ICU
MANAGEMENT & PRACTICE
VOLUME 17 - ISSUE 2 - SUMMER 2017

Cardiac Arrest

PLUS

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Peri-Operative Oxygenation: Novel Strategies to Optimize Oxygenation and Oxygen Delivery (DO_2)

Location: Room 4, PALEXPO Congress Center Geneva, Geneva, Switzerland

Date and Time: **Sunday June 4th • 12:15 - 13:45**
Lunch will be provided

Chairperson: **Prof. Jean-Louis Vincent**

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Presenters

The Importance of Individualized Oxygen Therapy: Harmful Effects of Hyperoxia in Postcardiac Arrest, Sepsis, Traumatic Brain Injury, or Stroke

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)
Brussels, Belgium

After All, Brain Oxygenation Is What Really Matters

Basil Matta, BA, BAO, BCh, MB, FRCA, FFICM
Divisional Director, MSK. Digestive Diseases, Major Trauma and Perioperative Care Medicine
Clinical Lead – Cambridge University Hospitals Trust
Consultant, Anaesthesia and Critical Care
Associate Lecturer, University of Cambridge
Cambridge, UK

Patient Customized Anaesthesia Care - Optimizing Blood, Oxygen and Fluids; Friends or Foes?

Aryeh Shander, MD, FCCM, FCCP
Chief Department of Anesthesiology
Pain Management and Hyperbaric Medicine
Englewood Hospital and Medical Center
Clinical Professor of Anesthesiology, Mount Sinai School of Medicine
Mount Sinai Hospital, New York

Detecting Dilutional Anemia : Why and How?

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

The Future of Noninvasive Monitoring - Beyond Pulse Oximetry: 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

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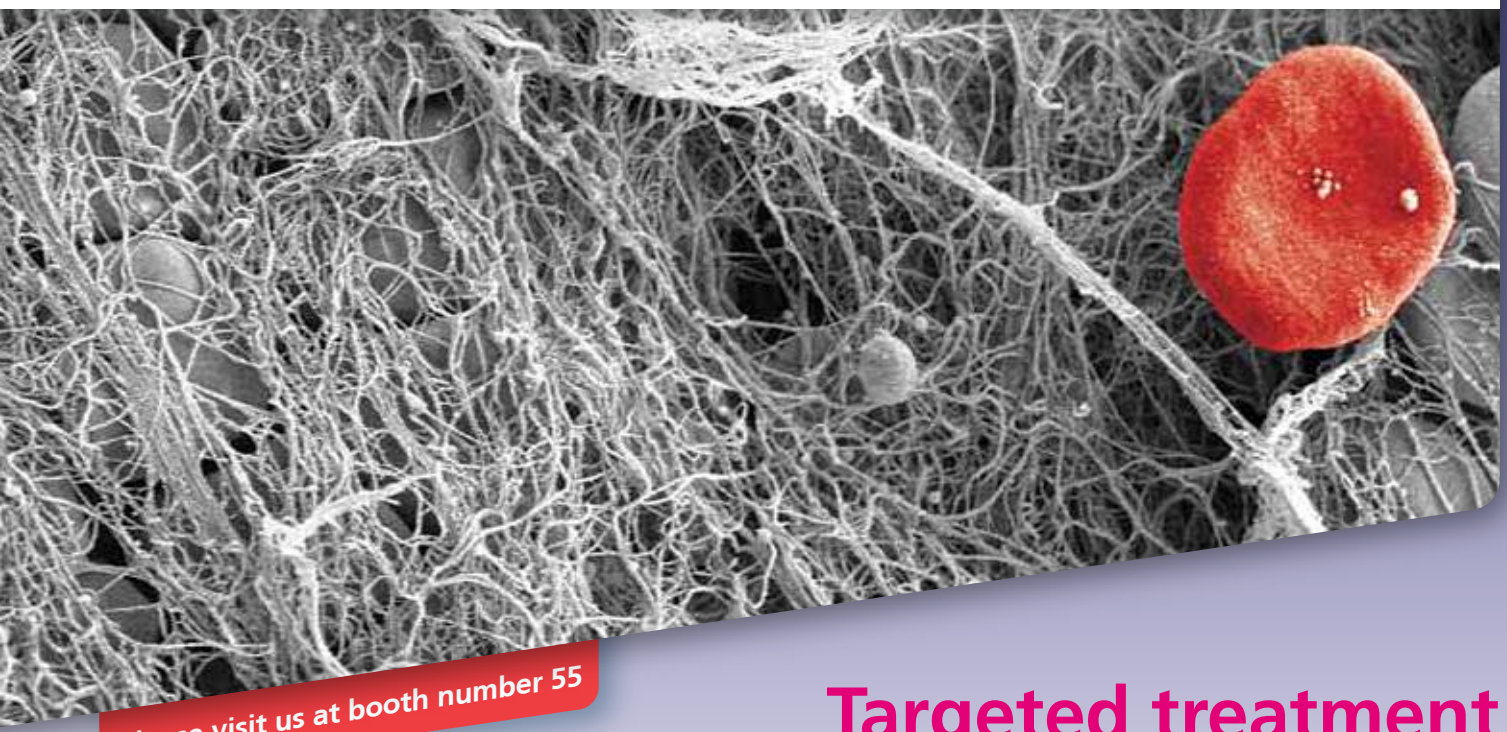

Please visit us at booth number 55

Targeted treatment to achieve haemostasis

Sunday 4 June 2017, 12:15–13:45

Room X, PalExpo, Geneva, Switzerland

CSL Behring-sponsored satellite symposium at Euroanaesthesia 2017

Programme

Chairs: *Donat R. Spahn (Switzerland) and Marco Ranucci (Italy)*

12:15 **Chairs' welcome**

Treatment of bleeding patients during therapy with non-vitamin K antagonists – Results from the French registry
Pierre Albaladejo (France)

Fibrinogen concentrate in elective complex cardiac surgery: a monocentric trial
Arno Nierich (The Netherlands)

The Fibcon study: Fibrinogen concentrate in paediatric cardiac surgery (a randomised cohort trial)
Shane Tibby (UK)

Treatment of trauma-induced coagulopathy with factor concentrates versus treatment with fresh frozen plasma
Petra Innerhofer (Austria)

Closing remarks

13:45 **Close of symposium**

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Lunch will be provided

Cardiac Arrest

The "chain of survival" metaphor for improving outcomes from sudden cardiac arrest (CA) was first coined in the 1980s. Since adopted by the American Heart Association and the International Liaison Committee on Resuscitation amongst others, it is a useful tool to concentrate efforts on how to optimise every link in the chain to improve survival and neurologically intact outcomes for CA patients. Mortality from out-of-hospital cardiac arrest (and indeed in-hospital) is still stubbornly high. Can we do better? At the "macro" level, initiatives to train lay people to perform cardiopulmonary resuscitation (CPR) will improve bystander resuscitation rates. Technology, such as apps to help bystanders locate automated external defibrillators, will also play a part. Organisational efforts, such as the "shock lab" at my own institution, bring together teams of emergency and intensive care medicine to optimise care. In other countries, intensivists go into the field to provide prehospital care.

In our cover story we consider several elements in the chain of survival.

Jerry Nolan summarises the advances made in improving the outcomes of cardiac arrest over the last 10-15 years—no longer is treatment an "exercise in futility". Next, Simon Schmidbauer and Hans Friberg outline the factors for improving prehospital care, namely the roles of first responders, emergency medical services and the importance of termination of resuscitation rules.

Martin Dünser and Daniel Dankl examine the pragmatic criteria for extracorporeal cardiopulmonary resuscitation, and note that it should only be used in carefully selected patients. Next, Glenn Eastwood and Rinaldo Bellomo, who are leading the Targeted Therapeutic Mild Hypercapnia After Resuscitated Cardiac Arrest (TAME) trial, explain the background, the rationale and the trial design. A poor neurologic outcome unfortunately is noted in a high percentage of survivors. Mena Farag and Shashank Patil review the latest evidence on prognostication and key principles in following a prognostication strategy.

David Kloeck, Peter Meaney and Walter Kloeck observe that international recommendations on CA often require adaptation due to cost or therapy. Particularly in South Africa, resuscitation training, adapted to local conditions, has increasingly been made available. Last, Hans van Schuppen makes the case for debriefing after resuscitation.

While airway pressure release ventilation has been available on ventilators for some time, evidence for its use in patients with ARDS is still lacking accumulated evidence from randomised controlled trials. In the Matrix section, Brian O'Gara and Daniel Talmor summarise the benefits and limitations of the technique and review the evidence supporting its use. Next, Daniel Martin and Helen McKenna describe how high altitude research is relevant to critical illness.

In the Management section Katherine Nugent and Craig Coopersmith begin by explaining the core principles of rounds, as well as who should be included, how to structure, how to optimise communication and accommodate the needs of learners. "Rounds should be enjoyable—and even fun—if at all possible", they conclude.

We are pleased to include a patient's perspective in this issue. Eileen Rubin writes about her experiences of critical illness, its effect on her and her family, and her motivation to co-found the ARDS Foundation.

The European Society of Anaesthesiology (ESA) has an active network for trainees. Three trainees, Mihai Ștefan, Liana Văleanu and Diogo Sobreira Fernandes, Chair of the ESA Trainee Committee, write about the goals of the network. A recent survey highlighted the heterogeneity of anaesthesiology training in Europe, as well as a keen interest in intensive care medicine.

What does your difficult airway trolley look like? Jonathan Gatward describes the trolley in use at Royal North Shore Hospital in Sydney, Australia, a design standardised across the emergency and operating departments and the ICU. Last, our sister journal, *HealthManagement.org The Journal*, recently published a cover story on value-based healthcare. Michelle Fakkert, Fred Van Eenennaam, Vincent Wiersma explain five points that show how VBHC can provide a common language for all stakeholders in healthcare.

This issue we have the bonus of two interviews with experts. John West is often described as the guru of hypoxia. We are delighted to bring you an interview, in which he talks about his discoveries, his serendipitous career, the promise of oxygen conditioning and why the avian lung is better than the human lung.

Research into organisational aspects of intensive care has yielded many important insights into improving outcomes. Jeremy Kahn is a leader in this field and shares his thoughts next.

We visit Tunisia for our Country Focus. Lamia Ouanes-Besbes, Mustapha Ferjani and Fekri Abroug write frankly about the issues facing the intensive care specialty in their country and outside, as there is a brain drain of specialists.

Intensivists and anaesthesiologists gather at Euroanaesthesia in Geneva this month, and will be joined by the ICU Management & Practice team. We hope to meet you there!

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

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IN EVERY ISSUE

COVER STORY

MATRIX

POINT OF VIEW

38th International Symposium on Intensive Care and Emergency Medicine

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MARCH 20-23, 2018

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ICU MANAGEMENT & PRACTICE VOLUME 17 - ISSUE 2 - SUMMER 2017

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Europe: Wide Variation in Severe Critical Events in Paediatric Anaesthesia

A Europe-wide observational study of anaesthesia practice in children has shown wide variation in severe critical events and a higher incidence than previously understood. The study was run by the European Society of Anaesthesiology and the results are published in *Lancet Respiratory Medicine*.

The **A**naesthesia **PR**actice **I**n **C**hildren **O**bservational **T**rial (APRICOT) included data from 261 centres across 33 countries that performed 31,127 perioperative anaesthetic procedures for 30,874 children from birth to 15 years of age. Data was collected on severe critical events, namely occurrence of respiratory, cardiac, allergic or neurological complications requiring immediate intervention that led or could have led to major disability and/or death.

Experience and Volume Count

There was a 20 to 30-time variation in incidence of severe critical events between the countries involved. More than 5% of children undergoing anaesthesia experienced at least one severe critical event. In 17% of these, additional anaesthesia treatments, prolonged treatment in hospital, or both were needed.

The incidence of perioperative severe critical events was 5.2% (95% CI 5.0-5.5). Respiratory critical events were highest at 3.1%, followed by cardiovascular instability (1.9%), and were more frequent in children aged up to 6 years.

The researchers found statistical evidence that experienced paediatric anaesthesiologists and teams with a higher volume of paediatric cases had significantly fewer severe critical events. Lead Investigator, Prof. Walid Habre, Head, Unit for Anaesthesiological Investigations, Senior Consultant Paediatric Anaesthesia, Geneva University Hospitals, Geneva, Switzerland, said that the study's findings reinforce the urgent need to elaborate and implement standardised training programmes and good clinical practice guidelines for paediatric anaesthesia management throughout Europe. The investigators suggest that the results also emphasise the need to establish a European register to monitor peri-anaesthetic morbidity and mortality in children. They recommend that below 3 years of age, children should be managed by more specialist services and centralisation of care may also be necessary for the youngest and most ill infants. ■

Reference

Habre W, Disma N, Virag K et al; APRICOT Group of the European Society of Anaesthesiology Clinical Trial Network (2017) Incidence of severe critical events in paediatric anaesthesia (APRICOT): a prospective multicentre observational study in 261 hospitals in Europe. Lancet Respir Med, 5(5):412-425.

Denmark: Increased Bystander CPR, Decreased Mortality in Out-of-Hospital Cardiac Arrest

A registry study from Denmark has investigated the 1-year risk of anoxic brain damage or nursing home admission and of mortality among patients who survived to day 30 after an out-of-hospital cardiac arrest. The risks were analysed according to whether bystander CPR or defibrillation was performed. The study is published in the *New England Journal of Medicine*.

The number of survivors to 30 days in the study period, 2001 through 2012, totalled 2855. OHCA incidence remained stable, but the percentage surviving to 30 days increased from 3.9% to 12.4%, with recipients of bystander CPR more likely to survive to 30 days. Of note, the rate of bystander CPR increased from 66.7% to 80.6% and all-cause mortality decreased from 18% to 7.9%. The risk of anoxic brain damage or nursing home admission was also significantly lower in those who received bystander CPR.

The authors write that their findings "underscore the need to implement or improve strategies that help bystanders initiate CPR and strategies that facilitate public access to automated external defibrillators."

ICU Management & Practice asked the study's first author, Kristian Kragholm, MD, PhD, Department of Departments of Cardiology and Epidemiology/Biostatistics, Aalborg University Hospital, Denmark, how other countries might replicate the success in optimising bystander CPR in Denmark.

He explained that in Denmark mandatory basic life support courses in elementary schools and when acquiring a driver's licence were introduced on a nationwide level in 2005 and 2006, respectively. The annual number of completed voluntary courses in basic life support nearly doubled in the past decade, and media commercials and annual awareness campaigns in later years may also have had an impact on the increased rates of bystander CPR from around 20% in 2001 to nearly 65% in 2014 (based on all included patients in the Danish Cardiac Arrest Registry during 2001-2014). Healthcare professionals were introduced in emergency dispatch centres in 2009 and on a nationwide level from 2011. These healthcare professionals are able to guide bystanders to recognise cardiac arrest and start CPR. *Continued on page 72*

ESA 2017 Industry Sponsored Symposium

CURRENT CHALLENGES IN PAEDIATRIC SEDATION
An Interactive Overview

PRIMEX PHARMACEUTICALS

Sunday 4th June 2017
12.15 – 13.45
Hall 1 / Room 3

Lunch will be served at 12.00 noon – no pre-registration needed

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Chairman: Dr Karin Becke, Nuremberg, Germany

12.15 Welcome and Introduction

PAEDIATRIC SEDATION – *current treatment options and challenges*
Karin Becke, Nuremberg, Germany

IN-HOSPITAL PAEDIATRIC SEDATION – *areas for improvement*
Claudia Höhne, Leipzig, Germany

A NOVEL ORAL SOLUTION *for paediatric sedation*
Michael Brackhahn, Hannover, Germany

Panel discussion and Chairmans' summary

13.45 Close

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PRIMEX PHARMACEUTICALS

4th June 2017
Geneva
Switzerland

Facilitating early defibrillation is also important, noted Dr. Kragholm. Between 2006 and 2011, the number of registered AEDs in Denmark increased from approximately 3,000 to nearly 15,000. An AED registry was formed in 2007 in Copenhagen that established a platform to register the location and accessibility of AEDs. This AED registry was expanded to a nationwide level in 2010. Information from the AED registry was integrated with emergency dispatch centres in Copenhagen beginning in 2010 and nationwide from 2011, enabling healthcare professionals to not only guide bystanders to initiate CPR but also to find and use the nearest available AED. The AED registry data is available through a smartphone app, so citizens can locate the nearest available AED. In Denmark, there has also been increased media attention directed towards placing AEDs outside buildings, thus making them accessible on a 24/7 basis.

"Our study underscores the importance of bringing an AED to the scene before emergency medical services personnel arrive. In Denmark, there are ongoing and future research studies planned on how to engage lay first responders in parallel with ambulances to increase CPR rates and use of AEDs before ambulance personnel arrival. Such interventions could be used in other settings but it should also be noted that it may be more sensible to engage fire fighter or police officers as first responders, depending on area coverage and AED availability and dissemination in the community," Dr. Kragholm observed.

The researchers are also investigating hospital costs, length of stay and admission to intensive care units in relation to early bystander efforts, and they will look at longer-term outcomes, including mortality and nursing home care, in comparison to the background population. ■

Reference

Kragholm K, Wissenberg M, Mortensen RN et al. (2017) Bystander efforts and 1-year outcomes in out-of-hospital cardiac arrest. N Engl J Med, 376(18): 1737-47.

Does Gender Matter in Resuscitation Teams?

A simulated study of cardiopulmonary resuscitation (CPR) that compared performance by male and female medical students found that the female students performed less efficiently and were less effective resuscitation team leaders. The researchers, from the University of Basel and University Hospital Basel, suggest that gender-specific training may be needed. The results are published in *Critical Care Medicine*.

Results

In this randomised, prospective observational study 216 fourth-year medical students (108 women and 108 men) were divided into groups of three. They took part in an emergency simulator-training workshop in the Simulation Center of the Medical ICU at University Hospital Basel, Switzerland. The students had previously completed basic life support training, including using defibrillators, during their medical school training. The students were not informed about the workshop's goal or content of the simulated scenarios.

The researchers documented and analysed the performance of the individual groups during a simulated cardiac arrest scenario, focusing on hands-on time, defined as the uninterrupted CPR time within the first three minutes after the onset of the cardiac arrest. They also noted how often the participants made clear leadership statements, i.e. verbal commands to assign tasks or clarify how something should be done.

"In comparison with male-only teams, the female groups showed less hands-on time and took longer overall to start the CPR," said Professor Sabina Hunziker, the study leader. The female-only teams also showed less leadership communication compared with the male-only teams. Leadership communication included assigning and distributing tasks, deciding what to do and how, commands, corrections and planning work ahead. Even in mixed teams, women made significantly fewer clear leadership statements than men. Female-only teams also had fewer unsolicited CPR measures, meaning situations in which a rescuer does something useful without prior order from another rescuer or prior announcement. Individually, in mixed teams, female gender was associated with a lower number of secure leadership statements.

The authors write that as far as they know theirs is the first study reporting unsolicited meaningful CPR measures as a predominantly male behaviour and as a main driver of gender differences in CPR.

The authors conclude that improving personal leadership skills is a good starting point in teaching medical emergencies. Female rescuers should be trained to show secure leadership behaviour and perform unsolicited CPR measures. Future research should find out if gender differences are still apparent in more mature and experienced physicians.

In an email to *ICU Management & Practice*, Hunziker noted that to improve cardiac arrest survival, on a resuscitation team level most important seems to be active leadership—i.e. one in the team needs to be in charge of the situation and guide the rest of the team. In mixed teams, this person should preferably be the one with the most experience—independent of gender. "In our studies it was interesting to see that in mixed teams females tended to turn over this active leadership position to their male colleague (although they had similar experience and knowledge)."

Sabina Hunziker

Hunziker confirmed that at Basel they will focus more on the importance of leadership and of taking the lead during CPR courses, particularly in medical school students and junior physicians. "It is important that females are aware of such shortcomings so they can improve their skills," she said. ■

Reference

Amacher SA, Schumacher C, Legeret C Tschan F, Semmer NK, Marsch S, Hunziker S (2017) Influence of gender on team performance of cardiopulmonary rescuers: a randomized, prospective simulator study. Crit Care Med, doi: 10.1097/CCM.0000000000002375 [Epub ahead of print]

Sepsis Detection and Management

New KLAS Report

Healthcare providers are increasingly turning to technology to detect sepsis and report on sepsis management. As most electronic medical record (EMR) providers do not offer easily deployed sepsis modules, healthcare providers report using solutions from infection control and surveillance vendors as well as specialised sepsis solutions.

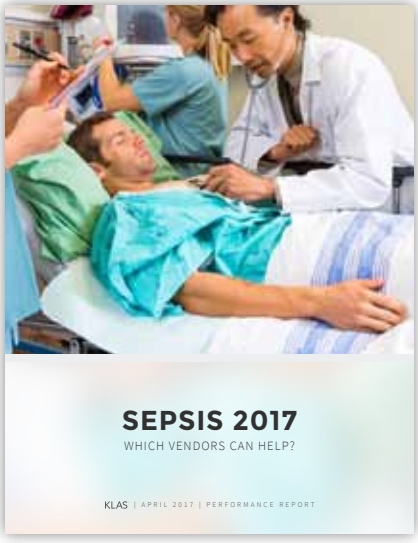
KLAS Research's new report, *Sepsis 2017: Which Vendors Can Help?*, provides clarity on which vendor solutions can help hospitals tackle sepsis. The report includes feedback from over 150 phone interviews with sepsis thought leaders on their strategy and utilisation in regard to sepsis technology and solutions.

Vendor Performance

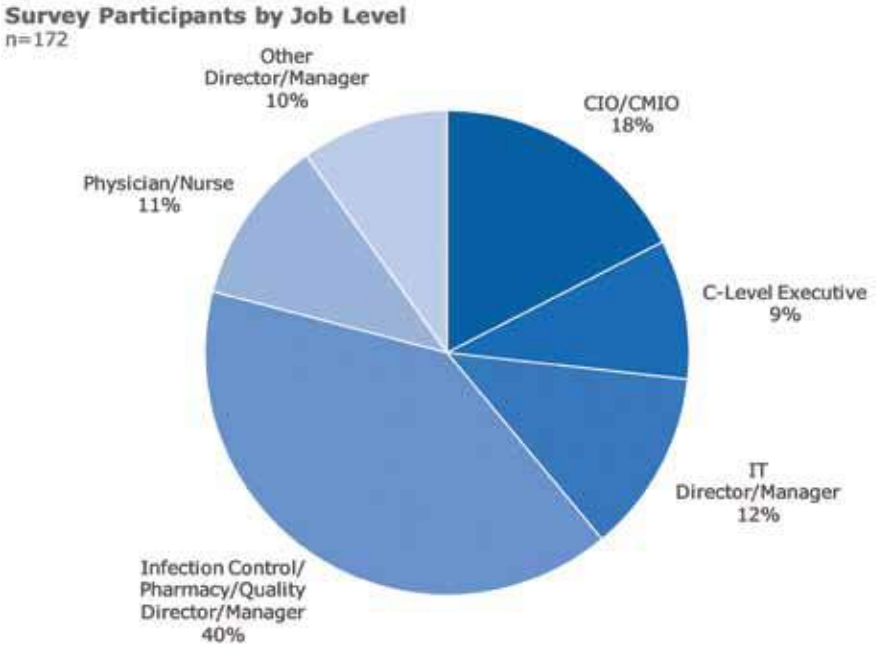
Vendors included in the report are Allscripts, Cerner, Epic, McKesson, MEDITECH, Iatric Systems, PeraHealth, Truven Health, VigiLanz, Wolters Kluwer, d2i, Health Catalyst, LogicStream, Iodine Software, Qualcomm, Uniphy Health and WPC Healthcare. KLAS note that they included vendor-supported sepsis technology and services in the report, but other providers may address sepsis more broadly via the automation of infection control. Most solutions offer real-time alerting; Health Catalyst and LogicStream provide retrospective reporting.

Healthcare providers did report positive outcomes in regard to compliance, mortality, length of stay, readmissions and cost. However, KLAS notes that their report is not designed to compare vendors in relation to outcomes, as this is not directly comparable.

Kody Hansen, Research Manager at KLAS, told *ICU Management & Practice* that the questionnaire administered in the interviews was derived from collaboration with sepsis thought leaders around the U.S.



> "evolving from being point solutions to proactive intelligence at the point of care"



Hansen confirmed that KLAS plans a follow-up study in 2018, which will delve into straightforward differentiation of the vendors by performance criteria. "In addition to tracking adoption and implementation of sepsis solutions, we will also try to determine who the standout players are and who is making the biggest difference for their clients in terms of tangible outcomes, effective alerting and helping to manage workflow and screening and many other processes that are inherent to effective sepsis management," he added.

"With these sepsis solutions, we are finally seeing some of the value realisation attributed to clinical decision support tools that has historically been lacking. These tools are evolving from being point solutions to proactive intelligence at the point of care," concluded Hansen. ■

More Information

Providers may receive a free copy of the full report by contacting Kody Hansen, Research Manager, KLAS Research, kody.hansen@klasresearch.com

Reducing Brain Injury After Cardiac Arrest

American Academy of Neurology Practice Guideline

Therapeutic hypothermia (TH) (32-34°C for 24 hours) should be mandatory practice for patients who are comatose after being resuscitated from out-of-hospital cardiac arrest, if the initial cardiac rhythm is either pulseless ventricular tachycardia (VT) or ventricular fibrillation (VF), according to the American Academy of Neurology (AAN)'s newly published practice guideline *Reducing brain injury following cardiopulmonary resuscitation.*

The guideline, which is endorsed by the Neurocritical Care Society and published online in *Neurology*, is based on the evidence from studies conducted over the last 50 years on ways to reduce brain injury in people who are comatose after resuscitation from cardiac arrest.

The recommendation for patients who are comatose following resuscitation from cardiac arrest, in whom the initial cardiac rhythm is either VT/VF or asystole/pulseless electrical activity (PEA) after OHCA is for targeted temperature management (36°C for 24 hours, followed by 8 hours of rewarming to 37°C, and temperature maintenance below 37.5°C until 72 hours). The recommendation is Level B "should do", and the guideline notes that it is an acceptable alternative to TH. The guideline also states that there is insufficient evidence to support or refute the use of 32°C vs 34°C.

