Editorial

Rosemarie Kearsley St Mary's Hospital, Imperial College Healthcare NHS Trust, London

Case reports in the COVID-19 pandemic: first responders to an emergency in evidencebased medicine

R Kearsley,¹ R Daly Guris,² LF Miles,^{3,4} CL Shelton^{5,6}

1 Consultant Anaesthetist, Department of Anaesthesia, St Mary's Hospital, Imperial College Healthcare NHS Trust, London,

2 Attending Physician, Department of Anaesthesia, Children's Hospital of Philadelphia, Philadelphia, USA

3 Staff Specialist, Department of Anaesthesia, Austin Health, Melbourne, Australia.4 Honorary Senior Fellow, Centre for Integrated Critical Care, The University of Melbourne, Melbourne, Australia

5 Consultant Anaesthetist, Department of Anaesthesia, Wythenshawe Hospital, Manchester University Hospitals NHS Foundation Trust, Manchester, UK

6 Senior Clinical Lecturer in Anaesthesia, Lancaster Medical School, Faculty of Health and Medicine, Lancaster University, Lancaster, UK.

Twitter:	<pre>@Rose_Kearsley @theRodrigoDaly @nyquistlimited @DrCliffShelton</pre>			
Correspondence to:	Rose Kearsley, <u>rosemariekearsley@gmail.com</u>			
Running title:	Case reports in the COVID-19 pandemic			
Key words (MeSH):	COVID-19 Evidence-Based Medicine Safety Patient-Centered Care Diffusion of Innovation			

Aliorum vulnus nostra sit cautio Let us take warning from another's wound

> Saint Jerome Letter 54, To Furia, AD 394

The role of the case report has evolved over time, reflecting the evolution of medicine itself. In ancient times, classical texts by physicians such as Hippocrates and Galen formed the basis of medical education. These reports, written with limited understanding of the underlying pathophysiology, provided a framework for the empirical treatment of disease. Over time, with a greater understanding of medical sciences and associated advances in technology and research methodology, the function of the case report was overtaken by 'higher' forms of evidence. While the randomised, double-blinded, clinical trial has come to epitomise the science underpinning our practice, the well-written case report continues to illuminate the subtleties of our art.

In 1979, the Canadian Task Force on Periodic Health Examination proposed a system that graded the effectiveness of specific interventions (from I to III) and the strength of their associated recommendation in best practice guidelines (from A to E) [1]. This system has subsequently been adopted worldwide and now forms a cornerstone of evidence-based medicine. Although this approach generally serves the medical community well, there are certain circumstances to which it is not well suited, namely: rare events for which it is difficult to assemble large patient cohorts; the reporting of early safety concerns involving medical devices, and; rapidly evolving situations where the assembly of higher levels of evidence is hindered by lack of available data. In the context of the COVID-19 pandemic, the potential severity of the disease, the speed and geographic extent of transmission of SARS-CoV-2, combined with limited knowledge of the pathogenesis and natural history of the infection positions the first wave of the pandemic firmly in the third category [1].

Such a highly contagious and unknown entity is an uncommon occurrence in modern medicine. Early in the pandemic, clinicians did not have the luxury of time to wait for the availability of rigorous research findings before acting to save lives. Early treatments, observations and outcomes were, therefore, shared formally and informally via personal communications, social media, correspondence articles and short papers. In disseminating the best available new knowledge regarding COVID-19, case reports become became the 'first responders' in the medical literature.

Under 'normal' circumstances, the case report has been perceived as the 'lowliest' form of peer reviewed evidence. However, the COVID-19 pandemic has demonstrated that these manuscripts are highly relevant when written with a scholarly approach and subjected to peer review. As anaesthetists and critical care physicians, we have treated patients with COVID-19 in the operating theatre, in the intensive care unit, in the emergency department and on the labour ward. We have provided assistance with airway management and other invasive procedures in virtually every other area of the hospital. As the pandemic progressed, reflecting on our lived experiences and those of our patients was paramount in providing relevant information to colleagues. In this editorial, we discuss the twelve COVID-19-related cases that *Anaesthesia Reports* has published to date, and present the themes that arise when considering these reports in aggregate.

