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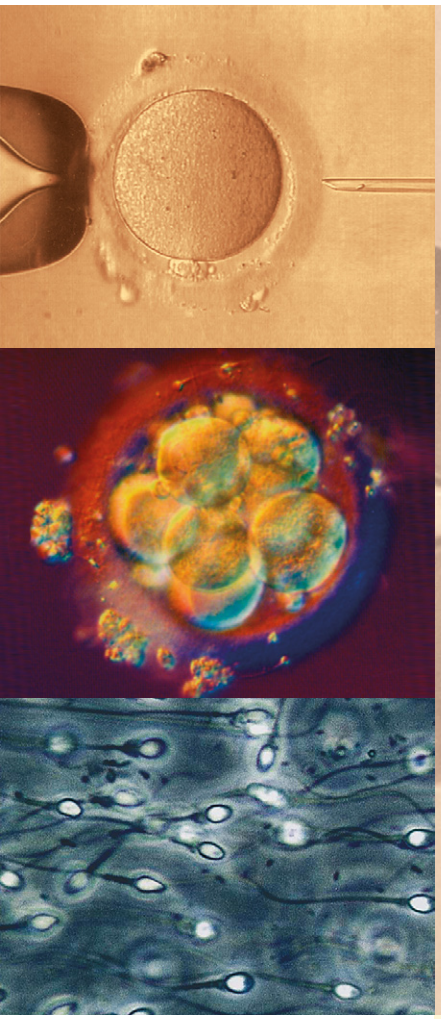

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Value of Malignancy Exclusion of Ovarian Cysts Prior to Laparoscopy

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Our aim was to evaluate the accuracy of preoperative tests for differentiating between benign and malignant ovarian cysts. We want to be able to detect cases of ovarian cancer at an early stage in order to give the most appropriate management and thereby decrease the mortality. ***J Reproduktionsmed Endokrinol 2008; 5 (2): 93–100.***

Key words: *laparoscopy, ovarian cysts, malignancy exclusion*

Ovarian cancer is one of the most frequent causes of death in the western world [1]. Every year, more than 5000 new cases are diagnosed in the UK and 22,000 in the United States. Four thousand women die each year of ovarian cancer in England and Wales and 13,000 die in the USA [2]. This poor prognosis is attributed to the fact that ovarian cancer is the "cancer that whispers" because it often occurs at menopause when ovaries have no physiological role and therefore abnormal ovarian function shows no clear-cut symptoms. If diagnosed at stage I (FIGO), when the disease is confined to the ovaries, the 5-year survival rate is > 80 %. Survival falls dramatically with each increasing stage of the disease with only a 10 % 5-year survival rate for stage-IV ovarian cancer [3].

The problem of early detection of ovarian cancer is intensified by the lack of detection of any one single screening tool which is specific, sensitive, non-invasive, easy to use and cost-effective. Recently, a significant amount of progress has been made in developing newer methods in ultrasound technology and a novel approach for interpreting Ca-125 results and other tumour markers has been studied. Amongst the new tumour markers a study of serum proteins (proteomics) is in progress and may lead to a breakthrough in the early detection of ovarian cancer. The purpose of this evaluation is to assess the current possibilities of pre- and intra-operative malignancy exclusion in the treatment of ovarian cysts.

Screening Tests

A test when used for the purpose of diagnosis at an early stage should have high sensitivity (probability of the test being positive in individuals with the disease) and high specificity (the probability of the test being negative in individuals without the disease). Unfortunately, an increase in the sensitivity of a test results in a reduction in specificity and vice versa [4]. It must also be remembered that although ovarian cancer is an important cause of mortality, it is still a relatively uncommon disease with an incidence no greater than 40 per 100,000 per year, even in postmenopausal women [5].

Therefore, any false positive test will result in a large number of surgeries and outweigh the benefits of early detection of ovarian cancer. Hence, specificity is an important consideration when deciding which test is best for diagnosis. To have a 10 % predictive value, a screening test for ovarian cancer should have a specificity of 99.6 %. This is a challenge for any one single test or marker and explains the need to combine various predictive factors.

Another requirement is to find a test which not only detects apparent ovarian cancer but detects it at an early stage of the disease. Many tumour markers have a high sensitivity for diagnosed cases of ovarian cancer [6]; but only a few have high sensitivity for the preclinical disease. Thus, an important parameter is the positive marker in the preclinical phase which at present is difficult to study. Maybe ongoing prospective trials will show encouraging results. Different modalities and tests are used to detect ovarian cancer in asymptomatic women which will be discussed in this article.

