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.

Perioperative risk evaluation in patients scheduled for elective surgery in close relation to their SARS-CoV-2 vaccination

Ulrich Limper[1,*], Jerome Defosse[1], Oliver Schildgen[2] and Frank Wappler[1]

[1]Department of Anesthesiology and Critical Care Medicine, Merheim Medical Center, Hospitals of Cologne, Witten/Herdecke University, Cologne, Germany and [2]Institute of Pathology, Merheim Medical Center, Hospitals of Cologne, Witten/Herdecke University, Cologne, Germany

*Corresponding author. E-mail: Ulrich.limper@dlr.de

Keywords: COVID-19; perioperative; risk; SARS-CoV-2; vaccination

Editor—A recent patient confronted us for the first time with the problem of the right timing of elective surgery in relation to SARS-CoV-2 vaccination. A 51-yr-old woman, who presented recently at our department for preoperative evaluation 4 days before her bariatric surgery, was at high risk for COVID-19 as a front-line worker. She had received the first shot of the AstraZeneca AB, Södertälje, Sweden SARS-CoV-2 vaccine just the day before and was scheduled to receive the second shot 48 days after the first one. At the vaccination clinic she had mentioned that she was to undergo major surgery 5 days later, but had been reassured that her inoculation would not interfere with her surgery.

Despite the availability of different vaccine platforms, including mRNA, adjuvanted proteins, inactivated viruses, and adenoviral vector vaccines, a general gap of knowledge exists about the interactions of immunisation, anaesthesia, and surgery. Major and minor problems can originate from the vaccination process in the perioperative phase. Most importantly: (1) the best timing of vaccination for optimal immune response to protect the patient from COVID-19 after surgery is unknown; (2) immunomodulatory effects caused by anaesthesia and surgical trauma may diminish immunisation; (3) side-effects of the vaccine, of live vaccines in particular, may be aggravated through perioperative immunomodulation; and (4) adverse events of the vaccine may be misinterpreted as postoperative complications.[1]

COVID-19, often a nosocomial infection, increases the perioperative risk of elective surgery, mainly because of increasing the rate of pulmonary complications. SARS-CoV-2-infected men >70 yr old who undergo major elective surgery are of particularly high risk of mortality.[2] So-called COVID-19-free surgical pathways have shown lower pulmonary complication rates, and immunisation against SARS-CoV-2 will foster these efforts. However, the SARS-CoV-2 vaccines have relevant differences in their minimum times to immunisation, and these times (Table 1) have not been investigated in the perioperative phase. If a patient undergoing elective surgery has the choice of different vaccines, consideration may be given to the one with the shortest time to full immunisation.

In order to avoid vaccine side-effects in the perioperative period, it is recommended to separate elective surgery and immunisation with inactivated and live vaccines 3–7 and 14–21 days, respectively.[3] However, recommendations derive mainly from paediatric anaesthesia and have been transferred to adult perioperative medicine. At present, the Royal College of Surgeons of England recommends that non-urgent elective surgery in adults can take place soon after vaccination and both events shall not be separated for more than 1 week.[4] In urgent cases, active boosting of immunisation must not be delayed, as in the case of the application of tetanus toxoid in trauma patients for example.[5] Yet, recommendations on the management of SARS-CoV-2 immunisation in the context of elective surgery have not been included into the pertinent guidelines of preoperative evaluation of the adult patient.[6]

The four different SARS-CoV-2 vaccines currently authorised in Europe are either DNA-vector-based or mRNA-based. They contain the genetic information for the immunodominant antigen only, the spike protein of SARS-CoV-2, which is, after i.m. application, expressed for a short time. Hence, these vaccines cannot elicit SARS-CoV-2 infection and are considered neither inactivated nor attenuated live virus vaccines. As mRNA-based therapeutics are novel and no systematic experience exists for their interactions with anaesthesia, this class of drugs will become more common in the future as cancer vaccines. The BioNTech-Pfizer BNT162b2 vaccine (BioNTech Manufacturing GmbH, Mainz, Germany), Comirnaty®, is a lipid nanoparticle-formulated, nucleoside-modified mRNA vaccine, encoding the SARS-CoV-2 spike protein modified by two proline mutations to keep it in the prefusion conformation. Two i.m. doses of the vaccine elicited high neutralising antibody titres and antigen-specific CD8+ and CD4+ T-cell responses with a lower antibody response in older compared with younger individuals,[7] although it remains unclear from the data published to date how much of the induced immunity is specific and which portion originates from vaccine-triggered unspecific innate immunity.[8] Longer observation periods will finally solve this issue. The US

Table 1 Scheduling of SARS-CoV-2 vaccines.

