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ORIGINAL ARTICLE

# Accuracy of 18FDG Positron Emission Computer Tomography (PET-CT) in Characterization and Preoperative Staging of Ovarian Cancer

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## ABSTRACT

**Background**: Ovarian cancer is a challenging disease. Accurate staging and restaging are critical for improving treatment outcomes and determining the prognosis. Imaging is an indispensable component of ovarian cancer management. Hybrid imaging modalities, including positron emission tomography/computed tomography (PET/CT), are emerging as potential non-invasive imaging tools for improved management of ovarian cancer.

**Methods**: This study involved 24 female patients exhibiting increasing CA-125 levels throughout clinical follow-up. All patients underwent comprehensive history-taking and clinical evaluation. Then all patients were evaluated using PET-CT scans, the histopathology results served as the gold standard against which the PET-CT results were compared.

**Results**: The CT specificity was 100% and its sensitivity was 75%. PET-CT had 92.9% sensitivity and a 100% specificity rate. When ROC curve analysis is performed on SUV max of the lesion to separate benign from malignant masses, it reveals a sensitivity of 89.29%, specificity of 100%, and AUC of 0.911 at the cut-off point of 4.2. When comparing differentiated from poorly differentiated malignant masses, using ROC curve analysis on SUV max to the lesion, the results show that the sensitivity is 70.83 percent, the specificity is 100%, and the AUC is 0.708 at a cutoff point of 6.7.

**Conclusion**: FDG PET/CT can greatly impact the evaluation of primary and recurrent ovarian cancer, leading to considerable changes in patient care.

**Keywords:** Positron emission, Computer tomography, Ovarian cancer.

## INTRODUCTION

One of the most prevalent gynecologic malignant tumors, epithelial ovarian cancer ranks third in incidence rate behind cervical and uterine carcinoma. Among gynecologic malignancies, ovarian cancer has the greatest death rate because of its sneaky early signs and the likelihood of metastasis and recurrence following the first chemotherapy and cytoreductive surgery. Within five years, 70% of individuals with ovarian cancer will experience metastasis and recurrence [1].

Histologically stated, OC is divided into three main subtypes: germ cell, stromal, and epithelial tumors [2]. It has been discovered that epithelial ovarian cancer (EOC) subtypes account for about 90% of ovarian cancer cases [3]. The usual course of treatment consists of chemotherapy and surgical resection [4].

The process of acquiring images, volume delineating, prescribing doses, and fractionations, assigning treatment fields and beam modifiers, assessing dose distribution, and ensuring quality control prior to treatment delivery approval is known as radiation therapy planning. To deliver therapeutic doses of radiation to the tumor while limiting the quantity of radiation to the surrounding healthy tissue, radiotherapy treatment planning is a complex process that significantly depends on imaging and computational technology [5].

Peptide-based emission tomography (PET) is a sophisticated technique of functional imaging. It is mostly utilized for a variety of cancer care tasks, including diagnosis, staging, prognostication, and

surveillance. Currently, the most common radiological procedures are CT or MRI-based imaging [6].

One of the main benefits of PET functional imaging is its superior accuracy in differentiating between normal and malignant tissues compared to CT or MRI, which rely on morphological markers for this purpose [7]. The use of fluorodeoxyglucose (FDG)-positron emission tomography (PET)/computed tomography (CT) is highly beneficial in the identification of individuals who are most likely to benefit from subsequent cytoreductive surgery as well as in the recurrence detection of ovarian cancer [8].

Pretreatment volume-based metabolic characteristics of 18 F-FDG-PET have been linked to the clinical results of patients with various malignancies, including ovarian cancer, based on meta-analysis and systematic review of literature data [9].

Because integrated PET/CT uses a metabolic tracer and simultaneously acquires anatomic data to pinpoint the precise site of lesions, it is more effective than anatomic imaging techniques like CT and MRI in detecting ovarian cancer relapses. Additionally, PET/CT is utilized to survey the complete body in contrast to anatomic imaging to detect recurrence in numerous areas, which is essential for therapy planning to prevent additional relapse [10].

