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Professor of Intensive Care Medicine
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Head, Dept of Intensive Care, Erasme Univ. Hospital
President, World Federation of Intensive and Critical Care Societies

Peri-operative Anemia, Bleeding and Blood Transfusion: New Methods of Assessing a Growing Problem

Juan Llau, MD, PhD

Department of Anaesthesiology and Critical Care
Hospital Clinic Universitari - Valencia
Associated Professor of Physiology, University of Valencia
Valencia, Spain

Non-Invasive Assessment of Fluid Responsiveness

Daniel A. Reuter, MD, PhD

Professor of Anaesthesiology and
Vice Chair Department of Anaesthesiology
Center of Anesthesiology and Intensive Care Medicine
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Patient Blood Management and Transfusion Optimization

Aryeh Shander, MD, FCCM, FCCP

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Clinical Advances in Brain Monitoring and Regional Oxygenation for Anaesthesia

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Expanding the Role of EEG Monitoring to Identify Unique Anaesthetic agent Signatures

Emery N. Brown, MD, PhD

Warren M. Zapol Professor of Anaesthesia
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Edward Hood Taplin Professor of Medical Engineering
Professor of Computational Neuroscience
Massachusetts Institute of Technology
Cambridge, Massachusetts

The Brain is Not Just a Number – Applications and Advances for Processed EEG Monitoring and Regional Oximetry in Anaesthesia

Michael Ramsay, MD, FRCA

Chairman Department of Anesthesiology and Pain Management
Baylor University Medical Center and Research Institute
President Baylor Research Institute, Dallas, Texas

Brain Function Monitoring: Where Do We Go From Here?

Pedro L. Gambus, MD, PhD

Department of Anaesthesiology, Hospital Clínic
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Prevention

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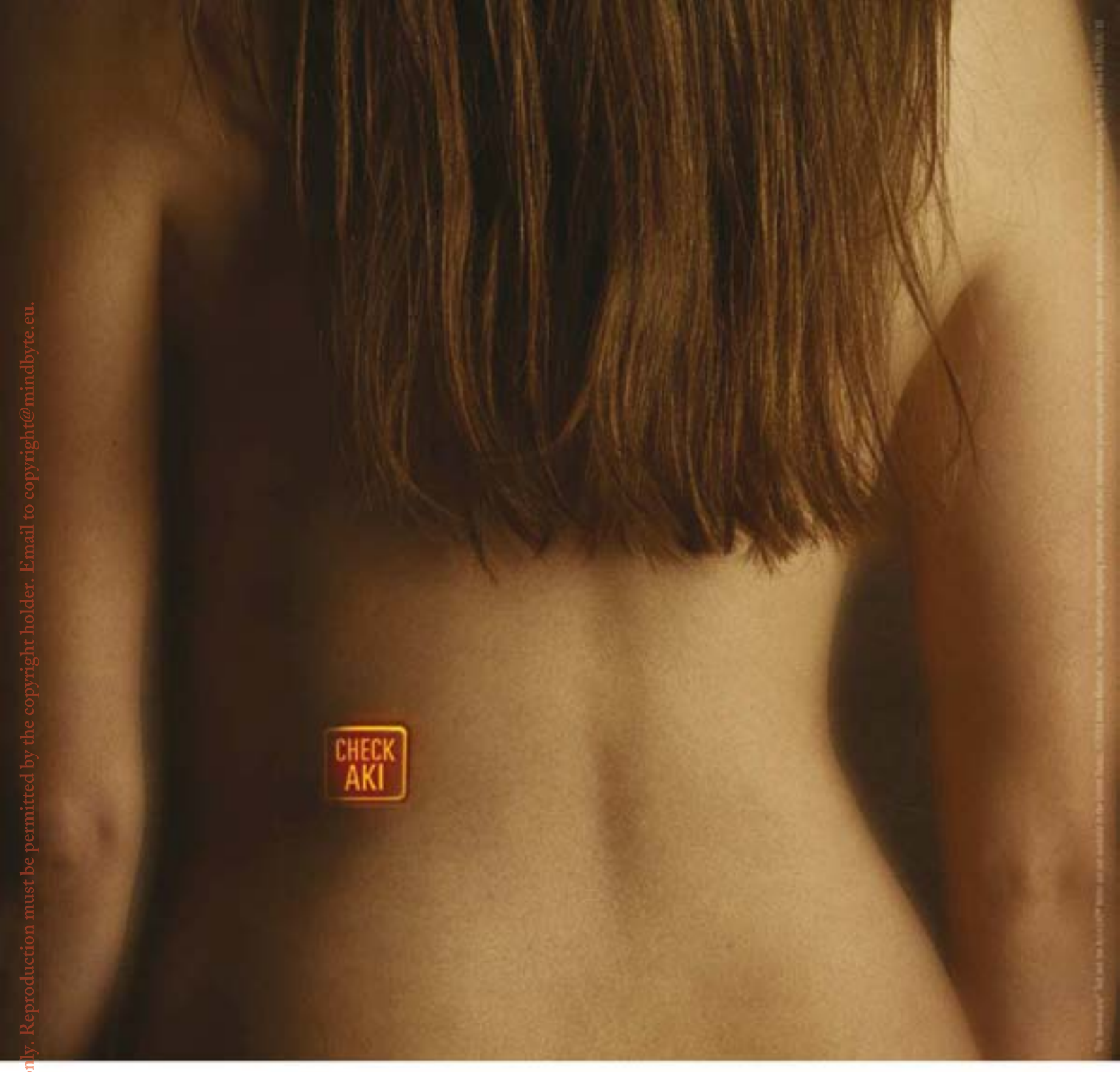

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PREVENTION

The intensive care unit is one of the most expensive parts of the hospital to run. While no intensivist would like to ration intensive care, there are possibilities for prevention and early recognition of critical illness, which can either prevent patients ending up in intensive care or make their stay shorter. In this issue, our cover story is Prevention. Firstly, I write about early recognition of sepsis, for which mortality rates are still far too high. Next, Rajit Basu and colleagues discuss the potential benefits of an AKI care bundle to standardise supportive care measures. They argue that the AKI epidemic requires a more logical and consistent approach to the disease process. Then Candelaria de Haro and Antonio Artigas consider preventive strategies for ARDS, and argue that early identification of patients at risk and control of hospital exposures seem to have most potential.

New advances in fluid responsiveness is the topic for the Fluids series. Xavier Monnet and Jean-Louis Teboul argue that central venous pressure and other static markers of cardiac preload should not be used to predict fluid responsiveness. They outline various tests that can be used for a dynamic approach.

In the Matrix section, first Tim Cook and colleagues look at airway management in the ICU. They argue that the ICU community needs to acknowledge airway dangers, and work on improvements in tracheostomy, capnography, videolaryngoscopy and human factors. Next, David Osman and Isabelle Boytchev review upper gastrointestinal bleeding and its management both before endoscopic diagnosis and after endoscopic diagnosis of ulcer and variceal bleeding. They consider the challenges that remain, including persistent and recurrent bleeding, management of antithrombotic therapy and transfusion management.

Current metabolic and nutritional isues in the ICU are discussed by Olav Rooyackers and Jan Wernerman. Finally, Alain Broccard and Damien Tagan consider the use of diaphragmatic ultrasonography in the ICU, a tool they consider to be underused when it comes to assessing patients with respiratory failure and/or difficulty weaning.

In the Management section, Courtenay Bruce and Janice Zimmerman review the definitions, causes and impact of moral distress, and suggest interventions at the individual and system level, which may help healthcare professionals experiencing moral distress.

John Marini is our interview subject, and shares his frank and sometimes controversial views on evidence-based care, ventilator management and more.

We visit India for our Country Focus. Shirish Prayag outlines the rapid development of the critical care discipline over the last 20 years, and Pravin Amin looks at the state of neurocritical care.

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

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RESEARCH NEWS

Maintaining Normal Day/Night Cycles in the ICU Could Benefit Heart Attack Patients

Normal day and night cycles could improve recovery from heart attack for hospitalised patients, according to researchers from the University of Guelph in Canada.

Their study shows for the first time that interrupting diurnal rhythms impairs healing immediately after a heart attack. Researchers already knew that circadian rhythms can affect timing of a heart attack. This study shows the importance of circadian rhythms during the few days after an attack.

"We have devised a simple way to better practise medicine to improve the outcome from heart attacks by considering normal circadian rhythms," said Prof. Tami Martino of the Department of Biomedical Sciences. She and PhD student Faisal Alibhai conducted the study with Dr. Michael Sole and clinician collaborators from the Peter Munk Cardiac Centre in Toronto, who are already looking at ways to use the results to change practices in intensive care units. "It has an immediate life application," said Martino.

The team induced heart attacks in mice, and then compared rodents held under normal light and dark cycles with others whose diurnal cycles were disrupted for five days after the attacks. Early heart repair and remodelling were impaired in the disrupted mice. Diurnal disruptions interfered with their normal inflammatory and immune responses crucial for scar formation and healing.

"These mice were likely to go more quickly to heart failure," said Martino. "Disrupting circadian rhythms for the first few days after a heart attack worsens the disease outcome."

Reference

Alibhai FJ, Tsimakouridze EV, Chinnappareddy N et al. (2014) Short term disruption of diurnal rhythms following murine myocardial infarction adversely affects long term myocardial structure and function. Circ Res, Apr 1. [Epub ahead of print].

CPR Instruction from Emergency Call Handlers Increases Child Survival

Children who suffer out-of-hospital cardiac arrest are more likely to survive and have good brain function if call handlers/ dispatchers instruct bystanders on CPR, according to a large Japanese study published in the Journal of the American Heart Association.

"Dispatcher-assisted bystander CPR increased bystander CPR delivery rate and was associated with improved one-month favourable neurological and overall outcome compared to no bystander CPR," said lead author Yoshikazu Goto, director of the section of Emergency Medicine at Kanazawa University Hospital in Kanazawa, Japan. "Survival rates increased from 8 percent to 12 percent with bystander CPR and dispatcher instruction, a significant difference."

In a prospective, population-based study conducted over three years, researchers analysed 5,009 children (infancy to 18 years) who received CPR. The children were divided into three groups: 2,019 who received bystander CPR with dispatcher instruction; 703 who received bystander CPR without dispatcher instruction; and 2,287 who didn't receive bystander CPR.

The study found one-month favorable neurological outcomes increased, compared to those who received no bystander CPR:

- 81 percent in those who received bystander CPR with dispatcher instruction;
- 68 percent in those who received bystander CPR without dispatcher instruction.

"Expectant mothers should learn how to perform bystander CPR before they give birth," said Goto, who is also associate professor of Emergency Medicine at Kanazawa University School of Medicine. "It is very important for parents, teachers and other adults who deal with children to learn how to deliver CPR to children."

The study findings also confirm that conventional CPR is preferred to chest compression-only CPR in children.

Reference

Goto Y, Maeda T, Goto Y (2014) Impact of dispatcher-assisted bystander cardiopulmonary resuscitation on neurological outcomes in children with out-of-hospital cardiac arrests: a prospective, nationwide, population-based cohort study. J Am Heart Assoc, 3(3): e000499. doi: 10.1161/JAHA.113.000499.

Not Enough Kidney Patients Receive Home Dialysis, Says Australian Study

Many kidney failure patients in Australia who could benefit from undergoing dialysis at home are being treated in hospitals and dialysis units, according to a study published in the Clinical Journal of the American Society of Nephrology (CJASN). This is creating significant costs for healthcare providers and causing unnecessary disruptions to patients' lives.

Home dialysis is more convenient for patients and can provide similar or better care than haemodialysis, which must be done in a clinic. Blair Grace, from the Australia and New Zealand Dialysis and Transplant Registry led a team that investigated the links between socioeconomic status and use of home dialysis (which includes peritoneal dialysis and home haemodialysis) in Australia. The researchers analysed 23,281 adult patients who started dialysis in Australia between 2000 and 2011.

Among the major findings:

- Socioeconomic status was not associated with use of home haemodialysis.
- Patients from the most advantaged areas were 37% less likely to commence peritoneal dialysis and 19% more likely to use in-centre haemodialysis than patients from the most disadvantaged areas.
- Rural areas were more disadvantaged and had higher rates of peritoneal dialysis, while privately-funded hospitals rarely used home dialysis.
- Patients from the most advantaged areas were nearly six times more likely to use private hospitals than those from the most disadvantaged areas.

"We expected to find that patients with more education and financial resources were more likely to use peritoneal dialysis and home haemodialysis, as has been demonstrated in other countries," said Dr. Grace. "Instead, we found that patients from socioeconomically advantaged areas were less likely to use peritoneal dialysis and more likely to use in-centre hemodialysis."

It's unclear why private hospitals in Australia rarely use home dialysis, and why patients from advantaged areas are more likely to use private hospitals.

"More research is required to determine if patients from advantaged areas choose private hospitals knowing they want to dialyse in centre, or whether they attend public hospitals then get directed towards in-center dialysis," added Grace.

Reference

Grace BS, Clayton PA, Gray NA et al. (2014) Socioeconomic differences in the uptake of home dialysis. Clin J Am Soc Nephrol, 9(5):929-35. doi: 10.2215/CJN.08770813.

Depression Hits More than One in Three Critical Illness Survivors

Depression affects more than one out of three survivors of critical illness, according to one of the largest studies to investigate the mental health and functional outcomes of critical care survivors, published in The Lancet Respiratory Medicine.

With around 5 million patients admitted to intensive care units (ICUs) in the United States alone, it is a major public health issue, according to James Jackson, assistant professor of Medicine at Vanderbilt University in Tennessee.

Weakness, appetite change and fatigue - all signs of somatic, or physical, depression - were present in two-thirds of the patients, as opposed to cognitive symptoms such as sadness, guilt or pessimism.

"We need to pay more attention to preventing and treating the physical rather than psychological symptoms of depression in ICU survivors," Jackson said. "The physical symptoms of depression are often resistant to standard treatment with antidepressant drugs, so we need to determine how best to enhance recovery with a new focus on physical and occupational rehabilitation."

The BRAIN-ICU study observed 821 critically ill patients ages 18-90 with respiratory failure or severe sepsis (blood poisoning) admitted to medical or surgical ICUs at Vanderbilt University Hospital and Saint Thomas Hospital. Vanderbilt researchers assessed survivors for depression, PTSD, functional disability and impact on quality of life at three-month and one-year intervals, reporting that 149 of the 407 patients (37 percent) assessed at three months had at least mild depression, while only 7 percent of patients experienced symptoms of PTSD.

"Depression symptoms were significantly more common than symptoms of PTSD," Jackson said. "And they occurred to a large degree across the entire age range. People tend to have a vision of a frail, older patient who goes to the ICU and is at risk for adverse mental health and, in particular, functional outcomes. But what people don't anticipate is someone in their 20s, 30s or 40s could go to the ICU and leave with functional disability, depression or PTSD. These problems are not really a function of old age."

One-third of the survivors who developed depression still had depressive symptoms at their one-year assessment, a statistic that Jackson said could, in part, be due to high expectations they set for rehabilitation.

"They have some arbitrary timeline set and they reach that date and they're still not better and, in some cases, not a lot better at all," he said. "Then what can happen is that depression can really worsen because they set this expectation that was really unrealistic and they feel like they have missed the goal.

So that's a big challenge, recalibrating expectations. This is especially hard for the many high-achieving, type A, patients that we might see who leave the ICU and want to get back to work right away, want to compete in the triathlon right away. They tend to have the hardest time," he said.

Jackson said study authors gained additional perspective on their patients by doing at-home assessments following discharge.

"Home visits were the really interesting part of this," Jackson said. "What it enabled us to do was to see patients in their real-life surroundings in actual circumstances in which they were sometimes a little more willing, I think, to disclose their problems. When you see someone in a hospital, the situation is a little more sterile. When you get to know them in their homes, we felt like you really get to know them and that was often the context where they told us about their depression.

"One thing we learned was that if people don't have significant social support, they are profoundly limited in their ability to access care or improve in key areas," he added.

Vanderbilt is now following ICU patients after discharge through the Vanderbilt ICU Recovery Center.

Reference

Jackson JC, Pandharipande PP, Girard TD et al. (2014) Depression, post-traumatic stress disorder, and functional disability in survivors of critical illness in the BRAIN-ICU study: a longitudinal cohort study. Lancet Respir Med, 2(5):369-79. doi: 10.1016/S2213-2600(14)70051-7.

EARLY RECOGNITION OF SEPSIS

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Patients with sepsis, now defined as a severe infection with some degree of associated organ dysfunction, make up a large proportion of the critically ill population and, although outcomes have improved over the last decade, mortality rates remain above 20-30%, and even close to 40% when shock is present. There are no effective specific anti-sepsis treatments, and management of patients with sepsis thus relies largely on early recognition allowing rapid institution of correct therapeutic measures, including administration of appropriate antibiotics, source control measures when necessary and effective resuscitation strategies with intravenous fluids and vasoactive agents when required. Additional therapies, such as corticosteroids or other immunomodulatory drugs, have a limited place (especially after the withdrawal of activated protein C from the drug market).

> *"The ability to accurately diagnose sepsis as soon as possible is, therefore, paramount"*

Early and aggressive management with appropriate antimicrobials and rapid and complete haemodynamic stabilisation has been shown to be associated with improved outcomes. The ability to accurately diagnose sepsis as soon as possible is, therefore, paramount. However, it is difficult to know in advance who will develop sepsis. A minor infection (even an apparently simple viral cold) can evolve into sepsis, but (fortunately!), not all people with minor infections will develop organ dysfunction and sepsis. Although advances in genomics and proteomics are providing some clues as to which patients may be more likely to develop sepsis than others, these techniques remain exploratory at present. For many years some people used the so-called systemic inflammatory response syndrome (SIRS) criteria (hypo- or hyperthermia, tachycardia, tachypnea, altered white blood cell count) to screen patients for possible sepsis, but these criteria are present in most critically ill patients, so have limited use in trying to distinguish those who have or will develop sepsis from other patients. These criteria are currently used to reflect the presence of infection and this is important; however, fever and other signs of infection are commonly present in acutely ill patients, and these patients are frequently already receiving antibiotics, such that microbiological cultures will be negative in as many as 50%. Imaging modalities to locate a source are also often unreliable, e.g. lung opacities may be due to infection, but could also be the result of atelectasis, or lung oedema due to acute respiratory distress syndrome (ARDS) or acute heart failure. Improved bioinformatics and microarray techniques may improve our ability to identify the presence of microorganisms, but these techniques are not yet available for routine clinical use. Various biomarkers have also been suggested to help in the diagnosis of sepsis, e.g. procalcitonin, C-reactive protein, interleukin-6 levels, but as yet none is specific for sepsis. Panels of multiple biomarkers may be more helpful, but further research is needed to define which biomarkers should be included in such panels.

Rather than focusing on signs or markers of infection to diagnose sepsis, it is perhaps better to focus on the presence or development of organ dysfunction, and to evaluate whether this may be due to sepsis. Any organ dysfunction without a clearly identifiable cause should always raise

Table 1. Sequential Organ Failure Assessment (SOFA) Score

SOFA score	0	1	2	3	4
Respiration					
PaO_2/FiO_2, mmHg	> 400	≤ 400	≤ 300	≤ 200 ------ with respiratory support ------	≤ 100
Coagulation					
Platelets x $10^3/mm^3$	> 150	≤ 150	≤ 100	≤ 50	≤ 20
Liver					
Bilirubin, mg/dL (µmol/L)	< 1.2 (< 20)	1.2 - 1.9 (20 - 32)	2.0 - 5.9 (33 - 101)	6.0 - 11.9 (102 - 204)	> 12.0 (> 204)
Cardiovascular					
Hypotension	No hypotension	MAP < 70 mmHg	dopamine ≤ 5 or dobutamine (any dose)*	dopamine > 5 or epinephrine ≤ 0.1 or norepinephrine ≤ 0.1*	dopamine > 15 or epinephrine > 0.1 or norepinephrine > 0.1*
Central nervous system					
Glasgow coma score	15	13 - 14	10 - 12	6 - 9	< 6
Renal					
Creatinine, mg/dL (µmol/L)	< 1.2 (< 110)	1.2 - 1.9 (110 - 170)	2.0 - 3.4 (171 - 299)	3.5 - 4.9 (300 - 440)	> 5.0 (> 440)
or urine output				or < 500 ml/d	or < 200 ml/d

* adrenergic agents administered for at least one hour (doses given are in mcg/kg/min)

Box 1. Signs of Organ Dysfunction That May Suggest Sepsis

Cardiovascular: hypotension, increased lactate levels
Respiratory: hypoxaemia, need for oxygen therapy
Neurological: disorientation, confusion, obtundation
Renal: oliguria, increased creatinine concentration
Haematological: decreased platelet count
Hepatic: jaundice, increased bilirubin

the possibility of sepsis, but six types may be particularly indicative (see Box 1). Importantly, because of the systemic nature of the sepsis response any organ system may be affected regardless of the source of the underlying infection. Respiratory dysfunction is particularly common, and may manifest simply by tachypnea or hypoxaemia, necessitating oxygen therapy or mechanical ventilation in more severe cases. Renal dysfunction often leads to reduced urine output and later to increased serum creatinine levels. Cardiovascular dysfunction can include tachycardia and hypotension and resultant poor tissue perfusion leading to increased blood lactate levels. Abnormalities in blood clotting are also common in patients with sepsis, and include a reduced platelet count as one of the early signs. Unexplained confusion and reduced alertness are signs of central nervous system dysfunction. Jaundice with raised bilirubin levels indicates liver dysfunction, although this occurs relatively late in the process.

