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The role of ^{18}F-FDG PET / CT in evaluation of therapy effectiveness and prognosis of lymphomas

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ABSTRACT

Aim. To determine the diagnostic value of positron emission tomography (PET) / computed tomography (CT) with F-18 fluorodeoxyglucose (^{18}F-FDG) for monitoring the effectiveness and prognosis of lymphoma therapy.

Materials and methods. Retrospective data of ^{18}F-FDG PET/CT (before treatment (PET1), after two cycles (PET2), and after completion of chemotherapy (PET3)) in 30 people with lymphomas were analyzed.

Results and discussion. A complete metabolic response in PET2 (PET2–) was observed in 21 patients (70%). In 9 patients in PET2–, a partial metabolic response (6 people), lack of metabolic response (2 people), or metabolic progression (1 person) were detected. These patients comprised the PET2+ group.

After chemotherapy, a complete metabolic response (PET3–) was diagnosed in 26 patients (87%). This effect was achieved in 21 patients (100%) with PET2– and in 5 patients (66%) with PET2+. Of the 9 patients in the PET2+ group, in 4 (44%) patients, a partial metabolic response or no metabolic response was diagnosed. Further monitoring of these patients showed that progression was detected in 2 cases, and in 2 patients, further treatment resulted in complete remission.

A two-year follow-up of patients revealed that remission was observed in 20 (67%) patients. The analysis of the results of PET2 showed that a relapse of the disease was observed in 6 (67%) PET2+ patients and remission was noted in 3 (33%) patients. In PET2– patients, a relapse was diagnosed in 4 (19%) persons, and remission was established in 17 (81%) patients.

Conclusion. Early PET / CT with ^{18}F-FDG allows to predict the effect of lymphoma treatment. The method can be recommended for monitoring lymphoma therapy.

Key words: Hodgkin's lymphoma, non-Hodgkin's lymphoma, computed tomography, positron emission tomography, monitoring of lymphoma therapy, prognosis of lymphoma therapy.

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Роль позитронной эмиссионной и компьютерной томографии с ^{18}F-флуоро-2-дезокси-D-глюкозой в оценке эффективности терапии и прогнозе лимфом

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РЕЗЮМЕ

Цель. Определение диагностической значимости позитронной эмиссионной и компьютерной томографии (ПЭТ/КТ) с меченной ^{18}F-флуоро-2-дезокси-D-глюкозой (^{18}F-ФДГ) в оценке эффективности и прогнозе лечения лимфом.

Материалы и методы. Проанализированы ретроспективные данные ПЭТ/КТ с ^{18}F-ФДГ 30 человек со злокачественными лимфомами: до лечения (ПЭТ1), через два курса (ПЭТ2) и после завершения полихимиотерапии (ПЭТ3).

Результаты и обсуждение. При анализе результатов ПЭТ2 полный метаболический ответ на два курса химиотерапии (ПЭТ2–) наблюдался у 21 (70%) пациента. У 9 пациентов через два цикла химиотерапии были установлены: частичный метаболический ответ (6 человек), отсутствие метаболического ответа (2 человека) или метаболическое прогрессировании (1 человек). Эти больные составили группу ПЭТ2+.

После окончания химиотерапии полный метаболический ответ (ПЭТ3–) был диагностирован у 26 (87%) пациентов. Такой эффект был достигнут у 21 (100%) больного с ПЭТ2– и 5 (66%) человек с ПЭТ2+. Из 9 пациентов группы ПЭТ2+ у 4 (44%) пациентов после завершения химиотерапии был диагностирован частичный метаболический ответ или его отсутствие. Дальнейшее наблюдение за этими пациентами показало, что в двух случаях было диагностировано прогрессирование, а у 2 больных последующее лечение привело к полной ремиссии.

При двухлетнем наблюдении за пациентами обнаружено, что ремиссия наблюдалась у 20 (67%) пациентов. Анализ результатов ПЭТ2 показал, что при ПЭТ2+ рецидив заболевания наблюдался в 6 (67%) случаях, ремиссия – в 3 (33%). В то время как при ПЭТ2– рецидив диагностирован у 4 (19%) человек, ремиссия установлена у 17 (81%).

Заключение. ПЭТ/КТ с ^{18}F-ФДГ, выполненная на ранних этапах химиотерапии, позволяет предсказать эффект лечения у пациентов со злокачественными лимфомами. Метод показан к широкому использованию в клинической практике на этапах терапии этой патологии.

Ключевые слова: лимфома Ходжкина, Неходжкинские лимфомы, компьютерная томография, позитронная эмиссионная томография, мониторинг терапии лимфом, прогноз терапии лимфом.

Конфликт интересов. Авторы заявляют об отсутствии явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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компьютерной томографии с ^{18}F-флуоро-2-дезокси-D-глюкозой в оценке эффективности терапии и прогнозе лимфом. *Бюллетень сибирской медицины.* 2021; 20 (2): 120–129. https://doi.org/10.20538/1682-0363-2021-2-120-129.

