Predicting a Positive Antibody Response After 2 SARS-CoV-2 mRNA Vaccines in Transplant Recipients: A Machine Learning Approach With External Validation

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Background. Solid organ transplant recipients (SOTRs) are less likely to mount an antibody response to SARS-CoV-2 mRNA vaccines. Understanding risk factors for impaired vaccine response can guide strategies for antibody testing and additional vaccine dose recommendations. **Methods.** Using a nationwide observational cohort of 1031 SOTRs, we created a machine learning model to explore, identify, rank, and quantify the association of 19 clinical factors with antibody responses to 2 doses of SARS-CoV-2 mRNA vaccines. External validation of the model was performed using a cohort of 512 SOTRs at Houston Methodist Hospital. **Results.** Mycophenolate mofetil use, a shorter time since transplant, and older age were the strongest predictors of a negative antibody response, collectively contributing to 76% of the model's prediction performance. Other clinical factors, including transplanted organ, vaccine type (mRNA-1273 versus BNT162b2), sex, race, and other immunosuppressants, showed comparatively weaker associations with an antibody response. This model showed moderate prediction performance, with an area under the receiver operating characteristic curve of 0.79 in our cohort and 0.67 in the external validation cohort. An online calculator based on our prediction model is available at http://transplantmodels.com/covidvaccine/. **Conclusions.** Our machine learning model helps understand which transplant patients need closer follow-up and additional doses of vaccine to achieve protective immunity. The online calculator based on this model can be incorporated into transplant providers' practice to facilitate patient-centric, precision risk stratification and inform vaccination strategies among SOTRs.

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INTRODUCTION

Approximately half of all solid organ transplant recipients (SOTRs) develop an antibody response after 2 doses of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) mRNA vaccines.[1,2] Additional doses may induce serologic responses in those who failed 2, 3, or 4 doses, but clinicians lack prediction models to guide personalized antibody testing and vaccination recommendations. Instead, the transplant community currently operates under a "one size fits all" recommendation for all SOTRs to receive at least 3 vaccine doses with vague guidance on timing or ideal platform selection for additional "booster" doses.[3-5] This may not be the most appropriate use of limited resources, particularly in the developing world where vaccines and routine antibody testing are not widely available.

Understanding the clinical factors associated with lack of antibody response after mRNA vaccination of SOTRs would inform subsequent vaccine platform number and selection, the role of antibody testing, intervals for additional doses, and potentially identify those to prioritize in global areas of limited vaccine access. Machine learning (ML) is a sophisticated alternative to traditional regression modeling and has been utilized for large registry data analyses in transplantation.[6,7] However, the utility of these methods in the prediction of SARS-CoV-2 vaccine response in SOTRs has not been explored.

In this study, we quantify risk factors and create a prediction model for positive antibody response to doses of SARS-CoV-2 mRNA vaccine (mRNA-1273 or BNT162b2). We analyzed a nationwide cohort of 1037 transplant recipients who completed the 2-dose mRNA vaccine series via an ML algorithm that can quantify non linear associations and characterize the interactions between predictors in a robust and comprehensive manner. Our prediction models' performances were evaluated using an external validation cohort from a tertiary transplant center.

MATERIALS AND METHODS

Study Population

SOTRs without a previously reported COVID-19 infection were recruited from across the United States to participate in this prospective cohort through a social media campaign.[1,2,4,5] SOTRs who reported receiving 2 doses of SARS-CoV-2 mRNA vaccine between December 16, 2020, and May 21, 2021, were followed through July 6, 2021. Semiquantitative anti-Spike antibody testing with the Roche Elecsys anti-SARS-CoV-2 S enzyme immunoassay, which tests for the receptor-binding domain of the SARS-CoV-2 spike protein, or the EUROIMMUN enzyme immunoassay, which tests for the S1 domain of the SARS-CoV-2 spike protein, were used. The study was approved by the Johns Hopkins Medical Institute (JHMI) Institutional Review Board (IRB), and participants provided informed consent electronically.

An external validation cohort was used to test the prediction performance of our models. The Houston Methodist J.C. Walter Jr. Transplant Center cohort included 512 SOTRs vaccinated between January 4, 2021, and May 31, 2021. Patients who reported transplant after vaccination, had no documented vaccine type or post-dose 2 antibody test result, or tested positive for anti–SARS-COV-2 nucleocapsid protein antigen (using the Roche Elecsys anti–SARS-CoV-2 serological assay) or qualitative PCR (titers >1:50 threshold is considered positive) were excluded. Data were collected with a waiver of informed consent approved by the Houston Methodist Research Institute (HMRI) IRB. De-identified data from HMRI were shared with JHMI after approval from both IRBs.

