Chapter 8

The Past, Present and Future of Diagnostic Imaging in Ovarian Cancer

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Additional information is available at the end of the chapter

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Abstract

Ovarian cancers (OC) include a group of diseases with variable prognoses. While most conventional imaging techniques rely on the detection of tumour burden and distant spread to identify treatment plans, more emphasis is now being placed on screening for early detection and also for more accurate staging using molecular imaging techniques. It is generally accepted that there are some incremental benefits of using serum CA125 levels coupled with cross-sectional diagnostic imaging to aid in the diagnosis, staging and treatment planning of OC. This chapter provides a review of tests and diagnostic imaging modalities that aid in the detection and staging of OC with a particular focus on F18-Fluorodeoxyglucose positron emission tomography/computed tomography (F18-FDG PET/CT) imaging. This chapter also proposes a diagnostic algorithm for the management of ovarian cancer. F18-FDG PET/CT imaging can act as a catalyst for the development of personalised medicine by stimulating advancements in targeted therapy. In conclusion, diagnostic imaging with particular focus in molecular imaging has the potential for altering management plans, which can ultimately help improve the prognosis of ovarian cancer.

Keywords: diagnostic imaging, MRI, PET/CT, molecular imaging, adnexal mass

1. Introduction

This chapter regarding diagnostic imaging aims to guide multidisciplinary teams to decide on further investigation of ovarian cancer (OC), by proposing a diagnostic imaging algorithm (**Figure 1**) for the detection and staging of this disease [1, 2]. Furthermore, it provides a special focus on the evolving utility of molecular imaging, specifically PET/CT imaging in the management of ovarian cancer [3].

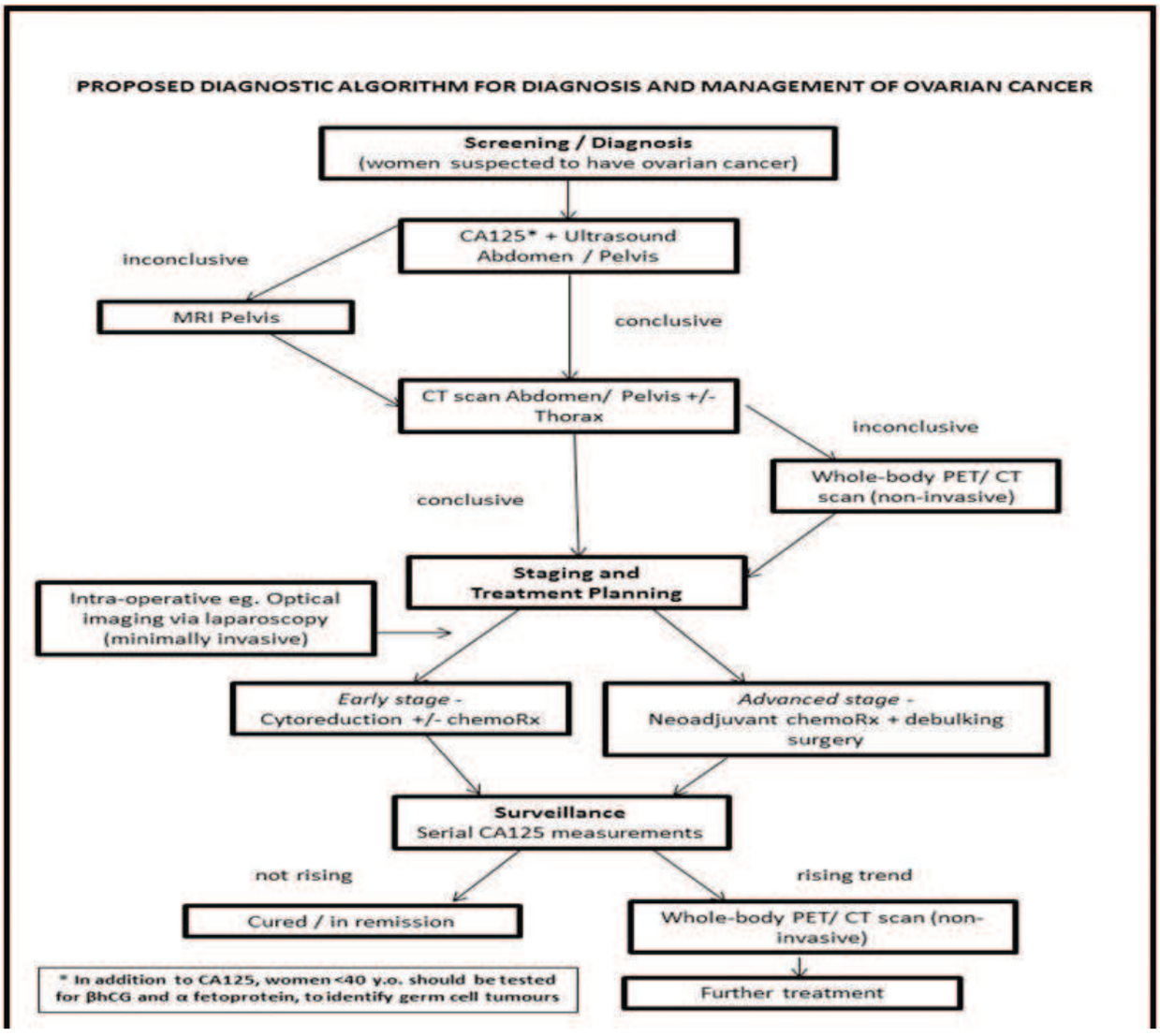

Figure 1. Diagnostic imaging algorithm for management of ovarian cancer (adapted from Suppiah et al. [1]).