Lower strength recommendations are for patients who are comatose with an initial rhythm of PEA/asystole, in whom the guideline states that TH possibly improves survival and functional neurologic outcome at discharge vs standard care and may be offered (Level C - "might" be done).

Prehospital cooling as an adjunct to TH is not recommended, as the available evidence is strong enough to say that it is highly likely to be ineffective in further improving neurologic outcome and survival. The guideline states that it should not be offered (Level A). In addition, other pharmacologic and nonpharmacologic strategies (applied with or without concomitant TH) are also reviewed.

> **"Prehospital cooling as an adjunct to TH is not recommended"**

The guideline recommends that future studies try to find optimal target temperatures and rates of cooling and rewarming the body as well as examining which cooling methods work best.

In an accompanying editorial, Gregory Kapinos, MD, MS, a neurointensivist at North Shore Long Island Jewish Health System and Assistant Professor, Hofstra Northwell School of Medicine and Lance B. Becker, MD, chair and professor of emergency medicine at the Hofstra Northwell School of Medicine, write, "The keen semantic nuances used in these AAN guidelines send the correct message to the neurologic community (Yes we cool!) to prevent ongoing misinterpretation of the study by Nielsen at al. [2013]." They suggest that the guidelines could have been "more precise" on prehospital cooling and should have only recommended against the methods that have been proven to be potentially deleterious: 4°C fluid loads or intranasal cooling, adding that it's "premature to close the door on all methods of preshospital TH induction." They write: "We concur with the AAN experts that less is not more and cooling should be harder, better, faster, stronger, in the sense that neurologists should be hardliners who embrace cooling as a default mode for nearly all cardiac arrest survivors, making it harder to exclude patients, while using cooling techniques that are the better ones, starting as quickly as possible after ROSC, and that 33°C is stronger than 36°C."

The AAN said that families of patients who have suffered cardiac arrest should ask if their loved one qualifies for therapeutic hypothermia. "People who are in a coma after being resuscitated from cardiac arrest require complex neurologic and medical care and neurologists can play a key role in improving outcomes by providing body cooling," said the chair of the guideline committee, Romergryko G. Geocadin, MD, of Johns Hopkins University School of Medicine in Baltimore, and a Fellow of the American Academy of Neurology. "This guideline recommends that cooling is used more often for patients who qualify."

Geocadin told *ICU Management & Practice* in an email, "We know that implementation of this therapy is really low (6% to 30% in the USA) despite the strong scientific evidence. Families need to know that they have this option—we are empowering families because cardiac arrest survivors are comatose and could not advocate for themselves." ■

References

Geocadin RG, Wijdicks E, Armstrong MJ et al. (2017) Practice guideline summary: Reducing brain injury following cardiopulmonary resuscitation: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology, 10 May. doi: 10.1212/WNL.0000000000003966. [Epub ahead of print]

Kapinos G, Becker LB (2017) The American Academy of Neurology affirms the revival of cooling for the revived. Neurology, 10 May. doi: 10.1212/WNL.0000000000003968. [Epub ahead of print]

Nielsen N, Wetterslev J, Cronberg T et al. (2013) Targeted temperature management at 33°C versus 36°C after cardiac arrest. N Engl J Med, 369(23): 2197-206.

Out-of-Hospital Cardiac Arrest

Bystander CPR Impact on Survival, Cost

Bystander cardiopulmonary resuscitation (CPR) is crucial to successful resuscitation following out-of-hospital cardiac arrest (OHCA). New research shows that bystander CPR was positively associated with long-term survival and appears cost-effective, with an incremental cost-effectiveness ratio of USD48,044 per quality-adjusted life year (QALY). The findings are published in *Resuscitation*.

Although early CPR has been associated with return of circulation and survival to hospital discharge, few studies have examined the long-term prognostic role of bystander CPR. In this study, researchers used information from a regional OHCA registry in Greater King County, Washington, USA, and a database of hospital costs to assess the association of bystander CPR with long-term survival and the cost of the incident OHCA hospitalisation in order to estimate the cost-effectiveness of bystander CPR. Cost-effectiveness was based on hospital costs divided by QALYs for a five-year follow-up window.

Investigators found that bystander CPR increased the adjusted odds of survival to hospital admission by 16%, survival to hospital discharge by 26%, and five-year survival by 30%. They estimated costs at USD75,175 for survivors and USD6,506 for those who died in hospital. They calculated an incremental cost-effectiveness ratio of bystander CPR of USD48,044 per QALY. This ratio was adjusted for cardiac arrest characteristics typically reported, supporting the generalisability of this intervention in most patients and settings.

First author, Guillaume Geri, MD, PhD, Post-doctoral fellow at the Li Ka Shing Knowledge Institute of St. Michael's Hospital, Toronto, Canada, told *ICU Management & Practice*, "Besides the effectiveness of a procedure, it is more and more important nowadays to evaluate costs associated with the management of our patients. We aimed to describe inpatient costs related to out-of-hospital cardiac arrest patients treated by emergency medical services and admitted to the hospital and to evaluate the impact of bystander CPR on costs. Interestingly, survival was the main driver of costs and it seemed important to simultaneously consider costs and effectiveness." Dr. Geri explained that in this study, survival was censored at five years post-OHCA as this enabled comprehensive ascertainment of vital status for the population-based cohort. He added that the research team strongly believes that (very) long-term outcome should be preferentially used in cardiac arrest patients, including social and professional events occurring in the survivors to have a clearer idea of the quality of life of such survivors.

The research team notes that the study was observational so that they cannot determine whether the relationship between bystander CPR and long-term survival is causal, despite efforts to account for potential confounders. ■

Guillaume Geri

Reference

Geri G, Fahrenbruch C, Meischke H et al. (2017) Effects of bystander CPR following out-of-hospital cardiac arrest on hospital costs and long-term survival. Resuscitation, 115: 129-34.

Professor Gian Maria Rossolini

The Impact of Fast MIC Evaluation on Antimicrobial Stewardship

A Case Report

Dealing with Antimicrobial Resistance

Recently antibiotic resistance has become a major public health issue with global dimensions, having a remarkable impact on morbidity, mortality and healthcare associated costs. Due to its increasing relevance, the "antibiotic resistance crisis" has entered the agenda of the WHO and other international agencies, scientific societies, governments and even the UN General Assembly.

Dealing with antimicrobial resistance requires a multitiered approach including the discovery and development of new antibiotics active against multidrug-resistant (MDR) and extremely drug-resistant (XDR) bacteria, the enforcement of effective infection control practices to limit the dissemination of these pathogens, and the implementation of antibiotic stewardship programs to improve patient outcomes while limiting the antibiotic pressure for selection.

Microbiological Diagnosis

Microbiological diagnosis plays an essential role in this complex scenario, by providing information on the presence and the nature of resistant pathogens in clinical specimens, which are crucial to both antimicrobial stewardship and infection control practices. However, the impact of microbiological diagnosis is largely dependent on the speed of results provided by the laboratory, whereby delayed microbiological reports will invariably have minimal impact on the selection/revision of antibiotic treatment. Even in the document addressing the US National Strategy to Combat Antibiotic Resistance, recently issued by the White House, an advancement of the development and use of rapid and innovative diagnostic tests for identification and characterisation of resistant bacteria is considered among the main goals.

> **"The impact of microbiological diagnosis is largely dependent on the speed of results"**

The Case Report

An example of the utility of rapid and innovative tests when treating patients with severe bacterial infections is briefly described by the case below.

A 65-year old patient was admitted to the ER with diagnosis of sepsis at 5 pm on day 1. The patient suffered from Type 2 diabetes for several years and had a history of recurrent urinary tract infections due to benign prostatic hyperplasia. The patient had been febrile for six days, and received oral ciprofloxacin as an empiric treatment for five days, with no clinical improvement and eventually a rapid worsening.

Upon hospital admission, blood culturing was performed, and the patient was empirically given meropenem (1 g tid) in consideration of the clinical history and the epidemiological setting, characterised by a high prevalence of ESBL production among *Enterobacteriaceae*. The patient was then transferred to the general ICU. The blood cultures turned positive after 14 hrs (8 am on day 2), with the presence of Gram-negative bacilli. After Gram-staining, positive blood cultures were processed according to the routine workflow followed in the laboratory (based on fast subculture,

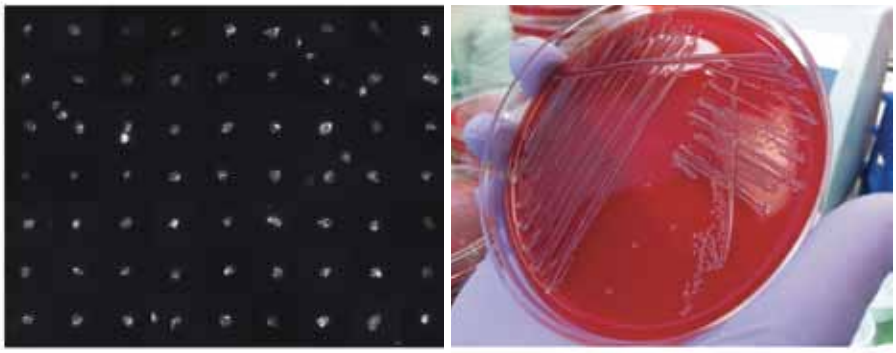


Image 1-2. Contrast of perspective - clones on an agar plate versus individual clones cropped from original dark field imagery during antimicrobial susceptibility testing.
Source: Accelerate Diagnostics

followed by MALDI-TOF identification and antibiogram with broth microdilution), and also with the Accelerate Pheno™ system. The Accelerate Pheno™ system returned an identification of *Escherichia coli* after 2 hrs (10:30 am on day 2), and an antibiogram 5 hours after identification (3:30 pm on day 2) shown in **Table 1**.

The rapid antibiogram revealed a resistance profile suggestive of ESBL production (resistance to cefepime, ceftazidime, ceftriaxone), with resistance also to fluoroquinolones, intermediate susceptibility to amikacin, and susceptibility to gentamicin, piperacillin-tazobactam, carbapenems and colistin. The conventional workflow confirmed the identification (with MALDI-TOF) after 7 hrs (3:30 pm on day 2), and returned the antibiogram on the following day (day 3). Results of the conventional antibiogram were overall consistent with those provided by the Accelerate Pheno™ system (**Table 1**).

Antibiotic	Accelerate Pheno™ System	Broth Microdilution
	MIC (mg/L)	MIC (mg/L)
Amikacin	16	16
Gentamicin	≤ 1	1
Ciprofloxacin	≥ 8	> 2
Cefepime	≥ 32	64
Ceftazidime	≥ 32	16
Ceftriaxone	≥ 8	32
Ertapenem	0.25	≤ 0.12
Meropenem	≤ 0.25	≤ 0.06
Piperacillin-Tazobactam	≤ 4	8
Tigecycline	N.A.	0.25
Colistin	≤ 0.5	0.25

Table 1. Results of antimicrobial susceptibility testing reported by the Accelerate Pheno™ system and by conventional broth microdilution with the E. coli strain isolated from blood culture.

Image 3. A resistant micro-colony growing from progenitor cells as seen by Morphokinetic Cellular Analysis. Source: Accelerate Diagnostics

Contributor's Commentary

In this case, the Accelerate Pheno™ system returned an antibiogram with MIC values for the infecting pathogen isolated from the blood culture on the day after admission, while the routine workflow adopted in the laboratory returned similar results two days after admission, despite using rapid subculture techniques. By comparison, if the laboratory had followed a more conventional approach, such as waiting for the growth of isolated colonies for identification followed by preparing an inoculum for the susceptibility testing, results would not have been available until three days after admission, at the earliest.

The increased speed of the antibiogram allowed de-escalation from empiric treatment to a carbapenem sparing regimen, like piperacilin-tazobactam, to be considered as early as the first day of treatment, offering antimicrobial stewardship advantages. Using conventional diagnostic workflows, the same information would have been available after two or three days of treatment, with a longer carbapenem exposure and a lower likelihood for treatment revision, especially if the patient was already improving.

On the other hand, a molecular test for rapid bacterial identification and detection of resistance determinants, carried out on the positive blood culture, could have returned identification in approximately the same time (1-2 hrs) but would have not provided comparably useful information about antibiotic de-escalation, since susceptibility to piperacillin-tazobactam cannot be directly extrapolated from a molecular antibiogram. ■

About Professor Gian Maria Rossolini

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Cardiac Arrest Management

The treatment of cardiac arrest has made significant progress over the last 10–15 years. This period marks a significant turning point, because the treatment of out-of-hospital cardiac arrest (OHCA) had often been considered an exercise in futility, with no improvement in outcome for the previous 30 years (Berdowski et al. 2010). In recent years, several investigators have documented marked improvements in survival after OHCA, particularly in those cases with an initial shockable rhythm (ventricular fibrillation (VF) or pulseless ventricular tachycardia (pVT) (Wissenberg et al. 2013; Daya et al. 2015; Chan et al. 2014).

Several interventions are likely responsible for the improving survival rates following OHCA. Bystander cardiopulmonary resuscitation (CPR) is associated with survival rates that are 2–3 times higher than those cases without bystander CPR (Hasselqvist-Ax et al. 2015; Rajan et al. 2016). Emergency medical services dispatchers are now better trained to efficiently ask the right questions to enable prompt recognition of cardiac arrest and then to instruct the caller to perform compression-only CPR (telephone CPR) (Bobrow et al. 2016). For shockable rhythms, reducing the delay to attempted defibrillation also improves outcome. Implementation of public access defibrillation (PAD) programs and dispatch of community first responders trained to use automated external defibrillators (AEDs) will reduce the time to defibrillation (Blom et al. 2014). Text alerts can be used to direct first responders to retrieve the nearest AED and then take it to the scene of a cardiac arrest (Zijlstra et al. 2014).

Once return of spontaneous circulation (ROSC) has been achieved, post-resuscitation management impacts significantly on the ultimate neurological outcome. European guidelines for the management of post-cardiac arrest patients were published in 2015 and describe the interventions that will optimise outcome (Nolan et al. 2015). Those patients who achieve ROSC and have ST-elevation (STE) on their ECG will require urgent coronary catheterisation because most of these will benefit from percutaneous coronary intervention (PCI) to restore coronary perfusion (Dumas et al. 2010). The immediate management of those without an obvious non-cardiac cause and without STE is controversial. Some experts advocate urgent coronary catheterisation in all such patients (Dumas et al. 2016). Current European guidance is that these patients should also be discussed with interventional cardiologists and considered for urgent coronary catheterisation (Nolan et al. 2015). Some centres will immediately catheterise cardiac arrest survivors without STE, but only if they had presented with a shockable rhythm.

> **“immediate management of those without an obvious non-cardiac cause and without STE is controversial”**

Cerebral autoregulation is disturbed in 35% of post-cardiac arrest patients and is particularly associated with pre-arrest hypertension (Ameloot et al. 2015a). The optimal target mean arterial pressure (MAP) post cardiac arrest is likely to vary between patients, but to avoid secondary brain ischaemia it has been suggested that the optimal MAP is likely to be in the range 85–105 mmHg, which is somewhat higher than the 65–70 mmHg that is widely used (Ameloot et al. 2015b).

Until recently, in the immediate period after ROSC (certainly prehospital and often in the emergency department) it has been common practice to ventilate the lungs of comatose post-cardiac arrest patients with 100% oxygen. This not unreasonably reflected concerns about harm from hypoxaemia and lack of awareness of harm from high-concentration oxygen. Animal studies have documented worse neurological outcome from the use of 100% oxygen immediately after ROSC, particularly during the first hour (Balan et al. 2006), and some observational studies using data from intensive care unit (ICU) registries have documented an association between hyperoxaemia and worse outcome among post-cardiac arrest patients. In a randomised controlled trial (RCT) the use of routine supplemental oxygen among patients with STE myocardial infarction (but not cardiac arrest), resulted in an increase in size of myocardial infarction compared with patients given oxygen only if hypoxaemic (Stub et al. 2015). A RCT of oxygen titrated to 90–94% versus 98–100% as soon as possible after ROSC and continued until ICU admission (EXACT phase 3 trial) will inform the optimal oxygenation strategy after ROSC (Nolan et al 2017). European guidelines recommend the use of a protective lung ventilation strategy in post-cardiac arrest patients, but this was based mainly on data extrapolated from patients with acute respiratory distress syndrome (Nolan et al. 2015). However, a recent observational study of OHCA patients using propensity matching has documented an association between the use of time-weighted average tidal volumes of < 8 mL kg^{-1} predicted body weight and better neurological outcome (Beitler et al. 2017). Mild hypercapnia may also be associated with better neurological outcome in post-cardiac arrest patients, possibly because it may increase blood flow to ischaemic brain. A phase 2 study comparing mild hypercapnia with normocapnia in 50 post-cardiac arrest patients documented a lesser increase in neuron-specific enolase (NSE)

values in the hypercapnia group (Eastwood et al. 2016). A RCT comparing post-cardiac arrest patients ventilated to either normocapnia or mild hypercapnia (6.6–7.3 kPa) starts recruiting soon (Targeted Therapeutic Mild Hypercapnia After Resuscitated Cardiac Arrest (TAME) [clinicaltrials.gov/ct2/show/NCT03114033]).

Mild hypothermia has been shown to improve neurological outcome from OHCA presenting with a shockable rhythm, but the two prospective studies documenting this are now considered to be of moderate to low quality (Bernard et al. 2002; Hypothermia After Cardiac Arrest Study Group 2002). The targeted temperature management (TTM) study showed no difference in neurological outcome between all-rhythm OHCA patients with ROSC who had their temperature controlled for 24 h at 33°C versus 36°C (Nielsen et al. 2013). Temperature control for comatose survivors of OHCA is still important, but within the range of 32–34°C there is no consensus on the optimal target temperature (Donnino et al. 2016). The Hypothermia or Normothermia-Targeted Temperature Management After Out-of-hospital Cardiac Arrest-trial (TTM-2 [clinicaltrials.gov/ct2/show/NCT02908308]) study will start recruiting soon and will randomise comatose OHCA survivors to temperature control at 33°C versus prevention of fever, with temperature control to a target of 37.5°C initiated only if the patient's temperature reaches 37.8°C.

The commonest mode of death in post-cardiac arrest patients who are admitted to ICU but do not survive is withdrawal of life-sustaining therapy (WLST) following determination of a poor neurological prognosis. We now recognise that in many cases these WLST decisions have been premature and that prognostic tests previously thought to be reliable are associated with unacceptably high false positive rates (Elmer et al. 2014; Cronberg et al. 2017). European guidelines for prognostication in comatose post-cardiac arrest patients advocate a multimodal approach that is delayed until at least 3 days after cardiac arrest (Sandroni et al. 2014). Those ICUs experienced in the management of post-cardiac arrest patients should have easy access to electroencephalography, including somatosensory evoked potentials, and to neurologists who can interpret the findings.

In some countries, regionalisation of post-cardiac arrest treatment has resulted in cardiac arrest centres with availability of 24/7 coronary catheterisation laboratories, intensive care teams experienced in post-resuscitation care and neurologists that can help in the interpretation of neuroprognostic tests (Spaite et al. 2014). The introduction of cardiac arrest centres where high volumes of post-cardiac arrest patients can be treated is associated with better outcomes, even when patients are transported for greater distances as they bypass local hospitals (Tranberg et al. 2017; Schober et al. 2016; Elmer et al. 2016). Investigators in London, UK are about to start recruiting to a study patients with ROSC after OHCA of likely cardiac cause but without STE on their 12-lead ECG, and will compare the outcome of patients randomised to be transported to the nearest acute hospital with those taken to a regional cardiac arrest centre (Patterson et al. 2017). This study will help to determine if all OHCAs of cardiac cause should be treated in a cardiac arrest centres and not just those patients with STE on their 12-lead ECG.

By strengthening every link in the chain of survival it is likely that survival from cardiac arrest can still be improved considerably. ■

Conflict of Interest

Jerry Nolan is Editor-in-Chief of *Resuscitation*. He has a UK National Institute of Health Research (NIHR) grant for the PARAMEDIC-2 study (adrenaline versus placebo in out of hospital cardiac arrest-OHCA) and for the AIRWAYS-2 study (i-gel versus tracheal intubation in OHCA).

Abbreviations

AED automated external defibrillator
ICU intensive care unit
MAP mean arterial pressure
NSE neuron-specific enolase
OHCA out-of-hospital cardiac arrest
PAD public access defibrillation
PCI percutaneous coronary intervention
pVT pulseless ventricular tachycardia
ROSC return of spontaneous circulation
RCT randomised controlled trial
STE ST-elevation
TTM targeted temperature management
VF ventricular fibrillation
WLST withdrawal of life-sustaining therapy

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Prehospital Care for Cardiac Arrest

How to Improve Outcome!

More patient lives have been saved after OHCA in recent years, but the numbers can improve further. Increased awareness, more education of laypersons and more first responders, in combination with reduced response times for the EMS and early defibrillation will save many lives.

The chances of surviving an out-of-hospital cardiac arrest (OHCA) and returning to a good life have increased in recent years, but the numbers are still disturbingly low, with large registry studies reporting survival rates around 10% (Chan et al. 2014; Strömsöe et al. 2015). Some regions, however, have survival rates of 20% or more and could serve as role models for improved care of OHCA patients (Lindner et al. 2011).

The increased survival rates after OHCA in recent years are a result of improved prehospital as well as hospital care. This review will focus on the prehospital setting and what we can do to improve care further. The vast majority of OHCA patients have a cardiac or a presumed cardiac cause of arrest and this review will mainly address these cases. Patients with a clear non-cardiac cause of arrest, such as trauma, accidental hypothermia, suffocation, hanging and drowning have grim prognoses and will not be addressed here.

The increased numbers of patients admitted to hospital alive after OHCA are believed to be an effect of more bystanders performing cardiopulmonary resuscitation (CPR) (Hasselqvist-Ax et al. 2015), thereby shortening the critical *no-flow time*, and by improved quality of CPR (*low-flow*) by the emergency medical services (EMS), including depth and frequency of chest compressions. Improvements in survival after OHCA have been most pronounced among patients with an initial shockable rhythm. Recent data from the Swedish Register of Cardiopulmonary Resuscitation show that one in three patients will eventually have a good outcome if the initial rhythm is shockable as compared to one in twenty-five if the initial rhythm is non-shockable (Strömsöe et al. 2015). A similar development is seen in Denmark (Wissenberg et al. 2013).

First Responders

What can be done to improve prehospital care further? As noted, an analysis of what measures have been taken in those regions with the highest survival rates could serve as a good role model for many. Increased education of laypersons in CPR, including programmes for school children at all levels, will increase the rate of bystander CPR in our society and improve survival rates.

Other measures that decrease no-flow times and improve low-flow will improve survival as well. In addition to more bystander-CPR, the involvement of first responders can markedly reduce no-flow times and time to first defibrillation (Nordberg et al. 2014). Established models for first responders include involvement of fire brigades and police units, and this can be expanded further in many regions (Malta Hansen et al. 2015). Modern technology, including a mobile-phone positioning system, could instantly locate and dispatch lay volunteers trained in CPR to the scene of a cardiac arrest patient (Ringh et al. 2015). It remains to be shown that lives can be saved as well, but few doubt it, especially if combined with a positioning system for automated external defibrillators (AEDs) that would allow for laypersons to deliver very early shocks as well (Zijlstra et al. 2014). Even remote delivery of AEDs using drones has been shown to be feasible (Claesson et al. 2016). A limiting factor is, however, that the majority of OHCAs occur at home (≈70%) as opposed to a public place, which is a potential practical and legal obstacle (Hansen et al. 2017).

Emergency Medical Services

Despite educational and technological advances enabling more effective bystander interventions, the time for the EMS to arrive to the scene of the arrest remains a crucial part in the chain of survival after OHCA (Rajan et al. 2016). The early measures by the EMS (as for fire brigades and police) should include immediate manual CPR and rhythm analysis, followed by defibrillation in patients with a shockable initial rhythm. If there is no immediate return of spontaneous circulation (ROSC), the cardiac arrest algorithm should be rigorously followed with repeated rhythm analysis every two minutes. If ROSC is achieved, the patient should be immediately transferred to a hospital, ideally with angiography facilities. If the initial rhythm is shock-

able and if ROSC is not achieved, there are two options. Either CPR is continued on site, or the patient is rapidly transported to hospital with ongoing CPR. With current evidence insufficient for a clear recommendation on which approach is preferable, this decision is likely to be influenced by a number of local or regional system-specific factors. Regardless of whether or not transport is initiated, CPR should be continued for at least 40 minutes, since ROSC may occur after prolonged CPR in patients with initial shockable rhythm (Grunau et al. 2016; Reynolds et al. 2016). In patients with initial asystole or pulseless electrical activity (PEA) on the other hand, there are very few survivors after 20 min of continued CPR, and CPR could therefore be terminated on scene in most cases in the absence of ROSC (Grunau et al. 2016; Reynolds et al. 2016). Patients with non-shockable rhythms, who do not recover ROSC in the field, should thus not routinely be transported to hospital. Unfortunately, the proportion of OHCA patients with an initial shockable rhythm at the EMS arrival is decreasing and may be as low as one in four (25%) (Strömsöe et al. 2015).

Termination of Resuscitation Rules

The original termination of resuscitation (TOR) guidelines were proposed in 2002 (Verbeek et al. 2002) and are now referred to as the *universal* TOR guidelines, validated in 2009 and onwards for OHCA of cardiac or unknown origin (Morrison et al. 2009; Grunau et al. 2017).

In short, the universal TOR guidelines recommend termination when there has been no ROSC at any time, no shocks have been administered and the arrest was not witnessed by EMS personnel. Patients with a shockable rhythm at any time during CPR and those who arrest with the EMS present, on the other hand, fulfil the universal TOR guideline for transport and should be brought to hospital, independently of whether field ROSC is achieved or not (Morrison et al. 2009). Transport should probably be initiated without unnecessary delay in most cases. In a recent analysis of a large multicentre database, Drennan and co-workers retrospectively evaluated the universal TOR guidelines in patients transported to hospital without having achieved ROSC in the field (Drennan et al. 2017). They found that patients who met the universal TOR criteria for transport had a survival rate of 3%, as compared to 0.7% among those fulfilling the universal TOR criteria for termination, thus highlighting the importance of a TOR rule more refined than solely a lack of field ROSC.

