



OVARIAN CYSTS IN POSTMENOPAUSAL WOMEN

1. Aim

The aim of this guideline is to provide information, based on clinical evidence where available, on the investigation and management of postmenopausal women with known ovarian cysts.

2. Introduction and background

Ovarian cysts are common in postmenopausal women, although the prevalence is lower than in premenopausal women. Of 20 000 healthy postmenopausal women screened in the Prostate, Lung, Colon and Ovarian Cancer Screening Trial,¹ 21.2% had abnormal ovarian morphology, either simple or complex. The greater use of ultrasound and other radiological investigations means that an increasing proportion of these cysts will come to the attention of gynaecologists. Ovarian cysts may be discovered either as a result of screening, as a result of investigations performed for a suspected pelvic mass or incidentally following investigations carried out for other reasons.

Before ultrasound was routinely available, the finding of a pelvic mass or a palpable ovary² in a postmenopausal woman was considered to be an indication for surgery. However, the large numbers of ovarian cysts now being discovered by ultrasound and the low risk of malignancy of many of these cysts suggests that they need not all be managed surgically. The further investigation and management of these women has implications for morbidity, mortality, resource allocation and tertiary referral patterns and, hence, provides the need for clear guidelines in this area.

3. Identification and assessment of evidence

A search of Medline, Embase from 1966 to 2001 and of the Cochrane Database of Systematic Reviews was conducted, looking for relevant randomised controlled trials, meta-analyses, other clinical trials and systematic reviews. The databases were searched using the relevant MeSH terms including all subheadings. This was combined with a key word search using 'ovarian,' 'cyst,' 'neoplasm,' 'pelvic mass' and 'adnexal mass'.

The definitions of the types of evidence used in this guideline originate from the US Agency for Health Care Research and Quality. Where possible, recommendations are based on, and explicitly linked to, the evidence that supports them.

4. Diagnosis and assessment of ovarian cysts

The finding of an ovarian cyst in a postmenopausal woman raises two questions. First, what is the most appropriate management and, second, where should this management take place?

The appropriate location for the management should reflect the new structure of cancer care in the UK.^{3,4} As the risk of malignancy increases, the appropriate location for management changes, so that while a general gynaecologist might manage women with a low risk of malignancy, those at intermediate risk should be managed in a cancer unit and those at high risk in a cancer centre.

The first aim should be to triage women in order to decide the most appropriate place for them to be managed. A decision can then be made as to the most appropriate management.

B It is recommended that ovarian cysts in postmenopausal women should be assessed using CA125 and transvaginal grey scale sonography. There is no routine role yet for Doppler, MRI, CT or PET.

In order to triage women, an estimate needs to be made as to the risk that the ovarian cyst is malignant. This needs to be done using tests that are easily available in routine gynaecological practice. At present, these tests are serum CA125 measurement and ultrasound. Serum CA125 is well established, being raised in over 80% of ovarian cancer cases and, if a cut-off of 30 u/ml is used, the test has a sensitivity of 81% and specificity of 75%.⁵ Ultrasound is also well established, achieving a sensitivity of 89% and specificity of 73% when using a morphology index.⁶

Ovarian cysts should normally be assessed using transvaginal ultrasound, as this appears to provide more detail and hence offers greater sensitivity than the transabdominal method.⁷ Larger cysts may also need to be assessed transabdominally. It has also been suggested that colour-flow Doppler sonography may be of benefit in assessing ovarian cysts.⁸ However, subsequent studies have not consistently confirmed this, in particular finding that any small decrease in the false positive rate over greyscale ultrasonography was at the cost of a large drop in sensitivity.⁹ There is therefore not yet a clearly established role for colour-flow Doppler in assessing ovarian cysts in post-menopausal women.

