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Axillary Lymph Node Uptake on ^{18}F-FDG PET/CT after COVID-19 Vaccination: A Direct Comparison Study with Influenza Vaccination

COVID-19 Aşısından Sonra ^{18}F-FDG PET/BT'de Aksiller Lenf Nodu Tutulumu: Grip Aşısı ile Doğrudan Karşılaştırma Çalışması

Yoichi Otomi[1], Takayoshi Shinya[1], Hiroto Kasai[1], Naoko Okada[2], Tomoki Matsushita[1], Kohei Higashi[1], Saya Matsuzaki[1], Yuka Hiroshima[1], Michiko Kubo[1], Hideki Otsuka[1], Masafumi Harada[1]

[1]*Tokushima University Hospital, Department of Radiology, Tokushima, Japan*
[2]*Tokushima Prefectural Central Hospital, Department of Radiology, Tokushima, Japan*

Abstract

Objectives: To compare vaccinated-side axillary lymph node uptake on ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) after coronavirus disease-2019 (COVID-19) and influenza vaccination.

Methods: We retrospectively analyzed 177 patients who underwent ^{18}F-FDG PET/CT after COVID-19 or influenza vaccination. We compared the uptake of the vaccinated-side axillary lymph nodes of 109 COVID-19 vaccinated patients with those of a lot of influenza-vaccinated patients. We also compared the uptake between 66 patients who received the first COVID-19 vaccination with 43 who received the second COVID-19 vaccination.

Results: ^{18}F-FDG-avid axillary lymph nodes on the vaccinated side were significantly more frequently observed in the COVID-19 group (45%) than in the influenza group (19%) ($p<0.001$). When the interval between vaccination to PET/CT was within 7 days, there was no significant difference in the frequency of ^{18}F-FDG-avid vaccinated-side axillary lymph nodes between the groups (COVID-19 group: 41% vs. influenza group: 45%, $p=0.724$). When the interval was over 7 days, ^{18}F-FDG-avid lymph nodes were much more frequent in the COVID-19 group (47%) than in the influenza group (7%) ($p<0.001$). Comparing the first and second COVID-19 groups, ^{18}F-FDG-avid lymph nodes were more frequent in the second vaccination group than in the first vaccination group, but the difference was not significant.

Conclusion: ^{18}F-FDG-avid vaccinated-side axillary lymph nodes were more frequently observed in the COVID-19 group than in the influenza group. In the case of the COVID-19 vaccine, a delay of ^{18}F-FDG PET/CT examination is recommended by a longer interval from vaccination than in the influenza vaccine.

Keywords: COVID-19, influenza, vaccination, ^{18}F-FDG PET/CT, axillary lymph node

Öz

Amaç: Koronavirüs hastalığı-2019 (COVID-19) aşısı ve grip aşısı sonra ^{18}F-florodeoksiglukoz (FDG) pozitron emisyon tomografisi/bilgisayarlı tomografi (PET/BT) ile aşılanan taraf aksiller lenf nodu tutulumunu karşılaştırmaktır.

Yöntemler: COVID-19 veya influenzaya yönelik aşılamadan sonra ^{18}F-FDG PET/BT uygulanan 177 hastayı retrospektif olarak inceledik. COVID-19 aşısı yapılan 109 hastanın aşılanmış taraftaki aksiller lenf nodlarındaki ^{18}F-FDG tutulumunu, grip aşısı yapılan hastalardaki tutulum ile karşılaştırdık. Ayrıca ilk COVID-19 aşısını olan 66 hasta ile ikinci COVID-19 aşısını olan 43 hasta arasındaki alımı karşılaştırdık.

Bulgular: Aşılanan taraftaki ^{18}F-FDG tutulumu olan aksiller lenf nodları, COVID-19 grubunda (%45) influenza grubuna (%19) göre anlamlı derecede daha sık gözlendi ($p<0,001$). PET/BT ile aşılama arasındaki aralık 7 gün içinde olduğunda, gruplar arasında ^{18}F-FDG tutulumu olan aşılı taraf aksiller

Address for Correspondence: Yoichi Otomi MD, Tokushima University Hospital, Department of Radiology, Tokushima, Japan
Phone: +81-88-633-7173 **E-mail:** otomi.yoichi@tokushima-u.ac.jp ORCID ID: https://orcid.org/0000-0002-8960-3662
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lenf nodu sıklığında anlamlı bir fark yoktu (COVID-19 grubu: %41 vs. influenza grubu: %45, p=0,724). Aralık 7 günden fazla olduğunda, ^{18}F-FDG tutulumlu lenf nodları, COVID-19 grubunda (%47) influenza grubuna (%7) göre çok daha sıktı (p<0,001). Birinci ve ikinci COVID-19 grupları karşılaştırıldığında, ^{18}F-FDG tutulumlu lenf nodları ikinci aşılama grubunda birinci aşılama grubuna göre daha sıktı ancak aradaki fark anlamlı değildi.

