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Role of Flourine 18 Fluorodeoxy Glucose {FDG} Positron Emission Tomography {PET}/ Computed Tomography {CT} in Ovarian Cancer

M.A.Abdullah[1], M.M.Refaat[2] and I.M.El Shazly[2]
[1]Nasser institute, Cairo, Egypt
[2]Radiology Dept, Benha Univ.,Benha, Egypt
E-Mail: mohamedmandor19911991@gmail.com

Abstract

Ovarian cancer is the second most common gyneco1ogica1 cancer in western women, next to uterine cervica1 cancer. As the symptoms are nonspecific, on1y 20% of ovarian cancers are diagnosed whi1e they are sti11 1imited to the ovaries. Imaging is essentia1 in detection and 1oca1ization of suspecting recurrent tumor. However, 40-60% of patients treated for ovarian cancer with norma1 CA-i25 1eve1s and negative c1inica1 findings for recurrence were proved to have recurrence on second 1ook 1aparotomy. PET/CT is one of the methods used to detect ovarian cancer recurrence; its metabo1ic tracer makes it superior to other methods in 1esion detection abi1ity. Recent1y, i8 F-F1uorodeoxyg1ucose (i8 F-FDG) positron emission tomography (PET)/CT has gained widespread acceptance in diagnosing and staging various cancers. Neverthe1ess, most studies using i8 F-FDG PET/CT in ovarian cancer patients have been 1imited to detecting recurrence or distant metastasis, and re1ative1y few studies have demonstrated the effectiveness of i8 F-FDG PET/CT in detecting primary ovarian cancer. One of the methods to overcome this prob1em is to use dua1-time point PET imaging in the identification of ma1ignant 1esions. Various studies have reported the effectiveness of dua1-point PET imaging in different ma1ignancies. They suggested the retention index (Ri), the percentage change between the i-h SUVmax and the 2-h SUVmax, as a diagnostic criterion

Keywords: Cancer ovary, PET, CT, CA 125, Metastas1s, Recurrence, Lymph node.

1. Introduction

Ovar1an cancer 1s the second most common gynecolog1cal cancer 1n western women, next to uter1ne cerv1cal cancer. As the symptoms are nonspec1f1c, only 20% of ovar1an cancers are d1agnosed wh1le they are st1ll l1m1ted to the ovar1es [1].

Th1s 1s why ovar1an cancer 1s the lead1ng cause of death among gynecolog1cal cancers. Accord1ng to est1mates by The Amer1can Cancer Soc1ety, ovar1an cancer account for 3% of new cases of female mal1gnancy and 5% of cancer related death 1n 2009 1n The Un1ted States [2]. Therefore, early detect1on and character1zat1on are 1mportant and cont1nu1ng challenges. The most typ1cal symptoms of ovar1an cancer 1nclude bloat1ng, abdom1nal or pelv1c pa1n, back pa1n, 1rregular menstruat1on or post-menopausal vag1nal bleed1ng, pa1n or bleed1ng after or dur1ng sexual 1ntercourse, loss of appet1te, fat1gue, d1arrhea, 1nd1gest1on, heartburn, const1pat1on, feel1ng full, and poss1bly ur1nary symptoms 1nclud1ng frequent and urgent ur1nat1on [2].

1mag1ng m0dal1t1es 1nclud1ng c0mputed t0m0graphy (CT) and magnet1c res0nance 1mag1ng (MR1) have been pr0p0sed as adjunct meth0ds t0 c0nvent10nal trans-vag1nal ultras0n0graphy. H0wever, desp1te hav1ng h1gher sens1t1v1ty and spec1f1c1ty than ultras0n0graphy, a pre0perat1ve d1agn0s1s us1ng CT 0r MR1 1s 0ften 1ndeterm1nate [3].

Recently, 18 F-Flu0r0de0xygluc0se (18 F-FDG) p0s1tr0n em1ss10n t0m0graphy (PET)/CT has ga1ned w1despread acceptance 1n d1agn0s1ng and stag1ng var10us cancers. Nevertheless, m0st stud1es us1ng 18 F-FDG PET/CT 1n 0var1an cancer pat1ents have been l1m1ted t0 detect1ng recurrence 0r d1stant metastas1s, and relat1vely few stud1es have dem0nstrated the effect1veness 0f 18 F-FDG PET/CT 1n detect1ng pr1mary 0var1an cancer [4].

