DIAGNOSTIC VALUE OF ^{18}F-FDG PET/CT IN THE ASSESSMENT OF OVARIAN LESIONS USING VISUAL AND SEMI-QUANTITATIVE ANALYSIS

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ABSTRACT

BACKGROUND: Ovarian cancer is prominent cause of death among gynecologic malignancies. The use of 18F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) provides a non-invasive method to diagnose ovarian malignancy due to its ability to detect increased glucose metabolism in cancerous cells, helping to avoid unnecessary treatments for non-cancerous conditions. Therefore, this study aims to determine a cut-off value for ^{18}F-FDG PET uptake that distinguishes between malignant and benign lesions.

METHODS: We retrospectively included 112 female patients with age range 14 – 74 years' old. The patients were referred to the Nuclear Medicine department in the royal medical service, Amman, Jordan, from January 2020 to March 2024 with suspected ovarian lesion detected on other radiological modalities such as pelvic Us, CT or MRI. Patients with a prior history of different cancer types or any past ovarian cancer treatment were not included in the study. Patients underwent 18F-FDG PET/CT scan followed by pathological confirmation. PET scans were analyzed using visual and semi-quantitative analysis. The semi-quantitative analysis was conducted using maximum standardized uptake value (SUVmax) for each ovarian lesion and evaluated as lesion-by-lesion analysis. For statistical evaluation, analysis of variance (ANOVA) and receiver operating characteristic curve (ROC) analyses were utilized, considering a p-value of less than 0.05 as significant.

RESULTS: In the study group consisting of 112 patients, 79 were confirmed to have ovarian cancer, and 33 had benign lesions. The average SUVmax was 9.7 ± 4.3 for ovarian cancer patients and 2.6 ± 1.2 for those with benign lesions. Using a cutoff of SUVmax > 3.15 as criterion for malignancy the study achieved an accuracy rate of 92%. Analysis of all cases revealed that ^{18}F-FDG-PET/CT had sensitivity, specificity, PPV, NPV, and accuracy rates of 92%, 62%, 88.76%, 69.57%, and 85%, respectively.

CONCLUSION: While additional research involving a larger group of patients is essential, the utilization of various semi-quantitative parameters and visual assessment of 18F-FDG PET/CT imaging plays a crucial role in identifying malignancies in patients with ovarian cancer.

KEYWORDS: Ovarian cancer; ^{18}F-FDG PET/CT scan; Maximum standardized uptake value(SUV_{max}).

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INTRODUCTION

As a leading cause of gynecological cancer related deaths, ovarian cancer has a profound impact on women's health[1]. The disease not only affects the physical well-being of patients but also poses significant psychological, social, and economic challenges for women and their families[2].Early diagnosis of ovarian cancer is associated with a remarkable 5-year survival rate of 93%[3]. This underscores the importance of timely detection for improving patient outcomes and increasing the likelihood of successful treatment and overall survival. Ovarian cancer is sometimes referred to as a "silent" disease due to its lack of distinctive symptoms in the early stages[4]. As a result, the disease can progress unnoticed until it reaches an advanced stage, making it harder to treat

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effectively and reducing the chances of a favorable outcome, which means that early diagnosis is crucial to achieving a high survival rate and decreasing the mortality rate[4]. Radiological imaging modalities such as computed tomography (CT), and magnetic resonance imaging (MRI) may not always provide definitive distinctions between malignant and benign ovarian tumors, despite having higher sensitivity and specificity than ultrasonography [5, 6]. Malignant and benign ovarian tumors can present with similar clinical features and imaging characteristics, making it challenging to differentiate between them before surgery[7]. Both types of tumors may manifest as pelvic masses, causing symptoms such as abdominal pain, bloating, and urinary symptoms[8].

The application of 18F-FDG PET/CT has shown clinical utility in diagnosing and staging various cancers, including lung, colorectal, lymphoma, and melanoma, among others[9]. This modality's versatility and accuracy have facilitated its integration into clinical guidelines as a significant tool in oncologic imaging [9]. Although research on the effectiveness of 18F-FDG PET/CT for detecting primary ovarian cancer lesions is limited, existing studies indicate promising outcomes. The main objective of this study was to assess the diagnostic accuracy of 18F-FDG PET/CT imaging in differentiating between ovarian cancer and benign ovarian lesions. This goal highlights the critical need for a reliable non-invasive imaging technique for precise diagnosis and effective management of ovarian masses.