PET/CT is not frequently utilized to define an adnexal mass because its utility is limited by the possibility of physiologic uptake in normal ovaries. Nonetheless, several writers have documented the effectiveness of PET/CT in identifying pelvic masses. Research indicates that PET CT can diagnose malignant ovarian tumors with 81–100% sensitivity and 93–95% specificity [11].

Although the aforementioned studies demonstrate the usefulness of PET CT in ovarian cancer diagnosis, its economic viability for this use is still up for debate. The most widely used imaging modalities at the moment for the identification and diagnosis of ovarian cancers are pelvic ultrasonography and magnetic resonance imaging (MR). This study aimed to evaluate the sensitivity and accuracy of diagnosis of combined PET/CT (positron emission tomography/computed tomography) in ovarian cancer patient detection and preoperative staging

## METHODS

This study was carried out on 24 adult female patients at the Oncology Department of Zagazig University Hospitals. The patients were sent to the Radio-Diagnosis Department for preoperative staging and characterization of adnexa masses. Histopathology results were used as the gold standard for comparison with PET-CT results, following the Institutional Review Board's (IRB) approval Committee (IRB no.: #10959).

The study was conducted between September 2023 and March 2024 and strictly adhered to the Declaration of Helsinki, which was established by the World Medical Association to safeguard the well-being of individuals involved in medical research.

The study included patients exhibiting increasing CA-125 levels throughout clinical follow-up. All patients have been pathologically confirmed to have ovarian cancer. While patients who were pregnant, had blood glucose levels over 200 mg/dl, inadequate PET/CT pictures due to artifacts, recent radiotherapy within 3 months, recent chemotherapy within 3 weeks, and non-cooperative patients were excluded from the study.

All patients underwent comprehensive history-taking and clinical evaluation. Examination of images was performed and the data was acquired utilizing a GE Discovery 690 scanner and a Siemens Bio-graph true point scanner. The specialized system combines a PET scanner with multi-section helical CT scanners to allow the collection of co-registered CT and PET imaging simultaneously.

***Protocol of Imaging:*** Patients were required to fast about 6 hours before the exam. Metallic objects were extracted from patients. Patients were instructed to void their bladder before the examination. All patients had their random blood glucose levels checked as part of a routine check to ensure they were within the acceptable range. An I.V. cannula was put into the arm of the patient to administer 18F-FDG. Prior to examination, patients were advised to refrain from engaging in intense activities to prevent physiological muscle uptake of FDG after the injection of the radioisotope. Patients were also urged to empty their bladder before the scan. Dosage Administration: Administer a dose of 10-20 millicuries (370 megabecquerels; approximate dose to patient, 3-5 megabecquerels per kilogram) of 18F. The FDG injection was administered 45-90 minutes prior to the assessment. This phase is the required duration for FDG to be sufficiently disseminated and

delivered into the cells of patients. Patients are instructed to set in a quiet environment free of distractions and to minimize their movements and chatting. This reduces the natural absorption of FDG by skeletal muscle, which could complicate the analysis of the scan. Patients must feel at ease and calm. Patients were positioned comfortably with their heads fixed and arms raised.

***CT Technique:*** The whole-body PET-CT scan started at the base of the skull and went down to the upper parts, covering the neck, chest, belly, and pelvis. The collimation width is 5.0 mm, the pitch is 1.5, the rotation time of the gantry is 0.8 seconds, the view field is 50 cm, and the gantry diameter is approximately 70 cm. The helical information is reconstructed retroactively at 1-millimeter intervals.

***Image analysis:*** A radiologist will visually evaluate the photographs. Increased FDG uptake will be compared with the equivalent anatomical findings on CT scan pictures. An atypical CT result showing an increase in FDG absorption will be considered indicative of recurrent illness. If a structural anomaly is detected on CT but does not show FDG uptake on PET imaging, it will be considered a negative result.

