require to be addressed in a positive manner.

- Early and accurate diagnosis needs to be fostered through educating primary health carers to be aware of the nuances of clinical presentation of ovarian cancer to optimise their interpretation of these and to follow sound referral pathways
- There is evidence that outcomes are directly related to the training of the surgeon, who understands the natural history of the disease and who is also trained to deal with any clinico-pathological situation which might arise at the time of the laparotomy.¹⁻⁵ Improvements in survival have been found both in women with early stage and advanced disease

MULTIDISCIPLINARY CARE FOR OVARIAN CANCER

Many diseases, including ovarian cancer, require a range of treatment modalities for optimal outcomes. The concept of multidisciplinary care, as a co-ordinated approach using a collaborative group of health professionals for the diagnosis, continuing management and palliative care has been evolving for ovarian cancer over the last decade or more. The team as a whole is responsible for the diagnosis, continuing management and palliative care of the woman with ovarian cancer.

No randomised clinical trial has been undertaken to compare outcomes for women managed by multidisciplinary teams versus individual clinicians. Audits show shortcomings in clinical practice despite published guidelines.⁶ The best evidence is from a comparison of patient outcomes from teaching hospitals versus non-teaching centres. Junor's paper reports that the decrease in risk of death at five years is 40% for women treated in teaching hospitals. This is independent of optimal surgery and reflects presumed benefit of multi-disciplinary management.¹

There is, however, a growing body of evidence^{1,7} to suggest that outcomes for a woman with ovarian cancer are improved if she is referred to be managed under the care of a Multidisciplinary Care team including:

- pathologists and nursing staff specially trained in the management of ovarian cancer;
- subspecialty-trained gynaecological oncologists; and
- medical and radiation oncologists with expertise in the management of ovarian cancer.

In the UK, the *National Health Service Executive Report on The Management of Women with Gynaecological Cancer July 1999*,⁸ responsible for all commissioning of cancer services in the UK, announced:

“Dedicated diagnostic and assessment services should be established in cancer units to which all women with suspected gynaecological cancer should be referred. There should be specialist gynaecological oncology teams based at the referral centres ...who are responsible for the management of all women with gynaecological malignancy”

While the ideal situation is for referral of the woman to a centre where all aspects of management, including surgery, pathology review, chemotherapy and on-going psychosocial support are available, there are several reasons why women are not referred to a multidisciplinary team for primary management of ovarian cancer. These may include that the diagnosis is not anticipated by the surgeon, who is not well trained to deal with the situation. Some surgeons may feel that comprehensive surgery is excessive and not warranted, especially in early stage disease.⁹ A comprehensive understanding of the disease is important, together with the mindset to perform as complete surgery as is possible.

Guideline - Multidisciplinary care for women with ovarian cancer	Level of Evidence	Refs
There is a growing body of evidence to suggest that outcomes for a woman with ovarian cancer are improved if she is referred to be managed under the care of a Multidisciplinary Care team. The ideal situation is for referral of the woman to a centre where all aspects of management, including surgery, pathology review, chemotherapy and on-going psychosocial support are available.	IV	1,7

THE AUSTRALIAN CONTEXT

Multidisciplinary care is not uniform across Australia. There may be multiple models which are still acceptable for good practice, depending on the local availability of resources, and external arrangements with larger multidisciplinary care units in the capital cities but the principles of multidisciplinary care should be promoted. The minimum standard, regardless of location, includes the presentation and discussion of individual women’s cases at a Multidisciplinary Care meeting, with expert pathology review and input from a gynaecological oncologist. This may take the form of a letter or telemedicine conference and in all cases the outcome of the discussion should be relayed directly to the woman and her referring doctor.

WHAT GROUPS SHOULD BE INVOLVED IN THE MULTIDISCIPLINARY TEAM FOR THE MANAGEMENT OF OVARIAN CANCER?