Before illustrating diagnostic imaging methods for detecting OC, it is best to understand the embryology of the disease. Given that there is a remarkable morphologic and molecular heterogeneity in OC, therefore it has been postulated that ovarian cancers can be divided into Type I (indolent) and Type II (aggressive) tumours [4]. Type I is composed of low-grade serous, low-grade endometrioid, clear cell, mucinous and transitional carcinomas. These tumours are confined to the ovary at presentation and are relatively genetically stable and the majority display KRAS, BRAF and ERBB2 mutations [5]. Type II tumours include high-grade serous carcinoma (HGSC), undifferentiated carcinoma, and malignant mixed mesodermal tumours (carcinosarcoma), are highly aggressive, evolve rapidly and almost always present at an advanced stage. They display TP53 mutations in over 80% of cases and rarely harbour the mutations found in Type I tumours. Type I is suggested to be of Müllerian-type of tissues in origin, whereas Type II tumours are mesothelium in source and are suspected to originate from the Fallopian tubes [5].

Currently there is no test which is entirely distinct and suitable to be used for population screening in women with low to moderate risk of developing OC. Serum tumour marker CA125 measurement has been studied, and include single cut-off points [6] and time-series algorithms [7]. Serum CA125 coupled with conventional imaging such as ultrasound scans have been used to stratify patients who may be at a higher risk of having OC. Magnetic resonance imaging (MRI) and Computed tomography (CT) imaging are useful in further characterising lesions and staging the disease respectively. Conversely, once diagnosed, intra-operative imaging such as optical imaging and hand-held spectroscopic devices can also guide in the detection of small cancers [8].

Furthermore, the advent of newer *in vitro* cancer models to assess for ovarian cancer specific biomarkers has paved the way for the development of potential novel therapeutics [9]. The study of micro-environmental cues in the regulation of miRNAs has also generated a growing need for advancement of *in vivo* functional tests that can help determine the phenotype and physiology of ovarian cancer. Functional imaging such as positron emission tomography/computed tomography (PET/CT) using radiopharmaceuticals, namely 18F-Fluorodeoxyglucose (FDG) enables non-invasive assessment of *in vivo* cellular metabolism.

2. Multimodality diagnostic imaging

Diagnostic tests to detect epithelial ovarian cancer include using serum tumour marker levels correlated with imaging findings. Diagnostic imaging modalities that are frequently used to detect, stage and monitor treatment of ovarian cancers include ultrasound, computed tomography, magnetic resonance imaging and positron emission computed tomography.

2.1. Serum tumour marker CA125

CA125 is a protein that is found in greater concentrations in ovarian cancer tumour cells than in other cells of the human body. Therefore, a simple blood test, using a sample taken from a peripheral vein, makes it possible for it to be used as a marker to detect the presence of ovarian cancer. Nevertheless, it is non-specific for ovarian cancer, as raised levels may also be found in other malignancies, e.g., breast, lung, colon and pancreatic cancer as well as in benign conditions such as in endometriosis, pelvic inflammatory disease and ovarian cysts [10]. CA125 has a high positive predictive value (PPV) of >95%, but a low negative predictive value (NPV) ranging from 50 to 60%, for the detection of OC [11]. Some studies have advocated the use of a single CA125 level measurement, frequently quoting the value 35 IU/ml as a cut-off point to indicate the presence of malignancy [12, 13]. Levels above this have a good positive predictive value, however many actual cancers may have lower levels of CA125 and can be missed [14].

The National Institute for Health and Care Excellence (NICE) clinical guidelines recommend further tests to be done if a CA125 level of >35 IU/ml is detected in a woman suspected to have ovarian cancer [2]. Conversely, when a cut-off of 30 IU/ml is used, the test has a sensitivity of 81% and specificity of 75% [15]. In general, one of the methods for assessment of treatment

response is by monitoring the CA125 levels. Moreover, longitudinal monitoring of CA125 levels can also provide additional information about survival in ovarian cancer [16].

2.2. Risk of malignancy index (RMI)

The risk of malignancy index (RMI) is a validated clinical tool that is used to assess the risk of having OC [2]. RMI combines three pre-surgical features which include serum CA125 levels using the unit IU/ml (CA125), menopausal status (M) and ultrasound score (U) for its assessment, using the formula: RMI = CA125 × M × U. The ultrasound result is scored 1 point for each of the following characteristics, namely the presence of multilocular cysts, solid areas, metastases, ascites and bilateral lesions. U = 0 (for an ultrasound score of 0), U = 1 (for an ultrasound score of 1), U = 3 (for an ultrasound score of 2–5). The menopausal status is scored as 1 = pre-menopausal and 3 = post-menopausal. The classification of 'post-menopausal' is a woman who has had no period for more than 1 year or a woman over 50 years of age and has had a hysterectomy [2].

According to the NICE guidelines, RMI scores are interpreted as low, moderate and high risk based on the total score [2]. Low-risk RMI is for scores <25 (noted in 40% of women, and the risk of cancer is <3%). Moderate-risk RMI is assigned for scores 25–250 (noted in 30% of women, and the risk of cancer is 20%), whereas scores >250 are associated with high-risk RMI (observed in 30% of women, and the risk of cancer is 75%). Women with moderate or intermediate risk are recommended to have an MRI for further evaluation of the ovarian lesion. Whereas, post-menopausal women with an RMI score of >250 should be referred to a cancer centre for further assessment and often undergo a staging computed tomography scan.