Vaginal Examination

Pelvic manual examination can detect ovarian cysts only in larger tumour masses. This is because of the deep anatomic location of the ovaries. Also, if detected, ovarian cysts are almost certainly at an advanced stage and therefore associated with a poor survival rate.

Tumour Markers

Non-invasive tests are more acceptable in a screening programme [4] and therefore many tumour markers for ovarian cancer have been investigated. Ideally, a tumour marker should be able to detect a subclinical disease, be useful in monitoring response to treatment and be able to identify early recurrence so that further treatment can be given.

There are various tumour markers, but the most useful tumour marker to date is Ca-125. Ca-125 is the antigenic determinant of a glycoprotein expressed by epithelial ovarian tumours and other tissues of Mullerian origin. It is recognised by a mouse monoclonal antibody. It is the most commonly used test in prospective studies for monitoring clinically diagnosed ovarian cancer. Serum levels of Ca-125 have been found to be elevated in 50 % of patients with stage-I disease and 90 % of those

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with stage-III epithelial ovarian cancer [7].

Unfortunately, the measurement of Ca-125 is neither specific nor sensitive for early detection of ovarian cancer. In stage-I disease, high tissue expression of Ca-125 antigen is found in 90 % of cases, but elevation is present in < 50 % of cases (normal < 35 U/ml) [8]. Elevation of serum Ca-125 levels is related more closely to factors influencing the release of the antigen into the circulation.

In addition, Ca-125 is elevated in conditions showing an alteration in normal tissue barriers, such as in fibroids, endometriosis, menstruation, haemorrhagic ovarian cysts, pregnancy (first trimester) and non-gynaecological conditions, such as acute pancreatitis, cirrhosis of liver and pericarditis. It is important to remember that the above conditions are infrequent in postmenopausal women who form the target population for ovarian cancer screening.

Despite the above problems there are a number of encouraging evidences of Ca-125. In the JANUS study, a retrospective analysis of stored serum from 39,300 healthy women, samples were tested for Ca-125. Ca-125 was elevated in 105 cases and the incidence of ovarian cancer in this population over a 12-year follow-up was 8.8 cases per year. Of the 195 women who developed ovarian cancer, Ca-125 levels were elevated 18 months before diagnosis [8].

In another study, 5500 healthy volunteers in Stockholm were examined for serial Ca-125, pelvic examination and ultrasound (TAS). Six cases were detected to have ovarian cancer and all were postmenopausal women [9]. Five of the 6 cases had a doubling of Ca-125 over the course of one year. It is important to assert that the rate at which Ca-125 levels increase is a more accurate method of detecting ovarian cancer than a single test. Also, the degree of elevation is an important marker. Minor elevations (35–50 U/ml) and levels that oscillate up and down are more likely to be associated with benign disease [8].

Considering this approach to improve sensitivity led to the development of a mathematical algorithm for interpretation of the pattern of change in Ca-125. Skates et al described this observation in a Risk of Cancer (ROC) algorithm which achieved both high sensitivity and specificity [10].

The same algorithm was applied in the London study examining 22,000 women. It confirmed the improvement in performance over interpretation of absolute levels alone.

In another UK study, Ca-125 was used as a first-line test with ultrasound as a second-line test if Ca-125 was abnormal. This multimodal approach achieved a specificity of 99.9 % and a sensitivity of 78 % and a positive predictive value of 26.8 % at one-year follow-up [11].

Despite these results Ca-125 has lower specificity in premenopausal than in postmenopausal women. It is not recommended for use alone as an early detection method of ovarian cancer. Combining it with transvaginal ultrasound lowers the number of false positive results.

Search for New Tumour Markers

Development in this field is ongoing. It has been found that a new substance, lysophosphatitic acid (LPA), stimulates proliferation of ovarian cancer cells and it has been found in fluids of ovarian cancer patients. Studies comparing Ca-125 and LPA in detection of ovarian cancer are being carried out.

One such study was carried out at the Cleveland Clinic in 1998 where LPA levels were investigated in 48 healthy women (control), 48 women with ovarian cancer, 36 with other gynaecological cancers, 17 with benign gynaecological disease, 11 with breast cancer and 5 women with leukaemia. Elevated plasma levels of LPA were detected in 9 out of 10 patients with stage-I ovarian cancer and in 24 out of 24 patients with stage-II, -III, and -IV cancer. Women in the ovarian cancer group had significantly higher levels of LPA. The researchers, however, stressed that these were preliminary results and ongoing studies will determine the use of LPA as a potential biomarker for ovarian cancer [12].