The input of specialists from several disciplines offers a broader perspective for the derivation of a care plan for a given woman’s disease. Protocols are established by

consensus and in the setting of a formalised training program; the discipline of adhering to the plan is much stronger in these circumstances.¹⁰

Care of the gynaecological oncology patient relies on all partners in the team – no one team member being less important than the other. Each has a role to play in the management and support of the woman, from those who deliver the primary care, to the staff, both medical and paramedical, to the support team in the community. All are important and should not lose sight of either their own role or the importance of others around them. Any specialist is welcome to be part of the discussion about any given woman with ovarian cancer, as is the initial referring doctor. The team may offer advice and help, but is always willing and motivated to work as a teaching resource and for tertiary referrals.

In general, consumers are in favour of ‘multidisciplinary teams, good teamwork and communication between professionals’.¹¹ It is worthwhile taking time to discuss the role of the team and each of its members with the woman. She may feel more comfortable discussing the management of her care with one particular member of the team and needs to know that each member of the team is equally valued, that the team members communicate and discuss the options for her care, and that any one of them can provide her with the best available advice and opinion.

Key point:

- Any member of the multidisciplinary team may, with the woman’s approval, become the lead person for on-going communication about her care.

THE MULTIDISCIPLINARY CARE TEAM FOR WOMEN WITH OVARIAN CANCER

- Gynaecological oncologist
- Gynaecological pathologist
- Medical oncologist with special experience in ovarian cancer
- Radiation oncologist with special experience in ovarian cancer
- Radiologist with a special interest in ovarian cancer
- General practitioners
- Specialist nurses
- Physiotherapists
- Pharmacists
- Psychologists, social workers
- Palliative Care specialists
- Geneticist
- Genetic counsellors

Key point:

- The involvement of a broad range of staff considering the care plan requirements for each patient will result in a planned approach that takes into consideration all the nuances of the woman, her disease and psychosocial situation.

ROLE OF THE GYNAECOLOGICAL ONCOLOGIST

Gynaecological Oncology is a sub-specialty of obstetrics and gynaecology. It was recognised as a sub-speciality by the National Academic Specialist Qualifications Advisory Committee (NASQAC) in 1988, as an advanced speciality credentialing process.

Gynaecological Oncologists are specialists in Obstetrics and Gynaecology who:

- hold a Fellowship with the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (FRANZCOG);
- have completed a formal three year training program in gynaecological cancer care;
- have passed the examination for the Certificate of Gynaecological Oncology (CGO);
- are actively practising in the field of gynaecology, with at least 66% of time spent in gynaecological oncology;
- are competent in the comprehensive management of women with a genital malignancy; and
- must submit for re-certification every three years.

(See Appendix 4 - Gynaecological oncology training requirements.)

The role of the certified gynaecological oncologist is clearly significant in the management of epithelial ovarian cancer (*see chapter 7 – Assessment of initial symptoms, chapter 8 – Management of a pelvic mass and Chapter 10 – Surgery for invasive ovarian cancer*).

In the National Institutes of Health Consensus Statement on Ovarian Cancer, it was noted that for surgery for ovarian cancer ‘...the procedure is best conducted by a qualified gynaecologic oncologist’.¹²

There is Level IV evidence for the influence of training of the surgeon on outcomes of treatment, especially surgery. A study from Scotland found an improved patient survival independent of other prognostic factors if operated on by specialist gynaecologist or by a gynaecological oncologist.¹³

An Australian report² follows this same trend, whilst an American study suggests that adequate staging only occurs when patients are operated on by specialists.³

Mayer⁴ *et al.* found a significantly better survival for women with stage I and II disease when they were staged by a gynaecological oncologist compared with those women who were operated on by a non-oncologist. Five-year actuarial survival was 83 ± 7% for the gynaecological oncologist group and 59 ± 11% for the non-oncologist group (p<0.05) and disease-free survival was 76 ± 8% and 39 ± 11% respectively (p<0.03).

Key point:

- The training of the surgeon has an effect on prognosis, especially in early stage disease, where careful staging can determine whether a woman needs additional therapy or not.