2.3. Ultrasound scan

Ultrasound (USS) is a safe, inexpensive and widely available diagnostic modality. Grey scale USS is a real-time imaging that detects the difference in the acoustic impedance (density × velocity of sound) of internal structures and can give excellent soft tissue detail for the evaluation of adnexal masses. Trans-abdominal scan (TAS) and transvaginal scan (TVS) are the first line diagnostic imaging modality for diagnosing OC. TAS utilises a low frequency (3.5–7 MHz) convex probe to characterise adnexal lesions that have grown beyond the pelvic brim. TVS uses a higher frequency (7.5–12 MHz) endocervical probe and gives better spatial resolution as it is placed closer to the ovaries; and is the first line modality of choice for small masses [16]. Nevertheless, a smaller field of view, leading to a possibility of overlooking a larger pelvic mass, is one of its limitations. Therefore, TAS is usually performed first followed by a TVS as a standard scan procedure.

In women suspected of having ovarian cancer, USS is indicated as a first line diagnostic imaging test. USS can diagnose the presence of an adnexal mass and help characterise it. The size, consistency, presence of loculations and solid component within a tumour; are some of the criteria used to characterise adnexal masses. A point to note is that an anechoic ovarian lesion detected in a postmenopausal woman should be considered as a physiological inclusion cyst, and not a pathological cyst if it was smaller than 10 mm and did not distort the ovary [17]. In certain occasions, the presence of bilateral lesions can be detected, and the pouch of Douglas is a common location for a left ovarian lesion (**Figure 2**).

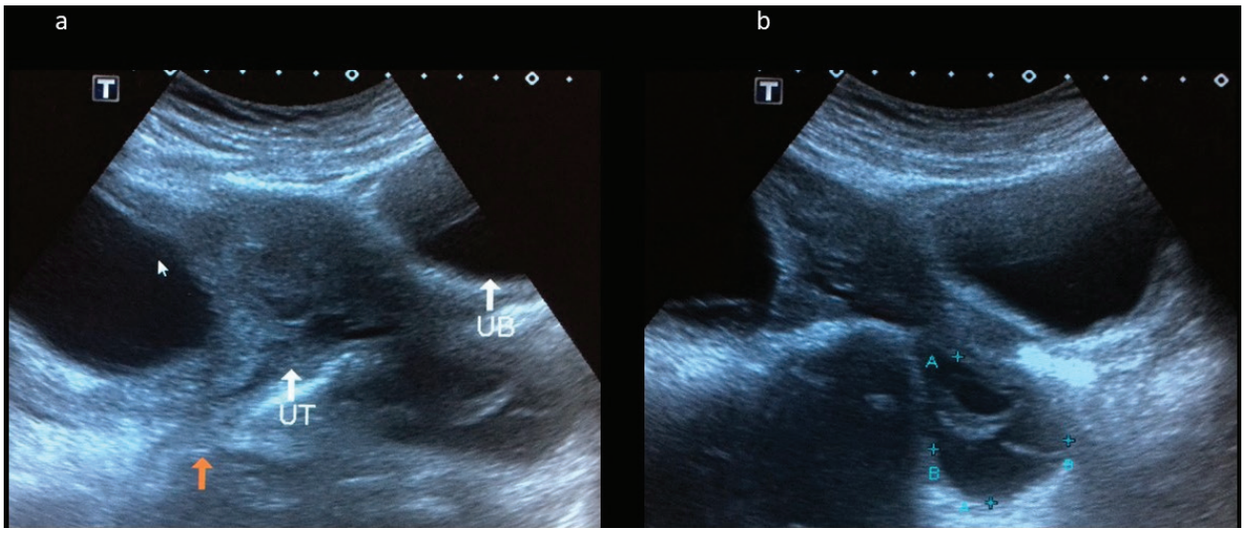

Figure 2. Grey scale ultrasound scans demonstrating suspicious bilateral large adnexal masses in a postmenopausal woman. The white arrow on the left indicates the uterus, the white arrow on the right indicates the urinary bladder and the orange arrow indicates the thick-walled right adnexal mass. Image (b) shows the dimensions of the left adnexal mass.

Figure 2a demonstrates a thick-walled, right adnexal lesion and **Figure 2b** demonstrates a multiseptated, left ovarian lesion in the pouch of Douglas.

2.4. Interpretation of ultrasound imaging

USS has improved specificity in detecting OC by the utility of simple ultrasound rules model [18]. In particular, by using the conventional technique of pattern recognition or subjective assessment by an experienced sonographer, the sensitivity and specificity were 83 and 90%. Whereas, by the technique of using the simple ultrasound rules (**Table 1**) was 92 and 96% respectively [19]. The rules comprised of five ultrasound features to predict a malignant tumour (M features) and five to predict a benign tumour (B features). These include features

Sonographic characteristics	Benign features (B features)	Malignant features (M features)
Tumour size	<100 mm	>100 mm
Loculations	Unilocular, smooth	Multilocular
Consistency	Cystic	Solid, mixed
Papillary projections	None/a few, thin	Multiple (at least 4), thick
Size of largest solid component	None/3–7 mm	Usually >7 mm
Wall	Thin, regular	Thick, irregular
Internal Doppler flow	None/minimal	Increased
Ascites	Absent	Present
Acoustic shadow	Present	Not applicable

Table 1. Sonographic characteristics of ovarian lesions based on simple ultrasound rules [18, 19].

of shape, size, solidity, and results of colour Doppler examination. Masses would be classified as malignant if one or more M features were present in the absence of a B feature. While if one or more B features were present in the absence of an M feature, the mass would be classified as benign. However, if both M features and B features were present, or if none of the features was present, the simple rules were considered inconclusive [20].

