




Vaccination Against SARS-CoV-2 Decreases Risk of Adverse Events in Patients who Develop COVID-19 Following Cancer Surgery

Nathaniel B. Verhagen, BS¹, Nicolas K. Koerber, BS¹, Aniko Szabo, PhD², Bradley Taylor, MBA³, J. Njeri Wainaina, MD⁴, Douglas B. Evans, MD¹, Anai N. Kothari, MD^{1,3} , and On behalf of the N3C Consortium

¹Division of Surgical Oncology, Department of Surgery, Medical College of Wisconsin, Milwaukee, WI; ²Department of Biostatistics, Medical College of Wisconsin, Milwaukee, WI; ³Clinical and Translational Science Institute of Southeastern Wisconsin, Froedtert and Medical College of Wisconsin Health Network, Milwaukee, WI; ⁴Division of Infectious Disease, Department of Medicine, Medical College of Wisconsin, Milwaukee, WI

Early in the COVID-19 pandemic, mortality rates were observed to exceed 25% in patients who developed postoperative SARS-CoV-2 infections.¹ This prompted numerous perioperative structural and process changes to mitigate this risk.^{2,3} As the pandemic has progressed, the emergence of novel therapeutic and preventative measures have proven effective in decreasing the overall burden of SARS-CoV-2 infection. These advances likely reduce the risk in surgical patients; however, this has not been reexamined at a population level. This study reports 30-day adverse postoperative event rates in patients who develop postoperative COVID-19 and measures the impact of vaccination on these outcomes.

METHODS

This was a retrospective cohort study using the National COVID Cohort Collaborative (N3C) Data Enclave. The study cohort included patients who underwent surgical resection for cancer. Patients positive for COVID-19 were identified based on a positive lab measurement (PCR or antigen) or a positive COVID-19 diagnosis (ICD10-CM

code U07.1). Postoperative COVID-19 was defined as a new SARS-CoV-2 infection that occurred within 30 days of surgery. Fully vaccinated patients were characterized as having at least two COVID-19 vaccines 14 days or more before surgery. This analysis included patients from January 2020 to August 2022.

Construction of the study cohort was executed using Observational Health Data Science and Informatics' (OHDSI) ATLAS tool. Patients with cancer were identified using the Malignant Neoplastic Disease standard concept and benign concepts were excluded.⁴ Major oncologic surgery concepts were created using standard codes obtained from ATLAS. Exclusion criteria included (1) endoscopic or natural orifice procedures; (2) percutaneous approaches; (3) diagnostic procedures (unless performed open); (4) cosmetic procedures; (5) nononcologic procedures; and (6) transplants.

The primary outcome of the study was composite adverse event that occurred within 30 days of surgery. Adverse events included mortality, hospital readmission, pneumonia, respiratory failure, pulmonary embolism, sepsis, cardiac arrhythmia, renal failure, urinary tract infection, and deep vein thrombosis. SNOMED concepts were used for defining surgical morbidity, because there is not a validated crosswalk to other surgical classification frameworks presently available in the N3C Data Enclave (i.e., Clavien-Dindo). Multivariable logistic regression models assessing postoperative outcomes were adjusted for relative surgical risk, comorbidities, age, sex, and race. All analyses were performed within the N3C Data Enclave.

This is a U.S. Government work and not under copyright protection in the US; foreign copyright protection may apply 2022