The most widely used system to assess organ dysfunction in critically ill patients is the sequential organ failure assessment (SOFA) score (see Table 1). This score quantifies organ dysfunction in six organ systems - respiratory, cardiovascular, hepatic, coagulation, renal and neurological – using a score from 1 (least dysfunction) to 4 (most dysfunction). Individual scores can be combined to give an overall indication of the degree of organ dysfunction in individual patients (range 0-24). The SOFA score on admission to the ICU is correlated with the development of bacteraemia. Higher scores are correlated with a higher risk of death, and changes in SOFA score over time can indicate response to therapy, with stable or increasing scores suggesting a worsening condition.

Increased awareness of sepsis and more rapid management of patients with sepsis have helped to improve outcomes in recent years, but mortality rates remain unacceptably high. While waiting for specific therapies to become available, continued emphasis must therefore be on the importance of early diagnosis allowing rapid infection control and organ support. ■

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Kaukonen KM, Bailey M, Suzuki S et al. (2014) Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000-2012. JAMA, 311: 1308-16.

Levy MM, Fink MP, Marshall JC et al. (2003) 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Crit Care Med, 31: 1250-6.

Vincent JL, Moreno R, Takala J et al. (1996) The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. Intensive Care Med, 22: 707-10.

Vincent JL, Opal SM, Marshall JC, Tracey KJ (2012) Sepsis definitions: time for change. Lancet, 381: 774-5.

Vincent JL, Beumier M (2013) Diagnostic and prognostic markers in sepsis. Expert Rev Anti Infect Ther, 11: 265-75.

BUNDLING MANAGEMENT OF ACUTE KIDNEY INJURY IN CRITICALLY ILL PATIENTS MAY MINIMISE TREATMENT VARIABILITY

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Acute kidney injury (AKI) is a significant problem in hospitalised patients, independently contributing to morbidity and increasing mortality. Prevention, risk assessment and supportive care, dependent on timely recognition of decreases in kidney function, are the mainstay of current treatment, as no singular therapy has proven effective at reducing AKI or improving associated negative outcomes. Additionally, although AKI severity-based care guidelines have been published, they have not yet been widely disseminated into clinical practice and AKI management continues to be highly variable. In this brief review, we discuss the potential benefits of an AKI care bundle to standardise supportive care measures. We suggest that incorporation of this bundle would help minimise practice variation, making possible the determination of effective disease- and patient-targeted therapy, and potentially lead to improved patient outcomes.

Introduction

Acute kidney injury (AKI) is an international epidemic and its incidence is increasing (Lameire et al. 2013; Rewa and Bagshaw 2014). Indeed, the incidence of AKI has grown at an alarming rate over the past 20 years and has been repeatedly shown to be associated with increased mortality, prolonged mechanical ventilation and longer hospital stay (Bellomo et al. 2012; Kellum et al. 2011; Hoste et al. 2010; Foretnberry et al. 2013). Increasing recognition of the negative impact of AKI has led to a paradigm shift – patients are not just dying with AKI, but from AKI (Hoste and Corte 2011). Since no therapy has yet proven to be effective to mitigate the deleterious effects associated with AKI, systematic risk assessment, preventive strategies and supportive care directed toward overall patient stability are the cornerstones of AKI management.

> *"Identifying patients with increased risk of AKI outside the ICU appears to be more challenging"*

AKI prevention depends on systematic risk and disease recognition. To date, no widely accepted and implemented practice parameters exist to identify and triage at-risk patients even though many AKI risk factors are known. Further, while AKI in intensive care units (ICUs) most commonly occurs secondary to other systemic injury (sepsis, trauma, post-surgical), the risk is not binary. Epidemiologic data strongly suggest that in the ICU degrees of risk exist and it is not homogeneously 'present or absent'. Stratifying the heterogeneity of patient risk is essential to implementation of a feasible AKI prediction strategy. Leveraging population analyses of risk factors in adults and children, the recently proposed renal angina methodology is the first attempt to use risk stratification to underscore patient risk and improve prediction of AKI (Goldstein and Chawla 2010).

Timely recognition of AKI has been challenged by limitations associated with the traditional parameters used for diagnosis. Changes in serum creatinine (SCr) and urine output (UOP) may lag behind injury, and are variable with regard to patient body habitus, gender, and age (Bagshaw and Gibney 2008). Thus, current AKI diagnostic strategy is often *reactive* to injury. By contrast, novel AKI biomarkers carry the potential to provide robust predictive ability in and may enable *proactive* therapy for incipient injury. Unfortunately, many of these biomarkers demonstrate inconsistent ability for AKI prediction in heterogeneous patient populations not stratified by risk (McCullough et al. 2013; Vanmassenhove et al. 2013; Basu et al. 2012). Although recent advances in bio-

Figure 1. The Renal Angina Index

RISK STRATA

Patient Description	Risk Level	Risk Score
Admitted to ICU, Post-Trauma, Post-Surgery	Moderate	1
Significant Co-Morbidities: Sepsis, Diabetes, Congestive Heart Failure, Transplant	High	3
Significant Current Illness: Mechanically Ventilated, Vasopressor Requirement	Very High	5

✖

INJURY STRATA

Change in Creatinine from Baseline	Flyid Overload	Risk Score
1x - 1.24x	0 - 4.9%	1
1.25x - 1.49x	5 - 9.9%	2
1.5x - 1.99x	10 - 19.99%	4
≥ 2x	≥ 20%	8

=

Renal Angina Index (Range: 1-40)

The theoretical construct of the renal angina index is to operationalise renal angina, a composite of risk and injury levels.
The tables above represent potential strata of both increasing risk and early injury, which can be quantified and used to calculate an index number (range 1-40).
Validation of a similar scoring methodology has been performed in critically ill children (Basu et al. 2014).

marker development focusing specifically on discovery in heterogeneous populations appear to show more promise (Kashani et al. 2013; Cruz and Mehta 2014; Bihorac et al. 2014), patient selection for biomarker measurement remains essential. Critically ill patients are already a high-risk group. Identifying patients with increased risk outside the ICU appears to be more challenging.

Current AKI management is supportive in nature and generally directed at the pathophysiologic drivers of injury. Large randomised controlled trials (RCTs) studying more individualised therapy - diuretics for oliguria, anti-inflammatory medication, continuous renal replacement therapy (CRRT) for fluid overload, and 'reno-selective' vasodilators such as fenoldopam to augment renal perfusion have been attempted, but demonstrate inconsistent outcomes (Nigwekar and Waikar 2011; Palevsky 2009; Landoni et al. 2007; Scrascia et al. 2014). The dustbin of AKI trials is filled with these therapies, which demonstrate the ability to alter the course of a single perturbation (ie increase diuresis in oliguric patients), but are unable to affect the ultimate outcome of interest (eg AKI or decreased mortality rates). Consequently, no consistent and standard protocol is followed for AKI management and treatment continues to be directed towards global injury.

Risk Recognition to Trigger Management

To improve global recognition of risk factors and unify the approach to the diagnosis and care of patients with AKI, the Kidney Diseases Improving Global Outcomes (KDIGO) AKI collaborative published stage-based AKI practice guidelines (Kidney Disease: Improving Global Outcomes Acute Kidney Injury Work Group 2012). These guidelines embody the efforts of the Agency for Healthcare Research and Quality (AHRQ) to standardise care for high-impact diseases by "reducing variations, improving outcomes, and reducing costs" (Agency for Healthcare Research and Quality 2013). There have been no published studies to date reporting on the implementation of these guidelines and outcomes from use.

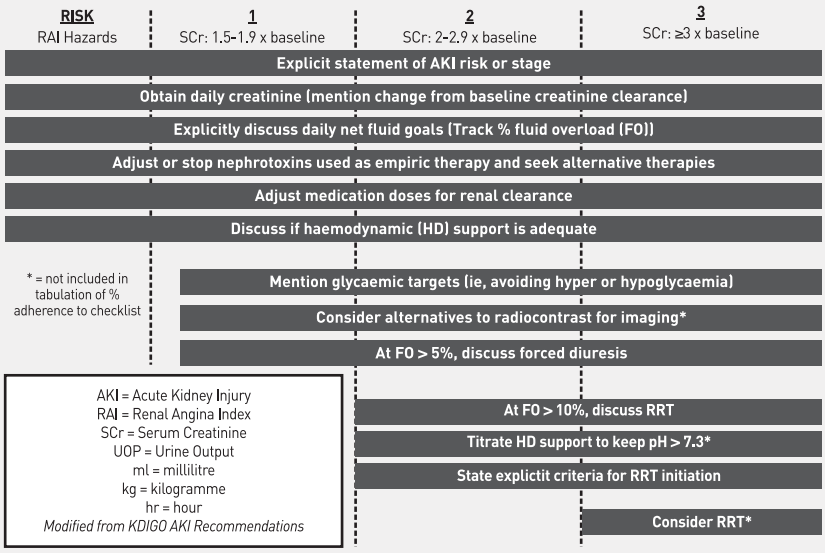
The KDIGO AKI management guidelines are predicated on identification of AKI risk or injury. Unfortunately, unlike acute coronary syndrome, stroke, infection and many other acute illnesses, AKI does not carry easily identifiable physical signs to expedite identification of injury and initiation of management. For instance, while respiratory failure often presents with shortness of breath and myocardial infarction with chest pain, AKI does not typically present in a way that brings patients to medical attention (ie symptomatically). Simply put, AKI does not hurt (Goldstein and Chawla 2010). Despite limitations mentioned earlier, however, small changes in SCr and UOP below the level of injury as classified by consensus criteria have been associated with high rates of progression to severe AKI and worse hospital outcomes (Basu et al. 2012; Cruz et al. 2014; Coca et al. 2007; Nin et al. 2010; Zappitelli et al. 2009). So while chest pain in the correct context (angina pectoris) may be the herald sign for a heart attack, injury diagnosed by small changes in SCr or UOP in the correct context (renal angina) may be a harbinger of a kidney attack (Kellum et al. 2012). To operationalise this concept, the renal angina index (RAI) was derived (see Figure 1), combining AKI risk factors and sub-clinical injury (Basu et al. 2014). Context-driven biomarker testing for detection of early myocardial injury has dramatically improved the outcomes of patients suffering heart attacks as it triggers the initiation of heart attack protocols and stage-based management. Context-driven biomarker testing for detection of early AKI, using renal angina or other validated methodologies to identify high-risk patients, may now be possible, and lends itself to direct integration with management guidelines.

> *"Increasing recognition of the negative impact of kidney attacks will drive the impetus for a more logical, consistent, and algorithmic approach to the disease process"*

AKI Bundle – Targeting Risk, Injury, and Standardising Care

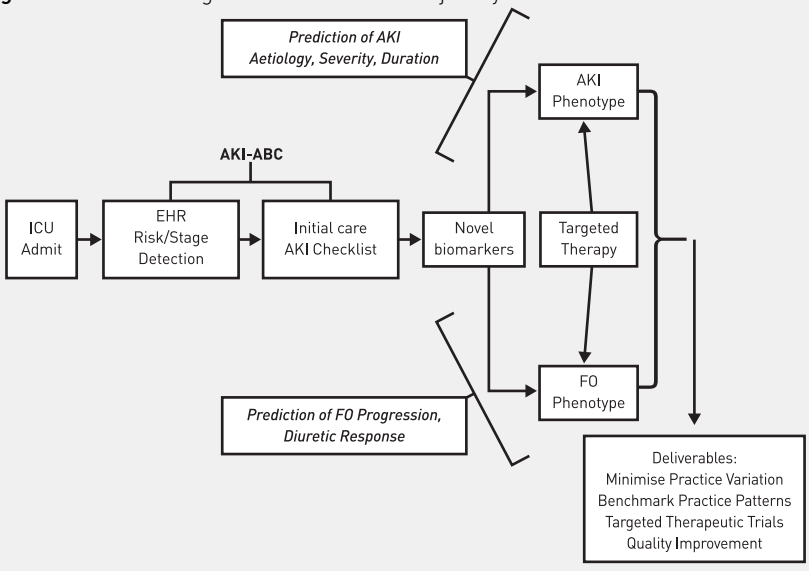
Improved outcomes in patients with AKI will rely on the development and incorporation of an automated AKI detection and management tool. Clinical decision support systems (CDSS) embedded within high functioning electronic health records (EHRs) are able to integrate patient information, laboratory data, and efficacy of available therapeutic options in real time. CDSS are currently being used to standardise management of several high impact disease processes to adhere to best practice guidelines (Cleveringa et al. 2007; Twiggs et al. 2004; Okelo et al. 2013).

Figure 2. The AKI - Acute Bundle of Care



Derived from the KDIGO AKI best practice management guidelines, the AKI Acute Bundle of Care (AKI-ABC) delineates the actions to be taken for a patient fulfilling either risk of AKI (defined by renal angina index (RAI) risk strata) or the KDIGO AKI stages 1-3 based on changes from baseline serum creatinine (SCr). RRT = renal replacement therapy.

Figure 3. The AKI Management and Research Trajectory



A care algorithm for approaching critically ill patients with AKI incorporates the AKI Acute Bundle of Care (AKI-ABC), novel biomarker prediction of AKI phenotype and fluid overload progression, ultimately leading to discrete deliverables. The anticipated net result of these outcomes is optimising AKI management by providing clinical decision support to direct targeted therapy.

CDSS to guide AKI prediction and management in the ICU have not yet been described, but an 'AKI Acute Bundle of Care' (AKI-ABC), incorporating risk stratification, renal angina, and AKI-stage-based management parameters can be designed and potentially incorporated into an EHR (see Figure 2). The integration of this bundle into patient workflow would theoretically occur during the initial stabilisation phase of admission and twice daily thereafter. The bundle explicitly incorporates the stages of AKI, including risk of AKI. The bundle focuses the attention of care providers on routine practices, which can both prevent AKI from occurring (such as discontinuing nephrotoxic agents or using alternatives to intravenous contrast) and mitigate the effects of AKI (limit the extent of fluid overload (FO)). Detection of vital patient elements and calculation of risk could be programmed using natural language processing or other advanced biomedical informatics technique (Campas et al. 2013; Byrd et al. 2013). Additionally, the bundle attempts to standardise the approach to initiation of renal replacement therapy (RRT), for which there currently is no consistent and universally accepted algorithm. Similar to the reported effect of an EHR-based trigger tool for detection of nephrotoxic-associated AKI triggering increased systematic kidney function surveillance, a reduction in the severity or duration of AKI, or the prevalence of AKI, would be anticipated with adherence to this bundle (Goldstein et al. 2013). The use of the bundle in critically ill patients would also standardise management and minimise practice variation, making it possible to systematically investigate new diagnostic strategies (e.g. combining biomarkers or attempting to phenotype AKI by pathophysiology) or targeted therapeutic interventions (Endre et al. 2013; McCullough et al. 2013). The incorporation of this checklist into the AKI research trajectory, studying EHR use, novel biomarker diagnosis, and creation of AKI-disease phenotypes (e.g. fluid overload), could then be used to benchmark practice patterns against the outcome of disease (see Figure 3). The development of quality improvement benchmarks for internal and external reporting would logically follow. For a global disease, the adoption of such standards would make side-by-side comparisons of AKI epidemiologic patterns and outcomes possible across not only institutions, but different socioeconomic and geographic areas.

Conclusion

The epidemic of AKI demands action; increasing recognition of the negative impact of kidney attacks will drive the impetus for a more logical, consistent, and algorithmic approach to the disease process. Use of the EHR to integrate risk stratification, disease severity and an initial AKI management bundle would be an example of a highly useful clinical decision support tool. Standardisation of the approach to AKI would minimise the variability of practice and potentially allow disease and patient-specific targeted therapeutic trials to be developed. This methodology may be the path forward. ■

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ACUTE RESPIRATORY DISTRESS SYNDROME THE ERA OF PREVENTION

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Acute respiratory distress syndrome (ARDS) results in increased use of critical care resources and the overall associated mortality remains high. The identification of patients at risk and the implementation of preventive strategies are necessary.

Introduction

Acute respiratory distress syndrome (ARDS) is common in critically ill patients admitted to intensive care units (ICU). ARDS is characterised by acute hypoxaemia and bilateral pulmonary infiltrates and pulmonary oedema due to an increased permeability without left cardiac failure (Rubenfeld and Herridge 2007; ARDS Definition Task Force 2012).

There is an incidence of 58.7 cases per 100,000 people/year (Rubenfeld et al. 2005). Data about mortality vary widely. A systematic review, which analysed mortality from ARDS from 1994 to 2006, selected all trials that included patients based on the American-European Consensus Conference definition, and concluded that mortality decreased over the last decade, with an overall mortality of 43%, in-hospital mortality of 48.7% and ICU mortality of 44.3% (Zambon and Vincent 2008). A recent analysis reports an overall mortality of 44.3% (Phua et al. 2009). ARDS involves a high health cost and high overall mortality. Several indicators of poorer prognosis in ARDS have been identified (Ware 2005; Stapleton et al. 2005). The most important factors related to mortality are co-morbidities, age, severity (Simplified Acute Physiology Score [SAPS] II) and shock and organ failure (mortality has a direct relation with the number of organ failures and increases up to 83% with three or more organ failures). Once treatment is initiated, prognostic factors are correlated with response to treatment.

Currently there is no specific treatment for ARDS. The best care emphasises adequate and correct supportive care focused on the treatment of the underlying cause and avoiding iatrogenic complications. Mechanical ventilation remains the most important support therapy in ARDS.

Patients At Risk of Development of ARDS

ARDS is rarely present at the hospital admission; rather, it develops in a short time period from hours to days in patients with predisposing factors. Patients with risk factors at admission for ARDS develop ARDS in a median of 2 days (interquartile range 1-4) (Gajic et al. 2011). A chain reaction based on multiple hits can be involved in the pathogenesis of ARDS development and/or the progression of severity (Pavord et al. 2006). Host predisposing conditions act as a first hit in healthy lungs, where multiple hits can induce ARDS. In the absence of these predisposing conditions, the probability that the other hits will result in ARDS is lower (de Haro et al. 2013).

Early identification of patients at risk for ARDS may represent a good opportunity for preventive strategies. Following the paradigm of early goal-directed therapy in sepsis, early identification and treatment of ARDS patients could improve surveillance.

Several predisposing factors have been ascribed to ARDS development. Hudson et al. evaluated the presence of one or more of eight clinical conditions (sepsis, aspiration, drug overdose, near drowning, pulmonary contusion, multiple transfusions, multiple fractures, cranial traumatism), determined in previous studies, in ARDS development, and they obtained a 79% sensitivity and 26% specificity (Hudson et al. 1995). Gong et al. demonstrated that a pulmonary aetiology of injury, haematologic failure, transfusion of eight or more units of concentrated red blood cells, respiratory rate > 33 rpm, haematocrit > 37.5%, arterial pH < 7.33, albumin ≤ 2.3g/dL and transfer from another hospital increase ARDS risk (Gong et al. 2005). Ferguson et al. (2007), in patients from hospital wards, determined that pulmonary risk factors had a higher rate of ARDS progression than non-pulmonary risk factors, but shock was the most potent predictor factor. Trillo-Alvarez et al. developed in 2011 a predictor index for ARDS, called the Lung Injury Prediction Score (LIPS), which identified patients at risk of ARDS before ICU admission (Trillo-Alvarez et al. 2011). Gajic et al. (2011), in a multicentre prospective observational trial, determined that ARDS development varies due to the presence of predisposing factors and that the LIPS model discriminates efficiently (AUC 0.80; CI 95%; 0.78-0.82) between those with a low risk of ARDS development and those who developed ARDS. If adjusted for severity and predisposing factors, ARDS development increases in-hospital mortality (OR 4.1; CI 95%; 2.9-5.7). A recent trial, which studied the role of potentially preventable hospital exposures in the development of ARDS, suggests that the avoidance of second hits can decrease the development of ARDS and improve safety and outcomes for critically ill patients (Ahmed et al. 2014). The hospital exposures with a strong

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**Compared to conventional mechanical ventilation

1. Xirouchaki N, Kondili E, Vaporidi K, et al. Proportional assist ventilation with load-adjustable gain factors in critically ill patients: comparison with pressure support. Int Care Med. 2008;34:2026-2034.
2. Younes, Magdy. Proportional Assist Ventilation, a New Approach to Ventilatory Support. AM REV RESPIR DIS 1992; 145:114-120.

association with development of ARDS were preventable medical and surgical adverse events, inadequate antimicrobial therapy, larger volumes of blood product and intravenous fluid administration and documented pulmonary aspiration (Ahmed et al. 2014).

