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# Ovarian cancer: the clinical role of US, CT, and MRI

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**Abstract** This article presents an overview of ovarian cancer, which addresses the clinical roles of imaging studies, including US, CT, and MR imaging in the course of diagnosis and treatment of this important disease. US is the modality of choice in the evaluation of patients with suspected adnexal masses. Although its accuracy is not sufficient to avert surgery, morphological analysis of adnexal masses with US helps narrow the differential diagnosis, determining the degree of suspicion for malignancy, usually in concert with a serum CA-125 level. Combined morphological and vascular imaging obtained by US appear to further improve the preoperative assessment of adnexal masses. For uncertain or problematic cases, MR imaging helps to distinguish benign from malignant, with an overall accuracy for the diagnosis of malignancy of 93%. The accuracy of MR imaging in the confident diagnosis of mature cystic teratoma, endometrial cysts, and leiomayomas is very high. CT is not indicated for differential diagnosis of adnexal masses because of poor soft tissue discrimination, except for fatty tissue and for calcification, and the disadvantages of irradiation. In the staging of ovarian cancer, CT, US, and MR imaging all have a similarly high accuracy. Although it is difficult to suggest a simple algorithm for evaluating the state of women with adnexal masses, the correct preoperative diagnosis and staging of ovarian cancer with the use of any of these imaging studies will lead to an appropriate referral to a specialist in gynecologic oncology and offer a significant survival advantage for patients with ovarian cancer.

**Keywords** Ovary neoplasm · US · CT · MR

## Introduction

Ovarian cancer is the second most common gynecologic malignancy, but has the highest mortality rate of all of the gynecologic malignancies with an overall 5-year survival rate of 46% [1]. Despite diagnostic and therapeutic advances in the care of women with ovarian cancer, the overall 5-year survival rate has changed little [1, 2, 3]. The major reason for this poor prognosis is that, at the time of diagnosis, approximately 75% of patients have diseases that are at an advanced stage [1, 2]. Because of the obvious significant differences in prognoses between early and advanced cancers, early detection with accurate staging is of paramount importance. The purpose of this article is to review the clinical role of imaging studies in ovarian cancer screening, in the evaluation of suspected adnexal masses, ovarian cancer staging, and recurrent tumor identification. We also introduce a clinical background that facilitates an understanding of this important issue, in addition to current investigations.

## Epidemiology

A total of 1.4% of all women will develop ovarian cancer during their lifetime compared with 11.1% for breast cancer [4, 5]. There is a high mortality rate in all gynecologic malignancies, with ovarian cancer being the main cause of death among gynecologic malignancies. Women with ovarian cancer have poor overall survival rates, largely because the disease is often detected at an advanced and less curable stage. The survival rate for patients with localized disease is 93%, whereas for regional and advanced diseases it is 55 and 25%, respectively [1].

The incidence and mortality rate of ovarian cancer increases with age. Risk factors are nulliparity, low parity, delayed childbearing, early onset of menses, late menopause, postmenopausal estrogen use for 10 or more years, and a family history of ovarian or breast cancer. The strongest risk factor for ovarian cancer is familial evidence of ovarian cancer, as reported in 3–7% of patients [6]. The American College of Radiology (ACR) recommends that women with a positive family history and a familial tendency for ovarian cancer should consult specialists in their early twenties about their risk, and undergo an actual clinical follow-up in their thirties [4]. A prophylactic bilateral oophorectomy is even recommended for women from families with a history of ovarian cancer and with BRCA mutations by the age of 35 years.

## Screening test

Ovarian cancer is a "silent" disease. The preclinical phase of ovarian cancer is estimated to be less than 2 years [4]. As noted by Scully, it appears that most ovarian cancers (particularly serious ones) develop as de novo sources, making early detection very difficult [7]. A negative US study is imperfect, and it is generally accepted that some women develop to an advanced stage of ovarian cancer within 12 months of a normal scan. A negative CA-125 is also imperfect, and, at the same time, a high false-positive rate persists with CA-125 and US techniques alone or in sequence. Although CA-125 is elevated (>35 U/ml) in more than 80% of patients with epithelial ovarian cancer, it is only 25% sensitive toward early disease [5, 6]. The level of CA-125 fluctuates following the menstrual cycle with more than 90% of findings being false-positive in premenopausal women. CA-125 can be elevated in many clinical conditions, including both malignancies and benign conditions (pregnancy, endometriosis, leiomyomas, and pelvic inflammatory diseases), or even just with the presence of peritoneal fluid; however, in postmenopausal women, we should be careful as levels exceeding 65 U/ml are predictive of malignancy in 75% of women with pelvic masses [4].

There is no evidence available that the currently used screening modalities of CA-125 and transvaginal US are effective for widespread screening in reducing mortality from ovarian cancer, nor that their use decreases rather than increases morbidity and mortality [8]. The detection rate of ovarian cancer is low, and a cost–benefit analysis of screening for epithelial ovarian cancer using CA-125 and US techniques, even in women at high risk for the disease, has indicated that routine screening is not cost-effective at present [6]. The efficacy of a screening program could only be established after a mega-study involving over 100,000 women carried out for a period of 15–20 years.

Although the efficacy of mass screening is not well established, women with three known hereditary syndromes (familial site-specific ovarian cancer syndrome, breast ovarian cancer syndrome, and Lynch syndrome) are at exceedingly high risk, and are recommended to have annual examinations with CA125 and transvaginal US [8]. In addition, even before the completion of a large study to evaluate the efficacy of mass screening, certain statements concerning transvaginal US screening for early stage ovarian cancer have been made and well accepted [9]. Transvaginal US can detect early stage ovarian cancer. Transvaginal US is better than pelvic examinations or CA-125 [9]. To identify early stage ovarian cancer with reasonable accuracy, the age of patients, their family history, their serum level of CA-125, and US findings should always be taken into account simultaneously.

## Imaging evaluation of suspected ovarian cancer

Analysis of ovarian masses: benign vs malignant

Transabdominal US, transvaginal US, or both are the modalities of choice in the evaluation of suspected adnexal masses. Transvaginal US has a markedly improved resolution and is essential for imaging adnexal masses. The follow-up examination is also very helpful for evaluating adnexal masses. If the lesion regresses or remains the same size, the lesion may be a functional cyst. US can help narrow the differential diagnosis, although it cannot always distinguish malignant from benign masses with an accuracy sufficient to avert surgery.

Adnexal masses are practically classified on US as simple cystic masses (which are anechoic with smooth thin walls and no internal architectures), solid, or complex adnexal masses [10]. The sonographic identification of a simple cystic mass indicates a benign process in 100% of premenopausal women and in 95% of postmenopausal women [11]. Even in postmenopausal women, cysts are identified at a frequency of 17%, which usually disappear or stablilize but may enlarge in 11% of the cases [12]. A follow-up study on US is essential for distinguishing benign from malignant, although there is no consensus regarding follow-up intervals for simple

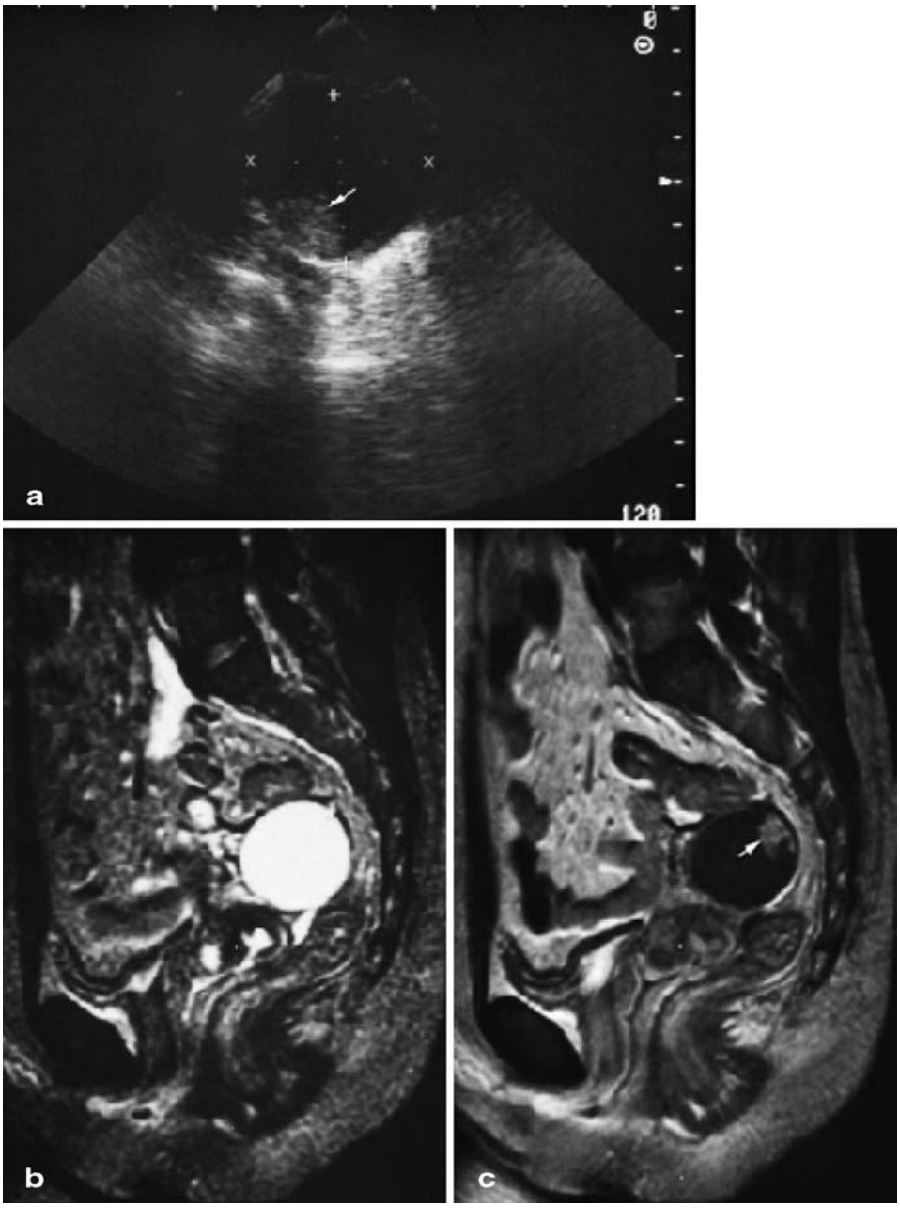


**Fig. 1a–c** Serous tumor of borderline malignancy. **a** transvaginal US displays small vegetation (*arrow*) in a cystic adnexal mass of 4 cm in diameter. **b, c** Contrast-enhanced sagittal MR image also clearly shows vegetation (**c**, *arrow*), whereas it is not clearly identifiable on T2-weighted MR image (**b**). Vegetations in serous tumors are frequently edematous and show high signal intensity on T2-weighted images and are markedly enhanced on contrast-enhanced images, making identification easier. As the imaging findings most predictive of malignancy are vegetation in a cystic tumor, contrast-enhanced images are important

cystic masses. Solid-appearing intraovarian masses on US include both benign ovarian tumors such as cystic teratomas, fibromas, thecomas, and ovarian cancer. Many cystic teratomas are identifiable by their typically bright, echogenic, and large focus. Complex adnexal masses are commonly hemorrhagic cysts or endometriomas, whereas the presence of internal structures, such as mural nodules or septations, indicates that an adnexal mass is a neoplasm (Fig. 1). Hemorrhagic corpus luteal cysts resolve within one or two menstrual cycles, whereas endometrial cysts persist.

