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RESEARCH ARTICLE

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Effects of nonsteroidal anti-inflammatory drugs on ultrasound findings of mRNA COVID-19 vaccine-related lymphadenopathy

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Abstract

Background: Previous studies reported axillary lymphadenopathy (LAP) as a side effect of the anti-COVID-19 vaccine. However, the effects of nonsteroidal anti-inflammatory drug (NSAID)s on mRNA COVID-19 vaccine-related LAP have not been investigated.

Purpose: We aimed to investigate the effects of NSAIDs on temporal changes in sonographic findings of COVID-19 vaccine-associated LAP.

Methods: Our single-center retrospective cohort study was conducted between October 2021 and April 2022. We included patients (aged ≥ 18 years) who applied with complaints of swelling in the ipsilateral axillary region after the COVID-19 vaccine and had axillary region ultrasound (US) scans in electronic medical records within 30 days pre-vaccination. The serial US was performed on the third, 10th, and 30th days post-vaccination.

Results: Our study included 38 patients with a median age of 36 (IQR, 32–43) years. In 18 (47.4%) patients used NSAIDs in the early post-vaccination period. Measurements of LAPs on ultrasound scans increased at day 3 post-vaccination compared with pre-vaccination both in NSAID users and non-users. On the 10th day, a statistically insignificant decrease in LAP diameters and cortical thickness was observed in NSAID users compared to non-users. On the post-vaccination 30th day, axillary LAPs regressed similarly in both groups.

Conclusion: In our study, post-vaccine NSAID use had no statistically significant effect on the course of axillary LAPs.

KEYWORDS
COVID-19, lymphadenopathy, nonsteroidal anti-inflammatory drug, ultrasound, vaccine

1 | INTRODUCTION

Following the worldwide spread of the COVID-19 infection, numerous studies began to develop effective COVID-19 vaccination programs. In the United States, the Food and Drug Administration (FDA) has authorized the emergency use of the new two messenger RNA (mRNA) COVID-19 vaccine (Moderna and Pfizer/BioNTech).[1] BNT162b2 (Pfizer-BioNTech) was formulated with a lipid nanoparticle encoding full-length spike protein 2.[2]

Although COVID-19 vaccines have many positive protective effects, the vaccine may sometimes be accompanied by undesirable side effects, which are usually temporary and insignificant.[3] Among these side effects, regional lymphadenopathy (LAP) can be seen,

Abbreviations: LAP, lymphadenopathy; mRNA, messenger RNA; NSAID, nonsteroidal anti-inflammatory drug.

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which in some cases can reach a frequency of one-third after conventional vaccines.[4] After vaccination, activated antigens migrate first to the injection site and then to the draining lymph nodes, causing the formation of LAPs.[5] COVID-19 vaccines are performed on the deltoid muscle, intramuscularly. Therefore, vaccine-associated LAPs are typically observed in the axilla and supraclavicular region.[6,7] Being aware of this relationship is very important, especially in cancer patients. While investigating patients with cancer for LAP, questioning their COVID-19 vaccination history may prevent unnecessary biopsies.

Anatomically, the COVID-19 vaccine-related LAPs are mostly located in the ipsilateral axilla, cervical, supraclavicular and infraclavicular regions. The Centers for Disease Control and Prevention reported that the onset of LAP associated with the COVID-19 vaccine is 1 to ~3 days after the vaccination, and the duration may take up to 16 days, depending on the type of vaccine.[8] But, in some studies much longer durations for LAPs have been reported.[1,9] COVID-19 vaccine-associated LAPs can be easily evaluated in serial follow-ups by ultrasonography (US).[10] Generally, "reactive" post-COVID-19 LAPs occur in typical lymph node regions and they have benign sonographic features such as oval-shaped, symmetric cortex with hilum evidence.[11] Sometimes they may be located in atypical sites and have "non-reactive" sonographic features like hypoechoic round nodes with increased (>3 mm) diffuse or asymmetric cortical thickness. In this case, they may mimic serious pathologies with a worse prognosis and be confused with malignancy.[1,11–13]

Non-steroidal anti-inflammatory drugs (NSAID) have been used frequently for many years to control acute side effects of vaccines or reactogenicity. Public health authorities recommend the usage of these drugs to treat symptoms associated with the COVID-19 vaccine. NSAIDs exert their therapeutic effects as a result of inhibition of inflammatory pathways including cyclooxygenase-1 (COX-1) and COX-2 activities and prostaglandin synthesis.[14]

In our study, we aimed to investigate the temporal sonographic changes of BNT162b2 (Pfizer-BioNTech) COVID-19 vaccine-associated LAPs at various time intervals and the effects of post-vaccine nonsteroidal anti-inflammatory drug (NSAID) usage on LAPs.