The 2015 European Resuscitation Council (ERC) guidelines recommend using the universal TOR rules for OHCA of cardiac or unknown origin (Soar et al. 2015), and so do the authors of this paper.

Automated Chest Compression Devices

Although automated chest compression devices like the Lund University Cardiac Assist System (LUCAS®) or the Autopulse® could not be shown to improve outcomes in randomised trials (Perkins et al. 2015; Rubertsson et al. 2014; Wik et al. 2014), their use is becoming increasingly popular. Current ERC guidelines (Soar et al. 2015) do not recommend their routine use, but conclude that automated chest compressions are a reasonable alternative in certain situations, for example in the cardiac catheterisation laboratory (Wagner et al. 2010) or during transport (Gässler et al. 2013). Drawbacks with automated chest compression devices include increased costs and a possible risk for delayed defibrillation (Hardig et al. 2017; Schmidbauer et al. 2017). Also, rib fractures have been shown to increase (Smekal et al. 2014), and other injuries like sternum fractures and injuries to soft tissues seem to be more prevalent (Englund et al. 2008; Truhlar et al. 2010).

Extracorporeal Cardiopulmonary Resuscitation (eCPR)

The exciting novel field of eCPR for OHCA deserves mentioning but should be viewed as exploratory. A major obstacle is to identify the limited number of patients that may benefit from this costly, invasive and labour intensive intervention (Xie et al. 2015). There are presently seven registered trials to be found on ClinicalTrials.gov, of which one is completed, two are recruiting patients and two are not yet recruiting. For the remaining, the status is unknown. This highlights the increasing interest for eCPR after OHCA, and confirms the urgent need for randomised studies and studies from large eCPR registries (Soar et al. 2015).

Formula for Improved Survival after OHCA

Time to initiation of CPR and to first defibrillation after OHCA are the critical factors for outcome and all efforts should be taken to shorten them. A strategy for educating more laypeople about preventive measures and how to perform high-quality CPR will save lives, as will deployment of public defibrillators and increased numbers of first responders. Police and fire brigades are obvious first responders in many regions, and in addition, trained volunteers can be dispatched using app-based positioning systems.

> **All efforts should be made to give immediate and optimal care to all OHCA patients**

While we encourage the use of large registries to compare OHCA care and survival rates between regions, one must also bear in mind that higher relative survival rates do not automatically equal more saved lives. It is thus reasonable to also compare and present numbers of saved lives after OHCA per 100,000 population between regions in addition to percentages (Strömsöe et al. 2015).

All efforts should be made to give immediate and optimal care to all OHCA patients, with the most resources concentrated to those patients with the best chances of a good outcome. Such a strategy would probably include early transport of all patients with an initial shockable rhythm to hospital, regardless of whether field ROSC is achieved. Many patients with refractory VT/VF should be brought immediately to the cardiac catheterisation laboratory without delay and with ongoing high-quality CPR when needed. It must again be stressed that the use of automated chest compression devices and early transport directives must not delay initial (manual) CPR, initial rhythm analysis and delivery of immediate shocks when feasible.

Our common goal should be survival rates after OHCA with good functional outcome at a level of the best performers or around 20%, which would mean a doubling of saved lives from today's levels. ■

Conflict of Interest

Simon Schmidbauer declares that he has no conflict of interest. Hans Friberg declares that he has no conflict of interest.

Abbreviations

AED automated external defibrillator
CPR cardiopulmonary resuscitation
eCPR extracorporeal cardiopulmonary resuscitation
EMS emergency medical services
ERC European Resuscitation Council
OHCA out-of-hospital cardiac arrest
PEA pulseless electrical activity
ROSC return of spontaneous circulation
TOR termination of resuscitation
VT/VF ventricular tachycardia/ventricular fibrillation

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Extracorporeal Cardiopulmonary Resuscitation

Who Could Benefit?

This article summarises the current ratio and scientific evidence on which cardiac arrest patients could benefit from extracorporeal cardiopulmonary resuscitation.

Acute cardiac arrest has a dismal prognosis even when advanced cardiac life support is initiated without delay. Extracorporeal cardiopulmonary resuscitation (eCPR) refers to a technique which uses an extracorporeal life support system to re-establish vital organ blood flow despite ongoing cardiac arrest. Although the technique was suggested for this indication already in the 1960s (Kennedy 1966), the use of eCPR in patients with cardiac arrest only became more common after the widespread availability of extracorporeal life support systems in response to the influenza H1N1 pandemics. In cardiac arrest patients undergoing eCPR, the femoral vein and artery are accessed with large bore cannulas during resuscitation. After insertion, the cannulas are connected to a pump-driven extracorporeal circuit,which drains blood from the inferior vena cava, passes it over a membrane oxygenator and delivers oxygenated and decarboxylated blood back into the abdominal aorta (Fagnoul et al. 2014). This re-establishes vital organ perfusion in patients with successful cannula placement. Even though return of spontaneous circulation occurs in several patients after extracorporeal (and by that, coronary) blood flow has been initiated, the cause of cardiac arrest is not reversed by eCPR. Therefore, this technique must always be combined with a diagnostic work-up to identify, and interventions to treat, the underlying pathology causing cardiac arrest. Current data suggest that eCPR is associated with good functional outcome in up to 30-40% of patients with cardiac arrest, especially when used in the in-hospital setting (Fagnoul 2014). A meta-analysis of nine studies including 3,098 cardiac arrest victims reported that the use of extracorporeal life support during cardiopulmonary resuscitation increased 30-day survival by 13% (absolute increase; CI 95% 6-20%, p<0.001, number needed to treat 7.7) and favourable neurological outcome by 14% (absolute increase, CI 95% 7-20%, p<0.0001, number needed to treat 7.1) compared to standard advanced cardiac life support (Ouweneel et al. 2016).

> **the question of which subgroup of patients is most likely to benefit from eCPR remains controversial**

Criteria for eCPR

In view of the fact that eCPR is highly invasive, resource-intensive and expensive, it should only be implemented in a carefully selected patient population. As only limited data are currently available, the question of which subgroup of patients is most likely to benefit from eCPR remains controversial. Pragmatically, four criteria must be fulfilled (**Table 1**).

As in other acute conditions, functional status before the critical illness delicately impacts outcome. Although a recent meta-analysis did not report age as an independent predictor of outcome from cardiac arrest managed with eCPR (Debaty et al. 2017), most ongoing trials have upper age limits as one of their inclusion criteria (**Table 2**). No comparisons of mortality have so far been made between children and adults undergoing eCPR. However, observational data suggest that the chances of good functional recovery are higher in children than adults (Wolf 2012).

Reversibility of the underlying cause of cardiac arrest is another prerequisite to initiate eCPR. Only in a few instances, such as in the in-hospital setting, has the underlying cause of cardiac arrest clearly been identified before eCPR is initiated. Therefore, reversibility has often been equated with the presence of a shockable rhythm (ventricular fibrillation or flutter, pulseless ventricular tachycardia). Intra-arrest echocardiography may be a valuable tool to identify patients with a potentially reversible cause of cardiac arrest who present with non-shockable rhythms (e.g. patients with pulmonary embolism). In the out-of-hospital setting, two further cardiac arrest circumstances have been considered potential indications for eCPR. Accidental hypothermia has traditionally been a condition for which eCPR has been

Table 1. Pragmatic criteria which need to be fulfilled before the decision to initiate eCPR is made

1.	An established eCPR programme is available in the hospital or can be reached within a reasonable time.
2.	The patient's functional status/physiologic reserve allows recovery from cardiac arrest.
3.	The underlying cause of cardiac arrest is reversible.
4.	The brain has not sustained severe hypoxic brain damage before extracorporeal circulation is established.

eCPR extracorporeal cardiopulmonary resuscitation

used for over three decades (Ruttmann et al. 2007). Similarly, case reports and smaller observational studies suggest that eCPR could be beneficial for patients with severe poisoning, particularly with sedative and/or cardiotoxic drugs (Reynolds and Judge 2015).

Another essential criterion to be met is the absence of severe hypoxic brain damage before extracorporeal blood flow is established. Extrapolation of data from general cardiac arrest populations in both children and adults suggests that only patients whose collapse has been observed and in whom chest compressions have been initiated within 10 minutes of the onset of cardiac arrest should be considered for eCPR. In addition, an increasingly solid amount of evidence indicates that good functional recovery becomes more likely if the time from collapse to start of extracorporeal blood flow does not exceed 60 minutes. While in patients experiencing in-hospital cardiac arrest this time limit can often be achieved, it requires a particularly tight and well-implemented protocol to install eCPR in patients who experience cardiac arrest in the out-of-hospital setting. Several strategies have been adopted in this patient population. Selected centres, for example, provide eCPR in the out-of-hospital setting and have reported reasonable outcomes (Lamhaut et al. 2017). Most centres, however, initiate eCPR in those patients only after admission to the emergency department. Further to careful patient selection, this approach relies even more on a straightforward selection and decision process on scene and a clear protocol in the receiving emergency department (Spangenberg et al. 2016). Patients who exhibit signs of life during cardiopulmonary resuscitation (e.g. spontaneous movements, gasping or breathing, CPR-induced consciousness) or experience repeated cardiac arrest episodes might be considered for eCPR even after prolonged periods of cardiopulmonary resuscitation.

European Resucitation Council Guidelines

The latest European Resuscitation Council guidelines suggest that eCPR be consid-

Table 2. Inclusion criteria of selected ongoing clinical studies testing the effect of eCPR on cardiac arrest outcome (clinicaltrials.gov)

Emergency Cardiopulmonary Bypass for Cardiac Arrest (ECBP4OHCA)

NCT01605409, randomised controlled trial, eCPR+ACLS vs. ACLS, Vienna/Austria, recruiting

- 18-75 years
- witnessed out-of-hospital cardiac arrest
- presumed cardiac cause
- immediate initiation of bystander CPR
- no ROSC after a minimum of 15 min of ACLS

Hyperinvasive Approach in Cardiac Arrest

NCT01511666, randomised controlled trial, prehospital mechanical compressions + intra-arrest cooling+hospital eCPR vs. ACLS, Prague/Czech Republic, recruiting

- 15-65 years
- witnessed out-of-hospital cardiac arrest
- presumed cardiac cause
- no ROSC after min of 5 min of ACLS (by EMS)
- unconsciousness (Glasgow Coma Scale <8)
- ECMO team and bed capacity in cardiac centre available

ECPR for Refractory Out-of-Hospital Cardiac Arrest (EROCA)

NCT03065647, randomised controlled trial, eCPR vs. ACLS, Michigan/USA, recruiting

- 18-70 years
- OHCA of presumed non-traumatic aetiology requiring CPR
- predicted arrival at eCPR-capable hospital within 30 minutes from 911 call or cardiac arrest onset (if witnessed)
- witnessed arrest or initial shockable rhythm (ventricular tachycardia or fibrillation)
- persistent cardiac arrest after initial rhythm analysis and shock (if shock is indicated)

Refractory Out-of-Hospital Cardiac Arrest Treated with Mechanical CPR, Hypothermia, ECMO and Early Reperfusion (CHEER)

NCT01186614, single arm observational study, Melbourne/Australia, recruiting

- 18-59 years
- OHCA due to presumed cardiac cause
- chest compressions commenced within 10 minutes by bystanders or EMS
- initial cardiac arrest rhythm of ventricular fibrillation
- remains in cardiac arrest at the scene at 20 minutes after standard paramedic ACLS
- Autopulse® machine is available
- within 10 minutes ambulance transport to the study centre
- during normal working hours
- ECMO commences within 60 minutes of the initial collapse

eCPR extracorporeal cardiopulmonary resuscitation ACLS advanced cardiac life support CPR cardiopulmonary resuscitation ROSC return of spontaneous circulation EMS, emergency medical system ECMO extracorporeal membrane oxygenation OHCA out-of-hospital cardiac arrest

ered as a rescue therapy for those patients in whom advanced cardiac life support measures are unsuccessful and/or to facilitate specific interventions such as coronary angiography and percutaneous coronary intervention or pulmonary thrombectomy for massive pulmonary embolism. The Council further underlines the urgent need for randomised controlled trials of eCPR and large eCPR registries (Soar et al. 2015). Several studies are currently enrolling patients to test whether implementation of eCPR in patients with cardiac arrest can improve outcome compared to conventional advanced cardiac life support. Inclusion criteria of selected ongoing clinical studies are displayed in **Table 2**.

Conclusion

eCPR represents an experimental but potentially interesting technique to improve survival from acute cardiac arrest. Pragmatic criteria (availability of an eCPR programme, preserved functional reserve before cardiac arrest, reversible underlying cause, and alleged absence of severe hypoxic brain injury before establishment of extracorporeal circulation) should be met before eCPR is used. The results of ongoing and future trials need to be awaited to clarify the outcome effects of eCPR and specifically define the appropriate patient population for this invasive intervention. ■

Conflict of Interest

Martin W. Dünser declares that he has no conflict of interest. Daniel Dankl declares that he has no conflict of interest.

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Targeted Therapeutic Mild Hypercapnia After Cardiac Arrest

Cardiac arrest (CA) causes ischaemic brain injury and persistent cerebral hypoperfusion and cerebral hypoxia during the early post-resuscitation period. $PaCO_2$ is the major physiological regulator of cerebral blood flow, is a modifiable component of care and mild hypercapnia may lead to improved neurological outcomes for resuscitated CA survivors. In order to evaluate the potential therapeutic role of $PaCO_2$, we will conduct the TAME Cardiac Arrest trial. If TTMH therapy, which is cost free, is shown to be effective, the lives of countless CA survivors will be improved, clinical practice will be transformed, and major financial and human cost savings will be realised.

Out-of-hospital cardiac arrest (OHCA) is a common, catastrophic event that represents a major public health problem around the world. In Australia, estimates of the incidence of OHCA are approximately 1 per 1,000 persons per year (approximately 25,000 individuals in Australia each year), with Australian mortality rates varying between 87 to 94% (Berdowski et al. 2010; Victorian Ambulance Cardiac Arrest Registry 2014). For resuscitated CA patients admitted to the Intensive Care Unit (ICU), devastating neurological injury leading to withdrawal of life support or clinically important neurological impairment are the most common outcomes following CA (Lemiale et al. 2013). Accordingly, while the initial problem is cardiac in nature, after ICU admission the main reason for such dismal outcomes is neurological injury. Thus a better neurological outcome is the logical and dominant therapeutic goal in this population (Schneider et al. 2013).

Previously, from a large, multicentre, retrospective observational study we reported the association of early $PaCO_2$ values (first 24 hours) with clinical outcomes in 16,542 CA patients admitted to 125 Australia and New Zealand ICUs between 2000 and 2011 (Schneider et al. 2013). Our findings demonstrated that the occurrence of hypocapnia ($PaCO_2$ <35 mmHg) carried a higher mortality rate and a lower likelihood of discharge home for survivors compared with normocapnia ($PaCO_2$ 35-45 mmHg). In contrast, hypercapnia ($PaCO_2$ >45 mmHg) was independently associated with a 16% increase in the likelihood that a CA survivor would be discharged home, thus suggesting both safety and potential neurological benefit. Other subsequent observational studies involving adult resuscitated CA patients admitted to ICU indicate that hypercapnia is independently associated with improved neurological outcomes among survivors, while hypocapnia is associated with worse neurological outcomes, thus providing further evidence of the likely safety and possible benefit of hypercapnia (Eastwood et al. 2014; Vaahersalo et al. 2014).

Cerebral Perfusion and Arterial Carbon Dioxide Following Cardiac Arrest

It is well understood that CA leads to immediate brain ischaemia and that resuscitation leads to reperfusion injury with acute neuronal damage (Wiklund et al. 2012). What is underappreciated is that a state of sustained cerebral hypoperfusion develops and persists even after successful immediate resuscitation, return of spontaneous circulation (ROSC), and admission to the ICU (Ahn et al. 2014; Buunk et al. 2000; Koch et al. 1984). In this regard, several investigations using technologies like positron emission tomography (Edgren et al. 2003), middle cerebral artery blood flow assessment via Doppler ultrasound (Sundgreen et al. 2001), jugular bulb oxygen saturation (Buunk et al. 1999) and cerebral oximetry (Storm et al. 2014), all consistently show sustained hypoperfusion and cerebral hypoxia. For example, observational studies measuring cerebral tissue oxygen saturation ($SctO_2$) by near-infrared spectroscopy in patients receiving post-resuscitation care have demonstrated persistent cerebral under-oxygenation and a statistically significant association between such lower $SctO_2$ values and higher mortality rates (Ahn et al. 2014).

A likely pathophysiological mechanism responsible for such sustained early hypoperfusion relates to impaired cerebrovascular

auto-regulation (Kock et al 1984; Sundgreen et al. 2001). Such impaired auto-regulation may, in turn, make even a normal arterial carbon dioxide tension ($PaCO_2$) insufficient to achieve and maintain adequate cerebral perfusion and, consequently, cerebral oxygenation. However, $PaCO_2$ is the major determinant of cerebral blood flow in humans (Curley et al. 2010; O'Croinin et al. 2005), and an increase in $PaCO_2$ (hypercapnia) markedly increases cerebral blood flow under normal physiological conditions (Curley et al. 2010). The rapid vasodilatory effect of hypercapnia appears related to changes in arterial pH and cerebral vascular resistance (Koch et al. 1984; Meng & Gelb 2015). Additionally, elevated $PaCO_2$ levels are known to have anti-convulsive, anti-inflammatory and antioxidant properties, which may attenuate the inflammatory component of reperfusion injury (Kavanagh and Laffey, 2006; Tolner et al. 2011). Conversely, hypocapnia is known to increase neuronal excitability, increase cerebral oxygen consumption, reduce cerebral blood flow and, thereby, potentially worsen reperfusion injury.

Crucially, $PaCO_2$ is an easily modifiable variable and therefore a potential therapeutic target for the maintenance of cerebral perfusion and oxygenation in resuscitated CA patients (Schneider et al. 2013).

Cerebral Oxygenation and the Potential Role of Targeted Mild Hypercapnia

Until recently, there was no direct evidence on the effect of targeted hypercapnia on cerebral oxygenation in resuscitated CA patients to provide the additional biological rationale for its therapeutic application. To address this, we investigated the impact of targeted mild hypercapnia on cerebral oxygenation by performing a prospective double crossover physiological clinical study (Eastwood et al. 2016a). We enrolled seven adult resuscitated CA patients within 36 hours of their CA and compared the effect of targeting mild hypercapnia ($PaCO_2$ 50-55 mmHg) to standard care (TN) ($PaCO_2$ 35-45 mmHg) on regional $SctO_2$. With a median time from CA to ROSC of 28 minutes, at a median of 26 hours 30 minutes after CA, during TN (a median $PaCO_2$ of 37 mmHg), the median right and left frontal lobe $SctO_2$ was low with a significant proportion of values clearly below normal. However, during targeted mild hypercapnia (a median $PaCO_2$ of 52 mmHg), the median $SctO_2$ had increased to normal or above normal. Such increases were substantial in magnitude and reliably occurred in every patient every time and were not associated with any adverse events. Such findings provide further evidence for the potential role of targeting mild hypercapnia to safely improve cerebral oxygenation.

Table 1. Participant Eligibility Criteria for the TAME Cardiac Arrest Trial

Eligibility	Specific items
Inclusion criteria	1. Adult (age ≥18 years or older) 2. Comatose non-traumatic out-of-hospital cardiac arrest 3. Presence of return of spontaneous circulation following cardiac arrest 4. Receiving invasive mechanical ventilation 5. Admitted to the ICU 6. Within six hours from the onset of the cardiac arrest 7. The treating clinician believes that the patient is at risk of hypoxic brain damage
Exclusion criteria	1. Female who is known or suspected to be pregnant 2. Not receiving invasive mechanical ventilation 3. Able to follow commands 4. Clinical or radiological suspicion of raised intracranial pressure 5. Clinical or radiological suspicion of an intracranial bleed 6. Severe chronic obstructive pulmonary disease 7. Known or suspected pulmonary hypertension 8. Severe metabolic acidosis (pH <7.1 and base excess <-6 mmol/L) uncorrected within the first six hours of ICU admission 9. Transferred from another healthcare facility 10. Participation declined by the treating clinician 11. Cardiac arrest secondary to asphyxia 12. Death considered imminent

> **$PaCO_2$ is a potential therapeutic target for the maintenance of cerebral perfusion and oxygenation in resuscitated CA patients**

Targeted Therapeutic Mild Hypercapnia After Cardiac Arrest

In late 2015, we completed a randomised, controlled, parallel group, multicentre, phase II trial (Eastwood et al. 2016b). This phase II trial sought to determine the preliminary biological efficacy, feasibility, safety of delivering TTMH to resuscitated CA patients compared to standard care (TN) for the 24 hours following ICU admission. This study allocated patients to either TTMH ($PaCO_2$ 50-55 mmHg) or standard care (TN) ($PaCO_2$ 35-45 mmHg). These targets were deliberately established to avoid episodes of hypocapnia in both arms. In order to achieve a target of 50 patients with full assessment of serum neuron-specific enolase (NSE) levels (baseline, 24 hour, 48 hour and 72 hour), 86 patients were randomised from four ICUs in Australia and New Zealand. NSE is a biomarker of neuronal injury. NSE is released into the bloodstream after injury, with lower concentrations over the first 72 hours following CA indicative of decreased neuronal injury. Thus, lower levels of NSE are associated with improved neurological outcome (Calderon et al. 2014).

The study population had a median age of 61 years (79% male) and the majority were

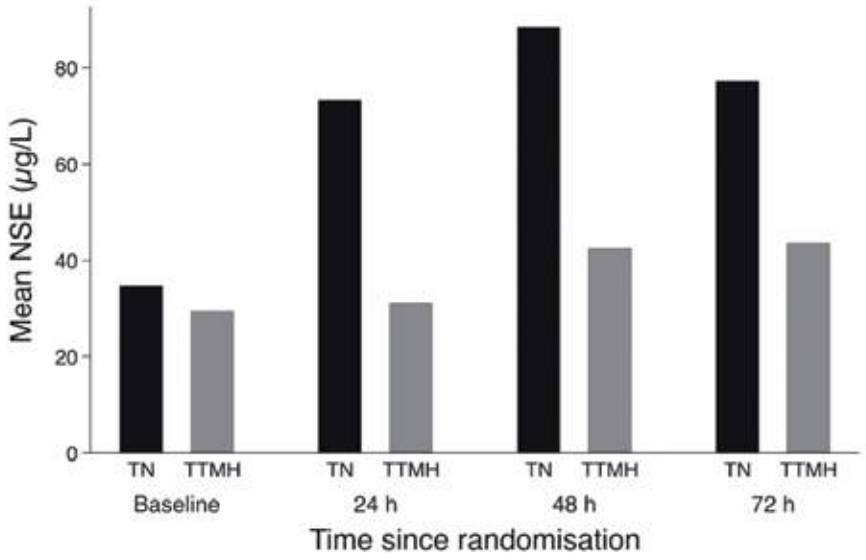

Figure 1. Mean neuron-specific enolase (NSE) concentrations at baseline, 24 hour, 48 hour, and 72 hour for patients allocated to targeted therapeutic mild hypercapnia (TTMH) and standard care (TN) who were enrolled into the CCC trial

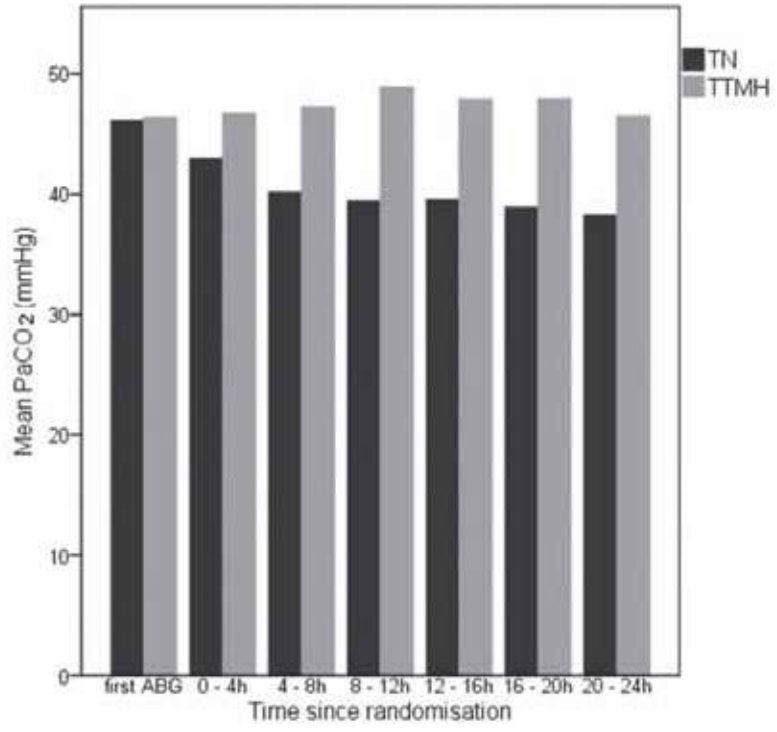

Figure 2. Time course of mean arterial carbon dioxide tension ($PaCO_2$) for patients allocated to targeted therapeutic mild hypercapnia (TTMH) and targeted normocapnia (TN) over the first 24 hours following admission to ICU for patients enrolled into the CCC trial

OHCA (78%). $PaCO_2$ separation was achieved and sustained throughout the first 24 hours following randomisation (**Figure 1**). Overall, we found TTMH significantly attenuated NSE release compared with standard care (TN) over the first 72 hours (**Figure 2**), with an identical pattern for OHCA patients, thus providing a robust signal of biological efficacy for TTMH, without differences in ventilation, temperature, or sedation management. Importantly, patients allocated to either group both avoided episodes of hypocapnia or severe hypercapnia and no clinical adverse events, sudden neurological deterioration, or clinical signs of raised intracranial pressure were reported, supporting the safety of TTMH. Most importantly, at 6 months, overall 23 (59%) TTMH patients had improved neurological outcomes compared with 18 (46%) TN patients (**Figure 3**). In addition, hospital mortality occurred in 11 (26%) TTMH patients compared with 15 (37%) TN patients (p = 0.31) (Eastwood et al. 2016b).