In addition to these simple criteria, many complex morphologic scoring systems have been proposed and have shown excellent results [13, 14]. Sassone et al. proposed a morphologic scoring system which included the evaluation of the inner wall structure, the wall thickness, the septa, and echogenicity, and demonstrated a sensitivity of 100% and a specificity of 83% in distinguishing benign from malignant ovarian lesions [13]. According to the level of complexity, the mass was assigned a scale ranging from 1 to 15, and a score of ≥9 was considered to be suspicious for malignancy. Generally, the sensitivity of morphologic analysis with US in predicting malignancy in ovarian tumors has been shown to be very high, possibly reaching 100%, whereas its specificity is relatively low [15].

Color flow and Doppler imaging have been proposed to help distinguish benign masses from malignant lesions

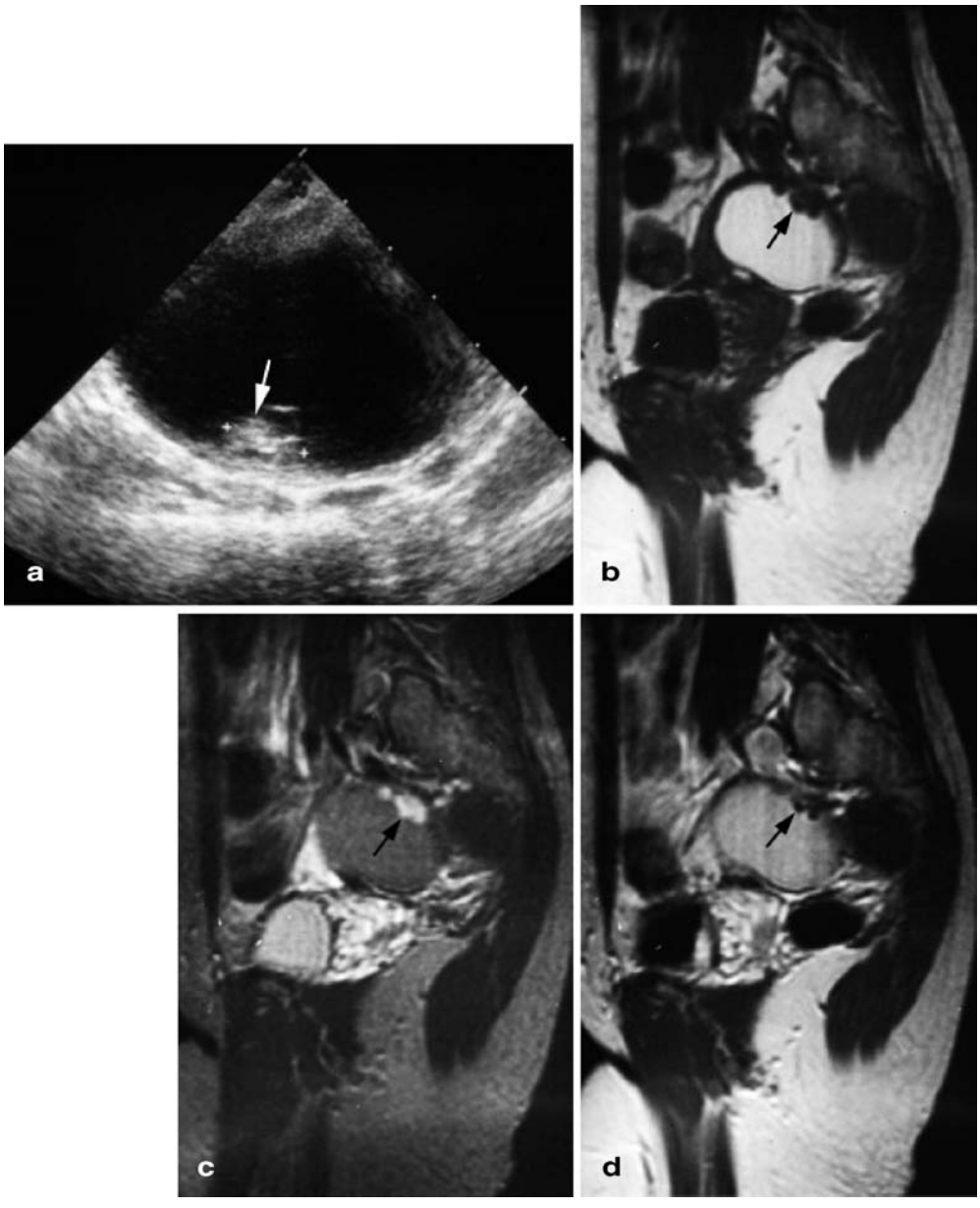


**Fig. 2a–d** Cancer mimic: endometrial cyst with internal clots. **a** US shows a hypoechoic cystic mass. The presence of mural nodules (*arrow*) raises the suspicion of an ovarian cancer. **b–d** MR images show a typical endometrial cyst filled with hemorrhagic fluids that exhibit prominently a high signal intensity on **b** T1-weighted image and low signal intensity on **c** T2-weighted image. Nodular tissue (*arrows* in **b–d**) shows a low signal intensity on a T1-weighted image and a high signal intensity on a T2-weighted image. It completely lacks enhancement on the **d** contrast-enhanced image, indicating that these are clots adhered to the wall

[16]. Malignant masses are usually vascular. Although the cut-off values are widely different among researchers and among machines used, a resistive index (RI) of less than 0.4–0.8 (84–90) and a pulsatility index (PI) of less than 1.0 are generally considered to be suspicious for malignancy [15]; however, a low-resistant Doppler waveform with low PI or RI seen in malignant lesions can also be demonstrated in inflammatory masses, vascular benign neoplasms, endometrial cysts, corpus luteal cysts, and ectopic pregnancies. A high PI or RI suggests benignity, but can be seen in some malignant tumors. The overlap of these indices in benign and malignant lesions limits the clinical usefulness of color and duplex Doppler imaging [17], and thus the morphologic characteristics remain the most important criteria at present. Doppler US alone has been shown to be inferior to MR imaging in the identification of malignancy [18].

The combined use of morphologic scoring and Doppler US may help overcome problems of color and duplex Doppler imaging and improve the assessment of adnexal masses [19, 20]. Twickler et al. have shown that the ovarian tumor index, which combines the patient's age with specific ultrasonographic markers, is an accurate method for predicting ovarian malignancy in cases with suspected adnexal masses [20]. The morphological characteristics were evaluated employing the Sassone morphologic scale