2 | MATERIALS AND METHODS

Our study was approved by the Ethical Committee of Amasya University Faculty of Medicine and was conducted according to the Declaration of Helsinki and Good Clinical Practice (12 May 2022, number: 50).

2.1 | Study population and data collection

Our study is a single-center retrospective analysis study of 38 patients (≥18 years) who were admitted with complaints of swelling in the axillary region after the COVID-19 vaccine (BioNTech) between October 2021 and April 2022. The data of patients who underwent axillary US scan within 30 days before vaccination and who underwent serial US follow-up for 30 days (3rd, 10th, and, 30th days) upon the clinician's request due to post-vaccination complaints were analyzed. Patients without the axillary US within pre-vaccination 30 days were excluded from the study. In addition, patients with suspicious pathological LAP features in the US pre-vaccination were excluded from the study. None of our patients included in the study had a history of active infection that may involve the axillary lymph node or malignancy during treatment. Demographic findings, malignancy history, vaccination dates, and post-vaccination symptoms of the patients were recorded. All of our patients received the second dose of the COVID-19 vaccine (BioNTech) on the left arm. In addition, patients were asked whether they used NSAIDs in the early post-vaccination period due to vaccination-related side effects. We grouped patients into NSAID users and non-users after the COVID-19 vaccine (BioNTech) and investigated temporal sonographic differences of axillary lymph nodes between groups.

2.2 | Imaging protocol and image analysis

In our study, the US scans were performed using Toshiba Aplio 500 ultrasound machine (Toshiba Medical Systems Corp, Tokyo, Japan). Two radiologists with 15 and 9 years of experience in general radiology (B.A. and A.T.K.) performed axillary US using a 4–14 MHz linear transducer (Frequency: 10 MHz; Range: 4–14 MHz; approximate field of view [FOV]: 58 mm).

Serial US scans were performed on all study populations at our hospital before and on the 3rd, 10th, and 30th days after vaccination. Lymph node count, long and short-axis diameters, max cortical thickness, and presence of fatty hilus were examined in all US scans. We

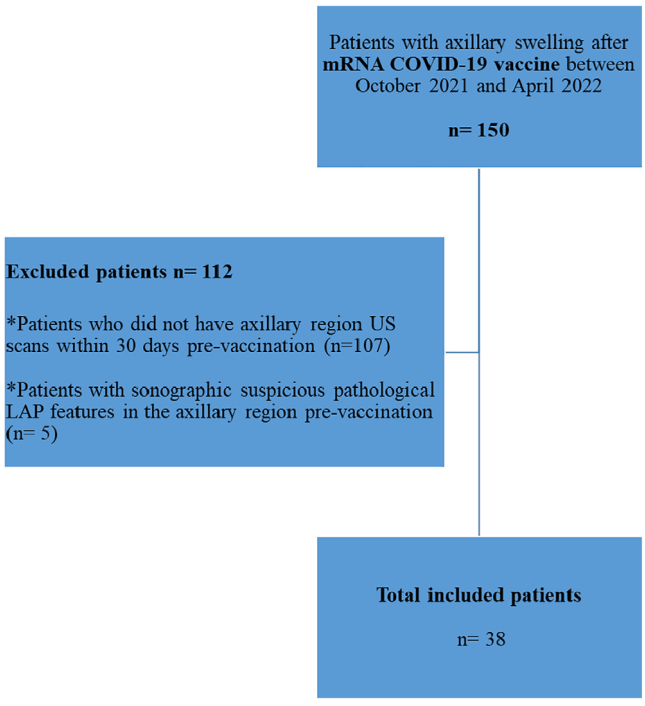


FIGURE 1 Flowchart for patient inclusion

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defined focal or diffuse cortical thickening when the max cortical thickness of the lymph node was ≥3 mm.[15]