## STATISTICAL ANALYSIS

The data was examined with IBM SPSS software version 20.0. Location: IBM Corp in Ammonk, NY Qualitative data were represented using numerical values and percentages. The significance of the results was assessed at a 5% level of confidence. The ROC Curve is an important instrument for evaluating the specificity and sensitivity of quantitative diagnostic measures that categorize instances into two categories. A P value below 0.05 was deemed statistically significant.

## RESULTS

This cross-section study included 24 female patients with suspected ovarian masses; all of them were evaluated with CT and PET-CT studies. As regards the site of the mass; the most frequent site was left ovarian mass in 12 patients (50%), while 6 patients (25%) had a right ovarian mass and 6 patients (25%) had bilateral ovarian masses. Among the 24 studied patients, 18 (75%) patients had a single mass, while 6 (25%) patients had bilateral masses. As regard CT findings; 9 masses (30%) were well-defined, while 21 masses (70%) were ill-defined. As regards PET-CT findings; Most of the masses were positive (93.3%), while (6.7%) were negative. With distal metastasis in (63.3%) of the masses and nodal metastasis in (70%) of the masses. As regards SUV max to lesion, it ranged from 2.5 to 20.5 with a median (IQR) of 6.44 (1.22), while SUV to nodal metastasis ranged from 2.90 to 17.9 with a median (IQR) of 12.08 (1.5) and SUV max to distant metastasis ranged from 2.39 to 13.7 with median (IQR) of 6.8 (1.7). As regard histopathological findings; only two masses (6.7%) were benign, while 28 masses (93.3%) were malignant in the form of 19 masses (63.3%) were adenocarcinoma, (13.3%) were invasive poorly differentiated adenocarcinoma, (10%) were ovarian carcinoma and (6.7%) were round cell tumor (**Table 1**).

The sensitivity of CT was 75%, its specificity was 100%, PPV was 100%, NPV was 72.2% & accuracy was 76.7%. While the sensitivity of PET-CT was 92.9%, its specificity was 100%, PPV was 100%, NPV was 50% and accuracy was 93.3% (**Table 2**).

On conducting ROC curve analysis on SUV max to the lesion for discriminating benign from malignant masses; at the cut-off point of 4.2, it shows a sensitivity of (89.29%), specificity of (100%) and AUC of (0.911) (**Figure 1**).

On conducting ROC curve analysis on SUV max to lesion for discriminating differentiated from poorly differentiated malignant masses; at cut off point of 6.7, it shows sensitivity of (70.83%), specificity of (100%) and AUC of (0.708) (**Figure 2**).

Large well defined mixed cystic and solid para median left adnexal region mass lesion looks to originate from the left ovary, the solid component is FDG avid, and such lesion is seen measuring about 65x49x65 mm achieving SUV max up 20.5 (**Figure 3**)

Abdomen & Pelvis:- – The left ovary is a seat of a large rather well defined hyper metabolic solid mass lesion, measuring 36x32.5 mm achieving SUV max up 11 (**Figure 4**)

Bilateral low-grade hyper metabolic adnexal lesions, the right one, measuring 20x20 mm achieving SUV max up 4.5. while that at the left measuring 28x25 mm achieving SUV max up 4.2 (**Figure 5**)

The left ovary is markedly enlarged, likely by virtue of a hyper-metabolic mass lesion measured 48x38 mm and achieving SUV max up to 12.4 associated with stranding of the surrounding fat planes (**Figure 6**).