METHODS:

This retrospective study is approved by the Jordan Royal Medical Services research ethics board.

Study population: Among patients referred to our Nuclear Medicine department in the Royal Medical Service, Amman, Jordan, with suspected ovarian mass from January 2020 to March 2024 only 112 female patients with age range 14 – 74 years' old were enrolled in this retrospective study collected from our system database. Only patients with a primary suspicion of ovarian lesion detected by gynecologist via either symptomatic presentation, tumor marker elevation or other radiological modalities such as pelvic Us, CT or MRI, without any pathological confirmation prior to our PET scan were included. Patients with a prior history of different cancer types or any past ovarian cancer treatment were excluded. Following the PET study the diagnosis of each case was confirmed via pathologic analysis of the surgical specimen in patients with resectable disease or by biopsy or cytological analysis of metastatic lesions and for some cases the diagnosis was made based on either clinical correlation with tumor markers and follow-up imaging.

^{18}F-FDG PET/CT procedure All patients fasted for a minimum 4-6 hours at least, ensuring their fasting blood sugar levels were below200 mg/dL. They were administered an intravenous injection of 296 –418MBq of ^{18}F-FDG. Following a 60-minute rest period in a quiet environment, a PET/CT scan was performed. The scan, from the skull base to the mid-thigh, was performed using PET/CT scanner (Discovery PET/CT 710mCT 64,GE Medical Systems). Transmission data were acquired using spiral CT (dose modulation with a quality reference of 210 mAs, 120 kV, a 512 × 512 matrix, 5 mm slice thickness, increment of 30 mm/s, rotation time of 0.5 s, and pitch index of 0.8) including the base of the skull to the proximal thighs. Consecutively, PET emission data was acquired in 3D-mode with a 200×200 matrix with 2 min emission time per bed position.

image interpretation and quantitation

All images were interpreted and analyzed by two experienced nuclear medicine physicians. For the visual assessment, we evaluated each ovarian lesion by using several parameters, including shape and metabolic intensity as compared to physiological uptake in the liver. The semi-quantitative analysis was conducted using maximum standardized uptake value (SUVmax) for each ovarian lesion as lesion-by-lesion analysis by outlining a region of interest (ROI) and comparing it to reference liver SUVmax (2.6±0.43). The SUVmax was obtained as the highest SUV of the pixels within the ROI. SUVmax = Tracer uptake in ROI/ (Injected activity / Patient weight) An SUVmax exceeding 3.15 was taken as an early sign for malignancy criterion. After histological analysis was completed, the ^{18}F-FDG PET/CT scans outcome were categories into true

positive (TP), false positive (FP), true negative (TN), and false negative (FN) categories. Statistical analysis An independent samples t-test was used to evaluate the data and compare the parametric results. The diagnostic performance of PET/CT for suspected ovarian malignancy was assessed as lesion-based by calculating its specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV) and accuracy. Statistical significance was determined by a P value below 0.05, and the data were represented as mean ± standard error of the mean (SEM).Also Receiver-operating characteristic curve (ROC) analysis was used to determine the optimal cutoff value of SUV max for detecting ovarian malignancies. SPSS version 29 was used to analyze data.

RESULT:

