P R A C E O R Y G I N A L N E
ginekologia

^{18}F-FDG PET-CT and USG/CT in benign and malignant ovarian tumors with postoperative histopathological correlation

Pozytonowa emisyjna tomografia komputerowa z ^{18}F-FDG, ultrasonografia i tomografia komputerowa w łagodnych i złośliwych guzach jajnika w korelacji z pooperacyjnym wynikiem histopatologicznym

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Abstract

Objectives: *The role of ^{18}F-FDG (^{18}F fluorodeoxyglucose) PET/CT** (Positron emission tomography) in the diagnosis, treatment and follow up of benign and malignant ovarian tumors had been investigated previously. The objective of the following study was to evaluate the predictive value of PET/CT in benign and malignant ovarian tumors and compare with computerized tomography and post-operative pathology.*

Materials and methods: *In this retrospective study, a total of sixty nine cases with benign or malignant pelvic masses underwent laparotomy at our clinic. Postoperative pathology of the patients was recorded and PET/CT results were compared with ultrasonography, computerized tomography and postoperative pathology.*

Results: *The ROCs and AUCs values four predictors were shown in Figure 1. The AUCs (95 % CI) values calculated for CA 125, ultrasonography (USG), PET/CT and CT were as follows: 0.855(0.752-0.958), 0.703(0.540-0.866), 0.681(0.514-0.848) and 0.631(0.463-0.799) respectively. CA 125 has the highest AUC value in order to predict the malignant potential of the patient. USG has the highest AUC value between the imaging techniques, following PET/CT and CT.*

Conclusion: *According to this study, among four modalities that distinguish malignant potential preoperatively; CA125 is the best parameter. USG and PET provide similar benefits in detecting malignant ovarian masses preoperatively. Both of these parameters are superior to CT. Combination of CA125, USG and PET/CT may be useful in detecting malignant ovarian masses preoperatively, resulting in less invasive surgeries.*

*** ^{18}F-FDG (^{18}F fluorodeoxyglucose) PET/CT will be used as the PET/CT, later in this article.*

Key words: **PET/CT** / **benign ovarian tumors** / **malignant ovarian tumors** / / **predictive value of tests** /

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Streszczenie

Cel pracy: *Rola 18F-FDG PET w diagnozowaniu łagodnych i złośliwych guzów jajnika w diagnozowaniu oraz obserwacji po leczeniu była już tematem badań. Celem tej pracy jest ocena wartości predykcyjnej PET/CT w łagodnych i złośliwych guzach jajnika i porównanie tej metody z tomografią komputerową i pooperacyjnym wynikiem histopatologicznym.*

Materiał i metody: *Badanie retrospektywne przeprowadzono na grupie 69 pacjentek z łagodną bądź złośliwą zmianą w miednicy mniejszej, które poddano laparotomii w naszej klinice. Wynik pooperacyjny histopatologiczny porównano z wynikiem badania PET/CT, USG, tomografią komputerową.*

Wyniki: *Obliczone wartości AUC (95%CI) dla CA125, USG, PET/CT i tomografii komputerowej wyniosły odpowiednio: 0,855 (0,752-0,958), 0,703 (0,540-0,866), 0,681 (0,514-0,848) i 0,631 (0,463-0,799). Marker CA125 miał najwyższą wartość AUC dla przewidywania złośliwych zmian. USG miało najwyższą wartość AUC wśród technik obrazowania, następnie PET/CT i tomografia komputerowa.*

Wnioski: *Według tego badania, spośród analizowanych czterech metod przedoperacyjnego prognozowania charakteru guza, CA125 jest najlepszym parametrem. USG i PET mają podobną siłę wykrywania zmian złośliwych przed operacją. Kombinacja badania CA125, USG i PET/CT może być przydatną metodą wykrywania złośliwych guzów jajnika przed operacją i wykonywania mniej inwazyjnych operacji.*

Słowa kluczowe: **pozytonowa emisyjna tomografia komputerowa** / / **tomografia komputerowa** / **nowotwory jajnika, łagodne, złośliwe** / / **wartość predykcyjna** /

Introduction

Preoperative imagining is one of the most important diagnostic steps in oncology. Computerized tomography (CT) and magnetic resonance imagining (MRI) are both used in evaluating abnormal masses, but they fail to supply data about the metabolic process of the lesion [1].