Immunogenicity

Negative titer levels were <0.8 U/mL (Roche) and ≤1.1 AU (EUROIMMUN), per manufacturer guidelines. We stratified positive antibody levels into "low" and "high" positive categories. Low-positive results were antibody titers >0.8 U/mL but ≤50 U/mL (Roche) or >1.1 AU but ≤4 AU (EUROIMMUN). High-positive titers were >50 U/mL (Roche) and >4 AU (EUROIMMUN). These high-positive cutoffs were based on the comprehensive analysis by Khoury et al, which estimated that an anti–receptor-binding domain titer of 54 U/mL with a 95% confidence interval (CI), 30–96 U/mL equated to approximately 50% protective neutralization against the ancestral variant, as well as the Food and Drug Administration recommended cutoffs of 132 U/mL (Roche) and 3.5 AU (EUROIMMUN).[8,9]

Prediction of Positive Versus Negative Antibody Response

We created a prediction model for positive versus negative antibody response using gradient boosting.[10] In this analysis, a positive response included both low- and high-positives. Gradient boosting is a general-purpose ML algorithm that generates a sequence of parsimonious prediction models based on the residual error of the previous models. This model included 19 predictors: age, sex, race (White versus non-White), organ transplanted, years since transplant, number of transplants, immunosuppressive medications (mycophenolate mofetil [MMF], tacrolimus, corticosteroids, azathioprine, sirolimus, and everolimus), and vaccine type (mRNA-1273 or BNT162b2).

Characterization of the Factors Associated With Positive Antibody Response

To quantify the association of the predictors and positive antibody response in a traditional regression framework, we performed a logistic regression using the same predictors as the gradient boosting described here against positive (versus negative) antibody response. Akaike information criterion was used to select predictors for this model and determine the ideal functional forms of the predictors. We incorporated predictor–predictor interactions using their product terms.

Prediction of Antibody Titer Category

To characterize the association of the predictors with low- and high-positive antibody response separately, we

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created an additional prediction model wherein the outcome was categorized into high-positive, low-positive, or negative. Like the previous model, gradient boosting was used with the same set of 19 predictors described previously, but this model used a multiclass objective function as opposed to a binary format.

Statistical Analysis

Variable importance and Shapley additive explanations (SHAP) were used to characterize the association between gradient boosting predictors and antibody response. Variable importance represents the contribution of each predictor to the overall model prediction performance.[11] SHAP values represent a specific predictor's impact on the predicted outcome in an individual patient.[12] First, we randomly permuted a predictor in our dataset to render it uninformative, used the modified dataset to create a new prediction model, and measured the decline in the prediction performance in the new model compared to the original. A greater decline in prediction performance indicates that the select predictor had a high variable importance. This procedure was repeated for every predictor in the original model, and the variable importance was presented in a relative scale. Second, we used SHAP values to visualize the predictor–outcome associations as well as the predictor–predictor interactions. SHAP values represent a specific predictor's impact on the predicted outcome in an individual participant.[12] In this study, SHAP values can be interpreted as the log odds of the outcome. Additionally, we conducted a preliminary evaluation of the model performance by measuring the area under the receiver operating characteristic (AUROC) curve via a 10-fold cross-validation.

Using the external validation cohort, we evaluated the prediction performance of the models in discrimination and calibration. Discrimination represents the model's ability to accurately assign higher predicted risk to those who had developed the outcome, and calibration represents the alignment between the predicted risk and the true risk.[13] Discrimination was measured using AUROC. Calibration was assessed using locally estimated scatterplot smoothing between the predicted log odds of the outcome and the observed outcome.[14]

Tuning parameters for the gradient boosting algorithm were selected via 10-fold cross-validations. Missing values were handled via multiple imputations during the gradient boosting procedure; for each iteration, the effect of the missing variable was predicted based on nonmissing parts of the data and the model. All analyses were performed using R version 4.0.4. Observational study data were collected and managed using REDCap electronic data capture tools hosted at JHMI.[15]

RESULTS

Population Characteristics

This study included 1031 participants who reported 2 doses of an mRNA vaccine and were tested for antibody response 1 mo after dose 2 (D2). Of these participants, 432 (42.1%) had negative, 223 (21.7%) had low-positive, and 372 (36.2%) had high-positive titers. Four participants reported positive serologic testing results, but their exact titers were unavailable. Compared with participants with negative titers, those with positive titers were more frequently liver transplant recipients (33.6% versus 9.0%), had a longer time since transplant (median; 9 versus 5 y), and less frequently reported MMF as a part of their immunosuppressive regimen (43.2% versus 86.1%) (Table 1).