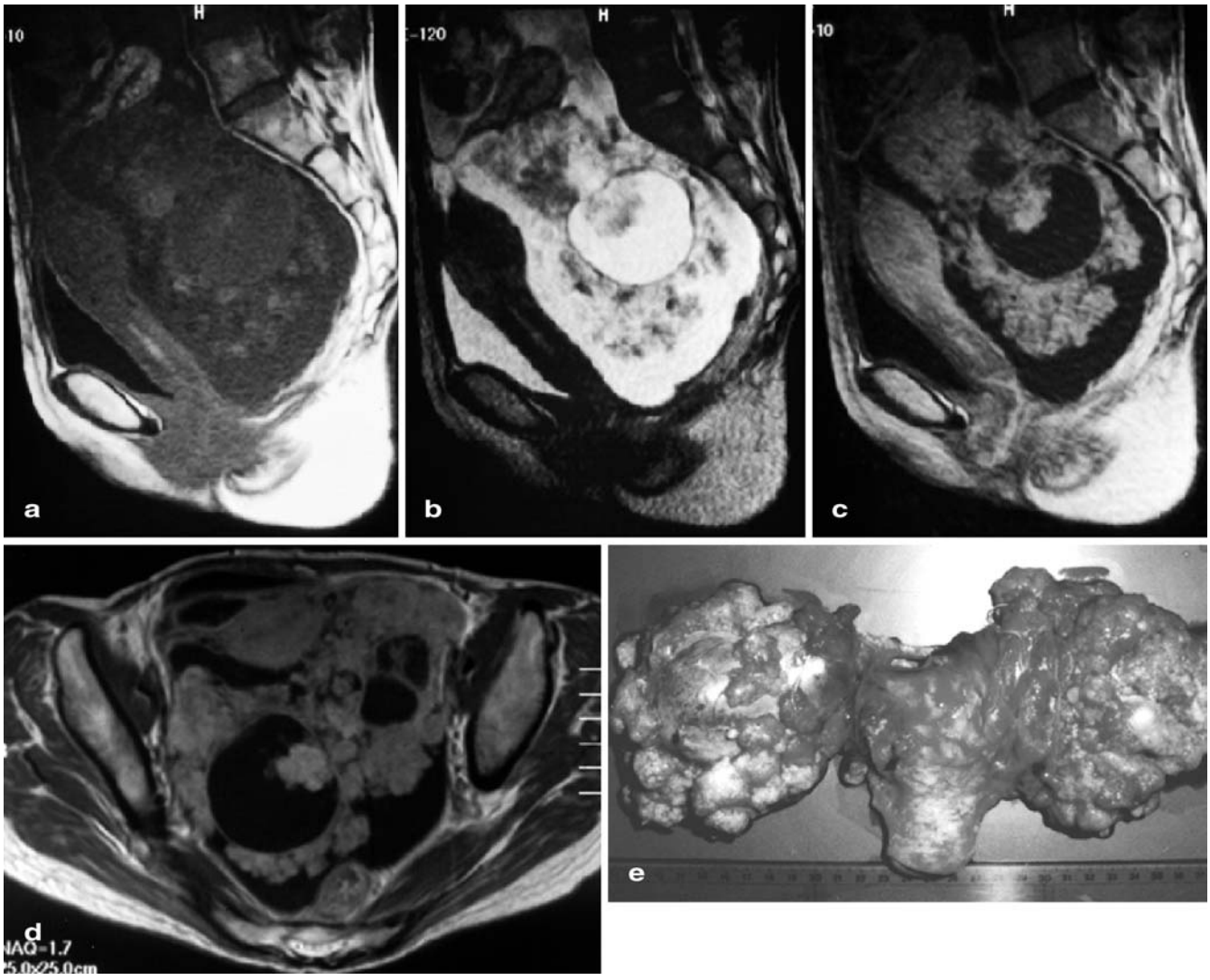


**Fig. 3a–e** Serous surface papillary adenocarcinoma. **a–c** T1- and T2-weighted images, and contrast-enhanced MR images, show a unilocular cystic mass with numerous papillary projections protruding both internally and externally. The projections are edematous, showing high signal intensity on the T2-weighted images and strong enhancement on the contrast-enhanced image. **d** Axial contrast-enhanced MR image also shows a unilocular cystic mass with numerous papillary projections protruding internally and externally. **e** Gross photograph shows the intact capsule with numerous surface papillary projections. The serous carcinomas range from predominantly cystic to entirely solid masses, often having papillary surfaces

[13]. An ovarian tumor index of higher than 90 has a 78% probability of malignancy (sensitivity of 11%, specificity of 99%, PPV 75%, NPV 89%), compared with an ovarian tumor index higher than 45 that has an estimated 12% probability of malignancy (sensitivity 85%, specificity 83%, PPV 41%, NPV, 98%) [20]. This probability assignment may be an alternative to absolute cut-off index.

MR imaging is a cost-effective next step when the results of the US evaluation are indeterminate [21, 22]. Although MR imaging is reliable and a reproducible modality, it is also more expensive. As a result, MR imaging is recommended as a problem-solving modality in the assessment of complex adnexal masses [23]. With a use of criteria based on signal intensity, the accuracy of MR imaging in the confident diagnosis of mature cystic teratoma, endometrial cysts, and leiomyomas is very high. Hricak et al. reported that gadolinium-enhanced MR imaging depicted 94% of adnexal masses, with an overall accuracy for the diagnosis of malignancy of 93% [23]. The MR findings most predictive of malignancy are vegetation in a cystic tumor and necrosis in a solid tumor (Fig. 1) [23]. Dissemination and adenopathy should also be carefully evaluated, as they can be a strong indicator of malignancy.

CT is usually not indicated in the evaluation of adnexal masses because of poor soft tissue discrimination and the hazards of ionizing irradiation. Only when the

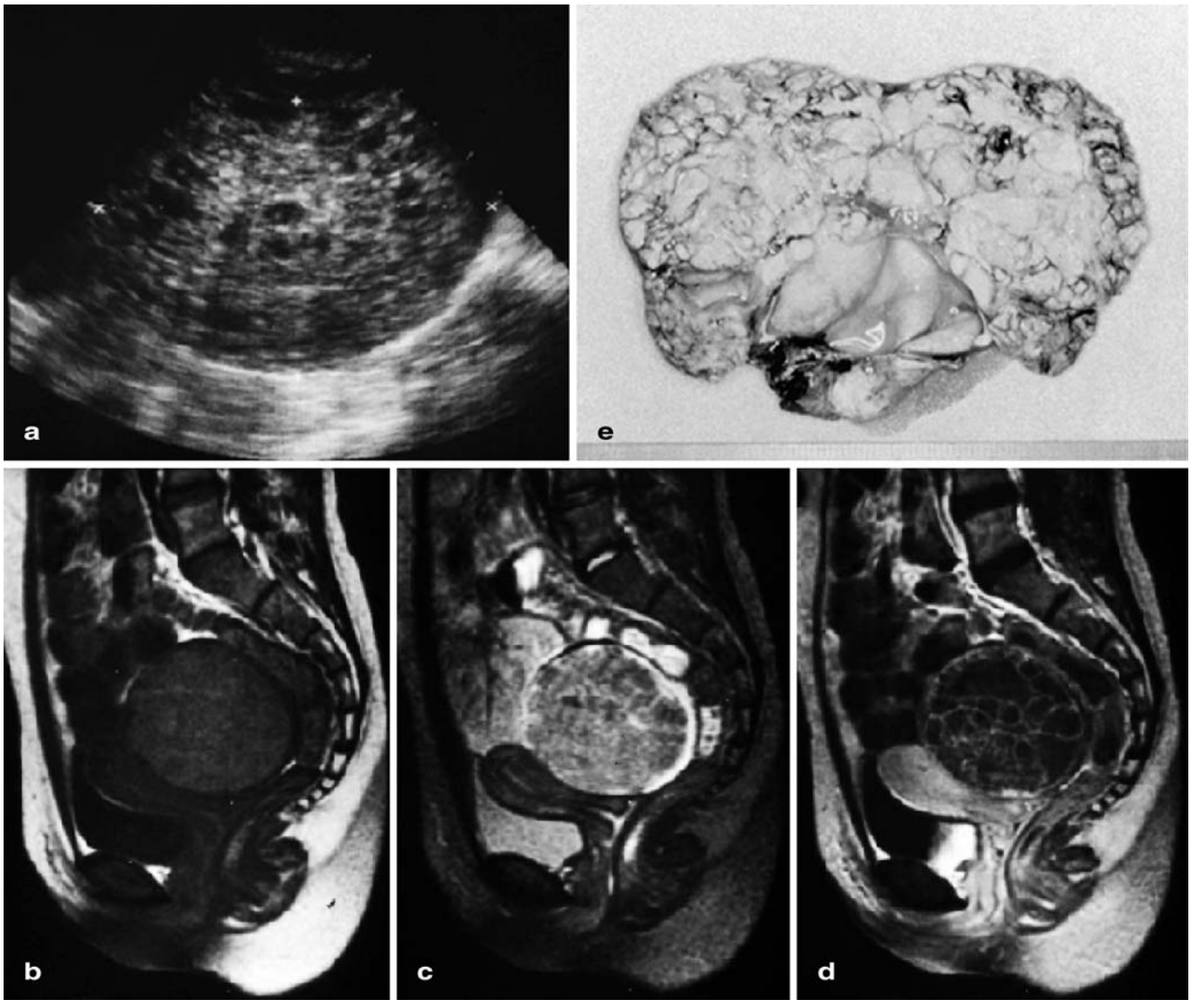


**Fig. 4a–e** Mucinous cystadenocarcinoma. **a** US displays a solid-appearing mass, in the presence of thick mucinous content. **b, c** T1- and T2-weighted images show a multi-locular cystic mass filled with thick contents which exhibit intermediate signal intensities on **b** T1-weighted image and low signal intensity on **c** T2-weighted image. **d** Contrast-enhanced MR image clearly displays numerous septi. **e** Photograph of a cut section of the l esion indicates that the content is extremely thick, remaining within the mass

diagnosis of the dermoid cyst is in doubt can CT clearly depict fat, teeth, and bony fragments, confirming the diagnosis as benign.

## Differential diagnosis of ovarian masses

MR imaging is frequently helpful in the further characterization of adnexal masses as its signal intensity reflects well the pathologic characteristics of the lesion. Numerous subtypes of ovarian cancers differ in their cellular line, mode of origin, growth speed, and in the feasibility of their early detection. It is important to have knowledge classifying these tumors and the corresponding imaging findings.

## Endometrial cysts

Endometrial cysts are unique retention cysts and typically exhibit multiple cystic masses with low level echoes on US. An identification of clots in the cyst frequently misleads the diagnosis of ovarian cancer on US, but can be distinguished on MR imaging. A high SI on T1-weighted images and a low SI on T2-weighted images is a specific finding in the diagnosis of endometrial cysts (Fig. 2) [24].