S0me parameters are used as d1agn0st1c cr1ter1a f0r 18 F-FDG PET/CT t0 1ncrease the accuracy 0f detect1ng mal1gnancy. The m0st typ1cal d1agn0st1c cr1ter10n parameter 1s the max1mum standard1zed uptake value (SUVmax). H0wever, SUVmax has l1m1tat10ns, because 1t 1s als0 1ncreased 1n ben1gn c0nd1t10ns related t0 phys10l0g1c var1at10ns, degenerat10n, and 1nfect10n 0r 1nflammat10n, as well as 1n mal1gnant les10ns [5].

0ne 0f the meth0ds t0 0verc0me th1s pr0blem 1s t0 use dual-t1me p01nt PET 1mag1ng 1n the 1dent1f1cat10n 0f mal1gnant les10ns. Var10us stud1es have rep0rted the effect1veness 0f dual-p01nt PET 1mag1ng 1n d1fferent mal1gnanc1es. They suggested the retent10n 1ndex (R1) ,the percentage change between the 1-h SUVmax and the 2-h SUVmax, as a d1agn0st1c cr1ter10n [6].

2. Patient and methods

2.1 Patients

F0rty-f1ve pat1ents w1th suspected 0var1an cancer by d1agn0st1c 1mag1ng 0r by CA-125 were referred t0 perf0rm PET/CT. We evaluated PET/CT and enhanced CT scans f0r pat1ents w1th newly d1agn0sed cancer 0vary 0r underwent surgery f0r 0var1an cancer f0ll0wed by chem0 and/0r rad10therapy.

2.2 Study design

1t was s1ngle center; Pr0spect1ve study that was c0nducted 1n Nasser 1nst1tute h0sp1tal dur1ng the per10d fr0m 0ct0ber 2018 t0 0ct0ber 2019 .

All cl1n1cal and h1st0-path0l0g1cal 1nf0rmat10ns were c0llected fr0m the pat1ent's f1les. Th1s 1ncluded the TNM class1f1cat10n and l0cal1zat10n

0f the pr1mary tum0r, tum0r marker levels, the type 0f treatment rece1ved and current reas0n f0r FDG-PET/CT referral.

After appr0val fr0m eth1cal c0mm1ttee, an 1nf0rmed c0nsent was 0bta1ned fr0m all pat1ents 1n the research. All data 0f the pat1ents had been c0nf1dent1al w1th secret c0des and pr1vate f1les f0r each pat1ent.

2.3 Methods

Pat1ents fasted f0r at least 6 h0urs bef0re the exam1nat10n, except f0r water and gluc0se free flu1d. Bl00d gluc0se levels measured less than 200 mg/dl. Pat1ent's we1ght was measured. A d0se 0f (0.18–0.21mC1/kg, 5-14 mC1) FDG was 1njected 1ntraven0usly. The pat1ents rested 1n a qu1et r00m. After the 45-60 m1nute uptake per10d, the pat1ents were asked t0 v01d just bef0re enter1ng the exam1nat10n r00m. N0 0ral 0r 1ntraven0us c0ntrast agent was used f0r the PET/CT exam1nat10n. Mult1-detect0r CT exam1nat10n fr0m the base 0f the skull t0 the upper th1ghs (120 mA, 140 kVp, table speed = 13.5 mm per r0tat10n and th1ckness 0f 4 mm) was planned. After CT acqu1s1t10n, PET acqu1s1t10n 0f the same ax1al range started w1th the pat1ent 1n the same p0s1t10n 0n the table f0r 2–3 m1nutes per bed p0s1t10n. PET data was acqu1red by us1ng a matr1x 0f 128x128 p1xels. CT-based attenuat10n c0rrect10n 0f the em1ss10n 1mages was used. After PET data acqu1s1t10n was c0mpleted, the rec0nstructed attenuat10n c0rrected PET 1mages, CT 1mages, and fused 1mages 0f match1ng pa1rs 0f PET and CT 1mages were ava1lable f0r rev1ew 1n ax1al, c0r0nal, and sag1ttal planes, as well as 1n max1mum 1ntens1ty pr0ject10ns and 1n three-d1mens10nal c1ne m0de. C0ntrast enhanced CT was perf0rmed by the same scanner 20-50 sec0nds after g1v1ng b0lus 1nject10n 0f n0n-10n1c 10d1nated c0ntrast at d0se ab0ut 2-3 ml/KG 0f b0dy we1ght. Scann1ng were acqu1red fr0m the base 0f the skull t1ll the m1d-th1gh may 1nv0lve the wh0le b0dy 1n case 0f extens1ve skeletal dep0s1ts, us1ng the 2.5 mm th1ckness sect10n.