Sonuç: ^{18}F-FDG tutulumlu aşılanmış taraf aksiller lenf nodları, COVID-19 grubunda influenza grubuna göre daha sık gözlendi. COVID-19 aşısı söz konusu olduğunda, ^{18}F-FDG PET/BT incelemesinin, grip aşısına göre daha uzun bir aralıkla ertelenmesi önerilir.

Anahtar Kelimeler: COVID-19, influenza, aşılama, ^{18}F-FDG PET/BT, aksiller lenf nodu

Introduction

The coronavirus disease-2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus-2 is rampant worldwide (1). Safe and effective vaccines are urgently needed against this disease (2,3). Currently, mass COVID-19 vaccination is being conducted worldwide (4). Recently, there have been many reports of increased uptake of axillary lymph nodes on the vaccinated side on ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) after COVID-19 vaccination (5,6,7,8,9,10,11,12,13). Apart from case reports, there are also comprehensive reports on the frequency and degree of uptake. Some studies have reported differences among the types of COVID-19 vaccines. Before the report of increased axillary lymph node uptake on ^{18}F-FDG PET/CT after COVID-19 vaccination, there were several reports on increased axillary lymph node uptake after influenza vaccination (14,15,16,17). The increased uptake of axillary lymph nodes after seasonal influenza vaccination on ^{18}F-FDG PET/CT has been reported, especially within 1 week after vaccination (14,15). However, in the case of the COVID-19 vaccine, it was observed more than 1 month or 6 weeks after vaccination (12,13). As aforementioned, some studies have compared uptake after influenza vaccination; however, there have been no reports directly comparing the uptake of axillary lymph nodes on ^{18}F-FDG PET/CT after COVID-19 vaccination and after influenza vaccination.

In this study, we compared axillary lymph node uptake on ^{18}F-FDG PET/CT after COVID-19 vaccination with that after influenza vaccination.

Materials and Methods

We retrospectively analyzed 177 patients who underwent ^{18}F-FDG PET/CT after COVID-19 vaccination (BNT162b2 mRNA vaccine, Pfizer) or influenza vaccination. We compared the uptake of the vaccinated side axillary lymph nodes of 109 patients who received COVID-19 vaccine with 68 patients who received influenza vaccine. To investigate the effect of the interval from vaccination to PET examination on the positive accumulation of axillary lymph nodes, the frequency of positive accumulation within 7 days and after 7 or more days was compared for each vaccine.

Before the above comparison, we also compared the uptake of vaccinated side axillary lymph nodes of 66 patients who received the first COVID-19 vaccination with those of 43 patients who received the second COVID-19 vaccination.

Patients

Based on the medical interview sheet for ^{18}F-FDG PET/CT examination, patients were placed in the COVID-19 and influenza vaccine groups. The COVID-19 vaccine group comprised patients who received COVID-19 vaccination within 50 days before undergoing ^{18}F-FDG PET/CT examination from May 10, 2021, to July 5, 2021. The influenza vaccine group comprised patients who received influenza vaccination within 50 days before undergoing ^{18}F-FDG PET/CT examination from October 1, 2020, to December 8, 2020. Patients with insufficient information on the date of vaccination and the vaccinated site were excluded. Patients with hyperglycemia (>150 mg/dL), suspected axillary lymph node metastases, or suspected malignant lymphoma lesions, and those with rheumatoid arthritis were excluded. A total of 109 patients (51 men and 58 women) after COVID-19 vaccination (after the first vaccination: 66 cases, after the second vaccination: 43 cases) and 68 patients after influenza vaccination (24 men and 44 women) were evaluated.

The Ethics Committee of Tokushima University Hospital approved this study (no: 4080). Informed consent was waived owing to the retrospective nature of the study.

