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Original Article, PET/CT.

^{18}F-FDG PET/CT Versus Contrast Enhanced CT in Detection of Mucinous ovarian Cancer Recurrence: Comparative Study.

Talaat O.[1], Amr M.[2], Ali I[3], Farouk Sh.[4], Abdelmaksoud B.[4], Nasr I.[4]

[1]Nuclear Medicine Unit & [2]Radiation Oncology Unit, National Cancer Institute, Cairo University [3]Radiology Department, Faculty of Medicine, & [4]Clinical Oncology and Nuclear Medicine Department, Faculty of Medicine, Zagazig University.

ABSTRACT:

Background: Mucinous ovarian carcinoma (MOC) is a unique and uncommon kind of ovarian cancer (OC). The diagnosis of tumor recurrence may be difficult to achieve with traditional imaging methods based on anatomical variations, such as the discovery of a new aberrant lesion or changes in the size of an existing lesion. **Aim** of the work by using fluorine-18-fluorodeoxyglucose (^{18}F-FDG) with PET/CT to assess the added value of ^{18}F-FDG PET/CT in the detection of MOC recurrence and its effect on patient management compared to contrast enhanced computerized tomography (CECT). **Methods:** All patients underwent ^{18}F-FDG PET/CT and CECT for detection of MOC recurrence. PET/CT and CT were interpreted separately and the significance of difference between them was evaluated. **Results:** The study included 59 patients, out of them 18 and 29 patients were proven to have local and distant recurrence respectively. PET/CT demonstrated lower false negative rate compared to CECT (1.7% vs. 11.9%) and greater sensitivity (SN) , positive predictive value (PPV), negative predictive value (NPV) and accuracy, but the same specificity (SP) in recurrence detection (97.9%, 90.2%, 87.5%, 89.8%, and 58.3%, vs. 85.1%, 88.9%, 50%, 79.7%, and 58.3%, respectively) and showed significantly higher sensitivity for detection of omento-peritoneal and LNs metastases (36 and 27 versus 22 and 18, p-0.0001 and 0.004, respectively). Both modalities were comparable in identifying distant organ metastases (p >0.05). PET/CT changed patient management in 25.4% of patients, from no therapy to local and systemic therapy in one and seven patients respectively, and from local to systemic therapy in another seven patients (p= 0.001).

Conclusion: ^{18}F-FDG PET/CT showed higher SN and accuracy than CECT in MOC recurrence detection, mainly the omento-peritoneal and nodal deposits, which allow better guidance for proper therapy planning.

Keywords: Mucinous ovarian cancer, ^{18}F-FDG PET/CT, CECT, and recurrence.

Corresponding author**: Omnia Talaat** E-mail**:** mony.talaat@yahoo.com

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INTRODUCTION:

There are about 22,000 newly diagnosed cases of OC every year and it is the most common reason of cancer-related deaths amongst women [1]. Mucinous ovarian carcinoma is a unique and uncommon kind of OC [2, 3]. It was previously believed that MOC accounted for a higher percentage of the diagnosed OC (≥10%) [4]. Presently MOC is considered as a rare form of OC as true primary MOC accounts for roughly 5% of OC cases [2,5]. Even with a good initial response, around 80% of patients eventually relapse and need further treatment [6].Clinical examination, assessment of the serum tumor marker (CA-125), and morphological imaging methods such computed tomography (CT), magnetic resonance imaging (MRI), and ultrasonography (US) are typically included in follow-up programs. These techniques do have certain drawbacks. The limits of the use of CA-125 are known as increased CA-125 levels cannot be used to distinguish between localized and diffuse tumor recurrence, nor normal CA-125 values can be used to rule out the existence of disease [7]. Furthermore, the diagnosis of tumor recurrence may be difficult to achieve with traditional imaging methods dependent on anatomical variations, such as the discovery of a new aberrant lesion or change in the size of an existing lesion. Furthermore, CT and MRI imaging cannot identify mets of normal-sized LNs and they are not very useful in accurately distinguishing a recurrence from a post-surgical change; neither immediately following treatment nor later on [8]. A solution to these issues has been suggested: fluorine-18-fluorodeoxyglucose (^{18}F-FDG) with Positron Emission Tomography (PET). It has been shown to be

extremely sensitive in identifying OC recurrence, particularly in individuals exhibiting an inexplicable rise in the level of tumor marker. It provides the advantages of both functional and anatomical imaging, and it has been applied to both the exclusion of illness in locations with residual structural abnormality and the localization of areas with elevated ^{18}F-FDG with greater anatomical specificity [9]. Precise localization of OC recurrence affect both patient's prognosis and therapy approach, according to Fulham et al, who evaluated the clinical effect of ^{18}F-FDG PET on therapy plans[10].

Aim of the study: To assess the added value of ^{18}F-FDG PET/CT in the detection of MOC recurrence and its effect on patient management compared to CECT.

