

PREDICTIVE VALUE OF ^{18}F -FDG ACCUMULATION IN VISCERAL FAT ACTIVITY TO DETECT EPITHELIAL OVARIAN CANCER METASTASES

A.F. SULEIMANOV¹, A.B. SADUAKASSOVA², D.V. VINNIKOV^{1,3}, V.S. POKROVSKY^{3,4}

¹Al-Farabi Kazakh National University, Almaty, the Republic of Kazakhstan;

²Medical Centre Hospital of President's Affairs Administration of the Republic of Kazakhstan, Nur-Sultan, the Republic of Kazakhstan;

³People's Friendship University of Russia, Moscow, Russian Federation;

⁴N.N. Blokhin National Medical Research Center of Oncology, Moscow, Russian Federation

ABSTRACT

Relevance: Epithelial ovarian cancer (EOC) is the most lethal gynecological malignancy, with relapse occurring in about 70% of advanced cases with poor prognosis.

The study aimed to assess functional visceral fat activity (VAT) evaluated by ^{18}F -fluorodeoxyglucose (^{18}F -FDG) positron emission tomography/computed tomography (PET/CT) as a predictor of metastases in epithelial ovarian cancer.

Methods: We assessed 53 patients with histologically confirmed EOC who underwent ^{18}F -FDG PET/CT after a surgical treatment and courses of chemotherapy. Age, histology, stage, and tumor grade were recorded. Functional VAT was measured by maximum standardized uptake value (SUV_{max}) using ^{18}F -FDG PET/CT and tested as a predictor of later metastases in eight abdominal locations and pelvis cavity in the adjusted regression models. We also identified the best areas under the curve (AUC) for SUV_{max} with the corresponding sensitivity (Se) and specificity (Sp).

Results: In both adjusted for regression models and ROC analysis, ^{18}F -FDG accumulation in RE (cut-off SUV_{max} 1.18; Se 64%; Sp 64%; AUC 0.669; $p=0.035$) could predict later metastases in EOC patients, as opposed to age, sex, primary tumor location, tumor grade, and histology.

Conclusions: VAT SUV_{max} is significantly associated with later metastases in EOC patients and can be used as their predictor.

Keywords: ^{18}F -fluorodeoxyglucose (^{18}F -FDG), positron emission tomography/computed tomography (PET/CT), epithelial ovarian cancer (EOC), predictive value.

Introduction: Ovarian cancer is the most commonly diagnosed gynecologic malignancy and the leading cause of cancer-related deaths in women [1, 2]. Epithelial ovarian cancer (EOC) is the most lethal gynecological malignancy, with relapse occurring in about 70% of advanced cases with poor prognoses [3]. EOC is the most lethal and silent gynecological tumor diagnosed at advanced stages (III-IV) in about 62% of cases [1, 3].

Positron-emission tomography/computed tomography (PET/CT) is used to evaluate the metabolic processes of the tissue at the molecular level in the tomographic mode. The advantage of PET/CT is that it can visualize viable tumor tissue and assess its biological activity by the degree of radiopharmaceutical agent accumulation in tissues and can be used to measure the hypermetabolic focus of visceral fat (VAT) activity. ^{18}F -Fluorodeoxyglucose (^{18}F -FDG) is now widely used to assess functional VAT activity during PET/CT; therefore, it can identify accumulation loci and detect metastases. Fluorine-18-2-fluoro-2-deoxy-d-glucose PET/CT (^{18}F -FDG PET/CT) is the most specific radiological imaging used to assess predictive value [3–5].

Although the predictive role of ^{18}F -FDG PET/CT in detecting metastases has been widely studied for a long time, the studies on its reported prognostic value for various cancer locations have yielded inconsistent findings. Thus, VAT has been shown to increase the risk of EOC; however, the relationship between VAT and the prognostic outcome in EOC is inconclusive. VAT is closely related to dysregulated visceral adipose tissue activity, which increases adipokines related to systemic inflammation and can play a role in tumorigenesis and metastasis. It is conceivable that increased inflamma-

tory condition of visceral adipose tissue activity might affect the status of LN in EOC patients.

Metabolic characterization of ovarian cancer by PET/CT has resulted in reports of several potential prognostic factors [2, 6, 7]. Y. Jiang et al. were among the few to retrospectively clinical study show SUV_{max} of peritoneal disease is valuable in predicting the recurrence of ovarian cancer [2]. In another multicenter study, F. Caobelli et al. showed the predictive value of ^{18}F -FDG PET/CT in restaging patients affected by ovarian carcinoma [8], whereas M. Mayoral et al. retrospectively showed the predictive value of ^{18}F -FDG PET/CT volumetric parameters in recurrent EOC [9].

Given that the findings of these studies have been inconsistent in showing the exact SUV_{max} readings indicative of a higher risk of metastases, more data is needed to verify whether ^{18}F -FDG PET/CT can assist in early metastases identification in EOC patients.

Therefore, this study aimed to assess functional visceral fat activity (VAT) evaluated by ^{18}F -FDG PET/CT as a predictor of metastases in epithelial ovarian cancer.

The study aimed to assess functional visceral fat activity (VAT) evaluated by ^{18}F -fluorodeoxyglucose (^{18}F -FDG) positron emission tomography/computed tomography (PET/CT) as a predictor of metastases in epithelial ovarian cancer.

