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.

research is warranted to determine whether intravenous iron therapy improves functional outcome after surgery.

Our study has several limitations. First, this was a substudy of a prospective cohort study and not primarily designed to answer the current research question. Second, WHODAS 2.0 was only recorded during follow-up and a comparison with preoperative results was not possible. Third, even though multivariable analysis demonstrated an association between nadir Hb level and the outcome parameters independently of underlying diseases or complexity of surgery, no conclusion on causation can be made. To conclude, early postoperative nadir Hb is associated with poor functional outcome after cardiac surgery in older patients.

Declarations of interest

RSM, TCDR, and PGN are currently conducting research on the effect of treatment of postoperative anaemia with intravenous iron on postsurgical disability. This research is sponsored by Pharmacosmos (Holbaek, Denmark), a company that develops and markets medicines for treatment of iron deficiency. LMV, RLNH, LV, MHE-V, OLC, and EPAD declare that they have no conflict of interest.

Funding

St. Antonius Onderzoeksfonds

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2022.04.017.

References

1. Gómez-Ramírez S, Bisbe E, Shander A, Spahn DR, Muñoz M. Management of perioperative iron deficiency anemia. *Acta Haematol* 2019; **142**: 21–9
2. Lasocki S, Krauspe R, Von Heymann C, Mezzacasa A, Chainey S, Spahn DR. PREPARE: the prevalence of perioperative anaemia and need for patient blood management in elective orthopaedic surgery: a multicentre, observational study. *Eur J Anaesthesiol* 2015; **32**: 160–7
3. Muñoz M, Acheson AG, Bisbe E, et al. An international consensus statement on the management of postoperative anaemia after major surgical procedures. *Anaesthesia* 2018; **73**: 1418–31
4. Hazen YJJM, Noordzij PG, Gerritse BM, et al. Preoperative anaemia and outcome after elective cardiac surgery: a Dutch national registry analysis. *Br J Anaesth* 2022; **128**: 636–43
5. Penninx BWJH, Pahor M, Cesari M, et al. Anemia is associated with disability and decreased physical performance and muscle strength in the elderly. *J Am Geriatr Soc* 2004; **52**: 719–24
6. Gill TM, Allore HG, Holford TR, Guo Z. Hospitalization, restricted activity, and the development of disability among older persons. *JAMA* 2004; **292**: 2115–24
7. Verwijmeren L, Noordzij PG, Daeter EJ, et al. Preoperative frailty and one-year functional recovery in elderly cardiac surgery patients. *J Thorac Cardiovasc Surg* https://doi.org/10.1016/j.jtcvs.2022.01.032. Advance Access published on February 3, 2022.
8. Khalafallah AA, Yan C, Al-Badri R, et al. Intravenous ferric carboxymaltose versus standard care in the management of postoperative anaemia: a prospective, open-label, randomised controlled trial. *Lancet Haematol* 2016; **3**: e415–25
9. Richards T, Baikady RR, Clevenger B, et al. Preoperative intravenous iron to treat anaemia before major abdominal surgery (PREVENTT): a randomised, double-blind, controlled trial. *Lancet* 2020; **396**: 1353–61
10. Ponikowski P, van Veldhuisen DJ, Comin-Colet J, et al. Beneficial effects of long-term intravenous iron therapy with ferric carboxymaltose in patients with symptomatic heart failure and iron deficiency. *Eur Heart J* 2015; **36**: 657–68

doi: 10.1016/j.bja.2022.04.017
Advance Access Publication Date: 28 May 2022

Evidence-based intraoperative infection control measures plus feedback are associated with attenuation of severe acute respiratory syndrome coronavirus-2 detection in operating rooms

Randy W. Loftus*, Franklin Dexter, Lance Evans, Alysha Robinson, Abby Odle and Stanley Perlman

Department of Anesthesia, University of Iowa, Iowa City, IA, USA

*Corresponding author. E-mail: randy-loftus@uiowa.edu

Keywords: COVID-19; infection control; infectivity; nucleic acid detection; perioperative cleaning; SARS-CoV-2