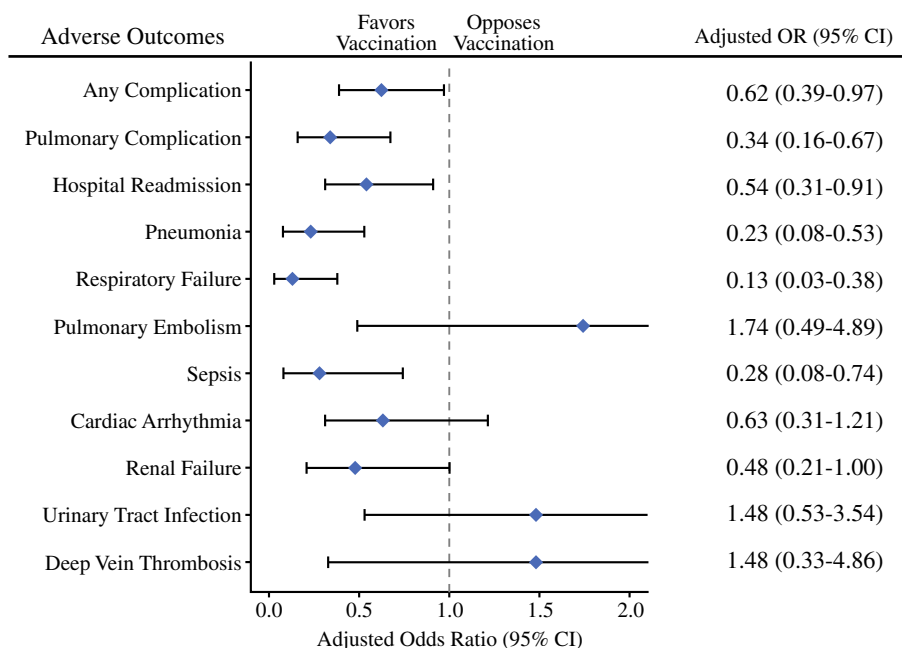
First Received: 9 November 2022

Accepted: 22 November 2022

Published Online: 7 December 2022

A. N. Kothari, MD
e-mail: akothari@mcw.edu

FIG. 1 Association between preoperative vaccination and adverse surgical outcomes in patients with postoperative COVID-19



RESULTS

Of 126,216 patients who underwent oncologic surgery, 1,091 (0.9%) developed a SARS-CoV-2 infection within 30 days after surgery. Patients who developed postoperative COVID-19 were at increased risk for 30-day readmission (47% vs. 15%, $P < 0.001$), pulmonary complications (20% vs. 4.4%, $P < 0.001$), nonfatal adverse events (47% vs. 20%, $P < 0.001$), and mortality (5.3% vs.

1.0%, $P < 0.001$). Following adjustment, postoperative COVID-19 was an independent risk factor and noted to increase the odds of all observed adverse events (Table 1).

At the time of surgery, 12,220 (9.7%) patients were fully vaccinated. Patients who were fully vaccinated did not have a decreased risk of developing postoperative COVID-19 (adjusted odds ratio [aOR] 1.12 [0.91–1.37]). Of patients with postoperative SARS-CoV-2 infection, 112 (10.2%) were fully vaccinated. These patients were observed to be at a decreased risk for 30-day readmission (aOR 0.54 [0.31–0.91]), pulmonary complications (aOR

TABLE 1 Risk of adverse 30-day outcomes following surgery in patients with and without postoperative SARS-CoV-2

Outcomes	No postoperative COVID-19 (N = 125,125)	Postoperative COVID-19 (N = 1,091)	P value	Adjusted OR (95% CI)
Mortality	1,239 (1.0%)	58 (5.3%)	< 0.001	5.73 (4.20-7.66)
Any complication	24,987 (20%)	510 (47%)	< 0.001	3.64 (3.18-4.17)
Pulmonary complication	5,474 (4.4%)	220 (20%)	< 0.001	5.99 (5.05-7.08)
Hospital readmission	14,767 (15%)	396 (47%)	< 0.001	5.17 (4.44-6.02)
Pneumonia	2,010 (1.6%)	168 (15%)	< 0.001	12.1 (9.99-14.6)
Respiratory failure	3,154 (2.5%)	145 (13%)	< 0.001	6.52 (5.33-7.92)
Pulmonary embolism	1,571 (1.3%)	30 (2.7%)	< 0.001	2.00 (1.30-2.93)
Sepsis	2,625 (2.1%)	118 (11%)	< 0.001	5.56 (4.46-6.88)
Cardiac arrhythmia	9,395 (7.5%)	168 (15%)	< 0.001	2.37 (1.96-2.85)
Renal failure	5,520 (4.4%)	149 (14%)	< 0.001	3.60 (2.95-4.37)
Urinary tract infection	2,819 (2.3%)	43 (3.9%)	< 0.001	1.81 (1.29-2.47)
Deep vein thrombosis	1,044 (0.8%)	21 (1.9%)	< 0.001	2.30 (1.42-3.50)