Focus on Prevention

Gajic et al. (2004), in a retrospective trial, hypothesised that one of the most important risk factors for ARDS development is mechanical ventilation with high tidal volumes. They demonstrated an increase of OR 1.3 per mL above 6 mL/kg predicted body weight (PBW) (Gajic et al. 2004). In 2010 Determann et al. conducted a trial, stopped at the interim analysis, in which patients ventilated with low tidal volumes (6mL/kg PBW versus 10 mL/kg PBW) developed less ARDS (13.5% vs. 2.6%; $p = 0.01$) (Determann et al. 2010). This trial supports the results of previous cohort trials suggesting that mechanical ventilation with traditional tidal volumes can contribute to the development of lung injury (Wrigge et al. 2004). Martin-Loeches et al. (2013) showed that protective ventilation strategies (plateau pressure < 30 cm H_2O) were associated with lower mortality in septic patients without ARDS. A recent multicentre trial demonstrated that the use of a lung-protective mechanical ventilation strategy during major abdominal surgery results in fewer pulmonary postoperative complications (Futier et al. 2013). A meta-analysis by Serpa Neto et al. (2012) showed that protective ventilation with lower tidal volume in patients without ARDS was associated with better clinical outcomes. Further prospective trials in critically ill patients are needed, but a protective mechanical ventilation strategy in patients at risk of ARDS seems to be a good prevention strategy.

Sepsis precipitates ARDS in 25% to 40% of cases, and the risk increases if a systemic inflammatory response, shock, or organ dysfunction is present. Early appropriate antibiotic therapy seems to be one of the most important preventive strategies, while there is no specific preventive treatment (Iscimen et al. 2008; Ferrer et al. 2008; Kumar et al. 2009).

Fluid balance has been identified in multiple trials as an important risk modifier in the development of ARDS. There are no specific trials evaluating a fluid strategy in patients without ARDS, but many trials support a conservative strategy in ARDS patients, with better outcomes (National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network 2006; Murphy et al. 2009). Fluid overload could be a preventable hospital exposure in patients at risk of development of ARDS.

There is an association between blood products and ARDS. This effect depends on the amount of red cell transfusions and alloimmunisation (Zilberberg et al. 2007; Gong et al. 2005; Toy et al. 2005). A policy of less transfusion is probably the best preventive strategy (Yilmaz et al. 2007).

Different pharmacologic treatments are under study, but as yet there are no results. Exposure to antiplatelet agents during the at-risk period was associated with a decreased risk of ARDS (Ahmed et al. 2014), but there are no prospective trials in human patients evaluating this treatment. Other treatments, such as activated protein C, inhaled corticosteroids, statins, mesenchymal stem cells and beta-2 adrenergic agonists have been tested in experimental studies, but have yet to show promising results in human patients (Maniatis et al. 2010; Chimenti et al. 2012; Levitt and Matthay 2012).

In conclusion, preventive strategies are a new field of research aiming to avoid the progression of ARDS. Early identification of patients at risk for ARDS and the control of hospital exposures (multiple hits) seem to be the best options for prevention of the disease or to avoid ARDS progression. ■

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FLUID RESPONSIVENESS
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Introduction

In case of acute circulatory failure, fluid is administered with the expectation that it will increase cardiac output. Nevertheless, this can occur only if cardiac output is dependent upon cardiac preload, ie if both ventricles operate on the ascending limb of the cardiac function curve (see Figure 1) (Monnet et al. 2013). If no test is used to predict fluid responsiveness, volume expansion results in the expected increase in cardiac output in only half of patients (Michard et al. 2002). Thus, fluid responsiveness should be detected before deciding to administer volume expansion or not. This should avoid fluid overload, which is an independent predictor of mortality in patients with septic shock (Vincent et al. 2006) and/or ARDS (Jozwiak et al. 2013).

> *"Central venous pressure and other 'static markers' of cardiac preload should be definitely abandoned for the prediction of fluid responsiveness"*

For predicting fluid responsiveness, 'static' markers of cardiac preload have been used for many years: central venous pressure, pulmonary artery occlusion pressure, left ventricular end-diastolic dimensions at echocardiography, for instance. However, a very large number of studies clearly demonstrate that such markers of preload are unable to predict fluid responsiveness (Monnet et al. 2013). This is mainly due to the physiological fact that a given value of preload could correspond to either a large or a negligible response of cardiac output to fluid administration, depending upon the slope of the Frank-Starling curve (see Figure 1). Today, using such static markers of preload for deciding to administer fluid or not should be definitely abandoned (Marik et al. 2013). Alternatively, a 'dynamic approach' allows assessment of preload dependency by observing the effects on cardiac output of changes in cardiac preload induced by various tests.

Respiratory Variations of Stroke Volume: a High Level of Evidence

During mechanical ventilation each insufflation decreases venous return and, if the right ventricle is preload-dependent, reduces the right ventricular outflow. Increase in right ventricular afterload induced by increased lung volume contributes to this reduction of right ventricular outflow. After the transit of blood through the lungs the left ventricular preload decreases. In the case of conventional ventilation, this should occur at expiration. If the left ventricle is also preload-dependent, the left ventricular stroke volume transiently decreases in response. Hence, a cyclic variation of stroke volume under mechanical ventilation indicates preload-dependency of both ventricles (Michard et al. 2000).

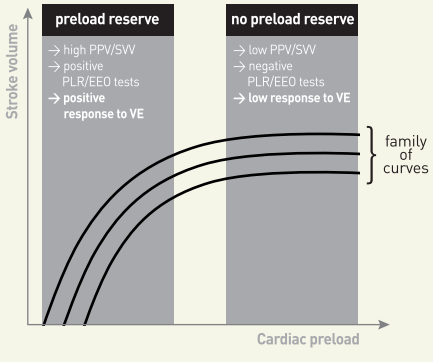
Surrogates of Stroke Volume

The arterial pulse pressure was the first index to be used to predict fluid responsiveness through its respiratory variation (Michard et al. 2000). Many other surrogates of stroke volume have been developed since, such as stroke volume estimated by pulse contour analysis, aortic blood flow measured by oesophageal Doppler, aortic blood flow with echocardiography and amplitude of the plethysmography signal with pulse oximetry (Monnet et al. 2013).

Limitations of the Respiratory Variations of Stroke Volume to Predict Fluid Responsiveness

It is important to always remember that the respiratory variation of haemodynamic signals cannot be used in some specific conditions. First, in case of spontaneous breathing activity, even in an intubated patient, variations of stroke volume relate more to the respiratory irregularity than to preload dependence (Heenen

Figure 1. Frank-Starling Relationship



Once the ventricle is functioning on the steep part of the Frank-Starling curve, there is a preload reserve. Volume expansion induces a significant increase in stroke volume. The pulse pressure (PPV) and stroke volume (SVV) variations are high (≥ 13%) and the passive leg raisng (PLR) and end-expiratory occlusion (EEO) tests are positive. By contrast, once the ventricle is operating near the flat part of the curve, there is no preload reserve and fluid has little effect on the stroke volume. There is a family of Frank-Starling curves depending upon the ventricular function.

et al. 2006, Monnet et al. 2006). The second obvious limitation is the presence of cardiac arrhythmias. The third limitation refers to ARDS. In such a case, the low tidal volume (De Backer et al. 2005) and/or the low lung compliance (Monnet et al. 2012), which reduces the transmission of changes in alveolar pressure to the intrathoracic structures, diminish the amplitude of the ventilation-induced changes of intravascular pressure. This should result in false negatives for the prediction of fluid responsiveness by pulse pressure variation (PPV). Open chest surgery, a low ratio of heart rate over respiratory rate (corresponding in fact to respiratory rates at 40 breaths/minute or more) or intra-abdominal hypertension are other circumstances in which PPV will be unreliable to predict fluid responsiveness (Marik et al. 2011).

The End-Expiratory Occlusion (EEO) Test

During mechanical ventilation each insufflation increases the intrathoracic pressure and impedes venous return. Thus, interrupting the respiratory cycle at end-expiration inhibits the cyclic impediment in venous return and transiently increases cardiac preload (see Figure 1). It has been demonstrated that if a 15 second EEO increases the arterial pulse pressure or the pulse contour-derived cardiac index by more than 5%, the response of cardiac output to a 500 mL saline infusion can be predicted with good sensitivity and specificity (Monnet et al. 2009).

Beyond its simplicity, the main advantage of the EEO test is that it exerts its haemodynamic effects over several cardiac cycles and thus remains valuable in case of cardiac arrhythmias (Monnet et al. 2009). It can also be used in patients with spontaneous breathing activity, unless a too marked triggering activity interrupts the 15-second EEO.

The 'Mini' Fluid Challenge

The disadvantage of the 'classical' fluid challenge is that it consists of the infusion of 300-500 mL of fluid (Vincent et al. 2006). This may obviously contribute to fluid overload if the test is negative.

A new method of 'mini fluid challenge' has been proposed as an alternative (Muller et al. 2011). It consists of administering 100 mL of colloid over 1 minute and observing the effects of this 'mini' increase in cardiac preload on stroke volume, measured by the subaortic velocity time index using transthoracic echocardiography (Muller et al. 2011).

A strong limitation of the mini fluid challenge may be that, even in cases of preload-dependency, such a small volume infusion will unavoidably induce only small changes in cardiac output. Thus, this test requires a very precise technique for measuring cardiac output.

The Passive Leg Raising (PLR) Test

In a subject lying down, raising the legs from the horizontal position passively transfers a significant volume of blood from the lower part of the body toward the cardiac chambers. This induces a reversible increase in cardiac preload (Monnet et al. 2006). Several studies have reported that the increase in cardiac output induced by this 'endogenous' volume challenge allows prediction of fluid responsiveness with reliability (Cavallaro et al. 2010). Interestingly, since the test exerts its effects over several cardiac cycles and since it is not related to heart-lung interactions, PLR remains a good predictor of fluid responsiveness in patients with spontaneous breathing activity, cardiac arrhythmias or ARDS (Monnet et al. 2006, Monnet et al. 2009).

Importantly, PLR must be started from the strict semi-recumbent position and not from the horizontal supine position. This mobilises blood coming not only from the inferior limbs but also from the large splanchnic compartment, and substantially increases sensitivity of the PLR test (Jabot et al. 2009).

Another important point concerns the method that can be used for measuring the changes in cardiac output during PLR (Monnet et al. 2008). Firstly, these effects cannot be assessed by observing the simple arterial pressure. Indeed, the PLR-induced changes in arterial pulse pressure are less accurate than the PLR-induced changes in cardiac output or stroke volume. Secondly, the PLR test requires a real-time measurement of cardiac output allowing tracking of haemodynamic changes in the timeframe of PLR effects, ie 30-90 seconds. This can be done by aortic blood flow measured by oesophageal Doppler, pulse contour analysis-derived cardiac output, cardiac output measured by bioreactance, subaortic velocity measured by echocardiography and even end-tidal carbon dioxide (Monnet et al. 2013).

Conclusions

Several tests have been developed to detect volume responsiveness before administering fluid. The choice between them should be made depending on the clinical setting and the patient's condition. Using such tests should avoid administering fluid if it is not haemodynamically effective. This should avoid fluid overload, a condition that increases mortality of critically ill patients, particularly in cases of sepsis and/or lung impairment. ■

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AIRWAY MANAGEMENT IN ICU

3 YEARS ON FROM NAP4 - WHAT'S NEW?

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By three methods we may learn wisdom: the first by reflection, which is the noblest; the second by imitation, which is the easiest; and third by experience which is the bitterest - Confucius.

The 4th National Audit Project of the Royal College of Anaesthetists and Difficult Airway Society; major complications of airway management in the UK (NAP4) reported that the intensive care unit (ICU), rather than being a place of safety for airway management, could instead be considered a place of danger (Cook et al. 2011a). Airway-related complications were more likely to occur on ICU than in theatre, and more likely to result in patient harm: the rate of airway-related complications on ICU was more than 50 times that during anaesthesia, and 50% of patients reported to NAP4 from ICU died, compared to 14% of those reported from theatres (Cook et al. 2011a; Whitaker 2011). Whereas most airway complications during anaesthesia arose at intubation (Cook et al. 2011a), the majority of life-threatening airway events on ICU involved accidental airway dislodgement, especially of tracheostomies. Difficulties associated with rapid sequence intubation and failures of airway rescue techniques were also seen.

> *"All modern ICUs should be prepared to manage the airway complications that will occur in their unit"*

Human factors were documented in 40% of reports to NAP4 (Cook et al. 2011a), and further analysis suggests the true figure is 100% (Flin et al. 2013). NAP4 highlighted organisational (latent) failings (e.g. lack of equipment, policies, training and staffing) and individual (active) errors (e.g. lack of knowledge or structured approach, omissions, loss of situation awareness, judgement errors), both of which were more prominent in cases occurring on ICU than during anaesthesia.

This article focuses on recent developments in four areas of ICU airway care identified in NAP4:

- Tracheostomy;
- Human factors;
- Capnography;
- Videolaryngoscopy.

Tracheostomy

Prior to NAP4, much of the focus of research around tracheostomy and ICU related to novel tracheostomy techniques, reducing procedural complications and determining optimum timing. In 2013 the TracMan study, which randomised patients to tracheostomy at <4 and >10 days, reported no differences in early or late all-cause mortality, length of ICU stay or procedural complications (6.3%) (Young et al. 2013). A recent meta-analysis also reported no effect on ventilator-associated pneumonia, ICU stay or mortality (Huang et al. 2014).

Remarkably, there is little data on the prevalence of tracheostomy in modern ICU care. A Swiss survey, in 2000, reported tracheostomy in 10% of patients ventilated >24 hours and 1.3% of all ICU patients (Fischler et al. 2000), while an English estimate in 2012 suggested tracheostomy formation in 9% of all adult ICU admissions (McGrath et al. 2012b). It is likely that practices have changed dramatically since then, and also vary across and within different European countries.

NAP4 identified tracheostomy-related complications, mainly tracheostomy displacement, particularly in obese patients, as important factors in major airway complications on ICU (Harper et al. 2011a).This built on previous work by Thomas and McGrath. In 2009 they reviewed >1000 ICU airway safety incidents submitted to the UK critical incident reporting system: 1 in 10 led to longer term harm, with the vast majority occurring after the airway had been established (Thomas and McGrath 2009). In their series, infants, equipment problems and tracheostomy were over-represented. Harm due to partial airway displacement and failure to use capnography were notable. They also examined ≈500 tracheostomy-related patient safety incidents on wards (McGrath and Thomas 2010). Displacement and blockage were prominent and patient harm was common, with long term harm in 19% cases. Of note, reporting systems usually underestimate safety incidents causing patient harm by up to 20-fold (Sari et al. 2007).

The variable design of tracheostomy tubes, particularly those suitable for obese patients, was highlighted by NAP4 (Harper et al. 2011b). Encouragingly equipment manufacturers are actively seeking to engage in redesign of tra-

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Concerns about management of tracheostomies extend beyond ICU, and several important quality improvement initiatives are in development. In the UK, the National Tracheostomy Safety Project (NTSP http://www.tracheostomy.org.uk/) has published multidisciplinary guidelines for the management of tracheostomy and laryngectomy airway emergencies (McGrath et al. 2012a). These algorithms describe a universal approach to managing tracheostomy emergencies, and are designed to be followed by first responders. Whilst these are strengths, the algorithms might be more suitable for wards than for ICU as they emphasise blockage over displacement, and capnography, while mentioned, is not emphasised. In June 2014, The National Confidential Enquiry into Patient Outcome and Death (NCEPOD http://www.ncepod.org.uk/trachy.htm) will publish the results of a two-year long study of tracheostomy care on ICU and wards, aiming to identify any remediable care failings. Finally, the Global Tracheostomy Collaborative (http://globaltrach.org/) will be launched in Boston, USA and London, UK in 2014. This multidisciplinary, international, not-for-profit collaborative aims to improve patient care by sharing best practices, supporting education and adopting integrated multidisciplinary care.

> *"It is notable that no national critical care organisation has yet provided guidelines on managing airway complications on ICU"*

We should be optimistic that in the next few years these considerable efforts will lead to better understanding of risk factors for complications associated with tracheostomies and, in the words of NTSP, lead to "improvements in infrastructure, competency and training, equipment provision, and communication."

Human Factors

Organisational Preparedness

Organisational preparedness involves organisations identifying predictable problems of airway management and putting in place solutions (e.g. equipment, staffing, procedures, training) that aid recognition and management of these risks and mitigate complications. NAP4 recorded that 20% of major airway complications occur outside theatres and the commonest events are failed intubation, accidental extubation and displacement of a tracheostomy.

An example is airway assessment to reduce unanticipated difficult intubation: 10% of ICU intubations require multiple attempts (Mort 2004), and life-threatening complications such as hypoxia, hypotension and cardiac arrest occur in up to 25% of cases (Leibowitz 2006). Organisational structures that make airway assessment routine on ICU (as in anaesthetic practice) and lead to adoption of clear airway strategies (Cook et al. 2011a) might be expected to reduce unanticipated difficulty and complications.

NAP4 recommended the adoption of an intubation checklist and the immediate availability of a difficult airway trolley. Previously, a 10-point checklist (including pre-oxygenation, fluid loading, rapid sequence intubation with ketamine or etomidate, capnography, vasopressors as required, early sedation and the presence or two operators) was shown to reduce complication rates by approximately one-third (Jaber et al. 2010). Senior supervision of intubation reduced complication rates fourfold (Schmidt et al. 2008).

Currently organisational preparedness is limited. A UK survey reported that 4% of patients admitted to ICU had been admitted for management of a primary airway problem, and 6.3% were predicted to have a difficult airway (Astin et al. 2012). Fewer than 1 in 5 of patients identified as 'at increased risk' had an individualised airway management plan in place. Action plans for unanticipated airway displacement were rarely available (tracheal tube displacement plans present in 7% of ICUs, tracheostomy displacement plans in 10% of ICUs), and often those available were anaesthesia guidelines (Henderson et al. 2004). Training and staffing were issues: only a small minority could describe the equipment available for emergency transtracheal access, and one-third of ICUs reported out-of-hours cover sometimes provided by junior doctors without basic anaesthesia competencies. An Australasian survey reported similar results (Husain et al. 2012).

Of further concern, recent changes in ICU management such as ventilating in the prone position, daily sedation holds and ventilation without sedation have the potential to increase the incidence of unanticipated extubations. ICU doctors are also increasingly from non-anaesthetic backgrounds. It is notable that no national critical care organisation has yet provided guidelines on managing airway complications on ICU. Whilst many national airway societies have published recommendations for managing anaesthetic airway difficulties, it is likely that underlying pathology, limited physiological reserve and the impracticality of waking the critically ill patient mean that airway crises in ICU require different solutions. National and European ICU organisations might usefully develop guidance.

All modern ICUs should be prepared to manage the airway complications that will occur in their unit. NAP4 made it clear that airway management on ICU can be complex, with rescue techniques being more likely to fail than in anaesthetic emergencies. Predefined protocols for intubation and unanticipated airway events and individualised airway strategies for high risk patients will facilitate planning and communication, and enable the appropriate equipment and staffing resources to be prepared. Training and audit should be in place. All form part of organisational preparedness.

Individual Preparedness

A high proportion of the events reported to NAP4 occurred out of hours, when ICUs are more likely to be staffed by fewer and less experienced doctors (Leibowitz 2006), who may not have anaesthetic training (Astin et al. 2012; Husain et al. 2012).

