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MANAGEMENT & PRACTICE

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VOLUME 16 - ISSUE 2 - SUMMER 2016

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Biomarkers for Acute Kidney Injury

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Presenters

High-Risk Surgical Patients: Oxygen Delivery and Hemodynamic Strategies

Jean-Louis Vincent, MD, PhD
Professor of Intensive Care Medicine (Université Libre de Bruxelles)
Department of Intensive Care, Erasme University Hospital
President, World Federation of Intensive and Critical Care Societies (WFSICCM)

Oxygen Reserve Index (ORI™): Validation and Application of a New Variable

Thomas W.L. Scheeren, MD, PhD
Professor of Anaesthesiology, Head Cardiothoracic Anaesthesia
Department of Anaesthesiology, University Medical Center Groningen
Groningen, The Netherlands

Oxygen Delivery (DO_2): An Oversimplified Concept?

Azriel Perel, MD
Professor of Anesthesiology and Intensive Care
Sheba Medical Center, Tel Aviv University
Tel Aviv, Israel

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Perioperative management of neonatal and paediatric patients

Chair: Prof. Isabelle Constant

Anaesthesia and ventilation strategies in children with asthma
Prof. Britta Regli-von Ungern Sternberg, Australia

Understanding anaesthesia devices in neonatal and paediatric ventilation
Dr. Erik Koomen, The Netherlands

Inhalational induction of paediatric anaesthesia: from natural spontaneous ventilation to target-controlled inhalational induction
Prof. Karine Nouette-Gaulain, France

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SAFETY

Jean-Louis Vincent

Editor-in-Chief
ICU Management & Practice

Professor
Department of Intensive Care
Erasme Hospital / Free University of Brussels
Brussels, Belgium

jlvincent@intensive.org

The publication of the landmark Institute of Medicine report *To Err is Human* shocked with its estimate that as many as 98,000 people die in U.S hospitals each year due to medical errors (Kohn et al. 2000). Has patient safety improved since the report's publication? Perhaps not as much as anticipated. A recent paper estimates that medical error is the 3rd leading cause of death in the United States (Makary and Daniel 2016). However, interpretation of what statistics there are on medical errors and harms should be approached with caution. Harmful events may not be reported, let alone counted.

Safety always comes back to 'culture'. Two reports marking the 15th anniversary of *To Err is Human* note the importance of leadership, at global, government, executive, board, clinical and community level, for promoting a safety culture. The authors of the *Patient Safety* 2030 report include leadership in their suggested patient safety toolbox as well as digital technology, education and training and stronger measurement methods (Yu et al. 2016). The U.S. National Patient Safety Foundation published *Free From Harm* (2015). Their recommendations cover leadership, patient safety oversight, safety metrics related to outcomes, research funding, safety across the care continuum, support for the healthcare workforce, patient and family involvement and safe and optimal use of technology.

Increased awareness, understanding and vigilance by all of us who work in intensive care as well as patients and their families can only help to contribute to a 'safety climate'. Our cover story looks at some important aspects of safety. Andreas Valentin outlines the key points to consider when transporting critically ill patients, starting with asking if the transport will likely result in benefit to the patient. Social media can play an important role in increasing awareness, and we feature an interview with the team behind patientsafe, which runs a Twitter account and a blog. Nancy Moureau and Vineet Chopra summarise the Michigan Appropriateness Guide to Intravenous Catheters (MAGIC), which provides evidence-based guidance on vascular access selection in critical care with the aim of reducing risk and improving safety. While healthcare-associated infections (HAIs) are already on the medical agenda, Frédéric Barbut and colleagues argue that *Clostridium difficile* in particular should be taken more seriously as a threat to patient safety. Last, Marck Haerkens and colleagues explain the concept of Crew Resource Management (CRM) training, which focuses on teamwork, threat and error management, and blame-free discussion of human mistake.

Our Biomarkers series continues with a look at kidney biomarkers. Marlies Ostermann and Kianoush Kashani explain the potential of the new biomarkers and how they may best be used in clinical practice.

In our Matrix section Thomas Hemmerling and Marilu Giacalone provide an overview of the application of mechanical and pharmacological robots to anaesthesia. Yuda Sutherasan and colleagues outline the optimal perioperative respiratory management of morbidly obese patients, recommending multimodal anesthesia and analgesia and protocols for perioperative care in order to reduce pulmonary complications and improve outcomes. The chain of survival concept for out-of-hospital cardiac arrest has been around since the 1980s, but only comparatively recently has the "fifth link" of post-cardiac arrest come to the fore. Takashi Tagami explains how post-resuscitation care was implemented in Aizu, Japan. In the last article in this section, Danielle Bear and Zudin Puthucheary look at potential nutritional strategies and schedules to reduce muscle wasting in the early stages of critical illness.

In our Management section, Vitaly Herasevich and colleagues consider the barriers and potential solutions for the future development of meaningful clinical scores derived from Big Data. Next we look at two more social media tools that are widely used in the ICU community. We hear about vodcasting from Claudio Ronco and Marta Scabardi and talk to Jonathan Downham about podcasting. Last, Fiona Kiernan writes about the role of public opinion and resource allocation in healthcare.

Our interview is with Sharon Einav, Chair of the Intensive Care Medicine Subcommittee of the European Society of Anaesthesiology. She has much to say about the interface of intensive care and anaesthesiology and what the disciplines might learn from each other.

Our Country Focus is Sri Lanka. Chulananda Goonasekera and colleagues, founder members of the Sri Lanka Society of Critical Care and Emergency Medicine, describe the evolution of critical care in their country.

The *ICU Management & Practice* team will be at Euroanaesthesia 2016 in London this month. If you will be attending, make sure to drop by and pick up your copy of the journal.

As always, if you would like to get in touch, please email **editorial@icu-management.org**

Jean-Louis Vincent

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Email: veronique.de.vlaeminck@intensive.org
Dept of Intensive Care,
Erasme University Hospital
Route de Lennik 808, B-1070 Brussels, Belgium
Phone 32 2 555 32 15/36 31, Email: sympicu@intensive.org

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CAREGIVERS OF ICU SURVIVORS AT HIGH RISK OF DEPRESSION

Image credit: UHN

Jill Cameron

A Canadian study has found that caregivers of ICU survivors experience symptoms of depression up to 1 year after their relative is discharged (Cameron et al. 2016). Factors associated with worse mental health symptoms included younger age and less social support and sense of control over life. Older caregivers caring for a spouse, with a higher income and better social support and sense of control had better health outcomes. No patient variables were consistently associated with caregiver outcomes over time.

In an email to *ICU Management & Practice*, lead author Jill Cameron, PhD, Affiliate Scientist at Toronto Rehabilitation Institute-University Health Network (UHN) and Associate Professor, Department of Occupational Science and Occupational Therapy, Graduate Department of Rehabilitation Science, Faculty of Medicine, University of Toronto, explained that the study is one of the first to take a comprehensive look at caregiver outcomes. The research team enrolled 280 caregivers of patients in 10 hospitals across Canada, who received 7 days or more of mechanical ventilation in an ICU.

"We simultaneously examined patient illness severity, aspects of the caregiving situation (e.g. amount of care provided, impact on everyday life of providing care), and aspects of the caregiver (e.g. their social support network, their ability to maintain control over situations). When you consider all factors at the same time, the most important seem to be those related to the caregiving situation and the caregiver. This suggests that even in situations where the illness is fairly mild, and the disability is low, caregivers without adequate supports, or who don't have good control over their situation may experience depression and need help", said Cameron.

Findings

- Caregivers' average age: 53
- Gender: 70% female
- Role: 61% caring for a spouse
- Depression symptoms:
  - 67% at 7 days
  - 43% at 1 year
- Improvement in depression symptoms: 84%

The next phase will focus on developing models of rehabilitation for patient recovery and a programme for caregivers to better prepare. Dr. Cameron said that many interventions have been developed and tested for different caregiving populations. She added: "We may be able to identify those caregivers most in need of support and target them for specific support. This would allow the healthcare system to make the best use of available resources and still meet the needs of those caregivers who need more support." ■

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PERSISTENT CRITICAL ILLNESS - THE 5 PERCENT

A study of over 1 million ICU patients has found that just 5 percent of patients account for 33 percent of ICU bed days. The researchers, led by Theodore Iwashyna, MD, Associate Professor of Internal Medicine at the University of Michigan (U-M) Health System and a member of the VA Center for Clinical Management Research and the U-M Institute for Healthcare Policy and Innovation, have identified these patients as having the condition of persistent critical illness (PerCI) (Iwashyna et al. 2016). The research team based their work on data from patients treated in 182 ICUs across Australia and New Zealand between 2000 and 2014.

Findings

Of the million patients 51,509 were found to have PerCI. PerCI patients spent more than a million days in ICU beds, and more than 2.2 million days in the hospital overall. Nearly one-quarter of the patients with PerCI died in the ICU. Just under half were able to go directly home from the hospital - compared with three-quarters of non-PerCI ICU patients.

The researchers looked at the patients' hospital records to see how well each patient's eventual outcome could be predicted. They found that after about 10 days in the ICU, the usual clinically-based prediction tools lost their power to predict risk of death. Who the patient was before he or she came to the hospital mattered more to their chance of dying. This point signals transition to PerCI, say the researchers.

Dr. Iwashyna confirmed that PerCI is a separate state that patients transition into: "you're there because you're there, stuck in this cascade that we can't get you out of," he said. He added: "The reason why these patients came in to the hospital in the first place doesn't matter nearly as much anymore - what matters is that they've been there, and some aspects of how well their body worked before they came in, such as age. These [patients] are the ones where no matter how hard we try, we can't get them balanced."

Next Steps

Carol Hodgson, PhD, a Monash University ICU physiotherapist and second author, explained that PerCI focuses on different characteristics of patients than other efforts used to describe long-stay patients, such as 'failure-to-wean'. "That label focuses the care team on the particular details of respiratory mechanics," she said. "Our clinical experience and our data suggest instead that the problem may be that PerCI patients may never even reach the point where ICU doctors are able to try to get them off a ventilator - they just keep cascading from new problem to new problem. These patients need particular strategies that may prevent or reduce PerCI within the ICU, and additional

resources to facilitate safe discharge from the ICU and hospital, with only 50% able to be discharged home."

Senior author Professor Rinaldo Bellomo commented that better understanding of PerCI could assist ICU teams in discussing prospects for patients who have been in the ICU a long time. "We need to help the fraction who are inevitably going to die do so with dignity, and at the same time help those who are not fated to die to get better treatment," he said. ■

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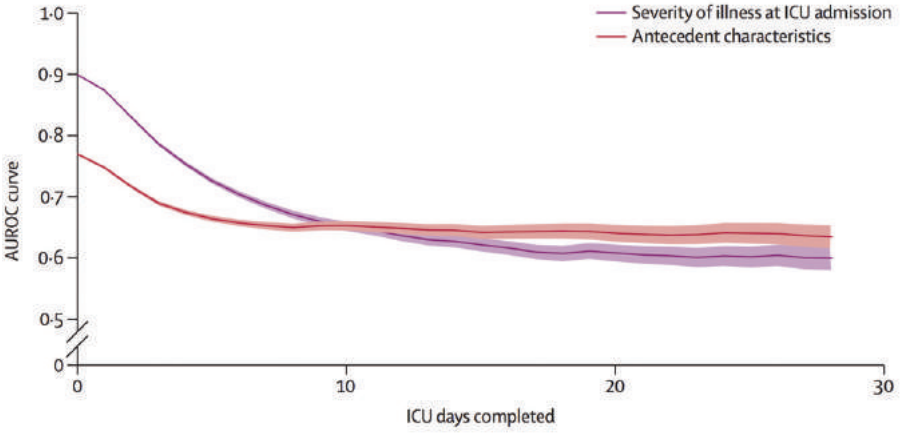

Image credit: University of Michigan and Monash University

Around Day 10 of an ICU stay, patients enter a state called persistent critical illness, or PerCI, where the reason they entered the hospital becomes less important than who they were before they became ill or injured

DEDICATED RESUSCITATION UNIT IMPROVES TRANSFER TIMES

Image credit: University of Maryland Medical System

Lewis Rubinson

A critical care resuscitation unit (CCRU) at the University of Maryland Medical Center (UMMC) has significantly improved transfer times for non-trauma critically ill patients, according to a recent study (Scalea et al. 2016).

In its first full year of operation, for the subset of adult patients admitted for critical care, transfers increased 64.5 percent compared to a previous year (2,228 vs. 1,354), with a 93.6% increase in critically ill surgical patients. Of the 2,228 patients, 1,318 (59.2%) were transferred to the CCRU; the remaining 910 patients were transferred directly to a UMMC ICU. More transfer patients required an operation during their hospital stay (46 percent vs. 31.1 %) and a higher percentage were in the operating room within 12 hours of arriving (41 % vs. 21.4 %). For patients requiring operations, median time to arrival and operating room (118 vs 223 minutes and 1,113 vs 3,424 minutes, respectively) and median hospital length of stay (13 vs 17 days) were reduced significantly. Patients arrived in nearly half the time (129 vs. 234 minutes). The CCRU also significantly decreased the percentage of lost admissions from 25.7 % to 14 % in this subset.

Co-author Lewis Rubinson, MD, PhD, Associate Professor of Medicine at University of Maryland School of Medicine, said in an email to *ICU Management & Practice*: "We believe this is a game changer. We have begun to emulate the trauma system for non-trauma time-sensitive critical care and believe this is a logical and powerful way for academic centres to coordinate all of their time-sensitive transfers rather than having them occur haphazardly."

Dr. Rubinson added: "Direct transfer to ICUs makes sense to reduce another round of handoffs. The dilemma is that availability for admissions must be 24/7. Workflow in ICUs works contrary to admissions when there are many patients to round on—either rounding gets short changed or the admission does not receive all hands on deck. When rounds are over, direct transfers could receive more attention but there is not always bed availability. In addition, most ICUs are not set up to take the referring facilities' information and establish a pre-arrival readiness posture to be able to optimise immediate evaluation, resuscitation and intervention for patients. Lastly, if we directly admitted to each specialty ICU than each would require 24/7 open staffed available beds to be able to meet emergent demand. We have 7 adult specialty ICUs and the amount of resources which would be required to make sure each individually is always ready for an emergent admission would be tremendous. Also, the different ICUs would not have optimal capability to take a patient outside of their specialty. The ability to move patients from receipt and resuscitation allows for an ongoing readiness posture to take the next patient." ■

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Andreas Valentin
Professor
Head of Medical Department
Kardinal Schwarzenberg Hospital
Schwarzach, Austria

andreas.valentin@kh-schwarzach.at

SAFE TRANSPORT OF CRITICALLY ILL PATIENTS

The transport of critically ill patients for diagnostic or therapeutic procedures carries a particular risk and requires therefore a careful risk-benefit assessment. Transport-related risks can be reduced by increased awareness and education, adequate staffing, proper choice and handling of equipment and the use of error-preventive tools like checklists.

Intensive Care Units (ICUs) have been developed to provide a safe environment staffed with highly educated and competent physicians and nurses using the most advanced medical technology and therapies for the critically ill patients. Even if this ideal of an ICU were perfectly realised it would be necessary for many if not most ICU patients to temporarily leave this paradigmatic world. The reason is simply the common need to perform a diagnostic or therapeutic procedure outside the ICU or the need to transfer a patient to another hospital with higher-level or more specialised critical care, or other medical service (e.g. heart surgery). These transports expose critically ill patients to an increased risk for errors and adverse events. ICU teams must aim to reduce this risk and related consequences as much as possible, or in other words to increase patient safety in this particular vulnerable situation.

What is a Safe Transport?

In an abstract perspective a safe transport would be defined by the absence of error with the potential for patient harm and ultimately by the absence of adverse events. In a more pragmatic approach a safe transport could be described by several aims like "patient arrives at least in the same condition as at departure", "no transport-related physiological deterioriation", "absence of critical events", "no equipment failure" and so on. Indeed, the opportunities for transport-related errors and events are numerous. To illustrate a few, a pathophysiological deterioriation might arise from the displacement of lines or drains, the loss of airway in a ventilated patient, a less sophisticated monitoring or treatment during transport (e.g. a more simple mode of ventilation), additional movements (e.g. lifting of a patient) or exposure to altered environmental conditions (temperature, altitude, acceleration), as well as limited diagnostic and therapeutic resources during transport frequently characterised by the lack of senior staff.

Risk Assessment and Safety Status of Transports

Although the number of publications in this field is increasing it remains difficult to come up with representative numbers. The reasons for this difficulty consist of different definitions of error, different types of transport (e.g. intrahospital and interhospital), and very frequently the missing information about the number of opportunities for error and the actual error (numerator and denominator). In a study on 184 mechanically ventilated ICU patients requiring 262 transports for CT, 26% of transports were associated with an adverse event affecting the patient (Parmentier-Decrucq et al. 2013). Interhospital transports carry a particular risk regarding the safe functioning of transport equipment. In a Dutch study involving 353 interhospital transports, 55 technical problems were encountered, ranging from problems with the gas supply and electricity to problems with the medical equipment and the trolleys, as well as with some functions of the ambulance car. Although there was only little impact on patient status, these problems led to delays or even cancellation of patient transports. In any case this study highlights the particular dependence on technical equipment during a period when the relatively safe environment of a hospital is left with a critically ill patient on board (Droogh et al. 2012).

> "the fastest route and means of transport will not always provide the best risk to benefit ratio for a patient"

Patient safety is not only a matter for the transport period; a transport might impact the patient status beyond arrival on or return to the ICU. In a French study it was shown that intrahospital transport increases the risk for complications in ventilated critically ill patients. Patients exposed to a transport had a higher risk for various complications including pneumothorax, atelectasis, ventilator-associated pneumonia, hypoglycaemia, hyperglycaemia, and hypernatraemia (Schwebel et al. 2013). The latter findings illustrate that the interruption of critical care processes like the continuous administration of medication might lead to pathophysiological derangements if no proper and time-sensitive adaption is performed.

An important question concerns the composition of the transport team. While it seems intuitively most likely that a dedicated transport team should be advantageous there are few data supporting this assumption. In a Scottish study on interhospital transfers of acutely ill patients the incidence of unsecured medical equipment and equipment failures in ventilated patients was significantly lower in dedicated transport teams (Fried et al. 2010). Obviously ventilated patients are to be considered as a group with increased risk during any kind of transport and a clear demand for skilled accompanying medical staff. To illustrate this point an example of a patient with decreasing oxygen saturation

might be helpful. The causes for a decreasing oxygen saturation might be trivial like the loss of the signal due to the displacement of the oxygen sensor, but could also be attributed to a life-threatening event like airway obstruction or pneumothorax, as well as technical problems like the breakdown of gas supply or defect hoses and valves, just to mention a few. It goes without saying that the fast and accurate workup and solution of this event will be much more challenging with a patient on the move, either on the street or in the air.

How to Minimise Transport-Associated Risks for Patients?

Assessment of the Patient & Decision for Transport

Considering the risks associated with the transport of critically ill patients the first principle must be "avoid any unnecessary transport" and ask the question "will this transport likely result in findings or procedures that will ultimately benefit this patient?". **Table 1** summarises the questions to be answered before any transport. Most importantly a careful assessment of the patient status must be performed before a final decision is reached to transport the patient (**Fig. 1**).

Setting & Equipment

As elaborated above the choice, maintenance and proper handling of equipment is a crucial factor in preventing critical events during transport. One of the paradigms in safety research is about system design and the risk of an environment and equipment that might rather promote than prevent the occurrence of error. It is therefore of uppermost importance to choose transport equipment that is built with a user-friendly and error-mitigating design. The user-machine interface makes a difference, as has been shown in a study on different types of transport ventilators (Templier et al. 2007). For intrahospital transports the ICU equipment already in use in a particular patient should be used as much as possible for the transport as well. There are many ICU ventilators available that will be applicable during transport, for example. Alternatively some transport ventilators will provide the exact similar ventilator mode as used with a particular ICU ventilator.

The placement of equipment during a transport should allow unhindered access to the patient, while at the same time patient safety must not be compromised by an insecurely stowed monitor, ventilator, perfusion pump etc. In most cases equipment is best mounted at or below the level of the patient, but the display of the monitor, ventilator and other devices must be visible and alarms should be as audible as possible.

At least for gas supply and power supply redundancy must be a principle. Calculations must consider unplanned delays during a transport and other scenarios like a higher demand for oxygen in a deteriorating patient.

Table 1. Questions to be Answered Before Patient Transport

Question	Domain	Responsible
What is the aim of the transport?	Organisation Medical Decision	ICU Physician
Will the results have clinical consequences?	Medical Decision	ICU Physician
Will the expected benefit outweigh the risks?	Risk Assessment	ICU Team
Is the patient stable enough? (see Fig. 1)	Medical Decision	ICU Physician
Is it the right point in time?	Organisation Medical Decision	ICU Team ICU Physician

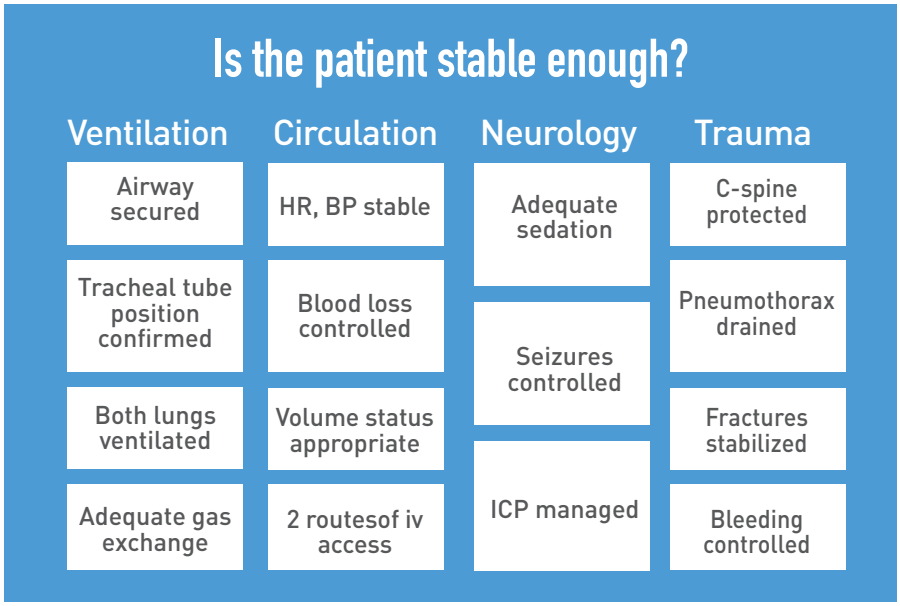

Figure 1.

Staffing

If we agree with the principle that the safety profile of a transport of a critically ill patient should resemble the conditions of an ICU as closely as possible then an intensive care physician or an emergency physician and at least one intensive care trained nurse are required for this transport. Depending on the character of the transport and the number of medical staff additional personnel like porters might be necessary.

Route & Means of Transport

The choice of route and the means of transports depend on several criteria like geographic circumstances and weather conditions (interhospital) or local structures (intrahospital). But first of all the patient's status of urgency and stability is the determining factor. Of note, the fastest route and means of transport will not always provide the best risk to benefit ratio for a patient.

Handover

Information transfer and the loss of significant information during medical processes are a major challenge in healthcare. This is particularly true for critically ill patients undergoing interhospital transports. A comprehensive medical report from the transferring ICU and a report from the transport team are essential tools to ensure continuity of care and avoid loss of relevant clinical information.

Checklists

Many of the issues elaborated above can be in part addressed by the use of checklists. The assessment of a patient before transport and the review of transport equipment are good examples. It has been shown that the use of checklists is associated with a reduction of incidents during the transport of critically ill patients (Bérubé et al. 2013). Other authors have published very useful checklists for the preparation and realisation of transports that can be considered as part of a programme to enhance patient safety (Fanara et al. 2010; Brunsveld-Reinders et al. 2015).

Conflict of Interest

Andreas Valentin confirms that he has no affiliations or involvement in any organisation or entity with any financial interest in the subject matter or materials discussed in this manuscript. ■

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ps

The patientsafe team

@patientsafe3

patientsafe.wordpress.com

PATIENT SAFETY AND SOCIAL MEDIA

Patientsafe represents a group of healthcare staff focused on introducing effective and sustainable healthcare solutions. *ICU Management & Practice* emailed the team to find out more about their Twitter account and blog.

Your Twitter strapline is "Front Line Staff Implementing Effective Safety Solutions" Who's behind patientsafe?

Patientsafe started as a small group of three critical care subspecialty doctors. Our group has gradually grown to incorporate several front-line staff—doctors, nurses, and technicians. We collaborate closely with leaders from several healthcare backgrounds.

We have a particular focus on patient safety from the human factors perspective. We believe this is an untapped and poorly understood field that could be of great benefit in reducing adverse events. We have all witnessed avoidable adverse events and are driven to prevent them recurring.

We would like to note the influence of Dr Terry Fairbanks (human factors) and Dr Ronald Heifetz (adaptive leadership) as having particular impact on our work.

How can social media help to bring patient safety "front of mind" to healthcare staff?

Our posts have two overall themes:

- The human factors approach to patient safety;
- Specific hazards that exist in the workplace.

Social media has enabled us to connect with numerous individuals and groups who share a similar interest. With their feedback they have in turn helped polish our work, which is continually evolving.

Why a blog about patient safety?

We have been bestowed with the knowledge that patient safety could and should be much better. Unfortunately with existing safety frameworks this can feel like a curse.

The continued presence of obvious hazards in the workplace enlightens us to the difficulties in improving patient safety systems.

Can you share any success stories where you have helped make a difference to patient safety?

We have had some success in removing hazards from individual hospitals, particularly Adjustable Pressure Limiting (APL) valves and almost colourless antiseptic solutions. We have exposed the difficulties in removing these from all healthcare workplaces using current safety systems.

We are aware that some hospitals have removed attachments that open to air from their central lines—a hazard that unnecessarily risks air emboli. We have discovered a central line that does not open to air and await Therapeutic Goods Administration (Australia) approval prior to trialling it.

We have developed a Hazard Feedback Framework (**https://iii.hm/32m**), which we believe may be used by any frontline staff member in developing a proposed solution to a safety hazard. Through its use we hope staff will become better educated about the human factors approach to healthcare safety, while helping to remove identified hazards from their workplace.

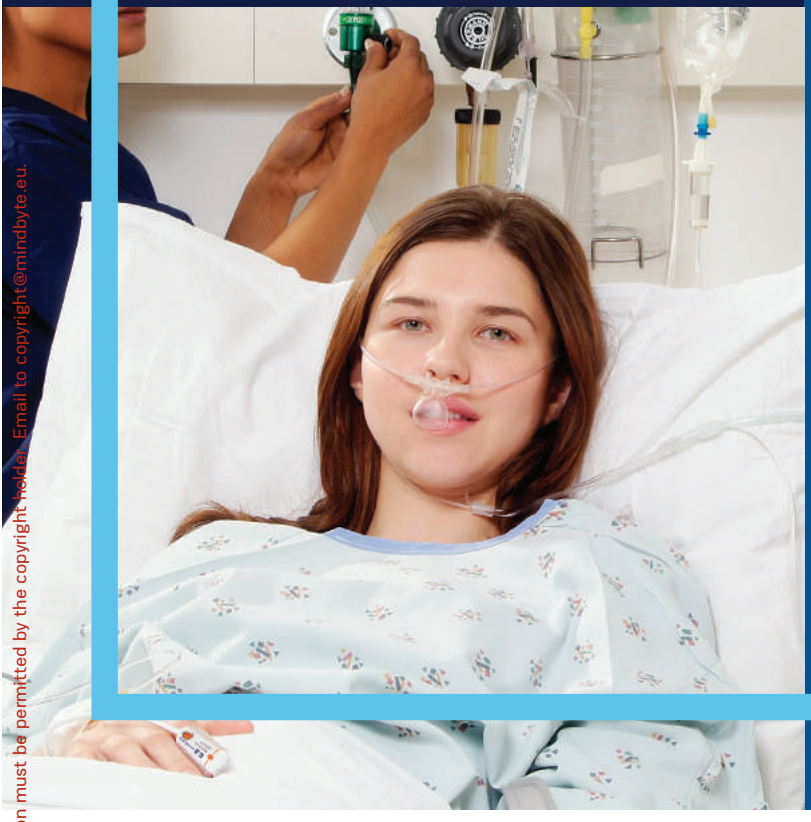
There are several specific safety hazards that we continue to work on, including:

- Ensuring immediate availability to adequate doses of Sugammadex in operating theatres;
- Central line management to reduce air embolus risk;
- Use of laryngoscopes that allow simultaneous video and direct laryngoscopy as first line for intubation.
- Replacement of forced air warmers with active warming blankets where appropriate.

