Correlation of Ki-67 Immunohistochemistry with SUV on 18F-FDG PET Uptake in Non-small Cell Lung Cancer

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Background

Ki-67 is a proliferation marker expressed in all phases of the cell cycle (G1, S, G2 and M) except in resting cells and is extensively used to assess proliferation rates of neoplasms. It is associated with high mitotic rate and higher histological grade tumours. Elevated Ki-67 has been reported to be an unfavourable prognostic factor in non-small cell lung cancers. Positron emission tomographic (PET) scanner with 2-^{18}F-fluorodeoxyglucose (FDG) provides physiologic information on glucose uptake and metabolism which is elevated in malignant cells and this effect increases with higher grades of malignancy. PET may provide useful prognostic information because higher-grade tumours, which are associated with poorer survival, exhibit highly elevated levels of 2-^{18}F-FDG uptake. The aim of the present study was to assess the role of standardised uptake value (SUV) on 2-^{18}F-FDG PET/CT in non-small cell lung cancer correlated with proliferative activity assessed by the Ki-67 index.

Methods

This study included 44 patients. All of them had a complete surgical resection at our Institution and were diagnosed based on the WHO classification of non-small cell lung cancer (22 adenocarcinomas including 2 bronchioloalveolar carcinomas, 12 squamous cell carcinomas, 5 large cell carcinomas, 1 typical carcinoid, 1 atypical carcinoid, 1 hamartoma, 1 leiomyosarcoma and 1 mucoepidermoid carcinoma). PET imaging was performed and the maximum standardised uptake value was calculated. Proliferating cell activity as indicated by the Ki-67 index was estimated in a representative section of the surgically resected lung specimen. We compared standardised uptake value with their corresponding Ki-67 index in the total group of tumours, in a subgroup with tumour size at least 2 cm in diameter and in squamous carcinoma and adenocarcinoma subgroup. The amount of Ki-67 positive cells and the standardised uptake values for 2-^{18}F-FDG were compared using linear regression analysis.

Results

2-^{18}F-FDG PET/CT allowed diagnosing the primary tumour in all cases. A low correlation was observed between 2-^{18}F-FDG standardised uptake value and Ki-67 index (r= 0,57; p=0.001) in the total group of 44 patients but a high correlation coefficient was observed in the subgroup of tumour size at least 2 cm in diameter (n=30, r=0,74; p=0.001), similar to previous reports. One case of squamous cell carcinoma with a diameter of 8 mm had Ki-67 rate of 30 % but a low 2-^{18}F-FDG uptake in the tumour (SUV:1'74) (Figure 1). A lymphoepithelioma-like carcinoma had a Ki-67 rate of 80 % and 2-^{18}F-FDG uptake was high in the tumour (SUV: 19) (Figure 2).

In typical carcinoid and hamartoma cases, standardised uptake value was < 2 and Ki-67 was < 1 %.
On the other hand we observed a low correlation coefficient in adenocarcinomas subgroup (n=22; r= 0,32) and in squamous carcinomas subgroup (n=12; r= 0,58) however those results were not statistically significant (p>0.05). A case of bronchioloalveolar carcinoma had a proliferation rate (Ki-67) of 5 % and the PET images showed high 2-^{18}F-FDG uptake in the tumour (SUV:12'1). A coexisting granulomatous lesion had an increased proliferation rate (Ki-67) of 20 % (Figure 3).

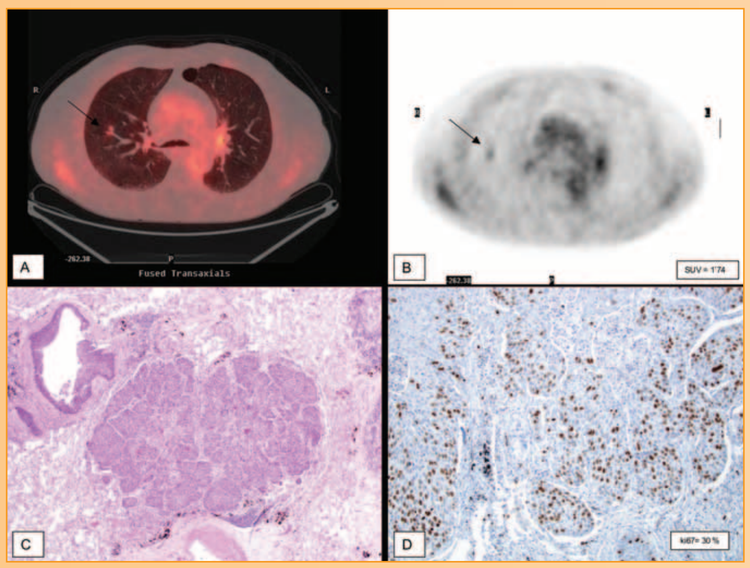

Figure 1. Radiological and immunohistochemical images of a a patient with Squamous cell carcinoma. A and B ^{18}F-FDG PET images demonstrate low FDG uptake in the tumour (SUV: 1'74). C Squamous cell carcinoma (8 mm diameter tumour) D Proliferation rate (Ki-67) of 30 %.