MATERIAL AND METHODS:

59 patients with probable recurrent MOC were included in the current analysis patients were referred from National Cancer Institute and the Zagazig university hospitals to the Nuclear Medicine Unit of the National Cancer Institute's to do PET/CT Our study was performed after receiving the institutional research board acceptance (protocol number: IRB#:11164-8-10-2023). Every patient gave his signed consent to share in this study after being informed.

Patient population: Patients with suspected MOC recurrence guided by the clinical, laboratory and/or radiological data fulfill the inclusion criteria. Exclusion criteria are ovarian cancer other than the mucinous type, concomitant cancer, uncontrolled diabetes, severe infections, and lacking definitive pathology data, as well as a suspected short life span of less than 6 months.

Patient preparation: Patients were instructed to avoid strenuous activity for few days before the exam to lessen ^{18}F-FDG uptake by skeletal muscles and follow a low-carb diet and fasting for 24 hours, and 4-6 hours before ^{18}F-FDG injection respectively. The peripheral blood glucose level should be verified to be less than 160 mg/dL. Oral diabetic drugs could be used as advised except prescriptions containing metformin, which should be stopped 48 hours before the study to lower the intestinal background activity produced by such medications. The day before the study, diabetic patients with type 1 diabetes mellitus should fast after midnight (except from drinking water) and

scheduled in the morning before taking insulin and their acceptable blood glucose level was to be maintained at less than 180 mg/d. If there was hypoglycemia with symptoms or if the glucose level was more than 200 mg/dL, the exam should be rescheduled. (Serum creatinine level was also done for all patients before IV contrast injection and should not exceed the level of 1.7 mg/dl).

Imaging Technique: After I.V. injection of ^{18}F-FDG by a dose of 240–380 MBq, all patients were instructed to spend 45–60 minutes in a dimly lit room with a warm atmosphere. Also, patients were instructed to move as little as possible and rest quietly; no speaking, chewing, or reading was allowed. The patients were asked to urinate before being put on the PET/CT scanner. Scanning began with a non-enhanced, low-dose CT scan extending from the skull base down to the upper thighs, with a field of view of 50cm, 120 kV and 60 mAs, 0.9 pitch, and a 5 mm slice thickness. CT data were used for attenuation correction and anatomical localization. A three-dimensional whole-body PET scan was started immediately after the CT at the same acquisition range with 6-7 bed positions (2 minutes/position) using an integrated PET/CT system (Philips Medical Systems, equipped with a 16-slice CT)). A standard iterative reconstruction approach was utilized to reconstruct PET images that had been corrected for attenuation. Diagnostic CECT scan was carried out in the same session covering the same field of view. Iodinated contrast material was injected in a dose of 1.5–2 ml/kg by an automated injector at a 4 ml/s flow rate through a patent venous line inserted in the ante-cubital vein. Imaging started 70-80 seconds post injection with acquisition parameters of 5.0 mm collimator width, 120 kV, 120 mAs, 0.9 second gantry rotation time, and 5 mm slice thickness. Coronal and sagittal reconstructions were produced using the obtained raw data. Fusion images were generated for every set of PET and CT data. The CECT data set was automatically fused with the 3D PET images to generate contrast-enhanced anatomical images superimposed with ^{18}F-FDG uptake using the integrated software interface supplied by the manufacturer company.

Image interpretation: A team of doctors with over 15 years of experience in nuclear medicine and radiology that were blind to the final pathology data and each other's assessments performed both visual and semi-quantitative analysis of the acquired PET/CT and CECT images for every patient. The

CECT image interpretation was done by radiologist at the radiology department, faculty of medicine Zagazig University. Using a region of interest drawn in the area of enhanced uptake, the maximum standardized uptake values (SUV max). for each pathological lesion have been determined for semi-quantitative assessment. Malignant lesions were identified on ^{18}F-FDG PET/CT imaging as lesions with an SUV max of at least 2.5 at the location of pathologic alterations[11]. The diagnostic criteria of CECT were the presence of surgical bed mass particularly if invading the nearby organs e.g. bladder, the rectum or the pelvis side wall that is suspected d if the disease is less than 3 mm from the muscular sidewall and there is invasion or encasement of the iliac vessels. Abnormal enhancement of the peritoneum, subtle thickening and fine reticular nodular pattern along the peritoneal surface are the early signs. Peritoneal deposits may be calcified. Advanced stage peritoneal disease most frequently presents as large nodular deposits early signs of sub-diaphragmatic disease are abnormal hepatic capsular or diaphragmatic enhancement progressing to nodular disease and dense plaque disease. Subtle early omental disease manifests as stranding, fine reticular nodular enhancement whilst more advanced disease is plaque like and forms the classical 'omental cake' appearance. Early mesenteric disease comprises of a misty stranded mesentery, small scattered nodules and advanced disease is plaque like with retraction and distortion of the bowel loops. Criteria of abdominal organs metastasis include Invasive serosal surface implants (most frequent) of parenchymal involvement of liver and spleen and these may invade the underlying liver parenchyma. Bowel involvement may be nodular or plaque like lesions along serosal and wall surfaces with or without bowel wall invasion. The nodal short axis diameter of 1 cm is used to suggest malignant lymphadenopathy.