We are always learning. We recognise that all healthcare staff are dedicated to patient safety and providing optimal outcomes. We would like to help in generating an environment which allows this to happen. ■

RESPIRATORY COMPROMISE

Euroanasthesia 2016, London



Monday, 30th May
12:15 – 13:45
Capital Suite 11

Chairman:
David Whitaker, Manchester, UK

Integrated Pulmonary Index after off-pump coronary surgery: is it helpful to assess recovery ?
Prof. Mikhail Kirov, Arkanglesk, Russia

Capnography for Sedation in Clinical Practice
Dr. Amit Prakash, Cambridge, UK

Opioid-induced respiratory depression in the perioperative patient: Risk, Incidence, Monitoring
Prof. Albert Dahan, Amsterdam, The Netherlands

Medtronic
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Nancy Moureau
Chief Executive Officer
PICC Excellence, Inc.

Vascular Access Specialist
Greenville Memorial University Medical Center
Greenville
South Carolina, USA

Adjunct Associate Professor
Alliance for Vascular Access Teaching and Research (AVATAR) Group
Centre for Health Practice Innovation
Menzies Health Institute Queensland
Griffith University
Brisbane, Australia

Nancy@piccexcellence.com

Vineet Chopra
Assistant Professor of Medicine and Research Scientist
University of Michigan Health System and VA Ann Arbor Health System
Ann Arbor
Michigan, USA

MAKING THE MAGIC

Guiding Vascular Access Selection for Intensive Care - a Summary of Michigan Appropriateness Guide for Intravenous Catheters (MAGIC)

Determining appropriateness for vascular access devices limits the risk of complications in critically ill patients. Michigan Appropriateness Guide to Intravenous Catheters (MAGIC) establishes evidence-based indications as summarised in this paper.

Safe and reliable venous access is the foundation for medication administration in critical and intensive care unit (ICU) patients. Several important issues surround vascular access in the ICU setting, including the need for multiple multi-lumen devices for delivery of concomitant drugs and the frequent sampling of blood from catheters. Risk factors associated with catheter-related complications in ICU patients are coma/immobility and the number of catheters present (Villamarín-Bello et al. 2016). The risk of complications associated with central venous catheters is higher in ICUs compared to other departments, with 35% greater prevalence in one prospective study evaluating peripherally inserted central catheters (Leroyer et al. 2013). Balancing the needs of clinically unstable patients with risks associated with numerous vascular devices requires a process for device selection, aseptic insertion, management and removal of devices when no longer necessary.

Central venous access devices commonly used in ICUs pose significant infectious and thrombotic risk to patients (Maki et al. 2006). Potential risk factors identified as contributing to the development of infectious and thrombotic complications are the patient's underlying disease, type of catheter, immobility, sedation and duration of catheter use (Richet et al. 1990). The concern for thrombosis includes lower extremities for immobile patients, but also heightened concern for upper extremity thrombosis from central venous access devices (CVAD) (Kearon et al. 2012; Clemence and Maneval 2014). Central devices inserted in the arm, such as peripherally inserted central catheters (PICCs), have a higher risk of thrombosis, with incidence in the literature ranging from 2-75% (Chopra et al. 2013a; Clemence and Maneval 2014; Fallouh et al. 2015). Increasing use of PICCs in intensive care has similarly led to greater levels of thrombosis in this patient population (Chopra et al. 2013a). The association between thrombosis, infections and central catheters highlights why use of devices such as PICCs should be considered only when indicated (Evans et al. 2010; Chopra et al. 2012a; Chopra et al. 2013a; Chopra et al. 2013b; Malinoski et al. 2013; Moureau 2013a; Marschall et al. 2014).

Guidance for selection with evidence-based indications for PICCs or other chest-inserted central catheters (CICC) has been lacking despite recommendations for hospitals to establish tighter criteria. The Society of Healthcare Epidemiology of America (SHEA) recommends providing clinicians with easy access to an evidence-based list of indications for CVC, prior to placement, to minimise unnecessary central catheters and limit risk of central line-associated bloodstream infections (CLABSI) (Marschall et al. 2014). In an effort to address the issues and potentially reduce vascular access device risk to patients, a multidisciplinary panel of national and international experts was convened to examine criteria for appropriate placement of peripherally inserted central catheters (PICCs) in comparison with other peripheral and central venous devices (Chopra et al. 2015). The *Michigan Appropriateness Guide for Intravenous Catheters (MAGIC): Results from a Multispecialty Panel Using the RAND/UCLA Appropriateness Method* reflects the in-depth evaluation of vascular access devices to provide the evidence needed to guide selection (Chopra, Flanders et al. 2015).

Methods

MAGIC was formulated using the RAND Corporation/University of California Los Angeles (RAND/UCLA) Appropriateness Method (Fitch et al. 2001). Following systematic reviews of the literature and compilation of available evidence, clinical scenarios were created to rate the appropriateness of insertion, maintenance and care of PICCs in comparison with other peripheral and central venous access devices. Using a conceptual framework of categories such as duration of use, type of infusate, patient, device and provider factors, scenarios were developed for ratings. In accordance with the RAND/UCLA method, the purpose of the panel was not to reach consensus, but rather evaluate why disagreement occurred in order to minimise misunderstandings when rating each scenario. A multi-specialty group of experts was selected to review the literature and rate the appropriateness of each of the scenarios for each of the devices including peripherally inserted central catheters (PICCs), ultrasonography-guided peripheral intravenous catheters, midline catheters, and peripheral intravenous catheters, non-tunnelled CVCs, tunnelled CVCs and ports.

Results of MAGIC

A summary of appropriate and inappropriate vascular access applications follows and is condensed in **Table 1 Vascular Access Dashboard**. For more detailed information on the results of MAGIC refer to the complete publication (Chopra et al. 2015).

Table 1. Vascular Access Dashboard

Device	PIV	USGPIV	MIDLINE	PICC	CVC non-tunnelled	Antimicrobial CVC	Tunnelled CVC	PORT
Indications	Immediate intravenous access, general infusions. Treatment with peripherally compatible infusion. Forearm placement more reliable	Difficult access patient (DIVA) with 1 or more attempts Treatment 5 days or less than 14 days (transition to midline). Requires longer peripheral catheter	Difficult access patient (DIVA) less than 14 days. More reliable than USGPIV and may be more appropriate in ICU setting	Central catheter indications for peripherally incompatible infusions/ irritants, vesicants, vasoactive medications. Measure vein size to approximate catheter to vein ratio of less than 45%.	Central catheter indications. Critically ill patients requiring vasopressors, haemodynamic monitoring. Subclavian preferred for lower infection risk.	Antimicrobial catheters reduce incidence of infections and may be most appropriate for ICU patients. Central catheter indications. For high risk patients or those with history of infections.	Central catheter indications. Longer term treatment for Parenteral nutrition, cancer, other	Central catheter indications. Longer term treatment for Parenteral nutrition, cancer, other
Treatment	Peripherally compatible infusions	Peripherally compatible infusions	Peripherally compatible infusions	Peripherally incompatible infusions or based on duration	Peripherally incompatible infusions or based on duration	Peripherally incompatible infusions with history of infection	Peripherally incompatible infusions and based on duration	Peripherally incompatible infusions and based on duration
Duration	Treatment 5 days or less. Clinically indicated removal policy may extend time if required and without complications for less than 6 days	Treatment less than 6 days or up to 14 days. Clinically indicated removal policy may extend time if required and without complications	Treatment exceeding 6 days and less than 14 days. Clinically indicated removal policy may extend time if required and without complications	Treatment with any infusion greater or equal to 15 days up to 30 days. Difficult access patient greater than 6 days. Preference for midline with less than 15 days. Any duration for peripherally incompatible infusions.	Treatment 6-14 days. Any duration for peripherally incompatible infusions. Preferred device for critically ill /unstable patients or if haemodynamic monitoring is needed.	Treatment up to 30 days. May be appropriate for catheter exchanges. Applies to PICC and chest inserted CVC (CICC)	Treatment 15-30 days or longer	Treatment 15-30 days or longer
Contra-indications	Circulatory impairment, or hemiparesis. For chronic renal failure (CKD) patients insertion focused on dorsum of the hand.	Circulatory impairment, or hemiparesis. For chronic renal failure (CKD) patients insertion focused on dorsum of the hand.	Circulatory impairment, or hemiparesis, history of upper extremity deep vein thrombosis. Not appropriate for CKD patients	Greater risk of thrombosis with unstable, hypercoagulable or patients with history of thrombosis.	Coagulopathies and other patient specific contraindications.	Sensitivity to chlorhexidine or other impregnations.	Without availability of trained inserter	Morbid obesity, coagulopathies
RISK LEVEL	0.2-0.5/1000 catheter days	0.2-0.5/1000 catheter days	0.2-0.8/1000 catheter days	2.1/1000 catheter days Higher risk in Intensive Care areas	2-5/1000 catheter days	1.2-1.6/1000 catheter days	1.6/1000 catheter days	0-0.4/1000 catheter days

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Peripherally Inserted Central Catheters (PICCs)

Peripherally inserted central catheters (PICCs) are currently used in all care settings with a reported volume of 2.9 million per year used in the USA market alone (iData Research 2014). Specific indications for PICCs in intensive care areas include administration of vasopressors, delivery of peripherally incompatible infusions, parenteral nutrition, frequent blood sampling of three times a day or more, need for invasive haemodynamic monitoring, or patients who may require infusions greater than 15 days (**Table 1 Vascular Access Dashboard**). Importantly several studies (including a recent randomised trial and a meta-analysis of 64 studies) suggest that the risk of upper-extremity thrombosis is higher for PICCs in critically ill patients (Chopra et al. 2013a). For this reason, non-tunnelled CVCs are rated as appropriate for use in ICU settings over PICCs when such use is proposed to last <14 days. In patients with chronic kidney disease (CKD) (glomerular filtration rate of less than 45 mL/

min, creatinine level greater than 3.0, those on dialysis or with stage 3b CKD or greater) peripheral access with PICCs is considered inappropriate and should be preceded by nephrology consultation (Hoggard et al. 2008; Drew and Weiner 2016). In patients with difficult access and no central infusion indications, MAGIC recommendations list a preference for ultrasound-guided peripheral catheters or midline devices rather than PICCs.

Short Peripheral, Ultrasound-Guided Peripheral and Midline Catheters

Indications for short peripheral catheters include immediate intravenous access for peripherally compatible infusions with treatment duration of 5 days or less. Short peripheral catheters are available in 1-6cm lengths with the longer 4-6cm catheters used with ultrasound-guided deeper catheter insertions. Specialists are often called upon when peripheral catheters fail or when multiple peripheral cannulation attempts are required (Helm et al. 2015). Ultrasound-guided peripheral catheters (USGPIV) are indicated for patients with difficult intravenous access (DIVA), defined as patients having one or more failed cannulation attempts. USGPIV or midlines are beneficial when central access devices are no longer necessary or indicated. Reports demonstrate 92-99% success with USGPIV cannulation when education, supervised insertions and competency assessment are established for inserters (Chinnock et al. 2007; Mills et al. 2007; Bauman et al. 2009; Gregg et al. 2010; White et al. 2010; Witting et al. 2010; Moureau 2013; Deutsch et al. 2014). In one study of 148 USGPIV insertions, 40 CVADs were discontinued and 34 CVADs avoided with placement of peripheral catheters using ultrasound guidance (Gregg et al. 2010).

While ultrasound can be used to place any intravenous catheter, we use the term USGPIVs to refer to the ultrasound needle-guided placement of catheters of greater length (4-6cm), owing to the greater depth needed for access (Keyes et al. 1999). USGPIV are appropriate for difficult access patients requiring treatment for 6 or fewer days or up to 14 days with peripherally compatible infusions. Midline catheters provide even greater catheter length for longer dwell. Midline catheters range from 8-20cm in length with the terminal tip in the basilic, brachial or cephalic veins. Notably midlines should not extend into the axillary vein or enter the chest (Gorski et al. 2016). Indications for midline catheters mirror USGPIV for indications of treatment up to 14 days. Additionally midlines may be a more reliable peripheral catheter for intensive care patients, owing to their longer dwell time and more stable upper arm placement (Anderson 2004; Mills et al. 2007; Garcia 2009; Alexandrou et al. 2011; Morrison 2012; Warrington et al. 2012; Baliad and Peterson 2013; Dawson and Moureau 2013). A policy ensuring that peripheral catheters are removed when clinically indicated rather than on a routine basis is also recommended by MAGIC. (Rickard et al. 2012; Webster et al. 2013; Tuffaha et al. 2014).

> “the risk of upper-extremity thrombosis is higher for PICCs in critically ill patients”

Chest Inserted Central Catheters (CICC)

MAGIC examined the appropriateness of non-tunnelled chest inserted central catheters, tunnelled catheters, as well as subcutaneously implanted ports in comparison with PICCs. Based on treatment, the peripheral compatibility of the infusate, proposed duration of infusion and other factors dictating the need for central administration, the use of non-tunnelled acute care catheters for 6-14 days was considered appropriate. Non-tunnelled catheters are preferred over PICCs when risk factors for thrombosis are present or when there is a history of deep vein thrombosis (Chakravarthy et al. 2005; Evans et al. 2010; Chopra et al. 2013a). Preference was given for non-tunnelled CVADs for patients who were haemodynamically unstable, actively receiving vasopressors or requiring urgent central venous access (Chopra et al. 2015). Tunnelled catheters were indicated when at least 3 months of treatment were needed. Ports were considered appropriate for treatment that required intravenous access for 6 months or more and neutral for treatment of 3-6 months.

Conclusion

Maintaining vascular access is a top priority in the intensive care patient population. The selection of vascular access devices for critically ill patients requires the clinician to consider many factors that impact patient risk and safety. With prolonged immobility and critical illness, the risk of thrombosis and infection must be factored into the equation when selecting a device. Selection criteria established within the MAGIC guide can help determine which device is associated with least risk and meets treatment needs of the patient (Anderson and Spencer 2003; Maki et al. 2006; Crowley et al. 2008; Chopra et al. 2012b; Clemence and Maneval 2014; Chopra et al. 2015). MAGIC provides guidance and measurement criteria through which to assess the appropriateness of PICCs and other vascular access devices for the intensive care patient (Chopra et al. 2015; Woller et al. 2015). Application of MAGIC by clinicians and providers within intensive care areas may assist hospitals in establishing reliable access, improving outcomes, achieving infection prevention goals and reducing burden of thrombosis.

Conflict of Interest

Nancy L. Moureau is the chief executive officer of PICC Excellence, Inc., a speaker and educational consultant with 3M, Access Scientific, Angiodynamics, Arrow/Teleflex, BD Carefusion, Chiesi, Cook, Entrotech, Excelsior, Fresenius Kabi, and Nexus; a research doctoral candidate with the Alliance for Vascular Access Teaching and Research at Griffith University, and clinician at Greenville Memorial University Medical Center. Vineet Chopra declares that he has no conflict of interest. ■

Abbreviations

CICC chest inserted central catheter
CKD chronic kidney disease
CLABSI central line-associated bloodstream infections
CVAD central venous access devices
CVC central venous catheter
DIVA difficult intravenous access
ICU intensive care unit
PICC peripherally inserted central catheters
MAGIC Michigan Appropriateness Guide for Intravenous Catheters
USGPIV ultrasound-guided peripheral catheters

For the full Michigan Appropriateness Guide for Intravenous Catheters see

Chopra V, Flanders SA, Saint S et al. (2015) The Michigan Appropriateness Guide for Intravenous Catheters (MAGIC): Results From a Multispecialty Panel Using the RAND/UCLA Appropriateness Method. Ann Intern Med, 163(6 Suppl): S1-40.

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Reference:
1. Ojito JW et al. J Extra Corpor Technol 2012;44:15-20.

CVOR: cardiovascular operating room

* Assumes eight arterial blood gas (ABG) tests being run in a four-hour operation and travel time to and from the blood analyser outside of the CVOR. Excludes delays due to human factors, or any equipment delays

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Roberto Oggioni
Director

roberto.oggioni@uslcentro.toscana.it

Margherita Labardi
Anaesthetist and Intensivist

Department of Anaesthesia and Intensive Care
S. Giovanni di Dio Hospital
Florence Health Authority
Florence, Italy

TREATING COMPLICATIONS FROM ABDOMINAL SURGERY

CASE REPORT USING NONBRONCHOSCOPIC BAL

Use of the HALYARD* Mini-BAL Sampling Catheter proved invaluable in the case of a patient experiencing complications from abdominal surgery. Dr. Roberto Oggioni has been director of the Department of Anaesthesia and Intensive Care at S. Giovanni di Dio Hospital since 2012, and wrote up the case with colleague Dr. Margherita Labardi for *ICU Management & Practice*.

Case Report from March 2014

Patient FN, aged 74 years, gender ♂

The patient was admitted to the emergency department for abdominal pain of a few days' duration. An abdominal CT scan was performed, showing marked pleural effusion of density similar to water collected from the left middle-basal area, associated with secondary atelectasis.

A lumbar hernia with intestinal loop involvement was observed in the area of the painful periumbilical swelling, associated with an extensive area of increased density of the adjacent subcutaneous adipose tissue. Immediately below this there was a further area of intestinal loop herniation, not associated with documentable CT signs of inflammation. After surgical evaluation, the patient was transferred to the operating theatre (OT) and underwent intestinal resection and intra-abdominal VAC (Vacuum-Assisted Closure® KCI, Houten, The Netherlands) therapy.

After the procedure the patient was transferred to intensive care sedated and intubated for monitoring and treatment. The following samples were taken for culture tests on admission: bronchial aspirate, blood cultures, urine culture, and nasal and rectal swabs. The patient was haemodynamically autonomous, without the need for vasoactives. Empirical antibiotic therapy was started with piperacillin-tazobactam and metronidazole owing to peritonitis.

The patient was kept intubated over the following days in anticipation of abdominal revision surgery.

Six days later he was transferred back to the operating theatre for second-look surgery.

On that date the bronchial lavage (BAL) collected by HALYARD* Mini-BAL Sampling Catheter (Halyard Health, Zaventem, Belgium), a protected, blinded telescoping catheter (cutoff 10^4), was negative.

The second procedure comprised a revision of the previous ileo-ileal anastomosis, appendectomy, and closure of the abdominal wall by a "Posterior component separation" technique; a biological prosthesis was introduced under the rectus muscle bellies.

The patient returned from the OT sedated and intubated, with pressure-controlled ventilation. Monitoring was started of intra-abdominal pressure (IAP).

The patient recovered his gastrointestinal motility on the third day. He was extubated on the fourth day. Noninvasive ventilatory assistance was continued for the next few days. Of note on the eighth postoperative day was a CT scan of the chest and abdomen, which documented abundant left pleural effusion with atelectasis of the adjacent pulmonary parenchyma, associated with slight effusion on the right. In the abdomen non-homogeneity was observed of the subcutaneous tissue below the xyphopubic wound with an oedematous-saturated appearance of the muscle layer in front of the abdominal prosthesis, where air bubbles were visible. No surgical indications were determined.

On the tenth postoperative day there was an episode of high frequency AF concomitantly with a fever spike, electrically cardioverted with sinus rhythm recovery.

On the fifteenth postoperative day the patient developed signs of respiratory failure with the need for orotracheal reintubation, probably related to right middle-basal bronchopneumonia; the empirical antibiotic therapy was then altered to linezolid, meropenem and fluconazole. The bronchopulmonary disorder was confirmed by a CT scan, which also showed suspected dehiscence of the surgical wound.

After reintubation, bronchoaspiration and a new BAL (HALYARD* Mini-BAL Sampling Catheter) were carried out. In the meantime the patient developed signs of severe sepsis due to pneumonia and surgical wound infection. A thoracocentesis performed was negative.

The BAL sample collected by HALYARD* Mini-BAL Sampling Catheter demonstrated the presence of *Klebsiella pneumoniae* while the tracheal aspirate proved to be negative. While awaiting the antibiotic sensitivity test result, antibiotic therapy was altered to tigecycline and meropenem. However, as the bacterium proved to be multisusceptible, de-escalation was then carried out leaving only fluconazole and meropenem.

During the subsequent 48 hours the patient needed a new infusion of vasoactive drugs and muscle relaxation to allow adequate ventilation and oxygenation. The patient also presented with hyperthermia for which he was cooled by physical means. A new bronchial aspirate sample was taken, which proved negative.

Past Medical History

2007
ischaemic heart disease treated by coronary angioplasty (PTCA) and stenting.

2011
intestinal perforation treated surgically with the creation of an ileostomy.

2012
episode of atrial flutter-fibrillation (AF) treated by elective electrical cardioversion.

2013
diagnosis of gastric ulcer.

October 2013
closure of ileostomy and lumbar hernia repair.

February 2014
admission to the medical ward for cardiac decompensation in a patient with known ischaemic heart disease.

March 2014
admission to the medical ward for acute anaemia during gastrointestinal bleeding in a patient with erosive gastropathy.

Receiving therapy at home with: diltiazem, ramipril, transdermal nitrates, clopidogrel, furosemide, potassium canrenoate, simvastatin, allopurinol, benzodiazepines.

On the 23rd postoperative day, the patient underwent percutaneous tracheostomy according to the Fantoni technique.

Over the next few days the signs of septic shock showed an improvement, with a progressive reduction in vasoactive support, and negative procalcitonin.

On the 26th postoperative day, vasoactive support and antibiotic therapy were discontinued, after a negative bronchial aspirate sample response. The patient then had a rectal swab showing KPC *Klebsiella pneumoniae* colonisation.

Unfortunately an episode of haematuria further complicated the postoperative course, and a three-way catheter had to be introduced with continuous bladder irrigation.

One month and ten days after the second operation, the tracheostomy cannula was removed, after a weaning period lasting approximately one week.

After one month and 18 days, the patient was transferred from intensive care to the medical ward; KPC *Klebsiella* colonisation was present in a rectal swab, not treated.

Conclusion

Bronchoalveolar lavage (BAL) using bronchoscopy is an accurate and reproducible method for the evaluation of suspected ventilator-associated pneumonia (VAP). However, bronchoscopy is an invasive technique that needs the continuous availability of a skilled physician. The HALYARD* Mini-BAL Sampling Catheter, a telescoping catheter, permits healthcare staff to carry out a BAL without using bronchoscopy. This device offers several advantages in comparison with invasive techniques: it can be performed directly at the bedside by an ICU nurse in a few minutes; it is protected inside another catheter to avoid bacterial contamination during the injection and aspiration; and it has a turning end to insert into the right or left main bronchus without disconnecting the patient from mechanical ventilation. Moreover what makes it distinctive is its ease of performance coupled with the major sensitivity of BAL (10^{4} cfu) versus tracheal aspirate (>10^{5} cfu). Thus this makes this, in case of a positive result, potentially reliable in the aim to ameliorate the sometimes difficult diagnosis of VAP and to start prompt and adequate targeted antibiotic therapy. This was the main difference in diagnosis and treatment concerning this patient in whom tracheal aspirate was negative.

When you suspect ventilator-associated pneumonia HALYARD* Mini-BAL Sampling Catheter makes more sense than tracheal aspirate, because it is quick, easy to perform, protected and less invasive than bronchoscopy. Although it is relatively costly compared to tracheal aspirate it has to be balanced against nursing time for sterilisation etc., service maintenance and any difficulties.

We have now added HALYARD* Mini-BAL Sampling Catheter in our VAP bundle strategy, as follows:

1. Daily assessment of sedation
2. Endotracheal tube with subglottic aspiration
3. Closed circuit aspiration
4. Oral hygiene with chlorexidine
5. Head of bed-elevated 30-45°

This strategy is carried out in all ICU patients after 72 hrs of mechanical ventilation. ■


HALYARD* Mini-BAL Sampling Catheter

Abbreviations

AF atrial fibrillation
BAL bronchoalveolar lavage
CFU colony forming unit
CT computed tomography
IAP intra-abdominal pressure
OT operating theatre
PTCA percutaneous transluminal coronary angioplasty
VAC vacuum-assisted closure
VAP ventilator-associated pneumonia

CLOSTRIDIUM DIFFICILE

A PUBLIC HEALTH THREAT THAT SHOULD BE ROUTINELY INCLUDED WITHIN CARE QUALITY AND PATIENT SAFETY PROGRAMMES

This paper provides an overview of the evidence confirming that CDI independently increases mortality risk in hospitalised patients, and argues for system-wide implementation of specific actions, including care bundles for management (not only infection control) and mandatory surveillance, to improve the quality of CDI care, and thereby reduce morbidity and mortality, in alignment with European policy initiatives.

Frédéric Barbut*
Head
National Reference Laboratory for *Clostridium difficile*
Clinical Research Group « EPIDIFF »
Faculty of Medicine
Pierre and Marie Curie University
AP-HP Saint-Antoine Hospital
Paris, France

frederic.barbut@sat.aphp.fr

Javier Cobo
Head of Section
Department of Infectious Diseases
University Hospital Ramón y Cajal
Ramón y Cajal Institute of Health Research (IRYCIS)
Madrid, Spain

javier.cobo@salud.madrid.org

Oliver A. Cornely
Professor
Head of Translational Platform and Principal Investigator
Department I of Internal Medicine
Clinical Trials Centre Cologne (ZKS Köln BMBF 01KN1106)
Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases
University of Cologne
Cologne, Germany

oliver.cornely@uk-koeln.de

Ed J. Kuijper
Professor of Experimental Bacteriology
Department of Medical Microbiology
Leiden University Medical Centre
Leiden, the Netherlands

Head
National Reference Centre for *C. difficile*
the Netherlands

Coordinator
European CDI Surveillance Network

E.J.Kuijper@lumc.nl

Nicola Petrosillo
Director of the Clinical and Research Department
National Institute for Infectious Diseases Lazzaro Spallanzani-INMI IRCCS
Rome, Italy

nicola.petrosillo@inmi.it

*corresponding author

Patient safety, defined as the freedom for patients from unnecessary or potential harm associated with healthcare (Council of the European Union 2009), is a central component of healthcare quality. Healthcare-associated infections (HAIs) are a leading threat to patient safety. On average, 6% of patients in European acute care hospitals have at least one HAI (European Centre for Disease Prevention and Control [ECDC] 2013). Annually these infections are estimated to cause 37,000 deaths and to incur costs of over €5.5 billion (Committee on the Environment, Public Health and Food Safety 2013). In 2009 the European Council recommended that Member States implement various measures to improve patient safety and HAI prevention and control in particular (Council of the European Union 2009). The implementation of these measures has been supported by the European Union Network for Patient Safety and Quality of Care Joint Action (pasq.eu). Progress has been made (European Commission 2012; European Commission 2014), and there is a raised level of awareness about patient safety at the political level. Nevertheless, the European Parliament has urged the Commission and Member States to step up their efforts and to place the issue near the top of the political agenda (Committee on the Environment, Public Health and Food Safety 2013), and the European Council has invited the Commission to continue supporting improvements in patient safety and HAIs and the Member States to intensify their efforts in these areas (Council of the European Union 2014). Specific considerations include the setting of national targets, resourcing, education and training of healthcare professionals, the promotion of good practice, information provision to patients, disease surveillance and research support.

Although figures vary between countries, *Clostridium difficile* (*C. difficile*) infection (CDI) accounts for almost 4% of all HAIs in Europe, and *C. difficile* accounts for 5.4% of isolated pathogens, being the eighth most common (ECDC 2013). CDI is increasingly common in many countries and the estimated annual number of 124,000 cases across Europe (ECDC 2013) is likely to be an underestimate owing to under-diagnosis (ECDC 2013; Davies et al. 2014). In the United States, a multistate prevalence survey concluded that *C. difficile* was the most commonly reported pathogen, causing 12% of all HAIs (Magill et al. 2014). The Centers for Disease Control and Prevention (CDC) estimates that 453,000 CDI cases occur annually in the U.S. (Lessa et al. 2015) and categorises CDI in the highest priority category of antimicrobial resistance threats (CDC 2013). In a systematic assessment of antimicrobial resistant threats based on 10 criteria, the public health agency of Canada also defined *C. difficile* as the second most important national priority (Garner et al. 2015). CDI typically adds approximately €4000–14,000 to inpatient costs, mainly as a result of extended hospitalisation (Weigand et al. 2012; Asensio et al. 2015; Heimann et al. 2014).

