(e) ISSN Online: 2321-9599

(p) ISSN Print: 2348-6805

ORIGINAL ARTICLE

CAN RAISED LEVELS OF CA–125 PREDICT THE EXTENT OF DISEASE BURDEN IN CASES OF RECURRENT OVARIAN CARCINOMA? – A CORRELATIVE STUDY WITH ^{18}F–FDG PET/CT IMAGING

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ABSTRACT:

Purpose: To evaluate if any linear relationship exists between CA–125 levels and degree of disease burden in suspected recurrent ovarian carcinoma cases on PET/CT and to establish a possible CA–125 cut-off value which could predict whether the active disease predominantly involves lymph nodal stations or intra-abdominal soft tissue sites.

Methods: This retrospective study involved 42 patients (35-74 years) with suspected disease recurrence based on raised CA–125 levels referred for PET/CT scan. Patients were classified into three groups based on the range of CA–125 levels. Number of lesions per patient was counted. Data analysis was done using appropriate statistical tests. **Results:** PET/CT detected a total of 57 lesions in Group A (n=18), 68 in Group B (n=14) and 65 lesions in Group C (n=10) respectively. No significant statistical difference was found in the total number of lesions detected in all the three groups. No significant statistical difference was seen when comparing total number of lesions detected on PET/CT in groups with marked difference in CA–125 levels. When the number of lesions detected on PET/CT in each patient was correlated, no correlation (r = 0.342) between the CA–125 levels and disease burden was observed. A cut-off CA–125 value of 350 U/ml was established to be significant (p-value <0.001) in suggesting whether the active disease predominantly involves lymph node or intra–abdominal soft tissue sites. **Conclusion:** There exists no relationship between CA–125 levels and degree of disease burden detected on PET/CT suggesting that higher degree of disease burden may be found in low levels of raised CA–125 levels and vice versa. A cut-off of 350 U/ml of CA–125 may be useful to predict the predominant disease distribution pattern i.e. lymph nodal stations versus soft tissue deposits in these patients.

Key words: CA -125, 18F-FDG PET/CT, Ovarion carcinoma.

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This article may be cited as: Sonik B, Sundaram PS, Sundaram PS. Can raised levels of CA–125 predict the extent of disease burden in cases of recurrent ovarian carcinoma? – A correlative study with ^{18}F–FDG PET/CT imaging. J Adv Med Dent Scie Res 2017;5(3):84-86.

Access this article online	
Quick Response Code	Website: www.jamdsr.com
	DOI: 10.21276/jamdsr.2017.5.3.19

INTRODUCTION

Ovarian cancer is one of the major causes of cancer death among women worldwide.[1] It also has an extraordinary probability of recurrence despite belligerent treatment plans.[2,3] Due to its high sensitivity when compared to computed tomography (CT) or magnetic resonance (MR) imaging, ^{18}Fluorine – Fluorodeoxyglucose (^{18}F - FDG) positron emission tomography (PET) combined with CT is useful for detection of recurrent or residual ovarian cancer and for monitoring response to therapy.

However, PET/CT has a tendency towards false-negative results especially in patients with small, necrotic, mucinous, cystic or low-grade tumors. In addition, in the post therapy setting, inflammatory and infectious processes may lead to false-positive PET/CT results. Despite these drawbacks, PET/CT is considered superior to CT and MR imaging for detection of recurrent disease.

Cancer antigen 125 (CA–125) is used for monitoring disease status in post treatment patients of ovarian cancer as rising concentrations predict recurrence in most cases[4]. Many studies[5-7] have demonstrated that ^{18}F–FDG PET/CT imaging is sensitive and a better modality when compared to conventional anatomical imaging in detection of recurrent disease in patients with raised CA–125 levels.

Thus, the present retrospective study was designed to determine:

1. Whether any linear relationship exists between CA–125 levels and degree of disease burden detected on PET/CT.
2. A possible CA–125 cut-off value which could predict whether the active disease predominantly

involves lymph nodal stations or intra-abdominal soft tissue (omental/peritoneal/mesenteric) sites.

METHODS

42 patients (35-74 years, Median 52 years) with suspected disease recurrence based on raised CA–125 levels referred for PET/CT scan were studied. Patients were classified into three groups based on the range of CA – 125 levels:

Group A (35 – 175)
Group B (175 – 350)
Group C (more than 350)

Number of lesions in patient was counted in the following manner:

a. Each lymph nodal station was given a score of 1.
b. Each segment of liver was given a score of 1
c. Peritoneal soft tissue deposit along the surface of an organ was given a score of 1 and omental, mesenteric and serosal deposits were assigned a score of 1 individually.
d. Any other lesion such as soft tissue deposit, pulmonary nodule and skeletal lesion was individually given a score of 1.

Data analysis was done using appropriate statistical tests. To arrive at a possible cut-off value for CA–125, various levels of CA–125 were analysed using Chi square test.

RESULTS

PET/CT detected a total of 57 lesions in Group A (n=18), 68 in Group B (n=14) and 65 lesions in Group C (n=10) respectively as shown in the Table 1. No significant statistical difference was found in the total number of lesions detected in all the three groups with different levels of CA–125, (One way ANOVA; p - value: 0.071).