Data Analysis: The SUV max values were recorded and locations with focally increased ^{18}F-FDG uptake were observed in order to conduct a qualitative and semi-quantitative analysis. The lesions were deemed abnormal if it showed greater ^{18}F-FDG uptake on the attenuation-corrected pictures than the activity of the hepatic blood pool. In order to exclude the potential of physiological ^{18}F-FDG uptake by specific organs such as adipose tissues, salivary glands and muscles, areas of ^{18}F-FDG uptake were compared with the corresponding CT images for anatomical localization. The imaging data were compared to the outcomes of the histopathology and/or to clinical, radiological and laboratory follow-up data. True positives (TP) were lesions that demonstrated a decrease in CA-125 levels during ovarian cancer therapy (chemotherapy or radiation

therapy) or that were validated by subsequent imaging methods like PET/CT. If the PET/CT scans were normal and no recurrence was seen during serial imaging and clinical follow-up, a true negative (TN) result was obtained. If further imaging modalities or clinical follow-up data demonstrated recurrence but the PET/CT scans were normal, the results were considered false-negative (FN). Positive PET/CT results that turned out to be benign or that were linked to a subsequent cancer were referred to as false-positive (FP) results. The criteria of recurrence on serial imaging include the presence of operative bed mass, enlarged abdominal lymph nodes with the short axis more than 1 cm as a cut-off value, the presence of peritoneal, mesenteric or omental nodules or plaques, abdominal parenchymal organ or distant organs metastasis as seen on follow up CT, MRI or PET/CT. The clinical follow up criteria of recurrence included Unusual abdominal pain, bloating, fatigue, Pain and other symptoms related to the spread of the cancer to other areas and increase in the CA-125 level.

Statistical Analysis: Both the continuous and categorical variables were expressed as the mean ± SD, median (range) and number (%). To confirm that continuous variables were normal, the Shapiro-Wilk test was employed. The Wilcoxon signed rank test was used to compare the non-normally distributed data in two dependent groups. **McNemar's** test was used to compare the matched data. The Stuart-Maxwell test, a version of the **McNemar** test, was used to determine the marginal homogeneity of a square table with more than two rows and columns. The validity of CT and PET/CT was determined by comparing the diagnostic performance of sample 2x2 contingency PET/CT versus CECT in ovarian cancer tables created with the golden standard test as a reference test for mucinous ovarian cancer recurrence. The associated 95% confidence intervals for the accuracies, PPV, NPV, SP and SN were computed. The inter-rater agreement (Cohen's Kappa) test was used to calculate the requirements for qualifying for the strength of agreement, and the results were as follows: (K<0.2 denotes poor quality), (K 0.21–0.40 fair), (K 0.41–0.60 moderate), (K 0.61–0.80 good), and (K 0.81–1.00 extremely good). P-value of less than 0.05 was deemed statistically significant for all two-sided tests. **MedCalc** Software bvba, and SPSS 22.0 for Windows were used to analyze all of the data.

RESULTS:

A total of 59 patients with MOC and a mean age of 55.0±13.0 years were enrolled in our study. Fifty-five (93.2%) underwent both surgery and chemotherapy, while four patients received chemotherapy alone. Forty-seven (79.6%) patients had recurrences, out of them 18 patients had local recurrences and 29 had distant recurrences. The mean CA-125 blood level as a tumor marker was 58.6±36.7, which was high in 36 (61%) patients and normal in 23 (39%). The mean value of CA-125 was significantly higher in patients with MOC recurrence than those without (68.3±34.6 versus 20.7±11.4,

respectively, p 0.001). On PET/CT and CECT, the mean maximal lesion size for the operative bed and lymph node recurrence was 5.7±3.3 and 1.8±1.9 cm, while the mean SUV max was 7.1±2.6 and 6.0±6.2, respectively **(Table 1)**.

Table (1): The characteristics of the studied mucinous ovarian carcinoma patients

Characteristics		Total No = 59		
		No.	%	Mead &SD
Age (years)				55.0±13.0
Primary therapy	Surgery + Chemotherapy.	55	93.2%	
	Chemotherapy only	4	6.8%	
CA125 level	Within normal	23	39%	
	Elevated	36	61%	
	For all patients			58.6±36.7
	With recurrence			68.3±34.6
	Without recurrence			20.7±11.4
Max. Lesion size	O. Bed			5.7±3.3
	LNs			1.8±1.9
SUV max	O. Bed			7.1±2.6
	LNs			6.0±6.2

