Journal of Positive School Psychology http://journalppw.com
2022, Vol. 6, No. 10, 3472-3482

Assessment Of Difference In Quality Of Life Due To PET/CT A Hybrid Imaging Modality In Advanced Epithelial Ovarian Cancer Patients In Complete Remission After Primary Treatment

Ramya Soundararajan[1], G. P. Bandopadhyaya[1], Rakesh Kumar[1], Lalit Kumar[2], Sunesh Kumar[3], Suhas Singla[1]

[1]Department of Nuclear Medicine
[2]Department of Medical Oncology
[3]Department of Obstetrics and gynaecology
All India Institute of Medical Sciences, New Delhi

ABSTRACT

AIM: To assess and compare the quality of life of advanced epithelial ovarian cancer patients with the impact of 18F-FDG PET/CT in detection of residual or persistent disease after primary treatment.

MATERIALS AND METHODS: Prospective observational study was done in 38 patients (mean age=48.1 ±10.6 years)from July 2010-July 2012).Patients on complete remission (CR) with normal CA-125 / computed tomography/ultrasound imaging after debulking surgery and primary adjuvant platinum-based chemotherapy were included and 18F-FDG PET/CT was done. 10mCi of 18F-FDG was injected i.v after 6 hrs fasting and whole-body scans were acquired after 45 - 60 minutes in Siemens Biograph 2 PET/CT scanner. Histopathology or follow up imaging/clinical follow up were kept as the reference standard. Patients were asked to fill up/complete quality of life(QOL) questionnaires at two points in the study, after completion of primary treatment and three months after PET/CT. QOL was measured using version 4 of the Functional Assessment of Cancer Therapy –Ovarian (FACT-O). Scores will be evaluated using FACT-O scoring model and QOL before and after PET/CT during the course of disease is evaluated.

RESULTS: Among total 38 patients, 18F-FDG PET/CT detected residual disease initially in 10 patients and were offered salvage chemotherapy. Hence the detection rate of residual disease in patients in CR by 18F-FDG PET/CT is 26% [95% CI = 4.79-18.39]. There was no statistically significant difference in the mean QOL score before PET-CT (p value = 0.800) and after PET-CT(p value = 0.103) for patients who had negative PET-CT scans compared to who had positive results in PET-CT. The present disease status of the patients and QOL of patients who underwent 18F-FDG PET/CT also was not influenced PET/CT results.

No statistically significant difference (p value = 0.602) was found in the mean QOL score before PET/CT in patients remained in CR compared to patients with progressive disease post salvage chemotherapy. Borderline statistically significant difference (p value = 0.051) is noted in the mean QOL score, three months after PET/CT had detected residual disease in patients with complete remission compared patients who had progressive disease.

Among the 28 patients with normal PET/CT scan post primary treatment no statistically significant difference (p value = 0.163) was found in the mean QOL score for patients in complete remission compared to patients who relapsed, However, the mean QOL score three months after PET-CT for patients in complete remission compared to patients who relapsed, the difference being statistically significant (p value < 0.001).

CONCLUSION: The Quality of Life (QOL) after three months of PET/CT scan was substantially lower in patients with progressive disease, who had abnormal PET/CT scan compared to baseline QOL after primary treatment, which supports the impact of PET/CT in QOL of the patients.

Keywords: Quality of Life(QOL), 18F- FDG PET/CT, Complete Remission(CR), Residual disease

Introduction:

Ovarian cancer is the second most common gynaecologic malignancy, and accounts for approximately half of all deaths related to gynaecologic cancer [1]. In India ovarian cancer has emerged as one of the most common malignancies in women. [2]. Majority of the patients, (70-75%) are diagnosed at an advanced stage [3]. Symptoms are non-specific such as abdominal pain or discomfort, an abdominal mass, bloating, back pain, urinary urgency, constipation, tiredness, pelvic pain, abnormal vaginal bleeding, fluid accumulation in the abdominal cavity or involuntary weight loss [4-6].. The overall survival at 1 and 5 years is 75 and 45%, respectively [3].