PET/CT imagining technique offers an opportunity to detect active metabolic processes and morphological features of the tissues in a single examination [2]. The most commonly used area of PET/CT imagining is oncology, and depends on the different, increased use of the ^{18}F-FDG by cancer cells when compared with the normal cells [3]. Kubato et al reported that the macrophages of tumor cells have a high uptake of ^{18}F-FDG [4].

In patients with ovarian carcinoma, PET/CT imagining can be used for staging, prognosis and diagnosis of recurrence [5-8]. In a study by Saif et al., reported that PET/CT imagining can be used as an initial method, staging, treatment monitoring and radiotherapy planning [9]. To the best of our knowledge, only two studies so far have compared the diagnostic accuracy of ultrasonography, CT and MRI [11], and Kurtz et al., also compared these modalities with postoperative histopathology in ovarian masses [11].

In this study, the authors aimed to evaluate the diagnostic accuracy of CA125, USG, CT, PET/CT and postoperative histopathology of the patients with ovarian tumors operated at our clinic.

Materials and methods

We performed this retrospective study at Dicle University School of Medicine, Department of Obstetrics and Gynecology, Division of Gynecological Oncology, from January 2006 to December 2009. Dicle University Hospital is a tertiary research and education hospital in southeastern Turkey. This is a referral center of gynecological oncology that most of the patients were referred to from the surrounding health centers.

A total of sixty nine patients with benign or malignant pelvic masses subjected to laparotomy were included into this study. The clinical characteristics of the enrolled patients are presented in Table 1.

Forty eight (69.5 %) of the patients had malignant ovarian tumors and twenty one (30.5 %) had benign ovarian tumors. The initial evaluation of the patients included gynecological and obstetric history, systemic examination, complete blood count, tumor markers, chest x ray, ultrasonography, CT and PET/CT imagining.

1. Conventional US Protocol

The system used was the Voluson 730 PRO Real Time 4D imaging technology (GE Medical System, Milwaukee, USA). This device has transabdominal and transvaginal probes with maximal frequencies of 2 and 7 MHz, respectively. It also has power and color Doppler capability. Morphological evaluation of the ovarian masses for benign and malignant differentiation was performed using the inner wall structure, wall thickness, presence of septa and their thickness and echogenicity according to the Sassone criteria [12] and Doppler velocimetry.

2. CT Protocol

The systems used for CT scanners were 4-slice MDCT (Somatom, Volume Zoom, Siemens, Germany) as follows: 4-slice MDCT: collimation 2.5mm; table movement 10mm; pitch 1, 120 kV, 60-100 mAs, with intravenous contrast medium administration; 3 mm slices of abdomen were obtained.

3. PET-CT Protocol

PET scanning was performed with a whole body PET system (Siemens Biograph 6 LSO). It takes 60 minutes to prepare the patient (fasting 6 hours prior to the examination, 200 Mbq FDG, 20 mg furosemid iv) and then scanning of the whole body (takes 43 minutes), including the abdomen and pelvis, was performed [13].

Table I. The clinical characteristics of the patientsgo.

Characteristics	
Age (year) $\bar{\chi}$ ± SD	57.2±14.0
Initial diagnose*	
Malignant ovarian masses	56 (66.6)
Benign ovarian masses	14 (16.6)

* Data presented as n (%).

Table II. Postoperative histopathology of the patients.