2.3 | Statistical analyzes

Statistical analyzes were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp. Released 2017. Armonk, NY). The conformity of the variables to the normal distribution was examined using Shapiro-Wilk test. In descriptive analyses, median and interquartile ranges (IQR) were used for non-normally distributed variables. Measurements of axillary lymph node parameters in pre- and post-vaccine US follow-ups did not meet the parametric test assumptions. For this reason, the statistical significance of the temporal changes of lymph nodes according to the use of NSAIDs was examined with the Friedman test. Pairwise comparisons were made using the Wilcoxon test. After Bonferroni's correction. $p < 0.017$ was considered statistically significant.

3 | RESULTS

First, we investigated the data of 150 patients who were admitted to our hospital with complaints of swelling in the axillary region after the COVID-19 vaccine (BioNTech). In total, 32 female and 75 male patients who did not have the axillary US in the last 30 days pre-vaccination were excluded from the study. Four female and one male patient with suspicious pathological LAP appearance in the US pre-vaccination were excluded from the study (Figure 1). Therefore, a total of 38 patients with a median age of 36 (IQR, 32–43) years were included in the study; 29 (76.3%) were female. The most common symptoms of the patients were muscle pain in 29 (76.3%) and weakness in 23 (60.5%) patients that started on the day of vaccination or the next day. One (2.6%) patient had a history of breast CA and 1 (2.6%) patient had a history of lung CA (Table 1). In total 18 (47.4%) patients took NSAIDs in the early post-vaccination period (post-vaccine first or second day) due to vaccination-related side effects and all of them were female (100%). The median age of NSAID users was 35 and NSAID non-users was 39.

TABLE 1 Demographic characteristics of study population, history of nonsteroidal anti-inflammatory drug (NSAID) usage and complaints after vaccine (Pfizer-BioNTech).

		Frequency	Percent (%)
Gender	Female	29	76.3
	Male	9	23.7
History of COVID-19	Absent	20	52.6
	Present	18	47.4
Using NSAIDs after vaccine (Pfizer-BioNTech)	Non-used	20	52.6
	Used	18	47.4
Family history of malignancy	Absent	29	76.3
	Breast CA	2	5.3
	Lung CA	4	10.5
	Other	3	7.9
History of Breast CA	Absent	37	97.4
	Present	1	2.6
History of Lung CA	Absent	37	97.4
	Present	1	2.6
Complaints after vaccine (Pfizer-BioNTech)			
Fever	Absent	29	76.3
	Present	9	23.7
Weakness	Absent	15	39.5
	Present	23	60.5
Muscle pain	Absent	9	23.7
	Present	29	76.3
Headache	Absent	21	55.3
	Present	17	44.7
Swelling at the injection site arm	Absent	27	71.1
	Present	11	28.9
Fatigue	Absent	18	47.4
	Present	20	52.6
Chill shiver	Absent	28	73.7
	Present	10	26.3

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TABLE 2 The comparison of the axillary lymph nodes' sonographic findings performed on the 3rd, 10th, and 30th days after the vaccination according to nonsteroidal anti-inflammatory drug (NSAID) usage.

