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Unilateral Axillary Lymphadenopathy Frequency and Follow-up Results After Inactivated COVID-19 Vaccination

İnaktive COVID-19 Aşısı Sonrası Unilateral Aksiller Lenfadenopati Sıklığı ve Takip Sonuçları

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Öz

Aşılarının yaygınlaşmasıyla birlikte aşıya bağlı ipsilateral aksiller lenfadenopati ile karşılaşılabilmektedir. Çalışmanın amacı inaktive COVİD-19 aşısı sonrası aksiller lenfadenopati sıklığını, lenf bezlerinin sonografik özelliklerini ve takip sonuçlarını değerlendirmektir. Mart-Nisan 2021 tarihleri arasında gerçekleştirilen prospektif çalışmaya toplam 127 katılımcı dahil edilmiştir. Tanımlayıcı ve çıkarımsal istatistiksel analizler SPSS kullanılarak gerçekleştirilmiştir. İkinci doz aşılamadan sonra 10-16 günlük süreçte 127 katılımcının (39.92±8.96 yaşında, %68.5'i erkek) ultrasonografi ile aksiller lenf nodu durumu değerlendirildi. Toplam 32 katılımcıda (%25.2) ilk ultrasonda ipsilateral aksiller lenfadenopati görüldü. Bu hastalardan yalnızca birinde 30 gün sonraki kontrol ultrasonda sebat eden lenfadenopati görüldü. Lenf nodu korteks kalınlığı en kalın yerinde aşılanan tarafta (2.63±2.12 mm) karşı tarafa (1.53±1.11 mm) göre anlamlı derecede yüksekti (p<.001). Lenfadenopati sayısı aşılanan tarafta karşı tarafa göre daha yüksekti (p<.001). Ayrıca COVİD-19 öyküsü ile ipsilateral lenfadenopati bulunmaması arasında anlamlı ilişki mevcuttu (p<.001). Lokal bir yan etki olarak inaktive COVİD-19 aşısının ikinci dozu sonrasında ipsilateral aksiller lenfadenopati görülebilmekte ve genellikle 1 ay içinde gerilemektedir. Ancak daha önce COVİD-19 enfeksiyonu geçiren bireylerde aşı sonrası aksiller lenfadenopati beklenmemektedir. Aksillayı ilgilendiren radyolojik incelemelerden önce hem enfeksiyon hem de aşılama geçmişinin bilinmesi, radyoloğun lenf nodu durumunu yanlış yorumlanmasını engelleyecektir. Aşıya bağlı ipsilateral aksiller lenfadenopatinin, koronavirus enfeksiyon öyküsü olmayan bireylerde inaktif COVİD-19 aşıları sonrasında görülebileceği ve tespit edildikten bir ay sonra çoğunlukla kaybolduğu akılda tutulmalıdır.

Anahtar Kelimeler: Aşılama, Covid-19, Kortikal Kalınlık, Lenfadenopati, Ultrasonografi

Abstract

Vaccine-induced ipsilateral axillary lymphadenopathy can be encountered with the widespread application of COVID-19 vaccines. The study aims to evaluate the frequency of axillary lymphadenopathy, sonographic features of axillary lymph nodes after administration of inactivated COVID-19 vaccine, and follow-up results. Between March and April 2021, a total of 127 participants were enrolled in this prospective study. Data were analyzed using both descriptive and exploratory test techniques with SPSS. A total of 127 participants (39.92±8.96 years, 68.5% men), who were between 10-16 days after the second dose vaccination, were evaluated for axillary lymph node status by initial ultrasound. A total of 32 participants (25.2%) had ipsilateral axillary lymphadenopathy in the initial ultrasound. Only one of these patients had persistent lymphadenopathy on the control ultrasound 30 days later. The widest cortical thickness was significantly higher on the ipsilateral side (2.63±2.12 mm) compared to the contralateral side (1.53±1.11 mm) (p<.001). The number of lymphadenopathies was higher on the vaccinated side compared to the contralateral side (p<.001). A significant relationship between the history of COVID-19 infection and the absence of ipsilateral lymphadenopathy was found (p<.001). As a local adverse effect, ipsilateral axillary lymphadenopathy following the second dose of inactivated COVID-19 vaccine can be seen, and it usually regresses within a month. However, during that period, axillary lymphadenopathy is not expected in vaccinated individuals who previously experienced COVID-19 infection. Awareness and questioning of both infection and vaccination history before radiological examinations involving the axilla should help the radiologist avoid the misinterpretation of lymphadenopathy. It should be kept in mind that vaccine-induced ipsilateral axillary lymphadenopathy can be seen after inactivated COVID-19 vaccines in individuals who don't have a history of coronavirus infection, and it regresses a month later after detection.