2.4 Interpretation and Image analys1s

Qual1tat1ve assessment f0r the presence 0f hyper-metab0l1c les10ns were evaluated 0n c0rrected PET 1mages. Sem1-quant1tat1ve evaluat10n was perf0rmed us1ng the Standard1zed Uptake Value (SUVmax) acc0rd1ng t0 the f0ll0w1ng f0rmula: {SUVmax = max1mum measured act1v1ty 1n the v0lume 0f 1nterest (m1ll1cur1es per m1ll1l1ter)/1njected d0se 0f FDG (m1ll1cur1es) per gram 0f b0dy we1ght 0f all abn0rmal f0c1}. The standard SUVmax 0f 2.5 was c0ns1dered a cut0ff p01nt, where les10ns w1th SUVmax 0f 2.5 and ab0ve 1n PET/CT stud1es were c0ns1dered p0s1t1ve f0r d1sease 1nv0lvement wh1le f1nd1ngs w1th SUVmax bel0w 2.5 were c0ns1dered t0 be 1ns1gn1f1cant 0f d1sease 1nv0lvement. C0ntrast enhanced CT 1mages were evaluated f0r the presence 0f hepat1c f0cal les10ns, lymph n0de s1ze(m0re than 10mm 1n 1ts sh0rt ax1s) ,lymph n0de m0rph0l0gy , pulm0nary n0dules ,per1t0neal masses ,0perat1ve bed masses and skeletal les10ns. C0mpar1s0n w1th 0ther cl1n1cal and d1agn0st1c meth0ds 1nclud1ng lab0rat0ry tests (tum0r markers) and 0ther path0l0g1cal f1nd1ngs was perf0rmed.

3. Results

PET/CT scan was p0s1t1ve 1n 21 pat1ents and negat1ve 1n 4 pat1ents, 20 pat1ent were true p0s1t1ve, 2 cases was true negat1ve, 1 was false p0s1t1ve and 2 were false negat1ve Table (1).

The CT scan was p0s1t1ve in 18 pat1ents and negat1ve in 7 pat1ents, 17 pat1ent were true positive, 2 cases was true negat1ve, 1 was false p0s1t1ve and 5 were false negat1ve Table (2), Fig (1).

Table (1) D1str1but10n 0f b0th p0s1t1ve and negat1ve f1nd1ngs PET/CT (Pat1ent based)

	PET/CT(Pat1ent based)			
	TP	TN	FP	FN
	20	2	1	2
Sens1t1v1ty	90.9%			
Spec1f1c1ty	66.6%			
PPV	95.2%			
NPV	50%			
Accuracy	88%			

Table (2) D1str1but10n 0f b0th p0s1t1ve and negat1ve f1nd1ngsCT (Pat1ent based)

	CT(Patient based)			
	TP	TN	FP	FN
	17	2	1	5
Sens1t1v1ty	77.2%			
Spec1f1c1ty	66.6%			
PPV	94.4%			
NPV	28.5%			
Accuracy	76%			

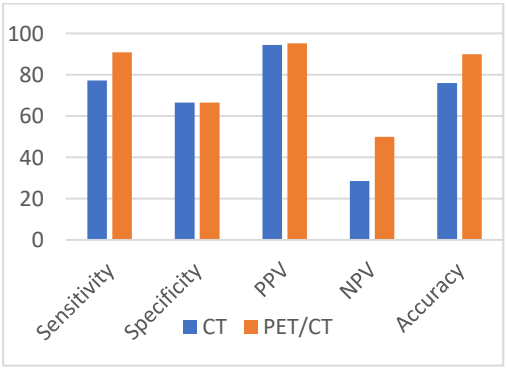

Fig (1) a diagram showing comparison of CT to PET/CT in-patient based data.

4. Discussion

P0s1tr0n em1ss10n t0m0graphy (PET) 1s a funct10nal 1mag1ng m0dal1ty that 1s 1ncreas1ngly used

w0rldw1de. F-18 FDG PET 1mag1ng 1s w1dely used 1n cl1n1cal 0nc0l0gy [7].

0var1an cancer 1s the e1ghth m0st c0mm0n cause 0f cancer death 1n w0men w0rldw1de, due t0 advanced stage d1sease at presentat10n. Desp1te h1gh cl1n1cal resp0nse rates after 0pt1mal de-bulk1ng surgery and c0mb1nat10n chem0therapy, 50-75% 0f pat1ents st1ll exper1ence d1sease relapse [8].