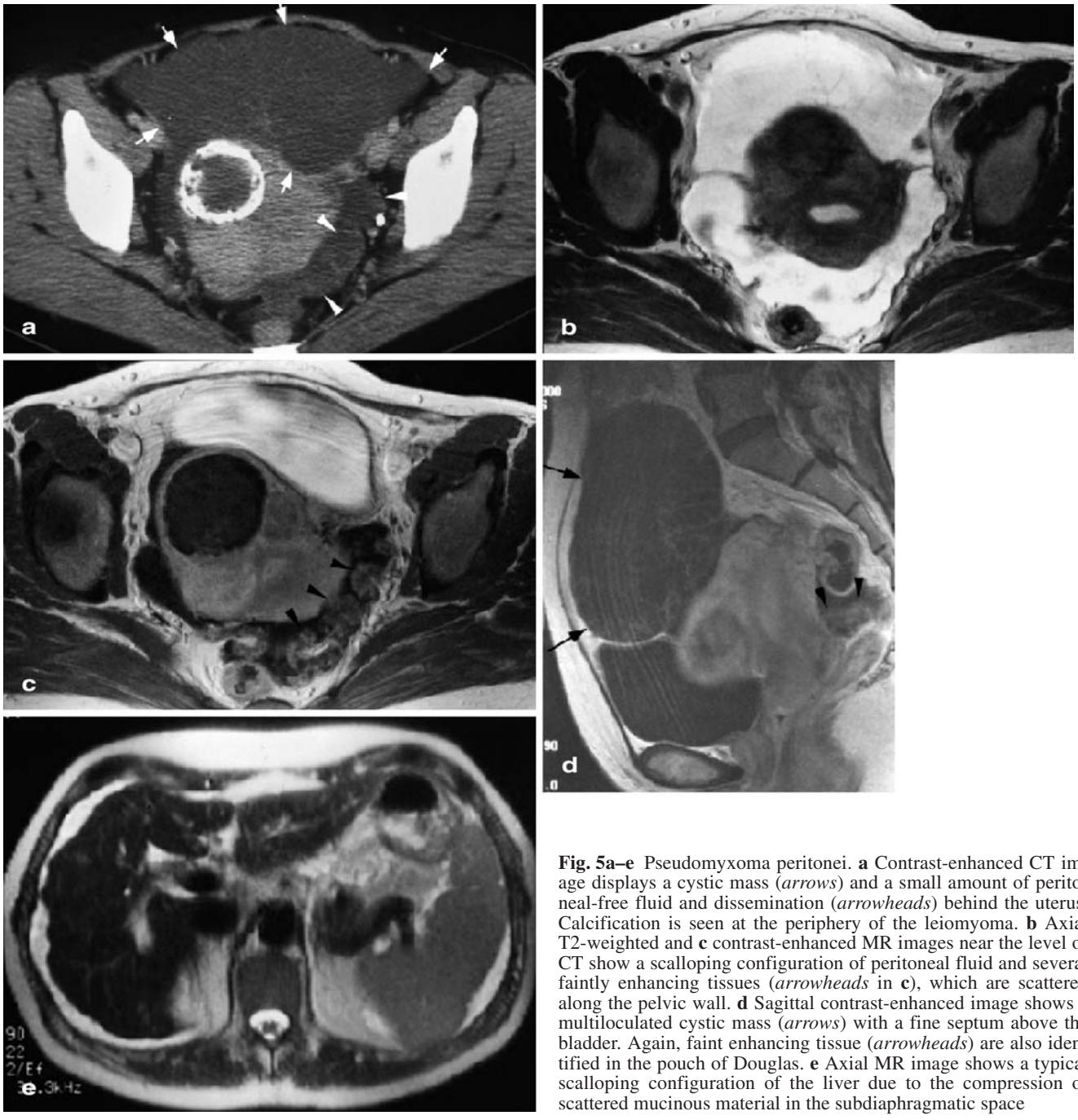


**Fig. 5a–e** Pseudomyxoma peritonei. **a** Contrast-enhanced CT image displays a cystic mass (*arrows*) and a small amount of peritoneal-free fluid and dissemination (*arrowheads*) behind the uterus. Calcification is seen at the periphery of the leiomyoma. **b** Axial T2-weighted and **c** contrast-enhanced MR images near the level of CT show a scalloping configuration of peritoneal fluid and several faintly enhancing tissues (*arrowheads* in **c**), which are scattered along the pelvic wall. **d** Sagittal contrast-enhanced image shows a multiloculated cystic mass (*arrows*) with a fine septum above the bladder. Again, faint enhancing tissue (*arrowheads*) are also identified in the pouch of Douglas. **e** Axial MR image shows a typical scalloping configuration of the liver due to the compression of scattered mucinous material in the subdiaphragmatic space

Tuboovarian abscess

Pelvic inflammatory disease (PID) is usually diagnosed with clinical findings and US; however, US findings are not always specific [25]. When the acute inflammation subsides into a subacute or chronic stage, signs and symptoms of inflammation are less overt [26]. Up to 20% of patients with tuboovarian abscess (TOA) lack clinical symptoms, and can occasionally be mistaken as having ovarian cancer. In such complicated cases, MR imaging may help distinguish tubovarian abscess from other ovarian tumors [26]. Reported findings include an ill-defined border of the mass, the presence of a “halo,” diffuse bowel wall thickening, a stranding of the fat plane, and adhesion.

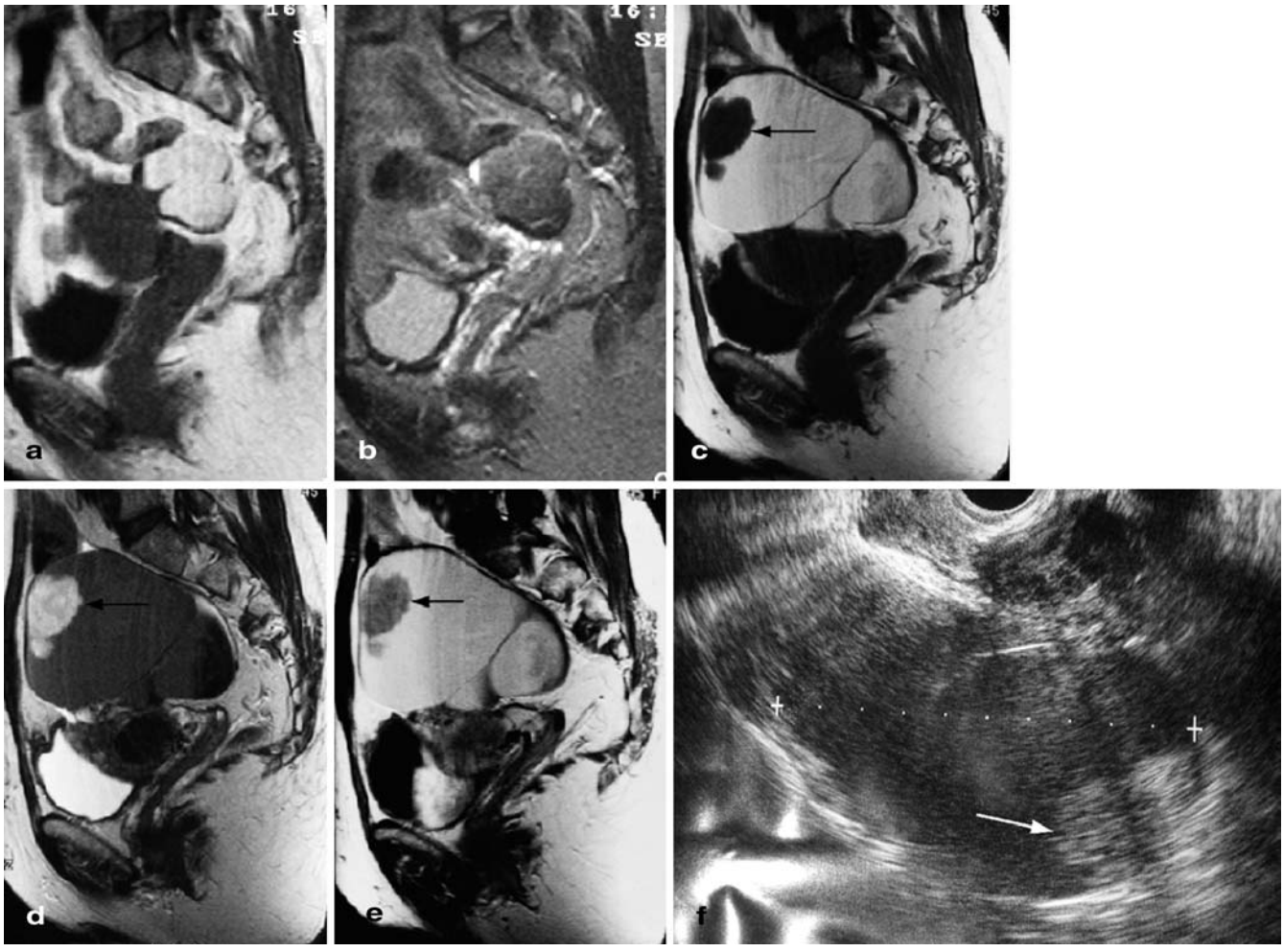


**Fig. 6a–f** Clear cell carcinoma arising within a preexisting endometrial cyst. **a** Sagittal T1- and **b** T2-weighted MR images at initial presentation show typical MR findings of endometrial cysts, which include prominent high signals on **a** T1-weighted images and heterogeneous low signals on **b** T2-weighted images. **c–e** Sagittal T1- and T2-weighted, and contrast-enhanced MR images obtained 2 years later. The lesion is enlarged and has an obvious solid mural nodule (*arrows*) within hermorrhagic contents. **f** US displays nodules along the wall (*arrow*) although it is not always easy to distinguish solid tissue from clot

## Surface epithelial tumors

Surface epithelial cancers are by far the most common type of malignant ovarian tumor, accounting for over 90% of the cases, but are rare before puberty. Surface epithelial cancers include serous, mucinous, clear cell, endometrioid, Brenner, and undifferentiated surface epithelial cancers. Most surface epithelial cancers (64%) are serous or undifferentiated in origin [3]. Seventy-three percent of serous and 78% of undifferentiated carcinomas arise de novo and spread rapidly, presenting clinically at advanced stages [3]. Primary lesions can only be microscopic, and are known as normal-sized ovarian carcinoma syndrome.

In the vast majority of tumors of surface epithelial origin, an increasing amount of solid tissue increases the possibility of malignancy. One of the findings most predictive of malignancy is vegetation in a cystic mass [23]. A wall thickness of 3 mm may be another useful value in order to identify suspect malignancies [14]. An exception to this rule is in the case of a Brenner tumor. Although benign, Brenner tumors are solids that are frequently associated with other cystic masses. Brenner tumors may be distinguished from other surface epithelial cancers, because fibrocollagenous stromas in Brenner tumors shows significantly lower signal intensities than do other non-fibrous ovarian tumors on T2-weighted images [27].