Keywords: Vaccination, Covid-19, Cortical Thickness, Lymphadenopathy, Ultrasound

Introduction

With the widespread usage of inactivated or mRNA COVID-19 vaccines worldwide, different side effects of vaccination have been identified (1,2). One of these side effects is vaccine-induced lymphadenopathy following deltoid vaccination administration. The axilla is one of the most common regions where lymphadenitis can be observed from 1 to 3 weeks after vaccine injection. Lymph node changes typically begin on the 8th day after vaccination, with maximal antibody response reached 15 days after vaccine administration (3). Vaccine-induced ipsilateral axillary lymphadenopathy has been detected using various imaging modalities such as ultrasound, CT, MRI, or FDG PET/CT following COVID-19 vaccine administration. This phenomenon poses diagnostic challenges, complicates patient management, leads to unnecessary biopsies or treatments, and causes patient anxiety (4-7). Understanding the frequency of axillary lymph node enlargement and its imaging features after COVID-19 vaccination should assist radiologists in interpreting findings. Additionally, awareness of vaccine-induced axillary

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lymphadenopathy among both radiologists and clinicians aids in scheduling radiological examinations and evaluating results for patient management. Most cases of ipsilateral axillary lymphadenopathy following deltoid mRNA COVID-19 vaccination have been observed primarily during breast screening or imaging of oncologic patients with PET-CT. The reported lymph nodes with pathological imaging features were almost exclusively observed after vaccination with mRNA COVID-19 vaccines (8). In a study, vaccine-associated hypermetabolic lymphadenopathy in PET-CT occurs more commonly after mRNA vaccination compared to inactivated vaccination (9). In a retrospective study, it is shown that mild and diffuse lymph node cortical thickness can be detected using ultrasound following administration of inactivated COVID-19 vaccines even when there are no clinical signs of lymph node enlargement (10). The study aims to evaluate the frequency of axillary lymphadenopathy, sonographic features of axillary lymph nodes, and follow-up results following administration of the inactivated SARS-CoV-2 vaccine (CoronaVac).

Material and Method

Muğla Sıtkı Koçman University Medical Faculty Ethics Committee approved this study (Approval Reference Date and Number: 31.03.2021 and 7/II). Informed consent was obtained from all volunteers before the ultrasound examination. Study participants were selected using the quota sampling method. Between March and April 2021, a total of 127 participants were enrolled in this prospective study. The study included participants who were between 10-16 days after receiving the second dose of the CoronaVac vaccine. Exclusion criteria were as follows: participants under 18 years of age, participants with a known history of immunodeficiency or malignancy, participants with a history of rheumatological diseases that could affect axillary lymph nodes, and participants with a history of axillary surgery. Real-time ultrasound examinations of all participants were performed by the same radiologist with 12 years of experience. A second radiologist with 15 years of experience reviewed all the images, and both radiologists reached a consensus on the final results of lymph node status, whether lymphadenopathy was present or not.