Maintaining staff safety

One of the greatest challenges that the COVID-19 pandemic presents is how to protect ourselves and our colleagues in the workplace [3]. Anaesthetists and critical care physicians –

by the very nature of the work we do – are involved in numerous high-risk clinical activities, often with the sickest patients [4]. It is unsurprising that many of the reports we have published emphasised staff safety. Broadly, these fell into three categories: strategies for the avoidance of aerosol generating procedures, such as the novel approach to spinal anaesthesia to facilitate prolonged surgery in a patient with SARS-CoV-2 infection reported by Oon and Ha [5]; modifying existing procedures to minimise aerosol generation, including the approaches to tracheostomy described by Smith et al and Harper et al [6, 7]; ensuring the proper availability, function and use of personal protective equipment (PPE), including Rotman et al's description of the vital role of team briefing in ensuring appropriate protection is worn by all team members during shared airway surgery in the context of COVID-19 [8]. The knowledge and awareness of the risks we faced as clinicians was seen in the personal account from Ramachandran [9], which also shows how the evolution of policies regarding PPE have changed over time.

The patient experience of COVID-19

The anxieties felt by clinicians facing the pandemic were mirrored by patients and their relatives, who were likewise facing a threat that was both potentially deadly and poorly-understood. This uncertainty was combined with the need for physical and social distancing and infection control measures, creating numerous conflicts with the usual best practices of patient experience. Nevertheless, understanding and optimising the experiences of patients has been a prominent feature of our reports, perhaps most notably in Ramachandran's account of his personal experience as a junior doctor with severe COVID-19, and his experiences of psychological and physical recovery [9]. Likewise, the report by Oon and Ha discusses the balance between staff safety and patient experience, which were both positive in this case [5]. The symptoms of COVID-19 were also described, including Hoshijima et al's description of a severely hypoxic but only minimally symptomatic patients [10], experiencing what has come to be known as silent or 'happy' hypoxia [11].

Complications and clinical risks

In addition to highlighting many aspects of staff safety, our reports also describe some of the risks to patients associated with COVID-19 and its clinical management. Hypercoagulability is now thought to be a significant factor in the pathogenesis of severe disease [12], but opinions remain divided on the correct approach to its management. With this in mind, Aaron et al discuss the dilemmas presented by the use of increased doses of anticoagulants in a critically ill patient with recurrent pulmonary emboli [13]. It was in order to prevent complications of mechanical ventilation with high-pressures that Tulley et al used extracorporeal carbon dioxide removal in a patient with COVID-19 and progressive acute respiratory distress syndrome [14]. Indeed, complications of tracheal intubation and invasive ventilation were seen in several cases, including McGuire et al's report of widespread surgical emphysema secondary to barotrauma, including extraconal orbital emphysema, pneumomediastinum, pneumopericardium and throughout the soft tissues with dissection into the peritoneum and retroperitoneum [15].

Anaesthetists as innovators

Innovation is a requirement in addressing a novel pathogen, and our published reports demonstrate widespread evidence of anaesthetists acting as innovators to overcome challenges presented during the crisis. Miles et al developed a simple 3D-printed device to allow powered air-purifying respirators (PAPRs) to be worn under protective gowns without obstruction of the air inlet [16]. Their report demonstrates the benefits of clinical-academic collaboration to develop a cheap, scalable and rapidly-implementable solution. Innovation occurred likewise in the clinical setting to adapt common techniques in response to challenges

presented by COVID-19. Hoshijima et al report the technique of rocuronium 'priming' to minimise the time from induction to tracheal intubation in patients with COVID-19, using a modified version of existing recommendations [10]. Ahmad et al described one of the first cases of awake tracheal intubation in COVID-19 and described various modifications to standard practice in order to safeguard staff safety [17]. With no previously published guidelines on this technique in the COVID-19 setting, their report demonstrated the feasibility of a procedure which remains vital in the management of predicted difficult airway.