Standard treatment of advanced ovarian cancer includes aggressive cytoreductive surgery followed by platinum or taxane-based chemotherapy [7]. After front-line therapy for ovarian cancer, which typically involves 6 to 8 cycles of platinum and taxane-based chemotherapy, the majority of patients (70-80%) experience a clinical, radiologic, and biochemical complete response [8].

Serial determination of the tumor marker CA-125 level is the most frequently used method for monitoring the disease. However, a CA-125 level within the normal range (0 to 35 U/ml), does not exclude the presence of microscopic disease and positive values cannot differentiate between localized and diffuse spread [9,10]. Normal CA-125 levels are associated with persistent disease in 36% to 73% of cases [8].

In addition to CA-125 estimation, imaging modalities like USG, CECT and MRI are an important component of the clinical management of patients with ovarian cancer. It is important for tumor detection, staging, restaging, treatment planning, and follow-up. Imaging findings assist in creating a specific treatment plan for each individual patient and accurate delineation of disease status [11]. CT and MRI, both are equivalent; in general small local recurrence, LN metastasis, small dissemination, and bone/muscle metastasis are difficult to detect with both CT and MRI [12].

Despite the fact that ovarian cancer is very sensitive to platinum-based chemotherapy, the 5-year survival rate for patients with advanced disease is only 17%, because of the high rate of persistent or recurrent disease [13 - 16]. The quality of life of such patients detoriate due to presence of persistent or recurrent disease. But almost in 50–75% of those with advanced disease whoobtain a complete response after first-line chemotherapy,disease will ultimately recur [17]. Therefore, it is necessary to identify the patients with persistent or residual disease after primary line of treatment, so if needed further consolidation therapy can be given and quality of life can be improved. Because of limited sensitivity of CT scan in imaging the residual disease after primary treatment and limited accuracy of CA-125 Integrated PET/ CTPositron Emission Tomography / Computed tomography with 2-[18F]fluoro-2-deoxy-D-glucose (FDG), which yields metabolic information by increased utilization of glucose by malignant cells may be helpful in the detection of a tumorand provides precise anatomic localization of suspicious areas of increased FDG uptake[14, 18].

In the present study we have prospectively evaluated and assessedthe quality of life of advanced epithelial ovarian cancer patients with the impact of ^{18}F-FDG PET/CT in detection of residual or persistent disease after primary treatment.

Materials and methods:

This is a Prospective observational study was conducted in Department of Nuclear Medicine, AIIMS, New Delhi with patients being refered from Gynaecology tumor clinic of Dr.BRA IRCH at All India Institute of Medical Sciences(July 2010 to June 2012). 38 patients were included in the study as per the criteria. The study was approved by ethics committee andinformed consent was obtained from all the patients. **All** Histologically proven cases of advanced epithelial ovarian carcinoma (EOC).Patients who have undergone surgery and completed six cycles of chemotherapy and in clinical remission(CR) i.e without any residual lesions on CT scan and having normal serum CA-125 after completion of chemotherapy, patients who gave consent to fill the questionnaire were included in the study.Patients who already have known residual/recurrent disease on other imaging techniques/tumor markers, patients not willing to give written informed consent, pregnant and lactating women, patients with uncontrolled diabetes, patients who have not completed six cycles of chemotherapy and histology other than epithelial ovarian carcinoma were excluded from the study.

All patients in clinical remission after primary treatment were evaluated with ^{18}F-FDG PET/CT for identification of residual disease. Histopathology (HPE)/clinical follow up/Follow up imaging and CA-125 was kept as the reference standard. Patients with residual disease identified by PET/CT were given three more cycles of salvage chemotherapy and patients with normal PET/CT scan were kept on follow up. All patients were followed up till June 2012.