Editor—A recent review in the *British Journal of Anaesthesia* described the impact of optimised, basic intraoperative infection control measures.[1] Feedback is a critical implementation feature for prevention of bacterial transmission and associated surgical site infections,[2,3] but the importance of feedback for viral pathogens is unknown. We have observed a low rate of *Staphylococcus aureus* [0% (0/108)] and severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) transmission [1% (1/108)] after implementation of recommended anaesthesia work area infection control measures.[1–5] Residual contamination of operating room environmental sites other than the anaesthesia machine occurring after surface disinfection (13.5% without and 5.6% with ultraviolet irradiation-C [UV-C]) indicated a need for improvement.[4] We aimed to assess residual environmental SARS-CoV-2 contamination with and without UV-C after implementation of feedback.[1–4]

A post-implementation study involving 31 patients positive for SARS-CoV-2 within 90 days of surgery (Table 1, baseline characteristics) was initiated 3 months after baseline analysis (November and December 2020) and completed over 4 months (March 24 to July 27, 2021) at the University of Iowa (Study Timeline, Supplementary Fig. S1).[4] The study was approved by the Institutional Review Board (202005391) without requirement for informed, written patient consent, and was registered at clinical trials.gov (NCT04443803). We chose 90 days to study viral transmission because patients can remain positive or become re-infected for up to 90 days after diagnosis.[6–8]

Recommended infection control procedures were implemented in March 2020 (Perioperative COVID-19 Defense Strategy, https://vimeo.com/409005129/4e1f2a0711) for all operating rooms (ORs), and (UV–C; Helios, Surfacide, Waukesha WI, USA) was implemented for ORs exposed to patients with COVID-19 (Supplementary material).[1–3,9–16]

The epidemiology of intraoperative SARS-CoV-2 transmission (Table 1) was observed in 11 ORs after implementation.[4] Vascular care, hand hygiene, and anaesthesia machine cleaning procedures were implemented effectively based on a low *S. aureus* (<12.5%) and viral transmission rate.[5] In contrast, there were many environmental sites with residual SARS-CoV-2 detection (Supplementary Table S2).[4] There were multiple meetings with the anaesthesia department, perioperative medicine leadership, and environmental services leadership throughout February 2021 regarding the overall magnitude and locations of intraoperative environmental SARS-CoV-2 contamination.

Wipes prepared manually during the acute COVID-19 period via the addition of hydrogen peroxide (Oxivir Tb; Diversey, Fort Mill, SC, USA), an *N*-alkyl compound (Virex plus, Diversey), or an *N*-alkyl compound with one type of alcohol (Asepticare Tb + II; Ecolab, St. Paul, MN, USA) solutions to dry wipes were replaced by February 2021 with surface disinfection wipes containing didecyl dimethyl ammonium chloride along with ethyl and isopropyl alcohol (Sani-Cloth Prime Germicidal Wipe; PDI, Woodcliff Lak, NJ, USA).[1–3] Wipes were used for routine between-case and terminal cleaning of the anaesthesia cart, equipment, surgical bed, mattress, and siderails, as supported by clinical trial results and reviews.[2,17,18]

The primary outcome was SARS-CoV-2 nucleic acid detection in frequently contaminated environmental sites after cleaning (after surface disinfection and after UV-C) including the top of the anaesthesia cart, anaesthesia cart handles, anaesthesia provider computer mouse, suction canister, circulating nurse computer mouse, surgical bed side, air return registers, walls, and floor at base of the bed.[4,19] We also evaluated for viral infectivity by culture. Sample size was based on baseline viral detection results: 17/126 (13.5%) without *vs* 6/108 (5.6%) with UV-C.[4] Comparing those two proportions using Fisher's exact test based on alpha=0.05 and 90% statistical power, there should be 297 locations sampled before and after UV-C, or a total of 594 locations. We compared the proportion of samples positive before feedback *vs* after feedback using Fisher's exact test.

A total of 31 operating room environments were enrolled and 587 samples were collected. Patient and procedural characteristics for the before and after periods are shown in Table 1. Sites involving SARS-CoV-2 nucleic acid or infectivity are shown in Supplementary Table S2. Whereas there was SARS-CoV-2 detected in 13.5% (17/126) of samples at baseline, there were 0% (0/587) with feedback resulting in process improvement ($P<0.0001$). Although there was no SARS-CoV-2 detected, there were more cases (compared with baseline period) with acute disease and more cases without acute disease, more patients without vaccination, and more patients with vaccination, etc. for the other eight characteristics in Table 1. We were unable to assess UV-C effect with zero viral nucleic acid detection and no positive viral cultures.

