

Axillary Adenopathy after COVID-19 Vaccine: No Reason to Delay Screening Mammogram

Stacey Wolfson, MD • Eric Kim, MD • Anastasia Plaunova, MD • Rita Bukhman, MD • Ruth D. Sarmiento, MD • Naziya Samreen, MD • Divya Awal, MD • Monica M. Sheth, MD • Hildegard B. Toth, MD • Linda Moy, MD • Beatriu Reig, MD, MPH

From the Department of Radiology, New York University Grossman School of Medicine, New York University Langone Health, Laura and Isaac Perlmutter Cancer Center, 160 E 34th St, 3rd Floor, New York, NY 10016 (S.W., E.K., A.P., R.B., R.D.S., N.S., D.A., M.M.S., H.B.T., L.M., B.R.); NYU Langone Radiology Associates, Staten Island, NY (R.B.); NYU Langone Radiology Associates, Mineola, NY (R.D.S., M.M.S.); Bernard and Irene Schwartz Center for Biomedical Imaging, Department of Radiology, NYU School of Medicine, New York, NY (L.M.); and NYU Vileck Institute of Graduate Biomedical Sciences, New York, NY (L.M.). From the 2021 RSNA Annual Meeting. Received December 20, 2021; revision requested January 6, 2022; final revision received January 24; accepted January 28. **Address correspondence to S.W.**

Conflicts of interest are listed at the end of this article.

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Unilateral lymphadenopathy, an adverse effect of the COVID-19 vaccines, has posed a diagnostic challenge in oncologic imaging (1–8). We sought to determine the outcomes of axillary lymphadenopathy after COVID-19 vaccination on breast imaging examinations.

Material and Methods

In this institutional review board–approved and Health Insurance Portability and Accountability Act–compliant retrospective study, we identified patients who received the COVID-19 vaccine and underwent breast imaging between December 30, 2020, and April 12, 2021, at 17 sites across one institution. Follow-up examinations were recorded through December 10, 2021. Seven radiologists extracted clinical-pathologic data and vaccine information from the medical records. The original radiology reports were used for imaging characteristics. Long-axis lymph node measurements were recorded. Statistics were calculated in Microsoft Excel and Mann-Whitney *U* tests in SPSS software (version 25, SPSS).

Results

Among the 1217 patients who received the COVID-19 vaccine and underwent breast imaging, 537 (44%) had lymphadenopathy identified during at least one imaging examination. A total of 823 patients (68%) presented for screening (Table E1 [online]). A total of 334 patients underwent mammography and sonography on the same day: 29 (9%) patients had lymphadenopathy identified with mammography alone, 203 (61%) patients with US alone, and 102 (30%) patients with both mammography and US. In patients with lymphadenopathy, the average node measured 1.8 cm (range, 0.5–4.2 cm). Charts

were reviewed for imaging and biopsy follow-up for 273 days (range, 253–348 days).

Among the patients with known vaccine manufacturer information, 459 patients received the Moderna vaccine (46% with lymphadenopathy) and 505 patients received the Pfizer vaccine (38% with lymphadenopathy) ($P = .007$).