Colour Doppler can identify the presence of colour flow, within the papillary or solid components of an ovarian tumour and has good PPV for detecting malignancy. Nevertheless, the absence of colour flow in smaller lesions potentially causes falsely negative observations. False positive findings of flow can also occur in ovarian cysts in the luteal phase in premenopausal women [21].

The sensitivity and specificity of grey scale USS alone has been reported as 88% and 96% respectively; whereas, with the addition of colour Doppler as 83% and 97% respectively [22]. Although the introduction of power 3D Doppler has been able to increase the PPV of detecting malignancy; the availability of instruments and necessary expertise for interpretation has limited the use of this technique [23].

Several scoring systems have been suggested based on USS morphology of ovarian lesions to calculate and determine scores for malignancy [15, 24]. The PPV of these systems are small because the morphology of many benign lesions overlaps with that of malignant disease [21]. Rarely, certain OC are detected in large cysts, usually >7.5 cm in diameter; but do not exhibit an apparent complex morphology on ultrasound [25].

2.5. Limitations and future research in ultrasound

Recently, some experiments have been conducted to evaluate the role of contrast-enhanced USS to help further characterise ovarian tumours [26]. The meta-analysis of 10 studies revealed a pooled sensitivity of 0.89 and specificity of 0.91 respectively [27]. The limitation of ultrasound is the low sensitivity for detection of peritoneal metastasis [28]. Furthermore, screening low-risk population by transvaginal ultrasound may incidentally detect indeterminate lesions and lead to unnecessary biopsies [29]. Therefore, it should not be considered as a standalone investigation to be used to screen the general population for OC.

2.6. Computed tomography (CT) scan

Computed tomography (CT) scan utilises ionising radiation (photon beams of X-ray) to create cross sectional images of the internal organs. CT scans can give detailed information regarding tumour extent and metastatic disease (**Figure 3**). **Figure 3** is a multiplanar CT scan of a patient in axial, coronal and sagittal views, demonstrating a large ovarian cancer with intra-abdominal extension (white arrow) as well as gross ascites (black arrow) and thickened peritoneum consistent with metastasis (red arrow).

It is the preferred modality for the staging of OC and detection of recurrence because it is more widely available and less costly compared to magnetic resonance imaging (MRI) [30]. The Response Evaluation Criteria in Solid Tumours (RECIST) is often used in assessing treatment response in follow up CT scans and may be employed alone or in combination with CA125, for

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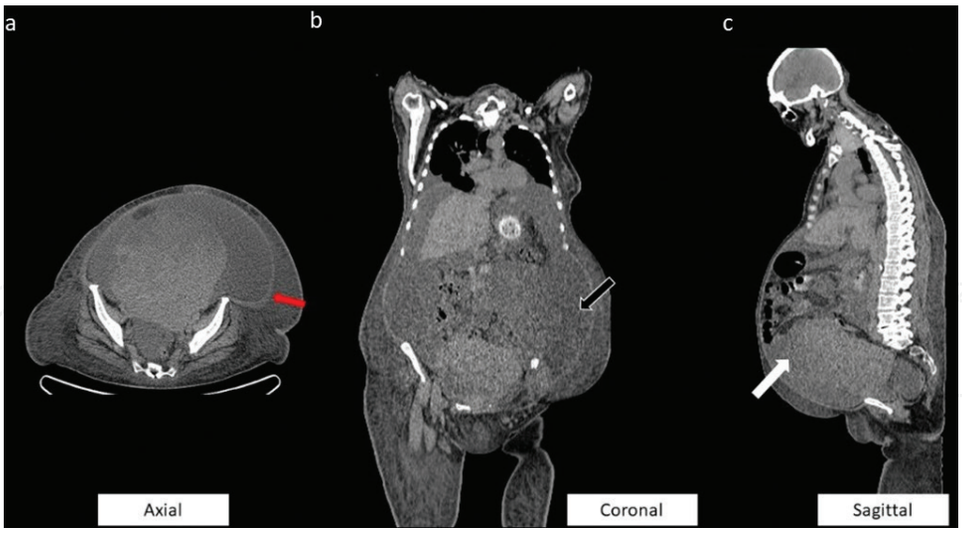

Figure 3. Multiplanar computed tomography scan demonstrating an ovarian cancer. The red arrow shows thickened peritoneum, black arrow shows gross ascites and white arrow shows a large adnexal mass.

evaluating the potential need to start or change the treatment regime [31]. Contrast-enhanced CT (CECT) studies have an added advantage compared to low dose non-enhanced CT scans, as they enable improved delineation of anatomical structures, and increased sensitivity for detection of pathological lesions [32]. Contrast-enhanced PET/CT is a more accurate imaging modality than PET using low dose CT for assessing OC recurrence [33].

Conventional CT has a limited and variable sensitivity of 40–93% and specificity of 50–98% for detection of recurrent disease [30]. Spiral CT can improve the detection of peritoneal lesions and implants, in particular in those with concurrent ascites. Obtaining a CT before secondary debulking may aid in surgical planning and to assess the feasibility of achieving maximum resectability [34].