In a recent review of patients in Utah with epithelial ovarian cancer from 1992-1998, it was shown that overall, a gynaecological oncologist saw only 39.3% of patients at some time during their diagnosis and/or treatment. Among cases diagnosed with advanced stage disease, those cases seen by gynaecologic oncologists had a significant survival advantage when compared to those who were not (median survival 26 and 15 months respectively, $p < 0.01$).⁵

A study of patterns of care in Victoria during 1993-1995,¹⁴ showed that primary surgery was performed by gynaecological oncologists in 47.2% of cases (205 women). Gynaecological oncologists were more likely to perform complete and adequate surgery; however the proportion of tumours optimally resected was relatively low, even when surgery was performed by gynaecological oncologists. The study did show, 'staging to be associated with improved survival when tumours were adequately staged'.

A population-based cohort study of all women undergoing surgery for ovarian cancer in Ontario, Canada between 1992 and 1998 showed there was a statistically significant association between 30-day postoperative survival, reoperation rate and overall survival and surgical specialty. The adjusted survival was improved if the initial surgery was done by a gynaecological oncologist (Hazard Reduction 0.70, CI 0.57 to 0.85) or by a gynaecologist (Hazard Reduction 0.65, CI 0.53 to 0.79).¹⁵

Guideline - Surgical care of women with ovarian cancer	Level of Evidence	Refs
Survival for women with ovarian cancer has been shown to be improved when the initial surgery has been done by a gynaecological oncologist. The surgical care of women with ovarian cancer is best directed, whenever possible, by a gynaecological oncologist.	IV	2,4,5, 13,15

The surgical care of the woman should be directed by state-of-the-art surgical staging. This is best directed, whenever possible, by a fully trained gynaecological oncologist, who has a full knowledge of the natural history of the disease, which includes an awareness of the likely sites of spread and who is trained to manage, intra-operatively, the range of pathology that may be encountered.

THE ROLE OF THE GENERAL PRACTITIONER

The general practitioner (GP) may play a number of roles in the management of the woman with ovarian cancer including: diagnosis, referral, treatment, and co-ordination of care, through all stages of the disease. The GP is also ideally placed to provide ongoing information and support to the woman with ovarian cancer and her family.

As a key member of the multidisciplinary team, the GP should provide all necessary information to specialists and allied health professionals involved in the care of the woman with ovarian cancer. The GP's role will be greatly supported by the receipt of timely letters from specialists involved in the woman's care, with adequate information about the management plan, pathology reports, other investigations etc.

THE ROLE OF THE GENERAL SURGEON

The general surgeon may encounter ovarian cancer unexpectedly or inadvertently at the time of laparotomy for other purposes in a rural or acute setting. In this case the minimum necessary surgery (e.g. relief of bowel obstruction) should be carried out. A biopsy should be undertaken for histological diagnosis and the woman referred for further evaluation and treatment recommended as appropriate by the multidisciplinary team (*see chapter 8 – Management of a pelvic mass*).

THE ROLE OF THE NURSE SPECIALIST

Nurses are essential to the delivery of a comprehensive service to women affected by ovarian cancer and play a significant part in the woman's cancer journey. Relatively little is known about women's experiences of having ovarian cancer or the impact of recurrent disease, and this limits the development and implementation of appropriate nursing interventions.¹⁶ A number of studies focussing on the care of women with breast cancer have shown that women cared for by a specialist nurse have better outcomes in relation to co-ordination of care, earlier referral to specialist services and improved psychological outcomes.^{17,18} These studies suggest that a similar outcome could be achieved by specialist gynaecological nurses.

There is limited information available about benefit of specialist nursing for gynaecological oncology patients, although a recent randomised controlled trial identified that sexual functioning and quality of life were improved for women in a specialist gynaecological nurse intervention group.¹⁹

ROLE OF THE PATHOLOGIST

Expert pathological reviews of ovarian cancers have found that 10% had a change in diagnosis, as a result of review. There was especial difficulty with borderline lesions.^{20,21} Cronje *et al.*²² reviewed 1718 slides from 454 patients with a diagnosis of granulosa cell tumours, and 111 (24%) were reclassified, mostly to classifications with a less good prognosis. In all, 206 were initially reported as granulosa cell tumours, but after review only 97 remained.