NAP4 recommended that airway experts should be rapidly available for ICU doctors without advanced airway skills: the surveys cited above provide little reassurance.

Teaching Anaesthetic Non-Technical Skills (ANTS) has gained increasing prominence throughout anaesthetic and ICU practice (Flin and Patey 2011). It describes understanding the cognitive, interpersonal and social attributes of an individual to improve overall performance, reduce human error and enhance patient safety. ANTS comprises four key skill categories: situation awareness, decision-making, task management, and team working/leadership (Flin et al. 2008). NAP4 and other studies have directly linked a lack of these skills, especially situation awareness, to the contributing factors underlying critical airway incidents in ICU (Flin et al. 2013). Intubation checklists and pre-prepared airway strategies have been proposed to improve situational awareness during airway interventions on the ICU (Cook et al. 2011b, Gaba et al. 1995; Hales and Pronovost 2006).

In our experience junior staff can be trained in a relatively short period to provide a basic level of airway competency. Closely monitored airway experience in elective anaesthetic cases, workplace-based simulation training and formal induction courses provide suitable learning opportunities (Bristol Medical Simulation Centre). The resources required are minimal. Low fidelity scenarios have been shown to rapidly improve the ability of inexperienced doctors to perform basic medical interventions (Grober et al. 2004). Airway competency should not be assumed, and airway strategies should recognise available skills (Mulcaster et al. 2003): more than 50 intubations are required to achieve >90% success rate, with I in 5 trainees still requiring assistance after 80 supervised intubations (Konrad et al. 1998). Emphasising simpler airway management techniques (e.g. i-gel® (Intersurgical®, Wokingham, UK) (Wharton et al. 2008) or Supreme LMA™ (Teleflex Medical, San Diego, CA, USA) insertion (Howes et al. 2010) and use of limited airway rescue algorithms (Kelly et al. 2013)) offers leaner solutions. Some suggest that a competency-based assessment should be undertaken by all new ICU staff (Association of Anaesthetists of Great Britain & Ireland).

Those working on modern ICUs should:

- know their own airway skillset and limitations;
- know when and how to call for assistance;
- have knowledge of local equipment, standard operating procedures (SOPs) and, algorithms;
- engage in audit and training.

All form part of individual preparedness.

Capnography

NAP4 reported that failure to use capnography contributed to >80% of airway-related deaths on ICU. The report recommended the use of continuous capnography for patients dependent on an artificial airway, and described this as the single change most likely to reduce complications and deaths (Cook et al. 2011b; Fischler et al. 2000). This recommendation was rapidly endorsed by national and European organisations (Association of Anaesthetists of Great Britain & Ireland; Thomas et al. 2012; European Board of Anaesthesiology 2011).

In 2003 a UK survey of capnography in adult ICUs focused on its use for confirming tracheal tube placement (Kannan and Manji 2003). One-quarter of units did not have a capnograph, and only one-fifth had one per bed. Capnography was used at intubation in only half of units which possessed one and routinely by only 1 in 4 units. Remarkably, half of respondents did not think that capnography should be mandatory for intubations outside the operating theatre. In 2010 Georgiou reported modest improvements: 25% ICUs used capnography for continuous monitoring during controlled ventilation, but 40% never used it (Georgiou et al. 2010). In paediatric practice capnography was used for all intubations in only 11% of ICUs (Cumming and McFadzean 2005). There is little published data on use of capnography in neonatal ICUs. However, fatal avoidable airway errors do occur in such settings (Higgins 2013).

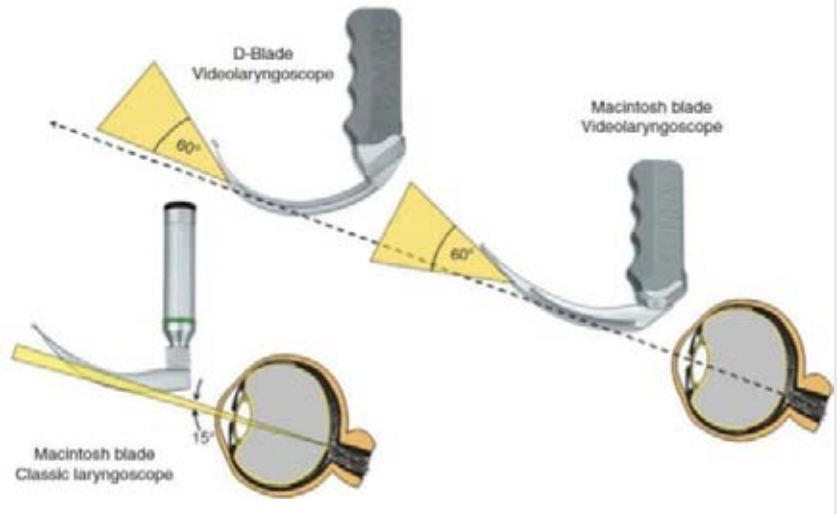
Surveys published after NAP4, but conducted before its final report, suggest further progress has been made. In 2012 a UK survey reported that 56% routinely used continuous waveform capnography for patients with artificial airways (Astin et al. 2012), and Husain from Australasia reported that capnography was used during tracheal intubation in 88% of ICUs and for continuous monitoring in 64% (Husain et al. 2012).

Capnography should be considered not only as a tool to confirm intubation, but (perhaps even more importantly) also as an airway and respiratory monitor. There is evidence that continuous capnography throughout a period of ventilatory support on adult ICU is becoming routine care in the UK (TM Cook, Unpublished data). Less is known about non-adult practice.

It is likely that the role of capnography in ICU can be developed further still. Opportunities for development and research include:

(i) making its use mandatory for patients dependent on an artificial airway;
(ii) ensuring that changes in adult practice reach paediatric and neonatal ICUs;
(iii) extending its use during non-invasive ventilation and sedation (Manifold et al. 2013);
(iv) exploring the diagnostic roles of qualitative and quantitative capnography trace analysis (e.g. assessing volume responsiveness (Young et al. 2013), lung recruitment manoeuvres (Tusman et al. 2014), monitoring bronchospasm (Yaron et al. 1996));
(v) exploring technical and non-technical methods to improve reliability of use of capnography (Hodges et al. 2012).

Figure 1. The effect of videolaryngoscopy with a Macintosh type and more angulated blade on the view and angle subtended during laryngoscopy.



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Videolaryngoscopy in ICU

The second commonest primary event leading to reports to NAP4 from ICU was failed intubation. Use of carefully selected videolaryngoscopy (VL) offers the potential to reduce intubation difficulty in general (Behringer and Kristensen 2011), including on ICU.

Videolaryngoscopes can be divided into three main groups (Niforopoulou et al. 2010):

1. **Macintosh-blade shaped videolaryngoscopes** (e.g. C-MAC (Karl Storz, Tuttligen, Germany), McGrath MAC (Aircraft Medical, Edinburgh, UK), AP Venner with Macblade (Venner Medical, Dänischenhagen, Germany)) can be used for conventional direct laryngoscopy (DL) or for indirect VL. The distally placed camera enables the operator to 'see around the corner' and to achieve a wider angle of view than with DL (see Figure 1).
2. **Angulated videolaryngoscopes** (e.g. Glidescope (Verathon, Bothell, WA, USA), McGrath 5 (Aircraft Medical, Edinburgh, UK), CMAC D blade ((Karl Storz, Tuttligen, Germany), AP Venner scope with 'standard blade' (Venner Medical, Dänischenhagen, Germany)) have more angulated blades than a standard Macintosh and only provide an indirect VL view of the larynx. They require the use of a stylet or a bougie.
3. **Channelled videolaryngoscopes** (e.g. Airtraq (Prodol Meditec, Vizcaya, Spain), Pentax-Airway Scope (Pentax Medical, Hamburg, Germany), AP Venner with difficult airway blade ((Venner Medical, Dänischenhagen, Germany)) have angulated blades and a guiding channel that directs the tracheal tube towards the glottic opening.

Use of VL improves the view at laryngoscopy (Behringer and Kristensen 2011), but the ad-

vantages of VL on ICU also include effects on teamwork, communication and situation awareness as much as on technical skills (Kelly and Cook 2014). Use of VL aids training of junior doctors (a supervising doctor can share the intubating doctor's view of the larynx on the screen, give advice to assist intubation and usually enable the junior doctor to complete the intubation themselves), training of ICU nurses (enabling nurses to monitor the effect of cricoid pressure and adjust it as needed), improves management of the unanticipated difficult airway because a videolaryngoscope is immediately to hand, and improves team working and situation awareness as the screen enables all staff involved to see what is happening and anticipate the next steps (Kelly and Cook 2014).

An important advantage of VL based on a Macintosh blade is that it uses the same skills as DL, thereby reducing the need for dedicated VL training. We have a dedicated C-MAC™ videolaryngoscope (Karl Storz, Culver City CA) on our ICU, and teach our trainees to use this as they would a standard MacIntosh blade. Initially the trainee is not allowed to see the VL screen (although the trainer watches this), but it is available if difficulty is encountered. In addition the intubation can be recorded for teaching after the event. A D-blade is immediately available when intubation is awkward or difficult. VL has become routine practice for all intubations on our ICU.

The overall impact of VL in the anaesthetic literature is confused due to marked heterogeneity in patient population, device studied, operator experience and confusion when manikin studies are included (Mihai et al. 2008). Whilst VL improves the ease of obtaining a view of the larynx, inserting a tracheal tube can be more difficult. Use of VLs on ICU is difficult to study for similar reasons, but is increasing in popularity (Mosier et al. 2013; De Jon et al. 2013; Lakticova et al. 2013). There is a need for randomised controlled trials (RCTs) of VL vs DL on ICU (Larsson and Dhonneur 2013): these need to be performed before VL use on ICU is so widespread that such a study is impractical. RCTs would help determine which devices are of greatest utility, and could study the impact of VL on both technical and human factors (Kelly and Cook 2014).

Conclusions

NAP4 showed that ICU can be a place of airway danger and that the quality of airway care falls short more often than in anaesthetic practice. This results in avoidable harm to patients. It is important the ICU community acknowledges this gap in quality of care and continues to work towards closing it. Understanding our patients' needs, understanding the limitations of our technical and non-technical skills, using appropriate monitoring of the airway throughout the patient's ICU stay and evaluating and embracing appropriate new technology will go a long way to closing this gap. ■

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UPPER GASTROINTESTINAL BLEEDING

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Intensivists are regularly confronted with the question of upper gastrointestinal bleeding, the mortality of which remains high, but should be reduced through recent diagnostic and therapeutic advances.

Introduction

Upper gastrointestinal bleeding (UGIB) is defined as a recent and sudden onset of haemorrhage originating from the oropharynx to the ligament of Treitz. In clinical practice, identification of lower versus UGIB can be difficult. UGIB usually presents as fresh blood or coffee ground haematemesis and/or melaena, but haematochezia may be the presenting sign in patients with massive bleeding. In a few cases, the haemorrhage is not overt and symptoms consist of a more or less severe anaemic syndrome. UGIB is usually divided into portal hypertension-related and unrelated causes. Peptic ulcer disease is the most common cause. UGIB is associated with a wide variety of severities, but remains a severe condition. Its mortality has probably not changed for 20 years, but could be reduced through recent diagnostic and therapeutic advances.

> *"Its mortality has probably not changed for 20 years, but could be reduced through recent diagnostic and therapeutic advances"*

Management Before Endoscopic Diagnosis

Delay Before Endoscopy

For overt or suspected UGIB, an oesophagogastroduodenoscopy (OGD) should always be performed (Barkun et al. 2010; Osman et al. 2013; de Franchis 2010). Its performance within 24 hours after admission was shown to be associated with a reduction in transfusion, second endoscopy and surgery requirement (Barkun et al.2010). When variceal bleeding is suspected, OGD is recommended in the first 12 hours (de Franchis 2010; Garcia-Tsao et al. 2010).

Earlier OGD (within 6 to 12 hours) is a matter of debate. A meta-analysis of three randomised trials showed no benefit of early endoscopy (Barkun et al. 2010). However, when active bleeding is suspected, early endoscopy may prove valuable and is usually recommended (Osman et al. 2013). One study identified fresh blood in gastric aspirates, haemodynamic instability and haemoglobin concentrate (Hb) <8 g/dL as predictors of the benefits of early OGD (Adamopoulos et al. 2003). A recent study demonstrated that in patients with a Glasgow-Blatchford score ≥ 12 the mortality rate was lower when OGD was performed within the first 13 hours (Lim et al. 2011). Pending endoscopy, appropriate management includes risk stratification (Srygley et al. 2012), pharmacological therapy and in some cases abdominal CT angiography.

Risk Stratification

Several scoring systems have been described. The Rockall score was found to be a good indicator of the risk of rebleeding (Rockall et al. 1996), but it comprises only endoscopic data, and may therefore be of limited utility in the acute setting. The Glasgow-Blatchford score (see Table 1) includes clinical and biochemical data, and has proven useful in predicting the need for hospitalisation, transfusion, surgery or death (Blatchford et al. 2000). It is commonly used to identify patients at high risk and refer them to an intensive care unit (Barkun et al. 2010; Osman et al. 2013). An easily calculated risk score (AIMS65) has been developed to predict mortality, but needs further validation (Saltzman et al. 2011). The role of nasogastric tube and aspirate inspection for risk assessment is debated. Presence of red blood in aspirates suggests undeniably active bleeding and should prompt urgent OGD, but it should be remembered that absence of blood cannot rule out severe UGIB (Palamidessi et al. 2010).

Pharmacological Therapy

Ulcer is the main cause of UGIB, and early administration of acid suppressive therapy is probably always reasonable (Osman et al. 2013). Pump proton inhibitors (PPIs) offer sustained and durable acid suppression. High dose of intravenous PPIs has become the dominant therapy for bleeding ulcers. A meta-analysis demonstrated that 'stan-

dard' doses of PPIs (in comparison with no treatment, placebo or H2-receptor antagonists) facilitated OGD by reducing the proportion of patients with active bleeding and the need for endoscopic haemostasis (Sreedharan et al. 2010). Another study established that administration of 'high' PPIs doses reduced transfusion requirement and rebleeding (Lau et al. 2007). This issue has not been examined by comparing 'high' and 'standard' doses. Once portal hypertension is suspected, a vasopressor agent active on the splanchnic circulation (terlipressin, somatostatin, somatostatin derivative) should be combined with PPis (Osman et al. 2013). By reducing portal hypertension, vasopressor agents stop variceal bleeding in 80% of cases (Garcia-Tsao et al. 2010), improve the quality of transport, and facilitate endoscopy (de Franchis 2010). To ensure emptying of gastric content, a prokinetic drug (erythromycin or metoclopramide) should be administered before OGD. A recent meta-analysis showed that the use of a prokinetic drug reduced the need for a second OGD (Barkun et al. 2010). If a nasogastric tube has been placed, gastric lavage is an effective alternative (Pateron et al. 2011).

Table 1. Glasgow-Blatchford Score

Admission Risk Marker		Score
Blood urea (mmol/L)	≥ 6.5 and < 8	2
	≥ 8 and < 10	3
	≥ 10 and < 25	4
	≥ 25	6
Haemoglobin (g/L) for men	≥ 120 and < 130	1
	≥ 100 and < 120	3
	< 10	6
Haemoglobin (g/L) for women	≥ 100 and < 120	1
	< 10	6
Systolic blood pressure (mmHg)	≥100 and < 109	1
	≥ 90 and < 100	2
	< 90	3
Other markers	Pulse ≥ 100	1
	Melaena	1
	Syncope	2
	Hepatic disease	2
	Cardiac failure	2

A total score more than 8 carries high risk justifying ICU admission

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Table 2. Prevalence and Outcomes of Bleeding Ulcers According to the Forrest Classification

	Class	Prevalence	Further bleeding
Clean base	III	42%	5%
Flat spot	IIc	20%	10%
Adherent clot	IIb	17%	22%
Non bleeding visible vessel	IIa	17%	43%
Active bleeding (oozing)	Ib	18%	55%
Active bleeding (spurting)	Ia		

Adapted from Laine L, Peterson WL (1994) Bleeding peptic ulcer. N Engl J Med, 331(11): 717-27.

Role of CT Angiography

Several studies have demonstrated the great value of abdominal CT angiography for topographic and aetiological diagnosis of UGIB (Duchat et al. 2010) and for guiding therapeutic decisions (Lim et al. 2011). Abdominal CT angiography should probably be performed in an emergency, when OGD cannot be done within the recommended timeframe, or in the rare cases where an aortoenteric fistula is suspected (Burks et al. 2001).

Management After Endoscopic Diagnosis of Ulcer Bleeding

Management of ulcer bleeding is well established, combining in most cases endoscopic and pharmacological therapies.

Endoscopic Therapy

The Forrest classification (see Table 2) is used to categorise the appearance of bleeding ulcers and to determine the type of endoscopic treatment needed. The natural history of ulcer disease shows a rebleeding rate < 5% in the presence of a Forrest type IIc or III lesion (Gralnek et al. 2008). Endoscopic haemostasis should not be used in such cases (Barkun et al. 2010; Osman et al. 2013). Two meta-analyses confirmed the value of endoscopic therapy compared with PPIs alone in a high-risk population (Forrest Ia, Ib, IIa), by demonstrating a significant decrease in rebleeding (Barkun et al. 2009) and mortality (Leontiadis et al. 2006). It is now demonstrated that endoscopic treatment must include epinephrine injections and clips or thermal treatment, and not epinephrine alone (Laine et al. 2009). In Forrest type IIb lesions (adherent clot), endoscopic haemostasis is recommended when it seems possible, ie when the clot is small (Osman et al. 2013). A meta-analysis suggested that adherent clot should be removed in order to perform endoscopic treatment of the underlying artery lesion (Kahi et al. 2005).

Pharmacological Therapy

In lesions at low risk of rebleeding, PPIs are recommended to be used at 'standard' doses. When a high risk is found (Ia to IIb), PPIs are usually recommended to be continued at 'high' doses for 72 hours (Barkun et al. 2010; Osman et al. 2013) even though in most studies 'high' doses were only compared to placebo (Lau et al. 2000; Leontiadis et al. 2007; Sung et al. 2009; Wang et al. 2010). The issue of *Helicobacter pylori* infection can rarely be resolved in the acute phase of UGIB, and there is probably no advantage in treating this infection on an emergency basis. If biopsy screening can be performed during the first OGD, without worsening bleeding, it is important to know that the sensitivity of rapid urease tests is lower in this setting (Tang et al. 2009). Although a meta-analysis clearly established that eradication of *Helicobacter pylori* reduced the long-term risk of recurrent bleeding, in comparison with antisecretory therapy alone (Gisbert et al. 2004), it has not been shown that eradication therapy was useful in case of early rebleeding.

Management After Endoscopic Diagnosis of Variceal Bleeding

Management of variceal bleeding includes in most cases endoscopic and pharmacological therapies.

Endoscopic Therapy

Endoscopic haemostasis of bleeding oesophageal varices is based on band ligation rather than sclerosis (Gross et al. 2001). Obturation using cyanoacrylate glue is the reference treatment for bleeding gastric varices (Lo et al. 2001).

Pharmacological Therapy

Combined treatment using vasoactive agents and endoscopic therapy has proven to be more effective than OGD alone in controlling bleeding (Sung et al. 1995; Avgerinos et al. 1997), and in survival without rebleeding (Besson et al. 1995; Cales et al. 2001). It is therefore recommended to continue vasoactive treatment using terlipressin or somatostatin or a somatostatin derivative for a period of three to five days after endoscopic therapy (de Franchis 2010; Osman et al. 2013). Early introduction of beta-blockers avoids rebound portal hypertension. A meta-analysis showed that combined treatment (ligation and beta-blocker introduced within a period of three days) significantly reduced rebleeding in comparison with endoscopic therapy or pharmacological therapy alone (Gonzalez et al. 2008).

Bacterial infections are observed in about 40% of cirrhotic patients in the seven days following their admission for UGIB (Bernard et al. 1995), and are independently associated with rebleeding and mortality (Goulis et al. 1998). A meta-analysis established that antibiotic prophylaxis significantly reduced mortality (Bernard et al. 1999). Third-generation cephalosporin or fluoroquinolone for five to seven days is generally recommended to be given to any cirrhotic patient with UGIB (de Franchis 2010; Osman et al. 2013).