When the OHCA patients (80% of the cohort) were assessed separately, this effect was even stronger, as hospital mortality occurred in 8 (29%) TTMH patients compared with 13 (61%) TN patients. In addition, 20 (65%) TTMH patients had improved neurological outcomes compared with 16 (50%) TN patients (p=0.16). Thus, TTMH was associated with a beneficial biological effect (attenuated NSE levels) and a pattern of improved neurological and clinical outcomes (Eastwood et al. 2016b).

The TAME Cardiac Arrest Trial

There is now compelling epidemiological, biological, physiological, and supportive clinical data suggesting that TTMH can deliver significant outcome improvements in resuscitated CA patients admitted to ICU. In their aggregate, these findings strengthen the need to perform a larger phase III trial to address the question of whether TTMH improves patient-centred outcomes in resuscitated CA patients admitted to the ICU. As such, on behalf of the Australian Resuscitation Outcomes Consortium (Aus-ROC) NHMRC Centre of Research Excellence, the Australian New Zealand Intensive Care Society (ANZICS) Clinical Trials Group, and the Australian and New Zealand Intensive Care Research Centre (ANZIC-RC), the Targeted Therapeutic Mild Hypercapnia After Resuscitated Cardiac Arrest: A Phase III Multi-Centre Randomised Controlled Trial (The TAME Cardiac Arrest Trial) was developed. The primary outcome measure for this study will be the proportion of patients with a favourable neurological outcome at 6 months as assessed using the Glasgow Outcomes Scale Extended (GOSE) (defined as a score ≥5) (Wilson et al. 1998).

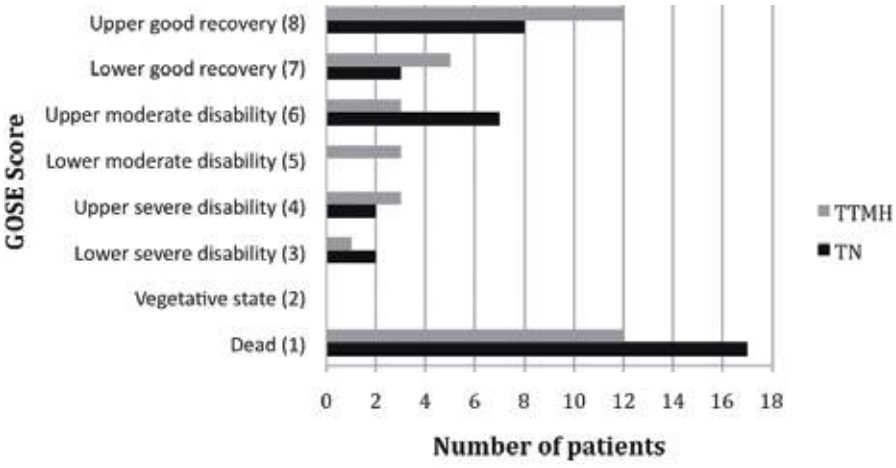

Figure 3. Glasgow outcome score extended (GOSE) assessment of patients allocated to targeted therapeutic mild hypercapnia (TTMH) and targeted normocapnia (TN) at 6 months following randomisation; with a score of >5 considered a favourable outcome for patients enrolled into the CCC trial

Five key secondary outcomes include mortality, functional recovery, cognitive functional recovery, quality of life and a health economic evaluation.

Briefly, the TAME Cardiac arrest trial will recruit 1,700 adult resuscitated OHCA patients from 30 ANZICS Clinical Trials Group member ICUs. All participating ICUs, stratified by site, will randomise patients via a website-enabled computer-generated code with permuted blocks. Eligibility criteria are shown in **Table 1**. Patients allocated to the TTMH protocol will be sedated to achieve moderate to deep sedation (a target Richmond Agitation Scale Score of –3 to –4). Arterial blood gases and end-tidal carbon dioxide levels will be measured at baseline and then used to guide respiratory rate adjustments of minute ventilation to remain within the target $PaCO_2$ range of 50-55 mmHg. Arterial blood gases will be repeated every 4 hours for 24 hours following randomisation or if end-tidal carbon dioxide values change >5 mmHg. While patients allocated to the TN protocol will be managed according to current practice in Australia and New Zealand (Schneider et al. 2013) and in accordance with ILCOR guidelines, which recommend maintaining normocapnia in these patients (Neumar et al. 2010). For both groups, ventilation management for all patients will be guided by arterial blood gas data assessed after adjustment to 37°C (alpha-stat) (standard care) (Eastwood et al. 2015) and, to ensure safety, the treating ICU physician can modify patient management, including the use of sedative agents, muscle relaxants and paralysis, as clinically indicated throughout the 24-hour intervention period. Importantly, all pre-hospital and pre-ICU care will be performed in accordance with state/territory best practice guidelines and existing local protocols. In addition, all post-ICU patient management will be at the discretion of the patient's ward-based treating physicians. ■

Conflict of interest

Glenn M. Eastwood declares that he has no conflict of interest. Rinaldo Bellomo declares that he has no conflict of interest.

Abbreviations

CA cardiac arrest
ICU intensive care unit
ILCOR International Liaison Committee on Resuscitation
NSE neuron-specific enolase
OHCA out-of-hospital cardiac arrest
$PaCO_2$ arterial carbon dioxide tension
ROSC return of spontaneous circulation
$SctO_2$ cerebral tissue oxygen saturation
TN targeted normocapnia
TTMH target therapeutic mild hypercapnia

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Prognostication Following Out-of-Hospital Cardiac Arrest

This article reviews the current evidence on prognostication after cardiac arrest.

Post-resuscitation care has developed and evolved significantly since 2003, following recommendations by the Advanced Life Support task force of the International Liaison Committee on Resuscitation to implement therapeutic hypothermia (TH) in unconscious survivors following out-of-hospital cardiac arrest (OHCA) (Nolan et al. 2003). The 2015 European Resuscitation Council (ERC) and European Society of Intensive Care Medicine (ESICM) guidelines on post-resuscitation care made strong recommendations to avoid severe hyperoxia (large amounts of oxygen) for patients following cardiac arrest (CA). This was primarily based on the evidence that severe hyperoxia is associated with increased in-hospital mortality (Kilgannon et al. 2011) and decreased survival to discharge (Elmer et al. 2015). Supplemental oxygen in absence of hypoxia is also associated with increased early myocardial injury and a large myocardial infarct size assessed at six months (Stub et al. 2015). The ERC-ESICM guidance also recommended emergency cardiac catheterisation and immediate percutaneous coronary intervention for adult patients with return of spontaneous circulation (ROSC) after OHCA of suspected cardiac origin and ST segment elevation on the electrocardiogram (ECG) (Nolan et al. 2015). A large randomised control trial demonstrated no additional benefit in survival following TH at 33˚C to targeted temperature management (TTM) of 36˚C following CA (Nielsen et al. 2013). However, the current ERC-ESIM guidance strongly recommends temperature management between 32˚C-36˚C. These recommendations were reinforced to decrease the pathological and clinical impact caused by CA, known as 'Post-Cardiac Arrest Syndrome' (Nolan et al. 2008).

> "essential that rapport and a good relationship is established with the next of kin"

The four key components of Post-Cardiac Arrest Syndrome were identified as:

I. Post-cardiac arrest brain injury;
II. Post-cardiac arrest myocardial dysfunction;
III. Systemic ischaemic / reperfusion injury;
IV. Persisting precipitating pathology.

Despite advances in post-resuscitation care management, about 50% of resuscitated patients from CA die or have a poor neurological prognosis. One of the major causes of mortality following CA is severe neurological damage due to post-anoxic brain injury (Sandroni and Nolan et al. 2015;). It is therefore essential to have a prognostication model that can predict poor neurological outcome and enable physicians to consider early withdrawal of life supporting treatment.

The Quality Standards Subcommittee of the American Academy of Neurology published a review in 2006 on prediction of neurological outcome in the comatose patient following CA (Wijdicks et al. 2006). However, the patients included in this review did not undergo TH or TTM, which was recommended subsequently. In 2015, ERC-ESICM recommended a multimodal prognostication approach for comatose survivors following CA (Sandroni et al. 2014).

Prognostication Strategy

At the recently concluded annual 37th International Symposium on Intensive Care and Emergency Medicine (ISICEM), Brussels, experts, who presented and published original studies on post-resuscitation care, explained their strategies in the workshop, *Prognostication in post-anoxic brain damage: my strategy* (37th ISICEM)

The key principles to follow are:

- early communication with the family
- delay prognostication
- multimodal evaluation, and
- be patient.

Early Communication

It is essential that rapport and a good relationship is established with the next of kin or family members at the earliest opportunity. There should be attempts to provide meaningful information and for them to be made aware of the critical nature of the patient's medical condition. This will also aid physicians to understand the expectations and goals of family members or patients. There should be regular interaction and it is vital for the family to understand that physicians will make the decision.

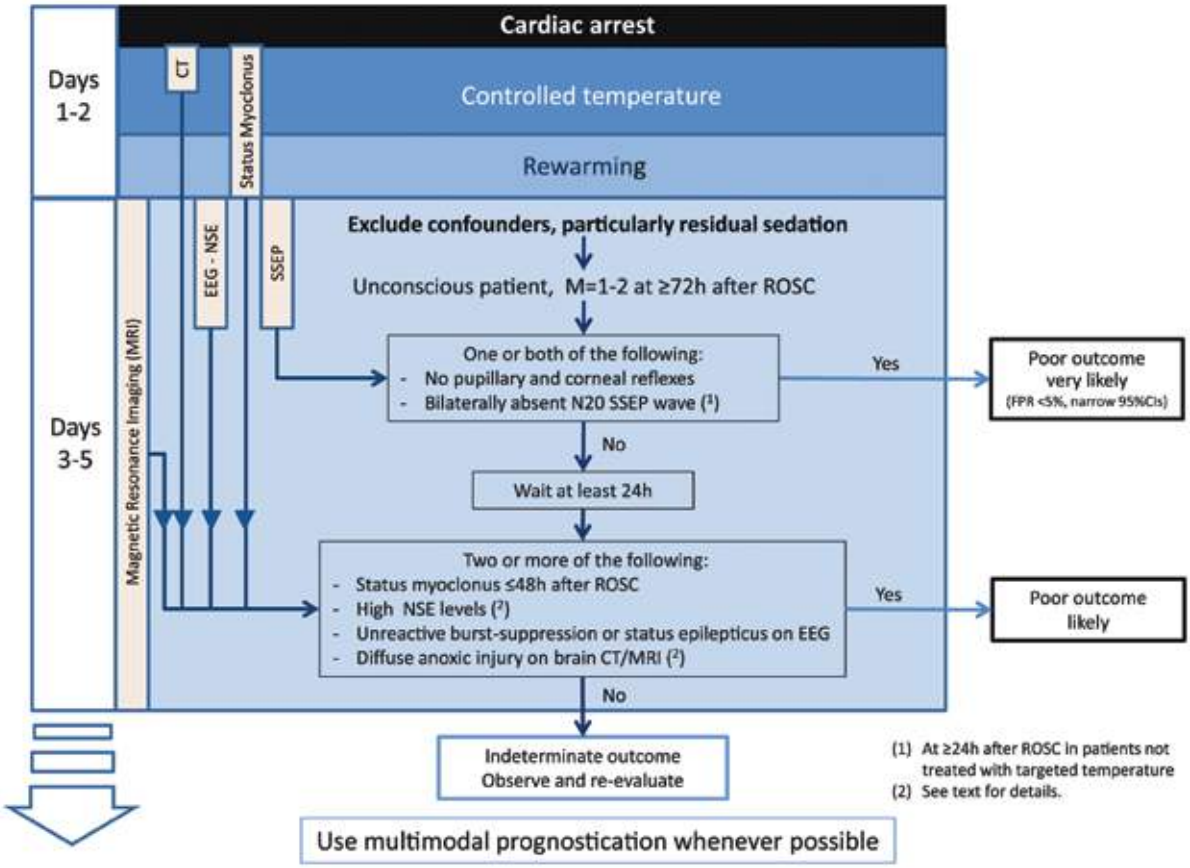

Figure 1. Suggested Prognostication Algorithm
The algorithm is entered ≥72 h after ROSC if, after the exclusion of confounders (particularly residual sedation), the patient remains unconscious with a Glasgow Motor Score of 1 or 2. The absence of pupillary and corneal reflexes, and/or bilaterally absent N20 SSEP wave, indicates a poor outcome is very likely. If neither of the features is present, wait at least 24 h before reassessing. At this stage, two or more of the following indicate that a poor outcome is likely: status myoclonus <48 h; high neuron-specific enolase values; unreactive EEG with burst suppression or status epilepticus; diffuse anoxic injury on brain CT and/or MRI. If none of these criteria are met consider continue to observe and re-evaluate. Source: Sandroni et al. 2014

Delay Prognostication

The current evidence supports the practice of first assessment after 72 or 24 hours, depending on whether patients received or did not receive temperature control management, respectively. This will help guide further management, and further prognostication can be carried out 24-48 hours later. However, the phenomenon of 'late awakening' has been described; there is a small subset of patients who will defy the 5-7 day recovery period and may wake up late and will have full neurological recovery. This is where the experience of the treating physician comes into action.

Multimodal Evaluation

The modalities for evaluation were described in the 2013 review (Sandroni et al. 2013) and are as follows:

I. Clinical examination (brainstem reflex, motor response, myoclonus);
II. Electrophysiology (burst suppression, seizures, flat or low amplitude electroencephalogram (EEG), non-reactive EEG, EEG grading, somato-sensory evoked potential (SSEP));
III. Biochemical markers (neuron-specific enolase (NSE), S-100B);
IV. Brain imaging (computed tomography (CT), magnetic resonance imaging (MRI)). It will be even more effective if this is performed by an intensivist alongside a neurologist.

Be Patient

This attribute is key and it is important to have a process. The process involves looking at all the previously described pre-, peri- and post-arrest factors, and continuous delivery of timely optimal care. It is therefore vital to be patient and to follow this process over a period of a week, even if there is no obvious visual recovery in the patient.

In 2014, an advisory statement on prognostication in comatose survivors following CA was published by the ERC and the ESICM (Sandroni et al. 2014). This statement updated and summarised the available evidence on this topic including that of TH-treated patients. The robust analysis of evidence provided practical recommendations on the most reliable prognostication strategies, and formed the basis of the ERC guidelines on resuscitation published in 2015.

The key recommendations are summarised below:

1. Clinical examination

- Using the bilateral pupillary and corneal reflexes at 72 h or more from ROSC to

predict poor outcome in comatose survivors from cardiac arrest, either TH or non-TH treated patients;
- Prolonging observation of clinical signs beyond 72 h when interference from residual sedation or paralysis is suspected, so that the possibility of obtaining false positive results is minimised;
- Not to use absent or extensor motor response to pain (M ≤ 2) alone to predict poor outcome as it has a high false-positive rate; it should be used in combination with other robust predictors.

2. Myoclonus and status myoclonus
- Using the term status myoclonus to indicate a continuous and generalised myoclonus persisting > 30 mins in comatose survivors of CA;
- Using the presence of a status myoclonus within 48 h from ROSC in combination with other predictors to predict poor outcome in comatose survivors of CA, either TH or non-TH treated;
- Evaluate patients with post-arrest status myoclonus off sedation whenever possible.

3. Bilateral absence of SSEP N20 wave
- Using bilateral absence of SSEP N20 wave at ≥72 h from ROSC to predict outcome in comatose survivors following CA treated with controlled temperature;
- There was suggestion to use SSEP at ≥ 24 h from ROSC to predict outcome in comatose survivors following CA not treated with controlled temperature.

4. Electroencephalogram (EEG)
- Absence of EEG reactivity to external stimuli, presence of burst suppression or status epilepticus at ≥ 72 h after ROSC to predict poor outcome in comatose survivors from CA;
- They should be used in combination along with other predictors as this criteria lacks standardisation and does not have very strong evidence.

5. Biomarkers

There is suggestion to use high NSE at 48-72 h from ROSC in combination with other predictors for prognosticating a poor neurological outcome in comatose survivors following CA, either TH or non-TH treated. However, no threshold enabling prediction with zero false-postive results can be recommended. Utmost care and preferably multiple sampling should be employed to avoid false positive results due to haemolysis.

6. Imaging

Using the presence of a marked reduction in grey matter/white matter ratio or sulcal effacement on brain CT within 24 hours after ROSC or presence of the extensive reduction in diffusion on brain MRI at 2-5 days after ROSC to predict a poor outcome in comatose survivors following CA both TH or non-TH treated. The brain CT or MRI should be used in combination with other predictors and only at centres where specific experience is available.

Figure 1 (Sandroni et al. 2014) suggests a prognostication algorithm approach.

Point-of-Care Focused Echocardiography

In a recent systematic review (Tsou et al. 2017), a total of 1695 patients in CA had point-of-care (POC) focused echocardiography performed during resuscitation. The study concluded POC focused echocardiography can be used to identify reversible causes and predict short-term outcome in patients with CA. In patients with a low pretest probability for ROSC, absence of spontaneous cardiac movement on echocardiography can predict a low likelihood of survival and guide the decision of resuscitation termination. It is very early to consider focused echocardiography, and it is currently not a part of prognostication strategies.

Conclusion

The current evidence suggests a delayed (post 72 h), multimodal prognostication approach for unconscious survivors who receive post-resuscitation care following cardiac arrest. ■

Conflict of Interest

Mena Farag declares that he has no conflict of interest. Shashank Patil declares that he has no conflict of interest.

Abbreviations

CA cardiac arrest
ECG electrocardiogram
EEG electroencephalogram
ERC European Resuscitation Council
ESCIM European Society of Intensive Care Medicine
NSE neuron-specific enolase
OHCA out-of-hospital cardiac arrest
ROSC return of spontaneous circulation
SSEP somatosensory evoked potential
TH therapeutic hypothermia
TTM targeted temperature management

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Resuscitation in Resource-Poor Settings

A Southern Africa Experience

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Worldwide, there are over 17 million cardiovascular deaths each year, and the prevalence of cardiovascular disease is increasing. Many regions in the world have seen mortality rates level off or improve; this is not the case for Sub-Saharan Africa (SSA). With only modest reductions in age-adjusted cardiovascular mortality, overshadowed by a blossoming and ageing population, increases in cardiovascular deaths in Africa have increased 80-101% from 1990 (Mensah et al. 2015).

Effective systems of care can have a significant impact on cardiac arrest in high-income countries (Peberdy et al. 2008; Perkins and Cooke 2012; Stiell et al. 2012), and can significantly reduce death and disability in low- and middle-income countries (Kobusingye et al. 2005). But while SSA shoulders 25% of the world's burden of sudden cardiac arrest, only 3% of the world's healthcare workforce are located there (Aufderheide et al. 2013). In SSA, prehospital emergency care systems have significant variation in quality. They range from well-developed systems of care that rival first world systems to informal community-based systems using taxi and bus drivers to community members that use wheelbarrows (Naidoo 2011) and even ox-wagon transfers (Hauswald and Yeoh 1997).

In Southern Africa, prior to 1987, there was no uniform resuscitation approach to the critically ill patient. Different organisations utilised different guidelines developed for either the least resourced (World Health Organization) or for developed health systems (American Heart Association, European Resuscitation Council, Japan). During a resuscitation attempt, healthcare professionals often differed on preferred resuscitation sequence and technique, leading to decreased team performance and concern for suboptimal patient outcomes. In March 1987, the Heart Foundation of Southern Africa convened the first South African National Basic Cardiopulmonary Resuscitation (CPR) Symposium, attended by 513 CPR Instructors from around the country, followed by a National Workshop a year later, where uniform standards and guidelines for the teaching, training and performance of basic life support were developed through consensus and provided the foundation for South Africa's national guidelines (Kloeck 1990). The Resuscitation Council of Southern Africa was formed to promote basic and advanced life support techniques relevant to all of Southern Africa: both South Africa as well as its resource-poor neighbouring countries.

International Involvement

In 1992 the American Heart Association held the National Conference on CPR and Emergency Cardiac Care. Recognising the expertise that existed within national and regional councils across the globe, the AHA invited representatives from existing councils from Europe, Australia, Canada and Southern Africa. Over 25 countries and 53 international organisations were represented, and 25% of the delegates came from outside the USA (Chamberlain and Cummins 1993). It was at this conference that the decision was made to form an International Liaison Committee on Resuscitation (ILCOR), which would offer support to develop effective emergency systems of care, a permanent infrastructure for collaboration and support for universal guidelines.

Since its formation, ILCOR has produced numerous statements to increase the impact of resuscitation (Chamberlain 2005). Unfortunately, many of the ILCOR statements require further adaptation by resource-limited countries, and often adaptations are necessary due to cost or therapy instead of cost-effectiveness of a functioning system. Examples include the relative lack of public access defibrillation and slow ambulance response time due to vast travel distances.

Local Developments

The implementation of basic and advanced adult and paediatric life support training has gained enormous popularity in Southern Africa. This contextualised training is based largely on the guidelines of the American Heart Association but modified to include the use of local devices and improvisation techniques. The high cost of training materials and equipment have been a major deterrent, particularly due to a lack of availability in most parts of Africa. The Resuscitation Council of Southern Africa has added to the improvement in resuscitation training with the addition of simple memory aids to improve resuscitation team performance and communication—namely the "9 ALS triads" (Kloeck 2001) and the "10 step zig-zag approach"—to the 5Hs and 5Ts in pulseless electrical activity management (Kloeck 1995).

Resuscitation Training

The 2015 ILCOR Resuscitation Guidelines review process looked at the PICO (Population

Kevin Mysore leading a resuscitation scenario for the PFCCS course in Gaborone, Botswana

Low fidelity simulation in another critically ill child for the second PFCCS course in Gaborone, Botswana

[Participants], Intervention, Comparator and Outcomes) question in the Education Implementation and Teams (EIT) Task Force – 634: Resuscitation training in low income countries (ilcor.org). The PICO question reviewed included students taking Basic Life Support (BLS) or Advanced Life Support (ALS) courses in a resource-limited educational setting using any educational approach, compared with other approaches. The comparison of approaches looked at the various outcomes of the effectiveness of resuscitation training. The outcomes reviewed were a change in clinical outcome, skill performance in actual resuscitations, skill performance at 1 year, skill performance at time between course conclusion and 1 year, skill performance at course conclusion and cognitive knowledge.

The review included 7 studies which met the GRADE evidence review process. The summary of findings revealed no "golden bullet approach" that would improve training in low-income settings. These findings are limited to the 7 studies reviewed and therefore did not include all the different training modalities available globally.

The recommendation from the ILCOR Task Force suggests "alternative instructional strategies would be reasonable for BLS or ALS teaching in low-income countries (weak recommendation, low quality of evidence). The optimal strategy has yet to be determined" (Finn et al 2015).

Some of the concerns around making recommendations in low-income countries are the cost of and access to training, which may play a large role in the ability of healthcare workers to receive training in BLS and ALS. The educational resources from one country to another as well as within a country (e.g. Johannesburg a "first world" city vs Manguzi a "developing city") vary and therefore a 'one size fits all approach' cannot be used.

> **"high cost of training materials and equipment have been a major deterrent"**

Does this mean that third world countries cannot use the developed world's courses and teaching approaches? We are proud to say "No!" Recently we were involved in running the Society of Critical Care Medicine (SCCM)'s Paediatric Fundamentals in Critical Care Support Course (PFCCS) in Gaborone (Botswana). This two-day short course includes pre-reading, a pre-test, practical and post-course evaluation and is considered a very intensive cognitive and skills-based course. Two PFCCS courses were conducted at the University of Botswana in February 2016. Thirty-five participants took part, and completed a brief demographic survey as well as the SCCM PFCCS pre-test and post-test at the end of the course.

Demographic data and matched test scores were de-identified for each participant and tabulated and evaluated. An increase in the score between the pre- and post-test was considered a measure of knowledge accrual. Data was reported as mean and standard deviation and compared using a paired t-test with statistical significance at 0.05.

Of 35 participants, there were 32 (91%) physicians and 3 (9%) nurses. Physician specialty groups were general paediatricians (69%), emergency medicine (9%), surgeons (3%), and anaesthesiologists (3%). 27 Participants worked in the major University-affiliated hospital (61%), 2 in a private hospital (6%) and 6 from district hospitals (17%). There was an improvement of mean test score results from 67% correct on the pre-test to 79% correct answers on the post-test [p value < 0.001].

Therefore in conclusion "participation in the PFCCS course led to increased knowledge accrual regardless of participant level of training or experience. Even in a resource-limited setting, the concepts of critical care imparted by this course could prove invaluable in improving outcomes in critically ill children" (preliminary data – Afonso et al.)

Currently in Southern Africa and extending to Central Africa is a programme originally designed by the American Heart Association's Pediatric Emergency Assessment Recognition and Stabilization Course (PEARS), which has been modified specifically to the needs and medical protocols of the Botswana Minstry of Health, and is known as the Saving Childrens' Lives programme (SCL). The SCL programme includes the base PEARS course, which is a two-day immersive instructor-led programme involving pre-reading, lectures, skills stations and real-time audience post-test evaluation. Under direction of this author group and ILCOR collaborators, Saving Children's Lives is a multifaceted implementation strategy designed to improve care of the acutely ill child in the community. It is based on embedding high

One of the final participant and instructor group photos, of the Saving Children's Lives (SCL) course to complete all the healthcare providers to be trained in the Kwaneng East and Kwaneng West provinces, held at Scottish Livingstone Hospital in the Molepolole District in Botswana

quality active in-service training with existing health management structures of quality improvement and resource allocation. Since inception in January 2014, preliminary data from the Ministry of Health and Wellness indicates the Saving Children's Lives programme has been associated with a 41% reduction in neonatal deaths, 57% reduction in infant (1m to 1 year of age) deaths, and 58% reduction in children aged 1-5 years. In contrast, non-participating district hospitals within the same system only averaged modest reductions in mortality (0.3%, 5.5%, and 37% respectively). There has been a 26% reduction in patient hospital days and 24% reduction in transfer to higher level facilities. There has been a shift of hospital admissions from the district hospital to the primary hospital, which may signify prompt treatment early, leading to less need for transfer to a higher level facility. Prior to SCL programme implementation, the district hospital had the highest infant mortality in Botswana. Now it has the third lowest infant mortality (preliminary data – Meaney and Kloeck).