The average age between the patients was 48.7 ± 15.2 years. In visual analysis, experts examine the PET images directly and uptake within ovarian lesion was correlated to liver background activity (SUVmax 2.6±0.43). Uptake higher than liver background was seen in 81 scans and equal or less than liver background in 31 scans. 12 benign lesions had FDG uptake higher than liver background. When applying visual analysis by calling any lesion with FDG uptake higher than liver background as potentially malignant, our data revealed sensitivity, specificity, and accuracy of 90%, 45.5%, and 81.3%, respectively (Table 1). In the ovarian cancer group, average SUVmax were 9.7 ± 4.3, while in the benign lesion group, the average SUVmax were 2.6 ± 1.2 (P < 0.05). There were significant differences in SUVmax between the ovarian cancer and benign group. The accuracy rate reached 85% for all patients. ROC analysis (Fig. 3) revealed that the ideal cutoff value for SUVmax for the differentiation of ovarian cancer from benign lesion was 3.15. The sensitivity, specificity, PPV, NPV, and accuracy rates were 92.00%, 62.00%, 88.76%, 69.57%, and 85.00%, respectively and area under ROC curve (AUC) of 0.882 (Fig 1). Out of 112 patients enrolled in the study, 79 were found to have ovarian cancer (Fig 2), and 33 had a benign lesion (Fig 3). Also 10 cases were of false positive (Fig 4), and 7 patients of false negative (Fig 5). of ovarian cancer. The maximum standardized

uptake value (SUVmax) is the most frequently employed diagnostic criterion in 18F-FDG PET/CT **DISCUSSION:**

^{18}F-FDG-PET/CT has emerged as powerful imaging modality in the diagnosis and management assessments. SUVmax indicates the peak level of FDG uptake within a lesion, reflecting its metabolic activity [11]. This dual-modality approach allows for precise localisation and characterisation of ovarian tumours, thereby facilitating accurate diagnosis and staging of the disease [12]. As the first Jordanian study to discuss diagnostic performance of PET/CT visual and semi quantitative analysis in the assessment of ovarian lesions, this study aimed to underscore the potential of ^{18}F-FDG PET/CT as an essential diagnostic tool and for determination of SUVmax cutoff value**.** Accurate

differentiation between malignant and benign ovarian lesions through PET/CT imaging can significantly impact clinical decision-making. In our study, most patients with biopsy-confirmed malignancy were found to have advanced disease, including peritoneal carcinomatosis and distant metastases. Around 49.3%of the patients had stage 3 and 4 disease, with the primary lesion SUVmax typically being greater than 9. Many studies investigated and addressed the value of cut-off SUVmax criterion in differentiation between benign and malignant like liver, lung, splenic lesions,..etc [13]. Our ROC analysis has revealed SUV > 3.15 as best criterion for malignancy. This criterion yielded sensitivity, specificity and accuracy of 92 %, 62 %, and 85 %, respectively. Our study confirms that 18F-FDG PET/CT exhibit high sensitivity and adequate specificity in detecting ovarian cancer. We observed a significant difference in FDG uptake between malignant and benign lesions, with higher metabolic activity in cancerous tissues enabling effective differentiation. This distinction crucially reduces the chances of false positives and negatives [14]. Taegyu Park et al. performed F-18 FDG PET on 51 peritoneal lesions. [15]. In that study visual assessment was the most significant parameter in differentiating malignancy from benign lesions in ovarian cancer patients, although other semi quantitative parameters including SUVmax1, SUVmax2, SUVmean1, SUVmean2, total lesion

glycolysis (TLG), and retention index (RI) of TLG were also identified as showing significant diagnostic value[15]. The results of Park et al. are in contrast to our results, as our study yielded a sensitivity, specificity and accuracy of semi-quantitaive analysis of 92% ,62% and 85% respectively, over visual analysis which sensitivity, specificity and accuracy was 90%,45.5 and 81.1% respectively. It is found that quantitive SUmax cut-off criterion was more reliable and accurate still
applying both to FDG PET/CT scan reporting will be of significant diagnostic value for malignancy detection and improve diagnostic report confidence. Moreover, SUVmax was significantly higher in patients with ovarian cancer compared to those with benign lesions. This distinction highlights SUVmax as a reliable marker for differentiating between malignant and benign ovarian tumors[16, 17]. All this improved accuracy not only aids in early detection and appropriate treatment planning but also minimizes unnecessary surgical interventions for benign conditions, enhancing patient care and resource allocation within the healthcare system. According to Chung et al., who studied 77 patients with suspected recurrent ovarian cancer, PET/CT showed accuracy of 94.8%. a sensitivity of 93.3%, and specificity of 96.9%[18]. The reduced in sensitivity and specificity is maybe due to the frequent occurrence of diseases like inflammation and endometrioma, which have high FDG uptake, in our region. Our results are in line with lee et al. who reported a distinct elevation in mean FDG uptake in malignant ovarian tumors compared to benign ones[19]. Studies have demonstrated that ^{18}FDG PET/CT can produce false-negative results during the early stages of the disease and when detecting recurrences in mucinous subtypes of ovarian cancer. According to Yuko et al., 6 of 11
(54.5%) clear cell ovarian cancers and 4 of 6 (66.7%) mucinous ovarian cancers exhibited ncreased FDG uptake[20], which were consistent with our findings. ^{18}F-DG PET/CT is considered a