Patients referred to Johns Hopkins Hospital for definitive therapy for cancer were studied.²³ In 6171 cases, the diagnosis was changed in 1.4%, but in gynaecological cases, 5.1% ($p < 0.0001$) were changed.

Where any doubt exists, the second opinion of a specialist pathologist should be

mandatory if patient safety and quality control is to be maintained.²³ This would expedite timely decision-making by the multidisciplinary team.

To ensure that the multidisciplinary team can fully discuss all aspects of a woman's case, it is helpful for the pathologist to ensure that the relevant slides are available for each multidisciplinary team meeting.

Key point:

- A pathologist with extra training in gynaecological malignancy pathology is an integral member of the multidisciplinary team.

CLINICAL TRIAL PARTICIPATION

Better outcomes have been reported for patients with other cancers taking part in clinical trials.^{24,25} Teams who take part in clinical trials are at the forefront of new knowledge and treatments and can offer these to their patients (*see chapter 17 – Clinical trials*).

Key point:

- Better outcomes have been reported for cancer patients who take part in clinical trials.

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7. ASSESSMENT OF INITIAL SYMPTOMS

While it is commonly reported that the presenting symptoms of ovarian cancer are frequently vague, and do not point to the ovary as the primary problem, some small retrospective studies, which relied on chart review, suggest that most women diagnosed with ovarian carcinoma do report symptoms, although they are not usually gynaecological in nature.^{1,2}

Data obtained from a survey of 1725 women showed that 95% of women reported symptoms prior to diagnosis. Only 11% of stage I and II and 3% of stage III and IV reported no symptoms prior to their diagnosis.³ Using a structured questionnaire to conduct interviews with over 750 women diagnosed with borderline or invasive epithelial ovarian cancer, Vine *et al.* reported that 92% of women with invasive ovarian tumours and 84% of borderline cases have symptoms, with a median duration of four months.⁴ In a group of 168 women who were interviewed shortly after diagnosis, nearly all the cases (93%) reported at least one symptom, compared with 42% of controls.⁵ In a study of Canadian women only 9% reported experiencing no symptoms whatsoever prior to diagnosis.⁶

OVARIAN CANCER SYMPTOMS

- Abdominal bloating
- Increased abdominal girth
- Indigestion, lack of appetite
- Change in bowel habits
- Constipation
- Urinary frequency or incontinence
- Fatigue
- Abdominal and/or pelvic pain

SYMPTOM CATEGORIES³

77%	Abdominal symptoms
70%	Gastro-intestinal
50%	Constitutional (e.g. fatigue)
34%	Urinary
26%	Pelvic

While symptoms reported by women can be extremely difficult to differentiate from symptoms experienced by women with more benign conditions, one study indicated that bloating, fullness and pressure in the abdomen was much more likely to be constant, rather than intermittent, in proven cases of ovarian cancer, compared with controls.⁵

In the survey conducted by Goff and colleagues, when women were asked about the diagnosis offered prior to the diagnosis of ovarian cancer, 13% of the survey participants responded that they were told that nothing was wrong, 6% were told they had depression and 12% stress.³

Key points:

- Ovarian cancer symptoms are frequently vague and non-specific eg bloating, fullness and a feeling of pressure in the abdomen. Persistence of symptoms for greater than one month must promote a high index of suspicion.⁷
- The thought that a woman may have a psychosomatic problem should not overrule clinical suspicion of malignancy in women with persistent symptoms.
- A high level of suspicion is a useful adjunct in making the diagnosis of ovarian cancer, particularly:
 - in women with a family history of ovarian cancer;
 - in women who are older than 45; or
 - where symptoms appear to persist in the absence of any alternative explanation.

INVESTIGATION OF WOMEN WITH SYMPTOMS

The cornerstone to assessing initial symptoms that may be ovarian cancer is the taking of a careful clinical history. The clinician should seek information about symptoms which either persist or regularly recur. The physical examination is of equal importance and must not be neglected in favour of radiological or blood studies. It is important that the woman is undressed sufficiently to provide access to the whole of the abdomen, unrestricted by constricting clothing.