Materials and Methods:

Study venue and patients

We prospectively reviewed 53 patients with a histologically confirmed diagnosis of EOC who underwent ^{18}F -FDG PET/CT in the Nuclear Medicine Department of the Diagnostic Center of the Medical Centre Hospital of President's Affairs Administration of the Republic of Kazakhstan (Nur-Sultan)

between January 2017 and February 2021.

The study included 53 patients (age 32–75; median 57 (interquartile range (IQR) 47–62) years; all patients are women) after a surgical treatment and courses of Folfiri and Folf-ox chemotherapy according to the regimen. During the initial screening for eligibility, patients with histologically unverified pelvis cancer or with metastases confirmed at the baseline examination were excluded from the study. We also excluded patients with concurrent cancers. TNM classification along with FIGO stages of recruited patients are presented in Table 1.

Table 1 shows the absence of patients with IV FIGO stage, whereas adenocarcinoma was identified in 39.6%, carcinoma in 28.3%, and cystadenocarcinoma in 32.1% of

patients. Of note, patients were classified into FIGO stages at their baseline examination, after which they were subjected to treatment and then underwent baseline PET/CT. By the time enrolled patients underwent baseline PET/CT, they had completed their treatment and had no signs of cancer or metastases, and this baseline PET/CT was considered day 0 of the study.

Patients underwent ¹⁸F-FDG PET/CT at enrollment and then again at a follow-up medical examination scheduled six months or more (median 12, IQR 6–32) after the baseline examination. All images were reconstructed using dedicated workstations and software. Patients' data were anonymized and de-identified prior to studies.

Table 1 - Overall baseline patient characteristics

PTL	Sex (Female) (n)	Age (Me)	T stage (n)	N stage (n)	M stage (n)	FIGO stage (n)	Histology (n)
Ovaries	53	57	T ₁ - 8 T ₂ - 15 T ₃ - 28 T ₄ - 2	N ₀ - 19 N ₁ - 9 N _x - 25	M ₀ - 53	I - 8 II - 13 III - 32	I - 21 II - 15 III - 17

Note: PTL - Primary Tumor Location. FIGO - International Federation of Gynecology and Obstetrics. Histology: I - Adenocarcinoma; II - Carcinoma; III - Cystadenocarcinoma.

¹⁸F-FDG PET/CT study protocol and image analysis

¹⁸F-FDG was produced at the Republican Diagnostic Center (Nur-Sultan, Kazakhstan) and was used on the study day due to the ultra-short shelf life (109 minutes). The whole-body ¹⁸F-FDG PET/CT images were completed using PET/CT scanner (Biograph TruePoint PET-CT, Siemens Medical Solutions USA Inc., USA) and carried out according to the approved ¹⁸F-FDG PET/CT examination clinical protocol. Prior to PET/CT procedure and the corresponding ¹⁸F-FDG injection, patients fasted for at least 6 hours, and the glucose serum level in all patients <11 mmol/l was confirmed. The average activity dose of the injected ¹⁸F-FDG was 255.6 MBk, ranging from 132.8 to 425.5 MBk. The average effective radiation dose was 8.6 mSv, ranging from 5.9 to 15.4 mSv. CT scans were obtained following PET emission scanning. PET/CT study protocol included a topogram, a low dose CT to correct attenuation and anatomical correlation, and the collection of PET data. The duration of PET data collection depends on the patient's height and weight but usually takes 25–40 minutes. Once PET data were obtained, CT and PET images were reconstructed and stored in the axial, coronal, and sagittal slices.

Image analysis was performed in a region of interest (ROI) using the extended Siemens workspace. We calculated the standardized uptake value (SUV) accumulation in VAT automatically with the software using the formula:

$$SUV = [ROI (MBq/g)] / [injected dose (MBq)] / [total body weight (g)]$$

VAT areas were identified by using predefined Hounsfield units (HU), ranging from [-70] to [-110] from background CT images. To measure the VAT activity, ROI (1.00 mm for each measured point) were divided into regions according to the topographic structure, including eight subdomains of abdominal regions (RE - Epigastric Region, RLH - Left Hypochondriac Region, RRL - Right Lumbar Region, RU - Umbilical Region, RLL - Left Lumbar Region, RRI - Right Inguinal Region, RP - Hypogastric (Pubic) Region, RLI - Left Inguinal Region) and pelvic cavity (P). They were located on three consecutive sections of the abdominal cavity to exclude excessive physiological absorption of ¹⁸F-FDG by the kidneys. We measured SUV_{max} in the axial plane for each area, and the average SUV_{max} of each

area was calculated separately. All images were reconstructed in axial, sagittal, and coronal multiplanar planes and read visually. The analysis was carried out with these functional parameters, taking into account the metastatic LN lesion status.

Data analysis and interpretation

The primary end-point of this analysis was SUV_{max} of selected nine locations at baseline and follow-up. Image analysis was performed by determining the maximum standardized uptake value (SUV_{max}) accumulation in VAT at each abdominal and pelvic cavity. Each measured point was 1.00 mm and varied depending on the visceral adipose tissue volume in the measured area. VAT areas were identified from background CT images, and SUV was defined on PET images, including a hypermetabolic focus on ¹⁸F-FDG-PET/CT. We report SUV_{max} values for nine locations of the VAT, whereas the SUV_{max} value at baseline and follow-up was a mean of several loci for each location with a 1-mm shift.