Post-dose 1 (D1) antibody titer data were available for 918 (89.4%) participants; 752 (81.9%) had negative, 129 (14.1%) had low-positive, and 37 (4.0%) had high-positive titers. Among the 752 participants with negative titers post-D1, 386 (51.3%) remained negative, 191 (25.4%) developed low-positive, and 175 (23.3%) developed high-positive titers post-D2. Among the 129 participants with low-positive titers post-D1, 1 (0.8%) decreased to negative, 7 (5.4%) maintained low-positive, and 121 (93.8%) developed high-positive titers post-D2. Among the 37 participants with high-positive titers post-D1, 1 (2.7%) decreased to negative and 38 (97.3%) maintained high-positive titers post-D2.

The external validation cohort included 512 participants. Of those participants, 220 (43.0%) had a positive antibody response after 2 mRNA vaccine doses (**Table S1, SDC,** http://links.lww.com/TP/C491). In the positive and negative subgroups, the external validation cohort included a higher proportion of male (64.1% and 56.8% versus 43.6% and 41.1%, respectively) and non-White recipients (24.5% and 25.0% versus 10.0% and 10.0%, respectively), as well as patients with less time since transplant (median, 3 and 2 y versus 9 and 5 y, respectively) than the primary cohort. Other characteristics were relatively similar between the primary and external validation cohorts.

Prediction of Any Positive Versus Negative Antibody Response

Among 19 predictors supplied to the ML algorithm, 16 were included in the final model, and 3 were eliminated. MMF (39.5%), time since transplant (23.6%), and age (13.1%) showed the highest variable importance, followed by liver transplant status (6.4%) and type of vaccine product (4.1%) (Table 2, left column).

A longer time since transplant was associated with higher odds of a positive antibody response; this association was stronger during the first several years post-transplant (Figure 1A). Time since transplant also showed some predictor–predictor interactions, specifically in liver transplant recipients and participants taking MMF. Although a longer time since transplant was associated with higher odds of a positive antibody response in both liver and non-liver transplant recipients, this association was less pronounced in liver transplant recipients (Figure 2A; shown in red). Additionally, beyond the 5th year post-transplant, the association of time since transplant with a positive antibody response was stronger among those using MMF than it was among those who were not (Figure 2B).

Older age was associated with lower odds of a positive antibody response, especially among those under 65 y of age (Figure 1B). MMF use was associated with lower odds of a positive antibody response (Figure 1C), whereas liver transplant status (versus non-liver transplant) was associated with higher odds of a positive antibody response (Figure 1D).

This model showed moderate prediction performance. In the primary cohort, this model showed a cross-validation

TABLE 1.

Cohort characteristics by antibody titer after 2-dose mRNA vaccine series

		Positive (n = 599)		
	Negative (n = 432)	All positives (n = 599)	Low-positive (n = 223[a])	High-positive (n = 372 [a])
Age (y)	62 (47–68)	59 (45–68)	63 (50–70)	58 (43–66)
Male sex	175 (41.0)	261 (43.9)	98 (45.0)	161 (43.3)
Non-White race	42 (9.8)	59 (9.9)	22 (10.1)	36 (9.7)
Transplanted organ (multiple-response allowed)				
Kidney	273 (63.2)	281 (46.9)	125 (56.1)	154 (41.4)
Liver	39 (9.0)	201 (33.6)	44 (19.7)	156 (41.9)
Pancreas	25 (5.8)	17 (2.8)	9 (4.0)	7 (1.9)
Heart	56 (13.0)	98 (16.4)	42 (18.8)	55 (14.8)
Lung	70 (16.2)	38 (6.3)	20 (9.0)	18 (4.8)
Intestine	2 (0.5)	2 (0.3)	0 (0.0)	2 (0.5)
Other	4 (0.9)	1 (0.2)	0 (0.0)	1 (0.3)
Time since transplant (y)	5 (2–11)	9 (4–16)	7 (3–15)	9 (5–16)
Immunosuppressive agents (multiple-response allowed)				
MMF	372 (86.1)	259 (43.2)	147 (65.9)	110 (29.6)
Tacrolimus	380 (88.0)	468 (78.1)	173 (77.6)	292 (78.5)
Corticosteroids	278 (64.4)	281 (46.9)	117 (52.5)	162 (43.5)
Azathioprine	11 (2.5)	63 (10.5)	16 (7.2)	47 (12.6)
Sirolimus	37 (8.6)	72 (12.0)	20 (9.0)	51 (13.7)
Everolimus	11 (2.5)	33 (5.5)	9 (4.0)	23 (6.2)
Vaccine product: MRNA-1273 (vs BNT162b2)	166 (38.4)	308 (51.4)	90 (40.4)	217 (58.3)
Total number of transplants				
1	395 (91.4)	566 (94.5)	208 (93.3)	355 (95.4)
2	37 (8.6)	28 (4.7)	13 (5.8)	14 (3.8)
3+	0 (0.0)	5 (0.8)	2 (0.9)	3 (0.8)

Continuous variables are shown in median (IQR) and categorical variables in N (%).
[a]Four recipients whose antibody response data were available only in a qualitative format were excluded from this stratified analysis.
MMF, mycophenolate mofetil.