In South Africa, over the past 5 years (2012–2016), a total of 14,440 Advanced Cardiovascular Life Support (ACLS) providers, 4826 Paediatric Advanced Life Support (PALS) providers and 1543 Neonatal Resuscitation Programme (NRP) providers have been trained in this internationally accepted intensive short course resuscitation training (resus.co.za). These numbers are under-reported totals as there are other International Training Centres (ITCs) not affiliated to the Resuscitation Council of Southern Africa (RCSA) offering these short courses, and therefore the numbers quoted are the minimum recorded trained by those centres affilated with the RCSA. These courses are attended and offered to all areas in Southern Africa from the major cities to the more primary (rural) and secondary level centres.

Other articles in this issue focus on the incredible "first world" directions in resuscitaion outcomes such as prognostication and extracorporeal support during resuscitation. South Africa is proud to report that we have successfully transported our first paediatric ECMO patient via our local helicopter emergency service in March this year. As one can see, some of the difficulties we have are the huge variations in what can be offered to patients, from ECMO transport to the ability of adequate BLS services within the same country.

From the above, there certainly are major attempts to improve resuscitation training in low-income areas. However, data is sparse on exactly the "how" but what is encouraging are the many local and international organisations who are trying to make a difference in resuscitation training and therefore outcomes in Southern Africa.

Conflict of Interest

David Kloeck declares that he has no conflict of interest. Peter Meaney declares that he has no conflict of interest. Walter Kloeck declares that he has no conflict of interest. ■

Abbreviations

ALS Advanced Life Support
BLS Basic Life Support
CPR cardiopulmonary resuscitation
ILCOR International Liaision Committee on Resuscitation
SSA Sub-Saharan Africa

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Why You Should Always Debrief Your Resuscitations

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Everyone who is active in resuscitation teams will admit: treating a patient in cardiac arrest is a challenge and often things will not go as you would like them to. This can lead to negative feelings when the resuscitation attempt has ended, either because the patient did not regain return of spontaneous circulation (ROSC) or the patient is transported to the cath lab for example. Negative feelings can lead to a somewhat pessimistic attitude, especially when no progress is made to improve the quality of care. I think it is obvious we should avoid these things for many reasons. I am convinced that always debriefing you resus will make a positive impact on the quality of your resuscitations, the way your team members feel afterwards and the culture in your department. And it's free. Dutch people love it when things are free.

Should we always debrief our cardiac arrests? I believe so. When you do not do it every time, you will miss opportunities to improve your system. But more importantly, when a case was really suboptimal, it is harder to get everyone together to debrief. I can remember working in an organisation where debriefing was not standard. When after a case someone asked: "Shall we evaluate this case?" Team members were surprised, and perhaps also a little afraid. Someone reacted: "Why? Everything went all right don't you agree?" From that moment on I decided to make it standard. And not call it an 'evaluation' but debriefing.

I can also remember a prehospital case where the fire department was involved. From a medical point of view, it was a straightforward case (not a cardiac arrest). And it was not complex for the fire department either. Still, the fire chief came to us afterwards and asked us: was the information of the dispatch center clear? How were things on route to the incident? Were you satisfied cooperating with the fire department? And was communication optimal? We looked a little surprised when we heard all his questions but answered all of them. He could tell on the looks on our faces this we were not used to this so he explained: "If we are not able to manage these simple incidents perfectly, we will not be able to handle difficult incidents." I knew he was right. It gave me the inspiration to debrief trauma cases even when there were no problems with the ABC's. Debriefing should be standard. It allows you to get the basics right every time.

Getting all your team members together for a debriefing is one of the biggest challenges. Most of the time, people will come and go from the resuscitation room. After regaining ROSC, and being rushed to the ICU, CT, OR, and/or the cath lab, many of the team members from the initial resuscitation are not in the room. In this setting, I usually mention a certain time when we will try and be back at the Emergency Department to debrief the case. Most of the time, I get around 80% of the team members present. When the patient does not regain ROSC, the team is usually complete when the decision is made to stop CPR. I usually announce the standard debriefing shortly after stopping CPR. Sometimes even in the same room.

There are different ways to debrief a case. Most common ways are: having every one state one good thing and one way to improve, using a checklist or to reflect on the case in a chronological order. Having every one mention the two things has the advantage of relative short time needed and you getting to know the most important things to keep and to change. A checklist has the advantage of gaining information on specific elements which you might want to know on an organisational level but can sometimes limit a real dialogue between the team members. Going over a case in chronological order gives a structure and a complete overview but will not guarantee every one will say something. So every way has its advantages and disadvantages. I usually debrief according to the first method with a checklist afterwards to see if everything is covered.

One of the things I love about the debriefing is letting every one say something, including interns, guests and everyone else who was present at that case. It can give valuable insight into how things looked from a distance. This also can help break down hierarchy and create an atmosphere where everyone has the right to express his/her feelings. As a team leader, I think it is important to give compliments as well. Recently I had a case of cardiac arrest with severe hypothermia. During the code, one of the nurses reminded me of the implications for the resuscitation. Being busy getting the resus started, I did not think of this yet. During the debriefing, I gave a big compliment to her. She gave an example of high performance team membership.

During the debriefing things will be mentioned that need improvement. It is important to acknowledge these things and try to figure out ways to make that improvement. My mindset is: how can we prevent this from happening the next time, when other people form the resuscitation team? Make these improvements, if possible, as practical as can be. Usually I ask the person who mentioned the improvement to arrange it as well. And to let the team know if the improvement is made. In this way, you will experience a more constructive culture and, more importantly, the next patient will hopefully have a better chance of surviving their cardiac arrest.

Let's debrief our resuscitations every single time. The best way is to agree on this on an organisational level but do not let this hold you back to start debriefing yourself. You can start with it today. I have experienced some great moments during debriefing and learned a lot. That is why I think we should debrief all our resuscitations. Missing a debriefing session is missing an opportunity to improve patient care. And it's free!

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Airway Pressure Release Ventilation

What's Good About It?

The use of APRV has many proposed benefits for patients with lung injury. However, quality evidence supporting the use of this technique is limited. This article summarises the purported benefits and limitations of routine use of the technique in the management of ARDS, and critically reviews the evidence supporting its use.

Airway pressure release ventilation (APRV) was originally described in 1987 (Downs and Stock 1987). Since its origin as a unique form of bi-level continuous positive airway pressure, APRV has become nearly ubiquitously available on mechanical ventilators over the course of 20 years. Increased use of the technique can be linked to presumptive benefits on oxygenation, patient comfort, and haemodynamics. To date, however, there is a dearth of quality investigational data to substantiate claims based largely on preclinical and observational studies that APRV should be the preferential ventilator mode used in patients with acute respiratory distress syndrome (ARDS).

Basic Overview of APRV

APRV is classically described as a form of pressure controlled ventilation with an inverse inspiratory:expiratory ratio (**Figure 1**). The clinician prescribes the upper limit of airway pressure to be held for a specified period (P_{high} and T_{high}), as well as the corresponding "releases" in P_{high} to a lower pressure for a predefined period (P_{low} and T_{low}). Spontaneous patient breaths are typically allowed at any time in the ventilator cycle. Thus, APRV can be defined as inverse ratio, pressure control – intermittent mandatory ventilation with unrestricted spontaneous breathing. To further improve on this classic model, numerous customisations have been described that seek to optimise synchronisation and limit de-recruitment, such as allowance of spontaneous triggering only during mandatory inspiratory cycles and initiating inspiration at various points along the expiratory flow curve according to measured pulmonary compliance.

> judgment should be reserved when considering its widespread use

Proposed Benefits

Improved Oxygenation

Perhaps the main intended benefit of APRV is achieving a higher mean airway pressure at lower peak and plateau pressures than conventional mechanical ventilation. Conceptually, this increased mean airway pressure will then better aerate recruitable lung units and improve oxygenation without leading to ventilator-induced lung injury (VILI). This concept was illustrated by Yoshida in a retrospective analysis of 18 patients with ARDS either with APRV or pressure support (PS) ventilation (Yoshida et al. 2009). Patients who received APRV were found to have more dramatic improvements at follow up in p:f ratio (median p:f 79 to 398 vs 96 to 249, p=0.018) and percentage gains in lung aeration (29 to 43%, p=0.008 vs 39 to 44%, p=ns) measured via computed tomography than patients who received PS. Similar findings of improved oxygenation have been demonstrated in additional small retrospective series, although it should be noted that the majority of publications evaluating APRV versus conventional ventilation illustrate that oxygenation between the two modes is largely similar, albeit with the benefit of lower peak airway pressures (Jain et al. 2016).

Spontaneous Ventilation

Active spontaneous breathing improves gas exchange through the optimisation of ventilation/perfusion matching in dependent lung regions (Putensen et al. 1999; Neumann et al. 2005). Given this, it is possible that the benefits seen in APRV could largely be attributed to effects of spontaneous ventilation. Putensen's group randomised 30 patients with multiple trauma to receive either APRV alone, or a 72-hour period of pressure-controlled ventilation (PCV) followed by a wean with APRV (Putensen et al. 2001). The patients in the PCV group were ventilated at the same mandatory pressure and time limits as the APRV group, but were given paralytics to prohibit spontaneous

respiration. Patients in the APRV alone group were found to have significantly higher p:f ratios through a 10-day follow-up period than their PCV counterparts, suggesting that spontaneous ventilation at APRV-type pressures may contribute to larger gains in gas exchange than an increase in mean airway pressure alone.

Another proposed benefit of spontaneous ventilation during APRV is increased patient comfort. As the main goals of sedation during mechanical ventilation are to optimise patient comfort and encourage synchrony, it follows that patients who breathe comfortably throughout the respiratory cycle may have reduced sedation requirements. The results from Putensen's study suggest that the increased patient comfort attributed to spontaneous ventilation leads directly to a reduced sedative requirement, and the authors link this finding to an observed decrease in both ventilator days (18 vs 25, p=0.011) and ICU stay (23 vs 30, p=0.032) for patients who were in the APRV group. Lastly, spontaneous ventilation during APRV may provide the additional haemodynamic benefit of increased venous return through diaphragmatic excursion. Patients in the APRV alone group in Putensen's study were found to have significantly higher cardiac indices as well as decreased dose requirements for vasopressors and inotropes, suggesting that spontaneous respirations were associated with improved haemodynamics.

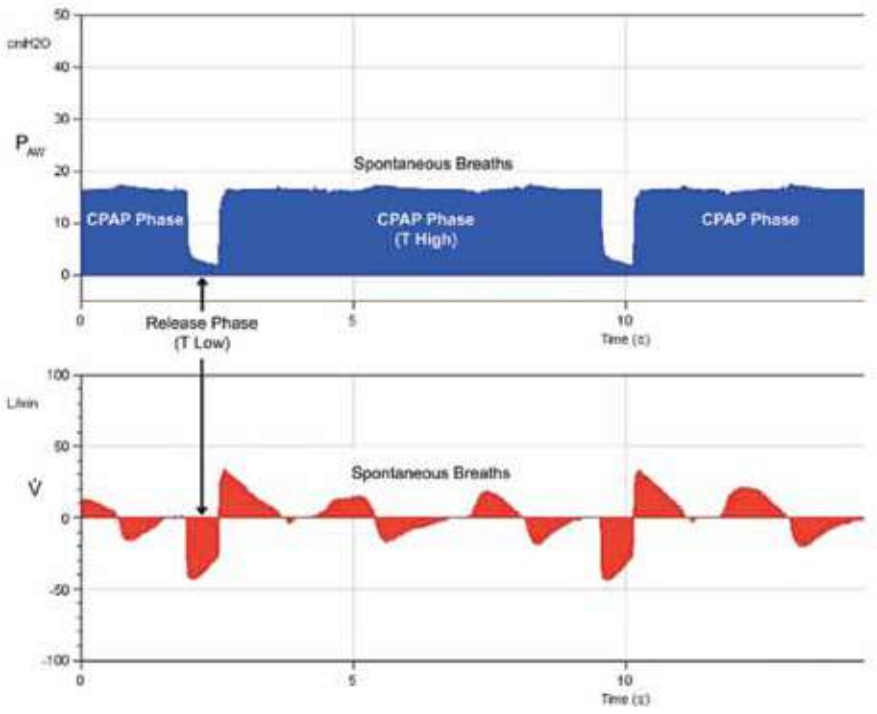

Figure 1. Ventilator tracing illustrating the typical pressure and flow characteristics of APRV

Limitations

Lack of Quality Data

Although the inferences made from the previously mentioned small retrospective series are encouraging, they do not carry the same scientific weight as evidence that would come from a randomised, controlled trial (RCT). Furthermore, the marked heterogeneity in APRV settings, stemming from a lack of commonly accepted APRV protocols, prohibits accurate meta-analyses of their outcomes. Perhaps the main limitation to APRV's inclusion in the routine management of ARDS is the lack of prospective evidence from an RCT comparing the technique to the current standard of care. As is the case in both Yoshida and Putensen's studies, the few randomised trials that have investigated the clinical impact of APRV have not compared it to the gold standard of lung-protective ventilation (LPV).

Maxwell's study in 2010 remains the only RCT to investigate whether APRV can improve outcomes for patients with ARDS when compared to LPV (Maxwell et al. 2010). 63 patients with polytrauma were randomised to receive either APRV or LPV. Of note, patients in the APRV group had significantly higher APACHE II scores. Through a 5 day follow-up period, the group did not find any significant differences between groups in p:f ratio, ventilator days, sedation requirements, ICU length of stay, or mortality. Although the study did not solely include patients with ARDS, it should be noted that 45% and 34% of patients in the APRV and LPV groups suffered from ARDS at baseline. One interpretation of the results of this trial therefore could be that APRV might neither be an effective preventative nor therapeutic management strategy for ARDS.

In contrast to Maxwell's findings, Andrews et al. published a retrospective observational review in 2013 that claimed to provide evidence of APRV's ability to prevent ARDS and possibly reduce mortality in trauma patients (Andrews et al. 2013). The authors performed a systematic review identifying studies with 100 or more trauma patients in which ARDS and mortality outcomes were reported, and then compared to those incidences to those from a single centre where trauma patients were routinely placed on APRV as a preventative strategy. The authors reported impressive differences in both ARDS incidence and mortality (14 vs 1.3 % and 14 vs 3.9% respectively). However, to suggest that APRV alone, as opposed to innumerable patient, clinical, or secular factors was the causative agent for such a dramatic difference in both outcomes is not scientifically responsible based on a comparison of observational data and class IV evidence.

Potential for Harm

As previously mentioned, spontaneous ventilation has many purported benefits. On the contrary, spontaneous ventilation can be harmful if dyssynchrony or breath stacking occur as a consequence of poor patient-ventilator interaction. Such can be

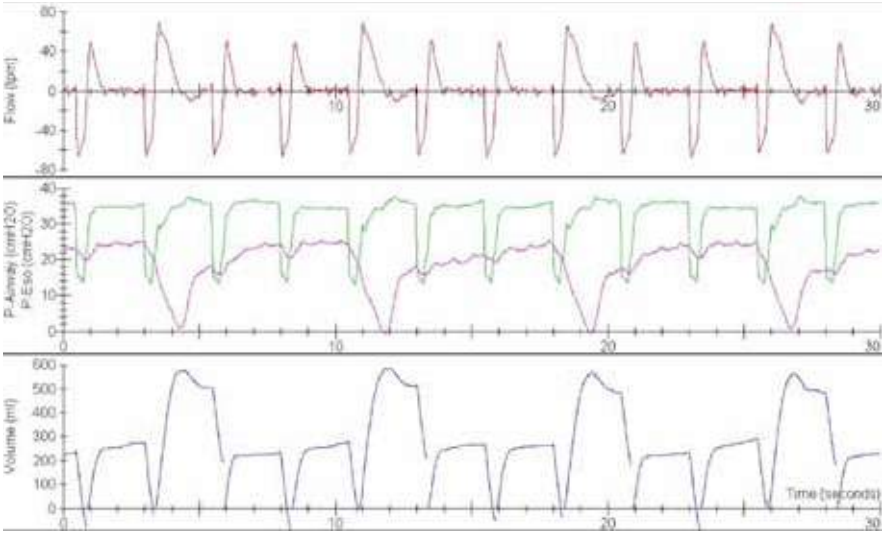

Figure 2. Ventilator tracing of a 60kg patient on APRV. Notable are the massive airway pressures (>35cm H20) and tidal volumes (nearly 10cc/kg) that can occur during spontaneous breathing, denoted by the downward deflections in inspiratory pressure (purple)

the case during APRV, despite its promise as a safe and comfortable mode of ventilation. As evident by the tracings in **Figure 2**, a patient breathing spontaneously during a period of P_{high} can be subjected to massive transpulmonary pressures and tidal volumes far exceeding the limits of conventional practice. As is the case for any mode of mechanical ventilation, close monitoring of the patient-ventilator interaction by an experienced clinician is necessary to prevent harm, especially in centres where experience in APRV is nascent.

Conclusion

Preclinical and observational data suggest that APRV has the potential to improve oxygenation without the associated cost of VILI from high airway pressures. Its utility in patients with ARDS must be rigorously evaluated through randomised, controlled trials that are powered for mortality and other clinically relevant outcomes before it can be recommended as a routine measure. As we have learned from recent investigations into the use of oscillatory ventilation, another example of a promising strategy predicated on maximising oxygenation via the open lung with minimal risk of VILI, attractive early results may not always translate to improved patient outcomes after rigorous study (Ferguson et al. 2013). Therefore, although APRV may ultimately prove to be useful for oxygenating the ARDS patient, judgment should be reserved when considering its widespread use until it achieves the level of scientific evidence available for both the standard of care and rescue therapies relied on by clinicians to improve outcomes in this challenging patient population. The authors await a number of large RCTs currently underway that may provide additional clarity to this important clinical question.

> **attractive early results may not always translate to improved patient outcomes after rigorous study**

Conflict of Interest

Brian O'Gara declares that he has no conflict of interest. Daniel Talmor declares that he has no conflict of interest. ■

Abbreviations

APRV airway pressure release ventilation
ARDS acute respiratory distress syndrome
LPV lung-protective ventilation
PCV pressure-controlled ventilation
PS pressure support
RCT randomised controlled trial
VILI ventilator-induced lung injury

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High Altitude Research and its Relevance to Critical Illness

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Critical illness can be considered as the body's failure to compensate for severe pathophysiological 'stress'. The result is a vicious circle of damage that ultimately ends in organ failure, permanent harm and, unfortunately for many, death. Fortunately, the human body is remarkably resilient. It has the ability to tolerate changes to its internal milieu and defend the cells that make up its vital organs. In the presence of a stressor, such as infection or inflammation, such tolerance occurs via the maintenance of 'normality' through multiple homeostatic mechanisms. However, the ability to preserve a cellular status quo is not unlimited, and if the stressor is sustained over time, or excessive in magnitude, other strategies are required to ensure survival. Adaptation is the process through which biological systems undergo change to tolerate a specific stressor, such as heat or cold.

Critical illness is a complex pathology, but one stressor commonly associated with it is hypoxia: a lack of oxygen for cellular metabolism. Understanding adaptation to hypoxia is vital to advancing the treatment of critically ill patients and all avenues should be explored to achieve this. One experimental model that has gained momentum during the last decade is the study of healthy volunteers ascending to high altitude, where they are subjected to a controllable 'dose' of hypoxia due to the reduced partial pressure of oxygen in the air there. Physiological and cellular responses can be measured and their relationship with performance at altitude studied. The ability to observe integrated human responses over time, through a systems biology approach, makes a high altitude laboratory a potentially fruitful model for mapping the complex phenomenon of human adaptation to hypoxia, and for testing interventions that have direct clinical applications for hypoxic critically ill patients. In essence, an external environmental stress (the atmospheric hypoxia experienced at high altitude) is used as a translational tool, comparable to that of an animal model, but allowing exploration of species-specific mechanisms. This novel paradigm for hypoxia in critical illness may provide clinically relevant biomarkers and identify novel therapeutic targets.

High Altitude and Acclimatisation

The key factor limiting ascent to high altitude is the exponential decline in the inspired partial pressure of oxygen that mirrors the change in atmospheric pressure. At the highest point on the surface of the Earth, the summit of Mount Everest (8848m), atmospheric pressure and oxygen partial pressure are approximately one third of that at sea level (West et al. 1983). It is unclear whether this pressure change itself has an independent and compounding effect (to that of the hypoxia) on human physiology (Coppel et al. 2015). By an interesting coincidence, the summit of Mount Everest appears to be the limit of human tolerance to hypoxia, and it is unlikely that humans could ascend much further (West 2009). The effectiveness of adaptation to altitude is in part determined by speed of ascent and the magnitude of altitude gained. Rapid ascent to very high altitude leaves inadequate time for effective adaptation, and can lead to unconsciousness and death (Ernsting 1963). Slow ascent, such as is achieved during a trek, allows sufficient time (days to weeks) for the process of acclimatisation to restore convective oxygen delivery through increases in heart rate (and therefore cardiac output), minute ventilation and haemoglobin concentration. This classic description of acclimatisation to altitude was formulated decades ago and has stood the test of time. However, it fails to explain inter-individual performance at altitude, as those with the greatest values for convective oxygen delivery do not necessarily cope best with altitude (Martin and Windsor 2008). Perhaps the reason for this is that beneath these overt and easily measurable systems lies a covert network of complex cellular adaptations to hypoxia, adjusting cells to their oxygen-scarce environment. These two distinct strategies (system level changes in organ function versus cellular alterations) help us to think clearly about the pathophysiology and management of clinical illness. On the one hand the body can restore oxygen delivery at altitude, but its long-term value is questionable, and requires additional energy consumption in an environment when it is in short supply. We emulate this on the intensive care unit (ICU) by augmenting cardiac output, blood pressure, oxygen saturation and haemoglobin concentration; again, often without demonstrable improvements in clinical outcomes

(Hayes et al. 1994). Cellular changes in response to hypoxia, however, tend to alter metabolism in a way that improves the efficiency with which oxygen is used and thus saves valuable energy. If these processes could be mimicked via a therapeutic intervention, new treatments targeting metabolism have the potential to benefit critically ill patients.

At the heart of cellular acclimatisation is the genetic transcription factor hypoxia-inducible factor (HIF), the master regulator of hypoxic responses (Semenza 2000). The HIF complex exists in every cell of the body; it proliferates in hypoxic conditions, and up-regulates many different genes involved with oxygen delivery and consumption, cell proliferation, and a vast array of metabolic processes. The importance of this oxygen sense-and-response system is highlighted by the fact that it is preserved throughout most living organisms on Earth (Iyer et al. 1998). We should, therefore, rest assured that HIF is constantly ready to protect us from hypoxia, through the initiation of a complex network of cellular changes. Of note, no such rescue system exists to protect us from hyperoxia-induced reactive oxygen species damage, beyond a limited supply of endogenous antioxidants.

The study of native high altitude populations, such as Andeans, Ethiopians and Tibetans, can provide fascinating insights into long-term hypoxic adaptation. Tibetans in particular display phenomenal adaptation to hypoxia, perhaps unsurprising given that their altitude ancestry stretches back over 20,000 years. Whilst genetic alterations that have occurred during this time have been reported (Simonson et al. 2010; 2012), the successful phenotype of this population remains elusive (Gilbert-Kawai et al. 2014). One thing that we can be certain of is that, contrary to popular belief, Tibetans do not have a raised haemoglobin concentration at altitude (Beall et al. 1984). Understanding more about the biology of Tibetans may also benefit critically ill patients, through interventions that reproduce their hypoxia survival strategies. Thus far, almost every genetic locus identified to be positively selected for in these ancestral high altitude populations appears to be involved in the HIF complex or its downstream target genes.

Examples of Translational Findings from High Altitude

Permissive Hypoxaemia

On 23 May 2007, four climbers descending from the summit of Mount Everest stopped at an altitude of 8400m to take femoral arterial blood gases from one another for rapid analysis in a standard benchtop analyser at 6400m (Grocott et al. 2009). The results revealed some of the lowest levels of blood oxygenation ever reported in humans, one of which was an incredible 19.1 mmHg. With the caveats that these were healthy, physically fit individuals known to perform well at altitude, these data allow us to speculate on whether normoxaemia is truly a necessary target for the critically ill (Martin and Grocott 2013). An intriguing coincidence is that similar levels of hypoxaemia are observed in every normally-developing human foetus, suggesting that all humans possess the innate ability to withstand significant hypoxaemia

> **“The paradigm of ascent to high altitude has now become accepted as an alternative to the mouse or petri dish”**

(Martin et al. 2010). Since these data were presented, a number of studies have been undertaken to explore the benefits of ‘permissive hypoxaemia’ (generally considered to be an SpO_2 of between 88-92%) in the critically ill (Suzuki et al. 2014; Panwar et al. 2016; Helmerhorst et al. 2016). Whilst the safety and efficacy of permissive hypoxaemia has yet to be fully elucidated this could lead to a substantial shift in practice with the potential to benefit critically ill patients.

The Microcirculation

There has been a great deal of interest in measuring microcirculatory blood flow for many years; reduced and heterogeneous flow in capillary beds has been associated with worse clinical outcomes in the critically ill (Bezemer et al. 2012). Microcirculatory flow index (MFI) in the sublingual microcirculation decreases on ascent to high altitude whilst capillary density increases (Martin et al. 2009; 2010). The reduction in blood flow may be due to the polycythaemia that accompanies acclimatisation, and may actually represent maladaptation. This hypothesis is supported by the fact that a reduction of flow is not observed in Sherpas (of Tibetan descent) when they ascend to altitude (Gilbert-Kawai et al. 1985). Tibetans have been shown to have more than double the forearm blood flow of low-altitude residents, resulting in greater than sea level oxygen delivery to tissues (Erzurum et al. 2007). From this it can be deduced that local capillary blood flow is a crucial component of convective oxygen delivery that may have a significant influence on performance.