**Table 1:** Findings among studied patients

| **Variable** *(N. %)* | **All masses (n=30)** |
|---|---|
| **CT findings** | |
| Well-defined | 9 (30%) |
| Ill-defined | 21 (70%) |
| **PET-CT findings** | |
| Distal metastasis | 19 (70%) |
| Nodal metastasis | 21 (70%) |
| FDG uptake<br>– Negative<br>– Positive | <br>2 (6.7%)<br>28 (93.3%) |
| **SUV findings** | |
| SUV max to the lesion<br>*Median (IQR)*<br>*Range* | <br>6.44 (1.22)<br>(2.5 – 20.5) |
| SUV max to nodal metastasis<br>*Median (IQR)*<br>*Range* | <br>12.08 (1.5)<br>(2.90 – 17.9) |
| SUV max to distant metastasis<br>*Median (IQR)*<br>*Range* | <br>6.8 (1.7)<br>(2.39 – 13.7) |
| **Histopathology findings** | |
| Benign | 2 (6.7%) |
| Malignant<br>– Adenocarcinoma<br>– Invasive poorly differentiated adenocarcinoma<br>– Ovarian carcinoma<br>– Round cell tumor | <br>19 (63.3%)<br><br>4 (13.3%)<br>3 (10%)<br>2 (6.7%) |

**Table 2:** Comparison between CT and PET-CT in differentiating benign from malignant masses.

| **Variables** | **Sensitivity (%)** | **Specificity (%)** | **PPV (%)** | **NPV (%)** | **Accuracy (%)** |
|---|---|---|---|---|---|
| **CT** | 75% | 100% | 100% | 72.2% | 76.7% |
| **PET-CT** | 92.9% | 100% | 100% | 50% | 93.3% |