TABLE 2.

Variable importance

	Model 1 (positive vs negative)		Model 2 (antibody titer category)	
Rank	Predictor	Importance	Predictor	Importance
1	MMF use	39.5%	MMF use	42.1%
2	Time since transplant	23.6%	Time since transplant	20.3%
3	Age	13.1%	Age	13.3%
4	Liver transplant	6.4%	Liver transplant	7.4%
5	Vaccine product (MRNA-1273 vs BNT162b2)	4.1%	Vaccine product (MRNA-1273 vs BNT162b2)	5.5%
6	Lung transplant	3.7%	Lung transplant	3.0%
7	Male sex	2.8%	Male sex	2.9%
8	Corticosteroids	1.6%	Sirolimus	1.4%
9	Kidney transplant	1.4%	Corticosteroids	1.2%
10	Tacrolimus	1.3%	Heart transplant	1.1%
11	Sirolimus	1.1%	Tacrolimus	0.6%
12	Pancreas transplant	0.5%	Kidney transplant	0.5%
13	Heart transplant	0.4%	Number of transplants	0.3%
14	Non-White race	0.3%	Pancreas transplant	0.2%
15	Everolimus	0.2%	Non-White race	0.1%
16	Number of transplants	0.1%	Everolimus	0.0%

The outcome (antibody response after vaccine dose 2) was processed as binary (positive vs negative) in model 1 and as categorical (high-positive vs low-positive vs negative) in model 2. Importance values were assessed via the permutation method and are shown in a relative scale across the predictors chosen in the final model.
MMF, mycophenolate mofetil.