Non-technical skills

Perhaps unsurprisingly given the prominence of non-technical skills in anaesthetic practice, we were presented with many examples highlighting the importance of team work, communication and situation awareness in the management of COVID-19. Several reports highlight the role of team briefing prior to undertaking modified procedures that are potentially both unfamiliar and high-risk [7,8]. Outside of the operating theatre environment, new collaborations with colleagues redeployed from other areas required teamwork to address new challenges. Smith et al describe their approach to the development of a dedicated percutaneous tracheostomy team comprising two ear, nose and throat surgeons and two anaesthetists who performed percutaneous tracheostomies in the intensive care setting [6]. The interplay between anaesthetists, intensivists and other specialties was demonstrated throughout the pandemic in the care of the most critically ill of these patients. McGrath et al discuss the risks involved in transferring a critically-ill patient to the radiology department for computed tomography scanning in the prone position [18]. An appropriately experienced team undertook the transfer after having first planned the logistics with radiology colleagues, facilitating the successful completion of a potentially challenging transfer and procedure.

Case reports can inform all aspects of clinical practice and, as we have described herein, frequently address multiple areas of practice simultaneously. In contrast to more systematic or larger studies, the case report is a nimble form of evidence which, by drawing on individual experiences in light of current evidence, can act as an academic 'rapid response' when facing unprecedented circumstances. Case reports demonstrate the capacity to rapidly disseminate clinical information and can form the basis of further research and innovation. Furthermore, the learning points generated by case reports inspire discussion and development in the workplace, and can be rapidly applied to 'real world' clinical situations, to the benefit of both clinicians and patients. The COVID-19 pandemic has generated an emergency in evidence-based medicine which we hope will abate as the scientific understanding of COVID-19 advances. Nevertheless, case reports have been an important part of our collective effort to address an unfolding crisis, cementing their place as an essential component in the toolbox of evidence-based medicine.

Acknowledgements

All authors are assistant editors of *Anaesthesia Reports*. No other interests or funding declared.