INTRODUCTION

Today, in Russia, the percentage of malignant neoplasms of the lymphatic and hematopoietic tissue accounts for 5% and 4.6% of tumors detected annually in men and women, respectively. In 2016, the incidence of this pathology in the Russian Federation was 19.58 per 100 thousand population, while the average annual growth rate was 1.78% [1]. Every year lymphomas become the cause of death in 5% of all patients with tumor diseases. Hodgkin's lymphoma (HL) is the most common lymphoproliferative disease (30%). Of non-Hodgkin's lymphomas (NHL), diffuse large B-cell lymphoma and follicular lymphoma are most commonly diagnosed (33% and 22%, respectively). The incidence of other types of lymphomas is less than 10% [2].

Usually the effect of lymphoma treatment is monitored by dynamic assessment of the tumor size using anatomical imaging techniques, most commonly computed tomography (CT). At the same time, CT is not optimal for this purpose. Thus, after completion of therapy, in more than 60% of patients with HL and 40% of patients with aggressive NHL, according to CT data, a residual tumor mass is visualized, which may contain areas of fibrosis and necrosis, as well as tumor cells [3]. At the same time, CT cannot differentiate a viable tumor mass from the residual scar tissue. In addition, anatomical imaging techniques usually do not allow to determine a tumor response at early stages of treatment, since reduction of the tumor volume takes time.

Therefore, there is a growing interest in new methods for diagnosing lymphoproliferative diseases. This fully applies to positron emission tomography (PET) with ^{18}F-fluoro-2-deoxy-d-glucose (^{18}F-FDG) [4, 5] and single-photon emission computed tomography (SPECT) with ^{99m}Tc-1-thio-d-glucose [6–8]. The data of modern studies show high efficiency and confirm the prognostic value of these methods, which makes it possible to determine the prevalence of lymphomas, assess the effectiveness of the therapy, and determine the presence or absence of indications for radiation therapy. Thus, according to the literature, PET with ^{18}F-FDG allows to visualize increased metabolic activity in 30–64% of patients with residual tumor masses after completion of the therapy [4]. The presence of such hypermetabolic formations in 62–100% of cases is accompanied by a relapse after the first-line chemotherapy [9].

The widespread use of PET in the Russian Federation is currently limited due to the high cost of the procedure and the insufficient number of PET centers, which are located mainly in the European part of the country. Considering high efficiency and demand for this method in recent years, modern PET centers have been built in the Eastern part of Russia, including the Nuclear Medicine Center of the Federal Siberian Research Clinical Center under FMBA of Russia (FSRCC FMBA of Russia) in Krasnoyarsk. The opening of this center made PET available to residents of the Siberian Federal District.

The aim of this study was to determine the diagnostic value of ^{18}F-FDG PET / CT in assessing the effectiveness and prognosis of lymphoma treatment.

MATERIALS AND METHODS

Retrospective data of ^{18}F-FDG PET / CT of 30 people with malignant lymphomas were analyzed: before treatment (PET1), after 2 cycles of polychemotherapy (PET2), and after completion (from 6 to 8 cycles) of polychemotherapy (PET3). PET2 was performed before the introduction of the third cycle of chemotherapy, and PET3 was performed 2 weeks after the last dose. In 12 cases, additional ^{18}F-FDG PET / CT (PET4) was performed at the stages of dynamic observation of patients (6–12 months after treatment completion). The examination was carried out at the Nuclear Medicine Center of the FSRCC FMBA of Russia (Krasnoyarsk) from 2015 to 2017. The study involved 13 men and 17 women aged 19–74 years (average age was 42 years). All patients underwent an immunohistochemical examination, according to which 12 patients had HL, and the remaining 18 had aggressive NHL: diffuse large B-cell lymphoma (11 cases) and follicular lymphoma (7 cases). In accordance with the data of the initial clinical and instrumental studies (clinical examination, CT, magnetic resonance imaging (MRI), ultrasound, bone marrow biopsy), stage I of the disease was established in 3 patients (10%), stage II – in 8 (27%) patients, stage III – in 8 (27%) patients, and stage IV – in 11 (36%) patients.

Reference methods for result verification were histological examination or, if it was impossible to perform it, long-term (at least a year) clinical monitoring of the patient with a series of control instrumental examinations (CT, MRI, ultrasound, ^{18}F-FDG PET / CT).

Most patients received R-CHOP treatment (14 patients) (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone). 9 patients had the BEACOPP regimen (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisolone), 4 patients underwent RB (rituximab, bendamustine) treatment, and 3 patients received ABVD (adriamycin, bleomycin, vinblastine, and dacarbazine) therapy.

Routine methods for assessing the effectiveness of treatment included a clinical examination of the patient, laboratory tests, and CT of the chest wall and abdominal cavity. This assessment was carried out after 2–3 cycles of chemotherapy and after completion of the entire treatment program. In accordance with the "Russian clinical guidelines for the diagnosis and treatment of lymphoproliferative diseases" [10], the patient's condition was assessed as complete remission (CR), uncertain complete remission (uCR), partial remission (PR), stabilization (St), relapse (after CR or uCR), or progression (after PR or St).