Prostasin is another new marker and is a serine protease normally secreted by the prostate gland. The combination of Ca-125 and prostasin in 37 patients with non-mucinous ovarian cancer and 100 control subjects resulted in a sensitivity of 92 % and specificity of 94 % in detection of ovarian cancer [13]. Osteopontin, identified by exploiting gene expression profiling techniques, is another new biomarker still being investigated.

Ki-OC-III was once our most successful monoclonal antibody [14] which selectively reacted with ovarian carcinoma but it was never further commercialized.

Ultrasound

A considerable amount of progress has been made using ultrasound to view ovaries and their abnormalities. In fact, greater use of ultrasound has increased the proportion of diagnosing ovarian cysts and thereby alerting gynaecologists. Ovaries can be visualized in more than 95 % of premenopausal women and in up to 85 % of postmenopausal patients.

In the past, transabdominal ultrasound (TAS) was extensively used and when evaluated prospectively in 5540 women had a high false positive rate of 5.4 % [15]. Of these false positive cases, 25.7 % had no ovarian pathology at a diagnostic operation. Various other trials using TAS (Tab. 1) were performed: specificity

Table 1. Value of transabdominal ultrasound for diagnosis of malignancy in adnexal mass

Authors	Patients (n)	Malignant tumours (n)	Specificity (%)	Sensitivity (%)
Herman et al [16]	304	50	94	82
Finkler et al [17]	106	37	95	62
Benacerraf et al [18]	100	30	87	80
Jacobs et al [19]	139	41	83	71
Buy et al [20]	108	43	92	60
Luxman et al [21]	102	29	42	93
Total	859	230	78	74

Table 2. Value of transvaginal ultrasound in diagnosis of malignancy in adnexal masses

Authors	Patients (n)	Malignant tumours (n)	Specificity (%)	Sensitivity (%)
Granberg et al [22]	50	16	82	100
Sassone et al [23]	143	13	83	100
Kurjak et al [24]	83	29	98	48
Hata et al [25]	63	27	69	85
Weiner et al [26]	53	17	69	94
Kawai et al [27]	109	40	65	90
Total	501	142	79	83

varies between 42–95 % and sensitivity between 60–93 % [16–21]. Thus, it is quite evident that it is difficult to distinguish between benign and malignant ovarian cysts using TAS.

However, with the advent of transvaginal ultrasound (TVS) it is easier to visualize ovaries as the method offers better resolution and thus greater sensitivity than transabdominal scanning. Efforts have been made to study the information obtained by TVS and thereby devise a morphological index which scores the findings, giving a risk of malignancy estimation. These criteria include internal borders, type of cysts, presence of septa, papillary projections, ovarian tissue echogenicity and ovarian volume, with cut offs of volume ranging from 10–20 ml, depending on menopausal status. Using TVS, a fair number of trials have been performed (Tab. 2). In these studies, it can be seen that TVS alone had a specificity varying between 65–98 % and a sensitivity between 48 and 100 % [22–27].

A long-standing trial was performed by van Nagell et al at the University of Kentucky in which they prospectively studied the efficacy of annual TVS in asymptomatic women deemed to be at risk for ovarian cancer [28].

The study population consisted of 14,469 asymptomatic women ≥ 50 years or ≥ 30 years of age with a family history of ovarian cancer. All women with abnormal TVS underwent a repeat sonogram 4–6 weeks later and if the abnormality persisted, surgery was recommended. In the 180 patients with persistent TVS abnormality who underwent exploratory laparotomy, 17 ovarian cancers were detected, 14 of which were stage I or II in diagnosis. Of the group without TVS abnormalities, 4 patients developed ovarian cancer within one year of negative scan, 2 of whom were at an early stage and 2 at an advanced stage.

Thus, in this study, TVS was associated with a sensitivity of 81 % and a specificity of 98.9 %. There was a positive predictive value of 9.4 % and negative predictive value of 99.9 %. Of the total 46,113 screening years there were 3 ovarian cancer deaths in the annually screened population. This study provides good evidence that TVS screening in the general population may be effective in detecting ovarian cancer when performed annually and may contribute to a decreased mortality from ovarian cancer.

However, the only concern is that the predictive value of any ultrasonographic investigation is correlated directly with the operator's experience and the degree of exactitude with which the criteria of malignancy are defined [14]. Also, the low positive predictive value is not acceptable when it comes to cost effectiveness and patient acceptance. Hence, TVS alone is not recommended as a single test for detection of ovarian cancer and should be combined with Ca-125 measurements for promising results [29–33].