Evidence level IIa

The roles of other imaging modalities, such as magnetic resonance imaging (MRI), computed tomography (CT) and positron emission tomography (PET), in the diagnosis of ovarian cancer have yet to be clearly established. One study indicated that MRI may be superior to CT and ultrasound in diagnosing an ovarian mass but there was no difference in the modalities' ability to distinguish between benign and malignant disease.¹⁰ In addition, in this study, there was little variation between the modalities in their ability to provide accurate staging. Another study found that ultrasound had greater sensitivity than either MRI or PET in distinguishing benign from malignant disease, at the expense of some specificity,¹¹ although the authors suggested that combining the imaging techniques may provide some overall improvement. However the lack of clear evidence of benefit, the relative expense and limited availability of these modalities, and the delay in referral and surgery that can result, mean that their routine use cannot yet be recommended.

B It is recommended that a 'risk of malignancy index' should be used to select those women who require primary surgery in a cancer centre by a gynaecological oncologist.

An effective way of triaging women into those who are at low, moderate, or high risk of malignancy and who hence may be managed by a general gynaecologist, or in a cancer unit or cancer centre respectively, is to use a risk of malignancy index. There are three well-documented risk of malignancy indices¹²⁻¹⁵ and Table 1 gives an example of one of these. This guideline is directed at postmenopausal women and therefore all will be allocated the same score for menopausal status.

Evidence level IIa

The best prognosis for women with ovarian cancer is offered if a laparotomy and full staging procedure is carried out by a trained gynaecological oncologist.¹⁴ This procedure is likely to be performed in a cancer centre. However, the large prevalence of ovarian cysts in the postmenopausal population and the increase in their diagnosis means that it would not be feasible

for all women with ovarian cysts that require surgery, whether benign or malignant, to be referred to a cancer centre. Women need to be triaged, so that a gynaecological oncologist in a cancer centre operates on those at high risk of having ovarian cancer, a lead clinician in a cancer unit operates on those at moderate risk, while those at low risk may be operated on by a general gynaecologist or offered conservative management. The high specificity and sensitivity of the risk of malignancy indices discussed makes them an ideal and simple way of triaging women for this purpose (Table 2 below gives an example of a reasonable protocol for triaging women using the risk of malignancy index, RMI). The three risk of malignancy indices produce similar results.¹⁵ Using a cut off point of 250, a sensitivity of 70% and specificity of 90% can be achieved. Thus the great majority of women with ovarian cancer will be dealt with by gynaecological oncologists in cancer centres, with only a small number of referrals of women with benign conditions. However, as most of the cysts will be benign, gynaecologists in units at more local level will perform the majority of surgery.

Evidence level IIa

It should be appreciated, however, that no currently available tests are perfect, offering 100% specificity and sensitivity. Ultrasound often fails to differentiate between benign and malignant lesions, and serum CA125 levels, although raised in over 80% of ovarian cancers, is raised in only 50% of stage I cases. In addition, levels can be raised in many other malignancies and in benign conditions, including benign cysts and endometriosis.

Those women who are at low risk of malignancy also need to be triaged into those where the risk of malignancy is sufficiently low to allow conservative management, and those who still require intervention of some form.

Table 1. Calculating the risk of malignancy index (RMI); these are modifications of the original RMI using modified scores

$$RMI = U \times M \times CA125$$

U = 0 (for ultrasound score of 0); **U** = 1 (for ultrasound score of 1); **U** = 3 (for ultrasound score of 2–5)

Ultrasound scans are scored one point for each of the following characteristics: multilocular cyst; evidence of solid areas; evidence of metastases; presence of ascites; bilateral lesions.

M = 3 for all postmenopausal women dealt with by this guideline

CA125 is serum CA125 measurement in u/ml

Table 2. An example of a protocol for triaging women using the risk of malignancy index (RMI); data from validation of RMI by Prys Davies *et al.*¹⁶

Risk	RMI	Women (%)	Risk of cancer (%)
Low	< 25	40	< 3
Moderate	25–250	30	20
High	> 250	30	75

5. Management of ovarian cysts

5.1. Conservative management

B Simple, unilateral, unilocular ovarian cysts, less than 5 cm in diameter, have a low risk of malignancy. It is recommended that, in the presence of a normal serum CA125 levels, they be managed conservatively.