^{18}F-FDG PET/CT Scanning

The patients fasted for at least 6 h before the ^{18}F-FDG PET/CT. after that, the patients received an intravenous injection of 3.0 MBq/kg of body weight of ^{18}F-FDG. ^{18}F-FDG PET/CT image acquisition was started 1 h after the ^{18}F-FDG injection with the patient in a relaxed supine position using an integrated PET/CT scanner (Discovery PET/CT 710; GE Healthcare, Milwaukee, WI, USA). A CT scan was obtained from the head to mid-thigh level, using a standardized protocol involving 120 kV, tube-rotation time of 0.6 s per rotation, and section thickness of 3.75 mm, and used for anatomical localization and attenuation correction. The PET acquisition time was 2 min per table position, with 7-9 bed

positions per patient. PET reconstructions were generated using penalized likelihood reconstruction (Q.Clear, GE Healthcare) with a β value of 550. All PET datasets were reconstructed with a 192×192 matrix using an ordered-subset expectation maximization iterative reconstruction algorithm.

Evaluating the ^{18}F-FDG Uptake of the Axillary Lymph Nodes of the Two Groups

A board-certified nuclear medicine physician with PET/CT experience of 12 years evaluated the ^{18}F-FDG PET/CT images. The maximum standardized uptake values (SUV_{max}) of the axillary lymph nodes with the highest uptake, normalized for body weight, were calculated on the viewer (AW server 2.0; GE Healthcare, Milwaukee, WI, USA). Positive axillary lymph node uptake was defined as a ratio ≥1.5 between SUV_{max} on the vaccinated side and the contralateral side, a method previously used (11,16). The size of the largest hypermetabolic lymph node was also measured on CT images in millimeters in short-axis diameter.

Statistical Analysis

Categorical variables are expressed as frequencies and percentages. Continuous variables are expressed as mean ± standard deviation. The normality of the distribution of variables was tested using Levene's test. The Student's t-test for normally distributed data and Welch's t-test or chi-square test for non-normally distributed data were applied to evaluate the differences in the variables. All statistical tests were performed using the SPSS Statistics software version 25 (IBM, Armonk, NY, USA). For all comparisons, a p value of < 0.05 was considered statistically significant.

Results

A comparison of the clinical characteristics related to PET/CT and vaccination of 66 patients from the post-first COVID-19 vaccination group and 43 from the post-second COVID-19 vaccination group are shown in Table 1. Sex, weight, height, blood glucose, ^{18}F-FDG dose on PET/CT examination, time interval PET/CT examination from last vaccination, rate of PET/CT examinations within 7 days from the last vaccination, and injected side of the upper arm of the vaccine were not significantly different between the two groups. The rate of patients with ^{18}F-FDG-avid axillary lymph nodes on the vaccinated side in the post-second COVID-19 vaccine group was higher than that in the post-first COVID-19 vaccine group, but not significantly (p=0.148). The average SUV_{max} of the ^{18}F-FDG-avid axillary lymph nodes on the vaccinated side in the second COVID-19 vaccine group was slightly higher than that in the first COVID-19 vaccine group, but not significantly (p=0.630). The average short-axis of the largest ^{18}F-FDG-avid axillary lymph nodes on the vaccinated side in the first and second COVID-19 vaccine groups was not significantly different (p=0.815).

The details of the clinical characteristics related to PET/CT and vaccination of 109 patients from the COVID-19 vaccine group and 68 from the influenza vaccine group are shown in Table 2. Patient age, sex, weight, height, blood glucose, ^{18}F-FDG dose, interval time to PET/CT exam from the last vaccination, and the rate of PET/CT examinations

Table 1. Comparison of post-first and-second COVID-19 vaccination groups

	Post first COVID-19 vaccination group (n=66)	Post second COVID-19 vaccination group (n=43)	p value
Patient age, years	72.2±8.6	69.5±13.2	0.240
Sex			
Female	35	23	0.132
Male	31	20	
Weight (kg)	55.3±10.2	56.7±10.0	0.473
Height (cm)	158.2±8.7	158.4±7.5	0.918
Blood glucose (mg/dL)	104.4±14.4	101.4±15.7	0.310
^{18}F-FDG (MBq)	165.9±31.2	168.8±31.0	0.630
Time interval to PET/CT exam from the last vaccination, days	12.0±7.8	15.5±11.9	0.094
Within 7 days from the last vaccination	18 (27%)	14 (33%)	0.554
Injected side of upper arm			
Right	7 (11%)	10 (23%)	0.075
Left	59 (89%)	33 (77%)	
Patients with ^{18}F-FDG-avid axillary LN of vaccinated-side	26 (39%)	23 (53%)	0.148
SUV_{max} of ^{18}F-FDG-avid axillary LN of vaccinated-side	5.1±2.9	5.5±3.1	0.630
Short-axis of the largest ^{18}F-FDG-avid axillary LN of vaccinated-side (mm)	5.3±1.4	5.2±1.5	0.815