We first tested all variables for normality using the Kolmogorov-Smirnov test. Quantitative variables following the regular distribution pattern were described using the mean (M) and standard deviation (SD); alternatively, we reported medians with the corresponding IQR. SUV_{max} values for different locations and at different periods (baseline or follow-up) were then compared using nonparametric tests, such as the Mann-Whitney U-test or Wilcoxon test, as appropriate. Since we selected a total of nine locations to report SUV_{max} values, we tested SUV_{max} values for each location in the univariate analyses with regard to sex, primary tumor location, and other variables, using either Mann-Whitney U-test (for two groups) or Kruskal-Wallis test (for three or more groups). We also used a similar approach to compare groups depending on metastases status, including patients who were positive for Lymphatic Metastasis (pLM) with metastases detected at a follow-up visit and patients who were negative for Lymphatic Metastasis (nLM) who showed no metastases. In this analysis, we compared baseline SUV_{max} as a predictor. In addition, we tested age and sex as predictors of showing pLM at follow-up. Localizations with significant differences between groups in SUV_{max} and other tested predictors (age, sex) showing significant associations with LM status were then tested in a logistic regression analysis, first crude, and then adjusted for other significant pre-

dictors, where we report the odds ratios (OR) of developing metastases at follow-up with the corresponding 95% confidence intervals (CI).

Finally, ROC analysis was used to assess the diagnostic performance of quantitative variables in predicting a categorical outcome. The optimal cut-off value of the quantitative variable was estimated using J. Youden's statistic. All statistical analyses were performed using StatTech v. 2.6.1 (StatTech LLC, Russia) and NCSS 2021, v. 21.0.3 (NCSS, LLC, USA).

This study was approved by the Local Bioethics Commission of the Medical Centre Hospital of President's Affairs Administration of the Republic of Kazakhstan (17/2020) and the

Local Ethical Commission of the Al-Farabi Kazakh National University (102 IRB – A102).

Results: The study group included women only with the PTL in the ovaries (n=53). The most prevalent staging was: T₃ (n=28), N_x (n=25), M₀ (n=53). With regard to FIGO tumor classification, most patients had stage III (n=32), with no patients at stage IV. At baseline, the overall mean SUV_{max} was 0.79; the highest accumulation level was found in RRL (0.96) and the lowest – in RRI (0.55). FIGO stage affected SUV_{max} in RRI (p=0.013) location. No differences related to sex, PTL, TNM, or histological grade were registered in baseline SUV_{max} in Mann-Whitney U-tests for the two groups (p<0.05) (Table 2).

Table 2 – Baseline patients' SUV_{max} stratified by sex, PTL, TNM, and FIGO stages

Variable	n (%)	SUV _{max}								
		RE	RLH	RRL	RU	RLL	RRI	RP	RLI	P
Sex										
Female	53 (100)	0.81	0.75	0.96	0.76	0.94	0.55	0.85	0.57	0.89
Primary Tumor Location										
Ovaries	53 (100)	0.81	0.75	0.96	0.76	0.94	0.55	0.85	0.57	0.89
T stage										
T ₁	8 (15.1)	0.79	0.81	0.72	0.81	0.88	0.54	0.78	0.58	0.95
T ₂	15 (28.3)	0.79	0.74	0.92	0.69	0.87	0.49	0.77	0.52	0.82
T ₃	28 (52.8)	0.83	0.72	0.97	0.81	0.99	0.64	0.94	0.58	0.90
T ₄	2 (3.8)	1.10	1.47	1.09	0.95	1.26	0.64	0.92	0.83	1.38
N stage										
N ₀	19 (35.8)	0.81	0.68	0.79	0.69	0.86	0.52	0.78	0.53	0.77
N ₁	9 (17.0)	0.87	0.78	0.90	0.86	1.19	0.58	0.92	0.56	1.17
N _x	25 (47.2)	0.73	0.78	1.02	0.75	0.97	0.66	1.00	0.60	0.86
M stage										
M ₀	53 (100)	0.81	0.75	0.96	0.76	0.94	0.55	0.85	0.57	0.89
FIGO stage										
I	8 (15.1)	0.79	0.81	0.72	0.81	0.88	0.54	0.78	0.58	0.95
II	13 (24.5)	0.77	0.62	0.82	0.68	0.86	0.45	0.74	0.51	0.78
III	32 (60.4)	0.85	0.78	1.04	0.90	1.00	0.70	0.96	0.60	0.93
Histology										
Adenocarcinoma	21 (39.6)	0.73	0.75	0.90	0.75	0.80	0.52	0.82	0.59	0.79
Carcinoma	15 (28.3)	0.94	0.97	1.06	0.83	0.92	0.58	0.92	0.58	0.98
Cystadenocarcinoma	17 (32.1)	0.79	0.68	0.96	0.72	1.01	0.55	0.83	0.56	0.95

Note: RE – Epigastric Region, RLH – Left Hypochondriac Region, RRL – Right Lumbar Region, RU – Umbilical Region, RLL – Left Lumbar Region, RRI – Right Inguinal Region, RP – Hypogastric (Pubic) Region, RLI – Left Inguinal Region, P – Pelvic cavity.

At follow-up examination, metastases developed in 28/53 (53%) of initially recruited patients. Those were classified as pLM, whereas the remaining 25 (47%) patients were nLM. The LNs were located in the neck, mediastinum, chest, peritoneum, retroperitoneum, and pelvis. We tested whether baseline SUV_{max} was different in those who developed metastases than those who did not. We did not find that such differences were statistically significant for all locations (Table 3).

