Lost in transition: use of SpO_2 in the Australian and New Zealand College of Anaesthetists transition tool. Reply to *Br J Anaesth* 2020; 125: e465–6

Adam Rehak[1,*], Nicholas Chrimes[2] and Andy Higgs[3]

[1]Department of Anaesthesia, Royal North Shore Hospital, St Leonards, Australia, [2]Department of Anaesthesia, Monash Medical Centre, Melbourne, Australia and [3]Department of Anaesthesia and Intensive Care Medicine, Warrington Teaching Hospitals NHS Foundation Trust, Warrington, Cheshire, UK

*Corresponding author. E-mail: adamrehak@yahoo.com.au

Keywords: airway management; cannot intubate; cannot oxygenate; cognitive aid; emergency front-of-neck airway; guideline; oxygenation

Editor—We thank Bradley[1] for his interest and comment in our recent article on the challenges of getting airway clinicians to move from the upper airway to the neck during an airway crisis.[2] Bradley seeks to clarify the rationale behind the inclusion of oxygen saturation (SaO_2) <90% as a trigger for declaring 'cannot intubate, cannot oxygenate' (CICO) on the Australian and New Zealand College of Anaesthetists (ANZCA) Transition to CICO cognitive aid.[3] One author of our article (AR) was also a co-author on the background document[4] supporting the ANZCA guideline and cognitive aid. As such, we can confirm that for the most part, the principles espoused in the ANZCA documents align closely with those in our article. However, the inclusion of a threshold SaO_2 as one of the criteria for declaring CICO is one we disagree on.

Bradley appears to agree with us that declaration of CICO and initiation of emergency front-of-neck airway (eFONA) should be based solely on completion of unsuccessful 'best efforts'[2] at each of the intubation, face mask ventilation, and supraglottic airway insertion upper airway options. He justifies inclusion of an SaO_2 threshold in the ANZCA cognitive aid[3] on the basis that SaO_2 remains relevant both to determining the time and number of attempts that are appropriate to invest before declaring a best effort at any of the upper airway options and to the need to expedite priming[2] for performance of eFONA. We wholeheartedly agree with this view. Our assertion that declaring CICO should not be linked to a specific SaO_2 threshold does not imply that the SaO_2 is irrelevant to decision-making in airway management.

The concept of a best effort is context dependent, and SaO_2 is one of a number of considerations informing the threshold for abandoning further attempts at a given upper airway option. What might constitute a reasonable suite of attempts at upper airway rescue in the context of high or slowly decreasing SaO_2 may be very different to the more limited number of attempts towards a 'best effort' in the context of critical desaturation. The trigger for declaration of CICO, however, remains a procedural rather than physiological one; it hinges on exhaustion of all reasonable efforts at intubation, facemask ventilation, and supraglottic airway insertion in a given context. There may be circumstances in which this is achieved rapidly in a well-preoxygenated patient, such that declaration of CICO and initiation of eFONA are indicated, despite saturations being well above the suggested threshold of 90%. Thus, the SaO_2 is relevant to defining what constitutes a best effort at any of the upper airway options but not to defining the trigger for declaring CICO *per se*.

Although the intention of the ANZCA cognitive aid may not be 'about insisting a desaturation should occur before declaring a CICO situation', the reality is that the utility of airway decision-support tools is dependent on the message conveyed rather than the message intended. We remain concerned that inclusion of 'SpO_2 <90%' on the ANZCA cognitive aid as one of four discrete criteria defining CICO will lead most clinicians to conclude that ALL these criteria must be satisfied for a CICO situation to be declared.

Our concerns with the ANZCA cognitive aid are based on the key tenet that airway decision-support tools should provide unambiguous triggers to facilitate decision making during the process of transition to CICO. Bradley's description of how SaO_2 may inform decision making during an airway crisis aligns with our own. Unfortunately, his description is inconsistent with the trigger for CICO as presented in the ANZCA cognitive aid. We feel that in its current form the ANZCA cognitive aid appears to contradict the guidelines that accompany it. This may lead to confusion and potential delays with regard to initiating eFONA.

Declaration of interest

The authors declare that they have no conflicts of interest.

References

1. Bradley P. Lost in transition: use of SpO_2 in the Australian and New Zealand College of Anaesthetists transition tool. Comment on *Br J Anaesth* 2020; 125: e38–46. *Br J Anaesth* 2020; **125**: e465–6
2. Chrimes N, Higgs A, Rehak A. Lost in transition: the challenges of getting airway clinicians to move from the upper airway to the neck during an airway crisis. *Br J Anaesth* 2020; **125**: E38–46

DOI of original article: 10.1016/j.bja.2020.09.007.