^{18}F-FDG PET/CT IMAGING PROTOCOL

^{18}F-FDG PET/CT images of the patients were acquired by setting appropriate parameters on a dedicated SIEMENS BIOGRAPH 2 PET/ CT scanner (Germany). PET/CT study was conducted in fasting conditions of at least 4-6 hours and patients with blood glucose levels less than 140mg/dl were considered for the study. Images were taken 45-60 minutes after 10 mCi FDG injection with additional pelvic views post 20mg furosemide i.v (if necessary) to overcome the difficulties due to high bladder activity by excretion of the radioactivity in these patients.

Analysis and interpretation of the PET, CT, and fused PET/CT images was done after displaying the images in transaxial, coronal and sagittal planes. Two experienced Nuclear Medicine physicians evaluated both the whole body and post furosemide scan findings independently and were blinded to the structural imaging and clinical findings. PET images were looked for area of increased radiotracer uptake and region of interest was marked around it for measurement of Standardised uptake value (SUVmax). Corresponding area in the CT images and fused PET-CT images were corroborated for identification of residual disease. SUVmax of the tumor tissue was measured. Liver was considered as background and SUVmax was measured. The lesion/background ratio was considered for comparison between baseline and post salvage chemotherapy PET/CT scans in patients with residual disease. Complete resolution of ^{18}F-FDG uptake within the lesion was considered as complete response. Reduction of minimum of 15% ± 25% in tumor^{18}F-FDG SUV after 1 cycle of chemotherapy, and > 25% after more than 1 treatment cycle was classified as having a partial response. Increase in ^{18}F-FDG tumor SUV of > 25% within tumor region defined on baseline scan; visible increase in extent of ^{18}F-FDG tumor uptake (20% in longest dimension) or appearance of new ^{18}F-FDG uptake in metastatic lesions constituted the evidence of progressive disease. All other responses were classified as stable disease and if neither progressive nor partial response is present [19]. In patients whom follow up PET/CT was done after salvage chemotherapy, the results of the baseline PET/CT was retrospectively confirmed.

Quality of Life (QOL)

Patients were asked to fill up/complete quality of life questionnaires at two points in the study, after completion of primary treatment and three months after PET/CT. QOL was measured using version 4 of the Functional Assessment of Cancer Therapy –Ovarian (FACT-O). This consists of a 33 item Functional Assessment of Cancer Therapy General (FACT-G) questionnaire, which is targeted to cancer patients generally, and 12 questions specific to issues faced by ovarian cancer patients. FACT-G questionnaire includes five subscales (physical well being, social well being, emotional well being, relationship with doctor and functional well being). All questionnaire were also explained in local and regional language as well to the patients. Scores will be evaluated using FACT-O scoring model and QOL before and after PET/CT during the course of disease is evaluated.

Study endpoints

- Residual disease detection after primary treatment.
- Comparison of Quality of life (QOL) of patients with normal PET/CT scan and patients with residual disease detected on PET/CT with their present disease status.

Observation and Analysis:

Thirty eight patients (n = 38) with advanced epithelial ovarian carcinoma, who were in complete remission after completing their primary treatment and who fulfilled the inclusion criteria underwent ^{18}F-FDG PET/CT to look for residual or persistent disease and assess the quality of life depending on the results.

PATIENT DEMOGRAPHICS

The age of patients ranged from 24 to 75 years. Mean age of the patients was 48.1 ±10.6 years and the median age was 47 years. Predominant Clinical presentation was abdominal pain and distension.Among total 38 patients, 32 (84.2%) patients had stage III and six (15.7%) patients were in stage IV.Serum CA-125 levels pretreatment ranged from 17.8 to 14,520 U/ml. Mean and median were 1685.1% and 931.9% respectively (Normal value = 0 to 35 U/ml).Among total 38 patients, 24 patients underwent debulking surgery and adjuvant chemotherapy (CT) and 14patients underwent neoadjuvant chemotherapy (NACT), debulking surgery and adjuvant chemotherapy.All patients achieved complete clinical, biochemical and radiological remission, before being referred for PET-CT examination in search of persistent or residual disease. The mean and median post treatment CA-125 values was 14.2 ± 9.7 U/ml and 10.7 U/ml respectively.