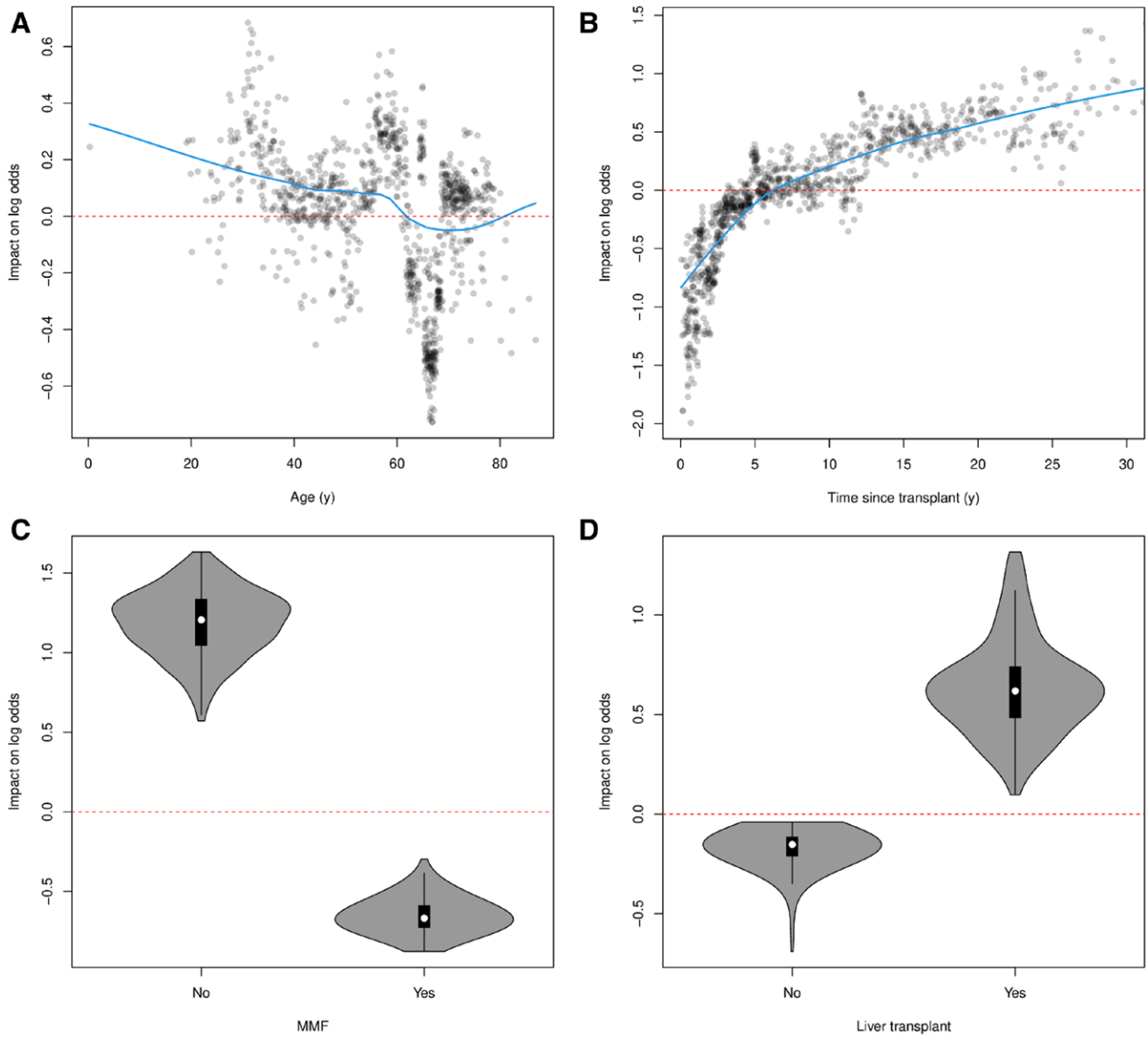

FIGURE 1. Association of key predictors with positive (vs negative) antibody response in a machine learning framework. For (A) and (B), markers indicate the impact of the predictor on the predicted log odds of the outcome in individual participants. For (C) and (D), the width of the plots represents the frequency of the data at the level, and the box and the white dot represent the interquartile range and the median value, respectively. A, Age. B, Time since transplant. C, MMF. D, Liver transplant (vs non-liver transplant). MMF, mycophenolate mofetil.

AUROC of 0.79. In the external validation cohort, the AUROC was 0.67 (95% CI, 0.62-0.72), and the calibration curve was relatively well aligned with the ideal line (y = x) (Figure 3).

Characterization of Factors Associated With Positive Antibody Response

The key results from our gradient boosting model were reproduced in our logistic regression. Specifically, predictors with higher variable importance in the gradient boosting model showed statistically significant associations with a positive antibody response in our logistic regression model (**Table S2, SDC,** http://links.lww.com/TP/C491). Each 1-y increase in time since transplant was associated with 1.27-fold odds (95% CI, 1.16-1.38) of a positive antibody response, up until 7 y since transplant, when the association became attenuated and was no longer statistically significant (adjusted odds ratio [aOR], 1.01; 95% CI, 0.98-1.05). Older age was associated with lower odds of positive antibody response (per 10 y increase; aOR, 0.89; 95% CI, 0.80-0.99). MMF use was associated with significantly lower odds of positive antibody response (aOR, 0.14; 95% CI, 0.10-0.20) and male sex (aOR, 1.38; 95% CI, 1.02-1.89) and receiving a liver transplant (aOR, 11.43; 95% CI, 4.70-29.17) with higher odds of positive antibody response. In addition, the statistically significant interaction between liver transplant and time since transplant (between 0 and 7 y since transplant) (p for interaction = 0.004), indicated that the association of time since transplant with positive antibody response was weaker among liver transplant recipients than it was among other organ transplant recipients.

Prediction of Antibody Titer Category

In our secondary gradient boosting model for prediction of category of antibody response (high-positive versus