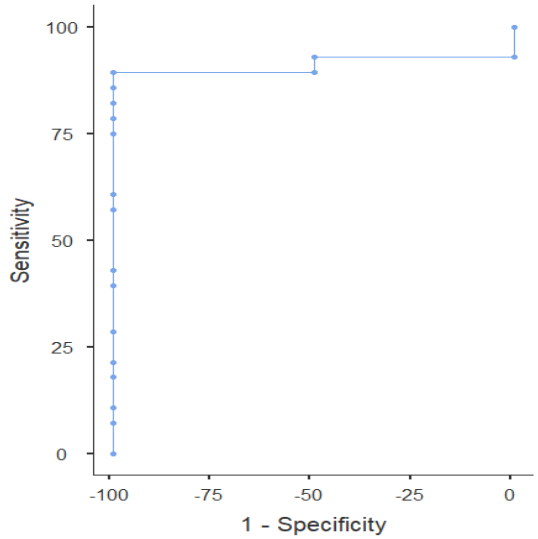


**Figure 1:** ROC curve analysis of SUV in differentiating benign from malignant masses

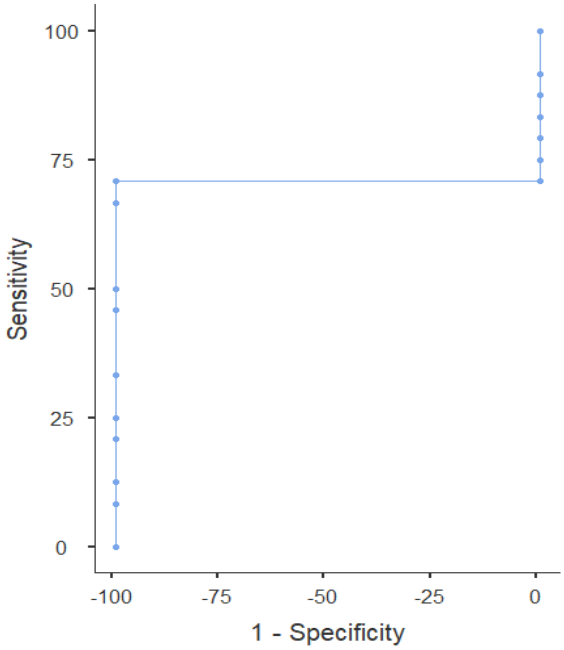


**Figure 2:** ROC curve analysis of SUV in differentiating differentiated from poorly differentiated malignant masses

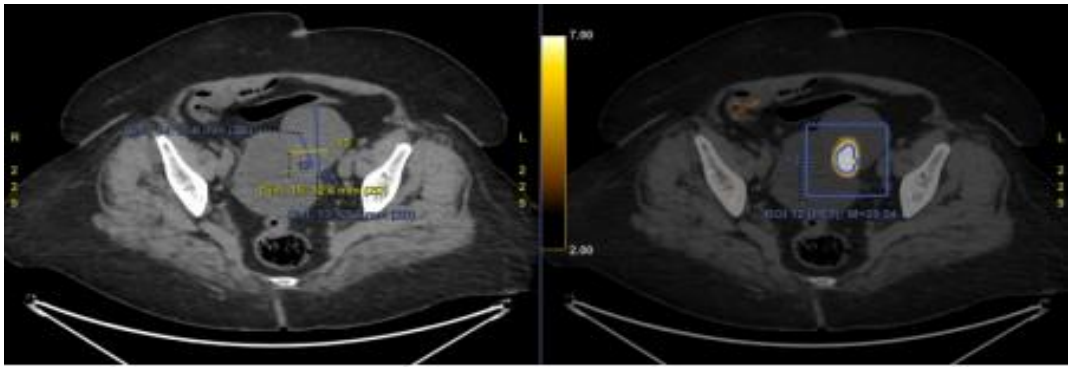

**Figure 3:** PET CT of 64 years old female patient, presented with a history of suspicious adnexal mass

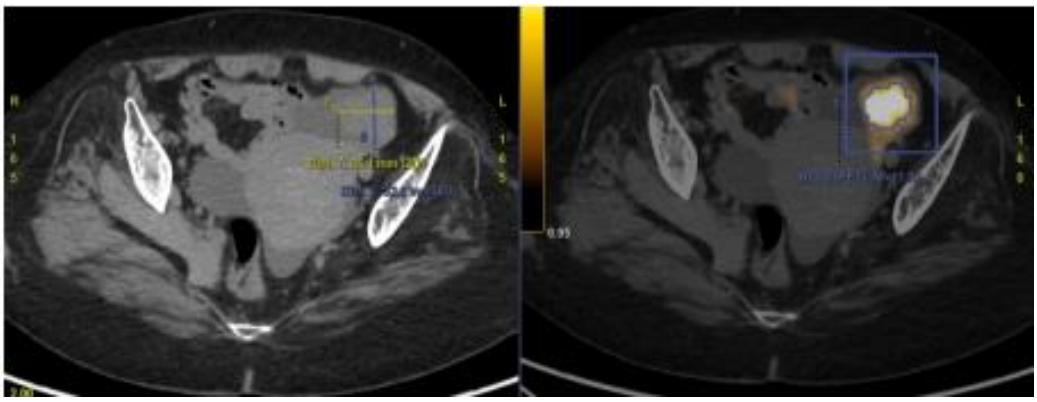

**Figure 4:** PET CT of 50 years old female patient, presented with a history of left mastectomy on therapy

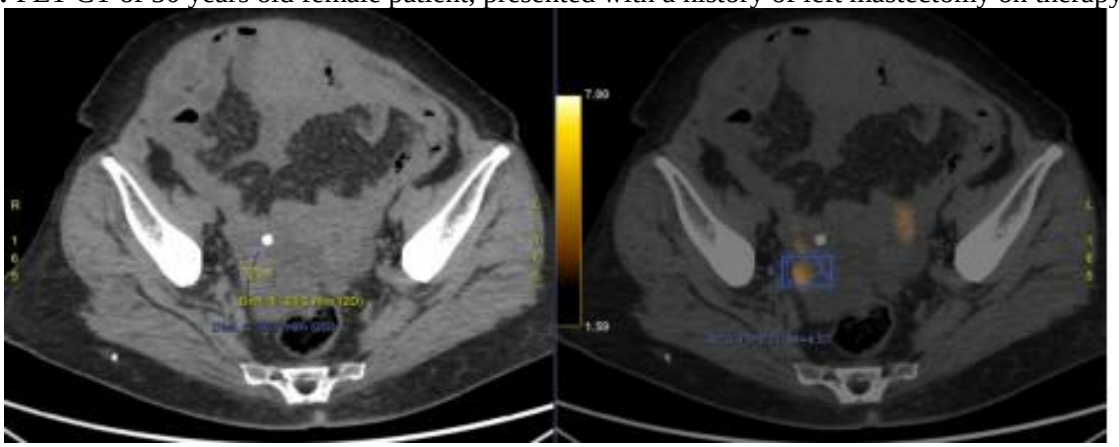

**Figure 5:** PET CT of 65 years old female patient, presented with a history of left ovarian mass

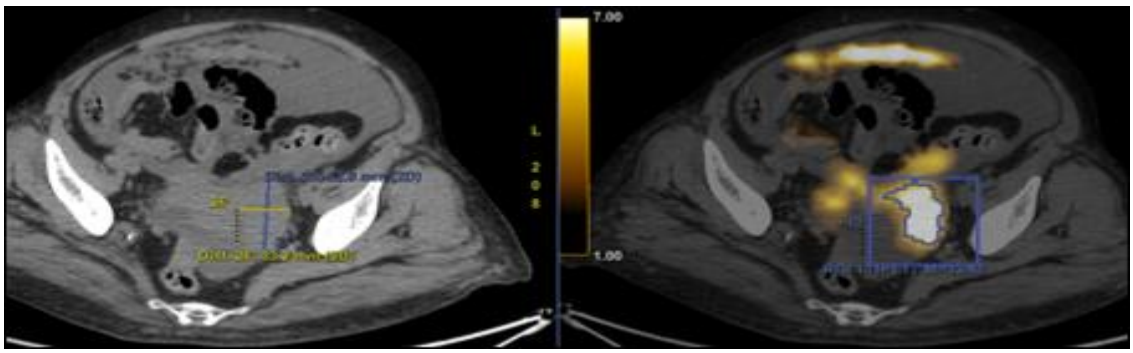

**Figure 6:** PET CT of 62 years old female patient, presented with suspected left adnexal mass with suggested peritoneal metastases

## DISCUSSION

This cross-sectional study was conducted in the Department of Radio-diagnosis at Zagazig University Hospitals involving 24 patients with suspected ovarian masses who underwent evaluation using CT and PET-CT scans. Our investigation found that PET-CT was more precise than CT in distinguishing between benign and malignant tumors. The CT scan has an accuracy rate of 76.7%. The accuracy of PET-CT was 93.3%. ROC curve analysis was performed on SUV