Contrast-enhanced CT scans (CECT) can detect the involvement of specific intra-abdominal sites recognised to reduce the chances of optimal debulking. These sites include suprarenal aortic lymph nodes, disease in the root of the mesentery, portal triad disease, or bulky liver disease [35]. Conversely, multidetector CECT scans often underestimates the extent of liver surface disease and infra-renal para-aortic lymph node involvement [36]. The reliability of CT assessment is also related to improvements in imaging techniques as well as scanner equipment and this can vary across different centres [37].

2.7. Interpretation of computed tomography scans

CECT provides improved contrast resolution in delineating suspicious adnexal masses [38]. CECT is helpful in characterising benign and malignant ovarian tumours by observation of certain characteristic features (**Table 2**). It can also help differentiate OC subtypes, albeit with some overlapping features, especially the commoner subtypes such as serous tumours. Serous tumours are usually unilocular but with multiple papillary projections and often present bilaterally [39]. Furthermore, peritoneal carcinomatosis is also seen more frequently in serous adenocarcinomas [40].

CT scan characteristics	Benign	Malignant
Size	<4 cm	>4 cm
Consistency	Cystic	Mixed/Solid
Papillary projections	Absent/a few	Multiple
Wall	Thin, regular	Thick, irregular
Internal calcifications	Occasionally present	Infrequently present
Pelvic lymphadenopathy	Absent	Present
Laterality	Unilateral	Bilateral
Ascites	Absent	Present
Peritoneal involvement	Absent	Present
Distant organ metastasis	Absent	Present

Table 2. Computed tomography characteristics of adnexal masses (adapted from Suppiah et al. [38] and Jung et al. [9]).

2.8. Limitations and future research in computed tomography

The main limitation of a CT scan is its inability to detect deposits on bowel serosa, mesentery and omental regions that are smaller than 5 mm; especially in the absence of ascites. However, this can be solved by pre-surgical laparoscopic assessment. The detection of subdiaphragmatic peritoneal deposits are also difficult, but can be aided by multiplanar reformatting of contrast-enhanced scans.

2.9. Magnetic resonance imaging (MRI)

Magnetic resonance imaging (MRI) uses a high strength magnetic field and pulsed radiofrequency waves to generate images with excellent soft tissue detail. It does not utilise ionising radiation and is relatively safe to use. It commonly involves acquiring T1-weighted, T2-weighted, fat-saturation spin echo, and usually, includes post-gadolinium contrast-enhanced T1-weighted fat-saturation sequences for the pelvic region. This protocol includes a full abdominal scan in three planes for the staging of ovarian cancer [41].

The ability of MRI to correctly stage ovarian cancer is excellent, providing a sensitivity and specificity of 98 and 88% respectively, as compared to 92 and 89% respectively for CECT [41]. MRI and CT have been noted to be more sensitive than ultrasound for detection of peritoneal metastases. The accuracy of MRI (76%) is also better than CT (57%) for detection of lymph nodes [28]. The improved soft tissue resolution achieved by MRI is able to better delineate the presence of pathological lymph nodes, both within the pelvic cavity as well as extra-pelvic spread. However, its limitations are that it is rather costly, time-consuming and often difficult to interpret due to breathing and bowel movement artefacts.

Therefore, the clinical utility of MRI is limited to evaluation of indeterminate pelvic lesions. MRI can detect haemorrhagic lesions and enhancement in papillary projections, as well as

identify the fatty tissue components within individual adnexal tumours. It can delineate ovarian lesions from uterine or urinary bladder involvement. MRI is also useful in cases where CECT is relatively contraindicated such as in the pregnant woman, in a patient with, a history of dye allergy or where giving iodinated contrast material is contraindicated, e.g., in renal impairment. Hence, a non-contrast-enhanced MRI scan should be performed instead.

2.10. Interpretation of magnetic resonance imaging

MRI is able to differentiate simple ovarian cysts from malignant lesions with solid internal components. Simple cysts return a low signal in the case of T1-weighted images and a high signal in T2-weighted images, whereas malignant lesions are often heterogeneous and show marked enhancement of its solid components. MRI is best to delineate the local extent of the tumour as well as detect pelvic nodal metastases.

2.11. Limitations and future research in magnetic resonance imaging

The utility of whole-body diffusion-weighted imaging in magnetic resonance imaging (WB-DWI/MRI) has shown some promising results. Diffusion-weighted imaging measures the Brownian motion of extracellular water and thereby approximates tissue cellularity and fluid viscosity, hence malignant tumours that have increased cellularity will have restricted diffusion, thus giving lower apparent diffusion coefficient (ADC) values. Interestingly, DWI/ADC sequences have shown 94% accuracy for primary tumour characterisation which is comparable with the results of 18F-Fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) [42].

WB-DWI/MRI has also shown an improved accuracy of 91% for peritoneal staging compared with CT (75%) and 18F-FDG PET/CT (71%). It also has higher accuracy (87%) for detecting retroperitoneal lymphadenopathies compared to CT scans (71%) [42]. However, this study was limited by the relatively small number of cases, the discrepancy between the ratio of MRI and PET/CT cases performed as well as the relatively large number of patients who presented with advanced disease, potentially increasing the pre-test likelihood of detecting metastases.