3. Australian and New Zealand College of Anaesthetists. *Guidelines for the management of evolving airway obstruction: transition to the can't intubate can't oxygenate airway emergency* 2017 July. Available from: https://www.anzca.edu.au/getattachment/71f54974-314a-4d96-bef2-c03f39c8a8e9/PS61-Guideline-for-the-management-of-evolving-airway-obstruction-transition-to-the-Can't-Intubate-Can't-Oxygenate-airway-emergency#page= (accessed December 2020)

4. Australian and New Zealand College of Anaesthetists. *Transition from supraglottic to infraglottic rescue in the "can't intubate, can't oxygenate" (CICO) scenario*. Report from the ANZCA Airway Management Working Group 2014, November. Available from, https://www.anzca.edu.au/resources/incident-reporting-docs/airway-docs/report-from-the-anzca-airway-management-working-gr (accessed December 2020)

doi: 10.1016/j.bja.2020.12.038
Advance Access Publication Date: 2 February 2021

Utilising mass cytometry with CD45 barcoding and standardised leucocyte phenotyping for immune trajectory assessment in critically ill patients

Matthew Fish[1,2], Richard Ellis[3], Cynthia Bishop[3], Katrina Todd[3], Nedyalko Petrov[3], Mervyn Singer[4], Chad M. Swanson[1] and Manu Shankar-Hari[1,2,*]

[1]Department of Infectious Diseases, School of Immunology and Microbial Sciences, King's College London, London, UK, [2]Department of Intensive Care Medicine, Guy's and St Thomas' NHS Foundation Trust, London, UK, [3]NIHR Guy's and St Thomas' Biomedical Research Centre at Guy's and St Thomas' NHS Foundation Trust and King's College London, London, UK and [4]Bloomsbury Institute of Intensive Care Medicine, University College London, London, UK

*Corresponding author. E-mail: manu.shankar-hari@kcl.ac.uk

Keywords: barcoding; critical care; CyTOF; immune phenotyping; immune response; leucocyte; sepsis

Editor—Critically ill patients have rapidly changing longitudinal immune responses (*immune trajectory*) to infection and tissue injury. If we can delineate this immune trajectory, then we can time treatments that stimulate or depress the immune system (*immunomodulation*) to mirror the dominant immune signal at distinct stages of critical illness.

These rapidly changing longitudinal immune responses generate two major inferential challenges. First, the signal for illness-specific alterations must be delineated from the noise of inter-experimental variation within a study. Second, lack of standardisation of immune cell phenotyping assays between studies makes it difficult to discern whether observed differences between studies represent signal or noise.[1] These challenges need addressing in sepsis, as innate and adaptive immune systems are profoundly altered, immune phenotyping is not standardised, and rapidly changing sepsis-specific immune trajectory remains poorly characterised, for optimal immunomodulation.[1,2]

To address the challenge of inter-sample and inter-experiment variability and to enable simultaneous leucocyte phenotyping in longitudinal samples from the same patient, we developed a multiplexing approach using the stably expressed pan-leucocyte cluster of differentiation 45 (CD45) antigen as the target (referred to as barcoding) and cytometry by time of flight (CyTOF) as the phenotyping method.[3] To address the non-standardised phenotyping challenge, we used markers proposed in the standardised human immunophenotyping panel[4] and included selected immune state markers that are treatment targets such as checkpoint molecules and the human leucocyte antigen DR isotype (HLA-DR).[5] This report summarises the development of CD45 barcoding, assessment of major cell populations with a standardised human immunophenotyping panel,[4] and comparison of individual to multiplexed samples.

For all experiments, cryopreserved peripheral blood mononuclear cells (PBMC) were isolated using Ficoll-Hypaque (Sigma-Aldrich, St. Louis, MO, USA) density gradient centrifugation. For CD45 barcoding, commercially available CD45 89Y (Fluidigm Corp., South San Francisco, CA, USA) and in-house conjugated metal isotopes (115In, 159Tb, 209Bi) to the CD45 antibody (BioLegend®, BioLegend Inc., San Diego, CA, USA) were used. PBMCs were thawed in a 37°C water bath, washed in Roswell Park Memorial Institute (RPMI) 1640 medium supplemented with 10% fetal bovine serum and 5% penicillin–streptomycin, resuspended in 1 ml, and counted. Then 3×10^6 cells from five donors were transferred to 5-ml polystyrene tubes for barcoding. Barcoded samples were washed once in phosphate-buffered saline (PBS), resuspended in 98 μl PBS, stained (1:100) with a unique combination of CD45 antibodies for 20 min, washed twice in 4 ml PBS, and combined into a single barcoded sample. The CD45 barcoding rationale, purpose, and novelty are summarised in Figure 1a.

For standardised leucocyte phenotyping, individual samples with 3×10^6 cells with combined barcoded samples were