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Imaging in the pre-operative staging of ovarian cancer

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Abstract

The main prognostic factor in ovarian cancer is the stage of disease at diagnosis. The staging system in use (FIGO classification, updated in 2014) is based on the surgical-pathological findings. Although surgical staging is the gold standard in ovarian cancer, the initial patient management depends on the imaging-based pre-surgical staging assessment, in order to identify unresectable or difficult to resect disease. Radiologists need to be aware of the strengths of the available imaging modalities, as well as the imaging pitfalls. Clear understanding of pattern of disease spread and review areas are critical for accurate staging and treatment planning. The current standard of care for pre-surgical staging is CT of the thorax, abdomen, and pelvis. This allows a rapid evaluation of disease extent and is fairly accurate in identifying bulky disease but has definite limitations in assessing the extent of small volume disease and in the confirmation of certain sites of disease beyond the abdomen. Functional MRI has been reported to be superior in detecting small peritoneal deposits. PET/CT may be used as a problem-solving tool in some patients where determination remains unclear, particularly in confirmation of advanced stage beyond the abdomen.

Key words: Ovarian cancer—Staging—Imaging—FIGO classification

Ovarian cancer causes 5% of cancer deaths among women and represents the fifth most common cause of cancer deaths in women in the United States after lung, breast, colorectal, and pancreatic cancer [1].

Stage remains the most important independent prognostic factor [2]. The 5-year survival rate for all ovarian cancers is estimated to be 46%, in both the US and UK, and is markedly variable depending on the stage, evaluated at 92% for patients diagnosed with localized disease, 75% for regional, 29% for distant-stage disease, and 25% for unstaged patient [1, 3, 4].

Despite significant efforts, there remains no reliable screening test for ovarian cancer and screening of asymptomatic women is not recommended. There is no significant mortality benefit between screened and non-screened women with average risk and screening may lead to harm, such as post-operative complications following surgery in women who ultimately do not have ovarian cancer [5–7]. Early-stage ovarian cancer may be associated with few or no symptoms and thus women are often diagnosed with advanced disease; more than 60% patients will have extrapelvic disease at presentation [1].

The WHO classification categorizes primary ovarian cancer in three main groups according to their cellular origin: epithelial, germ cell, and sex cord-stromal tumors [8]. Epithelial tumors are the most common, representing approximately 85%–90%, with serous carcinoma (usually high grade) as the most frequent subtype [9, 10]. Epithelial ovarian cancer will be the focus of this article. The majority of ovarian cancer cases are sporadic although a significant proportion, typically high-grade serous tumors, are genetic in origin with approximately 15% of all ovarian cancer patients harboring a germline BRCA 1 or 2 mutation [1, 11–14]. The stage at presentation and mortality rate vary depending on histological subtype (Table 1) [8, 10, 15–18]. The ovarian tumor staging system is based on the FIGO classification (Table 2) [10] which refers to the histopathological results of a staging laparotomy that includes a total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, pelvic and para-aortic lymphadenectomy, resection of visible peritoneal disease, or random sampling of multiple peritoneal sites if there is no visible peritoneal disease [2].

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Table 1. Typical stage at presentation and corresponding 5-year survival, based on the histological subtype

Histological type			Presentation		5-year survival	
Invasive epithelial tumors 90% of OC [10]	Serous	High grade 70% of EOC [10, 15]	Stage I	3.5%	–	
			Stage II	4.4%	–	
			Stage III	80.8%	40%	
			Stage IV	11.3%	–	
		Low grade <5% of EOC [10]	Stage I	–	–	
			Stage II	–	–	
			Stage III	–	70.7% [15]	
			Stage IV	–	–	
		All serous [8, 16]	Stage I	10%	80%	40%
			Stage II	7.4%		
			Stage III	54.5%	10%–20%	
			Stage IV	26.3%		
	Endometrioid adenocarcinoma 10% of EOC [8, 10]		Stage I	31%	78%	
			Stage II	20%	63%	
			Stage III	38%	24%	
			Stage IV	11%	6%	
	Clear cell adenocarcinoma 10% of EOC [8, 10]		Stage I	33%	69%	
			Stage II	19%	55%	
			Stage III	29%	14%	
			Stage IV	9%	4%	
	Mucinous 3% of EOC [8, 10, 17, 18]		Stage I	83%	91%	
			Stage II	17%	Poor prognosis	
			Stage III			
			Stage IV			
	Transitional cell carcinoma [8]		Stage II–IV in more than 2/3		35%	
	Malignant brenner tumor [8]		Stage I	80%	88% (stage IA)	
	Undifferentiated [8]		Stage I	6%	6%	
			Stage II	3%		
			Stage III	74%		
			Stage IV	17%		
	Mixed [8]		Stage I	93%	The dominant cell type dictates behavior	
Sex cord—stromal 1–2% of OC [9] [8]	Granulosa cell	Juvenile	Stage I	98%	98.5% in stage IA (Poor in stage II–IV)	
		Adult	Stage I	90%		
	Fibrosarcoma		Malignant course			
	Sertoli–Leydig cell		2%–3% of tumors have spread beyond the pelvis			
	Steroid cell		Sometimes with extensive intra-abdominal spread			

OC, ovarian cancer; EOC, epithelial ovarian carcinoma

Table 2. FIGO staging system for ovarian malignancies, updated in 2014

FIGO ovarian cancer staging (Effective Jan 1, 2014)	
Stage I: tumor confined to ovaries	
IA	Tumor limited to 1 ovary, capsule intact, no tumor on surface, negative washings
IB	Tumor involves both ovaries, capsule intact, no tumor on surface, negative washings
IC1	Tumor limited to 1 or both ovaries with surgical spill
IC2	Tumor limited to 1 or both ovaries with capsule rupture before surgery or tumor on ovarian surface
IC3	Tumor limited to 1 or both ovaries with malignant cells in the ascites or peritoneal washings
Stage II: tumor involves 1 or both ovaries with pelvic extension (below the pelvic brim) or primary peritoneal cancer	
IIA	Extension and/or implant on uterus and/or Fallopian tubes
IIB	Extension to other pelvic intraperitoneal tissues
Stage III: tumor involves 1 or both ovaries with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes	
IIIA1(i)	Positive retroperitoneal lymph nodes ≤ 10 mm
IIIA1(ii)	Positive retroperitoneal lymph nodes > 10 mm
IIIA2	Microscopic extrapelvic peritoneal metastasis beyond the pelvis ± positive retroperitoneal lymph nodes
IIIB	Macroscopic extrapelvic peritoneal metastasis ≤ 2 cm ± positive retroperitoneal lymph nodes. Includes extension to capsule of liver/spleen
IIIC	Macroscopic extrapelvic peritoneal metastasis > 2 cm ± positive retroperitoneal lymph nodes. Incudes extension to capsule of liver/spleen
Stage IV: distant metastasis excluding peritoneal metastasis	
IVA	Pleural effusion with positive cytology
IVB	Hepatic and/or splenic parenchymal metastasis, metastasis to extraabdominal organs (including inguinal lymph nodes and lymph nodes outside the abdominal cavity)