Challenges and Perspectives

Persistent and Recurrent bleeding

Treatment failure for UGIB covers two different aspects: persistent bleeding after haemostasis attempts and recurrence after primary success. From all causes, persistent bleeding occurs in approximately 10% of patients. The problem is particularly striking in Forrest Ia and Ib ulcer bleeding, where percutaneous arterial embolisation was demonstrated to be effective and is now recommended as a first-intention treatment (Osman et al. 2013). An analysis of 35 studies demonstrated that technical and clinical success rates of embolisation ranged from about 50% to 100% (Mirsadraee et al. 2011). Comparisons between surgery and embolisation showed equivalent results, although embolisation was applied to an older population. Interestingly, it has been shown that endoscopic marking with a metallic clip prior to embolisation enhanced the possibility of embolising the correct vessel (Eriksson et al. 2006). In variceal bleeding two studies demonstrated that early placement of a transjugular intrahepatic portosystemic shunt (TIPS) reduces the risk of persistent bleeding and rebleeding (Monescillo et al. 2004; Garcia Pagan et al. 2010). Improvement of survival following TIPS was also demonstrated in high-risk patients, defined as Child-Pugh class B patients with persistent bleeding at the time of OGD or Child-Pugh class C patients (Garcia Pagan et al. 2010). After endoscopic haemostasis of variceal bleeding, TIPS placement within 72 hours should therefore be considered in such patients (Osman et al. 2013).

In case of recurrent bleeding, whatever the cause, a second endoscopic attempt should first be proposed. Another approach is performing a second-look OGD in order to pre-empt recurrent bleeding. Second-look OGD is defined as an endoscopy scheduled for 16 to 24 hours after the initial OGD. A meta-analysis demonstrated in bleeding ulcer that second-look OGD with thermal coagulation reduced recurrent bleeding (without impact on the need for surgery, or mortality), but that second-look OGD with adrenaline injection had no beneficial effect (Tsoi et al. 2010). Another meta-analysis suggested that in ulcer bleeding, second-look endoscopy reduced the risk of rebleeding and surgery, but not mortality (Barkun et al. 2010). Therefore, recent guidelines proposed performing a second-look OGD in ulcer bleeding when high-risk stigmata have been observed (Osman et al. 2013). Evaluation of the clinical impact of a strategy involving pre-emptive embolisation after initial endoscopic control of ulcer bleeding is ongoing.

Management of Antithrombotic Therapy

Management of antiplatelet therapy in patients with UGIB is a clinical challenge. The decision to withhold or continue treatment should be discussed as soon as possible in a multidisciplinary setting. In ischaemic heart disease this issue is quite well codified. A meta-analysis demonstrated that discontinuing or not adhering to aspirin was associated with a three-fold higher risk of major cardiac events (Biondi-Zoccai et al. 2006). A randomised study in 156 patients with aspirin-induced ulcer bleeding receiving endoscopic therapy and PPIs showed that immediate re-introduction of aspirin was associated with a non-significant increased risk of rebleeding, while discontinuation of aspirin was associated with a significant increase in eight weeks' mortality (Sung et al. 2010). Consequently, in patients treated with antiplatelet therapy for ischaemic heart disease with UGIB, it is usually recommended to maintain aspirin (Osman et al. 2013). In dual antiplatelet therapy, clopidogrel is usually stopped until consultation with specialists. The new generation of oral anticoagulants (nOAC) might be associated with higher UGIB risk, especially in patients with altered renal function. It is important to note that no established antidote is available in cases of nOAC that complicate serious bleeding. Prothrombin complex concentrates and recombinant factor VIIa may improve haemostasis in patients in whom bleeding develops during treatment with a nOAC, but their efficacy is unproven.

Transfusion Management

The issue of transfusion strategy in UGIB is still poorly codified. Most guidelines recommend a policy of restricted blood transfusion (Barkun et al. 2010, de Franchis 2010, Osman et al. 2013). Transfusion management is particularly complex in cirrhotic patients, in whom increase in plasma volume seems to be linearly related to increase in portal pressure

(Castaneda et al. 2000), encouraging particular prudence during the resuscitation of such patients. A recent trial demonstrated that UGIB patients randomised to receive transfusion to an Hb of 9 g/dl had a significantly higher rebleeding rate and mortality, in comparison with patients allocated to receive transfusion with the objective of 7g/dl (Villanueva et al). The difference in survival was mainly observed in cirrhotic Child–Pugh class A or B patients. Platelet transfusion in severe bleeding is usually recommended when platelet count is < 50,000/mm3 (Rossaint et al. 2010; Souweine et al. 2010). No study has examined this question in the particular setting of UGIB in cirrhotic patients, where the risk of worsening portal hypertension has also been raised (Colle et al. 2011). Moreover, thrombocytopaenia is common during cirrhosis and is a poor indicator of haemorrhagic risk (de Franchis 2010). On the basis of these arguments, in cirrhotic patients, platelet transfusion is usually recommended for a platelet count < 30,000/mm3 and should not delay endoscopy.

In haemorrhagic shock due to trauma early treatment with fresh frozen plasma is recommended in massive bleeding (Rossaint R, Crit Care 2010). Again, and for the same reasons, it is much debated in cirrhotic patients (de Franchis 2010, Colle et al. 2011). Moreover, it is important to note that neither prothrombin time (PT), nor international normalised ratio (INR) are good indicators for coagulability in patients with cirrhosis. Administration of fresh frozen plasma, with the objective of correcting a coagulopathy, is therefore not recommended in cirrhotic patients with UGIB (Osman et al. 2013).

Conclusion

The management of patients with UGIB has significantly evolved throughout the past decade, and requires a multidisciplinary approach integrating pharmacological, endoscopic, and radiological options. Surgical treatment has become extremely rare. Future research is nevertheless needed to improve outcome in patients at high risk of rebleeding and to resolve current areas of uncertainty regarding transfusion and antithrombotic therapy management. ■

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METABOLIC AND NUTRITIONAL ISSUES IN THE ICU

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Background

Nutritional interventions in ICU patients are intended to influence outcome. However, there are often difficulties in interpreting outcome data, as selection of patients may not allow the results to be generally applied. There are no known mechanisms linking nutrition directly to outcome, and therefore designing outcome studies without completely understanding the possible relation between intervention and outcome is not easy. Feeding critically ill patients has repeatedly been questioned, primarily in the acute and often unstable phase, sometimes called the ebb phase. Hypothetically, preservation of body proteins, or perhaps better attenuation of the decrease in body proteins, may be the immediate target of a nutritional intervention. Consequently, assessment of body proteins may be used as a substitute marker for outcome. Here we discuss possibilities for this type of assessment with different techniques.

> *"A direct link between changes in biochemistry and in ultrasound imaging in individual subjects has not yet been presented, but such study protocols should be encouraged"*

Nutrition Studies

Several recently published clinical trials evaluating the effect of nutrition in critical illness are subject to conflicting interpretations (Casaer et al. 2011; Doig et al. 2013; Heidegger et al. 2013; National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network et al. 2012). To some extent the difficulty of defining patients at nutritional risk is the problem. Should all critically ill patients be given nutrition support? And at what time point? As mentioned there are a number of unknown steps from a nutritional intervention to mortality outcomes. Not surprisingly there are no prospective randomised studies in unselected ICU patients demonstrating survival advantages in relation to nutrition.

What should then be the target for nutritional intervention in ICU patients? Obviously long-term starvation leads to death, but what is optimal nutrition in critical illness? Will optimal nutrition be constant over time or may there also be a temporal component in optimal nutrition? At least one aspect of the efficacy of nutrition support is to save body proteins, and the key question becomes how to estimate body protein mass. Which techniques are applicable in everyday clinical practice with sufficient accuracy? Imaging may give information regarding tissue volume, while biochemical analyses may give information about possible mechanisms. Several different techniques together with measures of function need to be considered. When preservation of body proteins in the critically ill can be documented, prospective outcome studies should be performed to evaluate whether or not preservation of body proteins is a suitable proxy for core outcomes such as mortality and morbidity.

Muscle as an Index of Nutritional Status

The degree of muscle depletion relates to mortality and to post ICU quality of life. The loss of muscle proteins can be quantified (see Figure 1), but muscle biopsies are not possible in everyday clinical practice (Gamrin et al. 1997; Gamrin et al. 1996; Larsson et al. 2000). Therefore imaging is very attractive, in particular if imaging devises can be used bedside.

Ultrasound may be used to monitor sarcopenia in critically ill patients over time (Reid et al. 2004). It has also been possible to link the extent of the shrinkage of muscle cross section area to the severity of illness (Puthucheary et al. 2013). The technique is cheap and readily available, and it reflects the muscle loss objectively. A strict protocol for these measurements is needed to achieve reproducible results. The risk of large investigator-related variability is obvious. A direct link between changes in biochemistry and in ultrasound imaging in individual subjects has not yet been presented, but such study protocols should be encouraged.

When abdominal CT scans have been performed for other purposes, several investigators have utilised the images to diagnose sarcopenia and its progress over time (Baracos et al. 2010; Mourtzakis et al. 2008; Braunschweig et al. 2013; Moisey et al. 2013). Such imaging may also

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Figure 1. The Loss of Leg Muscle Mass in Critically Ill Patients During the Initial 2 Weeks of ICU Stay

This is reflected by (A) the protein content of the muscle (Gamrin et al. 1997), (B) muscle thickness as reflected by ultrasound examination (Reid et al. 2004), and (C) muscle volume as measured by CT scanning (Casaer et al. 2013). The patients represented by the three studies may not be immediately comparable, but the agreement of measures give a strong signal, and studies employing non-invasive techniques should be encouraged to aid decisions on optimal feeding.

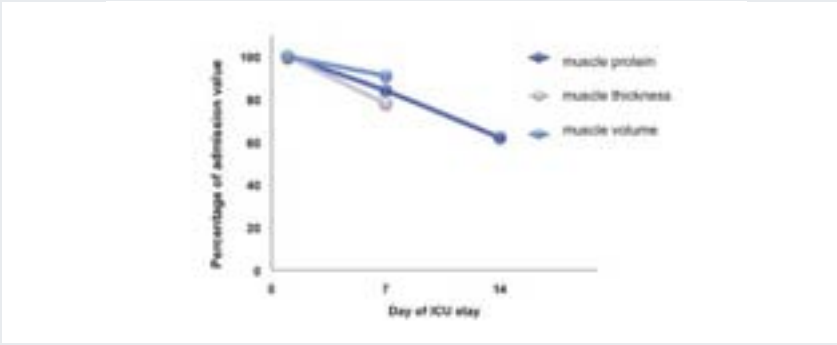
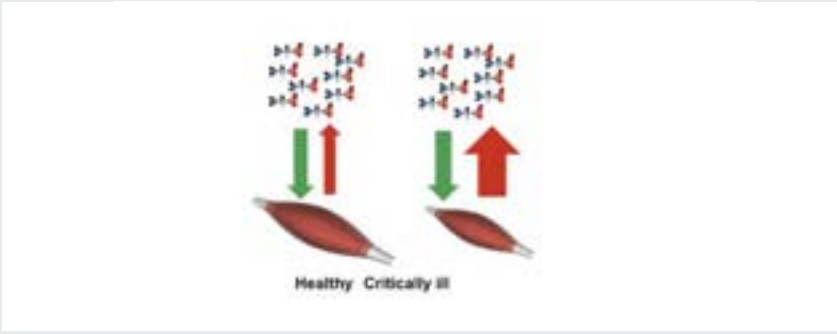


Figure 2. Muscle Protein Turnover in Healthy Volunteers and in Critically Ill Patients.

As reflected in the size of the arrows there is a similar muscle protein synthesis rate, but a different protein degradation rate, resulting in a different protein balance (Klaude et al. 2012). The figure illustrates the underlying mechanism behind the rapid development of sarcopenia in critical illness.



have a prognostic value (Weijs et al. 2014; Casaer et al. 2013). For the time being CT scanners are located outside the ICU, which limits accessibility and possibly imposes risks. However, the high resolution of modern CT scanners makes it a very promising tool. The literature contains reports of both leg muscle and abdominal muscle. A different time course of depletion may be at hand (Casaer et al. 2013). The investigator neutrality is attractive. More reports are warmly welcome, to elucidate the full potential of this technique.

The full value of imaging will become obvious when the image is directly linked to the results of biochemical alterations in the tissue, such as protein turnover, gene expression, and tissue signalling (Fredricksson et al. 2008; Klaude et al. 2012). In critically ill patients sarcopenia is driven by skeletal muscle degradation (Klaude et al. 2012; Klaude et al. 2005; Klaude et al. 2007), while protein synthesis rate in skeletal muscle is unaltered in most cases during critical illness and the development of sarcopenia (see Figure 2). This example also nicely illustrates the need to understand underlying mechanisms to direct intervention studies correctly. In this case, finding nutritional interventions to inhibit muscle breakdown will most likely have a better effect.

The development of sarcopenia and the temporal development of muscle depletion is attributable to many other factors beside nutrition, and the extrapolation of muscle mass to assess outcome risk and possibly be an indicator of a favourable response to nutrition must be viewed as hypothetical. The link between metabolic care and nutrition of the critically ill patients is challenging, and to monitor this by muscle mass seems very attractive.

Muscle Mass and Muscle Function

Muscle volume and muscle function are not closely correlated, and post ICU muscle function studies are sometimes difficult to interpret. Usually patient recruitment is quite selective and limited to patients able and motivated to participate in training activities (Poulsen et al. 2011). Nevertheless muscle mass may be a proxy for more than locomotor function in evaluations of post ICU quality of life, which usually rely upon questionnaires (Herridge et al. 2011; Griffiths et al. 2013). The possibility of an objective measurement is always attractive, but the relevance in post ICU care is still totally open. Sarcopenia during ICU stay is possibly a reflection of malnutrition, and a relation to mortality outcome has been reported (Weijs et al. 2014).

Conclusion

Nutrition and metabolic care of the critically ill should be targeted, and there is reasonable evidence linking preservation of body proteins to a favourable outcome. More mechanistic studies are needed to make this evidence stronger. If the connection between preservation of body proteins and favourable outcomes can be proven, then monitoring of body proteins becomes an important factor in guiding nutrition support. Here imaging of body proteins may be helpful. The possible link between nutrition and the preservation of body proteins may then be helpful when designing clinical trials to evaluate the effect of nutrition. It may help us to select the adequate patients and the optimal treatment in composition and in timing. ■

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DIAPHRAGMATIC ULTRASONOGRAPHY

AN UNDERUTILISED TOOL TO ASSESS ICU PATIENTS WITH RESPIRATORY FAILURE AND/OR DIFFICULTY WEANING

Point-of-care ultrasonography allows intensivists to non-invasively assess diaphragmatic function. We review here the key concepts and technical aspects needed to assess diaphragmatic dysfunction in the ICU and allow intensivists with prior ultrasound training to answer clinical questions related to the diaphragm. We anticipate that this and other novel applications of point-of-care ultrasound will continue to grow in the years to come.

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Introduction

Point-of-care ultrasonography (POCU) has changed the practice of emergency and critical care medicine. Until recently the emphasis has mainly been on using POCU to assist with percutaneous procedures and/or with the diagnosis and management of life-threatening conditions such as trauma, shock, pulmonary oedema or pneumothorax. More recently, new but not widely embraced ICU applications for POCU have emerged, which can better address important ICU clinical questions such as lung recruitability or diaphragmatic function.

Diaphragmatic dysfunction may lead to the need for mechanical ventilation, contribute to failure to wean from it or, as recently demonstrated, be the consequence of the ventilator strategy/mode applied (Powers et al. 2013). Bedside assessment of diaphragmatic function by physical exam is insensitive, while measurement of negative inspiratory pressure is effort-dependent. Alternative methods based on phrenic nerve stimulation, diaphragmatic electromyography or transdiaphragmatic pressure measurements are not widely available outside the research arena. The limited ability to identify diaphragmatic dysfunction in the ICU has likely caused underestimation of its contribution to the morbidity of ventilated patients. POCU now allows ultrasound-trained intensivists to elegantly and non-invasively assess the diaphragm by measuring active diaphragmatic excursion and inspiratory thickening.

Technical Aspects of POCU of the Diaphragm

An ultrasound unit with an M-mode option is needed, also ideally with an anatomic M-mode that allows the operator to steer the scan line to any angle rather than having the line in a strict vertical position. The recommended probe to image diaphragmatic excursion should have a low frequency range (3 to 7 MHz) and the transducer should be either a curvilinear or phase array probe. To measure diaphragmatic thickness, a high frequency (7 to 18 MHz) linear or microconvex probe is preferred. Posture is an important determinant of the breathing pattern: diaphragmatic breathing and excursion is more pronounced in the supine position and is best assessed supine. Normal reference values also differ depending on the position.

> *"The limited ability to identify diaphragmatic dysfunction in the ICU has likely caused underestimation of its contribution to the morbidity of ventilated patients"*

Measurement of Diaphragmatic Excursion

Prior to making any measurements, one needs to remove the patient from any positive pressure ventilation, providing it is safe to do so.

The right hemidiaphragm is best imaged through the hepatic window with a low frequency probe. It appears on ultrasound as an easy-to-recognise hyperechogenic (white) line that separates the liver from the lung (see Figure 1A). The left hemidiaphragm is slightly more challenging to visualise given that the splenic window is smaller and more difficult to find than the hepatic window. Two common approaches can

be used: anterior subcostal or lateral mid-axillary intercostal. In the anterior approach, the probe is aimed in a dorsal, medial and cephalad direction so that the beam reaches the posterior third of the diaphragm at a perpendicular angle (Boussuges et al. 2009). The beam direction is then adjusted to measure the maximal excursion of the hemidiaphragm. The lateral mid-axillary intercostal approach is often used to assess for pleural effusions and consists of a lateral and longitudinal cut of the hemidiaphragm. Given that the beam is not perpendicular to the diaphragm, the anatomic M-mode is required to adjust the angle accordingly (see Figure 1). The anterior approach is easy on the right side but not always feasible on the left one, due to the interposition of air in the stomach or bowel. Failure to get appropriate images on the left side is around 25% (Scott et al. 2006). For this reason we prefer the lateral approach. If the anatomic M-mode is not available, one can still measure diaphragmatic excursion from still images obtained at the peak of inspiration and expiration. On the first frames at end-expiration and at end-inspiration, a caliper is placed on the leading edge of the diaphragmatic line. The distance separating those two marks corresponds to diaphragmatic excursion.

The spontaneously breathing patient is assessed in the supine position to detect striking differences in excursion of the two hemidiaphragms. A cephalad movement during inspiration (paradoxical movement) is consistent with paralysis of one hemidiaphragm or diaphragmatic paralysis if the paradoxical movement is seen on both sides. If no significant asymmetry between the excursions of the two hemidiaphragms is identified, the greatest measured excursion of either hemidiaphragm is recorded for assessing global diaphragmatic function. Boussuges demonstrated that M-mode measurements are reproducible for assessing hemidiaphragmatic movement (Boussuges et al. 2009).

Diaphragmatic Thickening Measurement

A high frequency probe is placed on the mid-axillary line at the level of the costophrenic angle. The point of junction between the diaphragm and the chest wall is then identified to measure diaphragmatic thickening. The diaphragmatic muscle is easily identified underneath the intercostal muscles with its characteristic three-layer appearance (a central relatively thick hypoechogenic layer surrounded by two hyperechogenic fine lines corresponding to parietal pleura and peritoneum above and below the diaphragm, respectively) (see Figure 2A). The diaphragmatic muscle is thicker in its lower than its upper portions, and thickening should be measured at the point of maximum thickness using the M-mode (see Figure 2B). Although the measured dimensions are small, the values obtained appear to be reliable and reproducible (Baldwin et al. 2011).

Interpretation and Normal Values

Normal values for diaphragmatic excursion vary in the general population (Gerscovich et al. 2001). As a rule of thumb, the following values are worth remembering: the average excursion of the diaphragm during quiet spontaneous breathing is 20 mm (range: 2-23 mm)

Figure 1.
A. Right lateral mid-axillary intercostal scan: the anatomic M-mode (green line) allows ad justment of the angle so that the beam is as perpendicular as possible to the di aphragm.
B. M-mode view of diaphragm motion with measurement of leading edge to leading edge of maximal excursion (E).