Lymph nodes were classified and grouped as reactive or pathological based on the sonographic features described by Bedi et al. The cutoff value for lymphadenopathy was described as 3 mm (11). If a lymph node had cortical thickness less than 3 mm with an oval shape and visible echogenic hilum, it was described as a reactive lymph node. If the lymph node had cortical thickness more than 3 mm, didn't have a visible hilum, or was spherical shaped, it was noted as a pathological lymph node. The radiologists evaluated the lymph node status by considering both cortical thickness and morphological features of the lymph nodes. In case of disagreement between the radiologists, the lymph node was considered pathological. For both axillary regions, the short and long axis, cortical thickness and the number of reactive lymph nodes, the number and cortical thickness of spherical lymph nodes, and, also the short and long axis, cortical thickness, and the number of lymphadenopathies were separately measured. Then the widest cortical thickness of the lymph nodes containing both the reactive lymph node and lymphadenopathies for each axilla was noted for each patient. The pathological lymph node number, and the status of the axilla as positive or negative for the lymphadenopathy were also evaluated. The third radiologist (having a 3 year-experience) noted the age, weight, height of the patients, the site of the vaccination, presence, and duration of pain after vaccination, and history of a palpable mass detected by the patient.

If lymphadenopathy is detected on the initial ultrasound, participants are invited for a follow-up ultrasound a month later, following the recommendations of the Society of Breast Imaging Patient Care and Delivery Committee (12). The same radiologist performed the follow-up ultrasound without knowledge of the previous axillary status and recorded the same parameters. The contralateral axilla was used as a control group in our study.

Statistical Analysis

The distributions of the measured variables were assessed using the Shapiro-Wilk test for normality. Group-wise differences were evaluated with a t-test if the normality assumption was met, and with the Mann-Whitney U test if the normality assumption was violated. The Wilcoxon test was used to compare two related samples when the data were not normally distributed. Additionally, to explore the relationship between the number of lymph nodules, age, and BMI, the Pearson correlation coefficient was calculated. The relationship between categorical variables was examined using the Chi-square test to identify differences between sub-categories. Results were presented as mean and standard deviation for parametric data and as mean, median, and interquartile range for non-parametric data. Statistical analyses were performed using SPSS version 25 (developed by SPSS Incorporated, located in Chicago, Illinois, USA). The significance level was set at $p<.05$.

Results

A total of 127 participants, comprising 68.5% (87) men and 31.5% (40) women, participated in our study. Eleven volunteers were excluded from the study due to bilateral vaccination (n=4), history of

breast cancer (n=3), known axillary lymph node enlargement before vaccination (n=2), and a history of rheumatological diseases (n=2). The average age was recorded as 39.92±8.96 years. Among the participants, 30 (23.6%) had a history of COVID-19, while 97 (76.4%) had a negative history. Nineteen of them had mild, nine had moderate, and two had severe COVID-19 infection. For participants with a history of COVID-19, the time between the first diagnosis and the initial ultrasound for the study was found to be 96.6±20.5 days. Following the second dose of vaccination, the time between vaccination and the initial ultrasound examination ranged from 10 to 16 days, with a mean of 13.65±1.21 days. After the second vaccination of CoronaVac, the initial ultrasound revealed that a total of 38 patients (29.92%) had axillary lymphadenopathy. Of the participants, 25.2% (n=32) had only ipsilateral axillary lymphadenopathy on the injection side, while five participants had bilateral axillary lymphadenopathy, and only one participant had contralateral axillary lymphadenopathy on the initial ultrasound. For the contralateral side of the axilla, a total of six participants (4.72%) had lymphadenopathy.

The Chi-square test revealed no difference in terms of ipsilateral and contralateral lymph node status among male and female participants (p=0.487, 0.423, respectively). The relationship between age and contralateral axillary reactive lymph node cortex thickness is negative, with a low correlation coefficient of r=-0.222, and a significance level of p<0.05. Moreover, ipsilateral and contralateral axillary reactive lymph node cortex thickness exhibited a positive and moderate correlation, with a correlation coefficient of r=0.408 and a significance level of p<0.01.

According to the t-test results, the measured variables of "long axis of reactive lymph nodes and also short axis, long/short axis ratio, and cortical thickness of both the reactive lymph nodes and lymphadenopathy" were not significantly different between vaccinated ipsilateral and contralateral axilla. However, "the widest cortical thickness of all the lymph nodes in the axilla" was significantly higher in the "ipsilateral vaccinated side" group, with a mean of 2.63±2.12 compared to the "contralateral side" group, with a mean of 1.53±1.11 at p<0.001 (Table 1).