Colour Doppler

Neo-vascularisation is an obligate early event in tumour growth and neoplasia. Fast-growing tumours contain many new vessels which have less resistance to blood flow when compared to vessels in benign ovarian tumours.

Transvaginal colour Doppler simultaneously evaluates the morphologic aspects of an area of interest and also the blood flow within the uterus and adnexa. It can depict the relative impedance and velocity of flow within the vessels. Thus, it is possible to differentiate between vascular beds containing normal arterioles (resulting in relative high-impedance low-viscosity flow) from tumour beds with arteriolar venous shunting with a paucity of muscular media (resulting in low-impedance high-velocity flow). In various trials, the pulsatility index (PI)

$$PI = \frac{systolic\ peak - diastolic\ peak}{mean}$$

was used with the lowest pulsatility index taken as an indication of malignancy. Other vascular criteria, such as the resistance index (RI) were also analysed and the best cut-off value determined.

In a series of less than 680 tumours, Kurjak and Zalud found an RI of less than 0.4 in only one of 624 benign tumours, whereas an RI of less than 0.4 was found in 54 of 56 malignant tumours [34]. Fleischer et al examined 206 women using endovaginal colour flow Doppler; 164 patients were diagnosed as having an adnexal mass and 126 women underwent surgical removal. Of these, 26 were ovarian cancers. The overall sensitivity of endovaginal colour Doppler was 92 % and specificity 86 % [35]. Other authors, such as Weiner et al, have also suggested that a pulsatility index of < 1 points to malignancy [26].

Although Doppler studies appear to yield better results, there are a number of difficulties. Firstly, for a given tumour the flow varies according to the point at which it is recorded. Secondly, there can be an overlap in vascular resistance between two groups of tissue which prevents reliable separation of malignant from benign tumours. Finally, the optimal parameters and cut-off levels for pulsatility and resistance index which would predict malignancy have been difficult to define. Also, the cost of the equipment and the experience requirements may limit its universal application.

Other Imaging Modalities

The role of magnetic resonance imaging (MRI), computed tomography (CT) and positron emission tomography (PET) in the early diagnosis of early ovarian cancer has yet to be clearly established.

Table 3. Calculating the risk-of-malignancy index (RMI). Using a cut-off point of 250 u/ml, a sensitivity of 70 % and specificity of 90 % can be achieved as reported by Oram et al [37] (Tab. 4).

RMI = U × M × Ca-125

U = 0 (ultrasound score of 0); U = 1 (ultrasound score of 1); U = 3 (ultrasound score of 2–5). Ultrasound scans score one point each for the following characteristics: multilocular cysts, evidence of solid areas, evidence of metastases and presence of ascites bilateral lesions.
M = 3 for all postmenopausal women
Ca-125 is serum Ca-125 measurement in u/ml

Table 4. Protocol for triaging women using risk of malignancy by Oram et al [37]

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

In one study, MRI was found to be superior to CT and ultrasound in diagnosing an ovarian mass; but there was no difference in the modalities' ability to distinguish between malignant and benign disease. Recently, some studies have shown that the three-dimensional power Doppler examination may be more accurate than the two-dimensional ones. However, due to lack of clear evidence, relative expense and limited availability, these modalities are not routinely recommended.

Multimodal Approach

A multimodal screening approach involves a combination of tests and increases the sensitivity for early detection of ovarian cancer. A combination of serum tumour markers or computer modelling trends in serum markers, together with palpation and ultrasound, offers the best prerequisite for early diagnosis of ovarian cancer as well as high specificity and sensitivity [15].

Using multimodal screening, which involved sequential Ca-125 levels and pelvic ultrasound, a specificity of 99.9 % and positive predictive value of 26.8 % for the detection of ovarian and fallopian tube cancers was achieved in 22,000 postmenopausal women by Jacobs et al [36].

Ovarian cancer treatment is advised according to the risk category the patient belongs to. There are 3 well-documented risk-of-malignancy indices. Table 3 shows an example of one of these [37]. The patient's ultrasound findings, menopausal status and Ca-125 levels are scored.

A summary of trials using the multimodal strategy is given in Table 5 [36, 38–41].

Applying this method, it may be possible to predict with high accuracy the probability of ovarian malignancy in a patient with an ovarian mass, particularly among postmenopausal women.

Kiel Results

A total of 455 patients underwent laparoscopic treatment for benign adnexal masses in the period from 2003–2005 and a total of 480 cystic masses were removed. The age of the patients ranged from 16–73 years (Fig. 1). Sixty-eight percent of the patients were in the reproductive age group, with the highest number in the age group 31–40 years (37 %). The median age was 35 years.

