



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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

However, after adjusting for patient risk factors, surgical mortality was not different across regions of varying COVID-19 regional severity, suggesting that this finding was related to an inherently sicker patient population undergoing higher-risk surgeries, rather than impact from regional COVID-19 severity *per se*. Taken together, these findings support that the quality of care and safety of anaesthesia, surgery and perioperative medicine were maintained during the early phase of the pandemic.

## Acknowledgements

The authors thank the staff of the MPOG coordinating centre for the development of the technical, regulatory, and organisational infrastructure required for the establishment and sustenance of the work described. The authors gratefully acknowledge the valuable contributions to protocol and final manuscript review by the following MPOG collaborators: Leelynn Chen (University of California San Francisco), Catherine Chen (University of California San Francisco), Elizabeth Whitlock (University of California San Francisco), David Robinowitz (University of California San Francisco), Sarah Tingle (University of Arkansas), Anthony Yasick (Holland Hospital), Robert Freundlich (Vanderbilt University), Jose Soliz (University of Texas, MD Anderson Cancer Center), Richard Urman (Brigham and Women's Hospital), Shital Vachhani (University of Texas, MD Anderson Cancer Center), Germaine Cuff (New York University), Alvin Stewert (University of Arkansas), Vikas O'Reilly-Shah (University of Washington), Robert Schonberger (Yale University), Michael Godbold (University of Tennessee, Knoxville), Joseph Ruiz (MD Anderson Cancer Center), Brandon Togioka (Oregon Health and Science University), Brad Taicher (Duke University), Michael O'Connor (University of Chicago), Joel Kileny (St. Joseph Mercy Hospital, Ann Arbor, MI), Patrick McCormick (Memorial Sloan Kettering Cancer Center), Karen Domino (University of Washington), Sachin Kheterpal (University of Michigan).

## Declarations of interest

The authors declare no conflicts of interest.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.bja.2021.09.023>.

## References

1. Global guidance for surgical care during the COVID-19 pandemic. Available from: <https://pubmed.ncbi.nlm.nih.gov/32293715/> (accessed 10 August 2021).
2. Centers for Medicare & Medicaid Services CMS releases recommendations on adult elective surgeries, non-essential medical, surgical, and dental procedures during COVID-19 response 2020. Available from: <https://www.cms.gov/newsroom/press-releases/cms-releases-recommendations-adult-elective-surgeries-non-essential-medical-surgical-and-dental>. [Accessed 7 August 2020]
3. Pirracchio R, Mavrothalassitis O, Mathis M, Kheterpal S, Legrand M. Response of US hospitals to elective surgical cases in the COVID-19 pandemic. *Br J Anaesth* 2021; **126**: e46–8
4. Le Manach Y, Collins G, Rodseth R, et al. Preoperative Score to Predict Postoperative Mortality (POSPOM): derivation and validation. *Anesthesiology* 2016; **124**: 570–9
5. Doglietto F, Vezzoli M, Gheza F, et al. Factors associated with surgical mortality and complications among patients with and without coronavirus disease 2019 (COVID-19) in Italy. *JAMA Surg* 2020; **155**: 691–702
6. 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
7. Abbott TEF, Fowler AJ, Dobbs TD, et al. Mortality after surgery with SARS-CoV-2 infection in England: a population-wide epidemiological study. *Br J Anaesth* 2021; **127**: 205–14
8. Dobbs TD, Gibson JAG, Fowler AJ, et al. Surgical activity in England and Wales during the COVID-19 pandemic: a nationwide observational cohort study. *Br J Anaesth* 2021; **127**: 196–204

doi: 10.1016/j.bja.2021.09.026

Advance Access Publication Date: 1 October 2021

© 2021 British Journal of Anaesthesia. Published by Elsevier Ltd. All rights reserved.