^{18}F-FDG PET / CT was performed in the whole body mode (from the level of the eye sockets to the middle third of the thigh) with simultaneous low-dose CT to correct the attenuation. The study was carried out on a PET / CT scanner Discovery PET / CT 600. Eating was allowed no later than 6 hours before the study. The radiopharmaceutical ^{18}F-FDG was administered intravenously at a dose of 300–550 MBq, and after 60–90 minutes, scanning was performed. The obtained images were reconstructed using standard software. The results of all studies were interpreted and analyzed by specialists in nuclear medicine and radiology.

The results of PET2 and PET3 were assessed as follows: a complete metabolic response (1, 2, and 3 points on a five-point Deauville scale in lymph nodes or extranodal sites with or without residual tumor mass); a partial metabolic response (4 or 5 points on the Deauville scale with visually reduced uptake of the radiopharmaceutical compared to baseline and residual tumor mass of any size); lack of a metabolic response (4 or 5 points on the Deauville scale without a significant change in ^{18}F-FDG uptake compared to the baseline value), and metabolic progression (4 or 5 points on the Deauville scale with an increase in ^{18}F-FDG uptake compared to the baseline value and / or the emergence of new metabolically active foci associated with lymphoma) [11].

To study the prognostic value of the results of patients' examination at the stages of treatment, progression-free survival (the time from the diagnosis to the first signs of progression or a relapse or to disease-related death) (PFS) was chosen as an endpoint. The survival curves were constructed using the Kaplan – Meier method. The differences between the groups were analyzed using a log rank test.

RESULTS

According to the reference verification methods, 191 lymph nodes involved in the pathogenetic process were found in 30 patients with lymphoma. Most often, there was a lesion in the cervical (21%), supra- and subclavian (20%), mediastinal (13%), axillary (10%), and bronchopulmonary (10%) lymph nodes. Lesions in the mesenteric (6%), inguinal (6%), and paraaortic (5%) nodes were less commonly diagnosed.

According to PET / CT, pathological accumulation of ^{18}F-FDG in the lymph nodes was observed in all patients included in the study. 169 (88%) of 191 affected nodes were hypermetabolic. ^{18}F-FDG PET /CT was most effective in diagnosing the state of the iliac, mediastinal, mesenteric, and inguinal lymph nodes, when its sensitivity exceeded 90%.

In 16 patients, 33 extranodal lesions were diagnosed using reference verification methods. Most often, there was dissemination of malignant lymphomas in the lungs (10 patients), spleen (11 patients), and red bone marrow (7 patients); in individual cases, it was observed in the liver and soft tissues.

According to PET / CT, pathological ^{18}F-FDG uptake was observed in 30 (91%) of 33 extranodal foci. The PET / CT method was most effective in diagnosing the state of the red bone marrow, soft tissues, lungs, and spleen, when its sensitivity was 90% or more. When assessing the state of the liver, it was possible to visualize 2 pathological foci out of 3.

When analyzing the PET2 results, a complete metabolic response after two cycles of chemotherapy (PET2–) was observed in 21 patients (70%): in 9 patients (75%) with HL and 12 patients (67%) with NHL (Fig. 1). In this group of patients, patients with early stages of lymphoma (stages I-II) were more common, (9 (82%) out of 11), as well as persons without signs of extranodal lesions (11 (79%) out of 14). In stage III-IV lymphoma and in the presence of extranodal lesions, PET2– occurred in 12 (63%) and 10 (62%) patients, respectively (Table 1).

Table 1

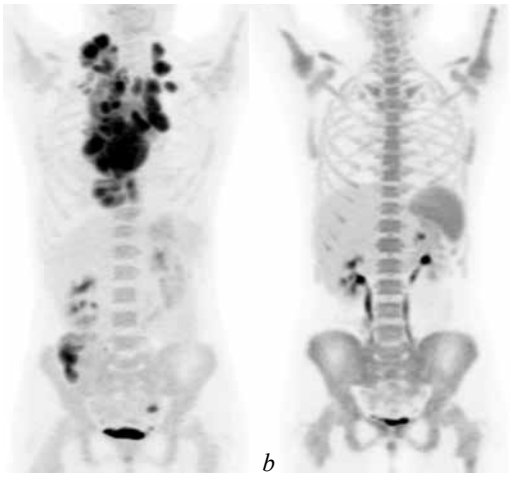
Interim ^{18}F-FDG PET/CT and ^{18}F-FDG PET/CT results after chemotherapy in lymphoma patients

Patients	LH		NLH		LH + NLH		Total
	PET2–	PET2+	PET2–	PET2+	PET2–	PET2+	
Total in the group	9	3	12	6	21	9	30
PET3–	9	2	12	3	21	5	26
PET3+	0	1	0	3	0	4	4
Early stages (I-II)	3	1	6	1	9	2	11
PET3–	3	1	6	0	9	1	10
PET3+	0	0	0	1	0	1	1
Advanced stages (III-IV)	6	2	6	5	12	7	19
PET3–	6	1	6	3	12	4	16
PET3+	0	1	0	2	0	3	3
Extranodal lesions –	5	1	6	2	11	3	14
PET3–	5	1	6	2	11	3	14
PET3+	0	0	0	0	0	0	0
Extranodal lesions +	4	2	6	4	10	6	16
PET3–	4	1	6	1	10	2	12
PET3+	0	1	0	3	0	4	4