TABLE 16: Demographic Profile

VARIABLES	N	Mean± SD	Median	Range
Age	38	48.1±10.1	47.0	24-75
CA125 Pre treatment	38	1685.1	931.9	17.8-14,520
CA 125 Post Treatment	38	14.2±9.4	10.7	2.2-35.4

(Variables are expressed as Mean ± SD, Median and Range)

STATISTICAL ANALYSIS

Numbers and percentages were used for categorical data. Mean, median, standard deviation, range and 25^{th} – 75^{th} percentile were described for continuous variables. Kolmogorov-Smirnov test was used to assess normality of data. Chi-square and Fisher's exact test were used to compare categorical

data. Fisher's exact test was used to analyse the diagnostic performance of ^{18}F-FDG PET/CT.

Statistical analysis of QOL

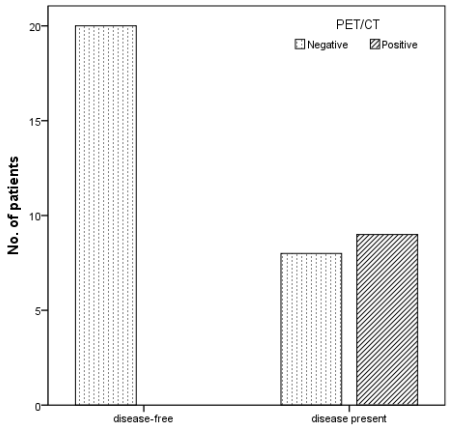
Comparison of QOL of patients before and three months after ^{18}F-FDG PET/CT with their present disease status is done using independent t – test. Mean QOL duration and p-value was derived.

DETECTION RATE OF RESIDUAL DISEASE BY ^{18}F-FDG PET/CT

Among total 38 patients, ^{18}F-FDG PET/CT detected residual disease initially in 10 patients in complete remission; PET/CT scan was normal in remaining 28 patients. Hence the detection rate of residual disease in patients in complete remission by ^{18}F-FDG PET/CT is 26% [95% CI = 4.79-18.39]. Histopathology (HPE)/clinical follow up/Follow up imaging and CA-125 was kept as the reference standard. Imaging guided FNAC was performed in five out of 10 patients and four patients were proven to have adenocarcinoma and for one patient the HPE result was doubtful for malignant cells.

Among the remaining five patients, four patients were followed up clinically and one patient was still under HPE investigation. Hence total 37 patients and nine out of 10 patients with residual disease detected on PET/CT were included for further analysis and follow up.

FIGURE 2: Bar diagram showing detection rate of PET/CT in patients of carcinoma ovary after completion of primary treatment



Among 10 patients with residual disease detected on ^{18}F-FDG PET/CT, nine patients received salvage chemotherapy. One patient was still under consideration for salvage chemotherapy.Follow up PET/CT scan was done after salvage chemotherapy in five out of nine patients and the follow up lesion SUVmax and lesion to background ratio was calculated. Three out of five patients were detected progressive disease in follow up PET/CT and remaining two patients had stable disease. Remaining four patients in whom PET/CT was not done were clinically followed up. The mean SUV max of lesion in those patients on follow up was 25.9 and mean lesion to background ratio was 2.7.Among total 38 patients present status of disease was known for 37 patients and one patient was still under investigation. Twenty three (62.2%) patients were in complete remission and 14 patients (37.8%) relapsed.All patients were followed till their last visit (date of censorship – 30.06.2012) at tumor clinic. The follow up duration ranged from 1.4-20.1 months. The median follow up duration was nine months.

Quality of Life

The mean quality of life score before PET-CT was 107.5 ±15.9 for patients who had negative PET-CT scans compared to 106.5±16.7 for patients who had positive results in PET-CT, the difference not being statistically significant (p = 0.858).The mean quality of life score three months after PET-CT scan was 108.6 ± 23.4 for patients with normal PET-CT scans and 93.7 ± 22 for patients with positive results on PET-CT, which was not statistically significant (p value = 0.103).The present disease status of the patients and QOL of patients who underwent ^{18}F-FDG PET/CT also was not influenced PET/CT results.

