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THE USE OF PET TO EVALUATE THE EFFECTIVENESS OF DRUG THERAPY FOR DISSEMINATED THE TUMOR BREAST CANCER

Akhmadova Maftuna Amin kizi - Assistant Professor of the Department of Medical Radiology and Nuclear Medicine at the Abu Ali ibn Sino Bukhara State Medical Institute
https://orcid.org/0009-0004-36117-4472

Resume. The current literature and the National Comprehensive Cancer Network (NCCN) guidelines state that 18F-FDG PET/CT is not routine for early diagnosis of breast cancer, and rather PET/CT scanning should be performed for patients with stage III disease or when conventional staging studies yield non-diagnostic or suspicious results because this modality has been shown to upstage patients compared to conventional imaging and thus has an impact on disease management and prognosis. Although 18F-FDG PET/CT mammography was able to detect axillary lymph node metastases with a high sensitivity, this method cannot soon be expected to replace the combination of clinical examination, ultrasound, and sentinel lymph node biopsy for axillary assessment. Drug therapy remains the main method of complex treatment at these stages. Positron emission tomography (PET) with fluorodeoxyglucose has now been used to assess the effect of the treatment. This method makes it possible to assess changes in the tumor at the cellular level long before morphological manifestations. Thus, a decrease in the accumulation of fluorodeoxyglucose in the tumor by more than 45% of the initial one predicts a complete pathomorphological response to drug therapy with great accuracy.

Key words: positron emission tomography (PET), fluorodeoxyglucoses, breast cancer, radiopharmaceutical

ИСПОЛЬЗОВАНИЕ ПЭТ ДЛЯ ОЦЕНКИ ЭФФЕКТИВНОСТИ ЛЕКАРСТВЕННОЙ ТЕРАПИИ ПРИ ДИССЕМИНИРОВАННОМ РАКЕ МОЛОЧНОЙ ЖЕЛЕЗЫ

Ахмадова Мафтуна Амин кизи - ассистент кафедры медицинской радиологии и ядерной медицины Бухарского государственногомедицинского института имени Абу Али ибн Сино
https://orcid.org/0009-0004-36117-4472

Резюме. Наши данные свидетельствуют о том, что протокол ПЭТ/КТ-маммографии всего тела с 18F-ФДГ может быть использован для определения стадии рака молочной железы за один сеанс. Эта первоначальная оценка протокола ПЭТ/КТ 18F-FDG показывает, что точность выявления раковых поражений молочной железы аналогична точности МРТ. Хотя МРТ, по-видимому, более точна при оценке Т-стадии опухоли, ПЭТ/КТ с 18F-ФДГ, по-видимому, позволяет более точно определить очаг поражения. Несмотря на то, что ПЭТ/КТ-маммография 18F-FDG позволяет с высокой чувствительностью выявлять метастазы в подмышечных лимфатических узлах, нельзя ожидать, что этот метод в скором времени заменит комбинацию

клинического обследования, ультразвукового исследования и биопсии контрольных лимфатических узлов для оценки состояния подмышечных лимфатических узлов. Медикаментозная терапия остается основным методом комплексного лечения на этих этапах. Для оценки эффекта лечения в настоящее время используется позитронно-эмиссионная томография (ПЭТ) с фтордезоксиглюкозой. Этот метод позволяет оценить изменения в опухоли на клеточном уровне задолго до морфологических проявлений. Таким образом, снижение накопления фтордезоксиглюкозы в опухоли более чем на 45% от исходного с большой точностью предсказывает полный патоморфологический ответ на медикаментозную терапию.

Ключевые слова: позитронно-эмиссионная томография (ПЭТ), фтордезоксиглюкозы, рак молочной железы, радиофармпрепарат