Data are presented as mean ± standard deviation. Statistical significance was set at p<0.05. COVID-19: Coronavirus disease-2019; FDG: Fluorodeoxyglucose, LN: Lymph node, SUV_{max}: Maximum standardized uptake value

Table 2. Comparison of COVID-19 and influenza vaccination groups

	COVID-19 vaccine group (n=109)	Influenza vaccine group (n=68)	p value
Patient age, years	71.1±10.6	67.3±13.7	0.056
Sex			
Female	58	44	0.132
Male	51	24	
Weight (kg)	55.8±10.1	57.6±13.7	0.363
Height (cm)	158.3±8.2	157.1±9.1	0.402
Blood glucose (mg/dL)	103.2±14.9	103.4±17.3	0.957
PET/CT indication			
Lung malignancy	23 (21%)	13 (19%)	
Breast malignancy	21 (19%)	21 (31%)	
Head and neck malignancy	18 (17%)	10 (15%)	
Digestive/gastrointestinal malignancy	12 (11%)	9 (13%)	
Hematological malignancy	7 (6%)	4 (6%)	
Gynecological malignancy	5 (5%)	4 (6%)	
Genitourinary malignancy	4 (4%)	4 (6%)	
Musculoskeletal malignancy	4 (4%)	1 (1%)	
Others	15 (14%)	2 (3%)	
^{18}F-FDG (MBq)	167.0±31.0	175.3±44.3	0.179
Interval time to PET/CT exam from the last vaccination, days	13.4±9.7	16.7±11.8	0.053
Within 7 days from the last vaccination	32 (29%)	22 (32%)	0.674
Injected side of the upper arm			
Right	17	20	0.028*
Left	92	48	
Patients with ^{18}F-FDG-avid axillary LN on the vaccinated-side	49 (45%)	13 (19%)	<0.001*
SUV_{max} of ^{18}F-FDG-avid axillary LN on the vaccinated-side	5.3±3.0	4.4±3.3	0.319
Short-axis of the largest ^{18}F-FDG-avid axillary LN on the vaccinated-side (mm)	5.2±1.4	5.0±1.6	0.647

Data are presented as mean ± standard deviation. *Statistical significance was set at p<0.05. COVID-19: Coronavirus disease-2019; FDG:Fluorodeoxyglucose, LN: Lymph node, SUV_{max}: Maximum standardized uptake value

within 7 days of the last vaccination were not significantly different between the two groups. There was a significant difference in the vaccine-injected side of the upper arm between the two groups. The number of patients with ^{18}F-FDG-avid axillary lymph nodes on the vaccinated side in the COVID-19 and influenza vaccine groups was 49 (45%) and 13 (19%), respectively (p<0.001).

The average SUV_{max} of the ^{18}F-FDG-avid axillary lymph node on the vaccinated side in the COVID-19 vaccine group was higher than that in the influenza vaccine group, but the difference was not significant (p=0.319). The average short-axis of the largest ^{18}F-FDG-avid axillary lymph node on the vaccinated side in the COVID-19 vaccine group was slightly larger than that in the influenza vaccine group, but not significantly (p=0.647). A comparison of the number of cases of ^{18}F-FDG-avid axillary lymph nodes on the vaccinated side by the interval from the last vaccination in the COVID-19 and influenza vaccine groups is shown in Table 3. Thirteen of the 32 patients (41%) with PET/CT performed within 7 days from the last vaccination in the COVID-19 vaccine group showed ^{18}F-FDG-avid axillary lymph node on the vaccinated side. Ten of the 22 patients (45%) with PET/CT performed within 7 days from the last vaccination in the influenza vaccine group showed ^{18}F-FDG-avid axillary lymph nodes on the vaccinated side. There was no significant difference between the two groups (p=0.724). Thirty-six of the 77 patients (47%) with PET/CT performed after over 7 days from the last vaccination in the COVID-19 vaccination group showed ^{18}F-FDG-avid axillary lymph nodes of the vaccinated side. Three of the 46 patients (7%) with PET/CT performed after over 7 days from the last vaccination in the influenza vaccination group showed ^{18}F-FDG-avid axillary lymph node on the vaccinated