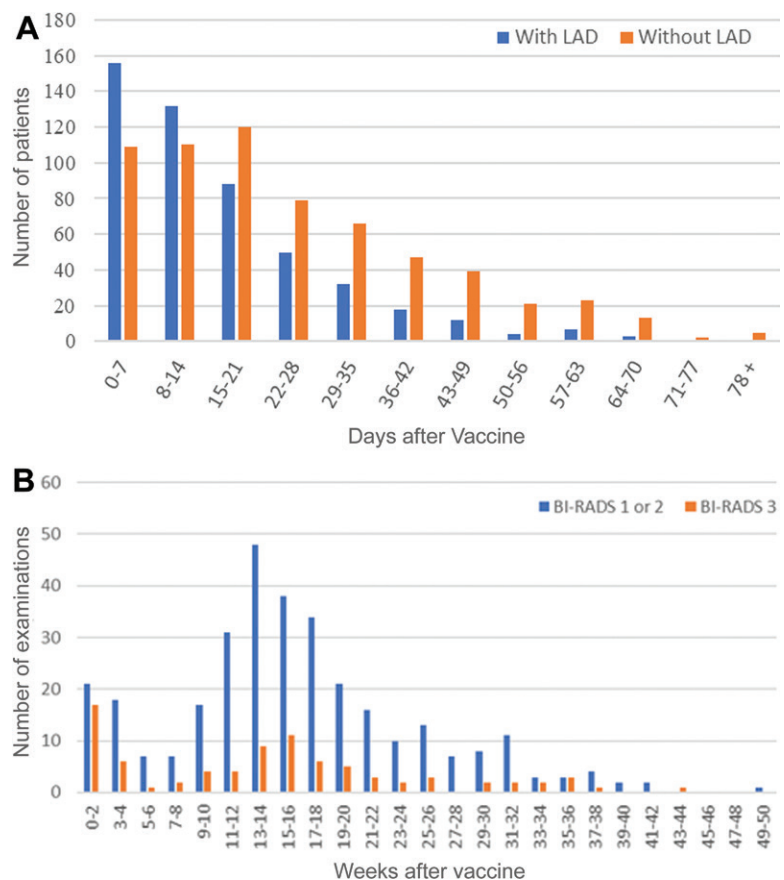


Figure 1: Graphs compare (A) patients with and without lymphadenopathy (LAD) at initial breast imaging after COVID-19 vaccination. Lymphadenopathy is seen most commonly in the first 2 weeks after vaccination, but can also persist at least 10 weeks. (B) Graphs compare patients with LAD and follow-up imaging. Bars show the number of examinations assigned Breast Imaging Reporting and Data System (BI-RADS) category 1 or 2 (negative or benign findings) versus BI-RADS 3 (probably benign finding; short-term follow-up is recommended) recommendations by time after the vaccination. Twenty-five percent of examinations performed at 0–12 weeks were given BI-RADS 3 recommendations, and none of these patients were subsequently diagnosed with a new malignancy.

Eighteen patients received the Johnson & Johnson vaccine (39% with lymphadenopathy) (Table E1 [online]).

Patients demonstrated lymphadenopathy as early as 1 day following the first dose and as late as 71 days following the second dose. The timing was different between the groups with and without lymphadenopathy. Lymphadenopathy was more likely to be seen within 14 days after vaccination and was rare after 50 days after the second dose (Fig 1A).

Eight percent (43 of 537) of patients underwent a biopsy; 34 (79%) had benign results (Fig 2) and nine (21%) had malignant results (Table E2 [online]). Four patients were diagnosed with metastatic breast cancer (Fig E1 [online]); all had suspicious concurrent mammographic findings in the ipsilateral breast. Four patients were diagnosed with lymphoma; three patients already had known diagnoses, and the fourth patient presented with bilateral lymphadenopathy

(Fig E2 [online]). One patient with a known history of lung cancer was diagnosed with lung cancer metastatic to an axillary lymph node.

In 387 (72%) patients with lymphadenopathy, there were 407 follow-up examinations, averaging 15.7 weeks after the initial examinations (range, 0.2–49 weeks). At follow-up imaging, 323 of 407 (79.4%) studies demonstrated decreased lymph node size and were assessed as benign. Eighty-four (20.6%) demonstrated stable findings and were assessed as probably benign with recommendation to undergo additional follow-up (Fig 1B). Among 135 patients with follow-up examinations within 12 weeks, 25% were given Breast Imaging Reporting and Data System, or BI-RADS, category 3 recommendations. No patients in the follow-up group were diagnosed with a subsequent malignancy. Persistent axillary lymphadenopathy was seen up to 43 weeks after vaccination.