Introduction. Effective management of breast cancer requires accurate diagnosis and determination of the extent of the disease to select the most effective treatment approach [3]. Breast cancer is very heterogenous and is characterized by different pathological features, with distinct responses to treatment and differences in long-term patient survival [4]. Approximately 70% of BC express the estrogen receptor (ER), and the majority of ER+ cancers also express the progesterone receptor (PR). Breast cancer occupies the first place both in the structure of morbidity and mortality in Russian and European women. Despite the successes achieved in the diagnosis and treatment of this suffering, the diagnosis of a locally spread or disseminated process is observed in almost every third patient. Drug therapy remains the main method of complex treatment at these stages. Positron emission tomography (PET) with fluorodeoxyglucose has now been used to assess the effect of the treatment. This method makes it possible to assess changes in the tumor at the cellular level long before morphological manifestations. Thus, a decrease in the accumulation of fluorodeoxyglucose in the tumor by more than 45% of the initial one predicts a complete pathomorphological response to drug therapy with great accuracy. Results showed that 32.1% of the diagnosed lesions did not change their SUV values, 39.3% were treated, 27.4% were new lesions do not present in the original PET-CT scan, and 1.2% for lesions that increased the value of the SUV. Moreover, the results also showed that left breast cancer was more responsive to treatment than right breast cancer, while chemotherapy was more effective than radiation therapy. In summary, the efficacy of chemotherapy and/or radiotherapy for both right and left breast cancer patients was evaluated using PET-CT technology. The effectiveness of drug therapy in patients with disseminated breast cancer using PET/CT is evaluated. It was found that the diagnostic value (SUVmax) for breast cancer metastases ranges from 1.5 to 3, and for the primary tumor – more than 2. As an illustration, the authors cite two clinical examples.

The incidence of breast cancer in 2024 in the Bukhara region was 382 per 100,000 population. In 24.5% of cases, the disease was diagnosed in stages III and IV. In 2024, 74.6% of patients, 29.6%, received combined or complex treatment of breast cancer using various drug therapy regimens. At the same time, mortality in

the first year after diagnosis was 5.8% [1,3]. Timely and accurate assessment of the effectiveness of drug therapy at various stages of treatment of disseminated breast cancer remains an urgent problem in oncology. Among the many diagnostic methods used in monitoring drug treatment of breast cancer, positron emission tomography combined with computed tomography (PET/CT) with radiopharmaceutical 18F-fluoro-2-deoxy-D-glucose (FDG) has now begun to be used [2,4].

This is a molecular imaging method that allows noninvasively monitoring the response of tumor cells to treatment at the cellular level long before structural changes in the tumor are detected by routine diagnostic methods such as mammography, ultrasound, CT and MRI [6,9]. At the same time, the level of FDG hyperfixation in the tumor focus can be considered a predictor of a complete pathomorphological response to treatment. Thus, according to a number of authors, a decrease in the accumulation of FDG by breast cancer cells during neoadjuvant drug therapy by more than 45% (SUV ≥ 45%), compared with baseline values, predicts with high accuracy a complete pathomorphological response and high effectiveness of systemic drug therapy for all molecular biological subtypes of breast cancer with The sensitivity of the method is 81.5%, the specificity is 77.8%. The degree of accumulation of FDG by breast cancer cells has a significant direct correlation with the large size of the primary neoplasm, high mitotic activity, and the absence of hormonal receptors in the tumor., It has a high Ki67 and is an early sensitive biological marker of the aggressiveness of the malignant process.In neoadjuvant chemotherapy for locally advanced breast cancer, clinical response criteria often do not allow evaluating the effectiveness of the treatment before surgery due to the difficulty in differentiating residual fibrous changes and active tumor tissue [8,11]. An important clinical problem of the HER2-positive subtype of invasive breast cancer remains the early identification of "responding" and "non-responding" patients after first-line chemotherapy with trastuzumab/cytostatic. In patients with metastatic breast cancer, therapeutic monitoring is difficult due to the inaccessibility of determining histopathological results. At the same time, PET/CT allows us to judge whether the patient is responding to the therapy or not, as well as predict the therapeutic result with high accuracy. In case of secondary damage to the bones of the PET skeleton/CT with FDG is the most accurate and optimal imaging method for assessing a tumor's response to treatment and may become the standard in evaluating the effectiveness of drug therapy in bone metastases. About 15% of patients have a basal-like (triple negative) subtype of breast cancer. This aggressive form of the disease is characterized by the highest glycolytic activity, an unfavorable clinical prognosis, and high sensitivity to chemotherapy. A decrease in the accumulation of fluorodeoxyglucose by breast cancer cells after the second course of chemotherapy by more than 50% of the initial one is a sensitive marker of the complete pathomorphological response of this subtype of breast cancer to treatment. Thus, the 3-year event-free survival rate was 76.5% in the group with a complete pathological response (SUV ≥ 42%) versus 45.1% in the group of patients who did not respond to treatment (SUV <42%). The luminal subtype of