Vaccine	Schedule	Total time to immunisation
BNT162b2/Corminaty (BioNTech-Pfizer)	Two doses 19–42 days apart	7 Days after the second dose → 26–49 days
mRNA-1273 (Moderna)	Two doses 28 days apart	14 Days after the second dose → 42 days
ChAdOx1-S/ Vaxzevria (AstraZeneca)	Two doses 28–84 days apart	15 Days after the second dose → 43–99 days
Ad26.COV2.S (Janssen-Cilag)	Single dose	Around 14 days

company Moderna, Cambridge, MA, USA) together with the US National Institutes of Health developed the similar mRNA-1273 vaccine, which is also a lipid nanoparticle-encapsulated mRNA vaccine encoding the prefusion stabilised spike glycoprotein.[9] AstraZeneca's ChAdOx1-S (recombinant) is a DNA-vector vaccine, made up of a modified, replication-deficient Chimpanzee adenovirus containing the gene for the SARS-CoV-2 spike glycoprotein.[10] The fourth, also vector-based, vaccine named Ad26.COV2.S (recombinant), manufactured by Janssen-Cilag International N.V., Beerse, Belgium, is currently the only available SARS-CoV-2 single-dose vaccine.

For all the vaccines, subacute symptoms have been reported to be common in the first days after immunisation, particularly after the second dose, which has initiated an in-depth review by the German Paul-Ehrlich-Institute. These symptoms mimic common postoperative conditions including pain (at the injection site), headache, nausea, vomiting, arthralgia, myalgia, pyrexia, chills, and fatigue. Lymphadenopathy and acute peripheral facial paralysis are less common. Although the manufacturers recommend postponing vaccination in individuals suffering from an acute severe febrile illness or acute infection, the presence of a minor infection or low-grade fever should not delay vaccination. These recommendations may be translated to the perioperative setting. SARS-CoV-2 immunisation in close proximity to major and minor elective surgery could be handled differently. However, no perioperative patients or immunocompromised patients were investigated in the clinical trials of the SARS-CoV-2 vaccines.

In our case we recommended delaying the highly elective procedure until 15 days after the second vaccine shot (Table 1). We reasoned that this would provide full protection against COVID-19 and therefore a significantly reduced postoperative risk. We suggest that anaesthesiologists respond to the current knowledge gaps regarding interaction of SARS-CoV-2 immunisation with the perioperative period by ensuring a proper gap between vaccination and elective surgery procedures.

Declarations of interest

UL received funding from the internal grant program (project IFF 2020-26) of the Faculty of Health at Witten/Herdecke University, Germany, during preparation of this work.

References

1. Siebert JN, Posfay-Barbe KM, Habre W, Siegrist CA. Influence of anesthesia on immune responses and its effect on vaccination in children: review of evidence. *Paed Anaesth* 2007; **17**: 410–20
2. COVIDSurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. *Lancet* 2020; **396**: 27–38
3. Bertolizio G, Astuto M, Ingelmo P. The implications of immunization in the daily practice of pediatric anesthesia. *Curr Opin Anaesthesiol* 2017; **30**: 368–75
4. Royal College of Surgeons of England. *Vaccinated patients guidance* 2021. Available from: https://www.rcseng.ac.uk/coronavirus/vaccinated-patients-guidance/. [Accessed 16 February 2021]
5. Rhee P, Nunley MK, Demetriades D, Velmahos G, Doucet JJ. Tetanus and trauma: a review and recommendations. *J Trauma* 2005; **58**: 1082–8
6. De Hert S, Imberger G, Carlisle J, et al. Preoperative evaluation of the adult patient undergoing non-cardiac surgery: guidelines from the European Society of Anaesthesiology. *Eur J Anaesthesiol* 2011; **28**: 684–722
7. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020; **383**: 2603–15
8. Lee YJ, Lee JY, Jang YH, Seo S-U, Chang J, Seong BL. Non-specific effect of vaccines: immediate protection against respiratory syncytial virus infection by a live attenuated influenza vaccine. *Front Microbiol* 2018; **9**: 83
9. Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med* 2021; **384**: 403–16
10. Ramasamy MN, Minassian AM, Ewer KJ, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. *Lancet* 2021; **396**: 1979–93

doi: 10.1016/j.bja.2021.03.007
Advance Access Publication Date: 20 March 2021