In women with ovarian cancer an omental mass may be felt as a firm resistance, or an unexpected fullness. Ascites may also be found as fullness which exhibits shifting dullness on percussion. A vaginal examination may also reveal a hard, irregular mass in the Pouch of Douglas, often more readily felt rectally, or adnexal masses.

Key points:

- The cornerstone to assessing initial symptoms that may be ovarian cancer is the taking of a careful clinical history. The physical examination is of equal importance and must not be neglected in favour of radiological or blood studies.
- It is important that the woman is undressed sufficiently to provide access to the whole of the abdomen, unrestricted by constricting clothing.

If on clinical examination, there is a suspicion of a mass, then radiological imaging, (using either ultrasound or CT, but not both), should be able to both confirm any findings, and also help elucidate its nature. The transvaginal ultrasound has a greater sensitivity for the detection of ovarian masses than transabdominal studies. Cysts less than 4 cm may be monitored, but cysts which are of a greater dimension, complex or solid should be referred for consideration of surgical exploration.

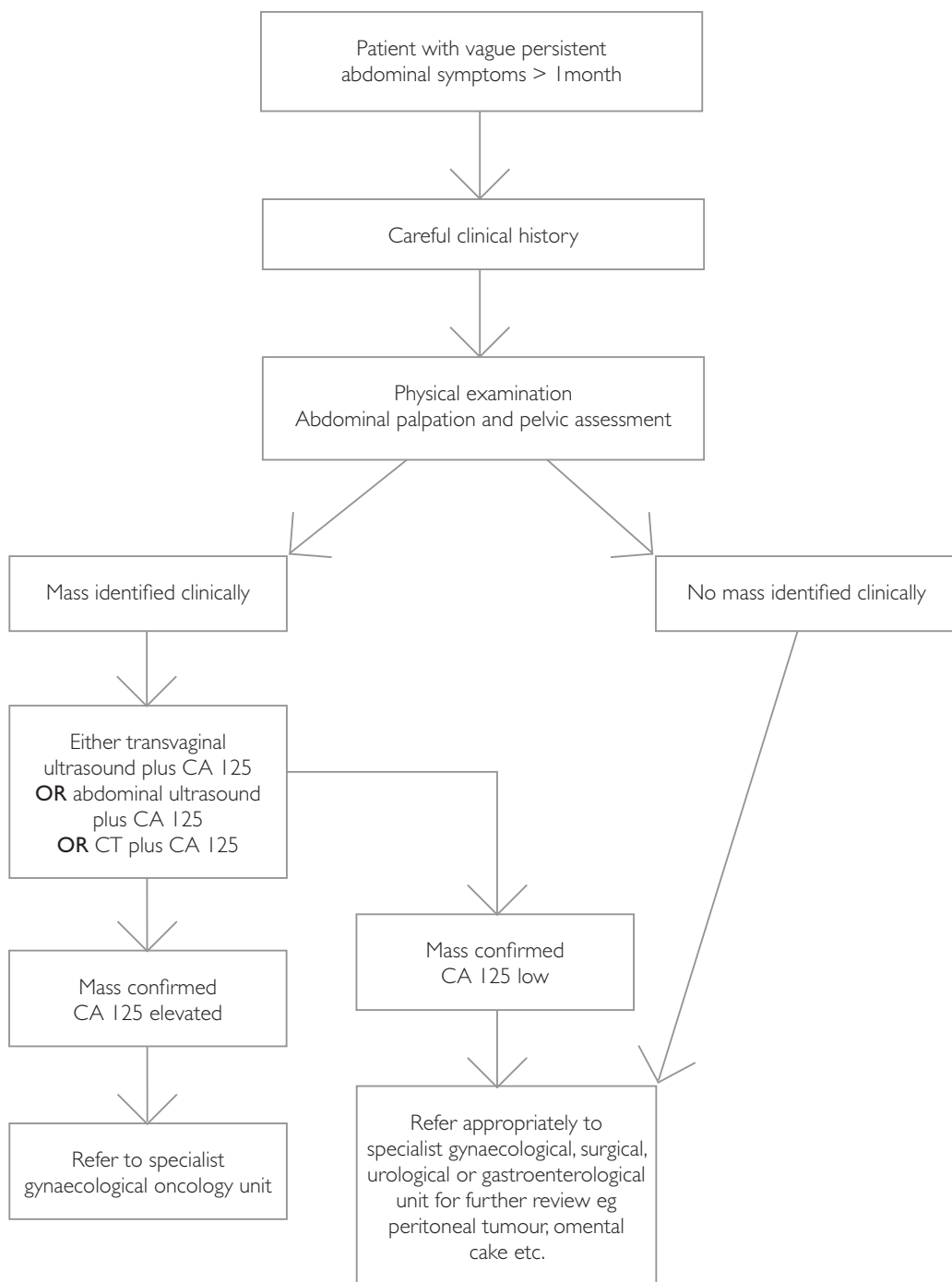
A blood test for CA125 may also contribute information, but whilst a very high value may assist in confirming the diagnosis, a low level is not helpful because of the non-specific nature of the test (*see chapter 3 – Screening for ovarian cancer and chapter 8 – Management of a pelvic mass*). CA125 should not be used to either rule in or rule out disease, as both false negative and false positive results can occur.