max to lesion to differentiate between benign and malignant masses. At a threshold of 4.2, the analysis yielded a sensitivity of 89.29%, a specificity of 100%, and an AUC of 0.911. ROC curve analysis was performed using SUV max to the lesion to differentiate between differentiated and poorly differentiated malignant masses. At a threshold of 6.7, the analysis yielded a sensitivity of 70.83%, a specificity of 100%, and an AUC of 0.708.

Sami et al [12] concurred with our findings, stating that 18F-FDG PET/CT is a sensitive and accurate noninvasive imaging technique for monitoring ovarian cancer. It can effectively detect ovarian

cancer recurrence in individuals with high CA-125 values, impacting the treatment strategy. The imaging of the Whole-body in PET/CT provides the benefit of detecting and accurately pinpointing recurring or metastatic areas in both abdominal and extra-abdominal locations. The study found that PET/CT had an estimated sensitivity of 95.6%, specificity of 75%, as well as total diagnosis accuracy of 94% in detecting recurrent ovarian cancer.

The higher sensitivity and diagnosis accuracy of PET/CT in our study align with the findings of Cengiz et al [13], who found a sensitivity of 94%, specificity of 75%, and accuracy of 96%. Fagotti et al [14] and Sari et al [15] also found good sensitivity and diagnostic accuracy in their trials.