Postoperative histopathology	N	%
Ovarian cancer		
Serous cystadenocarcinoma	36	42.8
Mucinous cystadenocarcinoma	3	3.5
Borderline ovarian tumor	8	9.5
Clear cell carcinoma	5	5.9
Others*	4	4.7
Benign ovarian masses		
Serous cystadenoma	7	8.3
Mucinous cystadenoma	2	2.3
Other pelvic masses$^{\alpha}$	5	5.9

* Dysgerminoma, granulosa cell tumor, immature teratoma and yolk sac tumor;
$^{\alpha}$ benign cystic teratoma, abscess

The operation types included total abdominal hysterectomy, bilateral salpingo-oophorectomy, peritoneal washing fluid samples, infracolic omentectomy, pelvic and paraaortic lymph node dissection, and appendectomy for ovarian cancer (if the frozen section revealed benign, pelvic mass extirpation was performed).

The post operative histopathological diagnosis of the cases were recorded and compared with preoperative CT and PET/CT results.

Statistical analysis

Means and standard deviations (SD) were calculated for continuous variables. The independent sample *t*-test was used to evaluate associations between the categorical and continuous variables. All variables were included in the backward stepwise procedure. Two-sided *p*-values were considered statistically significant at $p < 0.05$. Statistical analyses were carried out using the statistical packages for SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA).

The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of discrete variables, such as PET/CT and USG/CT, were calculated on the basis of postoperative histopathology. Differences in cumulative sensitivity and specificity between the imaging modalities were tested for statistical significance using the McNemar test. In addition, to compare the diagnostic accuracy of the imaging procedures, a receiver-operating-characteristic curve (ROC) analysis using the method of Metz [14] was performed, the ROCs and AUCs values were determined for PET/CT , USG, CT and CA 125. AUC value is known to have the ability of distinguishing malignant potential of the patients.

Results

A total of sixty nine cases with benign or malignant pelvic masses were subjected to laparotomy at our clinic. Forty eight (69.5%) of the patients had malignant ovarian tumors and twenty one (30.5%) cases had benign ovarian tumors. The mean age of the subjects was 57,2±14,0 years. Postoperative pathology of the cases is presented in Table II.

Thirty six (42.8%) of the cases turned out to be serous cystadenocarcinoma, eight (9.5%) borderline ovarian tumor, five (5.9%) clear cell carcinoma, three (3.5%) mucinous cystadenocarcinoma and four (4.7 %) other types (dysgerminoma, granulosa cell tumor, immature teratoma and yolk sac tumor). The benign histopathologies were seven (8.3%) cases of serous cystadenoma, two (2.3%) mucinous cystadenoma and five (5.9%) other types (benign cystic teratoma and abscess).

In this study the gold standard to detect the malignity were postoperative histopathological findings and diagnosis of pathological specimen (P.S). Eight patients according to USG, seven according to PET/CT and four according to CT were assessed to be malignant preoperatively but all of these patients were found to have benign histopathology.

Table III. Comparison of PET/CT with ultrasonography and tomography results with postoperative histopathological outcomes.

Patient Basis (n =69)	TP	TN	FP	FN	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
PET	49	7	9	4	43.75	92.45	63.63	84.48	81.16
USG	48	8	8	5	50.00	90.57	61.54	85.71	81.16
CT	47	6	10	6	37.50	88.69	50.00	82.46	76.81

TP = true-positive, TN = true-negative, FP = false-positive, FN = false-negative, PPV = positive predictive value, NPV = negative predictive value, PET= positron emission tomography, USG = ultrasonography, CT = computerized tomography

The true positive (TP), true negative (TN), false positive (FP), false negative (FN), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were calculated and the diagnostic power of the imaging modalities was compared. (Table III).

The accuracy of USG and PET/CT was the same (81.6%) and both was higher than CT. The ROCs and AUCs values four predictors were shown in Figure 1.

The AUCs (95% CI) values calculated for CA 125, USG, PET/CT and CT were as follows: 0.855(0.752-0.958), 0.703(0.540-0.866), 0.681(0.514-0.848) and 0.631(0.463-0.799), respectively. CA 125 has the highest AUC value in order to predict the malignant potential of the patient. USG has the highest AUC value between the imaging techniques, following PET/CT and CT.