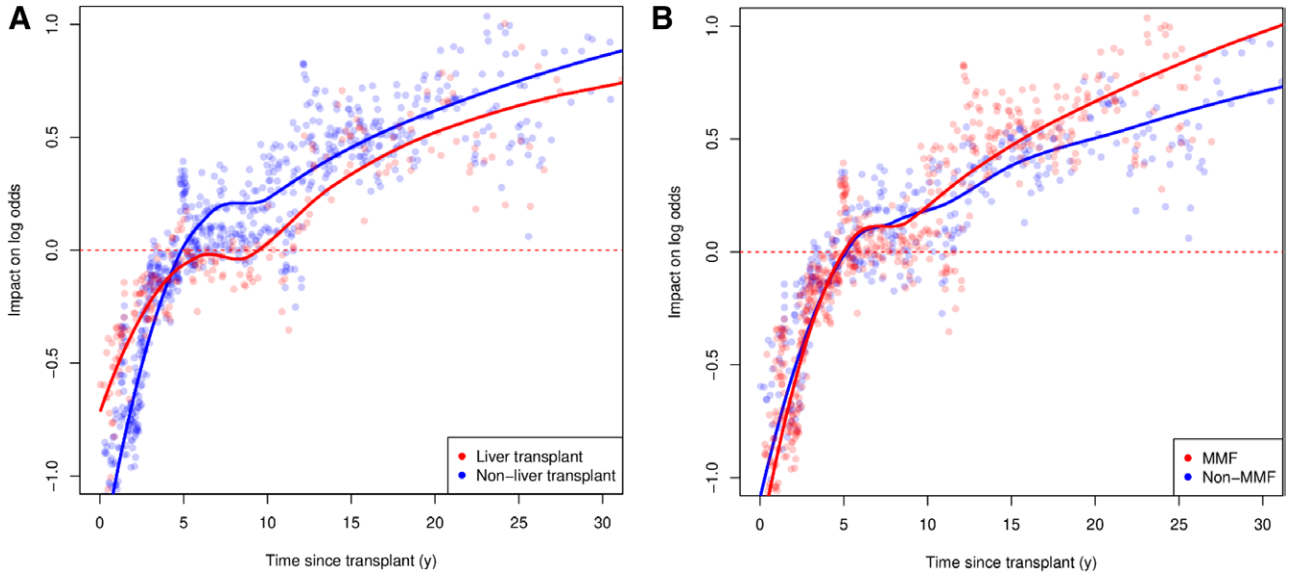

FIGURE 2. Notable predictor–predictor interactions in the prediction of positive (vs negative) antibody response. A, The increase in positive antibody response associated with time since transplant was more pronounced in non-liver recipients than it was in liver recipients. B, The increase in positive antibody response associated with time since transplant was more pronounced in MMF users than it was in MMF non-users. A, Time since transplant × liver (vs non-liver) transplant. B, Time since transplant × MMF. MMF, mycophenolate mofetil.

low-positive versus negative), MMF use (42.1%), time since transplant (20.3%), and age (13.3%) showed the highest variable importance, followed by liver transplant (7.4%) and vaccine type (5.5%) (Table 2, right column).

Of note, older age was associated with decreased odds of having a high-positive antibody response (Figure 4A), indicating that older recipients may remain at risk of COVID-19 due to having a suboptimal protection against infection even if they become seropositive after vaccination. In contrast, these trends were not observed in other key risk factors such as longer time since transplant (Figure 4B) and MMF use (Figure 4C); these risk factors were associated with decreased odds of having a high-positive antibody response to vaccination but showed no meaningful association with having a low-positive response.

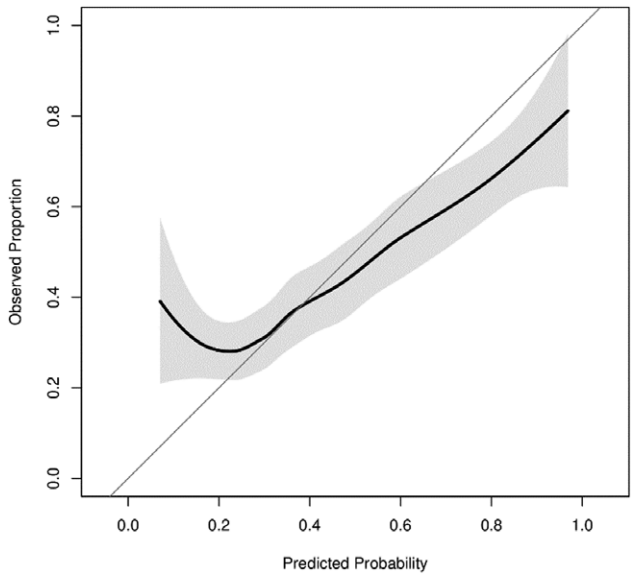

FIGURE 3. Calibration curves of the prediction model in the external validation set. The x-axis indicates the probability of a positive antibody response as predicted by our model. The y-axis indicates the actual proportion of a positive antibody response as observed in the external validation set. The calibration curve for a perfect model will overlap the identity line (y = x).

DISCUSSION

Using a nationwide observational study of 1031 COVID-19–naive SOTRs, we created and externally validated a sophisticated ML model to predict post-vaccine antibody response and the strength of that response. Among the 19 predictors investigated, MMF use, a shorter time since transplant, and older age were key risk factors that collectively contributed to 76% of the model's ability to predict failure to generate a positive antibody response. Our model showed a moderate prediction performance, with an AUROC of 0.79 in our primary cohort and 0.67 in an external validation cohort of 512 SOTRs from HM. An online risk calculator based on our model is publicly available at http://www.transplantmodels.com/covidvaccine/.