Quality of life	Before PET/CT	107.5 ±15.9	108.6 ± 23.4	0.858
	Three months after PET/CT	106.5±16.7	93.7 ± 22	0.103

Quality of life assessment in patients with residual disease detected in PET/CT

Among ten patients with residual disease detected by ^{18}F-FDG PET/CT, nine patients were offered salvage chemotherapy. Among them, three patients achieved complete remission (median follow up duration=13.43 months) and six patients had disease progression (median follow up = 13.59 months). One patient was under consideration for salvage chemotherapy and present status is not available. Hence only nine patients were considered for further analysis.

The mean quality of life score before PET/CT was 110.6 ± 5 in patients with CR compared to 106.5± 21 in patients with progressive disease, which was not statistically significant (p value = 0.602).

However, the mean quality of life score, three months after PET/CT had detected residual disease was 111 ± 4 in patients who was in complete remission post salvage chemotherapy compared to 85.1 ± 22 in patients who had progressive disease, which was borderline statistically significant (p value = 0.051).

Thus Borderline statistically significant difference was found in the QOL score after three months of PET/CT between patients in complete remission post salvage chemotherapy and patients with progressive disease.

Quality of life	**Before PET/CT**	110.6 ± 5	111 ± 4	0.602
	Three months after PET/CT	106.5± 21	85.1 ± 22	**0.051***
* P value considered as statistically significant.				

QOL assessment in patients with normal PET/CT after primary treatment:

Among 28 patients with normal PET-CT scan after primary treatment 20 (71%) patients were in complete remission (median follow up duration=6.5 months) and eight (29%) patients relapsed (median follow up duration= 9.5 months) .

Quality of Life before and after three months of PET-CT in patients with normal PET/CT results post primary treatment

The mean QOL total score before PET/CT, in this group of patients was 110.2 ± 14.2 for patients in complete remission compared to 100.8 ± 18.7 in patients who relapsed, the difference not being statistically significant (p value = 0.163). However, the mean QOL score

three months after PET-CT was 119.2 ± 14 for patients in complete remission compared to 82 ± 21 in patients who relapsed, the difference being statistically significant (p value < 0.001).

Thereforethere was statistically significant difference in the QOL three months after PET/CT for patients who relapsed compared to patients who are in complete remission inspite of normal PET/CT scan (p < 0.001).

Among 28 patients with normal PET-CT scan after primary treatment 20 (71%) patients were in complete remission (median follow up duration=6.5 months) and eight (29%) patients relapsed (median follow up duration= 9.5 months) **Quality of life**	**Before PET/CT**	110.2 ±14.2	100.8 ±18.7	0.163
	Three months after PET/CT	119.25 ± 14	82 ± 21	<0.001*
* P value is considered as statistically significant				

DISCUSSION

The corner stone of treatment of advanced ovarian epithelial cancer is primary cytoreductive surgery followed by six cycles of combination platinum - taxane based chemotherapy. Seventy five percent of patients achieve complete clinical response to this primary treatment. Due to residual disease majority of patients ultimately relapse, especially in two years following the first-line therapy. Even though the initial response is good, and it has been reported that 75% of ovarian cancer patients will experience disease relapse [20]. The 5-year survival ratefor patients with advanced disease is only 17%, because of high rate of residual orrecurrent disease [21].

Serial measurement of tumor marker CA-125 is routinely used to evaluate the response to chemotherapy, but it has limited reliability because elevation of CA-125 may indicate residual or recurrent disease, but normal values does not exclude the presence of microscopic residual disease[22].

Conventional morphological imaging modalities including TVUS, CT, and MRI have been widely used to evaluate the status of ovarian cancer, because anatomic localization of residual or recurrent disease is important for subsequent treatment planning and management and follow up of ovarian cancer [23,24,25]. CT is not much useful in detection of persistent disease. Combined with a normalization of initially elevated CA-125 levels, the predictive value of abdominal pelvic CT scanning for detecting persistent disease has been disappointingly low [26].