Although surgical staging is the gold standard staging system in ovarian cancer, pre-operative staging on imaging is essential as it allows evaluation of disease extent as well as demonstrating parenchymal organ metastases and sites of disease outside the peritoneal cavity, including the thorax, umbilical disease, or inguinal nodes,. The aim of surgery is to remove all visible sites of disease, known as complete macroscopic cytoreduction. However, in some cases, small sites of visible disease may remain and if these sites are less than 1cm in size, then the patient is considered to have had optimal cytoreduction. If residual sites of disease are larger than 1cm in size, then this is termed suboptimal cytoreduction. If it is thought that complete or optimal cytoreduction cannot be achieved, neo-adjuvant chemotherapy is considered to be the best choice of initial treatment, prior to consideration of delayed primary (so-called interval) cytoreductive surgery, usually after three cycles of chemotherapy. Imaging evaluation may help to determine the feasibility of cytoreductive surgery, demonstrating the volume of disease, as well as to assist in surgical planning by preoperatively identifying the sites of macroscopic disease that may be difficult to resect, including disease involving the small bowel mesentery, porta hepatis, and suprarenal nodal disease. Pre-operative imaging is also necessary to direct biopsy for histological diagnosis prior to starting neo-adjuvant chemotherapy in those patients that are considered unresectable.

Radiological staging

Technique

US

The primary imaging modality for patients with suspected adnexal masses is ultrasound. Transvaginal ultrasound provides high-resolution views of the adnexa in most cases and allows for adnexal mass characterization, evaluation of pelvic structures, and detection of ascites. Many ultrasound interpretation guidelines have been proposed; the highly validated International Ovarian Tumor Analysis (IOTA) simple rules are now widely used [19, 20]. According to IOTA simple rules, an adnexal mass is likely to be malignant if it has only M features which include an irregular solid tumor, presence of ascites, more than 4 papillary projections, irregular multilocular solid tumor larger than 10 cm, and very strong blood flow (color score 4) at color-Doppler evaluation. Benign tumor is likely if it has only B features which include a unilocular cyst, solid component less than 7 mm, acoustic shadowing, smooth multilocular tumor less than 10 cm, and no blood flow (color score 1) [21]. Indeterminate masses have M and B features or neither and require further characterization, which may be done with pelvic MRI. US remains the initial investigation for patients with ovarian masses and may be a useful adjunct to staging CT in early-stage disease.

CT

CT imaging with intravenous contrast enhancement from the thorax to the inguinal region is the current standard of care in pre-operative ovarian cancer staging [22, 23]. Optimal conspicuity of disease is achieved by scanning in the venous phase. Bowel may be opacified with positive contrast (for example, diluted Gastrografin or water soluble iodinated contrast) or negative contrast (i.e., water or VoLumen). However, it should be noted that positive contrast may sometimes obscure calcified peritoneal deposits. For this reason, negative contrast in the form of up to 1L of water within one hour of the scan is favored by many institutions [24]. CT imaging provides clinically relevant information including size and location of peritoneal deposits and enlarged nodes. The presence of ascites in advanced ovarian cancer is advantageous for CT as it makes identification of lesions easier as peritoneal surfaces and bowel loops are more clearly delineated against the fluid. The most important limitation is the identification of small-size peritoneal metastases, which have similar attenuation to adjacent normal structures (unless calcified) and may be too small to be confidently visualized.

MRI

Multi-parametric MRI may be used as an adjunct to CT as it performs better in the detection of subtle peritoneal disease. MRI may also be used when CT is contra-indicated due to iodine allergy, renal failure and in pregnancy as non-contrast sequences, including diffusion-weighted imaging, remain highly sensitive for detection of peritoneal disease. Although the imaging protocol varies from department to department, the protocol for the mapping of peritoneal disease should at least include contiguously stacked axial T1W, T2W, DWI, and T1W fat-suppressed pre-contrast and delayed post-contrast of the abdomen and pelvis if in addition to a breath-hold coronal T2 to view the diaphragms. To better evaluate for invasion of pelvic structures, high-resolution T2 images of the pelvis in the axial and sagittal planes may also be helpful.

PET-CT

PET-CT has limited utility in the initial ovarian cancer staging. FDG uptake varies depending on histological types and biological behavior of the underlying tumor. Nevertheless, it may be used as a problem-solving tool particularly in confirmation of stage IV disease, as in suspected mediastinal or thoracic disease; or in patients who cannot undergo MRI in case of inconclusive CT. Although the utility of PET/CT is not established in the initial imaging and staging of ovarian cancer, parameters such as SUV have been found by some investigators to be of prognostic value, for example in clear cell ovarian cancer [25]. However, published literature related to PET/CT in prediction of prognosis is fairly heterogenous [26].

Imaging stages

The majority of patients are formally staged at the time of presentation. The most recent staging data from Cancer Research UK indicate that approximately 15% of cases remain unstaged [27].

Stage I

In the UK, 31% of ovarian cancers are diagnosed at stage 1 [27]. Patients with a suspected pelvic mass should undergo ultrasound as the initial imaging test. Transvaginal ultrasound provides high-resolution detail of the adnexa in most patients.

In stage 1 ovarian cancer, tumor is limited to the ovaries. Stage IA (Fig. 1) tumor is unilateral with intact ovarian capsule and with no tumor on the ovarian surface. Imaging findings include a unilateral well-circumscribed solid or mixed solid and cystic mass, multiseptated with irregular septa > 3 mm thick. Solid tissues, which include enhancing irregular septations, papillary projections, or solid masses, are hallmarks of ovarian malignancy. The solid component and thick septa demonstrate vascularity on color Doppler on ultrasound and enhancement with CT or MRI [21, 28].