If all investigations and tests strongly suggest an ovarian malignancy, direct referral to a gynaecological oncology unit is the preferred option. If the CA125 is low, with a confirmed mass, one should consider other pelvic pathologies before deciding on the primary referral pathway; this might include colorectal and urological as well as gynaecological specialists. The final choice may still include a gynaecological oncologist, and will strongly be dependent on the presenting symptoms as well as any radiological findings. A woman with a suspicious or persistent complex adnexal mass needs surgical exploration. The surgeon of choice is one trained to understand the natural history of the disease who can anticipate and deal with any eventualities during surgery.⁸ Currently only a small percentage of women receive this optimal approach initially.

The more difficult situation is where the clinical examination is negative. The dilemma then is to decide which investigations to perform. Review of the symptoms and possibly radiological investigation of the whole abdomen may help suggest an appropriate referral line. Clinicians should be aware that primary peritoneal cancer may be a subtlety, whereby there are no pelvic masses, but ascites and an omental cake may still be found.

An algorithm has been developed to assist with an organised approach in assessing a woman presenting with vague and persistent abdominal symptoms. (*See Figure 11: Algorithm outlining the approach to assessment of women with vague and persistent abdominal symptoms*).

Figure 11 Algorithm outlining approach to assessment of women with vague and persistent abdominal symptoms



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8. MANAGEMENT OF A PELVIC MASS

When a woman presents with a pelvic mass, it is important to attempt to discriminate between a gynaecological and non-gynaecological mass in the first instance, and then whether the mass is benign or malignant.

Non-gynaecological masses will be diagnosed on the basis of history, physical findings, and special investigations such as colonoscopy.

If the mass is considered to be of ovarian origin, it is important to determine its likelihood of being malignant, because potentially malignant lesions should be referred to a gynaecological oncology unit where adequate surgical staging or cytoreduction can be performed (*see chapter 6 – Multidisciplinary management of women with ovarian cancer*). The best way to detect early ovarian cancer is for both the woman and her clinician to have a high index of suspicion of the diagnosis in a symptomatic woman.¹

There are a series of warning signs on both clinical assessment, biochemistry (CA125) and imaging that should raise suspicion that a pelvic mass is malignant. (For assessment of symptoms and diagnostic pathway, *see chapter 7 – Assessment of initial symptoms*.)

CA125

The CA125 titre in pre-menopausal women is commonly elevated in association with benign conditions such as endometriosis, pelvic inflammatory disease, fibroids adenomyosis, pregnancy and menstruation. Elevated CA125 titres are more suspicious in a post-menopausal woman,² however a normal CA125 measurement alone does not rule out ovarian cancer as it may be normal in 50% of women with stage I ovarian cancer and 20-25% of advanced cancers are also associated with normal values.