			Percentiles				
	Using NSAIDs after the vaccine	Days of US	25th (Median)	50th	75th	Comparisons	*p* value
Number of axillary lymph node	Non-used ($n = 20$)	Pre-vaccine	3	4	4	Pre-vaccine–Day 3	**0.003**
		Day 3	3.25	5	6	Day 3–10	***0.512***
		Day 10	4	5	5	Day 10–30	**0.003**
		Day 30	3	4	5		
	Used ($n = 18$)	Pre-vaccine	2	3	3	Pre-vaccine–Day 3	**0.001**
		Day 3	3	4	5	Day 3–10	0.131
		Day 10	3	4	5	Day 10–30	**0.008**
		Day 30	2	3	3.25		
	Total ($n = 38$)	Pre-vaccine	2	3	4	Pre-vaccine–Day 3	**<0.001**
		Day 3	3	5	5	Day 3–10Day	***0.7180***
		Day 10	3	4	5	Day 10–30	**<0.001**
		Day 30	3	3	4		
Axillary lymph node long-axis diameter	Non-used ($n = 20$)	Pre-vaccine	11.75	14.8	18.78	Pre-vaccine–Day 3	**<0.001**
		Day 3	14.43	19.6	24.28	Day 3–10	0.467
		Day 10	16.75	19.8	25.88	Day 10–30	**0.001**
		Day 30	13.48	16.4	22.28		
	Used ($n = 18$)	Pre-vaccine	11	15.85	19.05	Pre-vaccine–Day 3	**0.001**
		Day 3	17.3	21.2	25	Day 3–10	0.777
		Day 10	16.45	18.6	24.2	Day 10–30	**0.010**
		Day 30	14.88	16.95	18.53		
	Total ($n = 38$)	Pre-vaccine	11.20	15.50	18.93	Pre-vaccine–Day 3	**<0.001**
		Day 3	16.38	19.95	24.73	Day 3–10	0.7610
		Day 10	16.68	19.35	24.20	Day 10–30	**<0.001**
		Day 30	14.38	16.75	20.10		
Axillary lymph node short-axis diameter	Non-used ($n = 20$)	Pre-vaccine	5.03	6.55	8.28	Pre-vaccine–Day 3	**0.002**
		Day 3	6.73	8.6	10.28	Day 3–10	0.866
		Day 10	7.33	8.5	9.43	Day 10–30	**<0.001**
		Day 30	6.05	6.55	8.38		
	Used ($n = 18$)	Pre-vaccine	4.93	6.15	7.5	Pre-vaccine–Day 3	**0.001**
		Day 3	7.28	8.25	9.3	Day 3–10	***0.163***
		Day 10	6.38	7.55	9.23	Day 10–30	0.028
		Day 30	5.78	6.55	8.05		
	Total ($n = 38$)	Pre-vaccine	5	6.35	7.83	Pre-vaccine–Day 3	**<0.001**
		Day 3	7.20	8.45	9.60	Day 3–10	***0.4720***
		Day 10	6.98	8	9.28	Day 10–30	**<0.001**
		Day 30	6	6.55	8.13		

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TABLE 2 (Continued)

	Using NSAIDs after the vaccine	Days of US	Percentiles 25th (Median)	50th	75th	Comparisons	*p* value
Axillary lymph node max cortical thickness	Non-used ($n = 20$)	Pre-vaccine	1.15	2.05	2.85	Pre-vaccine–Day 3	0.017
		Day 3	1.65	2.9	3.58	Day 3–10	***0.294***
		Day 10	1.85	2.8	3.38	Day 10–30	**0.006**
		Day 30	1.23	2.05	2.7		
	Used ($n = 18$)	Pre-vaccine	1.18	1.5	2.33	Pre-vaccine–Day 3	**0.003**
		Day 3	2.18	3	3.35	Day 3–10	0.206
		Day 10	1.65	2.55	3.03	Day 10–30	**0.004**
		Day 30	1	1.89	2.9		
	Total ($n = 38$)	Pre-vaccine	1.18	1.75	2.70	Pre-vaccine–Day 3	**<0.001**
		Day 3	2.03	2.95	3.50	Day 3–10	0.096
		Day 10	1.78	2.60	3.23	Day 10–30	**<0.001**
		Day 30	1.10	1.90	2.80		

Note: The statistical significance of the temporal changes of lymph nodes according to the usage of NSAIDs was examined with the Friedman test. Pairwise comparisons were made using the Wilcoxon test. After Bonferroni correction. $p < 0.017$ was considered statistically significant. Therefore, p values of $p<0.017$ has be written in bold.

Abbreviations: max, maximum; NSAID, nonsteroidal anti-inflammatory drug; US, ultrasound.