When tumor is present in both ovaries, with intact ovarian capsule and no tumor on the ovarian surface, this corresponds to stage IB. This occurs in approximately 6 to 13% of the patients with stage I disease [29]. If there is ascites, this must be confirmed to be free of malignant cells by cytology upon surgical staging.

Image findings in stage IC may be similar to those described above, but may be up-staged due to spill of cyst contents during surgery (1C1), rupture of the capsule before surgery or tumor on ovarian surface (1C2), or the presence of malignant cells in ascites or peritoneal washings (IC3) (Fig. 2) [10]. In the case of cyst rupture prior to surgery, imaging may demonstrate free fluid or blood in the peritoneum and some collapse of the adnexal cyst.

Stage II

Stage II disease is limited to the true pelvis and is found in 5% of patients diagnosed with ovarian cancer [27]. Stage IIA involves one or both ovaries and fallopian tubes and/or direct extension or implantation to the surfaces of the uterus or fallopian tubes.

Involvement of other pelvic intraperitoneal tissues, including the serosal surface of the bladder or intrapelvic sigmoid colon, denotes stage IIB (Fig. 3). On imaging, local disease extension may lead to distortion of the infiltrated structure and loss of tissue planes. Some authorities consider tumor within 3 mm of the pelvic sidewall to be stage IIB [29].

Stage III

Stage III implies involvement of one or both ovaries or fallopian tubes with disease extension beyond the pelvis to the retroperitoneal nodes and/or peritoneum and accounts for 31% of new diagnoses [27]. Stage IIIA encompasses positive nodes (IIIA1) and microscopic peritoneal metastasis (IIIA2). While microscopic nodal metastases cannot be elucidated with imaging, nodal disease is subcategorized as IIIA1(i) for subcentimeter nodes and IIIA1(ii) for nodes larger than 1 cm in short axis, which can be diagnosed on imaging. The commonest site of nodal metastases is to the para-aortic and paracaval nodes at the level of the renal hila, following the anatomic lymphatic drainage of the ovaries [30].

Stage IIIB is characterized by macroscopic peritoneal metastasis beyond pelvis which are < 2 cm, with or without positive retroperitoneal lymph nodes. Careful and systematic search for subtle signs of peritoneal disease is crucial. There is preferential flow and subsequent tumor seeding along the right para-colic gutter, liver capsule, and diaphragm [30]; hence, these should be regarded as essential review areas. Subtle signs of peritoneal disease include peritoneal thickening at the pelvic peritoneal reflections and the para-colic gutters. Diaphragmatic disease is best evaluated on coronal CT or MR images. Ascites improves the conspicuity of subtle diaphragmatic and peritoneal deposits, where there may be irregularity of the peritoneal surface.

In stage IIIC (Figs. 4, 5), there is macroscopic peritoneal metastasis beyond the pelvis, > 2 cm in greatest dimension with or without positive retroperitoneal lymph nodes. Liver and spleen surface metastases are frequent but parenchymal metastases are rare. Liver and spleen serosal deposits are usually smooth, well defined, and have an elliptic or biconvex appearance and may extend along the falciform ligament. These should be differentiated from the parenchymal metastases which are less well defined and surrounded by liver parenchyma [30].

Stage IV

18% of women have stage IV disease (Fig. 6) at presentation [27]. Malignant pleural effusion (cytologically confirmed), visceral haematogenous metastases (such as liver or spleen parenchymal metastases), and disease outside the abdominal and pelvic cavity denote stage IV and confer the poorest prognosis. Cardiophrenic lymph nodes larger than 5 mm would be considered suspicious of stage IV [22, 29]. Involvement of the cardiophrenic