ULTRASOUND

Features of cancer on the ultrasound images that suggest malignancy include:

- Septation
- Papillary projections
- Solid areas
- Ascites

The presence of ascites has a positive predictive value of 95%. The absence of ascites is far less reliable in predicting a benign lesion. Less than 20% of early stage ovarian cancers have ascites present.³

Key points:

- The risk for ovarian cancer being present is related to older age (greater than 45 years), family history (positive for breast/ovarian cancer) (*see chapter 2 - Risk factors for ovarian cancer and chapter 4 - Familial aspects of ovarian cancer*), the level of the CA125 titre (>35U/ml), and characteristics on transvaginal ultrasonography⁴
- Any woman with a pelvic mass, in association with the following features should be considered for referral to a gynaecological oncology unit¹
 - Ascites
 - Nodular or fixed pelvic mass
 - Any evidence of abdominal or distant metastases
 - Family history of one or more first degree relatives with breast or ovarian cancer
 - Raised CA125 (or a very raised CA125 (>200U/ml) in a premenopausal woman)

RISK OF MALIGNANCY INDEX⁵

Efforts to standardise the information obtained from each modality have resulted in scoring systems that can be applied as a method of triage. One of these methods (the Risk of Malignancy Index) is a scoring system devised by Jacobs that can be applied as a useful triage for a woman with a pelvic mass.⁵ The algorithm includes assessment of the woman's menopausal status, the ultrasonic features and the serum CA125.

Criteria	Scoring System	Score
Menopausal status: Premenopausal Postmenopausal	1 3	A (1 or 3)
Ultrasonic features: Multiloculated Solid areas Bilaterality Ascites Metastasis	no features = 0 one feature = 1 > 1 feature = 3	B (0, 1 or 3)
Serum CA125	Absolute level	C
Risk Of Malignancy Index (RMI)		A x B x C

If a cut off value of 200 is used to discriminate benign from malignant ovarian masses, there is a good correlation, with a sensitivity of 87% and a specificity of 97%.

Key point:

- Use of a Risk of Malignancy Index in the presence of a pelvic mass is a useful triage to help determine which women would benefit from direct referral to a gynaecological oncology unit.

SURGERY FOR A PELVIC MASS

A woman with a suspicious or persistent complex adnexal mass needs surgical exploration. The surgeon of choice is a clinician, such as a gynaecological oncologist, who is trained to understand the natural history of the disease, who can appropriately stage and debulk ovarian cancer, and anticipate and deal with any eventualities during surgery.⁶ Currently only a small percentage of women receive this optimal approach initially.

Surgery should be performed in a hospital facility, such as a gynaecological oncology unit, that has the necessary support and consultative services, which will optimise the patient's outcome, such as preoperative counselling, psychosocial support services and intraoperative pathology assessment.

Prior to surgery, the woman should be counselled about the risks of ovarian cancer, the plans and options available during surgery and the possible need for radical surgery and staging, including the possible effect on fertility and menopause. If appropriate, consent should be obtained for removal of the uterus, tubes and ovaries and complete surgical staging.

If the woman has her primary surgery in a gynaecological oncology unit, she should have removal of the pelvic mass, as far as is technically possible. If the mass is confirmed as ovarian cancer, she should undergo complete surgical staging⁷⁻⁹ (*see FIGO Staging, Introduction, p3*)

Guideline - Surgical staging	Level of Evidence	Refs
Surgical staging for ovarian cancer always includes: <ul style="list-style-type: none">• peritoneal washings for cytology;• exploration of all peritoneal surfaces including the diaphragm, bowel serosa and Pouch of Douglas;• biopsy of any suspicious nodules;• infracolic omentectomy, multiple peritoneal biopsies; and• at least adequate sampling of pelvic and para-aortic lymph nodes	IV	7,8,9

When these procedures are performed on women with disease apparently confined to the pelvis, 28% of women with apparent stage I disease and 43% of women with apparent stage II disease will be upstaged, usually to stage III disease.⁸ This upstaging increases from 16% for Grade I lesions to 34% for Grade II and 46% for Grade III. The most common sites of metastatic disease are the omentum, diaphragm and retroperitoneal lymph nodes.⁹

In postmenopausal women, total abdominal hysterectomy and bilateral salpingo-oophorectomy should be performed.