In 9 patients, after 2 cycles of chemotherapy, a partial metabolic response (6 people), no metabolic response (2 people), or metabolic progression (1 person) were established (Fig. 2). These patients made up the PET2+ group. This group included 3 patients (25%) with HL and 6 patients (33%) with NHL. Signs of tumor metabolic activity on interim PET / CT scans were observed in 2 (18%) cases with early stages of lymphoma and in 7 (37%) patients with advanced stages of the disease. In addition, positive interim PET was more common in the presence of extranodal lesions (6 (38%) patients) than in their absence (3 (21%) patients) (Table 1). After the end of chemotherapy, a complete metabolic response (PET3–) was diagnosed in 26 patients (87%). This effect was achieved in 21 patients (100%) with PET2– and in 5 people (66%) with PET2+ (Fig. 3, Table 1).

In the PET2+ group after completion of chemotherapy, 4 (44%) patients had a partial metabolic response (3 people) or no metabolic response (1 person) (Fig. 1, Table 1). Follow-up of these patients showed that in 2 cases, progression was diagnosed, and in 2 patients, further treatment led to complete remission.

During a two-year follow-up of patients, it was found that remission was observed in 20 (67%) patients (complete remission in 15 people, uncertain complete remission in 5 patients). The "remission" group included 10 (83%) patients with HL and 10 (56%) individuals with NHL. The "relapse" group consisted of 10 (40%) people: 6 patients had a relapse of the disease, and 4 people had progression (Fig. 4, 5, Table 2). More often, a relapse or progression was observed in NHL – 8 (56%) cases, less often, in HL – in 2 (17%) patients (Fig. 6, Table 2). Patients with early stages of lymphoma more often were in the "remission" group than patients with advanced stages of the disease, 72% and 63%, respectively. It should also be noted that remission was more often observed in patients with no extranodal lesions (76%) than in those with extranodal lesions (56%) (Table 2).



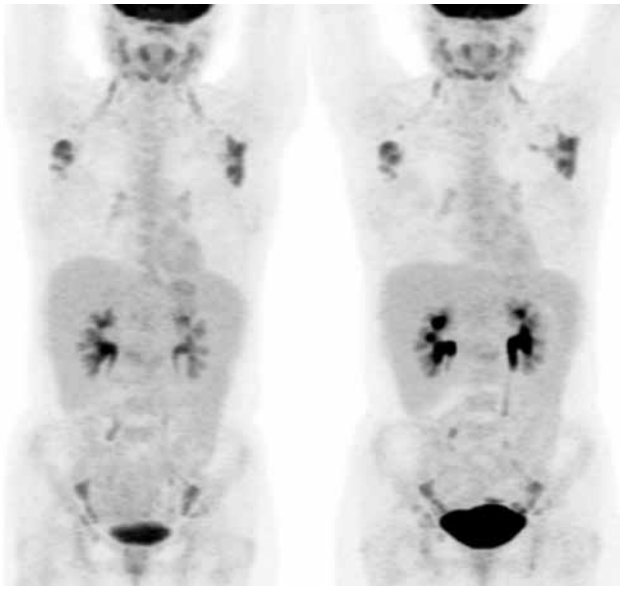
a *b*

Fig. 1. Patient T., 25 years old. Diagnosis: Hodgkin's lymphoma: *a* – PET1: signs of lymphoproliferative disease with multiple metabolically active lesions of the anterior and posterior mediastinum, cervical, supraclavicular and subclavian, bronchopulmonary, and intraperitoneal lymph nodes; *b* – PET2; complete metabolic regression

Table 2

Interim ^{18}F-FDG PET/CT and follow-up prognosis in lymphoma patients

Patients	LH		NLH		LH + NLH		Total
	PET2–	PET2+	PET2–	PET2+	PET2–	PET2+	
Total in the group	9	3	12	6	21	9	30
Remission	9	1	8	2	17	3	20
Relapse	0	2	4	4	4	6	10
Early stages (I-II)	3	1	6	1	9	2	11
Remission	3	0	4	1	7	1	8
Relapse	0	1	2	0	2	1	3
Advanced stages (III-IV)	6	2	6	5	12	7	19
Remission	6	1	4	1	10	2	12
Relapse	0	1	2	4	2	5	7
Extranodal lesions –	5	1	6	2	11	3	14
Remission	4	1	5	1	9	2	11
Relapse	1	0	1	1	2	1	3
Extranodal lesions +	4	2	6	4	10	6	16
Remission	3	0	4	2	7	2	9
Relapse	1	2	2	2	3	4	7



a *b*

Fig. 2. Patient C., 38 years old. Diagnosis: Hodgkin's lymphoma, nodular sclerosis: *a* – PET1: signs of lymphoproliferative disease with a metabolically active lesion of the cervical, axillary, iliac, and inguinal lymph nodes; *b* – PET2: compared to PET1– no changes

Analysis of the PET2 results showed that in patients with PET2+, a relapse was observed in 6 (67%) cases, and remission – in 3 (33%) cases. At the same time, in patients with PET2–, the opposite pattern took place: 4 (19%) people were diagnosed with a relapse and 17 (81%) had remission (Fig. 4, 5).