The median SUV_{max} of all locations increased from 0.79 at baseline to 1.11 at follow-up (p=0.005). When considering locations separately, we did not find a statistically significant increase in SUV_{max} in any location out of nine (Table 3), mainly because the sample size for each location was only 1/9 of the overall sample. When stratified to nLM and pLM, we found a significant SUV_{max} increase in all locations.

Table 3 - SUVmax change overall and two subgroups

Location	Overall (n=53)			nLM (n=25)			pLM (n=28)			p for baseline nLM vs pLM
	Baseline	Follow-up	p	Baseline	Follow-up	p	Baseline	Follow-up	p	
RE	0.81	1.17	<0.001	0.79	1.27	<0.001	0.83	1.10	0.03	0.82
RLH	0.75	1.17	<0.001	0.74	1.25	<0.001	0.77	1.10	<0.001	0.52
RRL	0.96	1.28	<0.001	1.05	1.55	0.03	0.91	1.14	<0.001	0.09
RU	0.76	1.12	<0.001	0.91	1.11	0.04	0.74	1.13	0.02	0.42
RLL	0.94	1.26	<0.001	0.94	1.26	<0.001	0.95	1.22	<0.001	0.36
RRI	0.55	0.77	<0.001	0.57	0.84	0.04	0.54	0.76	<0.001	0.40
RP	0.85	1.20	<0.001	0.92	1.23	0.03	0.80	1.19	<0.001	0.23
RLI	0.57	0.83	<0.001	0.68	0.89	0.08	0.54	0.80	<0.001	0.10
P	0.89	1.16	<0.001	0.96	1.16	0.02	0.80	1.14	<0.001	0.20
p-value	<0.001	<0.001		<0.001	<0.001		<0.001	<0.001		

Note: pLM - positive Lymphatic Metastasis; nLM - negative Lymphatic Metastasis; RE – Epigastric Region, RLH – Left Hypochondriac Region, RRL – Right Lumbar Region, RU – Umbilical Region, RLL – Left Lumbar Region, RRI – Right Inguinal Region, RP – Hypogastric (Pubic) Region, RLI – Left Inguinal Region, P – Pelvic cavity.

The RE AUC was the highest of the nine locations for which SUV_{max} as a metastasis predictor was tested at follow-up. SUV_{max} value with the highest AUC (0.669; 95% CI 0.521-0.816) for RE was 1.18, with sensitivity and specificity equaling 64%. This model was statistically

significant ($p=0.035$). Figure 1 illustrates AUC for this location. We observed a dramatic fall in specificity when reaching a high sensitivity of 80%. PTL, T and N stages, tumor grade, and LM staging did not affect SUV_{max} accumulation.

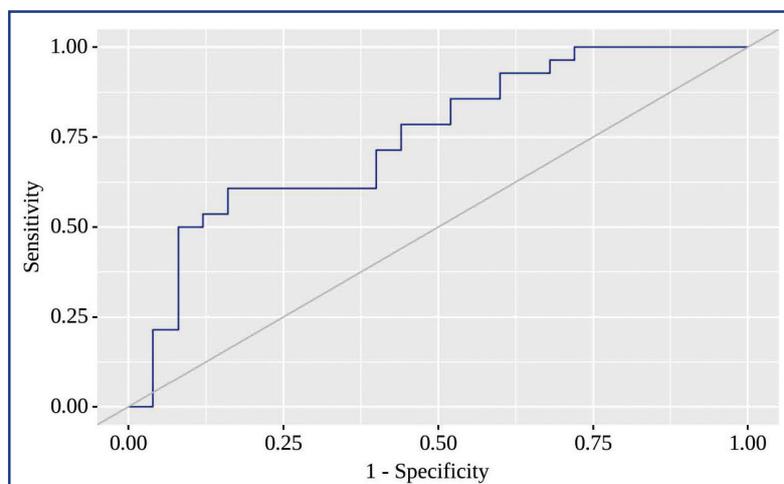


Figure 1 – ROC-curve showing AUC for a positive outcome in RE

Discussion: This prospective observational cohort study is one of the few to identify the localizations with more significant ^{18}F -FDG PET/CT accumulation increased by functional VAT as an early marker of later metastases that can affect the metastatic status in EOC patients. In a cohort of 53 patients adjusted for regression and ROC analysis, we show that ^{18}F -FDG PET/CT accumulation in RE can predict later metastasis in EOC patients with moderate but statistically significant sensitivity and specificity. Thus, a threshold RE SUV_{max} value of 1.18 has delivered the sensitivity and specificity of 64%. In our analysis, ^{18}F -FDG PET/CT accumulation in the remaining tested localizations was not associated with later metastasis risk.

The ^{18}F -FDG PET/CT prognostic value for EOC has been reported in several preceding studies at different SUV_{max} values. Y. Jiang et al. showed in a retrospective clinical study involving 82 ovarian cancer patients with a cut-off 2.0 obtained from the ROC curve analysis, the sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of SUV_{max} for predicting recurrence of peritoneal carcinomatosis at the level of 77.6%, 87.5%, 65.1%, 97.4%, and 38.9%, respectively [2]. In a multicenter study involving 168 patients, F. Caobelli et al. showed an essential ^{18}F -FDG PET/CT prognostic value in assessing the risk of ovarian carcinoma progression and mortality from this disease [8]. Finally, M. Mayoral et al. retrospectively showed that SUV_{max} was not a statistically significant predictor for recurrent EOC [9].