Table 3. Comparison of the number of cases of ^{18}F-FDG-avid axillary LNs on the vaccinated-side by time interval from the last vaccination to PET/CT in COVID-19 and influenza vaccination groups

	COVID-19 vaccine group (n=109)	Influenza vaccine group (n=68)	p value
0-7 days			
^{18}F-FDG-avid axillary LN (+)	13 (41%)	10 (45%)	0.724
^{18}F-FDG-avid axillary LN (-)	19 (59%)	12 (55%)	
>7 days			
^{18}F-FDG-avid axillary LN (+)	36 (47%)	3 (7%)	<0.001*
^{18}F-FDG-avid axillary LN (-)	41 (53%)	43 (93%)	

Data are presented as mean ± standard deviation. *Statistical significance was set at p<0.05. COVID-19: Coronavirus disease 2019, FDG: Fluorodeoxyglucose, LN: Lymph node

side. There was a significant difference between the two groups (p<0.001).

Figure 1 shows the PET/CT images of a patient after COVID-19 vaccination showing ^{18}F-FDG-avid vaccinated-side axillary lymph node. Figure 2 shows the PET/CT images of a patient after influenza vaccination showing ^{18}F-FDG-avid vaccinated-side axillary lymph node.

Discussion

^{18}F-FDG-avid axillary lymph node of the vaccinated side on PET/CT was significantly more frequent in the patients after COVID-19 vaccination than in those after influenza vaccination. Of the total, 45% of the patients showed ^{18}F-FDG-avid axillary lymph node on the vaccinated-side on PET/CT after COVID-19 vaccination and 19% of the patients after influenza vaccination. In a previous study, the frequency of ^{18}F-FDG-avid axillary lymph nodes on the vaccinated side on PET/CT after COVID-19 vaccination (Pfizer-BioNTech) was reported to be 43% (12). In another study, the type of COVID-19 vaccine was not specified, but the frequency of uptake was 45% (11). Yet another study reported a frequency of 45.6% (9). The results of COVID-19 vaccination in our study were similar to previous reports. Burger et al. (17) reported that 17 of the 58 (29.3%) patients who were vaccinated for influenza within 4 weeks before PET/CT (mean, 14.5±8.7 days) had ^{18}F-FDG-avid vaccinated-side axillary lymph nodes. The frequency of 29.3% in the previous report was higher than the result of our study on influenza vaccination. Skawran et al. (12) reported that ^{18}F-FDG PET/CT after COVID-19 vaccination had a higher frequency of ^{18}F-FDG-avid axillary lymph node compared with the findings of a previous paper on PET/CT after influenza vaccination. Since our study was a comparison between the axillary lymph node uptake after COVID-19 vaccination and influenza vaccination under the same imaging conditions with the same equipment in the same facility, the comparison of values, such as the frequency and SUV_{max} could be more accurate.

In comparison with PET examinations within 7 days from the last vaccination, there was no significant difference in the frequency of ^{18}F-FDG-avid axillary lymph nodes on the vaccinated side between the COVID-19 and influenza groups. On PET/CT, 41% of the patients showed ^{18}F-FDG-avid axillary lymph nodes on the vaccinated side after COVID-19 vaccination and 45% of the patients after influenza vaccination. However, compared with PET examinations over 7 days from the last vaccination, there was a significant difference in the frequency of ^{18}F-FDG-