CDI has been the focus of comprehensive and effective national-level control and surveillance interventions in some countries (e.g. United

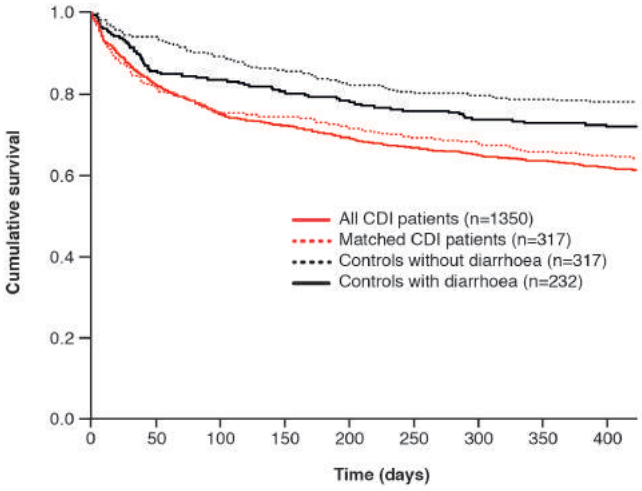
Kingdom), but remains under-recognised as a public health threat in many others. Indeed a discrepancy exists whereby, in many countries, efforts have focussed on multi-drug resistant Gram-negative pathogens and methicillin-resistant *Staphylococcus aureus*, while CDI presents a greater threat to public health (CDC 2013).

CDI and Mortality

Patients who acquire CDI in healthcare facilities are at high risk of death. Rates of all-cause 30-day mortality are estimated at 3–30% among all patients (Weigand et al. 2012; Wenisch et al. 2012; Hensgens et al. 2013; Schmid et al. 2013; Planche et al. 2013), and reach 40% among patients who undergo emergency surgery for fulminant CDI (Bhangu et al. 2012). However, as CDI is most common among patients who are elderly and suffering from severe underlying illnesses (Bauer et al. 2011), specific studies were necessary to confirm its independent contribution to the risk of death.

A European-wide epidemiological study conducted in 2008 found that CDI caused or contributed to death in 9% of 455 infected patients within 3 months of diagnosis. Expressed differently, CDI caused or contributed to 40% of all deaths occurring within 3 months (Bauer et al. 2011). More recently a large prospective cohort study in nine hospitals in the Netherlands showed that even in an endemic situation (i.e. in the absence of outbreaks), CDI independently increased the risk of 30-day mortality by 2.5-fold (95% confidence intervals [CI] 1.4–4.3), as compared with patients without diarrhoea, after adjustment for age, sex and underlying diseases (**Fig. 1**) (Hensgens et al. 2013). Similarly a single-centre, prospective cohort study in Austria found a relative risk for pre-discharge death among patients with CDI of 2.74 (95% CI 1.82–4.10; p<0.0001), as compared with patients without CDI (Wenisch et al. 2012).

In the Netherlands, patients with CDI were more likely to die within 30 days (hazard ratio 1.6; 95% CI 0.9–2.8) than were controls who had diarrhoea but a negative test for *C. difficile* toxins—indicating that CDI, rather than diarrhoea per se, increased the mortality risk (Hensgens et al. 2013). Similarly, a prospective multicentre study of over 6500 CDI episodes in the UK showed that patients whose unformed faecal samples tested positive for the *C. difficile* toxins had a higher 30-day mortality (after multivariate analysis to account for confounding factors) than those who were negative both for *C. difficile* toxins and cultures (odds ratio 1.61; 95% CI 1.12–2.31; p=0.01) (Planche et al. 2013).



	<30 days		<3 months		<6 months		<1 year	
Death, no (%)								
All CDI patients	177 / 1350	13.1%	319 / 1350	23.6%	401 / 1350	29.7%	497 / 1350	36.8%
Matched CDI patients	47 / 317	14.8%	74 / 317	23.3%	85 / 317	26.8%	109 / 317	34.4%
Controls without diarrhoea	17 / 317	5.4%	31 / 317	9.8%	51 / 317	16.1%	68 / 317	21.5%
Controls with diarrhoea	20 / 232	8.6%	38 / 232	16.4%	48 / 232	20.7%	63 / 232	27.2%

Figure 1. Mortality Rate of Patients with *Clostridium difficile* Infection (CDI) and a Matched Cohort.
Reproduced from Hensgens et al. (2013) with permission

Is CDI any worse than other types of infective diarrhoea? Researchers in Austria found that patients with CDI were twice as likely to die while in hospital or within 30 days than patients with other types of infective diarrhoea (caused by norovirus campylobacter, adenovirus, salmonella or rotavirus) after adjustment for age, comorbidities and other infections (Schmid et al. 2013). From a public health perspective, CDI is estimated to cause 70% of all deaths due to gastroenteritis in the United States—ten times more than the next leading gastroenteritis pathogen, norovirus (Hall et al. 2012). According to recent CDC figures, CDI is associated with 29,300 deaths annually in the US (Lessa et al. 2015).

> “care bundles and mandatory surveillance are needed both to control *Clostridium difficile* infection and to reduce mortality”

Mortality from CDI has been affected by changes in the epidemiology of the infection. The worldwide emergence of type 027 as a more virulent type with increased morbidity and mortality has been recognised since 2003 (Kuijper et al. 2006). Since then other highly virulent types have also been observed. These include types 018, 056 and 078 in Europe (Bauer et al. 2011; Walker et al. 2013), the last reportedly associated with higher mortality rates than type 027, and type 244 in Australia (Lim et al. 2014).

Reducing CDI-Related Mortality

CDI can affect patients in all medical specialties. Efforts to reduce its impact on patients and health systems must involve all healthcare professionals, hospital/health institution managers, ancillary staff (including janitors) and patients themselves, not merely microbiologists and infection specialists. Approaches to reducing CDI-related mortality include strategic, health system-wide measures to optimise diagnosis, therapy and infection control according to recommendations (Crobach et al. 2009; Debast et al. 2014; Vonberg et al. 2008; Dubberke et al. 2014).

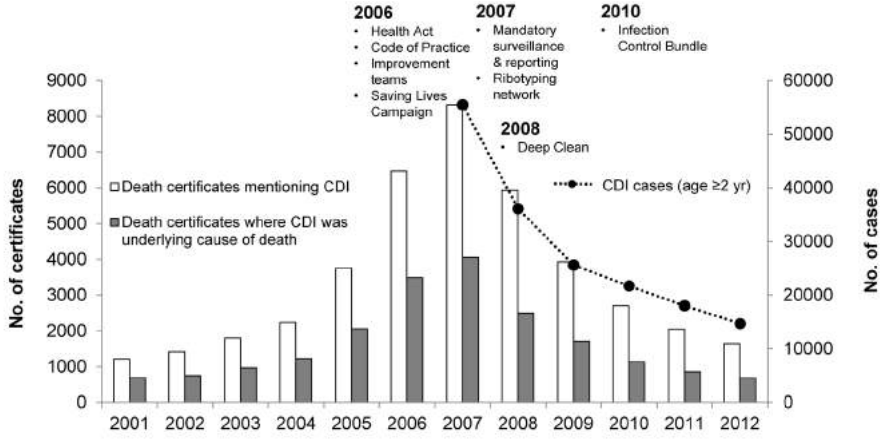


Figure 2. Annual number of death certificates mentioning *Clostridium difficile* infection (CDI), and where CDI was the underlying cause of death, and of toxin-positive CDI cases (based on mandatory surveillance from 2007) in hospitals in England and Wales, 2001–2012. Data from the Office for National Statistics (2013) and Public Health England (2015). Also shown are key elements of the national programme to reduce CDI cases (Department of Health 2010; UK National Audit Office 2009).

Diagnosis

Prompt CDI diagnosis can shorten the time to treatment and reduce empirical therapy, and enables infection control measures to be implemented (Barbut et al. 2014). A delay in CDI therapy owing to a failure of diagnosis may increase the risk of mortality, especially in patients with severe CDI (Berman et al. 2008). *C. difficile* testing policies and practices have improved in recent years, and yet almost a quarter of CDI episodes still go undiagnosed (Davies et al. 2014). Education directed to all healthcare staff regarding the appropriate management of patients with potentially infectious diarrhoea is therefore central to efforts to prevent and control CDI. For example, all staff members need to know that if they have a patient with potentially infectious diarrhoea, they should send a sample for laboratory testing, to include *C. difficile* tests, as soon as possible and manage the patient with appropriate infection control measures, e.g. contact precautions. Educating patients with regard to the possible implications of CDI and the need for them to report diarrhoea while in hospital, is also important.

Therapy

Various experimental treatments for CDI are in development, ranging from new antibiotics to humanised anti-toxin monoclonal antibodies and faecal transplantations (Oldfield et al. 2014). Clinical trials have not been designed or powered to assess the benefit of therapy for CDI on mortality. In any event, regulatory Phase III trials of new agents would not be the best tools to assess 'real-world' mortality benefits owing to the exclusion criteria employed. Retrospective observational evidence suggests that patients with CDI are more likely to die within 30 days if treatment fails to improve symptoms within 10 days (Kim et al. 2013). The use of oral vancomycin rather than metronidazole for severe CDI, as recommended (Debast et al. 2014), provides clinical benefit, although a numerical benefit on mortality did not reach statistical significance (Le et al. 2012). Recently, a large retrospective cohort study in the USA reported that patients with recurrent CDI had a 33% higher risk of death at 180 days compared with patients who had a primary CDI episode but no recurrence (hazard ratio 1.33; 95% CI 1.12–1.58; p=0.001) (Olsen et al. 2015). A prospective UK study also found that patients with recurrent CDI were more likely to die within 1 year from the first episode (9/55; 16.4%) than were patients with non-recurrent infection (1/184; 0.5%; p<0.001) (Taori et al. 2013).

> "almost a quarter of CDI episodes still go undiagnosed"

Data on real-world treatment patterns in Europe are scarce. However, evidence from the United States suggests that treatment and adherence to guidelines are suboptimal, especially in severe, complicated or recurrent CDI (Curtin et al. 2013). Although surgery can be life-saving in severe or complicated CDI (Bhangu et al. 2012), this depends critically on the indication, type and timing and further research is required.

Infection Control and Prevention

Adherence to recommended measures for the control and prevention of CDI (Vonberg et al. 2008; Dubberke et al. 2014) is essential to reduce the burden of infection. While these measures are common to other HAIs, CDI-specific procedures, such as careful handwashing using soap and water (rather than alcohol hand rubs), systematic glove wearing, sporicidal environmental decontamination and antibiotic stewardship, require specific education and resourcing. Importantly, antimicrobial stewardship programmes that reduce the use of high-risk antibiotics may contribute to a reduction in the rate of CDI cases. According to a recent meta-analysis of interventional studies, restrictive antibiotic stewardship policies halved the risk of CDI and had particular effect in elderly care settings (Feazel et al. 2014). Evidence suggests that gastric acid suppressants also increase the risk of CDI and should be considered in prevention strategies (Kwok et al. 2014).

Infection control and prevention bundles can reduce the incidence of CDI and control hospital outbreaks (Muto et al. 2007; Abbett et al. 2009). A bundle is a small set of evidence-based interventions for a defined patient segment/population and care setting that, when implemented together, will result in significantly better outcomes than when implemented individually (Resar et al. 2012). At a national level, a 'high impact intervention' bundle was implemented across the UK to prevent CDI and to control outbreaks caused by the type 027 strain (Department of Health 2010). This bundle (available online) combined elements of prudent antibiotic prescribing, correct hand hygiene, environmental contamination, personal protective equipment (e.g. gloves and aprons), and isolation or cohort nursing. It was introduced in 2010 as part of a national programme of actions (beginning in 2006) that include legislation on infection control in hospitals, hand hygiene campaigns, improvement teams, mandatory surveillance and reporting, diag-

nosis and testing guidelines and a network of ribotyping laboratories (UK National Audit Office 2009). The annual number of CDI cases in England has decreased by approximately 80% since mandatory reporting was introduced in 2007/8, with a corresponding fall in the number of deaths (**Fig. 2**) (Office for National Statistics 2012; Public Health England 2015).

Care Quality Bundle for CDI Management

While bundles exist for CDI prevention and infection control, there is a limited interventional evidence base for a corresponding bundle designed to improve CDI management in order to avoid complications, recurrence and mortality. Nevertheless, an intervention programme was recently reported to have reduced delays in the initiation of CDI therapy and increased adherence to practice guidelines (Jury et al. 2013). This programme comprised physician education on CDI diagnostic testing and treatment recommendations and a CDI order menu (including diagnostic and therapeutic recommendations) implemented in the electronic medical record system. A CDI stewardship team (comprising a nurse practitioner and an infectious-diseases physician, with intermittent assistance from an infectious-diseases fellow and an infectious-diseases pharmacist) was notified by the microbiology laboratory of all positive *C. difficile* test results. This team reviewed electronic medical records and either provided initial treatment recommendations or, if treatment was ordered, provided feedback to physicians if management was not in accordance with guidelines. Finally, medical records were reviewed for a sample of patients prescribed empirical CDI therapy, and feedback was provided to physicians on adherence to the relevant recommendation on empirical therapy. Other workers have described a severity-based treatment policy that increased vancomycin use (according to guidelines) and reduced the rate of refractory disease in patients with severe CDI (Jardin et al. 2013). Such a bundle is not a 'magic bullet', but is part of a proposed approach that offers particular benefit when current practice is poor. Further research is essential to define the elements that should be included in bundles to improve the quality of care for CDI.

Using CDI as a Care Quality Indicator

The implementation and effectiveness of a CDI care bundle should ideally be measured within quality improvement frameworks using both process indicators (e.g. the percentage of patients who commence treatment on the same day as diagnosis and the percentage of patients treated according to current guidelines) and outcome indicators (in-hospital or 30-day mortality and frequency of complications).

CDI is a healthcare facility-wide problem linked to all factors responsible for HAIs in general, including antimicrobial use and overuse, improper or inadequate handwashing, lapses in infection control procedures, poor decontamination of the healthcare environment, a lack of education and training and understaffing. The incidence of healthcare-associated CDI itself is a potentially useful routine marker of care quality and patient safety and yet it is little used in Europe. It has only been used as a national performance measure, and is mandatorily and publicly reported at hospital level, in the UK (since 2004) (Public Health England 2015; Department of

Health 2012). In Ireland, CDI has been an indicator in the national service plan since 2013 (F. Fitzpatrick, personal communication). Public reporting of CDI is also mandatory in Canada where in common with the UK it has been accompanied by a reduction in cases (Daneman et al. 2012). We would argue that mandatory, centralised, national collection and public reporting of hospital-level CDI incidence rates (with the origin or case, i.e. healthcare-associated or community-associated) would benefit CDI control, while acknowledging that such data should be collected using standardised methods and subject to risk adjustment and external audit.

There is a consensus among European infectious disease experts that public reporting of HAI indicators can benefit hospitals (Martin et al. 2013). Whether they directly benefit or influence patients themselves, and how indicators should be chosen and implemented, are more contentious questions. In 2009 the European Council recommended the development of a set of reliable and comparable patient safety indicators to help identify safety problems, evaluate the effectiveness of interventions aimed at improving safety, and facilitate mutual learning between Member States (Council of the European Union 2009). National performance indicators for HAIs in hospitals have since been developed by collaborative European projects (Cookson et al. 2011). However, according to the European Commission, in 2012 data on a limited and variable set of HAI indicators were made publicly available at the hospital level only in Denmark, France, Ireland, Luxembourg, Norway and the UK (European Commission 2012).

Generally, infection control experts are reported to favour structure indicators (e.g. the existence of national programmes, committees, guidelines and resources) and process indicators (e.g. alcohol-based hand-rub consumption) rather than outcome indicators (e.g. HAI incidence rates) (Martin et al. 2013). Concerns regarding outcomes data include the potential for mis-interpretation (due for example to inter-site differences in the patients monitored or the surveillance methods used) and under-reporting. Experts in France have proposed conditions for implementing and reporting performance indicators, namely a broad debate on their benefits and drawbacks, a test period, the avoidance of extra workload for infection control teams and the use of quality and validity control measures (French Society for Hospital Hygiene 2013).

Conclusion

There is now clear evidence that CDI increases the risk of death in hospitalised patients, especially among vulnerable groups such as the elderly and immunocompromised. This substantial and often preventable threat to patient safety warrants specific attention by healthcare policymakers, and this will become important as the population ages. Addressing

> **"the incidence of healthcare-associated CDI is a potentially useful routine marker of care quality and patient safety yet is little used in Europe"**

CDI is not a matter for microbiologists and infection specialists alone, as the infection threatens patients in all medical specialties and sites of care. It requires organisational leadership and commitment, with system-wide prioritisation of prompt and accurate diagnosis, and the implementation and audit of guidelines-led treatment and infection control measures, and continued European, national and local surveillance. Care bundles designed to improve CDI management and avoid complications, recurrence and mortality should be implemented within frameworks for improving quality and patient safety and monitored using appropriate indicators. We would also argue that mandatory centralised national collection and public reporting of hospital-level CDI incidence rates would benefit CDI control.

Conflict of Interest

FB has received fees as speaker and member of advisory boards from Pfizer, Novartis, Astellas Pharma Europe Ltd, MSD, Cepheid, bioMérieux and Summit. JC has received fees as speaker and member of advisory boards from Astellas Pharma Europe Ltd, AstraZeneca, Pfizer and Novartis. OAC is supported by the German Federal Ministry of Research and Education (BMBF grant 01KN1106) and the European Commission, and has received research grants from, is an advisor to, or received lecture honoraria from Actelion, Astellas Pharma Europe Ltd, Cubist, Genzyme, MSD, Optimer, Sanofi Pasteur, Summit, and Viropharma. EJK has received fees as speaker and/or member of advisory boards from Pfizer, Novartis, Astellas Pharma Europe Ltd and MSD. NP has received fees as speaker and member of advisory boards from Pfizer, Novartis, Astellas Pharma Europe Ltd, MSD, Johnson & Johnson and Carefusion.

Authors' Contributions

This paper was born from discussions at meetings of CDI Europe, an expert-led initiative aiming to translate research on CDI into meaningful policy responses to help improve patient outcomes, supported by Medline literature searches using relevant key words. All authors were involved at each stage, from the initial proposal, through review and input into the outline and multiple drafts to final approval.

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Abbreviations

CDI *Clostridium difficile* infection
CDC Centers for Disease Control and Prevention
CI confidence intervals
ECDC European Centre for Disease Prevention and Control
HAI healthcare-associated infection

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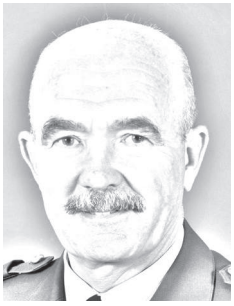

CJ Lorraine
Instructor Pilot, Senior Trainer
Wings of Care
Vught, the Netherlands

chris@wingsofcare.nl

TC Oud
Instructor Pilot, Senior Trainer
Wings of Care
Vught the Netherlands

Transavia Airlines
Schiphol Airport, the Netherlands

tames@wingsofcare.nl

P Pickkers
Professor of Intensive Care Medicine
Department of Intensive Care Medicine
Radboud University Medical Centre
Nijmegen, the Netherlands

JG van der Hoeven
Head of Department
Professor of Intensive Care Medicine
Department of Intensive Care Medicine
Radboud University Medical Centre
Nijmegen, the Netherlands

IMPLEMENTATION CHALLENGES OF CREW RESOURCE MANAGEMENT

Crew Resource Management (CRM) human factors awareness training is a useable tool in medicine and may fill a void in medical education curricula. Factors impacting CRM implementation into the clinical environment are identified.

Human factors (HF) account for the majority of adverse events in high-risk environments, and human factors awareness is therefore essential. Aviation-derived HF awareness training entitled Crew Resource Management (CRM) focuses on teamwork, threat and error management, and blame-free discussion of human mistakes.

In aviation, CRM is a multidisciplinary non-technical skills standard for aircrew. Any CRM-training has to meet U.S. Federal Aviation Authority (FAA) or European Aviation Safety Agency (EASA) regulations. Not only do these regulations define the various subjects and the extent to which each subject should be discussed, but they also set limits for refresher training and trainer requirements. This standardisation is a major contributing factor to the success of CRM. Crew Resource Management training for aircrew consists of 2-day, full-time, interdisciplinary training. The training syllabus consists of well-defined lectures in cognitive psychology and multiple interactive sessions, including case discussions.

Evidence is increasing that CRM HF training is also a promising format for safety climate change in the clinical environment, if well standardised and supported by leadership and effective follow-up (Pratt et al. 2007; McCulloch et al. 2009; Haerkens et al. 2015).

Medical HF training has no international standard yet, and training initiatives may vary in curriculum, duration, intensity, and follow-up support. It is important to realise that it took the professional aviation environment more than ten years to position CRM as an international aircrew operational standard and fully integrate CRM into training curricula.

Our Approach

The aim of our organisation is to generate an evidence-based standard for HF in medical training and operations in the Netherlands. To date we have implemented HF "culture-interventions" in more than 26 high-risk clinical departments in university and training hospitals.

Because the faculty of the clinical departments had no previous formal training in HF prior to this CRM initiative, we introduced a three–phase intervention approach, consisting of preparation, training and implementation.

1. *Preparation Phase*

During this phase the department's safety climate is assessed using the Safety Attitudes Questionnaire (**med.uth.edu/chqs/surveys/safety-attitudes-and-safety-climate-questionnaire**). All healthcare providers are asked to fill out this questionnaire. Process observations are conducted by CRM-trainers on site and video footage of critical communication moments is gathered. During this phase all training participants are informed of the upcoming CRM-training and implementation flow.

2. *Training Phase*

The basis of the training phase is 2 days classroom-based CRM training using lectures, video feedback and interactive exercises.

All training sessions are conducted by two trainers, and allow for a maximum of 15 participants with a mixed background (physicians, nurses, secretaries, etc). All training is held at a training facility at some distance from the hospital to minimise interference, and is delivered within a three-month window to maximise impact.

The training comprises a well-developed standard course, including lectures on HF and principles of CRM and multiple interactive sessions using realistic data such as case studies and video footage from the trained department.

The training emphasises nine key areas:

1. Situational awareness and recognition of adverse situations;
2. Human errors and non-punitive response;
3. Communication and briefing and debriefing techniques;
4. Providing and receiving performance feedback;

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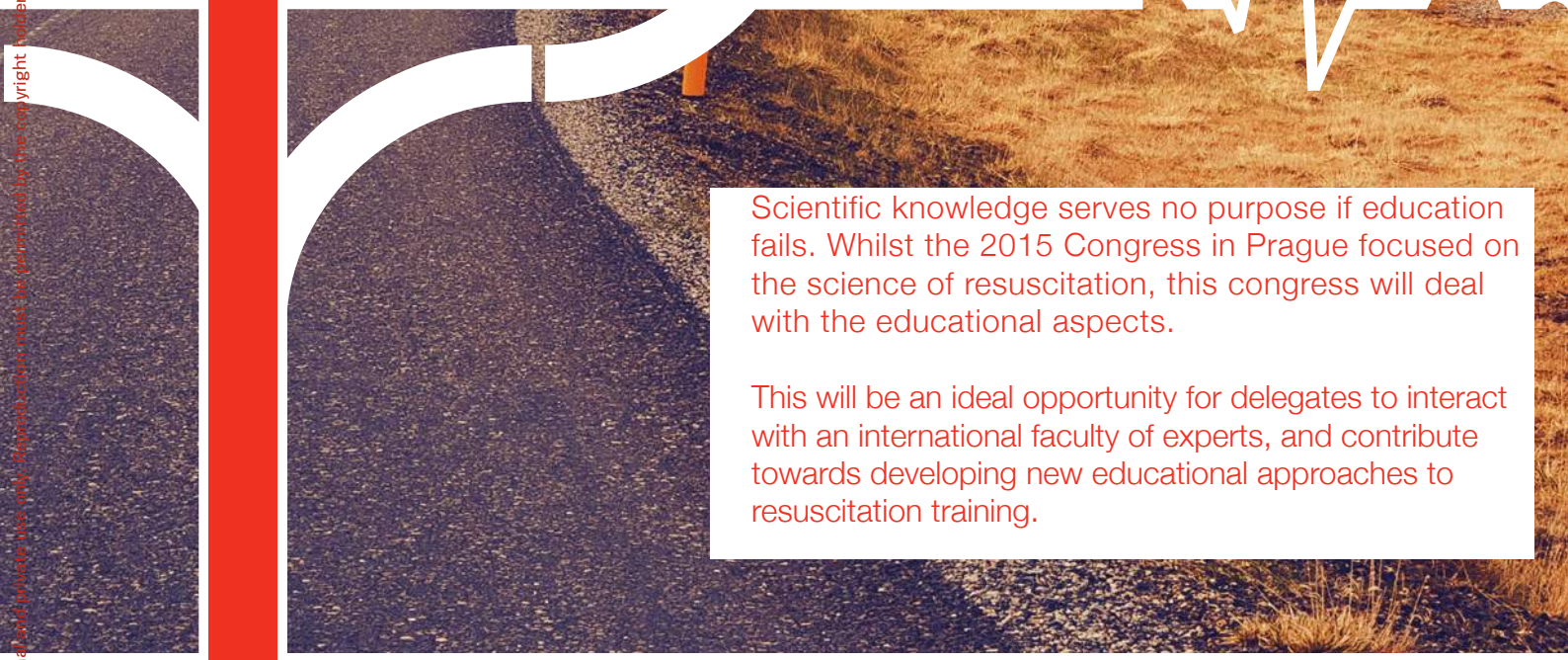

Scientific knowledge serves no purpose if education fails. Whilst the 2015 Congress in Prague focused on the science of resuscitation, this congress will deal with the educational aspects.

This will be an ideal opportunity for delegates to interact with an international faculty of experts, and contribute towards developing new educational approaches to resuscitation training.

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5. Management of stress, workload and fatigue;
6. Creating and maintaining team structure and climate;
7. Leadership;
8. Risk management;
9. Decision-making (Haerkens et al. 2012).

Each training group is challenged to produce a shortlist of practical action points to be used in the following implementation phase, during which the CRM principles should be forged into custom-made and practical clinical tools to be used in daily practice.

3. *Implementation Phase*

To be successful, the intended culture change should be supported by additional implementation measures.

A core group of clinical professionals is formed, and receives additional coaching during the year following the training. This way they will be able to integrate and develop the new way of professional interaction within the department. This group consists of clinical professionals and the patient safety officer from the trained department. They coordinate the efforts to convert the CRM action points into clinical practice, thereby creating joint ownership. Initiatives include:

- Hosting a plenary kick-off meeting for all personnel;
- Development of checklists, multidisciplinary standard operating procedures and briefing guides;
- Regular information bulletins on the department's intranet page;
- A yearly dedicated week of CRM during which extra attention is given to team performance by posters, lectures and internal coaching;
- Making CRM a standard agenda item in two-weekly staff meetings and in the yearly individual evaluations;
- Ensuring all new personnel receive the full CRM initial training.

Furthermore, even though CRM relies on intrinsic motivation to be effective, the department leadership needs to clarify to all staff in advance that CRM will become the professional standard, and that it is not optional but will serve as a yardstick for professional evaluation. This requires leadership by example.

Finally, simulation is encouraged as a follow-up measure. The effect of CRM-based culture change can be reinforced by the use of scenario-based team training, again derived from aviation simulation expertise. Simulation creates a zero-risk environment that allows medical teams to practise high-risk, low-frequency events without endangering patients. This training can be done in an artificial 'laboratory' environment or as in situ training, which is conducted on actual patient care units involving actual healthcare team members and actual organisation processes (Haerkens et al. 2012). Simulation—if well debriefed—has many advantages, but if used as a stand-alone modus without the basis of CRM-training there is a risk of focusing too much on technical skills and single-task performance. This could result in a limited impact on patient safety.