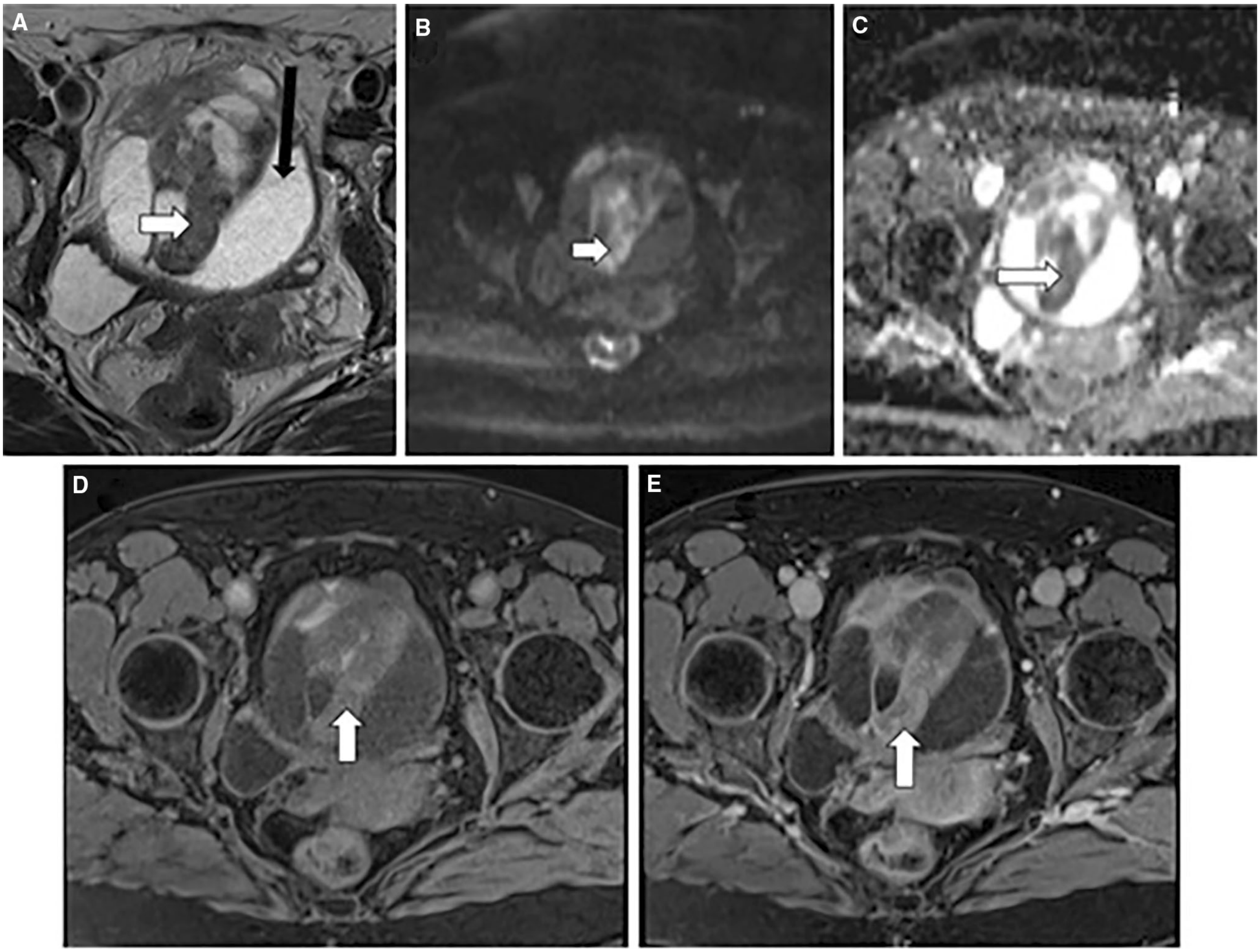

Fig. 1. T2WI, DWI, and ADC, pre- and post-contrast T1WI FS (**A**–**E**) images through the pelvis. This patient had a large complex adnexal mass with mixed solid (white arrows) and cystic components (black arrow). The solid components demonstrated restricted diffusion (**B**, **C**) and contrast enhancement (**E**) further raising the suspicion for malignancy. The entire mass was excised intact at surgery and found to be moderately differentiated mucinous adenocarcinoma. There was no tumor in the right ovary, uterus, and the fallopian tubes and ascitic cytology was negative. This was therefore stage IA despite the fairly large and complex mass.

nodes is thought to be through transdiaphragmatic spread rather than hematogenous spread. Umbilical metastases (Sister Mary Joseph nodule) and involved inguinal nodes also denote stage IV disease (Table 3).

Comparison of modalities with the review of the literature

Although CT remains routine for pre-operative staging of ovarian cancer, complementary MRI or PET/CT may be performed in some centers to improve diagnostic and staging accuracy [25, 31, 32]. MRI is well established as a tool for characterization of indeterminate adnexal masses and is increasingly being used in ovarian cancer staging, due to excellent tissue contrast, better detection of small peritoneal lesions, and better assessment of direct invasion of pelvic structures [33–35]. FDG-PET/CT is not widely used for initial staging but it may be utilized to evaluate suspicious CT findings which could up-stage to stage IV, particularly if a patient is unable to undergo MRI [36].

In 2011, the published *evidence paper for the development of the NICE ovarian cancer guidelines* [37] identified a relative lack of robust evidence to support CT as the modality of choice for the initial pre-treatment staging of ovarian cancer and it was felt that more evidence is needed to identify the most effective image-based staging modality for decision-making related to the best initial treatment choice. We searched the recent pubmed literature from 2011 to 2018 to identify further evidence for the use of each modality, including US, CT, MRI, and FDG-PET/CT in order to better evaluate the role of each technique, their strength, shortfalls, and capability to predict optimal cytoreduction, with particular regard to the more frequent sites of secondary

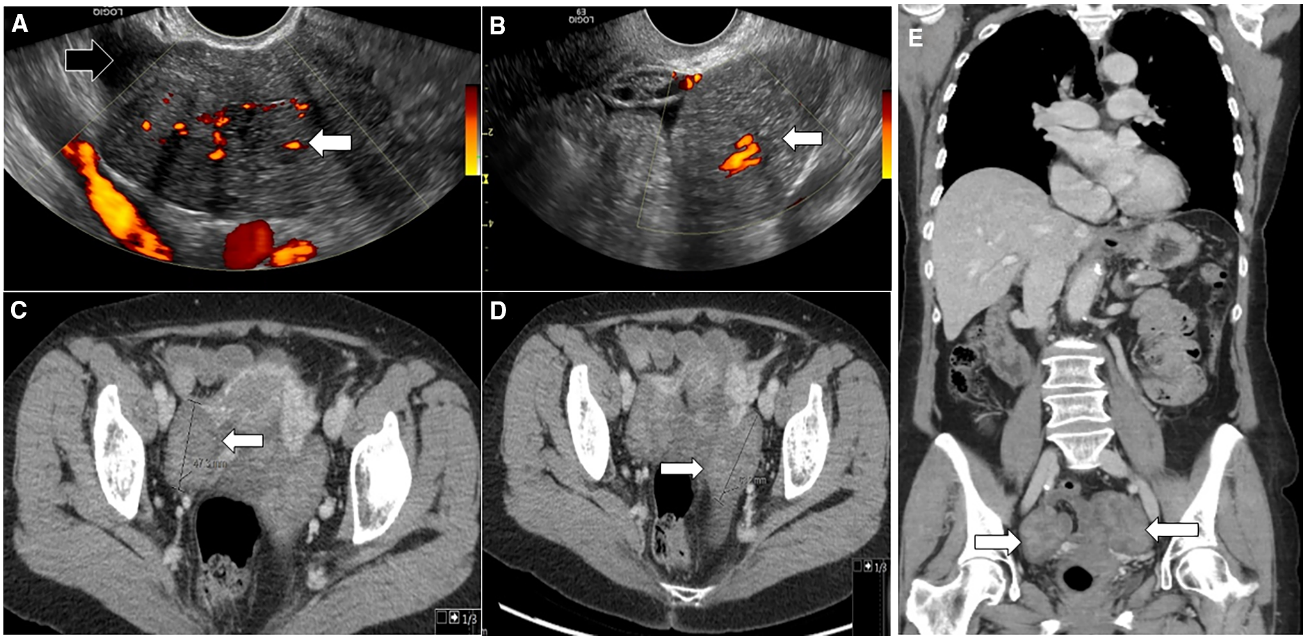

Fig. 2. The solid, vascular bilateral ovarian masses (**A**, **B**, **C**, **D**, **E**—white arrows) in this patient were first detected by transvaginal ultrasound (**A**, **B**). A small amount of fluid was also present during the ultrasound (black arrow). Histology after surgery confirmed this to be borderline seromucinous tumor with intraepithelial carcinoma in both ovaries, and the peritoneal fluid contained malignant cells on cytology. Final stage was IC3.

involvement that are likely to change clinical management.