When ovarian cancer is encountered in premenopausal women who are desirous of retaining fertility, with early stage disease and favourable pathology (that is, Grade I or II tumours), fertility-preserving surgery in association with appropriate follow-up can be safely undertaken.¹⁰⁻¹³

Guideline - Retaining fertility for premenopausal women	Level of Evidence	Refs
In premenopausal women, with invasive adenocarcinomas, early disease and favourable pathology (grade I or grade II, stage IA or IB tumours) fertility-preserving surgery in association with appropriate follow-up can be safely undertaken, if child bearing is desired.	IV	10-13

FOLLOW UP POST-FERTILITY PRESERVING SURGERY

In cases where the uterus and contralateral ovary are preserved, the patient should undergo three monthly measurements of CA125 and the remaining ovary should be monitored with transvaginal ultrasonography every six months. Consideration to remove the contralateral ovary should be given when childbearing has been completed.

Key points:

- In cases where the uterus and contralateral ovary are preserved, the patient should undergo three monthly measurements of CA125 and the remaining ovary be monitored with transvaginal ultrasonography every six months.
- Consideration to remove the contralateral ovary should be given when childbearing has been completed.

If an adnexal mass is removed by a specialist other than a gynaecological oncologist and intraoperative assessment indicates that ovarian cancer is present, no further surgical excision should be performed, unless consent for removal of the uterus and contralateral ovary has been obtained. If histological evaluation reveals an ovarian malignancy, the patient (with her histopathology slides) should be referred to a Gynaecological Cancer Centre for appropriate multidisciplinary evaluation (*see chapter 6 – Multidisciplinary management of women with ovarian cancer*). Avoidance of unnecessary fertility

destroying surgery is especially important in the case of younger women and in women where the final pathology may not confirm the indications for such treatment.

INADVERTENT DISCOVERY OF OVARIAN CANCER

There may be circumstances when the diagnosis of ovarian cancer is made unexpectedly or inadvertently at the time of laparotomy for other purposes, such as by general surgeons in rural or acute settings. If intraoperative consultation by a gynaecological oncologist is not available, it is suggested that the diagnosis be simply confirmed by appropriate biopsy such as of the omentum, that the acute situation be dealt with (for example, a bowel obstruction may be relieved), that minimal other surgery be carried out and that the patient be referred postoperatively to a gynaecological oncology unit.¹⁴ In such circumstances, good outcomes are obtained with individualised approaches such as using neoadjuvant chemotherapy and interval debulking surgery (*see chapter 10 – Surgery for invasive ovarian cancer and chapter 11 – Chemotherapy*). Referral also improves the opportunities for appropriate counselling and psychosocial support being made available to the patient.

Guideline - Inadvertent diagnosis of ovarian cancer	Level of Evidence	Refs
<p>In the event of an unexpected diagnosis of ovarian cancer at the time of surgery for other purposes:</p> <ul style="list-style-type: none"> • the diagnosis should be confirmed with a biopsy; • minimal additional surgery should be undertaken; • postoperative referral to a gynaecological oncology unit for definitive treatment should be arranged. 	IV	14

LAPAROSCOPIC SURGERY

Laparoscopic surgery is increasingly being used in the assessment of gynaecological symptoms. In recent years, reports have been published of undiagnosed ovarian cancer managed by laparoscopy with unfortunate consequences including dissemination of early stage disease and abdominal wall metastases. In view of these risks, laparoscopic surgery should not be performed when there is any significant risk of malignancy. If malignancy is encountered, then the patient should be referred promptly for immediate surgical staging and definitive treatment.^{15,16}

Key point:

- Laparoscopic surgery should not be performed when there is any significant risk of malignancy. If malignancy is encountered, then the patient should be referred promptly for immediate surgical staging and definitive treatment.

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