Nitric Oxide Biology

Ascent to altitude leads to an elevation in biomarkers of nitric oxide production (nitrate and nitrite) and activity (cGMP) (Levett et al. 2011). Furthermore, MFI correlates inversely with plasma nitrite concentration (Levett et al. 2011). When compared to lowland residents, Tibetans were seen to have more than ten times the circulating concentrations of bioactive nitric oxide products (plasma and red blood cell nitrate and nitroso proteins and plasma nitrite), suggesting this mechanism is advantageous in hypoxic adaptation. It is therefore conceivable that nitric oxide levels determine peripheral and microcirculatory blood flow and are central to the acclimatisation process. Therapies that manipulate nitric oxide biology may therefore be of value to the critically ill.

Metabolism

The ultimate consumers of oxygen are the mitochondria, whose ability to produce ATP is ultimately limited by the partial pressure of oxygen. Imbalance between mitochondrial oxygen supply and demand will not only reduce the energy available to drive cell functions, but also increase the local production of damaging reactive oxygen species (ROS), exacerbating dysfunction and cell death. Mitochondrial function in critical illness is known to influence mortality, with reduced ATP levels observed in the skeletal muscle of non-survivors of severe sepsis (Brealey et al. 2002), and early mitochondrial biogenesis

associated with recovery (Carre et al. 2010). During prolonged exposure to high altitude, humans demonstrate adaptation at the mitochondrial level, in both cardiac and skeletal muscle (Murray 2016). At altitudes >5500m there is a marked loss of mitochondrial density, and downregulation of specific respiratory complexes in skeletal muscle (Levett et al. 2012). It has been hypothesised that this reduction in mitochondrial numbers may reduce the oxygen demand of non-vital tissues, sparing oxygen for more vital organs, whilst also reducing the burden of oxidative stress by removing the principal source of reactive oxygen species (Howald and Hoppeler 2003). This seems to occur in regulated manner, with decreased density mirroring the reduction in mitochondrial biogenesis factor PGC-1α during prolonged exposure to high altitude (Levett et al. 2012). Compensatory changes have been observed to promote ATP production in the face of diminished oxygen availability and reduced mitochondrial numbers at high altitude. Remaining mitochondria appear to become more efficient. There is increased coupling between oxygen consumption and ATP generation; perhaps mediated by uncoupling protein (UCP) 3, which is shown to be downregulated at high altitude (Levett et al. 2012). A stoichiometric increase in the yield of ATP produced per molecule of oxygen consumed can be achieved by a switch away from fatty acid oxidation (Hinkle et al. 1991), and is observed in Sherpas (Hochachka et al. 1992).

Pathways underlying metabolic acclimatisation are potentially important targets for optimising outcomes in critical illness. HIF-target genes, whose levels are controlled in response to cellular oxygen levels, include many different metabolic enzymes and regulators, including the master regulator of fat metabolism, peroxisome proliferator-activated receptor alpha (PPAR-α) and its target proteins, enzymes of fatty acid oxidation and UCP3 (Narravula and Colgan 2001). Pharmacological manipulation of these metabolic pathways may allow us to boost the metabolic efficiency and oxidative stress defences of patients under conditions of hypoxic stress.

Conclusions

Recent studies of volunteers ascending to high altitude have focused attention on adaptation to hypoxia at a cellular level. Similar changes are likely to be occurring in critically ill patients and commonality in these responses may yield new programmes of clinical research and the development of novel biomarkers and treatments. The paradigm of ascent to high altitude has now become accepted as an alternative to the mouse or petri dish and is likely to continue shining light on an otherwise obscure pathophysiology that has yet to be tamed. ■

Conflict of Interest

Daniel Martin declares that he has no conflict of interest. Helen McKenna declares that she has no conflict of interest.

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How to Run Successful Rounds in the Intensive Care Unit

Rounds in the intensive care unit (ICU) allow for scheduled discussions in which healthcare providers review clinical information and develop care plans for critically ill patients. Despite this straightforward concept, there is widespread variability in numerous components of rounds. While some of these differences are culturally rooted and, as such, unavoidable, unintentional or unnecessary variability in key structures of rounds can lead to significant issues related to patient safety and dissatisfied patients, families and/or members of the multiprofessional ICU team. This article addresses some of the key components to successful ICU rounds with the goal to advance current practice patterns.

What are Core Principles of ICU Rounds?

First and foremost, the focus on rounds must be on the patient. While multiple elements of rounding will have to be tailored to a specific ICU, having the patient at the centre of all that happens on rounds must transcend differences in ICU structure and culture. Equally important, clear communication between team members is a requirement that positively impacts the quality and safety of patient care.

Which Healthcare Professionals Should Be On Rounds?

In 2015, the Society of Critical Care Medicine published practice guidelines focusing on processes of care and ICU structure (Weled et al. 2015). These guidelines strongly emphasise the importance of an intensivist-led multidisciplinary team. While a physician skilled in intensive care is a key component for successful rounds, we believe that a physician's presence, while critical, is insufficient. Although not every ICU will have all team members listed below, the more professionals with diverse and complementary skill sets, the more effective rounds will be.

Depending on the size of an ICU and patient acuity, an intensivist may spend 5-10 percent of their day (or less) with each individual patient. In contrast, based upon local staffing practices, the bedside nurse spends anywhere between 33-100 percent of their time with each patient. It therefore follows that the bedside nurse has a much better second to second knowledge of the patient's medical condition than the physician, and, as such, can often offer valuable insight that might be otherwise missed in developing the daily care plan. Furthermore, nurses also frequently have an in-depth knowledge of the humanistic concerns of patients and their families due to both increased contact time as well as a specific emphasis on this throughout their training. Adding this perspective to rounds brings an additional dimension that may otherwise be lacking. Finally, the bedside nurse is charged with directly carrying out many elements of the daily plan discussed on rounds, and direct communication is crucial towards its successful completion.

Critical care pharmacists assist clinicians with pharmacotherapy decision-making and dosing. They also play a crucial role in reducing medication errors and improving medication safety by identifying drug-drug interactions and assuring appropriate initiation and discontinuation of medications. Notably, a landmark study prospectively evaluated the impact of pharmacist participation during patient care rounds in a medical ICU on the rate of preventable adverse drug events, and found that the presence of a pharmacist on rounds was associated with a significant reduction in the total number of preventable adverse drug events (Leape et al. 1999). Studies have also shown improvements in infection control management, anticoagulation therapy, and sedation/analgesia utilisation in ICUs with critical care pharmacists (Preslaki et al. 2013).

Advanced practice practitioners (nurse practitioners and physician assistants) are increasingly being utilised in ICUs worldwide. These highly skilled practitioners have a diverse skill set and often function as the first-line bedside provider for patients, performing histories/physicals, developing differential diagnoses, constructing daily care plans, prescribing medications and performing procedures. Whereas physicians frequently

rotate to other responsibilities in the hospital and do not work full-time in the ICU in many parts of the world, advanced practice practitioners typically work full-time only in a single ICU and thus provide continuity that would otherwise be missing. Notably, outcomes in ICUs with advanced practice practitioners are at least equivalent to that provided by resident physicians (Kleinpell et al. 2008).

A large percentage of patients in the ICU require either invasive or noninvasive mechanical ventilation. In ICUs with dedicated respiratory care practitioners, they play a partnership role in determining the optimal way to ventilate a patient as well as physically manipulating ventilators. In addition, many ICUs have dedicated nutrition teams. In light of the multiple complex ways to feed patients enterally and parenterally, dietitians and others with specialised nutrition expertise play a vital role on rounds. Religious beliefs and the role those beliefs play vary widely between cultures; however, chaplains with specialised training to engage and support patients and their families in these often forgotten domains can have a significant impact on a wider view of patient care. Finally, every patient admitted to the ICU will eventually leave the ICU. Post-ICU options vary widely in the terms of locations to which a patient can go. For instance, in the United States, patients may be discharged to the hospital wards, long-term acute care facilities, nursing homes, skilled nursing rehabilitation, hospice, or (rarely) home. Navigating this complex array of potential locations, which is also dependent upon both availability and payer status, is an important portion of rounds in order to help the patient who no longer needs ICU services and the future patients who need an ICU bed in order to receive lifesaving critical care services. Social workers play a crucial role in planning and managing patient flow to optimise the location for patients following ICU discharge.

Should the Patient's Family Be On Rounds?

Although the primary focus of rounds should be on the critically ill patient, patients are rarely going through their ICU experience by themselves. Typically, their family is unprepared for the stress brought on by the acuity and complexity of an ICU admission. Exacerbating this stress is a general lack of understanding of what is happening to their loved ones.

Family participation on rounds represents an opportunity to improve collaboration and to engage in shared decision making with the ICU team. The American College of Critical Care Medicine's guidelines describing evidence-based best practices for patient- and family-centred care in the ICU recommend family participation in rounds as a way to improve bidirectional communication (Davidson et al. 2007). Family participation in rounds has multiple potential advantages. First, they allow family members to hear the daily plan of care. Understanding concrete daily goals can help make an ICU experience seem less overwhelming. Next, it allows transparency in care so families do not feel the medical team is hiding something from them (which unfortunately occurs frequently). It also allows for rapid communication of patients' wishes and concerns for patients unable to verbalise these to the rounding team. Finally, the family typically knows the patient's pre-morbid condition more accurately than the rounding team.

> "engaging the family interested in joining the rounding team in a culturally appropriate and respectful manner has numerous benefits that outweigh the associated challenges"

They also frequently know critical components of both the pre-ICU medical history and moment-to-moment experience in the ICU that would otherwise not be elucidated, which can in turn improve patient care and experience. While critics cite prolongation of rounds, reduced medical education opportunities, and avoidance of difficult clinical discussions as negative consequences when families join multidisciplinary rounds, the preponderance of the evidence supports families joining rounds. It is important to understand that this is not "one size fits all" and that some families prefer not to join rounds or to do so in a more limited fashion. It is important to note that we understand there is tremendous international variability related to the concept of families joining on rounds and several large countries have not instituted this concept, even on a pilot level. While we are respectful of these differences and the challenges associated with behaviour change, we respectfully submit that engaging the family interested in joining the rounding team in a culturally appropriate and respectful manner has numerous benefits that outweigh the associated challenges.

What is the Role for Standardised Rounding Structure?

In the practice of critical care, standardised protocols including evidence-based care bundles and order sets have led to improvements in a number of clinical endpoints. Standardisation of ICU rounding structure should be no different, and healthcare provider satisfaction has been shown to improve after implementation of a standardised rounding process and communication system (Lane et al. 2013). While there is no single optimal structure, standardisation of what time rounds start (should be the same 7 days a week) and location improves rounding effectiveness by facilitating greater participation among team members and improving team member attendance. Rounds should emphasise a systematic approach not only to patient data presentation but also to formation and documentation of treatment plans, timing of team member input, allowance for questions and clarifications, and summary of overall goals of care for the day.

What Makes a High-Functioning Team?

In addition to the construction of a multidisciplinary ICU team that has a standardised approach, there are several other factors needed to ensure such a team is highly functional and able to deliver the highest quality of patient care. Explicitly defining the role of each healthcare provider on the ICU team has been shown to increase patient-centredness and facilitate more effective discussions on rounds. Access to patient data for all health-

care providers and documentation of patient care goals are two key components reported by bedside providers to contribute to successful rounds (Lane et al. 2013). By definition, each member of the multidisciplinary team will have a different background and skill set, but it is imperative that all members support each other and treat each other with respect. Mutual respect optimises the clinical environment allowing for improved communication, collaboration, and teamwork. For instance, a study examining nurses' perspective on interprofessional communication in an ICU suggested that destruction of the hierarchical structure and power imbalance imposed on nurses by physicians creates more constructive clinical decision-making and improves information flow and communication between healthcare providers (Knoll et al. 2008). Anecdotally, this is why both of the authors of this article request that all members of the ICU team call them by their first name, regardless of their specialty. Empowering team members increases contributions during rounds and promotes a team-oriented approach to critical care management.

How Should Communication and Information Transfer Be Optimised?

Effective communication is vital to the successful care of critically ill patients. Communication failures are an important source of medical error, whereas conversely effective communication decreases medical errors and improves patient outcomes. This is especially important in the ICU where patients undergo numerous tests and treatments daily and have limited physiological reserve to tolerate even the smallest setback.

There is a strong association between provider understanding of the daily treatment plan and goals of care with provider satisfaction, perception of quality communication, adherence to practice guidelines and improved patient outcomes. By implementing a standardised rounding process, including documentation of patient daily goals at bedside or utilisation of daily goals checklists, barriers to communication are reduced and providers perceive a higher quality of communication between team members (Justice et al. 2016). All providers should be encouraged to speak clearly and audibly so all members of the care team can hear and have an opportunity to ask questions to clarify any points of confusion and practise closed-loop communication. Flow of information is critical, and just because something is said does not ensure it is understood. This is why a reiteration of the daily plan in some form (order readback from the person entering daily orders, reiterating the daily plan by either the team leader or those responsible for carrying out the plan) is critical to ensure that the plan has not only been heard by the team but also has been clearly communicated. Further, a "to do" list developed on rounds helps minimise lost information.

Other potential sources contributing to problematic or ineffective communication include interruptions during information transfer and rounds, lack of clear responsibilities and expectations for each team member, and insufficient understanding of patient care goals and daily treatment plans by all team members. Assigning roles to all team members involved in rounds allows for the ability to focus on one's specific responsibilities and remain engaged in discussion.

How Should Learners Be Integrated Into Rounds?

In academic medical centres in particular, ICU teams often consist of trainees from multiple specialties with different levels of training and exposure to critical care pathology. Learners may require some degree of individualised teaching and instruction, which can be difficult given the acuity of the ICU and the time constraints of other members of the team. While there is no single optimal approach to teaching, it is important to provide an interactive commitment to education focusing on maximising the engagement of all participants. Avoiding a condescending attitude towards trainees (and all team members) is crucial. While engaging trainees and simultaneously efficiently running patient-centred rounds can be challenging, the payoff for both trainer and learner can be enormous.

Conclusion

Although the concept of rounding in the ICU sounds simple, effective rounding requires considerable effort in numerous overlapping domains. Optimally, ICU rounds should be efficient, professional, interactive and educational. Finally, despite the very serious nature of our clinical environment, it is a tremendous privilege to work in the ICU, and rounds should be enjoyable—and even fun—if at all possible. ■

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From Independent Attorney to Critically Ill Patient

How Acute Respiratory Distress Syndrome Changed My Life in a Split Second

Life changed forever when Eileen Rubin was hospitalised with ARDS. After a slow recovery it was time to give something back, and Eileen went on to co-found the ARDS Foundation.

"I can't breathe. I think I'm dying." Those were the words I gasped to my mother less than two days after being admitted to the Medical Intensive Care Unit on 2 June 1995. I was thirty-three years old.

Immediately, my mother flew out of my room in search of help. She found my internist and repeated my words verbatim; he responded calmly, "She's anxious. It's nothing, I'm sure." My mother was insistent. She saw the pleading in my eyes; she knew I believed what I said.

Though he was quite reluctant, she convinced my doctor to enter my room. One glance at me and the machines connected to me and chaos ensued. He ordered visitors to leave. A code was called. Staff responded with urgency. And in the waiting room, my loved ones sat anxiously for nearly three hours before any information was forthcoming.

It was inconceivable that my last words could have been, "I can't breathe. I think I'm dying." And though they were not my final words, those were the last words I spoke for the next eight weeks. However, I was one of the lucky ones. Against the odds, I survived.

ARDS Diagnosed

When Acute Respiratory Distress Syndrome (ARDS) was diagnosed, my internist was so unfamiliar with ARDS, he often was observed doing research. My critical care physician explained this syndrome to my family with difficulty. It was just so hard to understand. Concern grew because doctors seemed very confused about their diagnosis and how to proceed. Often physicians were unavailable and my family had to ask nurses questions; they would not respond, and also declined to call physicians to offer answers or explanations. This left my family lost, confused, concerned and frightened. On a regular basis, my family was asked to sign documents providing consent for tests and procedures, often without fully understanding my condition. Lacking sufficient information to confidently authorise medical care that could result in potential life and death decisions was asking a lot of family. But often consent was necessary.

To complicate matters further, there were so many physicians. Each specialty had its own 'group.' Pulmonary had three; Infectious Disease had two. There were doctors from Psychiatry, Rheumatology, Cardiology, Neurology, Haematology, the ENT group, a Thoracic Surgeon and more. Aside from physicians, there were nurses, respiratory therapists, occupational therapists, physical therapists, speech therapists and a biofeedback specialist. The team seemed to include almost everyone. But it did not include my family. And later, it did not include me.

After two weeks, the hospital called a family meeting, attended by three physicians, the head of nursing, a social worker and my family. They alluded to what they believed: that I would never breathe on my own again, that I may have suffered brain damage and that this was a quality-of-life issue. They urged my family to consider removing life support, Doctors were told to do everything within their power to treat me. This meeting, initiated by the hospital, was arranged very quickly. To the contrary, when I asked for a family meeting in my ninth week, it was difficult to organise. Only two doctors showed, but one left early. There was one nurse, my mother and me. My 'team' had disappeared.

Although the hospital made it difficult to bring in a consulting specialist from another area hospital, my parents persisted and persevered. The consulting critical care specialist pored over my records, spoke to my doctors, examined me extensively, and reported to my family that my doctors were medically doing everything, but cautioned that he felt my doctors were 'giving up on me too soon.' He gave his cell number to my father, telling him to call anytime. That gesture, and this doctor's reassurance, offered renewed hope that the possibility of my survival existed. To this day, over twenty years later, my father still carries that slip of paper in his wallet.

I spent four weeks in a drug-induced coma. Doctors were certain I remembered nothing. I was certain they were wrong. Once out of the coma, when each physician came to my room, each stated their name and specialty. I already knew who he or she was. More than that, I also knew whether or not I liked that doctor.

Only days later, late at night, when a single room opened on the vent floor, a flurry of activity ensued. Before I realised what was happening, I was being transferred out of ICU. I panicked. I had grown 'comfortable' in the MICU. Why was I being moved so late at night. How would people find me? I was confused and frightened. This seemed wrong. I looked at my parents and sister with obvious anxiety. "This is good," they said. "This means you're getting better.'" I knew that was not true. Why would they move me from a place of comfort to the unknown? My distress grew. Then they

forced my family to leave. I felt completely alone in this unfamiliar place, with unfamiliar staff, unable to communicate, not by writing, not by speaking. I was terrified.

Shortly after, I suffered a serious case of delirium. I remember being unable to sleep, imagining fantasy weaved in with fact, resulting in bizarre, unbelievable stories that seemed so real. I heard everyone around me, mostly talking about me. After a couple of days, I had a neurology consult. But I was angry. I was upset they brought in another doctor. And I was so tired of being completely dependent. I could not move; I could not speak. I needed to exert some control. In this state of mind, I decided not to cooperate with the neurologist. I did not realise the potential consequences. The doctor grew frustrated. He asked my nurse if I cooperated with her. She said, "Sometimes." And then he raised my left arm above my head and let it drop. He did the same with my right arm. Excited, he announced to my family, "She protected her face!" He explained delirium to my family. He stayed the entire day, performed numerous tests and ruled out other possible causes. Finally at 11:30 pm, he reintroduced the morphine. When the fentanyl, morphine and other drugs were abruptly discontinued without weaning, along with being moved out of ICU, this contributed to my delirium. My neurologist was the first doctor at this hospital who made my family feel part of the team.

Slow Recovery

As I struggled with occupational and physical therapy, fought to wean from the vent, battled constant complications, I realised how many people were involved with my care. It was an army of clinicians but too often, they did not communicate with one another. Doctors offered contradictory information about my medical condition and progress. We expected to receive accurate, consistent information provided by the medical team. That failure created confusion, uncertainty and anxiety.

As a ventilated patient, unable to speak, but full of questions, I often wrote notes to doctors. One day, as I was writing follow up questions, my pulmonary doctor abruptly turned his back and started to walk out. In disbelief, I threw my pad of paper at him; my toss was too weak to make contact. Without noticing, he continued out of my room. I was infuriated to be treated with such disrespect.

In spite of often being treated as "the ARDS patient in room 704" rather than Eileen Rubin, I had many doctors, nurses, therapist and other staff who helped me survive ARDS, sepsis, and many related complications over my nine-week hospitalisation. When I was discharged on 4 August 1995, I walked out, albeit slowly, but on my own. I could not have done that but for my dedicated team of medical professionals, and because of those very people, I knew that one day I would have to give back.

> **"It was an army of clinicians but too often, they did not communicate with one another"**

Recovery was a slow, isolating process. People called and visited less, and then, not at all. Everyone around me went back to their daily routine, but my life was forever changed. I could no longer sleep through the night, but during the day I was exhausted. Ten months after my ICU admission, I went back to work part-time. I finally felt, physically and mentally, able to practise law. I fought depression occasionally, but on my two-year ARDS anniversary, I suffered post-traumatic stress disorder (PTSD). It was debilitating. Finding a therapist with experience treating patients suffering PTSD as a result of surviving critical care illness was challenging. Luckily, I found one who helped me out of the darkness.

ARDS Foundation Established

Five years after surviving ARDS, I looked at my children and thought, "If they got ARDS and I did nothing, I could not live with myself." I was ready to give back. With Paula Blonski, who lost her sister to ARDS, we cofounded ARDS Foundation, a nonprofit organisation, with the primary goal of creating an easy-to-read brochure. We wanted families to have more resources than our families had when doctors gave patients a diagnosis of ARDS. We wanted to ensure families received support when their loved one was critically ill, so we we created a website where people could go at any time of the day or night. Immediately, people contacted us from all over the world seeking information, wanting support. Almost everyone told us they never heard of ARDS until they or their loved one was diagnosed.

Sixteen years later, most people still say they never heard of ARDS before this syndrome entered their lives. No one asks to be part of the ARDS Community, but once someone 'joins' ARDS Foundation is available for information and support. Paula and I have volunteered our time since our inception in December 2000. We attend the American Thoracic Society (ATS)'s International Conferences every year. I represented ARDS Foundation on ATS's Public Advisory Roundtable for nine years. Over the years, I have been a member of numerous committees at ATS as well as others related to critical care research. As a patient speaker, I have presented at more than ten ATS sessions as well as at other events. I am currently the Society of Critical Care Medicine's Discovery Committee Chair of their Patient Engagement Workgroup.

ARDS Foundation has offered three partnership grants for medical research. We have given numerous travel grants. We have partnered to offer nursing scholarships in memory of Paula's sister, Marybeth Monaghan, to area nurses intending to work with critical care patients after they complete their master's degree. ARDS Foundation also facilitates many medical research surveys and projects. We are dedicated to providing education, information, awareness and support of Acute Respiratory Distress Syndrome to critical care patients and families and we are dedicated to the clinicians who continue to research these areas.

Conclusion

I have always felt that the addition of the patient and family voice was critically important in all areas of healthcare. Being respected, treated with dignity, included on the team, sharing our stories, expressing priorities related to medical research, working in concert with clinicians, is the ultimate goal.

After surviving ARDS, I had one doctor tell me I almost died five times; another doctor said that I am the sickest patient he has ever seen who lived. To be sure, my life changed forever when I was hospitalised with ARDS. Was it a blessing in disguise? I like to think it was. ■

Anaesthesiology Trainees

We Are Also Intensivists!

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In 2014, a few trainees from opposite corners of Europe had the somewhat bizarre idea that all anaesthesiology trainees should be able to communicate on a common platform. What followed was an almost immediate endorsement of this plan by the European Society of Anaesthesiology (ESA) Board of Directors, which led to the first European-wide survey on trainees´ needs, goals and expectations (Sobreira Fernandes 2015 et al., unpublished results). In parallel, the trainees mentioned above started to work on the foundation of the ESA Trainees Committee (ESATC) and on what became the first pan-continental Anaesthesiology trainee network – the ESA Trainee Network (Trainees Committee Policies, esahq.org).

The first shock we had while taking part in this endeavour was the heterogeneity in training systems, leading to somewhat diverging objectives in terms of end-of-training abilities and competencies. The same had been previously postulated by two trainees from Western Europe, as well as Eastern Europe, in a conference that took place at Euroanaesthesia 2015 (Longrois et al 2016). In the same year (2015), the National Village exhibition at Euroanaesthesia had as a theme the anaesthesiology residency formats throughout Europe (Filipescu 2015). After compiling the data from the 19 countries that presented their results, what we expected through our personal experience was confirmed by the numbers.

Regarding the training format we differ significantly, namely the period of time allocated to Anaesthesia, Intensive Care Medicine, Pain Therapy and Emergency Medicine. Concerning Intensive Care Medicine, it goes from 6 months of training in Greece, to a maximum of 24 in Hungary, with most countries requesting at least 12 months of training in Intensive Care Medicine. We also have very different admission processes and criteria (from interview-based forms to nationwide examinations), different in-residency evaluations, distinct duration of training (from 2 years in Ukraine, to 7-8 years in the United Kingdom) and finally, non-identical examinations for end-of-training assessment.

We continued to work, in order to expand our network (although it sometimes was more a pleasure than an obligation). To accomplish this goal, we used social networks (esatrainee.com), but also used the existent network built by the ESA National Anaesthesiology Societies Committee (NASC), in order to identify the existing European National Trainee Sections. We were astonished to realise that only 13 of the 37 European Countries associated to the ESA had such entities. After 2 years, we are proud to say that now the ESATN has 35 National Trainee Representatives (NTR). The first official meeting between more than 25 NTR and the ESA Trainees Committee (ESATC) is set to take place during Euroanaesthesia 2017 in Geneva.

Meanwhile, after analysing the results from the European Survey we ran, as mentioned above (Sobreira Fernandes et al., unpublished results), we found that despite many differences, we are surprisingly similar when it comes to our concerns and needs. For instance, we found the main field of interest of trainees that took the survey was Intensive Care Medicine, followed by Loco-regional Anaesthesia and Emergency Medicine, a top three that was the same for trainees from the four considered European regions. Furthermore, the trainees´ main concern was related to education/preparation for the European Diploma in Anaesthesia and Intensive Care (EDAIC).