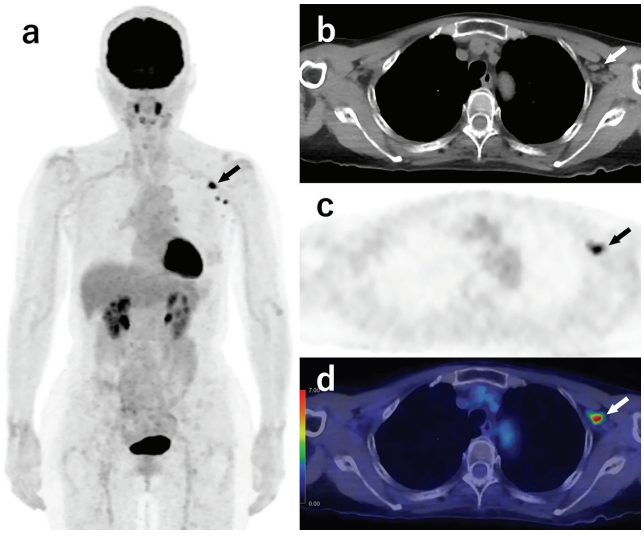

Figure 1. (a) MIP, (b) CT, (c) PET, and (d) fused PET/CT. ^{18}F-FDG PET/CT images of the representative case of a 67-year-old female in which ^{18}F-FDG uptake was observed in the axillary LN on the ipsilateral side to the COVID-19 vaccination arm (arrows). The interval time from vaccination to PET/CT exam was 19 days. The SUV_{max} was 11.2. The size of the largest hypermetabolic LN was 4.2 mm in short-axis diameter
MIP: Maximum intensity projection, PET: Positron emission tomography, CT: Computed tomography, FDG: Fluorodeoxyglucose, LN: Lymph node, COVID-19: Coronavirus disease-2019, SUV_{max}: Maximum standardized uptake value

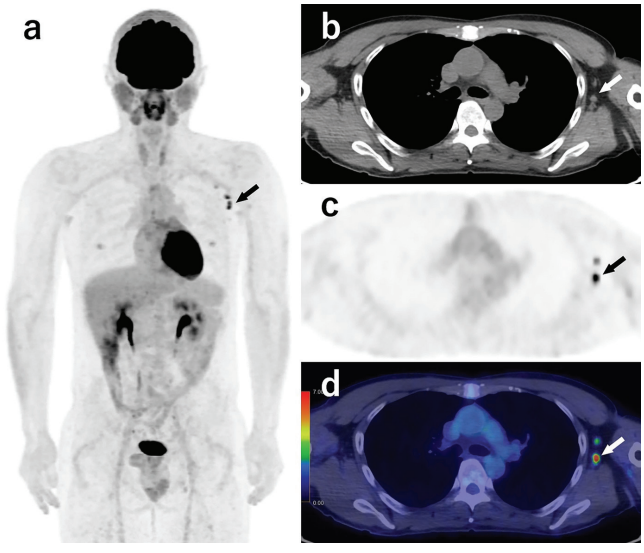

Figure 2. (a) MIP, (b) CT, (c) PET, and (d) fused PET/CT. ^{18}F-FDG PET/CT images of the representative case of a 39-year-old male in which ^{18}F-FDG uptake was observed in the axillary LN on the ipsilateral side to the influenza vaccination arm (arrows). The interval time from vaccination to PET/CT exam was 3 days. The SUV_{max} was 7.7. The size of the largest hypermetabolic LN was 5.2 mm in short-axis diameter
MIP: Maximum intensity projection, PET: Positron emission tomography, CT: Computed tomography, FDG: Fluorodeoxyglucose, LN: Lymph node, COVID-19: Coronavirus disease-2019, SUV_{max}: Maximum standardized uptake value

avid axillary lymph nodes on the vaccinated-side between the COVID-19 and influenza groups. Of the total, 47% of the patients showed ^{18}F-FDG-avid axillary lymph nodes on the vaccinated-side on PET/CT after COVID-19 vaccination and 7% of the patients after influenza vaccination.

Although ^{18}F-FDG PET/CT after COVID-19 vaccination had a higher frequency of ^{18}F-FDG-avid vaccinated-side axillary lymph nodes than that after influenza vaccination, there was no difference in the frequency of ^{18}F-FDG-avid vaccinated-side axillary lymph nodes on PET/CT examination in the COVID-19 vaccine group and the influenza vaccine group when the PET/CT was performed within 7 days after the vaccine. When there were long intervals of more than 7 days from vaccination to examination, ^{18}F-FDG-avid vaccinated-side axillary lymph nodes on PET/CT were much more frequently observed in the COVID-19 vaccine group than in the influenza vaccine group, suggesting that the lymphadenopathy status could last longer in COVID-19 vaccination. This could be the reason why PET/CT examination after COVID-19 vaccination showed a higher positive rate of axillary lymph nodes on the vaccinated side than after influenza vaccination. In addition to the frequency, we compared the SUV_{max} and size of the axillary lymph nodes in the COVID-19 and influenza groups and found that the SUV_{max} was higher and the size was slightly larger in the COVID-19 vaccination group than in the influenza group, although the difference was not significant. Based on these results, in the case of the COVID-19 vaccine, it should be better to leave a longer period from vaccination to ^{18}F-FDG PET/CT examination than in the case of the influenza vaccine. In the case of COVID-19 vaccination, ^{18}F-FDG PET/CT examination after vaccination should probably be performed with a delay of several weeks to one month or more if there is little risk of the progression of the disease. Ferrari et al. (18) recommended that, if possible, ^{18}F-FDG PET/CT be examined at least 20 days after vaccination because the frequency of vaccine-related ^{18}F-FDG-avid lymph nodes decreases when the period from COVID-19 vaccination to ^{18}F-FDG PET/CT examination exceeds 20 days. Additionally, the National Comprehensive Cancer Network guidelines recommend the delay in imaging studies by 4 to 6 weeks following the COVID-19 vaccine if it does not result in a delay that will affect patient outcomes (19). To perform ^{18}F-FDG PET/CT examination at an appropriate time to evaluate lymph nodes more correctly, it is necessary to correctly grasp the vaccination date and information on the vaccination-side in advance.