Serous tumors typically present as unilocular cystic masses, whereas mucinous tumors usually present as multiloculated cystic tumors (Figs. 3, 4, 5). Serous carcinomas range from predominantly cystic with vegetations to entirely solid masses. Vegetations are papillary in

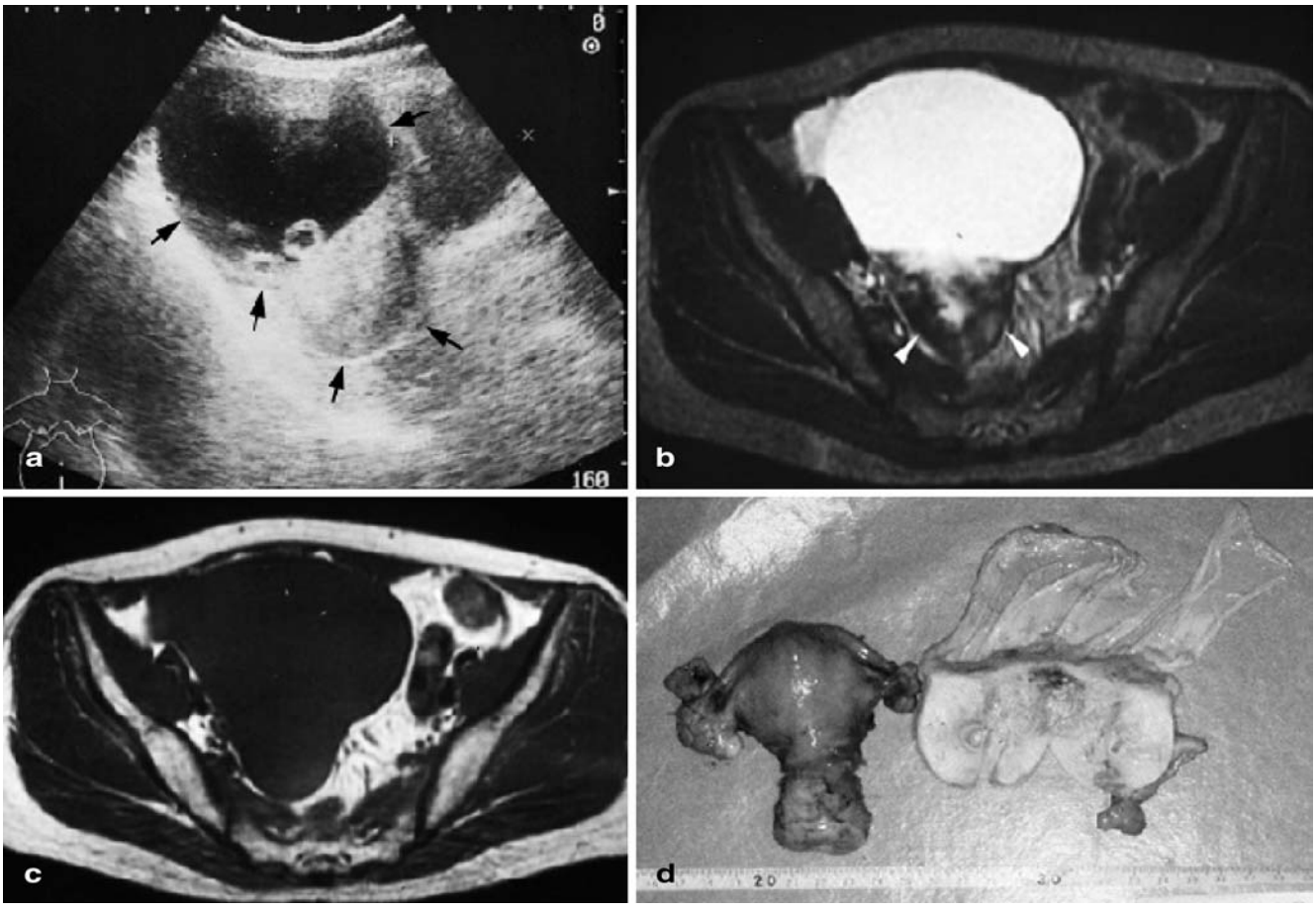


**Fig. 7a–d** Cancer mimic: fibroma. **a** Ultrasound displays a mixed solid and cystic mass (*arrows*) with cystic protrusions into a large cyst. The presence of solid tissue raises the suspicion of ovarian cancer. **b** Axial T2-weighted MR image reveals a distinct low signal intensity of solid tissue (*arrowheads*), indicating the fibrocollagenous nature of the lesion. Edema in the solid portion and an eccentric cyst are also in accordance with the diagnosis of fibroma. **c** Contrast-enhanced MR image shows an extremely weak enhancement in the solid tissue. **d** Gross section of the lesion shows white solid tissue typical of fibroma and peripheral cysts consisting of a thin wall and smooth inner surface

shape, protruding internally and/or externally. Surface papillary projections are important hallmarks of serous carcinomas (Fig. 3). Vegetations are frequently edematous, show high signal intensities on T2-weighted images, and are markedly enhanced on contrast-enhanced images (Fig. 3) [28]. In contrast, stained-glass appearances and daughter cysts are well-known imaging findings of mucinous tumors (Fig. 4). If the solid tissue is identified in otherwise typical endometriomas, the development of clear cell carcinomas or endometrioid carcinomas are highly suspected (Fig. 6) [29]. It is very important to distinguish clots adhered to the wall from viable mural nodules with the use of contrast enhancement.

## Gonadal stromal tumors

Gonadal stromal tumors are usually solid masses frequently associated with cysts. Estrogenic activities are commonly encountered in gonadal stromal tumors.

Fibromas and thecomas are benign but are frequently mistaken as ovarian cancer on US as they are solid. MR imaging displays lower signal intensities of solid tissue, representing their benign fibrocollagenous nature, than do other non-fibrous tumors on T2-weighted images (Fig. 7). Edema and cyst formations, which may be central or eccentric, are common [30]. As necrosis in a solid ovarian tumor is a reliable sign of malignancy, cysts within solid tissue should be carefully distinguished from necroses. Cysts have smooth inner surfaces, whereas necroses do not.

Granulosa cell tumors are the most common type of estrogenic tumor, and have malignant potential. Granulosa cell tumors usually present as solid tumors embedded with numerous cysts, which represent follicular and hemorrhagic cysts, and may show a honeycomb pattern.

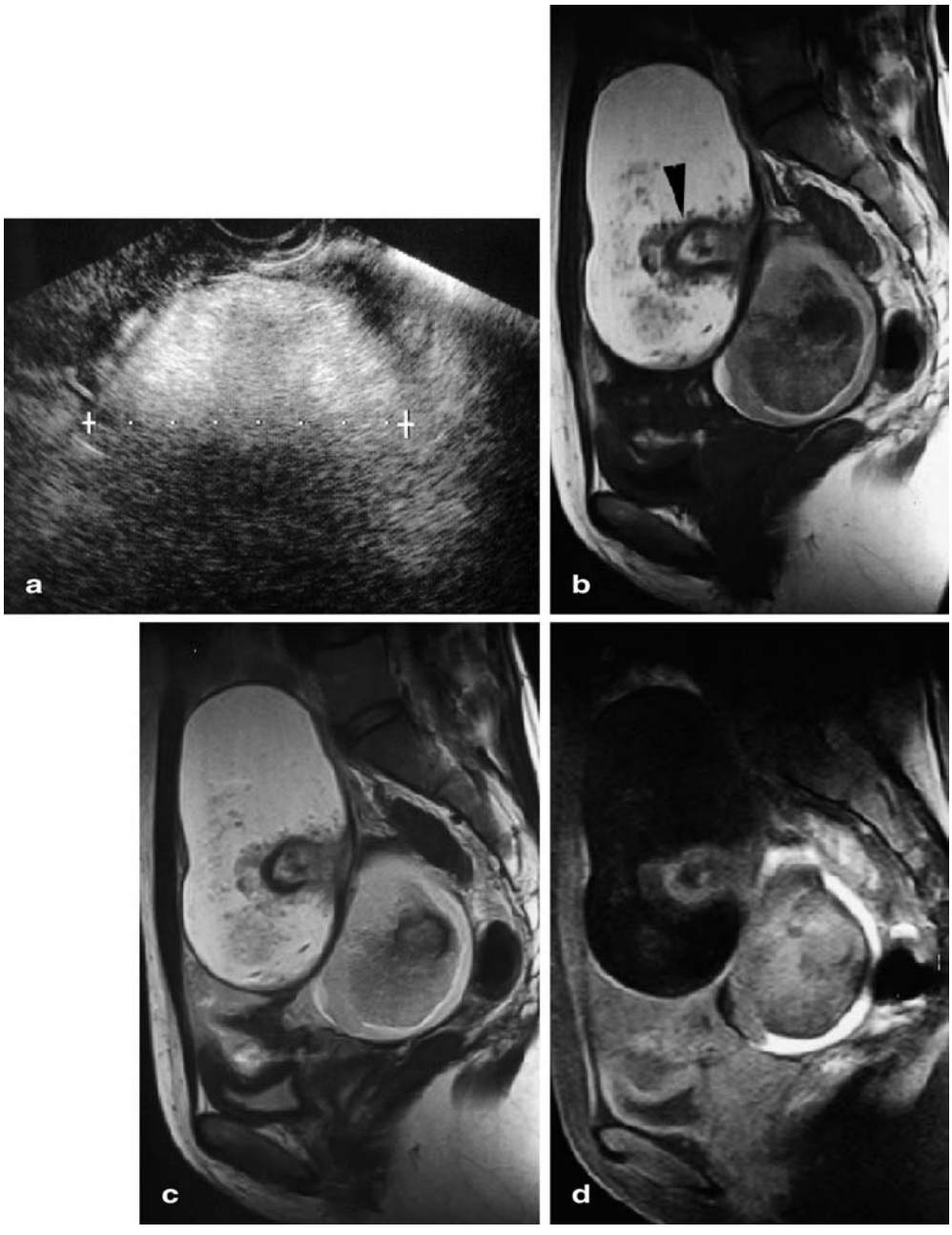


**Fig. 8a–d** Cancer mimic: dermoid cyst with Rokitansky protuberance. **a** US displays a huge mass of solid appearance with acoustic shadowing, suggestive of internal calcification with mass. It is considered a calcified mass including teratomas but is not confidently distinguishable from ovarian cancer. **b** Sagittal T1-weighted MR image displays a mass filled with prominently high signal intensity, representing sebaceous fluid or a hemorrhage. The solid-appearing protuberance is a Rokitansky protuberance (*arrowhead*). **c** T2-weighted MR image shows high signal intensity of the content. **d** Fat-suppressed image shows reduced signal intensity of the content, confirming the diagnosis of a dermoid cyst

## Germ cell tumors

Germ cell tumors include teratomas (mature and immature), dysgerminomas, yolk sac tumors, etc. Over 95% of germ cell tumors are benign dermoid cysts (mature cystic teratomas), and most of the remaining germ cell tumors are malignant [31]. Dysgerminomas are malignant, but the prognosis is usually excellent. Yolk sac tumors have poorer prognoses than do dysgerminomas. Sixty percent of ovarian tumors identified before the age of 21 years are of germ cell types, and one-third of these are malignant [31]. Many of the malignant germ cell tumors are associated with elevated serum marker levels. The serum level of LDH is elevated in up to 95% of dysgerminomas. Alpha-fetoprotein is prominently elevated in almost all patients with yolk sac tumors. To be noted is that benign dermoid cysts can be also associated with elevated CA 19–9 levels.