Table 5. Trials using multimodal approach for diagnosis of ovarian cancer

Study	Features and screening strategy	Patients screened (n)	Positive screens (n)	Operations for cancer (n)
Jacobs et al [36, 38]	Age ≥ 45 yrs, postmenopausal Serum Ca-125 TAS if Ca-125 increase	22,000	41	3.7
Jacobs et al [39]	Age ≥ 45 yrs, postmenopausal RCT, Serum Ca-125 TAS/TVS if Ca-125 increase	10,958 (3 annual screens)	29	4.8
Grover et al [40]	Age ≥ 40 yrs or with family history Serum Ca-125 TAS/TVS if Ca-125 increase	2550	16	16
Adonakis et al [41]	Age > 45 yrs Serum Ca-125 TVS, if Ca-125 increase	2000	15	15

The main indication for surgical intervention was attributable to ultrasound features of a persistent or significantly large adnexal mass (27 %), as shown in Figure 2, followed by symptomatic or complicated adnexal mass (20 %). Many patients were referred by their physician to our department with a prior diagnosed adnexal mass.

A total of 212 patients had undergone previous abdominal or pelvic surgery prior to laparoscopy. The median number of prior abdominopelvic procedure was zero, with a range of 0–6. In addition, 2.4 % of patients had undergone a previous hysterectomy, while 2.9 % underwent concurrent hysterectomy with this laparoscopy.

Of the patients, 57.8 % were nulliparous and the median parity was also zero, with a range of 0–5 (Fig. 3). The major medical risk factors in this series were hypertension and obesity, while 91.4 % of the cases analysed had no associated medical morbidities.

Laparoscopic diagnosis of simple cysts was made in 185 patients (40.7 %). This category includes serous, simple, functional and retention cysts (Fig. 4). Laparoscopy correctly identified 3 malignant masses in this series of reports (100 %). Six cases of borderline ovarian tumours were identified at laparoscopy, 4 of which were confirmed by frozen section and subsequently by histology. Two were reported benign (cystadenomas), one of which was later confirmed malignant by histology having been missed by frozen section. The patient was further appropriately managed as such.

Duration of surgery ranged between 20 and 210 minutes, the median duration being 70 minutes (Fig. 5). Of the surgical procedures, 69 % were accomplished between 30 and 90 minutes.

Various laparoscopic procedures were carried out, as influenced by patient's age, reproductive desires and nature of disease. In this review, cystectomy was performed in 297 patients (66.3 %), both intact cystectomy and fenestration of cyst wall (Fig. 6) and 22.3 % had bilateral or unilateral adnexectomy. The pre-

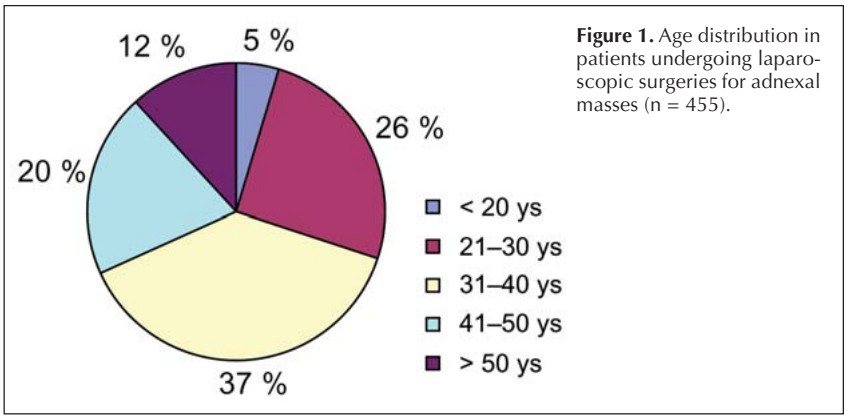

Figure 1. Age distribution in patients undergoing laparoscopic surgeries for adnexal masses (n = 455).