# Risk stratification of individuals undergoing surgery after COVID-19 recovery

Earlene Silvapulle<sup>1,\*</sup>, Douglas Johnson<sup>2,3</sup> and Jai N. Darvall<sup>1,4</sup>

<sup>1</sup>Department of Anaesthesia and Pain Management, Royal Melbourne Hospital, Parkville, VIC, Australia, <sup>2</sup>Victorian Infectious Diseases Service, Royal Melbourne Hospital, Parkville, VIC, Australia, <sup>3</sup>Department of Medicine, Royal Melbourne Hospital, Parkville, VIC, Australia and <sup>4</sup>Department of Critical Care, University of Melbourne, Parkville, VIC, Australia

\*Corresponding author. E-mail: [Earlene.Silvapulle@mh.org.au](mailto:Earlene.Silvapulle@mh.org.au)

**Keywords:** biomarker; COVID-19; perioperative complications; risk; SARS-CoV-2; surgery

Editor—The COVID-19 pandemic has had an immense impact on surgical procedures worldwide. Since January 1, 2021, England and Wales have seen a 38.6% reduction in elective surgery, resulting in more than 1.5 million cancelled emergency and elective operations.<sup>1</sup> As elective surgery resumes, clinicians will be faced with an increasing number of individuals recovering from COVID-19.

Individuals undergoing surgery after recovery from COVID-19 are at increased risk of postoperative pulmonary complications and mortality.<sup>2</sup> There is also a significant association between hospitalisation with COVID-19 and persistent multiorgan dysfunction after recovery.<sup>3</sup> As the time interval from diagnosis of SARS-CoV-2 infection to surgery increases, postoperative complications decrease progressively.<sup>4</sup> When surgery takes place >7 weeks after diagnosis, 30-day mortality rates are somewhat similar to those of individuals with no preoperative SARS-CoV-2 infection (2.0% and 1.4%, respectively).<sup>4</sup>

In light of the above findings, the recent interprofessional consensus statement including the Royal College of Anaesthetists and the Royal College of Surgeons of England recommended that, for individuals with asymptomatic SARS-CoV-2 infection or resolved symptoms, elective surgery should not be scheduled within 7 weeks from the time of diagnosis.<sup>5</sup> Individuals who were hospitalised, or those with persistent symptoms after COVID-19, may be at considerable risk of postoperative mortality, even when surgery is delayed for 7 weeks. In such cases, postponement beyond 7 weeks and a personalised plan for timing of surgery is recommended.<sup>5</sup> However, there is currently little guidance for stratifying risk in these individuals before surgery. Therefore, deciding the optimal timing of surgery, based on the risk–benefit of disease progression vs delaying surgery for optimisation, remains challenging.

Given the risks after mild COVID-19 appear to be minimal, the major question that remains is: *How can we accurately risk-stratify individuals with prior hospitalisation or persistent symptoms who are scheduled for surgery?* Data are lacking, but one approach may be to evaluate the predictive value of biomarkers and physiologic derangements in individuals with ‘long COVID’, a term used to describe signs and symptoms that continue or develop beyond 4 weeks after COVID-19 diagnosis.

The predictive value of acute phase reactants during acute COVID-19 illness has been studied extensively, and there are emerging data that these reactants may remain elevated after COVID-19 recovery. D-dimer, ferritin, and C-reactive protein (CRP) are three such biomarkers that have been found to be persistently elevated 6–8 weeks after hospital discharge.<sup>6</sup> In non-COVID-19 perioperative settings, CRP elevation is associated with postoperative complications; further studies are required to delineate the prognostic role of elevated CRP specifically after COVID-19 recovery.

Pulmonary fibrosis, impaired lung diffusing capacity, cardiac arrhythmias, ventricular dysfunction, and pulmonary hypertension are frequently observed after COVID-19 recovery.<sup>7,8</sup> High-sensitivity troponin and N-terminal-proB-type natriuretic peptide may be elevated in individuals with long COVID, although this may reflect the hyperinflammatory response, rather than specifically indicating myocardial injury.<sup>9</sup> The role of these cardiac biomarkers in long COVID remains to be elucidated. Similarly, persistently elevated inflammatory markers from the initial ‘cytokine storm’, such as interleukins and tumour necrosis factor- $\alpha$ ,<sup>10</sup> may be responsible for diminished myocardial performance and, therefore, may have

prognostic value in long COVID. However, these markers are not commonly available in clinical practice.<sup>7</sup>