We included papers reporting ovarian cancer stage based on imaging where the study population was 20 or more, with sufficient data quality and with histopathological results as the reference standard (Table 4).

In a prospective study involving 46 patients, Glaser et al. [38] evaluated CT accuracy of staging ovarian cancer demonstrating a low sensitivity and an high specificity for peritoneal (respectively 55.9% and 95%), large bowel (29% and 91%), mesenteric root (36% and 90%), and diaphragmatic disease (48% and 100%). Espada et al. [33] in a prospective study involving 34 patients evaluated the role of abdominal DWI-MRI in staging advanced (stage III and IV) ovarian cancer. They reported, for different sites of disease, a relatively high sensitivity (ranging from 69.2% to 100%) and specificity (from 81% to 96.6%). Nasser et al. [39] performed a retrospective study, involving 155 patients with either primary advanced (n = 105) or recurrent (n = 50) disease. CT findings were reported to be of high specificity for all sites of disease (ranging from 98% to 99%), but with a relatively lower sensitivity and specificity (respectively 67% and 78%) for retroperitoneal nodal metastases, due to the inability of CT to rule out microscopic tumor infiltration in normal-sized nodes and conversely overcall nodal involvement in the case of prominent benign inflammatory nodes.

Michielsen et al. [31] performed a prospective study involving 94 patients with primary ovarian cancer (stage I–IV) and compared the diagnostic performance of whole-body MRI and contrast-enhanced CT in prediction of suboptimal cytoreduction. They reported superiority of WB-MRI (accuracy 95.7% versus 71.3%) which was mainly attributed to more accurate evaluation of the peritoneum, nodes, duodenum, stomach, celiac trunk, mesenteric root, and distant metastases.

All studies identified consistently demonstrated that CT staging is associated with high specificity for predicting optimal cytoreduction but relatively poor sensitivity, particularly in identifying peritoneal, bowel, mesenteric, and diaphragmatic disease which are crucial sites in planning patient management and predicting surgical outcome.

In earlier literature, Coakley et al. [29] found that CT sensitivity is low for the detection of peritoneal disease sites smaller than 1 cm with results variable from 25% and 50% between the three readers. They suggest that CT is more likely to be accurate in cases of very advanced stage but it is not able to rule out diffuse disease when CT findings are negative in the peritoneum, resulting in frequent under-staging.

Considering the extensive evidence of false negative on CT for small volume peritoneal disease, there is the need for a further staging method with higher sensitivity. MRI-DWI has proved to increase accuracy in detecting peritoneal disease thanks to its ability to identify subcentimeter sites of disease (including some < 5 mm) due its high contrast resolution [40, 41]. Low et al. [34] highlighted how DCE and DWI increase accuracy

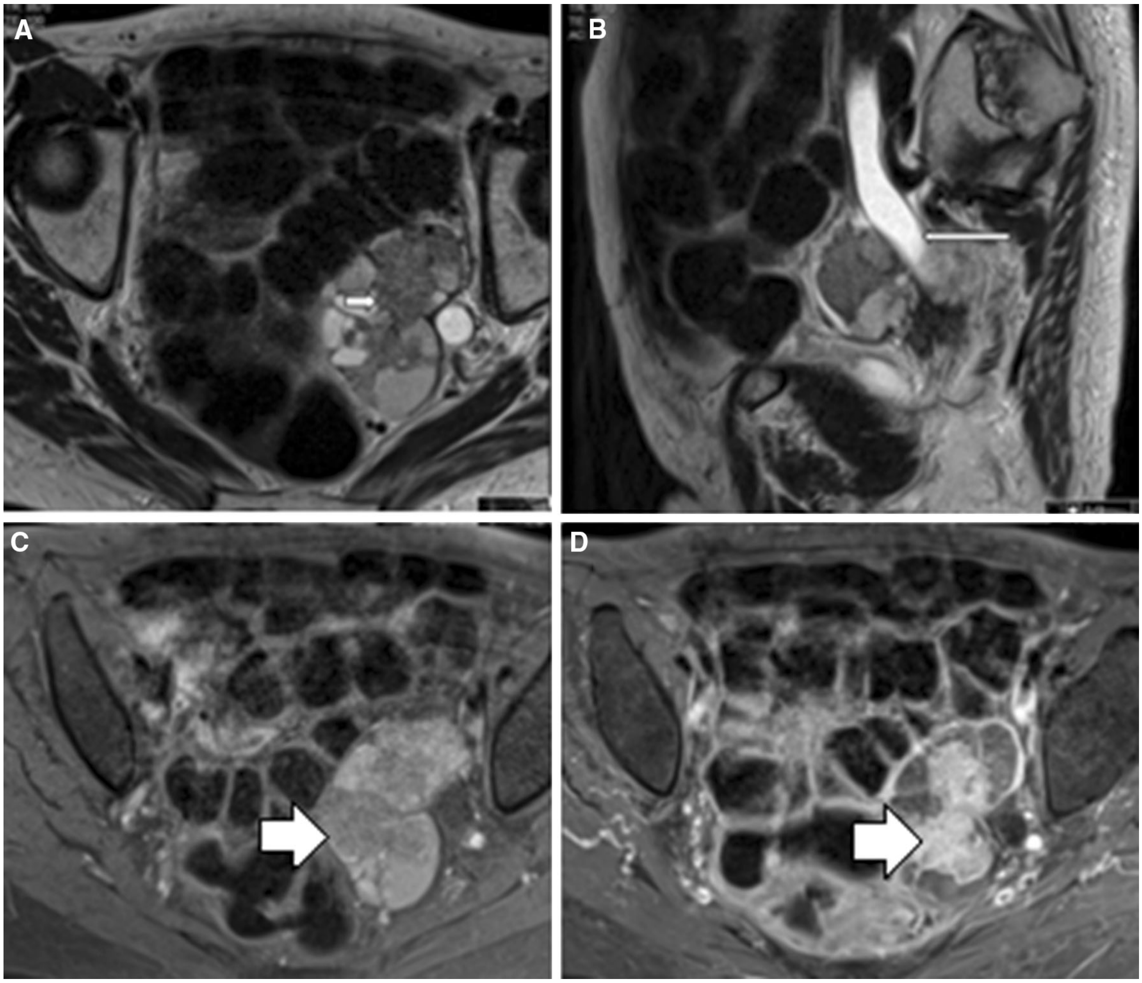

Fig. 3. The left ovarian mass (white arrows—**A**, **C**, **D**) in this patient had invaded the left pelvic sidewall and left distal ureter, resulting in left hydronephrosis (slender arrow—**B**). Histology specimen revealed endometrioid adenocarcinoma with evidence of invasion of the distal ureter. There were no other sites of disease—final histology stage was IIB.

compared with morphological images in patients with suspected peritoneal dissemination from abdominal tumors allowing an accurate prediction of peritoneal cancer index. The published literature to support the standardized use of functional MRI in ovarian cancer staging remains limited but continues to develop.