Numerous studies have looked at the risk of malignancy in ovarian cysts, comparing ultrasound morphology with either histology at subsequent surgery or by close follow up of those women managed conservatively. The risk of malignancy in these studies of cysts that are less than 5 cm,

Evidence level IIa

unilateral, unilocular and echo-free with no solid parts or papillary formations is less than 1%.^{9,17-30} In addition, more than 50% of these cysts will resolve spontaneously within three months.²⁴ Thus, it is reasonable to manage these cysts conservatively, with a follow-up ultrasound scan for cysts of 2-5 cm, a reasonable interval being four months. This, of course, depends upon the views and symptoms of the woman and on the gynaecologist's clinical assessment.

Evidence level IIa

5.2. Surgical management

Those women who do not fit the above criteria for conservative management should be offered surgical management in the most suitable location, and by the most suitable surgeon as determined by the risk of malignancy index. Initial surgical management that has been assessed includes aspiration of the cyst, laparoscopy and laparotomy.

5.2.1. Aspiration

B Aspiration is not recommended for the management of ovarian cysts in postmenopausal women.

Cytological examination of ovarian cyst fluid is poor at distinguishing between benign and malignant tumours, with sensitivities in most studies of around 25%.^{31,32} In addition, there is a risk of cyst rupture and, if the cyst is malignant, there is some evidence that cyst rupture during surgery has an unfavourable impact on disease free survival.³³ Aspiration, therefore, has no role in the management of asymptomatic ovarian cysts in postmenopausal women.

Evidence level IIa

5.2.2. Laparoscopy

C It is recommended that a 'risk of malignancy index' should be used to select women for laparoscopic surgery, to be undertaken by a suitably qualified surgeon.

The laparoscopic management of benign adnexal masses is well established. However, when managing ovarian cysts in postmenopausal women, it should be remembered that the main reason for operating is to exclude an ovarian malignancy. If an ovarian malignancy is present then the appropriate management in the postmenopausal woman is to perform a laparotomy and a total abdominal hysterectomy, bilateral salpingo-oophorectomy and full staging procedure. The laparoscopic approach should therefore be reserved for those women who are not eligible for conservative management but still have a relatively low risk of malignancy. Women who are at high risk of malignancy, as calculated using the risk of malignancy index, are likely to need a laparotomy and full staging procedure as their primary surgery. A suitably experienced surgeon may operate laparoscopically on those women that fall below this cut-off point.

Evidence level IV

C It is recommended that laparoscopic management of ovarian cysts in postmenopausal women should involve oophorectomy (usually bilateral) rather than cystectomy.

In a postmenopausal woman, the appropriate laparoscopic treatment for an ovarian cyst, which is not suitable for conservative management, is oophorectomy, with removal of the ovary intact in a bag without cyst rupture into the peritoneal cavity. This is the case even when the risk of malignancy is low. In most cases this is likely to be a bilateral oophorectomy, but this will be determined by the wishes of the woman. There is the risk of cyst rupture during cystectomy and, as described above, cyst rupture into the peritoneal cavity may have an unfavourable impact on disease-free survival in the small proportion of cases with an ovarian cancer. Women at intermediate risk undergoing laparoscopic oophorectomy should be counselled preoperatively that a full staging laparotomy would be required if evidence of malignancy is revealed.

Evidence level IV

C If a malignancy is revealed during laparoscopy or subsequent histology, it is recommended that the woman is referred to a cancer centre for further management.

If an ovarian cancer is discovered at surgery or on histology, a subsequent full staging procedure is likely to be required.

Evidence level IV

B A rapid referral to a cancer centre is recommended for those women who are found to have an ovarian malignancy. Secondary surgery at a centre should be performed as quickly as feasible.