Feedback is an important implementation feature for an evidence-based, multifaceted intraoperative infection control programme derived from a solid foundation of published evidence involving bacterial pathogens.[1–3] We learned in this study that feedback is also important for intraoperative control of SARS-CoV-2 disinfection. Feedback was remarkably practical, followed by only a change in surface disinfection wipes.

Table 1 Baseline characteristics of operating room environments.

Characteristic	Baseline* (*n*=11)	After (*n*=31)	More cases with characteristic	Most cases without characteristic
Acute infection, *n* (%)	5 (45)	9 (29)	After (9 *vs* 5)	After (22 *vs* 6)
Vaccinated, *n* (%)	0 (0)	6 (19)	After (6 *vs* 0)	After (25 *vs* 11)
Age <18 yr	0 (0)	2 (6)	After (2 *vs* 0)	After (29 *vs* 11)
Age ≥50 yr	7 (64)	12 (39)	After (12 *vs* 7)	After (19 *vs* 4)
Age ≥65 yr	4 (36)	7 (23)	After (7 *vs* 4)	After (24 *vs* 7)
Female, *n* (%)	7 (64)	11 (35)	After (11 *vs* 7)	After (20 *vs* 4)
General anaesthesia, *n* (%)	8 (73)	29 (94)	After (29 *vs* 8)	After (3 *vs* 2)
Negative pressure OR, *n* (%)	5 (45)	10 (33)	After (10 *vs* 5)	After (21 *vs* 6)
Case duration ≥2 h	6 (55)	20 (65)	After (20 *vs* 6)	After (11 *vs* 5)
Case duration ≥3 h	2 (18%)	13 (42)	After (13 *vs* 2)	After (18 *vs* 9)

*Results published.[4] Acute, ≤days from time of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) positivity to surgery.

We characterised the baseline epidemiology of intraoperative SARS-CoV-2 transmission, identifying high-risk environmental locations,[4] and leveraged that knowledge to test a data-driven process improvement strategy for environmental cleaning. The results can guide future research as the virus becomes endemic and preoperative testing is reduced. Future studies should use the reported model of intraoperative viral cross-contamination to assess the impact of intranasal povidone iodine on reduced aerosolisation of viral particles.[17] Given the negligible viral transmission rate after implementation of recommended cleaning procedures including feedback,[1,17,20] these findings should inspire implementation to improve patient and provider perioperative safety.

The validity of our findings is supported by a solid body of evidence for bacterial pathogens.[1–3,9,11] The results were not explained by vaccination, the number of patients with active infection, use of negative pressure rooms, or procedure duration. The purpose of feedback is to provide the impetus for process improvement such as a change in cleaning procedures. We were unable to assess the impact of UV-C given the lack of viral detection by nucleic acid or culture. Although we were unable to confirm infectivity by viral culture in either cohort, this may have been related to disinfectant exposure and does not exclude the possibility of aerosolisation of live virus before sampling. In conclusion, evidence-based feedback is an important and practical component for prevention of intraoperative SARS-CoV-2 spread.

Acknowledgements

The authors acknowledge Vrunda M. Patel for her contributions to sample collection and administration of UV-C.

Declarations of interest

RWL received research funding from Sage Medical Inc., BBraun, Draeger, and Kenall, has one or more patents pending, and is a partner of RDB Bioinformatics, LLC, and 1055 N 115th St #301 (Omaha, NE, USA) a company that owns OR PathTrac, and has spoken at educational meetings sponsored by Kenall (AORN) and BBraun (APIC). FD is Director of the Division of Management Consulting of the University of Iowa Department of Anesthesia, which provides consultations to corporations, hospitals, and individuals. He receives no funds personally other than his salary and allowable expense reimbursements from the University of Iowa. His family and he have no financial holdings in any company related to his work. A list of all the Division's consults is available in his posted *curriculum vitae* at FranklinDexter.net/Contact_Info.htm. One of the donors, Gunner Lyslo, is CEO/founder and partner of Surfacide (Naperville, IL, USA), the company that makes the Helios® UV-C Disinfection System.