OR odds ratio; CI confidence interval

0.34 [0.16–0.67]), and nonfatal adverse events (aOR 0.62 [0.39–0.97]) compared with those who were not fully vaccinated. Notably, patients that were fully vaccinated and developed COVID-19 after surgery did not have any 30-day mortality.

DISCUSSION

In this study of cancer patients undergoing surgical resection, postoperative SARS-CoV-2 infection remains a significant risk factor for mortality and morbidity. Vaccination decreases the risk of adverse postoperative events, however, does not prevent developing COVID-19 after surgery. While the incidence of postoperative COVID-19 infection is low, it remains a devastating complication in patients undergoing oncologic resection. Vaccination against SARS-CoV-2 provides a powerful, widely available measure to mitigate this risk and should be a mandatory part of preoperative optimization.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1245/s10434-022-12916-z>.

ACKNOWLEDGMENT The analyses described in this publication were conducted with data or tools accessed through the NCATS N3C Data Enclave covid.cd2h.org/enclave and supported by CD2H - The National COVID Cohort Collaborative (N3C) IDEa CTR Collaboration 3U24TR002306-04S2 NCATS U24 TR002306. This research was possible because of the patients whose information is included within the data from participating organizations (covid.cd2h.org/dtas) and the organizations and scientists (covid.cd2h.org/duas) who have contributed to the ongoing development of this community resource (cite this <https://doi.org/10.1093/jamia/ocaa196>). We gratefully acknowledge the following core contributors to N3C: Adam B. Wilcox, Adam M. Lee, Alexis Graves, Alfred (Jerrod) Anzalone, Amin Manna, Amit Saha, Amy Olex, Andrea Zhou, Andrew E. Williams, Andrew Southerland, Andrew T. Girvin, Anita Walden, Anjali A. Sharathkumar, Benjamin Amor, Benjamin Bates, Brian Hendricks, Brijesh Patel, Caleb Alexander, Carolyn Bramante, Cavin Ward-Caviness, Charisse Madlock-Brown, Christine Suver, Christopher Chute, Christopher Dillon, Chunlei Wu, Clare Schmitt, Cliff Takemoto, Dan Housman, Davera Gabriel, David A. Eichmann, Diego Mazzotti, Don Brown, Eilis Boudreau, Elaine Hill, Elizabeth Zampino, Emily Carlson Marti, Emily R. Pfaff, Evan French, Farrukh M Koraihsy, Federico Mariona, Fred Prior, George Sokos, Greg Martin, Harold Lehmann, Heidi Spratt, Hemalkumar Mehta, Hongfang Liu, Hythem Sidky, J.W. Awori Hayanga, Jami Pincavitch, Jaylyn Clark, Jeremy Richard Harper, Jessica Islam, Jin Ge, Joel Gagnier, Joel H. Saltz, Joel Saltz, Johanna Loomba, John Buse, Jomol Mathew, Joni L. Rutter, Julie A. McMurry, Justin Guinney, Justin Starren, Karen Crowley, Katie Rebecca Bradwell, Kellie M. Walters, Ken Wilkins, Kenneth R. Gersing, Kenrick Dwain Cato, Kimberly Murray, Kristin Kostka, Lavance Northington, Lee Allan Pyles, Leonie Misquitta, Lesley Cottrell, Lili Portilla, Mariam Deacy, Mark M. Bissell, Marshall Clark, Mary Emmett, Mary Morrison Saltz, Matvey B. Palchuk, Melissa A. Haendel, Meredith Adams, Meredith Temple-O'Connor, Michael G. Kurilla, Michele Morris, Nabeel Qureshi, Nasia Safdar, Nicole Garbarini, Noha Sharafeldin, Ofer Sadan, Patricia A. Francis, Penny Wung Burgoon, Peter Robinson, Philip R.O. Payne, Rafael Fuentes, Randeep Jawa,