Discussion

PET has an increasing role in the diagnosis, treatment and monitoring of malignant diseases. The first PET scanner was used in 1998. Following the development of PET imaging with the fluorine 18 (^{18}F)-labeled glucose analogue, ^{18}F fluorodeoxyglucose (FDG) started to be used [15].

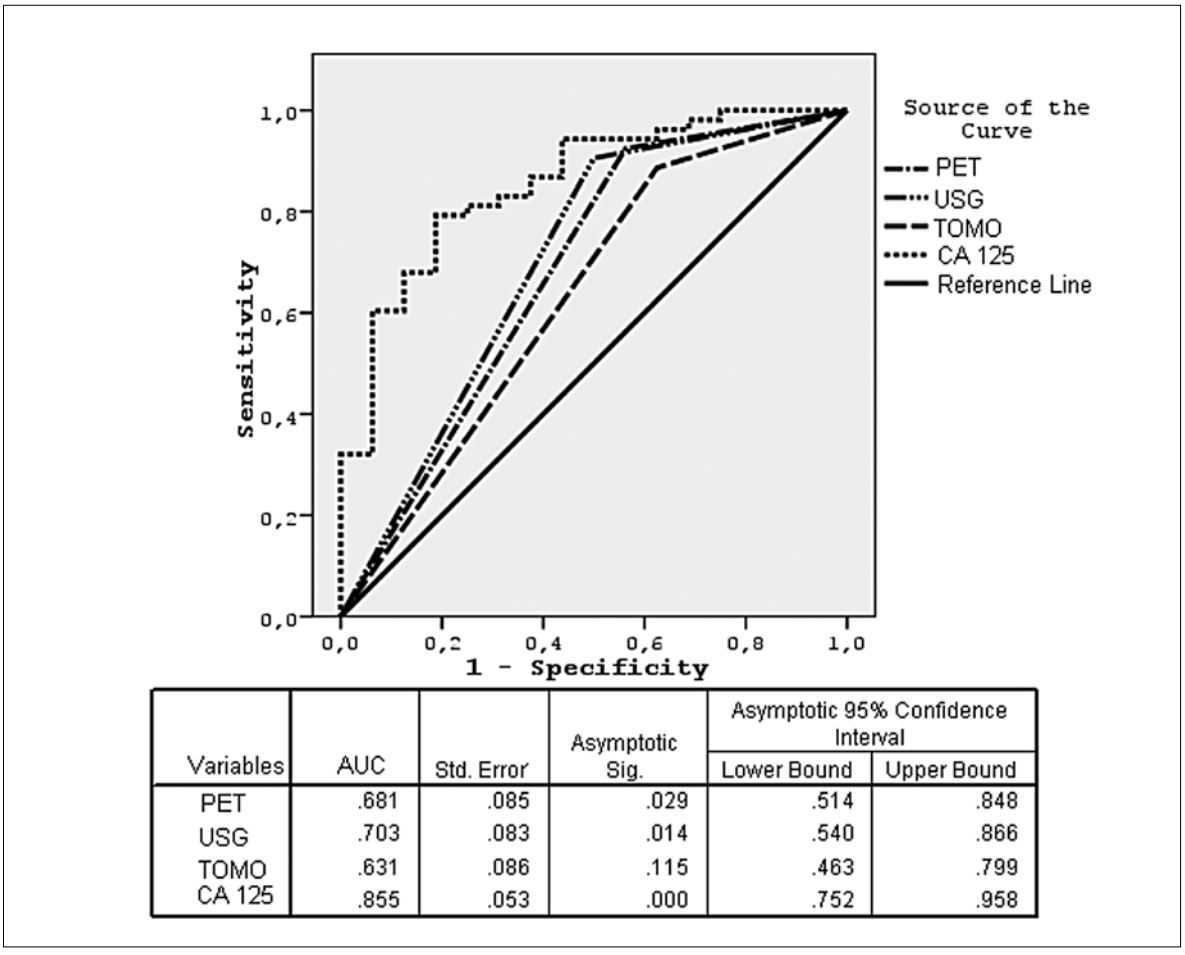
Adnexal masses are common problems of all women of all ages. The etiology of adnexal masses remains unknown.

