Streszczenie w języku angielskim

Head and neck cancer (HNC) are the sixth most common cancer in the world. Positron emission tomography (PET) using ^{18}F-labeled fluorodeoxyglucose (^{18}F-FDG) has an established role in the HNC patients diagnostic. Appropriate assessment of the clinical stage of the disease in newly diagnosed patients with HNC allows to estimate the prognosis of these patients and select the best treatment option. Apart from surgery, radiotherapy is the main therapeutic method in patients with HNC. The selection of the proper imaging method is essential for the precise determination of the target volumes. The modern ^{18}F-FDG-PET/MR hybrid combines excellent contrast of soft tissues and the possibility of multiplanar imaging obtained in MR with functional imaging based on PET images.

Purpose

The aim of the study was to verify the diagnostic accuracy and clinical usefulness of PET/MR with 18-fluorine-labeled fluorodeoxyglucose (^{18}F-FDG) in patients with squamous cell carcinoma of the oral cavity and/or oropharynx, including:

- assessment of ^{18}F-FDG-PET/MR diagnostic accuracy in preoperative diagnosis of patients with squamous cell carcinoma of the oral cavity and/or oropharynx, taking into account the correlation between the parameters of the primary tumor obtained in ^{18}F-FDG-PET/MR examination and the HPV and EBV infection status and biochemical parameters in the group of the oral cavity and/or oropharynx patients

- assessment of the usefulness and accuracy of ^{18}F-FDG-PET/MR in determining the volume of the primary tumor and metastatic lymph nodes in the process of radiotherapy planning in patients with head and neck cancers

Materials and methods

Thirty eight patients underwent both computed tomography (CT) and PET/MR examination, of whom 21 patients underwent surgical treatment as first-line therapy. The remaining patients received radiochemotherapy or radiotherapy alone as clinically indicated.

One of publications by Samołyk-Kogaczewska et al. (Cancers, 2020) discusses study which included a group of 21 surgically treated patients. Postsurgical tissue material was subjected to routine histopathological (HP) examination with additional evaluation of p16, human papillomavirus (HPV), Epstein-Barr virus (EBV) and Ki67 status. Agreement of clinical and pathological T staging, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) of CT and PET/MR in metastatic lymph nodes detection were defined. The verification of dependences between standardized uptake value (SUV value), tumor geometrical parameters, number of metastatic lymph nodes in PET/MR and CT, biochemical parameters, Ki67 index, p16, HPV and EBV status was made with statistical analysis of obtained results.

Another publication by Samołyk-Kogaczewska et al. (Strahlentherapie und Onkologie, 2019) concerned study which included group of 10 patients with squamous cell carcinoma of the tongue, undergoing radiochemotherapy or radiotherapy alone. In this group of patients gross tumor volume (GTV) for primary tumor and lymph nodes (nGTV) were defined on CT (GTV-CT/nGTV-CT) and compared to GTVs obtained from PET and MRI (GTV-MRI/nGTV-MRI) images. Two methods of GTV/nGTV determination were used: visual interpretation of CT, PET (GTV-PET/nGTV-PET) and MRI images and quantitative automatic method based on a chosen threshold value (20%, 30%, 40%, 50%) of standardized uptake values (SUVmax) from PET examination (GTV-PET20%/nGTV-PET20%, GTV-PET30%/nGTV-PET30%, etc.). Statistical analysis of differences in GTV/nGTV values obtained from CT, PET and MRI studies was performed. GTV-CT/nGTV-CT was used as a reference.

Moreover, spatial analysis between GTV-MRI, GTV-PET and GTV-CT was performed. The Dice similarity coefficient (DSC) and the modified Hausdorff distance (mHD) were calculated. Registration accuracy was qualitatively measured by the DSC and mHD computed on segmented tumors on CT (GTV-CT) and hybrid PET/MRI (GTV-PET/MRI) images.

The third publication by Samołyk-Kogaczewska et al. (Oncology and Radiotherapy, 2021) described the results of study with group of 15 patients with locally advanced cancers of the oral cavity and/or the oropharynx treated with radiochemotherapy or radiotherapy alone. Based on CT, MR and PET examinations, GTV volumes of the primary tumor were determined using the visual (GTV-CT, GTV-MR, GTV-PETvis) and automatic method (GTV-PET20%, GTV-PET30%, etc.) described above. Statistical analysis was performed and GTV-CT were the reference volumes. Spatial analysis between GTV obtained on CT, MR and PET examinations and between GTV-CT and GTV-PET/MR were determining with the DSC and mHD coefficients for individual pairs of measurements.

Results

The Samołyk-Kogaczewska et al. (Cancers, 2020) publication reported study which showed that hybrid PET/MR is characterized by better agreement in T staging, higher specificity, sensitivity, PPV and NPV of lymph nodes evaluation than CT imaging. Significant correlations were observed between SUVmax and maximal tumor diameter from PET/MR, between SUVmean and CT tumor volume, PET/MR tumor volume, maximal tumor diameter assessed in PET/MR. Other correlations were weak and insignificant.