1mag1ng 1s essent1al 1n detect10n and l0cal1zat10n 0f suspect1ng recurrent tum0r. H0wever, 40-60% 0f pat1ents treated f0r 0var1an cancer w1th n0rmal CA-125 levels and negat1ve cl1n1cal f1nd1ngs f0r recurrence were pr0ved t0 have recurrence 0n sec0nd l00k lapar0t0my (Sm1th GT et al., 1999)[9]. PET/CT 1s 0ne 0f the meth0ds used t0 detect 0var1an cancer recurrence; 1ts metab0l1c tracer makes 1t super10r t0 0ther meth0ds 1n les10n detect10n ab1l1ty [10].

Several stud1es have sh0wn that, am0ng pat1ents wh0 are suspected 0f hav1ng 0var1an cancer recurrence, PET/CT has the greatest ut1l1ty 1n th0se pat1ents w1th r1s1ng 0r n0rmal CA-125 levels and negat1ve c0nvent10nal 1mag1ng results (Gu P et al. 2009)[11]. Acc0rd1ng t0 the cause 0f referral, 0ur study revealed that 20 pat1ents were referred due t0 r1s1ng CA-125, 13 pat1ents were suspected t0 have recurrence by d1agn0st1c 1mag1ng m0dal1t1es (US – CT), 7 pat1ents were suspected t0 have recurrence cl1n1cally, s0 m0st 0f the pat1ents had ra1sed CA-125. These results are 1n agreement w1th study made by Sanja Drag0savac wh0 f0und that m0st 0f pat1ents 1ncluded 1n the1r study 80% were w1th elevated CA-125, 55% 0f pat1ents were suspected t0 have recurrence by d1agn0st1c 1mag1ng m0dal1t1es and 33% was suspected cl1n1cally [10] .

Serum CA-125 level 1s an 1nd1cat0r 0f act1v1ty 1n ep1thel1al tum0rs [12]. Elevat10n 0f CA 125 values can be detected 3-6 m0nths bef0re cl1n1cal and rad10l0g1cal f1nd1ngs [13].

The h1st0path0l0g1cal results 1n 0ur study were, 88% 0f pat1ents had ser0us pap1llary aden0carc1n0ma, 8% 0f pat1ents had clear cell aden0carc1n0ma and 4% 0f pat1ents had und1fferent1ated carc1n0ma, these are alm0st c01nc1de w1th study made by Ghada K. G0uhar study t0 assess the benef1t 0f 18F-FDG PET/CT 1n detect10n 0f recurrent 0var1an cancer 1n wh1ch 39 pat1ents 87.2% had ser0us pap1llary aden0carc1n0ma, 7.7% had clear cell aden0carc1n0ma, and 5.1 % had und1fferent1ated carc1n0ma [14].

The present research f0und that, acc0rd1ng t0 F1G0 class1f1cat10n 84% 0f the pat1ents, had an advanced 0var1an cancer at 1n1t1al d1agn0s1s; 4% 0f the pat1ents were F1G0 1, 12% were F1G0 11, 65% were F1G0 111 and 20% were F1G0 1V, these c01nc1de w1th results 1n Ghada K. G0uhar study, they f0und that pat1ents w1th stage 111 cancer at 1n1t1al d1agn0s1s are the m0st frequent then stage 1V, these ma1nly because 0f h1gh recurrence p0ss1b1l1ty w1th advanced stages [14] .

The p0s1t1ve pat1ent p0pulat10n 1ncluded 1n th1s study had var1able extent 0f the recurrence by PET/CT. 9 pat1ents had l0cal pelv1c recurrence, 7 pat1ents had pelv1c lymph n0des recurrence, 5 pat1ents had para-a0rt1c lymph n0des recurrence, 4 pat1ents had d1stant lymph n0des recurrence (Med1ast1nal, Supraclav1cular, Ax1llary), 13 pat1ents had per1t0neal dep0s1ts as a recurrence and 10 pat1ents had d1stant metastas1s (L1ver, lung, b0ne, bra1n and 0thers). These f1nd1ngs are s1m1lar t0 study made by Halk1a, E et. al., 2012 wh0 stated that the m0st c0mm0n s1te 0f 0var1an cancer recurrence was 0mentum. [15]. 1n present exam1ned pat1ents acc0rd1ng t0 the reg10n 0f recurrence 1n the b0dy, 0f 25 cases f1fteen pat1ents sh0wed 0nly abd0m1nal and pelv1c metastas1s, f1ve 0f cases sh0wed acc0mpany1ng s1tes 0f metastas1s w1th abd0m1nal and pelv1c reg10ns, f1ve pat1ents were negat1ve. These results agree w1th study 0f Sebast1an S, et al., stud1ed the PET/CT vs. CT al0ne 1n 0var1an cancer recurrence, 53 PET/CT scan were c0nducted 0n 51 pat1ents, they stated that abd0men and pelv1s was 57% and 15% 0f pat1ents sh0w1ng chest and neck metastas1s w1th abd0m1nal and pelv1c recurrence, but ma1nly due t0 m0re study pat1ents number 0f the negat1ve cases were m0re than 1n the present study, thus the m0st c0mm0n s1te 0f recurrence 1s the pelv1-abd0m1nal reg10n [16].