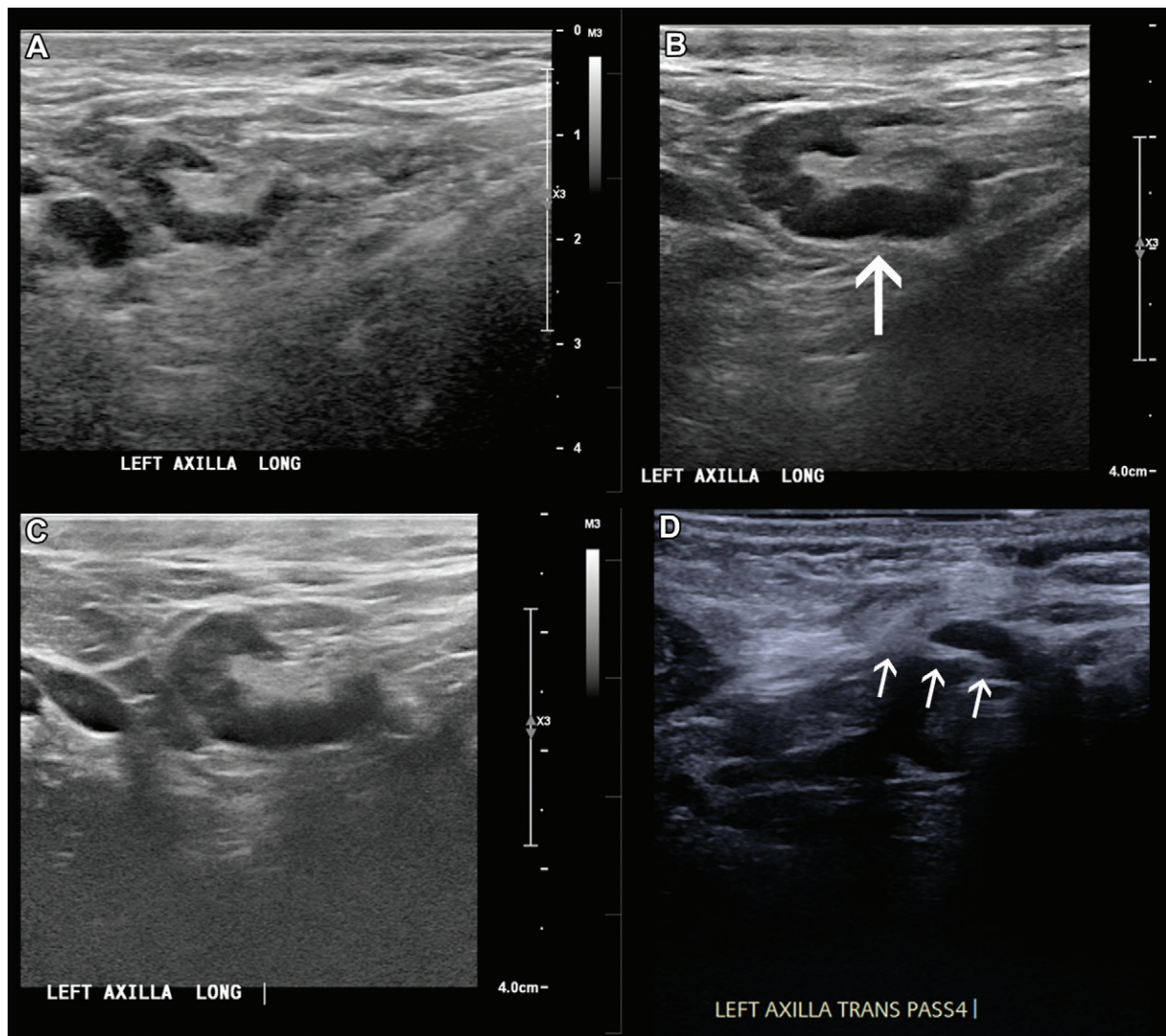


Figure 2: In a 46-year-old patient with a strong family history of breast cancer, (A) a screening US prior to COVID-19 vaccination demonstrated a morphologically normal left axillary lymph node. (B) Twenty-five days following the second dose of the COVID-19 vaccine, the patient presented with a palpable lump in the left axilla and US demonstrated enlarged lymph nodes with cortex measuring up to 6 mm in thickness (arrow). (C) Follow-up US 21 weeks following demonstrated stable axillary lymphadenopathy. (D) A US-guided core biopsy was then recommended and pathologic analysis demonstrated lymphoid cells negative for carcinoma. Arrows indicate the path of the needle.

Discussion

This is the largest study, to our knowledge, to evaluate axillary lymphadenopathy, with long-term follow-up of 6 months following COVID-19 vaccination. Adenopathy is a common adverse effect identified within 44% of our patients, with persistent lymphadenopathy seen up to 43 weeks after vaccination. Our findings suggest that patients should not delay their screening mammogram because they were recently vaccinated. The Moderna vaccine was significantly more associated with lymphadenopathy compared with Pfizer, consistent with a recent study (7) that evaluated axillary adenopathy on chest CT images (7). Prior to the COVID-19 vaccine era, axillary adenopathy in women with an otherwise normal mammogram was reported in 0.02%–0.04% of screening mammograms (4).

A minority of patients (8%) were recommended for biopsy, only nine (21%) with malignant results. All patients diagnosed with axillary metastases had suspicious imaging findings in the ipsilateral breast. Additional malignancies were detected either in patients with known cancer history or in patients presenting with bilateral lymphadenopathy. These results support the European Society of Breast Imaging guidelines (5) that recommend benign or probably benign assessment for patients without breast cancer history and no suspicious breast imaging findings, as well as the *Radiology* scientific expert panel guidelines (3) that recommend no default follow-up imaging in patients at low risk of axillary nodal metastases.

In our large cohort with extended follow-up, there were no new diagnoses of malignancy during the follow-up period. The time to resolution of reactive lymphadenopathy was variable, with persistent lymphadenopathy seen up to 43 weeks after vaccination. This is even longer than a case of persistent fluorodeoxyglucose PET/CT uptake at 70 days after the second dose of COVID-19 vaccination (8). Given the extended period of time to resolution, no short-term follow-up imaging should be recommended. This differs from current guidelines, which recommend a short-term follow-up examination in 4–12 weeks following the second vaccine dose (4).

Other studies with lower reported incidence of lymphadenopathy (3%–16%) are based on self-reported symptoms or detection solely on mammography; in contrast, our study had an incidence of 44%. This difference reflects our practice pattern that includes axillary adenopathy seen with either mammography or breast US in both the screening and diagnostic setting (2).

In conclusion, there should be no delay in screening mammograms due to recent vaccination and there is variable time to resolution of reactive lymphadenopathy. Lymphadenopathy should be interpreted in the context of patient risk factors with vigilance in patients with concurrent suspicious mammographic findings in the ipsilateral breast.

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