Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Words of Wisdom

Re: The Impact of COVID-19 Vaccine on Sperm Quality

Barda S, Laskov I, Grisaru D, et al

Int J Gynaecol Obstet. In press. https://doi.org/10.1002/ijgo.14135

Experts' summary:
Owing to concerns about the impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on male fertility and the potential analogous effects of the coronavirus vaccine, Barda and colleagues [1] evaluated the effects of two doses of the Pfizer SARS-CoV-2 vaccine (BNT162b) on sperm parameters. This prospective cohort study included 898 samples from 33 sperm donors, with each donor serving as his own control. Basic semen parameters (total sperm count, total motile count, percentage motile sperm) were assessed in 425 semen samples before the first vaccination and compared to 473 samples collected at least 72 d after receiving the second dose of the vaccine.

Total sperm count and total motile count increased after completion of two doses of the vaccine compared to samples obtained before vaccination, while the percentage of motile sperm remained unchanged. In addition, the authors evaluated whether vaccination would affect the quality of freeze-thawed semen samples. Findings showed that the BNT162b, SARS-CoV-2 vaccine did not negatively affect sperm quality after freezing.

According to the scientific literature, the virus triggers adverse effects on male sexual and reproductive health, while the vaccine appears to be safe, as evidenced by Barda et al [1]. Therefore, vaccine uptake is recommended, and patients and medical doctors should be counseled accordingly.

Experts' comments:
While most studies report the absence of SARS-CoV-2 in semen, prostatic secretions, and testicular tissues (which decreases the possibility of sexual transmission of the virus), there is evidence of association with testicular lesions and inflammatory infiltration, viral orchitis, altered seminal parameters, and increased sperm DNA fragmentation [2,3]. Collectively, these results suggest that SARS-CoV-2 infection may potentially cause fertility problems.

By contrast, Barda and colleagues [1] reported that vaccination has no harmful effects on semen parameters for fresh or cryopreserved samples. Their findings are similar to those reported by other groups [4–6]. Lifshitz et al [4] evaluated the effect of the Pfizer vaccine in 75 men with proven fertility (men who previously impregnated their partners without the use of assisted reproductive technology [ART]), and found that 74/75 samples exceeded the World Health Organization reference fifth percentiles for normal sperm concentration, progressive motility, total motile count, and morphology after vaccination. Reschini et al [5] retrospectively evaluated the effect of different vaccines (Pfizer n = 73, 69%; Moderna n = 20, 19%; Oxford/AstraZeneca n = 10, 9%; Janssen n = 1, 1%; and mixed vaccines n = 2, 2%) on the semen parameters of 106 men undergoing ART treatment, and observed no significant differences in semen parameters or fertilization rates after vaccination. Gonzalez et al [6] evaluated the effect of mRNA vaccines in 45 healthy volunteers (21 Pfizer and 24 Moderna) and found no significant decrease in any sperm parameter. Since the vaccines contain mRNA and not the live virus, it is unlikely that the vaccine would affect sperm parameters.

It is important to note that these studies only evaluated basic seminal parameters and that the effect of SARS-CoV-2 vaccines on sperm functional parameters, such as DNA fragmentation and mitochondrial membrane potential, have not been investigated. Furthermore, the potential effects on sperm biology, as well as the possible role of epigenetic changes, has also not been considered to date.

Taken together, these results suggest that the SARS-CoV-2 mRNA vaccine should be considered safe for men's reproductive health. Therefore, patients and medical doctors must be advised that, according to scientific evidence, vaccines can be administered safely and that their benefits outweigh the adverse effects of the virus on male sexual and reproductive health. Patients ought to be counseled accordingly and vaccine uptake should be recommended explicitly to men wishing to conceive.

Conflicts of interest: The authors have nothing to disclose.

References

[1] Barda S, Laskov I, Grisaru D, et al. The impact of COVID-19 vaccine on sperm quality. Int J Gynaecol Obstet 2022. https://doi.org/10.1002/ijgo.14135, In press.
[2] Yang M, Chen S, Huang B, et al. Pathological findings in the testes of COVID-19 patients: clinical implications. Eur Urol Focus 2020;6:1124–9.
[3] Omolaoye TS, Adeniji AA, Cardona Maya WD, du Plessis SS. SARS-COV-2 (COVID-19) and male fertility: where are we? Reprod Toxicol 2021;99:65–70.
[4] Lifshitz D, Haas J, Lebovitz O, Raviv G, Orvieto R, Aizer A. Does mRNA SARS-CoV-2 vaccine detrimentally affect male fertility, as reflected by semen analysis? Reprod Biomed Online 2022;44:145–9.

