In Response

We thank esteemed colleagues Drs Brull and Kopman,[1] both well-known experts in the field of neuromuscular monitoring and blockade for their interest in our article and their comments.

We would like to start by reiterating that our review[2] was aimed at presenting technologies and techniques for coronavirus disease 2019 (COVID-19) patients who needed the use of neuromuscular blocking agents (NMBA) outside the operating theater. In particular, the editorial focused on severe COVID-19 patients with acute respiratory distress syndrome (ARDS). NMBA were needed for either intubation in the intensive care unit (ICU) or emergency room (ER) or for sparing these drugs during prolonged invasive mechanical ventilation.[2] The creation of dedicated anesthesia intubation teams during the COVID-19 crisis as well as the increasing engagement of anesthesiologists in the ICU setting led us to believe that presenting basic principles of neuromuscular monitoring could be of interest for all readers.[2] We purposely adopted the terminology widely used in the setting of intensive care medicine[3] when we wrote about the train-of-four (TOF) monitoring. As a matter of fact, we deliberately referred to the way electric impulses are applied to a motor nerve. The TOF stimulation consists of applying 4 electric stimuli each separated by 0.5 s. Depending on the method of monitoring available, either qualitative—tactile or visual counting—or quantitative monitoring—using a specific monitoring device—is possible. In the former, the TOF count can be determined (1–4 twitches), or a definite ratio of T4/T1 ratio. The TOF ratio is the comparison of T4 (fourth twitch of the TOF) to T1 amplitude, expressed in percentage.[4] We left the choice of using either qualitative or quantitative monitoring to the discretion of the physicians working in the ICU because they could be not ICU trained.[2] In the operating room, quantitative monitoring devices are recommended as they give a more detailed and precise estimate of neuromuscular blockade (NMB).

NMB monitoring is not standard of care in the ICU, despite the infusion of NMBAs is common for adult with severe ARDS or during proning maneuvers. The best compromise between practicability, usefulness, and validity of monitoring seems to be the use of qualitative, handheld monitoring devices.[2] Handheld monitoring has limited value during intubation outside the ICU but it can be easily carried in the physician's pocket, and properly disinfected.[2] Monitoring is more frequently used during continuous infusion of NMBA and it can be done in seconds using facial or eye muscles, adductor pollicis muscle, or others.

The qualitative result can then be noted in the electronic patients' chart. The frequency and the site of placement of such monitoring is also discretion of the treating physician or the ICU guidelines.

The COVID-19 pandemic peak has significantly increased the workload in most ICUs and the frequency of TOF monitoring has been compromised at times. Even if 1 attempted quantitative monitoring in the ICU, validity of the results could be questioned because of the lack of standardization. Frequently asked questions are: shall one leave stimulating electrodes in the same place? How long could these stay on the skin without causing pressure damages? What position shall be used of the hand when monitoring is performed?

In that respect, again facial muscles are easier to monitor but they do not reflect NMB or neuromuscular transmission at the adductor pollicis muscle. We do not recommend the corrugator supercilii as the monitoring site of choice but wanted to point out that it best reflects NMB or neuromuscular transmission at the diaphragm or larynx, anatomic areas of particular interest for ICU physicians.

Drs Brull and Kopman[1] questioned the recommended target value of NMB in the ICU setting. The discussion of whether NMB is at all necessary for mechanical ventilation in the ICU is beyond the scope of our article. However, in a recent study,[3] a positive relationship was found between the depth and duration of NMB and ICU-acquired weakness.

The article entitled "Battle of the RSI Paralytics"[5] describes the long-standing discussion around the use of succinylcholine versus rocuronium for rapid sequence induction (RSI) from the perspective of emergency medical services. In terms of onset time and intubation conditions, rocuronium in a dose of more than 1 mg/kg and succinylcholine in a dose of 1 mg/kg are equally efficient.[6]