The key clinical factors identified by the ML model are congruent with findings from other studies. For example, the ML model identified a nonlinear association between the odds of a positive antibody response and time since transplant, with an initial rapid increase in the odds that gradually attenuated (Figure 1A). In addition, the ML model suggested that the impact of time since transplant varied with the use of MMF, especially after 5 y since transplant (Figure 2B). These associations have been previously reported (MMF use, age, time since transplant) to correlate with antibody response rates, but our ML model provides a more nuanced description of these associations, adding clinical relevance with the easy-to-use online clinical calculator.[2,16-20]

In addition to identifying key clinical factors associated with antibody responses, the ML model allows us to precisely predict the post-vaccine antibody response, identifying factors associated with the different categories of antibody response (negative, low-positive, and high-positive). An example of this was a longer time since transplant,

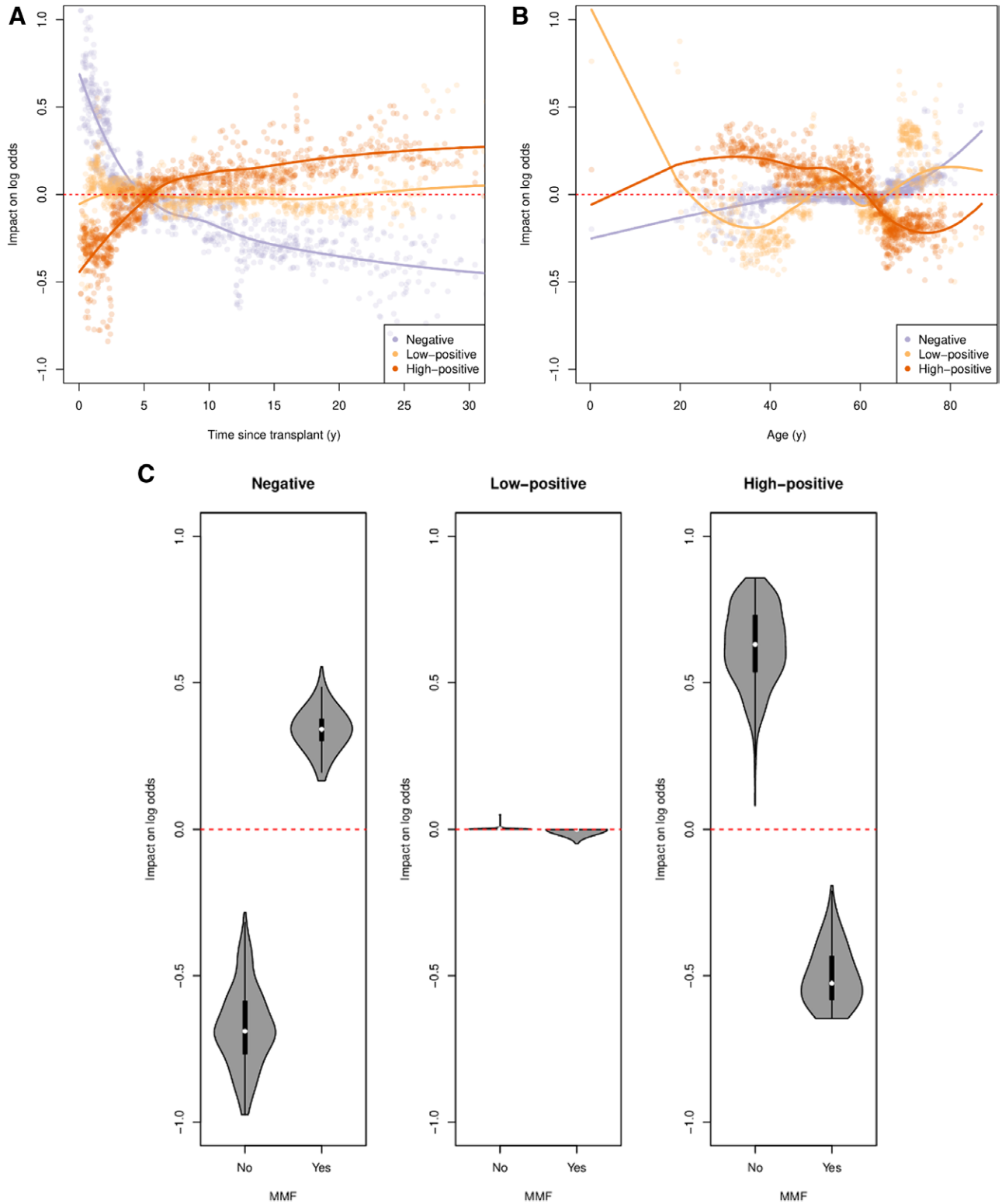

FIGURE 4. Odds of high- and low-positive antibody response by predictor levels. A, Longer time since transplant was associated with increasing odds of high-positive (dark orange) and decreasing odds of negative (light purple) antibody response over time. B, Older age was associated with increased odds of negative (light purple) or low-positive (light orange) but with decreasing odds of high-positive (dark orange) antibody response. C, MMF was associated with higher odds of negative antibody response (left panel) but with lower odds of high-positive (right panel) antibody response. A, Time since transplant. B, Age. C, Mycophenolate mofetil. MMF, mycophenolate mofetil.