breast cancer is characterized by low glycolytic activity and has the lowest basic SUV. In this regard, PET/CT with FDG has limited use for evaluating the effectiveness of hormone therapy for this subtype of breast cancer. However, according to B.B. Koolen et al., in some patients, SUV was a predictor of a complete pathomorphological response to treatment and had a prognostic value. This was mainly related to the luminal B subtype of breast cancer with a high Ki67 proliferative activity index. To evaluate the effectiveness of drug therapy for disseminated breast cancer in patients undergoing treatment at the Tambov Regional Oncological Clinical Dispensary, we used PET/CT with fluorodeoxyglucose [15,19]. The scan was performed strictly on an empty stomach (a 6-hour fast is required). In order to reduce the background activity of fluorodeoxyglucose, we used a water load. FDG was administered intravenously slowly, in a small amount of saline solution, at a rate of 3.4 MBq/kg. At the same time, the diagnostic dose of FDG ranged from 200 to 400 MBq. The radiation load on the whole body when the diagnostic dose was administered was 5-6 mSv. Scanning was started 60-90 minutes after administration of FDG. The duration of the study ranged from 14 to 16 minutes. The interpretation of the data during the "whole body" study was performed according to visual and quantitative criteria. Visual analysis of the images was performed in three projections using a gray scale. The intensity of FDG accumulation in the foci was also determined. Breast cancer is characterized by high glycolytic activity, which causes an intensive accumulation of FDG in the tumor tissue. The values of the standardized capture level were used as a quantitative criterion. This is a dimensionless quantity representing the ratio of the specific radioactivity in the measured area (kBq/cm3) to the amount of radioactivity introduced per body weight (MBq/kg). The value of the SUV is automatically calculated by the PET/CT scanner software package already in the process of image reconstruction, taking into account the physical half-life of the FDG. After analyzing the data obtained and comparing them with the results of other authors, we found that the diagnostic value of SUV for breast cancer metastases ranges from 1.5 to 3.0. For breast cancer, this indicator is more than 2.0. The indicator of SUV> 3.0 in the primary tumor before treatment indicates an unfavorable prognosis for survival. The permissible error of the SUV oscillation during treatment does not exceed 25% of the initial value. In complex differential diagnostic cases, we performed a "delayed" scan 2-3 hours after a single injection of FDG. The absence of a significant decrease or increase in SUV values in the lesion indicated its malignant nature. Breast cancer response to treatment was assessed by PET response criteria of PERCIST solid tumors[19] . A complete metabolic response was recorded in the absence of foci of increased FDG accumulation. A partial metabolic response is a decrease in SUVmax of > 30%. Progression is an increase in SUVmax > 30%, the appearance of new foci of FDG accumulation. Stabilization of the tumor process is none of the above criteria. Malignant tumors on PET/CT looked like areas of pathological hyperfixation of fluorodeoxyglucose of varying intensity, with clear or indistinct contours, rounded or irregular shapes. Below we present several clinical examples of the use of

PET/CT diagnostics in order to monitor the effectiveness of drug treatment of breast cancer.

Conclusion: With the growing interest in personalized medicine, including molecular targeted therapy, immunotherapy, and theranostics, the role of molecular imaging in breast cancer has evolved. PET/CT imaging has an emerging role in the identification of specific potential targets in the tumor-microenvironment and selecting patients who might benefit from novel molecular-targeted therapies, thus maximizing the therapeutic effect and minimizing toxicity. In this review, we will discuss the role of PET/CT imaging in the diagnosis, staging, prognostication, recurrence assessment, radiotherapy planning, restaging, and treatment response of patients with BC and in selecting patients eligible for novel targeted therapies. Applications of PET/CT in setting outside of the guidelines, such as in the setting of early stage breast cancer, are illustrated. Examples of 16-α[18F]-fluoro-17β-estradiol (FES) PET and 18F-fluorothymidine (FLT) PET scans are depicted with discussion of potential and future clinical applications.PET/Today, CT with FDG plays an important role in analyzing the results of drug treatment of breast cancer, especially in complex clinical situations. PET/CT with fluorodeoxyglucose is a promising biological marker for early evaluation of the effectiveness of drug therapy for disseminated breast cancer. It allows you to evaluate the effect of therapy in a timely manner, if necessary, to change, supplement or terminate it in time in case of progression. This will allow the doctor to carry out personalized treatment. Compared to other medical imaging methods PET/Full-body CT is particularly effective in evaluating the results of drug therapy for bone metastases. It can become a standard for evaluating the effectiveness of therapy.

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