Funding

An unrestricted donation from Gunner Lyslo to the University of Iowa. US National Institutes of Health (Bethesda, MD, USA; grants P01 AI060699, R01 AI129269 to SP and AO).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2022.04.018.

References

1. Loftus RW, Campos JH. The anaesthetists' role in perioperative infection control: what is the action plan? *Br J Anaesth* 2019; **123**: 531–4
2. Loftus RW, Dexter F, Goodheart MJ, et al. The effect of improving basic preventive measures in the perioperative arena on *Staphylococcus aureus* transmission and surgical site infections: a randomized clinical trial. *JAMA Netw Open* 2020; **2**: e201934
3. Wall RT, Datta Subhradeep, Dexter F, et al. Effectiveness and feasibility of an evidence-based intraoperative infection control program targeting improved basic measures: a post-implementation prospective case-cohort study. *J Clin Anesth* 2022; **77**: 110632
4. Loftus RW, Dexter F, Evans LC, Robinson ADM, Odle A, Perlman S. An assessment of the impact of recommended anesthesia work area cleaning procedures on intraoperative SARS-CoV-2 contamination, a case-series analysis. *J Clin Anesth* 2021; **73**: 110350
5. Dexter F, Ledolter J, Wall RT, Datta S, Loftus RW. Sample sizes for surveillance of *S. aureus* transmission to monitor effectiveness and provide feedback on intraoperative infection control including for COVID-19. *Perioper Care Oper Room Manag* 2020; **20**: 100115
6. Wang J, Hang X, Wei B, et al. Persistent SARS-CoV-2 RNA positivity in a patient for 92 days after disease onset. *Medicine* 2020; **99**, e21865
7. Dubelbeiss E, Silverberg M, White C, Jaspan DO, Goldberg J. Repeat positive severe acute respiratory syndrome coronavirus 2 (coronavirus disease 2019) testing ≥90 days apart in pregnant women. *Am J Obstet Gynecol MFM* 2021; **3**: 100331
8. Mills M. *Student and academic life. The 90-day post COVID-19 window explained*. Available from: http://uknow.uky.edu/student-and-academic-life/90-day-post-covid-19-window-explained. January 13, 2021 (accessed 3 December 2021).
9. Koff MD, Loftus RW, Burchman CC, et al. Reduction in intraoperative bacterial contamination of peripheral intravenous tubing through the use of a novel device. *Anesthesiology* 2009; **110**: 978–85
10. Clark C, Taenzer A, Charette K, Whitty M. Decreasing contamination of the anesthesia environment. *Am J Infect Control* 2014; **42**: 1223–5
11. Loftus RW, Brindeiro BS, Kispert DP, et al. Reduction in intraoperative bacterial contamination of peripheral intravenous tubing through the use of a passive catheter care system. *Anesth Analg* 2012; **115**: 1315–23
12. Eggers M, Koburger-Janssen T, Ward LS, Newby C, Müller S. Bactericidal and virucidal activity of povidone-iodine and chlorhexidine gluconate cleansers in an in vivo hand hygiene clinical simulation Study. *Infect Dis Ther* 2018; **7**: 235–47
13. Birnbach DJ, Rosen LF, Fitzpatrick M, Carling P, Arheart KL, Munoz-Price LS. Double gloves: a randomized trial to evaluate a simple strategy to reduce contamination in the operating room. *Anesth Analg* 2015; **120**: 848–52
14. ICT Infection Control Today. *New CDC study confirms effectiveness of UV-C disinfection to combat harmful pathogens* April 25, 2013. Environmental Hygiene, Purchasing, Clinical Interventions. Available from: https://www.infectioncontroltoday.com/environmental-hygiene/new-