which was associated with higher odds of a high-positive response, and has been previously described but until now not quantified using a large, diverse SOTR population.[20] Age had an inverse relationship with antibody response; older participants had higher odds of a low-positive antibody response. This suggests that the attenuation of the association between age and positive antibody response among older recipients, shown in our binary analysis (Figure 2B), might be a result of increasing low-positivity and decreasing high-positivity in this age group. The association between

younger age and positive antibody response was more pronounced in patients under 65 y of age, corroborating previous preliminary findings of an association between older age and shorter time since transplant with seronegativity.[2,20] Interestingly, male sex was found to have a small association (<3% in variable importance) with a positive seroresponse in this study. Although sex differences in vaccine-induced humoral responses have been described with other vaccines, there is a paucity of evidence to suggest any sex-based differences in COVID-19 vaccine immunogenicity.[21] Reporting of sex/gendered disaggregated data is an underdeveloped area of research within the scope of COVID-19 vaccine safety and efficacy. Further exploration of sex/gender differences in vaccine efficacy may be helpful in further clarifying mechanisms for vaccine responses, but this should not be specific to transplant patients.

ML has been used to predict vaccine immunogenicity and reactogenicity against other pathogens, but has not to our knowledge been applied to understand SARS-CoV-2 vaccine responses in SOTRs.[7] ML is particularly useful within the scope of vaccine development in instances where the pathogen displays genetic diversity, as SARS-CoV-2 has. Within the context of the SARS-CoV-2 pandemic, ML has the potential to augment predictions and our understanding of antibody response to current or future variant-specific vaccine formulations, patient-level risk factors (eg, medications and comorbidities), and identify high-risk individuals who may need more frequent, higher, or lower booster dosages to elicit an antibody response. Given that ML proved a useful tool to predict antibody response to 2 mRNA vaccines, further exploration into applying this method to predict third- and fourth-dose responses, including heterologous dosing strategies, is warranted.

Despite the strengths of our study, with internal prediction performance and external validity, there remain inherent limitations to consider. First, because of the observational design of our study, the associations and interactions characterized in our analyses may not necessarily represent causality between the predictors and the outcome. Second, the predictors included in this analysis were ascertained via self-report. However, we assess that the risk of information bias is relatively low, because this analysis only included basic clinical factors that were likely well-understood by the study participants. It is also important to remember that variable importance to the model does not equate to significance of certain clinical characteristics to the outcome. In addition, the C-statistic for our models was 0.79 in our cohort and 0.67 for the validation cohorts, indicating that they equally, if not out-performed, most conventional regression models that we use to predict other outcomes in transplantation.[22] Furthermore, these models analyze only responses to 2 mRNA vaccines in use in the United States (BNT162b2 and mRNA-1273) and may not directly translate to third doses, or those receiving non-mRNA vaccines, or heterologous vaccine combinations (though these were not recommended and should be limited for the first and second vaccine doses). Therefore, given the numerous additional vaccine platforms available internationally, the global applicability of our model is limited. Although all SOTRs are now recommended to undergo supplemental vaccination, these recommendations are blanket policies largely reflective of a lack of large-scale supportive data. Current US policy now recommends all SOTRs obtain 3 primary vaccine doses plus a first booster (fourth dose) with provisions for a second booster (fifth dose).[23] There is some encouraging evidence to support heterologous vaccination as a strategy to improve immune response rates among poor responders to the initial series, but further exploration of this strategy is needed.[24]

With this novel approach to predicting antibody response to mRNA SARS-CoV-2 vaccination in SOTRs, MMF use, older age, and a shorter time since transplant were the strongest factors associated with failure to generate an antibody response. In an era where universal antibody testing among transplant recipients has not yet been adopted, this model provides guidance for risk-based antibody testing. Given that a threshold for protective immunity has not yet been established, patients who exhibited a positive response may remain at risk for breakthrough SARS-CoV-2 infections. Patients and providers must remember that having an antibody response measuring "high" on a given immunoassay should not be equated with having strong protection against COVID-19 infection. Indeed, vaccination of SOTRs results in poorer protection against SARS-CoV-2 infection and mortality compared with the general population.[25] The antibody titers above which transplant patients would need to be protected from death due to SARS-CoV-2 still need to be identified. Further investigation into sequential dosing, immunosuppression modulation, and breakthrough infections in vaccinated SOTRs can guide vaccination policies in this at-risk population. This model both presents a mechanistic framework for evaluating, understanding, and better predicting future mRNA vaccine-induced immune responses in transplant patients and brings this model to the bedside via our online calculator, providing an opportunity for more precise vaccination strategies in this population.

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