The rate of surgical bed recurrence was found to be similar for both PET/CT and CECT (18 patients each) (p=1.00). Out of them, 6 patients on PET/CT and 5 on CECT showed invasion of the nearby structures (p value 1.00). PET/CT showed a significantly higher rate of distant metastases detection compared to CECT at the omento-peritoneal and LNs [36 (61%) and 27 (45.8%) versus 22 (37.3%) and 18 (30.5%), with p-values of 0.0001 and 0.004, respectively]. The rates of distant metastases diagnosis at the liver, lung, adrenals, bone, brain and PET/CT versus CECT in ovarian cancer subcutaneous tissue were comparable between both modalities, with an insignificant statistical difference (p >0.05) **(Table 2).**

Table (2): Comparison between CECT and PET/CT findings among the studied mucinous ovarian carcinoma patients

Findings		CECT (N=59)		PET/CT (N=59)		p-value
		No.	%	No.	%	
Operative bed recurrence	Absent	41	69.5%	41	69.5%	1.000[a]
	Present	18	30.5%	18	30.5%	
Nearby structures invasion	Absent	54	91.5%	53	89.8%	1.000[a]
	Present	5	8.5%	6	10.2%	
Sites of Nearby structures invasion	Absent	54	91.5%	53	89.8%	0.317[b]
	Uterus	2	3.4%	3	5.1%	
	Rectum	1	1.7%	1	1.7%	
	Bowel	2	3.4%	2	3.4%	
Omento-peritoneal metastases	Absent	37	62.7%	23	39%	<0.001[a]
	Present	22	37.3%	36	61%	
LNs metastases	Absent	41	69.5%	32	54.2%	0.004[a]
	Present	18	30.5%	27	45.8%	
Pelvic LNs metastases	Absent	45	76.3%	38	64.4%	0.016[a]
	Present	14	23.7%	21	35.6%	
Abdominal LNs metastases	Absent	48	81.4%	40	67.8%	0.008[a]
	Present	11	18.6%	19	32.2%	
Distant LNs metastases	Absent	57	96.6%	56	94.9%	1.000[a]
	Present	2	3.4%	3	5.1%	
Distant metastases	Absent	45	76.3%	44	74.6%	1.000[a]
	Present	14	23.7%	15	25.4%	
Liver metastases	Absent	55	93.2%	53	89.8%	0.500[a]
	Present	4	6.8%	6	10.2%	
Lung metastases	Absent	51	86.4%	51	86.4%	1.000[a]
	Present	8	13.6%	8	13.6%	
Adrenal metastases	Absent	57	96.6%	56	94.9%	0.003[a]
	Present	2	3.4%	3	5.1%	
Bone metastases	Absent	57	96.6%	57	96.6%	<0.001[a]
	Present	2	3.4%	2	3.4%	
Brain metastases	Absent	59	100%	58	98.3%	1.000[a]
	Present	0	0%	1	1.7%	
Subcutaneous nodule	Absent	58	98.3%	57	96.6%	1.000[a]
	Present	1	1.7%	2	3.4%	

PET/CT and CECT were highly concordant in the detection of both operative bed recurrence and nearby structure invasion (K 1.00 and 0.90, respectively, with p 0.001). There is only one (1.7%) discordant negative case on CECT, but positive on PET/CT (p <0.001). The detection of distant mets at the lung, bones, subcutaneous tissue and LNs

showed strong agreement between both modalities (K 0.69–1.0, p <0.001), while the omentoperitoneum and adrenals showed weak agreement (K.56 and 0.38, with p <0.001 and 0.003, respectively). For more details see (**Table 3)**.

Table (3): Agreement between CT and PET/CT findings among the studied mucinous ovarian carcinoma patients (N=59)