References

- 1. Canadian task force on the periodic health examination. The periodic health examination. *Canadian Medical Association Journal* 1979; **121**: 1193–1254.
- 2. Zdravkovic M, Berger-Estilita J, Zdravkovic B, Berger D. Scientific quality of COVID-19 and SARS CoV2 publications in the highest impact medical journals during the early phase of the pandemic: a case control study. *PLoS ONE* 2020; **15**: e0241826.
- 3. Cook T, Kursumovic E, Lennane S. Exclusive: Deaths of NHS staff from COVID-19 analysed, 2020. https://www.hsj.co.uk/exclusive-deaths-ofnhs-staff-from-covid-19-analysed/7027471.article (accessed 30/05/2020).
- 4. El-Boghdadly K, Wong DJN, Owen R, et al. Risks to healthcare workers following tracheal intubation of patients with COVID-19: a prospective international multicentre cohort study. *Anaesthesia* 2020; **75**: 1437-1447.
- 5. Oon Z, Ha C. A novel approach to spinal anaesthesia to avoid aerosol generating procedures in a patient with COVID-19 presenting for laser prostate surgery. *Anaesthesia Reports* 2020; **8**: 138–141.
- 6. Smith TG, Ahmad I, Takhar A, Surda P, El-Boghdadly K. Unconventional team strategy for tracheostomy in COVID-19. *Anaesthesia Reports* 2020; **8**: 176–180.
- Harper S, Robinson M, Manning G, Jones A, Hobson J, Shelton CL. Management of tracheostomy-related tracheomegaly in a patient with COVID-19 pneumonitis. *Anaesthesia Reports* 2020; 8: 157-160
- Rotman A, Dando AJ, Shorthouse J, Giris M, Nouraei SAR. Apnoeic ventilation for shared airway surgery during the COVID-19 pandemic. *Anaesthesia Reports* 2020; 8: 161–163.
- 9. Ramachandran S. A junior doctor's experience of critical illness: from treating patients to becoming a patient with COVID-19. *Anaesthesia Reports* 2020; **8**: 59-62.
- 10. Hoshijima H, Nagasaka H, Ozaki M, *et al*. Rocuronium priming for tracheal intubation in COVID-19 patients. *Anaesthesia Reports* 2020; **8**: 98-100.
- 11. Dhont S, Derom E, Van Braeckel E, et al. The pathophysiology of 'happy' hypoxemia in COVID-19. *Respiratory Research* 2020; **21**: 198.
- 12. Abou-Ismail MY, Diamond A, Kapoor S, Arafah Y, Nayak L. The hypercoagulable state in COVID-19: Incidence, pathophysiology, and management. *Thrombosis Research*. 2020; **194**: 101-115.
- 13. Aaron L, Welch M, Shah A, Thomas T, McKechnie SR. Recurrent massive pulmonary emboli in a critically ill patient with COVID-19. *Anaesthesia Reports* 2020; **8**: 94-97.
- Tully RP, Hopley N, Lawrence G. The successful use of extracorporeal carbon dioxide removal as a rescue therapy in a patient with severe COVID-19 pneumonitis. *Anaesthesia Reports* 2020; 8: 113-115
- 15. McGuire HD, Jennings C, Melvin M, Duggan M. Extraconal orbital emphysema secondary to barotrauma in a ventilated patient with COVID-19. *Anaesthesia Reports* 2020; **8:** 111-112.
- 16. Miles LF, Chuen J, Edwards L, et al. The design and manufacture of 3D-printed adjuncts for powered air-purifying respirators. *Anaesthesia Reports* 2020; **8**: 84-86.
- 17. Ahmad I, Wade S, Langdon A, Chamarette H, Walsh M, Surda P. Awake tracheal intubation in a suspected COVID-19 patient with critical airway obstruction. *Anaesthesia Reports* 2020; **8:** 28-31.
- 18. McGrath BA, Lowe R, Brady W, Sharman A, Felton T, Shelton CL. Computed tomography scanning in the prone position for a critically hypoxic patient with COVID-19. *Anaesthesia Reports* 2020; **8:** 71-2.

Caption for Table

Table 1: themes arising from the 12 COVID-19 casees published to date by Anaesthesia