Table 1. Descriptives of parametric variables and group-wise differences in initial ultrasound

Variable	Group	Mean	SD	MD	95%CI Lower	95%CI Upper	*p*
long axis of RL (mm)	Ipsilateral	16.57	4.77	-0.79	-2.32	0.73	.306
	Contralateral	17.37	5.91				
short axis of RL (mm)	Ipsilateral	7.25	1.86	-0.01	-0.57	0.56	.984
	Contralateral	7.26	2.12				
widest cortical thickness of RL (mm)	Ipsilateral	1.96	0.58	0.15	-0.01	0.31	.061
	Contralateral	1.80	0.55				
long/short axis ratio of RL	Ipsilateral	2.34	0.63	-0.08	-0.26	0.09	.352
	Contralateral	2.43	0.60				
short axis of LP (mm)	Ipsilateral	8.06	1.85	-0.27	-2.00	1.46	.753
	Contralateral	8.33	2.32				
cortical thickness of LP (mm)	Ipsilateral	3.95	0.75	0.54	-0.09	1.17	.093
	Contralateral	3.42	0.26				
long/short axis ratio of LP	Ipsilateral	2.27	0.58	-0.05	-0.56	0.46	.841
	Contralateral	2.32	0.47				
widest cortical thickness of all the lymph nodes in the axilla (mm)	Ipsilateral	2.63	2.12	1.10	0.68	1.52	.000
	Contralateral	1.53	1.11				

RL: Reactive lymph node, LP: Lymphadenopathy, Ipsilateral: Vaccinated side, Contralateral: Non-vaccinated side, SD: Standard Deviation, MD: Mean Difference, CI: Confidence Interval

On the other hand, "the number of reactive lymph nodes" and "the long axis of lymphadenopathy" were not found to be different between the "vaccinated side" and "other side" groups according to the Mann-Whitney U test. Nevertheless, the number of lymphadenopathies was significantly higher in the "vaccinated side" (0,1) compared to the "contralateral side" (0,0) at p<0.001, as detailed in Table 2.

Table 3 presents the number of observations in each group and indicates if there is a significant relationship between the groups, with the corresponding p-value on the right-hand side. We observed that "lymphadenopathy with thickened cortex" and "spheric lymph nodes" were more commonly observed on the vaccinated side,

accounting for 84.2% and 91.7% of the total, respectively. Moreover, the "status of axilla" was predominantly characterized as "lymphadenopathy" (86%) on the vaccinated side compared to the contralateral side (only 14%). Furthermore, the presence of pain in the arm was investigated in cases of "ipsilateral lymphadenopathy with thickened cortex". The results indicated that there was no arm pain in 81% (n=77) of cases with "lymphadenopathy", but arm pain was present in 19% (n=18) of cases. Additionally, when "lymphadenopathy with thickened cortex" was present, arm pain was absent in 59.4% (n=19) of cases, and present in 40.6% (n=13) of cases (p=0.014). There was a statistically significant relationship between COVID-19 history and the absence of ipsilateral lymphadenopathy with thickened cortex, as shown in Table 4 (p<0.001).

Table 2. Descriptives of non-parametric variables and group-wise differences in initial ultrasound

Variable	Group	Mean	Median	IQR	*p*
Number of RL	Ipsilateral	1.86	2	1.5	.947
	Contralateral	1.85	2	1.75	
The long axis of LP (mm)	Ipsilateral	18.06	17	6	.559
	Contralateral	18.83	20	8.25	
Number of thickened cortex lymh node	Ipsilateral	0.34	1	1	.000
	Contralateral	0.06	1	1	
Number of LP (with spherical lymph nodes)	Ipsilateral	0.43	0	1	.000
	Contralateral	0.07	0	0	