Secondary surgery should be performed as soon as feasible.³²⁻³³

Evidence level IIa

5.2.3. Laparotomy

All ovarian cysts that are suspicious of malignancy in a postmenopausal woman, as indicated by a high risk of malignancy index, clinical suspicion or findings at laparoscopy are likely to require a full laparotomy and staging procedure. This should be performed by an appropriate surgeon, working as part of a multidisciplinary team in a cancer centre, through an extended midline incision, and should include:³⁶

- cytology: ascites or washings
- laparotomy with clear documentation
- biopsies from adhesions and suspicious areas
- TAH, BSO and infra-colic omentectomy

The laparotomy and staging procedure may include bilateral selective pelvic and para-aortic lymphadenectomy.

Further details of the management of ovarian cancer are beyond the scope of this guideline. For example, some centres may make decisions about the extent of surgery on the basis of frozen section, according to local cancer centre protocol, and others may alter the timing of surgery in relation to chemotherapy in advanced cases, particularly with the advent of neoadjuvant chemotherapy.

In addition to the calculated risk of malignancy other factors will, of course, affect the decision as to whether a woman has surgery, what type of surgery is performed and where this takes place. These include a woman's anxiety, her desire to retain her ovaries and any other medical conditions affecting the risk of surgery.

6. Summary and suggested management protocol

LOW RISK: Less than 3% risk of cancer

- Management in a gynaecology unit.
- Simple cysts less than 5 cm in diameter with a serum CA125 level of less than 30 may be managed conservatively.
- Conservative management should entail repeat ultrasound scans and serum CA125 measurement every four months for one year.
- If the cyst does not fit the above criteria or if the woman requests surgery then laparoscopic oophorectomy is acceptable.

MODERATE RISK: approximately 20% risk of cancer

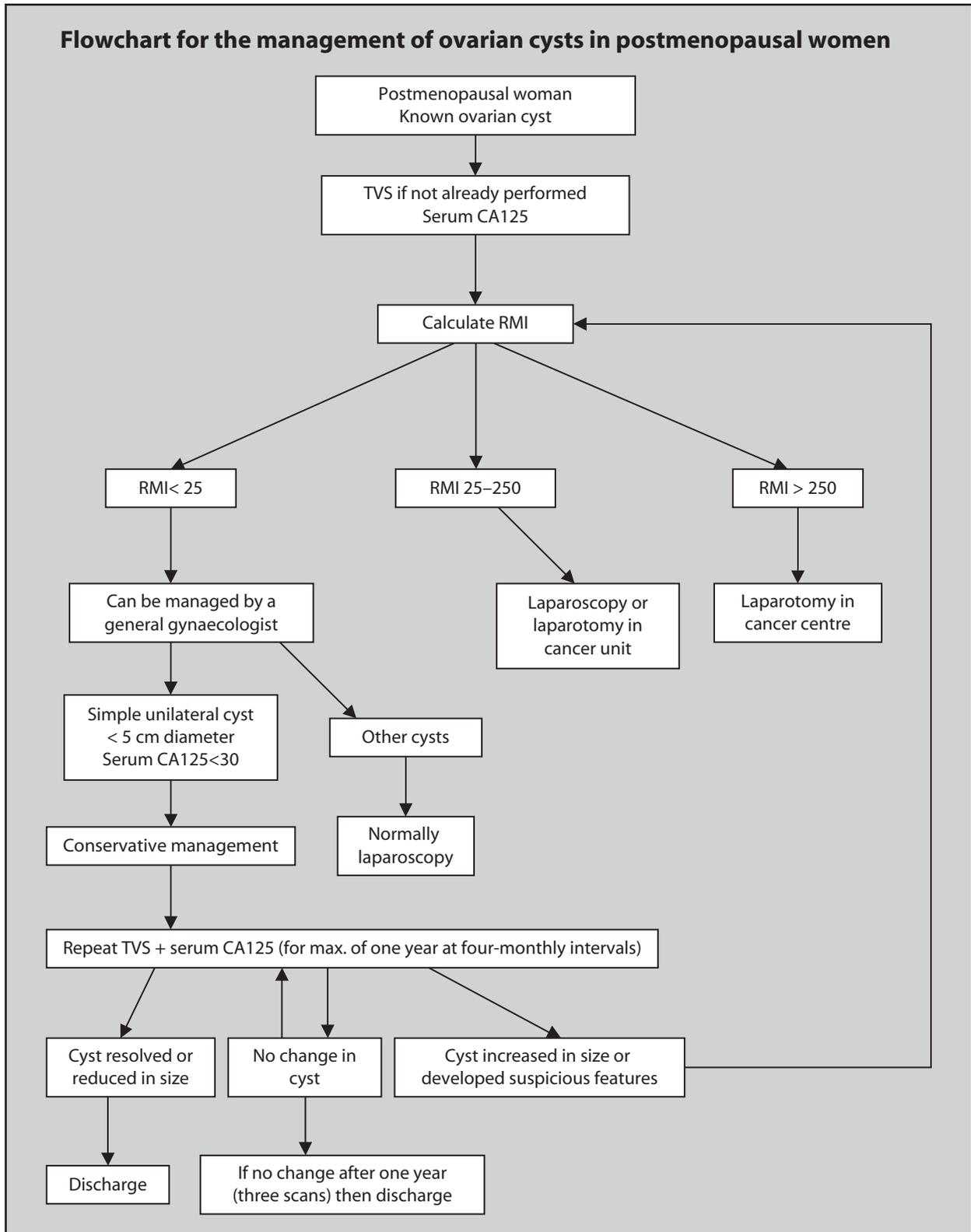
- Management in a cancer unit.
- Laparoscopic oophorectomy is acceptable in selected cases.
- If a malignancy is discovered then a full staging procedure should be undertaken in a cancer centre.