We followed up on our promise to further adapt the ESA resources to the trainees´ needs, and based on the results of our European Survey, we organised the first ever Euroanaesthesia Trainees´ Program during Euroanaesthesia 2016 in London, in collaboration with the Group of Anaesthetists in Training from the Association of Anaesthetists of Great Britain and Ireland (GAT-AAGBI). With the benevolence of Professors Mervyn Singer, Zsolt Molnár, Jean-Louis Teboul and Marc Leone, we had a hugely successful event (Symposium "ESATN: Networking with the Experts on Sepsis"), which confirmed that communication works, and trainees respond well to being asked what they want.

Our conclusion, after such positive experiences, is that ESA and the ESATN can contribute to enhance homogeneity of training in anaesthesiology throughout Europe, and respond to the needs of our future anaesthesiologists. The effective dissemination of information in a representative manner is an essential part to attain this goal, but can only be successfully done if it occurs both horizontally and vertically, amongst trainees and from educational stakeholders to trainees and vice versa.

That, we think, can change our future. We plan to see it happen. ■

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For full references, please email editorial@icu management.org or visit https://iii.hm/aqt

Standardised, Hospital-Wide Airway Trolleys

Inspired by the Difficult Airway Society Guidelines and the Vortex Cognitive Tool

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One of the main recommendations of the 4th National Audit Project of the UK Royal College of Anaesthetists and the Difficult Airway Society was that every intensive care unit (ICU) should have access to a difficult airway trolley, which should have the same content and layout as the one found in the operating department (Cook et al. 2011). At Royal North Shore Hospital in Sydney, Australia, we designed trolleys with standardised equipment for use in the ICU, emergency and operating departments.

The trolley consists of 4 drawers corresponding to Plans A, B, C and D of the Difficult Airway Society guidelines for the management of unanticipated difficult intubation (Frerk et al. 2015). The symbols used to depict these Plans are from the Vortex cognitive aid (**vortexapproach.org**) (Chrimes 2016).

The first drawer (Plan A, Endotracheal Tube) contains all the equipment necessary for endotracheal intubation by laryngoscopy, including Storz C-Mac® blades for use with the monitor attached to one of the upright poles on the back of the trolley.

The second drawer (Plan B, Supraglottic Airway Device, SAD) contains second-generation SADs (igel®, Intersurgical) for airway rescue. If circumstances allow (i.e the patient can be oxygenated via the SAD, and it is thought appropriate), the SAD can be converted to an endotracheal tube with the use of the Ambu® aScope™, using the monitor attached to the other upright pole, with or without the Aintree Intubating Catheter (AIC, Cook®). The AICs and bronchoscopes are located in the side baskets.

> **Every ICU should have access to a difficult airway trolley**

The third drawer (Plan C, Facemask) contains facemasks, nasopharyngeal and oropharyngeal airways of various sizes.

The fourth drawer (Plan D, CICO* rescue) contains equipment for cannula, surgical and Seldinger cricothyroidotomy techniques. It also contains an Airway Exchange Catheter and Staged Extubation Kit (Cook®).

For intensive care and emergency clinicians, the goal is almost always endotracheal intubation. We appreciate that this is not the case in the operating department, where a SAD may be the first choice. The drawers are arranged in the order outlined above for the sake of standardisation across the hospital.

On the side of the trolley is a file containing our Emergency Intubation Checklist and Emergency Airway Cognitive Tool, which combines the DAS and Vortex approaches to difficult airway management. We believe that the DAS guidelines should be used for forward planning and to help with the choice of techniques, while the Vortex cognitive aid helps the team with decision making, such as when to abandon a technique and move onto the next.

RNSH Airway Trolley

A detailed description of the airway trolley, checklist and cognitive tool mentioned above can be found at **ccam.net.au,** a website which serves as the pre-reading for the Critical Care Airway Management Course, a not-for-profit course run at our hospital twice a year. ■

**CICO = Can't Intubate, Can't Oxygenate*

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Five Reasons Why Value-Based Healthcare is Beneficial

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Patient-centered care is becoming a major topic in healthcare. Many initiatives have begun focusing their care around patients and their medical conditions. This requires focusing on patient value (Porter and Teisberg 2006). When focusing on value for patients, a few challenges may arise. Firstly, the meaning of value for patients varies widely among stakeholders in healthcare. Secondly, not all patients receive the same treatment for the same illness. Patients (and their families) want to be treated differently based on their preferences. Thirdly, the quality of care delivery in terms of patient relevant outcomes differs among hospitals. The diversity in measurements makes it difficult to compare.

I. Patient Value: A Common Definition

Doctors would base the meaning of patient value on the skills of a doctor, an improved medical lab result, or a well-performed surgery. These measurements are mainly based on the treatment or intervention perspective. On the other hand, a patient may base patient value on aspects such as the length of waiting lists, how kind the doctor was or perhaps how good the coffee or breakfast tasted. Most people would agree that both sets of measurements do not truly reflect the quality of care from a medical perspective.

Patients' perception: "They were so kind to me when performing the surgery seven times."

II. A Singular Language

Value-based healthcare provides a singular language that is comprehended by doctors, medical teams, patients and their families. Patient value is defined by an equation whereby patient-relevant outcome measurements are the numerator, and costs per patient in delivering those outcomes are the denominator. Patient value is defined for a specific medical condition over the full cycle of care (**Figure 1**).

Meetbaar Beter (winner of the VBHC Prize 2014) is a great example that transparently reports patient-relevant outcome measurements for specific medical conditions. They include coronary artery disease, atrial fibrillation, aortic valve disease and combined aortic valve disease and coronary artery disease (Meetbaar Beter 2012-2016). It is important to note that outcome measurements should be defined around a medical condition and should be manageable and actionable. Doctors and their teams are then intrinsically motivated to improve the quality of care they deliver to patients. All they need are the tools to measure and the ability to visualise accurate and valuable outcomes.

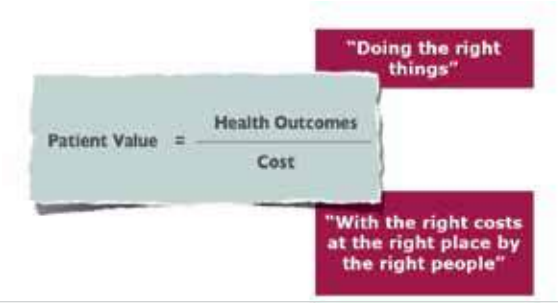

Figure 1. Patient value determined by the ratio of patient relevant outcome measurements to the costs per patient over the full cycle of care (Porter 2010)

III. Focused on Measurable Health Outcomes To Facilitate Improvement

Measuring outcomes in healthcare began in the 1950s (**Figure 3**), followed by a strong trend towards process and structure measurements. Some of the measurements focused on at that time were the length of waiting lists and the number of (certified) staff. This led to quality management based on the optimisation of processes, including Lean. All of these measurements are important in improving the internal process of care delivery. Patient and family perception only became important from a measurement perspective in the 1990s. Surprisingly, the healthcare sector took quite some time in realising the significance of patients in healthcare delivery. Luckily, healthcare providers are now able to present true patient-relevant outcome measurements to their colleagues and patients.

One of the most inspiring examples of improving measurable health outcomes is the Martini Klinik at the University Hospital Hamburg-Eppendorf (UKE) in Germany. Since the founding of the clinic in 2005, the Martini Klinik has focused on improving long-term health outcomes for patients with prostate cancer. The Martini Klinik massively improved their care by measuring patient-relevant outcomes (**Table 1**). The improved outcomes led to growth in volume and the Martini Klinik became the world's largest prostate cancer care clinic by 2013. It later received the VBHC European Inspirational Award in 2016 based on these inspiring results.

A second example is Meetbaar Beter. Meetbaar Beter has helped doctors learn from one another and improve care delivery based on reported outcomes. Over the last few years, impressive effects on patient-relevant outcomes have been achieved by looking at and learning from fellow cardiologists and cardiovascular surgeons.

IV. Protocols Do Not Fit Every Patient, But Patients Benefit From Protocols

Every patient is unique but they each walk a different path through the cycle of care. Protocols are very useful as they provide care delivery guidelines for patients with common medical conditions. In the St. Antonius hospital (winner of VBHC Cost-Effectiveness Award 2016), elderly patients with end-stage renal failure are guided towards their choice of treatment. Previously, protocols stated that patients with this medical condition should primarily be treated with dialysis. Dialysis is highly invasive (and costly) for elderly patients and it requires them to remain in hospital for long periods of time. Research made by Dr. Willem Jan Bos and his team found that conservative treatment is much better than dialysis (Verberne et al. 2016). By having discussions with patients, protocols can be changed and care delivery can be opitmised and adjusted to fit every individual.

V. Become a Patient-Centred, Fast-Learning Team

Value-based healthcare is centred around learning. Doctors who have a drive to show medical leadership and create a learning culture are key for the implementation of

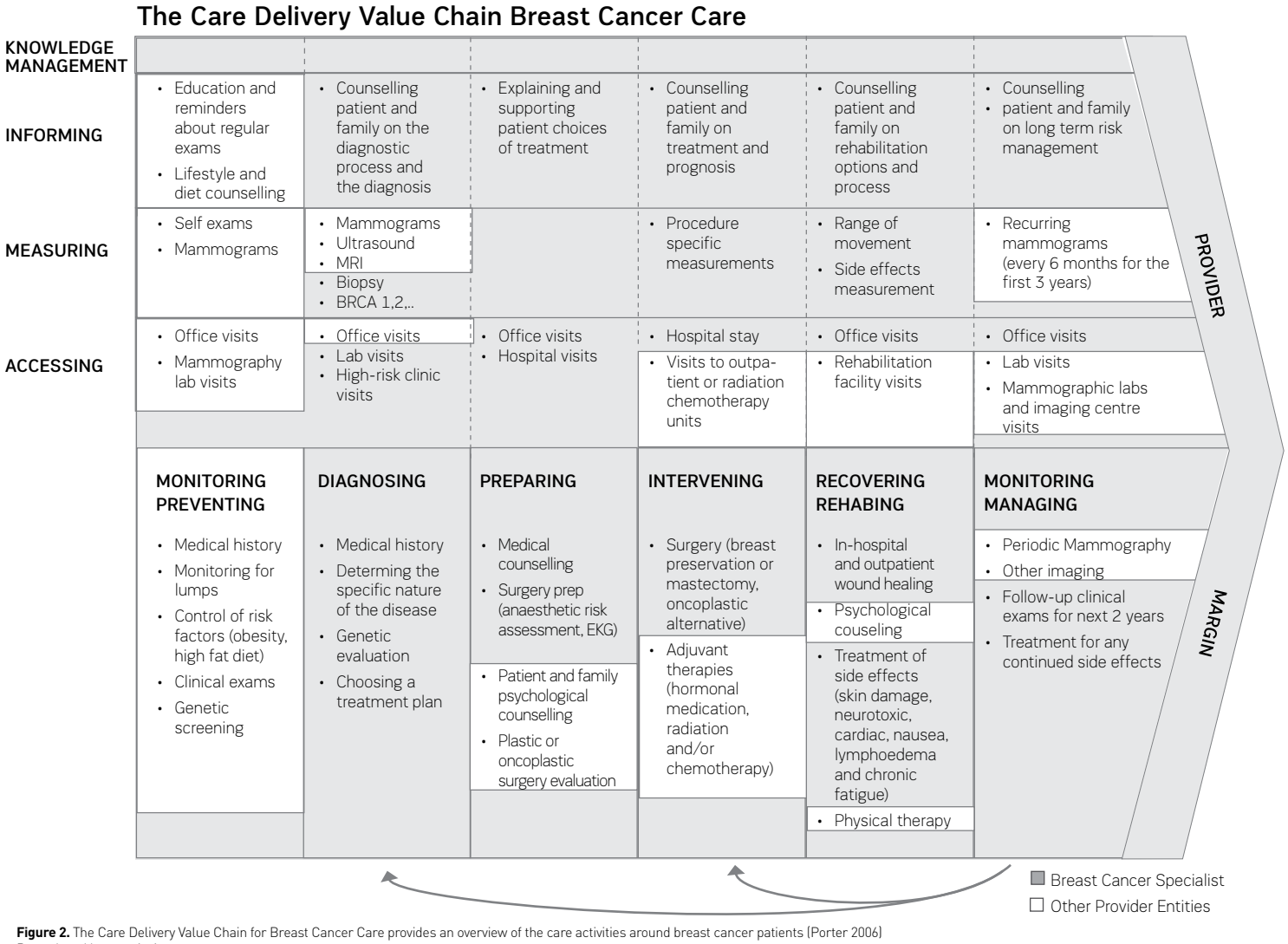

Figure 2. The Care Delivery Value Chain for Breast Cancer Care provides an overview of the care activities around breast cancer patients (Porter 2006)
Reproduced by permission.

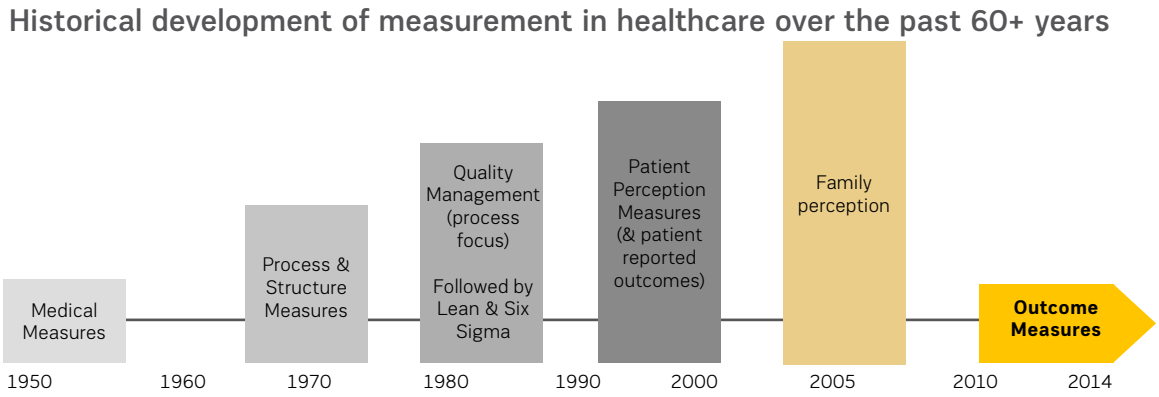

Figure 3. Historical development of measurements in healthcare. Started with medical measurements, followed by process and structure measurements, then quality measurements. Patient and family perception came into perspective in the 1990s. Currently, healthcare measurements are focusing on outcomes relevant for the patient (Van Eenennaam 2016)

"The Netherlands really is a remarkable example of what a country can do if the right culture, attitude, mindsets and knowledge base are really applied to actually changing how we deliver health care rather than just adding patches and bandages to try to stop the bleeding." Prof. Michael E. Porter (Honorary Chairman of VBHC Prize 2014-2017) (Value-Based Health Care Europe 2016)

Results	German average	Martini Clinic
Fully continent[1]	56.7%	93.5%[1]
Severe incontinence[2]	4.5%	0.4%
Severe erectile dysfuction (1 year)[3]	75.5%	34.7%
Ureteral injury	0.6%	0.04%
Sepsis	2.5 %	0.04%
Pulmonary embolism	0.8%	0.1%
Delayed wound healing	1.7%	0.9%
Rectal injury	1.7%	0.2%
Thrombosis	2.5%	0.4%

[1] Definition of fully continent: incontinence pads are unnecessary or are only used for safety
[2] More than 5 incontinence pads per day
[3] Including patients suffering from erectile dysfunction previous to the operation

Table 1. Patient-relevant outcome measurements of prostate cancer care at the Martini Klinik versus the German average. Source: Martini Klinik martini-klinik.de/en/results

"No protocol fits every patient and no protocol perfectly fits any patient." James Brent (Bohmer et al. 2002).

VBHC. Learning to improve value for patients provides satisfaction. This motivates doctors and their teams and also cuts costs. VBHC empowers doctors and their teams to do what they do best—provide excellent patient-value by using clinically relevant and evidence-based insights.

Creating Excellent Patient Value

- Patient-centred care is on the rise;
- VBHC provides a common definition for patient-value and a common language for all stakeholders in healthcare;
- VBHC puts the patients, their families, doctors and their teams at focus;
- Patients with similar medical conditions have different preferences and they each follow roughly similar care-paths;
- Care quality improves by measuring the right patient relevant outcome measures. This creates compelling learning cycles for the medical team.

Working towards excellent patient value has never been more optimistic than it is today! ■

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Reaching the Heights of Respiratory Physiology

Professor John B. West is a renowned respiratory physiologist and researcher. He joined the faculty of the University of California San Diego in 1969, where he is Distinguished Professor of Medicine and Physiology in the School of Medicine, where he still teaches first-year medical students. He is author of *Respiratory physiology - the essentials*, which has been translated into many languages, and is now in its 10th edition. His YouTube Lectures in Respiratory Physiology have attracted over 400,000 views and rave reviews. He is past president of the American Physiological Society, and was the founder Editor-in-Chief of the journal *High Altitude Medicine and Biology.* He has received numerous honours and awards from around the world for his research and teaching, and is the author of over 500 articles and 19 monographs.

Out of your many achievements what are you most proud of?

Firstly, the research we did leading to respiratory measurements on the top of Mount Everest. Second the measurements of the function of the lung in space, which we did for the first time with the NASA Programme. Finally, the effects of gravity on the lung, particularly the distribution of blood flow.

How has your research advanced critical care practice?

My work on pulmonary gas exchange that involved measuring ventilation-perfusion inequality in the lung added important information. In critical care medicine my research on the effects of gravity on the lung is important.

What is the most vexing unknown about respiratory physiology?

I wish we knew more about what determines the mechanical strength of pulmonary capillaries. We're not sure about that and I wish we were. I am also particularly interested in the function of permanent residents at high altitude, those people who have been at high altitude for generations. Have they completely adapted to severe hypoxia? They have severe hypoxaemia and the question is whether they are completely adapted to that or not. In particular, is their cognitive function as good as it would be if they were at a lower altitude? We don't know the answer to those important questions, and I think in a few years people will do some more research in this area.

You have donated your papers to the University of California San Diego Library, and you have written about the history of medicine (including West 2015a). Why is the history of medicine important?

Particularly in medicine, the work that has been done can illuminate a lot of the work done at the present time. If you don't know about history, you might make terrible mistakes. I have a special interest, because the archive at the University of California San Diego is a repository of high altitude medicine and physiology papers. It started with Griffith Pugh, the pioneer Everest physiologist, who went on the Everest expedition in 1953. I knew him well, and after he died I asked his widow whether I could have his papers, which she donated to the university. We have collected a lot of things since for this archive, and we welcome people from all over the world. In general, history is very important, and I like to think that we are contributing.

You joined Edmund Hillary's Silver Hut Everest expedition in a serendipitous way. It's a wonderful word and a wonderful concept—what part has serendipity played in your career?

There have been several very serendipitous events in my career. I was at a meeting of the British Physiological Society in London in 1960, and the woman sitting next to me told me that Edmund Hillary was planning an expedition to Mount Everest, which was physiological in its aim, and that the chief physiologist was Griffith Pugh. I was young at the time, but well trained in respiratory physiology. I didn't know anything about

high altitude, but I applied to join the expedition and I was very fortunate that I was accepted, even though I'd never been on a high mountain before. I've done a bit of skiing, but I am not a climber. That was the Silver Hut expedition in 1960-61, which turned out to be a very productive expedition (Milledge 2002). The idea was to study what happens to lowlanders, people who live at low altitude, when they go to a very high altitude, in this case 5,800 metres (19,000 feet), and spend several months there. Nobody had ever done that before, and I've not come across any other example. It was very new and we made a very extensive series of measurements. We had quite sophisticated equipment in a structure called the Silver Hut, because it was painted silver. It was a very successful expedition and I became very interested in high altitude as a result. At the end of the expedition, we went across to a mountain called Makalu, which is within 10 miles of Everest, and the climbers tried to climb it without supplementary oxygen. If they had been successful, it would have been the highest peak to be climbed without supplementary oxygen, but they were not successful. One of the climbers became acutely ill in the final stages and I helped in getting him off the mountain alive, because it was a desperate situation. The end result was I made some measurements with Michael Ward, another physiologist climber, at an altitude of 7,400 metres or so, which were the highest measurements at the time of physiological function. That experience in 1960 prompted me to wonder whether it would be possible to get measurements at the summit of Mount Everest, the highest point in the world. That was the objective of the 1981 American Medical Research Expedition to Everest (AMREE) that I led.

Another serendipitous event was when I was working at Hammersmith Hospital in London. There was a new respiratory physiology programme being developed, and Charles Fletcher, one of the principal physicians there, recommended that I go to the pneumoconiosis research facility in South Wales, learn some physiology and come back with ideas. When I came back, the Medical Research Council (MRC) cyclotron started on line and it produced radioactive oxygen with a half life of only two minutes. Nobody had used radioactive oxygen before in physiological measurements. So we inhaled the gas, and that was the beginning of my interest in the distribution of pulmonary blood flow, because we found that the radioactive gas was removed from the top of the lung much slower than from the bottom of the lung. It was a striking regional difference in blood flow, which had never really been described before; there had been intimations of it only, from bronchospirometry and other measurements. We made the first clear measurement of the uneven distribution of blood flow. That was an extremely serendipitous event.

> "I think oxygen conditioning has a great future for people living at high altitude"

You are a strong proponent of oxygen conditioning for people living at high altitude. Please explain.

As with so many things in medicine, this idea comes from advancements in technology. I have only recently realised that it is possible to reduce the physiological altitude of people by adding oxygen to inspired air on a large scale. I compare it with air conditioning, which has completely changed the wellbeing and productivity of people in hot places. Air conditioning in the USA is enormously important: 90% of new homes have air conditioning. Oxygen conditioning has the same potential. This has to do with improving the conditions at high altitude for visitors, and also what we call sojourners, who are people from low altitude who are living and working at high altitudes. All those people are certainly going to be improved by oxygen conditioning, which helps your physical and cognitive functions. Even adding oxygen to a single room has a potential benefit. In Peru you can go to a hotel and ask for an oxygen-enriched room, and oxygen conditioning is used in a mine in Chile and in China on the Qinghai-Tibet Railway, which travels to a 5000m altitude. Some people think it's going to be too expensive, but air conditioning is also expensive, but considered absolutely essential. Oxygen and air-conditioning share a number of features, and I think oxygen conditioning has a great future for people living at high altitude (West 2015b).

In the 1981 American Medical Research Expedition to Everest, the most important finding was hyperventilation. Could you elaborate on that please?

The objective of the American Medical Research Expedition to Mount Everest (AMREE)'s was to try and understand how someone from low altitude—sea level, or thereabouts—can possibly tolerate the extreme hypoxia on the summit of Mount Everest. The summit of Mount Everest is very interesting because it is right at the limit of human tolerance to oxygen deprivation. You may try to think of an evolutionary reason for that, but there is none of course. It's probably one of these cosmic coincidences. At the summit, the most important thing is that people develop extreme hyperventilation. For example, on the summit of Mount Everest, the alveolar PCO_2 we measured was between 7 and 8 mmHg as opposed to the normal value of 40 mmHg at sea level. So they were increasing their alveolar ventilation by about five times—a tremendous increase. One of the climbers had a tape recorder with him and he dictated the recording of barometric pressure for the first time. He was desperately short of breath, pausing between every one or two words. One of the things about the hyperventilation is that you get an extreme respiratory alkalosis, which we did not expect. We expected there would be hyperventilation because we'd done a modelling study. What we didn't realise is that the kidney, for reasons we still don't fully understand, was "reluctant" to excrete bicarbonate at these great altitudes. And the base excess changed only a small amount between 6,300 metres and the summit, 8,800 metres. For some reason, there was very little metabolic compensation of respiratory alkalosis. This was a very interesting situation. We think that may have to do with the fact that climbers are always volume depleted, always so dehydrated, that the kidney is not able to excrete bicarbon-

Michael Ward and John West assembling the stationary cycle to make measurements of maximal oxygen consumption at an altitude of 7440m (24,400 ft). These are the highest reported measurements to date.

ate. It turns out that this alkalosis is valuable because it increases the uptake of oxygen by the lung at this altitude. This is fascinating and it never occurred to us before. If you look at the whole animal kingdom, you find that all sorts of animals increase their oxygen affinity in their haemoglobin in hypoxic situations. And it's absolutely fascinating that the climber does the same thing by a completely different and unexpected method—the alkalosis.

You have written that a sound knowledge of respiratory physiology will always be necessary for the intelligent practice of medicine. Could you comment on that?

Some people are worried that physiology is passé, and some physiology departments have changed their name to human biology. It will never be passé. The study of medicine requires you to understand the function of the lung, and the whole system. It's absolutely critical that people in the intensive care environment understand gas exchange and mechanics. The work on the human genome and on molecular medicine is magnificent, but physiology has not lost its importance.

You have compared the features of the avian lung to the mammal lung and observed that many features of the bird lung are superior to those in mammals and that in the future we may be able to exploit some of these.

I'm interested in many aspects of physiology, including comparative physiology. I've done a lot of work on the bird lung, which is absolutely fascinating. For one thing, in the bird lung the gas exchange and ventilation functions have been separated. In the human lung, we use delicate alveoli for both gas exchange and pumping the air. If you think about this, it is a crazy solution. The alveoli walls have only a fraction of micron of thickness; why use those for pumping? Birds have air sacs, which do not take part in gas exchange; they don't have any capillaries. But the air sacs do the pumping and the gas exchange is done by another structure within the lung called the parabronchi, where you have the pulmonary capillaries. In many ways it's a much better design. Nowadays people are thinking about making artificial lungs that conceivably one of these days could take the place of diseased lungs. If you're going to bio-engineer a lung, you might want to take a close look at the bird lung because in my opinion it has a better design than the mammalian lung.

"If you're going to bio-engineer a lung, you might want to take a close look at the bird lung because in my opinion it has a better design than the mammalian lung"

You are renowned as an educator. Do you have any secrets to share?