Adnexal masses in adolescents and women of reproductive age are most commonly functional or benign neoplastic ovarian masses, whereas the risks of malignant ovarian tumors increase with age [16].

In spite of new chemotherapeutics, operative techniques and other auxiliary treatments, the 5-year survival is still low in malignant ovarian tumor. Therefore, early diagnosis and therapy are important to prolong the life and improve the life quality of epithelial ovarian cancer cases. Imaging techniques have played an important role in the clinical management of patients with ovarian cancer. It is important for tumor detection, staging, treatment planning, and follow-up [17].

In this study, the authors wished to evaluate and report their clinical experience of imaging techniques in benign and malignant adnexal masses. A total of sixty nine patients with pelvic masses subjected to laparotomy were included to this study. The clinical characteristics of the patients were presented in Table I.

Sixty nine cases with benign or malignant pelvic masses subjected to laparotomy at our clinic. Forty eight (69.5%) of the patients were malignant ovarian tumors and twenty one (30.5%) benign ovarian tumors. The initial evaluation of the patients included gynecological history, systemic physical examination, complete blood count, tumor markers, chest x rays, ultrasonography, CT and PET/CT imagining.



Variables	AUC	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
PET	.681	.085	.029	.514	.848
USG	.703	.083	.014	.540	.866
TOMO	.631	.086	.115	.463	.799
CA 125	.855	.053	.000	.752	.958

Figure 1. ROC curve for detecting malignancy by postoperative histopathology.

The AUCs (95% CI) values calculated for CA 125, USG, PET/CT and CT were as follows: 0.855(0.752-0.958), 0.703(0.540-0.866), 0.681(0.514-0.848) and 0.631(0.463-0.799), respectively. CA 125 has the highest AUC value in order to predict the malignant potential of the patient. USG has the highest AUC value between the imaging techniques, following PET/CT and CT.

Many previous reports discussed the application of PET/CT in malignant diseases. Ng et al. [17] reported their experience of PET/CT usage in oral cavity squamous cell carcinoma. Blodgett et al. [15] also described the cancers where PET/CT was used in the following cases: brain tumors, head and neck tumors, thyroid carcinoma, lung cancer, esophageal cancer, breast cancer, colorectal cancer, lymphomas, melanoma and also gynecological malignancies. Iagaru et al. [18] conducted a retrospective study and reported their experience of forty three women with ovarian cancer. They found that PET/CT imaging is a good diagnostic tool for both identification of residual/recurrent ovarian cancer and distant metastases localization.

In this study, by using the pathology results (79.1% of the patients) or clinical follow-up (20.9% of the cases) as the gold standard, they found PET-CT to have an overall per patient sensitivity of 88.4% (95% CI: 75.1–95.4) and specificity of 88.2% (95% CI: 64.4–97.9) for detection of ovarian cancer.

In other studies, in the primary diagnosis and staging of ovarian cancer, Hubner et al [19] reported a positive predictive value of 86% and a negative predictive value of 76% and Schroder et al [20] reported overall accuracy of 90%, with sensitivity of 96% and negative predictive value of 75%.

In our study, PET/CT imaging was found to have accuracy of 81.6%, with sensitivity of 92.45 % and negative predictive value of 84.48%.

Conclusion

In conclusion, PET-CT imaging is a useful imaging technique, especially in oncology. According to this study, it has no preponderance to USG. With the combination of CA125, USG and PET-CT better outcomes may be achieved.

Conflict Of Interest
The authors declare no conflict of interest.

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