COVID-19 patients who need intubation are predominantly suffering from multiple comorbidities.[7] This leaves us with the eternal question which muscle relaxant is better for the "can't intubate can't ventilate situation." Despite best efforts of preoxygenation, COVID-19 patients desaturate very quickly during the intubation process to alarming values of 70% or 60% or less within seconds. It is therefore important that intubation is provided by a dedicated team and mostly by the very experienced physicians, predominantly using videolaryngoscopy.[2] The procedure can be particularly challenging in COVID-19 patients. Naguib et al[8] found a significantly longer objectively measured duration of NMB after 1 mg/kg succinylcholine with 10 minutes versus 2 minutes after 1.2 mg/kg rocuronium followed 3 minutes later by 16 mg/kg sugammadex. As to the comments by Brull and Kopman[1] to the time it takes to get this amount of

sugammadex is ready, one can easily imagine the fractionated injection of sugammadex by the anesthesiologist, while a second person gets it ready. We argue that the time it takes to get sugammadex ready is not really an issue. However, no one can prove that the risks and benefits ratio of using rocuronium is better for those administering succinylcholine in these situations. Even when one looks at clinical parameters, such as a return to spontaneous ventilation, defined as respiratory rate of more than 8/min at a tidal volume of at least 3 mL/kg for 30 s, the combination of rocuronium/sugammadex is able to achieve this in half the time as succinylcholine.[9,10]

We finally would like to thank Drs Brull and Kopman[1] to allow us to elaborate a bit more on neuromuscular monitoring and NMB in critical care in the time of COVID-19 pandemic.

Francesca Rubulotta, MD, PhD, MBA, FRCA, FICM
Department of Anaesthesia and Intensive Care Medicine
Imperial College London
London, United Kingdom
francesca.rubulotta@nhs.net
Hatem Soliman-Aboumarie, MD, FEACVI, FASE, FHEA
Department of Anaesthetics and Critical Care
Harefield Hospital
Royal Brompton and Harefield NHS foundation trust
London, United Kingdom
Kevin Filbey, MD
Goetz Geldner, MD, PhD
Department of Anesthesia, Intensive Care Medicine, Chronic Pain and Emergency Medicine
Ludwigsburg Hospital
Ludwigsburg, Germany
Kai Kuck, PhD
Department of Anesthesiology and Bioengineering
University of Utah
Mario Ganau, MD, PhD, FEBNS, FACS
Department of Neurosurgery
John Radcliffe Hospital
Oxford University Hospitals NHS Foundation Trust
Oxford, United Kingdom
Thomas M. Hemmerling, MSc, MD, DEAA
Department of Anesthesia
McGill University
Montreal, Canada

ACKNOWLEDGMENT

The authors thank Umesh Patel for editing the content.

REFERENCES

1. Brull SJ, Kopman AF. Clarifications on technologies to optimize care of severe COVID-19 patients. *Anesth Analg*. In press.
2. Rubulotta F, Soliman-Aboumarie H, Filbey K, et al. Technologies to optimize the care of severe COVID-19 patients for healthcare providers challenged by limited resources. *Anesth Analg*. 2020.
3. Bouju P, Tadié JM, Barbarot N, et al. Clinical assessment and train-of-four measurements in critically ill patients treated with recommended doses of cisatracurium or atracurium for neuromuscular blockade: a prospective descriptive study. *Ann Intensive Care*. 2017;7:10.
4. McGrath CD, Hunter JM. Monitoring of neuromuscular block. *Continuing Educ Anaesth Crit Care Pain*. 2006;6:7–12.
5. https://www.jems.com/2019/05/13/succinylcholine-vs-rocuronium-battle-of-the-rsi-paralytics/.
6. Herbstritt A, Amarakone K. Towards evidence-based emergency medicine: best BETs from the Manchester Royal Infirmary. BET 3: is rocuronium as effective as succinylcholine at facilitating laryngoscopy during rapid sequence intubation? *Emerg Med J*. 2012;29:256–258.
7. Cheung JC, Ho LT, Cheng JV, Cham EYK, Lam KN. Staff safety during emergency airway management for COVID-19 in Hong Kong. *Lancet Respir Med*. 2020;8:e19.
8. Naguib M, Brewer L, LaPierre C, Kopman AF, Johnson KB. The myth of rescue reversal in "can't intubate, can't ventilate" scenarios. *Anesth Analg*. 2016;123:82–92.
9. Sørensen MK, Bretlau C, Gätke MR, Sørensen AM, Rasmussen LS. Rapid sequence induction and intubation with rocuronium-sugammadex compared with succinylcholine: a randomized trial. *Br J Anaesth*. 2012;108:682–689.
10. Rubulotta F, Rubulotta G, Occhipinti G, Naimo J, Gullo A. Comment on "Effects of neuromuscular block on systemic and cerebral hemodynamics and bispectral index during moderate or deep sedation in critically ill patients" by Inoue et al. *Intensive Care Med*. 2007;33:388–389.

DOI: 10.1213/ANE.0000000000005121