At my high school, Prince Alfred College in Adelaide, Australia I had a marvellous teacher, Ray Smith. I always like to mention that, because people often underestimate the importance of teachers. He taught me in my final years in high school. He had a wonderful ability to put himself in the place of the pupil, and that rubbed off on me as the secret of teaching. It's difficult for many teachers to do that for medical students. I teach the first year medical students here, and I get good reviews from them. I think the reason is that I realise their intellectual point of view as beginning medical students and I think that helps with teaching. I would like to put in a plug here for the American system, where there is a four-year college period between high school and medical school. It's a great idea. I went straight to medical school from high school at the age of 17, which is far too young. ■

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Evidenced-based ICU Organisation

Interview with Professor Jeremy Kahn

Jeremy Kahn is Professor of Critical Care, Medicine and Health Policy in the University of Pittsburgh School of Medicine and Graduate School of Public Health. As a core faculty member in the CRISMA Center in the Department of Critical Care Medicine, he directs the CRISMA Program on Critical Care Health Policy & Management. His research focuses on the organisation, management, and financing of critical care services. His group's work integrates approaches from the fields of epidemiology, health services research, health economics and operations management to investigate novel strategies for increasing the quality and efficiency of critical care. He directs several grants from the National Institutes of Health examining the effect of ICU organisation on the outcome of care for critical illness. Dr. Kahn spends his clinical time attending in the ICU of Magee Womens Hospital of University of Pittsburgh Medical Center.

On organising critical care for the 21st century, you suggested how to address the challenges (Costa and Kahn 2016). What would you say is most important? What is most difficult?

In our article for *JAMA*, we examined the major gaps in critical care delivery and suggested how to fix these gaps over the next 20 to 30 years. To me, the most important aspect is inter-professional critical care. Increasingly we recognise that critical care is not just a relationship between a physician and a patient, but there is an inter-professional care team that includes physical therapists, respiratory therapists, pharmacists, and nurses, who are at the bedside 24 hours a day. Family members are also part of the care team. The most important innovation of critical care in the last ten years and how we will continue to improve care moving forward is by emphasising the role of that inter-professional team including the family. To say critical care is a team sport feels like a platitude, but it is so true that one individual alone simply cannot deliver the level of critical care needed to consistently save lives and improve the experience of patients and families. I value my inter-professional care team deeply; I can't envision working in an ICU without them.

The most difficult thing to accomplish will be regionalised critical care, which means that the very high-risk, most severely ill patients should be systematically triaged and transferred to regional centres of excellence. I am an advocate of this approach, and although there is a lot of data to support it the political challenges are potentially too great and it may take many years to be fully realised. There are many people who develop critical illness while already in the hospital, and it is not clear if they should leave the clinicians that already know them and are experienced with them and move to these high quality centres. There are reimbursement issues also. While trauma care has been regionalised, it is very poorly reimbursed and community hospitals were relatively willing to give it up. Critical care is well reimbursed, and hospitals are not going to be so willing to have critical care patients transferred to regional centres. Also critical care supports so many other services in the hospital, such as oncology and cardiac surgery, that when you take critical care away from a small hospital it might be ultimately harmful. We need to recognise that regionalising critical care is difficult, and while pursuing it, think about ways to support quality in small hospitals in the absence of regionalisation.

You are principal investigator of the ConnECCT study: Contributors to Effective Critical Care Telemedicine. What can you tell us about this study?

The most salient observation in the ICU telemedicine literature is that telemedicine is a heterogeneous intervention with varying effects: sometimes it works and sometimes it doesn't. It is a very powerful tool for quality improvement, but it is just a tool. There is even data to suggest that introducing ICU telemedicine sometimes causes harm in hospitals. The most important question is not whether telemedicine is a good idea, but where and how it should be used.

The ConnECCT study, which is funded by the U.S. National Institutes of Health, acknowledges telemedicine's heterogeneity and asks: "Why are some hospitals very good at implementing telemedicine and why are some hospitals not implementing it very well?" We are visiting high performing and low performing hospitals to see if we can learn lessons from each, and we will develop an implementation toolkit to include how best to implement telemedicine and where to implement it.

Telemedicine is perhaps best suited for small, typically rural hospitals, where distance plays a large factor. Yet it is implemented quite frequently in large academic medical centres, unfortunately, for unclear reasons—maybe because they are well resourced and can afford telemedicine. However, the data might show that telemedicine improves outcomes more in smaller hospitals.

It is important for telemedicine to work well that the hospitals involved have pre-existing relationships. We have learned in our study the importance of trust: the nurses and clinicians at the bedside really have to trust the telemedicine doctors. You can't engender trust remotely if you have never met someone. It is very important to have face-to-face contact. In addition, we have found that telemedicine works best when the doctors in the telemedicine suite also work at the bedside. They have opportunities to develop trust with the nurses, because that is so important for quality.

Your study on implementation of evidence-based practice in Pennsylvania hospitals found variable implementation and also increases in some non-evidence based practices (Kohn et al. 2017). What are your thoughts on adoption and de-adoption of evidence?

I think adoption and de-adoption is going to be a central challenge in critical care in the next century. We are finally coming to a realisation that doctors are just human beings. As much as we want to believe that we can reliably deliver best practice, we have to admit to ourselves that as human beings we consistently fail. Understanding the reasons why we are good and why we are bad at adopting practice and understanding how to de-adopt more efficiently when evidence shows we shouldn't be doing something, will be a central challenge. It will take a multi-pronged approach, and we can learn lessons from behavioural economics and "nudge" concepts that can push us gently to adopting best practice. We can also take lessons from organisational behavior and theory to get teams to work together better. Traditional methods, such as education and guidelines dissemination, are not enough. Looking at implementation of the Surviving Sepsis guidelines there have been three studies showing that even after aggressive implementation only about a third of patients with sepsis were receiving the 6-hour resuscitation bundle. That demonstrates that we need more innovative and intense methods for implementation. Technology can also help—electronic screening for best practices and using the electronic health record to better translate evidence into practice can take us part of the way there, but ultimately it is going to be the human element and finding ways to get humans work together better.

> "I value my inter-professional care team deeply; I can't envision working in an ICU without them"

What research are you conducting into teamwork?

We are trying to take a different approach to understand the role of teamwork. Although everyone agrees that teamwork is important, it needs to be studied rigorously, because we don't know why it is important and therefore we don't know how to make it better. It is not enough to say that teamwork is important. We need to understand the mechanism in order to make teams function better, so that in ICUs where teams are not functioning we can intervene to make them more effective. Saying teamwork is important is like saying that the sky is blue. But if it is a cloudy day and I want to make the sky blue or a little bit more blue, how can I do that?

Issues in teamwork vary. There might be a dysfunctional leader, or 10 consultants who work in an ICU, of which 8 are fantastic and 2 are not so good. But we don't want high quality care 80% of the time. I hope that by understanding team learning as a mechanism for more effective teamwork in ICU we can recommend interventions. We can't assume that every intensivist is going to be a great leader naturally.

Do intensivists get enough training on leadership?

No. It is not part of the medical school curriculum, and there should be formal training in organisation and management, because so much of what we do as intensivists is management. The clinical decisions that we make and the science is a large, but not the entire part, of the skills of being an intensivist. For example, we are now just realising that end-of-life care is not something that comes naturally. Talking to a family member about end-of-life care is a learned skill. At Pittsburgh we are offering our fellows and intensivists formal training on how to communicate about end-of-life care. Why shouldn't we also provide formal training in communication strategies for teamwork and management? This is an extremely important part of intensivist training that has been neglected.

Your research interests include system and organisation-based interventions that you say can be as beneficial in improving outcomes as new technologies. Of the interventions you have researched, what would you say is the most promising?

Most promising for me is prompting for best practice, meaning having a very simple cue to a clinician that they have forgotten to do a practice and that they need to do it. There are two excellent studies on prompting information. One was a study at Northwestern Medicine in Chicago by Curtis Weiss and colleagues: they were using a checklist on rounds and they randomised two teams (Weiss et al. 2011). Both used the checklist, but in one team there was a human prompter on rounds, who spoke up whenever they noticed something on the checklist that was not discussed. That prompting intervention alone

was able to reduce mortality. In Pittsburgh we used a telehealth approach (Kahn et al. 2014), where we had a nurse screening each patient daily for evidence-based practice, and when they found it was missing they called the ICU and told the nurse and prompted them. Prompts are very powerful tools, because they are simple and targeted and not diffused. They are a just-in-time form of education that is potentially underutilised. However, human prompters are expensive, and we need ways to automate that system using technology. That has to be done smartly, because we don't want to have too many prompts, which may lead to alarm fatigue.

Please tell us about your research on a web-based patient-reported outcome system (Cox et al. 2016).

The critical care field is shifting towards greater examination of long-term outcomes and increased attention to ICU survivorship. Death is not the worst of all possible outcomes. We need to better understand the patient experience in recovery and how patient experience is affected by the therapies that we give them. Patient-reported outcomes are the very important next step to ensuring that our research is much more patient-centred. Just saying that a patient is alive one year after discharge is not enough anymore. And just measuring health-related quality of life using existing scales is not sufficient. To really improve long-term patient outcomes we need to understand and quantify outcomes as articulated by the patient. It's hard to follow up patients, and getting them to understand how to use patient-reported outcome systems is a challenge, but these are surmountable issues.

Do many ICUs in the U.S. have 24-hour visiting?

It is a mixture. The ICU I work in has 24-hour visitation, which is wonderful. On the other hand, I have had loved ones in ICUs recently where visiting was 1 hour in the morning and 1 hour in the evening. In the room my loved one was in, even if you could stay longer there was nowhere to sit. There was one chair and that was for the nurse, and the nurse made it very clear that it was not for family. I spoke to the hospital administration about it, and even gave them the consensus statements about the importance of 24 hours visitation. There is still the lingering old guard in some hospitals that work with the old mindset that the patient needs peace to recover. My belief is that we as clinicians are the visitors, we are the guests, and the family has a right to be there 24 hours a day.

What else will make critical care more patient-centred?

One of the depressing things that I see is that when we round as an inter-professional care team, we round outside in the hallway and not next to the patient's bed. This is because we have all the computers and the infection control issues and moving into the room is seen as too much of a challenge. Ultimately we become numbers doctors rather than people doctors. I am trying to think through ways that despite having all these computers on rounds we can bring rounds more frequently into the patient's room right by the bedside in order to engage the patient more.

We are moving towards less sedation and even patient-controlled sedation (there is a clinical trial underway (clinicaltrials.gov/ct2/show/NCT01606852). This will mean that patients are more awake and engaged. We are also facilitating ways for patients to speak when they are mechanically ventilated. These are major steps forward to more patient-centred critical care.

On big data you say you are a skeptic. Why?

I am a skeptic generally of technology, and I feel that big data as it is been applied is seen as a panacea that ultimately is going to potentially steer us wrong as much as it steers us right. The size of the data sets alone won't overcome bias. Moreover I don't believe that you can determine causation in an observational data set. Ultimately we can't abandon randomised clinical trials as a road to causation. I make my living with observational research, but I don't pretend I can infer causation from observational research. Time and time again there has been a difference between observational studies and clinical trials. A smart way to use big data is to use it to inform clinical trials to better understand disease phenotypes for randomisation into clinical trials to better understand the range of potential outcomes and to embed clinical trials into existing clinical care. An example of this is the Randomized, Embedded, Multifactorial Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP) clinical trial (clinicaltrials.gov/ct2/show/NCT02735707). But to say that the answer lies in big data I say is quite overly optimistic. ■

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Intensive Care in Tunisia

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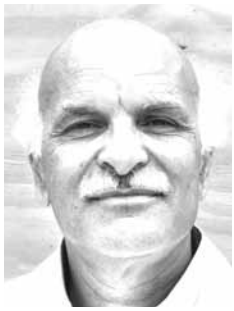

According to the World Bank classification, Tunisia is considered a lower middle-income country, corresponding to a country with a Gross National Income (GNI) per capita between USD1,026 and USD4,035 (World Bank 2015). The economic growth of Tunisia has been slowed following the 2011 Arab Spring, which was initiated in this country. Despite economic and political constraints, which have been exacerbated by the Arab Spring, Tunisia continues to capitalise on the choices made upon its independence in 1956, focusing on human development. Education and health for all was the leitmotif in that period, with free and compulsory public schooling, and free access to healthcare in its preventive and curative dimensions. As a result, the country still ranks among the first emerging countries in terms of the human development index (wealth), a composite of four components: life expectancy at birth, expected years of schooling, mean years of schooling, and GNI per capita. In 2016 Tunisia ranked 97 within the strata of countries with high human development (United Nations Development Programme 2016). As to health-related indicators, Tunisia performs among the best countries within its category, in terms of life expectancy (which rose from 70.3 years in 1990 to 75.6 in 2013), maternal mortality, fertility (which dropped from 5.2 children per woman in 1981 to 2.3 children by 2013), infant mortality etc. (GBD 2015 Child Mortality Collaborators 2016; GBD 2015 Maternal Mortality Collaborators 2016; GBD 2015 Risk Factors Collaborators 2016; GBD 2015 SDG Collaborators 2016; GBD 2015 Disease and Injury Incidence and Prevalence Collaborators 2016). Tunisia faces a striking epidemiological change with an important decline in communicable diseases and an increase in non-communicable diseases, including diabetes (one in six Tunisians suffers from diabetes in 2015), overweight (involving 60% of citizens over 35 years), vascular diseases, and cancer.

Intensivists and Intensive Care Societies

Four schools of medicine, distributed from the capital Tunis to the south, are in charge of the training of more than 1500 students each year, of whom almost one quarter specialise after MD graduation. Regarding intensive care medicine practice in Tunisia, there are two pathways of specialisation, which were started only by the early 1980s: anaesthesiology and surgical intensive care medicine, and medical intensive care medicine, with a curriculum of 5 years for the former and 4 years for the latter. This makes intensive care medicine the sole medical specialty with two parallel curricula, a scheme that is similar to that existing in France, although medical intensive care medicine has been a supra-specialty in France thus far. As a consequence, two societies of intensive care medicine exist in Tunisia: STAAR (Société Tunisienne d'Anesthésie Analgésie & Réanimation) for the first curriculum, and ATR (Association Tunisienne de Réanimation) for the medical intensivists. These societies have long ignored each other, and organise their own congresses, although a recent rapprochement has been made with the organisation of a common scientific day. Yet intensivists on both sides have common interests and challenges they could have addressed in a united way with the health authorities. Among the common problems are the lack of legislation defining intensive care medicine, the need for ICU beds, architectural standards, the minimal and maximal capacity of ICUs, the standards in terms of biomedical equipment, workforce, and operating procedures. Another area that could have brought the intensivists together is the lack of reimbursement for intensive care in the private sector, which imposes a monstrous out-of-pocket financial burden on citizens who choose this sector, and the undervaluation of reimbursement of an ICU admission in the public sector.

ICU Bed Capacity and Distribution

Tunisia's healthcare system includes three levels of care: primary, with a network of more than 2000 basic health centres; secondary, with 109 district hospitals; and tertiary, with 33 regional hospitals and 24 modern teaching hospitals (Centre Hospitalo-Universitaire) (République Tunisienne Ministère de la Santé 2016). Tunisia's private healthcare sector acccounts for no less than 49% of doctors in the country (split into more than 3100 general physicians, and more than 3600 specialised physicians), and more than 90 private clinics, with 75 new clinics expected to be built by 2025 (Oxford Business Group 2016). The public sector remains the primary healthcare provider in Tunisia with 31,936 beds, accounting for 87% of hospital bed capacity. The Tunisian health system counts around 500 ICU beds distributed between the public sector (240 beds corresponding to a ratio of 7.5/1000 acute care beds) and the private sector (around 280 beds corresponding to a ratio of 58/1000 acute care beds). Compared with global trends worldwide, this ratio for public/private ICU beds seems anachronistic, since the global trend is characterised by the gradual reduction in so-called "cold" beds with the increase in ICU beds, a figure that the private sector seems to have understood both in the

distribution of its beds offer, and in its functioning, aiming at minimising the frequency and duration of hospitalisation.

These beds are organised in ICUs of variable size and organisation. In the private sector ICU beds are usually assembled in open ICUs of small (4 beds) to medium-sized units (12 beds). These ICUs are usually managed by anaesthesiologists recruited on a full-time basis by the clinics, cumulating both the operative activity of anaesthesia within the operating room, and the management of cases (more or less rare) of patients requiring intensive care whether or not in relation to surgery. Anaesthesiologists working in the private sector have a close relationship with specialists from a variety of backgrounds, and perform all patient conditioning procedures (catheterisation, drainage etc.), together with the management of all aspects of artificial ventilation.

Things are quite different in the public sector and resemble more the European reality. In the teaching hospitals, the ICUs are usually bigger than in the private sector (at least 8 beds), and are staffed by substantially more intensivists. ICUs are more often specialised either in the surgical field (and managed by anaesthesiologists in this case), or in the medical field (and managed by medical intensivists therefore). In the largest university hospitals in the country (5-6 hospitals plus the principal military hospital in Tunis), these two types of ICUs usually coexist, in addition to the coronary care unit. In this case, surgical ICUs take care of all patients requiring intensive care in the perioperative period, in addition to trauma patients, whereas non-operative patients are admitted to the medical ICU. In smaller academic hospitals, as well as in non-university regional hospitals, only one type of ICU exists, which theoretically assures any kind of intensive care.

Quality of Care

The quality of patient care achieved in Tunisian ICUs can be inferred from two interesting studies. In a study aiming at the validation of severity scores in use in ICUs, Nouira et al. compared the performance of the scores Simplified Acute Physiology Score (SAPS II), Acute Physiology and Chronic Health Evaluation (APACHE II), Mortality Prediction Model (MPM0) and MPM24 in a Tunisian population of patients admitted to three ICUs (Nouira et al. 1998a). All models showed an acceptable discrimination power, but were inadequately calibrated. All models tended to underestimate actual mortality (high standardised mortality ratios [SMRs]). Beside an actual difference in the quality of care between Tunisian and western ICUs, some other factors might have accounted for the discrepancy between predicted and observed mortality rates. These might be putative differences in the disease leading to ICU admission (case mix), lead time bias, or availability of resources. Indeed, the main observed difference was the higher proportion of medical admissions in the Tunisian dataset (84.2%) in comparison to European and North American reports, a fact that might have contributed to an under-prediction of death, as it is acknowledged that surgical patients have actually lower mortality risks than medical patients.

An interesting benchmarking study compared variations in intensive care utilisation and outcome in relation to variations of costs in two large university hospitals (Monastir in Tunisia, and Créteil in France) (Nouira et al. 1998b). The working hypothesis was that since the Tunisian ICU medical staff had received post-doctoral training in that French unit and should have similar skills, any difference in the therapeutic approach should be due mainly to resource limitations as both countries had striking differences in GNI and the share of GNI spent in healthcare. This study showed that Tunisian patients received less treatment during a shorter length of stay, leading to overall lower

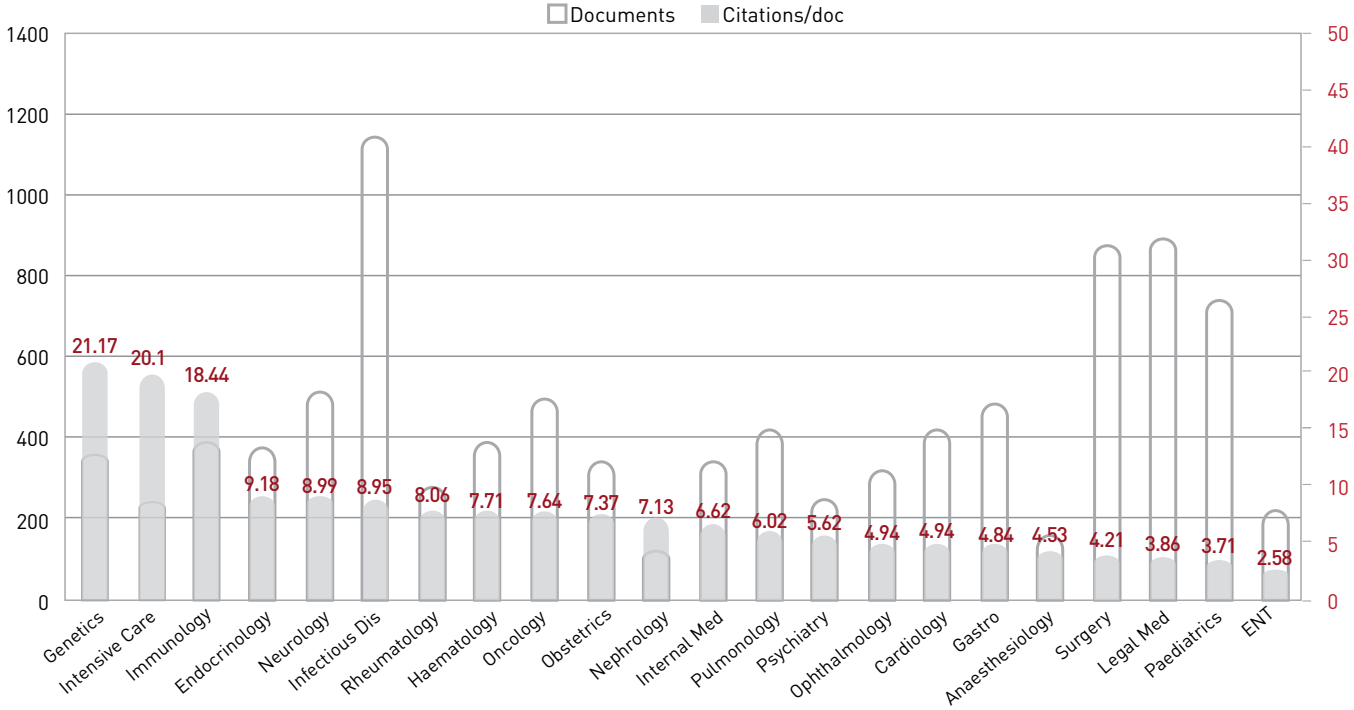

Figure 1. Publications from Tunisia Indexed in PubMed, by Specialty, 1996-2015

costs than French patients but with higher ICU mortality. Regarding cost-effectiveness profiles, it was similar in the low range severity group, but it was significantly poorer in Tunisia regarding the middle range of severity. However, in the highest severity range, there was a trend toward increased mortality and SMR in the Tunisian ICU, which could be viewed as more efficient from an economical standpoint. The study also showed an overall younger age and better prior health status of Tunisian ICU patients, reflecting a Tunisian policy of actively restricting ICU admission where the ICU bed shortage put a greater triage pressure on Tunisian physicians. The situation has probably changed nowadays with a high number of new ICU beds operated, at least in the private sector, making such benchmarking studies welcome.

Research and Research Networks

Despite its young age relative to well-established specialties, Tunisian intensive care medicine is one of the local disciplines with a strong tradition of research and publication. This research concerns both diseases with a high local prevalence/specificity (scorpionism, toxicology, traumatology), but also diseases that concern the whole community of intensivists throughout the world.

Figure 1 shows the distribution among major specialties of publications indexed in PubMed, both as an absolute production (white bars) over the period (1996-2015), and the average citation per paper (grey). Intensive care medicine has one of the best quality of publication with one of the highest ratios of citations/paper.

In spite of some sporadic attempts, there is no Tunisian research network in the intensive care field. We should admit that the culture of networking is almost non-existent in Tunisian medical research. This culture is indeed somewhat new worldwide, but nothing is done from the institutional side to federate skills in a specific field, or around a promising research project. There are neither financial incentives nor obligations favouring such groupings to be made. Nevertheless, many Tunisian teams have been involved in international networking, particularly on mechanical ventilation, with several international publications involving Tunisian teams (Esteban et al. 2008; Ferguson et al. 2005; Nin et al. 2017; Delclaux et al. 2000; Maggiore et al. 2010; Jolliet et al. 2017).

Challenges and Opportunities

Like many emerging countries throughout the world Tunisia faces the challenge of brain drain in the field of medicine and particularly in that of critical care medicine. At the end of their specialisation curriculum, Tunisian residents, especially those belonging to intensive care medicine, usually validate 1 to 2 years of their curriculum in a European country (usually France). While this mobility used to be informal, occurring through an arrangement between supervisors in both countries, it is now integrated within the framework of the French diploma of specialisation (DFMS), in which Tunisian (and more generally North African) residents pass a formal examination in the French Embassy and then are assigned to functional posts managed by the University of Strasbourg as required by local needs in the specialty workforce. This new system is considered a major regression when compared to the previous mode of exchange which, even if it was less well organised, was nevertheless satisfactory for the desire for training of the residents who were able to join medical teams in highly trained services in France, whereas with the new system, they find themselves more often in places lacking supervision where they provide services that are shunned by French physicians.

The brain drain continues even after the residency period with a strong attraction put on the young medical specialists of the country to join the French system through an equivalence contest where the performance of the Tunisian doctors is unanimously recognised. This brain drain is present in all disciplines, but is particularly high in high-stress specialties such as anaesthesiology and critical care medicine.

Another challenge intensive care medicine has to face in the next years is the unification of the curriculum leading to intensive care specialty. It seems illogical that residents come to the exercise of intensive care through two separate curriculums, that of anaesthesiology and surgical ICM, and the medical ICM curriculum. A unified way should be identified in order to have one single and efficient curriculum.

Conflict of Interest

Lamia Ouanes-Besbes declares that she has no conflict of interest. Mustapha Ferjani declares that he has no conflict of interest. Fekri Abroug declares that he has no conflict of interest. ■

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3-5 Euroanaesthesia 2017
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6-9 ESPNIC 2017
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8-9 Neurosciences in Intensive Care International Symposium
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12-13 CARE Convention 2017
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Milan, Italy
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JULY

27-30 16th International Conference on Complex Acute Illness - ICCAI
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31 Jul- 1 Aug 3rd World Congress & Exhibition on Antibiotics and Antibiotic Resistance
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SEPTEMBER

4-5 3rd International Symposium on Post Cardiac Arrest Care
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6-8 34th SSAI Congress
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9-13 ERS International Congress
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11-13 Sepsis 2017 Paris
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13-15 7th Congress of the European Shock Society
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23-27 ESICM LIVES
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23-27 XI European Congress of Emergency Medicine 2017
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