2.12. Positron emission tomography-computed tomography (PET/CT) scan

Molecular imaging, namely Positron Emission Tomography-Computed Tomography (PET/CT) scans are indicated for the detection of recurrence of OC as even small volume disease can easily be detected. It is considered by the European Society of Medical Oncology (ESMO) as an appropriate imaging modality to help in the selection of patients for secondary debulking surgery. PET/CT can alter the management plan in metastatic ovarian cancers by detecting additional sites of disease not seen on CT scans, and identifying locations that are not amenable to cytoreduction [1].

PET/CT can assess tumour aggressiveness by demonstrating an elevated level of the injected radiopharmaceutical, e.g., 18F-Fluorodeoxyglucose (18F-FDG) that is trapped in tumour cells, as quantified by standardised uptake values (SUV) [43]. Interestingly, elevated maximum

standardised uptake values (SUVmax) are frequently detected in the ovaries in the luteal phase of the menstrual cycle. This is considered as normal physiological FDG metabolism and should not be mistaken for pathology. Therefore, PET/CT scans should be scheduled right after the menstruation to minimise this observed effect in premenopausal women.

PET/CT scans are performed using a hybrid PET/CT scanner commonly using 3D lutetium oxy-orthosilicate crystals as detectors for the PET component. It is recommended that the examination include a diagnostic contrast-enhanced computed tomography (CECT) scan by the administration of low osmolar iodinated contrast media. Apart from enabling attenuation correction, and anatomical localisation; CECT is essential for performing diagnostic clinical staging [1]. Patients are instructed to fast for a minimum of 6 h before scanning, and blood glucose is checked before the scan. Subsequently, 18F-FDG will be administered and subjects are kept in a dark room for approximately 60 min to allow for uptake time. Subjects are given approximately 100 mL (2 ml/kg body weight) of iodinated contrast media during the CECT scan. Immediately after the CT, PET images acquisition will be performed over the same anatomic regions. The attenuation corrected CECT images will then be fused with PET images. The combined images will be utilised for visual interpretation, tumour size and maximum standard uptake value (SUVmax) measurements.

2.13. Interpretation of positron emission tomography-computed tomography (PET/CT) scans

Abnormal FDG hypermetabolism is analysed on the PET/CT images, starting from a survey of the maximum intensity projection (MIP) 3D image of the PET component. Regions commonly evaluated to detect nodal spread and distant metastases include the pelvic, abdominal and inguinal lymph nodes; the uterus, urinary bladder, peritoneum, omentum, bowel, liver, lungs and bones. Adnexal lesions frequently have a variable FDG uptake irrespective of their histopathological origin. For instance, mucinous carcinomas do not demonstrate avid FDG uptake compared to serous tumours [44]. It is postulated that indolent (Type I) and aggressive (Type II) ovarian cancers may arise from different cell lines [5]. Thus, Type I tumours do not demonstrate significantly elevated SUVmax values.

The sensitivity, specificity, PPV and NPV of PET/CT in detecting OC metastases are 87, 100, 81 and 100% respectively [45]. Moreover, PET/CT has improved accuracy at detecting peritoneal seeding, sub-diaphragmatic involvement, distant organ metastasis, bowel invasion and extra-abdominal lymph node involvement which has led to a reduction in the rate of second look surgery [46]. A negative PET/CT has NPV of 90% for detection of recurrence within a two-year follow-up period [2]. PET/CT scan in axial, coronal and sagittal views was able to detect bowel invasion (red arrow) in an advanced ovarian cancer disease (white arrow) (**Figure 4**). Therefore, it can aid in the decision-making for primary debulking surgery followed by platinum-based chemotherapy as opposed to treatment using neoadjuvant chemotherapy.

PET/CT is also able to demonstrate the heterogeneity of ovarian cancers. (**Figure 5**) There is moderate FDG uptake noted in serous adenocarcinomas of the ovary as seen in **Figure 5a**. Endometrioid adenocarcinomas often have multiple cystic areas within and can be associated

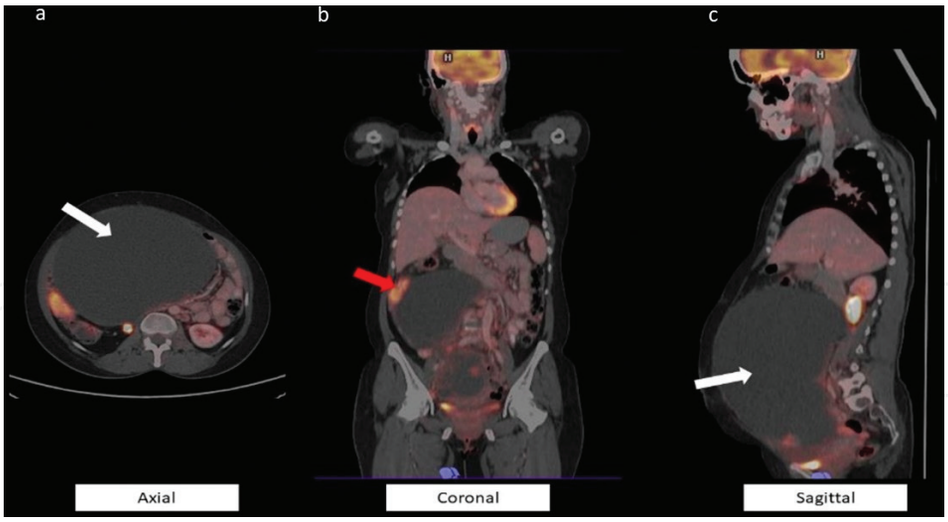

Figure 4. PET/CT scan demonstrating an advanced ovarian cancer. White arrows show a large adnexal tumour with heterogeneous FDG uptake. Red arrow shows bowel involvement.