The key to the success of scenario-based team training in healthcare is the identification of the domain-specific team skills required to manage routine and emergency scenarios. We suggest implementing two separate phases of simulation training: the first level of training should mainly focus on technical skills. After having followed classroom-based CRM-training participants may join second level simulation sessions that focus on nontechnical performance.

> "evidence is increasing that Crew Resource Management human factors training is also a promising format for safety climate change in the clinical environment - but a challenging one"

Our Experience

Our experience with CRM implementation in more than 26 high-risk clinical departments in Dutch hospitals is encouraging: the aviation-derived HF training concept was highly appreciated by medical professionals and identified as an important part of professional self-regulation. Overall, the healthcare providers' perceived safety climate usually improved (Haerkens et al. 2015).

Barriers

Important barriers to implementation still remain (Timmon et al. 2015). First, organisational structures and existing department cultures may induce a general reluctance to change ways of working, especially if they are thought to involve additional effort. Second, ever increasing financial and time constraints challenge the funding and time investment crucial for initial and refresher training and implementation efforts. Although one of our projects was awarded the Dutch Health Inspectorate's Patient Safety Award in 2013, to date Dutch national medical societies and health insurers have not yet agreed on funding for a national Human Factors training curriculum for healthcare professionals.

Third, the managerial challenges of integrating CRM into a department's cultural DNA should not be underestimated. Our approach to introduce CRM as an initiative led by clinicians requires a disengaged but supportive stance of the hospitals' management. This probably improves the acceptance by the professionals.

Nonetheless, managerial issues remain at both clinician and manager/administrator level. While clinicians are in general enthusiastic about initiating and leading CRM activities, they often become more ambivalent if it leads them into more formal 'managerial' activity. This deep-seated concern about managerial work may prove to be an obstacle to the development of HF in healthcare. Integrating managers/administrators into the CRM implementation process proved challenging, as expectations toward management's role varied. CRM trainees expected management to facilitate the development of an HF approach by allowing sufficient time and adequate funding, but also realised that implementing changes requires active support from and cooperation with managers, both local and corporate.

The bottom-up nature of our CRM-approach may in some cases have caused (lower) management to adopt a negative "not invented here" attitude and disengage from the implementation process, thus weakening the initiative.

Experience from past CRM / HF integration projects has helped us identify some key success factors as well as threats to success that may be of use to future clinical Crew Resource Management initiatives:

Success Factors

- The initiative is clinically-led.
- CRM training is delivered largely by clinicians with credible HF expertise.
- Confidentiality is maintained throughout the intervention.
- Participation is non-facultative – all staff members including residents and fellows are included.

- Training is conducted in multidisciplinary groups. This increases understanding of each other's problems and limitations whilst making it impossible to apportion blame to groups not represented in the training.
- Management in the hospital takes a supportive but hands-off stance.

Threats to Success

- Poorly managed expectations of the project, resulting in the idea that implementation of CRM/HF training will yield an immediate culture change. Improvement is unlikely to be seen within one year and requires dedication and tenacity from everyone involved (Haerkens et al. 2005; Kemper et al. 2011).
- Lack of a solid implementation plan and unrealistic timelines.
- Delay in initiating timely and noticeable improvements in daily practice.
- Insufficient accountable operational management.
- Disengagement of hospital management.
- CRM training is used as 'window-dressing' without adequate follow-up.

Conclusions

Aviation-based CRM/Human Factors awareness training is a useful tool in medicine. However, adapting the organisational context to fully integrate the Human Factors principles into daily operations remains a challenge. In the future an (inter)national standard for medical CRM training and evaluation is essential, and human factors should become a component of undergraduate curricula.

Conflict of Interest

MHTM Haerkens, a board-certified surgeon and retired Royal Netherlands Air Force pilot, founded the Dutch organisation "Wings of Care" with the goal to implement patient safety measures on a national level. All other authors have no competing interests to declare. ■

Abbreviations

CRM crew resource management
EASA European Aviation Safety Authority
FAA Federal Aviation Authority
HF human factors

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M Ostermann*
Consultant in Nephrology and Critical Care
King's College London
Guy's & St Thomas' Hospital
London, UK

Marlies.Ostermann@gstt.nhs.uk

K Kashani
Assistant Professor of Medicine
Assistant Professor of Medical Education
Mayo Clinic
Rochester, United States

* corresponding author

BIOMARKERS FOR ACUTE KIDNEY INJURY

WHERE ARE WE NOW?

Acute kidney injury (AKI) has been recognised as a major public health problem. It affects >50% of patients in the Intensive Care Unit (ICU) and is associated with serious short- and long-term complications, premature death and high financial healthcare costs (Mehta et al. 2015; Hoste et al. 2015; Lewington et al. 2013). The consensus definition of AKI has emerged from the Risk, Injury, Failure, Loss, End-stage (RIFLE) criteria in 2004 and the AKI Network classification in 2007 to the most recent Kidney Disease Improving Global Outcomes (KDIGO) classification in 2012 (Kidney Disease: Improving Global Outcomes 2012). Although these consensus criteria should be considered a major success towards the standardisation of AKI, they are solely based on serum creatinine and urine output, i.e. two markers which are not kidney-specific and have well-known limitations (Thomas et al. 2015). In particular, serum creatinine can take 24–36 hours to rise after a definite renal insult, may increase following administration of medications that inhibit tubular secretion despite no change in renal function, and is not reliable in patients with sepsis, liver disease, muscle wasting or fluid overload. It also does not provide any information regarding the underlying aetiology. As such, diagnosing AKI can be challenging, especially in critically ill patients. The failure to detect AKI early and the inaccuracy of AKI diagnosis are reasons why the management of AKI is often delayed and attempts to develop specific therapies for AKI have not been successful. There is general agreement that better tools are needed to improve risk assessment, early detection and management of AKI.

Types of Novel AKI Biomarkers

Biomarkers are defined as "characteristics that are objectively measured and evaluated as indicators of normal biologic or pathogenic processes, or pharmacologic responses to a therapeutic intervention" (Biomarkers Definition Working Group 2001). An ideal biomarker for AKI should be accurate, easy to measure at the point of care, correlate with severity of injury, be sensitive to early subclinical renal injury and affordable (Belcher et al. 2011).

In the last 10 years, numerous different substances in serum and urine have been identified and undergone evaluation as potential biomarkers for AKI (Ostermann et al. 2012; Charlton et al. 2014). They vary in their anatomical origin, physiological function, time of release after the onset of renal injury, kinetics and systemic distribution (**Table 1**). Based on their physiological role, they can be divided into markers of glomerular filtration (i.e. serum creatinine, cystatin C), glomerular integrity (i.e. albuminuria and proteinuria), tubular stress [i.e. insulin-like growth factor binding protein 7 (IGFBP-7), tissue inhibitor metalloproteinase 2 (TIMP-2)], tubular damage [i.e. neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), liver fatty acid-binding protein (L-FAB)] and intra-renal inflammation (i.e. interleukin-18) (**Table 1**).

Potential Benefits of Novel AKI Biomarkers

Biomarkers for AKI have been studied in various different patient cohorts, ranging from those with a clearly defined renal insult (i.e. coronary angiography or cardiac surgery) to patients presenting to the emergency department or critically ill patients in ICU where the onset of renal injury is less clear. Most investigations have focused on their ability to detect AKI earlier than serum creatinine. The results are most impressive in paediatric cohorts without comorbidities suffering from an illness with a defined onset of AKI, for instance in children after cardiac surgery. In more heterogeneous populations, where the onset of renal injury is not usually known and comorbid factors exist, the performance is more variable and sometimes equivalent to clinical evaluation and standard laboratory measurements (Vanmassenhove et al. 2013). Some biomarkers have also been shown to correlate better with severity of renal injury and important outcomes like mortality and need for renal replacement therapy than serum creatinine.

> "biomarkers should be regarded as a complement to routine assessment and be part of a decision tree"

An important finding has been the identification of patients with elevated biomarker levels but no detectable change in serum creatinine (Haase et al. 2011). These injury biomarker-positive, creatinine-negative patients appear to have a greater risk of complications, a longer stay in ICU and a higher mortality compared to patients without elevated biomarker level, which implies the existence of a state of 'subclinical AKI' where renal injury has occurred but the glomerular function is still preserved. Whether this phase of AKI represents a golden window

for effective therapeutic interventions will need to be investigated in future studies.

Finally the discovery of new functional and damage markers has broadened our understanding and provided invaluable insight into the pathophysiological processes involved in AKI from early injury to recovery. For instance, validation studies of the stress biomarkers IGFBP-7 and TIMP2 have highlighted the role of cell cycle and cell cycle arrest in the development and progress of AKI (Gomez et al. 2014).

Limitations of Novel Biomarkers

As indicators of normal biologic and pathogenic processes, the release of biomarkers following the original renal insult is dynamic and temporary. Therefore, the timing of measurement is very important and affects the interpretation of biomarker levels in serum or urine. Studies also vary in their chosen cut-offs for negative and positive predictive events related to AKI, which again contributes to the differences seen between reports. Another important limitation of biomarker research relates to the fact that in most studies the performance of novel biomarkers was compared with that of serum creatinine and oliguria, two markers which are not renal-specific and are considered to be inadequate for the diagnosis of AKI. So far, newer imaging techniques or methods to measure real-time glomerular filtration have not been used for the purpose of evaluating new biomarkers.

Use of Novel AKI Biomarkers in Clinical Practice

Some studies have shown very impressive results and clear indications that novel biomarkers have the potential to transform the way clinicians diagnose and manage patients with AKI. Commercial kits for measurement of cystatin C, NGAL, IGFBP7, and TIMP-2 are now available. However, some biomarkers of AKI, though approved for clinical utilisation, have not been extensively employed in the clinical setting. While reasonably good results are seen in the research setting, their performance in routine clinical practice is influenced by patient case mix, comorbidities, aetiology of AKI, the timing of renal insult, timing of biomarker measurement and the selected thresholds for diagnosis. The scarcity of evidence that biomarkers improve patient outcomes, the prohibitive cost and unavailability of point-of-care testing are additional barriers to their widespread routine use.

In the right setting, the new biomarkers have great potential. However, it is crucial to identify those patients who would benefit most. Some studies advertise the use of biomarkers in situations where the outcome already seems predictable based on clinical evaluation and standard physiological parameters (Vanmassenhove et al. 2013). Clearly, in this case, there is limited added benefit. Biomarkers should be regarded as a complement to routine assessment and be part of a decision tree. Indiscriminate application in patients at low risk of AKI would render the biomarker useless, as well as unnecessarily increase healthcare costs.

Future Roles of AKI Biomarkers

The discovery of new markers of glomerular and tubular function, tubular damage and inflammation allows a much better description and characterisation of AKI than traditional markers of renal function can offer. It is therefore very likely that they will be incorporated into future definitions and classifications of AKI, as proposed at the 10th Acute Dialysis Quality Initiative Consensus (ADQI) Conference (Murray et al. 2014) (**Fig. 1**).

As indicators of specific pathophysiological processes within the kidney, some of the new biomarkers also offer the opportunity to be used as diagnostic tools to identify the aetiology of AKI. However, a single biomarker is unlikely to be useful. Instead, a panel of functional and damage biomarkers in combination with traditional markers of renal function and clinical judgement will provide best results.

Table 1. Characteristics of Selected Biomarkers of AKI

AKI biomarker	Biological origin and role	Detection time after renal injury
Cystatin C	13 kDa cysteine protease inhibitor produced by all nucleated human cells and released into plasma at constant rate; freely filtered in glomeruli and completely re-absorbed by proximal tubular cells	12-24 hours post renal injury
Insulin-like growth factor binding protein-7 (IGFBP-7) and tissue metalloproteinase-2 (TIMP-2)	metalloproteinases involved in cell cycle arrest; released into urine following cell cycle arrest of tubular epithelial cells	within 12 hours
Interleukin-18 (IL-18)	18 kDa proinflammatory cytokine released into urine from proximal tubular cells following injury	6-24 hours after renal injury
Kidney Injury Molecule–1 (KIM-1)	transmembrane glycoprotein released into urine by proximal tubular cells after ischaemic or nephrotoxic injury	12-24 hours after renal injury
Liver-type fatty acid-binding protein (L-FABP)	14 kDa intracellular lipid chaperone produced in proximal tubular cells and hepatocytes; freely filtered in glomeruli and reabsorbed in proximal tubular cells; increased urinary excretion after tubular cell damage	1 hour after ischaemic tubular injury
Neutrophil gelatinase-associated lipocalin (NGAL)	At least 3 different sub-types: • monomeric NGAL (25 kDa glycoprotein); produced by neutrophils and epithelial cells of the gastrointestinal tract, bronchi, prostate and kidneys • homodimeric NGAL (45 kDa); produced by neutrophils • heterodimeric NGAL (135 kDa); produced by renal tubular cells	within 2-4 hours

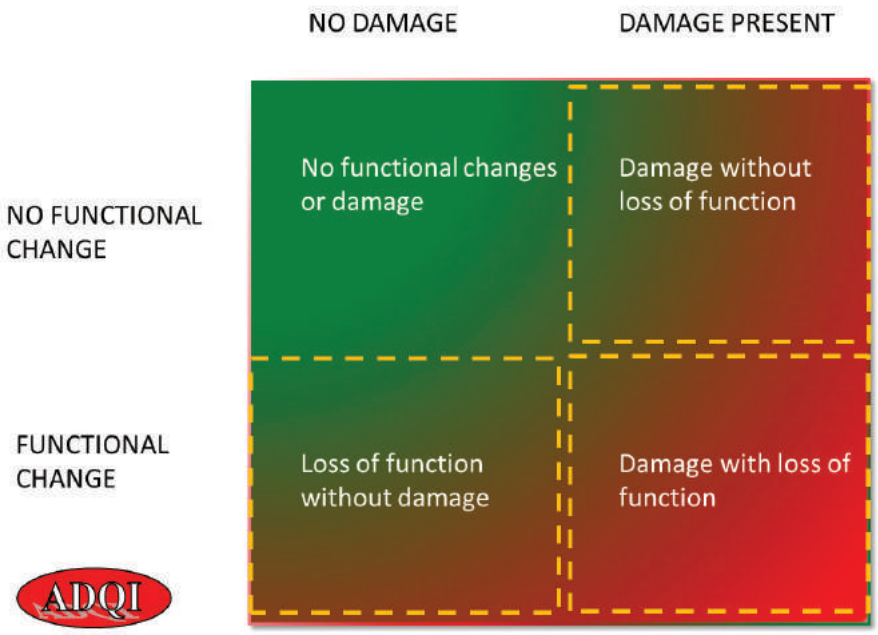

Figure 1. Definition of AKI Based on Functional and Damage Biomarkers

Source: Acute Dialysis Quality Initiative 10 adqi.org, licensed under CC BY 2.0 (creativecommons.org/licenses/by/2.0)

> potential to facilitate the development of new drugs by indicating renal injury earlier than conventional methods

Some of these biomarkers also have the potential to facilitate the development of new drugs by indicating renal injury earlier than conventional methods. Collaborations between international centres and major pharmaceutical companies, the U.S. Food and Drug Administration and the European Medicines Agency have already begun, and rodent urinary and plasma biomarkers have been accepted as surrogates for renal histology for initial evaluation and monitoring of nephrotoxicity in drug development. Finally, there is some hope that some of the novel molecules may not only serve as diagnostic tools but also as potential therapeutic targets for the treatment of AKI.

Conclusion

Numerous novel functional and damage biomarkers for AKI have been discovered and validated. Current evidence supports the concept that they have potential to facilitate the early detection, differential diagnosis and management of AKI in appropriately selected patients. More research including intervention studies based on biomarker results, identification of the most appropriate patient groups and standardisation of testing is necessary to incorporate utilisation of biomarkers into routine clinical practice.

Conflict of Interest

Marlies Ostermann declares that she has no conflict of interest. Kianoush Kashani declares that he has no conflict of interest. ■

Abbreviations

AKI acute kidney injury
IGFBP-7insulin-like growth factor binding protein 7
ICU intensive care unit
KDIGO Kidney Disease Improving Global Outcomes
KIM-1 kidney injury molecule-1
L-FAB liver fatty acid-binding protein
NGAL neutrophil gelatinase-associated lipocalin
RIFLE Risk, Injury, Failure, Loss, End-stage
TIMP2 tissue inhibitor metalloproteinase 2

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EARLY DIAGNOSIS AND PREDICTION OF ACUTE KIDNEY INJURY

PENKID – A DYNAMIC INFLAMMATION-INDEPENDENT BIOMARKER OF KIDNEY (DYS)FUNCTION

Dr. Andreas Bergmann

Founder & CEO of sphingotec GmbH

Hennigsdorf, Germany

bergmann@sphingotec.de

Early recognition and close monitoring of acute kidney injury (AKI) is vital in the ICU, given AKI's high prevalence and effect on length of stay and risk of re-hospitalisation and death (McCullough et al. 2013). As more becomes known about biomarkers, intensivists need to be well-informed about the benefits of currently available kidney biomarkers. While serum creatinine is still the standard method to determine kidney dysfunction, it has major limitations. It increases too slowly to detect worsening of kidney function in a timely manner and it decreases too slowly when kidney function is improving. In addition, it largely depends on other variables (McIlroy et al. 2010; Mårtensson et al. 2010). Most other biomarkers for acute kidney injury are affected by inflammation, and most AKI patients have inflammation, as sepsis and septic shock are the primary cause of AKI (Zarjou and Agarwal 2011). Hence, these biomarkers have failed to reliably predict AKI in ICU patients (Bell et al. 2015).

The sphingotest® penKid immunoassay measures the plasma level of penKid, a stable surrogate marker for the instable Enkephalins (Ernst et al. 2006). Enkephalins are endogenous peptide hormones that are highly expressed in the kidney and regulate renal excretion (Denning et al. 2008; Sezen et al. 1998). penKid is an inflammation-independent functional marker that indicates the actual kidney status by predicting the future change in serum creatinine. The highly dynamic nature of penKid enables close monitoring of the changes in kidney status, thereby supporting early clinical decision-making, e.g. regarding the use of nephrotoxic drugs, initiation of renal replacement therapy or discharge.

Clinical Studies

Inflammation-Independent Plasma Biomarker for Sepsis-Induced AKI

In a retrospective observational study, physicians from the Emergency Department (ED) Sant'Andrea Hospital, University of Rome Sapienza, analysed the blood of 101 patients admitted to the ED with sepsis (Marino et al. 2015). sphingotest® penKid was used to evaluate plasma levels of penKid and the results were compared to concentration levels of neutrophil gelatinase-associated lipocalin (NGAL). The results showed that penKid correlates with the severity of AKI in septic patients, as determined by RIFLE criteria, while sepsis patients without kidney failure display essentially normal penKid levels. NGAL is elevated above normal in patients with systemic inflammation, even without kidney injury.

Diagnosis of Kidney Dysfunction and Prediction of Adverse Cardiac Events

A UK study assessed the prognostic value of penKid levels in acute myocardial infarction (AMI) patients at admission for major adverse cardiac events (MACE) and death during follow-up of 2 years (Ng et al. 2014). N-terminal pro-B-type natriuretic peptide (NT-proBNP) and Global Registry of Acute Coronary Events (GRACE) scores were used as comparators. 1,141 AMI patients admitted to the University Hospitals of Leicester NHS Trust between August 2004 and April 2007 were included in the study. MACE is defined as a composite endpoint of all-cause mortality, heart failure, hospitalisation or recurrent acute myocardial infarction. Using a simple cut-off (99th percentile of normal range) penKid confirmed its significant predictive power for short-term mortality and MACE, as expected for a functional kidney marker. Univariate as well as multivariate models adjusted for ST elevation, age, sex, past history of hypertension, diabetes, IHD, eGFR, Killip class show that penKid predicts short-term (2 years) mortality and MACE stronger than NT-proBNP and Troponin. ■

penKid Key Points

- Plasma marker – in contrast to urine, plasma is easily available on ED/ICU;
- Functional kidney marker – indicates worsening or improvement of kidney function much earlier than mere markers of kidney damage;
- Indicates actual kidney status by predicting the future change in serum creatinine;
- Dynamic nature enables close monitoring;
- Unaffected by systemic inflammation;
- Simple cut-off for unambiguous results;
- Supports very early clinical decisions on nephrotoxic drugs, renal replacement therapy and discharge.

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Thomas M Hemmerling
Associate Professor
Department of Anesthesia
Division of Experimental Surgery
McGill University
Montreal, Canada

thomas.hemmerling@mcgill.ca

newanesthesia.com

Marilu Giacalone
Resident
Department of Anaesthesia
University of Pisa
Pisa, Italy

marilugiacalone@gmail.com

AN INTRODUCTION TO ROBOTS IN ANAESTHESIA

Technological advancement has made robots an integral part of several fields, including medicine. This article provides an overview of the application of robots to anaesthesia, highlighting recent developments. Pharmacological robots are closed-loop systems, able to precisely titrate the dose of anaesthetic drugs to a preset value, concerning hypnosis, analgesia and neuromuscular block. New evidence shows the possibility to feasibly control haemodynamic, respiratory and metabolic parameters. Mechanical robots automatically reproduce manual tasks, showing promising performance. Decision support systems and teleanaesthesia can improve clinical practice. The use of robots in anaesthesia shows the advantage of eliminating the repetitive part of the workload, allowing the anaesthesiologist to focus on patients. Additional studies will be addressed to test safety and refine algorithms of functioning, in order to maintain homeostasis through an automatic integrated control of all biological variables.

Background: the Rationale for Robots in Anaesthesia

The use of robots is part of the technological advancement in several aspects of our lives, from aviation to construction, from industry to medicine. Different definitions of robots have been presented (Hemmerling et al. 2011a). Automation, reproducibility and precision of an action are key elements of robots, which make their use advantageous. Recently this progress has involved the field of anaesthesia. The concepts of robotisation and automation have a potentially great impact on anaesthesia for different reasons. Essentially robots perform measurements, make decisions and perform actions accordingly, which represent what anaesthesiologists continuously do to maintain body homeostasis (Dumont and Ansermino 2013). The activity of anaesthesiologists is displayed in complex environments (operating room, intensive care unit) and requires technical and non-technical skills to be competently implemented (Smith and Greaves 2010). The repetitive implementation of technical and non-technical tasks (e.g., manual tasks, decision-making) during the day, or even in an emergency, may negatively affect the performance of further tasks, due to the accumulation of fatigue and drop in alertness, factors exacerbated by ageing and possible coexisting issues, with a variable safety outcome for patients (Atchabahian and Hemmerling 2014). Robots can eliminate the repetitive part of the workload, the acquisition of patient data, decision-making and manual tasks, and allow anaesthesiologists to efficiently focus on patients and the related perioperative issues (Cannesson and Rinehart 2014). Consequently, the workload is 'smartly' distributed and implemented as if the anaesthesiologist had a technological mental and physical 'extension'. In addition, several physiologic functions can be seen as a combination of automatic feedback circuitries, which can be controlled by robots in such terms. This change would mean the increase in accuracy and safety of the care being delivered, with robots assisting this process without replacing the conduct of anaesthesiologists. For these reasons, two main types of robots have been developed in anaesthesia: pharmacological robots and mechanical (or manual) robots (Hemmerling and Terrasini 2012). A third category is represented by decision support systems: they can be regarded as precursors of robots by helping anaesthesiologists in decision-making through relevant and updated information. This article will present an overview on the application of robotisation in anaesthesia, focusing on the latest advances.

Pharmacological Robots

Pharmacological robots are designed to correctly titrate anaesthetic drugs (Hemmerling and Terrasini 2012) and control biological parameters of anaesthetic concern. Robots exert a control, meaning the regulation of the functioning of a system in drug administration (Dumont and Ansermino 2013), which is performed by a closed-loop modality. Closed-loop or feedback control means that in predetermined time intervals a controller acquires measurements of a variable (controlled), which are compared to a desired target value (set point): if there is a difference, the controller modifies the manipulated variable in order to restore the controlled variable to the set point (Dumont and Ansermino 2013). On the basis of this model, three main elements are recognised: software (the controller), an effector (e.g., drug delivery system, ventilator) and some variables (usually one controlled and one manipulated, deriving from either the patient or the effector). Robots continuously adjust the administration of drugs and maintain a biological target without manual input (Hemmerling and Terrasini 2012). To date the closed-loop control has been applied to the three components of anaesthesia: hypnosis, analgesia and neuromuscular block. Recently, new applications concerning ventilation, haemodynamic

homeostasis, metabolism and temperature have been developed (Dumont and Ansermino 2013). These modern additions may allow anaesthesiologists to have complete feedback control of all aspects of human homeostasis (**Fig. 1**).

Management of General Anaesthesia

The idea of automation in anaesthesia is not new. The first trials date back to the 1950s when volatile anaesthetics were automatically administered using the electroencephalogram (EEG) (Bickford 1950). Schematically the relatively few works which followed were carried out on volatile anaesthetics using the EEG as input variable or on neuromuscular block. Limitations in the availability of means for monitoring, the advancement of systems for controlling (software), as well as the development of intravenous anaesthesia explain the initial slow development of automation. An important step was the introduction of the Bispectral Index (BIS) to objectively measure the depth of anaesthesia. The BIS was initially applied to isoflurane (Gentilini et al. 2001) or propofol general anaesthesia (Absalom and Kenny 2003). The closed loop was used for maintenance only in both cases, controlled by computer software. Other attempts at automation of anaesthesia were made, with more refined systems for control. A closed-loop anaesthesia delivery system (CLADS) has been successfully used for both induction and maintenance of total intravenous anaesthesia (TIVA), by intervening on the hypnotic component only (single loop) (Puri et al. 2007). The target BIS value was set at 50 and measurements were acquired every five seconds; the control algorithm adjusted propofol infusion according to these measurements and the last adjustments of dosing: the overall quantities of propofol were significantly lower in patients followed with CLADS than controls and these patients had a quicker recovery (Puri et al. 2007). This system was shown to function also in difficult environments, such as high altitude (Puri et al. 2012). A new closed-loop system for propofol administration was demonstrated to perform better than manual administration (Hemmerling et al. 2010a). It has an adaptive, rule-based algorithm, meaning that the administration takes into account a set of rules applied to modify the drug dose to achieve the target effect. These rules include different factors, i.e., previous adjustments, BIS trend, BIS artefacts, maximum and minimum allowance of dosing, etc. (Hemmerling et al. 2010a). In another study (Liu et al. 2011) BIS monitoring was applied to the control of the administration of both propofol and remifentanil. Due to the presence of two manipulated variables (dose of two drugs), the system is acknowledged to be dual loop, even if the controlled variable (depth of anaesthesia) is one, based on the assumption that painful operative stimuli cause cortical activation reflected by a reduction of the depth of hypnosis and analgesia and consequent increase of BIS. The control of hypnosis and analgesia was acceptable, with quicker extubation (Liu et al. 2011). This dual loop system was further refined by using the M-Entropy (GE Healthcare, Milwaukee, WI,

Table 1.