IQR:Interquartile range, RL: Reactive lymph node, LP: Lymphadenopathy

Table 3 presents the number of observations in each group and indicates if there is a significant relationship between the groups, with the corresponding p-value on the right-hand side. We observed that "lymphadenopathy with thickened cortex" and "spheric lymph nodes" were more commonly observed on the vaccinated side, accounting for 84.2% and 91.7% of the total, respectively. Moreover, the "status of axilla" was predominantly characterized as "lymphadenopathy" (86%) on the vaccinated side compared to the contralateral side (only 14%). Furthermore, the presence of pain in the arm was investigated in cases of "ipsilateral lymphadenopathy with thickened cortex". The results indicated that there was no arm pain in 81% (n=77) of cases with "lymphadenopathy", but arm pain was present in 19% (n=18) of cases. Additionally, when "lymphadenopathy with thickened cortex" was present, arm pain was absent in 59.4% (n=19) of cases, and present in 40.6% (n=13) of cases (p=0.014). There was a statistically significant relationship between COVID-19 history and the absence of ipsilateral lymphadenopathy with thickened cortex, as shown in Table 4 (p<0.001).

The measured variables of "ipsilateral axillary reactive lymph node cortex thickness", "ipsilateral axillary lymphadenopathy with thickened cortex", "contralateral axillary reactive lymph node cortex thickness", and "contralateral axillary lymphadenopathy with thickened cortex" were found to be 2.00±0.57, 4.08±0.79, 1.79±0.55, and 3.46±0.27 for females, and 1.85±0.59, 3.63±0.54, 1.83±0.55, and 3.2±n/a for males, respectively. Moreover, the differences between the two genders in these variables were not statistically significant, with p-values of 0.231, 0.132, 0.745, and 0.429, respectively.

Table 3. Number of observations for the vaccinated ipsilateral and contralateral side

		Group		
		Ipsilateral % (n)	Contralateral side % (n)	*p*
Reactive Lymph node	No	49.2% (30)	50.8% (31)	.883
	Present	50.3% (97)	49.7% (96)	
Lymphadenopathy with thickened cortex	No	44% (95)	56% (121)	.000
	Present	84.2% (32)	15.8% (6)	
Spheric Lymh Node	No	47.9% (116)	52.1% (126)	.003
	Present	91.7% (11)	8.3% (1)	
Conclusion of status of axilla	Normal	42.7% (90)	57.3% (121)	.000
	Lymphadenopathy	86% (37)	14% (6)	

n: number of observation. Note:p value is obtained with Chi-square test and significant at 0.05

Table 4. Relationship between COVID-19 history and ipsilateral axillary lymphadenopathy with thickened cortex

		Covid 19 History		
		Negative	Positive	*p*
Ipsilateral lymphadenopathy with thickened cortex	No	68% (65)	32% (30)	.000
	Present	100% (32)	%0 (0)	

Note:p value is obtained with Chi-square test and significant at 0.05

The control ultrasound was performed 30 days later for the 38 participants who had lymphadenopathy in the initial ultrasound. Among them, only 1 of the 38 participants had ipsilateral lymphadenopathy with a thickened cortex (3 mm cortex thickness) in the control ultrasound, while the second ultrasound revealed that all the other participants had reactive lymph nodes. The mean number of ipsilateral and contralateral axillary lymphadenopathy decreased over time from 1.45 to 0.03 and 0.24 to 0.00, respectively, at p<0.001 and p=0.011, respectively. The recorded time-wise differences are detailed in Table 5. According to the Wilcoxon test results, time-wise differences were explored in the cortex thickness of ipsilateral axillary lymphadenopathy from the initial to the control ultrasound at p<0.001, since the cortex thickness of ipsilateral axillary lymph nodes significantly decreased from the initial ultrasound to the control ultrasound (4.93 to 1.97 mm). Moreover, similar results were found for the cortex thickness of contralateral axillary lymph nodes as well, with a significant reduction from 2.10 to 1.47 mm (p=0.012). The cortex thickness of axillary lymphadenopathy in the control ultrasound 30 days after was found to be 1.97±0.78 mm for the vaccinated side and 1.47±0.95 mm for the other side, with a statistically significant difference at p=0.018. The number of axillary lymphadenopathies in the control ultrasound 30 days after was recorded as 0.03±0.16 for the vaccinated side and 0.00±0.00 for the other side, and therefore, was not significantly different (p=0.317). Another ultrasound was performed one month later on the patient who had a lymph node with thickened cortex, and it was found that the cortical thickness had reduced to 2.2 mm, which is under the cut-off value.