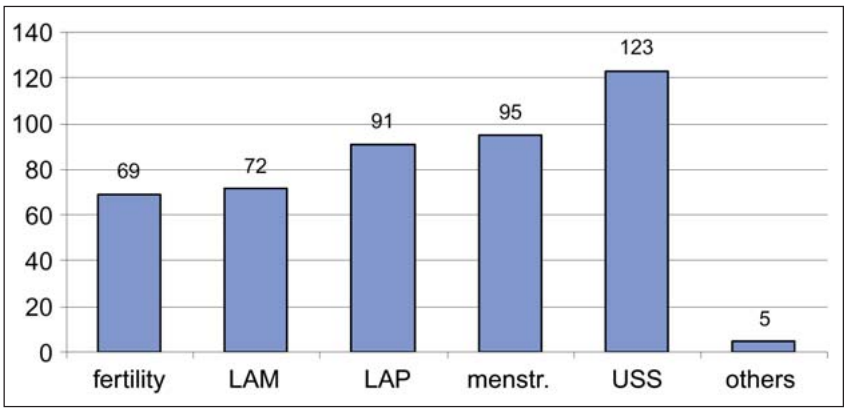

Figure 2. Distribution of patient's symptomatology and indications for laparoscopic treatment. (USS: routine ultrasound screening; menst.r: menstrual disorders; LAP: lower abdominal pain; LAM: lower abdominal mass and fertility disorders; n = 455)

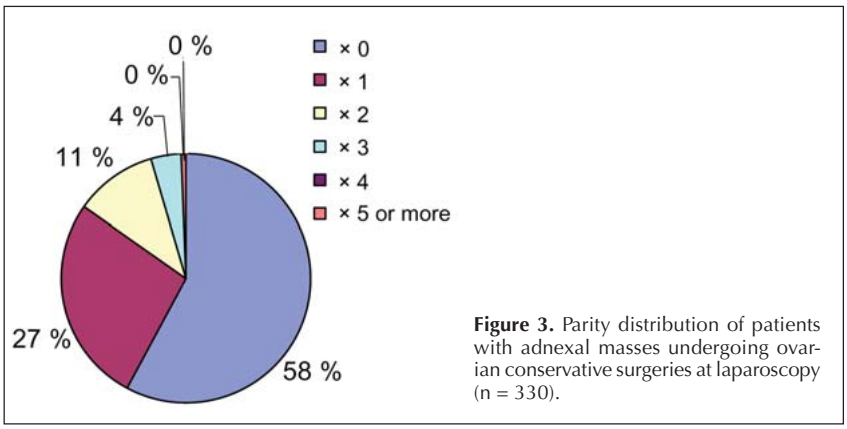

Figure 3. Parity distribution of patients with adnexal masses undergoing ovarian conservative surgeries at laparoscopy (n = 330).

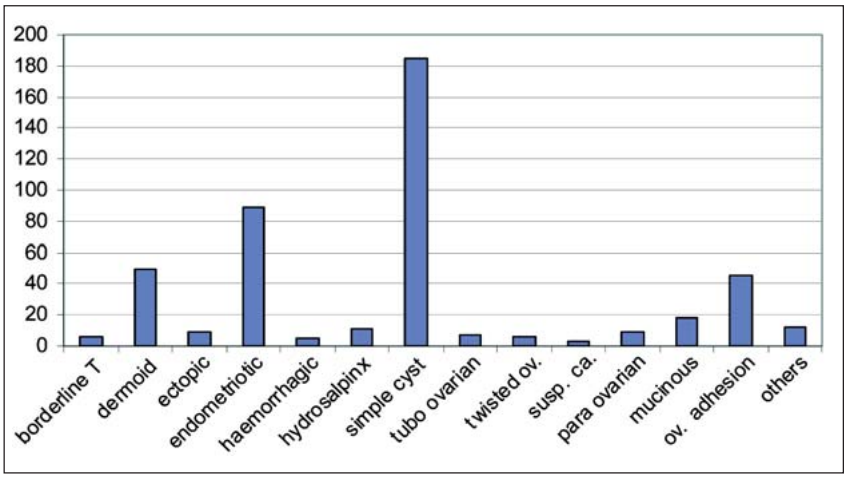

Figure 4. Laparoscopic diagnosis of adnexal mass (n = 455).

operative mass sizes ranged between 3.2 and 10 cm. The majority of the masses were between 4–8 cm, i.e. 260 patients (57.1 %). The mean maximum diameter was 4.8 cm.

A total of 398 patients (87.5 %) were premenopausal in status. In this period, only 50 surgical operations were carried out by trainee resident surgeons (11 %) while 405 cases (89 %) were performed by various specialist gynaecologists at consultant or intermediate level. Estimated blood loss was less than 250 ml in 98.2 % of patients. Hospital stays ranged from 1 to 7 days postoperatively. About 85 % of the patients were discharged home within 48 hours following the procedure.