HIGH RISK: greater than 75% risk of cancer

- Management in a cancer centre.
- Full staging procedure as described above.

7. Topics suitable for audit

- The proportion of women undergoing preoperative investigations with ultrasound and serum CA125 levels with use of RMI.
- The proportion of women managed at the correct location (gynaecological unit, cancer unit, cancer centre) according to risk of malignancy.
- The proportion of women in the cancer network with ovarian cancer referred to the cancer centre from cancer or gynaecological units **before** surgery.



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APPENDIX

Clinical guidelines are: 'systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions'. Each guideline is systematically developed using a standardised methodology. Exact details of this process can be found in Clinical Governance Advice No. 1: *Guidance for the Development of RCOG Green-top Guidelines* (available on the RCOG website at www.rcog.org.uk/clingov1). These recommendations are not intended to dictate an exclusive course of management or treatment. They must be evaluated with reference to individual patient needs, resources and limitations unique to the institution and variations in local populations. It is hoped that this process of local ownership will help to incorporate these guidelines into routine practice. Attention is drawn to areas of clinical uncertainty where further research may be indicated.

The evidence used in this guideline was graded using the scheme below and the recommendations formulated in a similar fashion with a standardised grading scheme.

Classification of evidence levels		Grades of recommendations	
Ia	Evidence obtained from meta-analysis of randomised controlled trials.	A	Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. (Evidence levels Ia, Ib)
Ib	Evidence obtained from at least one randomised controlled trial.		
IIa	Evidence obtained from at least one well-designed controlled study without randomisation.	B	Requires the availability of well controlled clinical studies but no randomised clinical trials on the topic of recommendations. (Evidence levels IIa, IIb, III)
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study.		
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.	C	Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV)
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.		
		Good practice point	
			Recommended best practice based on the clinical experience of the guideline development group.

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The final version is the responsibility of the Guidelines and Audit Committee of the RCOG.

Valid until October 2006
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