Table 5. Time-wise differences of ipsilateral and contralateral axillary lymphadenopathy

Variable	Mean	SD	Median	IQR	Paired	p
CTIL-i	4.93	2.38	4.00	2.03	CTIL-i- CTIL-30	.000
LNIL-i	1.45	0.80	1.00	1.00	LNIL-i - LNIL-30	.000
CTIL-30	1.97	0.78	2.15	0.90	CTCL-i - CTCL-30	.012
LNIL-30	0.03	0.16	0.00	0.00	LNCL-i - LNIL-30	.024
CTCL-i	2.10	1.37	2.10	1.15		
LNCL-i	0.24	0.59	0.00	0.00		
CTCL-30	1.47	0.95	1.85	1.20		
LNIL-30	0.00	0.00	0.00	0.00		

IQR:Interquartile range. The p-value is obtained with the Wilcoxon test for two-related samples. CTIL-i: cortex thickness of ipsilateral axillary lymphadenopathy in initial ultrasound. CTIL-30: cortex thickness of ipsilateral axillary lymphadenopathy in 30 days later. LNIL-i: lymph node number of ipsilateral axillary lymphadenopathy in initial ultrasound. LNIL-30: lymph node number of ipsilateral axillary lymphadenopathy in 30 days later. CTCL-i: cortex thickness of contralateral axillary lymphadenopathy in initial ultrasound

Discussion

Unilateral axillary lymphadenopathy causing misdiagnosis after mRNA COVID-19 vaccination has been demonstrated in several case reports and studies (4-8). Additionally, it has been proven that following administration of the first and second doses of the COVID-19 vaccine, the number of visible lymph nodes, maximum diameter, and cortical thickness significantly increased statistically, and in the follow-up, none of the participants returned to baseline values before vaccination (13). Our study indicates that ipsilateral axillary lymphadenopathy can also occur as a local adverse effect after administration of the inactivated COVID-19 vaccine, like what is observed after mRNA vaccines. It was observed that approximately one-fourth of the participants developed ipsilateral axillary lymphadenopathy within 2 weeks after the second dose of CoronaVac, and 97% of these participants had reactive lymph nodes in the control ultrasound performed 1 month later. Six weeks after the second dose of the inactivated COVID-19 vaccine, unilateral axillary lymphadenopathy is not expected to be detected. One of the significant findings of our study is that axillary lymphadenopathy is not expected in vaccinated patients who had a prior COVID-19 infection. This result underscores the importance of not only considering the vaccination history but also the history of COVID-19 infection when evaluating unilateral axillary lymph nodes in the era of COVID-19 vaccination.

The mean age of the 127 participants in our prospective study was 39.92±8.96, with a 23.6% history of COVID-19 infection, and 68.5% of them were men. We did not find a difference in lymph node status and cortical thickness of lymph nodes between sexes. A study that can be compared with ours investigated the occurrence of axillary lymphadenopathy similarly. In that study, 91 participants (79.1% women) with a mean age of 44, who received the mRNA COVID vaccine, were included, and 28% of the population had previously had the infection (13). While the frequency of unilateral axillary lymphadenopathy among participants after the second dose of the inactivated vaccine was 25.2% in our study, they demonstrated that the frequency was 81.3% after the mRNA vaccine, which is much higher than in our study. This difference in frequency may arise from the different types of vaccines, which elicit different

immune responses through different mechanisms. The high percentages of vaccine-induced hyperplasia of lymph nodes after COVID-19 vaccines are indicative of a robust immune response to these vaccines (14).

