COVID-19 vaccination not associated with increased risk of erectile dysfunction

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Abstract
Although mRNA COVID-19 vaccines have proven to be safe and effective against SARS-CoV-2, vaccination rates have slowed, with some individuals citing impotence as a concern. Therefore, we conducted a survey of the US males to evaluate the impact of COVID-19 vaccination on erectile function. We hypothesized that vaccinated men would not have a higher risk of ED compared to unvaccinated men. Amazon Mechanical Turk (MTurk) was utilized to survey the US adult male population between August 26 and September 2, 2021. Survey participation was open to 1000 males over the age of 18 and currently living in the United States regardless of vaccination status or the past medical history of COVID-19. Selection criteria included respondents ≥45 years old, no history of physician-diagnosed ED, biologically born, and identify as male. Participants completed an anonymous 16-question survey that included a multidimensional scale used to evaluate ED, the International Index of Erectile Function (IIEF-5). Among vaccinated men, the median IIEF-5 score was 20 [16–24] compared to 22 [17.5–25] in the unvaccinated group (p = 0.195). The multivariable-adjusted analysis demonstrated that vaccination against COVID-19 was not associated with increased risk of ED. Overall, this cross-sectional survey showed that COVID-19 vaccination was not associated with an increased risk of erectile dysfunction in males 45 years and older.

KEYWORDS
Coronavirus vaccine, COVID-19, erectile dysfunction, reproductive health, vaccine hesitancy

1 | INTRODUCTION

Although mRNA COVID-19 vaccines have proven safe and effective against SARS-CoV-2 and its respective variants, vaccination rates have slowed, with some individuals citing impotence as a concern (Center for Disease Control and Prevention [CDC], 2021; Fichera & Tulp, 2021). Following emergency use authorization of the Pfizer-BioNTech COVID-19 vaccine, Google searches related to male reproductive issues and COVID-19 vaccination increased by 34,900% (Sajjadi et al., 2021). While the COVID-19 vaccine has not been linked to erectile dysfunction (ED), various studies have identified COVID-19 infection as a potential etiology of ED (Davis et al., 2021; Kresch et al., 2021). Males infected with COVID-19 have a 3.3 times higher likelihood of experiencing ED when compared to males without COVID-19 (Katz et al., 2021). COVID-19 is hypothesized to cause ED through viral damage to penile endothelium explained by the ubiquitous presence of the target for SARS-CoV-2 uptake, ACE2 and TMPRSS2, in endothelial cells (Nassau et al., 2021). Briefly, replication of the virus in the cellular cytosol leads to damage of penile microvasculature and the subsequent development of ED (Nassau et al., 2021).
The resulting endothelial cell damage is typically a hallmark of vasculogenic ED (Pons et al., 2020). Additionally, COVID-19 particles have been identified in corpus cavernosa tissue after the resolution of COVID-19 infection, further supporting the hypothesis that SARS-CoV-2 damages penile endothelial tissue (Kresch et al., 2021). While no previous vaccination programmes have shown any association with ED, individuals have cited sexual dysfunction as a reason why they are hesitant to be vaccinated. Therefore, we conducted a survey to evaluate the risk of ED following vaccination in males 45 and over. Since there is no biological basis for vaccines affecting erectile function, we hypothesized that vaccinated men would not have a higher risk of ED compared to unvaccinated men.

2 MATERIALS AND METHODS

Amazon Mechanical Turk (MTurk, https://www.mturk.com/) was used to survey the United States adult male population between August 26 and September 2, 2021. Participation was voluntary and remained anonymous throughout the study. The “COVID Erectile Function Survey” was reviewed and approved by the Institutional Review Board of the University of Miami.

MTurk is a crowd-sourcing marketplace that allows online users to register and complete Human Intelligence Tasks (HIT) (e.g., online surveys) in exchange for monetary compensation (Diaz et al., 2021). Participants were compensated $0.50 for their participation based on an estimated completion time of 5–10 min. To eliminate the risk of automated computer programs, ballot-box stuffing, and task repetitions, users were required to enter their unique MTurk ID and complete the captcha verification. Users then reviewed an informed consent statement whereby clicking next implied voluntary agreement to study participation. Page 3 consisted of COVID-19 infection and vaccination history questions, including “have you ever tested positive for COVID-19?” and “have you received a dose of any COVID-19 vaccine?”. Respondents who answered “yes” were asked the follow-up questions: “how long ago did you test positive for COVID-19?” “how many doses of a COVID-19 vaccine have you received?” “which COVID-19 vaccine did you receive,” and “how long ago did you receive COVID-19 vaccine?”. This page included the command “write the word Coronavirus in the text box below” to evaluate participant inattention (Aguinis et al., 2021). Page 3 also included a question asking whether participants have ever been diagnosed with ED in the past and demographic questions, including age and assigned sex at birth. Survey page 4 consisted of the IIEF-5 questions survey assessing the following questions over the past 6 months:

- When you had erections with sexual stimulation, how often were your erections hard enough for penetration,” “during sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner,” “over the past six months: during sexual intercourse, how difficult was it

| TABLE 1 | Age breakdown and IIEF-5 categorization of survey respondents by COVID-19 vaccination status. Characteristics of survey respondents by COVID-19 vaccination status |
|-----------------|-----------------------------------------------------------------------------------------------------------|
| **Age group**   | **Overall n = 138 (100%)** | **Vaccinated n = 121 (87.7%)** | **Unvaccinated n = 17 (12.3%)** | **P-value** |
| 45–54 years     | 76 (55.1%) | 66 (54.5%) | 10 (58.8%) | |
| 55–64 years     | 37 (26.8%) | 34 (28.1%) | 3 (17.6%) | |
| >65 years       | 25 (18.1%) | 21 (17.4%) | 4 (23.5%) | 0.616 |
| IIEF-5 score    | 20 [16–24] | 20 [16–24] | 22 [17.5–25] | 0.195 |
| IIEF-5 category | **Severe 1–7** | 5 (4.1%) | 0 | |
|                | **Moderate 8–11** | 6 (5.0%) | 2 (11.8%) | |
|                | **Mild-to-moderate 12–16** | 28 (23.1%) | 1 (5.9%) | |
|                | **Mild 17–21** | 40 (33.1%) | 5 (29.4%) | |
|                | **No ED 22–25** | 42 (34.7%) | 9 (52.9%) | 0.248 |

Abbreviation: Median [Interquartile range: 25–75].
to maintain your erection to completion of intercourse” and “when you attempted sexual intercourse, how often was it satisfactory for you?

On the final page of the survey, participants were provided a randomized validation code to input into MTurk to receive compensation and submit their responses.

Statistical analysis was performed using the SPSS version 28. Categorical variables were compared with the Chi-squared test, and IIEF scores were calculated with the Mann-Whitney U test. A multivariable-adjusted logistic regression analysis was used to determine the association between ED and COVID-19 vaccine. A $p < 0.05$ was considered statistically significant.

3 | RESULTS

With an overall response rate of 81.8%, an exploratory analysis of 138 adult males who met selection criteria was performed. At the time of survey completion, 121 (87.7%) respondents were vaccinated against COVID-19 (18 men had one vaccine dose, 101 had two doses and 2 men had three doses), while 17 (12.3%) were unvaccinated. Overall, 76 (55.1%) of males were between 45 and 54 years of age, with similar overall age distribution between groups ($p = 0.616$) (Table 1). Of vaccinated men, the median IIEF-5 score was 20 [16–24] compared to 22 [17.5–25] in the unvaccinated group ($p = 0.195$) (Table 1). The multivariable-adjusted analysis demonstrated that vaccination against COVID-19 was not associated with an increased risk of ED (IIEF-5 < 22) (Odds ratio = $2.06; 95\% CI: 0.74–5.77, p = 0.169$). Among survey respondents, 67.3% (n = 93) admitted to ever having a positive COVID-19 test result, while 29.7% (n = 41) said “no” and 3% (n = 4) were “unsure.” Of those testing positive, 45.6% had COVID-19 in the past 6 months and 54.4% admitted infection more than 6 months prior to survey collection. Majority of respondents who met inclusion criteria received BioNTech, Pfizer vaccines (47%) followed by Moderna, NIAID (38.3%) and Johnson & Johnson (13.9%).

4 | DISCUSSION

In this cross-sectional survey, we demonstrated that COVID-19 vaccination was not associated with an increased risk of ED in males 45 years and older. It was found that the erectile function between vaccinated and unvaccinated survey individuals was not statistically different based on median IIEF-5 scores, with an average IIEF-5 score among vaccinated males of 20 and an average IIEF-5 score of 22 among unvaccinated males. Even though vaccinated males had lower IIEF-5 scores, associated with the mild ED category, this may be secondary to the cohort size differences (87.7% of respondents being vaccinated). Although men who were vaccinated reported mild ED, there does not appear to be a significant clinical or statistical difference from men who were not vaccinated.

This study is not without limitations, as the IIEF cannot accurately assess men who use erectile aids such as medications, injections, or vacuum devices. Secondly, self-misrepresentation and social desirability bias are well-documented limitations of the use of MTurk as a survey platform. It is important to note that the on-going COVID-19 pandemic paired with the previous COVID-19 infection history could be contributing to the IIEF scores observed to a higher degree than an individual’s vaccination status. Additionally, the number of total survey respondents was limited, and only 12% of total participants were unvaccinated against COVID-19. As such, the conclusions drawn from this research are based largely on COVID-19 vaccinated individuals and are to serve as an introduction to this important topic. Finally, while we only analysed males 45 years and older, younger men have lower vaccination rates, and the future studies may benefit from utilizing larger sample sizes and surveying males aged 18 and over (Hamel et al., 2021).

To date, there have been no studies examining the development of ED between individuals vaccinated and unvaccinated against COVID-19 using a standardized instrument. Thus, the results of this study could have wide-reaching effects on patient-informed decision-making and public health immunization campaigns amidst the current challenges of widespread myths, circulating variants, and vaccine hesitancy (Fichera & Tulp, 2021).

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CONFLICT OF INTEREST

The authors have nothing to disclose.

DATA AVAILABILITY STATEMENT

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

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SUPPORTING INFORMATION
Additional supporting information can be found online in the Supporting Information section at the end of this article.

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