Findings	Concordant	+ve/+ve	-ve/-ve	Discordant	+ve/-ve	-ve/+ve	K	95%CI	p-value
O. bed recurrence	59 (100%)	18 (30.5%)	41 (69.5%)	0 (0%)	0 (0%)	0 (0%)	1.000		<0.001
Nearby structures invasion	58 (98.3%)	5 (8.5)	53 (89.8)	1 (1.7%)	0 (0%)	1 (1.7%)	0.90	0.71 – 1.000	<0.001
Oment-peritoneal metastases	45 (76.3%)	22 (37.3%)	23 (38.9%)	14 (23.7%)	0 (0%)	14 (23.7%)	0.55	0.37 – 0.74	<0.001
LNs metastases	50 (84.7%)	18 (30.5%)	32 (54.2%)	9 (15.3%)	0 (0%)	9 (15.3%)	0.68	0.50 – 0.86	<0.001
Pelvic LNs	52 (88.1%)	14 (23.7%)	38 (64.4%)	7 (11.9%)	0 (0%)	7 (11.9%)	0.72	0.53 – 0.91	<0.001
Abd. LNs	51 (86.4%)	11 (18.6%)	40 (67.8%)	8 (13.6%)	0 (0%)	8 (13.6%)	0.65	0.44 – 0.86	<0.001
Distant LNs	58 (98.3%)	2 (3.4%)	56 (94.9%)	1 (1.7%)	0 (0%)	1 (1.7%)	0.79	0.40 – 1.00	<0.001
Distant metastases	52 (88.1%)	11 (18.6%)	41 (69.5%)	7 (11.9%)	3 (5.1%)	4 (6.8%)	0.68	0.46 – 0.90	<0.001
Liver metastases	57 (96.6%)	4 (6.8%)	53 (8.9%)	2 (3.4%)	0 (0%)	2 (3.4%)	0.78	0.49 – 0.98	<0.001
Lung metastases	55 (93.2%)	6 (10.1%)	49 (83.1%)	4 (6.8%)	2 (3.4%)	2 (3.4%)	0.71	0.44 – 0.98	<0.001
Adrenal metastases	56 (94.9%)	1 (1.7%)	55 (93.2%)	3 (5.1%)	1 (1.7%)	2 (3.4%)	0.38	0.00 – 0.93	0.003
Bone metastases	59 (100%)	2 (3.4%)	57 (96.6%)	0 (0%)	0 (0%)	0 (0%)	1.00		<0.001
Brain metastases	58 (98.3%)	0 (0%)	58 (98.3%)	1 (1.7%)	0 (0%)	1 (1.7%)	0.00		1.000
Subcutaneous Nodule	58 (98.3%)	1 (1.7%)	57 (96.6%)	1 (1.7%)	0 (0%)	1 (1.7%)	0.659	0.036 – 1.000	<0.001

PET/CT had a lower FN rate than CECT (1.7% vs. 11.9%) and demonstrated greater SN, PPV, NPV, and accuracy, but the same SP in recurrence detection (97.9%, 90.2%, 87.5%, 89.8% and 58.3%, vs. 85.1%, 88.9%, 50%, 79.7% and 58.3% respectively). On comparing the diagnostic

parameters with the gold standard PET/CT showed a lower P value than CECT (0.22 versus 0.77) (**table 4**).

Regarding the LNs metastases detection, PET/CT displayed higher SN (96.2%), NPV (96.9%) and accuracy (95%) compared to 65.4%, 78% and 83.1% for CECT respectively, while CECT has a higher SP (97%) versus 94% for PET/CT. CECT showed a high false negative rate (23.7%) in the diagnosis of peritoneal deposits but PET/CT did not **(table 4)**.

Table (4): Diagnostic performance of CECT and PET/CT in relation to the golden standard in diagnosis of mucinous ovarian carcinoma recurrence

Findings	TP No.(%)	FP No.(%)	TN No.(%)	FN No.(%)	SN% (95%CI)	SP% (95%CI)	PPV% (95%CI)	NPV% (95%CI)	Acc% (95%CI)	p-value
CECT Total no	40 (67.8%)	5 (8.4%)	7 (11.9%)	7 (11.9%)	85.1% (71.6-93.8)	58.3% (27.7-	88.9% (80.2-94)	50% (30.3-69.7)	79.7% (67.2-89)	0.774
PET/CT Total no	46 77.9%	5 8.4%	7 11.9%	1 1.7%	97.9%	58.3%	90.2%	87.5%	89.8%	0.219
CECT LNs metastases	17 28.8%	1 1.7%	32 54.2%	9 15.3%	65.4%	97%	94.4%	78%	83.1%	0.07
PET/CT LNs metastases	25 42.4%	2 3.4%	31 52.5%	1 1.7%	96.2%	94%	92.6%	96.9%	95%	1.00
CECT Perti. metastases	21 35.6%	1 1.7%	23 39%	14 23.7%	60%	96%	95.5%	62.2%	74.6%	0.001
PET/CT Perito metastases	35 59.3%	1 1.7%	23 39%	0 0.0%	100%	96%	97.2%	100%	98.3%	1.00

Qualitative data were expressed as a number (percentage); TP: True positive; TN: True negative; FP: False positive; FN: False negative; SN: Sensitivity; SP: Specificity; PPV: Positive Predictive Value; NPV: Negative Predictive Value; Acc: Accuracy; %CI: 95% Confidence Interval; p-value< 0.05 is significant.

PET/CT upgraded patient management in 25.4% of patients, from no therapy to local and systemic therapy in one and seven patients respectively, and from local to systemic therapy in another seven patients (p 0.001) **(Table 5)**.