FDG-PET-CT has some utility as a problem-solving modality when there are discrepancies between CT findings and clinical evidence or to better evaluate suspected stage IV disease. Nam et al. [42] in a prospective study with 95 patients reported a concordance between staging with FDG-PET/CT and surgical staging of 78%.

Pitfalls in ovarian cancer staging

Most of the pitfalls are due to inherent inability of the imaging modality to either identify the extent of disease resulting in under-staging, or conversely, due to physiological appearances which mimic disease and thus over-staging.

Small volume peritoneal disease

Small lesions less than 5 mm in the peritoneum are not readily identifiable on CT. Despite better tissue contrast with MRI, using DWI and post-contrast T1FS imaging, small peritoneal deposits may still be obscured by bowel. FDG-PET/CT is limited in identifying subcentimeter peritoneal deposits and detecting low-volume peritoneal involvement. Disease under the surface of the diaphragm may be overlooked if only the axial images are reviewed and it is essential to review the coronal and/or axial images as a routine (Fig 4G).

Nodal involvement

The use of size criteria in determining nodal disease is inaccurate as micrometastases cannot be ruled out in otherwise normal-sized nodes, while enlarged nodes may be reactive on histology. Para-cardiac, para-aortic, and pelvic lymph nodes are easily identified but delineating malignant from benign may not be reliable using mor-

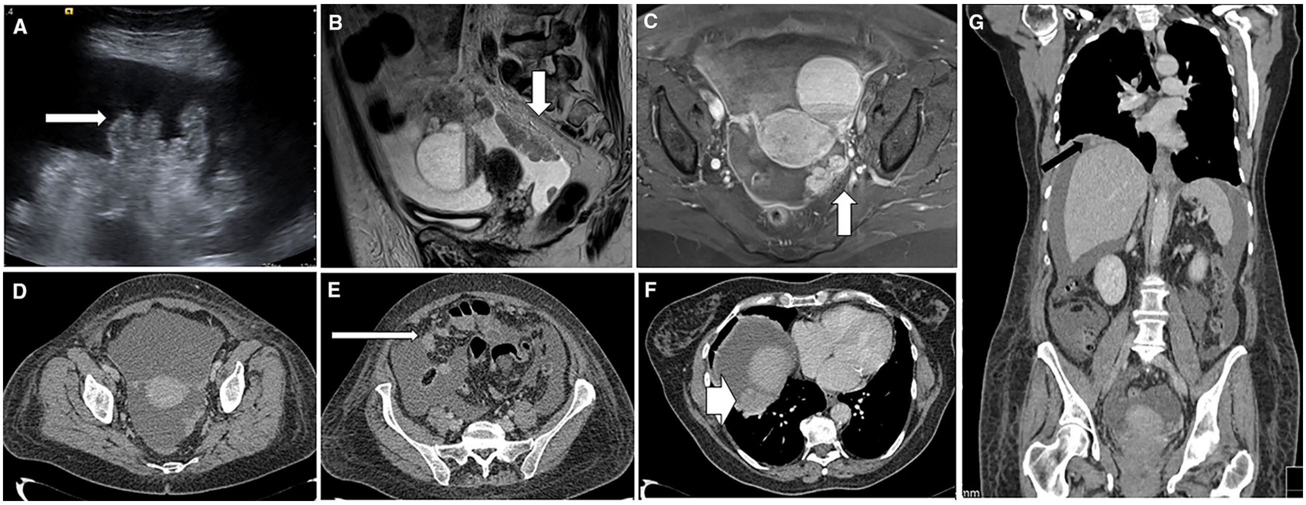

Fig. 4. The patient underwent initial evaluation with ultrasound which showed ascites and pelvic mass with papillary projections (**A**). Pelvis MRI revealed enhancing peritoneal deposits (**B**, **C**). CT chest, abdomen, and pelvis demonstrated further sites of peritoneal disease (**D**, **E**, **F**, **G**) and under the right hemidiaphragm (thick arrow—**F**). Coronal images are useful in demonstrating subdiaphragmatic disease (black arrow—**G**). This corresponds to stage IIIC.