Diagnostic Criteria	TP (n)	FP (n)	TN (n)	FN (n)	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
Visual analysis	81	12	10	9	90.00%	45.50%	81.10%	87.10%	53.00%
SUVmax > 3.15	79	10	16	7	92.00%	62.00%	85.00%	88.76%	69.57%

Table 1. Sensitivity, Specificity, Accuracy, PPV, and NPV for Visual Analysis, and SUVmax Semiquantitative Analysis Criteria (SUVmax > 3.15) Used in the Assessment of ovarian lesions.

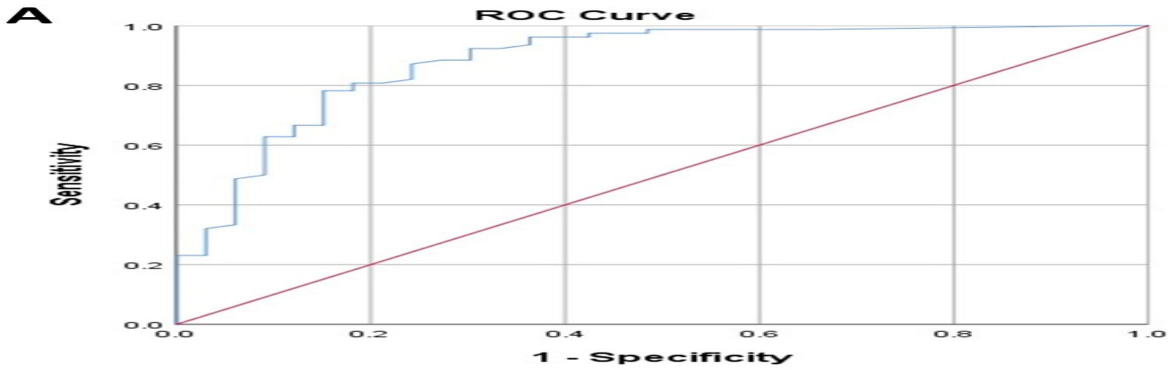
useful method for diagnosing ovarian cancer, but it
has limitations in detecting disseminated lesions
smaller than 1 cm[21]. Physiological activity in the
abdomen can reduce the specificity of the PET scan, while renal and urinary activity might obscure lesions, leading to false positives[22]. Finally, In
borderline tumors with low malignant potential and early-stage tumors, false-negative results can happen [23]. To ensure accurate diagnosis, conventional imaging should be performed to confirm pathological lesions in all areas of abnormal FDG accumulation. While our study provides valuable insights, its nonrandomized retrospective nature, the small sample size, particularly among non-ovarian cancer patients and being a single center experience , present significant limitations for our study. These factors introduce potential biases, limit the ability to control for confounding variables, and reduce the statistical power and generalized ability of our findings. Future research with larger, randomized, and prospective designs including other factors as tumor markers and family history of malignancy, would help to confirm these findings.

CONCLUSION

While visual analysis is essential, semi quantitative analysis complements it by providing quantitative data. This study revealed a clear benefit of semi-quantitative analysis over visual analysis, with higher specificity and accuracy while maintaining good sensitivity in the assessment of ovarian lesions and staging assessment of malignant ones. The use of 18F-FDG PET/CT and SUVmax semi-quantitative analysis using SUVmax 3.15 as a criterion for malignancy proved highly accurate in distinguishing ovarian cancer from benign lesions. **Acknowledgment** Appreciation for RN. biostatistician Anes Adel Hjazeen for his help in statistics review

Conflict of interest The authors declare that they have no conflict of interest.