Rebecca Erwin-Cohen, Rena Patel, Richard A. Moffitt, Richard L. Zhu, Rishi Kamaleswaran, Robert Hurley, Robert T. Miller, Saiju Pyarajan, Sam G. Michael, Samuel Bozzette, Sandeep Mallipattu, Satyanarayana Vedula, Scott Chapman, Shawn T. O'Neil, Soko Setoguchi, Stephanie S. Hong, Steve Johnson, Tellen D. Bennett, Tiffany Callahan, Umit Topaloglu, Usman Sheikh, Valery Gordon, Vignesh Subbian, Warren A. Kibbe, Wendy Hernandez, Will Beasley, Will Cooper, William Hillegass, Xiaohan Tanner Zhang. Details of contributions available at covid.cd2h.org/core-contributors. The following institutions whose data is released or pending: Available: Advocate Health Care Network — UL1TR002389: The Institute for Translational Medicine (ITM) • Boston University Medical Campus — UL1TR001430: Boston University Clinical and Translational Science Institute • Brown University — U54GM115677: Advance Clinical Translational Research (Advance-CTR) • Carilion Clinic — UL1TR003015: iTHRIV Integrated Translational health Research Institute of Virginia • Charleston Area Medical Center — U54GM104942: West Virginia Clinical and Translational Science Institute (WVCTSI) • Children's Hospital Colorado — UL1TR002535: Colorado Clinical and Translational Sciences Institute • Columbia University Irving Medical Center — UL1TR001873: Irving Institute for Clinical and Translational Research • Duke University — UL1TR002553: Duke Clinical and Translational Science Institute • George Washington Children's Research Institute — UL1TR001876: Clinical and Translational Science Institute at Children's National (CTSA-CN) • George Washington University — UL1TR001876: Clinical and Translational Science Institute at Children's National (CTSA-CN) • Indiana University School of Medicine — UL1TR002529: Indiana Clinical and Translational Science Institute • Johns Hopkins University — UL1TR003098: Johns Hopkins Institute for Clinical and Translational Research • Loyola Medicine — Loyola University Medical Center • Loyola University Medical Center — UL1TR002389: The Institute for Translational Medicine (ITM) • Maine Medical Center — U54GM115516: Northern New England Clinical & Translational Research (NNE-CTR) Network • Massachusetts General Brigham — UL1TR002541: Harvard Catalyst • Mayo Clinic Rochester — UL1TR002377: Mayo Clinic Center for Clinical and Translational Science (CCaTS) • Medical University of South Carolina — UL1TR001450: South Carolina Clinical & Translational Research Institute (SCTR) • Montefiore Medical Center — UL1TR002556: Institute for Clinical and Translational Research at Einstein and Montefiore • Nemours — U54GM104941: Delaware CTR ACCEL Program • NorthShore University HealthSystem — UL1TR002389: The Institute for Translational Medicine (ITM) • Northwestern University at Chicago — UL1TR001422: Northwestern University Clinical and Translational Science Institute (NUCATS) • OCHIN — INV-018455: Bill and Melinda Gates Foundation grant to Sage Bionetworks • Oregon Health & Science University — UL1TR002369: Oregon Clinical and Translational Research Institute • Penn State Health Milton S. Hershey Medical Center — UL1TR002014: Penn State Clinical and Translational Science Institute • Rush University Medical Center — UL1TR002389: The Institute for Translational Medicine (ITM) • Rutgers, The State University of New Jersey — UL1TR003017: New Jersey Alliance for Clinical and Translational Science • Stony Brook University — U24TR002306 • The Ohio State University — UL1TR002733: Center for Clinical and Translational Science • The State University of New York at Buffalo — UL1TR001412: Clinical and Translational Science Institute • The University of Chicago — UL1TR002389: The Institute for Translational Medicine (ITM) • The University of Iowa — UL1TR002537: Institute for Clinical and Translational Science • The University of Miami Leonard M. Miller School of Medicine — UL1TR002736: University of Miami Clinical and Translational Science Institute • The University of Michigan at Ann Arbor — UL1TR002240: Michigan Institute for Clinical and Health Research • The University of Texas Health Science Center at Houston —