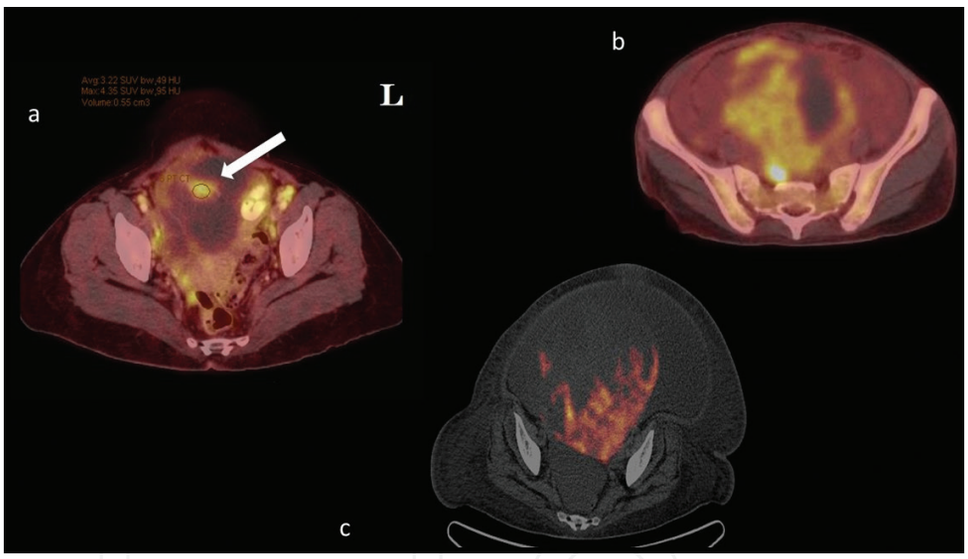

Figure 5. PET/CT scans in axial view demonstrating malignant ovarian tumours. White arrow shows markedly increased FDG uptake within the solid component of the tumour.

with internal calcifications as seen in **Figure 5b**. Mucinous adenocarcinomas often have low FDG uptake as seen in **Figure 5c** and represent a diagnostic caveat against dismissing them as benign lesions.

2.14. Limitations and future research in positron emission tomography-computed tomography (PET/CT) scans

The current theory postulates that high grade serous ovarian carcinoma (HGSC) originate from the fimbrial end of fallopian tubes [47]. It has sparked interest as to whether risk-reducing opportunistic salpingectomy could be performed to preserve fertility in a premenopausal

woman with high risk of developing ovarian cancer. There is a need to explore the role of PET/CT or rather MR/PET, which may be able to detect disease at an earlier stage especially when it is still localised to the fallopian tubes.

Apart from 18F-FDG, other tracers have also been studied to assess for recurrent or residual ovarian cancer. These include 11C-Choline which can help better delineate pelvic lesions [48]; as well as 16α-18F-fluoro-17β-estradiol (FES) which have the potential to evaluate the response to hormonal therapy for ovarian cancer [44]. Another tracer also in the experimental stage, is 3′-deoxy-3′-18F-fluorothymidine (FLT) that distributes rapidly in the extracellular fluid and is phosphorylated by thymidine kinase 1(TK-1) and becomes trapped in tumours with increased cellular proliferation activity. The role of FLT PET/CT may be in assessing and predicting response to an antitumour type of therapy, where it has been shown to be superior to 18F-FDG PET/CT [49].

2.15. Other research-based imaging techniques and work in progress

Positron Emission Tomography/Magnetic Resonance (PET/MR) is an emerging technique, which uses scanners that acquire MR and PET data either simultaneously or sequentially. Simultaneous acquisition devices, some called the mMR scanners, allow for concurrent imaging of the same body region. Alternatively, sequential scanning is done using two different scanners during one examination session, and the images are fused later. PET/MR acquisition protocol for assessment of a gynaecological tumour includes whole-body Dixon and a dedicated pelvic MRI exam that includes dynamic intravenous gadolinium administration [50]. It is suitable for assessment of the loco-regional extent of a pelvic tumour and evaluates the entire body for metastases, albeit having a very long scanning time of approximately 1.0–1.5 h [50].

Additionally, PET/MRI may be a more useful modality as compared to PET/CT for the detection of miliary disseminated metastases in cases of suspected OC recurrence [2]. As evident in **Figure 6** in which PET/MRI demonstrates FDG avid uptake in the para-aortic lymph nodes (**Figure 6**). Furthermore, PET/CT potentially gives high false negative results in the case of small volume disease which predisposes it to miss low-grade tumours and early adenocarcinomas [51]. Therefore, it is recommended to be used in conjunction with transvaginal ultrasound or MRI for characterisation of adnexal masses and the detection of OC.

PET/MRI ideally has added value in oncologic imaging due to its improved soft-tissue resolution. Furthermore, sophisticated sequences such as diffusion-weighted imaging, functional MRI, and MR spectroscopy can all be incorporated with molecular imaging, giving further information but with less radiation exposure. This can provide a significant reduction in radiation dose and exposure in patients who require follow-up imaging [3].

Some other imaging techniques are performed intra-operatively, namely the sentinel node procedure (SNP). SNP is sometimes conducted in patients with a high likelihood of having an OC in whom a median laparotomy and a frozen section analysis is planned. The concept of SNP is to determine whether the OC has spread to the very first lymph node (sentinel node). If the sentinel node is negative for cancer cells, then there is a high likelihood that the cancer has not spread to other lymph nodes [52]. Blue dye and radioactive colloid are injected into either the ovaries or the ovarian ligaments to perform the SNP [53].