DISCUSSION

The results of our study confirm the global experience of using ^{18}F-FDG PET / CT. In lymphomas, the metabolic activity of the tumor changes quite rapidly after the start of treatment, even before a change in tumor size is detected [12]. Many studies have shown that ^{18}F-FDG PET / CT performed at early stages of chemotherapy (interim ^{18}F-FDG PET / CT) predicts the effectiveness of treatment. Such stratification of patients makes it possible to personalize the treatment strategy and has a positive effect on the outcome of the disease [13]. In patients with lymphoma, an interim ^{18}F-FDG PET / CT scan is usually performed after one to four (as a rule two) chemotherapy cycles out of six to eight planned ones.

Interim ^{18}F-FDG PET / CT helps to differentiate between patients with favorable lymphoma who need standard therapy and high-risk patients who require more intensive treatment with high-dose chemotherapy regimens. The method has proven itself well in determining the sensitivity of tumor tissue to chemotherapy, especially in patients with an advanced stage of the disease and an unfavorable course of the lymphoproliferative process, who may need additional radiation therapy [14]. In addition, in low-risk patients, interim ^{18}F-FDG PET / CT can reduce side effects and unnecessary toxicity associated with treatment, making it possible to choose the gentlest protocols and reduce the number of cycles. According to the ESMO guidelines, in patients with HL [14], interim ^{18}F-FDG PET / CT after 1–2 cycles of chemotherapy can identify a group with a high probability of achieving a complete metabolic response after completion of treatment and without indications for consolidation radiotherapy [13]. At advanced stages of the disease, this method is used to identify patients who need to change the chemotherapy regimen.

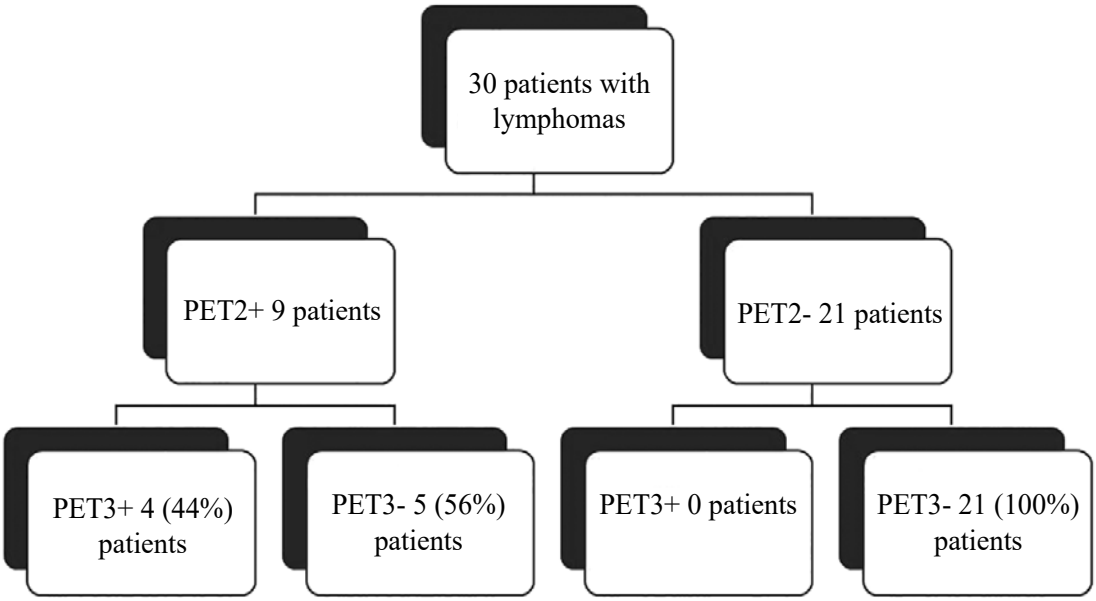


Fig. 3. Results of ^{18}F-FDG PET/CT after lymphoma chemotherapy in PET2+ and PET2– groups