Several previous studies reported the relationship between visceral obesity and the prognosis of other cancers, but not for EOC [10]. However, the results were diverse and discordant. These studies used CT to measure VAT volume as a surrogate marker of VAT activity. However, VAT volume is reportedly unrelated to visceral fat inflammation [11], whereas the determination of VAT volume by CT may not be sufficient to reflect the actual functional VAT activity [12]. Therefore, a functional imaging modality like ^{18}F -FDG PET/CT could be more suitable to assess functional VAT activity than CT.

The prognostic value of ^{18}F -FDG PET/CT for colorectal cancer (CRC) has been reported in several preceding studies, reporting different SUV_{max} values. Byung Wook Choi et al. retrospectively showed the prognostic value of metabol-

ic parameters on ^{18}F -FDG PET/CT in classical rectal adenocarcinoma in 149 patients on two models (AUC 0.778 and 0.762, $p=0.04$; 0.814 and 0.779, $p=0.83$) [13]. One more study of Sung Hoon Kim et al. retrospectively showed the predictive value of ^{18}F -FDG PET/CT for LN metastasis in rectal cancer in 166 patients, nodal SUV_{max} 2.356, AUC 0.698 ($p=0.04$), 0.720 (0.033), 0.806 ($p=0.04$) [14]. K. Pahk et al. retrospectively showed the predictive role of functional VAT activity assessed by preoperative ^{18}F -FDG PET/CT for regional LN or distant metastasis in 131 patients with CRC; however, the ratio of visceral fat to subcutaneous fat (VAT/SAT) was evaluated, while the ratio of SUV_{max} 1.88, AUC 0.862, sensitivity 84.6%, specificity 78.8%, $p<0.001$ [15]. E. Sokolović et al. showed the prognostic value of SUV_{max} of ^{18}F -FDG PET/CT in patients with metastatic CRC and concluded that SUV_{max} could be used as a novel prognostic marker of disease progression among patients with metastatic CRC. Average \pm SD progression-free survival in patients with SUV_{max} above 4.1 was 11.3 ± 9.37 months, and in patients with SUV_{max} below 4.1 was 19.6 ± 12.05 months ($p=0.001$) [16]. Finally, E. Arslan et al. showed the prognostic value of ^{18}F -FDG PET/CT and KRAS mutation in CRC, where the mean SUV_{max} of patients with primary tumor was estimated to be 21.1 ± 9.1 (range= 6.0-47.5) and mean tumor SUV_{max} of patients with a KRAS mutation (24.0 ± 9.0) was found to be significantly higher than those without KRAS mutation (17.7 ± 8.2) ($p=0.001$) [17].

Previous studies regarding functional VAT activity and ^{18}F -FDG PET/CT focused on systemic inflammatory diseases, such as atherosclerosis or chronic obstructive pulmonary disease [12, 18, 19]. L. Tong et al. showed the association between lung fluorodeoxyglucose metabolism and smoking history in 347 healthy adults with chronic obstructive pulmonary disease. In them, the lung SUV according to smoking status were analyzed. The mean SUV_{max} of current smokers was significantly higher than that of ex-smokers in patients with a medium (1.03 ± 0.14 vs 0.88 ± 0.16) or larger tobacco burden (1.08 ± 0.15 vs 0.89 ± 0.11) ($p=0.012$, $p<0.001$, respectively). However, there were no significant differences between the mean SUV_{max} of ex-smokers (0.91 ± 0.13) and current smokers (0.91 ± 0.16) with a smaller tobacco burden ($p=0.888$). The mean SUV_{max} of ex-smokers and

current smokers with less tobacco burden were both significantly higher than that of non-smokers (0.78±0.13) (p<0.001, p<0.001, respectively) [19].

In this study, ¹⁸F-FDG PET/CT was used to demonstrate the application of functional VAT activity for cancer, which can provide molecular information about inflammatory processes in EOC LM.

Our study had several limitations. Despite its prospective design, the study sample was limited, although patients were recruited for several years consecutively. Secondly, we could enroll only patients from one nuclear medicine center and one capital city. PET/CT is not yet available elsewhere in the country; the study sample included patients who had to travel to the capital city for this examination, so they represented the whole country's population. Thirdly, predictive value was evaluated for SUV_{max} only; other crucial factors like the primary tumor grade and location could not be analyzed. Further prospective studies with larger populations will be needed to validate our results.

Conclusion: Functional VAT activity assessed by ¹⁸F-FDG PET/CT is significantly associated with LM. Furthermore, it is a helpful factor in predicting LM. Implementation of the study results into medical practice will help practitioners choose tactics and control for EOC patients.

References:

1. Siegel R.L., Miller K.D., Fuchs H.E., Jemal A. Cancer statistics // *CA Cancer J. Clin.* – 2022. – Vol. 72. – P. 7-33. <https://doi.org/10.3322/caac.21708>;
2. Jiang Y., Hou G., Wu F., Zhu Z., Zhang W., Cheng W. The maximum standardized uptake value and extent of peritoneal involvement may predict the prognosis of patients with recurrent ovarian cancer after primary treatment: A retrospective clinical study // *Medicine (Baltimore)*. – 2020. – Vol. 99. – No. e19228. <http://dx.doi.org/10.1097/MD.00000000000019228>;
3. Perrone A.M., Dondi G., Lima G.M., Castellucci P., Tesi M., Coluccelli S., Gasparre G., Porcelli A.M., Nanni C., Fanti S., De Laco P. Potential Prognostic Role of 18F-FDG PET/CT in Invasive Epithelial Ovarian Cancer Relapse. A Preliminary Study // *Cancers*. – 2019. – Vol. 11. – P. 713. <https://doi.org/10.3390/cancers11050713>;
4. Fularz M., Adamiak P., Czepczyński R., Jarzqbek-Bielecka G., Kędzia W., Ruchala M. Positron emission tomography (PET) in malignant ovarian tumors // *Ginekol Pol.* – 2013. – Vol. 84(8). – #46000. <https://doi.org/10.17772/gp/1630>;
5. Chong G.O., Jeong S.Y., Lee Y.H., Lee H.J., Lee S.-W., Han H.S., Hong D.G., Lee Y.S. The ability of whole-body SUV_{max} in F-18 FDG PET/CT to predict sub-optimal cytoreduction during primary debulking surgery for advanced ovarian cancer // *J. Ovarian Res.* – 2019. – Vol. 12. – No. 12. <https://doi.org/10.1186/s13048-019-0488-2>;
6. Konishi H., Takehara K., Kojima A., Okame S., Yamamoto Y., Shiroyama Y., Yokoyama T., Nogawa T., Sugawara Y. Maximum standardized uptake value of fluorodeoxyglucose positron emission tomography/computed tomography is a prognostic factor in ovarian clear cell adenocarcinoma // *Int. J. Gynecol. Cancer.* – 2014. – Vol. 24. – P. 1190-1194. <http://dx.doi.org/10.1097/IGC.000000000000180>;

7. Reyners A.K.L., Broekman K.E., Glaudemans A.W.J.M., Brouwers A.H., Arts H.J.G., van der Zee A.G.J., de Vries E.G.E., Jalving M. Molecular imaging in ovarian cancer // *Ann. Oncol.* – 2016. – Vol. 27, Suppl. 1. – P. i23-i29. <https://doi.org/10.1093/annonc/mdw091>;
8. Caobelli F., Alongi P., Evangelista L., Picchio M., Saladini G., Rensi M., Geatti O., Castello A., Laghai I., Popescu C.E., Dolci C., Crivellaro C., Seghezzi S., Kirienco M., De Biasi V., Cocciolillo F., Quartuccio N., Young AIMN Working Group. Predictive value of ¹⁸F-FDG PET/CT in restaging patients affected by ovarian carcinoma: a multicentre study // *Eur. J. Nucl. Med. Mol. Imaging.* – 2016. – Vol. 43. – P. 404-413. <https://doi.org/10.1007/s00259-015-3184-5>;
9. Mayoral M., Fernandez-Martinez A., Vidal L., Fuster D., Aya F., Pavia J., Pons F., Lomena F., Paredes P. Prognostic value of ¹⁸F-FDG PET/CT volumetric parameters in recurrent epithelial ovarian cancer // *Rev. Espanola Med. Nucl. Imagen. Mol.* – 2016. – Vol. 35(2). – P. 88-95. <https://doi.org/10.1016/j.rem.2015.08.005>;
10. Rickles A.S., Iannuzzi J.C., Mironov O., Deeb A.-P., Sharma A., Fleming F.J., Monson J.R.T. Visceral obesity, and colorectal cancer: are we missing the boat with BMI? // *J. Gastrointest. Surg.* – 2013. – Vol. 17. – P. 133-143; discussion p. 143. <https://doi.org/10.1007/s11605-012-2045-9>;
11. Christen T., Sheikine Y., Rocha V.Z., Hurwitz S., Goldfine A.B., Di Carli M., Libby P. Increased glucose uptake in visceral versus subcutaneous adipose tissue revealed by PET imaging // *JACC Cardiovasc. Imaging.* – 2010. – Vol. 3. – P. 843-851. <https://doi.org/10.1016/j.jcmg.2010.06.004>;
12. Bucerius J., Vijgen G.H.E.J., Brans B., Bouvy N.D., Bauwens M., Rudd J.H.F., Havekes B., Fayad Z.A., van Marken Lichtebehn W.D., Motaghy F. Impact of Bariatric Surgery on Carotid Artery Inflammation and the Metabolic Activity in Different Adipose Tissues // *Medicine (Baltimore)*. – 2015. – Vol. 94. – P. e725. <https://doi.org/10.1097/MD.0000000000000725>;
13. Choi B.W., Kang S., Bae S.U., Jeong W.K., Bae S.U., Jeong W.K., Baek S.K., Song B.-I., Won K.S., Kim H.W. Prognostic value of metabolic parameters on 18F-fluorodeoxyglucose positron tomography/computed tomography in classical rectal adenocarcinoma // *Sci. Rep.* – 2021. – Vol. 11. – No. 12947. <https://doi.org/10.1038/s41598-021-92118-x>;
14. Xi Y., Xu P. Global colorectal cancer burden in 2020 and projections to 2040 // *Transl Oncol.* – 2021. – Vol. 14. – No. 101174. <https://doi.org/10.1016/j.tranon.2021.101174>;
15. Pahk K., Rhee S., Kim S., Choe J.G. Predictive Role of Functional Visceral Fat Activity Assessed by Preoperative F-18 FDG PET/CT for Regional Lymph Node or Distant Metastasis in Patients with Colorectal Cancer // *PloS One.* – 2016. – Vol. 11(2). – P. e0148776. <https://doi.org/10.1371/journal.pone.0148776>;
16. Sokolović E., Cerić T., Cerić Š., Bešlija S., Vegar-Zubović S., Bešlić N., Sečić-Pasić I., Pašić A. The Prognostic Value of SUV_{max} of 18F-FDG PET/CT in Patients with Metastatic Colorectal Cancer // *Acta Medica Acad.* – 2020. – Vol. 49(1). – P. 1-8. <https://doi.org/10.5644/ama2006-124.278>;
17. Arslan E., Aksoy T., Gürsu R.U., Dursun N., Çakar E., Çermik T.F. The Prognostic Value of 18F-FDG PET/CT and KRAS Mutation in Colorectal Cancers // *Mol. Imaging Radionucl. Ther.* – 2020. – Vol. 29. – P. 17-24. <https://doi.org/10.4274/mirt.galenos.2019.33866>;
18. Vanfleteren L.E.G.W., van Meerendonk A.M.G., Franssen F.M., Wouters E.F.M., Mottaghy F.M., van Kroonenburgh M.J., Bucerius J. A possible link between increased metabolic activity of fat tissue and aortic wall inflammation in subjects with COPD. A retrospective 18F-FDG-PET/CT pilot study // *Respir. Med.* – 2014. – Vol. 108, Issue 6. – P. 883-890. <http://dx.doi.org/10.1016/j.rmed.2014.04.001>;
19. Tong L., Sui Y., Jiang S., Yin Y. The Association Between Lung Fluorodeoxyglucose Metabolism and Smoking History in 347 Healthy Adults // *J. Asthma Allergy.* – 2021. – Vol. 14. – P. 301-308. <http://doi.org/10.2147/JAA.S302602>.