Controlled variable	Monitoring	Timing of measurement	Manipulated variable	Functioning	Additional features
Depth of anaesthesia	BIS	Every 5 seconds	Dose of propofol	Change of propofol IR according to BIS values (target value: 50)	Recognition of artefacts and previous adjustments, possibility to stop the infusion or administration of boli according to BIS mean values
Depth of analgesia	AnalgoScore	Every 2 seconds	Dose of remifentanil	Change of remifentanil IR according to MAP and HR (target value: 0)	Administration of a preset minimal dose in case of hypovolaemia (↑HR, ↔MAP) and vagal reactions (↓HR, ↔MAP)
Depth of neuromuscular block	Phonomyography/TOF	Every 15 minutes	Dose of rocuronium	Administration of rocuronium boli according to TOF ratio (target values <25%)	No administration of rocuronium if BIS>60 at induction or ventilation not possible, lockout time between two boli of 5 minutes, no administration 20 minutes before the end of the surgery

Basic principles of the closed loops embedded in McSleepy. The AnalgoScore is calculated on the basis of an increase of MAP and HR due to pain, ranging from -9 (very profound analgesia) to +9 (very superficial analgesia), with an optimal range included between -3 and +3. The use of the system is facilitated by a user-friendly interface and voice commands. The anaesthesiologists can intervene at any moment.
BIS bispectral index IR infusion rate MAP mean arterial pressure HR heart rate TOF train of four.
Symbols: ↑ increase; ↓ decrease; ↔ unchanged; < less than.
Source: Wehbe et al. 2014, with permission of Springer

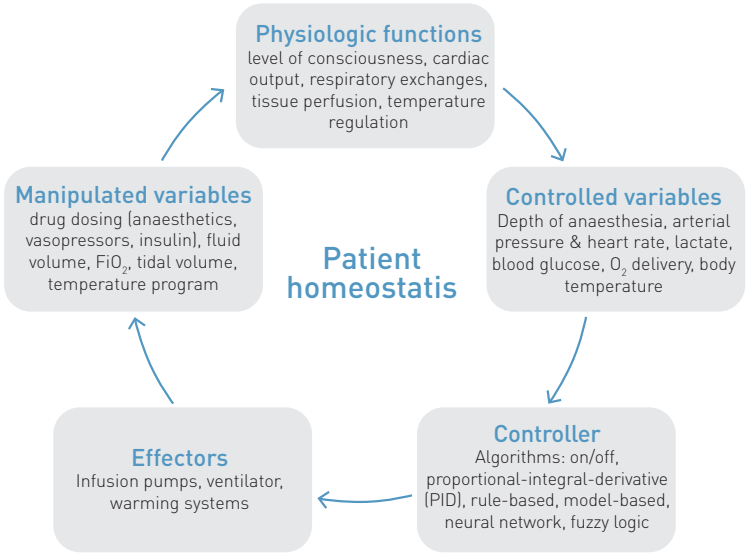

Figure 1. Functioning of closed-loop systems. The components of closed-loop systems are highlighted in bold on top of the boxes, below some examples. Note that the values of the controlled variables are acquired through monitoring, either noninvasive or invasive. To date, studies have mostly been based on noninvasive monitoring; elaboration of data deriving from invasive monitoring needs further study.

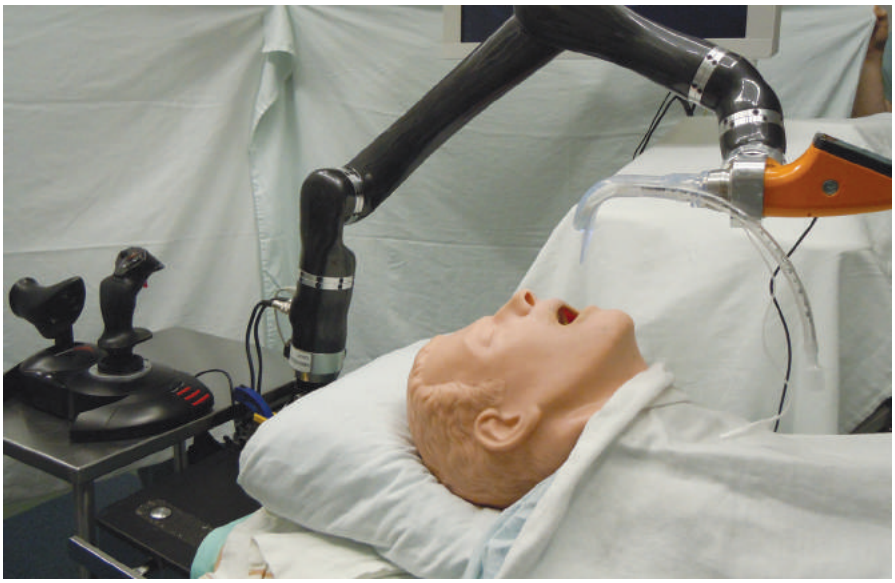

Figure 2. The Kepler Intubation System. The robotic arm is able to move into the 3 spatial plans, imitating the movements of arms and wrists. A camera is placed on it for live video feeding. On the left: the joystick.

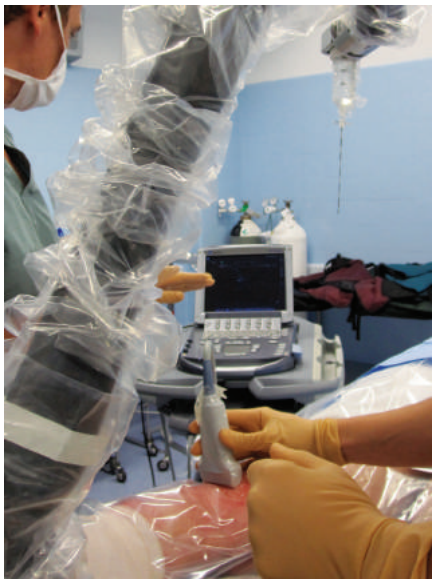

Figure 3. The Magellan System. Patient undergoing sciatic block at the popliteal fossa (posterior approach). The ultrasound images are transmitted to the cockpit (not shown) in real time to guide the robotic arm.

USA) as monitoring: similar to BIS, it is derived from EEG and elaborates two components, state and response entropy, one for hypnosis and one for analgesia, respectively (Liu et al. 2012). The management of general anaesthesia was better than expert manual control (Liu et al. 2012). A new system called McSleepy was introduced as a pharmacological robot able to autonomously control hypnosis, analgesia and neuromuscular block at the same time, in regard to induction, maintenance and emergence (Hemmerling et al. 2010b). Each variable has specific monitoring (BIS, AnalgoScore and train of four [TOF]/phonomyography, respectively) (**Table 1**). Total intravenous anaesthesia was successfully administered to 30 adult patients by McSleepy (Hemmerling et al. 2010b). Significantly more time with excellent control of hypnosis and good control of analgesia was obtained in comparison to the control group. A trial on a larger number of patients (185 overall) confirmed these data, showing a performance better than manual administration (Hemmerling et al. 2013a). McSleepy has some additional and safety features which make it a real robot for anaesthesia (**Table 1**) (Wehbe et al. 2014). The control of anaesthesia provided by McSleepy can be bypassed by the anaesthesiologist when needed (Wehbe et al. 2014). Other research has used monitoring other than BIS (NeuroSENSE Monitor (NeuroWave Systems Inc, Cleveland Heights, OH, USA) to administer propofol for general anaesthesia in closed loop (Dumont et al. 2011). This has been safely and effectively applied to the delivery of general anaesthesia to children, for both induction and maintenance, using appropriate kinetic and dynamic models (West et al. 2013). Recently, systems integrated into the anaesthesia workstation have been introduced to automatically adjust the fresh flow gas and the inspired concentration of inhaled anaesthetics to reach a set value of expired concentration (Singaravelu and Barclay 2013). A new trend is emerging in regard to closed-loop anaesthesia, which is the possibility to simulate the administration of anaesthetic drugs (in silico simulations). Computerised models have been developed to simulate patients and test closed-loop control of intravenous drugs, increasing the safety of the real administration (Fang et al. 2014; Liberman et al. 2013). This is now possible also for volatile anaesthetics, allowing a significant reduction of dosing by applying a low fresh gas flow (Luria et al. 2013). In addition, based on the precision of dosing, the use of closed-loop systems, unlike manual administration, allows performance of fine evaluations of the potency of drugs, for instance the comparison among three commercially available formulations of propofol (Le Guen et al. 2014). Recently the application of closed-loop systems has been extended to other components of the practice of anaesthesia. In a population of preterm infants receiving either invasive or noninvasive respiratory support and supplemental oxygen, the manual control of the inspired fraction of oxygen (FiO_2) was compared to the closed-loop control: with the closed loop, the percentage of time with the target arterial oxygen saturation was significantly higher than that with the manual control, achieving a reduced need for adjustments of FiO_2, even if not significant, and so a reduced repetitive workload (Hallenberger et al. 2014). Despite the current absence of compelling evidence, studies are being carried out to apply closed-loop systems to the control of mechanical ventilation and the performance of spontaneous breathing trials for weaning in adults (Burns et al. 2014). The development of noninvasive and refined means of haemodynamic monitoring as well as the superiority of goal-directed fluid therapy has also led to automation in these fields. A recent in silico study (Rinehart et al. 2012) shows that closed-loop systems for fluid resuscitation are effective in the maintenance of cardiac output, stroke volume and arterial pressure to the targets, detecting the need for fluid adjustments and vasopressors before anaesthesiologists, with fewer variations, and working well regardless of weight, heart contractility and initial volaemic state (Rinehart et al. 2013a). An in vivo study in pigs confirms these results (Rinehart et al. 2013b). For humans, closed-loop control of vasopressors (ephedrine and phenylephrine) was shown to perform better than manual control of hypotension in patients undergoing caesarean section under spinal anaesthesia (Sng et al. 2014). Closed-loop systems are also effective for controlling glycaemic levels in critically ill

simulated patients by adjusting the insulin delivery rate without significant fluctuations (Wang et al. 2014).

Management of Sedation

Sedasys® (Ethicon, Somerville, NJ, USA) is a computer-assisted personalised system intended for mild to moderate propofol sedation in healthy adults, managed by a non-anaesthetist member of staff (Banerjee et al. 2011). This device has been approved in Canada for colonoscopy (Banerjee et al. 2011) and in Australia, the European Union and the United States for colonoscopy and oesophagogastroduodenoscopy (Banerjee et al. 2011; Goudra et al. 2014). The system records patient data (e.g. arterial pressure, saturation, respiratory rate), automatically adjusts propofol rate infusion, oxygen flow and also gives cues to optimise patient responsiveness (Banerjee et al. 2011). Another system is the hybrid closed-loop sedation system (HSS), defined as hybrid since it includes a decision support system and a closed-loop control for propofol administration (Hemmerling et al. 2011b; Zaouter et al. 2016). It was tested in patients undergoing hip or knee arthroplasty under spinal anaesthesia and propofol sedation, monitored by the BIS. In the HSS group, the control of sedation showed more consistency and the control of adverse events (apnoea, hypotension) was more accurate than manual control (Hemmerling et al. 2011b).

Mechanical Robots

This kind of robot is designed to give support or replace manual gestures of anaesthesiologists. The two main fields of application are endotracheal intubation and regional anaesthesia. In regard to intubation, a first trial involved the use of the da Vinci® Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA, USA) in the performance of two simulated fibreoptic intubations, which were both successful even if technically difficult due to the robot design with multiple robotic arms (Tighe et al. 2010). The Kepler Intubation System (KIS) (Hemmerling et al. 2012a) is composed of one robotic arm linked to a standard videolaryngoscope at one end, and remotely controlled by a joystick controlled in turn by a specific software and interface (**Fig. 2**). Intubations can be performed automatically or semiautomatically, under direct vision or remotely: procedural time ranged overall from 40 to 60 seconds in 90 simulated intubations, which were successful at the first attempt (Hemmerling et al. 2012a). In a trial in 12 patients, the KIS showed a success rate of 91% with a mean procedural time of 93 seconds, without complications (Hemmerling et al. 2012b). In regard to regional anaesthesia, an attempt at ultrasound-guided nerve block and placement of a perineural catheter was carried out on a phantom using the DaVinci System, with the same constraints mentioned for intubations (Tighe et al. 2010). The Magellan system (Oceanic Medical Products, Inc., Atchison, KS, USA), has been developed to perform robot-assisted, ultrasound-guided nerve blocks by the use of a robotic arm, with a nerve block needle at the end, guided by a joystick and controlled by a specific software and interface (**Fig. 3**) (Tighe et al. 2013). A success rate of 100% was achieved on a standard ultrasound phantom (Tighe et al. 2013) and subsequently in 13 patients undergoing popliteal block with a maximum procedural time of 4 minutes (Hemmerling et al. 2013b). This system could be integrated with software which allows for the automatic recognition of the nerve on the ultrasound image, without human search (Wehbe et al. 2012). It is still under development after the first promising results (Wehbe et al. 2012). In addition, it has been recently shown that the use of robots for ultrasound-guided nerve blocks is associated with faster learning and a lower inter-subject variability than manual performance in a simulated setting (Morse et al. 2014).

> **"the workload is 'smartly' distributed and implemented as if the anaesthesiologist had a technological mental and physical 'extension'"**

Other Applications

Good clinical practice can be enhanced by the use of decision support systems (DSS) and telemedicine. Decision support systems are designed to provide the performer with updated clinical suggestions and options for treatment. They are precursors of robots, able to detect adverse events and enhance compliance with guidelines. It has been shown that DSS are effective in facilitating the achievement of haemodynamic (Sondergaard et al. 2012) and ventilation (Blum et al. 2013) set points, with a performance at least the same as the one of the anaesthesiologist. DSS improve the detection and the management of intraoperative hyper- and hypotension (Nair et al. 2014), critical events (respiratory and haemodynamic) during sedation (Zaouter et al. 2014) and epidural haematoma in patients under anticoagulant or antiplatelet therapy (Gupta 2014). Telemedicine is a form of delivery of healthcare using information and communication technologies when distance between the providers is significant (Chatrath et al. 2010). Many applications in anaesthesia are currently under development, ranging from pre- and intra- to post-operative applications, with promising results (Chatrath et al. 2010; Galvez et al. 2011). This is highly advantageous for some rural areas of the world where there may be a paucity of physicians and healthcare facilities (Chatrath et al. 2010), as well as an additional opportunity for training and learning (Galvez et al. 2011). The remote control of general anaesthesia has been successfully performed between two different countries (Canada and Italy) by using robots (McSleepy) (Hemmerling et al. 2013c). This pilot study in 20 patients undergoing thyroid surgery in Italy showed the feasibility of teleanaesthesia, with no additional risk of complications (Hemmerling et al. 2013c). Remote preoperative airway assessment between the same two countries has been demonstrated to be feasible as well (unpublished data).

Conclusions

Robots in anaesthesia are designed to eliminate the repetitive part of the workload. The objective is to safely and effectively deliver anaesthesia and have control of all biological variables involved in homeostasis, which is at the base of a good patient outcome. Robots can be helpful to exert this control continuously and simultaneously, with anaesthesiologists having the possibility to 'open the loop' when needed. The automatic management of general anaesthesia, sedation and manual tasks is not inferior to the conduct of anaesthesiologists, but can be even better. Decision support systems and teleanaesthesia can significantly improve the quality of care and the opportunity for training. Additional studies are needed to further test the safety of robots and to develop more refined systems of control and monitoring in order to integrate all components of the management of anaesthesia, augmenting their reliability and overcoming the possible limitations related to their use. ■

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PERIOPERATIVE RESPIRATORY MANAGEMENT OF MORBIDLY OBESE PATIENTS

Yuda Sutherasan
Physician
IRCCS AOU San Martino-IST
Department of Surgical Sciences
and Integrated Diagnostics
University of Genoa
Genoa, Italy

Division of Pulmonary and Critical
Care Medicine
Department of Medicine
Ramathibodi Hospital
Mahidol University
Bangkok, Thailand

sutherasan_yuda@yahoo.com

Lorenzo Ball
Physician
IRCCS AOU San Martino-IST
Department of Surgical Sciences
and Integrated Diagnostics
University of Genoa
Genoa, Italy

lorenzo.ball@edu.unige.it

Paolo Pelosi
Professor
IRCCS AOU San Martino-IST
Department of Surgical Sciences
and Integrated Diagnostics
University of Genoa
Genoa, Italy

ICU Management & Practice
Editorial Board Member

ppelosi@hotmail.com

Obese patients without other major co-morbidities are categorised as class II according to the American Society of Anesthesiologists (ASA) physical status classification (**https://iii.hm/38j**). If additional organ dysfunction is present they are categorised as ASA III. These patients are at increased risk for metabolic, cardiovascular and pulmonary complications. Postoperative pulmonary complications (PPCs), including atelectasis, respiratory failure and pneumonia are not uncommon conditions, and can develop in as much as 40% of high risk patients. Obesity affects the respiratory mechanics, causing a restrictive pattern due to adiposity, compromising both chest wall and lung compliance. The lung volume is decreased in obese patients, predominantly due to a reduction of functional residual capacity (FRC) (Bluth et al. 2016).

Co-Morbidities Related to Obesity

Regardless of the direct mechanical effect of obesity, the co-morbidities of obesity, i.e. obstructive sleep apnoea (OSA), obesity hypoventilation syndrome (OHS), pulmonary hypertension and difficult-to-control asthma may further cause deterioration of lung function (Bluth et al. 2016; Fernandez-Bustamante et al. 2015). These patients need to be carefully screened at the preoperative anaesthesiology visit. Peripheral oxygen saturation (SpO_2) should be always measured, while forced vital capacity and cardiopulmonary exercise testing should be performed in selected patients in order to identify high-risk subjects.

The prevalence of OSA is high in obese patients, and has been reported to be above 70% in patients scheduled for bariatric surgery (Fritscher et al. 2007). In obese patients, sleep apnoea is caused by upper airway collapsibility, and results in intermittent hypoxia and fragmented sleep (Chung et al. 2016). During the perioperative period, sedation and anaesthetic agents, especially neuromuscular blocking agents, opiates and benzodiazepines, facilitate the upper airway collapse and impair ventilatory status or arousal response. OSA increases the risk of postoperative hypoxaemia, ICU admission and increases hospital length of stay. The most relevant episodes of hypoxaemia are usually observed during the rapid eye movement (REM) sleep phase, due to unstable airway and muscle hypotonia; therefore this phase is a period at particularly high risk during the postoperative phase. As a result of the stress and inflammatory response, REM sleep episodes significantly reduce during postoperative nights 1 or 2. On the other hand, the REM sleep rebound occurs during recovery nights 3 to 5 (Vasu et al. 2012). The gold standard for the diagnosis of OSA is polysomnography, an expensive and time-consuming exam: it is not done routinely and this fact may lead to a high incidence of undiagnosed OSA in surgical patients. The STOP-BANG score assesses several parameters including snoring, tiredness, observed blood pressure, body mass index, age, neck circumference and gender and is a sensitive tool for predicting the diagnosis of moderate to severe OSA (Bluth et al. 2016). Not only OSA but also obesity hypoventilation syndrome (OHS) is associated with higher incidence of postoperative pulmonary complications. OHS is characterised by daytime hypercapnia in obese patients, and may be concomitant with chronic obstructive airway disease.

Obesity is a risk factor for asthma, is associated with the severity of the disease and often has a poor response to glucocorticoids. Chest wall fat accumulation leads to a reduction of lung volume, distal airway collapse with increase of closing capacity and reduced functional residual capacity. The incidence of perioperative bronchospasm is high, and should be taken into account.

Perioperative Management in Obese Patients

Airway management in obese patients can be challenging. Several studies have identified independent risk factors associated with difficult mask ventilation in obesity, including male gender, higher neck circumference, limited mandible protrusion, Mallampati score III or IV, OSA and reduced mobility of the cervical spine (Leoni et al. 2014). As a result of the decrease in FRC and expiratory reserve volume, the simple fact of placing the patient in supine position may

cause a rapid deoxygenation. Pre-oxygenation should be ideally performed in the head-up (reverse Trendelenburg), ramped or sitting position in order to limit the decrease in FRC and improve laryngoscopic view (Hodgson et al. 2015). A tight-fitting face mask is essential to ensure optimal pre-oxygenation.

The anaesthetic drugs should be titrated according to clinical effects. Dosing of several drugs should be based on lean body weight. The use of lipophilic drugs characterised by a rapid redistribution to adipose tissue compartments may lower the overall risk for accidental awareness (Bluth et al. 2016).

Perioperative Protective Ventilation

In obesity the airway pressure measured by the ventilator does not reflect the real stress and strain of lung tissue. In fact the decrease of compliance in obese patients with healthy lungs results from an increase in the chest wall elastance. An increase of BMI has a negative correlation with lung volume and lung compliance during general anaesthesia. These patients trend to have an increased incidence of intraoperative and postoperative atelectasis. Moreover an increase in intra-abdominal pressure causes an increase of chest wall elastance. Severely obese patients under mechanical ventilation are more likely to develop ventilator-induced lung injury and acute respiratory distress syndrome (ARDS) than non-obese patients. Obesity is undoubtedly a risk factor for receiving improperly high tidal volumes that should rather be titrated according to the predicted body weight (Fernandez-Bustamante et al. 2015; Serpa Neto et al. 2014). A recent meta-analysis demonstrated that a low tidal volume ventilation with 6-8 ml/kg predicted body weight with low to moderate levels of positive end-expiratory pressure (PEEP), with or without recruitment manoeuvres, can prevent postoperative pulmonary complications in non-obese patients undergoing surgery (Serpa Neto et al. 2015).

> **"multimodal anaesthesia and analgesia and protocols for perioperative care should be implemented in order to reduce pulmonary complications and improve outcome"**

The application of PEEP causes stabilisation of the alveoli, maintaining the patency of respiratory units and counteracting the airflow limitation and auto-PEEP (Fernandez-Bustamante et al. 2015). In morbidly obese patients with OSA undergoing bariatric surgery, the use of continuous positive airway pressure (CPAP) before the induction of anaesthesia, intraoperative PEEP plus recruitment manoeuvres and postoperative CPAP for at least 8 hours showed an improvement of respiratory function compared to conventional ventilation (Neligan et al. 2009). A combination of pre-oxygenation with noninvasive positive pressure ventilation (NIPPV) and recruitment manoeuvres after intubation showed an improvement of oxygenation and end-expiratory lung volume during anaesthesia compared with either oxygen or NIPPV alone in morbidly obese patients (Futier et al. 2011).

In obese patients with BMI above than 30 kg/m^2, a meta-analysis showed that an intraoperative ventilation strategy with recruitment manoeuvres with PEEP improved intraoperative oxygenation and compliance compared with PEEP alone (Aldenkortt et al. 2012). In patients without obesity, The Protective Ventilation using High versus Low positive end-expiratory pressure (PROVHILO) trial has investigated the effect of the open lung strategy with high PEEP and recruitment manoeuvres in short-term mechanical ventilation against PPCs. The authors demonstrated that high level of PEEP and recruitment manoeuvre does not

Table 1. Recommendations for Perioperative Respiratory Management in Obese Patients

Preoperative risk assessment

- Identify and treat early the pulmonary co-morbidities (asthma, OSA, OHS)
- Measure SpO_2 at baseline and spirometry
- Identify the risk of difficult airway management
- Prepare the equipment for management of difficult airway

Induction

- Head-up (reverse Trendelenburg), ramped or sitting position
- Consider CPAP/NIPPV pre-oxygenation
- Multimodal analgesic approach
- Limit the use of opiates, benzodiazepines and neuromuscular blockers if possible

Intraoperative period

- Tidal volume 6-8 ml/kg PBW, moderate levels of PEEP and consider recruitment manoeuvres
- Titrate respiratory rate to keep normal pH and normocapnia
- Minimise FiO_2 keeping SpO_2 more than 92%

Postoperative

- Monitoring driving pressure, chest wall elastance, transpulmonary pressure guided by the application of oesophageal catheter and intraabdominal pressure
- Head-up sitting position
- Respiratory physiotherapy including coughing, deep breathing and early mobilisation
- CPAP or NIPPV can be considered to relieve dyspnoea, or to prevent and treat acute respiratory failure

CPAP continuous positive airway pressure NIPPV noninvasive positive pressure ventilation OHS obesity hypoventilation syndrome OSA obstructive sleep apnoea PBW predicted body weight PEEP positive end-expiratory pressure SpO_2 oxygen saturation

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reduce PPCs (Hemmes et al. 2014). *Protective Ventilation with Higher versus Lower PEEP during General Anesthesia for Surgery in Obese Patients* (PROBESE), NCT02358512, is an ongoing randomised trial aimed at investigating the effect of higher PEEP levels and recruitment maneuvres compared with low PEEP levels on PPCs in patients at intermediate-to-high risk for PPCs (clinicaltrials.gov/ct2/show/NCT02148692). Pressure control ventilation (PCV) is often preferred to volume control ventilation (VCV), although clear benefits have not been demonstrated. Further studies are warranted to investigate the role of ventilator modes, namely PCV, VCV and other ventilator modes, including pressure-controlled ventilation volume-guaranteed in perioperative obese patients in terms of avoidance of either barotrauma or volutrauma (Dion et al. 2014). The high driving pressure during the intraoperative period and an increase in the level of PEEP that caused an increase in driving pressure are associated with more PPCs. The monitoring of driving pressure and the transpulmonary pressure with the application of an oesophageal balloon should be considered to titrate PEEP and adjust ventilator setting (Pelosi et al. 1998; Pelosi et al. 1999; Pelosi and Vargas 2012; Neto et al. 2016).

The intraoperative use of high inspiratory oxygen fraction might decrease the surgical site infection rate, but it might be associated with resorption atelectasis formation, potentially leading to PPCs. However, a recent randomised controlled trial failed to show differences in infection rates and PPCs between patients ventilated with 80% or 30% oxygen during and for 2 hours after surgery (Staehr et al. 2011).

Postoperative Period

The application of CPAP immediately after surgery can maintain lung function in patients after laparoscopic bariatric surgery (Neligan et al. 2009). Perioperative CPAP application is recommended in patients at risk for OSA (Chung et al. 2016). Respiratory physiotherapy, rehabilitation including coughing, deep breathing and early mobilisation should be initiated to reduce the incidence of PPCs. Practical recommendations for perioperative respiratory management in obese patients are summarised in **Table 1** (see p.102).

> **multidisciplinary teams must cooperate to achieve optimal management**

Summary

Obese patients present specific physiologic abnormalities challenging physicians during the perioperative period. A multimodal anaesthesia and analgesia approach and protocols for perioperative care should be implemented in order to reduce pulmonary complications and improve outcome. Lung protective ventilation with low tidal volume, adequate level of PEEP and appropriate use of oxygen concentration is recommended. Multidisciplinary teams including surgeons, anaesthesiologists and sleep and pulmonary physicians must cooperate to achieve optimal management of obese surgical patients.

Conflict of Interest

Yuda Sutherasan declares that she has no conflict of interest. Lorenzo Ball declares that he has no conflict of interest. Paolo Pelosi declares that he has no conflict of interest. ■

Abbreviations

ARDS acute respiratory distress syndrome
ASA American Society of Anesthesiologists
CPAP continuous positive airway pressure
FRC functional residual capacity
NIPPV noninvasive positive pressure ventilation
OHS obesity hypoventilation syndrome
OSA obstructive sleep apnoea
PCV pressure control ventilation
PEEP positive end-expiratory pressure
PPC postoperative pulmonary complications
REM rapid eye movement
SpO_2 peripheral oxygen saturation
VCV volume control ventilation

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CHAIN OF SURVIVAL AFTER OUT-OF-HOSPITAL CARDIAC ARREST

THE FINAL LINK

Takashi Tagami
Assistant Professor
Department of Emergency and Critical Care Medicine
Nippon Medical School Tama Nagayama Hospital
Tokyo, Japan

Department of Clinical Epidemiology and Health Economics
School of Public Health
University of Tokyo
Tokyo, Japan

t-tagami@nms.ac.jp

The "Chain of Survival" Concept after Out-of-Hospital Cardiac Arrest

To overcome a time-sensitive and severe condition with a low survival rate—out-of-hospital cardiac arrest (OHCA)—the following four links of the "chain of survival" concept were introduced by Newman in the 1980s (Newman 1989):

1. Early access to emergency medical care;
2. Early cardiopulmonary resuscitation;
3. Early defibrillation; and
4. Early advanced cardiac life support.

The American Heart Association (AHA) and the International Liaison Committee on Resuscitation adopted this concept in their guidelines in the early 1990s. Thereafter a similar concept was used globally until the publication of guidelines in 2005 (ECC Committee, Subcommittees and Task Forces of the American Heart Association 2005).

Even after spontaneous circulation is restored, most patients die within 2 days (Neumar et al. 2008). Post-cardiac arrest syndrome is a severe medical condition caused by prolonged complete whole-body ischaemia and reperfusion; thus the management of patients with post-cardiac arrest syndrome is challenging. Early arterial hypotension is common and associated with increased in-hospital mortality (Chang et al. 2007; Negovsky 1972). In addition to haemodynamic instability, pulmonary dysfunction is also common after cardiac arrest (Neumar et al. 2008). During this critical condition, several treatments are required to improve the outcome of cardiac arrest, including therapeutic hypothermia (targeted temperature management), percutaneous coronary intervention and other advanced interventions (**Fig. 1**) (see p.106).