[5] Reschini M, Pagliardini L, Boeri L, et al. COVID-19 Vaccination does not affect reproductive health parameters in men. Front Public Health 2022;10:839967.
[6] Gonzalez DC, Nassau DE, Khodamoradi K, et al. Sperm parameters before and after COVID-19 mRNA vaccination. JAMA 2021;326:273–4.

Walter D. Cardona Maya [a,*]
Temidayo S. Omolaoye [b]
Stefan S. du Plessis [b,c]

[a] *Reproduction Group, Department of Microbiology and Parasitology, Faculty of Medicine, Universidad de Antioquia, Medellín, Colombia*
[b] *Department of Basic Sciences, College of Medicine, Mohammed Bin Rashid University of Medicine and Health Sciences, Dubai, United Arab Emirates*
[c] *Division of Medical Physiology, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg, South Africa*

* Corresponding author. Reproduction Group, Department of Microbiology and Parasitology, Faculty of Medicine, Universidad de Antioquia, Medellín, Colombia.
E-mail address: wdario.cardona@udea.edu.co (W.D. Cardona Maya).

https://doi.org/10.1016/j.eururo.2022.06.021

Re: Effect of a Smoking and Alcohol Cessation Intervention Initiated Shortly Before Radical Cystectomy—the STOP-OP Study: A Randomised Clinical Trial

Lauridsen SV, Thomsen T, Jensen JB, et al

Eur Urol Focus. In press. https://doi.org/10.1016/j.euf.2022.02.005

Experts' summary:

Smoking is the leading cause of preventable disease and premature death worldwide; however, effective implementation of smoking cessation programs in our health care systems is a major challenge. In the randomized STOP-OP trial, the investigator assessed whether a preoperative smoking/alcohol cessation intervention reduced complications after cystectomy [1]. Half of 104 patients were randomized to receive five counseling sessions over a 6-wk period, while the control group followed the standard clinical care pathway. The proportion of patients experiencing at least one complication was similar in the two groups. Secondary outcome analyses suggested that patients in the intervention group had a lower number of complications, specifically fewer gastrointestinal complications, and were twice as likely to quit smoking or drinking alcohol before surgery.

Experts' comments:

Although this study did not meet its primary outcome, the authors should be applauded for conducting this work. In our view, there are two important methodological limitations that prevented the trial from being able to demonstrate the potential of prehabilitation: (1) the primary outcome chosen and (2) the time between the intervention and surgery.

First, instead of counting the number of patients experiencing any complication, we suggest that the Comprehensive Complication Index (CCI) is a more sensitive alternative for measuring overall morbidity. CCI is calculated as the sum of all Clavien-Dindo complications that are weighted for their severity. This yields a continuous scale that ranks the cumulative burden from any combination of complications from 0 to 100 in a single patient [2,3]. As a composite complication score, CCI has the advantage of reflecting the overall burden of the postoperative course that affects the health of patients and their quality of life. In addition, a continuous scale is a powerful endpoint in trials, because CCI as an outcome in trials allowed for a sample size up to nine times lower than the sample needed with traditional morbidity endpoints [3].

Second, the timing and intensity of cessation counseling are crucial. A Cochrane review of preoperative smoking cessation interventions reported that intensive interventions, consisting of weekly counseling starting 4–8 wk before surgery, had a significant effect on postoperative complications [4]. By contrast, counseling in the present study was rather late, as the median time from inclusion to surgery was only 8 d, translating to a median of only 2 d from smoking cessation to surgery.

Nevertheless, Lauridsen et al demonstrated proof of the concept, as most patients in the intervention group stopped smoking and there was no concerning safety signal among smokers stopping shortly before surgery. These results should encourage further implementation science trials studying the uptake of evidence-based medicine in routine clinical use and provide a framework for evaluating and improving practices. At our institution, we started a randomized controlled trial in which an advanced nurse practitioner screens patients scheduled for elective surgery and offers an intense smoking cessation program to smokers. The aim of the trial is to examine whether this practice decreases postoperative complications, length of stay, readmission rates, cancer-specific outcomes, and costs (NCT05192837).

Conflicts of interest: The authors have nothing to disclose.

References

[1] Lauridsen SV, Thomsen T, Jensen JB, et al. Effect of a smoking and alcohol cessation intervention initiated shortly before radical cystectomy—the STOP-OP study: a randomised clinical trial. Eur Urol Focus 2022. https://doi.org/10.1016/j.euf.2022.02.005, In press.
[2] Slankamenac K, Graf R, Barkun J, Puhan MA, Clavien PA. The Comprehensive Complication Index: a novel continuous scale to measure surgical morbidity. Ann Surg 2013;258:1–7.
[3] Slankamenac K, Nederlof N, Pessaux P, et al. The Comprehensive Complication Index: a novel and more sensitive endpoint for