Table (5): Comparison between therapy plan decisions based on CECT and PET/CT findings

		Decision based on PET/CT			Total
		No treatment	Local treatment	Systemic ttt	
Decision based on CECT	No treatment	6 (10.2%)	1 (1.7%)	7 (11.9%)	14 (23.7%)
	Local treatment	0 (0.0%)	10 (16.9%)	7 (11.9%)	17 (28.8%)
	Systemic ttt	0 (0.0%)	0 (0.0%)	28 (47.5%)	28 (47.5%)
	Total	6 (10.2%)	11 (18.6%)	42 (71.2%)	59 (100%)

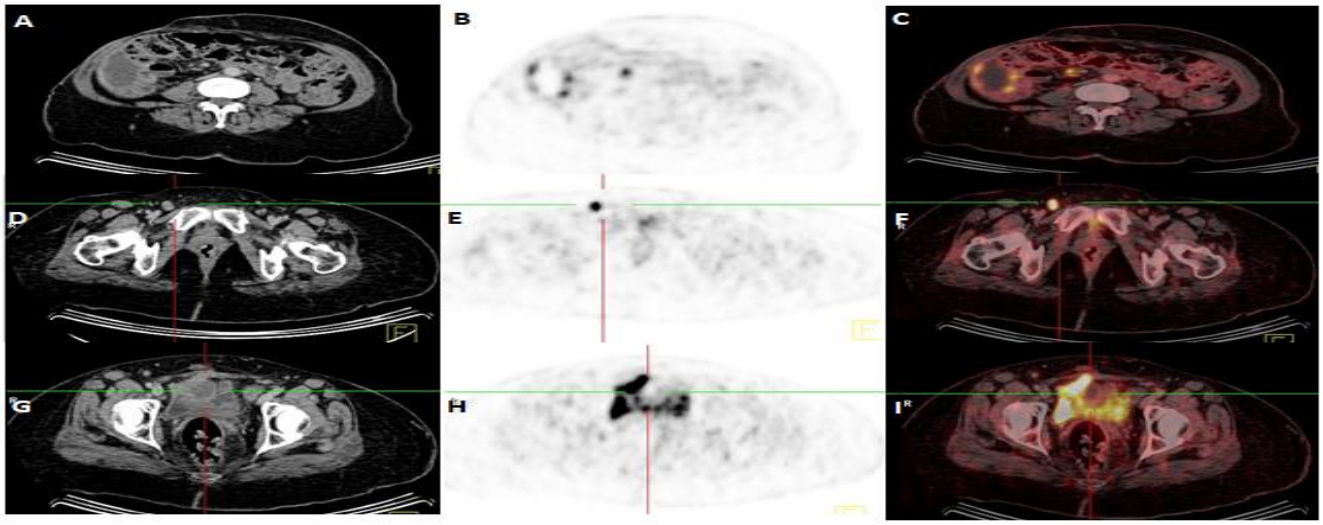

Fig (1): A 64yrs patient with ovarian cancer, received C/TH and referred for follow up. CECT (A, D, and G) images displayed a loculated right paracolic collection measuring 7.8x15.5 cm, small sub centimetric right inguinal LN, and a right pelvic cystic lesion with a solid component measuring 4.2x4.3 cm. PET and PET/CT scans showed diffuse FDG uptake at the loculated right paracolic collection (SUV max 8), the right ovarian mixed cystic and a solid lesion (SUV max 13). Also, FDG-avid omento-peritoneal infiltrative thickening, multiple nodularity and serosal implants (SUV max~11.2) were seen in addition to active FDG uptake at the small right inguinal LN (SUV max 5.5).