Thus the European Resuscitation Council revised the final link in the chain-of-survival concept from "early advanced cardiac life support" to provision for "post-resuscitation care" in 2005 (Nolan 2005). In 2010 the AHA guidelines implemented a "fifth link," which is "post-cardiac arrest care," in addition to the previous four links, as another critical link in the chain-of-survival concept (Peberdy et al. 2010). Although the introduction of the final link of the "chain-of-survival" concept was a rational approach, no direct evidence supported its implementation at the time of the publication of the guidelines (Peberdy et al. 2010; Nolan 2005).

> "high-quality and aggressive ICU management is needed to counteract post-cardiac arrest syndrome"

Aizu Chain-of-Survival Concept Campaign: From a Case to a Clinical Study

In spring 2008, a 58-year-old man suddenly lost consciousness and had a cardiac arrest. His wife immediately called emergency medical services and began chest compression. The emergency medical services provider found that he had ventricular fibrillation and performed defibrillation, which was unsuccessful. Our medical team participated in the resuscitation in progress and performed advanced cardiac life support, including adrenaline administration and intubation. We strictly followed the 2005 AHA Guidelines, which were the latest available at that time. However, it took 2.5 hours to achieve return of spontaneous circulation (ROSC). Immediately after achieving ROSC, his blood pressure decreased again in the emergency department. At that time, no consensus has been reached on the optimal treatment for post-cardiac arrest patients in our hospital. However, we provided what we believe was the most appropriate treatment for our patient (**Fig. 2**) (see p.106). Soon after the return of spontaneous circulation, he developed shock despite large doses of catecholamines. We therefore used venoarterial extracorporeal membrane oxygenation and an intra-aortic balloon pumping system with continuous renal replacement therapy. I spent several days and nights with him in the intensive care unit (ICU). After a month of aggressive intensive care in the ICU, he was discharged from our hospital with favourable neurological status.

The present case clarified two things. First, even if 150 minutes have passed before ROSC is achieved, the brain may not be completely impaired if the early links of the chain of survival are well conducted. Second, high-quality and aggressive ICU management is needed to counteract post-cardiac arrest syndrome.

During the patient's treatment the question "Could these treatments be performed outside the ICU?" arose, for which the answer is no. This led to the clinical question "Can patient outcomes improve if all patients with post-cardiac arrest syndrome in this region are treated at a single ICU?" To answer this clinical question, we performed a region-wide multicentre prospective study, the Aizu Chain of Survival Concept Campaign, to evaluate the effect of the final link in the chain of survival, which was defined as multidisciplinary post-resuscitation care (**Fig. 3**) (see p.108) (Tagami et al. 2012).

The Aizu region (Fukushima, Japan) is a suburban/rural area with 300,000 residents. All 12 emergency hospitals (one tertiary care and 11 non-tertiary care hospitals) in the region participated in the study. After the patients with OHCA achieved ROSC at each hospital, they were concentrated in one tertiary care hospital

and treated aggressively to focus on the fifth link. We used an advanced haemodynamic monitoring system (PiCCO monitoring system, PULSION, Germany) to measure several important haemodynamic and pulmonary variables for all the patients. The PiCCO system provides cardiac output and global end-diastolic volume as volumetric haemodynamic variables. It also provides extravascular lung water, which represents the degree of pulmonary oedema, and the pulmonary vascular permeability index, which can be used to differentiate between cardiogenic and non-cardiogenic pulmonary oedema. We performed individualised treatment, and optimised haemodynamic and respiratory instability by using these advanced variables, because every single patient has different cardiac function, fluid status, vascular permeability and previous medical history (including time from collapse to ROSC). After implementation of the fifth link, the proportion of survivors with a favourable neurological outcome increased significantly, and the fifth link was found to be an independent factor for a favourable neurological outcome (Tagami et al. 2012).

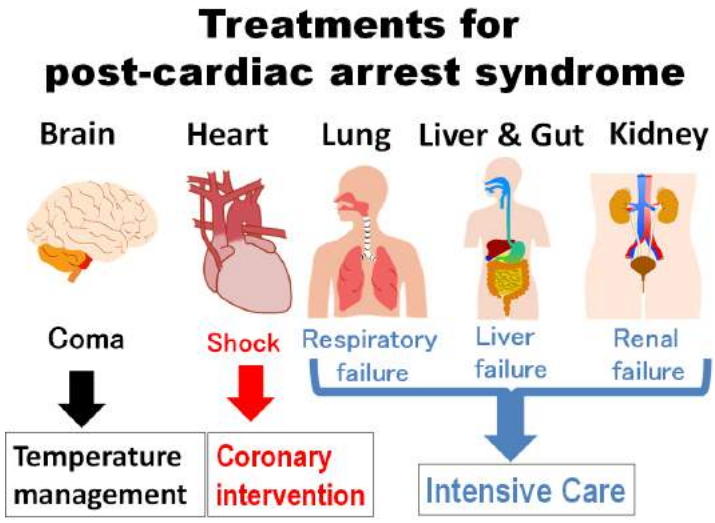

Figure 1.

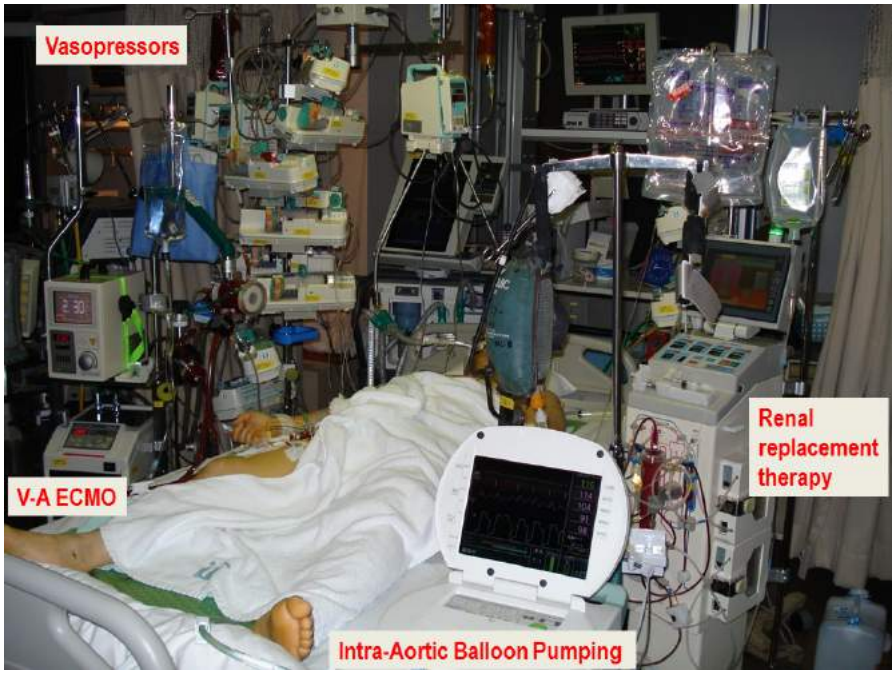

Figure 2.

Post-Resuscitation Care and Outcomes: Recent Evidence

The last decade has witnessed a significant reduction in OHCA-related mortality rate worldwide (SOS-KANTO 2012 Study Group 2015; Fugate et al. 2012; Wissenberg et al. 2013). Several large nationwide studies have suggested that the improvement in outcomes may be related to the provision of post-resuscitation care in addition to the improvement of the actions of bystanders and treatments before the ROSC (van der Wal et al. 2011; Fugate et al. 2012; Tagami et al. 2016; Kim et al. 2013). Fugate et al. reported that the in-hospital mortality rate of patients with cardiac arrest in the United States decreased by 11.8% from 2001 to 2009, based on the analysis of the American National Inpatient Sample database (Fugate et al. 2012). Van der Wal et al. reported that inducing a mild therapeutic hypothermia was associated with a 20% relative reduction in OHCA-related in-hospital mortality in the Netherlands (van der Wal et al. 2011). Kim et al. from Korea reported that provision of post-resuscitation care resulted in a significant improvement in patient outcome, and concluded that the systematic inclusion of the fifth link is recommended for improving patient outcomes (Kim et al. 2013). We recently reported that the provision of therapeutic hypothermia and percutaneous coronary intervention increased significantly among cardiogenic OHCA cases related to ventricular fibrillation over the period 2008 to 2012 in Japan (Tagami et al. 2016). We found that in-hospital mortality decreased significantly over the 5-year period. The results of logistic regression analyses using multiple propensity score analyses suggested that the decrease in mortality can be explained by the increase in the provision of both therapeutic hypothermia and percutaneous coronary intervention (Tagami et al. 2016).

Several studies have suggested that the level of care provided by institutions (i.e. tertiary care, level 1 vs. non-tertiary care, level 2 or 3) affects the outcome in post-resuscitation patients (Kajino et al. 2010; Soholm et al. 2015; Soholm et al. 2013; Stub et al. 2011). Among OHCA patients without field ROSC in Japan, those who were transported to tertiary-care centres had better survival than those transported to non-tertiary-care centres (Kajino et al.

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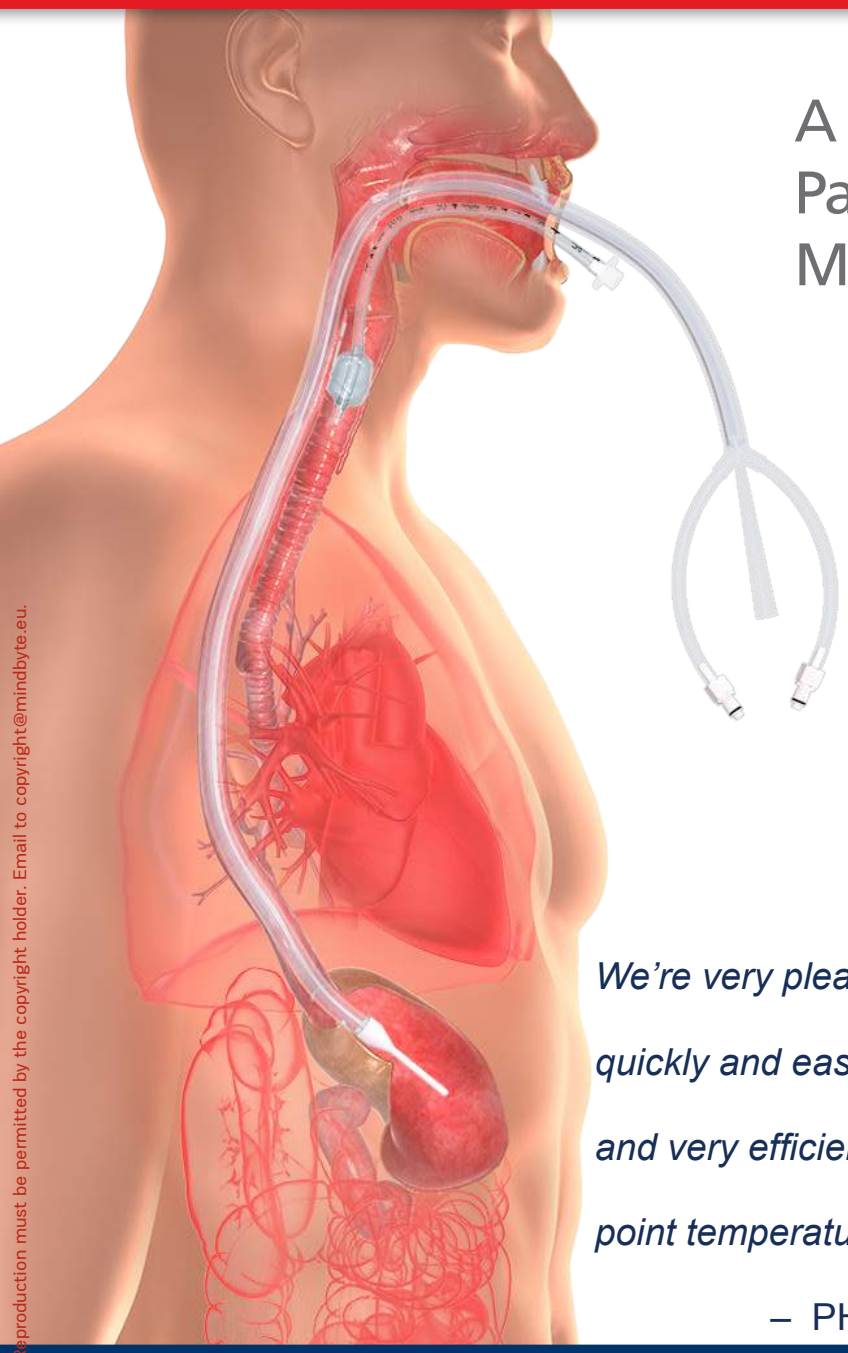

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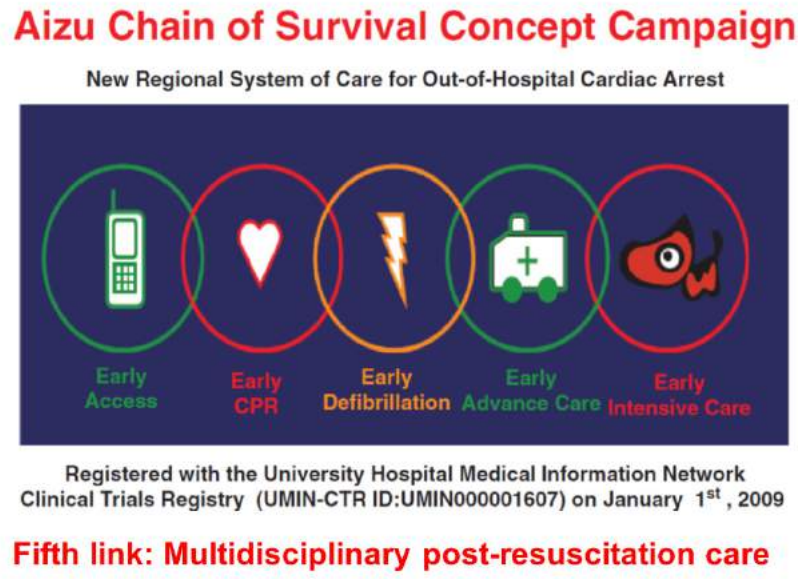

Figure 3.

2010). Similar results were reported from Denmark (Soholm et al. 2013; Soholm et al. 2015). Schober et al. evaluated the association among patient-related factors, comorbidities and intensive care measures and their impact on the outcome for patients treated after cardiac arrest in 87 Austrian ICUs (Schober et al. 2014). They reported that the high frequency of post-cardiac arrest care at an ICU seemed to be associated with improved outcome of patients who had a cardiac arrest (Schober et al. 2014). These studies suggest that admission to high-level-of-care centres and intensive care administration after OHCA are associated with a significantly higher survival rate even after adjustment for prognostic factors including pre-arrest comorbidity (Kajino et al. 2010; Soholm et al. 2015; Soholm et al. 2013; Stub et al. 2011; Schober et al. 2014).

Relay Baton of Survival

Recent evidence apparently indicates that the initial links before achieving ROSC are critically important. The final link can be initiated only if the previous links in the chain are well connected and patients achieved ROSC. Each link in the chain of survival could be represented as a relay baton. Therefore a relay baton should not be dropped before the final runner. However, if the baton is passed to the final runner, that specialist should perform as well as possible to achieve the goal of treatment. Our goal is not only to achieve spontaneous circulation but also to restore the patient's previous quality of life. Thus the true goal is located after completion of the final link. An emergency department physician must start the final link immediately after the patient achieves ROSC. Intensivists, cardiologists, neurocritical care physicians, nurses, medical engineers and all providers working in the ICU have the responsibility to complete the final chain in the survival link.

Conclusions

Several large nationwide studies have suggested that recent improvements in outcome are associated with the provision of post-resuscitation care. Recent studies also showed that admission to ICUs in high-level-of-care centres and administration of aggressive intensive care after OHCA were associated with better outcomes. Although randomised trials have not yet been performed, providing aggressive post-cardiac arrest care is a reasonable approach.

Conflict of Interest

Takashi Tagami declares that he has no conflict of interest. ■

Abbreviations

AHA American Heart Association
ICU intensive care unit
OHCA out-of-hospital cardiac arrest
ROSC return of spontaneous circulation

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POTENTIAL NUTRITIONAL STRATEGIES TO REDUCE MUSCLE WASTING IN EARLY CRITICAL ILLNESS

This review will briefly discuss the potential role of nutrition and the schedule of delivery on reducing skeletal muscle wasting in early critical illness.

Danielle E. Bear
Principal Critical Care Dietitian &
Health Education England / National Institute for Health Research Clinical Doctoral Fellow
Department of Nutrition & Dietetics
Department of Critical Care
Guy's and St Thomas' NHS Foundation Trust
London, UK

Danielle.Bear@gstt.nhs.uk

@danni_dietitian

Zudin Puthucheary
Consultant in Critical Care Medicine
Honorary Senior Lecturer
Institute of Sport Exercise Health
Division of Critical Care
University College London Hospitals
London, UK

zudin.puthucheary.09@ucl.ac.uk

Increasing numbers of patients are surviving critical illness due to treatment advances in the early management of acutely unwell patients. This survival advantage is reflected as an increase in the number of patients experiencing long-term functional disability post-critical illness (Cheung et al. 2006; Herridge et al. 2011; Hopkins et al. 2005; Iwashyna et al. 2010;), resulting in a higher frequency of discharges from hospital to rehabilitation facilities (Kaukonen et al. 2014).

Skeletal muscle weakness, termed ICU-acquired weakness (ICU-AW), contributes significantly to the physical and functional disability observed in these patients. This has been highlighted in the recent American Thoracic Society Consensus Statement (Fan et al. 2014), and skeletal muscle wasting has been identified as a contributing factor to ICU-AW (Puthucheary et al. 2010).

Interventions to reduce skeletal muscle wasting in critical illness are therefore urgently required and have been highlighted as recent research priorities in the United Kingdom (Reay et al. 2014).

Skeletal Muscle Wasting in Critical Illness

Although the pathogenesis remains poorly understood, translational data is emerging that has defined the trajectory of skeletal muscle wasting during the first week of critical illness. The MUSCLE-UK group has shown that muscle wasting occurs early and rapidly during the first week of critical illness, and is more severe in patients with multi-organ failure (Puthucheary et al. 2013). This study used muscle ultrasound of the rectus femoris cross-sectional area along with fibre cross-section from biopsies of the vastus lateralis muscle to confirm these findings. Furthermore, using leg protein turnover, they demonstrated that patients remain in a net catabolic balance at the end of the first week of critical illness as a consequence of persistently high levels of muscle protein breakdown and decreased muscle protein synthesis.

Potential Interventions

In health, skeletal muscle is maintained by a balance of muscle protein synthesis (MPS) and muscle protein breakdown (MPB). Any prolonged change in this balance will result in an increase or decrease in skeletal muscle (Morton et al. 2015). Resistance exercise is the most potent anabolic stimulus, including during bed rest (Ferrando et al. 1997; Fitts et al. 2007), and the dose, source and timing of protein ingestion can further influence gains in skeletal muscle in those undertaking this type of exercise (Atherton et al 2010; Bohe et al. 2001; Bohe et al. 2003).

It has been assumed that similar strategies may prove useful in the critically ill. However, resistance exercise is often not feasible in the early stages of critical illness due to the clinical instability of the patient. Additionally, there are no proven nutritional therapies to attenuate skeletal muscle wasting in the ICU and translational science in this area is severely lacking (Bear et al. 2013). When considering nutritional strategies to reduce muscle wasting in the critically ill, one must consider the timing, route of delivery and the amount of nutrient required to elicit a benefit. Each of these factors remains under debate for almost all areas of critical care nutrition.

Protein

Protein is the most obvious potential nutrient to reduce muscle wasting in this population, but data indicating a clear benefit to higher protein levels are lacking. Indeed a systematic review of protein provision in critical illness detailed the limited amount and poor quality of the available evidence and highlighted several shortcomings of studies investigating protein intakes in critically ill patients (Hoffer and Bistrian 2012).

The majority of randomised controlled trials (RCTs) investigating protein intake in critical illness were undertaken before 2000 (Greig et al. 1987; Iapichino et al. 1988; Ishibashi et al. 1998; Larsson et al. 1990; Long et al. 1976; Muller et al. 1995; Pitkanen et al. 1991; Shaw et al. 1987; Twyman et al. 1985; Wolfe et al. 1983), with very few undertaken after that time (Scheinkestel et al. 2003a; Scheinkestel et al. 2003b; Singer et al. 2007; Verbruggen et al. 2011). Protein doses of up to 3.5g/kg were studied and nearly all of these used parenteral

amino acids and reported nitrogen balance as the primary determinant of benefit from higher protein intakes. Notwithstanding the limitations of small sample size, the method of using whole body nitrogen balance is often flawed in the critically unwell due to the failure to account for losses in skin and faeces (Kopple 1987). Additionally, this method is not reflective of muscle mass, as the gastrointestinal and liver contributions remain unknown and are potentially high (Guillet et al. 2004). Whilst two studies measured protein turnover (Wolfe et al. 1983; Verbruggen et al. 2011), this was in fact whole body turnover, which also does not reflect muscle turnover itself.

Despite the lack of data from RCTs, current recommendations in the critically ill are for higher protein intakes ranging from 1.5-2.5g/kg/day (Hoffer and Bistrian 2012; Kreymann et al. 2006; McClave et al. 2016). These recommendations are based mainly on observational data and relate to a mortality benefit (Alberda et al. 2009; Allingstrup et al. 2012; Elke et al. 2014; Weijs et al. 2012; Weijs et al. 2014) rather than a reduction in the loss of lean body mass itself.

Only one study has investigated the effect of different protein intakes on patient-centred outcomes, including muscle wasting, in the critically ill. In the study by Ferrie and colleagues (2015), 119 patients were randomised to receive 0.8g/kg or 1.2g/kg protein from parenteral nutrition (PN). Despite a smaller than planned difference in the delivery of protein (0.9g/kg vs 1.1g/kg), they found a significant difference in the primary outcome of handgrip strength at day 7 along with improvements in secondary outcomes such as fatigue score and measures of forearm muscle thickness and rectus femoris cross-sectional area. These results indicate that higher protein intakes, at least when supplied via the parenteral route, may lead to reductions in muscle wasting during the first week of critical illness. However, this finding needs to be confirmed in larger studies, correcting for baseline heterogeneity, especially as these results are in stark contrast to observational data reported from two groups.

In two pre-planned sub-studies from the large EPaNIC Trial, early parenteral nutrition (PN) (and therefore higher provision of protein) was not found to reduce muscle wasting (Casaer et al. 2013; Hermans et al. 2013). In the first of these (Hermans et al. 2013), muscle atrophy, measured using muscle biopsies, was not different between the groups receiving early or late PN. In the second, repeated femoral and abdominal CT scans were obtained in 15 neurosurgical patients. Whilst early PN was shown to reduce the quality of the muscle, it did not affect the rates of wasting seen in this group of patients.

Puthucheary et al. (2013) used muscle ultrasound of the rectus femoris cross-sectional area to inform the trajectory of muscle wasting over a 10-day ICU stay in 63 patients. Muscle loss in this group was early and rapid, with patients losing on average 17% of their lean body mass over this time period. Additionally, patients with multi-organ failure experienced significantly more muscle loss than those patients with single organ failure (21.5% vs. 7.2%). This finding was confirmed by the data from muscle biopsies of the vastus lateralis. Protein tracer studies indicated that the muscle loss was due to increased protein catabolism and reduced protein synthesis over the first 7 days; however, muscle loss in this group was also found to be positively associated with protein intake over the study period.

> **"simply reducing the macronutrient deficit over the first week of critical illness may not be a useful strategy for reducing muscle loss"**

These studies indicate that simply reducing the macronutrient deficit over the first week of critical illness may not be a useful strategy for reducing muscle loss. It is likely that any nutrition intervention aimed at reducing muscle wasting will need to consider the delicate relationship between both energy and protein provision. Energy intake is a fundamental requirement for utilisation of amino acids and protein (Burke 2010; Calloway 1955; Kreymann et al. 2012). However, current trends are towards lower energy intakes in the first week of critical illness due to the potential for harm seen with aggressive early energy provision (Braunschweig et al. 2015; Casaer et al. 2011). Further, interventional trials increasing delivery of protein and calories will need to be designed with caution and consider the physiological mechanisms behind such strategies.

Feeding Schedule

The contradictory results and current controversies rest on the assumption that our current modes of delivery are best. A recent large study found no difference in mortality (30- or 90-day) or infectious complications when early PN was compared with early enteral nutrition (EN) (Harvey et al. 2014). Considering its non-nutritional benefits (McClave et al. 2014), EN remains the route of choice in early critical illness (McClave et al. 2016), despite the large degree of underfeeding associated with its use (Alberda et al. 2009). However, more fundamental to the route and volume of nutrition support is that each nutritional component needs to be delivered to the plasma from the gastrointestinal tract and then transported into cells to be utilised by the muscle. Gastrointestinal intolerance is common in critically ill patients, especially in terms of delayed gastric emptying (Nguyen et al. 2007). It has been shown that these patients experience impairments in both the rate and extent of nutrient absorption, even when post-pyloric feeding is utilised (Di Bartolomeo et al. 2012), which may confound any potential to see a positive impact of nutrition in preventing muscle wasting.

Additionally, it is possible that our current methods of continuous feeding may not be appropriate as a result of the muscle full effect. The concept of the muscle full effect has been studied in small groups of healthy individuals, where it has been found that upon ingestion of either whey protein (45g; Atherton et al. 2010) or commencement of intravenous amino acids (Bohe et al. 2001), a latent period of around 30-45 minutes exists where MPS then triples for up to 90 minutes before rapidly returning to post-absorptive rates. This reduction back to baseline MPS occurs despite continued availability of essential amino acids both intramuscularly and in the plasma. Additional amino acids were oxidised in both groups. These results indicate that, irrespective of the route of feeding, a simple overprovision of amino acids does not lead to continued increases in MPS. Although the muscle full effect has not been studied directly in critically ill patients, in a small group of critically ill patients studied over a 3-hour period, whole body protein balance was shown to increase due to synthesis, and amino acids were not oxidised at the equivalent of 1g/kg/day, indicating that amino acids at this level at least are utilised in these patients (Liebau et al. 2015). However, any direct relationship to muscle protein synthesis cannot be inferred due to the use of the whole

body protein turnover method whereby hepatic oxidation may fully account for these findings.

These data together suggest that continuous feeding may not allow physiological stimulation of intermittent MPS and that intermittent (bolus) feeding may be better (Atherton et al. 2010; Marik 2015). Intermittent feeding has been previously investigated in critical illness (Evans et al. 2016; MacLeod et al. 2007), but muscle mass and function were not measured. The Muscle-UK group is currently investigating the effect of this feeding schedule on changes in the rectus femoris cross-sectional area with results expected in 2017 (**Intermittent Versus Continuous Feeding in ICU Patients,** NCT02358512 **clinicaltrials.gov/ct2/show/NCT02358512**).

This review has not addressed specific amino acids (e.g. leucine), their metabolites (eg. ß-hydroxy-ß-methylbutyrate) or the post-ICU phase of critical illness. Discussions on these are beyond the scope of this article, but future studies may be aimed not at the acute phase, but in trying to rebuild the lost muscle. It is most likely that nutritional interventions are only one of several aspects needed for the increase in muscle mass and strength in the post-ICU phase and that when coupled with exercise, stronger benefits may be produced (Heyland et al. 2015).

Conclusion

Reducing muscle wasting and subsequent ICU-AW to improve the function and quality of life of ICU survivors are high priorities for critical care clinicians. No known intervention exists to achieve this at present, but several nutritional interventions may prove successful such as appropriate protein and energy provision and intermittent feeding. However, further translational science work, along with investigations into the patient group most likely to benefit are required before these interventions can be confirmed in large RCTs.

Conflict of Interest

Danielle Bear declares that she has no conflict of interest. Zudin Puthucheary declares that he has no conflict of interest. ■

Abbreviations

EN enteral nutrition
ICU intensive care unit
ICU-AW ICU-acquired weakness
MPB muscle protein breakdown
MPS muscle protein synthesis
PN parenteral nutrition

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Vitaly Herasevich
Associate Professor of
Anesthesiology and Medicine
Herasevich.vitaly@mayo.edu

Mark T Keegan
Professor of Anesthesiology

Brian W Pickering
Assistant Professor of Anesthesiology

Department of Anesthesiology
Division of Critical Care
Mayo Clinic
Rochester, USA

THE FUTURE OF ICU PREDICTION SCORES IN THE ERA OF "BIG DATA"

Fuelled by the growth in electronic medical record (EMR) adoption, the recent boom of Big Data analytics in healthcare affords unprecedented opportunities for developing new prediction scores for patients in the intensive care unit (ICU) and beyond. Based on a review of scientific literature reports, however, Big Data science has added no new scores to clinical practice in recent years. In this article, the authors will discuss barriers and potential solutions for the future development of meaningful clinical scores.