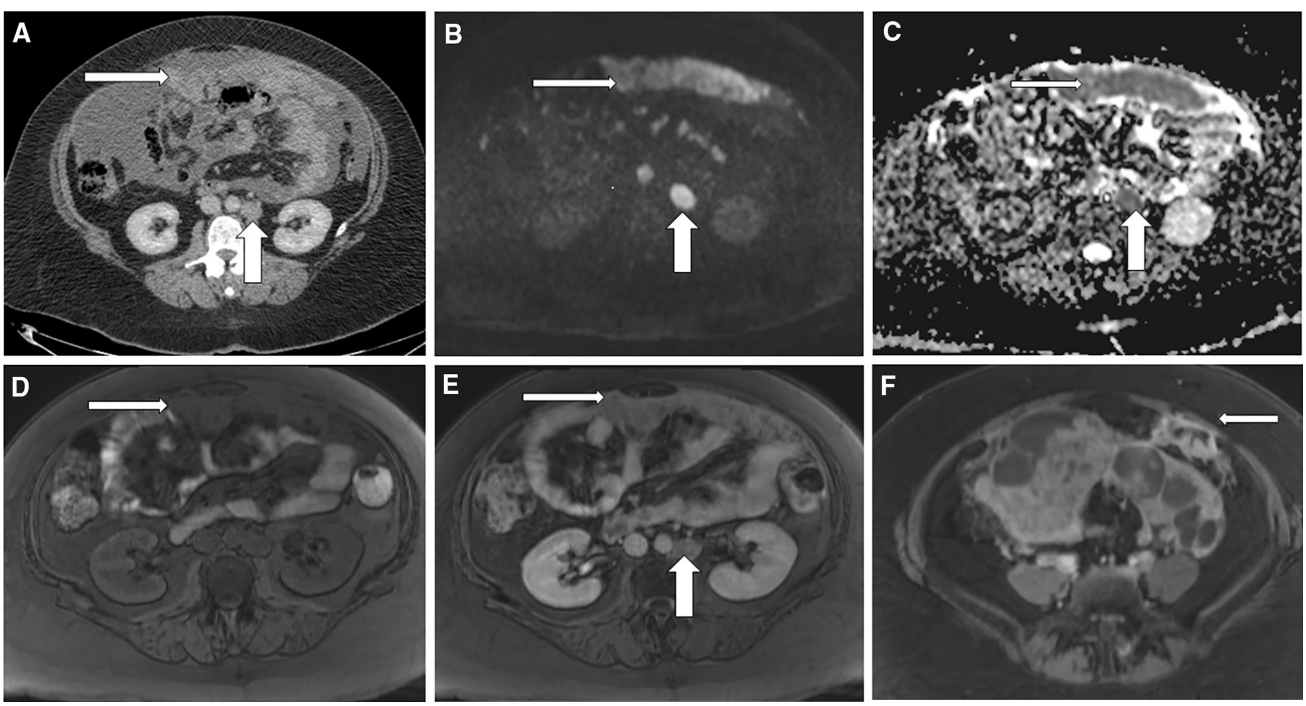

Fig. 5. This patient had bilateral ovarian masses. Staging CT (**A**) demonstrated omental cake (slender arrows), which showed restricted diffusion on MRI (**B**, **C**) and contrast enhancement (**D**-pre-contrast sequence; **E**, **F**-post-contrast sequences). Aortocaval and left para-aortic nodes also demonstrated restricted diffusion (vertical arrows). Histology was low-grade serous adenocarcinoma. This corresponds to stage IIIC.

phological criteria, size, and attenuation/signal characteristics. PET/CT would detect abnormal uptake in nodes greater than 8–10 mm in short axis with the caveat that metastatic nodes with necrosis, cystic, or mucinous degeneration may not be FDG avid PET imaging. Diffusion-weighted imaging has been reported to improve staging accuracy [31] but can also be challenging [43] as it is very sensitive but non-specific in detecting involved lymph nodes and some physiological appearances are difficult to confidently differentiate from tumor. In addition, DWI has poor anatomic localization and is more susceptible to image degradation by artifacts,

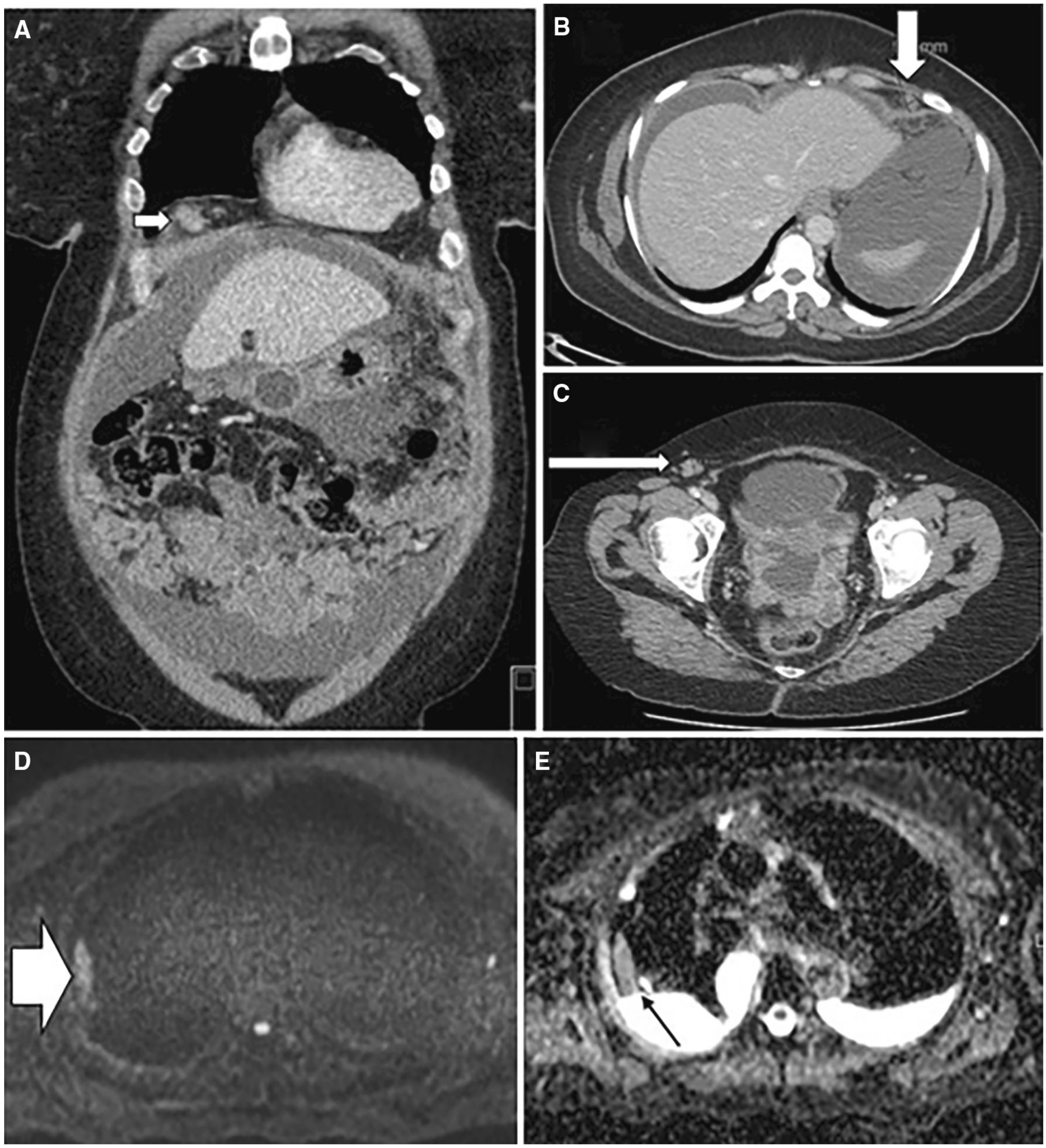

Fig. 6. Different sites of stage IV disease: CT demonstrates diaphragmatic nodes (**A**, **B**, white arrows) in a patient with disseminated peritoneal disease. Right inguinal histologically proven lymphadenopathy (**C**—different patient, white arrow). MRI through the lung bases of another patient (**D**, **E**) demonstrated solid pleural disease (arrows) which had restricted diffusion. Cytology of the pleural effusion was also positive for malignancy.