Wang et al [16] conducted a meta-analysis showing that the rate of false-negative of 18F-FDG PET/CT was 12%. The missing observations could be attributed to the lesion's close proximity to the urinary bladder, which has a higher concentration of excreted 18F-FDG, or a small-sized (< 1 cm) or hypo-metabolic lesion. Pannu et al [17] also showed a significantly decreased sensitivity with tumors smaller than 1 cm

Cengiz et al [13] found recurrent peritoneal and the retroperitoneal metastases in (79%) of patients. PET/CT was more effective than CT in identifying peritoneal nodules, particularly those located on the visceral surfaces.

Rubini et al [18] found similar specificity but poorer sensitivity and diagnostic accuracy.

Lopez et al [19] argued that PET/CT did not outperform CT in detecting peritoneal carcinomatosis from ovarian cancer before surgery. They suggested that the inconsistent outcomes in his study compared to other studies could be due to using intra-operative findings only as a reference approach.

Hynnimen et al [20] concluded that there was no benefit in conducting a PET/CT scan over a CT scan for assessing peritoneal deposits before surgery.

Kitajima et al [21] concurred with our findings, stating that integrated FDG-PET/contrast-enhanced CT is a superior imaging technique for staging ovarian cancer and aids in selecting the most suitable treatment compared to enhanced CT. The sensitivity of lesion-based detection increased from 37.6% (32 of 85) to 69.4% (59 of 85), specificity from 97.1% (578 out of 595) to 97.5% (580 out of 595), accuracy from 89.7% (610 of 680) to 94.0% (639 of 680) when comparing CT with PET/CT.

Several research publications on PET and PET/CT have distinguished between benign and malignant ovarian cancers, including those by Grab et al [22], Rieber et al [23], and Risum et al [24]. Yoshida et al [25] found that combining PET with independent CT scans improved diagnostic accuracy compared to using CT alone, with rates of 87% and 53% respectively, in a small sample of 15 patients with ovarian cancer.

Castellucci et al [26] found that the diagnosis accuracy of PET/CT was 69% compared to 53% for enhanced CT in 32 patients with ovarian cancer.

Kitajima et al [21] found that the sensitivity of PET/CT in detecting cancer involvement at six specific sites was below 60%. Sironi et al [27] showed that PET/CT accurately identified 32 out of 41 lesions in 17 patients with recurrent ovarian cancer. The lesions included peritoneal lesions, LNs, and pelvic lesions with sizes ranging from 0.3 to 3.2 cm (average size: 1.7 cm) and a sensitivity of 78%. They also determined that lesions larger than 0.5 cm were more likely to be detected.

Pannu et al [28] found that 50% of peritoneal lesions were bigger than 1 cm (n = 8) which was detected by PET/CT, but only 13% of peritoneal lesions not more than 1 cm (n = 23) were identifiable by PET/CT in patients with recurrent ovarian cancer. Bristow et al [29] found that PET/CT accurately diagnosed 24 out of 59 retroperitoneal LN metastases in 11 ovarian cancer recurrence patients, resulting in a sensitivity of 41%.

Tanizaki et al [30] studied the preoperative diagnostic efficacy of 18F-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography and computed tomography (PET/CT) in ovarian cancer patients. They concurred with us and stated that the SUVmax on FDG-PET/CT is valuable for distinguishing ovarian cancer from borderline or benign tumors with a good specificity & positive predictive value. A cutoff SUVmax of 2.9 was determined from the ROC curve analysis. The sensitivity, specificity, positive predictive value, and negative predictive value for identifying malignancy were 80.6%, 94.6%, 91.5%, and 87.1%, respectively. Positive FDG uptake (SUVmax Q 2.9) was observed in 89.5% of serous adenocarcinoma and 92.3% of endometrioid adenocarcinoma. Lower frequencies of high-quality FDG accumulation had been discovered in clear mobile phone adenocarcinoma (54.5%), mucinous adenocarcinoma (66.7%), and metastatic carcinoma (66.7%). The median SUVmax of these histological

kinds was once appreciably decreased in contrast to serous and endometrioid kinds. All patients with malignancy changes of mature cystic teratoma exhibited a positive FDG accumulation. Out of the 14 borderline malignant tumors, only 2 (14.3%) had positive FDG accumulation.