Do We Need Scores?

Clinical practice is concerned with resolving uncertainty around diagnosis, treatment options and prognosis. Clinical decisions are usually made by an individual such as a physician who has trained for many years in the science, art and practice of medicine. These individuals use their clinical experience to hone in on relevant cues from the patient history, physical examination, physiologic trends and laboratory and other diagnostic data. These cues often fall into some pattern the physician recognises, which forms the basis of a clinical diagnosis. The diagnosis informs treatment choices and the response to treatment determines prognosis.

The most useful prediction scores should combine medical signs, symptoms and other findings to reliably predict the probability of a specific disease or outcome (McGinn et al. 2000). Clinical scores became popular in the 1980s when computerisation of medical data made access and computation much easier than before. Electronic data could be processed more quickly, reliably and consistently than the equivalent manual process. Recently prediction models, clinical calculators and scores have attracted more attention as they become important parts of quality improvement initiatives and are used in administrative and financial management to standardise patient populations for comparison (Keegan et al. 2011).

We recently performed a systematic analysis of the peer-reviewed literature, and identified 176 validated clinical calculators used mostly in the specialities of critical care, emergency medicine and internal medicine (unpublished data). The most frequent outputs of clinical scores were outcome prediction, quantification of the severity of illness and estimation of disease progression as an aid to clinical decision-making. The most frequent computation technique utilised is branching logic with cutoff rules followed by regression analysis (unpublished data). The use of these techniques continues to grow in step with increases in computational power and availability of data.

Big Data Revolution

With the almost ubiquitous use of electronic medical records, clinical data have become accessible to analytics as never before. The more exotic potential applications of predictive analytics are almost within reach. The most important of those applications, in the authors' view, are those which will use large quantities of clinical data—collected and annotated automatically in data mining and machine learning algorithms—to build 'on-the-fly' predictive analytics tailored to the individual patient and to patient populations. The building blocks of these applications are well-established in industries which made an early switch from paper-based data storage and transfer to a business model in which electronic data processing is key (e.g. the banking and retail sectors). In these industries the tools are particularly focused on the prediction of future system and individual behaviours, on trajectory analysis, and on early detection of events which deviate from normal. Real-world examples include fraud detection in the banking industry and, in the retail sector, the prediction of what the customer might want to buy next. This often results in contact with the unsuspecting customer in the form of surprisingly relevant advertisements or phone calls. The success of Big Data analytics to deliver these results in other data-rich businesses, combined with the availability of clinical data in an electronic form, bodes well for the ability of machine-learning techniques to produce clinically important prediction models or scores. However, almost a decade into the Big Data revolution in healthcare we have not yet seen a new breakthrough described in the clinical scientific literature. Why?

Challenges and Potential Solutions

1. **Scoring systems need to be generalisable.** Data models developed based on a specific clinical setting tend to work best in that setting. When applied outside of the development environment they often

perform poorly. A universal scoring system requires clinical data from multiple healthcare settings. Notwithstanding the difficulties involved in the sharing of data among competing organisations, blended data can drag the performance of the model down to the lowest common denominator. Specific tools will perform better than universal tools. With further development of healthcare data mining tools and machine learning, combined with the availability of domain experts, it is likely that highly calibrated tools will be generated 'on the fly' for very narrow problems and specific settings.

2. **Prediction models developed from electronically captured data do not always represent the whole picture of healthcare delivery.** Observation of patients, discussion with clinical staff, patients and their families, and evaluation of the care delivery environment often provide essential information to decision-makers. Such information is typically poorly documented in the EMR. As new modalities of data capture (computer vision, radio-frequency identification (RFID) tags, accelerometers, social media, etc.) are integrated into the clinical record, Big Data analytic tools will have additional rich streams of data from which to generate predictions.
3. **Garbage in – garbage out.** Missing data, manually entered or delayed data and poorly validated data each play a role in decreasing the reliability of the final result. Often models work well on retrospective sets of data (collected and present as a single table), but when applied in real time suffer from delayed data presentation and cannot reliably predict an event earlier than a clinician at the bedside.
4. **Association is not causation.** Without biologic plausibility the 'black box' output from prediction models can be difficult to take seriously in the clinical setting where the stakes are very high. The incorporation of some basic hypothesis testing will add greatly to the credibility of 'black box' analytics.
5. **There are limits to the power of prediction.** As a clinician one needs to know that 'black box' predictions will not expose a patient to harm. With any test there are always false-positive and false-negative cases. Any diagnostic test can be described by its sensitivity and specificity. Prognostic scoring systems may be evaluated by assessment of discrimination and calibration. Big Data proponents have shied away from engaging with regulatory bodies, but must answer questions regarding test accuracy, safety, reliability and ease of implementation.
6. **Black box recommendations are poorly tolerated by clinicians.** Until artificial intelligence (AI) becomes standard in our lives, clinicians need to understand how the model produces a prediction. This is especially true if a model might be incorrect some of the time. Adjusting models to rule out true negative cases (for diagnostic models) and explanation of the steps behind survival predictions (for prognostic models) will enhance clinician acceptance. Engaging clinicians in model design and implementation are also useful intermediate steps on the path towards acceptance of AI recommendations.

> "the potential applications of predictive analytics are almost within reach"

7. **Actionable predictions will be highly valued by clinicians.** Predictions are most useful if they can be used by clinicians to correct course and prevent an adverse event or outcome for the patient. Clinicians do not highly value risk of dying or risk of deterioration predictions unless they come bundled with potential risk mitigation strategies or recommendations. Knowing that the elderly frail patient has a 45% chance of dying in the intensive care unit is not information that is actionable in most cases. When developing prediction algorithms, it is important that careful consideration be given to the associated expected course of action to reduce the risk of harm or suboptimal patient outcome.
8. **Presentation of final results.** Highly performing prediction models are useless if poorly implemented or presented (Ofoma et al. 2014). Careful consideration of the delivery mechanism of an alert will increase the likelihood that the output of a prediction model will be incorporated into clinical decision-making. Up-front consideration of "who, when, where and how" will greatly increase the potential impact of Big Data analytics predictions.

Although significant limitations exist in the current generation of EMRs, the move to a digital record opens up a world of possibilities for advanced analytics techniques. We have not yet seen significant breakthroughs at the bedside, but it is early days. As Big Data analytics experts from retail and finance incorporate learning from healthcare domain experts into their models, the complexity and human-centred nature of clinical care will become obvious. With these new insights and continuously advancing technology, clinicians and patients should expect to encounter ever more useful and meaningful tools supporting better health, better care and lower costs.

Conflict of Interest

Vitaly Herasevich declares that he has no conflict of interest. Mark T. Keegan declares that he hasno conflict of interest. Brian W. Pickering declares that he has no conflict of interest. ■

Abbreviations

AI artificial intelligence
EMR electronic medical record
ICU intensive care unit
RFID radio-frequency identification

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Claudio Ronco
Director

VODCASTING

THE STORY BEHIND CAPPUCCINO WITH CLAUDIO RONCO

Marta Scabardi
Executive Assistant

Department of Nephrology Dialysis and Transplantation
International Renal Research Institute Vicenza (IRRIV)
San Bortolo Hospital
Vicenza, Italy

info@irriv.com

irriv.com

Video on demand (VOD) is a popular way to keep updated in intensive care. *ICU Management & Practice* spoke to Prof. Claudio Ronco and Marta Scabardi, from the International Renal Research Institute, Vicenza Italy, about what's involved with their video subscription channel "Cappuccino with Claudio Ronco."

What's the idea behind Cappuccino with Claudio Ronco?

Marta Scabardi (MS): Dance is my big passion, and I keep up to date through social networks such as Instagram and YouTube. On YouTube an ex-ballerina opened a channel where she posts tutorials. That gave me the idea to record a short video of Prof. Ronco discussing his ideas about nephrology and his areas of research interest and posting it online in a YouTube channel. As Prof. Ronco's executive assistant, and one of the Vicenza Course meeting planners I cooperate with Prof Ronco every day and I know the energy and the power of his communication. Prof. Ronco loves new challenges, all kinds of technology and instruments for communication and he found this idea interesting. When I explained that the format should be short videos, starting and finishing in the same way every time, to be memorable for viewers, Prof. Ronco suggested sharing the morning coffee moment. Every morning Prof. Ronco, my colleague Anna Saccardo and I take a coffee together, and in these 10 minutes or so we discuss all the important topics and issues for our events. It's the morning briefing. Prof. Ronco noted that this is a very Italian way of working, so we decided to call our video channel "Take a Cappuccino with Claudio Ronco" (cappuccino is 100% more Italian than coffee!).

Claudio Ronco (CR): In Italy the cappuccino is a ritual two minutes' time dedicated to friendship and a small space in the day devoted to chatting in a real bar with real friends. I wanted to reproduce a space and time on YouTube with my videos, sharing with friends and followers two minutes' conversation on a hot topic in science, on a recently published paper, specific research or on recent results of a trial. I am Editor-in-Chief of *Blood Purification*; one paper every issue has the logo "Cappuccino with Claudio Ronco" and I make a virtual journal club for all our followers on that paper.

Other cappuccinos are shot in different locations around the world with experts and leading scientists to get their opinion on one specific question. Other times they describe the highlight of a congress or they express their frank opinion. Everything is designed to bring young physicians closer to their idols and mentors in research in the friendly environment of a virtual bar stand with cappuccino time. Young physicians are very busy with their routine, they have no time and they want some hints on new research at a glance. The two minutes of a cappuccino are ideal for that.

> "two minutes' conversation on a hot topic"

How often do you produce a video?

We do one per week most of the time, occasionally more. Sometimes we give some space between two cappuccinos to avoid burning the content of the previous one.

You have invited many distinguished doctors to take a cappuccino. Who is on your list to invite?

MS: We have no list as such due to Prof. Ronco's very tight schedule. He is often abroad for congresses where he meets esteemed researchers and doctors that over the years

have become friends. He personally invites them for a cappuccino, and they are always happy to do it.

CR: This is a dynamic club of friends. Imagine being in a worldwide university and you meet at the cafeteria the most important investigators of the moment. Whoever is leading research and has new stories to tell is a candidate for future cappuccinos. At the same time, sometimes I want to invite young fellows to express their wishes and their ideas in research. The meaning is to make this club alive and really entertaining.

Where have you filmed?

CR: I travel like crazy and we have filmed almost everywhere on all continents. The greetings at the beginning are in four languages, but I tend to insert the fifth of the place where the cappuccino is filmed (Japan, China, Greece etc).

MS: Some have even been filmed on vacation (sailing, on a mountain).

What were the set-up costs?

MS: There were no set-up costs: I shoot with my Iphone. We just invested in a better phone to give better resolution and microphone.

CR: The main actor comes for free ☺.

What has been the most watched video?

Currently it is no 77. The 2015 ERA-EDTA congress in London - **https://iii.hm/332**

What video is a particular favourite?

CR: My favourite cappuccino is the one I took before a hockey game (see picture on next page) where I was playing with the old glories and I spoke about traumatic AKI (No. 54: Polytrauma and AKI - **https://iii.hm/333**). Hockey is a brutal sport and sometimes trauma can occur. AKI in this type of sport is quite rare whilst in other traumatic situations this is frequent.

Whoever is leading research and has new stories to tell is a candidate

Prof. Ronco with *ICU Management & Practice* Editor-in-Chief Prof. Jean-Louis Vincent at ISICEM 2016 (https://iii.hm/33e)

Prof. Ronco playing hockey with the old glories (https://iii.hm/333)

Marta Scabardi with Prof. Claudio Ronco

Which YouTube channels do you follow?

- ERA-EDTA (European Renal Association - European Dialysis and Transplant Association) (**https://iii.hm/336**)
- International Society of Nephrology (**https://iii.hm/337**)

Further Information

Subscribe to Take a Cappuccino with Claudio Ronco at **https://iii.hm/338**

Prof. Ronco's Zoom On profile is published on the *ICU Management & Practice* website **https://iii.hm/37s**

Critical Care Channels

ICU Management & Practice I-I-I Interviews **https://iii.hm/3am**

ISICEM **https://iii.hm/339**

Society of Critical Care Medicine **https://iii.hm/33a**

Social Media and Critical Care (SMACC) **https://iii.hm/33c**

Critical Care Survival Guide – prepare for your ICU rotation (Indiana University) **https://iii.hm/33d** ■

PODCASTING

THE STORY BEHIND CRITICAL CARE PRACTITIONER

Jonathan Downham
contact@criticalcarepractitioner.co.uk
@ccpractitioner
criticalcarepractitioner.co.uk

Podcasts are audio files made available regularly to occasional listeners or subscribers (usually a free subscription). The 'pod' in the name comes from iPod, and although that device is no longer manufactured, podcasting goes from strength to strength. Listening to a podcast is as simple as clicking a link on a website, or subscribing via an Apple or Android app on to a smartphone or a tablet. You can then access a podcast when you like, either by downloading an episode on to your device or listening when you have an internet connection.

Podcasting is an ideal way to keep up-to-date in critical care and emergency medicine. Podcasts are just one part of the FOAMed free open access medical education and FOANed free open access nursing education movements, which have gathered together resources from around the world for the benefit of fellow practitioners.

ICU Management & Practice spoke to Jonathan Downham, who runs the website criticalcarepractitioner.co.uk, about the motivation behind the website and the practicalities of podcasting. Jonathan is an Advanced Clinical Practitioner in Emergency Medicine at Heartlands Hospital in Birmingham in the UK, who has also worked as an Advanced Clinical Practitioner in Critical Care. He teaches on the Masters-level Clinical Examination course at the University of Warwick, and established a degree level clinical examination course at the University of Staffordshire.

In a nutshell, what is Critical Care Practitioner?

It's a website I started around two years ago when I was qualifying as a critical care practitioner. It is a mixture of blog posts and podcasts about critical care. I have always been into 'gadgetry' and 'geekery', so I set up the website to share what I was learning with others. It started as a way of helping other people learn while I was learning, but it has grown and is designed as a resource for critical care and emergency medicine practitioners.

When I first started I approached fellow practitioners on Twitter. Twitter folk are very forthcoming on helping people out. I ping people and mostly they are very happy to talk to me. It's a very nice community to be part of – we're like a family.

I've had good feedback from both experienced staff and from learners. Footfall is gradually increasing, and it increased noticeably when I moved to my role in the emergency medicine department, while retaining a foot in the intensive care camp as well.

Who's your audience?

The website is aimed at critical care and emergency medicine practitioners. One of the drawbacks to podcasting is that the audience isn't very interactive. From the stats I get from the company that hosts the audio files, I know that 80% of my audience are in the U.S., of which 60% are in California, for some reason. With the website, again most of the audience is American. They have taken up the technology of podcasting more than we have in the UK.

> "mixture of blog posts and podcasts about critical care"

What's the critical care practitioner role in the UK?

The critical care practitioner role is relatively new in the UK. Before the critical practitioner role was introduced, a nurse in intensive care could get as far as senior sister level, then go either into education or management. There was not the opportunity to go further in a clinical role. Due to Modernising Medical Careers (specialtytraining.hee.nhs.uk) and the European working time directive, the junior doctors coming through intensive care spend 4-6 months maximum in the ICU before rotating elsewhere. That created problems as there was no consistency amongst the junior workforce and there were also gaps to fill, hence the decision to train senior nursing staff up to master's degree level with various other technical skills to enable them to work alongisde the junior medical staff and be part of the the medical rotation, taking on a lot of the tasks that the doctors used to do. It's been successful since it started in Devon around 7 years ago. My hospital was one of the early sites to do it. More and more centres are employing critical care practitioners. The advanced practitioner role is not just in critical care, it's in A&E, surgery, medicine, elderly care, frailty and so on. It's a role that's definitely here to stay.

What equipment do you use for Podcasting?

It cost me next to nothing to set up. You only need a computer with a microphone, a program to edit the sound files (I use Audacity, a free program) and iTunes. There is a cost for hosting sound files. If you host the sound files with your web company, it takes a lot of space on their servers, which is not ideal. So I pay a small fee to a company that hosts the sound files.

What has been your most popular podcast?

- One I did with Ollie Poole, a respiratory therapist in Canada. He does a series on YouTube (https://iii.hm/35i) where he talks to people about the way we can do mechanical ventilation, the various settings. We've produced three podcasts together on a similar vein: *CCP Podcast 018: Mechanical Ventilation* (https://iii.hm/35j); *CCP Podcast 024: Mechanical Ventilation…the basics* (https://iii.hm/35k) & *CCP Podcast 034: Mechanical Ventilation…Types of breath* (https://iii.hm/35l).

What medical podcasts do you listen to yourself?

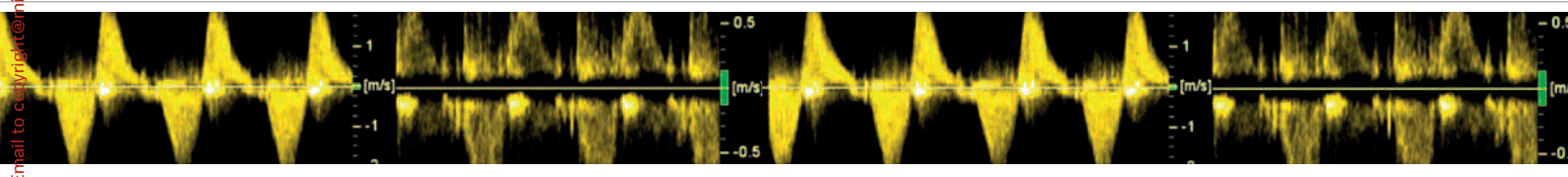
- *EMBasic:Your Boot Camp Guide to Emergency Medicine* - Steve Carroll (**embasic.org**). I like his style, because he presents information in a stuctured way.
- *EMCrit* - Scott Weingart (**emcrit.org**). Scott is well known in the podcasting world.
- *Pre-hospital emergency medicine* - Minh Le Cong (**prehospitalmed.com/category/prehospitalpodcast**). Minh is a flying doctor in Australia. I interviewed him for one of my podcasts, *CCP Podcast 010: Cricoid Pressure: Do it? Do it right? Or don't do it at all?* (**criticalcarepractitioner.co.uk/ccp-podcast-010-cricoid-pressure-do-it-do-it-right-or-dont-do-it-at-all**).

If our readers haven't listened to a podcast yet, where should they start?

- I don't recommend medical ones to start with. I suggest the first series of *Serial* (**serialpodcast.org/season-one**).

Further Information

- Subscribe to Critical Care Practitioner podcasts at:
  - iTunes - (**https://iii.hm/35m**)
  - Android – via the Stitcher app (**https://iii.hm/35n**)
- Subscribe to Critical Care Practitioner updates at **criticalcarepractitioner.co.uk**
- How to get a Podcast? **serialpodcast.org/how-to-listen**
- Audacity **audacityteam.org**



RESOURCE ALLOCATION IN HEALTHCARE

HAVE WE MISJUDGED SOCIETAL VALUES?

Fiona Kiernan
Consultant
Intensive Care Medicine
Beaumont Hospital
Dublin, Ireland

fionakiernan@rcsi.ie

Equitable Healthcare

With increased emphasis on financial constraint in healthcare, resource allocation discussions are heard more commonly in clinical departments. As agents of the patient, clinicians are faced with struggles to ensure that individual patients can receive costly treatments, despite growing demands for healthcare throughout society. It increasingly seems as though there is a conflict between the right of the individual to receive treatments, and the rights of society, who pay for it (Bulger et al. 1995). As this conflict grows, we should ask ourselves if the problem is in part due to our failings in understanding public preferences, as we may have misjudged societal values in the allocation of healthcare resources.

Innovations in healthcare have been responsible for a significant improvement in morbidity and mortality, resulting in an estimated seven-year increase in life expectancy between 1960 and 2000 in high income countries (Cutler et al. 2006). This comes at a price, however, as innovations in healthcare require a concurrent increase in healthcare expenditure. EU projections of spending on healthcare suggest that by 2060, average spending for the EU12 countries will reach 9 percent of gross domestic product (GDP) and 8.7 percent of GDP for the EU15 (Pryzwara 2010). Following the turbulence of a global economic crisis, together with rising healthcare expenditure, containing costs appears to have become the goal of both governments and private insurers. Yet in the face of rising costs and discussions about the sustainability of current levels of healthcare expenditure, it is even more important that decisions about necessary levels of spending, and how these resources should be distributed, should include the values of those who pay for it. Societal value judgments play an important role, now more than ever, in ensuring that the provision of healthcare is fair and equitable (Daniels 2013).

However, in reality society's opinion is rarely included. In areas of resource allocation within healthcare, the opinions of the public have consistently been shown to be different from those of healthcare professionals and politicians (Kinnunen 1998). In the emotive world of resource allocation in healthcare, we tend to assume that in order to provide care for an individual, we prevent other members of the public from accessing this care. In doing so we forget about the benefit that society gains through acts of altruism. In essence, we forget that society cares for the individual. Following are the steps through decision-making in resource allocation, which draw attention to the possibility that healthcare professionals may be wrong in assuming that we must trade off care for one against care for many. Furthermore, Big Data may have a role to play in helping us determine true societal values.

Equity-Efficiency Trade-Off

Fair resource allocation relies on the determination of an equitable and efficient trade-off, and is a focus of welfare economics. This trade-off can be long term, that is a trade-off between current and future generations, or it can be in the shorter term, between those requiring healthcare at a given point in time. The concern of all stakeholders is how to fairly balance the delivery of finite resources to one individual, therefore decreasing available healthcare for the rest of society. This balance is referred to as the equity-efficiency trade-off (Investopedia 2016). However, even the use of the term "trade-off" ignores the fact that society can benefit from delivering care to individuals. We know that individuals derive a benefit from altrusitic deeds, including blood donation, cadaveric organ donation and indeed stranger-to-stranger living organ donations (Steinberg 2006). We can assume that society and the public care about others' health, as demonstrated by the importance of healthcare on the political agenda, and the degree of funding delivered to medical charities (Hanson 2008). While economists argue that the most appropriate perspective for economic analyses is societal (Byford and Raftery 1998), the reality is that while the costs taken in these equations are societal, the benefit gained by society from helping individuals is not included in economic analyses within healthcare. In fact we examine benefits that accrue to the individual patient, their family or their community. If an equity-efficiency trade-off is required to appropriately distribute healthcare, then the preferences of and benefits to the public matter in determining how to allocate resources.

Agency Relationship

Decision-making in healthcare is undertaken by clinicians, who act as agents for the patient. Blomqvist went even further in describing them as triple agents in the delivery of resources, as they act for the patient, for society and to some extent in a self-interested way as their own agent (Blomqvist 1991). An additional agency relationship exists between society and policymakers, whose role should be to act in the best interests of the public. However, while both clinicians and policymakers appear to have similar stated beliefs regarding the optimal allocation of resources in healthcare, these differ from the opinions of the public. Evidence from Australia comparing the attitudes of various stakeholders within the healthcare system showed that doctors and the public differed in their attitudes to managing a healthcare system that was under substantial pressure due to costs (Robertson et al. 2011). For example, the public were more likely than doctors to believe that drug companies and lobby groups were responsible for increasing medical costs. However, the public were also more likely to believe that increasing costs were due to patients failing to take responsibility for their own health. In addition, fewer doctors than patients believed that the doctor should be responsible for educating the public regarding healthcare costs (Robertson et al. 2011).

In the face of such discrepancies in values, is the position of the policymaker and clinician as an agent of society untenable?

Measuring Societal Preferences

Rather than relying on an agent to understand societal values, perhaps we should rely on public opinion instead? This builds on the idea that decisions taken by a large group may be better than those taken by a small group, even when that small group is composed of experts (Surowiecki 2004). One of the major concerns with using societal/ public preferences is how to accurately measure them. We need to pay particular attention to how data regarding these preferences is obtained, as accurately measuring areas of public opinion is fraught with methodological concerns. Using survey questions targeted at a representative cross-section of the population to rank the priority of various health policies may appear, at first, to be a reliable source of data. Through surveying we can determine the stated preferences of that sample. However, using these stated preferences conflicts with aspects of both theoretical and experimental economic research, which suggests stated preferences do not represent true value judgements. For example when consumer choice is examined, the stated preference (the purchase a consumer tells us they would make) is less reliable than revealed preferences (the actual purchase they make) (Wardman 1988). Economists tend to reject the use of stated preferences in favour of revealed preferences. Studies examining the differences between stated and revealed preferences in healthcare have shown a discrepancy between the two groups, although they have mainly focused on willingness to pay studies (Blumenschein 2001).

Social Media as a Measure of Preferences

While it is relatively easy to determine an individual consumer's revealed preference for an individual purchase, examining the revealed preferences of a society for the distribution of a public good is clearly a different and more difficult scenario. Public discourse plays an important role in democracies, not only in forming values, but also in reflecting them (Della Carpini et al. 2004). Both the act of talking as an individual in public and conversations with fellow citizens allow the expression of views, the development of shared concerns and preferences, and enable society to reach a consensus about matters of public concern (Chambers 1996). Perhaps more importantly though, analysis of the most common topics of public discourse can show us what is of most concern to the public.

> "we may have underestimated the degree to which the public cares about individuals"

Increasingly people turn to social media to document events and issues that concern them, and in doing so they provide us with a real-time account of issues that concern the public. Social media monitoring has the ability to quantify positive and negative reactions to policy, including health policy. Analysis of social media is now a well-described method of analysis of public opinion (O'Connor et al. 2010), and allows unheard voices to enter the process of discussion of both policy and politics (Anstead and O'Loughlin 2015), of which resource allocation in healthcare is undoubtedly a feature. This is not a new use of social media content. It has previously been used to assess public responses to long-term political problems, including economic downturn (Gonzalez-Bailon et al. 2010). Along with public opinion, public mood can also be captured by analysis of social media, demonstrated by analysis of a Twitter feed in a study from the University of Bristol (Lansdall-Welfareet al. 2012). In this study, the researchers identified four key moods — anger, joy, fear and sadness — and linked these moods to words. They noticed that words associated with joy were particularly evident at Christmas, while words associated with a negative mood were found in mid-October 2010. The researchers noted that this corresponded to a time of large cuts in public spending. Furthermore, anger appeared to increase around the time of the summer riots in London in August 2011.

However, using Big Data methodology to analyse public opinion carries its own risks. The social value judgments recorded are likely to represent only a proportion of the population. According to the Oxford Internet Survey, social media users, in particular Twitter users, tend to be young, well-educated, and live in urban areas (Dutton et al. 2013). Analysing tweet data alone does not take into account the values of those who choose to engage by following the conversation, rather than entering it. Furthermore the number of tweets discussing a subject may not relate to the number of Twitter users who care about the issue — in an analysis of 26,000 uses between February and December 2011, it was found that 1 percent of users accounted for two thirds of tweets (Bruns, & Burgess 2012).

Conclusion

A combination of stated and revealed preferences may be the most acceptable means of determining social values. However, as healthcare professionals involved in resource allocation decisions, it is time for us to realise that what we consider to be a conflict between the right of the individual to healthcare and the right of society to those same resources, may not be a conflict for society itself. We may have underestimated the degree to which the public cares about individuals. Big Data has given us the opportunity to include revealed preferences in the equity-efficiency trade-off. Despite the uncertainty that it brings, we should welcome its inclusion in making decisions about resource allocation in healthcare. ■

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ANAESTHESIOLOGY AND INTENSIVE CARE MEDICINE

INTERVIEW WITH PROFESSOR SHARON EINAV

Professor Sharon Einav is Chair of the Intensive Care Medicine Subcommittee of the European Society of Anaesthesiology. She is Professor of Intensive Care, Hebrew University Faculty of Medicine, Director of Surgical Intensive Care and Chair of the Resuscitation Committee at Shaare Zedek Medical Center, Jerusalem, Israel. Prof. Einav is the Israel country representative for the European Society of Intensive Care Medicine, and is a member of the Steering Committee, Disaster Response Network, American College of Chest Physicians.