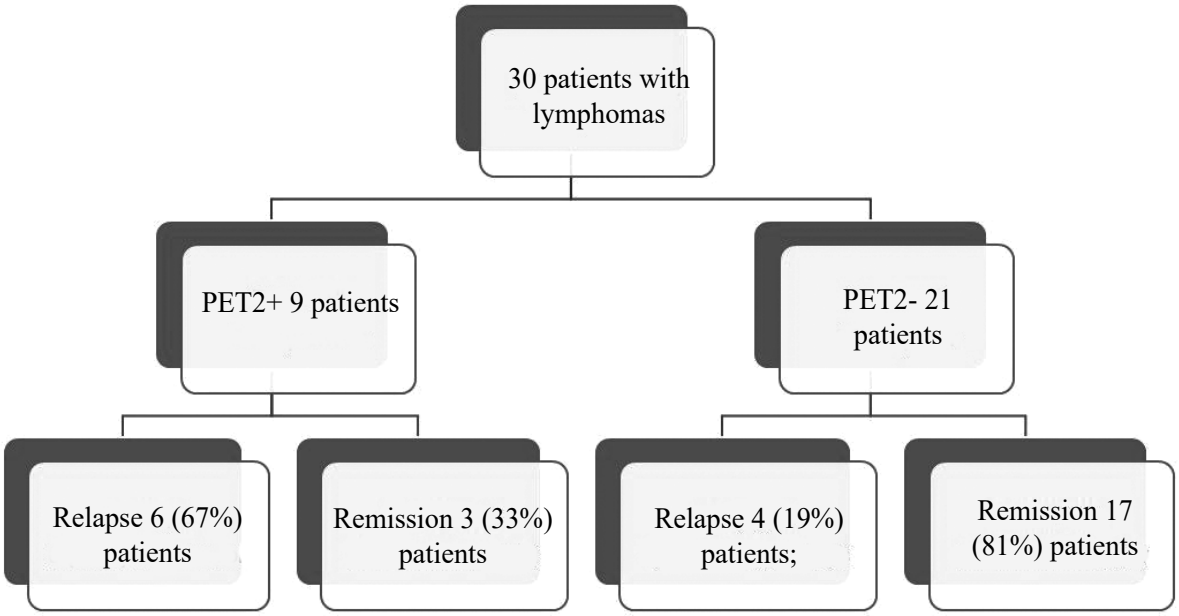


Fig. 4. Results of long-term follow-up of PET2+ and PET2– groups of lymphoma patients

According to a study by J. Radford et al. [13], performed on the basis of the analysis of the ^{18}F-FDG PET / CT findings in 602 patients with early stage HL who received ABVD chemotherapy, it was shown that if after 3 cycles the metabolic activity in the tumor foci was not detected, then further radiation therapy was unnecessary and progression-free survival (PFS) remained unchanged. A retrospective study of 260 HL patients treated with ABVD therapy confirmed the predictive role of interim ^{18}F-FDG PET/CT using Deauville's criteria for predicting a treatment response [16].

In another study, observation of patients with advanced stage HL showed that a complete metabolic tumor response after two cycles of ABVD chemotherapy had high negative predictive value (NPV) (94%) and positive predictive value (PPV) (73%) with predicting 3-year PFS [17]. Similar data were presented in an article by J. Markova et al., in which the analysis of the interim ^{18}F-FDG PET / CT findings in patients

with advanced HL after 4 cycles of BEACOPP chemotherapy demonstrated that a complete metabolic response in predicting 4-year PFS had NPV and PPV levels of 98% and 96%, respectively [18]. In addition to its high predictive value for assessing PFS, interim ^{18}F-FDG PET / CT can be used to determine the indications for consolidation radiotherapy [18].

CONCLUSION

Interim ^{18}F-FDG PET / CT with high accuracy allows to predict the effect of malignant lymphoma treatment. The method is recommended for widespread use in clinical practice for monitoring the stages of therapy for this pathology.

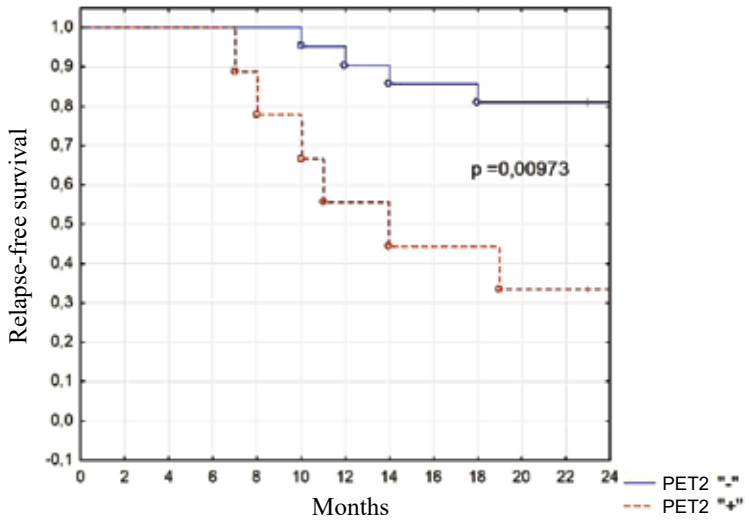
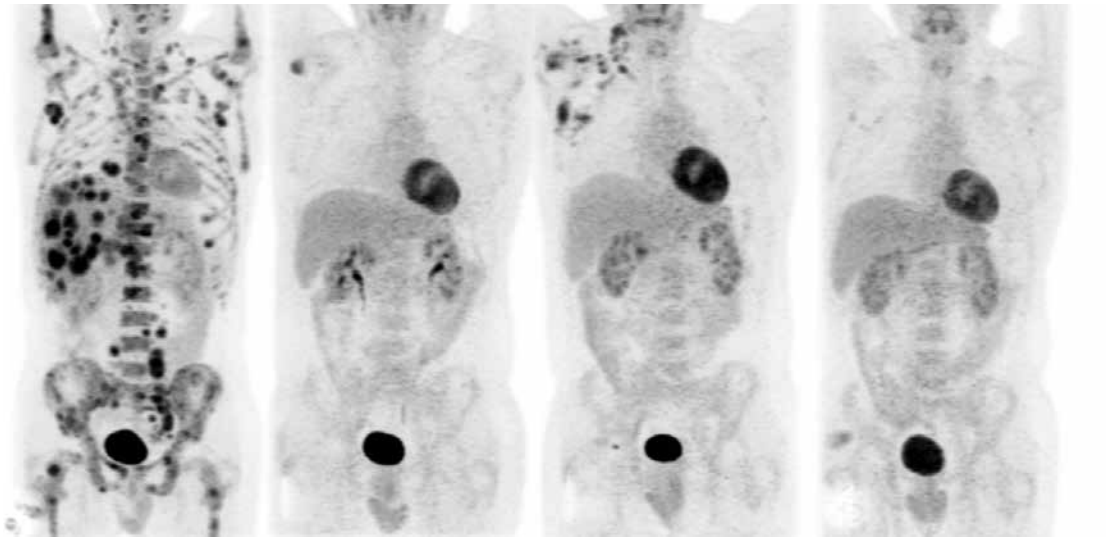