Dermoid cysts are commonly mistaken for ovarian cancer on US because their sonographic appearance is typically a complex, predominantly solid mass with echogenic foci [9]. CT is capable of detecting fat and calcification but has radiation hazards. On MR imaging, fat and sebaceous fluids are easily identifiable, since they show

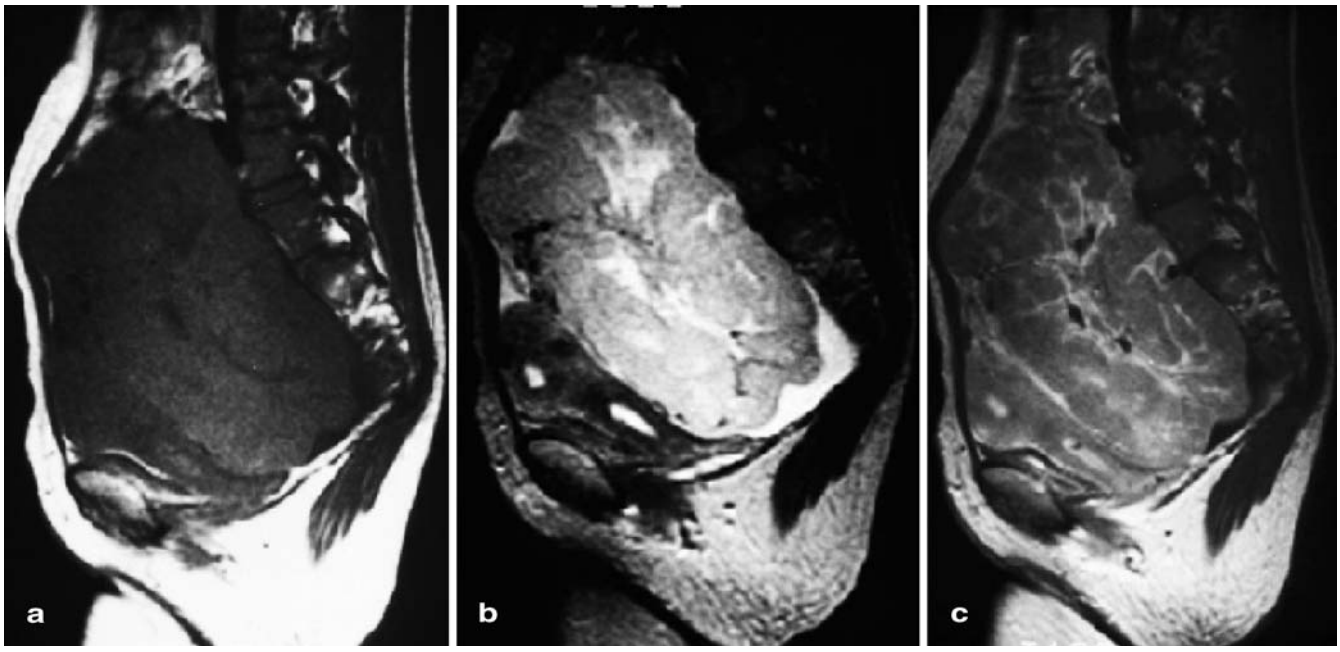


**Fig. 9a–c** Dysgerminoma. **a** Sagittal T1-weighted, **b** T2-weighted, and **c** contrast-enhanced MR images show an entirely solid tumor consisting of multiple nodules separated by bundles that exhibit high signal intensity on **b** T2-weighted images and prominent enhancement on **c** contrast-enhanced images. No area of high signal intensity is seen on the **a** T1-weighted image. **c** Contrast-enhanced image shows enhanced fibrous septa

high signal intensities on T1-weighted images and reduced signal intensities on fat-suppressed images (Fig. 8) [32]. The identification of a solid component in elderly patients is an important sign of malignant transformation [33]. The vast majority of supervening malignancies are squamous carcinomas. Solid components tend to penetrate into the tumor and involve adjacent organs.

Dysgerminomas present as solid tumors, consisting of multiple nodules separated by fibrovascular septa (Fig. 9) [34]. Fibrovascular septa exhibit either high signal intensities or low signal intensities on T2-weighted images, according to the proportion of fibrous material, and are usually well enhanced [34]. Foci of hemorrhages or necroses are rare. In contrast, yolk sac tumors may present as solid masses, almost always associated with hemorrhages or necroses, or as predominantly cystic masses with a lot of foci of hemorrhages or necroses. A prominent enhancement of the lesion, much stronger than that of the uterus, is another important MR finding [35].

## Metastasis

Ovarian metastases can be roughly divided into two groups: Krukenberg tumors and others. Krukenberg tumors are characterized by the presence of signet ring cells within a reactive proliferation of theca cells. They frequently (80%) result from gastric carcinomas, and are usually solid and bilateral. Typical MR findings of Krukenberg tumors are entirely solid masses showing low signal intensities on T2-weighted images, reflecting the presence of abundant theca cells (Fig. 10) [36, 37]. An important MR finding of Krukenberg tumors is the enhanced septa on contrast-enhanced images [37]. This finding may be helpful in distinguishing Krukenberg from fibrothecoma. An extensive edema with cyst formation is another characteristic of Krukenberg tumors.

Metastatic tumors other than Krukenberg tumor may show a variety of imaging findings; among them, metastases from colon carcinomas frequently present as multiloculated cystic tumors and are unilateral. An ovarian mass frequently presents as an initial manifestation of the disease, and is commonly mistaken as primary ovarian cancer [38]. Their gross findings closely resemble those of mucinous cystadenocarcinomas that are variable in content [38]. Thick mucinous or viscid gelatinous material occasionally exhibit a very low signal intensity on T2-weighted images (Fig. 11) [39].

## Summary of imaging evaluation of suspected adnexal masses

MR imaging is used to evaluate adnexal masses when US findings are indeterminate. CT is usually not indicated except when the diagnosis of a dermoid cyst is in doubt. MR imaging is highly accurate in the diagnosis of dermoid and endometrial cysts. If MR imaging confirms

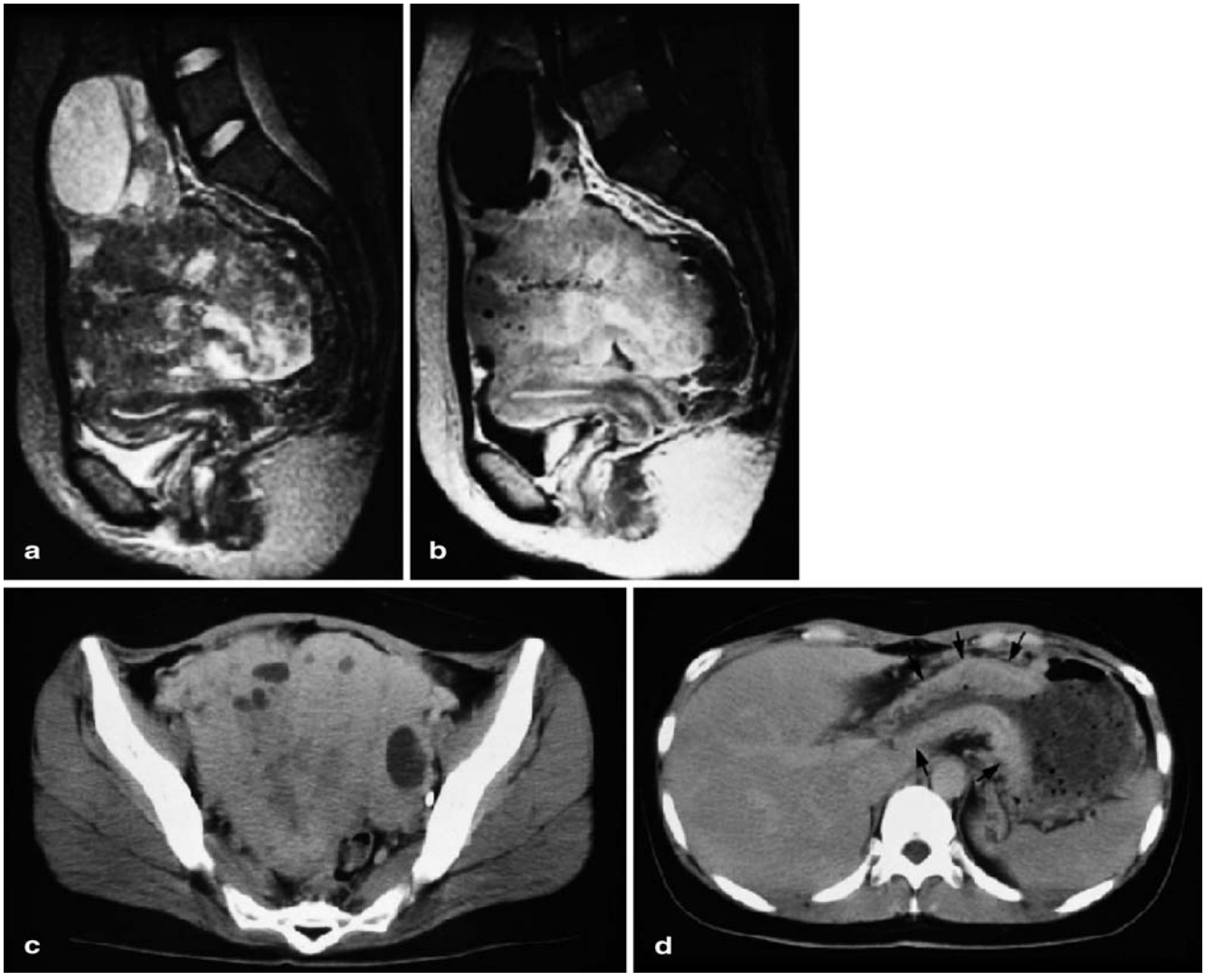


**Fig. 10a–d** Metastasis, Krukenberg tumor from gastric cancer. **a** Sagittal T2-weighted and **b** contrast-enhanced MR images show an almost entirely solid tumor embedded with several cysts at its periphery. The solid tissue exhibits relatively low signal intensity on the **b** T2-weighted image, indicating its fibrocollagenous nature. Low signal intensity and cyst formation are commonly observed findings in Krukenberg tumors. **c, d** Contrast-enhanced CT exhibits a nonspecific solid tumor in the **c** pelvis; however, diffuse wall thickening (*arrows* in **d**) of the stomach leads to the correct diagnosis: a metastatic ovarian tumor from gastric cancer

a dermoid or endometrial cyst, further diagnostic procedures are unnecessary [40]. If MR findings allow the unequivocal diagnosis of a dermoid or endometrial cyst, laparoscopy will safely be referred [40]. In all other cases, surgical evaluation should be considered at the time, and an intraoperative frozen section is the gold standard for patients with ovarian tumors.