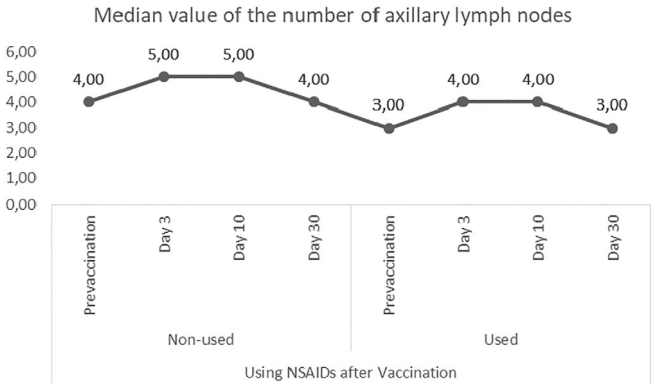


FIGURE 2 The statistical graphic shows the median axillary lymph node count before and on days 3, 10, and 30 post-vaccination for nonsteroidal anti-inflammatory drug (NSAID) users and non-users.

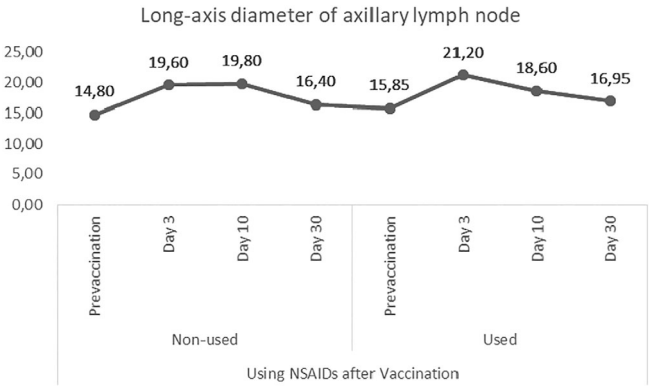


FIGURE 3 The statistical graphic shows the median long-axis diameter of axillary lymph before and on days 3, 10, and 30 post-vaccination for nonsteroidal anti-inflammatory drug (NSAID) users and non-users.

3.1 | Serial ultrasonography findings of axillary lymph nodes

All our patients had reactive oval-shaped lymph nodes with echogenic hilus on the US in the ipsilateral axillary region. None of our patients had LAPs with irregular contour, calcification, necrosis or rounded shape in the axillary region on the US. LAPs were considered radiologically and clinically benign as a result of regression in size and max cortical thickness in follow-up US scans and regression of clinical symptoms. Therefore, a biopsy was not required.

3.2 | Number of axillary lymph nodes

There was a statistically significant increase in the number of axillary lymph nodes between the pre-vaccine and third days after vaccination in both NSAID users ($p = 0.001$) and non-users ($p = 0.003$) (Table 2). The number of axillary lymph nodes gradually decreased over time. In both groups, the axillary lymph node count on the post-vaccination 10th day was the same as on the third day ($p = 0.131$). In both NSAID users and

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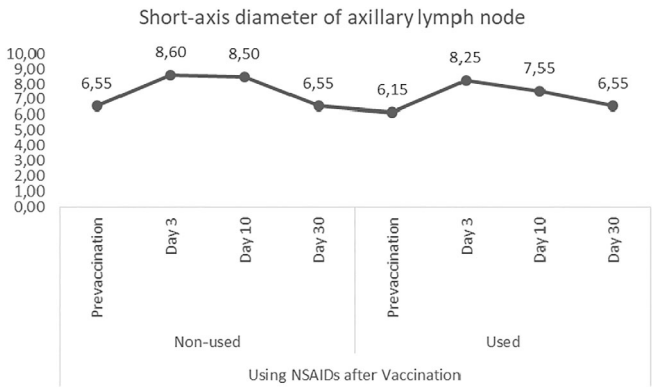


FIGURE 4 The statistical graphic shows the median short-axis diameter of axillary lymph nodes before and on days 3, 10, and 30 post-vaccination for nonsteroidal anti-inflammatory drug (NSAID) users and non-users.