There were 2 cases of re-exploration postoperatively following bleeding, one from divided adhesions between leaves of broad ligament and the other from the adhesiolysis site between omentum and anterior abdominal wall. Both patients had an uneventful recovery. There was one case of injury to the inferior epigastric vessels which was treated intraoperatively. There were 3 cases of readmission, for postoperative ileus which were managed conservatively, and an umbilical incision wound infection which was treated with antibiotics and local antiseptics. There was also a case of a 71-year-old patient who developed mental illness, depressive personality changes and anorexia on post-operative day 8. A detailed explanation was not explicitly given for her symptomatology. There were no cases of anaesthetic or surgical deaths. The overall complication rate was 1.3 %.

Conversion to laparotomy was required in 18 patients (3 of whom were mini-laparotomies) for reasons of malignancy (n = 5; 1.1 %), technical difficulty because of the large size of the tumours (n = 6; 1.3 %), dense adhesions (n = 5; 1.1 %) and bleeding (n = 2; 0.4 %). The overall conversion rate to laparotomy was 3.96 %.

There were 64 cases of rupture of cystic mass and spillage which accounted for 14 % of cases. As this was the highest untoward outcome in this series, significant association was sought for amongst predictor variables like size of cyst, hysterec-

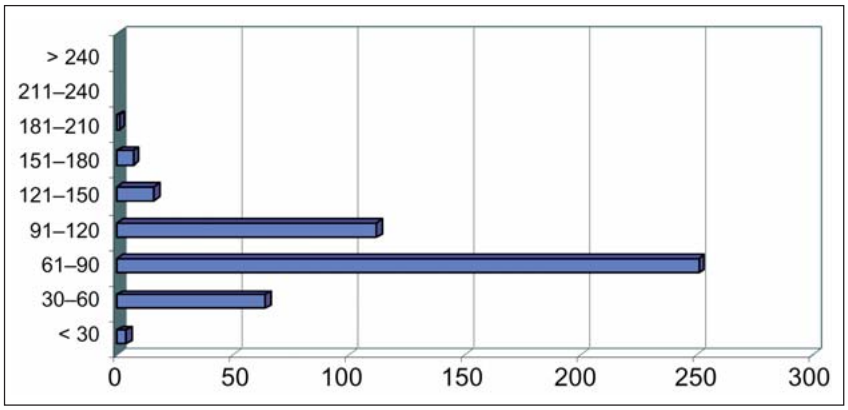

Figure 5. Distribution of duration of laparoscopic surgery in minutes on the Y-axis and the corresponding number of cases on the X-axis (n = 455).

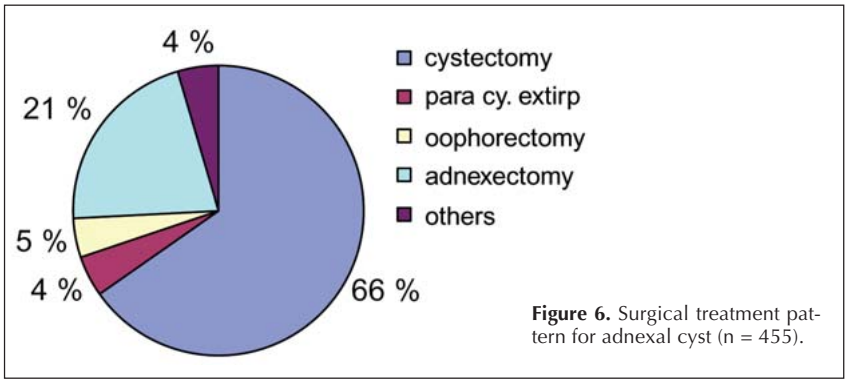

Figure 6. Surgical treatment pattern for adnexal cyst (n = 455).

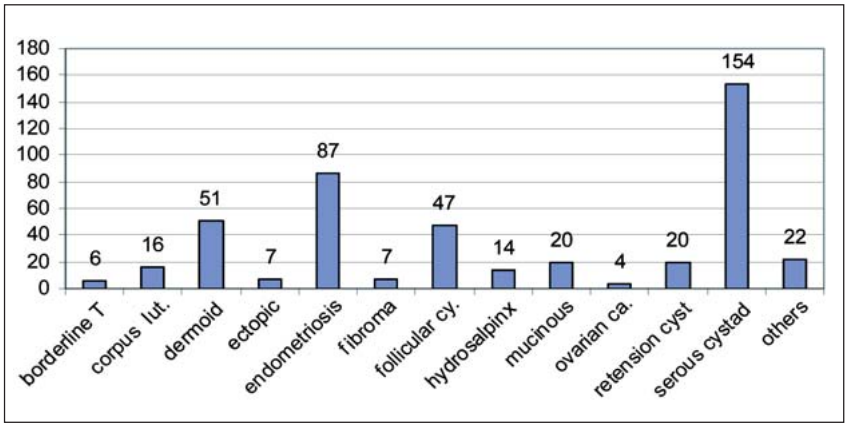

Figure 7. Pattern of histological diagnosis of adnexal masses (n = 455).