The frequency of ^{18}F-FDG-avid axillary lymph nodes on the vaccinated side in the post-second COVID-19 vaccine group was higher than that in the post-first COVID-19 vaccine group, but not significantly (53% in the second vaccination vs. 39% in the first vaccination group). Cohen et al. (9) reported that the frequency was significantly higher after the second vaccination (45.8%) than after the first vaccination (26.3%). In contrast, Skawran et al. (12) reported that the frequency was not significant in the Pfizer-BioNTech COVID-19 vaccination (44% after the second vaccination vs. 39% after the first vaccination). In addition to the frequency, we compared the SUV_{max} and size of the axillary lymph node in the post-first and post-second COVID-19 vaccine groups and found that the SUV_{max} was slightly higher in the post-second COVID-19 vaccination group than in the first group. There were no significant differences between the groups. The size was similar in both the groups.

Study Limitations

This study had some limitations. First, there was a selection bias because of the retrospective nature of the study. Second, the subject of this study was a PET/CT examination performed for cancer treatment, the results of which might be different from those of healthy individuals. The association between vaccinated-side axillary lymph node uptake, immune status, and hematologic malignancy has been reported in COVID-19 vaccinatio; however, but our study might include the effects of these factors (11,20). However, despite these limitations, this study is the first to directly compare vaccinated-side axillary lymph node uptake on ^{18}F-FDG PET/CT after COVID-19 vaccination and after influenza vaccination. This study revealed that there was no difference in the frequency of vaccinated-side axillary lymph node uptake on PET/CT examinations after COVID-19 vaccination and after influenza vaccination for a relatively short time interval of 7 days after the vaccination. It also revealed that the frequency was much higher on PET/CT after COVID-19 vaccination than after influenza vaccination for a longer interval time of over 7 days between the PET/CT and the vaccination. A more accurate interpretation of the axillary region could be expected by understanding the characteristics and differences of each type of vaccine, such as the frequency, uptake degree, and size of axillary lymph node uptake after vaccination.

Conclusion

There is no significant difference in the frequency of the ^{18}F-FDG-avid vaccinated-side axillary lymph nodes, SUV_{max}, or size between the first and second COVID-19 vaccinations. Therefore, careful interpretation of vaccinated-side axillary lymph nodes in ^{18}F-FDG PET/CT images after vaccination is required in both the first and second COVID-19 vaccinations.

To avoid false positives in the axillary lymph nodes, it is important to confirm the date of the recent vaccination

when scheduling an ^{18}F-FDG PET/CT examination. In the case of influenza vaccine, ^{18}F-FDG PET/CT examination should be performed at an interval of at least one week or more from vaccination. In the case of COVID-19 vaccine, ^{18}F-FDG PET/CT examination should probably be performed at a longer interval of several weeks to one month or more from vaccination. However, there are many cases where the early performance of ^{18}F-FDG PET/CT is necessary because treatment is urgent. In that case, it is better to perform without waiting.

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Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of Tokushima University Hospital (no: 4080).

Informed Consent: Informed consent was waived owing to the retrospective nature of the study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Medical Practices: Y.O., H.K., N.O., T.M., K.H., S.M., Y.H., M.K., Concept: Y.O., T.S., Design: Y.O., M.H., Data Collection, or Processing: Y.O., T.S., H.O., Analysis, or Interpretation: Y.O., T.S., M.K., H.O., M.H., Literature Search: Y.O., H.K., N.O., T.M., K.H., S.M., Writing: Y.O.

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