UL1TR003167: Center for Clinical and Translational Sciences (CCTS) • The University of Texas Medical Branch at Galveston — UL1TR001439: The Institute for Translational Sciences • The University of Utah — UL1TR002538: Uhealth Center for Clinical and Translational Science • Tufts Medical Center — UL1TR002544: Tufts Clinical and Translational Science Institute • Tulane University — UL1TR003096: Center for Clinical and Translational Science • University Medical Center New Orleans — U54GM104940: Louisiana Clinical and Translational Science (LA CaTS) Center • University of Alabama at Birmingham — UL1TR003096: Center for Clinical and Translational Science • University of Arkansas for Medical Sciences — UL1TR003107: UAMS Translational Research Institute • University of Cincinnati — UL1TR001425: Center for Clinical and Translational Science and Training • University of Colorado Denver, Anschutz Medical Campus — UL1TR002535: Colorado Clinical and Translational Sciences Institute • University of Illinois at Chicago — UL1TR002003: UIC Center for Clinical and Translational Science • University of Kansas Medical Center — UL1TR002366: Frontiers: University of Kansas Clinical and Translational Science Institute • University of Kentucky — UL1TR001998: UK Center for Clinical and Translational Science • University of Massachusetts Medical School Worcester — UL1TR001453: The UMass Center for Clinical and Translational Science (UMCCTS) • University of Minnesota — UL1TR002494: Clinical and Translational Science Institute • University of Mississippi Medical Center — U54GM115428: Mississippi Center for Clinical and Translational Research (CCTR) • University of Nebraska Medical Center — U54GM115458: Great Plains IDEa-Clinical & Translational Research • University of North Carolina at Chapel Hill — UL1TR002489: North Carolina Translational and Clinical Science Institute • University of Oklahoma Health Sciences Center — U54GM104938: Oklahoma Clinical and Translational Science Institute (OCTSI) • University of Rochester — UL1TR002001: UR Clinical & Translational Science Institute • University of Southern California — UL1TR001855: The Southern California Clinical and Translational Science Institute (SC CTSI) • University of Vermont — U54GM115516: Northern New England Clinical & Translational Research (NNE-CTR) Network • University of Virginia — UL1TR003015: iTHRIV Integrated Translational health Research Institute of Virginia • University of Washington — UL1TR002319: Institute of Translational Health Sciences • University of Wisconsin-Madison — UL1TR002373: UW Institute for Clinical and Translational Research • Vanderbilt University Medical Center — UL1TR002243: Vanderbilt Institute for Clinical and Translational Research • Virginia Commonwealth University — UL1TR002649: C. Kenneth and Dianne Wright Center for Clinical and Translational Research • Wake Forest University Health Sciences — UL1TR001420: Wake Forest Clinical and Translational Science Institute • Washington University in St. Louis — UL1TR002345: Institute of Clinical and Translational Sciences • Weill Medical College of Cornell University — UL1TR002384: Weill Cornell Medicine Clinical and Translational Science Center • West Virginia University — U54GM104942: West Virginia Clinical and Translational Science Institute (WVCTSI). Submitted: Icahn School of Medicine at Mount Sinai — UL1TR001433: ConduITS Institute for Translational Sciences • The University of Texas Health Science Center at Tyler — UL1TR003167: Center for Clinical and Translational Sciences (CCTS) • University of California, Davis — UL1TR001860: UC Davis Health Clinical and Translational Science Center • University of California, Irvine — UL1TR001414: The UC Irvine Institute for Clinical and Translational Science (ICTS) • University of California, Los Angeles — UL1TR001881: UCLA Clinical Translational Science Institute • University of California, San Diego — UL1TR001442: Altman Clinical and Translational Research Institute • University of California, San Francisco —