tomy status, presence of medical comorbidities, cadre of surgeons, menopausal status, operative findings of moderate to severe pelvic adhesions and previous surgery. Intraoperative rupture of cystic masses was significantly associated with prior and concurrent hysterectomy ($p < 0.001$; OR 8.81 with 95 %-CI: 4.22, 18.37), for trainee surgeon ($p < 0.001$; OR 53.89 with 95 %-CI: 30.55, 95.06), for size of mass ($p = 0.001$; OR 3.1 with 95 %-CI: 1.80, 5.37) and for pelvic adhesions ($p = 0.029$; OR 2.59 with 95 %-CI: 1.2, 4.70). There were no significant correlations with any other variables.

Histological reports revealed 445 benign tumours (97.8 %) while 10 cases were malignant or premalignant (Fig. 7). The 4 malignant cases were ovarian serous cystadenocarcinoma, 2 were stages 1c and the other 2 were stages 2a. 66 % of patients were treated by laparoscopic ovarian cyst enucleation (Fig. 6).

Transvaginal ultrasound revealed to be the primary imaging method for evaluating adnexal masses and is more reliable than the use of Ca-125 [24]. In this present study, ultrasound accurately identified 445 benign adnexal masses (97.8 %). In 10 patients (2.2 %), who had either a malignant or borderline tumour, the ultrasound report indicated a benign mass. This is similar to earlier reported series in this and many other centres [42–44].

Ongoing Trials for Ovarian Cancer Screening

The United Kingdom Collaborative Trial of Ovarian Cancer (UKCTOCS)
The trial started in January 2001 and should include 200,000 postmenopausal women aged 50–74 years. The women were randomised to ultrasound screening, multimodal screening and sequential Ca-125 tests followed by 1:1:2 ratios. Women will be tested annually 6 times and follow-up will continue for 7 years. This 10-year trial will not only investigate the impact of screening on mortality but also factors, such as target population, compliance, health economics and physical and psychological morbidities.

The NIHPLCO Study
This study aims to randomise 74,000 women > 60 years to either a control or a screening group which will undergo pelvic examination, ultrasound scanning and Ca-125 measurements. A positive result on testing initiates a referral to a gynaecological oncologist for further management.

The St Bartholomew's Hospital Study
A randomised controlled trial which will include 120,000 healthy postmenopausal women > 50 years in the UK. Women randomised to screening will undergo annual Ca-125 measurements and the results will be interpreted using the ROC algorithm described by Skates et al. Women with an elevated risk of ovarian cancer will be recalled for a TVS scan and will be referred for surgery if the results are abnormal.

Meta-Analysis (data published in 2006 and ongoing data collection)
In a meta-analysis [45], the major diagnostic methods evaluated were bimanual pelvic examination, ultrasound (morphology and Doppler velocimetry), MRI, CT, FDG-PET, Ca-125 and scoring systems that incorporated multiple clinical, laboratory and radiologic findings. A meta-analysis using a random effects

model was used to estimate pooled sensitivity and specificity for discriminating benign from malignant. Published models of the natural history of ovarian cancer were reviewed and the impact of assumptions about natural history on outcomes was detected.

Altogether, most diagnostic modalities showed trade-offs between sensitivity and specificity, but the available literature does not provide sufficient detail on relevant characteristics of study populations to allow confident estimation of the results of alternative diagnostic strategies. Although modelling studies may prove useful in evaluating diagnostic algorithms, further work is needed to explore the implications of uncertainty about the natural history of ovarian cancer.

Summary

Preoperative screening of every ovarian cyst is decisive for the following surgical intervention, particularly for laparoscopic ovarian cyst enucleation [46, 47]. It should be appreciated that in ovarian cyst malignancy exclusion there is no currently available test which is perfect and offers 100 % specificity and sensitivity. It is difficult to establish standards for early diagnosis. Triaging women with the use of risk of malignancy indices helps to identify women at low, moderate and high risk [37]. The multimodal strategy is promising and cost-effective. However, larger randomized controlled trials are being carried out and more research must be done to identify the premalignant phase of ovarian cancer.

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