## Staging

The majority of ovarian cancers present as advanced stage III–IV. Since an exploratory laparotomy is a gold standard at present for all patients with suspected ovarian cancer in order to confirm the diagnosis, the stage, and to reduce tumor volume, the role of imaging in staging ovarian cancer has been considered to be of limited use previously. Only chest radiography is used routinely to screen for pulmonary metastases, and barium enemas maintain a role in ovarian cancer staging to evaluate the invasion or to exclude the possibility of colon cancer presenting as a primary ovarian tumor; however, surgical staging itself has an inherent weakness: it cannot detect microscopic tumor seeding. An accurate preoperative depiction of possible sites of dissemination with imaging studies is mandatory for determining the sites for biopsy during surgery, in addition to referring the patient with an advanced stage of the disease to a cancer center [41].

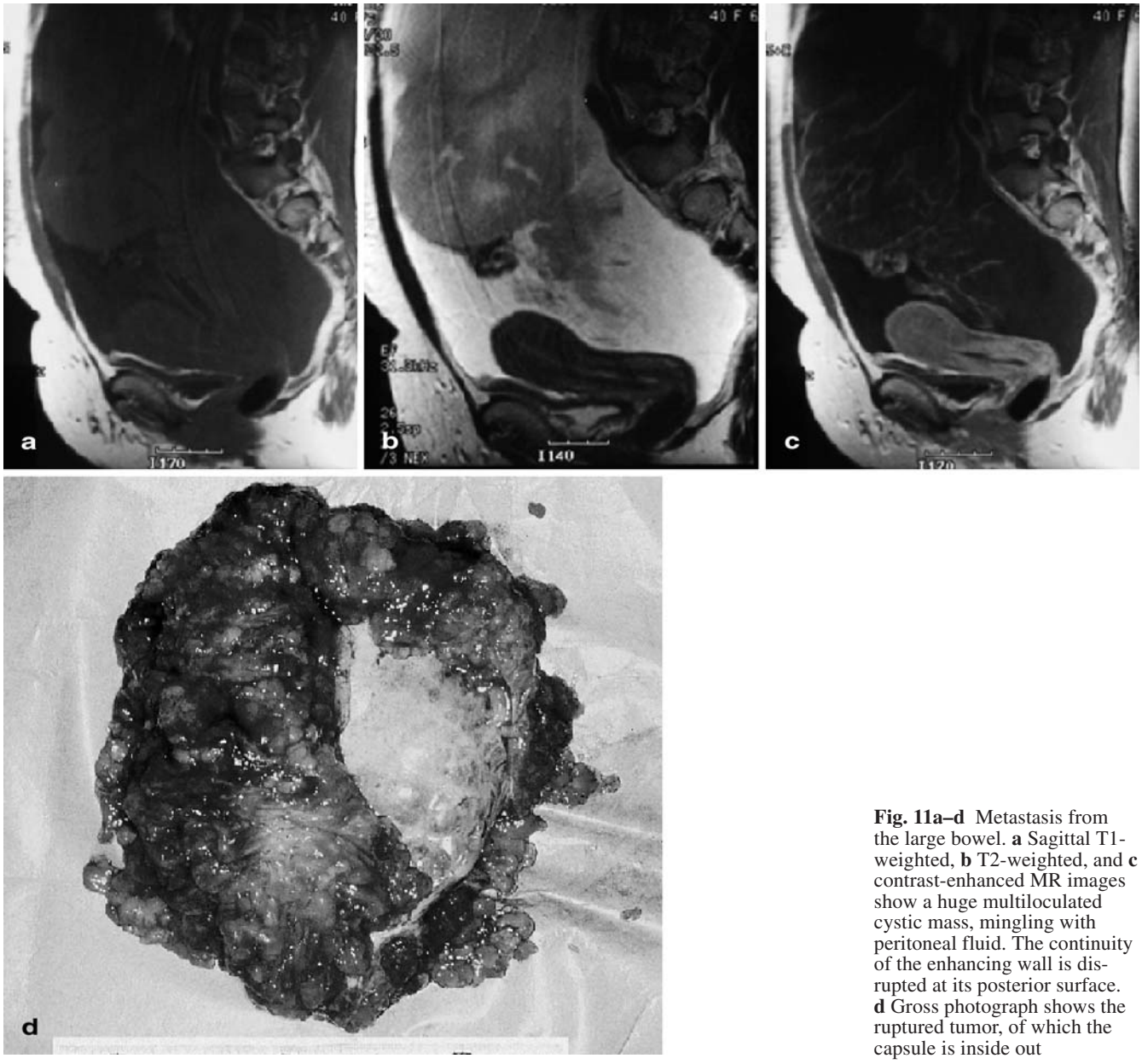


**Fig. 11a–d** Metastasis from the large bowel. **a** Sagittal T1-weighted, **b** T2-weighted, and **c** contrast-enhanced MR images show a huge multiloculated cystic mass, mingling with peritoneal fluid. The continuity of the enhancing wall is disrupted at its posterior surface. **d** Gross photograph shows the ruptured tumor, of which the capsule is inside out

CT has been demonstrated to be reasonably accurate in determining which patients may have tumor implants that can be optimally surgically debulked [42, 43]. Recent articles have also shown excellent results in CT and contrast-enhanced MR imaging in delineating small peritoneal diseases, with sensitivities of 95 and 92%, respectively [41]. Both modalities are equally accurate, and can be used to stage advanced ovarian cancer [41]. The most common sites of peritoneal disease are the omentum, followed by subphrenic spaces, the mesentery (large and small bowel), the anterior part of the abdomen, and the paracolic gutters (Figs. 12, 13) [41]. Ultrasound can be used to supplement CT or MR imaging, especially in hepatic substances and in the lymph nodes (Fig. 14) [41].

Another large study has shown little difference between US, CT, and MR in the staging of ovarian cancer with the highest specificity of 96% and the lowest sensitivity of 75% for US [18]. If an abdominal spread is detected with US, the accuracy of a diagnosis of a stage-III disease is high. Because of the importance of not understaging the abdominal malignancy as a disease limited to the pelvis, if stage-III cancer is not detected at the initial abdominal US, CT, or MR, imaging should be performed because of their higher sensitivities in staging [18].

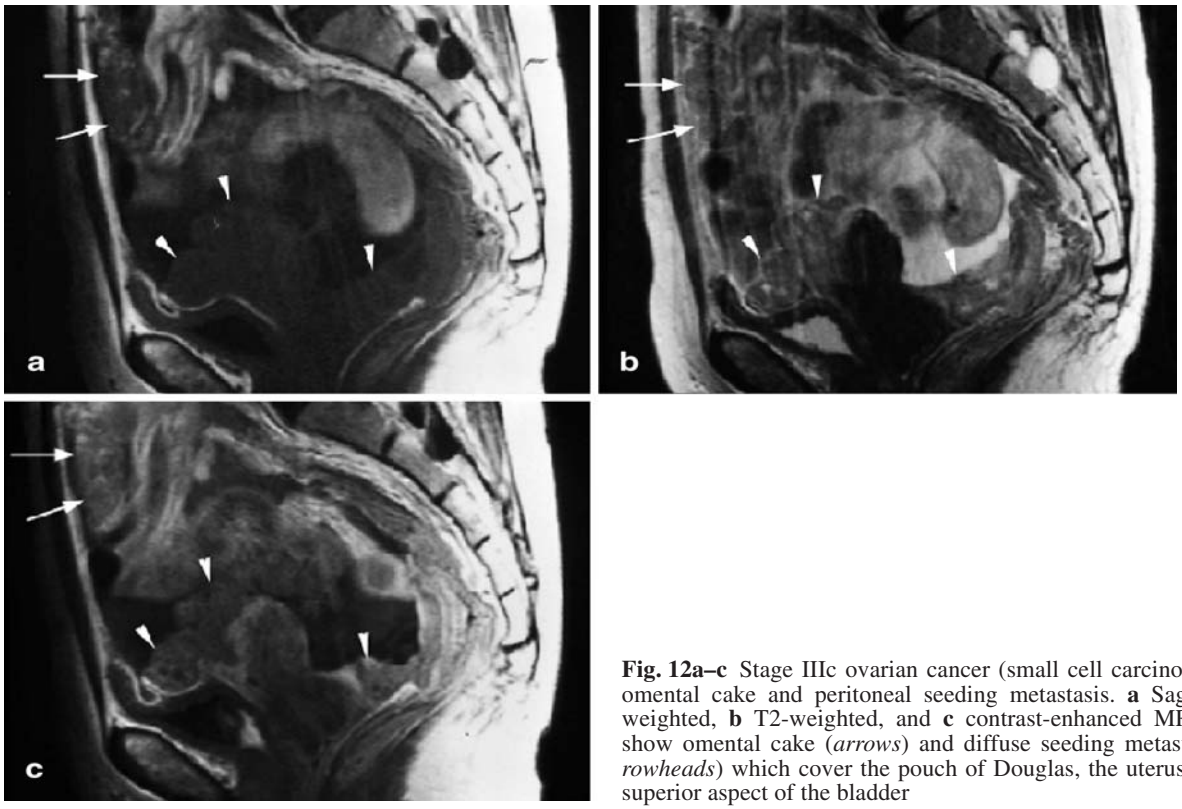


**Fig. 12a–c** Stage IIIc ovarian cancer (small cell carcinoma) with omental cake and peritoneal seeding metastasis. **a** Sagittal T1-weighted, **b** T2-weighted, and **c** contrast-enhanced MR images show omental cake (*arrows*) and diffuse seeding metastasis (*arrowheads*) which cover the pouch of Douglas, the uterus, and the superior aspect of the bladder

## Management strategy

Ovarian cancer should be diagnosed and staged surgically with a laparotomy according to the FIGO guidelines. To confirm the diagnosis and stage, and to reduce the tumor volume, an exploratory laparotomy is necessary for all patients with suspected ovarian cancer. Cytoreduction or debulking refers to an aggressive surgery to reduce the volume of a tumor, and its success enhances the effect of chemotherapy, prolonging survival [44]. A residual tumor of no greater than 1.5–2.0 cm in diameter is considered to be an optimal tumor for debulking, whereas a residual tumor greater than 2.0 cm is regarded as suboptimal for debulking [45]. The critical size for treatment planning is 2.0 cm [45], with smaller tumors usually best treated with chemotherapy. An unresectable tumor may be initially treated with chemotherapy followed by surgical debulking [44]. But in the vast majority of cases, surgery will precede any chemotherapy (platinum and paclitaxel-based adjuvant chemotherapy, with the optional use of intra-abdominal chemotherapy). The NIH conference has concluded that women with stage IA grade 1 and stage IB grade 1 ovarian cancer do not require postoperative adjuvant therapy, and that the remaining stage I patients and women with stages II, III, and IV epithelial ovarian cancer should receive postoperative chemotherapy (Table 1) [8]. Recent improvements in chemotherapy and hematologic support, including the use of G-CSF, have remarkably increased the treatment options for women with residual or recurrent tumors [8].