Morphological criteria and the size of lesions are used for assessment by conventional imaging modalities rather than the actual detection of metabolically active tissue. Therefore, CT has limited value in detecting

microscopic and small macroscopic disease, especially small peritoneal lesions, subcentimetric lymph nodes which are the most common sites of relapse [27, 28]. It is also difficult to distinguish benign postoperative changes from tumor relapse [29]. MR imaging is limited in its ability to depict small calcified peritoneal implants, which are common in patients with serous carcinoma [21].

To overcome these difficulties SLL is employed as a routine procedure in certain institutions, in patients without clinical evidence of disease to assess the response. But there is a growing acceptance that noninvasive evaluation of disease status would be beneficial, because SLL is an invasive procedure with surgical complications and also distant metastasis cannot be determined [30]. There is possibility of relapse even after negative SLL [31].

^{18}F-FDG PET/CT may overcome these limitations of anatomical imaging. FDG being a glucoseanalog it is a functional test of the glycolytic activity of the tumor and could potentially identify persistent ovarian carcinoma in tissues that appear anatomically normal on CT scan and determine the viability of anatomic CT scan findings. Ovarian cancer is generally characterized by a marked increase in glucose metabolism, which can be exploited as a target for imaging with PET/CT using FDG. The potential advantages of PET/CT for patients with ovarian cancer include increased lesion conspicuity, anatomic localization of lesions and differentiation of disease processes from physiologic activity [32].

In this study ^{18}F-FDG PET/CT detected residual disease in 10 patients and they were offered salvage chemotherapy. Hence detection rate of residual disease after primary treatment in patients in complete remission by FDG PET/CT is 26%, which had a subsequent bearing in management of those patients.

It is a fact that FDG PET/CT could enable the detection and localization of metastatic lymph nodes that are not enlarged and this is the area where FDG PET/CT overcomes the disadvantages of CT scan [26]. The same thing applies for this study as well. There was no gross areas of abnormal uptake in the remaining 28 patients.

Rose et al (2001)[22] evaluated the predictive value of stand alone PET in determining a complete pathological response in 22 patients in complete clinical response after chemotherapy. Persistent disease was found in 13(59%) patients. The sensitivity was only 10% and the specificity was 42%.

Among 28 patients with normal PET/CT results after primary treatment eight (29%) patients relapsed in spite of normal PET/CT scans. Among nine patients with residual disease detected by PET/CT and subsequently offered salvage chemotherapy, three (33%) achieved complete remission and six (67%) patients progressed when they were followed up for median duration of 13.59 months . Five out of six patients who progressed had new lesions diagnosed by conventional imaging modalities and/or FDG PET/CT and one patient had increase in size and uptake of FDG in the same site mentioned previously by FDG PET/CT study. More number of patients had progressed in this group which retrospectively confirmed the results of baseline PET/CT. In this group as well, present disease status of the patients was not influenced by any of the factors like age of the patient, stage of the disease, type of treatment and surgery, pre and post treatment CA-125 values and histopathology grade.

In patients with residual disease detected in PET/CT all three patients (100%) who underwent suboptimal debulking surgeryprogressed compared to three out of six (50%) who underwent optimal debulking. This explains the impact of residual disease after debulking surgery in determining the outcome of the patients.

The Quality of Life (QOL) score after three months of PET/CT scan was significantly lower in patients with progressive disease, who had abnormal PET/CT scan compared to baseline QOL score after primary treatment. Even though all patients with abnormal PET/CT scans received salvage chemotherapy

side effects of chemotherapy was encountered in none of the patients and possibly the deterioration in QOL was due to progressive disease, which supports the impact of PET/CT results in QOL of these patients.

But patients who relapsed even with normal PET/CT scan showed significant deterioration in quality of life compared to patients in complete remission, indirectly supporting the evidence that even patients with normal PET/CT scan should be kept under careful follow up.