Fig. 5. Two-year relapse-free survival in patients with lymphomas with (PET2–) and without (PET2+) a metabolic response to two cycles of chemotherapy



a *b* *c* *d*

Fig. 6. Patient K., 31 years old. Diagnosis: Hodgkin's lymphoma with damage to peripheral lymph nodes and skin: *a* – PET1: signs of lymphoproliferative disease with multiple metabolically active lesions of the liver, lymph nodes above and below the diaphragm, and bone marrow; *b* – PET2: signs of lymphoproliferative disease with a metabolically active lesion of the acromial process of the right scapula. Compared to PET1 – positive changes; *c* – PET3: metabolic activity in the cervical, supraclavicular, and axillary lymph nodes on the right, a single inguinal lymph node on the right, in the acromial process of the right scapula. Compared to PET2 – negative changes; *d* – PET4: a metabolically active lesion in single right axillary lymph nodes, regarded as a manifestation of Hodgkin's lymphoma. Compared to PET3 – positive changes

REFERENCES

1. Kaprin A.D., Starinskiy V.V., Petrova G.V. Malignant neoplasms in Russia in 2016 (morbidity and mortality). Moscow: P. Hertsen Moscow Oncology Research Institute of the NMRC Radiology of the Ministry of Health of the Russian Federation, 2018: 250 (in Russ.).
2. Rukavicin O.A. Hematology: national guidelines. Moscow: Geotar-Media. 2015: 912 (in Russ.).
3. Zucca E., Copie-Bergman C., Ricardi U., Thieblemont C., Raderer M., Ladetto M. Gastric marginal zone lymphoma of MALT type: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*. 2013; 24: 144–148. DOI: 10.1093/annonc/mdt343.
4. Chernov V.I., Dudnikova E.A., Gol'dberg V.E., Kravchuk T.L., Danilova A.V., Zel'chan R.V., Medvedeva A.A., Sinilkin I.G., Bragina O.D., Popova N.O., Gol'dberg A.V. Positron emission tomography in the diagnosis and monitoring of lymphoproliferative diseases. *Medical Radiology and Radiation Safety.* 2018; 6 (63): 41–50 (in Russ.). DOI: 10.12737/article_5c0b8d72a8bb98.40545646.
5. Chanchikova N.G., Dudnikova E.A., Karlova E.A., Savel'eva A.S., Silkina O.A., Zel'chan R.V., Sinilkin I.G., Bragina O.D., Medvedeva A.A., Chernov V.I. Possibilities of PET/CT with ^{18}F-FDG in the diagnosis and staging of lymphomas. *Problems in Oncology.* 2019; 65 (1):147–153 (in Russ.).
6. Chernov V.I., Dudnikova E.A., Zelchan R.V., Kravchuk T.L., Danilova A.V., Medvedeva A.A., Sinilkin I.G., Bragina O.D., Goldberg V.E., Goldberg A.V., Frolova I.G. The first experience of using 99mTc-1-thio-d-glucose for single-photon emission computed tomography imaging of lymphomas. *Siberian Journal of Oncology*. 2018; 17 (4): 81–87. DOI: 10.21294/1814-4861-2018-17-4-81-87.
7. Chernov V.I., Dudnikova E.A., Gol'dberg V.E., Kravchuk T.L., Danilova A.V., Zel'chan R.V., Medvedeva A.A., Sinilkin I.G., Bragina O.D., Belevich Ju.V., Koroleva E.S. Single-photon emission computed tomography in the diagnosis and monitoring of lymphoproliferative diseases. *Medical Radiology and Radiation Safety.* 2019; 64(3): 58–63 (in Russ.). DOI: 10.12737/article_5c0b8d72a8bb98.40545646.
8. Zelchan R., Chernov V., Medvedeva A., Sinilkin I., Stasyuk E., Rogov A., Il'ina E., Skuridin V., Bragina O. Study of a glucose derivative labeled with technetium-99m as potential radiopharmaceutical for cancer diagnosis EP634. *Eur. J. Nucl. Med. Mol. Imaging.* 2016; 43 (1): S466.
9. Sasaki M., Kuwabara Y., Koga H., Nakagawa M., Chen T., Kaneko K., Havashi K., Nakamura K., Masuda K. Clinical impact of whole body FDG-PET on the staging and therapeutic decision making for malignant lymphoma. *Annals of Nuclear Medicine.* 2002; 16 (5): 337–345. DOI: 10.1007/BF02988618.