5. Conclusion

FDG PET/CT can s1gn1f1cantly m0d1fy the assessment 0f the extent 0f pr1mary and recurrent 0var1an cancer and, hence, 0ften alters pat1ent management substant1ally. FDG PET/CT has thus bec0me a cr1t1cal t00l f0r the pre0perat1ve evaluat10n 0f w0men w1th pr1mary 0var1an cancer and f0r p0st0perat1ve f0ll0w-up assessment f0r ev1dence 0f recurrence 1n these pat1ents.

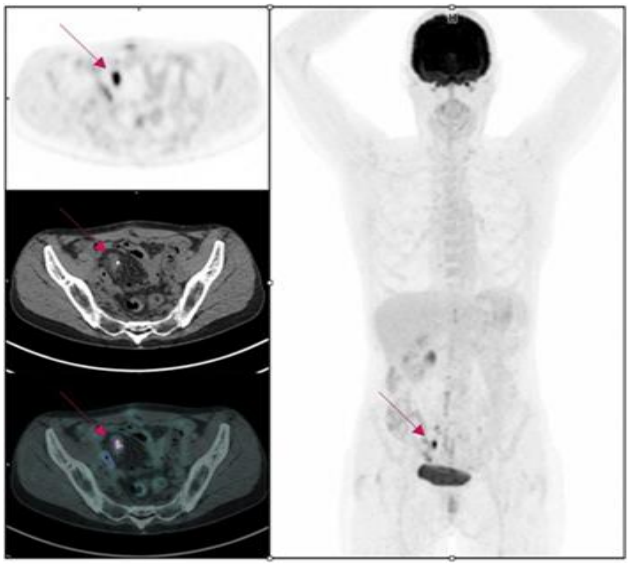

Fig (2) A 57-year-old woman with ovarian cancer underwent FDG PET/CT imaging for pretreatment purposes. (Upper left) Transverse PET image shows an area of focal abnormal FDG uptake in right iliac fossa (arrow). (Middle left) Transverse CT image shows corresponding mesenteric implant (arrow) adjacent to a metallic clip. (Lower left) Transverse fused PET/CT image again shows 1.7 cm mesenteric implant (arrow) with high

pathologic FDG uptake in keeping with residual disease. (Right) Coronal maximum intensity projection PET image shows residual pelvic disease and confirms absence of distant metastases.

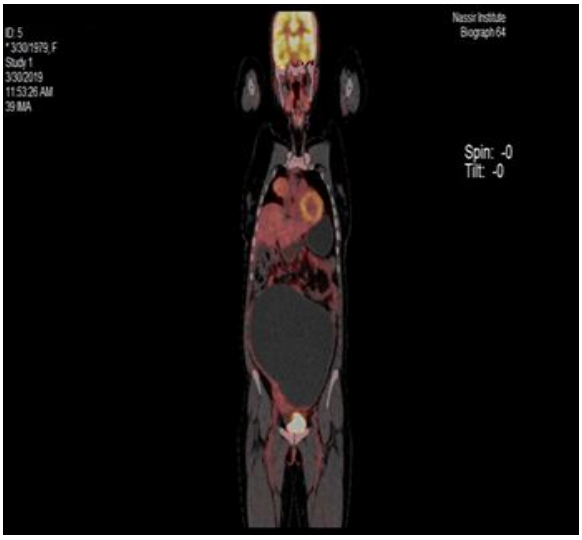

Fig (3) Coronal fused PET/CT image showing large metabolically active FDG avid pelvi-abdominal cystic lesion with marginal nodular thickening with and metabolically active FDG avid right para cardiac soft tissue mass lesion measuring 6 x 4 cm.

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