Other organ systems impacted substantially in individuals with long COVID include the neurologic, haematologic, renal, hepatic, and endocrine systems.<sup>11</sup> Memory loss, cognitive difficulties, thrombocytopenia, coagulation abnormalities, and impaired glucose metabolism have all been observed in individuals with long COVID.<sup>12</sup>

Further work is required to determine how these changes complicate recovery from surgery after COVID-19. Identification of measurements with prognostic importance should lead to refinement of predictive models to provide quantitative estimation of perioperative risk. We envisage an algorithm for preoperative risk stratification of recovered COVID-19 patients, whereby individuals are first classified on the basis of symptoms and hospitalisation. Those with asymptomatic disease or resolved symptoms are not considered to be at significantly increased perioperative risk as a result of recent COVID-19. Therefore, these individuals can proceed to elective surgery 7 weeks from COVID-19 diagnosis. Patients who were hospitalised, or those with persistent symptoms, should undergo targeted organ-specific assessment using a combination of echocardiography, lung function tests, and aforementioned biomarkers. With clarification of the importance of these biomarkers, better quantification of perioperative risk may then be weighed up against the risk of delaying surgery (and disease progression), assisting optimal timing of surgery.

In conclusion, further research is required to evaluate biomarkers and physiologic abnormalities in patients after COVID-19 recovery, and how these may predict postoperative outcomes. Future use of these variables for risk stratification may not only assist with deciding the optimal timing of surgery, but also with informed consent and shared decision-making.

## Declarations of interest

The authors declare that they have no conflicts of interest.

## References

1. Dobbs T, Gibson J, Fowler A, et al. Surgical activity in England and Wales during the COVID-19 pandemic: a nationwide observational cohort study. *Br J Anaesth* 2021; 127: 196–204
2. COVIDSurgCollaborative. Delaying surgery for patients with a previous SARS-CoV-2 infection. *Br J Surg* 2020; 107: e601–e2
3. Eochagain A, Hardman J, Buggy D. SARS-CoV-2 in perioperative medicine: lessons learnt. *Br J Anaesth* 2021; 126: E187–8
4. COVIDSurg Collaborative, GlobalSurg Collaborative. Timing of surgery following SARS-CoV-2 infection: an international prospective cohort study. *Anaesthesia* 2021; 76: 748–58
5. El-Boghdady K, Cook T, Goodacre T, et al. SARS-CoV-2 infection, COVID-19 and timing of elective surgery. A multidisciplinary consensus statement on behalf of the Association of Anaesthetists, the Centre for Peri-operative Care, the Federation of Surgical Specialty Associations, the Royal College of Anaesthetists and the Royal College of Surgeons of England. *Anaesthesia* 2021; 76: 940–6

6. Mandal S, Barnett J, Brill S, et al. 'Long-COVID': a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19. *Thorax* 2021; **76**: 396–8
7. Nalbandian A, Sehgal K, Wan E. Post-acute COVID-19 syndrome. *Nature* 2021; **27**: 601–15
8. Tudoran C, Tudoran M, Pop G, et al. Associations between the severity of the post-acute COVID-19 syndrome and echocardiographic abnormalities in previously healthy outpatients following infection with SARS-CoV-2. *Biology* 2021; **10**: 469
9. Giustino G, Croft L, Stefanini G, et al. Characterization of myocardial injury in patients with COVID-19. *J Am Coll Cardiol* 2020; **76**: 2043–55
10. Abou-Arab O, Bennis Y, Gauthier P, et al. Association between inflammation, angiotensin, and disease severity in critically ill COVID-19 patients: a prospective study. *Br J Anaesth* 2021; **12**: 3e127–e130
11. Sherren PB, Ostermann M, Agarwal S, Meadows CIS, Ioannou N, Camporota L. COVID-19-related organ dysfunction and management strategies on the intensive care unit: a narrative review. *Br J Anaesth* 2020; **125**: 912–25
12. Yan Z, Yang M, Lai C. Long COVID-19 syndrome: a comprehensive review of its effect on various organ systems and recommendation on rehabilitation plans. *Bio-medicines* 2021; **9**: 966

doi: 10.1016/j.bja.2021.09.026

Advance Access Publication Date: 9 October 2021

© 2021 British Journal of Anaesthesia. Published by Elsevier Ltd. All rights reserved.