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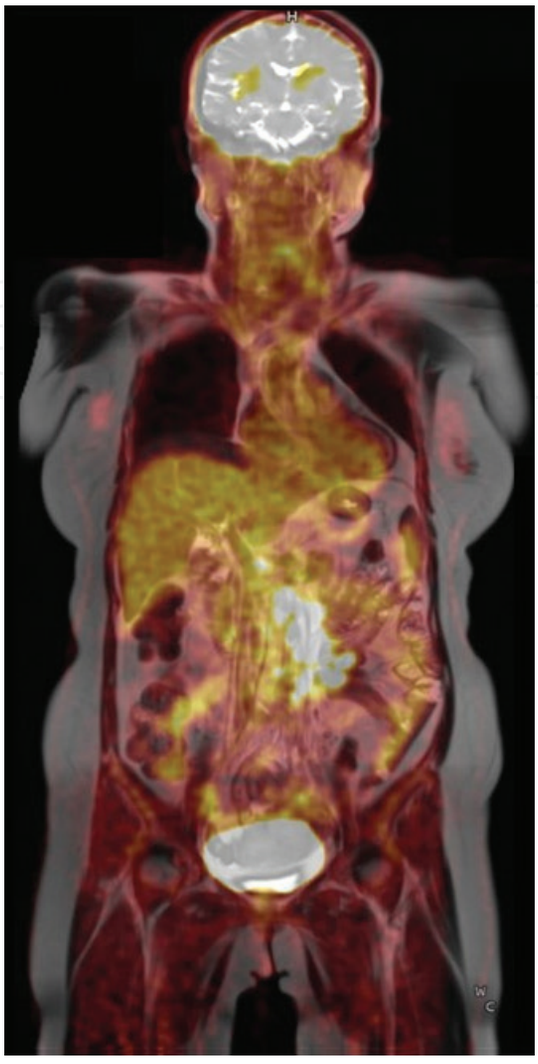

Figure 6. PET/MRI scan demonstrating recurrent ovarian cancer with para-aortic lymph nodes involvement. MRI gives good soft tissue resolution of the FDG avid lymph nodes noted at central abdomen.

After the incubation time, usually 10–15 min, the sentinel nodes can be visualised by either colorization (blue lymph nodes can be identified) and/or with a gamma probe that detects the radioactive tracer. The pathological examination of the sentinel node is an indication of the nodal status of the remaining nodes; when the sentinel node is negative, one can presume that the remaining nodes are also not involved. As a consequence, the patient may be spared from undergoing radical lymphadenectomy, and thus the morbidity associated with it.

Conventional diagnostic imaging modalities lack specificity and sensitivity in the detection of small primary and disseminated tumours in the peritoneal cavity. Using the knowledge that HER-2 receptors are overexpressed in ovarian tumours, a near infrared (NIR) optical imaging approach for detection of ovarian tumours using a HER-2 targeted nanoparticle-based imaging agent in an orthotopic mouse model of ovarian cancer has been conducted achieving improved detection of smaller lesions [54].

Furthermore, the overexpression of folate receptor-α (FR-α) in OC, has prompted the investigation of intra-operative tumour-specific fluorescence imaging. It has potential applications in

patients with OC for improved intra-operative staging and more radical cytoreductive surgery [55]. Additionally, optical coherence tomography (OCT) is another emerging high-resolution imaging technique that utilises an infrared light source directed to the tissues being examined. A novel prototype intra-operative OCT system combining positron detections; namely utilising Caesium (Tl204/Cs137) sources as well as 18F-FDG have shown potential for the development of a miniaturised laparoscopic probe to detect small volume disease of OC. This can offer simultaneous functional localisation and structural imaging for improved early cancer detection [56].

3. Conclusion

In summary, ovarian cancer is a heterogeneous spectrum of disease. Early detection and accurate staging using diagnostic imaging can help improve the prognosis of this condition. Prudent selection of the appropriate imaging modality can help expedite the correct treatment being instituted for the patients (**Table 3**). Molecular imaging, particularly 18F-FDG PET/CT can be a useful non-invasive biomarker to help stage the disease and detect recurrence based on the proposed diagnostic algorithm in this chapter.

Modality	Advantage	Disadvantage
Ultrasound	• Relatively cheap • Easily available • Does not involve ionising radiation	• Operator dependent • Unable to accurately stage the disease
CT scan	• Good for staging • Readily available	• Involves ionising radiation • Has pitfalls that lead to falsely negative findings
MRI	• Excellent soft tissue detail and able to characterise the pelvic lesion • Does not involve ionising radiation	• Relatively expensive • Longer scanning time • Requires specialised skills for interpretation
PET/CT	• Excellent for staging and detection of recurrence • Good for detection of extra-abdominal metastases	• Involves ionising radiation • Prone to false positive results • Requires specialised skills for interpretation
PET/MRI	• Excellent soft tissue detail and able to improve detection of nodal and peritoneal metastases • Slightly reduced radiation dose compared to pet/CT	• Expensive • Longer scanning time • Requires specialised skills for interpretation
Intra-operative devices	• Able to detect small volume disease • Able to delineate local extent of disease in a small region of interest	• Costly • Operator dependent • Requires specialised skills for interpretation

Table 3. Comparison of the diagnostic imaging modalities for the management of ovarian cancer.

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