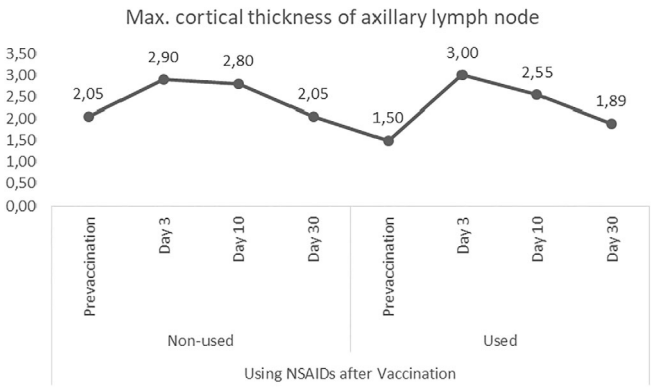


FIGURE 5 The statistical graphic shows the median max cortical thickness of axillary lymph nodes before and on days 3, 10, and 30 post-vaccination for nonsteroidal anti-inflammatory drug (NSAID) users and non-users.

non-users groups, the number of axillary lymph nodes decreased on the post-vaccination 30th day ($p = 0.008$, $p = 0.003$) (Figure 2).

3.3 | Long-axis diameter of axillary lymph nodes

There was a statistically significant increase in the long-axis diameter between pre-vaccine and third day after vaccination in both NSAID users ($p = 0.001$) and non-users ($p < 0.001$). The long-axis diameter gradually decreased over time. In NSAID users, a decrease in the median long-axis diameter of axillary lymph nodes was observed on the post-vaccination 10th day, but not statistically significant ($p = 0.777$). In both NSAID users and non-users groups, long-axis diameters decreased on the post-vaccination 30th day ($p = 0.01$, $p = 0.001$) (Figure 3).

3.4 | Short-axis diameter of axillary lymph nodes

All patients' median short-axis diameter of axillary lymph nodes increased on the post-vaccination third day compared to pre-vaccine. The median short-axis diameter was minimally decreased on the 10th day and on the 30th day; it decreased similar to the pre-vaccine diameter. The median short-axis diameter of axillary lymph nodes increased on the post-vaccination third day compared to pre-vaccine, in both NSAID users and non-users ($p = 0.001$, $p = 0.002$). NSAID users had a greater reduction in the median short-axis diameter than NSAID non-users on the 10th day after the vaccine, but it was not statistically significant. Short-axis diameters decreased in both groups at day 30 post-vaccination, similar to pre-vaccine measurements (Figure 4).

3.5 | Maximum cortical thickness of axillary lymph nodes

Of all patients, before the COVID-19 vaccine, 4 (10.5%) patients had axillary lymph nodes with focal or diffuse cortical thickening ≥3 mm. The number of patients who had lymph nodes with cortical thickening increased on the post-vaccination third day (50%). They decreased gradually on the 10th day (26.3%) and the 30th day (15.7%). The median value of max cortical thickness on the post-vaccine third day increased compared to pre-vaccine and slightly decreased on day 10 ($p = 0.096$). In 30 days after vaccination, the median value of max cortical thickness decreased significantly ($p < 0.001$). The median max cortical thickness of axillary lymph nodes increased on the post-vaccination third day compared to pre-vaccine in both NSAID users and non-users ($p = 0.003$, $p = 0.017$). NSAID users had a greater reduction in the median value of max cortical thickness than NSAID non-users on the post-vaccination 10th day, but it was not statistically significant ($p = 0.206$). In both groups, max cortical thickness decreased on the post-vaccination 30th day ($p = 0.004$, $p = 0.006$) (Figure 5).

4 | DISCUSSION

In our study, we aimed to investigate the temporal sonographic changes of LAPs associated with the BNT162b2 COVID-19 vaccine and the effects of post-vaccine NSAID usage on LAPs. In ultrasonography, the number, short, long-axis diameters and max cortical thickness of ipsilateral axillary lymph nodes increased on the third day after the second dose of COVID-19 vaccine (Pfizer-BioNTech) compared to the pre-vaccine. On the post-vaccine 30th day, the number, diameters, and max cortical thickness of LAPs decreased (Figure 6A–D). In both post-vaccine NSAID users and non-users, the sizes and max cortical thickness of axillary lymph nodes increased similarly on the post-vaccine third day. In NSAID users, a slight decrease in LAP dimensions and max cortical thickness was observed at day 10, but it was not statistically significant. No reduction was observed in NSAID non-users. On the post-vaccination 30th day, axillary LAPs were similarly regressed in both groups.