ICU Management & Practice spoke to Prof. Einav about the anaesthesiology/intensive care medicine interface, mass casualty events, monitoring, the key points of airway management and more in advance of the European Society of Anaesthesiology's annual congress, which will be held 28-30 May in London, UK.

What can anaesthesiologists bring to the multidisciplinary intensive care team?

Anaesthesiologists induce critical physiological dysbalance on a daily basis (often with the aid of our surgical counterparts). We then rapidly counterbalance the physiological derangement by providing appropriate support. In other words anaesthesiology training involves the management of an individual patient at a time of crisis. One learns to handle respiratory crises (e.g. hypoxia, apnoea), cardiovascular crises (sepsis, haemorrhage), neurological crises (spinal hypotension, loss of consciousness, arousal restlessness) and more.

This experience with 'extreme physiology'—live, at the bedside, and in the most difficult of situations—we carry over into the ICU. This includes familiarity with drugs that increase and decrease blood pressure or heart rate within minutes, familiarity with the fine balance between analgesia, amnesia, anaesthesia and muscle relaxation (if and when these are required), familiarity with the nuances of airway management in complex patients and a knowledge of the abilities and limitations of the devices that can be used for monitoring and support during these crises.

What are the advantages of training in both anaesthesiology and intensive care medicine?

First and foremost the ability to speak a common language. This can be very important for ensuring continuity of care in the perioperative period. Imagine two cooks baking a single cake: the first prepares the dough and places the cake in the oven. The second takes the cake out of the oven and makes the topping of the cake. Just as there is no single ideal baking technique, there is also rarely a single 'correct' way to manage a complex patient. Clearly this requires close collaboration. Ideally, the two would sit together and make a common plan. Alternatively they should have similar training and speak the same language. Sometimes, even if they do speak a common language, they may prefer different ingredients and have incompatible techniques.

The second advantage of training in both anaesthesiology and intensive care is the difference in perspective. Seeing the patient from only one perspective is like having two-dimensional vision. Seeing both perspectives gives the clinical picture a third dimension. Anaesthesia is directed by production pressure and patient safety, is very practical and looks at immediate results. Anaesthesiologists often lack information regarding the long-term implications of their practice, and in some places even perceive themselves solely as providers of a service. Intensive care doctors not only see the long-term implications of various practices but also view themselves as primary care physicians. On the other hand we do like theorising quite a bit…

What are the main challenges for anaesthesiologists working in intensive care?

Anaesthesiologists are accustomed to working alone (or in pairs, at most) and are rarely called upon to discuss their plans or impart information. Although we work with surgeons and operating room nurses, communication is minimal. So much so in fact that the 'time-out' was instituted to ensure that this small team has similar plans for their single patient.

In the ICU teamwork is the name of the game. One must develop excellent communication skills in order to share ideas, intentions and concerns with our colleagues, our peers and our nurses in a manner that is conducive to collaboration. One must also learn to conduct a formal learning/teaching round and deliver bad news to families.

You have researched critical care response to mass casualty incidents. What are the challenges for intensivists and anaesthesiologists?

Triage is traditionally considered the responsibility of the surgeon in the emergency room. However, in a mass casualty event an experienced anaesthesiologist or intensivist may sway the decision of a surgeon with less trauma experience regarding expectant care. This triage process does not end at the door of the emergency room (ER), but extends to the question of whether we should discharge one ICU patient in order to admit another. In a series of interviews we conducted on management of mass casualty events this was often cited as one of the most troubling aspects of patient care in such events (Einav et al. 2006).

Another major challenge is the need to separate politics from medicine. In this we are no different from our surgical colleagues. The care delivered to the patients must remain independent of our personal sentiments, opinions, preferences and value judgements. We must remain committed to the best interest of our patients regardless of whether they are perpetrator or victim and irrespective of the political and/or religious gulf that may lie between us.

Finally there is the issue of long-term ICU medical care. Long after the media have turned to new topics of interest and the surgeons have finished extolling the lifesaving heroic feats they performed in the operating rooms, intensivists are still caring for these patients and their families in the ICU. The fact that a patient has survived a mass casualty event does not mean he/she has gone home intact. Many of these patients suffer long-term sequelae. The realisation that their lives have probably been changed forever dawns on both the patient and their families during their ICU stay. And when they go through this process we go through it with them. By this time, there are no heroics and the glory of saving lives is all gone. All that remains is hard work and the challenge of continuing to hope for more improvement.

What can delegates expect from the intensive care track in the 2016 Euroanaesthesia congress?

The programme for the 2016 Euroanaesthesia congress was crafted to cover multiple aspects of intensive care as well as some general topics of interest. Some lectures are intended to provide practical tools for management of common clinical situations: septic shock, acute respiratory failure and antibiotic therapy. Other sessions cover more theoretical knowledge. For example, "Affairs of the Heart" will touch upon the interactions of the heart with the lungs and the brain and how these may affect outcomes. We also provide interest for those who wish to focus on research in a session with prominent "out of the box" speakers who will share their insights on the last decades of intensive care research with the audience ("Science, research, and intensive care"). We expect heated discussion when education and politics are intertwined in the session on "Anesthesia and intensive care - a love-hate relationship?". For those fond of technological tools we provide a glimpse into the future in the session "How can our computers serve us". The panel on "Oxygen!" will include much of the controversy surrounding oxygen administration in recent years. Finally, those who want an update on the most important publications in intensive care in the last year are welcome to join the "Best of Intensive Care" session.

> **"meaningful personal reflection is critical in the development of an expert"**

You are making a presentation at Euroanaesthesia 2016 on "Diagnosing death by resuscitation?" Please share your key points.

In-hospital cardiac arrest is often preceded by signs and symptoms of impending collapse that could be identified by professionals. It is expected that medical professionals would be able to recognise patient deterioration at an early stage. In reality, predicting the limits of patient tolerance represents one of the most challenging issues within hospitals in general and within critical care medicine in particular. Although approximately 60% of cardiac arrest events have at least one documented antecedent the medical response often occurs too late. Medical training and experience, it would seem, do not make the practitioner more sensitive to the nuances of physiological change prior to patient collapse. There are multiple causes for this phenomenon, some of which are discussed.

In addition, the ability to provide an effective response hinges not only on situation recognition but also on willingness and ability to respond. It is assumed that hospital staff are all willing and capable of performing cardiopulmonary resuscitation. However, there is very little data to prove the former and an accumulating amount of data suggesting quite the opposite regarding the latter. Despite extensive investment in staff training and introduction of standardised defibrillation equipment into most hospital wards, which should theoretically lead to excellent performance during resuscitations, performance remains poor and multiple errors occur. Almost a quarter of the cases entered into the American Heart Association (AHA)'s Get with the Guidelines National Registry of CPR (https://iii.hm/35g) reported some mistake occurring during resuscitation; during airway management, during defibrillation and certainly during administration of medication. Poor performance of chest compression is common and prolonged hands-off time occurs in more than a quarter of the patients. We are seeking a way to improve but things are more complicated than they seem. My talk will be accompanied by recordings of real resuscitations.

What are the key points in managing difficult airways? What are the most promising developments?

The last few decades have seen significant changes in airway management. The first occurred when anaesthesiologists recognised the risk of entrenchment in a specific airway management technique when it may not be appropriate. As a result all anaesthesiologists are expected to know the action flowchart, which includes the option of moving from one management option to another and one managing person to another. In terms of device development, there have been two major leaps forward—the first was the use of laryngeal mask airways and the second was the use of fibre-optic laryngoscopes.

Airway management of a patient with compromised gas exchange is an even greater challenge than airway management for surgery; when the patient has little reserve there is no place for indecision. With time, I believe we will continue to learn to use less and less invasive airway management.

However, until then, the key points of airway management in the ICU are:

(A) Do not let the patient take the lead. It is better to intubate before collapse occurs.

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(B) Always have options B and C ready and make sure everybody on the team knows what they are.
(C) "Failure to intubate" is only failure if you have lost the airway. If you let someone else try and they succeed—you may have saved the patient's life by not giving in to your ego.
(D) Do not hesitate to demand that the conditions for intubation be optimal (e.g. preoxygenation, patient position, depth of sedation, monitoring).

What role can anaesthesiologists take in pain management in the ICU?

Critically ill patients suffer a great degree of pain and discomfort: they are immobilised, they undergo multiple procedures and operations, they are invasively monitored and more. Not all anaesthesiologists are experts in pain management. However, anaesthesiologists are very experienced with drugs that provide analgesia through a variety of effects, some of which are better than others for specific situations (e.g. organ failure, respiratory, haemodynamic or neurological compromise). Anaesthesia training also includes the use of local and regional pain management techniques and modes of patient-controlled analgesia. These too can be put to good use to ease patient discomfort.

What are the most promising developments in invasive monitoring of critically ill patients?

This is very much a matter of personal opinion, but to my eyes noninvasive monitoring is much more promising than invasive monitoring. It carries less danger and discomfort for the patient and the data we can get with such methods is far from negligible. I cannot think of an invasive monitor that has led to the revolutions in clinical care that have resulted from the use of electrocardiography, pulse oximetry, capnography and echocardiography. The most exciting project that I am currently working on is with partners in the Department of Applied Physics in my university, the Hebrew University of Jerusalem, who have discovered that the human body emits a signal that we have been unaware of thus far. We are now attempting to correlate it with the physiological information we suspect it reflects. If we prove right the findings may well be revolutionary (Kurzweil-Segev 2014; Safrai et al. 2014).

What is the role of capnography in the ICU? Should it be routinely used?

At the very least capnography should be used to monitor patients as they are monitored in the operating room. It seems odd that when the patient moves from the OR to the ICU, where there is less individual supervision, there would be a step down in monitoring. This rarely occurs with other types of monitors, but occurs routinely with capnographs.

The American Society of Anesthesiologists (ASA)'s closed claims analysis (**asaclosedclaims.org**) has demonstrated a high proportion of cases with liability due to airway management problems that resulted in severe neurological injury. Introduction of mandatory capnography decreased the proportion of such cases significantly. Critically ill patients have more complications during intubation than do elective anaesthesia cases. Some studies have shown a complication rate exceeding 10% in ICU patients. Many of these can be prevented with appropriate airway monitoring.

Last but not least is the issue of blood sampling. Any tool that can be used to decrease the number of blood samples we take from our patient benefits them. Many practitioners hesitate to rely on capnography because of the arterial–alveolar gradient in CO_2. However the rules for that are simple: End tidal CO_2 is always lower than $PaCO_2$. An end tidal to arterial CO_2 difference of 2-5 mmHg is normal. If the gradient broadens your patient needs additional workup, since for some reason CO_2 removal (i.e. ventilation) is no longer keeping up with CO_2 production (i.e. metabolism). If the cause of the increased gradient is known, you can follow the gradient trend as an indirect indicator of response to treatment.

This interview will be published in *ICU Management and Practice's* issue with a cover story on Safety. Anaesthesiologists have been at the forefront in patient safety in healthcare. What still needs to be done in patient safety?

There is a need to standardise patient care across the operating room (OR) and ICU. For example, the use of similar syringe pumps would allow a simple exchange of pumps rather than transfer of a critical drug from one pump to another, which may result in inadvertent drug delivery changes. Similarly, standardisation of treatment plans across the board would result in fewer redundant procedures and drugs. A classic example is the insertion of a dedicated total parental nutrition (TPN) line in the OR when there is no intention of initiating TPN for the next week, or alternatively neglecting to insert a feeding jejunostomy in the OR during surgery of a malnourished patient.

Further Reading

Prof. Einav's Zoom On profile is published on the *ICU Management & Practice* website **https://iii.hm/35z** ■

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CRITICAL CARE MEDICINE IN SRI LANKA

AN EVOLVING SPECIALTY

Chulananda Goonasekera*

cgoonase@gmail.com

Rohan Dissanayake

Lakshman Karalliedde

Sumanasiri Kolombage

Chaminda Wickramaratne

Sri Lanka Society of Critical Care and Emergency Medicine

webadmin1@ssccem.com

ssccem.com

* corresponding author. The authors are all founder members of the Sri Lanka Society of Critical Care and Emergency Medicine

Sri Lanka is steadily progressing to establish critical care medicine as a separate specialty with fully trained intensivists and nurses playing pivotal roles, as in the developed world. Most general and teaching hospitals of the country already have fully equipped intensive care units. Establishment of an intermediate level diploma qualification for doctors in 2009, and recognition of critical care medicine as a separate specialty by the Government of Sri Lanka in 2011 are the recent milestones. With two academic societies, i.e. Sri Lanka Society of Critical Care Medicine and Emergency Medicine and Sri Lanka College of Anaesthesiologists enthusiastically prompting relevant teaching and training for doctors and nurses, conversion of current 'open' concept ICUs to 'closed' concept ones would soon follow. This article is about its path of evolution.

Historical Background: 1952–2002

Evolution of Surgical Recovery Units

The need to provide special care for patients who were critically ill was accepted by all clinicians in Sri Lanka. As with other developing countries, shortages of manpower and equipment enabled the provision of such care in sections of the general wards initially, where there was an increased ratio of nurses to patients and equipment to provide respiratory care in particular as well as limited equipment to monitor physiological parameters. During the early 1950s a separate section in the thoracic ward at the premier hospital in Sri Lanka, the General Hospital, Colombo, was designated a surgical recovery area, where an electrocardiography (ECG) monitor was available for immediate postoperative patient monitoring. In the early 1960s, an East Radcliffe ventilator was available in this recovery area while iron lungs were in use in some other hospitals, mainly for the management of patients with severe poliomyelitis.

The following years saw the establishment of more surgical 'recovery units' adjacent to operating theatres in larger general hospitals of the Ministry of Health with facilities for short-term mechanical ventilation. Later on, the recovery unit established in the General Hospital Colombo further expanded to include 2 beds for medical patients and neonates who needed to be ventilated. This facility was officially named the Surgical Intensive Care Unit (SICU) of the Colombo General Hospital in 1968. It had six beds equipped with ECG monitors, invasive blood pressure and central venous pressure (CVP) monitoring facilities, three Bennett Pressure cycled ventilators and a Radiometer blood gas machine (Jayawardene 2007). In the 1970s some hospitals reported successful short-term ventilation of patients manually or using an East Radcliffe ventilator, for example in the thoracic unit Jaffna post surgically, and in Kandy for patients with tetanus.

The country's first multidisciplinary intensive care unit was designed, built and equipped by the Japanese Government as a gift to the Government of Sri Lanka in 1980 at the new teaching hospital at Peradeniya. Its five-bed ICU was fully equipped with products of Japanese technology for remote patient monitoring and advanced ventilation along with on-site blood gas and electrolyte measurement facilities. In 1984 a six-bed intensive care unit was also installed at the General Hospital, Jaffna.

There was an increased demand for beds in intensive care units as the available beds served all specialties in the hospital and many with life-threatening disease states were deprived of necessary care. In this context 'Friends of Critical Care', established in Kandy in 1998, was an example of public support for such a venture. As a consequence, political interests grew to support development of critical care. In 2002 medical professionals from various specialties together founded the Sri Lankan Society of Critical Care and Emergency Medicine with the motto of being the "pulse of the critically ill". Installation of new services such as renal replacement therapy supported enhancement of medical services to new heights. The initiation of a national kidney transplant programme for children at Peradeniya in 2004 had a direct link to the availability of a continuous renal replacement therapy service in its critical

care unit (Abeysekera et al. 2007). Advancing critical care also contributed much needed research insight to enhance care for adults with organophosphate poisoning and envenoming (Karalliedde and Senanayake 1988; Munidasa et al. 2004). Most critical care units established around the country were multidisciplinary and some had facilities for children (Mudalige et al. 2009).

Current Status: 2002–2016

Sri Lankan Society of Critical Care and Emergency Medicine (SSCCEM)

At the outset, the founder members of SSCCEM comprised specialists from the major specialties of medicine, surgery, obstetrics and gynaecology, paediatrics and anaesthesiology. Over the years the society has grown to its current membership exceeding 200.

Since 2002, the SSCCEM (**ssccem.com**) has conducted numerous academic activities with the collaboration of intensivists and emergency physicians from around the globe, especially from the Australian College of Emergency Medicine, and the Indian Society of critical care medicine. Many Sri Lankan expatriates with an interest in the fields of critical care and emergency medicine also voluntarily contributed.

The Emergency Life Care (ELC) Sri Lanka, Basic Assessment & Support in Intensive Care (BASIC) course (**https://iii.hm/38x**) and WINFOCUS (**winfocus.org**) are some of the internationally recognised courses regularly conducted by the SSCCEM annually and biannually. Medical officers with postgraduate training in critical care medicine and emergency medicine actively participated in these activities of the SSCCEM.

With an unhindered commitment, members of the SSCCEM became the predominant force that persuaded policymakers of health services in Sri Lanka to accept the need for high-quality care for the critically ill patient. The national recognition of both intensive care medicine and emergency medicine as separate specialties in 2011 was a direct consequence. The SSCCEM's annual scientific sessions conducted every year since 2007 have become a much anticipated academic event in the local calendar with international participation. In 2011 the SSCCEM hosted the award-winning liver transplant team from the Mayo Clinic in the USA and conducted a comprehensive workshop on the subject.

In 2014 the SSCCEM hosted the15th scientific meeting of the Asia Ventilation Forum in Colombo. In July 2016 SSCCEM will be hosting the 2nd South Asian Association for Regional Cooperation (SAARC) critical care congress (**https://iii.hm/38y**), the scientific meeting of the Associations of SAARC critical care societies, which includes India, Sri Lanka, Pakistan, Nepal, Bangladesh, Bhutan, Maldives and Afghanistan. SSCCEM is now a dynamic society sharing knowledge and skills from experts in critical care and emergency medicine to provide the best care for the critically ill patient.

The SSCCEM has secured membership in many international bodies of critical care and emergency medicine including the World Federation of Societies in Critical Care Medicine, International Federation of Emergency Medicine, Asia Pacific Association of Critical Care Medicine, and the SAARCC Societies of Critical Care Medicine.

Postgraduate Institute of Medicine, Colombo

Critical care medicine has evolved on the principle that patients with serious illness are better managed when grouped to a separate area, and treated by a dedicated team of healthcare providers. Most countries in the developed world and many in the developing world installed dedicated intensive care training programs that produced intensivists. As a foundation for this process and promoting efficient and cost-effective 'closed' intensive care practice practice (Ghorra et al. 1999) in Sri Lanka, a Board of Study for Critical Care Medicine and Emergency Medicine was established in 2008. Sri Lanka did not have a professional category named intensivists. Thus the board was multidisciplinary and constituted clinicians of high academic standard with a special interest in critical care medicine (**https://iii.hm/38z**). Its main function was to expand critical care and emergency medicine teaching and training and produce required specialists for the country. To fulfil this need, as its first step, a Postgraduate Diploma in Critical Care Medicine was established in 2009 with an annual intake of 20 students (Rajapakse 2009). Its first batch of diplomates qualified in 2011. The College of Paediatricians of Sri Lanka formulated a comprehensive training programme to produce pediatric intensivists in a separate stream.

> **"Sri Lanka Society of Critical Care and Emergency Medicine...sharing knowledge and skills to provide the best care for the critically ill patient"**

Whilst PGIM was taking the lead in the development of critical care medicine, a journal, the *Sri Lanka Journal of Critical Care,* was also launched to support this cause (**sljcc.sljol.info**).

Sri Lanka College of Anaesthesiologists

In 2010 a Faculty of Critical Care Medicine was established under the College of Anaesthesiologists of Sri Lanka in 2010 (**criticalcare.lk**) that promoted the existing 'open' intensive care concept. In order to recognise its contribution to critical care the College was re-named in 2014 as the College of Anaesthesiologists and Intensivists of Sri Lanka. They too were devoted to enhance critical care practice through ongoing professional education.

In 2013 the Board of Study in Anaesthesiology of the Postgraduate Institute of Medicine of the University of Colombo developed a hybrid model of training for anaesthesiologists and general physicians to master the now clearly defined specialty of critical care, following their MD qualification.

*National Intensive Care Surveillance System (**nicslk.com**)*

National Intensive Care Surveillance was an initiative undertaken in 2012 to promote an ICU bed availability system and a critical care clinical registry for Sri Lanka. It was established with national and international collaboration led by the Ministry of Health, Sri Lanka. Its mission is to contribute to the improvement of critical care services through regular audit and standardisation of services to meet the needs and to introduce also a cost-effective bed management system.

National Audits and Standards

A national audit conducted in 2004 on intensive care services of Sri Lanka included 49 ICUs in the government sector hospitals (Yatawatte et al. 2008). 57.1% of those units were in the teaching hospitals and nearly half (51%) were 'general' ICU, i.e. serving patients of all specialties requiring care that was not available in the wards. A ventilator: bed ratio of 1:1 or more was seen only in 57% of units. This audit recognised that the standards and

management strategies practised in these ICUs varied widely, and suggested that the inability to establish closed-type ICUs in the country was a reflection of the non-availability of sufficient numbers of medical and nursing specialists in intensive care.

In 2012, another review was undertaken with an attempt to determine where Sri Lanka stands in the chain of evolution of critical care in the world. A cross-sectional observational study of all adult intensive care units in state sector hospitals in Sri Lanka recruited a total of 51 ICUs (Fernando et al. 2012). They concluded that hardly any changes had occurred in the areas of bed numbers, staffing, staff training and availability of allied facilities when compared to the audit of 2004 (Yatawatte et al. 2008). They also found that approximately 75% of ICUs were led by consultant anaesthetists, who had a major share of their work in the operating theatres. Amongst junior doctors, only 60% were dedicated for intensive care whilst the remaining 40% shared work as anaesthetists. The training and skills, seniority and competencies of both doctors and nurses were inconsistent due to ad-hoc training patterns. The researchers concluded that this working pattern was not conducive to efficient intensive care practice (Fernando et al. 2012). They also highlighted that Sri Lanka too should adopt regulations and recommendations to maintain the standards in a cost-effective manner as observed in other countries. In order to achieve this goal, qualified intensivists are needed to take a lead role, whilst intermediate-level training and certification is needed for both medical officers and nurses involved in critical care services (Briggs et al. 2006).

The Future: 2016 and beyond

Critical care medicine has two fundamental components in the provision of care: vital organ support and root cause identification and treatment. Although, traditionally, anaesthetists have been trained to provide vital organ support, respiratory and haemodynamic in particular, the world has moved towards a model of having dedicated trained intensive care specialists to improve outcomes. This is because prioritised multi-organ support is now an essential prerequisite for modern intensive care that requires multiple teams of expertise concurrently to manage extracorporeal systems such as extracorporeal membrane oxygenation (ECMO), continuous renal replacement therapy (CRRT) and install advanced monitoring such as intracranial pressure (ICP) and cerebral perfusion whilst also managing newer therapeutic environments such as hypothermia. Further, specialist anaesthetists with shared responsibilities elsewhere are unable to devote the time needed in the care of the critically ill and relevant continuing education.

Modern critical care is a separate specialty (Hawker 2009). While multi-monitoring, nursing and ventilator support facilities are essential on a 1:1 basis, an in-house laboratory with the capabilities of analysing blood gases, glucose, electrolytes, haemoglobin, lactate and clotting profile is deemed optimal (Hawker 2009). Around the clock support of the departments of physiotherapy, radiology, pathology, cardiology, microbiology and pharmacy cannot be undervalued.

Over the years, intensive care has moved from the 'open' ICUs concept, where physicians and anaesthetists with other commitments provided care to patients in a segregated area of the hospital, to 'closed' ICUs, with dedicated specialist doctors and nurses with focused critical care training (known as intensivists). It is mandatory that training of intensivists conforms to international standards and the arena should be a multidisciplinary, complementary participation. Conversion of intensive care to a 'closed 'model reduces complication and mortality rates (Ghorra et al. 1999). Sri Lanka is yet to move towards a 'closed' ICU concept managed by board-certified intensivists. In this context, promoting postgraduate education from critical care diploma to specialist level is now essential. ■

Statistics	
Gross national income per capita (PPP international $)	9,470
Life expectancy at birth m/f	72/78
Probability of dying between 15 and 60 years m/f (per 1 000 population)	184/75
Total expenditure on health per capita (Intl $)	304
Total expenditure on health as % of GDP	3.2

Source: World Health Organization who.int/countries/lka/en Statistics are for 2013

Directory	
College of Anaesthesiologists & Intensivists of Sri Lanka	anaesthesia.lk
Faculty of Critical Care Medicine, College of Anaesthesiologists & Intensivists of Sri Lanka	criticalcare.lk
National Intensive Care Surveillance System	nicslk.com
Sri Lankan Society of Critical Care and Emergency Medicine	ssccem.com
Sri Lankan Society of Critical Care Nurses	ssccninfo.com

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AGENDA

JUNE

30–1 July
TCS-ECMO
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JULY

6-10
Annual International Best of Brussels Symposium on Intensive Care and Emergency Medicine
Pune, India
isccmpune.com

31
SAARC Critical Care Congress
Sri Lanka
https://iii.hm/38y

AUGUST

10-14
International Conference on Complexity in Acute Illness
Pasadena, USA
iccai.org

27–31
ESC
Rome, Italy
escardio.org/ESC2016

28 – 2 Sept.
World Congress of Anaesthesiologists
Hong Kong, Hong Kong
wca2016.com

SEPTEMBER

3-7
European Respiratory Society International Congress
London, UK
erscongress.org

7-10
WINFOCUS World Congress on Ultrasound in Emergency and Critical Care
Ljubljana, Slovenia
winfocus.org

7-10
European Society of Regional Anaesthesia Congress
Maastricht, the Netherlands
esra2016.com

17-20
European Society for Clinical Nutrition and Metabolism
Copenhagen, Denmark
espen.org

22-24
Société Française d'Anesthésie et de Réanimation
Paris, France
sfar.org

22-24
26th Meeting of the European Society for Computing and Technology in Anaesthesia and Intensive Care
Timisoara, Romania
esctaic.org

24-25
Resuscitation 2016 - European Resuscitation Council Congress
Reykjavik, Iceland
congress2016.erc.edu

OCTOBER

1-5
ESICM-LIVES 2016
Milan, Italy
esicm.org

1-5
EuSEM: 10th European Congress on Emergency Medicine
Vienna, Austria
eusem.org

3-5
International Federation of Shock Societies Congress
Tokyo, Japan
congre.co.jp/ifss2016

12-15
19th Asia Pacific Conference on Critical Care Medicine 2016
Bangkok, Thailand
apcccm2016.com

20-22
41st ANZICS/ACCCN Intensive Care ASM
Perth, Australia
intensivecareasm2016.com.au

21-25
EAPS 2016: European Academy of Paediatric Societies
Geneva, Switzerland
paediatrics.kenes.com

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NATIONAL CORRESPONDENTS
Prof. Dr. Dominique Vandijck (Belgium) — dominique.vandijck@ugent.be

MANAGING EDITOR
Claire Pillar — editorial@icu-management.org

EDITORIAL ASSISTANT
Dana Ungureanu — office@healthmanagement.org

GUEST AUTHORS
Lorenzo Ball, Frédéric Barbut, Danielle E Bear, Andreas Bergmann, Vineet Chopra, Javier Cobo, Oliver A Cornely, Rohan Dissanayake, Jonathan Downham, Sharon Einav, Marilu Giacalone, Chulananda Goonasekera, MHTM Haerkens, Vitaly Herasevich, Thomas M Hemmerling, Lakshman Karalliedde, K Kashani, Mark T Keegan, Fiona Kiernan, Sumanasiri Kolombage, Ed JKuijper, Margherita Labardi, CJ Lorraine, Nancy Moureau, Roberto Oggioni, M Ostermann, TC Oud, patientsafe team, Paolo Pelosi, Nicola Petrosillo, Brian W Pickering, P Pickkers, Zudin Puthucheary, Claudio Ronco, Marta Scabardi, Yuda Sutherasan, Takashi Tagami, Andreas Valentin, JG van der Hoeven, Chaminda Wickramaratne

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MEDIA CONTACT, MARKETING, ADVERTISING
Katya Mitreva — k.m@icu-management.org

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General Organisation: MCO CONGRÈS - Information: contact@eusemcongress.org
Villa Gaby - 285 Corniche Kennedy - 13007 Marseille - France / Tel: +33 (0) 495 09 38 00