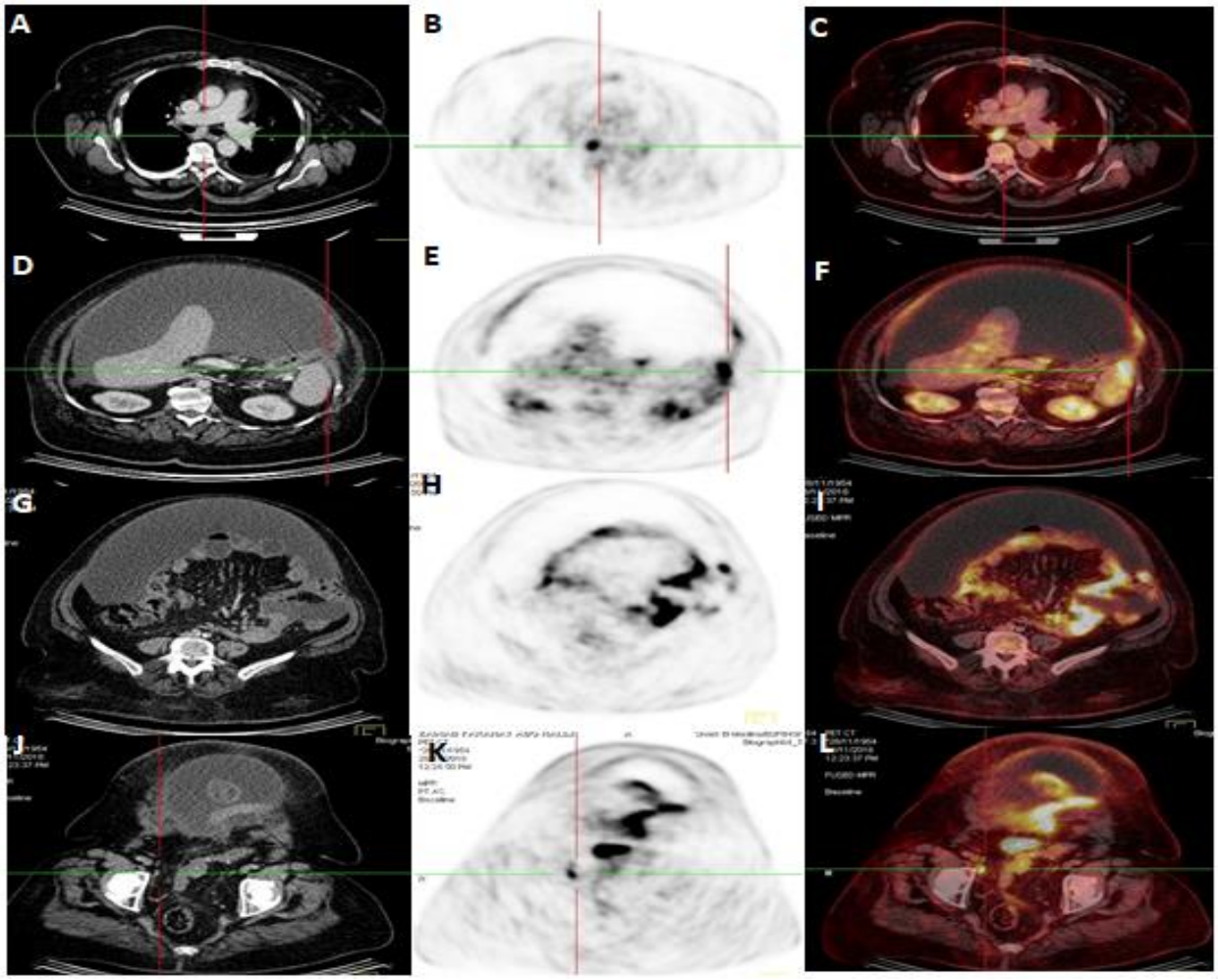

Fig. (2): A 58-yrs patient who had ovarian cancer was treated by pan-hysterectomy and chemotherapy.

CECT images (A, D, G and J) showed small calcified sub-carinal LN (8 mm), diffuse minimal abdomino-pelvic thickening, more pronounced at the left hypo chondrial area, diffuse and loculated abdominal ascites and sub centimetric right external iliac LN. PET and the fused PET/CT image revealed avid FDG uptake at the calcified sub carinal LN with SUV max 7.7 (C image). F and I images showed active diffuse omento-peritoneal thickening and nodularity with serosal implants, more prominent at Lt. hypo chondrium and left lateral region with SUV max 12 and 10.2. L images revealed sub-centimeteric FDG avid right external iliac LN with SUVmax~5.

DISCUSSION:

Despite effective treatment and complete response in patients with OC, the recurrence rate is high (50–80%). Early diagnosis of recurrence in these patients is important as it has a close relation with prognosis and the choice of appropriate treatment. [12-15]. Imaging techniques like CT and MRI can be used to detect OC recurrences. However, since OC metastases primarily affect the omento-peritoneal region rather than parenchymal organs, the detection of

small implanted metastases on the visceral surface is challenging [16-18]. Despite the limited value of F18-FDG PET-CT in evaluating the primary tumor, it has a particular value for identifying the LNs and distant metastases, particularly when it comes to extra-abdominal spread[19-20]. The value of 18FDG PET/CT is in detection of OC recurrence, as it is superior to both conventional imaging and the CA-125 assay. It has better SN and SP for both high and low-grade carcinomas [21, 22].

In addition to the higher efficiency of 18FDG PET/CT than CT and MRI in identifying recurrent OC, it can also identify recurrences of OC approximately six months before CT [23]. Consequently, 18FDG PET/CT can be used effectively for surveillance of treated OC patients, particularly when conventional imaging methods had negative results but there is an increase in the CA-125 level or the clinical examination may indicate recurrence or progression [24].

In the present study, 18FDG PET/CT showed higher SN than CECT (97.9% versus 85.1%) in detecting OC relapse at the patient level with a statistically insignificant difference when compared to the GS (P 0.77 and 0.21). These results support the findings of Sala et al who suggested that CECT and PET/CT may have comparable accuracy at detecting recurrent OC at the patient and regional levels [25]. Similar to our research, multiple studies (26-30) evaluated recurrent OC by directly comparing PET/CT with CECT. They discovered that PET/CT had a higher SN than CECT at the patient level (74%–100% vs. 53%–76%, respectively) [26, 27, 28, 31, 32]. In a recent meta-analysis, Gu et al [33] reported pooled accuracy, SN and SP of 96%, 91% and 88% respectively for PET/CT and 88%, 79% and 84%, respectively for CECT with significant differences in SN and accuracy. However, in the current study the difference was only insignificant at the regional not the patient level. Additionally, **Antunovic** et al. proposed that PET-CT is of higher efficacy (80%) than both traditional imaging (62%) and CA-125 (64%) in identifying recurrences of epithelial OC (34). Furthermore, the results of PET-CT are independent of the tumor's histology. Sebastian et al., stated that PET-CT is significantly more accurate than CT in detecting OC recurrence, with lower inter-observer variability of results in case of PET-CT [35].