LIMITATIONS OF PRESENT STUDY

The important limitation of the study was small sample size (n=38) especially in the group where PET/CT had detected residual disease (n=10). This was a single center study which may be a limitation, because of which large number of patients could not be recruited.

CONCLUSION

- ^{18}F-FDG PET/CT is a useful imaging modality in detecting residual disease in patients of advanced epithelial ovarian carcinoma after primary treatment who are in complete clinical, radiological and biochemical remission and it has a subsequent bearing on patients management.
- The Quality of Life (QOL) after three months of PET/CT scan was substantially lower in patients with progressive disease, who had abnormal PET/CT scan compared to baseline QOL after primary treatment, which supports the impact of PET/CT in QOL of the patients.

REFERENCES

1. Ozols RF, Rubin SC, Thomas GM, Robboy SJ: Epithelial ovarian cancer. In Principles and Practice of Gynecologic Oncology 4th edition.Edited by: William JH, Carlos AP, Robert CY. Philadelphia, LippincottWilliams & Wilkins; 2004:841-918.
2. Srinivasa Murthy N, Shalini S, Suman G, Pruthvish S, Mathew A. Changing Trends in Incidence of Ovarian Cancer - the Indian Scenario. Asian Pacific Journal of Cancer Prevention, 2009; 10:1025-30.
3. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T et al. Cancer statistics, 2008. CA Cancer J Clin 2008; 58(2):71–96.
4. Goff BA, Mandel L, Muntz HG, Melancon CH."Ovarian carcinoma diagnosis". Cancer 2000; 10:2068–75.
5. Bankhead CR, Kehoe ST, Austoker J. Symptoms associated with diagnosis of ovarian cancer: a systematic review. BJOG 2005; 112 (7):857–65.
6. Ryerson AB, Eheman C, Burton J, McCall N, Blackman D, Subramanian Set al.Symptoms, diagnoses, and time to key diagnostic procedures among older U.S. women with ovarian cancer . Obstet and Gynecol, 2007; 109(5):1053-61.
7. Chan YM, Ng TY, Ngan HY, Wong LC. Quality of life in women treated with neoadjuvant chemotherapy for advanced ovarian cancer: a prospective longitudinal study. Gynecol Oncol. 2003; 88:9–16.
8. Yen TC, and Lai CH. Positron Emission Tomography in Gynecologic Cancer. Semin Nucl Med. 2006; 36:93-104.
9. Bar-Am A, Kovner F, Lessing JB,Inbar M, Chaitchik S, Azem F et al. A second thought on second look laparotomy. Acta ObstetGynecol Scand. 1993; 72(5): 386–90.
10. Patsner B, Orr JW Jr, Mann WJ Jr, Taylor PT, Partridge E, Allmen T. Does serum CA 125 level prior to second-look laparotomy for invasive ovarian carcinoma predict size of