10. Poddubnaya I.V., Savchenko V.G. Russian clinical guidelines for the diagnosis and treatment of lymphoproliferative diseases. Moscow: MediaMedica, 2013:104 (in Russ.).
11. Cheson B.D., Fisher R.I., Barrington S.F., Cavalli F., Schwartz L.H., Zucca E., Lister T.F. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. *Journal of Clinical Oncology.* 2014; 32 (27): 3059–3068. DOI: 10.1200/JCO.2013.54.8800.
12. Romer W., Hanauske A.R., Ziegler S., Thodtmann R., Weber W., Fuchs C., Enne W., Herz M., Nerl C., Garbrecht M., Schwaiger M. Positron emission tomography in non-Hodgkin's lymphoma: assessment of chemotherapy with fluorodeoxyglucose. *Blood*. 1998; 91 (12): 4464–4471.
13. Radford J., Illidge T., Counsell N., Hancock B., Pettengell R., Johnson P., Wimperis J., Culligan D., Popova B., Smith P., McMillan A., Brownell A., Kruger A., Lister A., Hoskin P., O'Doherty M., Barrington S. Results of a Trial of PET-Directed Therapy for Early-Stage Hodgkin's Lymphoma. *New England Journal of Medicine*. 2015; 372 (17): 1598–1607. DOI: 10.1056/NEJMoa1408648.
14. Kostakoglu L., Cheson B.D. State-of-the-art research on "Lymphomas: Role of molecular imaging for staging, prognostic evaluation, and treatment response". *Front. Oncol.* 2013; 3: 212. DOI: 10.3389/fonc.2013.00212.
15. Dreyling M., Ghielmini M., Marcus R., Salles G., Vitolo U., Ladetto M., ESMO Guidelines Working Group. Newly diagnosed and relapsed follicular lymphoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Annals of Oncology.* 2014; 25 (3): 76–82. DOI: 10.1093/annonc/mdu200.
16. Gallamini A., Barrington S.F., Biggi A., Chauvie S., Kostakoglu L., Gregianin M., Meignan M., Mikhaeel G.N., Loft A., Zaucha J.M., Seymour J.F., Hofman M.S., Rigacci L., Pulsoni A., Coleman M., Dann E.J., Trentin L., Casasnovas O., Rusconi C., Brice P., Bolis S., Viviani S., Salvi F., Luminari S., Hutchings M. The predictive role of interim positron emission tomography for Hodgkin lymphoma treatment outcome is confirmed using the interpretation criteria of the Deauville five-point scale. *Haematologica.* 2014; 99 (6): 1107–1113. DOI: 10.3324/haematol.2013.103218.
17. Biggi A., Gallamini A., Chauvie S., Hutchings M., Kostakoglu L., Gregianin M., Meignan M., Malkowski B., Hofman M.S., Barrington S.F. International validation study for interim PET in ABVD-treated, advanced-stage hodgkin lymphoma: interpretation criteria and concordance rate among reviewers. *J. Nucl. Med.* 2013; 54 (5): 683–690. DOI: 10.2967/jnumed.112.110890.
18. Markova J., Kahraman D., Kobe C., Skopalova M., Mocikova H., Klaskova K., Dedeckova K., Eich H., Böll B., Dietlein M., Kozak T. Role of [18F]-fluoro-2-deoxy-D-glucose positron emission tomography in early and late therapy assessment of patients with advanced Hodgkin lymphoma treated with bleomycin, etoposide, adriamycin, cyclophosphamide, vincristine, procarbazine and prednisone. *Leuk. Lymphoma*. 2012; 53 (1): 64–70. DOI: 10.3109/10428194.2011.603444.

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Chanchikova N.G. – final approval of the manuscript for publication. Chernov V.I. – conception and design. Dudnikova E.A., Zelchan R.V., Bragina O.D., Medvedeva A.A., Berezneeva E.V. – analysis and interpretation of data. Karlova E.A., Savelyeva A.S., Silkina O.A. – substantiation of the manuscript, critical revision of the manuscript for important intellectual content.

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