COVID-19 vaccines can sometimes be accompanied by undesirable side effects, most of which are temporary and insignificant.[3] The most frequently reported systemic symptoms after vaccination were

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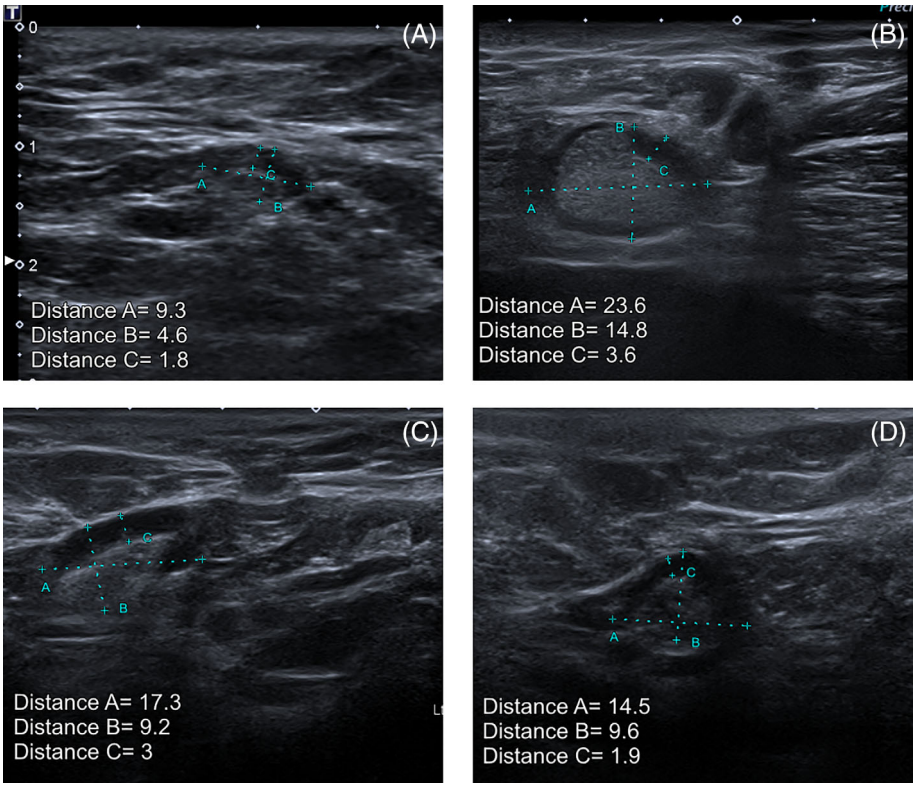


FIGURE 6 (A, B, C, D) A 30-year-old woman was admitted to our hospital with complaints of weakness, muscle pain and swelling in the ipsilateral axillary region 1 day after the COVID-19 vaccine (BioNTech). She used nonsteroidal anti-inflammatory drug (NSAID) in the early post-vaccination period due to vaccination-related side effects. The increases in the short and long-axis diameters and max cortical thickness of ipsilateral axillary lymph nodes were observed on US examinations performed on the third day after the COVID-19 vaccine. On the 10th day, a day minimal decrease was observed in measurements (A–C). On the 30th day after vaccination, the number, size, and max cortical thickness of the LAPs were decreased on US (D).

headache (39%–52%) and fatigue (34%–59%), which usually occurred post-vaccination first and second days. In the literature, both systemic side effects and injection site pain after vaccination have been reported more commonly in younger patients than elderly. In addition, vaccine-related adverse effects were observed more frequently after the second dose of the vaccine than after the first dose.[16] In our study, the most common symptoms of the patients were muscle pain, weakness, and fatigue that started on the day of the vaccination or the next day. Vaccine-associated reactive LAP is thought to result from a local adverse reaction to the vaccination and is more commonly seen after the administration of COVID-19 mRNA vaccines.[1,17–20] BNT162b2 (Pfizer-BioNTech), the vaccine administered to our study population, is a nucleoside-modified RNA vaccine. As in other vaccines, antigen-presenting cells in mRNA vaccines migrate to regional lymph nodes to reveal a humoral (B-cell) and cellular (T-cell) immune response. mRNA vaccines provide stronger and faster B cell proliferation in lymph nodes than protein-based vaccines, possibly increasing the incidence of LAP.[21,22] The COVID-19 vaccine-related LAPs are mostly located in the ipsilateral axilla, cervical, supraclavicular and infraclavicular areas.[8] In the literature, the imaging frequency of COVID-19 vaccine-related axillary LAP was reported at 15% after the BNT162b2 vaccine and 57% after the mRNA-1273 vaccine, respectively.[23] A recent study reported the incidence of axillary LAP associated with the COVID-19 vaccine in the US as 49%, and the most important factor for axillary LAP was receiving mRNA vaccine.[24] In our study, we included the patients who had axillary swelling complaints and had axillary LAP in the early period of post-vaccination.