 Reports

	Staff safety	Patient experience	Clinical risk	Innovation	Non-technical skills
Oon and Ha [5]	it is important to remember that no PPE is 100% effective and that every aerosol- generating procedure places healthcare staff at risk.	When questioned, he commented that he was comfortable throughout the entire operation.	the patient was SARS-CoV-2 positive and subjecting him to 3 h of invasive positive pressure ventilation could have potentially increased his risk of developing COVID-19 pneumonia	spinal anaesthesia was performed using a combination of adjuncts to prolong the effective duration of the block, and lidocaine was nebulised to prevent coughing during the procedure	
Smith et al [6]	We established mobile emergency rapid intubation teams (MERIT) early in the pandemic response, which follow specific protocols [to minimise] operator risk of infection		Anecdotally, percutaneous tracheostomies may be less prone to wound site infections and dislodgement in the presence of thick tenacious secretions in COVID-19.	our approach was distinct and unusual both in combining ENT surgeons with anaesthetists to form a tracheostomy team and, crucially, in this team undertaking percutaneous tracheostomies in the ICU	Our key multidisciplinary innovation was to then develop a dedicated tracheostomy team comprising two ear, nose and throat surgeons and two MERIT anaesthetists.
Harper et al [7]	concerns regarding aerosolised secretions may have led to staff feeling unable to tolerate even minor cuff leaks.		Computed tomography (CT) imaging on day 55 demonstrated new tracheomegaly with associated severe pneumomediastinum High cuff pressures can reduce local perfusion and damage tracheal mucosa and cartilage		In this already complex case, with the additional considerations of managing a patient recovering from COVID-19, team briefing and multidisciplinary co- ordination was of particular importance.
Rotman et al [8]	We recommend: a full team briefing where the risks are discussed; not allowing high- risk staff to include themselves; ensuring those remaining use appropriate [PPE]; minimising theatre staff numbers; and minimising movement in and out of the theatre		A [CT] scan demonstrated scarring at both lung apices, the lingula and the right middle lobe, some residual ground-glass change in the right lung, and a mass below the vocal folds nasendoscopy demonstrated granulomata of the subglottis	The first [learning point] relates to the successful use of THRIVE in a recovered patient with significant COVID-19, most notably multiple pulmonary emboli.	
Ramachandran [9]	it was clear to me that there was potential for me to be exposed to [SARS-CoV-2]. The infection prevention policy at my institution at the time permitted the use of [respirator masks] only when managing a patient with confirmed SARS- CoV-2.	When the physiotherapists and occupational therapists became involved I noticed a marked difference in my mood They encouraged me to self-function, accelerating my improvement	as a fit 26-year-old with no significant comorbidities, I was sure that if I was infected, the consequences were unlikely to be severe. Unfortunately, this was not to be the case.		much of my anxiety was dissipated by excellent communication from the critical care team. They provided opportunities for me to express my fears and addressed them appropriately
Hoshijima et al [10]		the patient could only maintain arterial oxygen saturations of approximately 85% However, clinically she was alert and orientated, with no obvious symptoms of respiratory distress.	we present two cases of tracheal intubation in COVID-19 patients where priming with a small dose of rocuronium caused hypoxia	We modified these recommendations by using the priming principle to further decrease time to tracheal intubation.	

Aaron et al [13]		Increased doses of anticoagulation must be weighed carefully against the risks of bleeding Our own experience has shown a bleeding rate of 12% in COVID-19 patients		Haematologists provided input throughout this patient's case with respect to optimal anticoagulation and monitoring Interventional radiology expertise was invaluable in deciding how and whether to provide thrombolysis
Tully et al [14]		The treating team felt that mechanical ventilation with dangerously high airway pressure was contributing to the progression of his ARDS	The treating team felt that mechanical ventilation with dangerously high airway pressure was contributing to the progression of his ARDS and therefore considered extracorporeal carbon dioxide removal as a rescue therapy.	
McGuire et al [15]		On [CT] scanning, a large pneumomediastinum, pneumopericardium and dissection of air into the peritoneum and retroperitoneum was observed. This was also noted in the patient's right eye		
Miles et al [16]	Caring for patients with coronavirus disease 2019 (COVID-19) may put healthcare workers at a risk of infection. This is especially true during aerosol-generating procedures		We describe the formation of a clinical-academic collaboration to develop a simple, cheap, scalable solution to this problem that could be manufactured rapidly.	Clinicians determined that a standoff to maintain separation between the gown and the filter intake was required A clinical- academic collaboration, with direct input from design engineers was formed.
Ahmad et al [17]	High-risk aerosol-generating procedures may put the anaesthetists, anaesthetic assistants and surgeons at risk of nosocomial infections, and this was at the forefront of the multidisciplinary discussion.	Meticulous planning of airway management and surgical tracheostomy in such patients must take into account the safety of the patient and that of all clinicians involved	To our knowledge this is the first reported case of an ATI in a suspected COVID-19–positive patient, therefore, we were unable to follow any previously published guidance specific to this scenario.	[Planning for failure] must happen before the procedure and a clear plan should be made and communicated. The surgical team were scrubbed and ready in the clean room in preparation for an emergency front-of-neck airway if required
McGrath et al [18]		the patient did not tolerate supine positioning for more than around 30 min, which was felt to represent an unacceptable risk Transfer in the prone position is itself not without risk		a dedicated experienced team undertook the transfer having first planned the logistics with radiology colleagues.