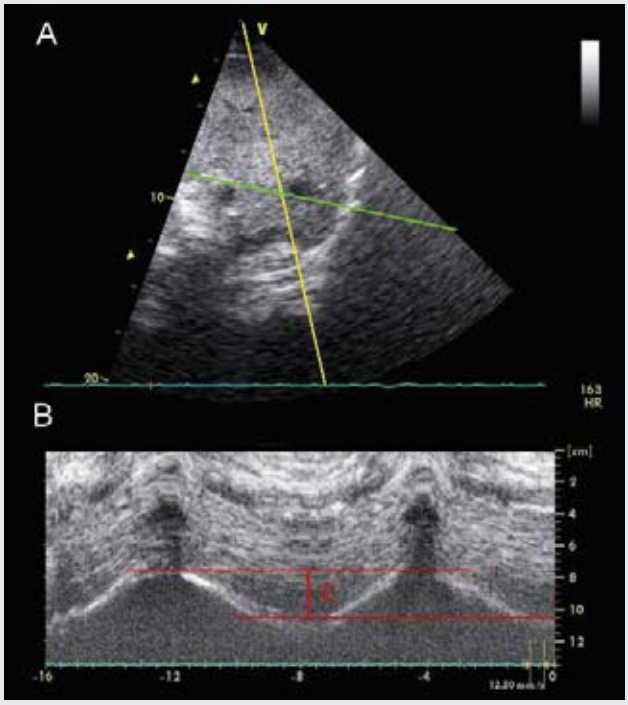
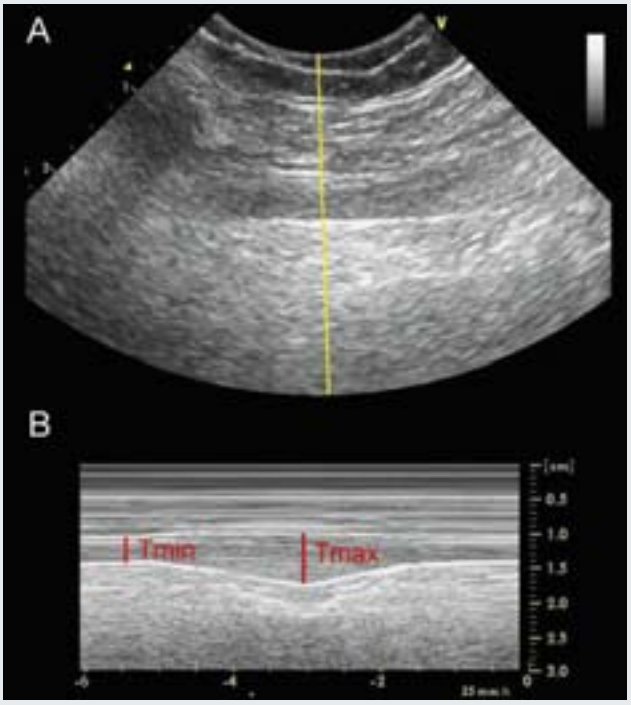


Figure 2.
A. Mid axillary line scan at the level of the costophrenic angle. The diaphragm muscle is located between the two yellow arrows.
B. M-mode allows precise measurement of muscle thickening.



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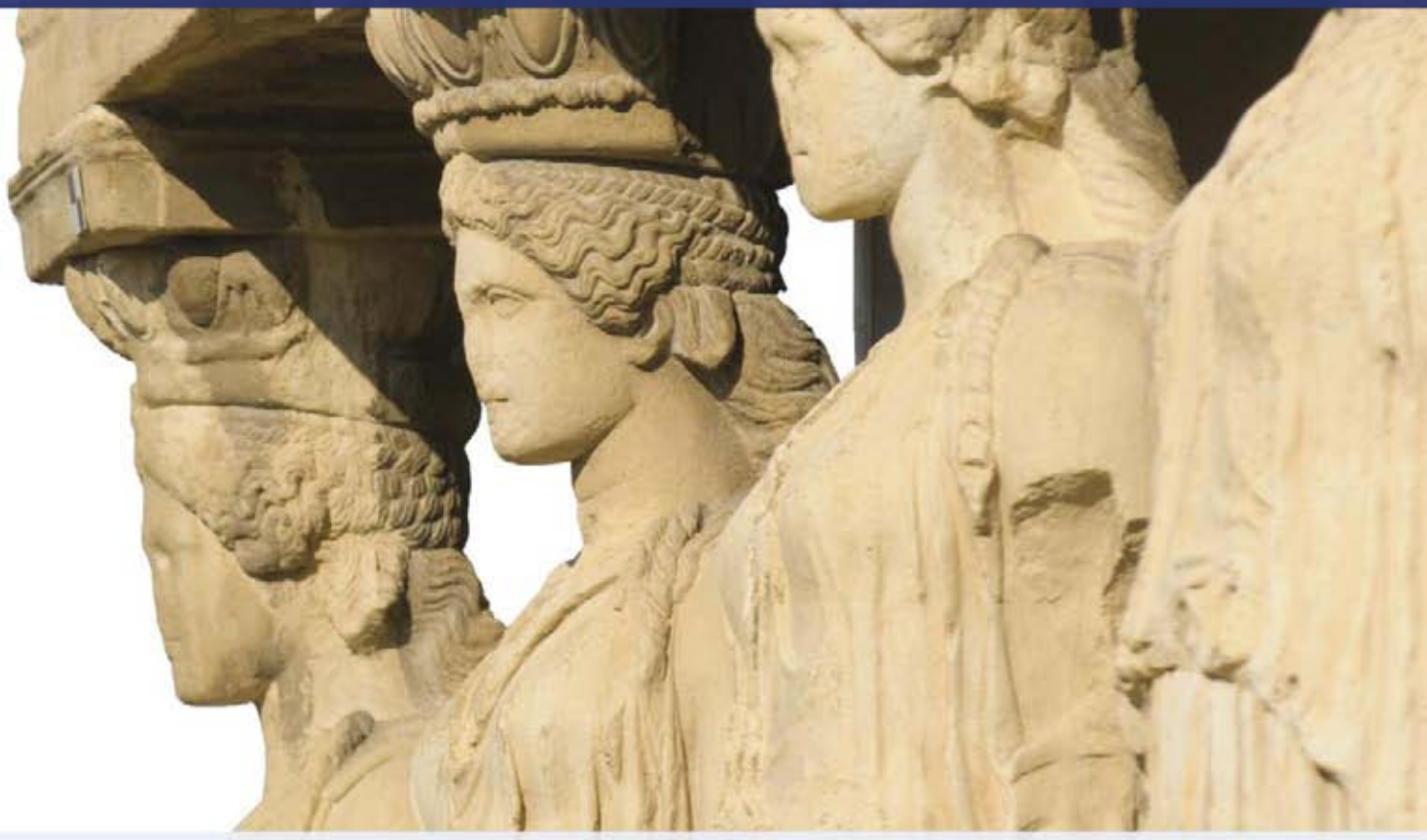

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and during deep breathing 60 mm (range: 40-90). Diaphragmatic excursion tends to be greater in males than in females and does not correlate well with age, height or weight. Although maximal excursions often differ between hemidiaphragms, a greater than twofold difference in excursion is to be considered abnormal.

Normal values for diaphragmatic thickening have been published during normal quiet and deep breathing (Harper et al. 2013; Boon et al. 2013). In the general population the average thickness of the diaphragm at its junction with the chest wall (measured at the end of expiration) is 3.0 mm (range, 1.2-12.0) with normal differences between right and left of less than 0.3 mm.

Diaphragmatic thickening may be expressed in two ways: a. thickening ratio (TR = Tmax / Tmin) or b. thickening index [Δtdi % = (end-inspiratory thickness - end-expiratory thickness) / end-expiration thickness]. In healthy subjects, the average TR is 1.2, but sometimes no thickening at all is observed during normal breathing. During a maximal inspiratory effort, the average reported TR is 2 but can vary between 1 and 4. Changes in the thickness of the diaphragm are proportional to its shortening, ie the change in thickness is proportional to the force that the muscle can generate.

Possible Clinical Applications and Words of Caution

When the aetiology of hypercapnic respiratory failure or severe shortness of breath is not fully understood, a neuromuscular cause, including diaphragmatic paralysis, must be considered, and can be assessed using ultrasound as described above. In the ICU, this tool is of great interest for predicting weaning success or failure and understanding the mechanism of failure to wean. Demonstration of diaphragmatic weakness or paralysis is an important clue to the possible cause of weaning difficulty. Ultrasound of the diaphragm also helps predict weaning outcome and compares favourably with traditional indices such as rapid shallow breathing (Jiang et al. 2004). This needs to be confirmed on a larger scale and in less expert hands. Ultrasound of the diaphragm may also be potentially helpful to detect asynchrony between spontaneous diaphragmatic movement and positive pressure ventilation (Matamis et al. 2013).

An important caveat when performing assessment of diaphragmatic excursion is that this requires the patient to be able to be disconnected from the ventilator to remove the confounding passive diaphragmatic movements induced by positive pressure ventilation. The patient must be able to tolerate at least a few minutes of T-piece and ideally to perform a maximal inspiratory effort on command. Under those conditions, a threshold value of 25 mm can identify patients with significant diaphragmatic dysfunction with good sensitivity and specificity (Lerolle et al. 2009). If patient cooperation cannot be obtained, the measure performed during baseline spontaneous breathing can still provide interesting clues. An excursion of less than 10 mm is usually due to diaphragmatic dysfunction and predictive of a difficult wean (Kim et al. 2011). In another study the average excursion in the patients who failed to wean was 8mm versus 21mm in the successfully weaned group (Giraldo et al. 2011). In obese patients, those measures are more difficult to obtain.

For thickening during maximum inspiration, the average Δtdi % of patients who failed to wean was 16%, versus 55% for those who were successfully weaned (Giraldo et al. 2011). In the study by Dinino et al. (2013) a Δtdi threshold <30% was found to discriminate patients at risk of failing with good sensitivity and specificity.

Thickness of diaphragm at the end of expiration is difficult to interpret and does not predict well strength or endurance. This measurement is highly variable from one individual to another so that the absolute value is of little interest. However, changes over time could indicate the development of diaphragmatic atrophy sometimes seen early after mechanical ventilation initiation. The prognostic value of this atrophy is not yet clear. In contrast, increasing diaphragmatic thickness over time appears to be a favourable prognostic factor for successful weaning from mechanical ventilation (Summerhill 2008).

Conclusion

Diaphragmatic utrasonography is an easy-to-learn and reproducible technique that complements heart and lung ultrasound to pinpoint potential causes for dyspnea, to predict weaning outcome and to assess cause for failure to do so. There is no current adequate substitute for the information provided non-invasively and at low cost by this method. We therefore strongly encourage intensivists to learn this new skill and to incorporate it into their practice. ICU administrators would be wise to budget for ultrasound devices and staff training as meaningful applications of ultrasonography will continue to grow in years to come. ■

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"LIKE FIREMEN GOING INTO A FIRE": MORAL DISTRESS IN THE INTENSIVE CARE UNIT

The definition, causes, and impact of healthcare professionals' moral distress in the intensive care unit (ICU) are reviewed. Individual and system strategies are proposed to mitigate the effects of moral distress.

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Introduction

After dealing with a long, protracted death of a patient, a critical care nurse remarks:

> *"Critical care physicians and nurses are like firemen going into a fire. We know we're going to get burned, yet we do it over and over again until the burns no longer hurt."*

This is a classic expression of moral distress. Moral distress occurs when a healthcare professional perceives an ethically preferable or morally right course of action to take, but they cannot take this course of action because internal or external constraints make it difficult (if not impossible) (Jameton 1984). Moral distress is often mistakenly equated with burnout, exhaustion, or an ethical dilemma, but it is distinct. For instance, in a classic ethical dilemma, there are two mutually opposing courses of action, and the clinician just does not know which course to take. With moral distress, the healthcare professional has identified the preferable course of action, but cannot act on it (Wilkinson 1987). When clinicians experience moral distress, they likely also experience burnout or psychological distress. Conversely, moral distress is not necessarily present when an individual suffers from burnout or stress. Distinguishing moral distress from other phenomena is important in order to recognise its impact on ICU team members and implement interventions to reduce its detrimental effects (Hamric 2012).

> *"Moral distress is often mistakenly equated with burnout, exhaustion, or an ethical dilemma, but it is distinct"*

Causes of Moral Distress

Moral distress has been studied over the past twenty years, particularly in the critical care context, but our understanding of this condition is still evolving (Hamric 2012; Lützén et al. 2006). Broadly, moral distress usually results from misalignment in goals and expectations between various stakeholders regarding treatment plans. This discordance can occur between patients/surrogate decision makers and healthcare professionals, between different healthcare professionals involved in a patient's care, or between patients and surrogates (or surrogates and other surrogates). Critical care physicians and nurses experience moral distress in a range of situations, but the specific clinical situations most likely to evoke moral distress centre on initiating or continuing aggressive measures at the request of patients or (more commonly) surrogate decision-makers, even where it might be medically inappropriate to do so. Here, critical care clinicians report feeling "ineffectual" and "hopeless" at directing the treatment plan in accordance with what they feel to be most ethically appropriate (Corley 2002). Discontinuation of treatment that is perceived to be appropriate or, alternatively, discontinuation of treatment in an inappropriate manner may also create moral distress for ICU clinicians.

Moral distress research has only recently conclusively determined that moral distress is experienced by all healthcare professionals, regardless of their disciplinary background or gender. The frequency and source of moral distress, however, might differ depending on professional background. A recent study found that social workers were distressed by discharge planning issues (Houston et al. 2013). Chaplains were distressed by feelings that life-sustaining treatment was withheld or withdrawn prematurely, a perception that was uniquely experienced

by chaplains for reasons that are unclear (Houston et al. 2013). Critical care nurses and physicians experienced moral distress from issues pertaining to continuation of aggressive measures where it was viewed as medically inappropriate, although nurses experienced this with greater frequency than physicians. A logical explanation for this finding may be that nurses have greater contact presence at the bedside and are unable to remove themselves from the distressing situation (Houston et al. 2013; Bruce et al. 2014a). Whether and to what extent moral distress manifests differently between various disciplines is worthy of further exploration.

Efforts are underway to build a more comprehensive knowledge base about root causes of moral distress and the interconnections between system, ICU-based, and individual factors (Hamric 2012). Presently we know that factors that affect moral distress intensity and frequency include: individual characteristics of a healthcare professional (discipline, years of experience, education, or belief system), ICU culture and organisation, institutional culture, and the healthcare environment, but the interconnections between these factors are not well understood (Hamric 2012; Lützén et al. 2006). For example, providing medically inappropriate treatment has consistently been identified as a major, if not the primary, root source of moral distress, as noted above.

> *"There are profound implications in allowing critical care professionals' moral distress to go unchecked and unmitigated"*

However, a more nuanced view might elucidate intra-team dynamics as a corollary root cause that somehow connects or influences feelings about medical appropriateness or inappropriateness of treatments. Some of our work suggests that discordance between team members regarding prognostic information or plans of treatment might exacerbate moral distress, whereas well-functioning teams with a supportive staff network might help in mitigating moral distress (Bruce et al. 2014b; Weinzimmer et al. 2014). More work is needed to characterise the interplay between team dynamics and individuals' moral distress

Impact of Moral Distress

Moral distress may have a significant impact on individual members of the ICU team, team dynamics and patient care. Others researchers' work and our own suggest that moral distress results in compromises in professional identity or integrity, surfacing in a variety of ways including emotional detachment or desensitisation (Bruce et al. 2014a; Epstein and Hamric 2009). Critical care clinicians have reported "stepping back" and "watching from the sidelines as the disaster unfolds" as a means of "self-protection" (Bruce et al 2014a; Weinzimmer et al. 2014). Efforts may be taken to transfer patients to different hospitals or services, change shift schedules or patient assignments, limit time with the patient and family or other similar strategies to remove healthcare professionals from morally distressing situations. These transitions could potentially affect quality of patient care and patient/family satisfaction. Aside from detachment, other symptoms suggestive of moral distress include frequent crying, physical illness, or a change in appetite or sleep patterns (Hamric 2010).

Repeated exposure to moral distress likely results in a cumulative building of the "residue" remaining from prior morally distressing cases, ultimately creating a new, higher baseline of moral distress (Epstein and Hamric 2009). With this cumulative buildup, professional integrity eventually erodes and clinicians opt to desensitise in order to, as one interviewee said, "inoculate" themselves. If this theory holds true, which has yet to be consistently demonstrated empirically, it is anticipated that experienced, senior clinicians might feel or have the appearance of becoming "jaded" or withdrawn in order to protect themselves from repeated exposure to morally distressing cases (Epstein and Hamric 2009).

Interventions to Mitigate Moral Distress

Given that moral distress is ubiquitous in ICUs, the question then becomes what to do to mitigate it. One option would be to ignore it, reasoning that some moral distress is acceptable because it indicates a healthy recognition of the moral domains of medicine. Such an approach, in our opinion, would be deleterious. Several studies have demonstrated at least an attenuated connection between moral distress and job dissatisfaction, and some studies have found links between moral distress and actually leaving one's profession (Beumer 2008; Elpern et al. 2005; Gordon and Hamric 2006). Ignoring a phenomenon that clearly impacts staff turnover and morale (and could affect patient care) only creates institutional risk.

Interventions to decrease moral distress could involve individual and system level strategies. One might assume that moral distress can only be addressed by the healthcare professional on an individual basis. While there are techniques that could be used individually (e.g. meditation, journalling, self-care, exercising), such approaches are limited in mitigating moral distress (Gordon and Hamric 2006; Hamric 2012). System strategies should supplement individual techniques in order to better and more fully support clinicians. System approaches to intervening on moral distress can take many forms, depending on organisational culture and resources, making it difficult to formulate generalisations, but they can generally be grouped according to three main activities: increasing education, cultivating mentoring networks, or conducting debriefing sessions.

Unfortunately, very little investigation has been done on system-level education interventions (Beumer 2008; Hamric 2012). Of the few studies that exist, most system-level interventions focus on increased bioethics education with mixed results. The premise for this is the belief that more education could help healthcare professionals identify moral distress and develop strategies to mitigate it. Regular inclusion of a bioethicist in

ICU rounds at our institution improved recognition of morally distressing cases, validated the clinicians' concerns, and facilitated intra-team communication (Bruce et al. 2014a), suggesting another means of education.

Alternatively, some system interventions encourage cultivating effective mentoring networks and setting up unit-based debriefing sessions (Gordon and Hamric 2006; Rushton 2006). The logistics of debriefing sessions and the means by which to facilitate mentoring networks are often context-dependent. Debriefing sessions could be facilitated by a chaplain, an ethicist, or an independent outside consultant. The topics of the sessions could range from orchestrating core content lessons to free-style 'venting' opportunities. The timing of the debriefing sessions could range from episodic meetings (e.g. during and after a particularly complex case) to regularly scheduled meetings not related to cases. A top-down approach wherein hospital leaders plan system interventions without essential input and buy-in from bedside clinicians will likely be perceived as authoritarian, heavy-handed, and unresponsive to the moral distress needs of clinicians. For this reason, involving bedside clinicians in shaping and selecting system approaches is prudent. More importantly, it is likely to lead to the selection and adoption of a plan that will be successful in particular ICUs.

Conclusion

In summary, there are profound implications in allowing critical care professionals' moral distress to go unchecked and unmitigated, especially given that is an experience that is shared by most—if not all—members of the ICU team. We lack a complete understanding about moral distress causes and the interconnections between system, ICU-based, and individual factors. Terminology and definitions have been inconsistent, further frustrating efforts to investigate moral distress. Intervention research is limited, and studies that exist often yield mixed results. Despite these limitations, recent efforts aimed at developing systematic approaches to studying moral distress suggest that inroads are being made to refine our understanding of this complex experience. ■

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EVIDENCE IN INTENSIVE CARE

AN INTERVIEW WITH PROFESSOR JOHN MARINI

Professor John Marini is Professor of Medicine at the University of Minnesota and director of translational research at Regions Hospital in St Paul, Minnesota in the United States.

You presented at ISICEM 2014 on the Round Table conference on "Evidence-based care: New directions". What were the key themes from this?

The rationale was to draw together experts from diverse areas to share ideas regarding how to do better in gathering the data needed to guide clinical practice of intensive care. As a field, we have made good progress toward improving rescue and survival, but not as well in restoring our patients to robust health. Many patients encounter chronic critical illness or lingering disabilities that follow them for months to years afterwards. We remain uncertain as to how much of this 'ICU hangover' is part of the innate process and how much is inadvertently caused by the care we administer. We have looked for guidance regarding patient care to randomised clinical trials (RCTs), observational studies and experimental laboratory work using models of disease. Often, the results of such work have been conflicting or misleading, and at times progress seems to be painfully slow. Population-based answers often do not apply to the specific problem of the individual. Interpretation of RCTs is tricky, and judicious application of population-based findings to decisions for the individual even more so. What we have been slow to understand is that we have imprecise definitions and imperfect models. At the same time, the problems we face involve patients who are heterogeneous in severity, susceptibility and responsiveness, pathologies and treatments that are complex and incompletely understood, and timing issues of the progressing condition that affect the effectiveness and side effects of our treatments.