Another publication by Samołyk-Kogaczewska et al. (Strahlentherapie und Onkologie, 2019) concerned study which results of primary tumor volumes evaluations showed that 80% of GTV-MRI and 40% of GTV-PET were larger than GTV-CT. Rest of of GTV-MRI and GTV-PET were smaller than GTV-CT. Taking into account all threshold measurements, 70% of volumes were smaller than GTV-CT. Volumes of GTV-PET30% were the most closely related

to GTV-CT from all threshold methods in 50% of patients. Manually determined GTV-PET generated the most similar volumes in relation to GTV-CT from all PET measurements. Statistical analysis confirmed those results. Compared to nGTV-CT, 70% of nGTV-MRI and 20% of nGTV-PET were larger. The remaining nGTV-MRI and nGTV-PET measurements were smaller than nGTV-CT. Measurements of all thresholds based nGTVs were smaller than nGTV-CTV in 52.5% of cases. Statistical analysis showed that nGTV-MRI, nGTV-PET30%, and nGTV-PET40% were significantly related with nGTV-CT.

The average value of DSC for GTV-CT and GTV-MRI was 0.74 (range 0.66–0.85) and for GTV-CT and GTV-PET—0.72 (range 0.57–0.79). Average mHD between GTV-CT and GTV-MRI was 13.2 mm (range 4–19 mm) and between GTV-CT and GTV-PET—12.4 mm (range 5–21 mm). The registration accuracy measurements in the form of mHD and DSC values for GTV-CT and GTV PET/MRI was in the range of 0–28 mm (average 16.2 mm) and 0–0.82 (average 0.55), respectively.

The results of the study described in in the third Samołyk-Kogaczewska et al. (Oncology and Radiotherapy, 2021) publication showed that 87% of GTV-MR and 80% of GTV-PETvis were larger than the reference GTV-CT. In the remaining cases, GTV-MRI and GTV-PETvis were similar to GTV-CT. In 32% of the GTV measurements obtained by the automatic method (mainly GTV-PET20% and GTV-PET30%) were larger than the GTV-CT. In contrast, 63% of the volumes based on specific SUVmax values (mainly GTV-PET40% and GTV-PET50%) were smaller than GTV-CT. Statistical analysis showed that the volumes of GTV-PETvis and GTV-PET30% were the closest to the reference GTV-CT. The remaining volumes differed significantly from GTV-CT.

In 27% of the cases, the increased FDG uptake occurred outside the GTV-MR contours. In the remaining cases (73%), the contours of GTV-PETvis and GTV-MR overlapped.

The mean DSC for GTV-CT and GTV-MRI was 0.74 (range 0.54-0.88) and for GTV-CT and GTV-PETvis - 0.78 (range 0.67-0.9). The mean mHD between GTV-CT and GTV-MRI was 17.4 mm (range 4-29 mm) and between GTV-CT and GTV-PETvis - 16.9 mm (range 5-28 mm). The mHD and DSC values for GTV-CT and GTV PET/MRI ranged from 0-24 mm (mean 13.3 mm) and 0-0.84 (mean 0.61), respectively.

Conclusions

The innovative PET/MR hybrid with 18-fluorine-labeled fluorodeoxyglucose (^{18}F-FDG) is useful in preoperative determination of clinical stage of the primary tumor (T feature) in patients with squamous cell carcinoma of the oral cavity and/or oropharynx. The results obtained on the basis of the ^{18}FDG-PET/MR examination are more consistent with the results of the histopathological examination of the postoperative material than those obtained on the basis of CT, which indicates the clinical usefulness of the ^{18}FDG-PET/MR examination.

PET/MR examination with the use of ^{18}F-fluorodeoxyglucose (^{18}F-FDG) is characterized by higher sensitivity, specificity, positive and negative predictive value in metastatic lymph nodes diagnostic, compared to the CT examination, which suggests the validity of the use of ^{18}FDG-PET/MR in clinical practice. The finding of significant correlations between SUVmax values and the maximum tumor size, as well as between SUVmean and the tumor volume and maximum tumor size assessed in ^{18}FDG-PET/MR indicates the possible usefulness of these parameters in clinical practice. The problem requires further research.

The presence of p16 protein, HPV and EBV infections is not significantly related with SUV values and tumor geometry parameters, as well as with number of metastatic lymph nodes in PET/MR examination using fluorodeoxyglucose labeled with ^{18}F fluorine, which excludes the use of ^{18}FDG-PET in diagnostic of tumors whose etiology is related to viral infections. This issue requires further research in the future. Combining PET with fluorodeoxyglucose labeled with ^{18}F and MR provides more information than other standard imaging methods, which may

increase the accuracy of primary tumor and metastatic lymph nodes volume determination during radiotherapy planning, but this issue requires further research in the future. Determination of GTV with ^{18}FDG-PET/MR requires a clearly defined methodology. The study showed that the most similar GTV volumes were obtained by using the 30% SUVmax threshold value for GTV determination, and 30% and 40% SUVmax for nGTV. Further prospective studies on a larger group of patients are needed to determine the best technique for GTV determination using the innovative ^{18}FDG-PET/MR hybrid.