Figure 1: (A) Receiver operating characteristics curve (ROC) curve used for differentiation between benign and malignant ovarian lesions based on maximum standardized uptake value (SUVmax), ROC analysis showed that the optimal cut-off value in these patients was 3.15; (B) area under the curve (AUC) = 0.882, P = 0.05.



B

Area Under the Curve

Test Result Variable(s): SUVmax

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.882	.038	.000	.808	.955

Fig 2: A representative image to demonstrate the true positive. 58 years old women with right ovarian cancer. (A) Axial CT and (C) axial hot iron FDG-PET (upper row), (B) axial fused 18F-FDG PET/CT images 18F-FDG PET/CT and (D) MIP whole-body maximum intensity projection images (lower row). Hypermetabolic right ovarian lesion (arrow)

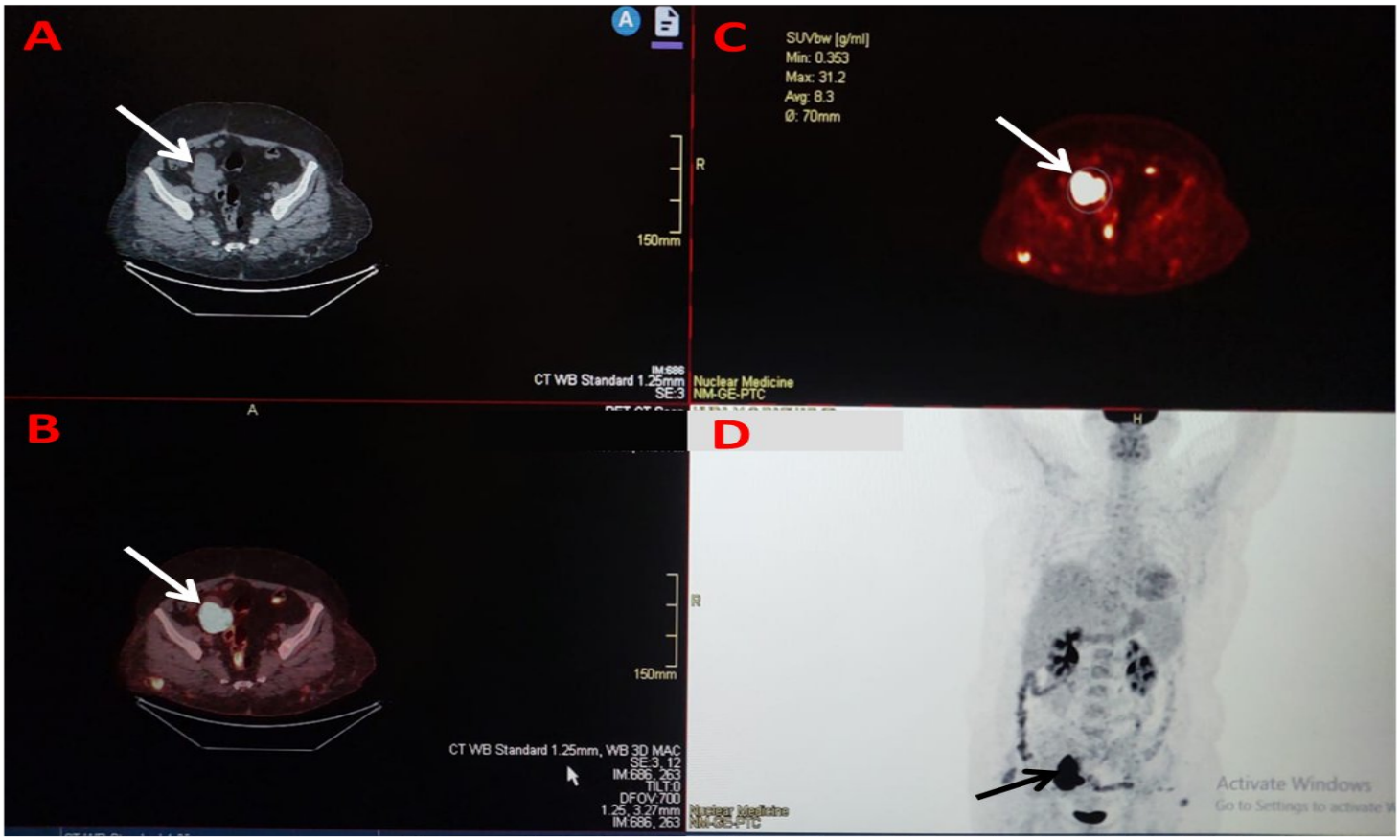


Fig 3: A representative image to demonstrate the true negative. 37 years old women with benign lesion, (A) coronal CT (B) coronal fused FDG PET/CT images showing right pelvic mostly ovarian mixed density lesion with calcifications (Dermoid cyst) showing no significant increased metabolic activity.

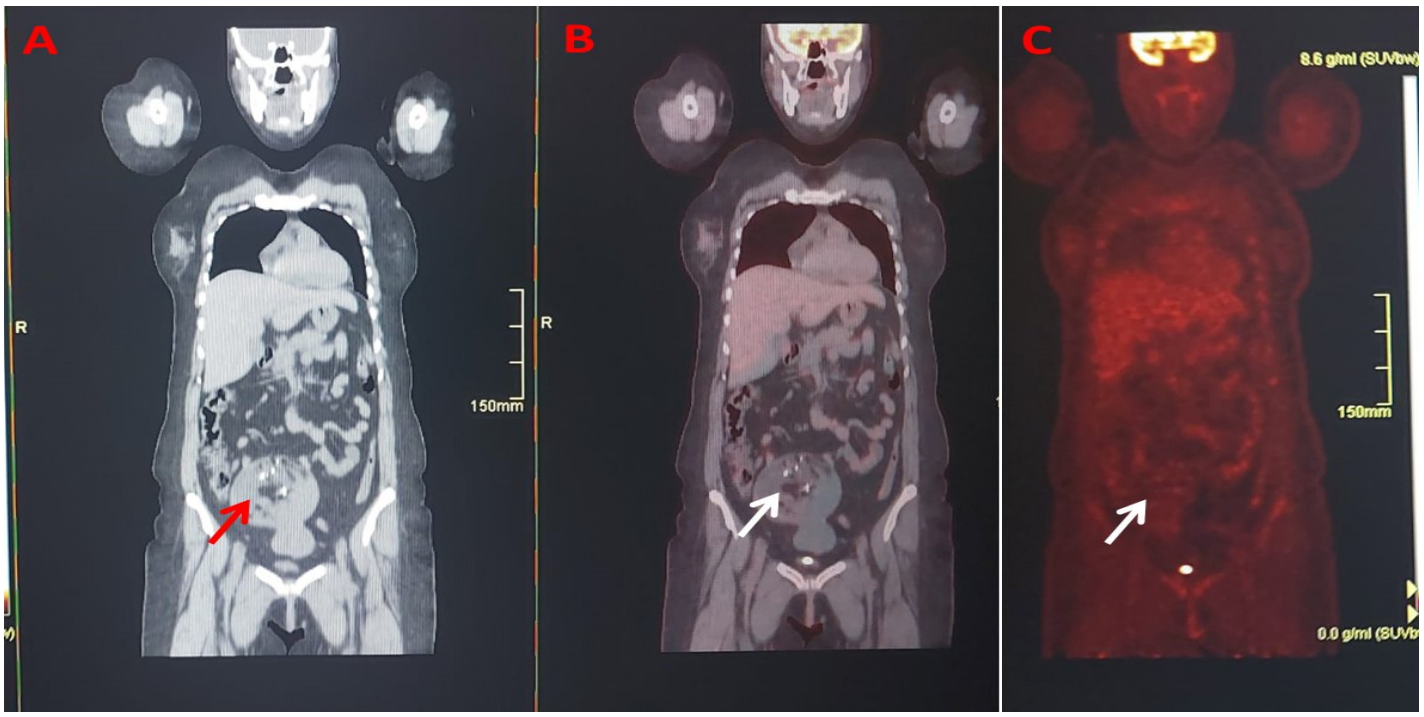


Fig 4: A representative image to demonstrate the false positive. 44 years old women with bilateral suppurative salpingitis (a) whole body mip, (b-d) axial ct, fused FDG PET/CT & hot iron axial pet images show peripherally hypermetabolic bilateral pelvic lesions (arrow).