Table 1	LYMPH NODAL LESIONS	SOFT TISSUE LESIONS	LIVER LESIONS	OTHER LESIONS	TOTAL
GROUP A	21	17	16	3	57
GROUP B	41	16	7	4	68
GROUP C	13	43	7	2	65
TOTAL	75	76	30	9	190

When comparing total number of lesions detected on PET/CT in groups with marked difference in CA–125 levels – Group A (CA–125: 35-175) and Group C (CA-125: >350), no significant statistical difference was seen (Proportional test; p – value: 0.380) as shown in Table 2.

Table 2	Test pairs	Z value	P value
Proportional Test	Group A – Group B	-1.201	0.230
	Group A – Group B	-0.879	0.380
	Group B – Group C	0.323	0.747

Also when the number of lesions detected on PET/CT in each patient was correlated with the respective CA–125 levels and data analysed using Spearman Correlation Coefficient, no correlation (r = 0.342) between the CA–125 levels and disease burden was observed as shown in Graph 1.

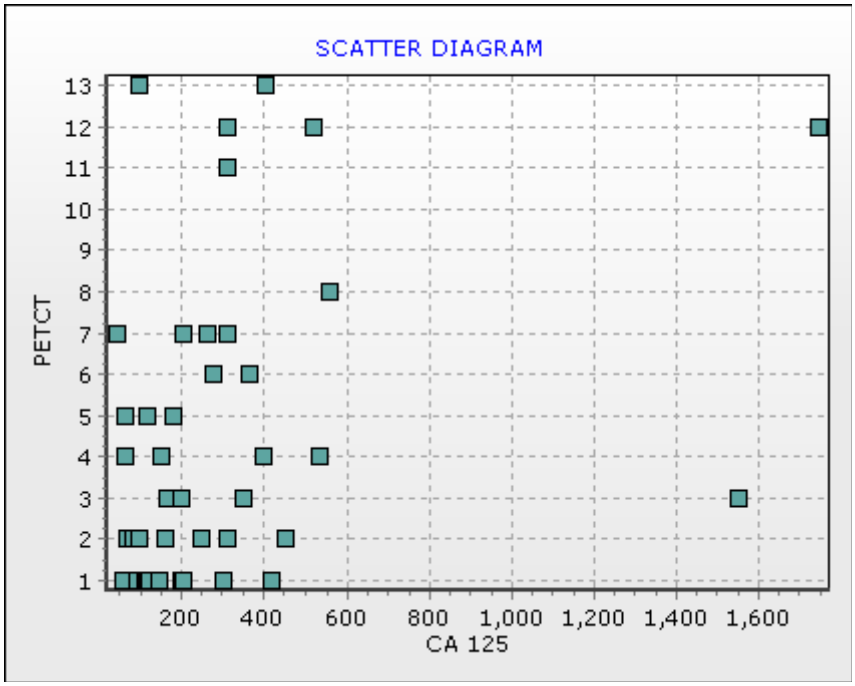

Table 3

Level	</= 350	>350	</= Median (200)	> Median	</=Mean (228)	> Mean
Lesion						
Lymph Nodes	62	13	26	49	33	42
Soft Tissues	33	43	21	55	22	54

Table 4

Cut off CA–125 levels	Chi – square	P – value
Median (200)	0.00255	0.960
Mean (228)	0.966	0.326
350	14.038	< 0.001 (significant)

Using Chi square test, a cut off CA–125 value of 350 U/ml was established to be significant (p-value <0.001) in suggesting whether the active disease predominantly involves lymph nodal or intra–abdominal soft tissue sites as shown in Tables 3 and 4.

In our study, lymph nodal metastases were more common in patients with CA–125 levels less than/equal to 350 U/ml (n=32/42, 76.2%) & soft tissue deposits were more common in patients with CA–125 levels more than 350 U/ml (n=10/42, 23.8%).

DISCUSSION

In most women who have been treated for ovarian cancer, serum concentrations of the tumour marker cancer antigen CA-125 will serially rise on average 4 months before they develop symptoms or signs of relapse. Positron emission tomography (PET) combined with CT is useful for detection of recurrent or residual ovarian cancer and for monitoring response to therapy.

In the present study, no significant statistical difference (p value 0.071) was seen in total number of lesions detected in all the three groups on PET/CT for different CA–125 levels.

Also, there exists no linear correlation (r = 0.342) between number of lesions detected on PET/CT in each patient when compared with their respective CA-125 levels. Hence, it was found that each test could report its individual significance and the value of one cannot be used to predict the disease burden that has to be found in the other.

A cut off CA–125 value of 350 U/ml was established to be significant (p-value <0.001) in suggesting whether the active disease predominantly involves lymph nodal stations or intra–abdominal soft tissue sites. This can serve as an important guide to detect the sites involved in metastasis and may also help as a predictor for response assessment / disease progression.

CONCLUSION

There exists no relationship between CA–125 levels and degree of disease burden detected on PET/CT suggesting that higher degree of disease burden may be found in low levels of raised CA–125 levels and vice versa. A cut-off of 350 U/ml of CA–125 may be useful to predict the predominant disease distribution pattern i.e. lymph nodal stations versus soft tissue deposits in these patients.

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Source of support: Nil **Conflict of interest:** None declared