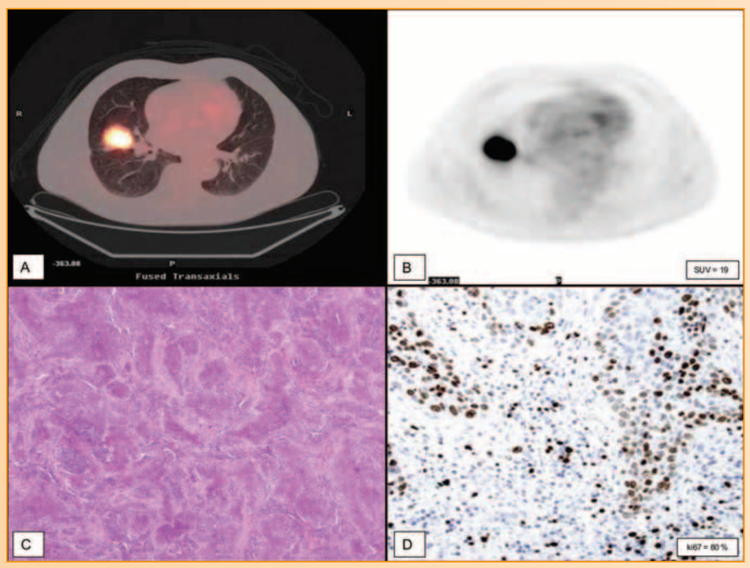

Figure 2. Radiological and immunohistochemical images of a a patient with a lymphoepitelioma-like carcinoma. A and B ^{18}F-FDG PET images demonstrate high FDG uptake in the tumour (SUV: 19). C and D Lymphoepitelioma-like carcinoma with a proliferation rate (Ki-67) of 80 %.

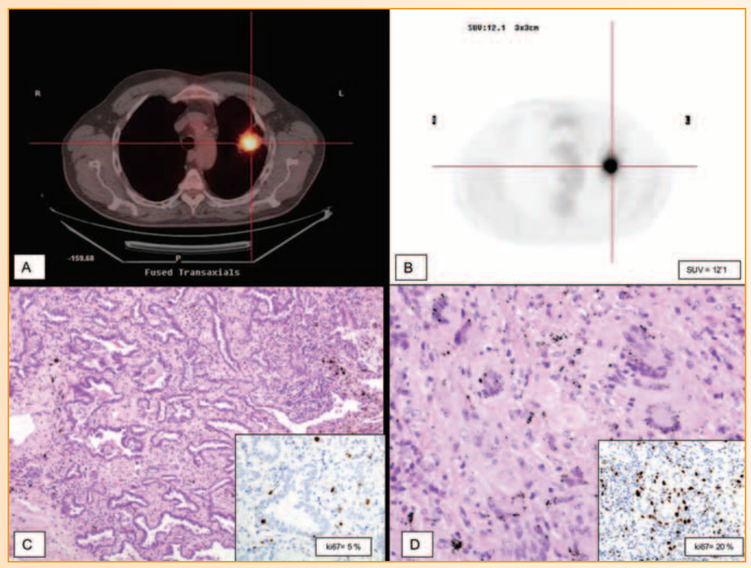

Figure 3. Radiological and immunohistochemical images of a a patient with bronchioloalveolar carcinoma. A and B ^{18}F-FDG PET images demonstrate high FDG uptake in the tumour (SUV: 12'1). C Bronchioloalveolar carcinoma with a proliferation rate (Ki-67) of 5 %. D Granulomatous lesion admixed with the tumour had an elevated proliferation rate (Ki-67) of 20 %.

Conclusions

The results of this preliminary study demonstrated that standardised uptake value on 2-^{18}F-FDG PET correlated significantly with proliferating cell activity assessed by the Ki-67 index, for primary staging in patients with non-small cell lung cancer when cases with tumour size < 2 cm in diameter were excluded.
Standardised uptake value on 2-^{18}F-FDG PET is underestimated in tumours < 2 cm in diameter.

References

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