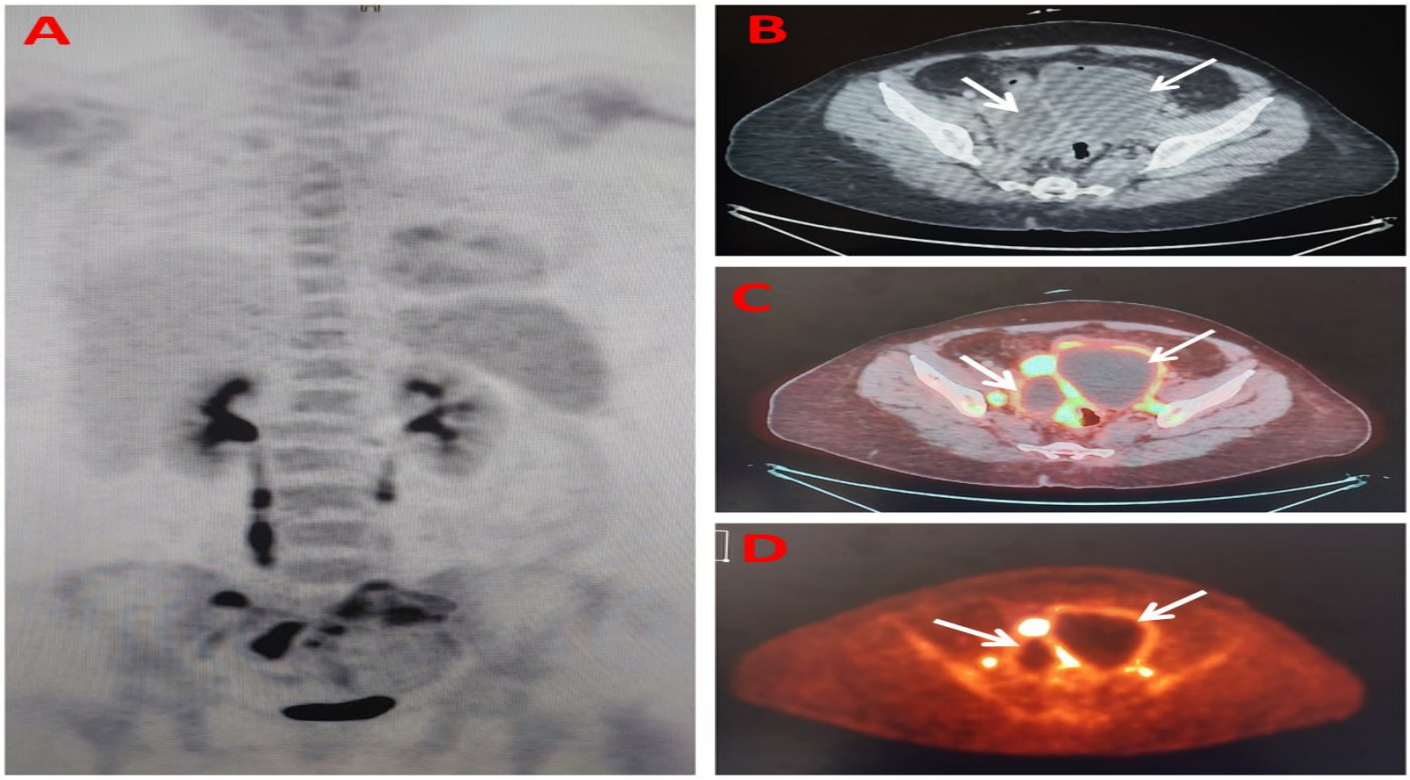
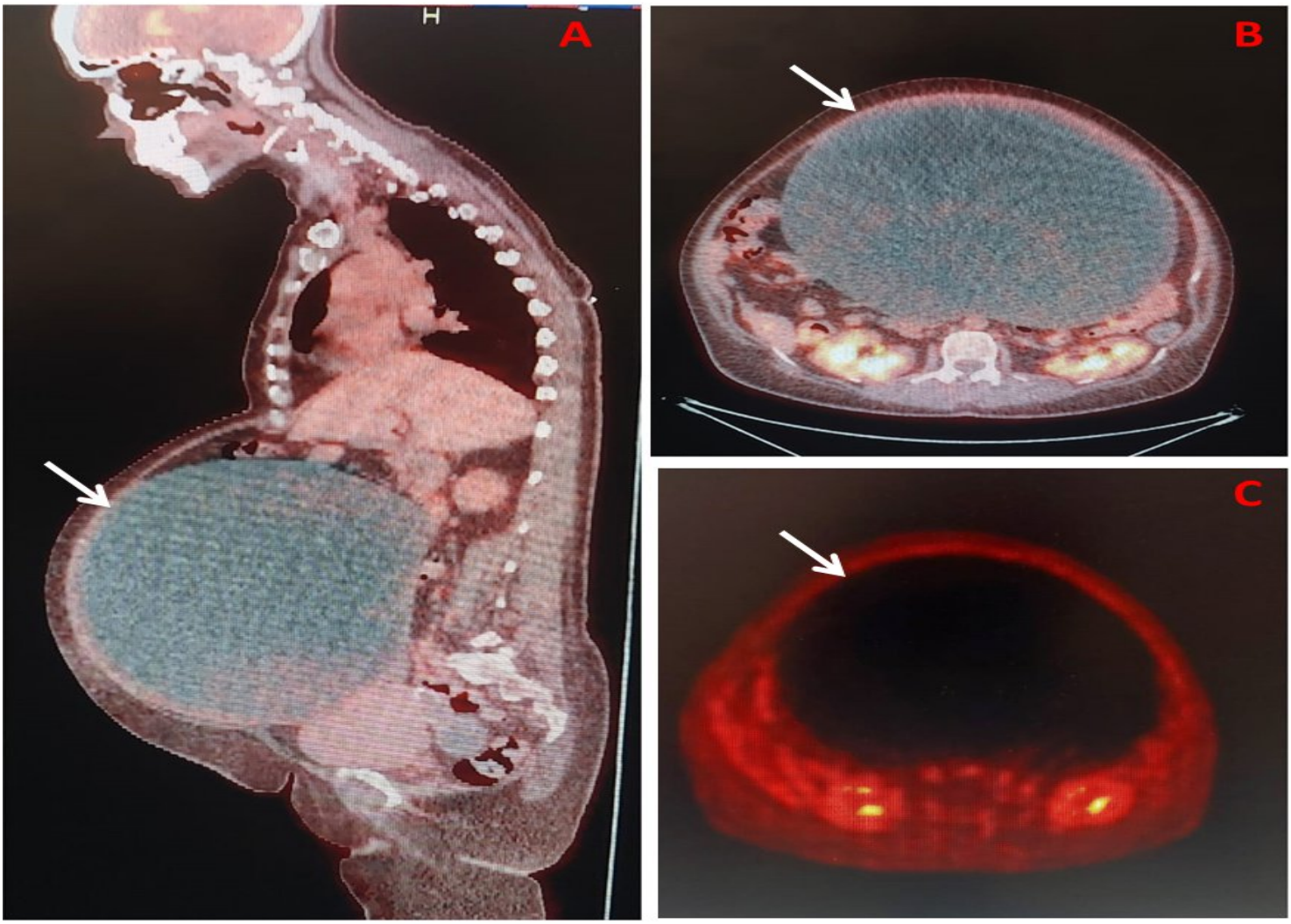


Fig 5: A representative image to demonstrate the false negative. 66 years woman with ovarian cancer. (a-b) sagittal & axial 18F-FDG fused PET/CT images of sizable ovarian lesion (arrow) with no significant increased fdg



uptake .

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