**Table 1** Treatment plan for epithelial carcinoma of the ovary (modified from NIH consensus conference [8]). *USO* unilateral salpingo-oophorectomy *TAH-BSO* total abdominal hysterectomy and bilateral salpingo-oophorectomy

| Tumor | Treatment plan |
|---|---|
| Stage IA grade 1 and most stage IB grade 1 | USO or TAH-BSO, depending on reproductive status. No adjuvant therapy |
| All other stage I | USO or TAH-BSO, depending on reproductive status. Postoperative adjuvant therapy |
| Stages II, III, and IV | Complete surgery with maximal cytoreduction. Postoperative systemic chemotherapy |

Specialists in cancer should perform these surgery and chemotherapy options. Patients, especially those with advanced disease, experience a significant survival advantage when a gynecologic oncologist is involved in their treatment [46]. Unfortunately, gynecologic oncologists see less than half of ovarian cancer patients [46]. Is

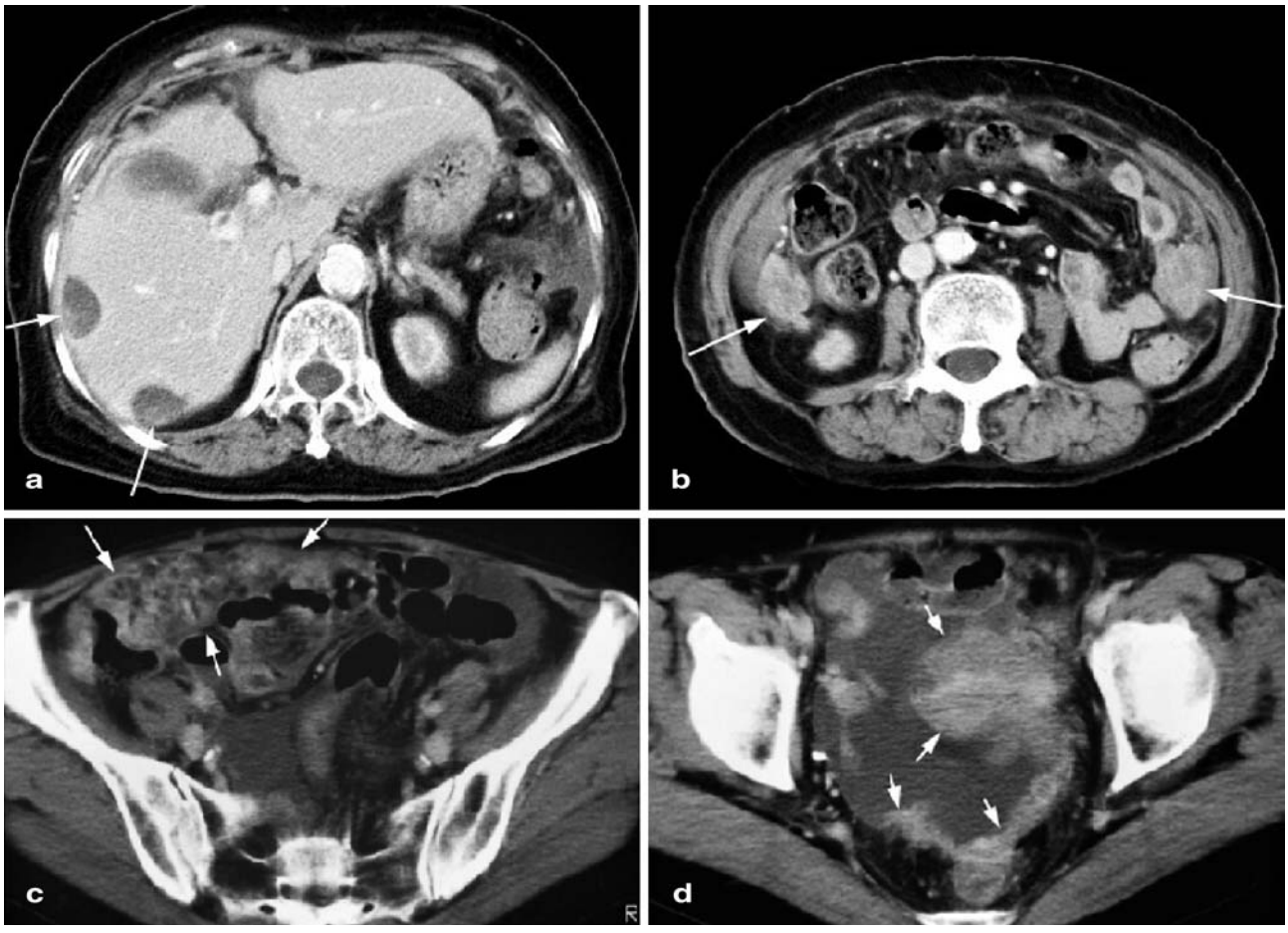


**Fig. 13a–d** Ovarian cancer stage IIIC, undifferentiated carcinoma with multiple dissemination. **a–d** Contrast-enhanced CT images show multiple dissemination (*arrows*) which are located in the **a** subdiaphragmatic space, **b** paracolic gutter, **c** omentum, and along the **d** pelvic wall. Lesions in the subdiaphragmatic space frequently grow into the liver and mimic liver metastasis

has been reported that up to 40% of cases are thought to actually be of a lower stage than they determined to be at their initial laparotomy [1, 47, 48, 49]. Whatever the modality used, the correct staging of ovarian cancer with imaging studies is important in the determination of the appropriate referral to gynecologic oncologists, and thus to obtain a longer survival [18].

After chemotherapy, second-look operations have conventionally been performed to assess tumor response to treatment and to excise residual tumors; however, in 1995, an NIH consensus conference raised suspicions about the routine use of the second-look operation. The role of second-look operations is discussed later.

## Evaluation of recurrent tumors

After the initial treatment, detecting a clinically occult tumor is critical in determining the appropriate treatment. Patients are traditionally followed up with serial measurements of serum CA-125 levels, since a doubling or halving of its value reflects well the response of the tumor to chemotherapy; however, a normal CA-125 level (<35 U/ml) does not necessarily exclude the presence of a recurrent tumor, with a negative predictive value of 38% [50]. In addition, the negative predictive value of second-look laparotomies is also limited (50%) and cannot improve the survival rate [51, 52]; thus, the NIH consensus conference proposed that a protocol should be developed to evaluate the benefits of consolidation therapy [8]. CT can help detect gross disease and obviate extensive repeat biopsies, and has been used to follow-up patients after primary cytoreductive surgery [15]. Recent imaging literature has addressed the usefulness of noninvasive imaging studies, including CT, MR, and PET, as possible alternatives to second-look surgery. Among them, contrast-enhanced MR imaging is proposed as a valuable clinical tool, having 91% sensitivity, 87% specificity, 90% accuracy, and a 72% negative predictive value, and is by far

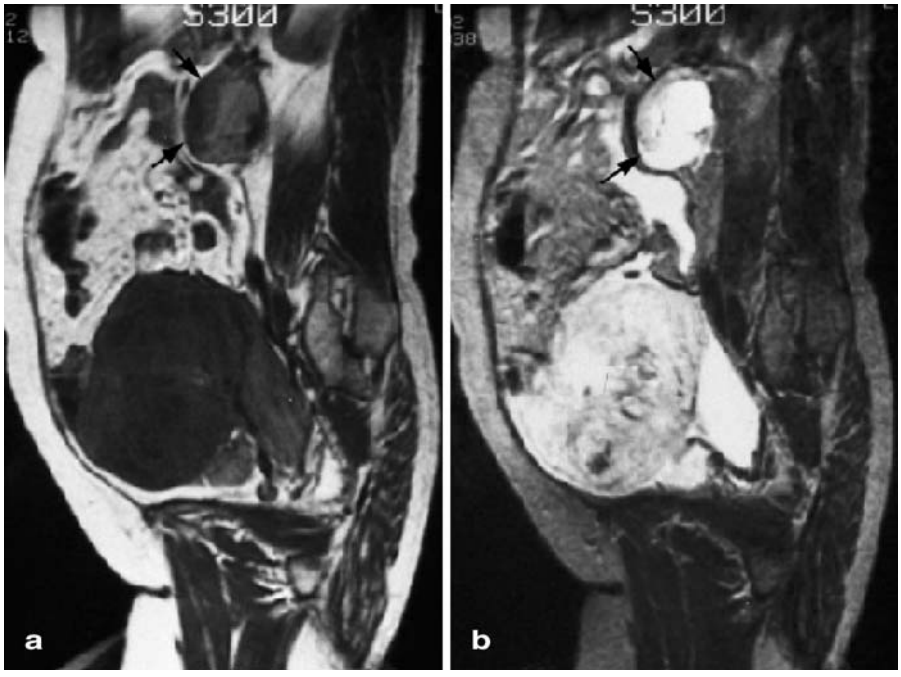


**Fig. 14a, b** Lymph node metastasis from ovarian cancer. **a** Sagittal T1-weighted and **b** T2-weighted MR images display a pelvic mass, bloody ascites, and para-aortic lymph node enlargement (*arrows*). The vast majority of lymph node metastasis of ovarian cancer are initially identified in this location

superior to serum CA-125 levels and equal to second-look laparotomy [53, 54]. A novel diagnostic tool, FDG-PET, is expected to be useful in detecting recurrent ovarian cancers with high specificity, compared with the conventional CT/MR morphologic imaging methods, or may be a complementary modality [40, 55].

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