residual disease? Gynecol Oncol 1990; 38:373–76.
11. Rustin GJS. Use of CA 125 to assess response to new agents in ovarian cancer Trials. J Clin Oncol 2003; 21:187s-193s.
12. Kitajima K, Murakami K, Sakamoto S, Kaji Y, Sugimura K. Present and future of FDG-PET/CT in ovarian cancer. Ann Nucl Med 2011; 25:155–64.
13. Omura GA, Brady MF, Homesley HD, Yordan E, Major FJ, Buchsbaum HJ et al. Long-term follow-up and prognostic factor analysis in advanced ovarian carcinoma: the Gynecologic Oncology Group experience. J Clin Oncol 1991; 9:1138– 50.
14. NIH Consensus Development Panel on Ovarian Cancer. Ovarian cancer: screening, treatment and follow-up. JAMA 1995; 273:491– 96.
15. Rose PG. Surgery for recurrent ovarian cancer. Semin Oncol 2000; 27:17–23.
16. Thigpen JT, Vance RB, Khansur T. Second- line chemotherapy for recurrent carcinoma of the ovary. Cancer 1993; 71: 1559–64.
17. Schwarz JK, Grigsby PW, Dehdashti F, Celbeke D. The role of ^{18}F-FDG PET in assessing therapy response in cancer of the cervix and ovaries. J Nucl Med. 2009; 50:64S–73S.
18. Beyer T, Townsend DW, Brun T, Kinahan PE, Charron M, Roddy R, et al. A combined PET/CT scanner for clinical oncology. J Nucl Med. 2000; 41:1369–79.
19. Young H, Baum R, Cremerius U, et al. Measurement of clinical and subclinical tumour response using [18F]-fluorodeoxyglucose and positron emission tomography: review and 1999 EORTC recommendations. European Organization for Research and Treatment of Cancer (EORTC) PET Study Group. Eur J Cancer. 1999; 35: 1773–82.
20. OzolsRF .Systemic therapy for ovarian cancer: current status and new treatments. Semin Oncol 2006; 33(Suppl 6):3–11
21. Sironi S, Messa C, Mangili G, Zangheri B, Aletti G, Garavaglia E et al. Integrated FDG PET/CT in patients with persistent ovarian cancer: correlation with histologic findings. Radiology.2004; 233(2):433-40.
22. Rose PG, Faulhaber P, Miraldi F, Abdul Karim FW. Positive Emission Tomography for Evaluating a Complete Clinical Response in Patients with Ovarian or Peritoneal Carcinoma: Correlation with Second-Look Laparotomy. Gynecol Oncol. 2001; 82**:**17–21.
23. Coakley FV, Choi PH, Gougoutas CA, Pothuri B, Venkatraman E, Chi D et al. Peritoneal metastases: detection with spiral CT in patients with ovarian cancer. Radiology 2002; 223: 495–99.
24. Pannu HK, Bristow RE, Montz FJ, Fishman EK. Multidetector CT of peritoneal carcinomatosis from ovarian cancer. RadioGraphics 2003; 23: 687–701.
25. Forstner R. Radiographical staging of ovarian cancer: imaging findings and contribution of CT and MRI. EurRadiol 2007; 17:3223–35.
26. Rose PG, Reuter K, Sirois J, Fournier L, Reale FR, Nelson BE et al. The impact of CA-125 on the sensitivity of abdominal/pelvic CT scan before second look laparotomy in ovarian cancer: Int J Gynecol Cancer 1996; 6:213–18.
27. Topuz E, Aydiner A, Saip P, Eralp Y, Tas F, Salihoglu Y et al. Correlation of serum CA125 level and computerized tomography (CT) imaging with laparotomic findings following intraperitoneal chemotherapy in patients with ovarian cancer. Eur J Gynaecol Oncol 2000; 21:599–602.

28. Zimny M, Siggelkow W, Schröder W, Nowak B, Biemann S, Rath W et al. 2-[Fluorine-18]-fluoro-2-deoxy-d-glucose positron emission tomography in the diagnosis of recurrent ovarian cancer. Gynecol Oncol. 2001; 83(2):310-15.
29. Kubik-Huch RA, Dorffler W, von Schulthess GK, Marincek B, Köchli OR, Seifert B et al. Value of FDG positron emission tomography, computed tomography, and magnetic resonance imaging in diagnosing primary and recurrent ovarian carcinoma. EurRadiol 2000; 10: 761–67.
30. De Rosa V, Stefano ML, Brunetti A, Caraco C, Graziano R, Gallo MS, et al. Computed tomography and second-look surgery in ovarian cancer patients. Correlation, actual role and limitations of CT scan. Eur J Gynaecol Oncol 1995; 16:123–29.
31. Cho SM, Ha HK, Byun JY, Lee JM, Kim CJ, Nam-Koong SE. Usefulness of FDG PET for assessment of early recurrent epithelial ovarian cancer. AJR.2002; 179:391–95.
32. Pannu HK, Cohade C, Bristow RE, Fishman EK, Wahl RL. PET–CT detection of abdominal recurrence of ovarian cancer: radiologic–surgical correlation. Abdom Imaging 2004; 39:398–403.