UL1TR001872: UCSF Clinical and Translational Science Institute. Pending: Arkansas Children's Hospital — UL1TR003107: UAMS Translational Research Institute • Baylor College of Medicine — None (Voluntary) • Children's Hospital of Philadelphia — UL1TR001878: Institute for Translational Medicine and Therapeutics • Cincinnati Children's Hospital Medical Center — UL1TR001425: Center for Clinical and Translational Science and Training • Emory University — UL1TR002378: Georgia Clinical and Translational Science Alliance • HonorHealth — None (Voluntary) • Loyola University Chicago — UL1TR002389: The Institute for Translational Medicine (ITM) • Medical College of Wisconsin — UL1TR001436: Clinical and Translational Science Institute of Southeast Wisconsin • MedStar Health Research Institute — UL1TR001409: The Georgetown-Howard Universities Center for Clinical and Translational Science (GHUCCTS) • MetroHealth — None (Voluntary) • Montana State University — U54GM115371: American Indian/Alaska Native CTR • NYU Langone Medical Center — UL1TR001445: Langone Health's Clinical and Translational Science Institute • Ochsner Medical Center — U54GM104940: Louisiana Clinical and Translational Science (LA CaTS) Center • Regenstrief Institute — UL1TR002529: Indiana Clinical and Translational Science Institute • Sanford Research — None (Voluntary) • Stanford University — UL1TR003142: Spectrum: The Stanford Center for Clinical and Translational Research and Education • The Rockefeller University — UL1TR001866: Center for Clinical and Translational Science • The Scripps Research Institute — UL1TR002550: Scripps Research Translational Institute • University of Florida — UL1TR001427: UF Clinical and Translational Science Institute • University of New Mexico Health Sciences Center — UL1TR001449: University of New Mexico Clinical and Translational Science Center • University of Texas Health Science Center at San Antonio — UL1TR002645: Institute for Integration of Medicine and Science • Yale New Haven Hospital — UL1TR001863: Yale Center for Clinical Investigation.

DISCLAIMER The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH. Authorship was determined using ICMJE recommendations.

REFERENCES

1. Nepogodiev D, Bhangu A, Glasbey JC, et al. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. *Lancet*. 2020;396(10243):27–38. [https://doi.org/10.1016/S0140-6736\(20\)31182-X](https://doi.org/10.1016/S0140-6736(20)31182-X).
2. Tzeng C-WD, Cao HST, Roland CL, et al. Surgical decision making and prioritization for cancer patients at the onset of the COVID-19 pandemic: a multidisciplinary approach. *Surg Oncol*. 2020;34:182–5.
3. Baiocchi G, Aguiar S Jr, Duprat JP, et al. Early postoperative outcomes among patients with delayed surgeries after preoperative positive test for SARS-CoV-2: a case-control study from a single institution. *J Surg Oncol*. 2021. <https://doi.org/10.1002/jso.26377>.
4. Sharafeldin N, Bates B, Song Q, et al. Outcomes of COVID-19 in patients with cancer: report from the National COVID Cohort Collaborative (N3C). *J Clin Oncol*. 2021;39(20):2232–46. <https://doi.org/10.1200/JCO.21.01074>.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.