The mean cortical thickness of ipsilateral lymph nodes (2.63 mm) was significantly wider compared to the contralateral side (1.53 mm) two weeks after receiving the inactivated vaccine. It has been shown that the mean cortical thickness of lymph nodes increased from 1.6 mm to 4.6 mm one week after receiving the mRNA vaccine (13). The mean contralateral cortical thickness in our study and the baseline cortical thickness in the other study are nearly the same, which can be assumed as the standard cortical thickness of normal axillary lymph nodes due to the lack of information about this issue. Taken together, it is evident that these vaccines cause cortical thickening regardless of whether they cause lymphadenopathy appearance on ultrasound or not.

One of the striking findings of our study, which correlates with the other study, is the paradoxical lymph node response in participants who experienced previous COVID-19 infection compared to naive participants (13). We believe that the localization and mechanism of the immune response are different in patients previously infected and those who are not. Further investigation into the changes due to immune response in the occurrence of COVID-19 is needed to prove this hypothesis. Several recommendations have been released in the era of COVID-19 vaccination, but the history of infection was not specifically mentioned in these recommendations (12,15). With the results of current and future studies, recommendations for patients with a history of COVID-19 infection or those requiring a booster dose may also be altered.

The cortical thickness of ipsilateral axillary lymphadenopathy significantly reduced between the initial and control ultrasounds in our study. However, cortical thickness on the ipsilateral side was still found to be statistically wider than the contralateral side in the control ultrasound. Only 1 of the 38 participants had cortex thickness in the control ultrasound that achieved normal thickness in the second control ultrasound 1 month later. In contrast, the other study showed that 53.1% of participants normalized cortex thickness within a month, and 9.4% continued presenting cortical thickness in the 4th month. Additionally, none of their participants reached basal cortical thickness in follow-ups (13). The wider cortical thickness on the ipsilateral side in the control ultrasound issued in our study, and the failure to reach basal levels in follow-ups in the other study, indicates that despite cortical thickness regressing over time, it remains thicker than before vaccination. The difference in normalization of cortical thickness between the two studies may depend on the difference in vaccine type and immune response. Monitoring the difference in normalization of lymphadenopathies among different COVID-19 vaccines closely in further studies is necessary to provide more accurate recommendations according to vaccine types.

The main limitation of our study is that we lack data on the axillary status of the participants before vaccination and after the first dose vaccination. We did not monitor the status of lymphadenopathies for short periods, and we conducted a control ultrasound only 1 month after detecting lymphadenopathies. Another limitation is that our study group received the inactivated COVID-19 vaccination, so we did not compare the frequency of axillary lymphadenopathy with other types of COVID-19 vaccines. Additionally, we did not evaluate the participants after the third dose, which may present new challenges with the widespread practice of booster doses. Furthermore, we did not assess the status of ipsilateral supraclavicular and cervical lymph nodes, where lymphadenopathy could also be observed after vaccination.

Conclusion

The widest cortical thickness of the lymph nodes and the number of lymphadenopathies are significantly higher on the ipsilateral side of vaccination compared to the contralateral side. As a local adverse effect of vaccination, ipsilateral axillary lymphadenopathy can be seen after the second dose of inactivated COVID-19 vaccine, and it mostly regresses within a month. However, during that period, axillary lymphadenopathy is not expected in vaccinated patients who previously experienced COVID-19 infection. The frequency of vaccine-induced axillary lymphadenopathy after inactivated COVID-19 vaccine is 25.2%, and it mostly regresses within a month. The timing of elective imaging such as screening containing the axillary region after vaccination would be appropriate approximately 6 weeks after receiving an inactivated COVID-19 vaccination. Ipsilateral lymphadenopathy after inactivated COVID-19 vaccine is not expected in individuals who had COVID-19 infection before the vaccination. Recommendations for individuals presenting with unilateral axillary lymphadenopathy after vaccination, with and without a history of COVID-19 infection, may vary. Before performing radiological examinations of the axilla, radiologists and clinicians need to be aware of and inquire about both COVID-19 infection and vaccination history and timing. This will help radiologists and clinicians avoid misinterpretation and mismanagement of unilateral lymphadenopathy.

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Conflict of interest statement

The authors declare that they have no known competing financial or personal relationships that could be viewed as influencing the work reported in this paper.

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