cdc-study-confirms-effectiveness-uv-c-disinfection-combat-harmful. [Accessed 3 December 2021].
15. Andersen BM, Bånrud H, Bøe E, Bjordal O, Drangsholt F. Comparison of UV-C light and chemicals for disinfection of surfaces in hospital isolation units. *Infect Control Hosp Epidemiol* 2006; **27**: 729–34
16. Bedell K, Buchaklian AH, Perlman S. Efficacy of an automated multiple emitter whole-room ultraviolet-C disinfection system against coronaviruses MHV and MERS-CoV. *Infect Control Hosp Epidemiol* 2016; **37**: 598–9
17. Dexter F, Parra MC, Brown JR, Loftus RW. Perioperative COVID-19 defense: an evidence-based approach for optimization of infection control and operating room management. *Anesth Analg* 2020; **131**: 37–42
18. Dexter F, Elhakim M, Loftus RW, Seering M, Epstein RH. Strategies for daily operating room management of ambulatory surgery centers following resolution of the acute phase of the COVID-19 pandemic. *J Clin Anesth* 2020; **64**: 109854
19. Wagner JA, Dexter F, Greeley DG, Schreiber K. Operating room air delivery design to protect patient and surgical site results in particles released at surgical table having greater concentration along walls of the room than at the instrument tray. *Am J Infect Control* 2021; **49**: 593–6
20. Eypasch E, Lefering R, Kum CK, Troidl H. Probability of adverse events that have not yet occurred: a statistical reminder. *BMJ* 1995; **311**: 619–20

doi: 10.1016/j.bja.2022.04.018
Advance Access Publication Date: 29 April 2022

Role of intraoperative ketamine in preventing severe rebound pain for patients undergoing ambulatory upper extremity surgery. Comment on *Br J Anaesth* 2022; 128: 734–41

Tim T. H. Jen[1,2,*], Aaron D. Victor[1,2] and Janny X. C. Ke[1,2,3]

[1]Department of Anesthesia, St Paul's Hospital/Providence Health Care, Vancouver, BC, Canada, [2]Department of Anesthesiology, Pharmacology and Therapeutics, University of British Columbia, Vancouver, BC, Canada and [3]Department of Anesthesia, Pain Management & Perioperative Medicine, Dalhousie University, Halifax, NS, Canada

*Corresponding author. E-mail: timothy929@gmail.com

Keywords: ambulatory surgery; brachial plexus block; ketamine; pain management; peripheral nerve block; rebound pain; regional anaesthesia; upper extremity surgery

Editor—We read the paper by Touil and colleagues[1] with interest. Their RCT sought to address the question of whether a single dose of intraoperative ketamine reduces the incidence of rebound pain. They also performed secondary analysis to evaluate potential risk factors for rebound pain. We thank the authors for contributing to our understanding on this important topic. However, there are three concerns regarding the internal validity of the study that would benefit from further clarification.

First, the study was underpowered to detect a difference in outcomes. The baseline incidence of rebound pain in the placebo group was 47% (in keeping with other published data[2,3]), which was higher than the 30% incidence from the authors' preliminary data used for sample size calculation. To detect a clinically important, absolute risk reduction of 20% from a baseline incidence of 47%, each group would require 91 subjects.[4] The conclusion that 'intraoperative ketamine at single anti-hyperalgesic doses does not prevent rebound pain after upper limb surgery' requires confirmation in an adequately powered study. Of note, in Table 2, the numbers of subjects who received intraoperative ketamine in the group with and without rebound pain should be 18 and 36, respectively, as reported in Table 1 and the Results section.

Second, findings from the secondary analysis of the RCT cohort data must be interpreted with caution, as the univariable logistic regression models used to identify possible risk factors for rebound pain did not adjust for potential confounding. The effect sizes may be overestimated or underestimated by the unadjusted odds ratios (ORs). For example, bone surgery was found to have an OR of 5.246 (95% confidence interval [CI]: 1.883–14.619) for rebound pain; yet, a larger cohort study previously identified a more modest adjusted OR of 1.823 (95% CI: 1.384–2.402).[2] This problem is compounded by a small cohort sample size and *P*-values that were not adjusted for multiple testing. Similarly, the finding of no association between positive Central Sensitisation Inventory and rebound pain might be susceptible to residual confounding. It would be helpful for the authors to report the OR from a multivariable analysis, along with E-value for residual confounding.[5] The statement that 'underlying central sensitisation does not play a major role in [rebound pain] development' thus warrants further investigation.

DOI of original article: 10.1016/j.bja.2021.11.043.