ТҰЖЫРЫМ

АНАЛЫҚ БЕЗДІҢ ЭПИТЕЛИЙ ОБЫРЫНЫҢ МЕТАСТАЗДАРЫН АНЫҚТАУ ҮШІН ВИСЦЕРАЛДЫ МАЙ ТІНДЕРІНІҢ БЕЛСЕНДІЛІГІНДЕ ¹⁸F-FDG ЖИНАҚТАЛУЫНЫҢ БОЛЖАМДЫ МӘНІ

А.Ф. Сулейманов¹, А.Б. Садуақасова², Д.В. Винников^{1,3}, В.С. Покровский^{3,4}

¹Әл-Фараби атындағы Қазақ ұлттық университеті, Алматы, Қазақстан Республикасы;

²Қазақстан Республикасы Президентінің Іс Басқармасы Медициналық орталығының ауруханасы, Нұр-Сұлтан, Қазақстан Республикасы;

³Халықтар достығы Ресей университеті, Мәскеу, Ресей Федерациясы;

⁴Н.Н. Блохин атындағы Ұлттық медициналық онкология зерттеу орталығы, Мәскеу, Ресей Федерациясы

Өзектілігі: Аналық бездің эпителий обыры (EOC) – бұл ең қауіпті гинекологиялық қатерлі ісік, ал рецидив дамыған жағдайлардың шамамен 70%-ында нашар болжаммен жүреді.

Зерттеудің мақсаты: ¹⁸F-фтордезоксиглюкозаның (¹⁸F-FDG) компьютерлік томографиямен біріктірілген позитронды-эмиссиялық томография (ПЭТ/КТ) әдісімен бағаланған висцералды май тінінің (VAT) функционалды белсенділігін аналық бездің эпителий обыры (EOC) метастазының болжаушысы ретінде бағалау.

Әдістері: Біз хирургиялық емдеуден және химиотерапия курстарынан кейін ¹⁸F-FDG ПЭТ/КТ-мен гистологиялық расталған EOC бар 53 пациентті тексердік. Науқастардың жасы, гистологиялық түрі, обыр сатысы мен дәрежесі талданды. Функционалды VAT ¹⁸F-

FDG ПЭТ/КТ көмегімен максималды стандартталған жинақталу мәнімен (SUV_{max}) өлшенді және түзетілген регрессиялық моделдерде іш қуысының сегіз жерінде және кіші жамбастағы кеіш метастаздардың болжаушысы ретінде сыналды. Сондай-ақ, SUV_{max} үшін қиыстықтың (AUC) астындағы ең жақсы аймақтар туралы тиісті сезімталдықпен (Se) және ерекшелікпен (Sp) хабарлаймыз.

Нәтижелері: Регрессиялық моделдерге түзету енгізу мен ROC талдау кезінде де RE-де ^{18}F -FDG жинақталуы (SUV_{max} 1,18; Se 64%; Sp 64%; AUC 0,669; $p=0,035$) EOC бар науқастарда жасына, жынысына, бастапқы обырдың орналасуына, обыр дәрежесіне және гистологияға қарағанда кейінгі метастаздарды болжай алады.

Қорытынды: SUV_{max} VAT негізінен EOC бар науқастарда кейінгі метастазбен байланысты және оларды болжаушы ретінде пайдалануға болады.

Түйінді сөздер: ^{18}F -фтордезоксиглюкоза, Компьютерлік томографиямен біріктірілген позитронды-эмиссиялық томография, Аналық бездің эпителий обыры, Болжамдық мәні.