Table 3. Typical sites of stage 4 disease

Supra diaphragmatic sites	Infradiaphragmatic sites	Other sites
i. Diaphragmatic/precardiac nodes ii. Malignant pleural effusion iii. Solid pleural deposits iv. Other mediastinal, supraclavicular, or axillary nodes	i. Visceral liver metastases ii. Visceral splenic metastases	i. Inguinal lymph nodes ii. Umbilical metastasis

Table 4. Recent literature evidences regarding imaging accuracy in staging ovarian cancer

Author	Date/study	Patients Total/staged	Stage	TP	FP	TN	FN	Sens	Spec	ACC	PPV	NPV
Peritoneal disease												
Contrast-enhanced CT												
Michielsen et al.	2017-prospective	161/94	I–IV	19	3	57	15	55.9%	95%	80.1%	86.4%	79.2%
Glaser et al.	2013-prospective	50/46	IIIc–IV	13	1	7	25	55.9%	95%	80.1%	86.4%	79.2%
DWI-MRI												
Espada et al.	2013-prospective	36/34	III–IV	9	4	17	4	69.2%	81%	–	69.2%	81%
Whole-body MRI												
Michielsen et al.	2017-prospective	161/94	I–IV	32	2	58	2	94.1%	96.7%	95.7%	94.1%	96.7%
Nodal disease (suprarenal RP)												
Contrast-enhanced CT												
Michielsen et al.	2017-prospective	161/94	I–IV	13	4	75	2	86.7%	94.9%	93.6%	76.5%	97.4%
Nasser et al.	2016-retrospective	155	POC ROC	35	22	77	21	63%	78%	–	61%	78%
DWI-MRI												
Espada et al. (LN > 1 cm)	2013-prospective	36/34	III–IV	5	4	25	0	100%	86.2%	–	55%	100%
Whole-body MRI												
Michielsen et al.	2017-prospective	161/94	I–IV	15	1	78	0	100%	98.7%	98.9%	93.8%	100%
Large bowel involvement												
Contrast-enhanced CT												
Nasser et al.	2016-retrospective	155	POC ROC	17	2	16	20	46%	98%	–	89%	85%
Glaser et al.	2013-prospective	50/46	IIIc–IV	10	1	10	25	29%	91%	–	–	–
Small bowel involvement												
Contrast-enhanced CT												
Nasser et al.	2016-retrospective	155/105	POC ROC	7	2	138	9	44%	99%	–	88%	94%
Mesenteric root and superior mesenteric artery												
Contrast-enhanced CT												
Michielsen et al.	2017-prospective	161/94	I–IV	3	0	86	5	37.5%	100%	94.7%	100%	94.5%
Gleaser et al.	2013-prospective	50/46	IIIc–IV	13	1	9	23	36%	90%	–	–	–
Nasser et al.	2016-retrospective	155	POC ROC	12	1	115	27	31%	99%	–	92%	81%
DWI-MRI												
Espada et al.	2013-prospective	36/34	III_IV	22	4	8	4	100%	84.6%	–	66.6%	100%
Whole-body MRI												
Michielsen et al	2017-prospective	161/94	I–IV	8	1	85	0	100%	98.8%	98.8%	88.9%	100%
Duodenum, stomach, celiac trunk												
Contrast-enhanced CT												
Michielsen et al.	2017-prospective	161/94	I–IV	11	1	77	5	68.8%	98.7%	93.6%	91.7%	93.9%
Whole-body MRI												
Michielsen et al.	2017-prospective	161/94	I–IV	15	1	77	1	93.8%	98.7%	97.9%	93.8%	98.7%
Diaphragmatic involvement												
Contrast-enhanced CT												
Nasser et al.	2016-retrospective	155	POC ROC	19	1	95	40	32%	99%	–	95%	70%
Glaser et al.	2013-prospective	50/46	IIIc–IV	15	0	15	16	48%	100%	–	–	–
DWI-MRI												
Espada et al.	2013-prospective	36/34	III–IV	4	1	28	1	80.0%	96.6%	–	80%	96.6%
Splenic disease												
Contrast-enhanced CT												
Nasser et al.	2016-retrospective	155	POC ROC	5	2	134	14	26%	99%	–	95%	70%
Glaser et al	2013-prospective	50/46	I–IV	1	2	43	0	100%	96%	–	–	–
Distant metastases												
Contrast-enhanced CT												
Michielsen et al.	2017-prospective	161/94	I–IV	20	10	49	15	57.1%	83.1%	73.4%	66.7%	76.6%
Whole-body MRI												
Michielsen et al.	2017-prospective	161/94	I–IV	34	1	58	15	97.1%	98.3%	97.9%	97.1%	98.3%
Prediction of suboptimal cytoreduction												
Contrast-enhanced CT												
Michielsen et al.	2017-prospective	161/94	I–IV	33	10	34	17	66.0%	77.3%	71.3%	76.7%	66.7%
Whole-body MRI												
Michielsen et al.	2017-prospective	161/94	I–IV	47	1	43	3	94.0%	97.7%	95.7%	97.9%	93.5%

POC, primary ovarian cancer; **ROC**, recurrent ovarian cancer; **LN**, lymph nodes which can be particularly problematic in the abdomen due to the presence of bowel gas.

Conclusion

Accurate and reliable radiological staging of ovarian cancer is an essential component of the work-up of women with newly diagnosed ovarian cancer. Surgical decision-making, operative planning, and the necessity and timing of systemic therapy all rely on radiological staging. Staging is also important in predicting survival outcomes. Radiologists should be familiar with radiological staging with regard to the optimal imaging modality, technique, and interpretation. Although not currently supported by robust evidence, functional MRI is developing and may be critical in the future of ovarian cancer imaging. On the basis of known patterns of disease spread, review areas should be given sufficient attention during image interpretation. Radiologists should also be aware of the limitations and potential pitfalls of imaging-based staging.

Compliance with ethical standards

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Ethical approval This article does not contain any studies with animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the paper.

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