Ultrasonography has advantages over other imaging methods such as not containing radiation and not requiring contrast material. Ultrasonography can be easily applied in the evaluation of lymph nodes in the axilla, supraclavicular and infraclavicular regions after the COVID-19 vaccine.[10] So in our study, serial follow-up US scans were performed on the patients with COVID-19 vaccine-associated reactive LAPs. In the US, some imaging findings are used to differentiate benign and malignant LAP. Round-shaped, irregular contours, changes in the shape of the LAP, and increases in volume and cortex thickness, including calcification and necrosis are findings supporting malignancy in the US.[25–28] In our study, LAPs were radiologically accepted as benign, as a result of regression in size and max cortical thickness in follow-up US scans, and because of their oval shape and smooth contours.

In Su Min Ha et al.'s study, serial US scans were applied to 88 healthy women with COVID-19 vaccine-related LAPs and they reported that LAPs were completely resolved in a median of 6 weeks.[10] In our study, we followed our patients 4 weeks after the vaccine and the number, size and max cortex thickness of LAPs regressed to pre-vaccine measurements.

Non-steroidal anti-inflammatory drugs are widely used as an anti-inflammatory, analgesic, and antipyretic agents in clinical practice, and public health authorities continue to recommend these drugs for treating the side effects of COVID-19 vaccines.[14] Studies have reported that NSAIDs inhibit cytokine synthesis or migration of leukocytes, either COX dependently[29] or independently.[30,31] Since the primary pathogenesis of vaccine-related side effects is increased cellular immunity, it was thought that the immunosuppressive effect of NSAIDs was responsible for the faster reduction of fever, headache, and general fatigue.[32] Diaz et al. reported that early administration of these drugs not only shortens the duration of vaccine-related systemic side effects but also may prevent serious complications such as post-vaccine

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myocarditis and pericarditis.[33] In the phase 2/3 data of the BNT162b2 vaccine, it has been shown that young people more frequently use antipyretic or analgesic drugs than older people after vaccination.[16] Also in our study NSAID users were younger than non-users, and were all female. To our knowledge, our study is the first to investigate the effect of NSAID usage after the COVID-19 vaccine (BioNTech), on the follow-up sonographic findings of the vaccine-related axillary LAPs.

Our study had some limitations. First, it was a single-center, retrospective study with small sample size. Therefore, a multicenter study with large sample size is needed for more validation. Second, biopsies were not performed on LAPs, and they were characterized as benign as a result of regression in size and max cortical thickness on follow-up US.

5 | CONCLUSION

The number, diameters, and max cortical thickness of vaccine-associated LAPs increased on the following third day after BNT162b2 COVID-19 vaccination on serial ultrasonography and decreased at day 30 post-vaccination, similar to pre-vaccine measurements. The use of NSAIDs after the COVID-19 vaccine resulted in an earlier slight reduction of the median values of diameters and max cortical thickness of ipsilateral vaccine-associated axillary LAP. However, this decrease was not statistically significant. On the 30th day after vaccination, statistically significant decreases were observed in the measurements in both groups. Therefore, in our study group, post-vaccine NSAID usage did not have a significant effect on the course of vaccine-related axillary LAPs.

AUTHOR CONTRIBUTIONS

Burcu Akman: Methodology, Investigation, Visualization, Writing-Reviewing and Editing, Supervision. Ahmet Turan Kaya: Data Curation, Conceptualization, Methodology, Supervision.

INFORMED CONSTENT

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author.

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