We discussed new methods for targeting the population tested in our trials, identifying and dissecting the interactions among the key variables and 'personalising' the treatments given. New methods for interpreting individual sensitivity and adaptive response were also of major interest. The novel tools we discussed included statistical approaches to data analysis and study design as well as molecular and genome-based diagnostic and monitoring methods. I think we all went away from the Round Table with sharpened awareness and fresh ideas regarding better directions for our work.

You have previously recommended against over-reliance on evidence. What is the role of evidence-based care in intensive care? How can intensivists be sure of new treatments, unless they have been tested in large RCTs?

If by the term evidence you mean the RCT, then I plead guilty as charged. But useful 'evidence' comes in many forms. When faced with a complex, quickly evolving and changeable clinical problem at the bedside, a logical approach based on mechanistic understanding, expert opinion and/or personal experience may be the best we have to guide us. Many factors interact to determine outcomes for individuals. In such a rapidly evolving and non-linear system, integrating all key information, making an informed, reasonable decision and then committing to short loop feedback and mid-course corrections is the way to go. In reality, this is an N-of-1 empirical trial, not an application of a deterministic one, as the RCT-guided approach would imply. Often, you cannot simply choose an option from a picklist or guideline, and then set it and forget it. I have long been concerned that we over-emphasise the results from RCTs. Within the data of any RCT you have patients who had neutral or contradictory responses to the group average. For example, prone positioning might be perfect for some but ineffective or dangerous for others. Lumping all results to draw one conclusion may be misleading for the appropriately selected subpopulation. It might seem that the question is simple and the choice clear—prone the ARDS patient or not? But we now understand that the dosing (hours per day and days prescribed) of prone positioning is important to its efficacy, as is the recruitability and severity of the lung disease (What exactly is 'ARDS', anyway?). That is not to say that certain specific problems should not be subjected to RCT—ones that are unambiguously defined, candidates appropriately identified, likely mechanisms for benefit or harm are known, and outcomes are directly traceable to the intervention. When RCTs are performed the question should be logical, the subject population sharply defined, the enrollment large, and the co-morbidities and co-interventions well controlled. These trials are expensive, usually take a long time to complete and publish, and, even when accurate, the results are relevant only to the specific patients and specific medical environment that was studied. Medicine often changes

impressively over time. RCTs are not the pinnacle of the evidence base for issues in critical care but rather a blunt tool that provides more questions than answers. They often make us stop, think and try to explain—a good thing. However, when published, their relative influence on practice is often both enormous and immediate. In my view, RCTs represent an overused research option that should be undertaken primarily when a serious question exists at the end of a more basic (and hopefully mechanism-defining) chain of observations and research that alone are not persuasive. When results are puzzling and/or practice changing, replication should be mandated.

What are the most serious challenges in ventilator management?

I hope to give a succinct answer. The goal of invasive ventilation is to provide cardiopulmonary support that is effective, safe, and comfortable. We currently do quite well in achieving life-sustaining CO_2 elimination and acceptable arterial oxygenation. Unfortunately, we do not do as well with safety and comfort. The potential damages that result from inappropriate and protracted sedation, ventilator and oxygen-associated lung injury, intubation-related infection and laryngeal dysfunction, psychic distress, interrupted communication, patient-ventilator asynchrony and excessive right ventricular afterload are always a challenge to prevent. We know that ventilatory support is often required, but when do we cross the line that demarcates harm from benefit? Sometimes taking full control is best; at other times we should aggressively transition to spontaneous breathing. Finding safe and effective ways of reducing the intensity of invasive ventilation (as by adapting the patient to permissive hypoxaemia as well as hypercapnia) or by using extrapulmonary gas exchange (ECMO, ECCO2R) hold promise. Our bedside processes of care must also be perfected—positioning, protocols, monitoring, early intervention etc. If I had to single out one all-encompassing challenge it would be to reduce the unintended consequences of mechanical ventilation.

Is it possible to ventilate obese patients? What are the challenges?

Learning the nuances of ventilating obese patients should be a priority for intensive caregivers, as the prevalence of obesity, already high, is slowly rising in all age groups and in every geographic sector and economic stratum of the world. The physiologic hazards that these folks confront are clear. The lungs operate at a low resting volume (FRC), so that they have limited oxygenation reserve. Many have baseline hypercapnia and most have a vulnerable upper airway that predisposes to obstructive apnea. Attention to CO_2 monitoring is especially important. The drive to breathe tends to be blunted. They often have pulmonary hypertension and are at risk for right ventricular decompensation when it rises further due to acidosis, hypoxemia, or excessive alveolar pressure. Obesity predisposes to venothrombosis, systemic hypertension, and oesophageal reflux. They encounter problems with airway closure in the usual supine, 30 degree position, and the heaviest should be managed in a more upright beach chair posture. After extubation, these patients are at higher risk for upper airway obstruction and sleep apnea due to abnormal neck anatomy—especially in the first post-extubation days, since they may slowly release fat-stored sedative agents. These many hazards pre-dispose to sudden, unexpected crises both during and after mechanical ventilation.

In an article on the future of critical care you noted emerging economic realities related to critical care that must be confronted in the future: fewer personnel, faster hospital throughput, increased needs for safety, timely intervention, quicker assessment of therapy and decision support (Marini et al. 2013). Which of these realities is the most challenging, and how can intensivists address it?

Among these, one of the most challenging is to better time what we do. In my opinion, many of our problems relate to our failure to first intervene quickly enough and then to time our 'therapeutic flip' toward withdrawal of supports and strengthening the rescued patient. The ability of the patient to adapt to the abnormal physiology that accompanies acute illness is really an underexplored but vitally important area. I strongly suspect that we do too much for too long, not only wasting resources but extending the duration of ICU stay, interfering with the patient's adaptive potential and unintentionally promoting chronic critical illness and encouraging lasting disabilities.

We can address efficiency issues and achieve better timing by deploying care extenders (e.g. nurse practitioners) and other helpers to attend to the mandated chores of modern medicine (e.g. documentation) that tend to disconnect us from the patients we treat. In principle, the electronic medical record and better monitoring systems can aid timely intervention, enable short loop feedback, and improve efficiency of hand-offs, but the obligation to document and to process communications electronically currently works in the other direction.

> *"What we have been slow to understand is that we have imprecise definitions and imperfect models"*

What is your view on prone positioning in ARDS, given recent findings?

My view today is almost exactly what it has been for the past 20 years. Prone positioning reduces the mechanical heterogeneity that predisposes to ventilator-induced lung injury, helps recruit the dorsal lung zones, improves oxygenation and contributes to effective airway secretion drainage. It is universally available, poses modest and preventable hazards, and once the turn has been made, requires little more personnel time to maintain than supine management. It can be life-saving for our most severely affected patients. Guérin and the PROSEVA team did intensive care a great service in showing its worth for the appropriately selected patients (Guérin 2013). Although some would disagree, I do not think that we can recommend proning for every ARDS patient—at least, not at this time.

By the way, the proning story is a good example of how misinterpretation of inconclusive RCTs can mislead us into discarding a valuable option. We need to

know the 'why', not just the 'what' behind these interventions and studies. I was recently asked by a journal editor why so many practitioners are now so willing to prone their ARDS patients whereas they were hesitant before. My answer: proning makes good mechanistic sense for these patients—always did. Moreover many physicians have seen positive results with those who were desperately ill. Now we have meta-analytic suggestions of whom to target and a strong RCT mandate to make it more routine.

> *"The ability of the patient to adapt to the abnormal physiology that accompanies acute illness is really an underexplored but vitally important area"*

You spoke at ISICEM 2014 in favour of plateau pressure's ability to guide ventilation in ARDS? What are the main arguments for this in your opinion?

Please bear in mind that the setting was an intentionally polarised 'pro-con' style debate. Plateau pressure is universally available, easy to measure, and potentially valuable. This number tends to relate more directly to injury risk than tidal volume, whose impact varies with the volumetric capacity of the injured lung. Clearly, plateau pressure is only one of the things to consider when trying to prevent ventilator-induced lung injury. For example, it may be misleadingly low when the patient makes strong breathing efforts and misleadingly high when the chest wall is stiff. It is risky to set a precise numerical guideline for what is a safe or hazardous plateau that applies across a diverse population of patients. However, the utility of the plateau pressure is still significant when caring for the individual patient. An increase or decrease of plateau pressure obtained under passive conditions tends to affect the maximum tidal stress and the driving pressure in the same direction, and both are linked to ventilator-induced lung injury risk. In fact, at sites of stress focusing, the potentially damaging tissue tension is a non-linear function of the plateau. An upward change of plateau disproportionally increases the tissue tension, and the opposite (disproportionate lowering of tension) will apply if the plateau can be reduced. When the patient is passive and the chest wall is normally compliant, plateau pressure—keeping PEEP and tidal volume the same—helps gauge the hazard, the trajectory of illness, and the progress toward recovery. I realise that for any airway pressure the associated stress we apply is not uniform in the injured lung and that the recordable parameter of most interest is not the plateau pressure but the average pressure across the lung—plateau minus pleural (oesophageal) pressure.

This interview will appear in the Summer issue of ICU Management, which focuses on prevention of critical illness. What do you see as the main challenges in prevention?

Some categories of life-threatening problems (for example those that develop from trauma, violence, mental illness, and self-abuse) will always be there. Improved public awareness of behavioural hazards, the benefits of exercise and good nutrition, and warning signs of impending disease will have a positive effect, as has already been amply shown. But a considerable volume of critical illness develops out of milder disorders that are mistakenly ignored or improperly treated. Deterioration can be targeted earlier, especially after the patient comes to medical attention. Within the hospital, for example, rapid response teams have really helped interrupt the downward spiral toward the need for ICU attention.

It can be argued that the biggest challenges in the prevention of critical illness are to address those of our own making. As medicine advances, our delivery system is inadvertently growing an ageing population of patients with multiple serious chronic diseases that often eventuate in repeated needs for intensive care. The associated costs are staggering. With notable exceptions, our transitions from intensive care to general inpatient care to outpatient care are clearly imperfect. We do not have delivery systems to 'catch' and strengthen rescued but fragile patients once they leave the ICU. As a result, recurrent ICU admissions are frequent. Expectations and incentives are aligned to quickly address problems with drugs and interventions. These folks are often seen by multiple specialty providers who place them on many different medications—often without the patient's understanding of what they are intended for, how they should be used, or whether they are still needed. In my country, the over prescription of narcotics for chronic pain and of beta blockers for non-essential conditions in the elderly provide a case in point, as both predispose to hypotension, altered mental status and blunted response to stress. Unnecessary ICU admissions often result. Better patient education, less medical meddling, more efficient access to medical help, and good follow-up will help, as will timely telecommunication and better integration of provider services. Perhaps most important of all in preventing critical illness, we need to re-establish and/or strengthen the connections between committed, caring, and well informed providers with the patient. In the hectic, rapidly changing and 'bottom line' oriented environment that surrounds us, achieving this ideal is indeed a major challenge that must be confronted at all stages of medical education and levels of practice. ■

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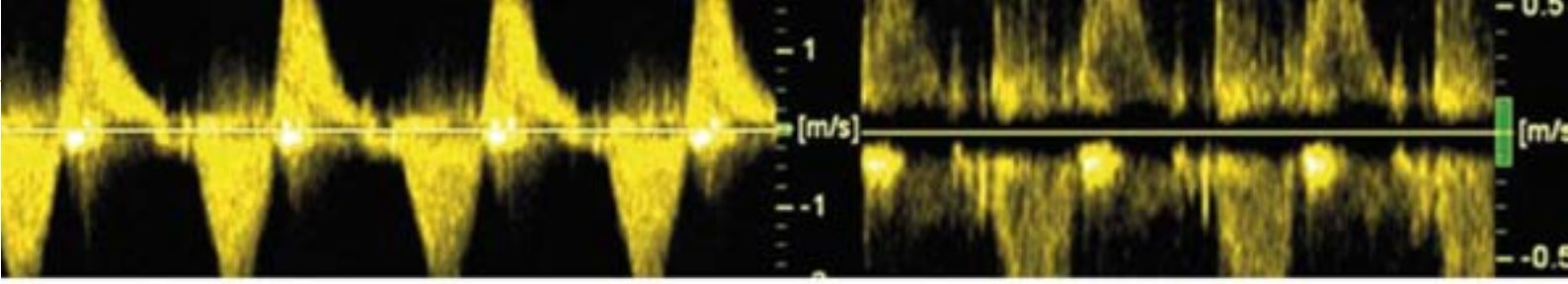

International Course

Echocardiography for Hemodynamic Monitoring 2014

with videotransmissions of live cases from the ICU

Brussels, November 18-20, 2014

Course directors

Daniel De Backer (Brussels, Belgium)
Michel Slama (Amiens, France)
Antoine Vieillard-Baron (Boulogne-Billancourt, France)

Special guest speakers:

Paul Mayo (New York, USA)
Anthony McLean (Sydney, Australia)

Other Faculty members:

Laurent Bodson (Paris, France)
Chantal Dedobbeleer (Brussels, Belgium)
Jan Poelaert (Brussels, Belgium)

Aim:

To promote the use of echocardiography in the hemodynamic evaluation of critically ill patients.

General description:

The course will be interactive, with a lot of time devoted to questions, hands-on sessions, and discussions of live video-transmissions.

The first day will be devoted to revising the basics of echocardiography; the second and third days will describe how to use this technique to evaluate the hemodynamic status of critically ill patient.

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CRITICAL CARE IN INDIA
PROGRESS OVER TWO DECADES

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Critical care in India has grown from a relatively small body of professionals to a fully-fledged active speciality. The Indian Society of Critical Care Medicine publishes a MEDLINE®-indexed monthly journal, hosts an increasingly popular annual congress, but more importantly runs an extremely successful training programme. All this has been a part of the phenomenal growth in the field of critical care in India. With a projected rise in medical tourism to India, critical care as a speciality is poised to grow even further. Future challenges will include giving the speciality a meaningfully socialist angle to serve the multitudes where critical care has not reached as yet. The era ahead seems promising and exciting

Introduction

The growth of the field of critical care medicine in India is a great story of how the economic changes in a country can lead to the evolution of a scientific subspecialty. It is a story of how the private hospital industry can accelerate the growth and development of a service-oriented sector in the community.

Like everywhere else in the world, critical care in India, in the beginning, was practised in major public hospitals as part of the general management of seriously ill patients, without being labelled as a separate service. Attempts to segregate seriously ill patients in specialised areas dedicated to advanced management began in 1968 with the development of coronary care units in Mumbai (Yeolekar 2008). Very soon the concept of attempting to save the life of a seriously ill patient with the help of a specialised unit consisting of special equipment and staff engulfed non-cardiac patients as well. The availability of ventilators was responsible to a significant extent for the development of this concept. The early 1970s saw the development of the first critical care units, again in Mumbai, dedicated to the management of critically ill non -cardiac patients as well (Prayag 2002). These units, like most other units in the world, were being run by dedicated staff, who had interest and enthusiasm for this field.

Statistics	
Total population	**1,240,000,000** (2012)
Gross national income per capita (PPP international $)	**3,910**
Life expectancy at birth m/f (years)	**64/68**
Probability of dying under five (per 1,000 live births, 2012)	**56**
Probability of dying between 15 and 60 years m/f (per 1,000 population, 2012)	**242/160**
Total expenditure on health per capita (Intl $)	**157**
Total expenditure on health as % of GDP	**4.1**
Population living in urban areas (%)	**31 (2011)**
Physicians per 10,000	**6.49 (2009)**

Source: World Health Organization Global Health Observatory http://apps.who.int/gho/data/node.country

Indian Society of Critical Care Medicine

The real impetus for the development and evolution of this speciality came in the early 1990s. A group of physicians, back in various cities of India after training in the western world, started the Indian Society of Critical Care Medicine (ISCCM) in 1993. Although it started off as a body of professionals, mainly for exchange of knowledge and discussions amongst the group, the leadership quickly realised that the main work it needed to do was to create an awareness of the speciality of critical care medicine. The popularity of the ISCCM can be seen from the growth in membership (see Figures 1 and 2) and the spread of the city units across the country over the last 20 years (see Figure 3). As of 2014, the membership stands at nearly 7000, and the number of city units is around 80.

Training

The need for developing a training programme for upcoming graduates was also felt quite strongly. Unfortunately, at that time in the 1990s, the universities and official licensing councils were not convinced about the need for developing a strong training programme in this upcoming speciality. ISCCM then took upon itself to start this training programme. It laid down the course curriculum, identification process of training institutes and their certification as well as a well structured exit examination. Initially a one-year certificate course was started, which soon evolved into a one-year diploma and a two-year fellowship course. Figure 4 shows the growth in the number of candidates registering for these courses over the last 16 years of these training programmes; Figure 5 shows the increasing number of training institutes for these courses.

The period of growth of the ISCCM coincided with the strong economic growth of India. The industrial policies of the country opened up, and as a result the healthcare sector grew significantly. The public sector, controlled by the government, has always been a smaller player in healthcare delivery in India. Private

healthcare organisations, predominantly for-profit organisations, form almost 80% of the total healthcare delivery sector (Prayag 2004). Because of the extra cost of equipment and specialised manpower, critical care is a hospital segment, which is heavily driven by high-end economics, and the growth in the critical care sector in India over the last two decades has been essentially in private sector organisations. The exact number of ICU beds in India is not available, since the registration of ICUs and hospitals is not a centralised process. There appears to be a shortage of beds in hospitals in most parts of the country compared to the population, the demands and also to western standards (Yengkhom 2013). With the increasing development of large multi-speciality hospitals and the growing penetration of health insurance, this deficit is expected to be reduced significantly over time. The centralised National Board of Medicine in India and the Medical Council of India approved the critical care training programmes only recently, and these are currently run in a limited number of centres in the country. The contribution of ISCCM is significant in this regard, since it could provide the bulk of a large number of trained specialists to staff these ICUs from the mid-1990s, at a time when there was a significant shortage of manpower.

Specialist Congresses with International Experts

One of the other major contributions in the growth of this speciality in India has come from the annual national congresses of ISCCM, which have been extremely successfully conducted over the last 20 years in various parts of the country. Many international stalwarts in the field of critical care have presented their latest work to the Indian audience at these congresses. In an era when very few Indian specialists could attend International meetings such as ISICEM, ESICM or SCCM, the presence of these specialists from all across the globe has done wonders to raise the scientific standards and act as appropriate role models for the average ICU physician of India. The currently started programme of "Best of Brussels" is also another significant step in the same direction since it carries the mini-programme of ISICEM into India.

Critical Care Research

Original research in critical care in India has been limited. Traditionally, Indian medical students have not been taught research methodology during medical school. The emphasis during training had always been on clinical medicine and patient care rather than research and publications. Despite the strong pool of good quality clinicians, original research therefore has been extremely poor in volume, as revealed by the fact that the SCOPUS database since 1977 revealed only 72 articles from India published in three major critical care journals (Divatia and Jog 2013). ISCCM has now developed its own research section, and data collection in various issues peculiar to ICUs across India has begun. The first corroborative study involving collection of data from Indian ICUs – INDICAPS – was presented in 2012. Indian ICUs have contributed significantly to data in various International studies, including EPIC II (Vincent et al. 2009) ICON, (Vincent et al. 2013), OSCILLATE, (Ferguson et al. 2013) PROWESS SHOCK (Ranieri et al. 2012), INICC data (Mehta et al. 2013) amongst others. Although this is a good beginning in the culture of research methodology, this really is not original work from India. Hence the Indian critical care community is now leaning towards making meaningful contribution towards the management of conditions peculiar to their subcontinent, and trying to publish this research. Patients with severe Dengue infections coming to ICU (Schmitz et al. 2011) or ARDS related to H1N1 epidemics managed with high frequency oscillatory ventilation (HFOV) (Jog et al. 2013) are amongst the examples of contributions which the Indian intensive care community is trying to make in the world of critical care. These kind of contributions will be extremely meaningful given the volumes of case material available in India and the maturing research abilities of the Indian critical care community.