Castellucci et colleagues [26] demonstrated that with a malignancy threshold of an SUVmax higher than 3.0, the sensitivity, specificity, and PPV were 87%, 100% & 100%, respectively, which supports our data.

In previous studies by Iagaru et al [32] and Bast et al [33], PET/CT showed sensitivity and specificity ranging from 70% to 100% and 80% to 100% for detecting ovarian cancer, respectively. These results suggest that PET/CT may outperform or be on par with MRI or US when paired with other serum indicators such as CA125. The differences in sensitivity and specificity among the studies may be influenced by factors such as the chosen SUV cutoff, the methodology of PET scanning and analysis, or the characteristics of the patient group.PET/CT is highly accurate in distinguishing ovary cancer from benign tumors, however, struggles to differentiate the malignant tumors.

Jung et al [34] demonstrated that the average Standardized Uptake Value (SUV) of 8 with ovary cancers was below 2.0. Yamamoto et al [35] demonstrated that there was no significant disparity in SUVmax values between benign and malignant tumors, despite the limited included cases.

Prakash et al [36] stated that FDG-PET/CT has limitations in detecting lesions smaller than 1 cm, especially those under 5 mm. The reduced FDG uptake in tumors in the current study could be attributed, partially, to the small solids component of tumors. For clinical therapy, it is necessary to perform a thorough surgical staging for patients with borderline malignant tumors. Therefore, preoperative imaging for predicting borderline malignancy could be highly valuable. Additional research involving a substantial number of patients is necessary to assess the effectiveness of PET/CT in diagnosing ovarian cancers. Ovarian carcinoma comprises various histological types with distinct biological characteristics.

Clear cell and mucinous histological results have been shown to exhibit a diminished response to chemotherapy and shorter survival rates when compared to serous or endometrioid types, according to Hess et al [37]. The variation in FDG absorption on PET/CT for every histological type has not been thoroughly researched.

Karantanis et al [38] revealed that FDG uptake in ovarian cancer is not correlated with tumor grade or histological subtype. However, the study had a limited patient number with clear cell (n = 2) and mucinous (n = 1) types. The uptake of FDG in a tumor is affected by various factors, including the presence of glucose transporters (GLUTs), the activity of cytoplasmic hexokinase, variations in cellular density, blood supply, hypoxia level, cellular growth, and enzyme systems that regulate the metabolic activity, as stated by Kurokawa et al [39].

These characteristics may be associated with both the variability of characterization and the varying FDG uptake in ovarian cancers. Yasuda et al [40] demonstrated a correlation between GLUT1 and hypoxia-inducible factor and the histological findings of ovary cancer. They discovered that GLUT1 expression was low in clear cell and mucinous carcinomas.

Itamochi et al [41] showed reduced cell proliferation in ovary clear cell carcinoma and the association with chemoresistance. Berger et al [42] demonstrated that lower tumor cellularity and high mucin levels were associated with reduced FDG uptake in mucinous carcinoma.

Kitajima et al [31] found that individuals with ovarian metastasis had varying SUVmax levels. Metastasis of breast cancer had the greatest SUV, whereas metastasis from gastrointestinal and pancreatic malignancies had very low SUV levels.

Liu (44) observed that benign ovarian tumors are frequently present in younger women, and physiological FDG uptake is routinely seen in the ovaries of premenopausal women during ovulation.

The study's limitations include being hospital-based, resulting in a small sample size, and a risk of publication bias due to not being multicentric. The study does not represent a specific community.

## CONCLUSION

FDG PET/CT can greatly impact the evaluation of primary and recurrent ovarian cancer, leading to considerable changes in patient care.

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