Most cases of relapsed ovarian cancer are multifocal and approximately 75% of cases are located in the peritoneal cavity and retroperitoneal space [36-38]. These findings are consistent with data from other literature that indicates the trans-coelomic spread is the most common method of OC dissemination [39]. **Kosinska** et al found that multifocal relapse of OC was present in 77.61% of cases with localization of cancer in the peritoneum and/or the retro peritoneum in 84.13%. Distant organs and supra-diaphragmatic LNs mets was seem in only 15.87% of cases [40]. These findings are in concordance with our study in which peritoneal metastases were seen in 59.3% and LN metastases in (44%) of patients. However, Elsayed et al., found that the most frequent site of disease relapse was LNs, mainly the abdomino-pelvic nodes with a prevalence of 64% [41]. Furthermore, **Dragosavac** et al. observed that the LNs were the main site for recurrent disease [42]. When it comes to identifying peritoneal implants with recurrent OC the SN and SP of 18FDG PET/CT are extremely high [43-46]. **Rubini** et al. stated that 18FDG PET/CT has higher SN (85%) and SP (92.31%) than CT and MRI [47].

Researchers in previous studies like our study directly compared CECT and PET/CT in the detection of OC recurrence at the regional level. They found that the accuracy and SN of PET/CT (92%–96% and 75%–97%, respectively) were greater to those of CECT (83%–93% and 61%–92%, respectively) (26-48). Like our study, exploratory surgery was not the gold standard. Coakley et al. showed 85–93% SN for peritoneal mets detection in OC through spiral CT with significantly lower SN for implants less than 1 cm [(49)]. The current study revealed PET/CT has significantly higher SN than CECT PET/CT versus CECT in ovarian cancer in the detection of omento-peritoneal and LN metastases, specifically the pelvic and abdominal LNs (100% and 96% versus 60% and 65%) with p-values of 0.0001 and 0.004 respectively, but PET-CT has not been found to be more effective than CECT in identifying LR or extra-abdominal metastases, especially bone metastases that may be due to the small patient's number who proved to have extra pelvic and distant metastases. The lower accuracy of CECT in the current study may be due to the smaller sample size. Sala et al. discovered, however, that while both CECT and PET/CT were successful in identifying lesions in the peritoneum and pelvic LNs, they were only moderately accurate in identifying pelvic LR, distant LNs invasion (above renal hila), distant liver and spleen metastases (46). Furthermore, **Sironi** et al. [(50)] found that pelvic LR was less sensitive to PET/CT than peritoneal and LNs metastases. But according to **Rusu** et al. [(24)] PET-CT is superior to traditional imaging for identifying distant and extra abdominal metastases, especially when there is involvement of the supra-diaphragmatic LNs. Additionally, Nam et al. demonstrated that 3.8% of cases with additional synchronous tumors and 15.8% of instances of unanticipated extra-abdominal LNs expansion could be identified by PET-CT [(51)].

In line with another study that assessed the clinical impact of FDG PET upon treatment strategy and found that accurate localization of OC recurrence impacts both patient outcome and treatment strategy (10). The current study demonstrated that PET-CT has a clinical impact on patient management, as the treatment strategy has been changed in 25.4% of patients based on the findings of FDG-PET/CT compared to CECT. In contrast to the current study and earlier studies results Cho et al observed that, PET/CT showed a low degree of SN (58.2%.). Moreover, they failed to find any statistically significant differences in the diagnostic accuracy of CT, FDG-PET, or the combination of CT and FDG-PET modalities [(52)].

LIMITIONS:

This analytical prospective study was carried out at a single center, which limit the selection criteria and may result in inherent selection bias. Our study focused on patients with MOC, which is uncommon histological type of ovarian cancer, resulting in a limited sample size. The gold standard (pathological confirmation) cannot be achieved for all lesions with enhanced contrast on CT and/or avid FDG uptake, as it is inappropriate and immoral.

CONCLUSIONS:

Despite the common use of CECT and its comparable results with ^{18}FDG-PET/CT in the evaluation of patients with suspected MOC recurrence, ^{18}FDG-PET/CT achieved higher SN and diagnostic accuracy in detection of MOC recurrence, mainly the omento-peritoneal and nodal deposits which allow better guidance for proper therapy planning in these patients. Our results encourage the use of 18FDG PET/CT as the preferred imaging modality for MOC recurrence detection.

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