АННОТАЦИЯ

ПРОГНОСТИЧЕСКАЯ ЦЕННОСТЬ УРОВНЯ НАКОПЛЕНИЯ ^{18}F -FDG В ВИСЦЕРАЛЬНОЙ ЖИРОВОЙ ТКАНИ ДЛЯ ОПРЕДЕЛЕНИЯ МЕТАСТАЗИРОВАНИЯ ПРИ ЭПИТЕЛИАЛЬНОМ РАКЕ ЯИЧНИКОВ

А.Ф. Сулейманов¹, А.Б. Садуақасова², Д.В. Винников^{1,3}, В.С. Покровский^{3,4}

¹Казахский национальный университет имени аль-Фараби, Алматы, Республика Казахстан;

²Больница Медицинского центра Управления делами президента Республики Казахстан, Нур-Султан, Республика Казахстан;

³Российский университет дружбы народов, Москва, Российская Федерация;

⁴Национальный медицинский исследовательский центр онкологии имени Н.Н. Блохина, Москва, Российская Федерация

Актуальность: Эпителиальный рак яичников (Epithelial Ovarian Cancer; EOC) является наиболее злокачественным гинекологическим новообразованием, рецидив которого происходит примерно в 70% запущенных случаев и отличается неблагоприятным прогнозом.

Цель исследования – оценить функциональную активность висцеральной жировой ткани (VAT) методом позитронно-эмиссионной томографии с ^{18}F -фтордезоксиглюкозой, совмещённой с компьютерной томографией (^{18}F -FDG ПЭТ/КТ) в качестве предиктора метастазирования EOC.

Методы: Нами были обследованы 53 пациента с гистологически верифицированным диагнозом EOC, которым была проведена ^{18}F -FDG ПЭТ/КТ после хирургического лечения и курсов химиотерапии. Оценке подверглись такие показатели, как возраст пациентов, гистологический тип, стадия и степень опухолевого процесса. Функциональная активность VAT была измерена с помощью показателя максимального стандартизованного уровня накопления (SUV_{max}) и полученный цифровой уровень накопления определен на скорректированных регрессионных моделях в качестве предиктора поздних метастазов брюшной полости и малого таза. Также были получены наилучшие показатели площади под кривой (AUC) для SUV_{max} с соответствующей чувствительностью (Se) и специфичностью (Sp).

Результаты: Накопление ^{18}F -FDG в RE (SUV_{max} 1,18; Se 64%; Sp 64%; AUC 0,669; $p=0,035$), как при корректировке регрессионных моделей, так и при анализе ROC-кривой, может предсказывать более поздние метастазы, чем возраст, пол, локализация первичной опухоли, степень рака и гистологический тип рака у пациентов с EOC.

Заключение: Уровень накопления SUV_{max} в VAT связан с поздним метастазированием в лимфатические узлы, что имеет прогностическую ценность для выбора тактики и контроля лечения у пациентов с EOC.

Ключевые слова: ^{18}F -фтордезоксиглюкоза (^{18}F -FDG); позитронно-эмиссионная томография, совмещённая с компьютерной томографией (ПЭТ/КТ); эпителиальный рак яичников (EOC); прогностическая ценность.

Transparency of the study – Authors take full responsibility for the content of this manuscript.

Conflict of interests – The authors declare no conflict of interest.

Financing: The authors declare no financing of the study.

Authors' Inputs: contribution to the study concept – Suleimanov A.F., Saduakassova A.B., Vinnikov D.V., Pokrovsky V.S.; study design – Vinnikov D.V., Pokrovsky V.S.; execution of the study – Suleimanov A.F.; interpretation of the study results – Suleimanov A.F., Saduakassova A.B., Vinnikov D.V., Pokrovsky V.S.; preparation of the manuscript – Suleimanov A.F., Vinnikov D.V.

Authors' Details:

Suleimanov Amil Fazil-Ogly (corresponding author) – Ph.D. student (Medicine), Department of Healthcare Policy and Organization, Faculty of Medicine and Health Care, Al-Farabi Kazakh National University, Al-Farabi Ave. 71, Almaty 050040, Kazakhstan, Tel. +77023838005, e-mail: amil134@mail.ru, ID ORCID: <https://orcid.org/0000-0003-2397-103X>;

Saduakassova Aigul Bolatovna – Doctor of Medicine, Head of the Nuclear Medicine Department of the Diagnostic Center, Hospital of the Medical Center of the Office of the President of the Republic of Kazakhstan, Nur-Sultan, Kazakhstan, Tel. +77019909993, e-mail: sadik.a@mail.ru, ID ORCID: <https://orcid.org/0000-0002-7412-8328>;

Vinnikov Denis Vladimirovich – Vinnikov Denis Vladimirovich – Doctor of Medicine, Ass. Prof. Department of Biostatistics, Epidemiology and Evidence Medicine, Faculty of Medicine and Healthcare; Head of the Health and Environment Scientific Research Laboratory, Al-Farabi Kazakh National University, Almaty, Kazakhstan, Tel. +77072068036, e-mail: denisvinnikov@mail.ru, ID ORCID: <https://orcid.org/0000-0003-0991-6237>;

Pokrovsky Vadim Sergeevich – Pokrovsky Vadim Sergeevich – Doctor of Medicine, Professor, Head of the Laboratory for Combination Therapy of Tumors at the Federal State Budgetary Institution "National Medical Research Center of Oncology named after N.N. Blokhin" of the Ministry of Health of Russia, Moscow, Russia, Head of the Biochemistry Department of the Peoples' Friendship University of Russia, Moscow, Russia, tel. +79151430391, e-mail: vadimpokrovsky@gmail.com, ID ORCID: <https://orcid.org/0000-0003-4006-9320>.