Publications

The Indian Journal of Critical Care Medicine (http://www.ijccm.org) was established in 1996, and has been indexed in MEDLINE® since 2007. It has evolved to become a strong representative mirror of the work of the critical care community in India. It is now published monthly, and gets a large number of articles from outside the Indian subcontinent. ISCCM has other publications, including a newsletter Critical Care Communications, an ICU protocol book, audio journal series podcast and now a textbook called the ICU Book. It has also published numerous guidelines (e.g. on catheter-related bloodstream infections, management of tropical infections,

Figure 1. Increase in Number of Members Over the Years

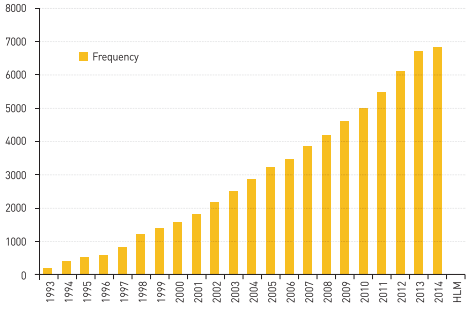


Figure 2. Number of New Members each Year

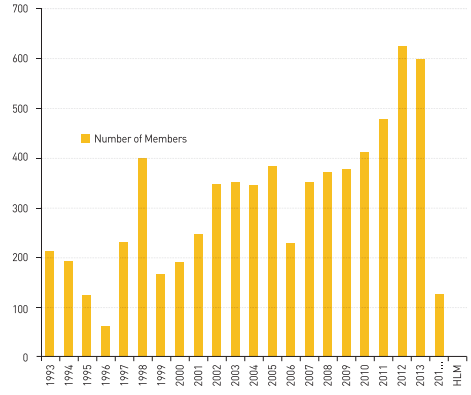


Figure 3. Spread of City Chapters of ISCCM

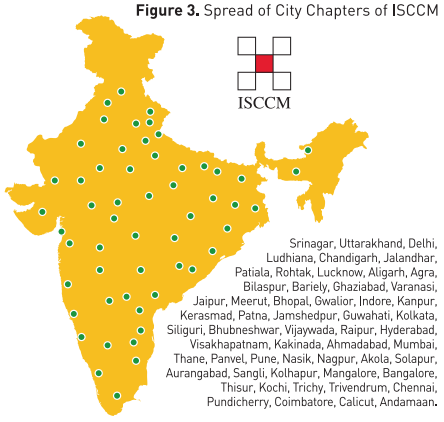


Figure 4. Students under Training

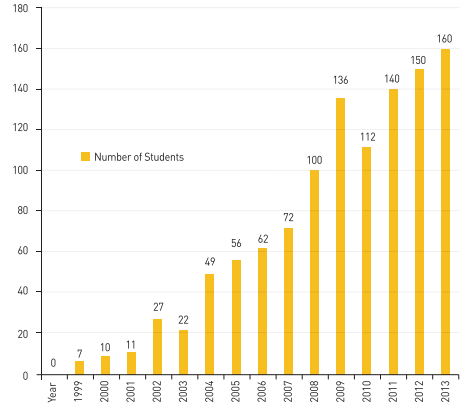


Figure 5. No. of Training Centres for Diploma Students

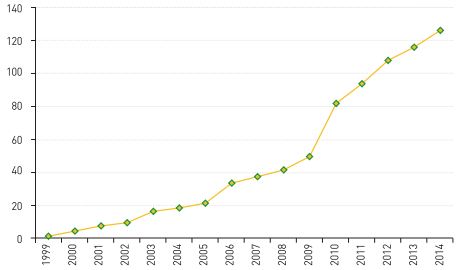
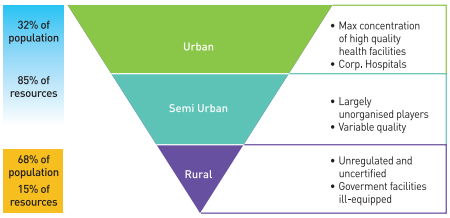


Figure 6. Delivery - Infrastructure Mismatch



end-of-life care, ICU planning and designing in India etc.) (Mani et al. 2012). These are substantial contributions to evolve the critical care community in India to a group of committed, meaningful, scientific group of physicians.

Conclusion

The increasingly important role of the Indian critical care community is being recognised all over the world. An Indian representative was elected on the Council of the World Federation of Societies for Intensive and Critical Care Medicine (WFSICCM) for the first time in 2001, and since then India continues to be present in the council. Asia Pacific critical care also has a significant contribution from India. An Indian consultant has become the Asia Pacific representative on the council of the European Society of Intensive Care Medicine (ESICM). India is now represented on the editorial boards of prestigious International journals like Intensive Care Medicine, ICU Management and Critical Care (in future).

Critical care in India has evolved very rapidly and significantly in the last two decades of its existence. Not only has the number of ICUs and the number of properly equipped beds increased, but the trained manpower has increased leaps and bounds. More importantly, there has been a meaningful pragmatic direction to this movement to make sure that this growth is in an extremely scientific, academically oriented atmosphere. Where will all this lead to in the future ? India is gearing up for a possible meaningful change in political leadership. This could add substance to the numerical economic growth which it has been experiencing. This meaningful growth, if and when it happens, will hopefully reach the multitude of masses which are still struggling below poverty line. A strong socialistic direction is needed in the modern way to really service the masses of critically ill patients struggling to get high quality care due to prohibitive costs (see Figure 6). Hopefully, India will be able to achieve a balance in the progress and its appropriate distribution. Unless that happens, critical care would remain a relatively exclusive service for the minority who can afford its ever increasing costs. This perhaps is the biggest challenge for the Indian critical care community for the future. Either way, we look forward to interesting and exciting times ahead. ■

For full references, please email **editorial@icu-management.org,** visit the website at **www.icu-management.org** or use the **QR code** at the top of the article.

NEUROCRITICAL CARE IN INDIA

Globally neurocritical care is a well-established field in medicine. In India this discipline has developed in the major cities. However, elsewhere it is found wanting. The high incidence of head trauma and stroke and advances in neurosurgical techniques clearly warrant the need for neurocritical care units. The morbidity and mortality associated with head trauma and stroke will certainly reduce if state-of-the art neurocritical care centres are established across the country.

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Introduction

India is a vast country with a population of over 1.2 billion people, still rising by about 18 million a year. Healthcare provision is not a centralised process. The government plays a very small role in healthcare delivery, nor does it have control over the non-governmental sector. Only a small proportion of publicly-funded government hospitals are able to provide state-of-the-art care, whereas a large percentage of public hospitals only provide basic care. This is due to the fact that India currently spends only 3.9 per cent of its GDP on publicly-funded healthcare. Most healthcare in India is currently provided via the private sector. Because of a lack of affordable insurance protection it is principally funded via out-of-pocket payments.

Understandably, private institutions provide most critical care services in this part of the world. There are large numbers of neurocritical centres across the country, but most neurocritical care patients are treated in general ICUs. In an Internet-based survey conducted by the author in 2013 with a web-based Indian Critical Care discussion group, of the 162 respondents 59 (36.42%) stated they had exclusive neurocritical care units (Amin 2014).

Critical care in India started in the early 1960s, and was introduced in the city of Mumbai. It slowly and gradually spread to other cities and towns. A formal society of critical care, the Indian Society of Critical Care Medicine (ISCCM) was formed in 1993, and now has around 7000 members.

The Neurological Society of India (NSI) was founded by eminent neurosurgeons and neurologists in 1951. The NSI currently has 2,565 members, of whom 1,983 are neurosurgeons and the rest are neurologists. In 1992 the neurol-

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Table 1. Nature of Head Injuries

	Total No.	Total%
Cerebral Concussion	2397	35.5
Cerebral Contusion	2182	32.3
Skull Fractures	787	11.7
Brain Haemorrhage	882	13.1
Unspecified	182	2.7
Crush Injury	5	0.1
Spinal Cord Injury	310	4.6
Total	6745	100

Source: Gururaj 2002; 2008

Table 2. Outcomes

	Total No.	Total%
Death	308	5.5
Persistent Vegetative State	206	3.7
Severe Disability	850	15.3
Moderate Disability	2597	46.3
Good Recovery	1593	28.7
Total	5554	100

Source: Gururaj 2008

Table 3. Stroke Prevalence Studies in India

First author	Year	Location	Sample size	Crude prevalence/ 100,000	Age-adjusted prevalence/ 100,000
Urban					
Bansal BC	1973	Rohtak	79 046	44	-
Bharucha NE	1988	Mumbai-Parsi	14 010	842	424
Dalal PM	1997	Mumbai	145 456	220	-
Banerjee TK	2001	Kolkata	50 291	147	334
Gourie-Devi M	2004	Bangalore	51 502	136	-
Rural					
Abraham J	1970	Tamil Nadu	258 576	57	84
Gourie-Devi M	1987	Karnataka	57 660	52	-
Razdan S	1989	Kashmir	63 645	143	244
Das SK	1996	West Bengal	37 286	126	-
Saha SP	2003	West Bengal	20 842	147	-
Gourie-Devi M	2004	Karnataka	51 055	165	262

Source: Gupta et al. 2008

Table 4. Morbidity and Mortality

Factors	Urban	Rural	P value
Crude Annual Incidence Rate	116/100,000	19/100,000	NS
Risk Factors Present	94.9%	94.1%	NS
Ischaemic Stroke	83.9%	82.3%	NS
Haemorrhagic Stroke	16.1%	17.7%	NS
Smoking (men)	22.8%	39.3%	0.013
3 or More Risk Factors	12.7%	20.8%	0.034
Imaging Available	71.9%	56.4%	0.003
28-Day Fatality Rate	24.5%	37.1%	0.011
28-Day Disability Rate-Mild	42.3%	43.2%	NS
Moderate Disability	42.3%	47.7%	NS
Severe Disability	15.4%	9.1%	NS

Source: Pandian and Sudhan 2013

ogists decided that they certainly had to have an identity of their own, which led to the formation of the Indian Academy of Neurology, which now has a membership of 1,323 (Ganapathy 2013).

For many years neurocritical care was considered to be essentially a part of the neurosurgical ICU or neurosurgical recovery room, with well-established protocols for managing such patients. It is believed that there may be 100 to 125 neurosurgical ICUs in India, but the distribution of these centres may not be uniform. For example, Chennai, a city in the southern part of India, has a population of nine million people with 110 neurosurgeons, which is also the number of neurosurgeons catering to 250 million people in North Eastern India.

Head Trauma

About 40 per cent of all deaths in India are still due to infections. The majority of the remainder is mainly due to non-communicable conditions. 11% of deaths in India from non-communicable diseases are due to injuries, of which 78% of injury deaths are due to road traffic accidents. Road traffic injuries are the leading cause (60%) of traumatic brain injury (TBI), followed by falls (20%-25%) and violence (10%). The World Health Organization (WHO) has projected that by 2020 road crashes will be a major killer in India, accounting for 546,000 deaths (Peden 2004). The only epidemiological study undertaken in Bangalore at the National Institute of Mental Health and Neurosciences (NIHMANS) has revealed that the incidence, mortality and case fatality rates were 150/1,00,000, 20/1,00,000 and 10%, respectively. NIMHANS provides care for nearly 60-70% of brain-injured persons in Bangalore city. 7,164 persons were enrolled into a Neurotrauma Registry during the year 2000 at NIMHANS (Gururaj 2002). The nature of head Injuries in this registry is shown in Table 1.

Information on duration of hospital stay was available for 5554 (82%) of the subjects. The outcomes of these patients are reflected in Table 2.

Due to the lack of adequate emergency medical services patients reach hospital late; this has a major impact on outcomes. At least one-third of potentially preventable deaths occur prior to arrival at hospital, and over half occur during the hospital reception and resuscitation phase of care. Over 80% of accident victims do not achieve access to medical care within one hour of the incident. A study from Mumbai noted that for severely injured patients, the time between the injury and hospital admission averaged 6 hours (Murlidhar and Roy 2004).

Stroke

There are eight stroke registries based in various states of India. Each registry independently set up its stroke surveillance systems, based on the WHO STEPS guidelines (http://www.who.int/chp/steps/en/). The Indian Council of Medical Research (ICMR) initiated several strategies to integrate the registries and develop a common population-based stroke registry for the country, but it is still under development (WHO 2006). Some registries are trying to conduct feasibility studies that would help establish this common population-based registry for stroke patients. Based on these registry data the prevalence of stroke is illustrated in Table 3. Table 4 demonstrates the morbidity and mortality from the Trivandrum registry.

The proportion of stroke patients reaching hospital within three hours in India is 15%. This is due to the unavailability of emergency ambulance services, especially in rural areas (Ghandehari 2011). In our web-based Indian Critical Care discussion group survey, to the question how many critical care physicians thrombolysed acute ischaemic stroke, as per the NINDS rt-PA study protocol (National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group 1995), of the 126 respondents 49 (38.89%) responded positively, and of these 11 (8.73%) also used intra-arterial thrombolysis performed by an interventional radiologist.

Despite a high prevalence of stroke in India, the number of stroke patients receiving recombinant tissue plasminogen activator (rtPA), as in other third world countries, is extremely low (Ghandehari 2011). Some of the most important barriers for thrombolysis in India are pre-hospital barriers, financial constraints and lack of Infrastructure.

There is a lack of knowledge about stroke thrombolysis among medical professionals. A study by Nandigam and colleagues (2003) demonstrated that a significant majority of general physicians in India are not aware of the beneficial effects of tissue plasminogen activator (tPA). A study from South India reported that 30% of stroke patients reached the hospital within three hours post event and 16% were

eligible for thrombolysis therapy, but all of these eligible patients belonged to a lower socioeconomic group and could not afford the therapy due to its high cost (Ghandehari 2011).

Intracerebral haemorrhage (ICH) is associated with high mortality and morbidity. Low Glasgow Coma Scale score, higher baseline ICH volume, presence of intraventricular haemorrhage and need for ventilatory assistance are independent predictors of mortality. In a 2013 study by Bhatia and colleagues, most of the patients with spontaneous ICH were disabled at discharge. Surgery did not improve mortality or outcome.

Stroke-associated early seizures (ES) often complicate the initial course of acute stroke. In a study in Kolkata, of the 441 patients (49.43% had haemorrhagic stroke), 79 (17.91%) suffered from ES. Alcoholism, haemorrhagic stroke, cortical and severe strokes predict development of ES. ES are an independent important risk factor for early mortality (Goswami et al. 2012).

Subarachnoid Haemorrhage (SAH)

Incidence of SAH in Kashmiri, a northern part of India, is high, being about 13/100,000 persons per year. SAH comprises 31.02% of total strokes and aneurysmal ruptures are the cause of 54.35% SAHs (Bhat et al. 2011).

In a study by Sharma and colleagues (2011) 168 aneurysms were coiled in 150 patients over a six-year study period. Procedure-related rupture during endovascular coiling occurred in 2.97% of procedures, and was responsible for 1.78% treatment-related deaths. Risk factors were small aneurysm size, previous SAH. The outcome of treatment of aneurysm with coiling is safe (Sharma et al. 2011). Aneurysm surgery is performed extensively in India.

Stroke Units

A stroke unit is a multidisciplinary team comprising medical, nursing, physiotherapy, occupational therapy, speech therapy, and social work staff. In India there are approximately 35 stroke units, and they are predominantly in private sector hospitals in the cities (Pandian and Sudhan 2013). According to the Mumbai registry study, only 306 of 456 (67.2%) patients with first-ever stroke were managed at a healthcare facility, and the remaining 150 (32.8%) patients were cared for at home or in nursing homes (Dalal et al. 2008).

Intracranial Pressure Monitoring (ICP)

ICP monitoring is routinely performed in very few centres in India. This is probably due to the assumption that ICP monitoring is technologically very demanding, and also because commercially available systems are extremely expensive in the Indian setting (Joseph 2003). The intraventricular drain, which is the most frequently used technique, is cost-effective and has shown a higher incidence of nosocomial meningitis. The more modern fibre optic devices are clearly more expensive. In the web survey regarding ICP monitoring and multimodal monitoring the observation is shown in Figure 2 and Figure 3.

Only 33 (26.19%) critical care consultants of the 126 respondents of the survey had facilities in their units to carry out continuous EEG monitoring in patients suspected to have status epilepticus. 49 respondents of the 126 were regularly doing transcranial Dopplers in their ICUs.

Conclusion

Neurocritical care is a well-established specialty in the developed world. The success of the speciality is due to integration of various sub-specialities, namely neurology, neurosurgery, neuro-anaesthesiology, interventional neuroradiology and neuro-critical care. The phenomenal progress demonstrated by general critical care in India was due to the contribution of ISCCM in increasing awareness to the medical community and the public at large. ISCCM over the years conducted seminars, continuing medical education, workshops, national and international conferences along with a curriculum to train young potential intensivists. For neurocritical care to move ahead a similar cohesive group or a subgroup of ISCCM needs to establish standards of neurocritical care practice and probably set up a curriculum for a diploma in neurocritical care.

For full references, please email **editorial@icu-management.org,** visit the website at **www.icu-management.org** or use the **QR code** at the top of the article.

Figure 1. Nationwide Numbers of Patients Treated with IV rtPA, 2009-2011

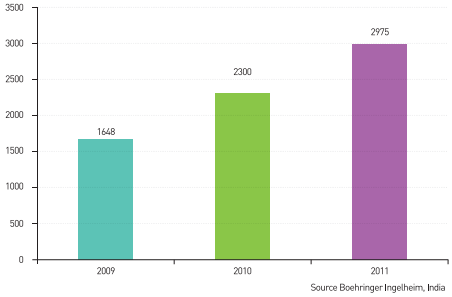
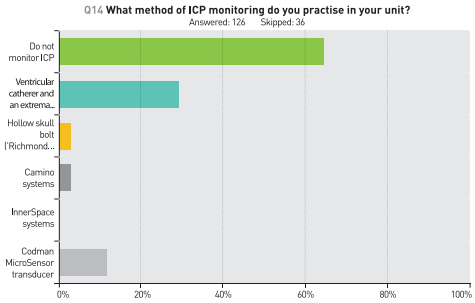
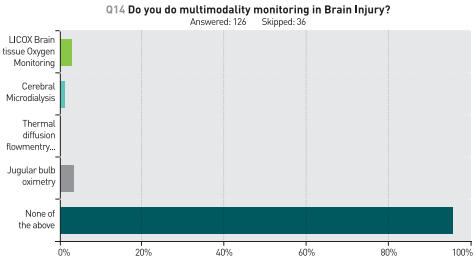


Figure 2. ICP Monitoring



Answer Choices	Responses	
Do not monitor ICP	**63.49%**	80
Ventricular catheter and an external transducer	**28.57%**	36
Hollow skull bolt ('Richmond screw')	**2.38%**	3
Camino systems	**2.38%**	3
InnerSpace systems	**0%**	0
Codman MicroSensor transducer	**11.11%**	14
Total Respondents: 126		Source: Amin 2014

Figure 3. Multimodality Monitoring in Brain Injury



Answer Choices	Responses	
LICOX Brain tissue Oxygen Monitoring	**2.38%**	3
Celebral Microdialysis	**0.79%**	1
Thermal diffusion flowmetry using Bowman perfusion	**0%**	0
Jugular bulb oximetry	**3.17%**	4
None of the above	**95.24%**	120
Total Respondents: 126		Source: Amin 2014

AGENDA

JUNE

31 May- 3 June	Euroanaesthesia Stockholm, Sweden www.esahq.org
3 – 4	Metabolic and Nutritional Issues in the ICU Brussels, Belgium www.intensive.org
5 – 6	4th Paris International Conference on Intensive Care Paris, France www.srlf.org
12-14	SESAM 2014 Poznan, Poland www.sesampoznan.eu
25-28	EAES 2014 Paris, France www.eaes-eur.org

JULY

7-8	2nd Annual International Best of Brussels Symposium on Intensive Care & Emergency Medicine (2014) Pune, India www.isccmpune.com
31 June– 3 August	13th International Conference on Complexity in Acute Illness Charlottesville, USA www.iccai.org

SEPTEMBER

4-6	21st Paediatric Critical Care Colloquium Huntington Beach, California, USA www.pcccolloquium.com
6-9	ESPEN Geneva, Switzerland www.espen.orggeneva-2014
27 Sept.- 1 October	27th ESICM LIVES 2014 Annual Congress Barcelona, Spain www.esicm.org

OCTOBER

9-11	ANZICS/ACCCN Intensive Care ASM Melbourne, Australia www.intensivecareasm.com.au
29 October– 1 November	Critical Care Canada Forum Toronto, Canada www.criticalcarecanada.com

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